Diseases of the Alimentary Tract: Nonruminant

7

Principles of Alimentary Tract Dysfunction

The primary functions of the alimentary tract are the **prehension**, **digestion** and **absorption of food and water,** and the **maintenance of the internal environment** by modification of the amount and nature of the materials absorbed.

The primary functions can be divided into four major modes and, correspondingly, there are four major modes of alimentary dysfunction. There may be abnormality of **motility**, **secretion**, **digestion,** or **absorption.** The procedure in diagnosis of alimentary tract dysfunction should be to determine which mode or modes of function are disturbed before proceeding to the determination of the site and nature of the lesion and ultimately of the specific cause.

MOTOR FUNCTION

NORMAL GASTROINTESTINAL MOTILITY

The form and function of the small intestine of farm animals are similar between species, but the stomachs and large intestines vary considerably. The motility patterns in both the small and large intestine are similar among the species. In the small intestine, the fundamental unit of electrical activity is the slow wave, which is a subthreshold fluctuation in membrane potential. Slow waves are constantly propagated from the stomach to the rectum. When an additional stimulus causes the membrane potential to exceed the excitation threshold, a spike or electrical response activity occurs, which is usually accompanied by contraction. Almost all spike activity in the intestine is superimposed on slow waves, which are important in controlling frequency and velocity at which

spiking events occur. The spiking activity, also known as the migrating myoelectric complex, is the myoelectric pattern in the stomach and small intestine of fasted nonruminants, fed and fasted ruminants, and pigs and horses fed ad libitum.[1] There are three phases of the migrating myoelectric complex:
- **Quiescent phase**, in which very little spike activity occurs
- **Irregular phase**, characterized by intermittent spike activity
- **Activity front**, characterized by intense, continuous spike activity

There is very little muscle contraction or transit of gut contents during the quiescent phase. During the irregular phase, contractions mix the intestinal contents and propel them in an aboral direction. The activity front is accompanied by intense muscular contraction that obliterates the lumen, preventing backflow of content as it propagates, or migrates, down the intestine.

In nonruminants, and pigs and horses fed periodically, feeding abolishes the migrating myoelectric complex for several hours. It is replaced by the fed pattern, characterized by intermittent spike activity resembling the irregular phase.

Normal cecal and colonic myoelectric activities, like those of the small intestine, are characterized by slow waves and spikes. However, unlike the small intestine, the patterns of spikes vary greatly with the species and the area of the large intestine.

Abnormalities of stomach and intestinal motility represent the most common consequence of gastrointestinal tract disease. Disruption in gastrointestinal tract motility can result in the following:

- Hypermotility or hypomotility
- Distension of segments of the tract
- Abdominal pain
- Dehydration and shock

HYPERMOTILITY AND HYPOMOTILITY

The most important functions of alimentary tract motility are the peristaltic movements that move ingesta from the esophagus to the rectum, the segmentation movements that churn and mix the ingesta, and the tone of the sphincters. In ruminants these movements are of major importance in the forestomach. Prehension, mastication, and swallowing are the other functions of alimentary tract motility that are essential for normal function. Eructation of ruminal gases is an additional crucial function of motility in ruminants.

Abnormal motor function can take the form of **increased or decreased motility.** Peristalsis and segmenting movements are usually affected equally and in the same manner. Motility depends on stimulation via the sympathetic and parasympathetic nervous systems, and is thus dependent on the activity of the central and peripheral parts of these systems and on the intestinal musculature and its intrinsic nervous plexuses. Autonomic imbalance, resulting in a relative dominance of one or other system, is manifested by hypermotility or hypomotility, and can arise as a result of stimulation or destruction of hypothalamic centers, the ganglia, or the efferent or afferent peripheral branches of the system. Debility, accompanied by weakness of the musculature, or severe inflammation, such as occurs in acute peritonitis or after trauma, or infarction, results in atony of the intestinal wall. Less severe inflammation, such as occurs in mild gastritis and enteritis, can result in an increase in muscular activity and increased propulsive activity. Abnormalities in intestinal motility can result in diarrhea or constipation and adversely affect digestion and absorption of ingesta.

Increased irritability at a particular intestinal segment increases its activity, and disturbs the normal downward gradient of activity that ensures the ingesta are passed from the esophagus to the rectum. Not only is the gradient toward the rectum made steeper, increasing the rate of passage of ingesta in that direction, but the increased potential activity of an irritated segment may be sufficiently high to produce a reverse gradient to the oral segments so that the directions of the peristaltic waves are reversed orally to the irritated segments.

DISTENSION

One of the major results of abnormality of motility is distension of one or more segments of the gastrointestinal tract. Distension can be the result of accumulation of gas, fluid, or ingesta. Much of the accumulated fluid represents saliva and gastric and intestinal juices secreted during normal digestion. Gas distension occurs as a result of failure to expel gas, by eructation or as flatulence, which is produced either as a result of normal digestive processes or abnormal fermentation.

Distension causes pain and, reflexively, increased spasm and motility of adjoining gut segments. Distension also stimulates further secretion of fluid into the lumen of the intestine, and this exaggerates the distension. When the distension passes a critical point, the ability of the musculature of the wall to respond diminishes, the initial pain disappears, and a state of paralytic ileus develops in which much muscle tone is lost.

ABDOMINAL PAIN

Visceral pain can arise in any abdominal viscus or organ, but the mode of its development is always the same, and alimentary tract disease is the major cause of visceral and, more specifically, of abdominal pain. The **most important mechanism is stretching of the wall of the viscus**, which stimulates free pain endings of the autonomic nerves in the wall. Contraction does not itself cause pain but does so by causing direct and reflex distension of neighboring segments. Thus spasm, an exaggerated segmenting contraction of one section of intestine, will result in distension of the immediately oral segment of intestine when a peristaltic wave arrives. When there is increased motility for any reason, excessive segmentation and peristalsis cause abdominal pain, and the frequent occurrence of intermittent bouts of pain depends on the periodic increases in muscle tone that are typical of the alimentary tract wall. Other factors that have some stimulating effect on the pain of end organs are edema and failure of local blood supply, such as occurs in local embolism or in intestinal accidents accompanied by twisting of the mesentery. A secondary mechanism in the production of abdominal pain is the stretching and inflammation of serous membranes.

Clinically, abdominal pain can be detected by palpation and the eliciting of pain responses. However, it is unknown if the response elicited is caused by involvement of underlying organs or by referred pain. It is difficult to decide if referred pain occurs in animals. In humans it is largely a subjective sensation, although often accompanied by local hyperalgesia. There are no known examples of referred pain that are of diagnostic importance in animals, and a local pain response on palpation of the abdomen is accepted as evidence of pain in the serous membranes or viscera that underlie the point of palpation.

DEHYDRATION AND SHOCK

An immediate effect of distension of the stomach or small intestine by the accumulation of saliva and normal gastric and intestinal secretions is the stimulation of further secretion of fluid and electrolytes into the oral segments. The stimulation is self-perpetuating, and creates a vicious cycle resulting in loss of fluid and electrolytes to the point where fatal dehydration can occur. The dehydration is accompanied by acidosis or alkalosis, depending on whether the obstruction is in the intestine and accompanied by loss of alkali, or in the stomach and accompanied by a large loss of acid radicals. The net effect is the same whether the fluid is lost by vomiting or is retained in the gut.

The same cycle of events occurs in ruminants that gorge on grain, but here the precipitating mechanism is not distension but a gross increase in osmotic pressure of the ingesta caused by the accumulation of osmotically active compounds, including lactic acid. Dehydration is also of major importance in diarrhea, irrespective of the cause. An important additional factor in the production of shock, when there is distension of alimentary segments, is a marked reflex depression of vasomotor, cardiovascular, and respiratory functions. In diarrhea in calves in which there is no septicemia or toxemia associated with bacteria, the endpoint in the phase of dehydration can be cardiac failure caused by severe metabolic acidosis and electrolyte abnormalities. Renal ischemia leading to azotemia or uremia can result from decreased circulating blood volume and also contribute to a fatal outcome. These matters are discussed in detail in Chapters 5 and 6.

SECRETORY FUNCTION

Diseases caused by abnormalities of secretion of digestive enzymes are not generally recognized in farm animals. In humans, and to a lesser extent in small animals, defects of gastric and pancreatic secretion produce syndromes that are readily recognized, but they depend on clinical pathologic examination for diagnosis. If they do occur in farm animals, they have so far only been recognized as aberrations of motility caused by the defects of secretion. However, it is reasonable to assume that some neonates are deficient

in lactase activity, which results in dietetic diarrhea. Undigested lactose causes diarrhea by its hyperosmotic effect, and some of the lactose can be fermented in the large intestine, the products of which fermentation exaggerates the diarrhea. A deficiency of lactase activity has been suspected in foals affected with diarrhea of undetermined origin when the definitive diagnosis has not been made. The intestinal lactase activity of foals is at its highest level at birth, gradually declines until the fourth month of age, and then disappears from adults before their fourth year.

DIGESTIVE FUNCTION

The ability of the alimentary tract to digest food depends on its motor and secretory functions and, in herbivores, on the activity of the microflora that inhabits the forestomachs of ruminants or cecum and colon of Equidae. The flora of the forestomachs of ruminants is capable of digesting cellulose, of fermenting the end products of other carbohydrates to volatile fatty acids, and of converting nitrogenous substances to ammonia and protein. In a number of circumstances, the activity of the flora can be modified so that digestion is abnormal or ceases. Failure to provide the correct diet, prolonged starvation or inappetence, and hyperacidity such as occurs in engorgement on grain all result in impairment of microbial digestion. The bacteria, yeasts, and protozoa may also be adversely affected by the oral administration of antibiotic and sulfonamide drugs or drugs that drastically alter the pH of the rumen content.

Diseases of the stomach of ruminants are presented in Chapter 8. Information about the digestive and absorptive capacities of the equine gut is not exhaustive, but some basic data are available. The rate of passage of ingesta through the stomach and intestines is rapid but varies widely depending on the physical characteristics of the ingesta and dissolved material passaging more rapidly than particulate material; 75% of a liquid marker can be emptied from the stomach in 30 minutes and be in the cecum in 2 hours. Passage through the large bowel is much slower, especially in the latter part of the colon in which much of the fluid is absorbed. There is an obvious relationship between the great activity of the small intestine and the effect of a complete obstruction of it: the pain is very severe and often uncontrollable with standard analgesics; fluid loss into the obstructed parts is rapid; and dehydration, loss of electrolytes, and disturbances of acid-base balance are acute, severe, and life-threatening.

ABSORPTIVE FUNCTION

Absorption of fluids and the dissolved end products of digestion can be adversely affected by increased motility or by disease of the intestinal mucosa. In most instances, the two occur together but, occasionally, as with some helminth infestations, lesions occur in the intestinal wall without accompanying changes in motility.

Manifestations of Alimentary Tract Dysfunction

Inanition is the major physiologic effect of alimentary dysfunction when the disease is chronic, dehydration is the major effect in acute diseases, and shock is the important physiologic disturbance in hyperacute diseases. Some degree of abdominal pain is usual in most diseases of the alimentary tract, with the severity varying with the nature of the lesion. Other manifestations include abnormalities of prehension, mastication, and swallowing; and vomiting, diarrhea, hemorrhage, constipation, and scant feces.

ABNORMALITIES OF PREHENSION, MASTICATION, AND SWALLOWING

Prehension is the act of grasping for food with the mouth (lips, tongue, and teeth). It includes the ability to drink. Causes of faulty prehension include:

Paralysis of the muscles of the jaw or tongue
Malposition of incisor teeth caused by the following:
- Inherited skeletal defect (inherited displaced molar teeth, inherited mandibular prognathism, inherited congenital osteopetrosis)
- Rickets
Absence of some incisor teeth
Pain in the mouth caused by the following:
- Stomatitis, glossitis
- Foreign body in mouth
- Decayed teeth, e.g., fluorosis
Congenital abnormalities of tongue and lips:
- Inherited harelip
- Inherited smooth tongue of cattle

A simple examination of the mouth usually reveals the causative lesion. Paralysis is indicated by the behavior of the animal as it attempts to ingest feed without success. In all cases, unless there is anorexia caused by systemic disease, the animal is hungry and attempts to feed but cannot do so.

Mastication may be painful and is manifested by slow jaw movements interrupted by pauses and expressions of pain if the cause is a bad tooth, but in a painful stomatitis there is usually complete refusal to chew. Incomplete mastication is evidenced by the dropping of food from the mouth while eating and the passage of large quantities of undigested material in the feces.

Swallowing is a complex act governed by reflexes mediated through the glossopharyngeal, trigeminal, hypoglossal, and vagal nerves. It has been described endoscopically and fluoroscopically in the horse. The mechanism of the act includes closure of all exits from the pharynx, the creation of pressure to force the bolus into the esophagus, and involuntary movements of the musculature of the esophageal wall to carry the bolus to the stomach. A defect in nervous control of the reflex or a narrowing of the lumen of the pharynx or esophagus may interfere with swallowing. It is difficult to differentiate clinically between physical and functional causes of dysphagia (difficulty in eating/swallowing).

Dysphagia is manifested by forceful attempts to swallow accompanied initially by extension of the head, followed by forceful flexion and violent contractions of the muscles of the neck and abdomen. Inability to swallow is usually caused by the same lesions as dysphagia, but to a greater degree. If the animal attempts to swallow, the results depend on the site of the obstruction. Lesions in the pharynx cause regurgitation through the nostrils or coughing up of the material. In the latter instance, there is danger that some of the material is aspirated into the lungs and could cause acute respiratory and cardiac failure or aspiration pneumonia. When the obstruction is at a low level in the esophagus, a large amount of material can be swallowed and then regurgitated. It is necessary to differentiate between material regurgitated from the esophagus and vomitus: the former is usually slightly alkaline and the latter is acid.

CAUSES OF DYSPHAGIA AND INABILITY TO SWALLOW

- Foreign body, tumor, or inflammatory swelling in pharynx or esophagus
- Painful condition of pharynx or esophagus
- Esophageal obstruction by impacted feed material
- Esophageal dilatation caused by paralysis
- Esophageal diverticulum
- Esophageal spasm at site of mucosal erosion (achalasia of cardia not encountered)

DROOLING OF SALIVA AND EXCESSIVE SALIVATION

Drooling saliva from the mouth, distinct from frothing such as occurs during convulsions, can be caused by pain in the mouth and by an inability to swallow. Excessive salivation is caused by stimulation of saliva production by systemic toxins, especially fungal toxins, or by hyperthermia. With systemic poisonings the increased salivation is often accompanied by lacrimation.

LOCAL CAUSES OF DROOLING

- Foreign body in mouth or pharynx
- Ulceration, deep erosion or vesicular eruption of the oral mucosa
- Inability to swallow (esophageal abnormality)

SYSTEMIC CAUSES OF EXCESSIVE SALIVATION

- Poisonous trees: *Oleander* spp., *Andromeda* spp. (rhododendron)
- Other poisonous plants: kikuyu grass (or an attendant fungus)
- Fungal toxins, e.g., slaframine and those causing hyperthermia, e.g., *Claviceps purpurea* and *Acremonium coenophialum*
- Iodism
- Watery mouth of lambs
- Sweating sickness
- Methiocarb poisoning

VOMITING AND REGURGITATION

VOMITING

Vomiting is the forceful ejection of contents of the stomach and the proximal small intestine through the mouth, and is a complex motor disturbance of the alimentary tract. It is a vigorously active motion signaled by hypersalivation, retching, and forceful contractions of the abdominal muscles and diaphragm. Vomiting is essentially a protective mechanism with the function of removing excessive quantities of ingesta or toxic materials from the stomach. Note that vomition is exceedingly rare in horses and is usually a terminal event. Vomition occurs in two forms: **projectile** and **true vomiting**.

Projectile Vomiting

This is not accompanied by retching movements, and large amounts of fluid material are ejected with little effort. It is almost always as a result of overloading of the stomach or forestomach with feed or fluid.

True Vomiting

As it occurs in monogastric animals like the dog and cat, true vomiting is accompanied by retching movements including contraction of the abdominal wall and of the neck muscles and extension of the head. The movements are commonly prolonged and repeated, and the vomitus is usually small in amount and of porridge-like or pasty consistency. It is usually a result of irritation of the gastric mucosa. Vomiting is commonly designated as being either peripheral or central in origin depending on whether the stimulation arises centrally at the vomiting center or peripherally by overloading of the stomach or inflammation of the gastric mucosa, or by the presence of foreign bodies in the pharynx, esophagus, or esophageal groove. Central stimulation of vomiting by apomorphine and in nephritis and hepatitis are typical examples, but vomiting occurs rarely, if at all, in these diseases in farm animals.

Vomiting can have serious effects on fluid and electrolyte balance because of the losses of gastric and intestinal contents. Aspiration pneumonia and laryngeal obstruction are potentially serious consequences of vomiting. Examination of any suspected vomitus to determine its site of origin should always be performed.

True vomiting is rare in farm animals except in pigs with gastroenteritis and some systemic diseases. True vomiting does not occur in ruminants but abnormal regurgitation does (see later). **True vomiting is not a feature of gastric disease in the horse for two reasons.** First, the strong cardiac sphincter inhibits the release of stomach contents; in horses rupture of the stomach is more likely to occur before vomiting takes place. Second, the soft palate and epiglottis combine to affect a seal between the oral and nasal parts of the pharynx so that any vomited stomach contents must be discharged through the nasal cavities and not through the mouth. Spontaneous nasal regurgitation or vomiting does occur occasionally, as manifested by the production of green stomach contents at the nostrils. This suggests extreme gastric distension or a dilated esophagus and cardiac sphincter and perhaps some underlying neurologic deficit. Thus vomiting of large quantities of material in the horse is usually a terminal event and suggests gastric rupture.

REGURGITATION

Regurgitation is the expulsion through the mouth or nasal cavities of feed, saliva, and other substances that have not yet reached the stomach. In most cases it is caused by abnormalities of the esophagus that interfere with swallowing. A common example in large animals is the regurgitation of feed, saliva, and perhaps bloodstained fluid from the esophagus of the horse with esophageal obstruction. Esophagitis is also a common cause of regurgitation.

Ruminants regurgitate rumen contents as part of rumination, but the material is not expelled from the mouth or into the nasal cavities. The regurgitation of rumen contents through the mouth does occur in cattle occasionally, is abnormal, and is a dramatic event. It is usually associated with loss of tone of the cardia or inflammation of the cardia (see examples in the following sections).

Nasogastric regurgitation or gastric reflux occurs in the horse. Stomach contents flow into the esophagus, and usually into the nasopharynx and nasal cavities, as a result of distension of the stomach with fluid (which usually originates in the small intestine). This involuntary process is usually slow and gradual, unlike true vomiting. Gastric reflux in the horse can be elicited by nasogastric intubation. Spontaneous efflux of stomach contents is indicative of high-volume and high-pressure fluid distension of the stomach. On other occasions the presence of sequestrated gastric fluids can be confirmed only by the creation of a siphon, using the nasogastric tube to infuse a volume of fluid then disconnecting its supply to retrieve the **nasogastric reflux.**

Causes of vomiting and regurgitation include the following:

- Terminal vomiting in horses with acute gastric dilatation
- "Vomiting" in cattle is really *regurgitation* of large quantities of rumen contents through the mouth. Causes include the following:
  - Third-stage milk fever (loss of tone in the cardia)
  - Arsenic poisoning (acute inflammation of the cardia)
  - Poisoning by plants including *Eupatorium rugosum, Geigeria* spp., *Hymenoxys* spp., *Andromeda* spp., *Oleander* spp., and *Conium maculatum*
  - Veterinary administration of large quantities of fluids into the rumen (regurgitation occurs while the stomach tube is in place)
  - Use of a large-bore stomach tube
  - Cud-dropping: a special case of regurgitation usually associated with abnormality of the cardia
- Vomiting in pigs may be caused by the following:
  - Transmissible gastroenteritis (TGE)
  - Acute chemical intoxications
  - Poisoning by the fungus *Fusarium* spp., which also causes off-feed effects suspected to be analogous to nausea in humans
- Regurgitation in all diseases causing dysphagia or paralysis of swallowing

DIARRHEA, CONSTIPATION, AND SCANT FECES

Diarrhea and constipation are the most commonly observed abnormalities in **fecal consistency**, **composition,** and **frequency of defecation**.

DIARRHEA

Diarrhea is the increased frequency of defecation accompanied by feces that contain an increased concentration n of water and decrease in dry matter content. The consistency of the feces varies from soft to liquid.

Abnormalities of peristalsis and segmentation usually occur together, and when there is a general increase in peristaltic activity there is increased caudal flow, resulting in a decrease in intestinal transit time and diarrhea. Because of a lack of absorption of fluid the feces are usually softer than normal, the dry matter content is below the normal range, and the total amount of feces passed per day is increased. The frequency of

defecation is usually also increased. Common causes of diarrhea are
- Enteritis, including secretory enteropathy
- Malabsorption, e.g., caused by villous atrophy and in hypocuprosis (caused by molybdenum excess)
- Neurogenic diarrhea as in excitement
- Local structural lesions of the stomach or intestine, including the following:
  - Ulcer, e.g., of the abomasum or stomach
  - Tumor, e.g., intestinal adenocarcinoma
- Indigestible diet, e.g., lactose intolerance in foals
- Carbohydrate engorgement in cattle
- In some cases of ileal hypertrophy, ileitis, diverticulitis, and adenomatosis
- Terminal stages of congestive heart failure (visceral edema)
- Endotoxic mastitis in cattle (splanchnic congestion)
  - Small colon impaction in horses
  - Sand colic in horses
- Chronic and acute undifferentiated diarrhea in horses
- Vagus indigestion in cows causes pasty feces but bulk is reduced; these cases may be mistaken initially for other causes of diarrhea

Malabsorption Syndromes

Malabsorption syndromes are being recognized with increased frequency in monogastric farm animals. For example, in recently weaned pigs, there is villous atrophy with a resulting loss in secretory and absorptive function. Inefficient digestion originating in this way may or may not be manifested by diarrhea, but in malabsorption there is usually diarrhea. There is always failure to grow or maintain body weight (BW), in spite of an apparently normal appetite and an adequate diet. In horses, the lesions associated with malabsorption, which can be with or without diarrhea, include villous atrophy, edema and/or necrosis of the lamina propria of the gut wall, and nodular tracts and aggregations of eosinophils indicating damage by migrating strongyle larvae. Special tests are now detailed for the examination of digestive efficiency in the horse. These are listed in the next section. Increased venous pressure in the portal circuit caused by congestive heart failure or hepatic fibrosis also causes diarrhea.

The question of whether or not enteritis in animals causes intestinal hypermotility and increased peristalsis, resulting in diarrhea, remains unresolved. If hypermotility and increased peristalsis cause diarrhea, antimotility drugs may be indicated in some causes of acute infectious diarrhea. Current concepts on the pathophysiology of the common diarrheas associated with infectious agents (such as enterotoxigenic *Escherichia coli*) indicate that there is a net increase in the flow of intestinal fluid into the lumen and a decrease in outflow back into the systemic circulation, which causes distension of the intestine with fluid. The hydraulic effect of the distension can cause diarrhea, and hypermotility is probably not necessary. In addition, because of the temporary malabsorption that exists in infectious enteritides, and the presence of infectious agents and enterotoxins in the lumen of the intestine, the emphasis should be on evacuation of the intestinal contents and not on the use of anticholinergic drugs to inhibit evacuation. Furthermore, it is unlikely that the anticholinergics will have any significant effect on the secretory-absorptive mechanisms that have been altered by an enteropathogen.

CONSTIPATION

Constipation is the **decreased frequency of defecation** accompanied by feces that contain a decreased concentration of water. The feces vary in consistency from being hard to dry and of small bulk. True constipation, as it occurs in humans, is usually characterized by failure to defecate and impaction of the rectum with feces. When the motility of the intestine is reduced, the alimentary transit time is prolonged and constipation or scant feces occurs. Because of the increased time afforded for fluid absorption, the feces are dry, hard, of small bulk, and are passed at infrequent intervals. Constipation may also occur when defecation is painful, such as in cattle with acute traumatic reticuloperitonitis.

SCANT FECES

Scant feces are small quantities of feces, which may be dry or soft. Scant feces are most common in cattle with abnormalities of the forestomach or abomasum resulting in the movement of only small quantities of ingesta into the small and large intestines (**an outflow abnormality**). The details are available in Chapter 8. When there is complete intestinal stasis the rectum may be empty except for blood-tinged, thick, pasty material.

Common causes of constipation or scant feces are as follows:
- Diseases of the forestomach and abomasum causing failure of outflow
- Impaction of the large intestine in the horse and the sow
- Severe debility, as in old age
- Deficient dietary bulk, usually fiber
- Chronic dehydration
- Partial obstruction of large intestine
- Painful conditions of the anus
- Paralytic ileus
- Grass sickness in horses
  - Cauda equina syndrome in any species
  - Polyneuritis equi
- Chronic zinc poisoning in cattle
- Terminal stages of pregnancy in cows.

ILEUS (ADYNAMIC AND DYNAMIC ILEUS)

Ileus is a state of **functional obstruction** of the intestines or failure of peristalsis. It is also known as **paralytic ileus** or **adynamic ileus. Dynamic or mechanical ileus** is a state of physical obstruction. In paralytic ileus there is loss of intestinal tone and motility as a result of reflex inhibition. This can occur in acute peritonitis, excessive handling of viscera during surgery, and prolonged and severe distension of the intestines as in intestinal obstruction or enteritis. Ileus can also be caused by acid-base imbalance, dehydration, electrolyte imbalances such as hypocalcemia and hypokalemia, and toxemia. Ileus can affect the stomach, causing delayed gastric emptying and subsequent dilatation with fluid and gas. The effect of ileus on the intestines is to cause failure of orocaudal movement of fluid, gas, and ingesta and accumulation of these substances, which results in intestinal distension and varying degrees of abdominal pain, dehydration, and a marked reduction in the amount of feces. Distension of the abdomen, fluid-tinkling, fluid-splashing sounds, and pings on percussion of the abdomen are common clinical findings. Impaction of the large intestine of horses is a form of ileus.

Postoperative ileus of the small and large intestines is a common complication of surgical treatment for colic in the horse.[2-5] The clinical findings include gastric reflux because of gastric distension with fluid, absence of or minimal intestinal peristaltic sounds, an absence of feces, abdominal pain, distended loops of intestine palpable per rectum, and varying degrees of shock and dehydration as a result of intestinal fluid sequestration and a decrease in fluid absorption. **Infarction of the intestinal wall** associated with an acute mechanical obstruction of the intestine also results in ileus. In thromboembolic colic caused by verminous mesenteric arteritis in the horse, large segments of the large colon and cecum can become infarcted, resulting in irreversible ileus.

The etiology and pathogenesis of ileus in farm animals are not well understood. Sympathetic hyperactivity is thought to be a factor. The gastroileal reflex is one example of the influence of the activity of one part of the digestive tract on that of another; inhibition of gastric motility when the ileum is distended is called ileogastric reflex. Immediate cessation of all intestinal movement (adynamic ileus) follows distension of an intestinal segment, rough handling of the intestine during abdominal surgery, or peritoneal irritation. Adynamic ileus operates through three pathways: general sympathetic discharge of the peripheral reflex pathway through the iliac and mesenteric plexuses and the intramural plexuses. The treatment of ileus depends on the original

Table 7-1 Medications with potential prokinetic actions in horses (see text for references)

Drug	Mechanism of action	Proposed dose	Potential indications
Parasympathomimetics			
Bethanechol	Direct acting muscarinic receptor agonist	0.025 mg/kg BW, IV or SC every 4–6 h	Disorders requiring promotion of gastric or cecal emptying. Postoperative ileus, gastroesophageal reflux in foals
Neostigmine	Indirect acting cholinesterase	0.0044–0.022 mg/kg BW, IV, IM or SC; 4 mg SC every 6 h; 2 mg SC every 2 h	Caecal and large colon impactions inhibitor
Benzamides			
Metoclopramide	5-HT4 agonist, 5-HT3 and D2 antagonist	0.04 mg/kg BW/h, IV CRI	Disorders requiring promotion of gastric and small intestinal motility, post-operative ileus, anterior enteritis
Cisapride	5-HT4 agonist, 5-HT1 antagonist	0.1–0.25 mg/kg BW/h, IV over 60 min; 0.1 mg/kg BW, IM	Disorders requiring promotion of gastric and small intestinal motility, post-operative ileus, anterior enteritis
Mosapride	5-HT4 agonist	1–2 mg/kg BW, PO, every 24 h	Gastric impactions, small intestinal ileus, cecal impactions
Tegaserod	5-HT agonist	0.27 mg/kg BW, PO every 12 h	Large colon impactions
Sodium channel blockers			
Lidocaine	Unknown	1.3 mg/kg BW, IV (loading dose) followed by 0.05 mg/kg BW/min CRI	Post-operative ileus, anterior enteritis
Macrolide antimicrobials			
Erythromycin	Stimulation of motilin receptors	0.5–1 mg/kg BW in saline, IV over 60 min	Disorders requiring promotion of gastric and small intestinal motility, post-operative ileus, cecal impactions
Dopamine antagonists			
Domperidone	D2-receptor antagonist	0.2 mg/kg BW, IV	Disorders requiring promotion of gastric and small intestinal motility, post-operative ileus
α-Adrenergic antagonists			
Yohimbine	α2-Adrenergic receptors antagonist	0.15 mg/kg BW, IV every 3 h 0.25 mg/kg BW in saline, IV over 60 min	Post-operative ileus
Tolazoline	α2-Adrenergic receptors antagonist	1 mg/kg BW in saline, IV	Unknown over 60 min
Atipamezole	α2-Adrenergic receptors antagonist	0.03–0.06 mg/kg BW, IM	Unknown; possible prevention of α-adrenergic–induced ileus
Acepromazine	Nonspecific α-adrenergic receptors antagonist	0.01 mg/kg BW, IV or IM 4 h	Post-operative ileus
Opioid antagonists			
Naloxone	Opioid antagonist	0.05 mg/kg BW, IV	Unknown, possible large colon impactions, opioid-induced ileus
N-methylnaltrexone	Opioid antagonist	0.75 mg/kg BW, IV every 12 h	Unknown, possible large colon impactions, opioid-induced ileus

BW, body weight; IM, intramuscularly; IV, intravenously; PO, orally; SC, subcutaneously; CRI, constant rate infusion.

cause. Physical obstruction of the intestines and torsion of the stomach must be corrected surgically.

Management of postoperative ileus and ileus associated with proximal duodenitis–jejunitis (anterior enteritis) includes correction of fluid and electrolyte abnormalities, relief of gastric distension, and administration of prokinetic drugs. Lidocaine (lignocaine, loading dose 1.5 mg/kg followed by 0.033 mg/kg/min intravenously) administered prophylactically to horses undergoing exploratory laparotomy because of abdominal pain reduces the severity and duration of postoperative ileus.[4,6]

Motility of the gastrointestinal tract can be modified by administration of a number of compounds (Table 7-1).[7-11] Clinical utility is documented for administration of lidocaine to horses with postoperative ileus (see earlier information) and for erythromycin in cattle following surgery for abomasal disease.[7,8]

ALIMENTARY TRACT HEMORRHAGE

Hemorrhage into the stomach or intestine is a common occurrence in farm animals. The main causes include the following:
- Gastric or abomasal (rarely duodenal) ulcers
- Severe hemorrhagic enteritis
- Structural lesions of the intestinal wall, e.g., adenomatosis, neoplasia
- Infestation with blood-sucking nematodes, e.g., bunostomiasis,
- Local vascular engorgement or obstruction as in intussusception and verminous thrombosis

Hemorrhage into the stomach results in the formation of **acid hematin,** which makes vomitus a dark brown color like coffee grounds, and feces have a black or very dark brown, tarry appearance (**melena**). The change in appearance of the feces caused by hemorrhage into the intestine varies with the level at which the hemorrhage occurs. If the blood originates in the **small intestine,** the feces may be **brown-black**, but if it originates in the **colon or cecum**, the blood is unchanged and gives the feces an **even red**

color. Hemorrhage into the **lower colon and rectum** may cause the voiding of feces containing or consisting entirely of **clots of whole blood (hematochezia).**

If there is any doubt about the presence of blood in the feces or vomitus, biochemical tests should be performed. The hemorrhage may be sufficiently severe to cause anemia and, in particularly severe cases, acute peripheral circulatory failure. In cattle the most sensitive test is one using a dilute alcoholic solution of guaiac as the test reagent. It is capable of detecting a daily blood loss into the abomasum of as small a volume as 70 mL. Transit time of blood from abomasum to rectum in normal cows varies from 7 to 19 hours.

ABDOMINAL PAIN

The pain associated with diseases of the abdominal viscera causes similar signs regardless of the viscus or organ involved and careful clinical examination is necessary to locate the site of the lesion. The manifestations of abdominal pain vary with the species, with horses being particularly sensitive, but they are comprised largely of abnormalities of behavior and posture. Pain as a systemic state is presented in general terms in Chapter 5, including its effects on body systems and methods for its detection.

Readily identifiable syndromes of abdominal pain referable to the alimentary tract include the following.

Horses
- Acute pain: Pawing, flank-watching, rolling
- Subacute pain: Lesser degree of flank-watching, often excessive pawing, lying down frequently without rolling, stretching out as if to urinate, males may extrude the penis, walking backward, dog-sitting posture, lying on back, impulsive walking
- Peritoneal pain: Rigidity of the abdominal wall, pain on palpation.

Cattle
- Acute pain: Downward arching of back with treading of the hind feet, lying down (rolling is uncommon), calves will lie down and bellow with severe abdominal pain, as in abomasal torsion
- Subacute pain, including peritoneal pain: Back arched upward, grunting on walking or lying down, grunting on deep palpation of the abdomen, immobility

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DIFFERENTIAL DIAGNOSIS

The disease states likely to be mistaken for the above categories of alimentary tract pain are
- Acute pain: Paresthesia, e.g., in photosensitive dermatitis of cows; pleuropneumonia in the horse; uterine torsion in the mare and cow; urticaria as in milk allergy in cows; renal and urethral colic; compulsive walking, e.g., in hepatic disease; lead poisoning; dysuria or obstruction of urinary tract generally; laminitis; and lactation tetany in mares
- Subacute pain: Encephalopathy, possibly hepatic insufficiency

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COMMON CAUSES OF ALIMENTARY TRACT PAIN
Horses
- Acute pain: All causes of intestinal obstruction, gastric dilatation, enteritis generally, acute colitis, rarely salmonellosis
- Subacute pain: Thromboembolic colic, impaction of the large intestine, ileal hypertrophy

Cattle
- Acute pain: Intestinal obstruction, especially by phytobezoars; poisoning by kikuyu grass, *Andromeda* sp., *Oleander* sp., and water hemlock (*Cicuta* sp.)
- Subacute pain: Traumatic reticuloperitonitis and peritonitis generally, abomasal volvulus

TENESMUS

Tenesmus, or persistent straining, is common in many diseases of the organs of the pelvic cavity; therefore, it is not necessarily a diagnostic sign of disease in the lower alimentary tract. It is sometimes associated with frequent defecation caused by neurologic stimulation of peristalsis. Common causes of tenesmus are listed by species in the following sections.

Cattle
- Lower alimentary tract disease, e.g., colitis and proctitis caused by coccidiosis
- Genital tract disease, e.g., severe vaginitis, retained placenta
- Estrogen toxicity in steers, e.g., estrogen implantation, fusariotoxicosis
- 4-Aminopyridine poisoning, methiocarb poisoning
- Lower spinal cord lesions: spinal cord abscess, rabies
- Idiopathic

Horses
- Tenesmus does not usually occur except during parturition.

Pigs
- Constipation in parturient sows; also dystocia

SHOCK AND DEHYDRATION

Acute rapid distension of the intestine or stomach causes reflex effects on the heart, lungs, and blood vessels. The blood pressure falls abruptly, the temperature falls below normal, and there is a marked increase in heart rate. In acute intestinal accidents in horses that terminate fatally in 6 to 12 hours, shock is the major cause of death. There appears to be some species difference in the susceptibility to shock because similar accidents in cattle rarely cause death in less than 3 to 4 days; acute ruminal tympany is an exception and may exert its effects rapidly, causing death in a very short time after its onset. Less severe distension, vomiting, and diarrhea cause clinically recognizable dehydration and abnormalities of electrolyte concentration and acid-base balance. Determination of the relative importance of shock and dehydration in a particular case at a particular time is one of the challenges in gastroenterology. The subject is considered in detail in a later section.

ABDOMINAL DISTENSION

Distension of the abdomen is a common manifestation of disease of the alimentary tract. Generally, abdominal distension associated with the alimentary tract is caused by **distension of viscera** with **gas** or **fluid**. The degree of abdominal distension depends on the viscera that are distended, the species involved, and the age of the animal. Abdominal distension is most pronounced when large viscera of adult cattle and horses are distended. Distension of the small intestines in adult cattle and horses is not reliably detected on rectal examination but can be detected by percutaneous ultrasound examination of the abdomen.[12-14]

Occasional cases of abdominal distension are caused by **pneumoperitoneum**, which usually follows abdominal surgery. In ruminants the most common causes are distension of the rumen, abomasum, cecum, and large intestine, and the details of which are presented in Chapter 8. Abdominal distension in horses and pigs is usually caused by distension of the large intestine. Gastric dilatation of the horse does not cause abdominal distension. Ascites is a cause of abdominal distension in all species but can be difficult to detect in horses.

Abdominal distension can be symmetric, asymmetric, or more pronounced dorsally or ventrally on one or both sides. The severity can vary from mild and barely detectable to so severe that the skin over the abdominal wall has sufficient tension that it cannot be picked up or "tented." Determination of the cause of the distension requires careful examination of the abdomen by inspection, palpation, percussion, and simultaneous auscultation. Rectal palpation is used to determine the location and nature of

distended viscera. Diseases of other body systems that cause abdominal distension and must be considered in the differential diagnosis include advanced pregnancy and hydrops allantois.

The alimentary tract diseases of simple-stomached animals in which abdominal distension can be a manifestation include the following:

- Intestinal tympany: Caused by excessive gas production caused by abnormal fermentation in the large intestine of horses and pigs
- Obstruction of the large intestine: In horses and pigs as a result of their torsion or miscellaneous constrictions caused by adhesions, usually as a result of peritonitis
- Retention of the meconium: In foals this is often accompanied by severe distension of the colon and abdomen

Obstruction of the small intestine may cause abdominal distension but not to the degree that occurs in distension of the large intestine. In all the previously mentioned diseases, acute abdominal pain is common.

ABNORMAL NUTRITION

Failure of normal motor, secretory, digestive, or absorptive functions causes impairment of the nutrient supply to body tissues. Inanition or partial starvation results, and the animal fails to grow, loses BW, or shows other signs of specific nutritional deficiencies. Ancillary effects include decreased appetite when gut motility is decreased; in many cases in which motility is increased and there is no toxemia, the appetite is increased and may be voracious.

Special Examination

The general aspects of the clinical examination of the alimentary tract and abdomen of farm animals are described in Chapter 1. Some additional or special examination techniques and procedures are included in the following sections.

NASOGASTRIC INTUBATION

RUMEN OF CATTLE

Examination of the rumen contents is often essential to assist in determination of the state of the rumen environment and digesta. Passage of a stomach tube into the rumen will determine the patency of the esophagus and if there is increased intraruminal pressure associated with a frothy or free-gas bloat. In a free-gas bloat, large quantities of gas are usually released within a minute. In a frothy bloat, the ruminal end of the tube may become occluded by the froth and very little if any gas is released. Moving the tube back and forth within the rumen and blowing air into the tube to clear the ruminal end may result in the release of some gas.

When the tube is in the rumen, some **rumen juice** can be siphoned or pumped out and collected in an open beaker for field and laboratory analysis. The **color**, depending on the feed to a limited extent, will be green, olive-green or brown-green. In cattle on **pasture** or being fed good quality hay, the color is **dark green**. When **silage or straw** is the diet the color is **yellow-brown**. In grain overload the color is **milky gray**, and in rumen stasis of long duration with putrefaction, the color is **greenish-black**. The **consistency of the rumen contents** is normally slightly viscid, and watery rumen content is indicative of inactive bacteria and protozoa. **Excess froth** is associated with frothy bloat as in primary ruminal tympany or vagus indigestion. The **odor** of the rumen contents is normally aromatic and, although somewhat pungent, not objectionable to the nose. A **moldy, rotting odor** usually indicates protein putrefaction, and an intensely sour odor indicates an excess of lactic acid formation caused by grain or carbohydrate engorgement. The **pH of the rumen juice** varies according to the type of feed and the time interval between the last feeding and taking a sample for pH examination. The normal range, however, is between 6.2 and 7.2. The pH of rumen juice should be examined immediately after the sample is obtained, using a wide range pH (1–11) paper. **High pH values** (**8–10**) will be observed when putrefaction of protein is occurring in the rumen or if the sample is mixed with saliva. Low pH values (4–5) are found after the feeding of carbohydrates. Generally, a **pH below 5** indicates **carbohydrate engorgement**; this pH level will be maintained between 6 and 24 hours after the animal has actually consumed the carbohydrate diet. Microscopic examination of a few drops of rumen fluid on a glass slide with a low-power field will reveal the level of protozoon activity. Normally five to seven protozoans are active per low-power field. In lactic acidosis the protozoa are usually absent or a few dead ones are visible.

DECOMPRESSION OF DISTENDED RUMEN

In adult cattle with severe abdominal distension caused by gross distension of the rumen it is difficult, if not impossible, to assess the status of the abdomen. To determine whether the rumen is distended and/or to relieve the pressure a large-bore stomach tube should be passed (Colorado Kingman tube: 2 m long and 3-cm inside diameter). In vagus indigestion, the rumen may be grossly distended with fluid contents, which will gush out through a large-bore tube. In some cases 100 to 150 L of rumen contents may be released. If no contents are released the contents may be frothy or mushy and the rumen end of the tube will plug almost instantly. Rumen lavage may then be attempted using a water hose to deliver 20 to 40 L of water at a time followed by back drainage using gravity flow. After the rumen is partially emptied it is usually possible to more accurately assess the rumen and the abdomen.

DECOMPRESSION OF THE HORSE'S STOMACH

Attempts to pass a nasogastric tube in the horse will usually detect complete or partial obstruction of the esophagus. In gross distension of the stomach in the horse, there is an immediate rush of fluid contents as soon as the cardia is passed (**gastric reflux**). The technique of gastric decompression is therapeutic and diagnostic. Gastric distension is a highly painful feature of some colic cases, and the mere pain relief of gastric decompression facilitates the clinical examination. The retrieval of significant volumes (2 L or more) of sequestered gastric fluid is also an extremely specific indicator of intestinal obstruction, especially small-intestinal obstruction, and a reasonably specific indicator that surgical intervention is necessary.

MEDICAL IMAGING

RADIOGRAPHY

Because of their large size, and the presence of substantial amounts of gas in the large intestine, abdominal radiography has not been used routinely as a diagnostic aid in mature horses with abdominal pain. Similarly, in mature cattle the sheer size of the abdomen and the gas in the rumen has not favored abdominal radiography except for identifying the presence of metal objects in the reticulum. **Esophageal radiography** is, however, useful for the diagnosis of disorders of swallowing in horses.

Foals, calves, and small horses are too small to be palpated per rectum, and abdominal radiography, with and without contrast media, has been used diagnostically in colic of foals. A standard lateral abdominal radiography is a valuable diagnostic aid in the foal with colic. The site of the lesion, whether gastric, small, or large intestinal, or a combination of all three, can be determined from the radiographs. The **sensitivity of radiography** in detecting gastrointestinal lesions in neonatal foals was found to be 96%, and the specificity was 71%.

Knowledge of the radiographic appearance of the normal neonatal abdomen is important before lesions can be reliably detected. The standing lateral radiographic of the normal abdomen of the neonatal foal is characterized by the following:

- A gas cap over fluid and ingesta in the stomach
- Small collections of gas in the small intestine in the cranial and midcentral abdomen

- Gas caps over fluid and ingesta in the cecum and large colon, seen in the caudodorsal abdomen
- Small amounts of gas in the small colon and inconsistent gas in the rectum, seen at the pelvic inlet

Abdominal radiography has also been used for the diagnosis of enterolithiasis and sand accumulation as causes of colic.[15-18] The technique provides a high positive predictive value and is cost-effective in high-prevalence areas.

ABDOMINAL ULTRASONOGRAPHY

Abdominal ultrasonography has been used to identify small intestine intussusceptions, large-colon displacements, abdominal viscera, and neoplasms. The technique requires only several minutes in the hands of an experienced clinician.[14]

Horse

Abdominal ultrasonography is a diagnostic aid that is used for evaluation of equine colic and to assist in differentiation of medical from surgical colics.[19-21]

It is accurate in identifying horses with abnormal small intestines. Completely distended small intestine is associated with an increased risk of strangulating obstruction (odds ratio [OR] 6.3), inability to visualize the left kidney (OR 31 for left dorsal displacement), and thickened large colon (OR 12 for large-colon strangulating volvulus).[22] Detecting increased thickness of the wall of the large intestine during ultrasonography is a reproducible and accurate preoperative test for large-colon torsion in horses with surgical colic localized to the large colon.[20] The duodenum of the horse can be evaluated by ultrasonography. The technique has been used to detect large-intestinal sand accumulations.[23] Gastrointestinal activity patterns have been evaluated in healthy horses using B-mode and Doppler ultrasonography.[24] The anatomy and biometric analysis of the thoracic and abdominal organs in healthy foals from birth to age 6 months have been evaluated with ultrasonography.[25]

Cattle

Abdominal ultrasonography is an ideal diagnostic aid for the investigation of gastrointestinal diseases, the most common of which include traumatic reticuloperitonitis, left and right displacement of the abomasum, duodenal obstruction, hemorrhagic bowel syndrome, omasal disease, ileus of the small intestine, and dilatation and displacement of the cecum.[12,13,26] The various divisions of the small intestine can be differentiated from one another with the exception that the ileum cannot be differentiated from the jejunum. In normal cows, in which the intestine is full of ingesta, all parts of the intestine have a relatively large diameter. In cows with ileus, the loops of intestine proximal to the ileus are distended, and those distal to the ileus are empty.

ENDOSCOPY

Gastroscopic examination is limited to monogastric animals and has particular utility in horses and foals. It is useful in confirming the presence or absence of gastric ulcers, impaction, neoplasia, and inflammatory disease. The procedure involves passage of a flexible endoscope of at least 3 m in length for the adult horse and approximately 13 mm in diameter.[27] Case preparation is important to ensure that the stomach and proximal duodenum can be completely visualized. Feed should be withheld for approximately 16 hours and water for no less than 1 hour. Horses are usually sedated before commencing the examination. Insufflation of the stomach is essential for a thorough examination, although it has been associated with segmental volvulus in a small number of cases.[28]

A complete examination of the stomach is important, and the presence or absence of squamous ulceration cannot be used as a predictor for the presence or absence of glandular ulceration.[27] Observation of the squamous mucosa is relatively easy, whereas passage through to the pyloric antrum is more technically demanding. However, observation of the pyloric antrum is critical because the majority of glandular ulceration occurs in this region.[29-31] Observation of the most ventral portion of the fundus is typically not possible because of the presence of fluid. The fluid can be suctioned out via the biopsy channel of the gastroscope; however, this is usually not necessary because ulceration in this region is rare.[27]

LAPAROSCOPY

In this procedure a laparoscope is passed through an incision in the abdominal wall of either the left or right paralumbar fossa. Feed must be withheld for 36 hours, analgesia is provided during the procedure, and abdominal insufflation with carbon dioxide is required to separate the viscera for viewing. Laparoscopy in standing horses is a valuable diagnostic aid for examination of the structures in the dorsal regions of the abdomen. In the standing horse, the anatomic structures of importance that can be viewed in the left half of the abdomen are the hepatic duct, left lateral and quadrate lobes of the liver, stomach, left kidney with associated nephrosplenic ligament, segments of the jejunum, descending colon and ascending colon, left side of the male and female reproductive tracts, urinary bladder, vaginal ring, and mesorchium. The important structures observable in the right side of the abdomen are the common hepatic duct, left lateral, quadrate and right lobes of the liver, caudate process of the liver, stomach, duodenum, right dorsal colon, epiploic foramen, omental bursa, right kidney, base of the cecum, segments of jejunum, descending colon and ascending colon, urinary bladder, right half of the male and female reproductive tracts, and rectum.

In the dorsally recumbent horse under general anesthesia, with laparoscopy the main structures of diagnostic relevance in the caudal region of the abdomen are the urinary bladder, mesorchium, ductus deferens (left and right), left and right vaginal rings, insertion of the prepubic tendon, random segments of jejunum and descending colon, the pelvic flexure of the ascending colon, body of the cecum, and cecocolic fold. The main structures observed in the cranial region of the abdomen are the ventral surface of the diaphragm; falciform ligament and round ligaments of the liver; ventral portion of the left lateral, left medial, quadrate, and right lateral lobes of the liver; spleen; right and left ventral colons; sternal flexure of the ascending colon; apex of the cecum; and stomach. Alterations in cardiovascular and respiratory functions in response to the pneumoperitoneum and various positional changes indicated a need for continuous and thorough anesthetic monitoring and support.

EXPLORATORY LAPAROTOMY (CELIOTOMY)

An exploratory laparotomy is useful for palpating and inspecting the abdominal viscera as a diagnostic aid in cattle, sheep, and horses of all ages. Cost and time are important factors, but if abdominal disease is suspected and other diagnostic techniques cannot identify the location and nature of the abnormality, a laparotomy is highly desirable.

TESTS OF DIGESTION AND ABSORPTION

Digestion and absorption of nutrients are complex, interrelated functions of the gastrointestinal tract. Failure in one or more of normal motility and enzymatic digestion of food and absorption of simple sugars, fat, and protein by the small intestine can result in inadequate assimilation of nutrients from the gastrointestinal tract. Tests of small-intestinal digestion, absorption, or both have been devised for use in monogastrics. These tests take advantage of the rapid appearance in blood of products of digestion, or of compounds that are readily absorbed without digestion.

Indications for these tests include the following:

- Weight loss of undetermined cause suspected to be from failure of absorption of food by the small intestine
- Diarrhea of suckling foals suspected to be from failure of the foal to digest lactose (lactase deficiency)

- Suspected protein-losing enteropathy of older foals and adult horses

Low serum protein and albumin concentrations with small-intestinal disease can be caused by failure of digestion of proteins and absorption of amino acids or leakage of plasma proteins into the intestine. Some horses with protein-losing enteropathy have abnormal tests of intestinal digestion and absorption of sugars. **Contraindications** include the presence of obstructive lesions of the gastrointestinal tract, risk of worsening the disease process by the period of fasting required for most of the tests (such as in ponies with hyperlipemia), or known adverse reactions of the animal to any of the test substances.

Interpretation of the test is based on the concentration of the variable of interest (usually glucose or xylose) in blood over a period of time after administration of the test meal (usually by nasogastric intubation). Concentration of the metabolite or marker of interest in blood is plotted against time, and the shape of the curve, highest concentration attained, time to attain the highest concentration, and elevation over baseline values (i.e., those measured immediately before administration of the test meal) are compared against values obtained from clinically normal horses or foals. Blood concentrations of glucose or xylose that are lower than expected (so called "flat curve") can be indicative of alterations in gastrointestinal function that hinder propulsion, digestion, or absorption of nutrients. Thus tests of digestion and absorption alone rarely provided sufficient information to make a definitive diagnosis of the functional disorder. The exception to this rule is the modified lactose tolerance test in foals (see later). Interpretation of the results of oral tests of absorption is often confounded by factors that alter gastrointestinal function, such as feed withholding or enteritis or conditions that alter removal of the test compound from blood like reduced insulin sensitivity. This is particularly the case for tests that depend on measurement of blood glucose concentration. Blood glucose concentrations are determined in the absorptive state by the difference in rates of absorption of glucose from the small intestine into blood and removal of glucose from blood by uptake into muscle, adipose tissue, and metabolically active tissues. Conditions that enhance glucose uptake from the blood can result in low peak blood glucose concentrations, and conditions that decrease insulin sensitivity (as is seen in fat horses) can result in high blood glucose concentrations. The use of D-xylose as an indicator of small-intestinal absorption is intended to avoid these effects of variable glucose disposal. Therefore the values obtained with oral tests of absorption and digestion should be interpreted with caution and should be considered in light of all clinical and laboratory data available for the animal. Sedation does not affect D-xylose uptake in horses.[32]

GLUCOSE ABSORPTION TEST

The oral glucose tolerance test is one of the simplest tests of small-intestinal absorptive capacity to perform. However, because of the many factors that affect blood glucose concentration, including factors not related to small-intestinal absorptive capacity, results of the test can on occasion be difficult to interpret. Oral glucose tolerance testing can produce abnormal results in horses with diseases that do not involve the small intestine, such as lower motor neuron disease or polysaccharide storage myopathy. On the other hand, the oral glucose tolerance test is often used because of the ready availability of glucose for oral administration and routine nature of measurement of blood glucose concentrations.

The main indications for performing oral glucose tolerance testing include unexplained weight loss believed to be associated with gastrointestinal disease and suspected protein-losing enteropathy. Contraindications are those listed previously. In addition, care should be exercised in performing the test in horses at increased risk of laminitis, because rapid passage of unabsorbed glucose into the large colon and cecum can cause laminitis.

Horses undergoing oral glucose tolerance testing are first fasted for 12 to 18 hours. Access to water should be provided. Glucose is given by stomach tube at 1 g/kg BW of anhydrous glucose (or comparable) as a 10% to 20% solution in water. Blood for measurement of glucose concentration is collected immediately before and every 30 minutes for 4 to 6 hours after glucose administration. Some protocols involve less frequent (hourly) collection of blood. One protocol requires collection of blood samples before and 120 minutes after administration of glucose. This last protocol is not recommended because early or delayed peaks in blood concentration are not detected. The blood glucose concentration in the normal horse increases by at least 85% (from 90 up to 180 mg/dL [5.0–10.0 mmol/L]) with peak blood concentrations attained 90 to 150 minutes after administration of glucose. Horses with partial malabsorption have increases in blood glucose concentration of 15% to 85% of baseline values, and horses with complete malabsorption have no increase or less than 15% increase in blood glucose concentration by 2 hours. Blood concentrations of glucose in normal horses return to resting values in approximately 6 hours. The shape of the curve is affected by the horse's previous diet, and the curve is much lower in horses fed on stored feeds such as hay and grain compared with horses eating pasture of clover and grass.

Horses with weight loss and complete failure of absorption of glucose are likely to have extensive infiltrative disease of the small intestine such as lymphosarcoma or granulomatous enteritis. Of 25 horses with partial failure of glucose absorption, 18 (62%) had structural abnormalities of the small intestine. Clearly abnormal results of the oral glucose tolerance test appear to be fairly specific for severe and widespread small-intestinal disease. Care should be taken when interpreting results that deviate only marginally from normal values.

STARCH DIGESTION TEST

A suitable test for the evaluation of gastric, small-intestinal, and pancreatic function is the starch digestion test. The test relies on the presence of amylase in the small intestine with subsequent cleavage of starch into glucose, which is then absorbed into the blood. The horse is fasted for 18 hours and then given corn starch (1 kg in 4 L of water or 2 g/kg BW) by stomach tube. A pretreatment blood sample is matched with others taken at 15, 30, 60, 90, and 120 minutes and then hourly to 6 hours.

In the normal horse there is an increase in blood glucose levels of about 30 mg/dL (1.7 mmol/L; from 90 up to 120 mg/dL [5.0–6.7 mmol/L]), with the peak occurring at 1 to 2 hours and the curve returned to pretreatment level at 3 hours. The test can be affected by the diet of the horse before testing.

LACTOSE DIGESTION TEST

Newborn animals rely on ingestion of milk sugar (lactose) as an important source of energy until weaning. Lactose is digested in the proximal small intestine by lactase, a disaccharidase present in the brush border of intestinal epithelial cells that cleaves lactose into glucose and galactose. Loss of small-intestinal production of lactase, such as occurs in some bacterial and viral enteritides including rotavirus infection, results in failure to cleave lactose and passage of the sugar to the hind gut. Fermentation of lactose in the hind gut causes acute and sometimes severe osmotic diarrhea. A prime indication for the oral lactose tolerance test is therefore acute diarrhea in neonates being fed milk. The test is also important because a positive test (i.e., demonstration of lactose intolerance) provides a clear indication for feeding lactose-free milk or providing supplemental lactase in the animal's diet.

An oral lactose digestion test has been devised for foals. Lactose (1 g/kg BW) is given by stomach tube in a 20% solution to a foal that has been fasted for 2 to 4 hours. In foals and young horses up to 3 years of age there is a rise in blood glucose levels from 86 ± 11 mg/dL (4.8 ± 0.1 mmol/L) up to 153 ± 24 mg/dL (8.5 ± 1.3 mmol/L), with a peak achieved in 90 minutes, and the level returns to pretreatment levels in 5 hours. In foals of 1 to 12 weeks of age the plasma glucose concentration should rise by at least 35 mg/dL

(1.9 mmol/L) and peak within 40 minutes of the administration of the lactose. With this test no changes in blood sugar levels occur in horses over 4 years of age. Instead there is abdominal discomfort followed by diarrhea, with feces the consistency of cow feces for the next 24 hours. Sucrose and maltose are readily digested by the intestine of the adult horse, but not by newborn foals. Maximum levels of the relevant intestinal disaccharidases (sucrase and maltase) are not achieved until 7 months of age. The oral lactose digestion test is likely to be of value as a monitor of epithelial damage in young horses. In humans the ability to hydrolyze lactose is one of the first functions of the intestinal mucosa to be lost in which there is epithelial damage in the gut. It is also one of the last functions to return in the recovering patient. The loss of intestinal lactase may be the pathogenetic basis of the diarrhea that occurs in rotavirus infections in neonates. Lactase digestion is impaired in calves with mild diarrhea. Calves with acute diarrhea are in a catabolic state and respond with a larger increase in plasma glucose concentration to a given amount of glucose than do healthy calves.

A modification of the oral lactose tolerance test in foals includes a second evaluation in foals in which there is failure of blood glucose concentrations to increase by the appropriate amount after oral administration of lactose. At least 8 hours after the first test, foals are fed a meal of lactose-free milk, or of milk to which lactase has been added. Blood glucose concentrations are measured, and an increase of at least 35 mg/dL (1.9 mmol/L) is interpreted as evidence of lactase deficiency. Such animals can then be maintained on a diet of lactose-free milk. Diarrhea usually resolves in 24 hours but returns within hours of feeding milk containing lactose.

An alternative to the lactose tolerance tests described earlier is to simply feed the foal lactose free milk for several days. The foal must not have access to mare's milk or milk-based feed supplements during this time. Some foals have prompt resolution of diarrhea when fed only lactose-free milk.

XYLOSE ABSORPTION TEST

D-Xylose is used to evaluate small-intestinal absorptive function because it is not metabolized by tissues, which is an advantage over the oral glucose tolerance test. D-xylose absorbed from the intestinal tract is excreted unchanged in the urine within 15 hours of dosing. Concentrations of D-xylose in blood are therefore dependent only on the rate of absorption from the intestine and rate of excretion into the urine. However, the compound is more expensive than glucose, and measurement of D-xylose in blood requires a particular analysis that might not be readily available. Indications for the test are the same as those for the oral glucose tolerance test described earlier.

D-Xylose, at a dose rate of 0.5 g/kg BW as a 10% solution, is administered by stomach tube after a starve of 18 hours. A maximum blood xylose level of 30 mg/dL (2.0 mmol/L) at 1.5 hours is a normal result in adult horses. In normal foals the peak blood concentration of xylose is reached in 30 to 60 minutes, and the level attained varies with age, being highest (47 mg/dL [3.14 mmol/L]) at 1 month of age and lowest (19 mg/dL [1.25 mmol/L]) at 3 months (the pretreatment reading should be zero). In abnormal horses the xylose curve is flat (a peak of 7–13 mg/dL [0.5 mmol/L] at 60 to 210 minutes) contrasted with a peak of 20 mg/dL [1.3 mmol/L] at 60 minutes in normal horses. As an initial checking test, one postdosing sample at 2 hours is recommended.

Interpretation of the test is influenced by the customary diet of tested animals and feed deprivation. Horses receiving a high-energy diet have a lower absorption curve than horses on a low-energy diet. The test is also affected by the duration of deprivation of feed. In mares deprived of feed for 72 and 96 hours, the rate of D-xylose absorption and the maximum concentrations of D-xylose in plasma were reduced. For example, apparent low absorption can be caused by increased transit time through the gut, perhaps from to excitement.

Low blood concentrations of xylose occur in horses with small-intestinal infiltrative disease, such as lymphosarcoma or granulomatous enteritis. The test appears to be quite specific (low false-positive rate) for small-intestinal disease, but the sensitivity (false-negative rate) is unknown. Peak xylose concentration is significantly ($P = 0.048$) higher in horses with suspected inflammatory bowel disease that survive (1.36 ± 0.44 mmol/L) than nonsurvivors (0.94 ± 0.36 mmol/L).[33]

A D-xylose absorption curve has been determined for cattle. The xylose (0.5 g/kg BW) is deposited in the abomasum by abomasocentesis, and a peak of blood glucose is attained in about 90 minutes.

SUCROSE ABSORPTION TEST

The sucrose absorption test differs from the other tests in this section in that abnormal results are associated with detection of sucrose in blood or urine of horses. Sucrose is not normally absorbed intact; it is usually cleaved by disaccharidases in the small intestine into glucose and fructose, which are then absorbed. Intact sucrose is absorbed across compromised gastric mucosa, and detection of sucrose in blood or urine indicates the presence of gastric ulceration, because mammals neither synthesize nor metabolize sucrose. The sucrose absorption test involves administration of 250 g of sucrose to an adult horse that has been fasted overnight. Blood samples for measurement of serum sucrose concentration are collected at 0, 15, 30, 45, 60, and 90 minutes after

dosing. Alternatively, a urine sample is collected 2 hours after dosing (the bladder must be emptied immediately before dosing). Peak serum sucrose concentrations occur 45 minutes after administration, and peak values correlate with the severity of gastric ulceration. Horses with minimal lesions have serum sucrose concentrations of 103 pg/μL, whereas horses with the most severe lesions have concentrations of 3400 pg/μL.

RADIOACTIVE ISOTOPES

A technique used for determining whether a protein-losing enteropathy is present is based on the examination of feces for radioactivity after the intravenous administration of a radioactive agent. ^{51}Cr ^{13}C-labeled plasma protein has been used for this purpose. Similarly, administration of radioactively labeled leukocytes reveals the presence of small-intestinal inflammatory disease in horses. The test is quite specific, in that false-positive tests are uncommon, but not very sensitive.

ABDOMINOCENTESIS FOR PERITONEAL FLUID

Peritoneal fluid reflects the pathophysiological state of the parietal and visceral mesothelial surfaces of the peritoneum. Collecting a sample of peritoneal fluid is useful in the diagnosis of diseases of the peritoneum and the abdominal segment of the alimentary tract. It is of vital importance in horses in the differential diagnosis and prognosis of colic and in cattle in the diagnosis of peritonitis.

EQUINE AND BOVINE PERITONEAL FLUID

Normal peritoneal fluid is a transudate with properties as summarized in Tables 7-2 and 7-3. It has functions similar to those of other tissue fluids. It contains mesothelial cells, lymphocytes, neutrophils, a few erythrocytes, and occasional monocytes and eosinophils. The following general comments apply:
- It can be examined in terms of physical characteristics, especially color, translucence, specific gravity, clotting time, biochemical composition, cell volume, cell morphology, and cell type.
- Examination of the fluid may help determine the presence in the peritoneal cavity of
  - Peritonitis (chemical or infectious)
  - Infarction of a segment of gut wall
  - Perforation of the alimentary tract wall
  - Rupture of the urinary bladder
  - Leakage from the biliary system
  - Intraperitoneal hemorrhage
  - Peritoneal neoplasia
- The reaction of the peritoneum varies with time, and a single examination can be dangerously misleading. A series of examinations may be necessary, for example, in acute cases at intervals of as short as an hour.

Table 7-2 Guidelines for the classification and interpretation of bovine peritoneal fluid

Classification of fluid	Physical appearance	Total protein (g/dL)	Specific gravity	Total RBC × 10^6/μL	Total WBC × 10^6/μL	Differential WBC count	Bacteria	Particulate matter (plant fiber)	Interpretation
Normal	Amber, crystal clear 1–5 mL per sample	0.1–3.1 (1.6) Does not clot	1.005–1.015	Few from puncture of capillaries during sampling	0.3–5.3	Polymorphonuclear and mononuclear cells, ratio 1:1	None	None	Increased amounts in late gestation, congestive heart failure
Moderate inflammation	Amber to pink, slightly turbid	2.8–7.3 (4.5) May clot	1.016–1.025	0.1–0.2	2.7–40.7 (8.7)	Nontoxic neutrophils, 50%–90%; macrophages may predominate in chronic peritonitis	None	None	Early stages of strangulation, destruction of intestine; traumatic reticuloperitonitis; ruptured bladder; chronic peritonitis
Severe inflammation	Serosanguineous, turbid, viscous 10–20 mL per sample	3.1–5.8 (4.2) Commonly clots	1.026–1.040	0.3–0.5	2.0–31.1 (8.0)	Segmented neutrophils, 70%–90%; presence of (toxic) degenerate neutrophils containing bacteria	Usually present	May be present	Advanced stages of strangulation obstruction; acute diffuse peritonitis; perforation of abomasal ulcer; rupture of uterus, stomachs, or intestine

RBC, red blood cell; WBC, white blood cell.

Table 7-3 Characteristics of equine peritoneal fluid in selected diseases of horses

Disease	Protein concentration	Total nucleated cell count	Cytological comments	Other variables	Comments
Normal horse	<2.1 g/dL <21 g/L	<9 × 10^9 cells/L <9 × 10^3 cells/μL (TNCC is usually substantially lower in clinically normal horses)	Approximately 50% each of nondegenerate neutrophils and mononuclear cells	Lactate <1 mmol/L (always < plasma (lactate)); Glucose <2.0 mmol/L different from blood glucose; pH > 7.45; fibrinogen < 300 mg/dL (3 g/L) Creatinine = serum creatinine No red blood cells	Clear and slightly yellow Not malodorous Culture does not yield growth
Normal late gestation mare	<2.5 g/dL <25 g/L	<0.9 × 10^9 cells/L <900 cells/μL	<40% neutrophils; no degenerative changes. <20% lymphocytes	Fluid usually readily obtained; clear and slightly yellow	
Normal postpartum (<7 days) mare	<2.5 g/dL <25 g/L	<5.0 × 10^9 cells/L <5.0 × 10^3 cells/μL	<50% neutrophils; no degenerative changes <10% lymphocytes	Fluid usually readily obtained; clear and slightly yellow	
Dystocia but clinically normal mare (1 day)	<2.5 g/dL <25 g/L	2.7 × 10^9 (3.9) cells/L* 2.7 × 10^3 (3.9) cells/μL	50%–90% nondegenerate neutrophils; 40% mononuclear cells and 10% lymphocytes	Fluid clear and yellow Essentially normal fluid with small increases in TNCC and protein concentration	
Dystocia and clinically abnormal mare (uterine rupture, vaginal tear)	4.4 (1.3) g/dL* 44 (13) g/L	27 × 10^9 (35) cells/L* 27 × 10^3 (35) cells/μL	70%–100% neutrophils, some of which are degenerate, <10% mononuclear cells and <10% lymphocytes	Increased red blood cell count	Fluid yellow or serosanguinous and cloudy; can be malodorous; culture can yield variety of bacteria; red cell count in mares with middle uterine artery rupture is high with normal TNCC

Table 7-3 Characteristics of equine peritoneal fluid in selected diseases of horses—cont'd

Disease	Protein concentration	Total nucleated cell count	Cytological comments	Other variables	Comments
Peritonitis, septic	5.2 (4.0–6.0) g/dL[†] 50 (40–60) g/L	131 (7–700) × 10^9 cells/L[†] 131 (7–700) × 10^3 cells/μL	Almost all neutrophils, many of which have degenerative changes Some neutrophils contain bacteria in many cases; plant material with rupture of intestine	pH < that of blood; glucose < blood (difference < 2.0 mmol/L or 50 mg/dL); peritoneal glucose < 30 mg/dL (1.5 mmol/L); fibrinogen > 200 mg/dL (2.0 g/L)	Fluid usually dark yellow, brown, or serosanguinous Can be green if severe rupture of intestine or stomach; cloudy. Malodorous; culture yields bacteria
Peritonitis, nonseptic (e.g., nonstrangulating, nonischemic obstructive lesion of the bowel)	2.7 (0.7–4.9) g/dL[†] 27 (7–49) g/L	13 (0.4–516) × 10^9 cells/L[†] 13 (0.4–516) × 10^3 cells/μL	Mostly neutrophils (>50%) Nondegenerate No bacteria detected No plant or foreign material	No abnormalities pH ≥ that of blood	Fluid yellow and clear Not malodorous; no bacteria isolated on culture
Strangulating intestinal lesion or ruptured intraabdominal viscus	5.2 (4.0–6.0) g/dL[†] 50 (40–60) g/L	131 (7–700) × 10^9 cells/L[†] 131 (7–700) × 10^3 cells/μL	Almost all neutrophils, many of which have degenerative changes Some neutrophils contain bacteria in many cases; plant material with rupture of intestine	Lactate 8.5 ± 5.5 mmol/L	Serosanguinous fluid Cloudy if ruptured
Nonstrangulating obstruction				Lactate 2.1 ± 2.1 mmol/L	
Peritonitis caused by *Actinobacillus equuli*	2.5–8.4 g/dL 25–84 g/L	46–810 × 10^9 cells/L 46–810 × 10^3 cells/μL	>80% neutrophils, most of which do not have signs of degeneration Low numbers of gram-negative pleomorphic rods, both intracellular and extracellular		Cream, orange, brown or red fluid; turbid; not malodorous; growth of *Actinobacillus equuli* on culture
Intraabdominal abscess	>2.5 g/dL >25 g/L	>10 × 10^9 cells/L >10 × 10^3 cells/μL	>80% nondegenerate neutrophils; usually no bacteria detected on Gram stain		Yellow to white; slightly cloudy; culture will occasionally yield × causative bacteria (usually *Streptococcus equi*)
Hemoperitoneum	3.2–6.3 g/dL 32–63 g/L	<10 × 10^9 cells/L <10 × 10^3 cells/μL	Differential similar to blood Mostly nondegenerate neutrophils, erythrophages, and hemosiderophages as hemorrhage resolves	High red cell count (2.4–8.6 × 10^{12} cells/L, 2.4–8.6 × 10^6 cells/μL)	Serosanguinous to frankly bloody
Intraabdominal neoplasia (lymphosarcoma, gastric squamous cell carcinoma)	<2.5 g/dL <25 g/L	<10 × 10^9 cells/L <10 × 10^3 cells/μL	Abnormal cells not detected in most cases Care should be taken not to mistake reactive lymphocytes for neoplastic lymphocytes		Clear and yellow; often subjective assessment of increased quantity (increased ease of collection of a large quantity of fluid)
Uroperitoneum	<2.5 g/dL <25 g/L	<10 × 10^9 cells/L <10 × 10^3 cells/μL	Normal differential, might see calcium carbonate crystals in adult horses with uroperitoneum	Creatinine > serum creatinine concentration Urea nitrogen > serum urea nitrogen concentration Potassium > serum potassium concentration	Large amount of fluid Clear to very pale yellow Uriniferous odor

Data from Frazer G. et al. Theriogenology 1997; 48:919; van Hoogmoed L. et al. J Am Vet Med Assoc 1996; 209:1280; van Hoogmoed L. et al. J Am Vet Med Assoc 1999; 214:1032; Pusterla N et al. J Vet Intern Med 2005; 19:344; Latson KM et al. Equine Vet J 2005; 37:342; Matthews S et al. Aust Vet J 2001; 79:536.
TNCC, Total nucleated cell count.
*Mean (standard deviation [SD]).
†Median (range).

- A significant reaction in the peritoneal cavity may be quite localized, so a normal sample of fluid collected at one point in the cavity may not be representative of the entire cavity.
- Changes in peritoneal fluid, especially its chemical composition, e.g., lactate level, may be a reflection of a systemic change. The examination of a concurrently collected peripheral blood sample will make it possible to determine whether the changes are in fact restricted to the peritoneal cavity.
- As in any clinicopathologic examination the results must be interpreted with caution and only in conjunction with the history and clinical findings.

Specific Properties of Peritoneal Fluid (Normal and Abnormal)

Color

Normal fluid is crystal clear, straw-colored to yellow. Turbidity indicates the presence of increased leukocytes and protein, which may include fine strands of fibrin.

A **green color** suggests food material; intense orange-green indicates rupture of the biliary system. A **pink-red color** indicates presence of hemoglobin; degenerated erythrocytes; entire erythrocytes; and damage to the vascular system by infarction, perforation, or hydrostatic pressure. A **red-brown color** indicates the late stages of necrosis of the gut wall, the presence of degenerated blood and hemoglobin, and damage to gut wall with hemorrhage.

Whole blood, clear fluid streaked with blood, or heavily bloodstained fluid indicates that the sample has been collected from the spleen or a blood vessel or that there is hemoperitoneum. Rupture of the uterus or bladder or dicoumarol poisoning are also possibilities.

A dark green sample containing motile protozoa with very few leukocytes and no mesothelial cells indicates that the sample has been collected from the gut lumen. Enterocentesis has little apparent clinical affect in normal horses, although an occasional horse will show a transient fever. However, puncture of a devitalized loop of intestine may lead to extensive leakage of gut contents and fatal peritonitis. The effect of enterocentesis of normal gut on peritoneal fluid is consistently to increase the neutrophilic count, which persists for several days.

Cellular and Other Properties

Surgical manipulation of the intestinal tract during exploratory laparotomy or intestinal resection and anastomosis in the horse results in a significant and rapid postoperative peritoneal inflammatory reaction. Manipulation of the viscera causes injury to the mesothelial surfaces. Total and differential nucleated cell counts, red blood cell numbers, and total protein and fibrinogen concentrations were all elevated on the first day after the surgery and remained elevated for up to 7 days in a study of this phenomenon.

In cattle, exploratory celiotomy and omentopexy result in an increase in the total nucleated cell count by a factor of 5 to 8, minor increases in specific gravity, and increases in total protein concentration by a factor of up to 2. These changes appear by 2 days after surgery and continue to increase through to day 6.

Particulate matter in peritoneal fluid suggests either fibrin clots/strands or gut contents caused by leakage from a perforated or ruptured gut wall.

High specific gravity and **high protein content** are indicative of vascular damage and leakage of plasma protein, as in peritonitis or mural infarction.

The **volume** and viscosity of fluid varies. A normal flow is 1 to 5 mL per sample. A continuous flow with 10 to 20 mL per sample indicates excess fluid caused by a ruptured bladder or ascites (clear yellow), acute diffuse peritonitis (yellow, turbid), and infarction or necrosis of gut wall (thin, red-tinged). The higher the protein content, as the peritoneal fluid shifts from being a transudate to an inflammatory exudate, the higher the viscosity becomes. Highly viscous fluid may clot.

Cells

A rapid staining method, using a modified Wright's stain, makes a stained slide ready for examination within 5 minutes. The value of the technique is in indicating the number of leukocytes and other cells present, and in differentiating the types of cell.

An **increase in total white cell count** of the fluid including a disproportionate number of polymorphonuclear cells indicates acute inflammation, which may have an infectious origin or else be sterile. An increase in mononuclear phagocytes from the peritoneum is an indication of chronic peritonitis. **Degenerate and toxic neutrophils** suggest the probability of infection being present. An increase in the number of **mesothelial cells** with the distinctive presence of actively dividing mitotic figures suggests neoplasia.

Bacteria found as **phagocytosed inclusions in leukocytes,** or by culture of fluid, indicate an infective peritonitis, which may arise by hematogenous spread, in which case the infection is likely to be a specific one. If there has been leakage from a peritoneal abscess the same comment applies, but if there is leakage through a segment of devitalized or perforated bowel wall there is likely to be a mixed infection and possibly particulate matter from bowel contents.

Entire erythrocytes, often accompanied by some hemoglobin, indicate either hemoperitoneum, in which case there should be active phagocytosis of erythrocytes, or that the sample has been inadvertently collected from the spleen. The blood is likely to be concentrated if there has been sufficient time for fluid resorption across the peritoneum. Splenic blood has a higher packed cell volume (PCV) also, but there is no erythrophagocytosis evident in the sample. A **PCV of less than 5%** in peritoneal fluid suggests extravasation of blood from an infarcted or inflamed gut wall; a PCV of more than 20% suggests a significant hemorrhage.

Abdominocentesis in Horses

In the horse the recommended site for paracentesis is on the ventral midline, 25 cm caudal to the xiphoid (or midway between the xiphoid and the umbilicus). Following surgical preparation and subcutaneous infiltration of an anesthetic, a stab incision is made through the skin and subcutaneous tissues and into the linea alba. A 9-cm long blunt-pointed bovine teat cannula, or similar metal catheter, with the tip wrapped in a sterile swab to avoid blood and skin contamination, is inserted into the wound and manipulated until the incision into the linea alba can be felt. With a quick thrust the cannula is pushed through the linea alba into the peritoneal cavity. A "pop" is often heard on entry into the peritoneal cavity. Failure to incise into the linea alba first will cause many cannulas to bend and break.

In most horses (about 75%) a sample of fluid is readily obtained. In others it takes a moment or two before the fluid runs out, usually spurting synchronously with the respiratory movements. Applying suction with a syringe may yield some fluid if there is no spontaneous flow. Normal fluid is clear, yellow, and flows easily through an 18-gauge needle. Two samples are collected, one in a plain tube and one in a tube with an anticoagulant. If the fluid clots readily a few drops should be placed and smeared out on a glass slide and allowed to dry for staining purposes.

In peritonitis, the total leukocyte count will increase markedly, but wide variation in the total count can occur between horses with similar conditions, and in the same horse within a period of hours. Variations are caused by the nature and stage of the lesion and by the total amount of exudate in the peritoneal cavity, which has a diluting effect on the total count. Total leukocyte counts ranging from 10,000 to 150,000 μL have been recorded in peritonitis and in infarction of the intestine in horses. Experimentally, the intravenous injection of endotoxin into horses causes marked changes in the peripheral blood cellular components, but there are no changes in the total white cell count of the peritoneal fluid.

In **healthy foals** the reference values for peritoneal fluid are different from adult horses. The maximum peritoneal fluid nucleated cell counts in foals are much lower than in adult horses (1.5×10 /L versus 5.0×10 /L). Nucleated cell counts greater than 1.5×10 /L should be interpreted as elevated.

Peritoneal fluid abnormalities in mares within a week of foaling should be attributed to a systemic or gastrointestinal abnormality and not to the foaling event. The nucleated cell count, protein concentration, fibrinogen concentration, and specific gravity of peritoneal fluid from recently foaled mares should be normal; however, differential cell counts may be abnormal for up to 1 week after foaling.

Risks
Abdominocentesis is not without some danger, especially the risk of introducing fecal contents into the peritoneal cavity and causing peritonitis. This appears to be of major importance only if there are loops of distended atonic intestine situated on the ventral abdominal wall. This is a common occurrence in the later stages of intestinal obstruction that is still amenable to surgery. Puncture of a devitalized loop of intestine may cause a leakage of intestinal contents and acute diffuse peritonitis, which is rapidly fatal. Penetration of a normal loop of intestine occurs often enough to lead to the conclusion that it appears to have no ill effects. If a sample of peritoneal fluid is an important diagnostic need in a particular case, and the first attempt at paracentesis causes penetration of the gut, it is recommended that the attempt be repeated, if necessary two or three times, at more posterior sites. Repeated abdominocentesis does not cause alterations in peritoneal fluid constituents, and any significant changes are likely caused by alterations in the disease state present. The technique most likely to cause bowel penetration is the use of a sharp needle instead of the blunt cannula recommended, and forcibly thrusting the cannula through the linea alba without a prior incision. When the suggested incision is made in the linea alba, the cannula can be pushed gently through while rotating it.

Abdominocentesis in Cattle
The choice of sites for paracentesis is a problem, because the rumen covers such a large portion of the ventral abdominal wall, and avoiding penetration of it is difficult. Cattle have a low volume of peritoneal fluid, and failure to obtain a sample is not unusual. The most profitable sites are those that, on an anatomic basis, consist of recesses between the forestomachs, abomasum, diaphragm, and liver. These are usually caudal to the xiphoid sternum and 4 to 10 cm lateral to the midline. Another recommended site is left of the midline, 3 to 4 cm medial, and 5 to 7 cm cranial to the foramen for the left subcutaneous abdominal vein. A teat cannula similar to the one described for use in the horse is recommended but, with care and caution, a 16-gauge 5-cm hypodermic needle may also be used. The needle or cannula is pushed carefully and slowly through the abdominal wall, which will twitch when the peritoneum is punctured. When this happens the fluid will usually run out into a vial without the aid of a vacuum. However, if it does not, a syringe may be used and the needle may be moved backward and forward in a search for fluid, with the piston of the syringe withdrawn. A further site is the right caudoventral abdominal wall medial to the fold of the flank, using a 3.8-cm 15-gauge needle.

In calves, a reliable technique includes the use of sedation with intravenous xylazine hydrochloride and diazepam. The animal is placed in left lateral recumbency with the right hindlimb pulled dorsally and caudally. One site slightly dorsal and caudal to the umbilicus is prepared together with another site in the center of the inguinal region. The site is prepared with local anesthetic, and a 14-gauge needle is introduced and directed slightly caudally and toward the midline while keeping it parallel to the inner abdominal wall once the peritoneal cavity is entered. A 3.5-gauge urinary catheter (1.2 mm × 56 cm sterile feeding tube) is inserted through the needle, and a 3-mL sterile syringe is attached to the catheter. Gentle suction is applied. The fluid is placed in a 2-mL tube containing tripotassium ethylenediaminetetraacetic acid (EDTA). A 14-gauge over-the-needle catheter can also be used, followed by insertion of a 3.5 French feeding tube. If fluid cannot be obtained from the first site, the inguinal site is used using the same basic technique and with the catheter directed slightly cranially toward the midline.

Failure to obtain a sample does not preclude the possibility that peritonitis may be present: the exudate may be very thick and contain large masses of fibrin, or the peritonitis may be localized. Also, animals that are dehydrated may have less peritoneal fluid than normal. Most animals from which samples cannot be obtained, however, are in fact normal. In animals in which peritonitis is strongly suspected for clinical reasons, up to four attempts at paracentesis should be made before aborting the procedure. The fluid should be collected into an anticoagulant, preferably EDTA, to avoid clotting.

Abnormal peritoneal fluid in cattle is a highly sensitive indicator of peritoneal disease, but not a good indicator of the *nature* of the disease. The most pronounced abnormalities occur in acute diseases of the peritoneum; chronic peritonitis may be accompanied by peritoneal fluid that is almost normal.

Examination of the fluid should take into account the following characteristics:
- Large amounts (10–20 mL) of serosanguineous fluid suggest infarction or necrosis of the gut wall.
- Heavily bloodstained fluid, whole blood, or fluid with streaks of blood through it are more likely to result from puncture of a blood vessel or from bleeding into the cavity, as in dicoumarol poisoning or with a neoplasm of the vascular system.
- The same sort of bloodstained fluid as previously discussed may accompany a ruptured uterus or bladder or severe congestive heart failure.
- Large quantities of yellowish-colored turbid fluid suggest acute diffuse peritonitis. The degree of turbidity depends on the number of cells and the amount of fibrin present.
- Particulate food material in the sample indicates perforation or rupture of the gut, except that penetration of the gut with the instrument during collection may be misleading. Such samples are usually heavily fecal in appearance and contain no mesothelial cells.
- Laboratory examination is necessary to derive full benefit from the sample. This will include assessment of the number and type of **leukocytes** present (the number is increased in peritonitis), neutrophils predominating in acute peritonitis, and monocytes in chronic forms; the number of **erythrocytes** present; whether **bacteria** are present inside or outside the neutrophils; and **total protein** content.

The significant values for these items are included in Table 7-2.

Reference values for peritoneal fluid constituents of normal adult cattle may be inappropriate for interpretation of peritoneal fluid analysis in calves of up to 8 weeks of age. The peritoneal fluid nucleated cell count and mononuclear cell counts are higher in calves, and the eosinophil counts are lower than in adult cows.

INTESTINAL AND LIVER BIOPSY

An intestinal biopsy may be obtained from an exploratory laparotomy but is costly and time-consuming. Rectal biopsy is easily done and of low cost. It is a valuable diagnostic aid for evaluating certain intestinal diseases of the horse. Biopsy specimens are taken using minimal restraint and unaided by proctoscopic visualization in the standing horse. A rectal biopsy forceps is used to obtain the biopsy from the floor of the rectum approximately 30 cm proximal to the anal sphincter. The technique for liver biopsy is presented in Chapter 9.

Principles of Treatment in Alimentary Tract Disease

Removal of the primary cause of the disease is essential, but a major part of the treatment of diseases of the alimentary tract is supportive and symptomatic. This is aimed at relieving pain and distension, replacement of fluids and electrolytes, correcting abnormal motility, and relieving tenesmus and reconstitution of the digestive flora if necessary. Specific treatment for individual diseases is

presented with each disease throughout this book. General principles are outlined here.

RELIEF OF ABDOMINAL PAIN

The relief of abdominal pain is of prime importance from a humane aspect, to prevent the animal from self-injury associated with falling and throwing itself against a wall or other solid objects, and to allay the concerns of the owner. No single analgesic is completely satisfactory for every situation. Nonnarcotic and narcotic analgesics that are in general use and the analgesics used in the important subject of equine colic are presented later.

RELIEF OF DISTENSION

The relief of distension of the gastrointestinal viscera is a critical principle to minimize shock and to prevent rupture of the viscus. **Relief of distension of the stomach of the horse with colic is accomplished by nasogastric intubation**. Distension caused by bloat in cattle can be relieved by stomach tube or trocarization of the rumen. Relief of distension of the large colon by percutaneous or per rectal trocarization is used in horses. Either technique can be useful in relieving distension and signs of abdominal pain, but potential complications include peritonitis, infection, and abscessation at the site of trocarization.[34,35]

Relief of distension may be possible by medical means alone with the use of laxatives and purgatives when there is accumulation of ingesta without a physical obstruction. Surgical intervention is often necessary when the distension is associated with a physical obstruction. In functional distension (paralytic ileus), relief of the atony or spasm can be effected by the use of drugs such as metoclopramide. Distension caused by intestinal or gastric accidents requires surgical correction.

REPLACEMENT OF FLUIDS AND ELECTROLYTES

Replacement of fluid and electrolytes lost in gastrointestinal disease is one of the most important principles of treatment. In gastric or intestinal obstruction, or when diarrhea is severe, it is necessary to replace lost fluids and electrolytes by the parenteral administration of large quantities of isotonic glucose–saline or other physiologically normal electrolyte solutions. The amount of fluid lost may be very large and fluids must be given in quantities to replace losses and to support continuing losses and maintenance requirements. In acute, severe dehydration in horses, such as occurs in acute intestinal obstruction, the amount of fluid required before and during surgery ranges from 50 to 100 mL/kg BW per 24 hours. It is critical that administration of fluid is commenced at the earliest possible time because of the need to maintain homeostasis. Details of fluid therapy are given in Chapter 5.

In young animals the need is much greater still and amounts of 100 mL/kg BW, given slowly intravenously, are commonly necessary and not excessive. The treatment of shock is also presented in Chapters 2 and 9 and includes the administration of fluids, plasma or blood, and nonsteroidal antiinflammatory drugs (NSAIDs). The use of intravenous administration of hypertonic saline followed by the ingestion of large quantities of water by the animal is another aspect of fluid therapy in gastrointestinal disease (see Chapter 5).

CORRECTION OF ABNORMAL MOTILITY

INCREASED MOTILITY

When motility is increased, the administration of atropine or other spasmolytics such as dipyrone or proquamezine is usually followed by the disappearance of the abdominal pain and a diminution of fluid loss. Meperidine, butorphanol, and pentazocine inhibit regular cyclic myoelectric activity in the jejunum. There is a need for some scientific clinical investigation into the desirability of treating intestinal hypermotility, if it does exist in enteritis, for example, and the efficacy of anticholinergics. Loperamide has an antidiarrheal effect in experimentally induced diarrhea in calves, but the mechanism of action does not involve changes in intestinal motility.

DECREASED MOTILITY

When gastrointestinal motility is decreased, the usual practice is to administer parasympathomimetic drugs or purgatives, usually combined with an analgesic. Prokinetic drugs such as metoclopramide hydrochloride and cisapride monohydrate increase the movement of ingesta through the gastrointestinal tract. They are useful because they induce coordinated motility patterns.

Metoclopramide

Metoclopramide, acting in the upper gastrointestinal tract, increases acetylcholine release from neurons and increases cholinergic receptor sensitivity to acetylcholine. It is a dopamine antagonist and stimulates and coordinates esophageal, gastric, pyloric, and duodenal motor activity. It increases lower esophageal sphincter tone and stimulates gastric contractions, while relaxing the pylorus and duodenum. This results in accelerated gastric emptying and reduced esophageal reflux. The transit time of ingested material from the duodenum to the ileocecal valve is reduced because of increased jejunal peristalsis. It has little or no effect on colonic motility. The pharmacokinetics of metoclopramide in cattle has been studied.

Metoclopramide crosses the blood-brain barrier, where its dopamine antagonist activity at the chemoreceptor trigger zone can result in an antiemetic effect. It can also result in involuntary activity including tremors, restlessness, and aggressive behavior characterized by charging and jumping walls. This can be reversed by the use of an anticholinergic such as diphenhydramine hydrochloride intravenously at 0.5 to 2.0 mg/kg BW.

Indications for metoclopramide include reflux esophagitis and gastritis, chronic gastritis associated with delayed emptying, abomasal emptying defects in ruminants, gastric stasis following gastric dilatation and volvulus surgery, and **postoperative ileus**. It is contraindicated in animals with physical obstruction of the gastrointestinal tract.

In horses, the dose is 0.125 to 0.25 mg/kg BW diluted in multiple electrolyte solution and given intravenously over 60 minutes. It is used for stimulating equine gastric and small-intestinal activity at dose rates of 0.25 mg/kg BW per hour when there is intestinal hypomotility. Given as continuous intravenous infusion of 0.04 (mg/kg)/h it can decrease the incidence and severity of persistent postoperative ileus following resection and anastomosis of the small intestine in horses without serious side effects.

In cattle and sheep metoclopramide is used at 0.3 mg/kg BW subcutaneously every 6 to 8 hours. Metoclopramide did not alter cecocolic myoelectrical activity in cattle.

Cisapride

Cisapride promotes gastrointestinal motility by enhancing the release of acetylcholine from postganglionic nerve endings of the myenteric plexus. It is more potent and has broader prokinetic activity than metoclopramide by increasing the motility of the colon as well as the esophagus, stomach, and small intestine. It is does not have dopaminergic effects and does not have either the antiemetic or the extrapyramidal effects of metoclopramide. Cisapride is useful for the treatment of gastric stasis, gastroesophageal reflux, and postoperative ileus. In horses, it increases left dorsal colon motility and improves ileocecal junction coordination. The suggested dose is 0.1 mg/kg BW orally every 8 hours. Cisapride may have some value in the clinical management of cecal dilatation in cattle.

Xylazine and Naloxone

Although **xylazine** is used for alleviation of visceral pain in horses and cattle, it is not indicated in cecal dilatation in cattle because it reduces the myoelectric activity of the cecum and proximal loop of the ascending colon. **Naloxone**, a widely used opiate antagonist with a high affinity for μ-receptors, is also not indicated for medical treatment of cecal dilatation when hypomotility must be reversed.

Bethanechol and Neostigmine

Bethanechol is a methyl derivative of carbachol and classified as a direct-acting cholinomimetic drug. Its action is more specific on the gastrointestinal tract and urinary bladder. **Neostigmine**, a cholinesterase inhibitor, is an indirect-acting cholinergic drug with motor-stimulating activities but only on the gastrointestinal tract. Bethanechol at 0.07 mg/kg BW intramuscularly may be useful for medical treatment of cecal dilatation in cattle in which hypomotility of the cecum and proximal loop of the ascending colon must be reversed. Neostigmine at 0.02 mg/kg BW intramuscularly increased the number of propagated spike sequences, but they were uncoordinated.

RELIEF OF TENESMUS

Tenesmus can be difficult to treat effectively. Long-acting epidural anesthesia and sedation are in common use. Combinations of xylazine and lidocaine may be used. Irrigation of the rectum with water and the application of topical anesthetic in a jelly-like base are also used.

RECONSTITUTION OF RUMEN FLORA AND CORRECTION OF ACIDITY OR ALKALINITY

When prolonged anorexia or acute indigestion occurs in ruminants, the rumen flora may be seriously reduced. In convalescence, the reconstitution of the flora can be hastened by the oral administration of a suspension of ruminal contents from a normal cow, or of dried ruminal contents, which contain viable bacteria and yeasts and the substances necessary for growth of the organisms.

The pH of the rumen affects the growth of rumen organisms, and hyperacidity (such as occurs on overeating of grain), or hyperalkalinity (such as occurs on overeating of protein-rich feeds), should be corrected by the administration of alkalinizing or acidifying drugs as needed.

FURTHER READING

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Diseases of the Buccal Cavity and Associated Organs

DISEASES OF THE MUZZLE

Severe dermatitis with scab formation, development of fissures, and sloughing and gangrene of the skin of the muzzle are common lesions in cattle affected with photosensitive dermatitis, bovine malignant catarrh, bovine virus diarrhea, and rinderpest.

In sheep severe lesions of the muzzle are less common, but occur in bluetongue and ecthyma.

In pigs, only the vesicular diseases—vesicular exanthema of swine (VES), swine vesicular disease, and FMD—cause such lesions on the snout and on other sites. The lesions are vesicular initially, and confusion has arisen in recent years because of isolated incidents in Australia and New Zealand in which such outbreaks occurred but no pathogenic agent was identified.

Congenital lesions of solely the muzzle are rare; the congenital defect of harelip can be contiguous with a cleft palate.

STOMATITIS

Stomatitis is inflammation of the oral mucosa and includes **glossitis** (inflammation of the tongue), **palatitis** (lampas; inflammation of the palate), and **gingivitis** (inflammation of the mucosa of the gums). Clinically it is characterized by partial or complete loss of appetite, smacking of the lips, and profuse salivation. It is commonly an accompaniment of systemic disease.

ETIOLOGY

Stomatitis can be caused by physical, chemical, or infectious agents, with the last being the largest group of causes. The agents are listed next.

Physical Agents

- Trauma while dosing orally with a balling gun or similar instruments.[1]
- Laceration of the tongue.
- Foreign body injury.
- Malocclusion of teeth.
- Sharp awns or spines on plants. The most common lesions are on the gums of cattle and sheep just below the corner incisors where tough grass is pulled around the corner of the incisor arcade. In spear grass country the alveoli are often stuffed full of grass seeds. Very young animals, e.g., 1- to 6-week-old lambs, are particularly susceptible to traumatic injury from abrasive feed. Among the most dramatic lesions are those in the mouths of horses. They are large (2–3 cm long and 5 mm wide) and linear in shape. They can be caused in horses or cattle by eating hairy caterpillars that infest pasture,[2] or by the awns in hay or chaff made from triticale (a hybrid of wheat and rye) and a yellow bristle grass (*Setaria lutescens*).[3] Foxtail awns can cause multiple painful nodules on the lips of horses that have eaten hay contaminated with the awns,[4] as can the seedheads of mouse barley (*Hordeum murinum*).[5]
- The strength and thickness of the awn in dwarf barley cultivars used to make silage fed to feedlot cattle in some regions is associated with mouth lesions. The incidence of tongue lesions in slaughter cattle in some areas can be about 19%, and the incidence is higher in cattle finished on silage from semidwarf rough awn (29.3%) compared with normal-stem rough awn (13.5%) and normal-stem smooth awn barley (11.8%).
- Eating frozen feed and drinking hot water are recorded, but seem highly improbable.
- Ulcers of the soft palate of horses can be caused by mechanical trauma associated with dorsal displacement of the soft palate.

Chemical Agents

- Irritant drugs, e.g., chloral hydrate, administered in excessive concentrations.
- Counterirritants applied to skin, left unprotected, and licked by the animal, including mercury and cantharides compounds.
- Irritant substances administered by mistake, including acids, alkalis, and phenolic compounds.
- Manifestation of systemic poisoning, e.g., chronic mercury poisoning. Poisoning with bracken, *Heracleum mantegazzianum,* furazolidone, and some fungi (*Stachybotrys, Fusarium* spp., and mushrooms) cause a combination of focal hemorrhages and necrotic ulcers

or erosions. They are a common cause of confusion with vesicular or erosive disease.

- Lesions associated with uremia syndrome in horses.

Infectious Agents
Cattle
- Oral necrobacillosis associated with *Fusobacterium necrophorum.*
- Actinobacillosis of the bovine tongue is not a stomatitis, but there can be one or two ulcers on the dorsum and sides of the tongue and on the lips. Characteristically, there is initially an acute diffuse myositis of the muscle of the tongue, followed by the development of multiple granulomas and subsequently fibrosis and shrinkage.
- Ulcerative, granulomatous lesions may occur on the gums in cases of actinomycosis.
- Stomatitis with vesicles occurs in FMD and in vesicular stomatitis (VS).
- Erosive, with some secondary ulcerative, stomatitis occurs in bovine viral diarrhea (mucosal disease), bovine malignant catarrh, rinderpest. and rarely in bluetongue. Cases of infectious bovine rhinotracheitis in young calves may have similar lesions.
- Proliferative lesions occur in papular stomatitis, proliferative stomatitis, and rare cases of rhinosporidiosis and papillomatosis where the oral mucosa is invaded.
- Oral mucosal necrosis in bovine sweating sickness.
- Nondescript lesions varying from erosions to ulcers occur late in the stages of many of the previously mentioned diseases when secondary bacteria have invaded the breaches in the mucosa. In some cases the involvement goes deeper still and a phlegmonous condition or a cellulitis may develop. Thus lesions that were initially vesicular are converted to what look like bacterial ulcers. Secondary infection with fungi, especially *Monilia* spp., may also occur.

Sheep
- Erosive lesions in bluetongue, rinderpest, and peste de petits ruminantes.
- Vesicular lesions rarely in foot-and-mouth disease (FMD).
- Granulomatous lesions caused by ecthyma are not unusual in the mouth, especially in young lambs. Similarly, oral lesions occur in bad cases of sheep pox, ulcerative dermatosis, coital exanthema, and mycotic dermatitis.

Horses
- Cheilitis and gingivitis (inflammatory nodules of the lips and gums caused by plant awns)

- Vesicular lesions in VS
- Lingual abscess associated with *Actinobacillus* spp.

Pigs
- The vesicular diseases: FMD, VS, VES, and swine vesicular disease.

Bullous Stomatitis
- Bullous stomatitis has been reported in the horse and can be associated with a paraneoplastic pemphigus syndrome.

Many other causes of stomatitis have been suggested, but the relationship of these conditions to the specific diseases listed previously is unknown. It is common to find stomatitides that cannot be defined as belonging to any of these etiologic groups. An example is necrotic glossitis reported in feeder steers in the United States in which the necrotic lesions are confined to the anterior part of the tongue.

PATHOGENESIS
The lesions of stomatitis are produced by the causative agents being applied directly to the mucosa, or gaining entrance to it by way of minor abrasions, or by localization in the mucosa from a viremia. In the first two instances, the stomatitis is designated as primary. In the third, it is usually described as secondary because of the common occurrence of similar lesions in other organs or on other parts of the body, and the presence of a systemic disease. The clinical signs of stomatitis are caused by the inflammation or erosion of the mucosa and the signs vary in severity with the degree of inflammation.

CLINICAL FINDINGS
There is partial or complete anorexia and slow, painful mastication. Chewing movements and smacking of the lips are accompanied by salivation, either frothy and in small amounts, or profuse and drooling if the animal does not swallow normally. The saliva may contain pus or shreds of epithelial tissue. A fetid odor is present on the breath only if bacterial invasion of the lesion has occurred. Enlargement of local lymph nodes may also occur if bacteria invade the lesions. Swelling of the face is observed only in cases where a cellulitis or phlegmon has extended to involve the soft tissues. An increased desire for water is apparent and the animal resents manipulation and examination of the mouth.

Toxemia may be present when the stomatitis is secondary to a systemic disease or where tissue necrosis occurs. This is a feature of oral necrobacillosis and many of the systemic viremias. In some of the specific diseases, lesions may be present on other parts of the body, especially at the coronets and mucocutaneous junctions.

Several different lesions of the oral cavity may be present and their characteristic appearances are as follows. The importance

of vesicular diseases such as FMD means that the recognition and differentiation of these lesions assumes major importance.

Erosions are shallow, usually discrete, areas of necrosis, which are not readily seen in the early stages. They tend to occur most often on the lingual mucosa and at the commissures of the mouth. The necrotic tissue may remain in situ but is usually shed, leaving a very shallow discontinuity of the mucosa with a dark red base that is more readily seen. If recovery occurs, these lesions heal very quickly.

Vesicles are thin-walled swellings 1 to 2 cm in diameter filled with clear serous fluid. They are very painful and rupture readily to leave sharp-edged, shallow ulcers.

Ulcerative lesions penetrate more deeply to the lamina propria and are painful, such as in necrotic stomatitis in calves associated with *F. necrophorum.* In lambs the tongue may be swollen and contain many microabscesses infected with *Actinomyces (Corynebacterium) pyogenes.* There is an accompanying abscessation of the pharyngeal lymph nodes.

Proliferative lesions are characterized by an abnormality raised above the surface of the mucous membrane such as in oral papillomatosis. **Traumatic lesions** are usually solitary and characterized by a discontinuity in the mucous membrane often with evidence of healing and the presence of granulation tissue.

Catarrhal stomatitis is manifested by a diffuse inflammation of the buccal mucosa and is commonly the result of direct injury by chemical or physical agents. **Mycotic stomatitis** is characterized by a heavy, white velvety deposit with little obvious inflammation or damage to the mucosa.

Deformity of or loss of tissue at the tip of the tongue may result in a chronic syndrome of chewing and swallowing food in such a way that food is always oozing from between the lips. In sheep this may cause permanent staining of the hair around the mouth, creating an appearance similar to that of a tobacco chewer. Loss of the tip is usually the result of predator attack on a newborn or sick lamb.

Laceration of the tongue can result in complete or partial severance of the organ, with the severed portion protruding from the oral cavity. In cattle, glossectomy interferes with prehension and the animal is unable to eat. Excessive loss of saliva is common because of interference with swallowing.

Ulceration of the soft palate of horses may occur in 16% of horses with dorsal displacement of the soft palate and is characterized clinically by reduced exercise tolerance, respiratory noise during light exercise or racing, dysphagia, and coughing after exercising. The ulcers can be viewed by upper respiratory airway videoendoscopy. **Bullous stomatitis** in the horse is characterized by intact or ruptured vesicles on the peripheral

margin of the tongue, the sublingual region, and the mucosa of the oral cavity and lips.

CLINICAL PATHOLOGY

Material collected from lesions of stomatitis should be examined for the presence of pathogenic bacteria and fungi. Transmission experiments may be undertaken with filtrates of swabs or scrapings if the disease is thought to be caused by a viral agent.

NECROPSY FINDINGS

Oral lesions are easily observed, but complete necropsy examinations should be performed on all fatally affected animals to determine whether the oral lesions are primary or are local manifestations of a systemic disease.

DIFFERENTIAL DIAGNOSIS

- Particularly in cattle, and to a lesser extent in sheep, the diagnosis of stomatitis is most important because of the occurrence of oral lesions in a number of highly infectious viral diseases. The diseases are listed under etiology and their differentiation is described under their specific headings elsewhere in this book.
- Careful clinical and necropsy examinations are necessary to define the type and extent of the lesions if any attempt at field diagnosis is to be made.
- In cattle, lymphoma of the ramus of the mandible may spread extensively through the submucosal tissues of the mouth causing marked swelling of the gums, spreading of the teeth, inability to close the mouth, and profuse salivation. There is no discontinuity or inflammation of the buccal mucosa, but gross enlargement of the cranial lymph nodes is usual.
- The differentiation of causes of hypersalivation must depend on a careful examination of the mouth (the causative gingivitis is often surprisingly moderate in horses) and an awareness of the volume of increased saliva output caused by toxic hyperthermia, e.g., in fescue and ergot poisonings.
- Poisoning by the mycotoxin slaframine also causes hypersalivation.

TREATMENT

Affected animals should be isolated and fed and watered from separate utensils if an infectious agent is suspected. Specific treatments are described under the headings of the individual diseases. Nonspecific treatment includes frequent application of a mild antiseptic collutory such as a 2% solution of copper sulfate, a 2% suspension of borax, or a 1% suspension of a sulfonamide in glycerin. Indolent ulcers require more vigorous treatment and respond well to curettage or cauterization with a silver nitrate stick or tincture of iodine.

In stomatitis caused by trauma, the teeth might need attention. In all cases, soft, appetizing food should be offered and feeding by stomach tube or intravenous alimentation may be resorted to in severe, prolonged cases. If the disease is infectious, care should be exercised to ensure that it is not transmitted by the hands or dosing implements.

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DISEASES OF THE TEETH

Surgical diseases of the teeth of animals are presented in textbooks of surgery. Some of the medical aspects of diseases of the teeth of farm animals are described here.

ETIOLOGY

The causes may be congenital or acquired.

Congenital Defects

- Polyodontia (excessive number of teeth) occurs in many species. It is detected in 2.3% of donkeys.[1]
- Malocclusion of sufficient degree to interfere with prehension and mastication
- Red-brown staining of inherited porphyrinuria of cattle
- Defective enamel formation on all teeth combined with excessive mobility of joints is an inherited defect of collagen metabolism in Holstein/Friesian cattle identified as bovine osteogenesis imperfecta. The teeth are pink and abnormal in appearance. This defect is also recorded in a foal with severe epitheliogenesis imperfecta.

Dental Fluorosis

The teeth are damaged before they erupt and show erosion of the enamel.

Enamel Erosion

The feeding of acidic by-product feed such as sweet potato cannery waste, which is acidic because of the presence of lactic acid, can cause erosion of the enamel of the incisors of cattle. Exposure of incisor teeth in vitro to a supernatant of cannery waste or lactic acid at pH 3.2 results in removal of calcium from the surface enamel of bovine teeth. Neutralizing the cannery waste to a pH of 5.5 does not cause detectable etching of the teeth. Feeding cattle with heavily compacted silage is also associated with loss of incisor enamel and severe incisor wear.

Premature Wear and Loss of Teeth in Sheep (Periodontal Disease)

Premature loss of incisor teeth or "broken mouth" causes concern because of the early age at which affected sheep have to be culled. Broken mouth is a chronic inflammatory disease of the tissue supports of the tooth. Between 60% and 70% of ewes sold at slaughter in England and Scotland have loose or missing incisor teeth. Broken mouth is geographically specific and it seems that once the disease is established on a particular farm, the animals are permanently susceptible. Many sheep are culled before the end of their useful reproductive life because of broken mouth. The problem is particularly severe in New Zealand and the hill country in Scotland. The cause is uncertain, but environmental factors that result in periodontal disease are probably important. Broken mouth is associated with abnormal bacterial flora in the mouth with affected sheep having a preponderance of *Mannheimia ruminalis* and *Moraxella caprae* compared with sheep with healthy mouths.[2] *Porphyromonas* (*Bacteroides*) *gingivalis,* an organism that is found in plaque from sheep's teeth, has been found with increased frequency in diseased compared with unaffected animals. The depths of the gingival crevice of sheep are heritable and it is possible that deeper crevices may already be harboring greater numbers of periodontally pathogenic bacteria so that when the animals are exposed to a broken-mouth environment they may be more prone to the changes. Although nutrition and mineral deficiencies influence dental development and tooth eruption of sheep, there is no significant difference in calcium or phosphorus status between control and affected populations of sheep. Low planes of nutrition have delayed eruption of the permanent dentition and retarded mandibular growth, but these changes are not seen in broken mouth in sheep. The occurrence of this periodontal disease is higher in some soil types than on others. The ingestion of irritating materials such as sand and spiny grass seeds has been suggested as causes, but they are considered to be secondary complications in a preexisting disease.

Another dental disease of sheep is also recorded on an extensive scale in New Zealand. There is excessive wear of deciduous incisors but no change in the rate of wear of the molar teeth. The incisor wear is episodic and is not caused by any change in the supportive tissues, and there is no change in the intrinsic resistance to wear of the incisor teeth. The disease is not related to an inadequate dietary intake of copper or vitamin D and is thought to be caused by the ingestion of soil particles. The two New Zealand diseases do not occur together and have no apparent effect on body condition score.

Dentigerous cysts have been described in ewes in the South Island of New Zealand with a prevalence of 0.91%.

PATHOGENESIS

There are some limitations to the use of number of incisors for determining age in

sheep. In mixed-age female sheep flocks, the median age when two, four, six, and eight incisors come into wear is 15, 23, 30, and 42 months of age, respectively. Errors will be made by assuming that all sheep gain a pair of permanent incisors at annual intervals between 1.5 and 4.5 years of age.

In periodontal disease or broken-mouth disease of sheep the primary lesion is an acute gingivitis around permanent incisors and premolars at the time of their eruption. This subsides leaving a chronic gingivitis and an accumulation of subgingival plaque. On some farms, for reasons not understood, this gingivitis penetrates down into the alveoli, causing a severe periodontitis and eventual shedding of the teeth. The severity of the gingivitis can vary between farms. The disease is episodic in nature, with discrete acute inflammatory incidents leading to periodontal injury that may resolve by healing. The balance between repair and the various short- and long-term acute episodes probably accounts for the large variation in incidence and age onset of tooth loss both within and between flocks. The inflammatory periodontal disease markedly affects the tooth's mobility. Collagen fibrils supporting the tooth become abnormal. The deepened periodontal pocket resulting from inflammation removes the major area of support for the tooth and abnormal loads are applied to fibers deeper within the tissue. Although the incisor teeth are usually most severely affected, the cheek teeth are also involved. In some unusual circumstances the gingivitis appears to arise from heavy deposits of dental calculus. In the Scottish disease there is local alveolar bone loss but no accompanying general skeletal deficiency.

CLINICAL FINDINGS

The most obvious evidence of broken-mouth disease is incisor tooth loss, which usually occurs when sheep are between 3.5 and 6.6 years; normal sheep without broken mouth will retain their teeth beyond 7 years of age. Several dental health indices can assist to assess the amount of gingivitis, tooth movement, gum recession, and pocketing. Gingivitis is characterized by redness and edema of the attached gingiva. Bleeding from the gingivae is also a feature. Clinical gingivitis is evident as soon as the permanent teeth erupt. Chronic gingivitis results in a downward retreat of the gum margin; loss of its normal, scalloped shape; and fibrosis of the gingiva. Within a year before tooth loss, tissue damage around the incisors leads to deepening of the gingival sulcus and the formation of pockets, which are readily detected by the use of graduated dental measuring probes. The normal sulcus is 0.5 to 1.0 mm deep labially and up to 4 mm deep lingually; pockets may be over 1.0 cm in depth before tooth loss. Crown lengthening, protrusion, hemorrhages, loosening, and lingual periodontitis are characteristic. If sheep affected with broken mouth periodontal disease are examined over a 12-month period, only a few animals undergo clinically significant destruction. The relationship between periodontal disease and body condition score in sheep is variable.

Secondary starvation occurs even with a plentiful feed supply. Inspection of the mouth may reveal the worn or damaged incisor teeth, but the molar teeth are not easily inspected in the living animal and tooth lesions can be missed. Because it is common to find that both incisors and molars are affected, damage to incisors should lead the clinician to suspect that molar disease is also present.

Cattle fed sweet potato cannery waste develop black, stained teeth with severe enamel erosion.

An abattoir survey of dental defects in cull cows, all over 30 months of age, found that 14.6% had one or more missing incisors, most of which were acquired losses. Rotation and overlapping of rostral teeth were common, as was attrition. Congenitally absent first lower premolars; other missing teeth; large and often multiple interdental spaces; and a few cases of macrodontia, cavitation, multiple defects, and fractures were observed in cheek tooth arcades. There were also some unusual patterns of premolar and molar attrition, often attributable to malocclusion, one result of which was the formation of a hook at the posterior extremity of the third maxillary molar.

CLINICAL PATHOLOGY
None definitive.

TREATMENT AND CONTROL
There is no reliable treatment and control for broken mouth in sheep. The use of dental prosthetics glued to the incisors when the ewe has three pairs of incisors in place is being investigated. The use of antimicrobials has been proposed to control the gingivitis, but there is no apparent effect on the periodontal disease. Cutting the incisor teeth of ewes to control premature tooth loss has been explored, but the practice has been banned in the UK.

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DISEASES OF THE PAROTID SALIVARY GLANDS

Disease of the parotid gland includes parotitis, which can be septic or associated with sialolithiasis, congenital abnormalities including brachial cyst remnants, neoplasia, and trauma. Inflammation of the salivary glands (sialadenitis) can be secondary to sialolithiasis.

ETIOLOGY
Parotitis can be parenchymatous, when the glandular tissue is diffusely inflamed, or it may be a local suppurative process. There are no specific causes in farm animals, with cases occurring only sporadically and usually caused by localization of a blood-borne infection, invasion up the salivary ducts associated with stomatitis, irritation by grass awns in the duct, or salivary calculi. Avitaminosis A often appears to be a predisposing cause in cattle.

Septic sialadenitis of horses is an uncommon disease that causes pain, inappetence, dysphagia, and localized swelling of the parotid or submandibular salivary glands.[1] Some cases (one third) are associated with the presence of sialoliths.[1] Sialoliths can form around foreign bodies, such as grass seeds or grains.[2]

Local suppurative lesions are caused usually by penetrating wounds or extension from a retropharyngeal cellulitis or lymph node abscess. Neoplasia of the parotid glands of cattle, horses, and sheep occurs both as a primary tumor (adenocarcinoma and peripheral nerve sheath tumor), manifestation of a systemic tumor (lymphoma), or local extension of neoplasia in an adjacent structure, such as ocular squamous cell carcinoma.[3-7]

Trauma can injure the gland or draining duct.[8]

PATHOGENESIS
In most cases only one gland is involved. There is no loss of salivary function and the signs are restricted to those of inflammation of the gland.

CLINICAL FINDINGS
In the early stages, there is diffuse enlargement of the gland accompanied by warmth and pain on palpation. The pain can interfere with mastication and swallowing and induce abnormal carriage of the head and resentment when attempts are made to move the head. There can be marked local edema in severe cases. Diffuse parenchymatous parotitis usually subsides with systemic and local treatment within a few days, but suppurative lesions can discharge externally and form permanent salivary fistulae.

Examination should include careful oral examination and ultrasonographic examination of the gland and associated ducts.[1]

Treatment for septic sialolithiasis includes correction of the underlying defect (abnormal dentition or sialolith) and administration of antimicrobials.

CLINICAL PATHOLOGY
Bacteriologic examination of pus from discharging abscesses in horses reveals *Fusobacterium* sp. and a variety of other bacteria.[1]

NECROPSY FINDINGS
Death occurs rarely and necropsy findings are restricted to local involvement of the

gland or to primary lesions elsewhere in the case of secondary parotitis.

TREATMENT

Systemic treatment with sulfonamides or antibiotics is required in acute cases, especially if there is a systemic reaction. Abscesses might require draining. A salivary fistula is a common sequel.

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Diseases of the Pharynx and Esophagus

PHARYNGITIS

Pharyngitis is inflammation of the pharynx and is characterized clinically by coughing, painful swallowing, and a variable appetite. Regurgitation through the nostrils and drooling of saliva may occur in severe cases.

ETIOLOGY

Pharyngitis in farm animals is usually traumatic. Infectious pharyngitis is often part of a syndrome with other more obvious signs.

Physical Causes

- Injury while giving oral treatment with balling or drenching gun or following endotracheal intubation. The administration of intraruminal anthelmintic coils to calves under a minimum BW have also been associated with pharyngeal and esophageal perforation.
- Improper administration of a reticular magnet, resulting in a retropharyngeal abscess.
- Accidental administration or ingestion of irritant or hot or cold substances.
- Foreign bodies, including grass and cereal awns, wire, bones, and gelatin capsules lodged in the pharynx or suprapharyngeal diverticulum of pigs.

Infectious Causes
Cattle
- Oral necrobacillosis and actinobacillosis as a granuloma rather than the more usual lymphadenitis
- Infectious bovine rhinotracheitis
- Pharyngeal phlegmon or intermandibular cellulitis is a severe, often fatal, necrosis of the wall of the pharynx and peripharyngeal tissues without actually causing pharyngitis. *F. necrophorum* is a common isolate from the lesions.

Horses
- As part of strangles or anthrax
- Viral infections of the upper respiratory tract, including equine herpesvirus-1, Hoppengarten cough, parainfluenza virus, adenovirus, rhinovirus, viral arteritis, and influenza-1A/E1 and 1A/E2, cause pharyngitis.
- Chronic follicular pharyngitis with hyperplasia of lymphoid tissue in pharyngeal mucosa giving it a granular, nodular appearance with whitish tips on the lymphoid follicles.[1]

Pigs
- As part of anthrax in this species and in some outbreaks of Aujeszky's disease.

PATHOGENESIS

Inflammation of the pharynx is attended by painful swallowing and disinclination to eat. If the swelling of the mucosa and wall is severe, there may be virtual obstruction of the pharynx. This is especially so if the retropharyngeal lymph node is enlarged, as it is likely to be in equine viral infections such as rhinovirus.

In balling-gun–induced trauma of feedlot cattle treated for respiratory disease with boluses of sulfonamides, perforations of the pharynx and esophagus may occur with the development of periesophageal diverticulations with accumulations of ruminal ingesta and cellulitis. Improper administration of a magnet to a mature cow can result in a retropharyngeal abscess.

Pharyngeal lymphoid hyperplasia in horses can be graded into four grades (I–IV) of severity based on the size of the lymphoid follicles and their distribution over the pharyngeal wall.[2]

CLINICAL FINDINGS

The animal may refuse to eat or drink or it may swallow reluctantly and with evident pain. Opening of the jaws to examine the mouth is resented and manual compression of the throat from the exterior causes paroxysmal coughing. There may be a mucopurulent nasal discharge, sometimes containing blood, spontaneous cough and, in severe cases, regurgitation of fluid and food through the nostrils. Oral medication in such cases may be impossible. Affected animals often stand with the head extended, drool saliva, and make frequent tentative jaw movements. If the local swelling is severe, there may be obstruction of respiration and visible swelling of the throat. The retropharyngeal and parotid lymph nodes are commonly enlarged.

In "**pharyngeal phlegmon**" in cattle there is an acute onset with high fever (41–41.5°C [106–107°F]), rapid heart rate, profound depression, and severe swelling of the soft tissues within and posterior to the mandible to the point where dyspnea is pronounced. Death usually occurs 36 to 48 hours after the first signs of illness.

In **traumatic pharyngitis in cattle**, visual examination of the pharynx through the oral cavity reveals hyperemia, lymphoid hyperplasia, and erosions covered by diphtheritic membranes. Pharyngeal lacerations are visible, and palpation of these reveals the presence of accumulated ruminal ingesta in diverticula on either side of the glottis. External palpation of the most proximal aspect of the neck reveals firm swellings, which represent the diverticula containing rumen contents. A retropharyngeal abscess secondary to an improperly administered magnet can result in marked diffuse painful swelling of the cranial cervical region. Ultrasonographic examination of the swelling may reveal the magnet within the abscess.

Palpation of the pharynx may be performed in cattle with the use of a gag if a foreign body is suspected, and endoscopic examination through the nasal cavity is possible in the horse.

Most acute cases recover in several days but chronic cases may persist for many weeks, especially if there is ulceration, a persistent foreign body, or abscess formation.

Pharyngeal lymphoid hyperplasia is the most commonly recognized abnormality of the upper respiratory tract of the horse.[2-4] The disorder is characterized by chronic hyperplasia of lymphoid tissue in the pharynx of young horses evident as multiple, often coalescing, raised nodules in the pharynx. Up to 60% of Thoroughbred horses are affected and without apparent association with performance.[2] The disease is not associated with other abnormalities of the upper airway in sport horses.[3] If secondary bacterial infection is present a purulent exudate is seen on the pharyngeal mucosa and in the nostrils.

CLINICAL PATHOLOGY

Nasal discharge or swabs taken from accompanying oral lesions may assist in the identification of the causative agent. *Moraxella* spp. and *Streptococcus zooepidemicus* can be isolated in large numbers from horses with

lymphoid follicular hyperplasia grades III and IV.

NECROPSY FINDINGS

Deaths are rare in primary pharyngitis and necropsy examinations are usually undertaken only in those animals dying of specific diseases. In pharyngeal phlegmon there is edema, hemorrhage, and abscessation of the affected area, and on incision of the area a foul-smelling liquid and some gas usually escapes.

DIFFERENTIAL DIAGNOSIS

- Pharyngitis is manifested by an acute onset and local pain.
- In pharyngeal paralysis, the onset is usually slow.
- Acute obstruction by a foreign body can occur rapidly and cause severe distress and continuous, expulsive coughing, but there are no systemic signs.
- Endoscopic examination of the pharyngeal mucous membranes is often diagnostic.

TREATMENT

The primary disease must be treated, usually parenterally, by the use of antimicrobials. Pharyngeal phlegmon in cattle is frequently fatal and early, intensive antimicrobial treatment is indicated.

Pharyngeal lymphoid hyperplasia is not generally susceptible to antimicrobials or medical therapy and resolves as young horses age.

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PHARYNGEAL OBSTRUCTION

Obstruction of the pharynx is accompanied by stertorous respiration, coughing, and difficult swallowing.

ETIOLOGY

Foreign bodies or tissue swellings are the usual causes.

Foreign Bodies

Foreign bodies include bones, corn cobs, and pieces of wire. Although horses are considered discriminating eaters in comparison to cattle, they will occasionally pick up pieces of metal while eating.

Tissue Swellings
Cattle
- Retropharyngeal lymphadenopathy or abscess caused by tuberculosis, actinobacillosis, or bovine viral leukosis

- Fibrous or mucoid polyps are usually pedunculated because of traction during swallowing and can cause intermittent obstruction of air and food intake.

Horses
- Retropharyngeal lymph node hyperplasia and lymphoid granulomas as part of pharyngeal lymphoid hyperplasia
- Retropharyngeal abscess and cellulitis
- Retropharyngeal lymphadenitis caused by strangles
- Pharyngeal cysts in the subepiglottic area of the pharynx, probably of thyroglossal duct origin, and fibroma; also similar cysts on the soft palate and pharyngeal dorsum, the latter probably being remnants of the craniopharyngeal ducts
- Dermoid cysts and goitrous thyroids

Pigs
- Diffuse lymphoid enlargement in the pharyngeal wall and soft palate
- Food and foreign-body impaction in the suprapharyngeal diverticulum

PATHOGENESIS

Reduction in caliber of the pharyngeal lumen interferes with swallowing and respiration.

CLINICAL FINDINGS

There is difficulty in swallowing and animals can be hungry enough to eat but, when they attempt to swallow, cannot do so and the food is coughed up through the mouth. Drinking is usually managed successfully. There is no dilatation of the esophagus and usually little or no regurgitation through the nostrils. An obvious sign is a snoring inspiration, often loud enough to be heard some yards away. The inspiration is prolonged and accompanied by marked abdominal effort. Auscultation over the pharynx reveals loud inspiratory stertor. Manual examination of the pharynx can reveal the nature of the lesion, but an examination with a fiberoptic endoscope is likely to be much more informative. When the disease runs a long course, emaciation usually follows. Rupture of abscessed lymph nodes can occur when a nasal tube is passed and can result in aspiration pneumonia.

In horses with metallic foreign bodies in the oral cavity or pharynx, the clinical findings include purulent nasal discharge, dysphagia, halitosis, changes in phonation, laceration of the tongue and stertorous breathing. In case studies, most horses were affected with clinical signs for more than 2 weeks and had been treated with antimicrobials with only temporary improvement.

CLINICAL PATHOLOGY

A tuberculin test might be advisable in bovine cases in areas where bovine tuberculosis is endemic. Nasal swabs can contain

S. equi when there is streptococcal lymphadenitis in horses.

NECROPSY FINDINGS

Death occurs rarely and in fatal cases the physical lesion is apparent.

DIFFERENTIAL DIAGNOSIS

- Signs of the primary disease can aid in the diagnosis in tuberculosis, actinobacillosis, and strangles.
- Pharyngitis is accompanied by severe pain, systemic signs are common, and there is usually stertor.
- It is of particular importance to differentiate between obstruction and pharyngeal paralysis when rabies occurs in the area. Esophageal obstruction is also accompanied by the rejection of ingested food, but there is no respiratory distress. Laryngeal stenosis can cause a comparable stertor, but swallowing is not impeded. Nasal obstruction is manifested by noisy breathing, but the volume of breath from one or both nostrils is reduced and the respiratory noise is more wheezing than snoring.
- Radiography is useful for the identification of metallic foreign bodies.

TREATMENT

Removal of a foreign body can be accomplished through the mouth. Treatment of actinobacillary lymphadenitis with iodides is usually successful and some reduction in size often occurs in tuberculous enlargement of the glands, but complete recovery is unlikely to occur. Parenteral treatment of strangles abscesses with penicillin can affect a cure. Surgical treatment has been highly successful in cases caused by medial retropharyngeal abscess.

PHARYNGEAL PARALYSIS

Pharyngeal paralysis is manifested by inability to swallow and an absence of signs of pain and respiratory obstruction.

ETIOLOGY

Pharyngeal paralysis occurs sporadically, caused by peripheral nerve injury, and in some encephalitides with central lesions.

Peripheral Nerve Injury
- Guttural pouch infections in horses
- Trauma to the throat region

Secondary to Specific Diseases
- Rabies and other encephalitides
- Botulism
- African horse sickness
- As an idiopathic disease in neonatal foals[1]

PATHOGENESIS

Inability to swallow and regurgitation are the major manifestations of the disease. There may be an associated laryngeal paralysis, accompanied by "roaring." The condition known as "cud-dropping" in cattle might be a partial pharyngeal paralysis because there is difficulty in controlling the regurgitated bolus, which is often dropped from the mouth. In these circumstances, aspiration pneumonia is likely to develop.

CLINICAL FINDINGS

The animal is usually hungry but, on prehension of food or water, attempts at swallowing are followed by dropping of the food from the mouth, coughing, and the expulsion of food or regurgitation through the nostrils. Salivation occurs constantly and swallowing cannot be stimulated by external compression of the pharynx. The swallowing reflex is a complex one controlled by a number of nerves and the signs can be expected to vary greatly depending on which nerves are involved and to what degree. There is rapid loss of condition and dehydration. Clinical signs of the primary disease may be evident but, in cases of primary pharyngeal paralysis, there is no systemic reaction. Pneumonia may follow aspiration of food material into the lungs and produces loud gurgling sounds on auscultation.

In cud-dropping in cattle, the animals are normal except that regurgitated boluses are dropped from the mouth, usually in the form of flattened disks of fibrous food material. Affected animals may lose weight but the condition is usually transient, lasting for only a few days. On the other hand, complete pharyngeal paralysis is usually permanent and fatal.

Pharyngeal dysfunction in neonatal foals is characterized by the inability to nurse with discharge of milk from the nares. Affected foals are often premature or have signs of neonatal maladjustment syndrome. Diagnostic testing, including imaging studies, does not reveal abnormalities beyond a flaccid pharynx, persistent frequent dorsal displacement of the soft palate, laryngeal paralysis (unilateral or bilateral), and inability to swallow.[1]

CLINICAL PATHOLOGY

The use of clinicopathologic examinations is restricted to the identification of the primary specific diseases.

NECROPSY FINDINGS

If the primary lesion is physical, it can be detected on gross examination.

DIFFERENTIAL DIAGNOSIS

- In all species, often the first clinical impression is the presence of a foreign body in the mouth or pharynx, and this can only be determined by physical examination.

- Pharyngeal paralysis is a typical sign in rabies and botulism, but there are other clinical findings that suggest the presence of these diseases.
- Neonatal dysphagia in foals results from cleft palate or soft palate masses, esophageal disease including megaesophagus or esophageal stricture, or primary muscle or central neurological disease, including hyperkalemic periodic paralysis.[1]
- Absence of pain and respiratory obstruction are usually sufficient evidence to eliminate the possibility of pharyngitis or pharyngeal obstruction.
- Endoscopic examination of the guttural pouch is a useful diagnostic aid in the horse.

TREATMENT

Treatment is supportive in most cases in addition to management of any inciting disease, such as guttural pouch infection. Feeding by nasogastric tube allows for recovery of the ability to swallow in most (>90%) affected foals in 7 to 10 days.

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ESOPHAGITIS

Inflammation of the esophagus is accompanied initially by clinical findings of spasm and obstruction, pain on swallowing and palpation, and regurgitation of bloodstained slimy material.

ETIOLOGY

Primary esophagitis caused by the ingestion of chemical or physical irritants is usually accompanied by stomatitis and pharyngitis. Laceration of the mucosa by a foreign body or complications of nasogastric intubation can occur. Nasogastric intubation is associated with a higher risk of pharyngeal and esophageal injury when performed in horses examined for colic. This can be related to the use of larger diameter nasogastric tubes to provide more effective gastric decompression, the longer duration of intubation in some horses, or the presence of gastric distension resulting in increased resistance to tube passage at the cardia.[1] In a series of six horses with esophageal trauma the lesions were detected 5 and 20 cm from the cranial esophageal opening.

Death of *Hypoderma lineatum* larvae in the submucosa of the esophagus of cattle can cause acute local inflammation and subsequent gangrene.

Inflammation of the esophagus occurs commonly in many specific diseases, particularly those that cause stomatitis, but the other clinical signs of these diseases dominate those of esophagitis.

PATHOGENESIS

Inflammation of the esophagus combined with local edema and swelling results in a functional obstruction and difficulty in swallowing.

CLINICAL FINDINGS

In the acute esophagitis, there is salivation and attempts to swallow, which cause severe pain, particularly in horses. In some cases, attempts at swallowing are followed by regurgitation and coughing, pain, retching activities, and vigorous contractions of the cervical and abdominal muscles. If the esophagitis is in the cervical region, palpation in the jugular furrow causes pain and edematous tissues around the esophagus can be palpable. In specific diseases such as mucosal disease and bovine malignant catarrh, there are no obvious clinical findings of esophagitis, because the lesions are mainly erosive.

Endoscopy of the esophagus will usually reveal the location and severity of the lesion.

CLINICAL PATHOLOGY

In severe esophagitis of traumatic origin a marked neutrophilia can occur, suggesting active inflammation.

NECROPSY FINDINGS

Pathologic findings are restricted to those pertaining to the various specific diseases in which esophagitis occur. In traumatic lesions or those caused by irritant substances, there is gross edema, inflammation and, in some cases, perforation.

DIFFERENTIAL DIAGNOSIS

- Esophagitis must be differentiated from pharyngitis, in which attempted swallowing is not as marked and coughing is more likely to occur. Palpation can also help to localize the lesion; however, pharyngitis and esophagitis usually occur together.

TREATMENT

Feed should be withheld for 2 to 3 days and fluid and electrolyte therapy can be necessary for several days. Parenteral antimicrobials are indicated, especially if laceration or perforation has occurred. Reintroduction to feed should be monitored carefully and all feed should be moistened to avoid the possible accumulation of dry feed in the esophagus, which might not be fully functional.

ESOPHAGEAL RUPTURE

Rupture of the esophagus is usually traumatic and can be life-threatening.

ETIOLOGY

Rupture of the esophagus occurs from localized ischemia and necrosis secondary to

long-standing impaction or obstruction by foreign bodies or feed material, external trauma, nasogastric intubation, and perforation of ulcers in horses and cattle and death of *Hypoderma lineatum* larvae in cattle. In a series of six horses with esophageal trauma the lesions were detected 5 and 20 cm from the cranial esophageal opening. Spontaneous rupture can occur in horses with idiopathic muscular hypertrophy of the esophagus.[1] The case–fatality rate is high, approaching 100% for horses treated conservatively (without surgery), and somewhat better for horses subject to surgical intervention early in the disease.[2,3]

The administration of sustained-release anthelmintic boluses to young calves not large enough for the size of the bolus used can cause esophageal injury and perforation. The boluses are 8.5 cm in length and 2.5 cm in diameter and the calves 100 to 150 kg. The minimum BW for these boluses is 100 kg, but in the study some calves were younger than the recommended age and were also fractious when handled, which can have contributed to the injury.

PATHOGENESIS

Traumatic injury to the esophagus results in edema, hemorrhage, laceration of the mucosa, and possible perforation of the esophagus, resulting in periesophageal cellulitis, which spreads proximally and distally along the esophagus in fascial planes from the site of perforation. Perforation of the thoracic esophagus can result in severe and fatal pleuritis. There is extensive edema and accumulation of swallowed or regurgitated ingesta along with gas. The extensive cellulitis and the presence of ingesta results in severe toxemia, and dysphagia can cause aspiration pneumonia.

CLINICAL FINDINGS

In the acute injury of the esophagus, there is salivation and attempts to swallow, which cause severe pain, particularly in horses. In some cases, attempts at swallowing are followed by regurgitation and coughing, pain, retching activities, and vigorous contractions of the cervical and abdominal muscles. Marked drooling of saliva, grinding of the teeth, coughing, and profuse nasal discharge are common in the horse with esophageal trauma with complications following nasogastric intubation. Regurgitation can occur and the regurgitus contains mucus and some fresh blood.

If the esophageal rupture is in the cervical region, palpation in the jugular furrow causes pain and edematous tissues around the esophagus can be palpable. When perforation has occurred, there is local pain and swelling and often crepitus and swelling can extend to involve the head. Local cervical cellulitis can cause rupture through the skin and development of an esophageal fistula, or infiltration along fascial planes with resulting compression obstruction of the esophagus, and toxemia. Perforation of the thoracic esophagus can lead to fatal pleuritis. Animals that recover from esophageal traumatic injury are commonly affected by chronic esophageal stenosis with distension above the stenosis. Fistulae are usually persistent, but spontaneous healing can occur.

Endoscopy of the esophagus will usually reveal the location and severity of the lesion. Lateral cervical radiographs can reveal foreign bodies and extensive soft tissue swelling with pockets of gas.

CLINICAL PATHOLOGY

There is often hematological evidence of inflammation, dehydration, metabolic alkalosis, and toxemia.[2]

NECROPSY FINDINGS

Gross necropsy findings are consistent with esophageal perforation and cellulitis.

DIFFERENTIAL DIAGNOSIS

- Tracheal laceration and subcutaneous emphysema
  - Skin wounds over the axilla with subsequent subcutaneous emphysema
  - Severe guttural pouch empyema
- Clostridial myositis secondary to puncture wounds of the neck or cervical intramuscular injections
- Pharyngeal phlegmon in cattle

TREATMENT

Treatment involves effective drainage of the site over the esophageal perforation, prevention of further contamination, control of infection and inflammation, and provision of water and food.

Surgical treatment involves fasciotomy to provide drainage and access to the perforated esophagus. The perforation in the esophagus is debrided through a ventral fasciotomy. The fasciotomy wound is dressed and managed as an open wound. A stomach tube, of similar size as that used to perform nasogastric intubation on the animal (14–20 mm), is inserted through a separate incision in the esophagus in the midcervical region. The tip is placed in the distal esophagus. The horse is provided food (a pellet-based slurry) and water through this tube, as well as being offered water to drink. The tube remains in place until the esophageal perforation has sealed (5–7 days) and then removed.[2,3]

Loss of saliva can cause important abnormalities in electrolyte and acid-base status, and horses should be supplemented with sodium and potassium chloride while there is significant loss of saliva from the fistula.

Broad-spectrum antimicrobials and tetanus prophylaxis should be administered. Pain and swelling can be controlled by administration of NSAIDs.

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ESOPHAGEAL OBSTRUCTION

Esophageal obstruction can be acute or chronic and is characterized clinically by the inability to swallow, regurgitation of feed and water, continuous drooling of saliva, and bloat in ruminants. Acute cases are accompanied by signs of distress including retching and extension of the head. Horses with choke commonly regurgitate a mixture of saliva, feed, and water through the nostrils because of the anatomic characteristics of the equine soft palate.

ETIOLOGY

Obstruction can be **intraluminal** and caused by swallowed material or **extraluminal** caused by pressure on the esophagus by surrounding organs or tissues. Esophageal paralysis can also result in obstruction, for example, in horses with grass sickness.

Intraluminal Obstructions

Intraluminal obstructions are usually caused by ingestion of materials that are of inappropriate size and that then become lodged in the esophagus:

- Solid obstructions, especially in cattle, by turnips, onions, potatoes, peaches, apples, oranges, and similar objects.
- Fifteen-gram gelatin capsules in Shetland ponies.
- Feedstuffs are a common cause of obstruction in horses and occasionally in other species.[1] Most impactions are caused by routine feedstuffs.[2] Improperly soaked sugarbeet pulp, inadvertent access to dry sugarbeet pulp, and cubed and pelleted feed can cause the disease in horses when eaten quickly.
- Eating while sedated
- Foreign bodies in horses include pieces of wood, antimicrobial boluses, and fragments of nasogastric tubes.
- A trichobezoar can cause esophageal obstruction cattle.
- Poor dentition is often mooted as a cause[2] and, although sensible, there is no objective evidence of an association between dental abnormalities and esophageal obstruction.

Extraluminal Obstructions

- Enlarged lymph nodes in the mediastinum (tuberculosis, neoplasia, *Rhodococcus equi, Corynebacterium* spp., strangles, and secondary to pleuritis)
- Cervical or mediastinal abscess
- Persistent right aortic arch

- Thymoma
- Megaesophagus and caudal esophageal muscle hypertrophy in Friesian horses can cause esophageal obstruction.[3]
- Secondary to esophageal strictures, which can occur subsequent to esophageal trauma or performation.[6]

Esophageal Paralysis

Esophageal paralysis can be caused by **congenital or acquired abnormalities of the esophagus,** and there are many examples of such abnormalities that interfere with swallowing and cause varying degrees of obstruction, even though it may be possible to pass a stomach tube through the esophagus into the stomach or rumen.

Esophageal paralysis, diverticulum, or megaesophagus has been recorded in horses and in cattle. Congenital hypertrophy of esophageal musculature and esophagotracheal fistula has been found in calves. Congenital esophageal ectasia is recognized in foals, caused by degeneration of musculature and reduced ganglion cells in the myenteric plexus. Congenital esophageal dysfunction has also occurred in foals with no detectable histopathological lesion but with prolonged simultaneous contractions throughout the esophagus.

Megaesophagus

Megaesophagus is a dilatation and atony of the body of the esophagus usually associated with asynchronous function of the esophagus and the caudal esophageal sphincter. It occurs sporadically in cattle and in horses with preexisting esophageal disease. It is usually a congenital condition that causes regurgitation and aspiration pneumonia. A mild esophagitis has been observed in some cases and congenital stenosis of the esophagus in a foal has been associated with megaesophagus. Megaesophagus and caudal esophageal muscular hypertrophy occur in Friesian horses.[3]

Esophageal Strictures

These arise as a result of cicatricial or granulation tissue deposition, usually as result of previous laceration or trauma of the esophagus. They can occur in the adult horse with a history of previous obstruction. Esophageal strictures resulting in obstruction occur in foals from 1 to 6 months of age without any history of ingestion of a foreign body. An esophageal stricture has also been described in a goat.

Other Causes of Obstruction

- **Carcinoma of stomach** causing obstruction of cardia
- Squamous cell carcinoma of the esophagus of a horse
- Esophageal hiatus hernia in cattle
- Paraesophageal cyst in a horse
- Combined esophageal and tracheal duplication cyst in a young horse
- Esophageal duplication in a horse
- Tubular duplication of the cervical portion of the esophagus in a foal
- Cranial esophageal pulsion (pushing outward) diverticulum in a horse
- Esophageal phytobezoar in a horse
- Esophageal mucosal granuloma
- Traumatic rupture of the esophagus from an external injury (e.g., a kick or striking the neck during transportation in a float involved in a motor vehicle accident or similar causing sudden slowing or stopping) or during treatment using a nasogastric tube
- Esophageal paralysis can also be associated with lesions of encephalitis, especially in the brainstem

The **case–fatality rate** for simple choke treated in the field is approximately 2%, while that in presumably more severe cases treated in referral institutions is approximately 12%. Approximately 8% of horses (60 of 758) examined by one author in primary care practice were caused by esophageal obstruction.[2]

Arabian horses and ponies appear to be overrepresented and Thoroughbreds underrepresented among equids with choke.[2,4] There is no readily apparent sex predilection. Equids can be affected at any age.

PATHOGENESIS

An **esophageal obstruction** results in a physical inability to swallow and, in cattle, inability to eructate, with resulting bloat. In acute obstruction, there is initial spasm at the site of obstruction and forceful, painful peristalsis and swallowing movements. Complications of esophageal obstruction include laceration and rupture of the esophagus, esophagitis, stricture and stenosis, and the development of a diverticulum.

Acquired esophageal diverticula can occur in the horse. A traction diverticulum occurs following periesophageal scarring and is of little consequence. An esophageal pulsion diverticulum is a circumscribed sac of mucosa protruding through a defect in the muscular layer of the esophagus. Causes that have been proposed to explain pulsion diverticula include excessive intraluminal pressure from impacted feed, fluctuations in esophageal pressure, and external trauma. Complications associated with esophageal diverticula include peridiverticulitis, pulmonary adhesions, abscesses, and mediastinitis. Esophageal stricture and subsequent obstruction secondary to impaction of a diverticulum can also occur.

In **megaesophagus**, the esophagus is dysfunctional, dilated, and filled with saliva, feed, and water. This results in regurgitation and can lead to aspiration pneumonia. It can be congenital or secondary to other lesions and has been associated with gastric ulceration in foals.

Using esophageal manometry, the normal values for esophageal pressure profiles in healthy horses, cows, and sheep have been recorded. The body of the equine and bovine esophagus has two functionally different regions: the caudal portion and the remainder of the esophageal body (cranial portion).

CLINICAL FINDINGS
Acute Obstruction or Choke
Cattle

The obstruction is usually in the cervical esophagus just above the larynx or at the thoracic inlet. Obstructions can also occur at the base of the heart or the cardia. The animal suddenly stops eating and shows anxiety and restlessness. There are forceful attempts to swallow and regurgitate, salivation, coughing, and continuous chewing movements. If obstruction is complete, bloating occurs rapidly and adds to the animal's discomfort. Ruminal movements are continuous and forceful and there can be a systolic murmur audible on auscultation of the heart. However, rarely is the bloat severe enough to seriously affect the cardiovascular system of the animal, such as occurs in primary leguminous (frothy) bloat.

The acute signs, other than bloat, usually disappear within a few hours. This is caused by relaxation of the initial esophageal spasm and can or cannot be accompanied by onward passage of the obstruction. Many obstructions pass on spontaneously, but others can persist for several days and up to a week. In these cases, there is **inability to swallow**, **salivation,** and **continued bloat**. Passage of a nasogastric tube is impossible. Persistent obstruction causes pressure necrosis of the mucosa and can result in perforation or subsequent stenosis caused by fibrous tissue construction.

Horse

In the horse with esophageal obstruction caused by feed, the obstruction can occur at any level of the esophagus from the upper cervical region all the way to the thoracic portion. The ingestion of large quantities of grain or pelleted feed can cause obstruction over a long portion of the esophagus.

The clinical findings vary with the location, nature, extent, and duration of the obstruction. Typically, the major clinical finding is **dysphagia** with **nasal reflux of saliva, feed, and water**. Affected horses will usually not attempt further eating but will drink and attempt to swallow water. External palpation of the **cervical esophagus** can reveal a **firm cylindrical swelling** along the course of the neck on the left side when the esophagus is obstructed with feed.[2] In cases of foreign-body obstruction such as a piece of wood, there can be no palpable abnormality.

Horses with acute esophageal obstruction are commonly difficult to handle because they are panicky and make forceful attempts to swallow or retch.[2] They often vigorously extend and flex their necks and stamp their front feet. In some horses it can be difficult to

pass a nasogastric tube because they resist the procedure. During these episodes of hyperactivity they can sweat profusely, tachycardia can be present, and they can appear to be in abdominal pain. Such clinical findings on first examination can resemble colic, but attempted passage of a nasogastric tube as part of the examination of a horse with colic reveals the obstruction.

Passage of a nasogastric tube is necessary to make the diagnosis and to assess the level of the obstruction. The level of obstruction can be approximated by the amount of tube that has been passed. Care must be taken not to push the tube more than gently to avoid injury to the esophagus. Occasionally, a foreign body or bolus of feed will move distally into the stomach as the tube is gently advanced.

The nature of the obstruction can be assessed more adequately with a fiberoptic endoscope, but visualization of the entire esophagus of an adult horse requires an endoscope of 2.5 m length. The endoscope allows determination of the rostral but not the distal limit of the obstruction. Endoscopic examination of the esophagus after relief of the obstruction is useful in identifying any preexisting abnormalities or injuries caused by the obstruction. If radiographic equipment is available, standing lateral radiographs of the cervical and thoracic esophagus along with contrast media may be required to determine the extent and nature of an obstruction.

Persistent obstruction can occur in the horse and death can occur in either species from subsequent aspiration pneumonia or, when the obstruction persists, from dehydration. In **foals** with esophageal obstruction the clinical findings include **nasal reflux of saliva**, feed, and milk; reluctance to eat solid feed; and dyspnea if aspiration pneumonia has occurred. Unthriftiness occurs if the obstruction has been present for a few weeks. Affected foals can have had several episodes of choke within the previous few weeks from which they appeared to recover spontaneously. Passage of a nasogastric tube can be possible in some and not in others.

Chronic Obstruction

No acute signs of obstruction are evident and in cattle the earliest sign is chronic bloat, which is usually of moderate severity and can persist for several days without the appearance of other signs. Rumen contractions can be within the normal range. In horses and in cattle in which the obstruction is sufficiently severe to interfere with swallowing, a characteristic syndrome develops. Swallowing movements are usually normal until the bolus reaches the obstruction, when they are replaced by more forceful movements. Dilatation of the esophagus can cause a pronounced swelling at the base of the neck. The swallowed material either passes slowly through the stenotic area or accumulates and is then regurgitated. Projectile expulsion of

ingested material occurs with esophageal diverticula, but water is retained and there is no impedance to the passage of the stomach tube. In the later stages, there can be no attempt made to eat solid food, but fluids can be taken and swallowed satisfactorily.

When there is **paralysis of the esophagus**, as in megaesophagus, regurgitation does not occur, but the esophagus fills and overflows, and saliva drools from the mouth and nostrils. Aspiration into the lungs can follow. Passage of a stomach tube or probang is obstructed by stenosis but can be unimpeded by paralysis.

Complications Following Esophageal Obstruction

The risk of complications increases proportionate to the duration of obstruction.[4] Complications following an esophageal obstruction are most common in the horse and include esophagitis, mucosal ulceration, esophageal perforation and esophageal stricture, and aspiration pneumonia.[4] Complications developed in 51% of 109 horses hospitalized, with choke and the most frequent complication was aspiration pneumonia (39 of 109 horses).[4] The complication rate is much lower among horses treated in the field and in which resolution of the choke occurs within 24 hours.[2]

Mild cases of esophagitis heal spontaneously. Circumferential full-thickness mucosal ulceration can result in a stricture, which will be clinically evident in 2 to 5 weeks and can require surgical correction or balloon dilation.[5] Esophageal perforation can occur and is characterized by diffuse cellulitis of the periesophageal tissues, often with subcutaneous emphysema, and a fistula can develop.

CLINICAL PATHOLOGY

Laboratory tests are not used in diagnosis, although radiographic examination is helpful to outline the site of stenosis, diverticulum, or dilatation, even in animals as large as the horse. Radiologic examination after a barium swallow is a practicable procedure if the obstruction is in the cervical esophagus. Viewing of the internal lumen of the esophagus with a fiberoptic endoscope has completely revolutionized the diagnosis of esophageal malfunction. Biopsy samples of lesions and tumor masses can be taken using the endoscope. Electromyography has been used to localize the area of paralysis of the esophagus in a cow with functional megaesophagus.

TREATMENT
Conservative Approach

Many obstructions will resolve spontaneously and a careful conservative approach is recommended. Of 60 cases first treated in the field, 45 resolved within 12 hours, 51 within 24 hours, and 58 in 48 hours.[2] If there is a history of prolonged choke with considerable nasal reflux having occurred, the

animal should be examined carefully for evidence of foreign material in the upper respiratory tract and the risk of aspiration pneumonia. It can require several hours of monitoring, reexamination, and repeated sedation before the obstruction is resolved. During this time, the animal should not have access to feed and water.

Sedation

In acute obstruction, if there is marked anxiety and distress, the animal should be sedated before proceeding with specific treatment. Administration of a sedative such as an α-2 receptor agonist, with or without an opiod, can also help to relax the esophageal spasm and allow passage of the impacted material. For sedation and esophageal relaxation in the horse, one of the following is recommended:

- Acepromazine 0.05 mg/kg BW intravenously
- Xylazine 0.5 to 1.0 mg/kg BW intravenously
- Detomidine 0.01 to 0.02 mg/kg BW intravenously
- Romifidine 0.04 to 0.12 mg/kg intravenously.

DIFFERENTIAL DIAGNOSIS

- The clinical findings of acute esophageal obstruction in cattle and horses are usually typical but can be similar to those of esophagitis, in which local pain is more apparent and there is often an accompanying stomatitis and pharyngitis.
- The excitement, sweating, and tachycardia observed in acute choke in the horse often suggests colic. Passage of a nasogastric tube reveals the obstruction. The use of a fiberoptic endoscope will usually locate the obstruction for visualization, and obstructions are easiest to see when the endoscope is being withdrawn rather than advanced.

Chronic obstruction
- Differentiation of the causes of chronic obstruction can be difficult. A history of previous esophagitis or acute obstruction suggests cicatricial stenosis. Contrast radiography of the esophagus is valuable in the investigation of horses with dysphagia, choke, and nasogastric reflux. The use of the sedative detomidine can affect the function of the esophagus and make interpretation of barium swallowing studies difficult.
- Persistent right aortic arch is rare and confined to young animals.
- Mediastinal lymph node enlargement is usually accompanied by other signs of tuberculosis or lymphomatosis.
- Chronic ruminal tympany in cattle can be caused by ruminal atony, in which case there is an absence of normal ruminal movements.

- Diaphragmatic hernia can also be a cause of chronic ruminal tympany in cattle and is sometimes accompanied by obstruction of the esophagus with incompletely regurgitated ingesta. This condition and vagus indigestion, another cause of chronic tympany, are usually accompanied by a systolic cardiac murmur, but passage of a stomach tube is unimpeded. Dysphagia can also result from purely neurogenic defects. Thus early paralytic rabies "choke" is often suspected, with dire results for the examining veterinarian.
- Equine encephalomyelitis and botulism are other diseases in which there is difficulty in swallowing.
- Cleft palate is a cause of recurrent nasal regurgitation in foals.

For esophageal relaxation, analgesia and antiinflammatory effect hyoscine: dipyrone 0.5:0.22 mg/kg BW intravenously can be used and for analgesia and antiinflammatory effect flunixin meglumine 1.1 mg/kg BW intravenously or phenylbutazone 2 to 4 mg/kg intravenously are suggested. For analgesia butorphanol 0.02 to 0.1 mg/kg intravenously can be administered.

Pass a Stomach Tube and Allow Object to Move Into Stomach
The passage of the nasogastric tube is always necessary to locate the obstruction. Gentle attempts can be made to push the obstruction caudad, but care must be taken to avoid damage to the esophageal mucosa. A fiberoptic endoscope can be used to determine the presence of an obstruction, its nature, and the extent of any injury to the esophageal mucosa.

If the previously discussed simple procedures are unsuccessful it is then necessary to proceed to more vigorous methods. In cattle, it is usual to attempt further measures immediately, partly because of the animal's distress and the risk of self-injury and partly because of bloat. However, rarely is the bloat associated with esophageal obstruction life-threatening. The important decision is whether to proceed and risk damaging the esophagus or wait and allow the esophageal spasm to relax and the obstruction to pass spontaneously. This problem is most important in the horse. Attempts to push the obstruction too vigorously can injure the mucosa, causing esophagitis and even esophageal perforation. Alternatively, leaving a large obstruction in place can restrict blood flow to the local area of mucosa and result in ischemic necrosis. Complications such as strictures and diverticula can occur but are uncommon. As a guide in the horse it is suggested that conservative measures (principally sedation, waiting, and lavaging the esophagus) be continued for several hours before attempting radical procedures such as general anesthesia and manipulation or esophagotomy.

Removal by Endoscope
If a specific foreign body, such as a piece of wood, is the cause of the obstruction, it can be removed by endoscopy. The foreign body must be visible endoscopically, and suitable forceps or a snare through the scope is required. In some cases, impacted feed anterior to the foreign object must be lavaged out before the object is retrieved.

Manual Removal Through Oral Cavity in Cattle
Solid obstructions in the upper esophagus of cattle can be reached by passing the hand into the pharynx with the aid of a speculum and having an assistant press the foreign body up toward the mouth. Because of slippery saliva, it is often difficult to grasp the obstruction sufficiently strongly to be able to extricate it from the esophagus. A long piece of strong wire bent into a loop can be passed over the object and an attempt made to pull it up into the pharynx. The use of Thygesens probang with a cutting loop is a simple and effective method of relieving choke in cattle that have attempted to swallow beets and other similar-sized vegetables and fruits. If both methods fail, it is advisable to leave the object in situ and use treatments aimed at relaxing the esophagus. In such cases in cattle it can be necessary to trocarize the rumen and leave the cannula in place until the obstruction is relieved. However, this should not be undertaken unless specifically required.

General Anesthesia in the Horse
In horses, attempts to manually remove solid obstructions from the cranial portion of the esophagus require a general anesthetic, a speculum in the mouth, and a manipulator with a small hand. The fauces are much narrower in the horse than in the cow and it is only with difficulty that the hand can be advanced through the pharynx to the beginning of the esophagus. Fragments of nasogastric tubes have been retrieved from the esophagus of horses using sedation with xylazine and butorphanol intravenously and the use of a fiberoptic endoscope.

Esophageal Lavage in the Horse
Accumulations of feedstuffs, which are most common in the horse, can be removed by careful lavage or flushing of the obstructed esophagus. Lavage can be performed in the **standing horse** or in **lateral recumbency under general anesthesia.** Small quantities of warm water, 0.5 to 1 L each time, are pumped through a nasogastric tube passed to the point of obstruction, and then the tube is disconnected from the pump and the liquid material is allowed to siphon out through the tube by gravity flow. Return of the fluid through the oral cavity and nostrils is minimized by ensuring that the tube is not plugged by returning material and by using only small quantities of fluid for each input of the lavage. Throughout the procedure, the tube is gently manipulated against the impaction. The use of a transparent tube assists in helping to see the amount and nature of the material coming through the tube. This is repeated many times until the fluid becomes clear. This procedure can require a few hours, but perseverance will be successful. After each lavage the tube can be advanced caudad a few centimeters and eventually all the way to the stomach. Care must be taken to avoid overflowing the esophagus and causing aspiration into the lungs. This is a constant hazard whenever irrigative removal is attempted and the animal's head must always be kept as low as possible to avoid aspiration. Following relief of obstruction the horse can be offered water to drink and a wet mash of feed for several days.

Lavage is similar in the recumbent horse under general anesthesia. A cuffed endotracheal tube is used to maintain an airway and to prevent aspiration of foreign material. Lavage under general anesthesia provides relaxation of the esophagus, which can enhance the procedure and allow a greater volume of water to be used.

Surgical Removal of Foreign Bodies
Surgical removal by esophagostomy can be necessary if other measures fail. Gastrotomy or rumenotomy can be necessary to relieve obstructions of the caudal portion of the esophagus adjacent to the cardia. Although stricture or fistula formation is often associated with esophageal surgery, complications do not occur in every case and healing by secondary intention is common.

Repeated Siphonage in Chronic Cases
In chronic cases, especially those caused by paralysis, repeated siphonage can be necessary to remove fluid accumulations. Successful results are reported in foals using resection and anastomosis of the esophagus and in a horse using esophagomyotomy, but the treatment of chronic obstruction is usually unsuccessful.

Cervical Esophagostomy Alimentation
Alimentation of horses with esophageal ruptures can be attempted by various means. Maintenance of nasogastric tubes through the nostrils is difficult but possible. Tube feeding through a **cervical esophagostomy** has some disadvantages, but it is a reasonably satisfactory procedure in any situation where continued extraoral alimentation is required in the horse. However, the death rate is higher than with nasogastric tube feeding. When the obstruction is caused by circumferential esophageal ulceration, the lumen is smallest at about 50 days and begins to dilate at that

point so that it is normal again at about 60 days.

Antimicrobial Administration

Animals with prolonged obstruction (>12–24 hours), fever, abnormal lung sounds, ultrasonographic or radiographic evidence of aspiration, or in which there is a suspicion of aspiration of regurgitus should be administered broad-spectrum antimicrobials for 5 to 7 days.

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Diseases of the Nonruminant Stomach and Intestines

Diseases that are accompanied by physical lesions, such as displacement or strangulation, or disturbances of motility, such as ileus, are presented first for the horse and pig. Bacterial and viral infectious diseases specific to the pig are then discussed, followed by bacterial infectious diseases of large animals (including horses, pigs, and neonatal and adult ruminants) such as salmonellosis and viral diseases of large animals such as VS. Bacterial, viral, and parasitic infectious diseases of the stomach and intestine are then presented for the foal; piglet; and neonatal calf, lamb, and kid. Diseases of the stomach and intestine for the horse and pig, as well as neonatal and adult ruminants, caused by toxins or those that are caused by congenital or inherited disease, are discussed last. Diseases associated with functional disturbances of secretion are not recognized in animals. Deficiencies of biliary and pancreatic secretion are dealt with in Chapter 9. Those diseases of the stomach and intestines peculiar to adult ruminants are dealt with separately in Chapter 8.

GASTRITIS

Inflammation of the stomach is manifested clinically by vomiting and is commonly associated with enteritis in gastroenteritis.

ETIOLOGY

Gastritis may be acute or chronic, but both forms of the disease may be caused by the same etiologic agents acting with varying degrees of severity and for varying periods. The inflammation may be associated with physical, chemical, bacterial, viral, or metazoan agents.

Cattle and Sheep

Diseases of the rumen and abomasum are presented in Chapter 8. For comparative purposes the causes of abomasitis are listed here. For sheep there is no information other than about parasites. They are listed with cattle for convenience sake.

Physical Agents

Physical agents such as frosted feeds affect only the rumen. In calves, gross overeating and the ingestion of foreign materials may cause abomasitis. In adults, there is a very low incidence of foreign bodies in the abomasum, and half the cases are associated with traumatic reticulitis.

Chemical Agents

All of the irritant and caustic poisons (including arsenic, mercury, copper, phosphorus, and lead) cause abomasitis. Fungal toxins cause abomasal irritation, especially those of *Fusarium* spp. and *Stachybotrys alternans*. Acute lactic acidosis caused by engorgement on carbohydrate-rich food causes rumenitis with some runoff into the abomasum and the development of some abomasitis/enteritis.

Infectious Agents

Only the viruses of rinderpest, bovine virus diarrhea, and bovine malignant catarrh cause abomasal erosions. Bacterial causes are very rare and include sporadic cases of extension from oral necrobacillosis and hemorrhagic enterotoxemia caused by *Clostridium perfringens* Types A, B, C, rarely as an adjunct to colibacillosis and its enteric lesion in calves. Fungi, e.g., *Mucor* spp. and *Aspergillus* spp. complicate abomasal ulcers from other causes.

Metazoan Agents

Metazoan agents include nematodes such as *Trichostrongylus axei*, *Ostertagia* spp., *Haemonchus* spp., and larval paramphistomes migrating to the rumen.

Pigs

Most often lesions are associated with ulceration of the pars esophagea (PE), which is discussed under the separate topic of gastric ulceration.

Physical Agents

Foreign bodies, bedding, frosted feeds, moldy and fermented feeds are all possible causes. In older pigs, particularly outdoor sows, the presence of stones is a common feature and in some cases may be so bad as to be heard when sows move because considerable loss of weight is associated with the gastric fill. It may be one of the causes of the thin sow syndrome.

Chemical Agents

As listed under cattle, these are also possible causes of gastritis in pigs. It may also occur in the achlorhydria associated with diarrhea.

Pigs are extremely inquisitive and will investigate all compounds, but hopefully in this day and age there should be more care over on-farm storage. Bitterweed and blister beetle will also cause gastritis in pigs.

Infectious Agents

Venous hyperemia and infarction of the gastric mucosa occur in erysipelas, salmonellosis, porcine dermatitis and nephropathy syndrome (PDNS), TGE, swine dysentery and acute colibacillosis in weaned pigs. Similar lesions occur in classical swine fever, African swine fever, and swine influenza. Fungal gastritis also occurs secondarily particularly to antibiotic therapy.

Metazoan Agents

The red stomach worm, *Hyostrongylus rubidus*, and the thick stomach worms *Ascarops strongylina* and *Physocephalus sexalatus* are of low pathogenicity but cannot be disregarded as causes of gastritis in pigs. *Simondsia* spp. are found in Europe, Asia, and Australia and cause nodular gastritis. *Gnathostoma* spp. occur in Asia and produce cysts in the submucosa. On most commercial units, especially if outdoors, routine medication is practiced, but backyard pigs are seldom treated because of unawareness. These agents are also found in many wild boar and feral pigs.

Horses

Physical and chemical agents as listed under cattle rarely may cause gastritis. Infectious causes of gastritis are rare in the horse, but emphysematous gastritis associated with *C. perfringens* has been recorded.

Metazoan agents causing gastritis in horses include massive infestation with botfly larvae (*Gasterophilus* spp.); *Habronema muscae* and *H. microstoma* infestation; *H. megastoma* causes granulomatous and ulcerative lesions and can lead to perforation and peritonitis.

PATHOGENESIS

Gastritis does not often occur in animals without involvement of other parts of the alimentary tract. Even in parasitic infestations in which the nematodes are relatively selective in their habitat, infestation with one nematode is usually accompanied by infestation with others, and gastroenteritis is produced. It is dealt with as a specific entity here because it may occur as such, and enteritis is common without gastric involvement. The net effects of gastroenteritis can be determined by a summation of the effects of gastritis and enteritis.

The reactions of the stomach to inflammation include increased motility and increased secretion. There is an increase in the secretion of mucus, which protects the mucosa to some extent but also delays digestion and may allow putrefactive breakdown of the ingesta. This abnormal digestion

may cause further inflammation and favors spread of the inflammation to the intestines. In acute gastritis, the major effect is on motility, and in chronic gastritis it is on secretion. In acute gastritis there is an increase in motility, causing abdominal pain and more rapid emptying of the stomach, either by vomiting or via the pylorus in animals unable to vomit. In chronic gastritis, the emptying of the stomach is prolonged because of the delay in digestion caused by excessive secretion of mucus. This may result in chronic gastric dilatation. The motility is not necessarily diminished and there may be subacute abdominal pain or a depraved appetite caused by increased stomach contractions equivalent to hunger pains.

CLINICAL FINDINGS
Acute Gastritis
When the inflammation is severe, pigs and, rarely, horses and ruminants vomit (or ruminants regurgitate excessive quantities of rumen contents). In monogastric animals, such as pigs, the vomitus contains a great deal of mucus, sometimes blood, and is small in amount, and vomiting is repeated with forceful retching movements. The appetite is always reduced, and often absent, but thirst is usually excessive and pigs affected with gastroenteritis may stand continually lapping water or even licking cool objects. The breath has an offensive odor and there may be abdominal pain. Diarrhea is not marked unless there is accompanying enteritis, but the feces are usually pasty and soft. Additional signs are usually evident when gastritis is part of a primary disease syndrome. Dehydration and alkalosis with tetany and rapid breathing may develop if vomiting is excessive.

Chronic Gastritis
Chronic gastritis is much less severe. The appetite is depressed or depraved and vomiting occurs only sporadically, usually after feeding. The vomitus contains much viscid mucus. Abdominal pain is minor and dehydration is unlikely to occur, but the animal becomes emaciated through lack of food intake and incomplete digestion.

Anorexia, tympanites, gastritis, pyloric stenosis, and gastric ulcers are the clinical manifestations of abomasal foreign body in cattle.

CLINICAL PATHOLOGY
Specimens taken for laboratory examination are usually for the purpose of identifying the causative agent in specific diseases. Estimations of gastric acidity are not usually undertaken, but samples of vomitus should be collected if a chemical poison is suspected.

NECROPSY FINDINGS
The signs of inflammation vary in severity from a diffuse catarrhal gastritis to severe hemorrhagic and ulcerative erosion of the mucosa. In the mucosal diseases there are discrete erosive lesions. In parasitic gastritis there is usually marked thickening and edema of the wall if the process has been in existence for some time. Chemical inflammation is usually most marked on the tips of the rugae and in the pyloric region. In severe cases the stomach contents may be hemorrhagic; in chronic cases the wall is thickened and the contents contain much mucus and have a rancid odor suggestive of a prolonged sojourn and putrefaction of the food.

It is important to differentiate between gastritis and the erythematous flush of normal gastric mucosa in animals that have died suddenly. Venous infarction in the stomach wall occurs in a number of bacterial and viral septicemias of pigs and causes extensive submucosal hemorrhages, which may easily be mistaken for hemorrhagic gastritis.

DIFFERENTIAL DIAGNOSIS

- Gastritis and gastric dilatation have many similarities, but in the latter the vomitus is more profuse and vomiting is of a more projectile nature, although this difference is not so marked in the horse, in which any form of vomiting is severe.
- Gastritis in the horse is not usually accompanied by vomiting but may occur in gastric dilatation.
- In esophageal obstruction, the vomitus is neutral in reaction and does not have the rancid odor of stomach contents.
- Intestinal obstruction may be accompanied by vomiting and, although the vomitus is alkaline and may contain bile or even fecal material, this may also be the case in gastritis when intestinal contents are regurgitated into the stomach.
- Vomiting of central origin is extremely rare in farm animals.
- Determination of the cause of gastritis may be difficult, but the presence of signs of the specific diseases and history of access to poisons or physical agents listed under etiology may provide the necessary clues.
- Analysis of vomitus or food materials may have diagnostic value if chemical poisoning is suspected.

TREATMENT
Treatment of the primary disease is the first principle and requires a specific diagnosis. Ancillary treatment includes the withholding of feed, the use of gastric sedatives, the administration of electrolyte solutions to replace fluids and electrolytes lost by vomiting, and stimulation of normal stomach motility in the convalescent period.

In horses and pigs, gastric lavage may be attempted to remove irritant chemicals. Gastric sedatives usually contain insoluble magnesium hydroxide or carbonate, kaolin, pectin, or charcoal. Frequent dosing at intervals of 2 to 3 hours is advisable. If purgatives are used to empty the alimentary tract, they should be bland preparations such as mineral oil to avoid further irritation to the mucosa.

If vomiting is severe, large quantities of electrolyte solution should be administered parenterally. Details of the available solutions are given under the heading of disturbances of body water. If the liquids can be given orally without vomiting occurring, this route of administration is satisfactory.

During convalescence, the animal should be offered only soft, palatable, highly nutritious foods. Bran mashes for cattle and horses and gruels for calves and pigs are most suitable and are relished by the animal.

ENTERITIS (INCLUDING MALABSORPTION, ENTEROPATHY, AND DIARRHEA)
The term enteritis is used to describe inflammation of the intestinal mucosa resulting in diarrhea and sometimes dysentery, abdominal pain occasionally, and varying degrees of dehydration and acid-base imbalance, depending on the cause of the lesion, its severity, and location. In many cases, gastritis also occurs together with enteritis.

There are several diseases of the intestines of farm animals in which diarrhea and dehydration are major clinical findings, but classical inflammation of the mucosa may not be present. The best example of this is the diarrhea associated with enterotoxigenic *E. coli* (ETEC) which elaborates an enterotoxin that causes a large net increase of secretion of fluids into the lumen of the gut, with very minor, if any, structural changes in the intestinal mucosa. This suggests that a word other than enteritis may be necessary to describe alterations in the intestinal secretory and absorptive mechanisms that result in diarrhea but in which pathologic lesions are not present. However, with these qualifications, for convenience, the term enteritis is used to describe those diseases in which diarrhea is a major clinical finding caused by malabsorption in the intestinal tract.

ETIOLOGY AND EPIDEMIOLOGY
There are many causes of enteritis or malabsorption in farm animals and the disease varies considerably in its severity depending on the causative agent. Enteropathogens include bacteria, viruses, fungi, protozoa, and helminths. Many chemicals and toxins can also cause enteritis (Tables 7-4 to 7-7). In addition to the primary etiologic agents of enteritis, there are many epidemiologic characteristics of the animal and the environment that are important in facilitating or suppressing the ability of the causative agent to cause enteritis. Thus newborn calves and piglets deficient in colostral immunoglobulins are much more susceptible to diarrhea, and have a higher case–fatality rate from diarrhea than animals with adequate

Table 7-4 Epidemiological and clinical features of diseases of cattle in which diarrhea is a significant clinical finding

Etiological agent or disease	Age and class of animal affected and important epidemiological factors	Major clinical findings and diagnostic criteria
Bacteria		
Enterotoxigenic *Escherichia coli*	Newborn calves <3–5 days of age, colostral immune status determines survival; outbreaks common	Acute profuse watery diarrhea, dehydration and acidosis Culture feces for enteropathogenic type
Salmonella spp.	All ages; outbreaks occur; stress induced	Acute diarrhea, dysentery, fever, and high mortality possible Culture feces
Clostridium perfringens types B and C	Young well-nourished calves <10 days of age	Severe hemorrhagic enterotoxemia, rapid death; fecal smear
Mycobacterium avium subsp. *paratuberculosis*	Mature cattle, sporadic, single animal	Chronic diarrhea with loss of weight, long course No response to therapy; special tests
Proteus spp. and *Pseudomonas* spp.	Calves treated for diarrhea with prolonged course of antibiotics	Chronic to subacute diarrhea, poor response to treatment, progressive loss of weight; culture feces
Fungi		
Candida spp.	Young calves following prolonged use of oral antibacterials	Chronic diarrhea, no response to treatment; fecal smears
Viruses		
Rotavirus and coronavirus	Newborn calves, 5–21 days old, explosive outbreaks	Acute profuse watery diarrhea; demonstrate virus in feces
Winter dysentery (Coronavirus)	Mature housed cows, explosive outbreaks	Acute epizootic of transient diarrhea and dysentery lasting 24 h; definitive diagnosis not possible currently
Bovine virus diarrhea (mucosal disease)	Young cattle 8 months to 2 years; usually sporadic but epidemics occur	Erosive gastroenteritis and stomatitis; usually fatal; virus isolation
Rinderpest	Highly contagious, occurs in plague form	Erosive stomatitis and gastroenteritis; high morbidity and mortality
Bovine malignant catarrh	Usually mature cattle, sporadic but small outbreaks occur	Erosive stomatitis and gastroenteritis, enlarged lymph nodes, ocular lesions, hematuria and terminal encephalitis Transmission with whole blood
Helminths		
Ostertagiasis	Young cattle on pasture	Acute or chronic diarrhea, dehydration, and hypoproteinemia Fecal examination; plasma pepsinogen
Protozoa		
Eimeria spp.	Calves over 3 weeks old and cattle up to 12 months of age; outbreaks common	Dysentery, tenesmus, nervous signs; Fecal examination diagnostic
Cryptosporidium spp.	Calves 5–35 days of age	Diarrhea; fecal smear and special stain
Chemical agents		
Arsenic, fluorine, copper, sodium chloride, mercury, molybdenum, nitrates, poisonous plants, mycotoxicoses	All ages, history of access to substance Outbreaks occur	All severities of diarrhea, dysentery, abdominal pain, in some cases nervous signs, dehydration, toxemia; fecal and tissue analyses
Physical agents		
Sand, soil, silage, and feed containing lactic acid (sour brewers' grains)	Usually mature cattle, history of access; outbreaks occur	Acute, subacute diarrhea, and toxemia; see sand in feces Rumen pH
Nutritional deficiency		
Copper deficiency, conditioned by excess molybdenum	Usually mature cattle on pasture with high levels of molybdenum	Subacute and chronic diarrhea, osteodystrophy, no systemic effects, hair color changes; liver and blood analyses
Dietary		
Overfeeding	Young calves overfed on milk	Mild diarrhea, feces voluminous and pale yellow; clinical diagnosis
Simple indigestion	Change of ration of mature cows (hay to silage) or grain to feedlot cattle	Subacute diarrhea; normal in 24 h; Clinical diagnosis usually sufficient
Inferior milk replacers	Heat-denatured skim milk used in manufacturing of milk replacers for calves	Subacute to chronic diarrhea, progressive emaciation, no response to conventional treatment except cow's whole milk Clotting tests on milk replacer
Miscellaneous or uncertain etiology		
Intestinal disaccharidase deficiency	May occur in young calves. Sporadic	Subacute diarrhea unresponsive to usual therapy except withdrawal of milk; lactose digestion tests
Congestive heart failure	Sporadic; mature cattle	Profuse watery diarrhea associated with visceral edema
Toxemia (peracute coliform mastitis)	Sporadic	Acute diarrhea caused by endotoxemia from peracute mastitis Culture milk

Table 7-5 Epidemiological and clinical features of horses with diarrhea

Etiological agent or disease	Age and class of animal affected and important epidemiological factors	Major clinical findings; *diagnostic criteria*
Bacteria		
Salmonella spp.	Young foals; mature horses, following stress	Acute profuse diarrhea, severe dehydration, foul-smelling feces; leukopenia and neutropenia, culture feces, hyponatremia
Rhodococcus equi	Foals 2–5 months of age, some with history of respiratory disease	Diarrhea associated with *R. equi* pneumonia; culture respiratory tract
Clostridium perfringens or *C. difficile*	Mature horses administered antibiotics; young foals	Profuse, watery diarrhea, hypovolemia, hyponatremia. Fecal culture and demonstration of toxin in feces
Aeromonas spp.	Adult horses, tends to be more common in summer; often isolated from horses with diarrhea Definitive etiological role not proved	Febrile, acute diarrhea; culture feces
Viruses and rickettsia		
Neorickettsia risticii (formerly *Ehrlichia risticii*)	Endemic to certain regions in North and South America and Europe; ingestion of organism spread by insects (mayflies)	Profuse watery diarrhea, fever, laminitis; IFA, PCR
Parasites		
Cyathostomes and large strongyles	Individual horses; poor deworming history Seasonal occurrence of larval cyathostomiosis	Acute to chronic diarrhea. *Patent infections evident by fecal examination for parasite eggs*
Physical		
Sand accumulation	Individual horses or farm problem; Ingestion of sand or gravel	Watery diarrhea, not malodorous, not profuse; *abdominal radiography or ultrasonography, examination of feces*
Overdosing of cathartics (DSS, MgSO$_4$, NaSO$_4$, castor oil)	Treated animals	Moderate to profuse diarrhea; *historical confirmation of administration of compounds*
Miscellaneous or unknown		
Colitis X	Single animal; adult horses; high death rate	Acute, pyrexic diarrhea, hypovolemia, leukopenia; *postmortem examination*
Granulomatous or eosinophilic colitis	Single animal; adults	Chronic diarrhea; *necropsy or colonic biopsy*
Right dorsal colitis/ phenylbutazone toxicity	Administration of NSAIDs in large doses or prolonged administration	Mild diarrhea; low-grade fever; Mild colic; hypoproteinemia, hyponatremia; *necropsy, surgery*
Antibiotic-induced diarrhea	History of antimicrobial administration; high case–fatality rate	Acute onset diarrhea with or without fever; leukopenia, hypovolemia; *history*

DSS, dioctyl sodium sulfosuccinate; IFA, indirect fluorescence antibody test; NSAIDs, nonsteroidal antiinflammatory drugs; PCR, polymerase chain reaction.

Table 7-6 Epidemiological and clinical features of diseases of the pig in which diarrhea is a significant clinical finding

Etiological agent or disease epidemiological factors	Age and class of animal affected and important	Major clinical findings and diagnostic criteria
Viruses		
Classical and African swine fever	Hemorrhagic diarrhea at any age	Many other signs (pyrexia); a variety of lab tests (isolation, ELISA, PCR etc.)
Transmissible gastroenteritis	Explosive outbreaks in newborn piglets; high morbidity and mortality	Acute diarrhea, vomition, dehydration, and death; no response to treatment (lab tests include virus isolation, ELISA, EM, FATs)
Rotavirus and coronavirus (epidemic diarrhea)	Outbreaks in newborn piglets and weaned piglets May occur in well-managed herds	Acute diarrhea and dehydration; may continue to suck the sow; death in 2–4 days; virus isolation and pathology of gut, EM, FATs (PED); PAGE for rotavirus
Bacteria		
Enterotoxigenic *Escherichia coli*	Common disease of newborn, 3-week-old and weaned piglets; outbreaks; colostral immune status important	Acute diarrhea, dehydration; responds to early treatment Fecal culture and serotype; virulence factor determination
Salmonella spp.	All ages; most common in feeder pigs	Acute septicemia or chronic diarrhea; responds to early treatment; culture and serotyping

Table 7-6 Epidemiological and clinical features of diseases of the pig in which diarrhea is a significant clinical finding—cont'd

Etiological agent or disease epidemiological factors	Age and class of animal affected and important	Major clinical findings and diagnostic criteria
Clostridium perfringens type C	Newborn piglets; high mortality	Acute and peracute hemorrhagic enterotoxemia; toxin demonstration and culture
C. perfringens type A	Slightly older pigs, first week of life, lower mortality	As previously mentioned
C. difficile	Diarrhea in preweaned pigs	Smears of colon wall, culture, FAT, PCR
Brachyspira hyodysenteriae (swine dysentery)	Usually feeder pigs; outbreaks common	Dysentery, acute to subacute, fever; responds to treatment Culture, FATs, PCR on mucosal smears
Lawsonia *intracellularis* (PIA, PHE)	Growing and mature pigs; outbreaks common	Acute dysentery and death; MZN on mucosal smears, PCR, silver-stained sections
Brachyspira pilosicoli	Usually weaned pigs	PCR
Protozoa		
Isospora spp.	Newborn piglets 5–14 days of age; high morbidity, low mortality	Acute diarrhea; poor response to therapy with amprolium Fecal examination for oocysts
Other species (*Eimeria*)	In older pigs	Histology of gut sections
Parasites		
Ascaris suum and	Young pigs	
A. lumbricoides	All ages, usually older pigs	Mild diarrhea for few days; worm egg count
Trichuris suis		Diarrhea, dysentery, and loss of weight; fecal examination and gross pathology
Nutritional deficiency		
Iron deficiency	Young piglets 6–8 weeks; not common in well-managed swine herds	Mild diarrhea and anemia

ELISA, enzyme-linked immunoassay; EM, electron micrograph; FAT, fluorescence antibody transfer; MZN, modified Ziehl–Neilson; PAGE, polyacrylamide gel electrophoresis; PCR, polymerase chain reaction; PED, porcine epidemic diarrhea; PHE, proliferative hemorrhagic enteropathy; PIA, porcine intestinal adenomatosis.

Table 7-7 Epidemiological and clinical features of the diseases of sheep and goats in which diarrhea is a significant clinical finding

Etiological agent or disease	Age and class of animal affected and important epidemiological factors	Major clinical findings and diagnostic criteria
Bacteria		
Enterotoxigenic *Escherichia coli* (colibacillosis)	Newborn lambs in crowded lambing sheds; cold chilling weather; outbreaks; inadequate colostrum. Mismothering problems; poor udder development	Acute diarrhea (yellow feces), septicemia, and rapid death Culture feces for enterotoxigenic *E. coli*
Clostridium perfringens type B (lamb dysentery)	Newborn lambs up to 10 days of age; overcrowded lambing sheds	Sudden death, diarrhea, dysentery, and toxemia; fecal smear
C. perfringens type D (enterotoxemia)	Adult lactating does	Peracute, acute, and chronic forms occur; enterocolitis; watery diarrhea with feces containing blood and mucus, weakness, abdominal colic
Salmonella spp.	Newborn lambs; adult sheep in pregnancy	Acute diarrhea and dysentery in lambs; acute toxemia, diarrhea in ewes followed by abortion; fecal culture and pathology
Mycobacterium paratuberculosis	Mature sheep and goats; several animals may be affected	Loss of weight, chronic diarrhea, long course, no response to therapy; serological tests
Viruses		
Rotavirus and coronavirus	Newborn lambs; many lambs affected	Acute profuse watery diarrhea; no toxemia; usually recover spontaneously if no secondary complications; virus isolation
Parasites		
Nematodirus spp.	Lambs 4–10 weeks of age on pasture Sudden onset; outbreaks; ideal environmental conditions for parasite are necessary	Anorexia, diarrhea, thirsty, 10%–20% of lambs may die if not treated; fecal examination
Ostertagia spp.	Lambs 10 weeks of age and older lambs and young Ewes on grass; types I and II	Many lambs develop diarrhea, weight loss; abomasitis
Trichostrongylus spp.	Older lambs 4–9 months of age	Dull, anorexic, loss of weight and chronic diarrhea; fecal examination

Table 7-7 Epidemiological and clinical features of the diseases of sheep and goats in which diarrhea is a significant clinical finding—cont'd

Etiological agent or disease	Age and class of animal affected and important epidemiological factors	Major clinical findings and diagnostic criteria
Protozoa		
Eimeria spp.	Overstocking on pasture and overcrowding indoors, poor sanitation, and hygiene; commonly occurs following weaning and introduction into feedlot	Acute and subacute diarrhea and dysentery; loss of weight Mortality may be high; fecal examination
Cryptosporidium	Lambs 7–10 days of age	Dullness, anorexia, afebrile, diarrhea, may die in 2–3 days, survivors may be unthrifty; examination of feces and intestinal mucosa; no specific treatment

levels. Enteric salmonellosis is commonly precipitated by the stressors of transportation or deprivation of feed and water. The stress of weaning in pigs is a risk factor for PWD. The prolonged use of antimicrobials orally in all species may alter the intestinal microflora and allow the development of a superinfection by organisms that would not normally cause disease.

The salient epidemiologic characteristics and clinical findings of the diseases in which diarrhea, caused by enteritis or malabsorption, is a principal clinical finding in each species are summarized by species in Tables 7-4 to 7-7. There are many other diseases in which diarrhea might be present but in which it is only of minor importance.

PATHOGENESIS
Normal Intestinal Absorption
Under normal conditions, a large quantity of fluid enters the small intestine from the saliva, stomach, pancreas, liver, and intestinal mucosa. This fluid and its electrolytes and other nutrients must be absorbed, mainly by the small intestines, although large quantities move into the large intestine for digestion and absorption, especially in the horse. The brush border membrane of the villous epithelial cells is of paramount importance for the absorption of water, electrolytes, and nutrients.

Details of the physiology and pathophysiology of epithelial secretion in the gastrointestinal tract are becoming clear, leading to new models of the mechanisms underlying diarrhea. The enteric nervous system is a critical component of the mechanism regulating fluid secretion in the normal intestine and a key element in the pathophysiology of diarrhea. Neural reflex pathways increase epithelial fluid secretion in response to several enteric pathogens of veterinary importance such as *Salmonella* spp., *Cryptosporidium parvum,* rotavirus, and *C. difficile.* The enteric nervous system also has an important role in epithelial secretion triggered by products of activated leukocytes during inflammation.

Mechanisms of Diarrhea
Any dysfunction of the intestines will result in failure of adequate absorption and diarrhea. Depending on the causative agent, intestinal malabsorption may be the result of at least four different mechanisms:
• Osmotic diarrhea
• Exudative diarrhea
• Secretory diarrhea
• Abnormal intestinal motility

Osmotic Diarrhea
There may be an osmotic effect when substances within the lumen of the intestine increase the osmotic pressure over a greater than normal length of intestine, resulting in an osmotic movement of an excessive amount of fluid into the lumen of the intestine. The fluid is not reabsorbed and accumulates in the lumen. Examples include **saline purgatives**, **overfeeding**, **indigestible feeds,** and **disaccharidase deficiencies**. A deficiency of a disaccharidase leads to incomplete digestion and the accumulation of large quantities of undigested material, which acts as a hypertonic solution.

Malabsorption is associated with several epitheliotropic viruses that affect the villous absorptive cells, causing a disaccharidase deficiency. Examples include the TGE virus in newborn piglets and rotavirus and coronavirus infections in newborn calves and other species. The usual pathogenetic sequence of events is selective destruction of villous absorptive cells, villous atrophy, loss of digestive and absorptive capacities (malabsorption), diarrhea, crypt hyperplasia, and recovery. Recovery depends on the severity of the lesion, the relative injury done to the villous cells and crypt epithelium, and the age of the animal. Newborn piglets affected with TGE commonly die of dehydration and starvation before there is sufficient time for regeneration of the villous cells from the crypt epithelium. In contrast, older pigs have a greater capacity for regeneration of the villous cells and the diarrhea may be only transient.

Exudative Diarrhea
Acute or chronic inflammation or necrosis of the intestinal mucosa results in a net increase in fluid production; inflammatory products, including loss of serum proteins; and a reduction in absorption of fluids and electrolytes. Examples include many of the diseases associated with bacteria, viruses, fungi, protozoa, chemical agents, and tumors that are summarized in Tables 7-4 to 7-7. The classic example is enteric salmonellosis, in which there is severe inflammation with the production of fibrinous, hemorrhagic enteritis. Other notable examples include swine dysentery, bovine virus diarrhea, and inorganic arsenic poisoning.

Secretory Diarrhea
A **secretory–absorptive imbalance** results in a large net increase in fluid secretion with little if any structural change in the mucosal cells. The enterotoxin elaborated by ETEC results in intestinal hypersecretion. The villi, along with their digestive and absorptive capabilities, remain intact. The crypts also remain intact; however, their secretion is increased beyond the absorptive capacity of the intestines, resulting in diarrhea. The increased secretion is caused by an increase in cyclic adenosine monophosphate, which in turn may be stimulated by prostaglandins. The integrity of the mucosal structure is maintained and the secreted fluid is isotonic, electrolyte-rich, alkaline, and free of exudates. This is useful diagnostically in enterotoxic colibacillosis.

An important therapeutic principle can be applied in secretory diarrhea disease. Whenever possible, because of the cost of parenteral fluid therapy, fluids and electrolytes should be given orally. The mucosa remains relatively intact and retains normal absorptive capacity. Fluid replacement solutions containing water, glucose, and amino acids can be given orally and are absorbed efficiently. Glucose and amino acids enhance the absorption of sodium and water, replacing or diminishing fluid and electrolyte losses.

There is also evidence that active electrolyte secretion occurs in enterocolitis caused by salmonellosis in several species of animal. In diseases such as swine dysentery, the permeability of the colon may remain normal or even decrease, but the absorption of water and electrolytes is decreased. This suggests that the primary cause of fluid and electrolyte loss in some diseases of the colon may be failure of the affected epithelium to absorb fluids and electrolytes.

Abnormal Intestinal Motility
Hyperexcitability, convulsions, and the stress of unexpected sudden confinement may result in diarrhea, which may be caused by increased peristalsis, resulting in "**intestinal hurry**" and reduced intestinal absorption caused by rapid passage of intestinal fluids in an otherwise normal intestine. This can occur in animals that are being assembled for transportation and during transportation.

Location of Lesion
The location of the lesion in the intestinal tract may also influence the severity of the enteritis or malabsorption. Lesions involving the small intestine are considered to be more acute and severe than those in the large intestine, because approximately 75% to 80% of the intestinal fluids are absorbed by the small intestine and much lesser quantities by the large intestine. Generally, when lesions of the large intestine predominate, the fluid and electrolyte losses are not as acute or as severe as when the lesions of the small intestine predominate. However, the horse is an exception. The total amount of fluid entering the large intestine from the small intestine, plus the amount entering from the mucosa of the large intestine, is equal to the animal's total extracellular fluid volume, and 95% of this is reabsorbed by the large intestine. This illustrates the major importance of the large intestine of the horse in absorbing a large quantity of fluid originating from saliva, the stomach, liver, pancreas, and small and large intestine. Any significant dysfunction of the absorptive mechanism of the large intestine of the horse results in large losses of fluids and electrolytes. This may explain the rapid dehydration and circulatory collapse that occurs in horses with colitis X. Moderate to severe ulcerative colitis of the right dorsal colon in horses treated with phenylbutazone results in marked dehydration, endotoxic shock, and death.

Dehydration, Electrolyte, and Acid-Base Imbalance
The net effect of an increase in the total amount of fluid in the intestinal lumen and a reduction in intestinal absorption is a loss of fluids and electrolytes at the expense of body fluids and electrolytes and the normal intestinal juices. The fluid that is lost consists primarily of water; the electrolytes sodium, chloride, potassium, and bicarbonate; and

varying quantities of protein. Protein is lost (protein-losing enteropathy) in both acute and chronic inflammation, leading to hypoproteinemia in some cases. The loss of bicarbonate results in **metabolic acidosis**, which is of major importance in acute diarrhea. The loss of sodium, chloride, and potassium results in **serum electrolyte imbalances**. In the horse with enteric salmonellosis, there is severe dehydration and marked hyponatremia. In the calf with neonatal diarrhea there are varying **degrees of dehydration** and a moderate loss of all electrolytes. With acute severe diarrhea, there is severe acidosis and reduced circulating blood volume, resulting in reduced perfusion of the liver and kidney and of peripheral tissues. This results in uremia, anaerobic oxidation, and lactic acidosis, which accentuates the metabolic acidosis. Hyperventilation occurs in some animals in an attempt to compensate for the acidosis.

In acute diarrhea, large quantities of intestinal fluid are lost in the feces and large quantities are present in the intestinal lumen (**intraluminal dehydration**), which accounts for the remarkable clinical dehydration in some affected animals. The fluid moves out of the intravascular compartment first, then out of the extravascular compartment (interstitial spaces), followed last by fluid from the intracellular space. Thus in acute diarrhea of sudden onset the actual degree of dehydration present initially may be much more severe than is recognizable clinically; as the diarrhea continues, the degree of clinical dehydration becomes much more evident.

Chronic Enteritis
In chronic enteritis, as a sequel to acute enteritis or developing insidiously, the intestinal wall becomes thickened and mucus secretion is stimulated, the absorption of intestinal fluids is also decreased but not of the same magnitude as in acute enteritis. In chronic enteritis there is a negative nutrient balance because of decreased digestion of nutrients and decreased absorption, resulting in body wasting. The animal may continue to drink and maintain almost normal hydration. In some cases of chronic enteritis, depending on the cause, there is continuous loss of protein, leading to clinical hypoproteinemia. Intestinal helminthiasis of all species, Johne's disease of ruminants, and chronic diarrheas of the horse are examples. Lymphocytic plasmacytic enteritis causing chronic weight loss occurs in the horse.

Regional ileitis is a functional obstruction of the lower ileum associated with granulation tissue proliferation in the lamina propria and submucosa, with or without ulceration of the mucosa, and a massive muscular hypertrophy of the wall of affected areas of the intestine. It has been recognized with increased frequency in recent years in pigs, horses, and lambs. The lesion undoubtedly interferes with normal digestion and

absorption, but diarrhea is not a common clinical finding.

Replacement of Villous Epithelial Cells
The villous absorptive epithelial cells of the small intestine are involved in almost every type of enteritis or malabsorptive syndrome. These cells that line the villi and face the lumen of the intestine contain important digestive enzymes such as the disaccharidases. They are also involved in absorption of fluids, electrolytes, monosaccharides such as glucose, and amino acids, and in the transport of fat micelles. Their replacement time is up to several days in the newborn calf and piglet, and only a few days when these animals are older (at 3 weeks). This may explain the relatively greater susceptibility of the newborn to the viral enteritides, such as TGE in piglets and rotavirus infection in all newborn farm animal species. Almost any noxious influence can increase the rate of extrusion of these cells, which are then replaced by cells that are immature and not fully functional. The villi become shortened (villous atrophy) and chronic malabsorption similar to the "sprue gut" of humans may be the result. The destruction of villous epithelial cells explains the long recovery period of several days in some animals with acute enteritis and the chronic diarrhea in others with chronic villous atrophy.

The literature on the mechanisms of intestinal mucosal repair has been reviewed.

Role of Neutrophils in Intestinal Mucosal Injury
Neutrophils are critical elements of the cascade of events that culminates in mucosal injury in many inflammatory diseases of the gastrointestinal tract, including ischemia and reperfusion injury. Neutrophils mediate their detrimental actions by several mechanisms, especially physical disruption of the epithelium. These findings have resulted in consideration of strategies to attenuate neutrophil-mediated mucosal injury by preventing neutrophil transendothelial migration into the intestinal mucosa and subsequent activation during inflammation. Newer pharmacologic drugs that inhibit -β-2-integrin activation, and therefore β-2-integrin function, may be useful clinically to inhibit neutrophil-mediated injury during inflammation.

Intestinal Motility in Enteritis
The motility of the intestinal tract in animals with enteritis has not been sufficiently examined and little information is available. It was thought for many years that intestinal hypermotility, and increased frequency and amplitude of peristalsis, was present in most enteritides as a response to the enteritis and that the hypermotility accounted for the reduced absorption. However, when the pathogenesis of the infectious enteritides is

considered, for example, the unique secretory effect of enterotoxin, it seems more likely that, if hypermotility is present, it is a response to the distension of the intestinal lumen with fluid rather than a response to irritation. With a fluid-filled intestinal lumen, very little intestinal peristalsis would be necessary to move large quantities of fluid down the intestinal tract. This may explain the fluid-rushing sounds that are audible on auscultation of the abdomen in animals with enteritis. It is possible that the intestines may be in a state of relative hypomotility rather than hypermotility, which makes the use of antimotility drugs for the treatment of enteritis questionable.

Concurrent Gastritis

Gastritis commonly accompanies enteritis but does not cause vomition except perhaps in the pig. Gastritis (or abomasitis) may also be the primary lesion, resulting in a profuse diarrhea without lesions of the intestines. Examples are ostertagiasis and abomasal ulceration in cattle. Presumably the excessive amount of fluid secreted into the affected abomasum cannot be reabsorbed by the intestines.

Effects of Enteritis on Pharmacodynamics of Drugs

Enteritis may alter the pharmacodynamics of orally administered drugs. In acute diarrheal states there is delayed or impaired absorption, resulting in subtherapeutic plasma concentration. In chronic malabsorption states, decreased, increased, or delayed absorption may occur, depending on the drug. Also, gastric antacids, anticholinergic drugs, and opiates, administered orally for the treatment of diarrhea, may impair absorption of other drugs by altering solubility or delaying gastric emptying time.

CLINICAL FINDINGS

The major clinical finding in enteritis or malabsorption is **diarrhea**. **Dehydration**, **abdominal pain**, **septicemia,** and **toxemia** with **fever** occur commonly and their degree of severity depends on the causative agent, the age, the species of the animal, and the stage of the disease.

In **acute enteritis**, the feces are soft or fluid in consistency and may have an unpleasant odor. They may contain blood (**dysentery**), fibrinous casts, and mucus or obvious foreign material such as sand. The color of the feces will vary considerably: they are usually pale yellow because of the dilution of the brown bile pigments, but almost any color other than the normal is possible and, with the exception of frank blood (**hematochezia**) or **melena** (**black tarry feces**), the color of the feces is usually not representative of a particular disease. When the feces are watery, they may escape notice on clinical examination. Some indication of the nature of the enteritis may be obtained from the

distribution of the feces on the animal's perineum. Thus in calves, the smudge pattern may suggest coccidiosis when both the staining that accompanies it and the feces are smeared horizontally across the ischial tuberosities and the adjoining tail, or helminth infestation when there is little smearing on the pinbones, but the tail and insides of the hocks are liberally coated with feces. Straining may occur, especially in calves, and be followed by rectal prolapse, particularly when the lesions are present in the colon and rectum. Intussusception may occur when the enteritis involves the small intestine.

There are a number of diseases in which **dysentery** with or without toxemia occurs and death may occur rapidly. These include lamb dysentery, hemorrhagic enterotoxemia of calves, acute swine dysentery, and hemorrhagic bowel syndrome of pigs.

Acute intraluminal hemorrhage caused by ulceration of unknown etiology in the small intestine has been recorded in adult cows. Duodenal ulceration may also occur in cattle in association with left-side displacement of the abomasum.

Systemic Effects

The **systemic effects in enteritis** vary considerably. Septicemia, toxemia, and fever are common in the infectious enteritides. An increased body temperature may return to normal following the onset of diarrhea or if circulatory collapse and shock are imminent. **Dehydration** will vary from being just barely detectable at 4% to 6% of BW up to 10% to 12% of BW, when it is clinically very evident. The degree of dehydration can be best assessed by tenting the skin of the upper eyelid or neck and determining the time taken for the skin fold to return to normal. The degree of recession of the eyeball is also a useful aid. In the early stages of acute enteritis, the degree of clinical dehydration may be underestimated because of the time required for fluid to shift from the interstitial and intracellular spaces to the intravascular space to replace fluids already lost. Dehydration is usually evident by 10 to 12 hours following the onset of acute enteritis and clinically obvious by 18 to 24 hours. Peripheral circulatory collapse (**shock**) occurs commonly in acute and peracute cases. There may be tachycardia or bradycardia and arrhythmia depending on the degree of acidosis and electrolyte imbalance. In acute enteritis, there may be severe abdominal pain, which is most severe in the horse and is often sufficient in this species to cause rolling and kicking at the abdomen. Abdominal pain in enteritis is unusual in the other species although it does occur in heavy inorganic metal poisonings, such as arsenic and lead, and in acute salmonellosis in cattle. Some severe cases of enteric colibacillosis in calves are characterized by abdominal pain evidenced by intermittent bouts of stretching and kicking at the abdomen. The passage

of intestinal gas also occurs commonly in horses with acute and chronic diarrhea.

Intestinal Sounds in Enteritis

Auscultation of the abdomen usually reveals sounds of **increased peristalsis** and **fluid-rushing sounds** in the early stages of acute enteritis. Later there may be **paralytic ileus** and an absence of peristaltic sounds with only fluid and gas tinkling sounds. The abdomen may be distended in the early stages because of distension of intestines and gaunt in the later stages when the fluid has been passed out in the feces. Pain may be evidenced on palpation of the abdomen in young animals.

Chronic Enteritis

In **chronic enteritis,** the feces are usually soft and homogeneous in consistency, contain considerable mucus, and usually do not have a grossly abnormal odor. Progressive weight loss and emaciation or "runting" are common and there are usually no systemic abnormalities. Animals with chronic enteritis will often drink and absorb sufficient water to maintain clinical hydration, but there may be laboratory evidence of dehydration and electrolyte loss. In parasitic enteritis and abomasitis there may be hypoproteinemia and subcutaneous edema. In terminal ileitis, there is usually chronic progressive weight loss and occasionally some mild diarrhea. The lesion is usually recognized only at necropsy. Intestinal adenomatosis of pigs, rectal strictures in pigs, granulomatous enteritis of horses, and lymphosarcoma of the intestine of horses are examples of enteric disease causing chronic anorexia and progressive weight loss, usually without clinical evidence of diarrhea. These are commonly referred to as malabsorption syndromes.

CLINICAL PATHOLOGY

The laboratory testing of animals to obtain an etiologic diagnosis of enteritis can be a complex and expensive procedure, which requires careful consideration of the history, the clinical findings, and the number of animals affected. In outbreaks of enteric syndromes, it may be important to submit samples from both affected and normal animals. The details of the sampling techniques and the tissues required for the diagnosis of diseases of the digestive tract caused by feeding mismanagement, infections, toxins, and other agents have been outlined and this is recommended as a reference.

Fecal Examination

Examination of the feces to determine the presence of causative **bacteria**, **helminths**, **protozoa**, **viruses,** and **chemical agents** is described under specific diseases throughout this book. It is important that fecal specimens are taken as the differentiation of the etiologic groups depends on laboratory

examinations. In outbreaks of diarrhea, fecal samples should also be taken from a representative number of normal animals in the same group as the affected animals. Comparison of the fecal examination results between affected and normal animals will improve the accuracy of interpretation.

Fecal samples can be examined for the presence of leukocytes and epithelial cells, which occur in exudative enteritis.

Intestinal Tissue Samples

In outbreaks of diarrhea, especially in neonates, it may be useful to do necropsies on selected early untreated cases of acute diarrhea. The lesions associated with the enteropathogens are well known, and a provisional etiologic diagnosis may be possible by gross and histopathological examination of the intestinal mucosa.

Hematology and Serum Biochemistry

With increasing sophistication in diagnostic laboratories and in large-animal practice, it is becoming common to do considerable laboratory evaluation to determine the actual changes that are present for purposes of a more rational approach to therapy. For each specific enteritis there are changes in the hemogram and serum biochemistry that aid in the diagnosis and differential diagnosis. In bacterial enteritis, such as acute enteric salmonellosis in the horse, there may be marked changes in the total and differential leukocyte count, which is a useful diagnostic aid. In most cases of acute enteritis there is hemoconcentration, metabolic acidosis, an increase in total serum solids concentration, a decrease in plasma bicarbonate, hyponatremia, hypochloremia, and hypokalemia. However, abnormalities in body fluid compartments caused by diarrhea depend on the pathogenetic mechanisms involved and the duration of the diarrhea. In horses with diarrhea of less than 6 days' duration, the most common abnormality may be a combined anion gap, metabolic acidosis, and metabolic alkalosis characterized by hyponatremia, hypochloremia, and hyperkalemia. The **acid-base imbalances** may vary considerably from case to case, and it is suggested that optimal fluid therapy should be based on laboratory evaluation of the animal's blood gas and electrolytes. **Hyperkalemia** may occur in severe acidosis. An increase in serum creatinine may be caused by inadequate renal perfusion associated with the dehydration and circulatory failure.

Digestion/Absorption Tests

Digestion and absorption tests are available for the investigation of chronic malabsorptive conditions, particularly in the horse. Intestinal biopsy may be necessary for a definitive diagnosis of chronic intestinal lesions that cannot be determined by the usual diagnostic tests. Examples include intestinal lymphosarcoma, granulomatous enteritis, and perhaps Johne's disease. Serum electrophoresis and the administration of radioactively labeled albumin may be necessary to determine the presence of a protein-losing enteropathy.

NECROPSY FINDINGS

The pathology of enteritis or malabsorption varies considerably depending on the cause. There may be an absence of grossly visible changes of the mucosa, but the intestinal lumen will be fluid-filled or relatively empty, depending on the stage of examination in enterotoxigenic colibacillosis. When there is gross evidence of inflammation of the mucosa there will be varying degrees of edema, hyperemia, hemorrhage, foul-smelling intestinal contents, fibrinous inflammation, ulceration, and necrosis of the mucosa. With acute necrosis there is evidence of frank blood, fibrinous casts, and epithelial shreds. The mesenteric lymph nodes show varying degrees of enlargement, edema and congestion, and secondary involvement of spleen and liver is not unusual. In chronic enteritis, the epithelium may appear relatively normal, but the wall is usually thickened and may be edematous. In some specific diseases there are lesions typical of the particular disease.

DIFFERENTIAL DIAGNOSIS

Approach
- The approach to the diagnosis of diarrhea requires consideration of the epidemiological history and the nature and severity of the clinical findings. With the exception of acute enteritides in newborn farm animals, most of the other common enteritides have reasonably distinct epidemiological and clinical features.
- In some cases, a necropsy on an untreated case of diarrhea in the early stages of the disease can be very useful.
- If possible, a hemogram should be obtained to assist in determining the presence or absence of infection.

Appearance of feces
- The gross appearance of the feces may provide some clues about the cause of the diarrhea. Generally, diarrhea caused by lesions of the small intestine are profuse and the feces are liquid and sometimes as clear as water. The diarrhea associated with lesions of the large intestine are characterized by small volumes of soft feces, often containing excess quantities of mucus.
- The presence of toxemia and fever-marked changes in the total and differential leukocyte count suggest bacterial enteritis, possibly with septicemia. This is of particular importance in horses and cattle with salmonellosis.
- The presence of frank blood and/or fibrinous casts in the feces usually indicates a severe inflammatory lesion of the intestines. In sand-induced diarrhea in horses the feces may contain sand.

Weight loss
- Chronic diarrhea with a history of chronic weight loss in a mature cow suggests Johne's disease.
- Chronic weight loss and chronic diarrhea, or even the absence of diarrhea, in the horse may indicate the presence of granulomatous enteritis, chronic eosinophilic gastroenteritis, alimentary lymphosarcoma, tuberculosis, and histoplasmosis.

Dietary diarrhea and toxicities
- In dietary diarrhea the feces are usually voluminous, soft, and odoriferous. The animal is usually bright and alert and there are minimal systemic effects. An examination of the diet will usually reveal if the composition of the diet or irregular feeding practices are responsible for the diarrhea. Analysis of samples of new feed may be necessary to determine the presence of toxic chemical agents.
- Arsenic poisoning is characterized by dysentery, toxemia, normal temperature, and nervous signs.
- Copper deficiency conditioned by an excess of molybdenum causes a moderately profuse diarrhea with soft feces and moderate weight loss. There is usually normal hydration and possibly depigmentation of hair.

Parasitism
- Intestinal helminthiasis such as ostertagiasis causes a profuse diarrhea and marked loss of weight; the temperature is normal and there is no toxemia.

Miscellaneous causes
- In cattle, the oral cavity must be examined for evidence of lesions characteristic of viral diseases.
- Many diseases of the stomach, including ulceration, parasitism, gastritis, and tumors, may result in diarrhea and must be considered in the differential diagnosis of chronic diarrhea.
- The soft scant feces associated with some cases of incomplete obstruction of the digestive tract of cattle affected with the complications of traumatic reticuloperitonitis must not be confused with diarrhea.

TREATMENT

The principles of treatment of enteritis include the following:

- Removal of the causative agent
- Alteration of the diet
- Fluids and electrolytes
- Intestinal protectants and adsorbents
- Antidiarrheal drugs

Removal of Causative Agent

Specific treatment is usually directed at intestinal helminthiasis with anthelmintics, antiprotozoan agents against diseases such as coccidiosis, and antimicrobial agents against the bacterial enteritides. There are no specific treatments available for the viral enteritides in farm animals.

Although a considerable number of investigations have been done on the enteritides on farm animals, the emphasis has been on the immunology, pathology, microbiology, and body fluid dynamics, each with different emphasis in different species. For example, there is considerable information on the microbiology and immunology of the common enteritides in calves and piglets in addition to the extensive knowledge of the body fluid dynamics in calves. In the horse there is some information on body fluid dynamics, but the microbiology of the diarrheas is not well understood. In none of the species is there sufficient information on the effects of antibiotics on the intestinal microflora.

Antimicrobials

The use of antimicrobials, either orally or parenterally, or by both routes simultaneously, for the treatment of bacterial enteritides is a controversial subject in both human and veterinary medicine. Those who support their use in acute bacterial enteritis claim that they are necessary to help reduce the overgrowth of pathogenic bacteria responsible for the enteritis and to prevent or treat bacteremia or septicemia that may occur secondary to an enteritis. Those who suggest that they are contraindicated or unnecessary in bacterial enteritis suggest that the drugs may eliminate a significant proportion of the intestinal flora in addition to the pathogenic flora. This may reduce the effect of competitive antagonism in the intestine, which in turn may permit the development of a superinfection (the appearance of bacteriologic and clinical evidence of a new infection during the chemotherapy of a primary one). Also, the use of antimicrobials in infectious enteric disease allows the development of **multiple drug resistance**, which is a major public health concern. The use of antimicrobials may also increase the length of time over which affected animals excrete the organisms which, for example, may occur in enteric salmonellosis.

Many different antimicrobial preparations for both oral and parenteral administration are available. The choice will depend on previous experience, the disease suspected, and the results of culture and drug sensitivity tests. Parenteral preparations are indicated in animals with acute diarrhea, toxemia, and fever. Many antimicrobials, when given parenterally, are excreted by the liver into the lumen of the intestine and oral preparations may not be necessary. In cases of subacute diarrhea with minimal systemic effects, the use of an oral preparation may be sufficient. However, oral preparations should not be used for more than 3 days to avoid a superinfection. The preparations and doses of the antimicrobials commonly used in bacterial enteritides are described under each disease.

Mass Medication of Feed and Water Supplies

Mass medication of the drinking water supply with antimicrobials for the treatment of outbreaks of specific infectious enteritides in animals is used commonly and with success. One of the best examples is the use of antimicrobials in the drinking water of pigs affected with swine dysentery. However, not all affected animals will drink a sufficient quantity of the medicated water and daily intake must be monitored carefully. Severely affected animals in an outbreak need individual treatment.

Alteration of the Diet

If the cause of the diarrhea is dietary in origin the feed should be removed until the animal has fully recovered; feed should then be replaced by another source or reintroduced gradually. The question of whether or not a normally digestible diet should be removed temporarily or the total daily intake reduced in animals with acute enteritis is a difficult one. The rationale is that in acute enteritis the digestibility of nutrients is reduced considerably and undigested feed provides a substrate for fermentation and putrefaction to occur, the products of which may accentuate the malabsorptive state. However, temporary withdrawal of feed presents practical problems, especially in the young. For example, the temporary removal from the sow of newborn piglets affected with acute enteritis presents practical problems and is of doubtful value, which is similar with beef calves nursing cows on pasture. With foals it is relatively easy to muzzle them for 24 hours. With weaned piglets affected with weanling diarrhea and feeder pigs with swine dysentery, it is common practice to reduce the normal daily intake by half for a few days until recovery is apparent. Mature horses affected with diarrhea should not have access to any feed for at least 24 hours. During the period of temporary starvation, the oral intake of fluids containing glucose and electrolytes is desirable and necessary to assist in maintaining hydration. In newborn calves with diarrhea, if oral fluid intake is maintained, the total loss of water from feces and through the kidney is not significantly greater than in normal calves, because in diarrheic calves the kidney will effectively compensate for fecal losses. When recovery is apparent, the animal's usual diet may be reintroduced gradually over a period of a few days.

Fluids and Electrolytes

The initial goals of fluid and electrolyte therapy for the effects of enteritis are the restoration of the body fluids to normal volume, effective osmolality, and composition and acid-base balance. The quality and quantity of fluids required to achieve these goals depend on the characteristics of the dehydration and acid-base electrolyte imbalance. Under ideal conditions when a laboratory is available, the determination of PCV, total serum proteins, plasma bicarbonate, blood pH, serum electrolytes, and a hemogram would provide the clinician with a laboratory evaluation initially and throughout the course of therapy to assess the effectiveness of the treatment. However, such laboratory service is expensive and usually not readily available. The clinician must therefore assess the degree of clinical dehydration and, based on the history and clinical findings, estimate the degree of acidosis and electrolyte deficits that are likely to be present. A practical approach to fluid therapy in the horse has been described. Fluids should be given orally whenever possible to save time and expense and to avoid the complications that can arise from long-term parenteral fluid therapy. Also, fluids should be given as early as possible to minimize the degree of dehydration. With good kidney function there is a wider safe latitude in the solution used.

The three major abnormalities of **dehydration**, **acidosis,** and **electrolyte deficit** are usually corrected simultaneously with fluid therapy. When severe acidosis is suspected, this should be corrected immediately with a hypertonic (5%) solution of bicarbonate given intravenously at the rate of 5 to 7 mL/kg BW at a speed of about 100 mL/min. This is followed by the administration of electrolyte solutions in quantities necessary to correct the dehydration. With severe dehydration, equivalent to 10% of BW, large amounts of fluids are necessary (Table 7-8).

The initial hydration therapy should be given over the first 4 to 6 hours by continuous intravenous infusion, followed by maintenance therapy for the next 20 to 24 hours, or for the duration of the diarrhea if severe, at a rate of 100 to 150 mL/kg BW per 24 hours. Horses with acute enteritis have severe hyponatremia and following fluid therapy may become severely hypokalemic, as evidenced by weakness and muscular tremors. The hypertonic solution of sodium bicarbonate will assist in correcting the hyponatremia, but potassium chloride may need to be added to the large quantity of

Table 7-8 Fluid deficits (L) in horses, foals and calves with 10% dehydration

Animal	Dehydration (%)	Fluid deficit (L)
500-kg horse	10	50
75-kg foal	10	7.5
45-kg calf	10	4.5

fluids given for dehydration; 1 g of potassium chloride added to each liter of fluid will provide an additional 14 mOsm/L (14 mmol/L) of potassium. In preruminant calves with diarrhea, the fluids and electrolytes required for maintenance may be given orally in divided doses every few hours. In the early stage of acute diarrhea and for animals that are not severely dehydrated, the oral route can also be used successfully to correct dehydration and prevent it from becoming worse. The formula of oral glucose–electrolyte solutions are given in the section Colibacillosis. Piglets and lambs affected with dehydration are most effectively treated using balanced electrolyte solutions given subcutaneously at the dose rates of 20 mL/kg BW every 4 hours and orally at 20 mL/kg BW every 2 hours. Details of the treatment of fluid and electrolyte disturbances are given in Chapter 5.

Intestinal Protectants and Adsorbents
Kaolin and pectin mixtures are used widely to coat the intestinal mucosa, inhibit secretions, and increase the bulk of the feces in animals with enteritis. In children with diarrhea, kaolin and pectin will result in formed rather than watery feces, but the water content of the feces is unchanged. It is not possible at this time to make a recommendation on their use in animals.

Antidiarrheal Drugs
Antimotility Drugs
Anticholinergic drugs and opiates are available to decrease intestinal motility. The anticholinergic drugs block the action of acetylcholine on smooth muscle and glands. This results in decreased gastric secretion and emptying and a reduction on both segmental and propulsive movements of the intestines. Dosages of anticholinergics necessary to produce effectiveness may also cause side effects such as xerostomia, photophobia, tachycardia, urinary retention, and neuromuscular paralysis. The opiates function by producing an increase in segmentation while reducing propulsive movements in the intestine. The net effect is an increase in resistance to passage of intestinal contents, and more complete absorption of both water and nutrients occurs with a subsequent decrease in the frequency of defecation. There are no published reports of clinical trials using antimotility drugs for the treatment of diarrhea in farm animals; therefore at the present time

they cannot be recommended with any assurance of effectiveness.

Antisecretory Drugs
Antisecretory drugs are also available for the treatment of diarrhea caused by the hypersecretory activity of enterotoxin produced by bacteria such as ETEC. Loperamide hydrochloride given orally to calves with experimentally induced diarrhea can delay the onset of diarrhea by its inhibition of fluid secretion. Antisecretory drugs include chlorpromazine, opiates, atropine, and prostaglandin inhibitors. These have not yet been adequately evaluated and the provision of balanced fluids and electrolytes, containing sodium chloride, sodium bicarbonate, potassium chloride, and glucose, given both parenterally and orally, are considered to be adequate and effective for treating the effects of the hypersecretion.

Because prostaglandins have an important reparative role in the intestine, NSAIDs may retard recovery of ischemic-injured intestine and are contraindicated.

CONTROL
The control and prevention of enteritis in farm animals is a major topic and activity of large-animal practice. The control of each specific enteritis is presented under each specific disease in Part II of this book. The principles of control include the following:
- Reduce infection pressure by controlling population density
- Ensure adequate nonspecific resistance by adequate colostrum intake of neonatal farm animals and maintaining adequate nutritional status
- Vaccinate for those diseases for which there is an effective vaccine
- Minimize managerial and environmental stressors
- Monitor morbidity and mortality and ensure that a diagnosis is obtained so that control measures for newly introduced diseases into a herd can be instituted

INTESTINAL HYPERMOTILITY

A functional increase in intestinal motility seems to be the basis of a number of diseases of animals. Clinically there is some abdominal pain and, on auscultation, an increase in alimentary tract sounds and, in some cases, diarrhea. Affected animals do not usually die and necropsy lesions cannot be defined, but it is probable that the classification as it is used here includes many of the diseases often referred to as catarrhal enteritis or indigestion.

The major occurrence of intestinal hypermotility is spasmodic colic of the horse. Other circumstances in which hypermotility and diarrhea occur without evidence of enteritis include allergic and anaphylactic states and a change of feed to lush pasture.

DIETARY DIARRHEA

Dietary diarrhea occurs in all species and all ages but is most common in neonatal animals in which there is either absolute or relative inability to digest food or to which inappropriate food is provided. An absolute inability to digest food occurs in primary, or severe secondary, lactose intolerance in which the neonate does not have intestinal lactase activity. The result is failure to cleave lactose to its constituent monosaccharides and therefore fermentation of lactose in the small or large intestine. Bacterial fermentation of lactose causes osmotic diarrhea. Relative lactose deficiency presumably occurs in neonates that ingest large quantities of milk that then exceed the digestive capacity of the intestine. The frequency with which this occurs is unclear and withholding or restricting of feed to neonates should be approached with caution. The feeding of indigestible feedstuffs, such as inferior milk replacers, can cause diarrhea.

ETIOLOGY
Milk Replacers
The use of inferior-quality milk replacers in young calves under 3 weeks of age is one of the most common causes of dietary diarrhea. The quality of the milk replacer may be affected by the use of skim-milk powder that was heat denatured during processing, resulting in a decrease in the concentration of noncasein proteins. This results in ineffective clotting in the abomasum and reduced digestibility. The use of excessive quantities of nonmilk carbohydrates and proteins in milk replacers for calves is also associated with a high incidence of diarrhea, loss of weight, emaciation, and starvation. The use of large quantities of soybean protein and fish protein concentration in milk replacers for calves will result in chronic diarrhea and poor growth rates.

Most attempts to raise calves on diets based on large amounts of certain soybean products, such as heated soybean flour, have been unsuccessful because the animals developed diarrhea, lost appetite, and had lower weight or inferior growth rate. Preruminant calves develop gastrointestinal hypersensitive responses to certain soybean products because major proteases of the digestive tract do not denature soluble antigenic constituents of the soybean protein.

Diarrhea of nutritional origin has become one of the most important problems in which large numbers of calves are raised under intensive conditions. Because of the relatively high cost of good-quality skim-milk powder, large quantities of both nonmilk proteins and carbohydrates are used in formulating milk replacers. Although some calves in these large units can satisfactorily digest the nutrients in these milk replacers, many cannot, and this leads to a high incidence of diarrhea and secondary colibacillosis and enteric salmonellosis.

Milk replacers made from bovine milk and milk by-products used to feed orphan piglets, lambs, and foals may cause nutritional diarrhea for the same reasons given earlier. In milk-replacer–fed calves, increasing the total daily fluid intake as a percentage of BW causes a greater incidence of loose feces, dehydration, and dullness than lower levels of fluid intake and higher dry matter concentration. This suggests that a greater amount of fluid intake increases the passage rate of dry matter and decreases absorption. The concentration of solids in the liquid diet should range between 10% and 13% and should be offered at 8% of BW in calves fed milk replacer once daily and allowed free access to calf starter.

Overfeeding of Milk

The feeding of excessive amounts of cows' whole milk to hand-fed calves will result in large amounts of abnormal feces but usually not a profuse watery diarrhea with dehydration and loss of weight. This suggests that simple overfeeding of milk might not be a cause of acute neonatal diarrhea of calves. There is some limited evidence that dietary diarrhea can occur in nursing beef calves ingesting milk that does not clot properly. Only the milk from cows with diarrheic calves showed evidence of impaired clotting in an in vitro test.

The ingestion of excessive quantities of sows' milk by piglets at 3 weeks of age is thought to be a contributory cause of 3-week diarrhea of piglets. This could be caused by the sow reaching peak production at 3 weeks.

Beef calves suckling high-producing cows grazing on lush pasture are often affected with a mild diarrhea at about 3 weeks of age. The cause is thought to be simple overconsumption of milk. Similarly, vigorous lambs sucking high-producing ewes can develop diarrhea.

Foals commonly have diarrhea at about 9 days of age, which coincides with the foal heat of the mare. It has been thought for many years that the cause was a sudden change in the composition of the mare's milk, but this has not been supported by analyses of mares' milk at that time. Diarrhea is associated with age-related changes in the microbiota of the foals' gastrointestinal tract.[1]

There is considerable interest in the optimal conditions for feeding liquid diets to young calves. The temperature of the liquid when fed, feeding once or twice daily, and the amount of dry matter intake can affect the performance of calves. However, there is a range of safety in which the performance of the calves will not be significantly affected if management is good.

Change of Diet

Dietary diarrhea also occurs in all species following a sudden change in diet, but particularly in animals at weaning time. This is particularly important in the pig weaned at 3 weeks of age and not adjusted to the post-weaning ration. Diarrhea occurs commonly when animals are moved from a dry pasture to a lush pasture and when first introduced to liberal quantities of concentrates containing a large percentage of the common cereal grains.

PATHOGENESIS
Digestion of Milk

In calves, the ingestion of excessive quantities of cows' whole milk after several hours of no intake causes gross distension of the abomasum and possibly of the rumen. Under these conditions, the milk-clotting capacity of the abomasum may be limited, resulting in incomplete clotting. The flow of nutrients from the abomasum is more uniform in calves fed twice daily than once daily, which suggests that twice-daily feeding allows for more effective clotting and digestion.

Under normal conditions, the milk clot forms in the abomasum within minutes after feeding, and the whey moves to the duodenum 5 to 10 minutes later. The dilution of cows' whole milk will result in increased clotting time when treated with rennin (chymosin). Overfeeding could result in whole milk or excessive quantities of whey entering the duodenum, which cannot digest whole milk or satisfactorily digest and hydrolyze the substrates in whey. The presence of excessive quantities of such substrate, especially lactose, in the intestinal lumen would serve as a hydragogue and result in a large increase in intestinal fluid, failure of complete absorption, and abnormal feces. The speed of drinking is probably also important. Prolongation of drinking time results in dilution of the milk with saliva and the production of a more easily digested milk clot. Failure of the esophageal reflex in pail-fed calves may also be important. The milk enters the rumen, where it undergoes putrefaction.

Milk Replacers and Diarrhea

The pathogenesis of diarrhea in calves fed inferior-quality milk replacers is well known. In calves fed low-heat–treated skim-milk powder milk replacer, curd formation in the abomasum, compared with no curd formation, slows down the passage of total abomasal content (retained matter from the last feeding, residual matter from the penultimate feeding, saliva, and gastric secretions), dry matter, crude protein, and fat from the abomasum to the intestine. Heat-denatured skim-milk powder is incompletely clotted in the abomasum, leading to reduced digestibility.

Nonmilk carbohydrates and nonmilk proteins are not well digested by preruminant calves under 3 weeks of age because their amylase, maltase, and sucrase activities are insignificant, and their pepsin-HCl activity is not well developed until at least 3 weeks of age. Following the ingestion of these nutrients, there is reduced digestibility, malabsorption, and diarrhea. This results in a negative nutrient balance, loss of BW, and gradual starvation, all of which are reversible by the feeding of cows' whole milk. The digestion of fat is particularly affected, resulting in varying degrees of steatorrhea. Preruminant calves fed milk replacer containing corn oil will have diarrhea.

The mechanism for the diarrhea, which may occur in all species following a sudden change in diet, is not well understood. However, several days may be necessary for the necessary qualitative and quantitative changes to occur in the digestive enzyme capacity. Not much is known about the development of intestinal enzymes in the fetus and newborn, but this is likely to be of importance in individual animals. In calves, lactase activity is fully developed at birth and in the period between birth and weaning there are significant changes in enzyme activity, some of which are influenced by the presence or absence of dietary substances.

In dietary diarrhea, the presence of undigested substrate in the intestine can result in marked changes of the bacterial flora, which could result in excess fermentation of carbohydrates and putrefaction of protein, the products of which accentuate the malabsorption.

CLINICAL FINDINGS
Nursing Beef Calves

Dietary diarrhea of beef calves at 3 weeks of age on pasture is characterized by the passage of light yellow feces that is foul smelling and soft. The perineum and tail are usually smudged with feces. The calves are bright and alert and usually recover spontaneously without treatment in a few days.

Hand-Fed Dairy Calves

When overfed on cow's whole milk these animals are usually dull and anorexic and their feces are voluminous, foul smelling, and contain considerable mucus. The abdomen may be distended because of distension of the abomasum and intestines. Secondary enteric colibacillosis and salmonellosis may occur, resulting in severe dehydration. Most uncomplicated cases will respond to oral fluid therapy and withdrawal from or deprivation of milk.

Milk-Replacer Diarrhea

In calves fed inferior-quality milk replacers, there will be a chronic diarrhea with gradual weight loss. The calves are bright and alert, they usually drink normally, appear distended after drinking, and spend considerable time in recumbency. Not uncommonly, many treatments will have been tried unsuccessfully. The diarrhea and weight loss continues and in 2 to 4 weeks emaciation is evident and death from starvation may occur. Affected calves will often have a depraved appetite and eat bedding and other

indigestible materials, which further accentuates the condition. When large numbers of calves are involved, the incidence of enteric colibacillosis and salmonellosis may become high and the case mortality very high. This is a common situation in veal-calf–rearing units.

Alopecia occurs occasionally in calves fed a milk replacer, but the cause is unknown.

CLINICAL PATHOLOGY
Laboratory evaluation of the animals with dietary diarrhea is usually not necessary other than for elimination of other possible causes of the diarrhea. When milk replacers are being used the determination of the rennet-clotting time of the milk replacer compared with whole milk is a useful aid in assessing the quality of the skim-milk powder for calves.

NECROPSY FINDINGS
Emaciation, an absence of body fat, dehydration, and serous atrophy are present in calves that have died from diarrhea and starvation while being fed inferior-quality milk replacers.

DIFFERENTIAL DIAGNOSIS

- Dietary diarrhea occurs following a change in diet, the consumption of too much feed at once, or poor quality feed. There are usually no systemic signs and recovery occurs spontaneously when the dietary abnormality is corrected or the animal adapts to a new diet.
- Dietary diarrhea must be differentiated from all other common causes of diarrhea in a particular age group within each species.
- Examination of the recent dietary history and examination of the diet and its components will usually provide the evidence for a dietary diarrhea.

TREATMENT
Alter Diet of Hand-Fed Calves
In hand-fed calves affected with dietary diarrhea, milk feeding should be stopped and oral electrolyte solutions given for 24 hours. Milk is then gradually reintroduced. If milk replacers are being used their nutrient composition and quality should be examined for evidence of indigestible nutrients. The feeding practices should be examined and the necessary adjustments made.

The care and management of hand-fed calves to minimize the incidence of dietary diarrhea is an art. Much has been said about the use of slow-flowing nipple bottles and pails to reduce dietary diarrhea, but they are not a replacement for good management. Calves that are raised for herd replacements should be fed on whole milk if possible for up to 3 weeks. When large numbers of calves are reared for veal or for feedlots the milk replacer used should be formulated using the highest quality milk and milk by-products economically possible. The more inferior the milk replacer the more impeccable the management must become.

Monitor Beef Calves With Dietary Diarrhea
Beef calves affected with dietary diarrhea while sucking the cow and running on pasture do not usually require treatment unless complications develop. They must be observed daily for evidence of dullness, anorexia, inactivity, and profuse watery diarrhea, at which point they need some medical care.

REFERENCE
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ABDOMINAL FAT NECROSIS (LIPOMATOSIS)
Abdominal fat necrosis is a variant of generalized steatitis and is dealt with in more detail in Chapter 17. The **hard masses of necrotic fat** that occur relatively commonly in the peritoneal cavity of adult cattle, especially the Channel Island breeds and possibly Aberdeen Angus, are commonly mistaken for a developing fetus and can cause intestinal obstruction. The latter usually develops slowly, resulting in the appearance of attacks of moderate abdominal pain and the passage of small amounts of feces. Many cases are detected during routine rectal examination of normal animals. The lipomatous masses are located in the small and large omentum and mesentery in cattle and more diffusely to other parts of the body in sheep and goats. The composition of the fatty deposits is identical with the fat of normal cows and there is no suggestion that the disease is neoplastic. Sporadic cases are most common but there are reports of a herd prevalence as high as 67%. The cause is unknown, but there appears to be a relationship between such high prevalence and the grazing of tall fescue grass, and an inherited predisposition is suggested. The rate of occurrence increases with age with the peak occurrence at 7 years of age. It has been suggested that excessive fattiness of abdominal adipose tissue may predispose cattle to fat necrosis. An unusual form of the disease with many lesions in subcutaneous sites has been recorded in Holstein Friesian cattle and is regarded as being inherited. There is no treatment and affected animals should be salvaged. A generalized steatitis has been reported in pony foals.

Pedunculated lipomas provide a special problem, especially in older horses. Their pedicles can be 20 to 30 cm long, and during periods of active gut motility these pedicles can become tied around a loop of intestine anywhere from the pylorus to the rectum. At the pylorus they cause acute intestinal obstruction with gastric dilatation. At the rectum they cause subacute colic and a characteristic inability to enter the rectum with the hand. This is accompanied by a folded coning down of the mucosa, not unlike that in a torsion of the uterus. Early diagnosis and surgical intervention can produce a resolution, but delay in the acute disease is associated with a poor prognosis because the blood supply is compromised. Less acute disease causing small-colon impaction or recurrent colic occurs.[1,2]

REFERENCES
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2. Verwilghen D, et al. *Equine Vet Educ.* 2013;25:451.

Diseases of the Peritoneum

PERITONITIS
Inflammation of the peritoneum is accompanied by abdominal pain, fever, toxemia, and a reduction in the amount of feces. Signs vary in degree with the severity and extent of the peritonitis.

ETIOLOGY
Peritonitis can occur as a primary disease affecting the peritoneum or secondarily as part of a disease affecting primarily other organs with secondary involvement of the peritoneum.[1] Primary diseases of the peritoneum include malignancies of the peritoneum, *Actinobaccillus equuli* infection in horses, *Haemophilus suis* in pigs, or *Pasteurella multocida* infection in calves.[2,3] Primary causes of peritonitis are much less frequent than causes of secondary peritonitis. Secondary peritonitis occurs most commonly from loss of integrity of the visceral peritoneum, often from injury to the alimentary tract within the abdomen, allowing gastrointestinal contents to enter the peritoneal cavity. Less common is perforation of the abdominal wall from the exterior from traumatic injury, perforation of the reproductive tract, or the introduction of pathogens or irritating substances as a result of injections into the peritoneal cavity or exploratory laparotomy. Some of the more common individual causes are as follows.

Cattle
- Traumatic reticuloperitonitis, which also occurs in camelids[4,5]
- Secondary to ruminal trocarization
- Perforation or leakage of abomasal ulcer
- Concurrent abomasal displacement and perforating ulcer
- Necrosis and rupture of abomasal wall after abomasal volvulus
- Rumenitis of cattle subsequent to acute carbohydrate indigestion

- Complication of cesarean section
- Rupture of vagina in young heifers during coitus
- Deposition of semen into the peritoneal cavity, for example, during traumatic artificial insemination
- Injection of sterile solutions, e.g., calcium preparations for milk fever or vitamin/mineral supplements (selenium)[6]
- Transection of small intestine when it becomes pinched between the uterus and the pelvic cavity at parturition
- Intraperitoneal injection of nonsterile solutions
- Spontaneous uterine rupture during parturition, or during manual correction of dystocia
- Sadistic rupture of vagina or rectum[7]
- Spontaneous rupture of rectum at calving
- As part of specific diseases such as tuberculosis, pasteurellosis,[3] or algal peritonitis[8]

Horses

Peritonitis in horses is often secondary to gastrointestinal disease (colic) and can be a major complication after abdominal surgery. These diseases are discussed under the appropriate topic in the sections of this text dealing with equine colic. If cases attributable to gastrointestinal disease are excluded, most cases are idiopathic.[9] Primary causes are infrequent and include infection associated with *A. equuli*.[2,10] Peritonitis can be secondary to infectious, chemical, or parasitic peritoneal injuries:

- Rupture of dorsal sac of cecum or colon at foaling
- Cecal rupture in foals subjected to anesthesia and gastric endoscopy
- Cecal rupture of adult horses[11]
- As a sequela to cecal trocarization[12]
- Secondary to torsion and infarction of a liver lobe[13]
- Rectal rupture or tear during rectal examination, predisposed to by inflammation of mucosa and overenthusiasm by the operator; this subject is presented separately in the section **Rectal Tears**
- Extension from a retroperitoneal infection or intraabdominal abscess,[14] e.g., *S. equi,* as a result of metastatic strangles, *R. equi* in foals under 1 year of age,
- Gastric erosion or rupture related to ulceration associated with larvae of *Gasterophilus* or *Habronema* spp. or gastric ulceration (a rare sequel of gastric ulceration in adult horses)[15]
- Colonic perforation associated with aberrant migration of *Gasterophilus intestinalis*
- Leakage from a cecal perforation apparently associated with a heavy infestation of *Anoplocephala perfoliata* tapeworms
- Spontaneous gastric rupture
- *A. equuli* infection, in some cases secondary to immunodeficiency[10,16,17]
- Secondary to penetrating gastrointestinal foreign bodies[18]
- Rupture of the bladder or urinary tract[9]
- Periorchitis[19]
- Pancreatitis[20]

Pigs

- Ileal perforation in regional ileitis
- Glasser's disease associated with *H. suis.*

Sheep

- Spread from intestinal wall abscess following infestation with *Esophagostomum* sp. larvae
- Serositis-arthritis associated with *Mycoplasma* sp.
  - Intraperitoneal injection of selenium[6]

Goats

- Serositis-arthritis associated with *Mycoplasma* sp.

All Species

- Traumatic perforation from the exterior of the abdominal wall by horn gore or stake wound
- Faulty asepsis at laparotomy, peritoneal injection, or trocarization for tympany of rumen or cecum
- Leakage through wall of infarcted gut segment
- Spread from subperitoneal sites in spleen, liver, and umbilical vessels

PATHOGENESIS

At least six factors account for the clinical findings and the various consequences of peritonitis: toxemia or septicemia, shock and hemorrhage, abdominal pain, paralytic ileus, accumulation of fluid exudate, and the development of adhesions.

Toxemia and Septicemia

Toxins produced by bacteria and by the breakdown of tissue are absorbed readily through the peritoneum. The resulting toxemia is the most important factor in the production of clinical illness, and its severity is usually governed by the size of the area of peritoneum involved. In **acute diffuse peritonitis**, the toxemia is profound, but in local inflammation, it is negligible. The type of infection present is obviously important because of variations between bacteria in their virulence and toxin production.

With rupture of the alimentary tract wall and the spillage of a large quantity of gut contents into the peritoneal cavity, some acute peritonitis does develop, but death is usually too sudden, within 2 to 3 hours in horses, for more than an early lesion to develop. These animals die of endotoxic shock caused by absorption of toxins from the gut contents. In acute diffuse peritonitis caused solely by bacterial contamination from the gut, the reaction depends on the bacteria that gain entry, the capacity of the omentum to deal with the peritonitis, and the amount of body movement that the animal has to perform. Cows that suffer penetration of the reticular wall at calving have lowered immunologic competence, a greater than normal negative pressure in the peritoneal cavity; are invaded by *F. necrophorum, Corynebacterium* spp., and *E. coli*; and are required to walk to the milking parlor, to the feed supply, and so on. They are likely to develop a massive diffuse purulent peritonitis and a profound toxemia and die within 24 hours. In contrast, horses that develop acute peritonitis from streptococci or *A. equuli* show little toxemia and manifest only abdominal pain caused by the inflammatory reaction of the peritoneum.

Shock and Hemorrhage

The shock caused by sudden deposition of gut contents, or infected uterine contents, into the peritoneal cavity, plus the hemorrhage resulting from the rupture, may be significant contributors to the common fatal outcome when an infected viscus ruptures. Following rupture of the uterus in cows, the shock and hemorrhage may be minor and peritonitis may not develop if the uterine contents are not contaminated. Failure of the uterus to heal or be repaired may be followed by peritonitis several days later.

Abdominal Pain

Abdominal pain is a variable sign in peritonitis. In acute, diffuse peritonitis, the toxemia may be sufficiently severe to depress the response of the animal to pain stimuli, but in less severe cases the animal usually adopts an arched-back posture and shows evidence of pain on palpation of the abdominal wall. Inflammation of the serous surfaces of the peritoneum causes pain, which may be severe enough to result in rigidity of the abdominal wall and the assumption of an abnormal humped-up posture.

Paralytic Ileus

Paralytic ileus occurs as a result of reflex inhibition of alimentary tract tone and movement in acute peritonitis. It is also an important sequel to intestinal obstruction and to traumatic abdominal surgery, in which much handling of viscera is unavoidable. Rarely, it arises because of ganglionitis and a loss of neural control of peristalsis, similar to the idiopathic intestinal pseudoobstruction of humans. The net effect is **functional obstruction of the intestine**, which, if persistent, will increase the likelihood of death. The end result is a complete

absence of defecation, often with no feces present in the rectum.

Accumulation of Fluid Exudate

Accumulation of large quantities of inflammatory exudate in the peritoneal cavity may cause visible abdominal distension and, if severe enough, interfere with respiration by obstruction of diaphragmatic movement. It is a comparatively rare occurrence but needs to be considered in the differential diagnosis of abdominal distension.

Adhesions

Trauma to the peritoneum results in a serosanguineous exudate, which contains two closely bound proteins, fibrinogen and plasminogen. **Fibrinogen** is converted by thrombin to fibrin, forming an early fibrinous adhesion. **Plasminogen** may be converted by plasminogen activators to plasmin, a specific fibrinolytic enzyme favoring lysis of the early adhesion. Peritoneal mesothelial cells are a source of plasminogen activators and each species of domestic animal has its own baseline peritoneal plasminogen activity. Cattle have a high capacity to respond to trauma with fibrin deposition. Intraabdominal fibrin deposition and adhesion formation is the most important factor in localizing peritonitis after peritoneal trauma from penetrating foreign bodies or abomasal ulcers. However, these adhesions can cause mechanical or functional intestinal obstruction.

In **chronic peritonitis**, the formation of adhesions is more important than either of the two preceding pathogenetic mechanisms. Adhesions are an essential part of the healing process and are important to localize the inflammation to a particular segment of the peritoneum. If this healing process is developing satisfactorily and the signs of peritonitis are diminishing, it is common to find that vigorous exercise causes breakdown of the adhesions, spread of the peritonitis, and return of the clinical signs. Thus a cow treated conservatively for traumatic reticuloperitonitis by immobilization might show an excellent recovery by the third day but, if allowed to go out to pasture at this time, could suffer an acute relapse. The secondary adverse effects of adhesions may cause partial or complete **obstruction of the intestine** or stomach, or fixation to the body wall, interfering with normal gut motility. Adhesions are important in the pathogenesis of vagus indigestion in cattle.

CLINICAL FINDINGS

Peritonitis is common in cattle, less common in horses and rarely, if ever, identified clinically in sheep, pigs, or goats. There are general signs applicable to all species and most forms of the disease in a general way. In addition, there are special findings peculiar to individual species and to various forms of the disease.

Acute and Subacute Peritonitis

Inappetence and Anorexia

Inappetence occurs in less severe and chronic cases, and complete anorexia in acute diffuse peritonitis.

Toxemia and Fever

Toxemia, usually with a fever, is often present, but the severity varies depending on the area of peritoneum involved, the identity of the pathogens, and the amount of tissue injury. For example, in cattle with acute local peritonitis the temperature will be elevated (39.5°C [103°F]) for the first 24 to 36 hours, but then return to normal even though the animal may still be partly or completely anorexic. A high fever (up to 41.5°C [106°F]) suggests an acute diffuse peritonitis, but in the terminal stages the temperature usually falls to subnormal. It is most noteworthy that a normal temperature does not preclude the presence of peritonitis. In horses with peritonitis, the temperature will usually exceed 38.5°C, but the fever may be intermittent. There is usually a moderate increase in heart and respiratory rates, and the latter is contributed to by the relative fixation of the abdominal wall because of pain. In some cases there is spontaneous grunting at the end of each expiratory movement.

Feces

The amount and composition of feces is usually abnormal. The transit time of ingesta through the alimentary tract is increased and the dry matter content of the feces increases. The amount of feces is reduced, although in the early stages there may be a transient period of increased frequency of passage of small volumes of soft feces, which may give the false impression of increased fecal output. In some horses with peritonitis, periods of diarrhea can occur but the feces are usually reduced in amount. Feces may be completely absent for periods of up to 3 days, even in animals that recover, and the rectum may be so dry and tacky, because of the presence of small amounts of tenacious mucus, that it is difficult to do a rectal examination. This might suggest a complete intestinal obstruction.

In pastured cattle with peritonitis the feces are characteristically scant, dark, and like small fecal balls accompanied by thick, jelly-like mucus. The feces may alternatively have a thick, sludge-like consistency, be tenacious and difficult to remove from a rubber glove, and have a foul smell.

Alimentary Tract Stasis

As well as absence of feces, there are other indicators of intestinal stasis. In cows with acute peritonitis ruminal contractions are reduced or absent; in chronic peritonitis the contractions may be present but are weaker than normal. In the horse, intestinal stasis is evidenced by an absence or reduction of typical intestinal peristaltic sounds on auscultation, although the tinkling sounds of paralytic ileus may be audible. It is very important to differentiate the two.

Abdominal Pain Evidenced by Posture and Movement

In cattle with acute peritonitis there is a disinclination to move, disinclination to lie down, lying down with great care, and grunting with pain. The posture includes a characteristically arched back and a shuffling and cautious gait with the back held rigid and arched. Grunting at each step and when feces or urine are passed is common, and when urine is eventually passed it is usually in a very large volume. Sudden movements are avoided and there is an absence of kicking or bellowing or licking the coat.

In horses these overt signs of peritonitis that characterize the condition in cattle are uncommon, which makes the diagnosis difficult. In the horse peritonitis is often manifested as an episode of abdominal pain including flank watching, kicking at the belly, and going down and rolling, which suggests colic caused by intestinal obstruction.

In a series of 51 cases of peritonitis associated with *A. equuli* in horses, most had tachycardia, increased respiratory rates, fever, and reduced intestinal borborygmi. Affected horses were depressed, lethargic, and inappetent. Mild to moderate abdominal pain was manifested as reluctance to move, pawing on the ground, lying down, or splinting of the abdominal musculature. The onset of clinical signs was acute (<24 hours) in 30 horses, 1 to 4 days in eight horses, or longer and associated with weight loss in three horses. In 10 horses, there was no record of the duration of clinical signs. The disease is usually primary although recurrent or chronic cases can be attributable to immunodeficiency, such as common variable immunodeficiency of aged horses.[17]

Abdominal Pain as Evidenced by Deep Palpation

In cattle, deep firm palpation of the abdominal wall elicits an easily recognized pain response. It may be possible to elicit pain over the entire abdominal wall if the peritonitis is widespread. If it is localized the response may be detectable over only a very small area. Increased tenseness of the abdominal wall is not usually detectable in the cow, although it is responsible for the characteristic arched-back posture and apparent gauntness of the abdomen, because the wall is already tightly stretched anyway.

Several methods are used to elicit a grunt in cattle with abdominal pain. In average-sized cows with acute local peritonitis (most commonly traumatic reticuloperitonitis), while listening over the trachea with a stethoscope, a controlled upward push with the closed fist of the ventral body wall caudal to the xiphoid sternum is most successful. In large bulls, especially if the peritonitis is

subsiding, it may be difficult to elicit a grunt with this method. In these cases, the best technique is to use a heavy pole held horizontally under the area immediately caudal to the xiphoid sternum to provide a sharp lift given by assistants holding the pole on either side. **Pinching of the withers** while auscultating over the trachea is also used and with some clinical experience is highly reliable.

In horses with acute or subacute peritonitis, it is usually easy to elicit a pain response manifested by the animal lifting its leg and turning its head with anger when its lower flank is firmly lifted, but not punched. The abdominal wall also feels tense if it is lifted firmly with the heel of the hand. In all cases of peritonitis in all species a pain response is always much more evident in the early stages of the disease, and severe chronic peritonitis can be present without pain being detected on palpation.

Rectal Examination
The general absence of feces is characteristic. In cattle, it may be possible to palpate slightly distended, saggy, thick-walled loops of intestine in some cases. Also, it may be possible to feel fibrinous adhesions separating as the intestines are manipulated. Adhesions are not often palpable, and their absence should not be interpreted as precluding the presence of peritonitis. Only adhesions in the caudal part of the abdomen may be palpable. Tough, fibrous adhesions may be present in long-standing cases. In horses, there are no specific rectal findings, other than a reduced fecal output, to indicate the presence of peritonitis. Distension of segments of both the small and large intestines may provide indirect evidence of paralytic ileus. However, there is a lack of clarity as to what can be felt in chronic cases because of the presence of fibrin deposits and thickening of the peritoneum. There may also be more than usual pain when an inflamed area is palpated or a mesenteric band or adhesion is manipulated.

In rupture of the rectum associated with a difficult dystocia, the rupture is usually easily palpable rectally in the ventral aspect of the rectum deep in the abdomen. Distended loops of intestine may become entrapped in the rectal tear.

Peracute Diffuse Peritonitis
In those cases in which profound toxemia occurs, especially in cows immediately after calving or when rupture of the alimentary tract occurs, the syndrome is quite different. There is severe weakness, depression, and circulatory failure. The animal is recumbent and often unable to rise, depressed almost to the point of coma, has a subnormal temperature of 37 to 37.5°C (99–100°F), a high heart rate (110–120 beats/min), and a weak pulse. No abdominal pain is evidenced spontaneously or on palpation of the abdominal wall.

In mares that rupture the dorsal sac of the cecum during foaling, the owner observes that the mare has been straining and getting results when suddenly she stops making violent muscular contractions, and progress toward expelling the foal ceases. Moderate abdominal pain followed by shock is a characteristic development. Death follows 4 to 15 hours after the rupture.

The outcome in cases of acute, diffuse peritonitis varies with the severity. Peracute cases accompanied by severe toxemia usually die within 24 to 48 hours. The more common, less severe cases may be fatal in 4 to 7 days, but adequate treatment may result in recovery in about the same length of time.

In a series of 31 cases of generalized peritonitis in cattle most cases occurred peripartum. The most consistent clinical findings were depression, anorexia, decreased fecal output, and varying degrees of dehydration. The duration of illness ranged from 1 to 90 days with a median of 4 days. In 19 animals, the duration of clinical disease was less than 1 week, and in 12 cases the duration of illness was more than 1 week. All animals died or were euthanized.

Chronic Peritonitis
Cattle
The development of adhesions, which interfere with normal alimentary tract movements, and the gradual spread of infection as adhesions break down combine to produce a chronic syndrome of indigestion and toxemia punctuated by short, recurrent attacks of more severe illness. The adhesions may be detectable on rectal examination, but they are usually situated in the anterior abdomen and are impalpable. If partial intestinal obstruction occurs, the bouts of pain are usually accompanied by a marked increase in alimentary tract sounds and palpable distension of intestinal loops with gas and fluid. The course in chronic peritonitis may be several weeks and the prognosis is not favorable because of the presence of physical lesions caused by scar tissue and adhesions. In some cases there is marked abdominal distension with many liters of turbid-infected fluid present. This may be restricted in its location to the omental bursa. Detection of fluid in the peritoneal cavity of a cow is not easy because of the fluid nature of the ruminal contents. Results obtained by testing for a fluid wave should be interpreted cautiously. Collection of fluid by paracentesis abdominis is the critical test.

Horses
Horses with chronic peritonitis usually have a history of ill-thrift for a period of several weeks. Weight loss is severe and there are usually intermittent episodes of abdominal pain suggesting intestinal colic. Gut sounds are greatly diminished or absent, and subcutaneous edema of the ventral abdominal wall occurs in some cases. There may also be a contiguous pleurisy. Identification of the cause of the colic depends on the examination of a sample of peritoneal fluid.

Diagnostic Medical Imaging
In cattle with traumatic reticuloperitonitis, inflammatory fibrinous changes, and abscesses can be imaged (see also Chapter 8).

In cattle, standing reticular radiography is a useful aid for the diagnosis and management of traumatic reticuloperitonitis. It can accurately detect the presence of a foreign body and in most instances if the foreign body is perforating the reticular wall.

CLINICAL PATHOLOGY
Hematology
The total and differential leukocyte count is a useful aid in the diagnosis of peritonitis and in assessing its severity. In acute diffuse peritonitis with toxemia there is usually a leukopenia, neutropenia, and a marked increase in immature neutrophils (a degenerative left shift). There is "toxic" granulation of neutrophils. In less severe forms of acute peritonitis of a few days' duration there may be a leukocytosis caused by a neutrophilia with the appearance of immature neutrophils. In acute local peritonitis, commonly seen in acute traumatic reticuloperitonitis in cattle, there is commonly a normal total leukocyte count, or a slight increase, with regenerative left shift. In chronic peritonitis, depending on the extent of the lesion (diffuse or local), the total and differential leukocyte count may be normal, or there may be a leukocytosis with a marked neutrophilia and occasionally an increase in the total numbers of lymphocytes and monocytes. The plasma fibrinogen levels in cattle generally tend to increase as the severity of acute peritonitis increases and may be a useful adjunct to the cell counts for assessing severity.

In horses with peritonitis associated with *A. equuli,* there is hemoconcentration, hypoproteinemia, and a neutrophilia count with a left shift.

Abdominocentesis and Peritoneal Fluid
Examination of peritoneal fluid obtained by paracentesis is a valuable aid in the diagnosis of peritonitis and in assessing its severity. It can also provide an indication of the kind of antibacterial treatment required. The values in healthy horses and horses with various intestinal or peritoneal diseases are provided in Table 7-3. The maximum peritoneal fluid nucleated cell count in healthy foals is much lower than reported maximum values for adult horses and similarly for calves. Particular attention should be paid to the following:

- The ease of collection of the sample as a guide to the amount of fluid present
- Whether it is bloodstained, indicating damage to a wall of the viscus

- The presence of feed or fecal material, indicating intestinal ischemic necrosis or rupture
- Whether it clots and has a high protein content, indicating inflammation rather than simple transudation
- The number and kinds of leukocytes present, as an indication of the presence of inflammation, and also its duration
- Microbiological examination

When these results are available they should be interpreted in conjunction with the history, clinical signs, and other results, including hematology, serum chemistry, and possibly radiology. In particular, it must be noted that failure to obtain a sample does not preclude a possible diagnosis of peritonitis.

Interpretation of peritoneal fluid is also influenced by simple manipulation of the abdominal viscera, and the response is greater than that following opening and closing of the abdomen without manipulation of the viscera. Surgical manipulation results in a significant and rapid postoperative peritoneal inflammatory reaction.

In peritonitis in horses associated with *A. equuli,* the peritoneal fluid was turbid and had an abnormal color in 98% of cases. The protein content was elevated above normal in 50 samples (range 25–84 g/L, mean 44 g/L, normal <20 g/L). Total nucleated cell count was elevated in all samples (range 46–810 × 10 cells/L, mean 230 × 10 cells/L, normal <10 × 10 cells/L). A nucleated cell count above 100 × 10 cells/L, was present in 88% of animals. Pleomorphic gram-negative rods were seen on cytology in 53% of samples, and a positive culture of *A. equuli* was obtained in 72% of samples.

Experimentally, resection and anastomosis of the small colon in healthy horses causes a different inflammatory response than does manipulation. Absolute values in the peritoneal fluid for cell count, total protein, and differential count are inadequate to differentiate between a normal surgical reaction and a postoperative infection. Cytologic examination of peritoneal fluid is necessary to demonstrate degenerative cell changes and the presence of bacteria and ingesta. The peripheral leukon and fibrinogen concentration should always be compared with the peritoneal fluid for evidence of postsurgical infection. The nucleated cell and red blood counts of peritoneal fluid are commonly elevated for several days in horses following open castration. These elevated counts may be mistaken for peritonitis.

Septic Peritonitis in the Horse

Diagnosis of septic peritonitis is routinely made on the basis of physical examination and hematologic findings and peritoneal fluid analysis. After abdominal surgery, differentiation between septic peritonitis and other postoperative complications can be difficult using physical and hematological findings alone. As a result of the exploratory process itself, diagnosis of septic peritonitis is often complicated in horses after surgery because the total nucleated cell count and protein concentration in the peritoneal fluid are often high. Consequently, identification of bacteria on cytologic evaluation or isolation of bacteria from peritoneal fluid is a more definitive indicator of septic peritonitis, but sometimes there are false-negative results. Although bacterial cultures are considered the standard criterion for the diagnosis of sepsis, positive results may not always be obtained and results may be delayed by a minimum of 24 hours for aerobic organisms and up to 10 to 14 days for anaerobic organisms. Thus ancillary tests such as pH, glucose concentrations, and lactate dehydrogenase (LDH) activity in equine pleural and synovial fluid have been used to detect sepsis with the potential advantages of speed, ease of measurement, and lower cost relative to bacterial cultures.

Horses with septic peritonitis have significantly lower peritoneal fluid pH and glucose concentrations than horses with nonseptic peritonitis and healthy horses. Compared with other tests, serum-to-peritoneal fluid glucose concentration differences of more than 50 mg/dL had the highest diagnostic use for detection of septic peritonitis. A peritoneal fluid pH below 7.3, a glucose concentration below 30 mg/dL, and a fibrinogen concentration above 200 mg/dL were also highly indicative of septic peritonitis.

Peritonitis in Cattle

Tests for total protein, albumin, glucose, cholesterol, fibrinogen, L-lactate, D-dimer, LDH, alkaline phosphatase, creatine phosphokinase, white blood cells, and red blood cells are sometimes used to detect peritonitis in cattle. Peritoneal fluid D-dimer is most accurate in diagnosing peritonitis in cows (sensitivity and specificity >95.0% for concentrations <0.60 mg/L), LDH and LDH ratio in serum and peritoneal fluid, and the serum-ascites albumin concentration gradient have sensitivities between 49.0% and 67.1% and specificities between 88.4% and 95.5%.[21] A low-peritoneal fluid glucose concentration is highly indicative of septic peritonitis, as it is in horses.[21]

NECROPSY FINDINGS

In acute diffuse peritonitis, the entire peritoneum is involved, but the most severe lesions are usually in the ventral abdomen. Gross hemorrhage into the subserosa, exudation, and fibrin deposits in the peritoneal cavity and fresh adhesions that are easily broken down are present. In less acute cases, the exudate is purulent and may be less fluid, often forming a thick, cheesy covering over most of the viscera. In cattle, *F. necrophorum* and *Actinomyces (Corynebacterium) pyogenes* are often present in large numbers and produce a typical, nauseating odor. Acute local peritonitis and chronic peritonitis are not usually fatal, and the lesions are discovered only if the animal dies of intercurrent disease such as traumatic pericarditis or intestinal obstruction.

DIAGNOSIS

The diagnosis of peritonitis can be difficult because the predominant clinical findings are often common in other diseases. The clinical features that are the most reliable as indicators of peritonitis include the following:

- Abnormal feces, in amount and composition
- Alimentary tract stasis based on auscultation and evaluation of the passage of feces
- Abdominal pain evinced as a groan with each respiration or on light or deep percussion of the abdomen
- Abnormality of intestines on rectal palpation
- Fibrinous or fibrous adhesions on rectal palpation
- Abnormal peritoneal fluid with an increased leukocyte count collected by paracentesis
- A normal or low blood leukocyte count with a degenerative left shift
- The peritonitis may be chemical, and although microbiological examination usually yields positive results, these are not essential to a diagnosis of peritonitis

PROGNOSIS

Case–Fatality Rate in Horses

Peritonitis in the horse is a potentially life-threatening disease that must be treated promptly and aggressively.[1,22] Therapy must be aimed at reducing systemic shock and hypovolemia, correction of the primary cause, antibiotic therapy, and abdominal drainage and lavage. The case–fatality rates for peritonitis of any cause in horses range from 30% to 67%, although this includes cases with peritonitis secondary to colic, which have a worse prognosis than idiopathic cases or those caused by *A. equuli.* The case–fatality rate in horses with peritonitis not related to colic or rupture of the gastrointestinal tract is approximately 14%.[9] In a series of 67 cases of peritonitis in horses, of those that developed peritonitis after abdominal surgery, the case fatality was 56%. Peritonitis not associated with intestinal rupture or abdominal surgery had a lower case–fatality rate of 43%. Horses that died had higher heart rates, red blood cell count, serum creatinine concentration, PCV, and anion gap; lower venous blood pH; and a greater number of bacterial species cultured from the peritoneal fluid compared with survivors. Those that died were more likely to have clinical evidence of abdominal pain, shock, and bacteria in the peritoneal fluid.

TREATMENT

The specific cause must be treated in each case, and the treatments used are described under the specific diseases listed earlier. An exploratory laparotomy may be indicated to determine the cause of the peritonitis and to effect repair. The literature on the treatment of peritonitis in horses has been reviewed.

Antimicrobials

Broad-spectrum antimicrobials given intravenously or intramuscularly are indicated for the infection and toxemia. However, there are no published reports of clinical trials to evaluate the effectiveness of various antimicrobials for the treatment of peritonitis in cattle or horses. Thus the recommendations are empirical. Generally, **peritonitis in cattle** is commonly treated with any of the broad-spectrum antimicrobials, with the choice dependent on ease of administration and drug withdrawal times necessary in lactating dairy cattle. Treatment for traumatic reticuloperitonitis has commonly been restricted to the use of antimicrobials; supportive therapy has not been indicated with the exception of diffuse peritonitis.

Peritonitis in horses associated with abdominal surgery or rupture of the gastrointestinal tract is likely be accompanied by a mixed flora of bacteria, and broad-spectrum antimicrobials are necessary. They must be given at doses high enough to achieve high blood and tissue levels and maintained daily until recovery has occurred. In a series of cases of peritonitis in horses, the most commonly used antimicrobials were gentamicin at 2.2 to 3.3 mg/kg BW intravenously every 8 to 12 hours or 6.6 mg/kg BW intravenously every 24 hours, and penicillin at 22000 IU/kg BW intravenously or intramuscularly every 6 to 12 hours. Metronidazole given orally at 15 to 25 mg/kg BW has also been used in horses with peritonitis.

Horses with peritonitis associated with *A. equuli* respond quickly to treatment with penicillin at 22,000 units/kg BW intramuscularly twice daily for 5 days to 2 weeks. Most isolates of the organism are sensitive to penicillin, but some are resistant and gentamicin sulfate at 6.6 mg/kg BW intravenously once daily for 5 days to 2 weeks in combination with the penicillin has also been used successfully. In a series of 51 cases in horses, the recovery rate following treatment with penicillin and gentamicin and supportive therapy was 100%. Most horses responded favorably within 48 hours following commencement of treatment.

Administration of antimicrobials into the peritoneal cavity has been attempted on the basis that higher levels of the drug may be achieved at the site of the inflammation. However, there is no scientific evidence that it is superior to daily parenteral administration, and there is some danger of causing adhesions and subsequent intestinal obstruction.

Fluid and Electrolytes

Intensive intravenous fluid and electrolyte therapy are a vital part of treatment of peritonitis when accompanied by severe toxemia and shock, especially during the first 24 to 72 hours following abdominal surgery in the horse. It is continued until recovery is apparent and the animal is drinking water voluntarily; water can then be supplemented with electrolytes (see Chapter 5).

Nonsteroidal Antiinflammatory Drugs

Flunixin meglumine is recommended at 0.25 to 1.1 mg/kg BW intravenously every 8 to 12 hours when the peritonitis is accompanied by shock. However, no information is available on efficacy.

Lavage

Peritoneal lavage with large volumes of fluid containing antimicrobials is rational and has been attempted when large quantities of exudate are present. However, it is not easy to maintain the patency of drains, especially in cattle. Also, the peritoneum is highly susceptible to inflammation, and chemical peritonitis is common following the introduction of certain materials into the peritoneal cavity. Peritoneal lavage of ponies with saline and antimicrobials induces a mild, transient inflammatory response with minimal change visible at necropsy. Solutions containing povidone iodine-induced chemical peritonitis, which was severe when 10% povidone iodine solution was used. A 3% solution also causes peritonitis, and the use of these solutions is not recommended. Extreme caution is required when foreign materials are introduced into the cavity to avoid exacerbating the existing inflammation. The peritoneum is also a very vascular organ and toxic material is rapidly absorbed from it.

An **active intraabdominal drain** has been used successfully to treat abdominal contamination in horses. Closed-suction abdominal drains were placed, mostly under general anesthesia. Abdominal lavage was done every 4 to 12 hours, and about 83% of the peritoneal lavage solution was retrieved.

Prevention of Adhesions

Attempts can be made to prevent the development of adhesions but the efficacy has not been demonstrated.

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Abdominal Diseases of the Horse Including Colic and Diarrhea

GENERAL PRINCIPLES

Abdominal pain in horses, evident as a constellation of clinical and behavioral signs

Table 7-9 Origin and examples of visceral pain in the horse

Origin	Example: acute	Example: chronic
Thorax		
Lung	Pleuropneumonia	Pleural abscessation
Pleura	Choke	Neoplasia
Esophagus	Trauma	Pericarditis
Heart	Pericarditis	
Abdomen		
Stomach	Most causes of acute colic	Inflammatory bowel diseases
Small intestine	Pancreatitis	Enterolithiasis
Large intestine	Nephrolithiasis	Chronic diarrhea
Cecum	Uterine artery hematoma, rupture	Nephrolithiasis
Large colon	Metritis	Neoplasia
Small colon	Cholelithiasis	Cholelithiasis
Spleen	Uterine torsion	
Liver		
Pancreas		
Kidneys		
Ureters		
Ovaries		
Uterus		
Pelvis		
Bladder	Cystitis	Cystitis
Testicles	Urolithiasis	Urolithiasis
Rectum	Rectal tear	Neoplasia
Anus	Foaling trauma	
Vagina	Necrotic vaginitis	

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are often referred to as having "spasmodic colic," and this is the most common diagnosis at the primary presentation of horses with colic (24%–35%).[3] Large-colon impaction (20%) and undiagnosed (13%–25%) are the other largest diagnostic categories.[1,3]

SYNOPSIS

Etiology See Tables 7-9 to 7-11 and 7-13.

Epidemiology Incidence of 2 to 30 cases per 100 horse-years, mortality of 0.5 to 0.7 cases per 100 horse-years, and case–fatality rate of 7% to 13%. Any age predisposition is weak, although certain diseases (e.g., meconium impaction, strangulation by pedunculated lipoma) have specific age distributions. Consumption of a diet high in concentrate increases the risk of colic, as does a poor parasite control program.

Clinical signs Signs of abdominal pain include agitation, flank watching, flank biting, pawing, frequent lying down, kicking at the abdomen, frequent attempts to urinate or defecate, and rolling. Tachycardia is common. Normal gut sounds are absent and replaced by tympanitic sounds. Abdominal distension may develop. Reflux through a nasogastric tube may occur. Rectal examination may reveal abnormalities.

Clinical pathology Few changes have diagnostic significance but many are used to monitor the severity of the disease. Hemoconcentration, azotemia, and metabolic acidosis are frequent findings. Peritoneal fluid may have increased protein **and leukocyte concentration.**

Lesions Consistent with the particular disease.

Diagnostic confirmation Physical examination, exploratory laparotomy, necropsy.

Treatment Analgesia (Table 7-15), correction of fluid, acid-base and electrolyte abnormalities (Chapter 5), gastric decompression via nasogastric intubation, administration of fecal softeners or lubricants (Table 7-16), surgical correction of the lesion.

Control Parasite control. Ensure adequate roughage in the diet.

described next, is commonly referred to as colic. Colic is most often caused by gastrointestinal disease, although it can manifest as a result of disease in any intraabdominal organ (Table 7-9). The discussion in this section deals with colic caused by gastrointestinal disease, which is a frequent and important cause of death and is considered the most important disease of horses encountered by practicing veterinarians. It is estimated to cost the horse industry in the United States approximately $115,000,000 annually.[1]

ETIOLOGY

Several classification systems of equine colic have been described including a disease-based system (Table 7-10) classifying the cause of colic as

- **Obstructive, nonstrangulating:** Aboral movement of ingesta and secretions is prevented or hindered by luminal or extraluminal obstructions without a physiologically important reduction in blood flow to the gastrointestinal tract during the early stages of the disease (e.g., impaction of the large colon). Distension of the stomach or intestines can reduce blood flow in later stages of the disease.

- **Obstructive and strangulating:** Obstruction of aboral movement of ingesta and secretions with impairment of blood flow caused by mechanical compression of the vessels (arterial, venous, or both). Both the obstruction and impairment of blood flow occur at the same time (e.g., small-intestinal volvulus).
- **Nonstrangulating infarctive:** Reduction in nutritive blood supply (infarction) that is not attributable to mechanical compression of the vessels (e.g., thromboembolic colic).
- **Inflammatory** (peritonitis, enteritis): Inflammation of the stomach, intestines, or parietal and visceral peritoneum (e.g., colitis, peritonitis).

Colic cases can also be classified on the basis of the duration of the disease: **acute** (<24–36 hours), **chronic** (>24–36 hours), and **recurrent** (multiple episodes separated by periods of >2 days of normality). Another classification system is anatomically based and is listed in Table 7-11.

Regardless of the classification system used, some estimates are that fewer than >25% of colic cases seen in the field do not have a definitive diagnosis.[3] Horses with acute transient colic relieved by analgesics

EPIDEMIOLOGY

Most studies of the epidemiology of colic do not provide details of specific diseases; instead they consider colic as one disease. This inclusion of many diseases into one category, wile maximizing the statistical power of the studies, is unfortunate because it can obscure important details regarding the occurrence and risk factors of individual diseases. Furthermore, much of the information related to incidence, treatments, and outcome of horses with colic is derived from studies of horses examined at referral centers. Horses examined at these centers are in all

Table 7-10 Etiological classification of equine colic

Type of colic	Etiology	Lesion	Typical clinical signs	Diagnosis
Simple obstruction (not infarctive)	Luminal obstruction	Impaction of stomach, ileum or large intestine with dry ingesta Concretion-type body, e.g., fecalith, meconium, phytobezoar, enterolith, foreign body, sand colic, congenital atresia	Mild to moderate pain, heart rate mildly increased initially, moderate dehydration Mild to moderate pain, moderate dehydration	Usually subacute course Diagnosis on rectal exam or imaging; exploratory celiotomy Subacute to acute course Diagnosis on rectal exam or imaging; exploratory celiotomy
	Mural blockage	Hematoma, neoplasm, idiopathic muscular hypertrophy	Pain, moderate dehydration	Rectal exam, reflux through nasogastric tube; exploratory celiotomy
	Extramural blockage	Large colon displacement	Mild to moderate pain, mild dehydration, abdominal distension	Rectal exam; exploratory celiotomy
	Functional	Spasm (spasmodic colic) Paralytic ileus Gastric reflux (acute gastric dilatation, gastric ulcer, anterior enteritis)	Moderate to severe pain, moderate to severe signs of hypovolemia	Rectal exam, gut sounds, nasogastric intubation, ultrasonographic examination
Inflammation (irritation of peritoneal pain receptors)	Infectious (e.g., *Salmonella* spp., *Actinobacillus equuli*), chemical irritation (urine, ingesta)	Peritonitis Enteritis	Mild pain, fever, toxemia, tachycardia, hypovolemia	Leukocytosis, abdominal paracentesis, diarrhea
Simple infarction (no obstruction)	Infarction; ischemia	Thromboembolic colic (verminous arteritis), arterial occlusion (pedunculated lipoma around mesentery), detachment of mesentery (traumatic or congenital)	Mild to severe pain, toxemia Possibly blood loss	Abdominal paracentesis, total white cell count; exploratory celiotomy
Obstruction plus infarction	Intestinal accidents	Intussusception Torsion Strangulation (epiploic foramen, diaphragmatic, inguinal hernias, mesenteric tear or congenital defect, pedunculated lipoma)	Intractable pain followed by profound depression, toxemia, severe tachycardia, hypovolemia	Rectal exam; abdominal paracentesis, packed cell volume, total white cell count, nasogastric intubation, ultrasonographic examination

Table 7-11 Disorders of the equine gastrointestinal tract causing colic, by anatomical site

SITE	DISORDER

Stomach	Gastric dilatation
	    Primary
	    Secondary to outflow obstruction, pyloric stenosis, ileus, or anterior enteritis

	Gastric impaction
	Gastroduodenal ulceration
Small intestine	Volvulus

	Intussusception
	    Ileocecal
	    Jejunojejunal

	Infarction or ischemia
	    Thromboembolic disease
	    Disruption of blood supply by mesenteric tear

	Strangulation, including entrapment through the epiploic foramen, mesenteric rents (including cecocolic fold, splenic ligament, uterine ligaments, spermatic cord), Meckel's diverticulum and hernias (diaphragmatic, inguinal/scrotal, umbilical)
	Strangulation by pedunculated lipoma

	Luminal obstruction
	    Foreign bodies
	    Ascarids

	Luminal compression
	    Lipomas
	    Intramural masses such as *Pythium* spp. and neoplasms (adenocarcinoma, lymphoma, eosinophilic enteritis)

	Adhesions
	Enteritis

Table 7-11 Disorders of the equine gastrointestinal tract causing colic, by anatomical site—cont'd

SITE	DISORDER
Cecum	Impaction
	Rupture and perforation
	Intussusception Cecocolic Cecocecal
	Cecal torsion
	Infarction (thromboembolic disease, necrotizing enterocolitis)
	Typhlitis
	Tympany
Ascending (large) colon	Impaction
	Intestinal tympany
	Volvulus
	Displacement, including left dorsal (renosplenic or nephrosplenic), right dorsal, cranial displacement of pelvic flexure
	Infarction (verminous mesenteric arteritis, necrotizing enterocolitis)
	Luminal obstruction Sand accumulation Enterolith
	Right dorsal ulcerative colitis
	Colitis
	Necrotizing enterocolitis
Descending (small) colon	Impaction
	Luminal obstruction Fecalith Enterolith
	Luminal compression Pedunculated lipoma Intramural hematoma Perirectal abscess Perirectal tumor (melanoma)
	Avulsion of mesocolon and rectal prolapse in mares at parturition
	Strangulation

likelihood not representative of horses with colic that are not referred for examination by specialists. Details of the epidemiology of specific etiologic entities are included under those headings. Only general principles are included here.

Occurrence

Equine colic occurs worldwide, although there are regional differences in the types of colic (for example, enterolithiasis), and is a common and important disease of horses. For cases of equine colic recognized in the field, as distinct from those referred for specialized treatment, the **incidence** rate ranges between 3.5 and 10.6 cases per 100 horse years, although individual farms can have rates as high as 30 or more cases per 100 horse years. Owners of horses in the UK report annual prevalence of colic, as a proportion of all health concerns, of 2.1% to 5.6%.[4] These estimates are self-reported by owners and are not based on systematic reporting or collection of data. Estimates using a population of insured horses in Japan

identified an annual incidence rate for colic of 18.6% (of ~45,000 horses).[5] **Mortality** from colic is estimated to be between 0.5 and 0.7 deaths per 100 horse years in the United States and 0.7% in Japan, representing 28% of overall horse deaths (2.5 deaths per 100 horse years) in both populations.[1,5] The **case–fatality rate** is 6% to 13% of field cases, although a lower rate of 3.6% is reported for insured horses in Japan.[5] Approximately 1% to 2% of colic events in the United States and the British Isles result in surgery. It should be borne in mind that these estimates of incidence and mortality are highly influenced by the population of horses studied and can be biased or unduly influenced by inclusion of farms or groups of horses with an extremely high, or low, incidence of colic.

Risk Factors

Risk factors for colic can be categorized as (1) intrinsic horse characteristics, (2) those associated with feeding practices, (3) management, (4) medical history, (5) parasite control, and (6) season.[6]

Horse Characteristics

Age

There are conflicting results of studies that examine the association of colic and age. The conflicting results might be the result of varying study populations, study design, presence of varying confounding factors, and interpretation of data. Confounding factors are those that alter with the age of the horse, such as use, feeding, and management of horses, and mask an effect of age or give the impression of an effect of age when in fact such an effect is not present. Horses 2 to 10 years of age are 2.8 times more likely to develop colic that horses less than 2 years. One large-scale study reported that foals less than 6 months of age had an incidence of 0.2 cases of colic per 100 horses per year, whereas horses more than 6 months of age had an incidence of approximately 4 to 6 colic-affected horses per 100 horse years, with the incidence varying to a limited extent among older age groups. The mortality rate varies widely among insured horses in Japan, with a much higher incidence of death from colic

in older horses: 9% in horses >21 years of age compared with 1.5% in foals and yearlings.[5] Other studies have not found a similar effect of age. However, each age group has a particular set of diseases unique or common to it. Newborn foals can have congenital colon or anal atresia or meconium impaction (see the section Colic in Foals), diseases that do not affect older horses, whereas strangulating or obstructive lesions caused by pedunculated lipomas are found only in older horses.

Sex

There is no overall effect of gender on risk of colic, but certain diseases are restricted by gender. For instance, inguinal hernias occur only in males, whereas entrapment of intestine in the mesometrium is restricted to mares. Mares that have had a foal are at increased risk of developing volvulus of the large colon (adjusted OR of 12.9, 95% confidence interval [CI] 3.2–52).[7]

Breed

There is a generally consistent, although not universal, finding that Arabian horses are at increased risk of colic, but the reason for this apparently greater risk has not been determined. Thoroughbreds are reported to be at increased risk of colic, independent of their use.

Diet and Feeding Practices

Horses on pasture are at a lower risk of developing colic than are **stabled horses** fed concentrate feeds. The risk of colic increases with the amount of concentrate fed,[8] such that a horse fed 5 kg of concentrated feed per day has six times as great a risk of developing colic as a horse not fed concentrate.[1] However, another report did not detect an effect of diet composition on risk of colic. Changes to the horse's diet through changes in quantity and quality of feed, feeding frequency, or time of feeding increase the risk of colic by two to five times.

Management
Watering

Horses without constant **access to water** are at increased risk of developing colic,[8] whereas horses with access to ponds or dams have a reduced risk of colic compared with horses provided with water from buckets or troughs. This might represent a confounding effect of pasturing, in that horses with access to dams are probably on pasture and benefit from the lower risk of colic associated with that management practice. Alternatively, horses provided with water from buckets could be at greater risk of having periods when water is not available.

Housing

Increased duration of stabling per day is associated with an increased risk of colic.

Horses cared for by their owner and horses in stables with large numbers of horses are less likely to develop colic. Horses with more than three carers are at greater risk of developing large-colon volvulus.[7]

Exercise

Overall, there appears to be an increased risk of colic among horses undertaking physical activity or that have a recent change in the amount of physical activity. However, the finding of this association should be considered in the context of other differences that exist between active and inactive horses, such as in feeding practices, housing (stabling versus pasture), and transportation. Increased stabling is associated with an increased risk of large-colon volvulus (5.5, 95% CI 1.03–29).[7]

Colic during the hours after endurance racing occurs in approximately 1.6% (47 of 2832) of horses with small-intestinal volvulus common (13 of 15 horses) among those horses requiring surgery.[9] Most horses with colic associated with endurance racing do not require surgical exploration of the abdomen or correction of abnormalities.[10] The etiology is unclear but could be associated with an exercise-induced reduction in intestinal blood flow.

Colic associated with swimming is an important cause of colic in Thoroughbred horses in training with a 3-year incidence rate of 0.08%.[11] Over a 3-year period, 38% (136) of 361 colic cases were associated with swimming, of which 131 resolved spontaneously or with medical care.[11]

Season and Weather

There appears to be a seasonal distribution or pattern to some types of colic both in the field and in those examined at a referral hospital, with epiploic foramen entrapment, large-colon impaction and/or torsion, and medical colic having an apparent seasonal distribution.[5,12] There were increases in incidence of colic in early spring and autumn in the UK and increases in cases of acute abdomen during the summer in horses in Japan.[5,12] The seasonal pattern might represent changes in management and use of horses rather than a direct effect of weather. Despite the widespread belief that colic is associated with changes in weather, particularly thunderstorms, there is no conclusive evidence of such an association.

Medical History

Horses with a history of colic are more likely to have another episode, and horses that have had colic surgery are approximately five times more likely to have another episode of colic than are horses that have not had colic. There is no association between dental care and incidence of colic, although horses that "quid" (drop partially masticated food when eating) are at increased (7.8, 95% CI 1.8–33) risk of large-colon volvulus,[7] or

recent vaccination and colic. Horses with a history of **crib biting or wind sucking** are at markedly increased risk of developing colic (~2-fold risk) and more specifically epiploic entrapment of the small intestine (adjusted OR 72, 95% CI 14–359).[6,13] A history of colic in the past 12 months (5.1, 95% CI 1.4–18.9), increased stabling in the past 4 weeks (3.7, 95% CI 1.4–9.7), and increased height (1.07, 95% CI 1.01–1.12 per cm) are also being significantly associated with increased risk of colic caused by epiploic entrapment.[6] Similarly, horses that have had colic in the previous 12 months are at increased risk of a large-colon volvulus (adjusted OR of 8.7, 95% CI 1.8–43).[7]

Hospitalized horses are at increased risk of developing colic (see the section Cecal Impaction) and among horses hospitalized for treatment of ocular disease 21% developed signs of colic with 14% of those horses having a cecal impaction.[14] Duration of hospitalization (>8 days) was a strong risk factor for colic.[14]

Parasite Control

Inadequate parasite control programs have been estimated to put horses at two to nine times greater risk of developing colic, although other studies have not demonstrated a relationship between anthelmintic administration and colic. The presence of tapeworms (assessed by examination of feces) is associated with a three times greater risk of ileal impaction and 16 times increased risk of colic[15] likely because *A. perfoliata* infestation causes lesions at the ileocecal junction of horses.[16] The detection of exposure to *A. perfoliata* by detecting specific antibodies in the blood is either not associated, or weakly associated, with the risk of colic.[15,17]

Infestation by roundworms (*Parascaris equorum*) is associated with severe colic in young horses as a result of impaction or obstruction of the small intestine.[18] Approximately 75% of the affected horses had been administered anthelmintics in the previous 24 hours, suggesting that death or paralysis of a large burden of ascarids resulted in obstruction of the lumen of the small intestine by the dead or dying parasites.

There is an increased incidence of colic in horses on farms on which rotation of anthelmintics is practiced. This apparently paradoxical finding may be because farms with a higher incidence of colic are more likely to alter rotation of anthelmintics as a result of having more horses with colic. The apparently conflicting results of some of the epidemiologic studies should not deter veterinarians from recommending effective parasite control programs for horses, given the clear association at an individual level of the presence of tapeworms, cyathostomes, and/or large strongyles and ileocecal disease, diarrhea and ill-thrift, and verminous arteritis, respectively.

Importance

Losses caused by colic in horses are due almost entirely to death of the patient. However, the cost of treatment and the emotional trauma to the owners of their horse being afflicted with a potentially fatal disease are important considerations. A 1989 survey of veterinarians in the United States rated colic the most serious medical disease in horses, ahead of viral respiratory disease, and recent studies estimated the cost of colic to the horse industry in the United States at $115,000,000 annually.

PATHOGENESIS

The pathogenesis of equine colic is variable depending on the cause and severity of the inciting disease. A horse with a strangulating lesion involving 50% of its small intestine has a much more rapidly evolving disease, with severe abnormalities, than does a horse affected with mild spasmodic colic or impaction of the pelvic flexure of the large colon. Although equine colic often involves changes in many body systems, notably the gastrointestinal, cardiovascular, metabolic, and endocrine systems, there are several features and mechanisms that are common to most causes of colic that depend only on the severity of the disease for the magnitude of their change. The features common to severe colic, and often present to a lesser degree in milder colic, are pain, gastrointestinal dysfunction, intestinal ischemia, endotoxemia or toxemia, compromised cardiovascular function (shock), and metabolic abnormalities.

Pain

Pain is the **hallmark of gastrointestinal disease** in horses and is attributable to distension of the gastrointestinal tract and stimulation of stretch receptors in the bowel wall and mesentery; stretching of mesentery by displaced or entrapped bowel; and inflammation and irritation of the bowel, peritoneum, or mesentery. Methods for objectively assessing and scoring pain in horses have been developed but as yet have not been rigorously tested and validated in large numbers of horses in varying situations.[19-21] Scoring systems that provide a composite score, and for which there is good interrater and intrarater agreement, have usefulness in developing prognostic criteria, for monitoring response to treatment, and for determining the need and efficacy of analgesia/hypalgesia.

The **intensity of the pain** is often, but not always, related to the severity of the inciting disease. Horses with mild impaction of the large colon of short duration (<24 hours) often have very mild pain, whereas a horse with a strangulating lesion of the small intestine will have very severe pain. Horses that recovered from gastrointestinal tract surgery (colic surgery) had lower pain scores after surgery than did horses that did not survive.[19]

Gastrointestinal pain has an inhibitory effect on normal gastrointestinal function, causing a feedback loop in which the pain inhibits normal gut motility and function, allowing accumulation of ingesta and fluid, resulting in distension and further pain. Horses can respond very violently to abdominal pain and may injure themselves when rolling or thrashing.

Gastrointestinal Dysfunction

Colic is almost invariably associated with impaired gastrointestinal function, usually alterations to **motility** or **absorptive** function. Gastrointestinal motility may be increased, as is presumed to be the case in spasmodic colic, altered in its character or coordination, as in some cases of impaction colic, or absent, such as in ileus secondary to inflammation or ischemia of the bowel or to the presence of endotoxemia. Increased or uncoordinated gastrointestinal motility probably causes pain through excessive contraction of individual segments of bowel or distension of bowel because of the loss of normal propulsive activity. **Ileus** is associated with fluid distension of the small intestine and stomach and fluid and gas distension of the large colon, both of which cause severe pain and can lead to gastric or colonic rupture. The absorptive function of the intestine may be decreased by inflammation or ischemia, which results in distension of the small intestine or large colon, pain, and potentially rupture of the stomach or colon.

Impairment of the **barrier function** of the gastrointestinal mucosa by inflammation or ischemia can result in leakage of endotoxin and other toxic compounds into peritoneal fluid with subsequent endotoxemia, toxemia, and systemic inflammatory response syndrome (see the section Endotoxemia).

Ischemia of the Intestinal Wall

Ultimately, most forms of lethal colic involve some degree of ischemia of the intestine, with subsequent loss of barrier function, evident in its most extreme form as rupture of the viscus, endotoxemia, bacteremia, cardiovascular collapse, and death. Ischemia may be the result of impaired blood flow to or from the intestine because of torsion or volvulus of the intestine, entrapment of the intestine and associated mesentery in rents or hernias, strangulation such as by a pedunculated lipoma, or thromboembolic disease. Ischemia may also result from severe gastrointestinal distension, such as occurs in the terminal stage of severe colon impaction. Mild ischemia probably impairs normal intestinal motility and function. The role of reperfusion injury in pathogenesis of ischemic disease is uncertain at this time.

Endotoxemia

Death in fatal cases of colic in which the affected viscus ruptures secondary to distension, or when ischemia and/or infarction damages a segment of bowel wall, is caused by the absorption of endotoxins and other compounds from the gut lumen into the systemic circulation (see the section Endotoxemia). Endotoxin absorption causes increased concentrations of tumor necrosis factor and interleukin (IL)-6 in peritoneal fluid and blood concentrations.

Rupture of the stomach or intestine is also a characteristic termination of distension of the intestine in the horse. The resulting deposition of large quantities of highly toxic ingesta or fecal contents into the peritoneal cavity causes profound shock and death within a few hours.

Shock

The usual cause of death in severe colic is cardiovascular collapse secondary to endotoxemia/toxemia and hypovolemia. In less severe colic, hypovolemia and cardiovascular dysfunction may contribute to the development of the disease, and rapid correction of hypovolemia is central to the effective treatment of colic.

Hypovolemia is caused by the loss of fluid and electrolytes into the lumen of the gastrointestinal tract or loss of protein from the vascular space with subsequent reduction in the circulating blood volume. Hypovolemia impairs venous return to the heart and therefore cardiac output, arterial blood pressure, and oxygen delivery to tissues. Not surprisingly, measures of circulatory status are good predictors of the outcome of colic (see the section Prognosis).

Cardiorespiratory function is impaired if there is severe distension of gut, such as in large-colon torsion, because of restricted respiration by pressure on the diaphragm and reduced venous return to the heart because of pressure on the caudal vena cava. Cardiac function is impaired in some horses with colic, as indicated by the high incidence of arrhythmias, elevated serum concentrations of troponin, and abnormal contractile function detected by echocardiographic examination.[22-25] The reduction in myocardial function is most evident as an increase in the ratio of preejection time to ejection time for the left ventricle.[24]

Coagulation and Fibrinolysis

Severe colic, especially that involving ischemia or necrosis of intestine, is associated with abnormalities in coagulation and fibrinolysis characterized by hypercoagulation or hypocoagulation of blood and abnormal fibrinolysis.[26-28] The particular abnormalities present at a point in time depend on the severity of disease and its duration. Initial increases in coagulability or fibrinolysis can progress to hypocoagulable and hypofibrinolytic states as the severity of the disease increases.[28]

Disseminated intravascular coagulation is common among horses with ischemia or necrosis of the gut and is a good prognostic indicator of survival.[26,27] Changes in coagulation and fibrinolysis include decreases in

antithrombin activity and fibrinogen concentration and increases in prothrombin time, activated partial thromboplastin time, and concentration of thrombin–antithrombin complexes in plasma.[27,29] Dynamic measures of clotting function or fibrinolysis also reveal that hypocoagulation, indicated by abnormalities in one or more measures by thromboelastography, is indicative of a poor prognosis.[27] However, changes in these variables do not always correlate well with more dynamic measures of clotting function, such as thromboelastography.[27,29]

Overview of the Pathogenesis of Common Colics

Simple Obstructive

Simple obstructive colics are those in which there is obstruction to the aboral passage of ingesta but no ischemia or strangulation of bowel. In the terminal stages there is often ischemia caused by distension of the intestine.

Small-intestinal obstructive lesions include ileal hypertrophy, ileocecal intussusception, and foreign-body obstruction of the lumen. The course of the disease is often 24 to 72 hours, and sometimes longer depending on the extent of the obstruction, and partial obstructions have much less severe signs and disease of longer duration. The principal abnormality is reduced aboral flow of ingesta, with subsequent distension of intestine cranial to the obstruction, causing pain and, if the distension is severe, gastric rupture.

Large-intestinal obstructive lesions include impaction and simple (nonstrangulating) displacements of the large colon. The course of disease is prolonged, often more than 72 hours. Signs of abdominal pain are caused by distension of the bowel. There is progressive distension with fluid and gas and ultimately ischemia of the bowel and rupture.

Obstructive and Strangulating

Diseases that cause both obstruction and strangulation as an initial event, such as torsion of the small intestine or volvulus of the large colon, result in severe and unrelenting pain that is difficult to relieve with analgesics. Obstruction causes distension and strangulation causes ischemia, loss of barrier function, and endotoxemia. These diseases have a short course, usually less than 24 hours and sometimes as short as 6 hours, and profound clinical signs. Endotoxemia/toxemia, systemic inflammation, and cardiovascular collapse are characteristic of these diseases.

Infarctive

Infarctive diseases, such as thromboembolic colic, are characterized by ischemia of the intestinal wall with subsequent alterations in motility and absorptive and barrier functions. Ileus causes distension of the intestines

Behavior	Score
Depression	1
Flank watching Weight shifting	2
Restlessness Kicking abdomen Pawing Stretching Sternal recumbency	3
Attempting to lie down Lateral recumbency	4
Rolling Collapse	5

Table 7-12 Criteria for evaluation of pain in horses[30]

and stomach and altered barrier function causes endotoxemia. The course of the disease is usually less than 48 hours and is terminated by cardiovascular collapse and death.

Inflammatory

Inflammation of the intestine or peritoneum alters gastrointestinal motility and absorptive function leading to accumulation of fluid and ingesta, distension, and abdominal pain.

CLINICAL FINDINGS

The bulk of the following description is generally applicable to severe acute colic. Clinical findings characteristic of each etiologic type of colic are dealt with under their individual headings. The purposes of the clinical examination are **diagnostic**—to determine whether the pain is caused gastrointestinal tract disease and, if so, to determine the nature of the lesion—and **prognostic**—to provide some estimate of the likely outcome of the disease. Veterinary clinicians are able to accurately predict the site of lesions (small intestine versus large intestine), type of lesion (simple obstructive versus strangulating or infarctive), and outcome. The ability to predict these events increases with training and experience.

Accurate diagnosis of the cause of the colic has some prognostic usefulness, but assessment of the horse's physiologic state by measurement of heart and respiratory rates, mucous membrane color and refill time, arterial blood pressure, hematocrit and serum total protein concentration, as well as other measures, allows more accurate prognostication. Furthermore, the cause of colic is determined in only approximately 20% of field cases.

Visual Examination

Behavior

Pain is manifested by **pawing, stamping, or kicking** at the belly or by restlessness evident as pacing in small circles and repeatedly getting up and lying down, often with exaggerated care. Methodology for identifying and rating pain has been validated for horses and has high intraobserver ($\kappa = 0.9$) and interobserver (intraclass correlation coefficient 0.8) values indicating the repeatability of the assessments either by the same observer or by different observers. The pain scale also has good sensitivity and specificity for outcome (lived versus died, 70% and 71%) and treatment (medical, surgical, euthanasia, 70% and 57%)[30] (Table 7-12).

Other signs are looking or nipping at the flank, **rolling**, and lying on the back. Often the penis is protruded without urinating or with frequent urination of small volumes. Continuous playing with water without actually drinking (sham drinking) is common.

Pain may be continuous or, more commonly, intermittent with bouts of pain lasting as long as 10 minutes interspersed with similar periods of relaxation. Generally, the intensity of the pain is of about the same severity for the duration of the illness; sudden exacerbations may indicate a change in the disease status or the development of another abnormality, such as a horse with impaction of the large colon developing a displacement of the colon or horses with diarrhea developing necrotizing enteritis. Horses in the terminal phase of the disease may have a marked diminution of pain associated with relief of pressure after rupture of distended bowel and depression caused by toxemia and shock. Pain responses in colic can be so severe, and uncontrolled movements so violent, that the horse might do

itself serious injury. Other causes of pain, such as pleuritis or rhabdomyositis, can be confused with colic, although a horse that goes down and rolls almost certainly has alimentary tract colic.

Posture

The posture is often abnormal, with the horse standing stretched out with the forefeet more cranial and the hindfeet more caudal than normal or the so-called "sawhorse" stance. Some horses lie down on their backs with their legs in the air, suggesting a need to relieve tension on the mesentery.

Abdomen Size

Distension of the abdomen is an uncommon but important diagnostic sign. **Symmetric, severe distension** is usually caused by distension of the colon, sometimes including the cecum, secondary to colon torsion, or impaction of the large or small colon and subsequent fluid and gas accumulation. If only the cecum is distended the abdomen can show an **asymmetric enlargement** in the right sublumbar fossa. Maximum distension of stomach or small intestines does not cause appreciable distension of the abdomen.

Vomiting

Projectile vomiting or regurgitation of intestinal contents through the nose is very unusual in horses and is a serious sign suggesting severe gastric distension and impending rupture.

Defecation and Feces

Defecation patterns can be misleading. It is often mistakenly assumed that there is no complete obstruction because feces are still being passed, but in the very early stages of acute intestinal obstruction there can be normal feces in the rectum, and the animal might defecate several times before the more usual sign of an empty rectum with a sticky mucosa is observed.

Physical Examination
Heart and Respiratory Rates

The **heart rate** is a useful indicator of the severity of the disease and its progression but has little diagnostic usefulness. Horses with heart rates less than 40 beats/min usually have mild disease, whereas horses with heart rates above 120 beats/min are usually in the terminal stages of severe disease. Horses with obstructive, nonstrangulating disease often have heart rates between 40 and 60 beats/min, whereas horses with strangulating disease or necrotic bowel will usually have heart rates over 80 beats/min. However, heart rate is not an infallible indicator of disease severity, as horses with torsion of the colon can have heart rates of 40 to 50 beats/min.

The **respiratory rate** is variable and can be as high as 80 beats/min during periods of severe pain.

Mucous Membranes and Extremities

Mucous membranes of normal horses and of horses without significantly impaired cardiovascular function are pink, moist, and regain their normal color within 2 seconds after firm digital pressure is removed. Dehydrated horses have dry mucous membranes, although the capillary refill time and color are normal. Horses with impaired cardiovascular function have pale, dry mucous membranes with delayed capillary refill (>2 seconds). Endotoxemic horses will often have bright red mucous membranes with normal or delayed capillary refill. As the disease becomes more severe the mucous membranes develop a bluish tint and capillary refill is longer than 3 seconds. **Terminal** stages of disease are associated with cold, purple, dry mucous membranes with a capillary refill time of more than 3 seconds; necrosis of the mucosa of the gingival margins of the gums, the so-called "toxic line," is often seen.

Cool extremities can be indicative of compromised cardiovascular function but should be interpreted with caution and only in the context of the rest of the clinical examination. **Sweating** is common in horses with severe abdominal pain and, when present in a horse with cool extremities and signs of cardiovascular collapse, is indicative of a poor prognosis.

Auscultation and Percussion

Auscultation of the abdomen can provide useful diagnostic and prognostic information and should be performed thoroughly and without haste. All four quadrants (dorsal and ventral, left and right sides) of the abdomen should be examined for at least 1 minute at each site. Attention should be paid to the intensity, frequency, and characteristics of the spontaneous gut sounds (borborygmi). Repeated observations are often necessary to detect intermittent or rapid changes in the character of the borborygmi.

Continuous, loud borborygmi distributed in all or most quadrants are indicative of intestinal hypermotility and consistent with spasmodic colic, impending diarrhea, or the very early stages of a small-intestinal obstructive/strangulating lesion. The **absence of sounds**, or the presence of occasional high-pitched, brief sounds, sometimes with a splashing character, is consistent with ileus. These sounds should not be mistaken for the rolling, prolonged sounds of normal peristalsis.

Combined percussion and auscultation is a valuable procedure for defining the presence of extensive gas caps; a flick or abrupt tap with a finger while auscultating with a stethoscope will elicit a **pinging** sound similar to that made by flicking an inflated balloon. The detection of such sounds indicates the presence of tightly gas-distended bowel near the body wall. Such bowel is almost always large colon or cecum and is consistent with gas distension secondary to ileus, small or large-colon impaction, gas colic, or colon displacement, including torsion.

Rectal Examination

A careful rectal examination is probably the most important part of the clinical examination in colic and should not be neglected. The examiner must know the anatomy of the posterior abdomen to make reasonably accurate decisions about the location of various organs. Recognition that an important abnormality exists is a critical factor in the decision to refer the horse for specialized evaluation and care.

Normal Anatomy

The horse should be restrained so that the examination can be performed with minimal risk to both the examiner and patient. Fractious or horses in pain should be tranquilized. A twitch should be applied to all but the most cooperative horses to minimize straining and the chance of kicking. Rectal examination in small or unruly horses should be approached with caution.

Only approximately 40% of the abdomen can be examined in a mature horse, because the cranial and ventral structures are outside the reach of the examiner. In the normal 425-kg (1000-lb) horse there should not be any distended intestine and the small intestine should not be palpable. The **cecum** is readily palpable in the right caudal abdomen, with its ventral band running from the dorsal right quadrant ventrally and slightly to the left. The base of the cecum may be palpable as a soft, compressible structure containing fluid and gas. The caudal border of the **spleen** is readily palpable as it lies on the left side of the abdomen against the body wall. There should be no bowel between the spleen and the body wall, although occasionally the small colon can be detected dorsal to the spleen. Dorsal and medial to the spleen, the **left kidney** should be readily palpable, as should the **nephrosplenic ligament** and **space**. There should be no bowel in the nephrosplenic space, although some horses have portions of small colon in the region of the nephrosplenic space. Portions of **large colon**, especially the pelvic flexure, can be palpated in the caudal ventral abdomen if they contain ingesta. The inguinal rings may be palpated in males. The ovaries and uterus can be palpated in mares. The bladder can be palpated if it contains urine.

Abnormal Findings

Abnormalities associated with specific diseases are discussed under those headings (Table 7-13). One should be able to recognize gas and fluid distension of the cecum and colon, fluid distension of the small intestine, impaction of the large and small colon, and displacement of the large colon.

Small-intestinal distension is evident as loops of tubular structures of up to 10 to

Table 7-13 Rectal findings and associated causes of equine colic

Rectal abnormality	Disease	Clinical characteristics	Treatment
Distended small intestine	Proximal jejunitis/duodenitis, anterior enteritis	Small intestine mildly to moderately distended; voluminous gastric reflux; marked pain relief on gastric decompression Normal peritoneal fluid in most cases	Supportive; repetitive decompression of stomach
	Strangulating intestinal lesion; small intestinal volvulus or entrapment	Severe, tight distension of small intestine; gastric reflux Severe pain not relieved by gastric decompression; abnormal peritoneal fluid	Surgery
	Ileal impaction	Mild and progressive pain; gastric reflux only late in disease Impaction occasionally palpable per rectum	Medical initially, then surgery if no resolution
	Ileal hypertrophy	Mild to moderate chronic pain occurring after feeding Hypertrophy may be palpable	Surgical resection
	Ileocecal intussusception	Moderate to severe pain; gastric reflux later in disease Usually young horse	Surgical correction
Large colon distension	Colon torsion	Tenia dorsal in some cases; cecum displaced medially Severe pain; abdominal distension; no gastric reflux Short disease course	Surgical correction
	Left dorsal colon displacement (renosplenic entrapment)	Mild to moderate pain; bands on rectal examination leading to renosplenic space; ultrasonographic confirmation	Replacement by rolling horse Surgery
	Right dorsal displacement of colon	Moderate to severe pain; bands leading ventral to right dorsal quadrant; colon lateral to base of cecum	Surgical correction
	Impaction of large colon	Impaction palpable per rectum	Fecal softeners and lubricants, oral and intravenous fluids Surgery in refractory cases
	Enterolith	Obstruction usually of right dorsal or transverse colon Not palpable rectally; refractory pain; radiography	Surgical removal
	Gas colic	Gas distension of large colon; pain readily relieved with analgesics; short course with rapid recovery; major differential is colon torsion	Analgesics, mineral oil
	Sand colic	Mild to moderate pain; Sand auscultable in ventral abdomen; sand in feces; occasional watery feces	Analgesics, psyllium orally
Cecal distension	Cecal impaction	Mild to moderate pain, course of several days with sudden deterioration when cecum ruptures	Analgesics, lubricants, fecal softeners; surgical correction
	Cecal torsion	Acute, severe pain; rare	Surgical removal or correction
Displaced spleen	Renosplenic entrapment of large colon	See previously	
	Large colon displacement	Mild to moderate pain; ultrasonographic diagnosis	Analgesics; surgery
Intraabdominal masses	Mesenteric abscess	Fever, mild chronic or intermittent abdominal pain Increased leukocyte numbers in blood and peritoneal fluid	Long-term antibiotics
	Neoplasia	Neoplastic cells in peritoneal fluid; exploratory laparotomy	None

15 cm in diameter that may extend as far caudally as the pelvic canal. The structure is often compressible, akin to squeezing a fluid-filled tubular balloon, and slightly moveable. The presence of distended small intestine is an important sign suggestive of a small-intestinal obstructive lesion or anterior enteritis.

Colonic distension, impaction and displacement can be evident on rectal palpation. Gas and fluid distension of the **large colon** is evident as large (>20 cm) taut structures often extending into the pelvic canal. Tenial bands are often not palpable because of the distension. The distended bowel may extend into the pelvic canal, preventing examination of the caudal abdomen. **Impaction** is evident as columns of firm ingesta in the large or small colon. The most common site is the pelvic flexure in the caudoventral abdomen and the inlet to the pelvic canal. The impacted material remains indented when pressed with the finger tips.

Distension of the small colon is detectable as loops of tubular structures in the caudal abdomen. The loops of intestine have a prominent antimesenteric band, a feature not present on small intestine.

Displacement of the large colon is evident rectally as tight bands extending from the ventral abdomen cranially, dorsally, and to the left or cranially, dorsally, and to the right in left and right displacements of the colon, respectively. Displacement of the colon, if it obstructs aboral flow of ingesta and gas, may cause distension.

Nasogastric Intubation

Passage of a nasogastric tube is an essential part of the examination of a horse with colic because of the diagnostic information it provides and because relief of gastric distension can be life-saving.

The nasogastric tube **must** be passed into the stomach. This is usually evident by the release of a small amount of sweet-smelling gas as the stomach is entered. The tube should then be advanced further into the stomach

and, if reflux of material does not occur spontaneously, a siphon should be established by filling the tube with approximately 500 mL of water and rapidly dropping the end of the tube below the level of the horse's stomach. This procedure should be repeated at least three or four times if reflux is not obtained. If **reflux** is obtained, its volume and character should be noted. The volume should be measured, and anything more than 2 L of net reflux is likely important. If reflux is obtained, the nasogastric tube should be left in place or replaced frequently (1-hour intervals) until the colic resolves. If there is no reflux but the horse remains colicky, then repeated attempts should be made to obtain reflux. **Oral medications** should not be given to horses with nasogastric reflux.

Ancillary Diagnostic Techniques
Ultrasonography
Ultrasonographic examination of the abdomen of adult horses is useful in identifying a number of abnormalities, including small-intestinal distension, ileocecal intussusception, gastric distension, gastric squamous cell carcinoma, diaphragmatic hernia, peritoneal effusion, and other conditions.[31-35] Ultrasonographic examination is useful for detecting small-intestinal distension (such as occurs with anterior enteritis or small-intestinal accidents), reduced motility (anterior enteritis, enteritis, and obstruction), thickening of intestinal wall (>4 mm, enteritis, right dorsal colitis), volume and characteristics of peritoneal fluid (peritonitis and hemoperitoneum[36]), abnormalities in intestinal contents (such as presence of sand or excessively fluid ingesta), the presence of sacculations of the ventral colon (absence indicates distension), abnormalities in intestinal architecture (intussusceptions), and the presence of abnormal structures (neoplasia[37] and abscess[38]). Detection of colonic mesenteric vessels in an abnormal location (lateral or ventral to the colon) is strongly associated with a diagnosis of colon displacement or volvulus.[32,39] Ultrasonographic detection of small-intestinal distension is more sensitive than is rectal examination. (Fig. 7-1, A–D[33]).

Abdominal ultrasonography can be used for the accurate definitive diagnosis of some small-intestinal and large-intestinal diseases. Distended and nonmotile small-intestinal loops are associated with strangulated obstruction. Failure to visualize the left kidney is associated with renosplenic entrapment, and thickened large colon is associated with strangulating volvulus.[40]

Ultrasonographic examination reveals colon with a mural thickness of 9 mm or greater in horses with colon torsion. The test has a sensitivity of approximately 67% (i.e., correctly predicts the presence of colon torsion in two-thirds of horses that have the disease) and specificity of 100% (correctly rules out the diagnosis in 100% of horses that do not have the disease). Similarly, ultrasonography has a sensitivity of 80% and a specificity of 98% for detection of dilated small intestine.[33]

The abdomen should be examined in a systematic fashion with a 2.0 to 3.5-mHz transducer, and a procedure allowing rapid examination of the abdomen of horses has been proposed (Table 7-14).[33] The value of this protocol is that it ensures a systematic and thorough examination of the abdomen and thorax for signs of the cause of colic. The normal ultrasonographic anatomy of equids is described.[34]

Radiology
The large size of the adult horse precludes detailed radiographic examination of intra-abdominal structures. Enteroliths can be detected by computed radiography with a sensitivity of 85% and a specificity of 93%. Sensitivity is lower for small-colon enteroliths than for large-colon enteroliths (50% and 94.5%, respectively) and is significantly affected by gas distension.[41] Computed (digital) radiography provides some improvement in sensitivity over analog radiography, but both are useful techniques in diagnosis of enterolithiasis. Sand accumulation can be detected by radiographic examination of the abdomen.[42,43] Diaphragmatic hernias can be detected by radiographic (or ultrasonographic) examination of the thorax.

Arterial Blood Pressure
Arterial blood pressure is a very good indicator of the degree of shock in colic, and the availability of a simple technique makes it a practical aid in assessing prognosis in a clinical case. If normal systolic pressure is about 100 mm Hg (13.3 kPa), a pressure below 80 mm Hg (10.6 kPa) indicates a critical situation (it can be as low as 50 mm Hg [6.6 kPa]). In horses with very severe pain but not shock, the systolic pressure is likely to be very high, up to 250 mm Hg (33.3 kPa).

Course of the Disease
The course of the disease depends on its cause and the severity of the associated lesions. Spasmodic and gas colic usually resolves within hours of onset. Horses with
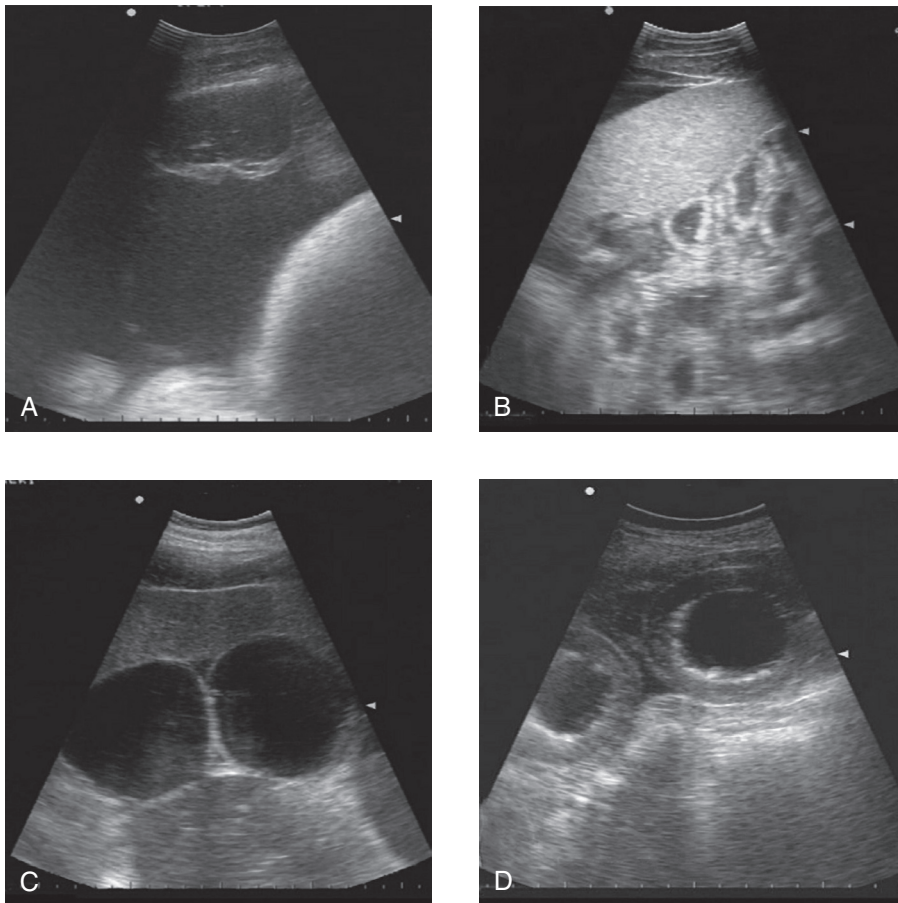
Fig. 7-1 **A,** Ultrasonographic image obtained at site 1: an abnormal amount of anechoic fluid is visible. **B,** Ultrasonographic image showing nonturgid fluid-filled small-intestinal loops. **C,** Ultrasonographic image showing turgid small-intestinal loops without wall thickening in a horse with small-intestinal obstruction. **D,** Ultrasonographic image showing turgid small-intestinal loops with marked wall thickening in a horse with strangulated small-intestinal obstruction.

Table 7-14 Method for brief examination of the abdomen of a horse with colic

Side	Site	Scanning procedure
Left	Ventral abdomen	Place the probe just caudal to the sternum and move caudally to assess the most gravity-dependent area of the abdomen.
	Gastric window	Visualize the stomach at the level of the 10th left ICS in the middle third (dorsoventrally) of the abdomen and then move the probe in the 2–3 ICSs cranial and caudal to the 10th one.
	Splenorenal window	Place the probe between dorsal and middle third of the abdomen at the level of the 17th ICS.
	Left middle third of the abdomen	Freely move the probe around in the middle third of the abdomen.
Right	Duodenal window	Place the probe in the 14–15th right ICS in the dorsal part of the middle third (dorsoventrally) of the abdomen.
	Right middle third of the abdomen	Freely move the probe around in the middle third of the abdomen.
	Cranial ventral thorax	Place the probe on the cranial ventral thorax just caudal to the triceps muscle.

Reproduced with permission from XX[33]
ICS, intercostal space.

strangulating lesions have severe clinical signs and usually die within 24 hours of the onset of signs. Horses with nonstrangulating obstructive lesions have longer courses, often 48 hours to 1 week, and die when distension causes bowel to become devitalized and rupture.

When intestinal rupture does occur, there is a sudden onset of shock and toxemia, the acute pain that preceded it disappears, and the horse becomes quiet and immobile. The terminal stages after rupture of the intestine or stomach, or from profound endotoxemia, are very distressing. The horse might be recumbent but most continue to stand until the last few minutes, when they can literally drop dead. The respiration is sobbing and there is gross muscle tremor and profuse sweating, and there is often a delirious, staggering wandering. Euthanasia should be performed before this stage is reached.

CLINICAL PATHOLOGY

Examination of various clinical pathology variables is useful in assessing the severity of the changes occurring as a consequence of the disease rather than in providing a definitive diagnosis. Therefore some of these variables have prognostic significance (see "Prognosis") and should be monitored repeatedly in severe cases.

Hematology and Serum Biochemistry

Measurement of **hematocrit** and **plasma total protein** concentration is useful in assessing hydration status (see Chapter 5). Hematocrit increases as a consequence of splenic contraction or dehydration, making the use of this variable as a sole indicator of hydration status unreliable. However, increases in both hematocrit and total protein concentration indicate dehydration,

and these variables can be used as crude estimates of response to fluid therapy. Plasma total protein concentrations may decline if there is significant loss of protein into the gut lumen or peritoneal space.

Measurement of the **blood leukocyte count** has little diagnostic significance, with the exception that the combination of leukopenia and a left shift are consistent with the endotoxemia that accompanies devitalized bowel, enteritis, or peritonitis. Serum concentrations of amyloid A, an acute phase protein, are higher in horses with colic than in healthy horses.[44]

Horses with severe colic often have abnormalities in coagulation, with nonsurviving horses and horses with strangulating lesions having the most severe changes, characterized by low antithrombin activity and prolonged prothrombin and activated partial thromboplastin times.[26,27,29] Disseminated intravascular coagulation is common among horses with ischemia or necrosis of the gut and is a good prognostic indicator of survival.[26,27] Changes in coagulation and fibrinolysis include decreases in antithrombin activity and fibrinogen concentration and increases in prothrombin time, activated partial thromboplastin time, and concentrations of D-dimer and thrombin–antithrombin complexes in plasma.[26,27,29,45] Dynamic measures of clotting function or fibrinolysis also reveal that hypocoagulation, indicated by abnormalities in one or more measures by thromboelastography, is indicative of a poor prognosis.[27] However, changes in these variables do not always correlate well with more dynamic measures of clotting function, such as thromboelastography.[27,29]

There is evidence of abnormal cardiac function or cardiac injury in up to one-half of horses with severe colic.[25,46] Plasma concentrations of cardiac troponin I (cTnI)

exceed the reference range for healthy horses in horses with strangulating or non-strangulating obstructive lesions of the small or large intestine or inflammatory (noninfarctive) lesions of the intestines or peritoneum.[25,46] The cTnI concentration exceeded the upper reference range (>0.03 ng/mL) in 36% (9/25) horses with strangulating lesions and 47% (9/19) with nonstrangulating inflammatory (9/19 [47%]) disease.[25] The proportion of horses with high cTnI concentration was significantly greater among nonsurvivors (12/24 [50%]) than among survivors (10/45 [22%]).[25] Concentrations are higher in horses that do not survive and are negatively correlated with hematocrit and blood lactate concentration and negatively with left ventricular ejection time (a measure of cardiac function in which a shorter ejection time indicates compromised function).[25]

Measures of **serum electrolyte concentration** are important in providing an assessment of the horse's electrolyte status and in tailoring fluid therapy (see Chapter 5). The nature of the abnormalities depends to some extent on the cause of the disease, but is more markedly affected by the severity of the disease. Mild hyponatremia is not uncommon but is clinically unimportant in the vast majority of cases.[47] **Hyperkalemia** is common in horses with severe acidosis and large sections of devitalized intestine.

Hypokalemia is common in horses with more long-standing colic, for instance impaction of the large colon, that have not eaten for several days. **Hypocalcemia** and **hypomagnesemia** are common in horses with colic, especially horses with severe colic.[47,48] Measurement of total concentrations (ionized plus nonionized) can be misleading in that reductions in concentration of the physiologically important ionized component can be present in horses with normal concentrations of the total ion. Hospitalized horses with colic or diarrhea are more likely to have hypomagnesemia than are horses with other diagnoses.

Serum enzyme activities are rarely useful in aiding diagnosis or treatment of horses with colic, with the exception that **serum γ-glutamyl transferase (GGT)** activity is elevated in approximately 50% of horses with right dorsal displacement of the colon, whereas such elevations are rare in horses with left dorsal displacement. The elevated GGT, and less commonly serum bilirubin concentration, in horses with right dorsal displacement is attributable to compression of the common bile duct in the hepatoduodenal ligament by the displaced colon. Serum and peritoneal **alkaline phosphatase** activities are higher in horses with ischemic or inflammatory bowel disease than in horses with other forms of colic, although the differences are not sufficiently large as to be useful diagnostically. Serum creatine kinase activity above the normal range (385 U/L) is

associated with a fourfold increase in the likelihood that a horse with colic has small-intestinal ischemia.

Serum **urea nitrogen** and **creatinine** concentrations are useful indicators of hydration status and renal function. Prerenal azotemia is common in horses with colic, and can progress to acute renal failure in severe cases of colic of sufficient duration. High plasma concentrations of intestinal fatty acid binding protein (>100 pg/mL) are associated with increased need for surgery in horses with colic.

Hyperglycemia is common in horses with colic examined in referral institutions with 45% of cases having blood glucose concentrations about the reference range.[49] Blood glucose concentrations are indicative of the severity of disease with more severely ill horses having higher concentrations of glucose in blood.[49,50]

Horses that die of colic have higher circulating concentrations of epinephrine, cortisol, and lactate than do horses that survive, indicating a greater degree of sympathetic and adrenal cortical activation.[51]

Acid-Base Status

Most horses with severe colic have **metabolic acidosis**, although respiratory acidosis and metabolic alkalosis also occur. Horses with less severe disease, such as simple obstructive disease or spasmodic colic, might not have abnormalities in acid-base status.

Metabolic acidosis, when severe, is usually but not always attributable to L-lactic acidosis. Lactate is present as the L-isomer, which is produced by mammalian metabolism, and the D-isomer, which is produced only by bacterial metabolism. L-Lactate accumulates as a result of increased production or decreased clearance of L-lactate by the animal. D-Lactate accumulates because of the production of this isomer in the blood or peritoneal fluid as a result of the presence of bacterial infection of these anatomic spaces or because of leakage of D-lactate produced by bacteria in the gastrointestinal tract into the circulation through compromised mucosa or as a result of a ruptured viscus.[52] Increases in blood and peritoneal fluid D-lactate concentrations are signs of a poor prognosis.[52]

L-Lactate concentrations can be estimated by calculating the anion gap:

$$Anion\ gap = (sodium + potassium) \\ - (bicarbonate + chloride).$$

(If bicarbonate concentrations are not available, total serum carbon dioxide can be substituted.) However, the increasing availability of laboratory-based or stall side (point-of-care) L-lactate analyzers means that direct measurement of plasma or blood L-lactate concentrations is feasible in a variety of clinical situations.[53-56] Samples should be analyzed within minutes of collection unless collected into evacuated tubes containing sodium fluoride/potassium oxalate in which case lactate concentration in plasma is stable in refrigerated samples for up to 6 hours (and perhaps longer).[55] Measurement of plasma lactate concentration is useful in assessing disease severity and likelihood of survival with one study documenting a 29% increase in odds of death (OR 1.20, 95% CI 1.2–1.4) for every 1 mmol/L increase in plasma lactate concentration.[54] Others report similar evidence in horses with surgical lesions of the small or large intestine.[46] Similarly, increases in plasma lactate concentration over time are indicative of a worsening prognosis.[46,54]

Anion gap of less than 20 mEq/L (mmol/L) is associated with 81% survival, 20 to 24.9 mEq/L (mmol/L) with 47% survival, and 25 mEq/L (mmol/L) or more with 0% survival.[1]

Abdominocentesis

Analysis of peritoneal fluid is an important component of the complete examination of a horse with colic. Details of the technique and interpretation of the results were discussed previously but, briefly, if there is an increase in the total protein concentration, a change in the color to red or blood-tinged, and an increase in the leukocyte count in peritoneal fluid, it is likely that there is some insult to intraabdominal structures. The color of peritoneal fluid is also indicative of its L-lactate concentration, with yellow fluid an indicator of a low lactate concentration and red fluid having the highest concentrations.[50] **Total protein concentration** increases when there is an insult to the gastrointestinal tract that compromises the serosal surface of the bowel, for instance strangulating lesions of the small intestine or in the terminal stages of an impaction colic in which the bowel wall is devitalized.

Increased concentrations of **D-lactate or L-lactate** are associated with more severe disease and decreased chances of survival.[50,52] Peritoneal lactate concentrations increase with increasing disease such that 55% to 60% of horses with peritoneal lactate concentrations <2.0 mmol/L die, whereas 100% of horses with peritoneal lactate concentrations >10 mmol/L die.[50]

Concentrations of D-dimers in peritoneal fluid are increased in horses with increased fibrinolytic activity as a result of inflammation of the peritoneum or impaired intestinal blood flow.[45,57] D-dimer concentrations in peritoneal fluid are highest in horses with endotoxin in the peritoneal fluid.[45] Prognosis for survival declines with increasing D-dimer concentration.

The presence of intracellular bacteria, plant material, and degenerate neutrophils is indicative of gastrointestinal rupture provided that one is *certain* that the sample came from the peritoneal space and not from the bowel lumen (by inadvertent enterocentesis).

PROTOCOL FOR EVALUATING A COLIC PATIENT

When evaluating a horse with colic the aims are to

- Determine the nature and cause of the lesion
- Establish a prognosis
- Determine the most appropriate therapy, including consideration of euthanasia
- Determine the need for referral for specialized care, including surgery

The suggested protocol for evaluating a horse with colic is discussed in the following sections. The time intervals between repeated examinations depend on a number of factors, including severity of the disease and the accessibility of the horse. For a horse with a possible intestinal obstruction this should be every hour, for a horse with probable colonic impaction examinations every 4 hours are adequate, and for a chronic colic with ileal hypertrophy an examination every day is usual. The following observations should be made.

Behavior

The following should be assessed: severity of pain, frequency and duration of attacks, whether food is taken, amount and character of feces, and frequency of urination.

Clinical and Clinicopathologic Observations

- **Elevated pulse rate** with a fall in **pulse amplitude** are among the most reliable indicators of the state of dehydration or shock. They can be temporarily misleading in a horse that is excited because it is in strange surroundings, or separated from its dam, foal, or close companion. They may also be marginally influenced by a bout of pain. A rate of more than 60 beats/min and a steady climb in heart rate of about 20 beats/min at each hour in a series of monitoring examinations signal a deterioration in prognosis. A high rate that continues to worsen during a period of analgesia as a result of medication also indicates a bad outcome. A small-amplitude, "thready" pulse characterizes severe shock.
- **Mucous membrane color** and **capillary refill time** are assessed. Deep congestion (dark red) or cyanosis (purple) and capillary refill times much longer than 2 seconds are indicators of peripheral circulatory failure.
- **Temperature** is infrequently taken unless there is some positive indication, such as suspicion of peritonitis, to do so.
- **Respiratory rate**, also of minor importance except as an indicator of severity of pain, or in terminal stages of endotoxic shock or dehydration, when it becomes gasping.
- **Intestinal sounds**. The disappearance of intestinal sounds indicates ileus.

Hypermotility is usually a sign of less serious disease, except in the very early stages of a small-intestinal accident. The development of a ping on auscultation–percussion indicates accumulation of gas under some pressure.

- **Rectal findings**. The development of palpable abnormalities is an ominous finding. A decision to intervene surgically is often made at this point. The inherent inadequacy of the rectal examination is that only the caudal half of the abdominal cavity can be reached. Therefore large bowel and terminal ileal problems are more easily detected. With anterior abdomen small-intestinal lesions, distended loops do not usually come into reach until 6 hours after colic commences. They may reach back as far as the pelvis by 18 hours.
- Amount and nature of **feces** is important. Failure to defecate within 12 hours of treatment is a bad sign. The empty rectum with a dry, tacky feel, or with a smear of mucus and degenerated blood some hours after the last defecation, presages a completely blocked intestine. The passage of oil but no feces suggests a partial blockage of large bowel that will permit the passage of oil but not fecal balls.
- **Reflux** through a nasogastric tube. Acute gastric dilatation or small-intestinal regurgitation of fluid sufficient to cause reflux of fluid via the stomach tube is a grim development. Large-bowel distension is also associated with fluid accumulations in the stomach. A negative test in a case suggestive of small-intestinal obstruction should be followed by repeated tests; reflux from a lesion well down in the small intestine may take some hours to reach the stomach. In ileocecal valve impaction gastric reflux may not develop until 24 hours after the commencement of the colic.
- **Abdominal paracentesis**. Repeated examinations are without serious risk and can herald the development of infarction and necrosis of gut wall, leakage and the development of peritonitis, or rupture and death caused by endotoxic shock.
- Visible **distension** of the abdomen.
- **PCV** and **plasma protein**. A rise in PCV of 5% (i.e., from 55%–60%) in an hour is a serious sign. A rise in PCV with a stable or declining serum protein concentration is often indicative of loss of capillary integrity and leakage of vascular proteins into extravascular spaces, such as the intestinal lumen. This is a sign of a poor prognosis.
- **Skin tenting** on its own can be a very misleading indicator of the state of a horse's dehydration, but significant changes from one examination to another are likely to confirm deductions made on the basis of heart rate and mucosal color.
- **Arterial blood pressure** is one of the most reliable prognostic indicators in cases of colic.
- Response to **analgesics**. Diminution in the relief of pain after administration of detomidine, xylazine, butorphanol, or flunixin meglumine can be interpreted as a serious decline in the status of the affected intestine.

When to Refer the Patient

The decision to refer a horse for specialist care and evaluation is often difficult. Most referrals occur because of the need for specialized medical or surgical treatment and therefore involve considerable expense and inconvenience to the owner. However, early referral is critical because of the improved chances of survival associated with early medical and surgical therapy of horses with severe colic.[58]

The criteria for referral include:
- Severe persistent pain without identifiable cause for more than 24 hours. Referral should be sooner if there is evidence of compromised cardiovascular function, or any of the signs described next.
- Recurrent attacks of colic over a period as long as several months.
- Failure of an efficient analgesic to provide analgesia or relief for at least 20 minutes.
- A rectally palpable lesion including distended small intestine, large colon, or small colon, or impaction of the large colon that does not resolve in 24 hours.
- Reflux of more than 4 L of fluid through a nasogastric tube.
- Abdominal distension.
- Blood-tinged, high-protein peritoneal fluid with a high white cell count.
- A rapid worsening of the pain and vital signs during a period of 2 to 4 hours

Not all of these criteria need to be fulfilled to warrant a decision to refer, and in most cases the presence of one of these findings is sufficient to justify a recommendation to the owner to refer the horse for further evaluation and specialized care.

Important in the decision to refer, or to perform a laparotomy, is the client's understanding of the **costs** involved and the **likely outcomes**. Because decisions to refer are often complicated by the emotional pressures on the owner and the need to make a decision quickly, it is important to take the time to fully inform the owner of the likely costs and outcomes before a final commitment is made to refer. **If there is doubt—refer it!**

Surgery

The **decision to perform surgery** is best made by trained specialists and is usually based on a variety of clinical and clinicopathologic findings with most weight given to the presence of severe unrelenting or intermittent pain, severe abdominal distension, large quantities of reflux through a nasogastric tube, intestinal distension palpable per rectum, serosanguinous peritoneal fluid, evidence of cardiovascular compromise including a high (>60 beats/min) and increasing heart rate, poor capillary refill, discolored mucous membranes, and the absence of borborygmi. The presence of abnormal abdominal fluid (turbid or serosanguinous) and peritoneal fluid with an elevated total protein concentration has good sensitivity (92%) and moderate specificity (74%) for the need for surgery. Formal modeling of the need for surgery in horses with colic at referral institutions provides a numerical estimate of the need for surgery, but is seldom used in most referral practices.

Prognosis

Given the enormous emotional and financial costs of having a severely ill horse with colic, there is an obvious need for accurate prognostication. The prognosis is heavily dependent on the underlying disease, and efforts to determine the diagnosis are useful in improving the accuracy of the estimate of prognosis. For instance, strangulating infarctive lesions carry a poorer prognosis than does an uncomplicated impaction of the large colon, and a much worse prognosis than spasmodic colic. The case–fatality rates for the various causes of colic are provided in the sections addressing those diseases.

Aside from the importance to prognostication of determining an accurate diagnosis, much effort has been devoted to determining the prognostic value of various clinical and clinicopathologic factors.[59] Overall best predictors of survival are those clinical and clinicopathologic factors that assess cardiovascular and metabolic status. The important factors include arterial blood pressure or its clinical correlates, pulse pressure and/or capillary refill time, pulse rate, mucous membrane color, indicators of hydration status (hematocrit and serum urea nitrogen concentration), blood lactate concentration, and anion gap.

Arterial systolic blood pressure is one of the best predictors of survival, with horses with systolic pressures of 90 mm Hg (12 kPa) having a 50% chance of survival, whereas fewer than 20% of horses with a pressure below 80 mm Hg (10.6 kPa) survive.

Capillary refill time, the clinical manifestation of arterial blood pressure, is also a good predictor of the probability of survival. Capillary refill times of 3 seconds or more associated with a survival rate of 30%. Similarly, increasing **heart rate** is associated with diminishing chances of survival—a horse with a heart rate of 80 beats/min has a 50% chance of survival, whereas one with a heart rate of 50 beats/min has a 90% chance of survival. Increasing blood lactate

concentration and anion gap (see the section Clinical Pathology) are associated with increased chance of death. Measures of hydration status are also good indicators of prognosis. A **hematocrit** of 50% (0.50 L/L) is associated with a 50% chance of survival, whereas the chance of surviving drops to 15% when the hematocrit is 60% (0.60 L/L). Horses with high circulating epinephrine, cortisol, or lactate concentrations are at greater risk of death.

Although individual variables can be good prognostic indicators, their predictive utility improves when they are combined, although this introduces the need for either remembering models or keeping the model close at hand, something often not easily accomplished in the field. Furthermore, these models have been developed from cases at specific referral institutions and are likely not be applicable to field cases or even cases at other referral sites. However, the general principles probably apply in all circumstances even if the precise weighting appropriate for each variable does not.

NECROPSY FINDINGS

The nature of the necropsy findings depends on the underlying disease.

DIFFERENTIAL DIAGNOSIS

Differential diagnostic features of common causes of equine colic are provided in Table 7-15. The following diseases may be mistaken for colic:

- Laminitis
- Pleuritis
- Enterocolitis
- Rhabdomyolysis
- Obstructive urolithiasis
- Uroperitoneum
- Foaling and dystocia
- Uterine torsion
- Peritonitis
- Cholelithiasis
- Ovulation and ovarian pain
- Esophageal obstruction
- Duodenitis-proximal jejunitis
- Gastric ulceration
- Anthrax
- Testicular torsion
- Lactation tetany
- Tetanus
- Rabies
- Botulism
- Grass sickness
- Purpura hemorrhagica
- Clostridial myonecrosis (gas gangrene)
- Psychogenic colic

TREATMENT
Medical Treatment

The specific treatment of each case of colic varies and depends on the nature of the lesion and the severity of the disease. However, several principles are common to the treatment of most colic:

- Provision of analgesia
- Correction of fluid, electrolyte, acid-base and hemostatic abnormalities
- Gastrointestinal lubrication or administration of fecal softeners
- Treatment of underlying disease

Analgesia[2]

Analgesia is important in that it relieves the horse's discomfort; minimizes the physiologic consequences of pain, including the pain-induced reduction in gastrointestinal motility; permits a thorough clinical examination; and reduces the likelihood of the horse injuring itself while rolling or thrashing. Analgesics can be broadly divided into NSAIDs, sedating analgesics, opiates, and spasmolytics. The doses of these drugs are provided in Table 7-15.

The analgesic and its dose rate should be chosen such that the horse's pain is relieved, but signs of progressive cardiovascular compromise indicative of the need for more

Table 7-15 Analgesics and spasmolytics for use in equine colic			
Drug class	**Drug**	**Dose**	**Comments**
NSAIDs	Flunixin meglumine	0.25–1.0 mg/kg, IV or IM every 8–24 h	Potent analgesic for up to 12 h May mask signs of surgical disease
	Ketoprofen	2.2 mg/kg, IV every 12 h	Potent analgesic for up to 12 h
	Phenylbutazone	2.2–4.4 mg/kg, IV or PO every 12 h	Weak analgesic for gastrointestinal pain Minimal effect on motility
	Dipyrone	10 mg/kg, IV or IM every 4–6 h	Weak analgesic; often combined with hyoscine in commercial preparations (Buscopan compositum)
Opiates	Butorphanol	0.025–0.1 mg/kg, IV or IM as required	Potent analgesia for 30–90 min; safe. Often combined with an α-2 agonist May cause ataxia
	Meperidine (pethidine)	0.2–2.0 mg/kg, slowly IV or IM as required	Moderate analgesia for 0.5–4 h; can cause excitement and/or ataxia
	Pentazocine	0.5–1.0 mg/kg, IV or IM as required	Moderate analgesia; may cause ataxia
	Morphine sulfate	0.05–0.1 mg/kg slowly IV or IM as required	Potent analgesia; can cause excitement
α-2 Agonists	Xylazine	0.1–1.0 mg/kg, IV or IM, as needed	Potent analgesia and sedation for up to 30 min; decreases intestinal motility Often combined with butorphanol
	Detomidine	10–40 μg/kg, IV or IM as needed	Potent analgesia and sedation for up to 120 min
	Romifidine	0.04 to 0.12 mg/kg, IV or IM	Potent analgesia and sedation
	Medetomidine	0.01–0.02 mg/kg, IV or IM	Potent analgesia for up to 120 min Sedation
Spasmolytics	Atropine	0.01–0.04 mg/kg IV or IM	Do not use because of induction of ileus
	Hyoscine butylbromide	0.1–0.4 mg/kg, IV or IM every 6–12 h	Reduces gastrointestinal motility; mild analgesic; often combined with dipyrone
Other	Acetylpromazine	0.02–0.04 mg/kg, IV or IM every 6–24 h	No analgesia but marked sedation; potent hypotensive agent; do not use
	Lidocaine	1.5 mg/kg IV loading dose followed by 0.05 (mg/kg)/min IV infusion	substance P inhibitor; analgesic, antiinflammatory, promotility agent

IM, intramuscularly; IV, intravenously; NSAIDs, nonsteroidal antiinflammatory drugs; PO, orally.

aggressive therapy or surgery are not masked. **Acupuncture** does not provide effective analgesia in horses with colic and should not be used in these animals.

Nonsteroidal Antiinflammatory Drugs

Flunixin meglumine is a potent, long-acting analgesic with the ability to mask signs of surgical disease, with the consequence that surgery might be delayed and the chance of recovery diminished. Flunixin meglumine should only be used to control pain when the diagnosis is clear or when surgical intervention is not an option. It should not be used routinely in horses being monitored for progression of disease unless such monitoring is frequent and thorough, which might not be the situation in field colics. A horse that remains painful 30 minutes after the administration of flunixin meglumine is likely to have severe gastrointestinal disease and should be further evaluated.

Comments similar to flunixin meglumine apply to **ketoprofen** but not to **phenylbutazone**, which has relatively weak analgesic effects in colic patients (as opposed to its potent analgesic effects in musculoskeletal disease). **Dipyrone** is a weak analgesic that is useful in treatment of mild cases of colic.

Flunixin meglumine and etodolac retard recovery of equine jejunum and barrier function and flunixin inhibits electrical activity in the ventral colon. However, these effects detected in vitro have not been demonstrated to have practical relevance to treatment of horses with colic with NSAIDs. Horses in pain should not, based on current information, be deprived of these drugs.

α-2 Agonists

The **α-2 agonists** (xylazine, detomidine, and romifidine) provide potent analgesia, especially when combined with the opiate **butorphanol**. Duration is relatively short (up to 90 minutes for detomidine), which means that signs of progressive disease are readily detectable. The effect of β-2 agonists in reducing gastrointestinal motility is not clinically important in most colic cases and should not discourage use of these very useful drugs.

Opiates

Opiates, including butorphanol, meperidine (pethidine), morphine, and pentazocine, are potent analgesics useful in the management of abdominal pain in the horse. These drugs are often combined with an α-2 agonist. Morphine and meperidine can cause excitement or urticaria in some horses. All are drugs with the potential for human abuse and the consequent limitation on their availability limits their use in horses.

Other Agents

Acetylpromazine has almost no analgesic properties, although it is a potent sedative, and should not be used in the routine treatment of colic. It is a potent hypotensive agent and should not be administered to any horse that is dehydrated or has compromised cardiovascular function.

Hyoscine butylbromide, a parasympatholytic drug, is widely used in certain parts of the world as the drug of choice in the initial treatment of field cases of colic. It is often combined with dipyrone and is effective in the field treatment of mild, uncomplicated colic.

Atropine causes gastrointestinal stasis in horses and should not be used in the routine treatment of colic.

Lidocaine is a potent analgesic when administered systemically, but must be given by constant intravenous infusion. Overdosing results in central nervous system (CNS) excitement.

Prophylaxis and Treatment of Endotoxemia

Treatment of endotoxemia is provided elsewhere (see Chapter 4). Administration of plasma from horses **hyperimmunized** with *Salmonella typhimurium* or *E. coli* reduces the severity of clinical signs and shortens the duration of disease in horses with endotoxemia secondary to enterocolitis or colic. **Polymyxin** (5000 IU/kg intravenously every 8–12 hours) attenuates the effect of endotoxin in experimental disease and is used for the prevention and treatment of endotoxemia in hospitalized horses. Its efficacy in clinical settings has not been determined. **Aspirin** (10 mg/kg orally every 48 hours) is administered to diminish platelet aggregation around intravenous catheters. **Flunixin meglumine** (1 mg/kg intravenously every 8–12 hours) or **phenylbutazone** (2.2 mg/kg intravenously every 12 hours) is given for analgesia and to prevent endotoxin-induced increases in plasma prostaglandins. **Pentoxifylline** (8 mg/kg orally every 8 hours) is administered for its putative effective in attenuating the effects of endotoxemia. The efficacy of these treatments in a clinical setting and their effect on measures of outcome of disease, such as duration of illness, case–fatality rate, or incidence of complications, has not been determined, with the exception of hyperimmune plasma or serum.

Antibiotics are often administered to horses with severe colic and evidence of toxemia because of presumed bacteremia. The antibiotics of choice should have a broad spectrum including gram-negative, gram-positive, and anaerobic bacteria. A suitable regimen includes an aminoglycoside and a penicillin, possibly combined with metronidazole. NSAIDs are administered to prevent the increased production of prostaglandins induced by endotoxin and the associated clinical abnormalities including fever, malaise, and tachycardia. However, the effect of NSAIDs in improving survival or shortening the duration of treatment has not been demonstrated.

Fluid and Electrolyte Therapy

Horses with evidence of dehydration, compromised cardiovascular function, or electrolyte imbalances should be administered fluids intravenously, preferably a balanced, isotonic, polyionic fluid such as lactated Ringer's solution. Horses with severe colic and signs of cardiovascular collapse require urgent resuscitation by intravenous administration of large quantities of fluids or administration of hypertonic saline followed by administration of isotonic fluids. Horses with hypoproteinemia could benefit from administration of plasma or colloidal fluids such as hetastarch (see Chapter 4 for details on fluid therapy and the section on Shock for a discussion of the treatment of this syndrome.)

Intestinal Lubricants and Fecal Softeners

The intestinal lubricant of choice is **mineral oil** (Table 7-16). It should be given only through a nasogastric tube because its aspiration is associated with severe and usually fatal pneumonia. Mineral oil is useful in cases of mild impaction colic and is often administered when the cause of the colic is not known, provided that there is no reflux of gastric contents through the nasogastric tube.

Dioctyl sodium sulfosuccinate is a fecal softener with the potential to be toxic at therapeutic doses, and its use is now not generally recommended. **Magnesium sulfate** is an effective fecal softener useful in the treatment of impaction colic. However, it can cause hypermagnesemia and toxicosis characterized by depression and signs of CNS dysfunction. **Sodium sulfate** is a safe and effective fecal softener, although it can induce mild hypernatremia and hypokalemia.

Other Treatments

Promotility agents (see Table 7-16) may be used in cases of ileus or large-colon impaction. Postoperative ileus is a common complication of surgical colic and should be treated by maintenance of hydration and electrolyte status and the administration of promotility agents.[60] **Cisapride** is apparently effective in reducing the incidence of postoperative ileus and may be useful in the treatment of ileus from other causes. The clinical efficacy of other putative promotility agents has not been demonstrated.

Heparin and low molecular weight heparins have been recommended for the treatment and prevention of coagulopathies associated with severe colic. The use of heparin or low molecular weight heparin is associated with increased risk of hemorrhage and heparin use causes a decrease in hematocrit. The efficacy of this treatment

Table 7-16 Promotility agents, lubricants, and fecal softeners for use in horses with colic

Drug group	Drug	Dose	Comments
Lubricants	Mineral oil	10–15 mL/kg, via nasogastric tube, every 12–24 h	Safe; lubricant only, does not soften feces; usually passed in 12–36 h*
Fecal softeners	Dioctyl sodium sulfosuccinate	12–25 mg/kg, via nasogastric tube, every 24 h	No more than two doses; toxic at higher doses*
	Magnesium sulfate	0.5–1.0 g/kg, via nasogastric tube, in water	Osmotic cathartic; toxic (CNS signs caused by hypermagnesemia) with repeated dosing*
	Sodium sulfate	1.0 g/kg, via nasogastric tube, in water, every 12 h	Osmotic cathartic; mild hypernatremia; safe*
	Psyllium	1 g/kg, orally, every 24 h	Bulk laxative; used for treatment of sand accumulation; efficacy uncertain but widely used*
Promotility agents	Lidocaine	1.5 mg/kg slow IV, then 0.05 mg/kg/min infusion	Analgesic, antiinflammatory, promotility; used to treat ileus; toxicity evident as CNS signs
	Metoclopramide	0.25 mg/kg IV slowly over 30 min every 12 h	Toxic; minimally effective
	Erythromycin	1 (mg/kg)/h IV	Questionable efficacy; may induce colitis
	Cisapride	0.1 mg/kg, IV every 8 h	Effective in prevention and treatment of postoperative ileus; may prolong cardiac Q-T interval (importance unknown)
	Neostigmine	0.02 mg/kg, IM or SC, every 8–12 h	Increases large-colon motility, decreases small-intestine motility; may cause colon rupture around hard impaction

CNS, central nervous system; IM, intramuscularly; IV, intravenously; SC, subcutaneously.
*None of these agents should be given if there is reflux through the nasogastric tube.

in improving survival has not been demonstrated.

Trocarization

Occasionally in severe cases of flatulent (gas) colic or in cases of colon torsion in which the abdominal distension is impairing respiration, it may be necessary to relieve the gas distension of the colon or cecum by trocarization. Trocarization is usually performed through the **right paralumbar fossa** immediately caudal to the last rib. The exact place for trocarization can be located by simultaneously flicking the body wall with a finger and listening with a stethoscope. The area of loudest ping will indicate the point of insertion of the trocar. A suitable trocar is a 12.5- to 15-cm 14- to 16-gauge needle. The needle is inserted through the skin and advanced into the abdomen until there is an audible expulsion of gas through the trocar. The trocar should be kept in position as long as gas is escaping. It may need to be replaced as the bowel is decompressed and moves away from the trocar. The procedure is reasonably safe but will cause inflammatory changes in the peritoneal fluid. The major danger is laceration of the colon or cecum and leakage of ingesta. It is advisable to administer systemic antibiotics to horses that have been trocarized.

A device for facilitating transrectal decompression of intestinal tympany is described with encouraging results.[61] However, this technique cannot be recommended until there are further studies of its efficacy and safety.

Management of Field Colic

Initial treatment of field cases of colic that do not have signs indicative of the need for referral or surgery usually includes administration of an analgesic and an intestinal lubricant. Analgesics suitable for the initial treatment of colic in the field are an α-2 agonist, such as xylazine, hyoscine butylbromide, dipyrone, butorphanol, or phenylbutazone. If there is no reflux through the nasogastric tube, then mineral oil should be administered. Fluids should be administered intravenously if there are signs of dehydration, cardiovascular compromise, or electrolyte imbalance. The response to this therapy should be monitored as described under the section "**Protocol for Evaluating a Colic Patient**" in this chapter. Further doses of analgesic can be given as required, and the horse should be monitored for any evidence of deterioration. If referral is contemplated, the referral institution should be contacted for advice on analgesia during transportation. Horses should be transported with a nasogastric tube in place.

Surgery

The only definitive treatment for many causes of equine colic is surgical correction or removal of the lesion. The availability of surgical facilities staffed by appropriately trained personnel has increased over the past two decades and there is often the opportunity to refer horses for examination by personnel with specialist training. Gastrointestinal surgery should not be attempted by those untrained or inexperienced in the necessary techniques or without the facilities to provide postoperative care.

The decision to perform an exploratory laparotomy on a horse with colic is based on a number of factors, including the provisional diagnosis, findings on physical and laboratory examination, and degree of pain. Horses with severe pain refractory to treatment with analgesics should have an exploratory laparotomy even if no other significant abnormalities can be detected. Algorithms for the decision to perform surgery have been developed, but are not perfect and do not replace the opinion of an appropriately trained and experienced examiner. Examination of peritoneal fluid contributes to the decision to perform surgery. The survival rate for horses undergoing surgical correction of lesions depends on the nature and location of the underlying disease and its duration. However, survival rates range from 50% to 75%, with approximately two-thirds of horses returning to their intended use.[62] The survival rate of horses with small-intestinal lesions is less than that of horses with large-intestinal disease, and the survival rate for horses with strangulating disease is much less than that of horses with nonstrangulating disease.[59] Thoroughbred racehorses that return to racing after colic surgery do so successfully.[63]

Prevention

Minimization of colic episodes depends on management factors, including ensuring adequate parasite control, feeding large quantities of forage and minimizing the

amount of concentrate fed, and providing dental care. However, most cases of colic not attributable to parasites or dietary factors cannot be prevented.

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COLIC IN THE PREGNANT AND POSTPARTURIENT MARE

Diagnosis and management of colic in pregnant and immediately postparturient mares is challenging because of the variety of conditions that can cause the disease, the difficulty in examination of intraabdominal organs in late-term mares, and concern about the viability of the fetus. There are also substantial technical challenges in surgical correction of abnormalities of either the gastrointestinal tract or reproductive tract in the presence of a gravid uterus. Colic in late-term mares can be caused by any of the causes of colic in adult horses (see the section Equine Colic), but some disorders are more common in late-term mares and, in addition to abnormalities of the reproductive tract, can cause signs of colic.[1] Causes of colic in the late-term mare include:

- Idiopathic, chronic, or recurrent, low-grade colic
- Large colon torsion
- Large colon impaction
- Incarceration of small intestine through a mesenteric rent
- Rupture of the cecum or colon
- Uterine torsion
- Uterine rupture
- Middle uterine or uteroovarian artery rupture
- Abdominal wall hernia
- Diaphragmatic hernia
- Dystocia
- Hydrops
- Imminent foaling

A common presentation of colic in late-term mares is chronic or recurrent, low-grade abdominal pain that is not associated with any signs of compromised cardiovascular or gastrointestinal function. It is assumed that the large gravid uterus interferes with normal motility or positioning of bowel, with subsequent pain. Severe colic in late-term mares is rarely associated with the uterus, with the exception of uterine torsion.

Colic in immediately postparturient mares (<24 hours after foaling) include:

- Cramping associated with uterine contractions and involution, often coincident with nursing or administration of oxytocin
- Rupture of the cecum or colon
- Primary idiopathic ileus and gastric rupture[2]
- Incarceration of the small intestine through a mesenteric rent
- Rupture of the mesocolon with segmental ischemia of the small colon
- Rectal prolapse
- Uterine tear, with or without prolapse of intestine
- Uterine prolapse
- Inversion of uterine horn
- Bladder prolapse through urethra
- Hemorrhage from uterine or uteroovarian artery
- Retained fetal membranes
- Uroperitoneum, usually secondary to rupture of the bladder

Colic in postparturient mares that is anything more than transient and associated with passage of placenta or nursing of the foal should be considered important and the mare should be examined closely and, if the colic does not resolve, repeatedly.

Idiopathic primary ileus and gastric rupture refers to a specific syndrome in postparturient mares that present with moderate to severe colic secondary to gastric and small-intestinal distension and ileus. There can be rupture of the stomach and death. The disease is most common in mares with 1 week of foaling, but can occur up to 2 months after parturition. The colic is acute and moderate to severe. Nasogastric intubation returns excess gas and fluid, and rectal or ultrasonographic examination reveals distended loops of atonic small intestine. Treatment is by relief of gastric distension by nasogastric intubation and supportive therapy (fluids and pain relief). Approximately 50% of mares require surgical exploration of the abdomen to confirm the diagnosis and allow decompression of the small intestine and stomach. Survival rate is approximately 90% with appropriate treatment.[2]

Survival rates for colic associated with anatomic abnormalities in late-term or postparturient mares are 50% and 30%, respectively.

Clinical examination of late-term or postparturient mares with colic uses the same principles as applied to examination of nonpregnant adult horses with colic. Monitoring of vital signs, passage of a nasogastric tube, rectal examination, and collection of peritoneal fluid should all be performed as indicated. However, the presence of a gravid uterus in late-term mares impairs rectal examination of the abdomen and often makes collection of peritoneal fluid impossible. Manual and visual (through a speculum) examination of the vagina and cervix should be performed.

Rectal examination should be performed and careful attention should be paid to examination of the uterus, including

position and viability of the fetus and broad ligaments. Uterine torsion can be detected by examination of the broad ligaments, which in mares with uterine torsion will be taut and spiral in the direction of the torsion. Hemorrhage into the broad ligament, which can extend into the uterus and perivaginal regions, is detectable as swelling in these structures. Additionally, affected mares will have signs of hemorrhagic shock, including tachycardia, sweating, and pallor of mucous membranes. Palpation of gastrointestinal structures per rectum is limited in the late-term mare, although the cecum and small colon should be palpable. The spleen and left kidney can be palpated in almost all normal late-term mares.

The reduced uterine size in postparturient mares permits more thorough per rectum examination of the caudal abdomen. Again, careful attention should be given to palpation of the uterus and associated structures for evidence of hemorrhage, prolapse, or rupture. **Rectal prolapse** and eversion of the small colon in a postparturient mare is an ominous finding because it is usually associated with rupture of the mesocolon and ischemic necrosis of the small colon, a condition that is almost always fatal. Prolapse of small amounts of anal or perirectal tissue is not a serious concern.

The **abdominal silhouette** should be examined for evidence of abdominal distension, such as can occur with colon torsion or uterine hydrops, and abnormalities in contour caused by rupture of the prepubic tendon and herniation of abdominal contents.

Vaginal and cervical examination can reveal discharge associated with impending abortion or parturition. Vaginal examination for uterine torsion is of limited value because the torsion almost always occurs cranial to the cervix so that, unlike the cow, the torsion is not apparent as deformation of the cervix. Manual examination of the vagina, cervix, and uterus of postparturient mares with colic is important to detect uterine, cervical and vaginal trauma, uterine inversion, and retained fetal membranes.

Ultrasonographic examination of the abdomen in the late-term mare, both per rectum and percutaneously, allows examination of structures not palpable per rectum. The presence and any abnormalities in structure, location, and motility of bowel should be noted. For example, small-intestinal distension caused by entrapment through a mesenteric rent may not be palpable per rectum but can be imaged. Peritoneal fluid should be examined for quantity and echogenicity. Intraabdominal hemorrhage caused by uterine artery rupture is evident as large quantities of echogenic fluid that has a characteristic swirling pattern similar to turbulent blood flow imaged ultrasonographically in the cardiac ventricles of some

horses. The position, number, and viability of the fetus or fetuses should be ascertained. The nature of allantoic fluid should be noted.

Collection of **peritoneal fluid** from late-term mares can be difficult because of contact between the gravid uterus and the ventral abdominal wall. Ultrasonographic examination can be useful in locating pockets of fluid for collection. Collection of peritoneal fluid is more readily accomplished in the postpartum mare. Peritoneal fluid from late-term and postpartum mares, even those with assisted vaginal delivery, should have protein and cell concentrations within the reference range of normal horses. Abnormalities in peritoneal fluid in late-term or postparturient mares should be considered to be indicative of intraabdominal disease.

The **differential diagnosis** of colic is similar to that of nonpregnant horses except as indicated previously.

Treatment of colic depends on its cause. Horses with low-grade to moderate, recurrent colic respond to administration of low doses of NSAIDs, mineral oil, or fecal softeners. Clenbuterol is sometimes administered for its tocolytic effect,[3] but the efficacy of this practice is unclear. Progestins are sometimes administered in an attempt to prevent abortion of mares after resolution of colic, but there is evidence of their lack of efficacy in this respect.[4]

The **risk of abortion** in mares with colic is partially dependent on the severity of the colic and it cause, necessity for surgical intervention, the duration of colic, and the stage of gestation.[3-6] Abortion rates in pregnant mares treated for colic at referral institutions vary from ~20% to 50% depending on the particular disease.[3-6] Severely ill mares with signs of toxemia have abortion rates of almost 70%, whereas mares with less severe disease have abortion rates of 8% to 18%, which is not markedly different from the rate in mares without colic.[3] Mares treated surgically have a greater relative risk of abortion (3.5, 95% CI 1.7–7.3) than mares treated medically. For mares treated surgically, hypotension during surgery and prolonged anesthesia are significant risk factors for abortion.[4] The need for surgical intervention, hypotension during surgery, and prolonged anesthesia are likely indicative of more severe disease, which could account for the higher abortion rate in these mares.[4]

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COLIC IN FOALS

SYNOPSIS

Etiology See Table 7-17.

Epidemiology Sporadic. Some causes are congenital, others heritable. Inguinal and scrotal hernias occur only in males.

Clinical signs Abdominal pain evidenced by kicking at the abdomen, flank watching, repeated tail movements as if chasing flies, repeated aborted attempts to suck, frequent lying down and standing within a short period, and rolling and lying in dorsal recumbency. Abdominal distension in some diseases and straining to defecate with meconium impaction. Radiography and ultrasonography are useful in identifying affected bowel.

Clinical pathology Nonspecific.

Lesions Are of the causative disease

Diagnostic confirmation Physical examination, radiography, ultrasonography, laparotomy, and necropsy

Treatment Pain control, fluid therapy, supportive care including consideration of the foal's nutritional requirements, and treatment of causative disease

ETIOLOGY

Diseases that cause colic in horses less than 1 year of age include both congenital and acquired conditions and are listed in Table 7-17. Fifty percent of neonatal Thoroughbred foals subjected to exploratory laparotomy had nonstrangulating lesions and 30% had enteritis. Among foals 2 weeks to 6 months of age, 30% of foals subjected to exploratory laparotomy had gastric ulcer disease, 27% strangulating lesions, 21% nonstrangulating lesions, and 17% enteritis.[1] The most common causes of colic in foals less than 30 days of age examined at a referral institution were enterocolitis (27%), meconium-associated colic (20%), transient colic of undetermined cause (19%), and necrotizing enterocolitis (16%).[2] Eight percent of foals examined had small-intestinal infarctive/obstructive lesions and 7% had other lesions, with 1.5% having overo lethal white syndrome.[2]

Diaphragmatic hernia is an uncommon cause of colic in newborn foals and can be congenital or acquired.[3-5] Intestinal accidents including displacements of the large colon and extraluminal obstruction of the small colon by ovarian pedicle are uncommon.[6,7] Herniation of the large colon through umbilical hernia is reported.[16] Pancreatitis in foals can cause signs of colic.[8] Intestinal hyperammonemia can cause colic, diarrhea, and signs of neurologic disease in foals.[9]

Table 7-17 Diseases causing colic in foals

Congenital anomalies	Anal atresia
	Colonic atresia
	Rectal atresia
	Ileocolonic agangliosis
	Myenteric hypogangliosis
	Inguinal hernia
	Diaphragmatic hernia
	Umbilical hernia
	Scrotal hernia
Gastrointestinal obstruction with or without infarction	Meconium impaction
	Ileus, secondary to extraintestinal disease including neonatal hypoxia
	Small-intestinal volvulus
	Large-intestinal volvulus
	Intussusception
	Jejunojejunal
	Ileocecal
	Small colon obstruction
	Fecalith
	Impaction
	Meconium
	Entrapment in hernia, mesenteric rents
	Large colon obstruction
	Impaction
	Intussusception
	Torsion
	Necrotizing enterocolitis
	Adhesions
	Colonic stricture
	Ileal impaction: foreign body
	Ascarid impaction: small intestine
	Phytobezoar
Other	Gastric ulcer
	Duodenal ulcer
	Abdominal abscess
	Umbilical abscess
	Peritonitis
	Tyzzer's disease (*Clostridium piliforme*)[1]
	Uroperitoneum
	Enteritis
	Ovarian torsion[2]

EPIDEMIOLOGY

Risk factors vary with the cause of colic, although congenital conditions such as **ileocolonic aganglionosis** in white progeny of overo spotted horses are clearly heritable, whereas others, such as "short colon" are not.[10] Most conditions occur sporadically, although **meconium impaction** is more common in colt foals and occurs only in the newborn foal, **intussusceptions** are most common in foals of 3 to 5 weeks of age and particularly those with diarrhea or extraintestinal illness, and impaction of the small colon by **fecaliths** is common in miniature horse foals.[1] Impaction by roundworms (*P. equorum*) is a common cause of small-intestinal obstruction in foals.[11] **Inguinal and scrotal hernias** occur only in male foals.

Case–fatality rate varies with the underlying disease, but 75% of foals treated at a referral institution survived to discharge from hospital, with similar survival rates for medically and surgically treated foals.[2]

Foals with clinical or clinicopathologic signs of more severe disease (greater pain, absent borborygmi, abdominal distension, and evidence of hypoperfusion) had a lower survival rate.[2] The long-term survival rate and suitability for use is excellent for most foals that have recovered from colic (93%).[2] The **mortality rate** attributable to colic in foals in Japan was 1.5% (74/4843).[12]

PATHOPHYSIOLOGY

The pathophysiology of colic in foals does not differ qualitatively from that of adult horses (see the section Equine Colic). The importance of pain, gastrointestinal distension, motility, and absorptive disturbances and loss of barrier function are all similar in foals and adults. Additionally, in young foals gastrointestinal disease may prevent nursing and ingestion of colostrum, causing failure of transfer of passive immunity (FTPI) to the foal. Failure to nurse also results in hypoglycemia and dehydration, which may exacerbate the abnormalities induced directly by the disease causing colic.

CLINICAL FINDINGS

Pain is the cardinal feature of gastrointestinal disease of foals. Foals with mild **abdominal pain** are apprehensive and walk continuously with frequent but brief (<1 min) periods of sternal or lateral recumbency. Affected foals make frequent attempts to nurse but do not continue to suckle and may butt the mare's udder even though there is a letdown of milk. The foal vigorously moves its tail as if chasing flies, looks at the abdomen, and may nip at its flanks. There are often frequent attempts to urinate or defecate but without passage of significant quantities of urine or feces. Severely affected foals will roll, often violently, and may spend considerable periods of time in dorsal recumbency, often propped up against walls or fences.

Severely affected foals are **tachycardic** (>100 beats/min) and **tachypneic** (<40 beats/min; recall that young foals have higher heart and respiratory rates and rectal temperature than do older foals and adults). **Mucous membrane color** and **capillary refill time** are similar to that of adult horses, and changes can be interpreted in the same manner as for adults.

The **external abdomen** should be examined closely for the presence of inguinal, scrotal, or umbilical hernias. Abdominal distension in foals can be the result of large-colon or small-intestinal distension (or uroperitoneum), although the abdominal distension is greater with large-colon distension. Abdominal circumference should be monitored frequently by direct measurement to detect changes in the degree of abdominal distension.

Auscultation of the abdomen may reveal increased or decreased borborygmi and, if there is gas distension of the large colon or cecum, pinging sounds on simultaneous flicking and auscultation of the abdomen.

Rectal examination in foals is limited to exploration of the rectum with one or two fingers. The presence or absence of feces should be noted. Lack of fecal staining of the rectum suggests a complete obstruction such as intestinal agenesis.

Nasogastric intubation should be performed. The presence of more than 300 mL of reflux in a foal is significant and suggestive of gastric dilatation secondary to an outflow obstruction or regurgitation of small-intestinal fluid into the stomach because of a small-intestinal obstruction.

Meconium is usually passed within the first 10 to 12 hours (usually 3 hours) after birth. **Retention of meconium** is evident as signs of colic and the presence of firm meconium in the rectum. Palpation of the caudal abdomen may reveal firm material in the small colon. Enemas (see the section Treatment) usually provide rapid relief and confirmation of the diagnosis.

Ancillary Diagnostic Tests
Diagnostic Imaging
Radiography is useful in the evaluation of foals with colic, although it seldom provides a definitive diagnosis, with the possible exception of meconium impaction and contrast studies of foals with lesions of the small or large colon, or gastric outflow obstructions. **Retrograde contrast radiography** of the lower gastrointestinal tract of foals less than 30 days old is a sensitive technique for detection of anatomic anomalies such as **atresia coli** and obstruction of the **small colon**. The technique is performed by the intrarectal infusion of up to 20 mL/kg of barium sulfate (30% w/v) in sedated, laterally recumbent foals. **Meconium impaction** can be evident as a mass of radiopaque material in the caudal abdomen with accumulation of fluid and gas oral to the obstruction. Upper gastrointestinal contrast radiography is useful to detect abnormalities of the stomach and small intestine, in particular gastric outflow obstructions.

Ultrasonographic examination of the foal abdomen can demonstrate intussusceptions, the presence of excessive peritoneal fluid (such as urine or blood), edematous intestine, hernias, and colonic impaction. The presence of atonic, distended small intestine suggests the presence of ileus, possibly secondary to a small-intestinal strangulating lesion. However, early ultrasonographic differentiation of ileus secondary to enteritis from that accompanying a strangulating lesion is difficult. Detection of gas within the wall of the small or large intestine (pneumatosis intestinalis) is indicative of a poor prognosis and the presence of necrotizing enterocolitis.[13] There is a high prevalence of asymptomatic intussusceptions (~50%) detected in healthy neonatal foals by ultrasonographic examination.[14] Detection of an intussusception in this way should be considered in light of the foal's other clinical signs and in a healthy foal should not necessarily provoke more extensive examination.

Endoscopy
Endoscopic examination of the stomach is indicated in any foal with recurrent or continuous mild to moderate colic, bruxism, or ptyalism suggestive of gastric or duodenal ulceration. Gastroscopy reveals the presence of any ulcers and their extent and severity.

CLINICAL PATHOLOGY
There are few changes detected by routine hematological or serum biochemical examination of foals with colic that provide a definitive diagnosis. However, changes in the hemogram and serum biochemical profile are useful in evaluating the physiologic state of the foal and the severity of the disease. Principles used in the evaluation of these variables in adult horses apply to foals. It should be appreciated that the normal range of values for many clinical pathology variables in foals is age dependent and markedly different from that of adult horses.

Profound leukopenia is more likely to be indicative of enteritis and colic secondary to ileus than of small-intestinal strangulating obstructions. Similarly, hyponatremia is uncommon with strangulating obstructions but is a common finding in foals with enteritis.

Newborn foals with colic should have the adequacy of transfer of passive immunity examined by measurement of serum IgG concentration, or an equivalent test.

Examination of abdominal fluid is useful in the assessment of colic in foals, as it is in adults. The normal values for abdominal fluid in foals differs from that of adult horses and white cell counts greater than 1500 cells/μL (1.5×10 cells/L) should be considered abnormal.

NECROPSY FINDINGS
The findings on necropsy examination depend on the nature of the disease.

TREATMENT
The principles of treatment of foals with colic are the same as those for adult horses: relief of pain, correction of fluid and electrolyte abnormalities, and treatment of the underlying disease. In addition, foals with **FTPI** should receive plasma.

Foals with gastrointestinal disease that cannot eat may require **parenteral nutrition** to ensure adequate caloric intake.

Meconium impaction can be treated by administration of an enema of soap and warm water, commercial enema preparations, or acetylcysteine. Soap and water enemas can be administered at a rate of 5 mL/kg through a soft Foley catheter inserted into the rectum. **Acetylcysteine** (8 g in 200 mL of water with 20 g sodium bicarbonate) has the advantage of actually dissolving part of the meconium, enhancing passage of the meconium. Affected foals may require analgesics to control pain, intravenous fluids to correct or prevent dehydration, oral laxatives such as mineral oil (300 mL via nasogastric tube), and plasma to correct FTPI. Surgical correction of the impaction is rarely required.

Surgical Treatment
The proportion of foals surviving varies with the disease and age of the foal.[15] Younger foals (<6 months of age) appear to have a worse prognosis after surgical correction of intestinal lesions than do older foals. Fewer foals having surgery for colic live to race than do their normal cohorts, although affected foals that do race have similar racing careers.[1] Others have reported no adverse effect of surgical treatment for colic on surviving foals.[2] Foals with nonstrangulating lesions and enteritis are more likely to survive than foals with gastric ulcer disease or strangulating lesions. Suckling foals are at greatest risk of development of postoperative adhesions and need for repeated celiotomy.[1]

PREVENTION
Although not proven, the suspected association between diarrhea and small-intestinal surgical lesions in foals suggests that measures to reduce the incidence of enteritis in foals could reduce the incidence of colic. Adequate deworming programs that reduce or eliminate infestation with parasites should be implemented. Care should be taken when deworming foals with heavy infestations of *P. equorum,* as rapid killing or paralysis of the ascarids can lead to impaction and obstruction of the small intestine.[11]

Table 7-18 Differential diagnosis of common foal colics

Disease	History	Clinical findings	Clinical pathology	Treatment
Intestinal atresia or hypoganglionosis	White progeny of overo horses; Otherwise sporadic Newborn foals <4 days old	Failure to pass feces Abdominal distension pain	None specific	None
Small-intestinal volvulus	Any age but more common at 3–6 months; abrupt-onset abdominal pain; diarrhea	Severe pain; nasogastric reflux; abdominal distension Ultrasonography: distended, atonic intestine Radiography: gas and fluid distension of small bowel	Increased protein and leukocytes in abdominal fluid	Surgical; low survival rate
Small-intestinal intussusception	Any age, but usually 3–6 weeks; diarrhea	Severe pain, abrupt onset Nasogastric reflux Ultrasonography: intussusception Radiography: gas and fluid distension of small bowel	Increased protein and leukocytes in abdominal fluid	Surgery; 40% survival rate
Ascarid impaction	More than 3 months of age Recent history (<3 days) of anthelmintic administration	Severe pain; nasogastric reflux Ultrasonography: distended, atonic bowel, ascarids	Nonspecific	Medical therapy; lubricants and analgesics; surgery
Meconium impaction	Newborn; no passage of meconium; more common in males	Mild pain initially, becoming more severe; Abdominal distension Ultrasonography: distended large colon, may see impaction Radiography: contrast may outline impaction	Nonspecific	Warm soapy enemas Acetylcysteine; mineral oil orally; surgery for refractory cases
Large-colon torsion	Sporadic	Severe pain and abdominal distension Ultrasonography: gas-distended colon Radiography: gas-distended colon	Nonspecific	Surgery; 20% recovery rate
Large-colon impaction	Sporadic; poor diet, eating sand-polluted feed	Mild to moderate pain initially Progressive abdominal distension Ultrasonography: distended colon with impacted material	Nonspecific	Medical treatment of lubricants, fecal softeners and analgesics; surgery
Small-colon impaction	Common in Miniature horses	Moderate to marked pain Lack of feces; abdominal distension Ultrasonography: gas-distended colon Radiography: impaction of small colon	Nonspecific	Medical as previously; surgery
Gastroduodenal ulcer	Common in foals with other disease or stress	Usually clinically inapparent Colic, inappetence, teeth grinding, excessive salivation, diarrhea; gastroscopy diagnostic	None diagnostic	Antacids and antiulcer compounds (Table 7-20) Rarely surgery to correct gastric outflow obstruction

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GASTRIC DILATION IN THE HORSE

SYNOPSIS

Etiology Gastric outflow obstruction. Idiopathic. Ingestion of excess fluid or feedstuffs

Epidemiology Sporadic. No age, breed, or sex predilection

Clinical signs Colic. Reflux from nasogastric tube. Gastric rupture, acute severe peritonitis, and death

Clinical pathology Nondiagnostic. Inflammatory cells and ingesta in peritoneal fluid of horses with gastric rupture

Diagnostic confirmation Nasogastric reflux without other identifiable cause

Lesions Gastric dilatation. Gastric rupture with hemorrhage at margins of rupture

Treatment Gastric decompression. Treat underlying disease.

Control Prevent overeating. Control inciting diseases.

ETIOLOGY

Chronic gastric dilatation can be caused by the following:
- Outflow obstruction, such as cicatricial constriction of the pylorus secondary to gastroduodenal ulceration or pressure by a tumor
- Gastric atony in older horses or wind-sucking (aerophagic) horses

Acute gastric dilatation is associated with:

- Reflux of intestinal contents secondary to acute intestinal obstruction, e.g., anterior enteritis, small-intestinal strangulation, or ileus
- Ingestion of excess fluid or feedstuffs such as whey or grain
- Acute idiopathic dilatation after racing

EPIDEMIOLOGY

The incidence of gastric rupture, the most severe sequela to gastric dilatation, in horses with colic is approximately 5%, although in horses subjected to exploratory laparotomy the rate may be as high as 11%.[1] There is no detectable effect of age, breed, or season on the risk of gastric rupture. Risk factors for gastric dilatation include consumption of excess grain, although horses routinely fed grain are at lower risk, and ingestion of palatable fluids such as whey has been implicated. **Acute idiopathic dilatation** of the stomach occurs sporadically and is a common cause of gastric rupture, representing between 16% and 60% of cases of gastric rupture. **Chronic dilatation** secondary to pyloric obstruction caused by a tumor is a sporadic occurrence in older horses, whereas cicatricial obstruction secondary to gastroduodenal ulceration is more common in younger horses and those at risk of developing gastroduodenal ulcers.

Acute dilatation occurs secondarily to acute obstruction of the small intestine.

PATHOGENESIS

Acute obstruction of outflow from the stomach or aboral passage of ingesta and secretions through the small intestine results in gastric dilatation. This causes severe pain and signs of shock, including elevated heart rate, sweating, and delayed mucosal capillary refill time. Gastric rupture can occur within hours and death shortly thereafter. Chronic dilatation results from partial obstruction and delayed gastric emptying. The disease is more prolonged and clinical signs can be related to the primary disease.

The obstruction can be as aboral as the ileocecal valve. Gastric distension with fluid also occurs late in the course of impaction of the large or small colon. Horses with large-intestinal volvulus have accumulation of fluid in the proximal small intestine and stomach because of tension on the duodenocolic fold causing extramural compression of the duodenum.

Gastric distension causes severe pain and there is often dehydration and hypochloremia as a result of sequestration of gastric secretions. Experimental distension of the stomach of healthy horses with water increases the intraabdominal pressure from -2.7 cmH$_2$O (i.e., subatmospheric) to $+3.1$ cmH$_2$O after instillation of 20 L of water. Whether similar increases occur during gastric distension associated with gastrointestinal disease and its contribution to intraabdominal hypertension awaits clinical studies.[2]

Engorgement of a readily fermentable carbohydrate, such as wheat, glucose, or calf feeds, results in a syndrome characterized by shock, ileus, and laminitis. Gastric dilatation can occur secondary to grain engorgement, but the clinical signs of gastric dilatation are often masked by more severe signs secondary to endotoxemia.

CLINICAL FINDINGS

The clinical findings in gastric distension depend in large part on the underlying disease. However, horses with primary gastric distension have abdominal pain, often of 12 to 36 hours' duration, that progressively worsens. The heart and respiratory rates increase progressively as the distension worsens, and the horse may sweat and exhibit signs of increasingly severe abdominal pain. Paradoxically, some horses with gastric distension, especially the type that develops over several days or in horses recovering from intestinal surgery and being treated with analgesics, may not exhibit any but the most subtle signs until rupture of the stomach occurs.

Vomition in horses is very rare, is always associated with gastric distension, and is usually a terminal event.

In **grain engorgement dilatation** abdominal pain is usually severe. Dehydration and shock develop rapidly, often within 6 to 8 hours of ingestion of the grain, and can be severe. Death from gastric rupture can occur within 18 hours.

Passage of a nasogastric tube usually results in the evacuation of large quantities of foul-smelling fluid, except in cases of grain engorgement, in which the fluid is absorbed by the grain. However, significant and life-threatening gastric dilatation can be present even though there is no reflux through a nasogastric tube. If gastric dilatation is suspected then repeated, persistent efforts should be made to obtain reflux. The nasogastric tube should be left in situ until the disease has resolved.

Acute postrace dilatation occurring immediately after racing is accompanied by more serious and acute signs. There is abdominal distension, coughing, and dyspnea. Tympany is also detectable on percussion of the anterior abdomen and large amounts of foul-smelling gas, and usually fluid, are passed via the stomach tube. This immediately relieves the animal's distress.

In **chronic dilatation** there is anorexia; mild pain, which is either continuous or recurrent; scanty feces; and gradual loss of BW persisting for a period of months. Vomiting and bouts of pain may occur after feeding, but they are not usually severe. Dehydration may be present but is usually only of moderate degree.

The distended stomach cannot be palpated on **rectal examination**, but the presence of distended loops of small intestine should alert the clinician to the probability of gastric distension. Rupture of the stomach, or other viscus, is characterized during rectal examination by a negative pressure in the abdomen and the presence of particulate matter on the serosal surface of intestine.

Ultrasonographic examination will reveal a distended stomach containing large quantities of fluid or ingesta and can reveal evidence of the predisposing lesion, such as the presence of distended small intestine. **Radiographic examination**, with or without a barium meal, can be of diagnostic value in young animals with chronic outflow obstruction. **Gastroscopy** performed after the stomach has been emptied can reveal lesions consistent with obstructed outflow, such as gastric squamous cell carcinoma or pyloric abnormalities secondary to gastric ulcer disease in foals.

CLINICAL PATHOLOGY

Horses with severe gastric dilatation often, but not always, have slightly **low serum chloride concentrations**. Metabolic alkalosis, metabolic acidosis, or mixed disturbances can be present. Other abnormalities depend on the underlying disease.

Abdominal fluid of horses with gastric dilatation is normal, whereas that of horses with gastric rupture is characterized by an elevated total protein concentration (>2.5 g/dL, 25 g/L) and leukocyte count (>10,000 cells/µL, 10×10 cells/L) which is predominantly composed of degenerate neutrophils. Microscopic examination of the fluid reveals intracellular and extracellular bacteria and plant material.

NECROPSY FINDINGS

After grain engorgement in horses, the stomach is distended with a doughy, malodorous mass of ingesta. In acute gastric dilatation caused by other causes, the stomach is grossly distended with fluid and the wall shows patchy hemorrhages. Rupture, when it occurs, is usually along the greater curvature and results in gross contamination of the abdominal cavity with ingesta.

DIFFERENTIAL DIAGNOSIS

See Table 7-19.

TREATMENT

Relief of the gastric distension should be considered an **emergency** because gastric rupture invariably causes death. Passage of a nasogastric tube, important in diagnosing the accumulation of fluid within the stomach, also provides a means for relieving the distension. Repetition and persistence may be needed to relieve the gastric distension.

Table 7-19 Differential diagnosis of common equine colics

	Epidemiology and history	Clinical findings	Clinical pathology	Response to treatment
Acute gastric dilatation	Feeding on grain or whey; Outflow obstruction Lipoma at pylorus Reflux with proximal enteritis	Acute severe pain, gut sounds negative, rectal negative; voluminous reflux through nasogastric tube and relief of pain; regurgitation	Depends on underlying disease; no diagnostic changes	Good to relief of gastric distension; prognosis guarded and depends on underlying disease
Acute obstruction and infarction of small intestine	Sporadic	Acute, severe intractable pain, no gut sounds, rectal exam reveals distended loops of small intestine, tight bands of mesentery at 12 h; no feces after 12 h; nasogastric reflux	Hypovolemia; toxemia late in disease Packed cell volume (PCV) more than 50% after 12 h Blood-tinged peritoneal fluid	Pain intractable; surgical correction
Acute obstruction of large intestine	As previously	As previously except abdomen visibly distended; rectal exam impeded by large loops of distended large colon	As previously	As previously
Ileocecal valve impaction	Feed includes finely chopped oat straw, or sorghum, Sudan grass, coastal Bermuda grass; infestation with *Anoplocephala perfoliata*	Subacute pain for 24 h as small intestine descends; then as for small intestinal obstruction; impaction palpable rectally	PCV normal first 24 h No characteristic changes	Medical therapy initially, then surgery for refractory cases
Spasmodic/tympanic colic	Sporadic; increased incidence with poor worm control	Acute moderate pain but heart rate up to 80 Loud and gassy gut sounds; rectal exam and feces normal, recovers spontaneously, lasts only 1–2 h	Normal	Xylazine, detomidine, butorphanol, hyoscine all effective; mineral oil orally
Impaction of large intestine	Old horse, debilitated, poor teeth, indigestible feed; inadequate access to water; excessive consumption of low-energy grass	Moderate pain, depressed or absent gut sounds, rectally long columns of dry hard fecal material, distinct from individual balls	Normal	Responds well to standard analgesics, mineral oil, fecal softeners, and fluid therapy
Verminous mesenteric arteritis (thromboembolic colic)	Poor worm control; rare	Subacute pain continues for 3–4 days; no gut sounds; rectally slightly distended loops; paralytic ileus	Slight leukocytosis and shift to left Paracentesis yields bloody fluid	Irreversible even if surgery performed Prevention includes adequate parasite control
Enteroliths, colonic foreign bodies, phytobezoars	Endemic in some areas	Subacute or recurrent colic of moderate severity only; masses palpable in small colon	No changes	Surgery only
Subacute obstruction of small intestine (adhesions, neoplasm, idiopathic muscular hypertrophy of ileum, etc.*	History of recurrent moderate or persistent mild colic	Moderate pain; distended loops of small intestine on rectal exam; point of obstruction may be palpable; gut sounds normal to loud	No changes	Excellent to surgery
Sand colic	Access to polluted feed; grazing on sandy country when feed sparse; salt deficiency or boredom leading to soil eating or licking	May be severe pain with acute impaction or chronic mild pain, often with intermittent bouts of diarrhea; may palpate impacted loops containing sand; auscultate sand in ventral abdomen; radiography; ultrasonography	Normal; mixture of feces and water allowed to stand shows heavy sand sediment	Analgesia and psyllium orally; prevent ingestion of sand
Flatulent colic	Mostly on succulent green feed Some secondary to physical obstruction of large intestine	Severe acute pain; visibly distended abdomen Loud gut sounds present early; rectal exam difficult because of size of loops	Not recorded	Trocarization through right flank or exploratory laparotomy if time and analgesia not successful

Table 7-19 Differential diagnosis of common equine colics—cont'd

	Epidemiology and history	Clinical findings	Clinical pathology	Response to treatment
Dorsal displacement left colon (nephrosplenic ligament entrapment)	Sporadic	Intractable moderate pain continues for days Pelvic flexure of colon missing, spleen displaced medially	No changes No changes	Rolling of anesthetized patient to replace colon very successful; jogging with or without administration of phenylephrine
Small intestine or colon strangulation by lipoma	Only horses older than 10 years Sudden onset	Sudden onset moderate pain without toxemia May be palpable per rectum	No changes	Surgery

The clinical picture varies with time: descriptions relate to clinical signs at 12–24 h of illness.
*Chronic intussusception, terminal ileal hypertrophy, constructive adhesions, Meckel's diverticulum, and fibroma at the root of the mesentery.

Passage of the nasogastric tube through the cardia can be difficult in horses with gastric distension. Blowing into the tube to dilate the esophagus or instillation of lidocaine (20 mL of 2% solution) can facilitate passage of the tube. If there is no spontaneous reflux of material, a siphon should be formed by filling the tube with 500 mL of water and rapidly lowering the end of the tube below the level of the horse's stomach. The nasogastric tube should be left in place until there are no longer clinically significant quantities of reflux (1–2 L every 3 hours for an adult 425-kg horse).

Gastric dilatation caused by overeating of grain, bread, or similar material may be impossible to resolve through a nasogastric tube because of the consistency of the material. Gastric lavage using water or isotonic saline administered through a large-bore nasogastric tube may aid in removal of inspissated ingesta. Surgical decompression may be attempted in refractory cases, but is technically demanding because of the position of the stomach in the adult horse.

The underlying disease should be treated to restore normal gastric emptying or stop reflux from the small intestine. Supportive therapy, including restoration of hydration and normal electrolyte and acid-base status, should be provided (see Chapter 5). Horses at risk of inhalation pneumonia should be treated with broad-spectrum antibiotics for at least 3 days.

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GASTRIC IMPACTION IN HORSES

Primary gastric impaction is a usual primary cause of colic in adult horses, comprising approximately 1.4% of 857 colic cases in one report and 20 of 653 (3.0%) horses with colic and 20/6097 admissions (0.3%) in another.[1,2] The case–fatality rate is 10% to 50%.[1,2] There does not appear to be a breed or gender predisposition, and the disease occurs in mature horses.[2]

The etiology of gastric impaction is unclear in most cases, with poor dentition, rapid food intake, inadequate intake of water, and abnormal gastric motility being mooted as causes of the disease.[1] Gastric impaction occurs secondary to hepatic fibrosis and insufficiency associated with poisoning with *Senecio jacobaea.*[3] Ingestion of persimmon (*Diospyros virginiana*) causes gastric impaction, ulceration, and rupture in horses because of the formation of phytobezoars.[4] Ingestion of thorn apple (*Datura stramonium* and other species of *Datura*) cause colic and acute gastric rupture in horses.[5] For cases of undetermined cause, there is usually a history of a diet of mature grass, alfalfa hay, corn, sorghum fodder, or ensilage. Other causes include insufficient access to water, poor teeth causing poor digestion, or the atony of old age. Some affected horses have histologic abnormalities of the stomach or intestine, but the clinical importance of these lesions in development of the disease is unclear.[1,2]

Horses can present with acute, chronic, or recurrent colic. Horses with acute disease usually have clinical signs of <3 days' duration, and half have had previous episodes of colic.[2] The most common clinical sign is inappetence with or without colic.[1,2] Heart rate and respiratory rate are usually not markedly elevated and rectal examination does not reveal diagnostic abnormalities. If the stomach has ruptured, there will be signs of septic peritonitis with toxemia and cardiovascular compromise including sweating, tachycardia, delayed mucous membrane capillary refill time, and discolored mucous membranes. Signs of long-term (chronic) disease include weight loss; intermittent colic; anorexia; dullness; and passage of small amounts of hard, dry feces.

Gastroscopy confirms the diagnosis by visualization of large amounts of ingesta in the stomach or phytobezoars, although visualization of the stomach is impaired by the presence of large quantities of ingesta causing the impaction. At exploratory laparotomy the stomach is enlarged with dry, fibrous feed material but is not grossly or acutely distended, and the intestines are relatively empty.

Clinicopathologic examination commonly reveals leucopenia and hyperfibrinogenemia,[1,2] although these findings are not consistent and present in every case.

Treatment includes restoration of normal hydration, which can aid in passage of the impaction. Judicious administration of lubricants (mineral oil) or osmotic cathartics (magnesium sulfate and sodium sulfate) or water might aid in softening the impaction. Phytobezoars associated with ingestion of persimmon can be treated medically by the administration of fluids (intravenous or, if tolerated, oral), intragastric administration of cola or diet cola beverages, and feeding of pelleted food.[4] Analgesia should be provided as needed preferably by use of drugs that do not inhibit gastrointestinal motility. Exploratory laparotomy with gastrotomy and removal of the impacted material might be required in a small proportion of cases.[1,2,6] Rupture of the stomach can occur and is invariably fatal.[1]

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GASTRIC (GASTRODUODENAL) ULCER IN FOALS

SYNOPSIS
Etiology Unknown in most cases
Epidemiology Foals from 1 day of age; 50% of normal foals have gastric mucosal ulceration. Clinical disease in 0.5% of foals. More severe ulceration in stressed foals or foals with other diseases
Clinical signs None in most foals. Teeth grinding, excessive salivation, colic, diarrhea, inappetence, and weight loss. Ulcers in glandular mucosa are considered most clinically important. Sudden death with perforation. Ulcers present on gastroduodenoscopy
Clinical pathology Nondiagnostic
Lesions Gastric mucosal ulceration, duodenal ulceration and stenosis, and esophagitis. Peracute septic peritonitis
Diagnostic confirmation Gastroscopic demonstration of ulcers in foals with appropriate clinical signs
Treatment Treatment should be reserved for foals with clinically important disease. Ranitidine 6.6 mg/kg, orally every 8 to 12 h, *or* cimetidine 6.6 to 20 mg/kg orally or intravenously every 6 h, *or* omeprazole 1 to 4 mg/kg orally or intravenously every 24 h
Control Minimize occurrence of inciting or exacerbating diseases. Do not administer antiulcer medications as prophylaxis.

Gastroduodenal ulcer disease in young equids has a variety of manifestations. Disease in neonates is characterized by ulceration of the glandular mucosa and occurs in foals that have other disease or are exposed to physiologically important stressors. Disease in suckling foals occurs in either or both of the squamous and glandular mucosa of the stomach and/or the duodenal mucosa. The disease in this age group can progress to scarring of the gastric outflow tract with subsequent gastritis, dysphagia, and esophageal ulceration leading to inappetence, ptyalism, and death. Disease in weanlings usually affects the gastric squamous mucosa. There is no evidence that the widespread occurrence of lesions of the gastric squamous mucosa is clinically important in weanlings.[1]

ETIOLOGY

There is no established etiology, although there is an association with stress (see later). There is no evidence of an infectious etiology, for instance, *Helicobacter* sp., in the development of ulcers in neonates or suckling or weanling foals. Nonsteroidal medications administered above recommended doses can induce gastroduodenal ulceration.

There is no evidence that at recommended therapeutic doses they are a common cause of gastric ulcers.[2]

EPIDEMIOLOGY
Occurrence
Gastric ulcers are reported in foals in North America, Europe, and Australia and probably occur worldwide. The **prevalence** of erosion and ulcers of the gastric glandular and nonglandular mucosa, detected by gastroscopic examination, averages 50% in foals less than 2 months of age that do not have signs of gastric ulcer disease.[3] Lesions of the squamous mucosa are present in 45% of foals, whereas lesions in the glandular mucosa occur in fewer than 10% of foals less than 4 months of age. Fifty percent of asymptomatic weanling foals (5–7.5 months of age) have gastric mucosal lesions evident on gastroscopy.[1]

Ulceration of the gastric and/or duodenal mucosa is evident in 22% (155 of 691) of foals at necropsy examination.[4] The study was performed at a referral institution, and the foals were examined as a result of their death or euthanasia at that institution. The relevance of these results to asymptomatic foals or foals that recovered from their illness is unknown. Foals examined were all less than 6 months of age and lesions were most common in the nonglandular gastric mucosa (70 of 155 foals). Twenty-five of 155 foals had lesions only in the glandular mucosa, 25 had lesions in both glandular and nonglandular mucosa, and 20 had lesions in both squamous and duodenal mucosa. There was no association of age with lesion distribution or prevalence.[4] Gastric ulcers were significantly associated with the presence of other gastrointestinal disease, but not with the presence of any other disease category.

Disease attributable to gastric or duodenal ulcers occurs in approximately 0.5% of foals, although the prevalence is greater in foals with comorbid diseases such as pneumonia and septicemia.

Estimates of case–fatality rate are not available for any of the forms of gastroduodenal ulcer disease in foals.

Risk Factors
Age and Sex
Age is an important risk factor for ulceration of the squamous epithelium, with 88% of foals less than 9 days of age affected compared with 30% of foals more than 70 days of age. These estimates should be considered with caution, because findings considered as lesions in earlier studies (desquamation [sheeting] of the squamous mucosa) are not now considered to be abnormal or indicative of disease.[4] Gastric lesions occur in fewer than 10% of foals over 90 days of age. There does not appear to be an effect of age on the prevalence of ulceration of the gastric glandular mucosa, which is considered a much more clinically significant lesion.

There is no effect of **gender** on the prevalence of ulcers.

Stress and Disease
Stress and disease are important risk factors for development of ulcers of the glandular mucosa. Lesions of the gastric glandular mucosa occur in 27% of foals with another disease but in 3% of otherwise healthy foals.

PATHOGENESIS
The pathogenesis of gastric ulceration in foals has not been definitively determined and much is extrapolated from the disease in humans and other animals. It is assumed that ulcers occur because of an imbalance between the erosive capability of the **low gastric pH** and the **protective mechanisms** of the gastric mucosa. Low gastric pH was considered essential for the development of a gastric ulcer, but there is less certainty about this now that it is recognized that critically ill foals, and especially those that are premature or recumbent, often have high (less acid to alkaline) and highly variable gastric pH.[5] Additionally, administration of omeprazole to weanlings is effective in reducing the prevalence of lesions of the gastric squamous mucosa but might worsen lesions of the glandular mucosa.[1]

The conventional wisdom is that preservation of adequate mucosal blood flow and the presence of an intact, bicarbonate-rich layer of mucus over the epithelium are essential to maintaining the resistance of the epithelium to digestion by gastric acid and pepsin. Mucosal blood flow and bicarbonate secretion into the protective mucous layer are dependent in part on normal prostaglandin E concentrations in the mucosa. Factors that inhibit prostaglandin E production, such as NSAIDs and ischemia, could contribute to the development of ulcers. Trauma to the gastric epithelium can disrupt the protective layer and allow an ulcer to develop, as can the presence of compounds in duodenal fluid, such as bile salts that intermittently reflux into the stomach of normal foals.

Normal foals develop the capacity for secretion of gastric acid and the ability to achieve gastric pH less than 4 within 1 to 2 days of birth. Ingestion of milk increases gastric pH, and it is a generally held belief that frequent ingestion of milk provides a protective effect against the adverse effects of low pH on gastric mucosa. However, the development of gastric lesions in foals is not solely a result of prolonged exposure to low pH, although this might be a necessary factor, because ill neonatal foals that are at high risk of gastric erosion or ulceration have gastric pH that is often greater than 5 to 6.[3] The elevated pH, which can be alkaline in severely ill foals at greatest risk of death, is not consistent with development of gastric lesions.

Most ulcers do not produce clinical signs. **Severe ulceration** is associated with delayed gastric emptying, gastric distension, gastroesophageal reflux, and subsequent reflux esophagitis and pain. Ulcers can perforate the stomach wall and cause a peracute, septic peritonitis or erode into a large blood vessel with subsequent hemorrhage and occasional exsanguination. Ulcers and the attendant inflammation and pain might cause gastroparesis and delay gastric emptying, and chronic lesions can result in both functional and physical obstructions to gastric emptying with subsequent gastric dilatation and reflux esophagitis.

CLINICAL FINDINGS

There are six syndromes associated with gastroduodenal ulcers in foals[3]:

1. Ulceration or epithelial desquamation of the squamous mucosa of the greater curvature and area adjacent to the margo plicatus. These lesions are very common in foals less than 60 days of age and usually do not cause clinical signs. The lesions heal without treatment and are now considered variations of normal.[4]
2. Ulceration of the squamous epithelium of the lesser curvature and fundus. This is more common in older foals (>60 days) and is sometimes associated with clinical signs including diarrhea, inappetence, and colic.
3. Ulceration of the glandular mucosa, sometimes extending into the pylorus. This lesion occurs in foals of any age and is most common in foals with a comorbid disease. Clinical signs caused by the ulcer can be severe and include teeth grinding, excessive salivation, inappetence, colic, and diarrhea. There is often reflux esophagitis.
4. Gastric outflow obstruction caused by pyloric or duodenal stricture secondary to pyloric or duodenal ulceration. This occurs in 2- to 5-month-old foals and is evident as colic, inappetence, weight loss, gastric dilatation, gastroesophageal reflux, excessive salivation, and teeth grinding.
5. Peracute peritonitis secondary to gastric perforation. This usually occurs in foals that do not have a history of signs of gastric ulceration. Clinical signs include unexpected death, shock, dehydration, sweating, and an increased respiratory rate.
6. Hemorrhagic shock secondary to blood loss into the gastrointestinal tract from a bleeding gastric ulcer. This is an unusual presentation.
7. The typical signs of gastric ulcers in foals include depression, teeth grinding, excessive salivation, and abdominal pain that can range in intensity from very mild to acute and severe, similar to that of a foal with an acute intestinal accident. Diarrhea, with or without mild to moderate abdominal pain, is often associated with gastric ulcer disease in foals. Treatment with antiulcer drugs is sometimes associated with resolution of diarrhea and signs of gastric ulcer disease. There might be pain evinced by deep palpation of the cranial abdomen, but this is not a reliable diagnostic sign.

Definitive diagnosis is provided by **gastroscopic examination**. The endoscope should be 2 m in length, although a 1-m endoscope might allow partial examination of the stomach of young or small foals. Diameter of the endoscope should be less than 1 cm. Foals can usually be examined without sedation, although sedation might facilitate examination in larger or fractious foals. Ideally, older foals should have food withheld for 12 hours before the examination but this might not be necessary or advisable in sick foals. Young foals (those relying on milk intake for their caloric needs) should have food withheld for 1 to 2 hours. Adequate examination of the nonglandular stomach can usually be achieved without fasting, especially in younger foals, but thorough examination of the glandular mucosa and pylorus requires fasting.

Nasogastric intubation might cause pain and cause affected foals to gag. Foals with gastric outflow obstruction, caused either by pyloric or duodenal stricture or by gastroparesis, will have reflux of material through a nasogastric tube.

Contrast **radiographic** examination is useful in defining gastric outflow obstruction and can demonstrate filling defects in the gastric wall that are consistent with ulcers. The principal use of radiography is to establish delays in gastric emptying. Normal foals have complete emptying of barium sulfate (10–20 mL/kg BW administered through a nasoesophageal or nasogastric tube) from the stomach within 2 hours of administration. Gastric ulcers are occasionally apparent as filling defects, but contrast radiography is not sufficiently sensitive to justify its routine use for diagnosis of gastric ulceration.

CLINICAL PATHOLOGY

There are no diagnostic changes in the hemogram or serum biochemical profile. Serum pepsinogen values are of no use in diagnosing gastric ulcers in foals. Testing for fecal occult blood is not sensitive to or specific for gastric ulceration in foals. Foals with perforation of the stomach have changes consistent with septic peritonitis. Measurement of an isoform of α1-antitrypsin in serum is reported to be sensitive and specific for detection of gastric ulcers in foals, but these results have not been validated and the test is not widely available.[6]

NECROPSY FINDINGS

Gastric ulcers and erosions are common findings in foals dying of unrelated disease and their presence should not be overinterpreted.[4] The gross characteristics of the gastric lesions were described earlier. Foals dying of gastric ulcer disease do so from peracute diffuse peritonitis, exsanguination, or starvation secondary to the gastric outflow obstruction.

DIAGNOSTIC CONFIRMATION

The combination of compatible clinical signs, endoscopic demonstration of gastric ulcers, a favorable response to antacid therapy, and the elimination of other diseases permits a diagnosis of gastric ulcer disease.

> **DIFFERENTIAL DIAGNOSIS**
>
> The combination of teeth grinding, excessive salivation, depression, inappetence, and colic in foals is virtually diagnostic of gastric ulcer disease. Other causes of colic in foals are listed in Table 7-17.

TREATMENT

Treatment of clinically important gastric ulcer disease must be differentiated from prophylaxis of animals considered to be at high risk of disease or those in which lesions have been detected incidentally. The principles of treatment of clinically important gastroduodenal ulcer disease in foals include the following:

- Promotion of healing by reducing gastric acidity and enhancing mucosal protection
- Enhancement of gastric emptying
- Provision of nutritional and metabolic support
- Treatment of comorbid disease

Reduction of gastric acidity is achieved by the administration of one of several drugs that reduce secretion of gastric acid and increase gastric pH (Table 7-20). These drugs are either histamine type 2 (H_2) receptor antagonists or inhibitors of the proton pump in the gastric parietal cells. Administration of ranitidine (6.6 mg/kg orally every 8 hour) effectively increases gastric pH in normal neonatal foals but does not affect gastric pH in hospitalized neonates.[3] Omeprazole (4 mg/kg orally every 24 hours), a proton pump inhibitor, increases gastric pH within 2 hours of administration and for 24 hours in clinically normal neonatal foals and in clinically ill neonatal foals.[7] Omeprazole enhances healing of spontaneous ulcers in foals older than 28 days and is usually considered not to have important or frequent adverse effects. However, recent evidence suggests that administration of omeprazole to clinically normal weanlings is associated with increased severity of lesions in the glandular mucosa.[1]

Sucralfate is used to provide protection of denuded gastric epithelium, although its

Table 7-20 Drugs used in the treatment of *clinically important* gastroduodenal ulcer disease of foals and adult horses and recommendations for treatment (not prophylaxis)

Drug class	Drug	Dose, route, and frequency	Comments
H$_2$-antagonists	Cimetidine	6.6–20 mg/kg PO every 6 h	Potent acid suppression; short elimination half-life necessitates frequent administration Preferably use at the higher dose rate
	Cimetidine	6.6 mg/kg IV every 6 h	Rapid and potent acid suppression; use when oral administration is not feasible or rapid effect is required
	Ranitidine	0.9–2.0 mg/kg IV or 6.6–8.8 mg/kg PO every 8–12 h	Potent acid suppression and rapid resolution of clinical signs
Proton pump inhibitor	Omeprazole	4 mg/kg PO as paste every 24 h	Potent, rapid onset and long-lasting acid suppression
	Pantoprazole	1.5 mg/kg IV every 12–24 h	Potent acid suppression in foals
Protectants	Sucralfate	40 mg/kg PO every 6 h	Can be given at the same time as inhibitors of acid secretion
Prostaglandin analogs	Misoprostol	5 µg/kg PO every 12 h	Causes diarrhea and mild colic Effective as a prophylactic for NSAID-induced ulcers in humans but minimal efficacy in enhancing healing of existing ulcers
Antacids	Aluminum hydroxide	1–2 g PO every 4–6 h	Ineffective; do not use
	Magnesium hydroxide	1–2 g PO every 4–6 h	Ineffective; do not use
	Calcium carbonate	1–2 g PO every 4–6 h	Ineffective; do not use
Promotility agents	Bethanechol	0.025 mg/kg SC every 6 h	Enhances gastric motility with minimally increased gastric acid secretion; used to treat gastroparesis; contraindicated if physical outflow obstruction exists

H$_2$, histamine type 2 receptor; IV, intravenously; NSAID, nonsteroidal antiinflammatory drug; PO, orally; SC, subcutaneously.

efficacy in preventing lesions or enhancing healing of existing lesions in foals with spontaneous disease is doubted.

A common **treatment protocol** involves administration of an H$_2$ antagonist or omeprazole. Treatment should begin as soon as the presence of a clinically relevant ulcer is suspected and should continue for at least 1 week after the resolution of clinical signs or until there is endoscopic confirmation of healing. Foals are often treated for 2 to 6 weeks.

Foals with gastroparesis secondary to severe gastroduodenal ulceration or gastritis can benefit from the administration of bethanechol (see Table 7-20) to increase gastric motility and enhance gastric emptying. Surgical bypass of pyloric or duodenal strictures can be necessary in foals with physical obstructions to gastric emptying, and when performed by experienced surgeons have a reasonable (>50%) prognosis for recovery and survival to discharge from hospital.[8]

Nonsteroidal antiinflammatory drugs such as phenylbutazone or flunixin meglumine are ulcerogenic at high doses and should be used sparingly and at recommended doses in sick foals. There is no evidence that these compounds predispose or cause gastric ulcers when used at the recommended dose rate.[2] It would be prudent to minimize their use in foals with gastric or duodenal ulcers.

Nutritional and metabolic support should be provided as necessary to foals that are unable to eat or drink or that have abnormalities of fluid and electrolyte status.

CONTROL

Control of diseases that predispose foals to gastroduodenal ulcer might reduce the incidence or severity of ulcer disease. Prophylactic treatment of sick or stressed foals with H$_2$ antagonists, sucralfate, or omeprazole is widely practiced but has been questioned because the efficacy of pharmacologic prophylaxis in prevention of disease or death caused by gastric ulceration has not been demonstrated.[9] Indeed, suppression of gastric acidity (increasing gastric pH) in either sick or normal foals might be unwise because of the protective effect of low gastric pH on gastric colonization of bacteria. Foals in an intensive care unit administered acid suppressive medication were 2.0 (95% CI 1.4–2.9) times as likely to develop diarrhea as those not administered these drugs.[9] Furthermore, the presence of detected ulcers was not different between foals administered antiulcer medication (15%) and those not administered these medications (21%).[9]

Administration of omeprazole to clinically normal weanlings is not recommended at this time.[1] Body condition score and BW of weanlings was not improved by administration of omeprazole, despite a reduction in prevalence of lesions in the squamous mucosa, and was associated with an increase in severity of lesions in the glandular mucosa.[1]

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GASTRIC ULCER IN ADULT HORSES

Ulceration of the esophageal, gastric squamous, gastric glandular, or duodenal mucosa, either alone or in various combinations, occurs in adult horses. This constellation of lesions has been labeled the equine gastric ulcer syndrome (EGUS).[1] However, this label does not provide sufficient granularity to descriptions of the syndrome, which is composed of a variety of diseases each with its own etiology and pathogenesis, to permit focused discussion of the risk factors, etiology, prognosis, and treatment of each disease.[1,2] For instance, ulceration and gastritis of the gastric squamous mucosa associated with intense training programs has a different presentation and etiology from ulceration of the gastric glandular mucosa caused by injudicious use of NSAIDs. The etiopathogenesis of lesions of the gastric squamous mucosa might well differ from that of lesions of the glandular mucosa; therefore the presence and severity of lesions in each site should be specified.[2,3] Furthermore, it is likely that optimal treatment of lesions of the squamous mucosa differs from that of lesions of the glandular mucosa.

There is not sufficient information to warrant a separate description of each disease (with the exception of NSAID toxicosis). For this reason, the syndrome is described rather than having separate discussions of each disease or circumstances in which the disease occurs. However, there are differences among the various diseases and the discussion should be interpreted in that light.

ETIOLOGY

The etiology of the most common occurrence of gastric ulcers in the horse is unknown but several risk factors have been identified, which are described in the section Epidemiology.

SYNOPSIS

Etiology Unknown in most cases. Nonsteroidal antiinflammatory drug intoxication. Not associated with *Helicobacter* sp. infection

Epidemiology Common in horses in intense training programs and used in competitive endeavors such as Thoroughbred, Standardbred, and Quarter horses in racing or training and horses used for endurance racing. Common in horses with colic, but clinical importance in most cases is unclear. Associated with periods of feed deprivation or intermittent feeding, such as can occur with stabling or housing on dirt lots

Clinical signs None in most horses. Poor appetite, failure to bloom, and mild colic in some horses. Ulcers or erosions present on gastroduodenoscopy

Clinical pathology Nondiagnostic. Sucrose absorption test has potential utility.

Necropsy lesions Gastritis and/or gastric ulceration, which is rarely a cause of death

Diagnostic confirmation Gastroscopic demonstration of ulcers

Treatment Omeprazole 1 to 4 mg/kg orally once daily. Ranitidine and cimetidine are used but are less efficacious and convenient.

Control Minimize risk factors, including confinement and intermittent feeding. Prolonged administration of omeprazole to at-risk horses

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Individual cases of gastric ulcers are associated with parasitic gastritis, such as in horses infested with *Gasterophilus* spp. and *H. megastoma* larvae. Tumors of the stomach, such as gastric squamous cell carcinoma or lymphosarcoma, cause ulceration of the gastric mucosa. Gastric phytobezoars and persimmon seeds (*D. virginiana*) have been associated with gastric impaction, ulceration, and perforation of the glandular portion of the stomach of a horse.[4] Administration of NSAIDs at recommended dosages is not associated with increased risk of gastric ulcers.[5]

There is only weak evidence that infection by *Helicobacter* spp. or similar organisms are associated with gastric ulcer disease in horses.[5,7] A convenience sample of 20 racehorses euthanized because of fractures of the limb during racing revealed that 18 (90%) had lesions of either or both of ulceration of the gastric mucosa or gastritis.[7] Spiral-shaped bacteria were detected in lesions in two of the seven horses with ulcers, four of seven animals with gastritis, and five of six horses with both lesions. *Helicobacter* DNA was detected by PCR in a similar proportion of lesions and in one of the two horses that did not have lesions. Importantly, this study demonstrated the presence of the bacterium but not its causal role in the disease; it might be that similar proportions of horses that do not have gastric lesions are infected. A study of 63 horses slaughtered for human consumption revealed gastric mucosal lesions in 36 but no evidence of infection by *Helicobacter* spp. demonstrated by urease or fluorescence in situ hybridization testing.[5] There is at present no convincing evidence for a role of *Helicobacter* spp. infection in the etiopathogenesis of gastric ulcer disease in horses. However, further studies that clearly define the disease being studied are needed.

EPIDEMIOLOGY
Occurrence

The occurrence of gastric ulceration is detected by either postmortem examination or gastroscopic examination. The frequency with which gastric ulcers are detected depends on the method of examination, the group of horses examined, and the reasons for examining them. It is not uncommon for studies of large numbers of horses (>100) to report prevalence of gastric ulcers equal to or greater than 80%, although this is not universal.[8,9] Studies reporting on incidence of gastric ulceration in horses with clinical abnormalities or at necropsy revealed a high frequency of gastric lesions in horses with colic (49%).[10] More recent studies have examined large numbers of horses without clinical signs of gastric ulcer disease but from populations at risk and have demonstrated a high prevalence in horses undertaking strenuous exercise on a regular basis.[9,11-13]

Gastric ulcer disease in horses is a recently recognized disease, with most reports originating after 1990 and coinciding with the widespread availability of endoscopes of sufficient length to permit examination of the stomach of adult horses. However, a longitudinal study of horses submitted for postmortem examination in Sweden demonstrated that horses have been affected with gastric ulcers since 1924.[14]

The condition is common in racehorses and other breeds of horse used for athletic events, and this population represents the most important occurrence of the disease. That said, less active horses and horses on pasture can be affected and with relatively high prevalence.[3,11,15,16] Broodmares on pasture can have a high prevalence of gastric ulcers (71%, 44 of 62 horses examined) with 42 of the 44 affected horses having ulcers only in the squamous mucosa.[16] There was no difference in prevalence of ulcers between pregnant and nonpregnant mares or between pregnant and recently foaled mares.[16] The presence of ulcers was not correlated with the weight of foals or placenta, raising the issue of the clinical importance of the presence of the ulcers. Over 60% of a nonrandom selection of horses kept on pasture in Denmark had gastric ulcer lesions ≥2.[3]

Thoroughbred and Standardbred horses in training or racing have a high prevalence of gastric lesions.[8,9,11,12] Gastroscopic studies of convenience samples of clinically normal Thoroughbred racehorses in training reveal a prevalence of lesions of the gastric mucosa of 82% to 93%. Gastric lesions are detected in 52% to 87% of Standardbred horses in training and actively racing.[9] Postmortem examination of Thoroughbred racehorses in Hong Kong, where many horses that retire from racing are examined postmortem, reveals a prevalence of gastric lesions of 66%, with the prevalence increasing to 80% when only horses that had raced recently were considered. Among racehorses selected for gastroscopic examination because of clinical abnormalities, including inappetence, failure to race to expectation, poor hair coat, or poor body condition, lesions of the gastric mucosa were detected in 86% to 90%.[14]

Lesions of the gastric mucosa occur in approximately 80% of **endurance horses** between racing seasons and in over 90% during racing.[13] Gastric lesions were present in 58% of **show horses** that had competed in the 30 days before gastroscopic examination.[14]

Lesions of the Squamous Versus Glandular Mucosa

The frequency of ulcers of the squamous mucosa is usually, but not invariably,[17] greater than that of ulcers of the glandular mucosa with many horses having lesions at both sites. For example, of 201 horses of various breeds and uses examined in Denmark, 43% had lesions of both glandular and nonglandular gastric mucosa, 15% had lesions of only the glandular mucosa, and 26% had lesions of only the nonglandular mucosa.[3] The majority (86%) of severe lesions (greater than or equal to grade 2, using a simplified grading system) were in the squamous mucosa. Most lesions are located adjacent to the margo plicatus. Lesions of the glandular mucosa are *considered* to be of greater clinical importance than are lesions of the squamous mucosa, although severe lesions (EGUS > 2) of the squamous mucosa are *considered* clinically important. However, clear evidence of the importance of ulcers at either site, or of the relative

importance of ulcers of varying severity, is lacking.

Risk Factors

Risk factors for gastric lesions in horses include being in training for an athletic event, exercise and the amount of time exercising, and colic. Suspected risk factors include the disposition of the horse (nervous horses are at greater risk),[17] diet, feeding practices, housing (pasture versus stall), stress (although the definition of stress is often not clear), and administration of NSAIDs such as phenylbutazone. Although each of these risk factors can be considered separately, it is likely that many are related and act in concert to increase the risk of development of lesions of the gastric mucosa. For instance, being in training often coincides with confined housing, intermittent feeding, daily bouts of strenuous exercise, and administration of NSAIDs. The combination of these factors, even without NSAID administration, reliably induces ulcers in Thoroughbred racehorses. Young horses (2 years old) that had arrived at the track within the month before first gastroscopic examination had a marked increase in severity of lesions at the time of a second gastroscopic examination 1 month later.

Animal Risk Factors

Among adult horses, age and gender are the only weak risk factors, if at all, for presence of gastric lesions.[17] Gastric lesions tend to be more severe in older horses. Among Standardbred racehorses, trotters are twice as likely as pacers to have gastric lesions. Horses with gastric lesions are more likely to have a nervous disposition, exacerbated stress hormone response to novel stimuli, and to paw more frequently.[17] Nonsteroidal antiinflammatory drugs are ulcerogenic at high doses and often administered to horses in training. The impact of NSAIDs on gastric permeability varies among drugs,[19] although the risk of any NSAIDs causing gastric ulcers at doses effective for treatment of musculoskeletal pain appears to be minimal.[5] Furthermore, among Thoroughbred racehorses there is no clear association between administration of these drugs and the risk of having gastric lesions.[14,17]

Colic is associated with presence of gastric lesions, although a cause and effect relationship is often not clear in individual cases. In a series of 111 horses with clinical evidence of abdominal discomfort of varying duration and severity, 91 had endoscopic evidence of gastric ulceration. Other abnormalities of the gastrointestinal tract or abdominal viscera were not found in 57 of the 91 horses with gastric ulcers. Thus gastric ulceration was the primary cause of colic, based on lack of concurrent abnormalities, clinical response to treatment with H_2 antagonists, and confirmation of improvement or resolution of gastric ulceration by endoscopy. However,

34 of the 91 horses with gastric ulceration had concurrent abnormalities of the gastrointestinal tract, demonstrating that gastric lesions can develop in horses with colic. Thus colic can cause gastric lesions and gastric ulcers can cause colic.

Management and Environmental Risk Factors

Racehorses in **training** have a higher prevalence of ulcers than do racehorses that are spelling (not in active training), and horses that are racing regularly have a higher prevalence than resting horses or horses in training but not racing. Standardbred racehorses in training are 2.2 times more likely to have gastric lesions, and those racing regularly are 9.3 times more likely to have gastric lesions, than are horses not training or racing. Increasing time in training is associated with greater severity of gastric lesions in Thoroughbred racehorses.[20] Although, as discussed previously, many factors can contribute to the likelihood of a horse having gastric lesions, such as exercise. This is probably because of the increase in intragastric pressure and decrease in pH in the proximal (nonglandular) stomach that occurs during exercise.

Feed withholding causes gastric ulcers in horses, probably because of the lack of buffering of acid produced during periods when the stomach is empty. It is likely that the intermittent access to feed that occurs in many stables results in periods of time during each day when horses do not have feed within the stomach. The loss of buffering is caused by lack of feed material in the stomach and by decreased production of saliva, which normally buffers gastric acid. Intragastric pH declines during periods of feed withholding in horses, which provides an explanation for the mechanism of increased acid exposure as a consequence of management practices.[21] Horses grazing on pasture eat frequently and have food in the stomach almost all the time.

Diet is suggested to be a risk factor for development of gastric ulcers, but definitive studies are lacking. Horses in training for racing are usually fed diets high in concentrated rations, and this is suspected to predispose these horses to gastric ulcers. Feeding of alfalfa hay and grain was associated with fewer gastric lesions in six research horses than was feeding brome grass hay.

Confinement to stalls is associated with an increased prevalence of gastric lesions, although lesions do occur frequently in some groups of horses kept on pasture. Although horses with gastric lesions during confinement have healing of these lesions when they are pastured, this change is not explained by a higher pH in horses on pasture.[15] Horses on pasture do not have a higher pH of the proximal or ventral stomach than when the same horses are fed ad libitum in stalls,[15] suggesting that it is not the environment that is

affecting intragastric pH. Again, there is considerable confounding among the various risk factors, because housing on pasture is associated with constant access to feed; thus there are no periods of feed withholding, changes in diet from that rich in concentrates to that predominated by grasses, and, often, cessation of forced exercise.

PATHOGENESIS

The equine stomach is comparatively small relative to the size of the gastrointestinal tract. The stomach mucosa is divided into two parts. The proventricular part is glistening white in color, is composed of thick **stratified squamous epithelium,** and contains no glands. It covers approximately one-third of the mucosal area and ends abruptly at the margo plicatus, a slightly raised irregular serrated border with the glandular mucosa. Most gastric lesions in horses occur in squamous mucosa.

The **glandular mucosa** has a velvet-like structure and is usually covered by a thick layer of viscous mucus. The mucosa contains three main gland types: mucous-secreting cardiac glands; fundic glands, which contain mucous-secreting cells, hydrochloric-acid–producing parietal cells and pepsinogen-secreting chief cells; and pyloric glands, which consist largely of mucous-secreting cells. The stratified squamous epithelial mucosa has minimal resistance to gastric acid. The glandular epithelium has elaborate mechanisms, including the mucus–bicarbonate barrier, prostaglandins, mucosal blood flow, and cellular restitution, to protect itself from peptic injury. Hydrochloric acid and pepsinogens, which are converted to the proteolytic enzyme pepsin in an acidic environment, are secreted in the glandular mucosa by parietal cells and chief cells, respectively. The horse is a continuous, variable hydrochloric acid secretor, and the pH of equine gastric contents in the pylorus and antrum is often less than 2.0. Gastric pH is lowest, and acidity highest, when horses have been deprived of feed or have voluntarily stopped eating, often for as little as 2 hours. Thus there are periods during the day when gastric acidity is high (notably during the nighttime hours from midnight to 9 am).[15,21] Periods of prolonged high gastric acidity (pH <2.0) can be induced in horses by intermittent deprivation of feed, which often results in severe ulceration in the gastric squamous epithelial mucosa. Concurrent administration of the H_2 antagonist ranitidine during feed deprivation substantially reduces the area of lesion in the gastric squamous epithelial mucosa.

The pathogenesis of gastric ulcer is uncertain. It is proposed that the stratified squamous epithelium reacts to excessive acidic exposure by thickening and becoming para/hyperkeratotic.[22] Sloughing of superficial layers then predisposes to secondary infection when opportunistic bacteria and

inflammatory cells migrate to the area. The lesion deepens and progresses from an erosion to ulceration, exposing unprotected tissue to acid contents.[22] Subsequent healing might occur depending on factors influencing acidity and healing capabilities of the individual animal.[22] Exposure of squamous mucosa to acid is probably involved in the development of ulcers in most horses and there is in vitro evidence that volatile fatty acids, in combination with hydrochloric acid, are important in the development of ulcers in the nonglandular mucosa.[23]

A particular circumstance appears to favor the development of gastritis and ulceration in horses that undertake intense exercise. During exercise intragastric pressure increases from approximately 14 mm Hg at rest to as high as 50 mm Hg, stomach volume decreases, and the acidity of fluid within the proximal part of the stomach declines from pH 5 to 7 to pH 2 to 4. The combination of reduced blood flow and exposure to low pH increases the likelihood of mucosal damage, loss of protective mechanisms, and development of gastric mucosal lesions.[14]

Other factors, including physical injury to gastric mucosa, reflux of bile acids from the duodenum, and the presence of volatile fatty acids in the stomach all can contribute to the development of gastric lesions, but the definitive roles, if any, of each of these factors have not been determined.

CLINICAL FINDINGS

The vast majority of horses with lesions of the gastric mucosa, including ulceration, do not have clinical signs. Among racehorses, signs of poor performance,[24] feed refusal, fussy eating (not consuming all of the meal at a constant rate), and poor body condition have been associated with the presence of gastric ulcers. Of these signs only poor hair coat and poor body condition have been demonstrated to be associated with gastric ulcers, although the association of lower body condition scores with the presence of gastric lesions is not consistent across studies.[9,17] The high prevalence of some of the clinical signs, for instance, failure to perform to expectation, and gastric ulcers means that there is a high likelihood that horses with a given clinical sign will have an ulcer by chance. However, clinical experience indicates that horses with more extensive or severe lesions will have more severe clinical signs, including colic and failure to perform.

Colic is associated with the presence of lesions of the gastric mucosa, including ulceration. Ulceration can result from lesions elsewhere in the gastrointestinal tract, probably because of feed withholding or feed refusal by horses with colic. Alternatively, gastric ulceration can cause colic. The four criteria to determine whether gastric ulceration is the primary cause of colic in horses include the following:

1. Endoscopic confirmation of gastric ulceration
2. Absence of another alimentary tract abnormality
3. Clinical response to treatment that effectively suppresses or neutralizes gastric acidity
4. Confirmation of improvement or complete healing of gastric lesions

Most gastric ulcers in horses are not associated with hemorrhage and so signs of anemia or melena are unusual in horses. Horses with severe gastric ulceration and reflux esophagitis often have bruxism and retching. Rupture of gastric ulcers, perforation and subsequent peritonitis, and exsanguination from a bleeding ulcer are rare in adult horses.

Involvement of the spleen in the horse with a perforating gastric ulcer, a rare event, results in fever, anorexia, toxemia, pain on deep palpation over the left flank, and leukocytosis with a left shift.

Gastroscopic examination is the only means of demonstrating gastric lesions and assessing their extent and severity. Gastroscopic examination of the adult horse requires an endoscope of at least 2.5 m in length, although 3 m is preferable. The presence of feed material within the stomach prevents complete examination of the gastric mucosa, and in particular of the pylorus and antrum. The horse should be prepared by having feed withheld for at least 12 hours and water withheld for 4 hours before examination. If the horse is stabled on edible material, such as straw or shavings, it should be muzzled to prevent it eating this material. The horse may need to be sedated before examination (xylazine hydrochloride 0.1–0.3 mg/kg intravenously) and a twitch applied. The gastric mucosa is examined in a systematic fashion. As the end of the endoscope passes through the cardia the greater curvature and margo plicatus are examined. The endoscope is then advanced and rotated so that the lesser curvature and cardia are examined. The stomach should be inflated with air during the procedure. Excess fluid in the pylorus and antrum can be aspirated to allow better visualization of these regions. Careful attention should be paid to the margo plicatus because this is the most common site for lesions. The gastric glandular mucosa should be examined carefully for lesions because they are easily missed in this region. Material adherent to the mucosa should be washed away by flushing water through the endoscope. The endoscope can be passed into the duodenum to permit complete examination of the antrum. Endoscopic examination usually underestimates the number of gastric ulcers, compared with necropsy examination, and does not accurately predict the severity or depth of ulcers.

Small-intestinal segmental volvulus occurs infrequently (0.3%–3.2% of examinations) in horses after gastroscopic examination.[25] Signs of colic develop 10 min to 3 hours after gastroscopy and are caused by nonstrangulating segmental volvulus of gas-distended small intestine. The cause is speculated to be gas distension of the small intestine, although this is not confirmed. Movement of air from the stomach into the small intestine after instillation of air into the stomach is a common occurance.[26] It is prudent to evacuate as much air as possible at completion of the gastroscopy.

A number of grading systems for description of gastric lesions in horses have been developed and proposed. Few have been validated and tested for diagnostic utility. The Gastric Ulcer Number/Severity score has been validated and compared with an unvalidated system proposed by a group of experts.[27] Notably, neither grading system makes explicit the anatomic location of the lesions. As this information is likely to be of diagnostic or prognostic importance, it should be recorded.[3] Specifically, esophageal lesions, gastric squamous lesions, gastric glandular mucosal lesions, and duodenal lesions should each be scored for location and severity regardless of the scoring system used.

The simplified scoring system, when used by three experienced observers, has greater agreement among observers (intraclass correlation coefficient [ICC] of 0.97) than does the number/severity system (ICC = 0.94 for number of lesions and 0.93 for severity).[27] The κ values for agreement among observers were significantly lower when using the number/severity system.[27] The simplified system was reported by the observers to be quick and easy to use.[27] The simplified system appears to offer a useful method of classifying the severity of gastric lesions in horses, with the caveat that the site of the lesions should be recorded.[2]

Gastric ulcer number/severity score		
Score	Number of lesions	Gastric ulcer severity
0	No lesions	No lesions
1	1–2 localized lesions	Appears superficial
2	3–5 localized lesions	Deeper structures involved (deeper than 1)
3	6–10 lesions	Multiple lesions and variable severity
4	>10 lesions	Same as 2 and in addition the presence of hyperemia or darkened lesion crater
5	>10 lesions	Same as 4 but hemorrhage or blood clot adherent to ulcer

Continued

Score	Description
0	Intact mucosal epithelium
1	Intact mucosal epithelium with reddening or hyperkeratosis
2	Small single or small multifocal lesions
3	Large single or large multifocal lesions or extensive superficial lesions
4	Extensive often coalescing lesions with areas of apparent deep ulceration

Most lesions in racehorses are in the gastric squamous mucosa with less than 20% of lesions in the glandular mucosa. The situation is different in hospitalized adult horses, in which lesions in the squamous and glandular mucosa occur with about the same frequency (58%). Most lesions in the glandular mucosa of hospitalized horses occur in the antrum or pylorus, as opposed to the glandular mucosa of the body of the stomach.

Idiopathic gastroesophageal reflux disease occurs sporadically and rarely in adult horses. Affected horses have bruxism and ptyalism that can be severe. Endoscopic examination reveals ulceration and erosion of the esophagus that is more severe in the distal esophagus. Often there is no evidence of impaired gastric outflow, as is common in foals with this disease.

CLINICAL PATHOLOGY

Horses with gastric ulcers are reported to have higher concentrations of creatinine and activity of alkaline phosphatase in serum than do unaffected horses, but these differences are not sufficient to be clinically useful.[14] Horses with gastric ulcer disease are typically not anemic.

Permeability of the gastric mucosa can be assessed by measurement of concentrations of sucrose in blood (serum) or urine. Sucrose, a disaccharide, is degraded by sucrase in the small intestine to its component monosaccharides glucose and fructose, which are then absorbed. Sucrose is not absorbed intact in healthy animals. Abnormal gastric permeability allows passage of sucrose from the stomach into the blood with subsequent excretion in the urine. In horses with gastric lesions, sucrose concentrations in blood (serum) after nasogastric administration of 250 g of sucrose (table sugar) as a 10% solution in tap water increase after 30 minutes, with peak levels at 45 minutes. The magnitude of the increase correlates with the severity of the lesions.[28] This test is quite sensitive for detection of abnormalities in permeability of gastric mucosa as evidenced by abnormal concentrations of sucrose in serum in the absence of lesions detectable by endoscopic examination in horses after administration of high doses of phenylbutazone

(4.4 mg/kg PO q12h day 1, 2.2 mg/kg PO q12h for 4 days, 2.2 mg/kg PO q24h for 9 days).[19] A test using concentrations of sucrose greater than 0.7 mg/dL in urine after intragastric administration of a 10% sucrose solution (1 g/kg orally after feeding) has a sensitivity and specificity of 83% and 90%, respectively, for detection of gastric ulceration.[14]

NECROPSY FINDINGS

Ulcers may be singular or multiple and are most commonly located in the squamous epithelial mucosa adjacent to the margo plicatus along the lesser curvature of the stomach. They can be linear or irregular in shape; with the exception of those in the glandular mucosa, they are rarely circular in appearance. Ulcers in the squamous mucosa often have slightly raised brown-stained keratinized borders and contain small amounts of necrotic material at their base; frank blood is uncommon. Ulcers in the glandular zone are usually circular or oval depressions surrounded by an intense zone of inflammation. Classification of lesions within the squamous region included hyperkeratosis, punctate scars, diffuse erosions/ulcerations, and margo injuria, and within the glandular region included hyperemia, focal erosions, ulcerations, and glandular metaplasia.[22]

When perforation has occurred, there is an area of local peritonitis, the stomach wall is adherent to the tip of the spleen, and an extensive suppurative splenitis may be present. In some cases, especially when the stomach is full at the time of perforation, a long tear develops in the wall and large quantities of ingesta spill into the peritoneal cavity. Tumor masses can be present and accompanied by several glandular ulcers.

> **DIFFERENTIAL DIAGNOSIS**
>
> Gastric ulceration of adult horses must be differentiated from the common causes of recurrent colic.

TREATMENT

The goals of treatment of horses with gastric ulcer disease are healing of the ulcer, suppression of pain, and prevention of ulcer recurrence. The principle underlying treatment of gastric ulcers in horses is suppression of gastric acidity (increase intragastric pH). This can be achieved by inhibiting acid production or increasing buffering of acid. Mucosal protectants are administered with the aim of preventing exposure of damaged mucosa to acid. Management changes may reduce the risk of horses developing disease.

Acid Suppression

The agents available to suppress acid production are compounds including omeprazole

and lansoprazole, which block the proton pump on the luminal surface of gastric parietal cells, and H_2 receptor antagonists including cimetidine, ranitidine, and famotidine.

Omeprazole

Omeprazole is currently the favored treatment for gastric ulcer disease in horses. The pharmacokinetics, pharmacodynamics, safety, and efficacy of the drug have been extensively investigated in horses under a variety of conditions and management systems. Omeprazole (4 mg/kg BW orally every 24 hours) is effective in promoting healing of ulcers of the squamous mucosa in horses that continue to train or race, a situation in which ulcers will not heal spontaneously. Omeprazole is safe and no adverse effects from its administration have been reported. Omeprazole at a dosage of 4.0 mg/kg once daily is more effective at healing ulcers of both the squamous and glandular portions of the stomach than is a dosage of 0.8 mg/kg.[29] However, omeprazole is less efficacious at healing ulcers of the glandular mucosa than the squamous mucosa.[29] A frequently used treatment regimen is omeprazole 4 mg/kg once daily for 14 days followed by maintenance therapy of 1 to 2 mg/kg once daily for as long as the horse is at risk of developing gastric ulcers. Administration of omeprazole (4 mg/kg once daily either before or after exercise) resulted in healing of 80% of squamous ulcers versus 21% of glandular ulcers ($P = 0.0002$), and improvement in 96% of squamous ulcers versus 53% of glandular ulcers ($P = 0.001$).[30] Omeprazole paste administered at 1 mg/kg orally once daily is effective in both preventing development of ulcers in horses entering race training and preventing recurrence of ulcers in horses in which ulcers have healed during treatment with a higher dose of omeprazole.[31,32] Omeprazole (0.5 mg/kg once daily) is as efficacious as 1 mg/kg once daily in treating Thoroughbred racehorses with ulcers in training. However, there was no untreated control group, or group administered a higher dose of omeprazole, and results might have reflected healing that could be expected without medication.[33] Administration of omeprazole (1 mg/kg) as an enteric-coated formulation is as effective as administration of omeprazole (4 mg/kg) as a paste in a nonplacebo controlled crossover trial. Administration of the enteric-coated formulation resulted in lower plasma omeprazole concentrations than those achieved with the higher dose of the paste formulation.[34]

Rectal administration of omeprazole does not reliably decrease gastric pH.[35] Intravenous administration of omeprazole (0.5 mg/kg) significantly increases intragastric pH within 1 hour and appears to enhance healing of nonglandular ulcers.[36]

The addition of trimethoprim-sulfonamide to treatment with omeprazole does

not enhance healing of ulcers of the glandular mucosa.[37]

The composition of the excipients and form of omeprazole is important in determining efficacy. Forms of omeprazole other than that in the commercial preparation are associated with reduced or nil efficacy. Omeprazole is more effective than cimetidine (20 mg/kg orally every 8 hours) for treatment of gastric ulcers in racehorses.

Esomeprazole (0.5 mg/kg intravenously every 24 hours) is effective in raising intragastric pH in adult horses.[38] Its efficacy in treatment or prevention of gastric lesions has not been determined.

Cimetidine

Cimetidine is the prototypical H_2 receptor antagonist. It acts by blocking action of histamine on the basilar membrane of the gastric parietal cells. It is used for treatment of gastric ulcer disease in horses, for which is must be administered frequently and in high doses (20–25 mg/kg orally every 6–8 hours). The drug has variable absorption after oral administration to horses. It is usually cheaper than omeprazole, but is less effective. Cimetidine can be administered intravenously (7 mg/kg every 6 hours) if rapid action is needed or the animal cannot take medication orally (e.g., a horse with colic).

Ranitidine and Famotidine

Ranitidine (6.6 mg/kg orally every 8 hours) effectively suppresses gastric acidity and prevents development of ulcers in horses deprived of feed. Ranitidine does not affect rates of gastric emptying.[39] Commercial preparations for its use in horses are marketed in some countries.

Famotidine is an H_2 receptor antagonist marketed for use in humans. It is effective in suppressing gastric acidity in horses (3 mg/kg orally every 12 hours or 0.3 mg/kg intravenously every 12 hours) but is expensive.

Gastric Antacids

Gastric antacids given orally neutralize stomach acid to form water and a neutral salt. They are not absorbed and decrease pepsin activity, binding to bile salts in the stomach, and stimulate local prostaglandin. One oral dose of 30 g of aluminum hydroxide and 15 g of magnesium hydroxide can result in a significant increase in gastric pH for up to 4 hours. The short duration of action, minimal and transient effect on gastric pH, and need for administration of large volumes orally render these products less than optimal. Moreover, there is evidence that antacids are not effective in treatment of gastric ulcers in racehorses.

Protectants and Other Treatments

Sucralfate is an antiulcer drug with a cytoprotective effect on the gastric mucosa. Sucralfate dissociates in gastric acid to sucrose octasulfate and aluminum hydroxide. The aluminum hydroxide acts as an antacid and the sucrose octasulfate polymerizes to a viscous, sticky substance that creates a protective effect by binding to ulcerated mucosa. This prevents back diffusion of hydrogen ions, inactivates pepsin, and absorbs bile acid. Sucralfate is administered to horses (22 mg/kg orally every 8 hours) but is not effective in promoting healing in induced disease or associated with a lower risk of gastric ulcers in racehorses administered the compound.

Pectin–lecithin complexes are not effective in treatment of gastric ulcer disease in horses. A combination of pectin, lecithin, and bicarbonate in unspecified amounts fed as a supplement demonstrated limited efficacy in reducing gastric ulcer scores induced by feed deprivation.[40]

Administration of concentrates or extracts of sea buckthorn berries (*Hippophae rhamnoides*) does not reduce the incidence of nonglandular gastric lesions in horses with experimentally induced (intermittent feed deprivation) gastric ulcerative disease.[41]

Misoprostol, a prostaglandin E analog, is administered for treatment of gastric and other enteric lesions,[42] and especially those attributable to NSAID toxicosis. However, its efficacy in treating or preventing gastric ulceration in horses has not been determined. It does appear to be safe to administer to pregnant mares.[43]

Management Changes

Horses with gastric ulcers experience spontaneous healing when removed from training and kept on pasture. These management changes are not appropriate in most instances, and emphasis should be placed on feeding diets that have a low ulcerogenic potential (such as alfalfa hay) and using feeding practices that minimize or eliminate periods when the horse does not have access to feed. Hay should be constantly available to horses, if at all possible.

Overview of Treatment

The usual approach to treatment is to promote healing of the ulcer by administration of effective agents (omeprazole or possibly ranitidine) at high dose until the ulcer has healed, as demonstrated by gastroscopy. The horse is then administered omeprazole at a lower dose (1–2 mg/kg orally every 24 hours) for the duration of time that it is at risk of developing gastric ulcers. Changes in management, including feeding practices and diet, should be instituted at the start of treatment. While not statistically associated with risk of gastric ulceration, use of phenylbutazone or other NSAIDs should be minimized in horses at high risk of disease.

CONTROL

Prevention of gastric ulcer disease in athletic horses centers on minimizing the effect of factors that promote ulcer development. This might involve the chronic administration of omeprazole (1 mg/kg orally once daily),[32] but should include attention to dietary and feeding practices (discussed previously) that minimize the time that horses have no feed in their stomach. Ideally, horses at risk would be kept on pasture, but this is not feasible under many management or husbandry systems and it does not reliably prevent the development of ulcers.[16] All horses in athletic training and confined to stalls should be considered at high risk of development of gastric ulcers and should be managed accordingly. Detailed recommendations about feeding practices are available.[44]

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INTESTINAL OBSTRUCTION IN HORSES

Intestinal obstruction is an important cause of colic in horses, and can involve the small intestine, cecum, large (ascending) colon, or small (descending) colon. Because the clinical characteristics of obstruction of the various bowel segments are quite different, intestinal obstruction is discussed based on the site affected (small intestine, cecum, and large or small colon).

SMALL-INTESTINAL OBSTRUCTION IN HORSES

SYNOPSIS

Etiology Volvulus; intussusception; incarceration and strangulation in epiploic foramen, Meckel's diverticulum, mesenteric rents, or umbilical, inguinal, or diaphragmatic hernia, or by pedunculated lipoma; obstruction caused by foreign bodies or ascarids, intramural tumors including hematomas, eosinophilic infiltrates, neoplasms, and abscesses; ileal hypertrophy; ileal impaction

Epidemiology Mostly sporadic diseases, although the age affected can vary with the disease

Clinical signs Strangulating lesions cause acute, severe disease with intense pain, tachycardia, dehydration and hemoconcentration, and usually distended loops of small intestine palpable rectally or detectable by ultrasonographic examination; death occurs in untreated horses within 48 h; obstructive, nonstrangulating lesions cause less severe pain and clinical abnormalities and have a longer course until death

Clinical pathology Nondiagnostic; hemoconcentration and azotemia are indicative of dehydration; increases in blood (plasma) and/or peritoneal fluid lactate concentrations are useful for prognostication; leukopenia and left shift are consistent with endotoxemia and peritonitis; peritoneal fluid can be serosanguinous with infarcted intestine

Lesions Consistent with the disease

Diagnostic confirmation Surgical exploration or necropsy

Treatment Surgical correction of lesion; analgesia; correction of fluid, electrolyte, and acid-base abnormalities

ETIOLOGY

A working classification is outlined next.[1]

Obstruction With Infarction
- Volvulus or torsion of the mesentery
- Incarceration in or strangulation by
  - Mesenteric rents
  - Epiploic foramen
  - Meckel's diverticulum
  - Pedunculated lipoma
  - Neoplastic lesions (teratoma)[2]
  - Adhesions
  - Inguinal hernia
  - Umbilical hernia
  - Diaphragmatic hernia
  - Rents in mesentery or intraabdominal ligaments (e.g., gastrosplenic) or spleen
  - Spermatic cord in geldings
  - Developmental defects in mesentery

Obstruction Without Infarction
- Intussusception:
  - Jejunojejunal, ileoileal, and other small intestinal intussusceptions
  - Acute and chronic ileocecal
- Foreign body:
  - Wood chip or fencing material impaction of duodenum or jejunum
  - Phytobezoars[3]
  - Linear foreign bodies such as string or baling twine
  - Impaction of the duodenum or jejunum by molasses-containing feedblocks
- Impaction by *P. equorum*[4,5]
- Impaction of the terminal ileum
- Muscular hypertrophy of the terminal ileum
- Intramural masses such as neoplasms (intestinal adenocarcinoma, focal lymphosarcoma, and leiomyoma), hematomas, abscesses and fungal infections (intestinal pythiosis), focal eosinophilic enteritis,[6] and Lawsonia *intracellularis* (LI) proliferative enteropathy
- Compression of intestine by intraabdominal masses including abscesses and neoplastic tumors

Functional Obstruction
- Anterior enteritis
- Postoperative ileus
- Myenteric ganglioneuritis
- Intestinal ischemia of any cause (thromboembolic colic, mesenteric accidents, and postexertional ileus)

The classification used above should be used only as a guide, because the actual clinical presentations vary. For instance, intussusceptions usually result in infarction of the intussuscepted segment but, because this segment is effectively isolated from the body, the clinical signs are often not characteristic of a horse with an infarctive lesion. Similarly, horses with small intestine entrapped in the epiploic foramen often have less severe clinical signs than anticipated for the severity of the lesion.

EPIDEMIOLOGY

The epidemiology of colic is covered in a previous section. There are no recognized risk factors for small-intestinal volvulus and for many small-intestinal accidents. Epidemiologic information is available for some small-intestinal obstructive diseases and is presented later. Obstructive diseases of the small intestine compromise approximately 20% of colic cases referred for further evaluation and treatment. For small-intestinal diseases requiring surgical correction, the case–fatality rate is 100% if surgery is not performed. Short-term survival of horses undergoing surgical correction of small-intestinal obstruction is 34% to 74%. The fatality rate is greatest in the perioperative period. Survival rates vary depending on the nature and severity of the lesion, with long-term survival rates lower for horses that require resection of the intestine, especially for resections of more than 2 m or more than one surgery. Prognosis might be improved by accurate identification of compromised, but viable, intestine and its preservation rather than resection.[7]

Intestinal Herniation Through the Epiploic Foramen

This occurs in approximately 5% of horses with small-intestinal disease requiring surgery. Geldings are four times more likely than mares to be affected. Thoroughbreds were overrepresented in two studies, suggesting a breed predisposition, and there was no effect of age on incidence. There appears to be an increased in incidence of the disease between October and March in Britain. Horses in the UK with a history of crib biting or wind sucking (adjusted OR 72, 95% CI 14–359), with a history of colic in the past 12 months (5.1, 95% CI 1.4–18.9), increased stabling in the past 4 weeks (3.7, 95% CI 1.4–9.7), and increased height (1.07, 95% CI 1.01–1.12 per centimeter) are at markedly increased risk of developing epiploic entrapment of the small intestine.[8] Similar risk factors are identified in horses from the United States, Ireland, and UK.[9] Horses with colic that crib (a behavioral abnormality in which horses grasp a fixed object such as a fence rail or post with the incisors, flex the neck, and draw air into the esophagus) are more likely to have herniation of the small intestine through the epiploic foramen than are horses that do not crib.[1,8,9] The reason for this association is not known but might be related to factors that predispose horses to both cribbing and intestinal herniation through the epiploic foramen, such as diet, exercise, or housing. Alternatively, cribbing might cause changes in intraabdominal pressure that favor herniation. There is no age predisposition to development of this disorder.

The **case–fatality rate** for horses subjected to surgery is between 30% and 50%, although older reports of the disease had a much higher case–fatality rate.[10]

Pedunculated Lipomas

The prevalence of colic caused by pedunculated lipoma is 1% to 2.6% of horses with colic and 1% to 17% of all horses that have a celiotomy because of small-intestinal disease. The prevalence varies depending on the population of horses studied. The proportion of horses with colic caused by pedunculated lipomas increases with age, and the median age of affected horses is 19 years. Pedunculated lipomas cause small-intestinal obstruction in older horses (>8 years) with geldings (2×) and ponies (4×) being at increased risk. Pedunculated lipomas occasionally (5 of 75 cases) cause strangulating obstructive lesions of the small colon. The case–fatality rate for horses subjected to surgery is over 60%.

Inguinal Hernias

Inguinal hernias occur only in males. **Congenital inguinal hernias** are usually self-limiting, do not require medical or surgical therapy, and resolve by the time foals are 3 to 6 months of age. Congenital inguinal hernias rarely cause a strangulating lesion of the small intestine (see the section Colic in Foals). **Acquired inguinal hernias** occur almost exclusively in stallions, and the disease is rare in geldings. There is no apparent breed or age predilection. The case–fatality rate for horses subjected to surgery is 25%.

Intussusception

Small-intestinal intussusception is more common in young horses and foals but also occurs in adult horses. Approximately 50% of intussusceptions in adult horses are associated with a luminal or mural mass, whereas this is not the case in younger horses and foals. The case–fatality rate of horses subjected to surgery is 25% to 60%.

Both acute and chronic **ileocecal intussusceptions** occur more commonly in young (6–30 months) horses, although they are rare in foals. There is no breed or gender predilection. The disease is acute in approximately 70% of cases and chronic in the remainder. Ileocecal intussusceptions constitute approximately 75% of all intussusceptions involving the small intestine and 60% of all intussusceptions. The **case–fatality rate** for horses with acute ileocecal intussusception when surgery is available is approximately 70%, whereas that for chronic intussusception is less than 10%. There is strong evidence of an association between tapeworm (*A. perfoliata*) infestation and ileocecal disease causing colic in horses.[11,12]

Foreign Body

Foreign-body obstructions occur most frequently in foals and yearlings, possibly because of their tendency to explore and eat unusual items. Impaction by *P. equorum* occurs in foals between 3 and 18 months of age and is often associated with the administration of anthelmintics to previously untreated foals.[4,5] Small-intestinal obstructions by feedblocks containing molasses is associated with ingestion of large quantities of the material.

Impaction

Ileal impaction is more common in mares and only in animals over 1 year of age. The disease represented 7% of surgical colic cases in one series. The case–fatality rate is as low as 8% in animals treated at a referral institution,[13] although older reports are of much lower survival rates.[1] The disease is attributed to the feeding of finely ground, high-fiber feed such as Coastal Bermuda hay, but this is not the only cause. Horses with colic that have been fed coastal Bermuda hay are approximately three times more likely to have ileal impaction than are horses with colic that have not been fed this feedstuff. Similarly, lack of administration of a compound effective against tapeworms is associated with a three times greater risk of ileal impaction among horses with colic, and tapeworm infestation is associated with an increased incidence of spasmodic colic and ileocecal impaction in Thoroughbred racehorses.

Mesenteric Rents

Incarceration of small intestine through mesenteric rents is a cause of colic in approximately 2% of colic patients undergoing exploratory celiotomy. The long-term survival rate is approximately 40%. There are no identified age, breed, or gender predilections.

PATHOGENESIS

The effects of intestinal obstruction and the particular influence of the related endotoxemia in horses were detailed earlier. The type of lesion is important, depending on whether the blood supply to a large section of intestine is occluded or whether effective circulation is maintained. Obstructions that do not cause widespread intestinal ischemia, such as those caused by focal external pressure or with some form of disease caused by pedunculated lipomas or caused by internal foreign bodies such as phytobezoars, are less acutely lethal and do not cause as severe signs as volvulus and forms of intussusception that result in ischemia of large sections of intestine. In the latter case, endotoxins from the gut lumen pass through the devitalized tissues of the gut wall into the circulation, resulting in signs of toxemia and cardiovascular collapse. There does not appear to be an important role for translocation of intestinal bacteria into the bloodstream in horses with small-intestinal lesions.[14]

CLINICAL FINDINGS

Acute Disease: Infarctive Lesions

In acute, complete obstructions of the small intestine, with intestinal ischemia caused by volvulus, intussusception, or strangulation, there is usually an almost immediate onset of severe abdominal pain. The pain can be minimally or only transiently responsive to administration of analgesics. During this early stage intestinal sounds are still present and feces still passed. The pulse rate increases to 60 to 80 beats/min, the respiratory rate can be as high as 80 beats/min, and sweating begins in many horses. It might be 8 to 12 hours before distended loops of intestine are palpable on rectal examination, and it is about the same time that clinical and laboratory evidence of hypovolemia is first apparent. Depending on the site of the obstruction there can be reflux of fluid on passage of a nasogastric tube. More proximal lesions result in distension of the stomach earlier in the course of the disease. Small-intestinal distension is readily detected by percutaneous or rectal ultrasonographic examination. The sensitivity and specificity of ultrasonographic examination for detecting small-intestinal distension (98% and 84%, respectively) is greater than that of rectal examination (50% and 98%, respectively).[1,15]

In the period 12 to 24 hours after obstruction commences, the pulse rate rises to 80 to 100 beats/min, loops of distended intestine can be palpated per rectum, gut sounds and defecation cease, and the rectum is empty and sticky to the touch. Abdominal paracentesis yields bloodstained fluid. From 24 hours onward, signs of hypovolemia and toxic shock become marked, but the pain may not worsen. The horse will often appear depressed and poorly responsive to external stimuli. Sweating may persist. The heart rate increases to 100 to 120 beats/min, intestinal loops are easily palpable, and reflux filling of the stomach occurs, with a great deal of fluid evacuated via the stomach tube; the horse may vomit. Death from endotoxemia or rupture of the intestine usually occurs within 48 hours. The terminal stage is one of severe endotoxic shock, with or without intestinal rupture and peracute diffuse peritonitis.

Subacute Cases: Noninfarctive Lesions

If there is no vascular involvement in the small-intestinal obstruction, such as occurs with ileal impaction, the pain is less severe than for horses with infarctive lesions, it is usually responsive to analgesics, and the heart rate is only mildly elevated (50–60 beats/min). The pain can be low-level continuous or intermittent with moderate attacks of pain alternating with periods of uneasiness without signs of overt pain. Pain is usually responsive to the administration of analgesics. The duration of colic in these cases can be several days to several weeks. Palpable intestinal distension and clinical and laboratory evidence of hypovolemia can be evident; for example, ileal impaction is detectable by rectal examination in approximately 25% of affected horses.[13] Surgical intervention becomes an option because of the failure of the horse to improve.

Intussusception of the Small Intestine

This can cause a syndrome of acute, subacute, or chronic colic, depending on the degree of involvement of the blood supply. Horses with **acute ileocecal intussusception** have an abrupt onset of moderate to severe abdominal pain, tachycardia, reflux through a nasogastric tube, complete absence of borborygmi, and tightly distended small intestine evident on rectal palpation. The course of the disease is usually less than 24 hours. Horses with **chronic ileocecal intussusception** have a history of chronic, intermittent colic occurring after feeding, weight loss, and reduced fecal volume. The abdominal pain is mild and intermittent and the horses are not dehydrated or tachycardic. Rectal examination may reveal the presence of mildly distended small intestine, especially after a meal, and in approximately 25% of cases the intussusception can be palpated per rectum. Mild abdominal pain can be present for weeks without an abdominal crisis occurring. Ultrasonographic examination may reveal the intussusception in the right flank.

Volvulus of the Small Intestine

This presents a typical syndrome of acute intestinal obstruction and infarction. The onset of signs is abrupt and there is severe pain, tachycardia, sweating, and a rapid deterioration in the horse's clinical condition.

Strangulated Inguinal Hernia

This entity is often missed in the early stages because the distension of the scrotum is easily overlooked unless a specific examination of that area is performed. Severe pain in an intact male, even when distended loops of small intestine are not palpable, should prompt a thorough examination of the scrotum and, per rectum, the internal inguinal rings.

Strangulated Diaphragmatic Hernia

When acquired after birth, this lesion has no distinguishing characteristics and will be identified only on thoracic radiography or exploratory laparotomy.[16] There is often a history of trauma, such as dystocia or, in adults, a fall or being hit by a car. The clinical course is characteristic of any acute, strangulating intestinal lesion. Small intestine or large colon can herniate into the thoracic cavity and be evident on radiographic or ultrasonographic examination of the thorax.

Epiploic Foramen Entrapment

Entrapment of small intestine in the epiploic foramen is associated with an array of clinical signs, some of which are subtle. Strangulation of small intestine through the epiploic foramen typically causes signs of acute abdominal pain with reflux of material through a nasogastric tube. However, approximately 40% of affected horses do not have signs of abdominal pain when examined at a referral center and 52% do not have nasogastric reflux. Horses with less severe clinical signs presumably have shorter lengths of incarcerated small intestine or incomplete obstructions to passage of luminal material or blood flow. Herniation of the parietal (antimesenteric) margin of the small intestine is sometimes associated with incomplete obstruction of the small intestine and signs of mild disease. Because of the anterior location of the lesion, distended small intestine cannot usually be palpated per rectum and is not identifiable without ultrasonographic examination or surgical intervention. A fatal complication of epiploic foraminal herniation is rupture of the portal vein, leading to sudden death from internal hemorrhage. Tension by the incarcerated section of gut on the portal vein causes tearing of the wall and subsequent hemorrhage. Hemoperitoneum in a horse with colic should prompt consideration of entrapment of small intestine in the epiploic foramen as a cause of the disease. The outcome of this combination of diseases is almost always fatal.

Functional Obstruction

Functional obstructions caused by anterior enteritis, intestinal ischemia, or postoperative ileus can be difficult to discriminate from obstructive lesions of the small intestine that require surgical correction. Postoperative ileus is characterized by continued pain and reflux through a nasogastric tube after surgical correction of an intestinal lesion. The ileus is probably a result of the diffuse peritonitis and inflammation of the intestine that results from surgical exploration of the abdomen. If sufficient doubt exists over the cause of a horse's signs of intestinal obstruction, then laparotomy or repeat laparotomy should be performed.

Foreign Body

Foreign-body impaction of the duodenum by agglomerations of chewed wood or cracked corn kernels cause signs of acute obstruction but without the endotoxemia caused by infarction.

Ileocecal Valve Impaction

Impaction of the ileocecal valve is manifest as an initial period of 8 to 12 hours of subacute abdominal pain with mild increases in heart rate. Intestinal sounds are increased in frequency and intensity. Rectal examination may reveal the enlarged, impacted ileum in the upper right flank at the base of the cecum in approximately 10% of cases. It is easily confused with an impaction of the small colon. Reflux on nasogastric intubation occurs in approximately 50% of cases. After 24 to 36 hours the pain increases in severity. There is severe depression, patchy sweating, and coldness of the extremities, and the animal stands with its head hung down, sits on its haunches, and rolls and struggles violently. The abdominal pain becomes severe and continuous, the pulse rate rises to between 80 and 120 beats/min, and the pulse is weak. The abdominal sounds are absent and there is reflux of sanguineous fluid through a nasogastric tube. On rectal examination the small intestine is tightly distended with gas and fluid. Death usually occurs within 36 to 48 hours after the onset of illness without surgical or effective medical intervention.

Idiopathic Muscular Hypertrophy (Terminal Ileal Hypertrophy)

This causes a long-term chronic or mild intermittent colic, with reduced appetite and weight loss, which persists over a period of weeks, sometimes months, in horses more than 5 years and up to 18 years old. Colic pain is associated with feeding. On rectal examination the greatly thickened ileum can be palpated at the base of the cecum, and there may also be distended loops of thick-walled ileum.

Difficulty can be experienced in differentiating ileal hypertrophy from chronic intussusception, especially of the terminal ileum into the cecum. Fluid ingesta can pass the much constricted lumen of an intussusception so that mural hypertrophy occurs orally. A similar clinical picture results from stenosis of the small intestine by adhesions, usually resulting from verminous migration. In all three diseases there is increased motility of the small intestine and there is no interference with the blood supply.

Caudal Abdominal Obstructions

Obstructive lesions of the small intestine in the caudal abdomen, and therefore more likely to be palpable, include strangulation through tears in the mesentery, through a defect in the gastrosplenic ligament, entrapment behind the ventral ligament of the bladder, or through a tear in the broad ligament of the uterus.

Radiography is not useful in diagnosing the cause of small-intestinal obstruction in adult horses, but **ultrasonographic** examination of the abdomen is rewarding and has greater sensitivity for detection of distended loops of small intestine than does rectal examination. If available, ultrasonographic examination is indicated in the initial or second examination of all horses with colic. Ultrasonographic examination can detect, in addition to distended small intestine, reductions in or absence of motility associated with ileus, thickening of the intestinal wall, intussusceptions, increased volume of peritoneal fluid, and abnormalities in the echogenicity of peritoneal fluid.

CLINICAL PATHOLOGY

Although laboratory examinations of animals with intestinal obstruction may not be used in the diagnosis of the obstruction, they are useful in assessing its severity and providing an indication of survival. Generally, the

laboratory findings in acute intestinal obstruction include the following:

- Hemoconcentration (the PCV usually exceeds 50%)
- Increase in serum creatinine concentration (depending on severity of the decrease in circulating blood volume)
- Decreases in plasma bicarbonate and pH, with increases in lactate concentration and anion gap
- Leukopenia and neutropenia caused by devitalization of infarcted intestine and the development of endotoxemia and, in some cases, peritonitis
- An increase in the total number of leukocytes, erythrocytes, and the protein concentration in the **peritoneal fluid** obtained by paracentesis. In acute intestinal obstruction with infarction, the peritoneal fluid will be bloodstained. As necrosis and gangrene develop there is an increase in the total number of leukocytes with an increase in the number of immature neutrophils. As devitalization proceeds, but before perforation of the gut wall, intracellular and extracellular bacteria may be seen in the fluid. Peritoneal fluid from horses with intestinal infarctive lesions has a higher alkaline phosphatase activity than fluid from horses with nonstrangulating obstructions. Peritoneal fluid lactate concentrations can be measured and are associated with probability of survival. Lactate concentrations in peritoneal fluid of horses with colic of 1, 6, 12, and 16 mM were associated with death rates of 11, 29, 63, and 82% in horses without strangulating lesions and 25, 52, 82, and 92% in horses with strangulating lesions.[17]
- Serum alcohol dehydrogenase activity increases in horses with colic, with concentrations increasing from (median range) of 10.5 (8.7–11 u/L) in healthy horses, 16.5 (13.8–18 u/L) in horses with colon impaction, 40 (20–74.9 u/L) in horses with small-intestinal strangulation, and 63.2 (40–78 u/L) in horses with colon torsion.[18]

NECROPSY FINDINGS

The physical lesions are characteristic of the disease.

DIFFERENTIAL DIAGNOSIS

Other diseases that may mimic pain caused by gastrointestinal disease are listed under differential diagnosis in the Equine Colic section. Gastrointestinal causes of colic that must be differentiated from small intestinal obstructive disease include:

- Enteritis and acute diarrhea
- Equine neorickettsiosis (Potomac horse fever)
- Anterior enteritis
- Gastric ulcer in foals and adults
- Disorders of the large or small colon
- Intestinal tympany (gas colic)
- Thromboembolic colic
  See also Table 7-10.

TREATMENT

The principles of treatment of horses with small-intestinal obstructive lesions are similar to those of any colic (see the section Equine Colic).

Every attempt should be made to relieve the horse's pain using appropriate doses of effective analgesics (see Table 7-15). Care should be taken when using flunixin meglumine that signs of a lesion requiring surgical correction are not masked until the severity of the disease makes successful treatment unlikely.

Almost all obstructive lesions of the small intestine require surgical correction. Surgical techniques including the need to resect small intestine vary with the physical lesion and viability of the intestine.[19,20] In addition to surgery, attention should be paid to maintaining the horse's fluid and acid-base and electrolyte status (see the section Equine Colic). Treatment of postoperative ileus should be aggressive and include correction of acid-base, fluid, and electrolyte abnormalities; continued gastric decompression through a nasogastric tube; and administration of promotility drugs such as cisapride, lidocaine, erythromycin, and metoclopramide (see Table 7-16).

Ileal impactions can be treated medically by the administration of intravenous fluids, gastric decompression, and administration of mineral oil. Horses treated medically should be closely monitored as prompt surgical intervention may be necessary if the horse's condition deteriorates.

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DUODENITIS-PROXIMAL JEJUNITIS (ANTERIOR ENTERITIS, PROXIMAL ENTERITIS)

Duodenitis-proximal jejunitis is a syndrome of small-intestinal ileus characterized clinically by acute onset of abdominal pain and production of copious amounts of nasogastric reflux. It is idiopathic and associated with lesions in the duodenum and/or proximal jejunum.

SYNOPSIS

Etiology Unknown—suspect strains of *Clostridium difficile*

Epidemiology Sporadic disease. Case–fatality rate highly variable (6%–75%)

Clinical signs Colic, voluminous reflux on nasogastric intubation, mild fever, resolution of pain on gastric decompression

Clinical pathology Nondiagnostic

Lesions Duodenitis, proximal jejunitis, gastric and small intestinal distension

Diagnostic confirmation None antemortem, resolution of disease

Treatment Gastric decompression, correction of fluid and electrolyte abnormalities

ETIOLOGY

The etiology of duodenitis-proximal jejunitis is unknown with both infectious (*Salmonella* spp. and *C. difficile*) and toxigenic (aflatoxicosis, fusariotoxicosis) as putative causes. *Salmonella* spp. are isolated from some horses with duodenitis-proximal jejunitis, but this is not a consistent finding. *C. difficile* might be involved as evidenced by detection of toxigenic strains of *C. difficile* from nasogastric reflux fluid of all 10 horses with duodenitis-proximal enteritis sampled but from only one of 16 horses with other diseases causing nasogastric reflux.[1] This observation is based on a small number of cases and demonstrates an association rather than causation and should be interpreted in that light. Experimental intoxication with culture media of *F. moniliforme* produces histologic, but not clinical, signs consistent with the disease.

EPIDEMIOLOGY

The disease is reported from the United States and Europe,[2] and there are anecdotal reports of it occurring in Australia and other countries. There is no apparent effect of age, with the exception that the disease is not reported in horses less than 1 year of age and is uncommon in horses less than 2 years of age. There is no demonstrated breed or gender predilection for the disease.[3]

Feeding of large amounts of concentrated feeds to horses is a risk factor for the disease, as is grazing.[3] Duodenitis-proximal jejunitis occurs more commonly in the warmer months.

There are anecdotal reports of farms with a high incidence of the disease, especially among , suggesting an unidentified cause or risk factor. There are no reports of the incidence, or morbidity/mortality rates of duodenitis-proximal jejunitis. The **case–fatality rate** varies from 6% to 75% but in referral institutions is likely about 10%.[4]

PATHOGENESIS

The primary lesion is inflammation and edema of the duodenum and jejunum with sloughing of villous epithelium and villous atrophy. These lesions are probably associated with ileus and failure of small-intestinal absorptive function. Fluid accumulation in the atonic small intestine causes distension and pain and reflux of alkaline small-intestinal contents into the stomach. Sequestration of fluid, electrolytes, and bicarbonate in the stomach and small intestine causes a reduction in blood volume, shock, and metabolic acidosis. Gastric and small-intestinal distension and hypovolemia cause tachycardia. Disruption of the small-intestinal mucosal barrier allows absorption of toxins, including endotoxins, which further compromise cardiovascular and metabolic function. Death in untreated cases results from acute, diffuse peritonitis secondary to gastric rupture, or shock and metabolic disturbances secondary to hypovolemia and endotoxemia. Laminitis and persistent nasogastric reflux are causes of death (including euthanasia) in hospitalized horses.[5]

CLINICAL FINDINGS

The onset of clinical signs is usually abrupt and characterized by mild to severe colic. Affected horses are **depressed**, **dehydrated,** and have prolonged capillary refill time and heart rates between 50 and 80 beats/min. The respiratory rate is variable. The horse might sweat profusely and there are muscle fasciculations in severely affected cases. Approximately two-thirds of cases are pyrexic.[5] **Borborygmi are absent,** although there can be tinkling sounds of gas bubbling in fluid-filled atonic intestine. **Rectal examination** usually reveals the presence of multiple loops of moderately to severely distended small intestine. **Reflux of fluid** through a nasogastric tube is a consistent finding, and usually results in marked relief of pain and resolution of tachycardia. The fluid is often sanguineous, malodorous, alkaline, and of large (10–12 L) volume.

Gastric decompression and intravenous administration of fluids results in marked improvement of clinical signs, although affected horses can continue to have nasogastric reflux for 24 hours to 10 days. Most cases resolve within 5 days. If untreated, horses develop severe gastric distension with subsequent rupture and death from peracute, diffuse peritonitis, or die as a result of hypovolemia and toxemia. A common sequela is the development of laminitis (approximately 8%). Approximately 10% of horses with duodenitis-proximal jejunitis have cardiac arrhythmias, including ventricular depolarizations and atrioventricular conduction disturbances. Arrhythmia resolves with resolution of the duodenitis-proximal jejunitis or correction of hypokalemia and acid-base disturbances.

CLINICAL PATHOLOGY

There is hemoconcentration with hematocrits as high as 0.70 L/L (70%) and total serum protein as high as 96 g/L (9.6 g/dL) in severely affected horses. The leukogram is variable and not diagnostic, and leukocytosis and left shift are common. Serum potassium concentration can be mildly low and blood bicarbonate concentration and pH are low in most cases. Horses with duodenitis-proximal jejunitis have serum bilirubin concentrations and serum GGT, aspartate aminotransferase, and alkaline phosphatase activities higher than horses with small-intestinal infarctive lesions. However, the differences are not sufficiently large for these variables to be useful in the differentiation of horses with duodenitis-proximal jejunitis from horses with small-intestinal infarctive lesions.

Peritoneal fluid has a normal nucleated cell count in 65% of cases; in the remaining cases it is increased. Peritoneal fluid protein concentration is often normal in cases sampled early in the disease but can be increased in more severe or prolonged disease and is a useful prognostic indicator.

NECROPSY FINDINGS

Gross lesions are restricted to the stomach, duodenum, and jejunum in most cases. The affected stomach and small intestine are distended, and the serosal surface has numerous petechial and ecchymotic hemorrhages. The mucosa is deep red and contains petechial hemorrhages and occasional foci of necrosis and ulceration. Histologic changes include neutrophilic inflammation, edema, hyperemia, epithelial sloughing, and villous atrophy. There is necrosis of mucosa, fibrin-rich edema and heavy neutrophil infiltration of the submucosa, and extensive hemorrhage in the tunica muscularis and serosa. A proportion of horses with duodenitis-proximal jejunitis have biochemical and histologic evidence of liver disease, including hepatocellular vacuolization and neutrophilic inflammation. Some horses with duodenitis-proximal jejunitis have myocarditis.

> **DIFFERENTIAL DIAGNOSIS**
>
> The most important differential diagnosis is a small intestinal obstructive lesion.

DIAGNOSTIC CONFIRMATION

Horses with small-intestinal obstructive lesions require urgent surgical correction, whereas most horses with duodenitis-proximal jejunitis respond well to medical therapy. The differentiation of duodenitis-proximal jejunitis and a small-intestinal obstructive lesion on clinical grounds is difficult, and there is no one variable that allows the distinction to be made reliably. Horses with duodenitis-proximal jejunitis have a lower heart rate, higher rectal temperature (fever), lower volume of gastric reflux, and less turgid small intestine on rectal examination than do horses with obstructive lesions, although others report that horses with duodenitis-proximal jejunitis have a higher volume of reflux at first examination and during the first 24 hours of disease. However, these differences are not sufficiently great to be conclusive. Horses with duodenitis-proximal jejunitis more often have normal peritoneal fluid than do horses with small-intestinal obstructive lesions. The response to gastric decompression and intravenous administration of fluids is useful in discriminating between diseases because horses with duodenitis-proximal jejunitis have marked resolution of abdominal pain and tachycardia within minutes of gastric decompression, whereas horses with small-intestinal obstruction have minimal or no resolution of these signs. Generally, horses with a heart rate below 60 beats/min after gastric decompression, mildly to moderately distended loops of small intestine, resolution of abdominal pain after gastric decompression, and normal peritoneal fluid probably have duodenitis-proximal jejunitis. However, horses should be examined frequently for changes in clinical condition. Worsening pain and cardiovascular status in the face of adequate fluid therapy warrant reconsideration of a diagnosis of duodenitis-proximal jejunitis.

TREATMENT

The principles of treatment of duodenitis-proximal jejunitis are gastric decompression; correction of fluid, acid-base, and electrolyte abnormalities and provision of maintenance fluid and electrolytes; relief of pain; and prophylaxis of laminitis. The decision on whether to elect surgical treatment for affected horses is dependent on the availability of surgical expertise and experience of clinicians in managing such cases medically or with surgical intervention. Horses for which surgical intervention is more likely are those with more severe signs of pain and absence of fever (each of which increases the likelihood of a small-intestinal obstructive lesion that requires surgical intervention for correction).[5] The duration of hospitalization is not different for horses treated medically (10 ± 4 days) or surgically (10 ± 6 days), although the survival rate for surgically treated horses is lower (75% versus 91%).[5] This could be a result of treatment modality,

Table 7-21 Agents used to treat ileus in horses with duodenitis and proximal jejunitis

Medication	Dosing	Comments	Recommendation
Lidocaine	1.3 mg/kg slow IV, then 0.05 mg/kg infusion	Analgesic, antiinflammatory, promotility; used to treat ileus; toxicity evident as central nervous system signs	R2
Metoclopramide	0.25 mg/kg IV slowly over 30 min every 12 h	Toxic; minimally effective	R3
Erythromycin	1 (mg/kg)/h IV	Questionable efficacy; might induce colitis	R3
Cisapride	0.1 mg/kg, IV every 8 h	Effective in prevention and treatment of postoperative ileus; can prolong cardiac Q-T interval (importance unknown); availability very limited	R3

IV, intravenously.

but it could also be related to the selection of horses for surgical treatment. Surgically treated horses are more likely to develop diarrhea (12% versus 28%).[5]

Gastric decompression is an urgent need in affected horses and can be accomplished by nasogastric intubation. The nasogastric tube should be left in place, or replaced frequently, for as long as there is reflux of clinically significant quantities of fluid (more than 2–4 L/4 h in a 425-kg horse). Discontinuation of gastric siphonage should be approached cautiously and the horse monitored for any increase in heart rate, development of abdominal pain, or ultrasonographic evidence of gastric or small-intestinal distension that could indicate recurrence of gastric distension. After the nasogastric tube is removed, the horse should be reintroduced cautiously to oral fluids and food. Small amounts (1–2 L) of water should be offered frequently (every 1–2 hours) during the first 12 to 24 hours. Horses should not be given immediate access to ad libitum water because some horses in the early convalescent period from duodenitis-proximal jejunitis will consume a large quantity of water and develop gastric dilatation and colic. Feed should be reintroduced gradually over 24 to 48 hours.

Complications of prolonged or repeated gastric siphonage through a nasogastric tube are pharyngitis, esophagitis, esophageal stricture, and esophageal perforation with subsequent cellulitis.

Fluid, electrolyte, and acid-base abnormalities should be corrected by the intravenous administration of isotonic, polyionic fluids such as lactated Ringer's solution. Affected horses lose considerable chloride and potassium in reflux fluid necessitating supplementation of fluids with potassium (up to 20 mEq/L of administered fluids).

Analgesia can be provided by administration of any of a number of drugs, including flunixin meglumine or ketoprofen. If the diagnosis of duodenitis-proximal jejunitis is uncertain, potent analgesics such as flunixin meglumine should be used judiciously until there is no possibility that a lesion requiring surgical correction exists.

Promotility agents such as lidocaine and cisapride (Table 7-21) and antacids such as cimetidine are sometimes administered. The efficacy of cimetidine has not been determined. There is evidence that lidocaine (lignocaine) is efficacious in reducing the duration of reflux, the amount of reflux, and the duration of hospitalization in horses with ileus of undermined cause (some of which presumably had duodenitis-proximal jejunitis) or after surgical correction of colic.[6]

Antibiotics, such as penicillin and an aminoglycoside, are often administered to affected horses because of the presumed bacteremia associated with the disease.

Surgical treatment of the disease is described and the outcomes were discussed previously.[5]

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DISEASES OF THE CECUM

ETIOLOGY

- Cecal impaction
- Cecal rupture
- Cecocecal and cecocolic intussusceptions
- Cecal torsion
- Cecal tympany
- Cecal infarction
  - Congenital abnormalities (cecal duplication)[1]
  - Ileocecal intussusception is discussed as an obstructive disease of the small intestine (see section on Small Intestinal Obstruction in Horses)

There is strong support for a role of *A. perfoliata* infestation in cecal disease of horses. Infestation with *A. perfoliata* results in edema, hyperemia, and hemorrhagic foci in the ileocecal valve mucosa with light parasitism through regional necrotizing enteritis, with extension of lesions to the muscularis mucosa and eosinophilic inflammation around arterioles and submucosal neural plexus with heavy parasitism.[2,3] The lesions are associated with local and systemic production of specific IgE and IgG(T) antibodies.[2]

SYNOPSIS

Etiology Cecal impaction, perforation, cecocecal and cecocolic intussusceptions, cecal torsion, and cecal tympany.

Epidemiology Sporadic diseases with exception of association with *Anoplocephala perfoliata* infestation. Cecal impaction and cecal perforation are reported in horses and foals hospitalized for unrelated conditions. Cecal rupture occurs in mares during parturition.

Clinical signs Cecal impaction is evident as mild, intermittent colic that might not be noticed by a casual observer. Cecal perforation or rupture is evident as acute shock, sweating, and tachycardia secondary to diffuse peritonitis. Cecocolic intussusception causes acute severe colic and cecocecal intussusception causes mild, intermittent colic. Rectal examination and/or rectal or percutaneous ultrasonographic examination can be diagnostic.

Clinical pathology Nondiagnostic.

Lesions Gross lesions consistent with the disease.

Diagnostic confirmation Physical examination, exploratory laparotomy, or necropsy examination.

Treatment Cecal impaction treated medically with overhydration, fecal softeners, and analgesics. No treatment for cecal rupture or perforation. Surgical correction of some cecal impactions and all cecocecal and cecocolic intussusceptions

Larval cyathostomiosis is also associated with cecocolic and cecocecal intussusception in young horses. Other causes include intramural and extramural masses, including cecal abscesses and accumulations of fatty tissue (lipomatosis)[4] or neoplasia[5] that alter cecal motility and passage of ingesta as well as other alterations in cecal and colonic motility.

Cecal rupture occurs in foals with a reported age range of 1 to 6 months that have an association with previous anesthesia and administration of antiinflammatory drugs.[6] Rupture is not exclusively associated with impaction of the cecum in affected foals.[6]

Disturbed cecal motility or dehydration of cecal contents secondary to dietary changes are thought to be the cause of most cases of cecal impaction and rupture. Horses with recurrent cecal impaction have lower neuron densities in muscle layers of the base of the cecum and cecal body than do normal horses, supporting the hypothesis that disturbed motility secondary to neuronal abnormalities is a cause of the disease. Administration of drugs that interfere with cecal motility or secretory function has the potential to increase the risk of cecal disease.

EPIDEMIOLOGY

Cecal disease accounts for approximately 4% to 10% of colic in horses examined for abdominal pain at referral centers.

Cecal Impaction

Cecal impaction is the cause of colic in approximately 2% to 5% of horses treated for colic in referral institutions.[7] This estimate probably reflects a selection bias, with horses with less severe disease not being referred for further examination. Cecal impaction is therefore probably much less common as a cause of colic in field cases. Cecal impaction is the most common cause of cecal disease (40%–50% of cases) and 5% of horses with intestinal impaction.[3,7]

There is no gender predisposition to the disease, although there are reports of a high proportion (22%) of affected mares having foaled within the previous 90 days or being pregnant (20%).[7] Older horses are disproportionately affected with 50% of affected horses being between 10 and 17 years of age.[7] Horses over 15 years are at increased risk compared with horses less than 7 years of age.[3] The disease occurs sporadically but is reported in horses and foals hospitalized or treated for an unrelated disease, and it is speculated that anesthesia, surgery, and/or administration of NSAIDs are risk factors for the disease.[3,6-8] Hospitalization and treatment for ocular disease are risk factors for impaction colic, with 10 of 72 (14%) of such horses in one study developing impaction of the cecum.[9] Fasting, poor dentition, poor-quality feed, and restricted water intake might also be risk factors for the disease. The **case–fatality rate** is approximately 30% to 50%.[7]

A particular form of cecal impaction is that involving only the cecal base (cecal cupula) without accumulation of impacted material in the cecal apex or body of the cecum.[10] There are no identified risk factors, and the outcome of surgical treatment is good (100% survival of 7 horses treated).[10] The disease had a frequency of 0.45% of horses undergoing exploratory laparotomy.[10]

Cecal Perforation or Rupture

Cecal rupture at parturition occurs in 0.1% of mares. It represents approximately 27% of cecal disease in horses, and that associated with concurrent but apparently unrelated disease is the most common (13%). Cecal rupture or perforation is otherwise a sporadic disease that is often, but not always, a sequela to cecal impaction. The case–fatality rate is 100%. Cecal rupture, often without recognized preexisting disease, is a complication of anesthesia and NSAID (usually phenylbutazone) administration. As with other cecal diseases, infestation with *A. perfoliata* has been implicated as a cause of cecal rupture, although not all horses with cecal rupture have tapeworms.

Cecocecal or Cecocolic Intussusceptions

Cecocolic and cecocecal intussusceptions are the cause of 1% of colic cases treated surgically and approximately 3% to 7% of cecal disease. The case–fatality rate is approximately 50% to 70%.[3,11] There are no recognized epidemiologic patterns to the occurrence of **cecal or cecocolic intussusceptions**, with the exception that younger horses (<3 years) and Standardbreds are disproportionately affected. Cecocolic and cecocecal intussusceptions appear to disproportionately affect younger horses (range 6 months to 12 years of age) in New Zealand.[11] This could represent a biologic effect or selection of cases presented to the referral institution. Infestation with tapeworm (*A. perfoliata*) is suspected to increase the risk of cecal intussusceptions, although this suspicion is not universal.

Cecal Torsion

Cecal torsion occurs rarely and is associated with hypoplasia of the cecocolic fold in some but not all cases.

Primary **cecal tympany** is rare. Cecal infarction is caused by thromboembolic disease secondary to *Strongylus vulgaris* arteritis or necrotizing enterocolitis.

PATHOGENESIS

Cecal impaction is probably a result of impaired or altered cecal motility, with resultant reduced cecal emptying into the right ventral colon. Accumulation of feed material causes cecal distension and excessive tension in the wall of the cecum with ischemia, necrosis, and rupture. Infestation by tapeworms, including *A. perfoliata,* causes disruption of the cecal mucosa and submucosa, necrosis, and inflammation—changes that contribute to cecal dysfunction. Death results from peracute diffuse peritonitis.

Cecal rupture at parturition is probably the result of high intraabdominal pressures associated with expulsion of the fetus. The pathogenesis of cecal rupture without cecal impaction is unknown.

CLINICAL FINDINGS
Cecal Distension and Impaction

There are a variety of classification schemes for cecal distension and impaction, including the time frame for development of the disease (acute or chronic), the presence of identifiable risk factors (hospitalization, antiinflammatory drug administration, and the presence of *A. perfoliata*), and the nature of the material distending the cecum (impacted ingesta and fluid).[10] Each provides the opportunity to emphasize a particular aspect of the disease(s) and is useful in that respect. The simplified classification used previously with continue to be used.[3]

Cecal distension occurs as two clinical syndromes: one caused by impaction of the cecum with inspissated feed material and the other caused by acute distension of the cecum by a mixture of fluid and ingesta.

Cases in which the cecum is **impacted** and distended with inspissated feed material usually have signs of mild to moderate abdominal pain that is often intermittent over a 1- to 4-day period. The signs of pain can be mild enough to be missed by a casual observer. Affected horses are usually mildly depressed and have a diminished appetite. The heart rate is 40 to 60 beats/min, borborygmi are reduced, and there can be mild dehydration. Nasogastric intubation yields reflux fluid only late in the course of the disease. Rectal examination reveals a doughy mass in the right caudal abdomen permitting diagnosis in approximately 85% of cases.[7] The ventral, and occasionally the medial, tenia of the cecum are palpable, as is firm feed material in the base and body of the cecum. The mass extends cranially, ventrally, and across the midline of the abdomen. If not treated, the cecum ruptures, causing an acute onset of tachycardia, sweating, delayed capillary refill, and shock, with death occurring in hours. It is not unusual for the initial signs of the disease to be missed and the problem to be recognized only after the cecum ruptures.

The outcome of horses with cecal impaction depends on the disease and its stage at presentation. The prognosis for horses treated medically is good with 81% surviving to discharge from hospital. This likely reflects that horses treated medically are metabolically stable (and therefore do not have a ruptured cecum) and have less severe impaction. Exploratory laparotomy results in diagnosis of cecal rupture in approximately one-quarter of horses,[7] all of which die, and a survival rate of approximately 65% to 90% in those horses allowed to recover from anesthesia.[7,8]

Horses with chronic, **recurrent cecal impaction** have a mild disease characterized by recurrent subtle to moderate signs of colic, reduced food intake, weight loss, and loose feces.

Impaction of the **base of the cecum** (the cecal cupula) by ingesta causes a mild colic

of several days' duration. Affected horses are metabolically stable and there are no diagnostic findings on rectal examination. Diagnosis is achieved during exploratory laparotomy.

Cecal distension also occurs as a syndrome in which **fluid** accumulates in the cecum. This disease has a much more acute course and is characterized by severe abdominal pain, tachycardia, and signs consistent with toxemia. Rectal examination demonstrates a cecum tightly distended with fluid ingesta. Without surgical intervention the outcome is cecal rupture and death.

Perforation and Rupture

Cecal perforation occurs secondary to cecal distension or as a primary entity. There are usually only very mild premonitory signs in either adults or foals, and the disease becomes apparent when the cecum ruptures and acute diffuse peritonitis develops.[6] Twenty-five percent of horses with cecal impaction develop cecal perforation or rupture.[7] Detection of serosa with a gritty feel and free gas in the abdomen on rectal examination is diagnostic of a ruptured viscus and diffuse peritonitis. Subserosal and retroperitoneal emphysema in the region of the base of the cecum can be indicative of cecal perforation or rupture.[12]

Intussusception

Cecocecal intussusception is the invagination of the cecal apex into the body of the cecum and usually presents as a mild intermittent colic, depending on the degree of involvement of the apex of the cecum. Small intussusceptions that cause little obstruction and no infarction of the invaginated section cause only mild pain.

Signs of cecocolic intussusception, in which the inverted cecum (the intussusceptum) progresses through the cecocolic orifice into the right ventral colon, occur over 1 to 7 days, and vary from mild and recurrent to acute and persisting. Rectal examination can reveal a mass in the right dorsal quadrant, lack of a cecum, and pain on palpation of the right dorsal quadrant. Ultrasonographic examination of the right flank reveals the presence of the cecum in the colon, which is apparent in cross section as a "target-like" pattern or taurus.[11]

CLINICAL PATHOLOGY

Cecal impaction with feed material is usually associated with mild hemoconcentration. Cecal perforation results in severe leukopenia and left shift, hemoconcentration (hematocrit > 50%, 0.50 L/L), and azotemia.

Peritoneal fluid from horses with cecal impaction is usually normal. However, if the cecum becomes ischemic, then the fluid is sanguineous with an elevated white blood cell count (>8000 cells/μL, 8 × 10 cells/L) and protein concentration (>2.5 g/dL, 25 g/L). Cecal perforation is evident as a high proportion of degenerate neutrophils, intracellular and extracellular bacteria, and plant material. Peritoneal fluid is abnormal in 81% of horses with cecocolic intussusception and 67% of cases with cecocecal intussusception.[11]

NECROPSY FINDINGS

The distended cecum and diffuse peritonitis are readily apparent. Cases of cecal perforation without distension will have diffuse peritonitis, but the cause is only apparent on close examination of the intestinal tract.

DIFFERENTIAL DIAGNOSIS

See Table 7-10 for causes of colic.

TREATMENT

Medical treatment of cecal impaction involves control of pain, restoration of normal fluid, acid-base and electrolyte status (see Chapter 5), and administration of fecal softeners such as sodium sulfate. Mineral oil, although frequently used, is not sufficient alone to facilitate passage of the impaction because it does not cause fecal softening.

Intravenous administration of fluid at two to three times maintenance needs is often used in an attempt to hasten fecal softening by increasing secretion of water into the impaction. **Oral administration** of large quantities of water (4 L every 2 hours for 24 hours) may soften the impaction.

Horses with cecal impaction should be **closely monitored** for signs of deterioration, and especially for cecal ischemia, by frequent physical examinations and repeated abdominocentesis. Lack of resolution within 24 hours or signs of deterioration should prompt surgical exploration with typhlotomy and evacuation of the cecum and possible partial cecal bypass. The results of surgical treatment of horses with cecal impaction are good with survival rates of 65% to 90% reported for horses that are recovered from surgery.

Cecocecal and cecocolic intussusceptions must be corrected surgically. The survival rate for horses with cecocecal or cecocolic intussusceptions is approximately 50%, although estimates are variable because of the small number of animals reported.[11]

Horses with **cecal perforation** always die and should be euthanized without delay.

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DISPLACEMENT AND/OR VOLVULUS OF THE LARGE (ASCENDING) COLON

Displacement and volvulus of the large (ascending) colon are evident as nephrosplenic entrapment, renosplenic entrapment, left dorsal displacement of the large colon, or right dorsal displacement of the large colon.

ETIOLOGY

- Left dorsal displacement of the large colon (renosplenic or nephrosplenic entrapment and entrapment of the large colon lateral to the spleen)
- Right dorsal displacement of the large colon
- Volvulus (both strangulating and nonstrangulating)

SYNOPSIS

Etiology Unknown, probably involves disturbance of colonic motility

Epidemiology Volvulus is more common in mares during late gestation or after parturition. Left dorsal displacement (renosplenic entrapment) may be more common in large male horses.

Clinical signs Left displacement of the large colon causes signs of mild to moderate colic. Rectal examination reveals large colon in the renosplenic space, and ultrasonographic examination confirms the diagnosis. Right dorsal colon displacement causes mild to moderate colic. Rectal examination reveals colon lateral to the base of the cecum. Volvulus of the large colon causes mild to extremely severe abdominal pain, tachycardia, shock, and abdominal distension. Rectal examination reveals the distended, displaced colon.

Clinical pathology Nondiagnostic.

Lesions Displaced large colon.

Diagnostic confirmation Physical examination, laparotomy, and necropsy examination.

Treatment Volvulus and right dorsal displacement should be treated by surgical correction. Left dorsal displacement can be corrected by rolling the anesthetized horse or jogging the horse after administration of phenylephrine.

The etiology of these conditions is unknown but presumably involves some disturbance to normal colonic motility. Other causes of obstruction of the large colon include congenital abnormalities of the right ventral colon, cystic duplication of the ascending colon, defects in the mesocolon, and incarceration in epiploic foramen or gastrosplenic ligament. Intussusception of the large colon causes infarction and severe colic.

The term volvulus refers to rotation of the segment of bowel about the long axis of its mesentery, and torsion refers to rotation about the long axis of the bowel. Because of the anatomic arrangement of the mesocolon, either term may be correctly used to describe displacements of the large intestine.

EPIDEMIOLOGY

Left dorsal displacement of the large colon (Figs. 7-2 and 7-3) is the cause of 2% to 10% of colic cases referred for specialist treatment. There is no breed, age, or gender predisposition, although some authors suggest that males and large horses are more likely to be affected. The case–fatality rate is approximately 5% for horses treated correctly.

Right dorsal displacement of the large colon (Fig. 7-4) occurs sporadically and without recognized risk factors. The case–fatality rate is reported to be as high as 43%.

Risk factors for noninfarctive displacement of the large colon include cribbing or wind sucking (OR = 90), number of hours stabled per day (OR for 24-hour stabling = 35), lack of regular exercise (OR 3.3), change in exercise program (OR 9), lack of anthelmintic administration (OR 13), and history of transport in the previous 24 hours (OR 17).

Volvulus of the large colon is the cause of colic in 11% to 17% of colic cases in which abdominal surgery is performed. The disease occurs commonly in mares, especially those late in gestation or having recently foaled. Risk factors for volvulus of the large colon include being a broodmare (OR 2.5 versus male horse), greater height, colic in the past 12 months (OR 2.17), having a greater number of carers, larger number of horses on the premises, and a number of variables related to feed quality or quantity.[1] The disease has a recurrence rate of up to 15% in broodmares. The disease occurs in horses from 2 days of age and there does not appear to be an effect of breed on occurrence of the disease. The **case–fatality rate** varies depending on the extent of the volvulus, with lesser degrees of volvulus (<270°) having a 30% fatality rate and volvulus of 360 degrees or more having a 65% fatality rate. The case–fatality rate for horses with strangulating large-colon volvulus treated surgically is approximately 30% (survival to hospital discharge), 52% at 1 year, and 67% at 2 years.[2]

PATHOGENESIS

Proximate factors leading to volvulus or displacement are unknown, although risk
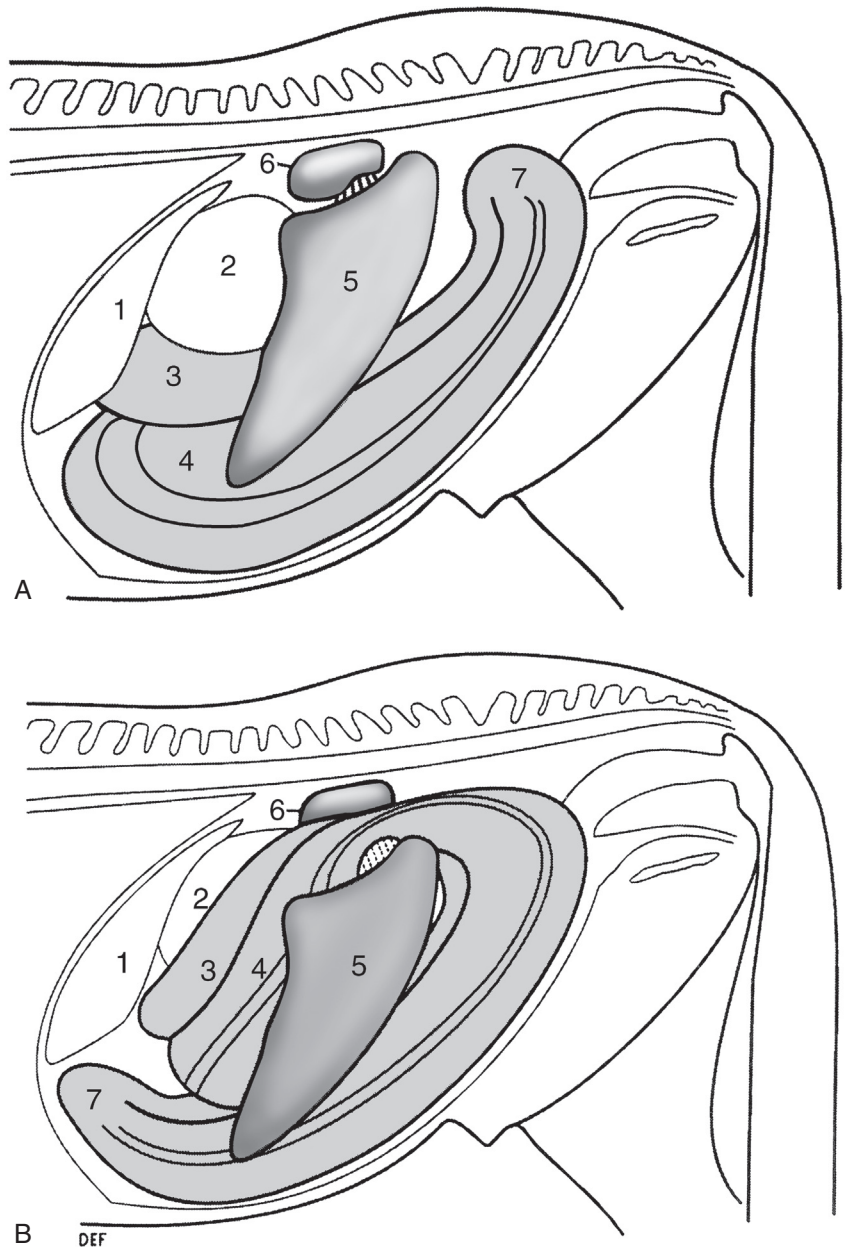
Fig. 7-2 A, Left lateral view of abdomen of a normal horse. **B,** Left dorsal displacement of the left colon, left lateral view. The left ventral and dorsal colon is displaced lateral and dorsal to the spleen and occupies the renosplenic space. *1,* liver; *2,* stomach; *3,* left dorsal colon; *4,* left ventral colon; *5,* spleen; *6,* left kidney and renosplenic ligament; *7,* pelvic flexure. (With permission from Johnston JK, Freeman DE. *Vet Clin North Am Equine Pract* 1997;13:317.)

factors have been identified (see earlier discussion). A plausible scenario is that altered colonic motility and subsequent distension with gas or ingesta predisposes the colon to displacement, either spontaneously or as a result of the horse rolling or lying down in response to abdominal pain.

Left dorsal and right dorsal displacements of the colon rarely compromise colon blood flow and represent nonstrangulating obstructive lesions (see section Pathogenesis in Equine Colic). The displacement of the large colon (see Figs. 7-2 and 7-3) impedes

aboral movement of ingesta and gas and may result in colonic distension. Should the distension become sufficiently severe, colon blood flow will be impaired and cause ischemia and necrosis of the colon. The obstruction to blood flow is predominantly in venous drainage, resulting in hemorrhagic strangulating obstruction with progressive development of intramural edema, extravasation of red blood cells, microvascular thrombosis, mesothelial cell loss from the serosal surface, and mucosal necrosis with loss of colonic epithelium.
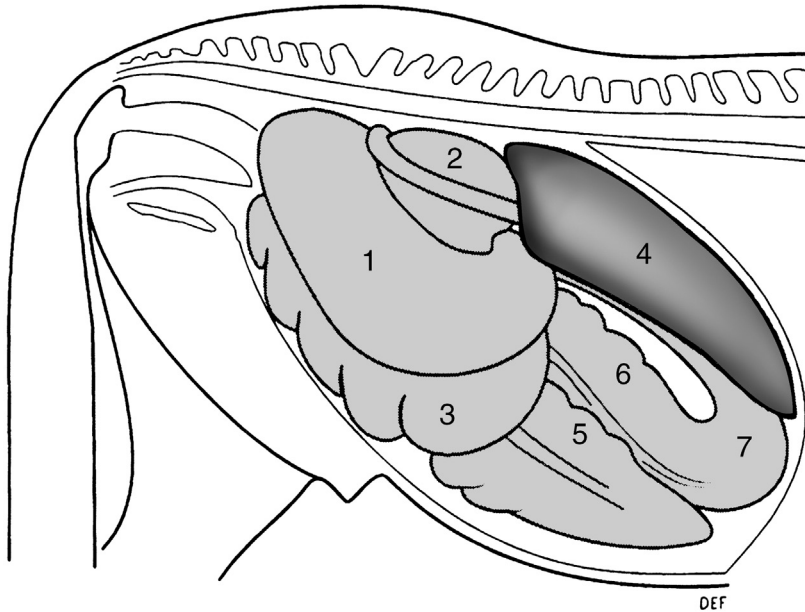
Fig. 7-3 Right dorsal displacement of the colon, right lateral view. The colon has passed lateral to the cecum, the pelvic flexure is displaced cranially, and the sternal and diaphragmatic flexures are displaced caudally. *1,* right dorsal colon; *2,* base of cecum; *3,* right ventral colon; *4,* liver; *5,* cecum; *6,* left ventral colon; *7,* pelvic flexure. (With permission from Johnston JK, Freeman DE. *Vet Clin North Am Equine Pract* 1997;13:317.)
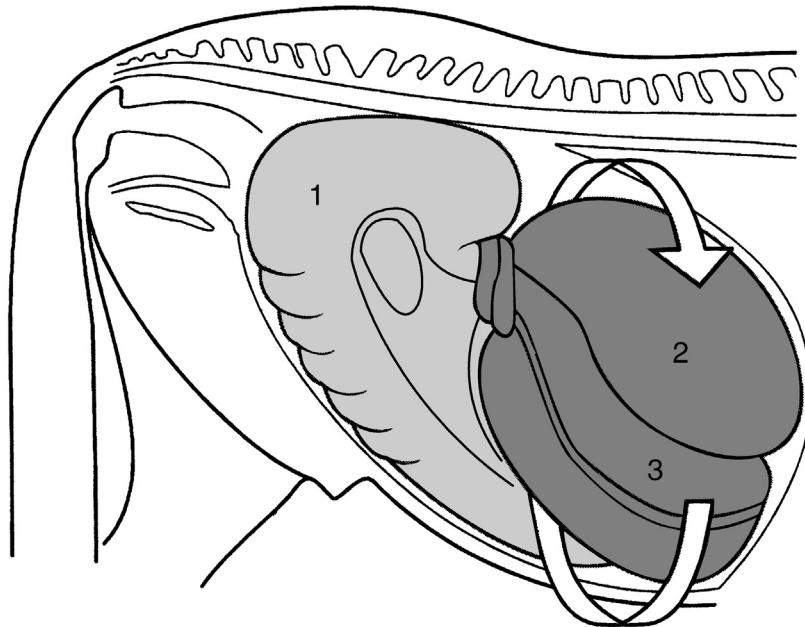
Fig. 7-4 A 360° clockwise volvulus of the colon viewed from the right side. The volvulus has occurred in the direction of the arrow. *1,* cecum; *2,* right dorsal colon; *3,* right ventral colon. (With permission from Johnston JK, Freeman DE. *Vet Clin North Am Equine Pract* 1997;13:317.)

Volvulus of the large colon of less than 270 degrees does not compromise blood supply but does impede aboral movement of ingesta and gas. Volvulus of 360 degrees or more causes ischemia through occlusion of both arterial and venous circulation of the involved large colon with rapid loss of colonic mucosal integrity and colon viability. There is reduced microvascular perfusion in horses with large-colon volvulus.[3] Irreversible mucosal damage occurs after 3 to 4 hours of ischemia. Loss of mucosal integrity impairs normal barrier function and permits toxins and substances normally confined to the colonic lumen to enter the systemic circulation. Additionally, loss of barrier function allows leakage of vascular proteins and in severe cases red blood cells into the colonic lumen. Subsequent signs are typical of strangulating obstruction (see section Equine Colic) with development of toxemia, cardiovascular collapse, and death within 12 to 18 hours.

The most common displacement is medial and dorsal movement of the ventral colon to complete a 360-degree volvulus of the large intestine (see Fig. 7-4). Lateral and dorsal displacement of the ventral colon is much less common. The volvulus is usually at the level of the cecocolic fold, although volvulus involving the cecum or at the diaphragmatic and sternal flexures does occur.

CLINICAL FINDINGS
Left Dorsal Displacement (Renosplenic Entrapment)
Left dorsal displacement usually has an acute onset and a duration of up to 4 days, although it can be a cause of chronic, recurrent colic. Abdominal pain in the initial stages is mild to moderate and becomes progressively more severe as distension of the large colon develops. The heart rate is usually between 50 and 70 beats/min, but may be as low as 30 beats/min. Rectal temperature is within normal limits. Mucous membrane color and refill time are usually normal provided there is no ischemia of the colon. **Abdominal distension** is appreciable in some affected horses. There is more than 2 L of reflux from a **nasogastric tube** in approximately 28% of cases, although rarely is there profuse reflux. **Rectal examination** reveals the presence of bowel in the renosplenic space in approximately 70% of cases with the typical finding of tenia of the ventral colon being traced into that space. Distension of the large colon may impair detection of bowel in the nephrosplenic space. The spleen is usually displaced caudally, medially, and ventrally from its normal position against the left body wall (see Fig. 7-2).

Ultrasonographic demonstration of colon in the renosplenic space confirms the diagnosis with an accuracy of 88%. Gas in the displaced colon obscures the left kidney and dorsal border of the spleen normally visible on ultrasonographic examination of the left paralumbar region.

Approximately 8% of horses with nephrosplenic entrapment have an additional lesion. Entrapment in which the sternal and diaphragmatic flexures are displaced cranial to the stomach and liver occurs in less than 3% of cases.

Right Dorsal Displacement
Severity of colic varies from mild to severe in horses with right dorsal displacement of the colon. Tachycardia (50–80 beats/min) and mild abdominal distension are characteristic provided that the entrapped bowel

is not ischemic. There is usually no reflux from a nasogastric tube, although as the disease progresses gastric distension may occur. **Rectal examination** reveals the presence of large colon lateral to the base of the cecum, although colonic distension may make detection of the displaced bowel difficult. Right dorsal displacement is a common sequela to impaction of the pelvic flexure.

Volvulus

The onset of pain is abrupt and the duration of the disease ranges from hours, in horses with strangulating lesions, to days in horses with torsion of less than 270 degrees. The pain ranges from mild to severe and intractable, with the horse violently throwing itself to the ground. Pain in horses with a volvulus of 360 degrees or greater is often unresponsive to any analgesics. Heart rate is variable and may be less than 40 beats/min in horses with severe disease, although usually it is more than 60 beats/min and increases with severity of the disease. Rectal temperature is within normal range. The mucous membranes are dark red to blue and capillary refill time is more than 3 seconds in severely affected horses. Abdominal distension is marked, usually severe, and may impair respiration in horses with a 360-degree or greater volvulus. **Auscultation** of the abdomen reveals a lack of borborygmi and the presence of high-pitched, tympanitic pings on simultaneous percussion and auscultation. The pings are caused by the presence of gas in a tightly distended large colon or cecum. There is usually no reflux through a nasogastric tube. **Rectal examination** may be limited by the distended, gas-filled colon occupying the caudal abdomen. In untreated cases death occurs within 12 to 24 hours from cardiovascular collapse. **Ultrasonographic** examination reveals colon with a mural thickness of 9 mm or greater in horses with colon torsion. The test has a sensitivity of approximately 67% (i.e., correctly predicts the presence of colon torsion in two-thirds of horses that have the disease) and specificity of 100% (correctly rules out the diagnosis in 100% of horses that do not have the disease).

CLINICAL PATHOLOGY

Changes in the hemogram, serum biochemical profile, and peritoneal fluid are nonexistent to mild in horses with uncomplicated left dorsal displacement, right dorsal displacement, and volvulus of less than 270 degrees. Horses with ischemic colon as a result of strangulation usually have a leukopenia with left shift, hemoconcentration, and increased anion gap.

Serum GGT activity is elevated in approximately 50% of horses with right dorsal displacement of the colon, whereas such elevations are rare in horses with left dorsal displacement. The elevated GGT, and less commonly serum bilirubin concentration, in horses with right dorsal displacement is attributable to compression of the common bile duct in the hepatoduodenal ligament by the displaced colon.

Horses with large-colon volvulus have a high prevalence of abnormalities in hemostatic variables, including thrombin–antithrombin concentration, D-dimer concentration, antithrombin activity, prothrombin time, and platelet count. Nonsurviving horses have lower platelet counts, increased prothrombin time, and reduced antithrombin activity.

Peritoneal fluid often has an increased total protein concentration (>25 g/L, 2.5 g/dL) and white blood cell count (>8000 cells/μL, 8×10 cells/L) in horses with compromised bowel. Examination of peritoneal fluid is often not necessary to achieve a diagnosis in horses with colon torsion, although it does have prognostic value in that horses with blood-tinged peritoneal fluid have a poor prognosis. The risk of inadvertent enterocentesis is increased in horses with severe distension of the colon, and abdominocentesis should be attempted with caution in such cases. Use of a bovine teat cannula or similar blunt instrument is preferred to the use of a needle.

NECROPSY FINDINGS

The colon is displaced as described earlier for each of the diseases. Death usually results from ischemic necrosis of the colon and the associated peritonitis, endotoxemia, and shock. Histologic lesions in horses dying of colon volvulus are more severe than of those that survive and are characterized by hemorrhage into the lamina propria, edema, and loss of the mucosal cells and crypt architecture.

DIFFERENTIAL DIAGNOSIS

See Table 7-19.
   Less common conditions of the large colon include:
- Entrapment of the pelvic flexure in the epiploic foramen
- Colocolic intussusceptions
- Colonic adenocarcinoma

TREATMENT

Treatment should consist of pain control; correction of fluid, acid-base, and electrolyte abnormalities; support of cardiovascular function; and correction of the underlying disease (see the section Equine Colic). Decompression by trocarization of gas-distended colon or cecum may be beneficial. Correction of colon volvulus or right dorsal displacement of the colon requires surgical exploration of the abdomen and manual correction of the displacement.

Left Displacement

Correction of left dorsal displacement can be achieved by either nonsurgical or surgical means. **Nonsurgical correction** is achieved by either rolling the anesthetized horse in a particular sequence that causes the displaced colon to return to its normal position in the abdomen or exercise after intravenous administration of phenylephrine.[4] Nonsurgical correction is successful in approximately 80% of cases, although complications are reported, and is recommended as the initial definitive treatment for horses with uncomplicated left dorsal displacement.

Rolling of anesthetized horses after intravenous administration of phenylephrine has a somewhat higher success rate (42/50, 84%) than exercise (trotting) after administration of phenylephrine (24/38, 63%).[4] The sequence of events following diagnosis of the condition is depicted in Fig. 7-5. **Phenylephrine** (0.02–0.04 mg/kg, intravenously as a 10-minute infusion) causes splenic contraction and is thought to increase the chances of the colon returning to its normal position. The horse is anesthetized within 10 minutes of phenylephrine administration and placed in right lateral recumbency. The horse is then slowly rolled into dorsal recumbency, and the abdomen is vigorously massaged in an attempt to cause the colon to move ventrally and medially. If a hoist is available the horse can be lifted into dorsal recumbency. The sequence ends with the horse being rolled into left lateral recumbency and a rectal or ultrasound examination being performed to determine the position of the colon. Fatal hemoperitoneum can occur after phenylephrine administration.

An alternative means of nonsurgical correction involves administration of phenylephrine (0.01 mg/kg, intravenously, slowly) and then jogging the horse. This technique was successful in correcting the displacement in 11 of 12 horses. It might be advantageous to relieve large-colon distension by percutaneous or per rectum trocarization before jogging.[5]

Cases that are refractory to nonsurgical treatment require laparotomy (ventral midline or left flank) and manual correction of the displacement. Recurrence of the displacement occurs in 3% to 7% of cases. Horses with recurrent disease can benefit from surgical ablation of the nephrosplenic space.

Right Dorsal Displacement and Colon Volvulus

Right dorsal displacement and colon volvulus require surgical correction of the anatomic abnormality.

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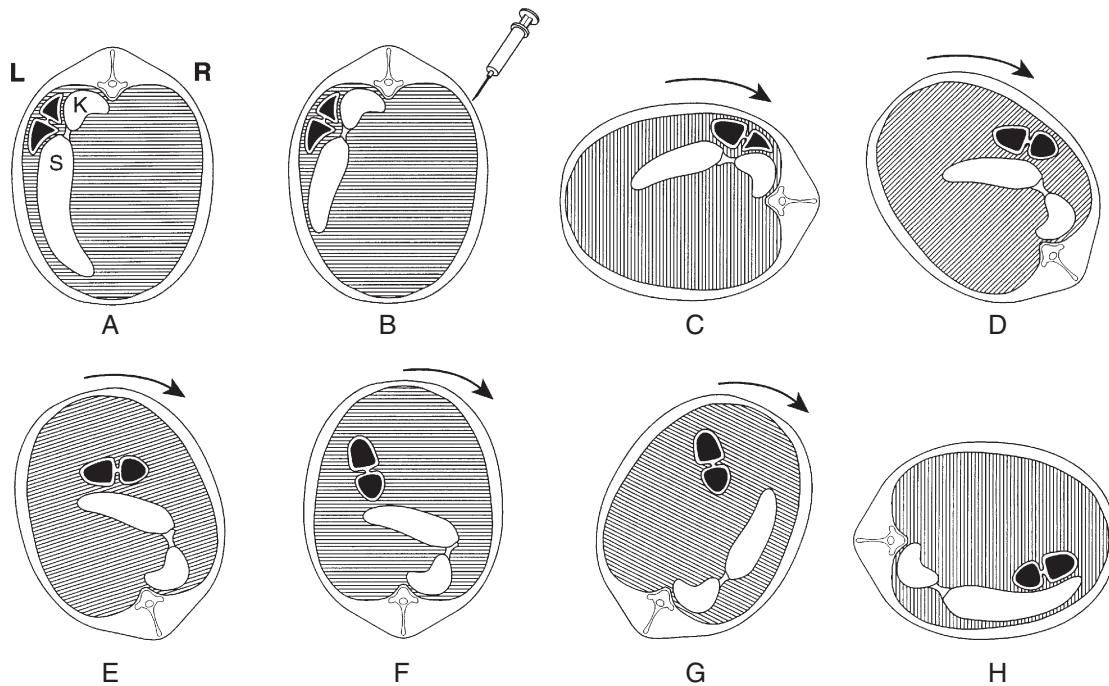
Fig. 7-5 Steps in correction of left dorsal displacement of the colon (renosplenic entrapment). **A,** Caudal view of abdomen of horse with left dorsal displacement of the colon. Entrapped colon is shown in black. *K,* left kidney; *S,* spleen. **B,** Injection of phenylephrine and contraction of spleen. **C,** Horse anesthetized and placed in right lateral recumbency. **D–H,** Horse rolled through dorsal recumbency to left lateral recumbency. Entrapped colon moves ventrally and then medially to the contracted spleen. (Modified with permission from Kalsbeek HC. *Equine Vet J* 1989;21:442.)

IMPACTION OF THE LARGE (ASCENDING) COLON OF HORSES

SYNOPSIS

Etiology Idiopathic, often associated with restricted exercise, poor-quality diet, or restricted access to water

Epidemiology Sporadic. Accounts for approximately 10% to 15% of colic cases at referral institutions and in primary practice. Case–fatality rate of 10%

Clinical signs Mild to moderate colic often of several days duration. Rectal examination reveals impacted, distended large colon.

Clinical pathology No diagnostic changes

Lesions Impaction of large colon, usually pelvic flexure or right dorsal colon

Diagnostic confirmation Physical examination

Treatment Pain control. Administration of fecal softeners (sodium sulfate). Oral administration of water or isotonic polyionic fluids or intravenous administration of isotonic fluids at 100 ml/kg/day

Impaction of the large (ascending) colon is a common disease of horses sometimes referred to as simple colonic obstruction and distension (SCOD). This does not include causes of colon obstruction caused by strangulation, volvulus, or displacement of the colon.

ETIOLOGY
The cause of most impactions of the large colon is unknown. Known or speculated causes include the following:
- Poor dentition, such as occurs in older horses
- Poor feeding regimens, such as infrequent feeding of stalled horses
- Horses not fed, in preparation for surgery or racing, and then given unrestricted access to feed or allowed to eat bedding materials
- Horses fed diets too high in fiber, e.g., mature sorghum or maize plants, or even mature Bermuda grass (*Cynodon* spp.) meadow hay, especially if their water intake is limited; ingestion of large volumes of indigestible seeds, e.g., *Crataegus crusgalli* (cockspur hawthorn), may cause outbreaks of impaction of the right dorsal colon
- Horses that come into loose boxes and are offered hard feed after being on soft grass on pasture are also likely to develop impaction colic.
- American Miniature horses develop impaction of the colon
- General debility
- Enteroliths and fiber balls may also cause obstruction of the large intestine and usually result in recurrent attacks of colic.
- Amitraz, a formamidine acaricide for cattle, causes impaction colic in horses.
- Retention of the meconium in foals (see section Colic in Foals)
- Administration of NSAIDs, which alter colonic motility and might predispose to impaction, although epidemiologic support of this etiology is not available
- Restricted water intake, such as during winter when watering points freeze or water is unpalatable

EPIDEMIOLOGY
Simple colon obstruction and distension occurs in horses of any age. It might be slightly less common in females,[1] although this is not a consistent finding in across studies of the disease. There does not appear to be a breed predisposition. The disease is more common in winter in the UK (41% of cases). The disease represented 13% of colic cases treated at a referral facility and approximately 10% of colic cases seen in private practice in the UK.[1] An important risk factor is a change in management, especially one that involves a reduction in exercise and change in diet.[1] Risk factors for SCOD include cribbing or wind sucking, stabling with the risk increasing with the number of hours stabled per day, change in regular exercise program, travel within the previous 24 hours, and lack of anthelmintic administration. A recent or current musculoskeletal injury is common in horses with SCOD.[1]

Among 118 cases of SCOD examined in primary care practice in the UK, 53% resolved with minimal or no treatment, 37% required multiple visits or hospitalization,

and 9% required surgical intervention or died.[1] The **case–fatality rate** is approximately 10%.[1]

The disease is common in donkeys occurring at a frequency of 3.2 per 100 donkeys per year and is the most common cause of colic in donkeys.[2,3] Important risk factors were increasing age (OR 1.1 per year), lower BW (0.98 per kg), previous colic (6.80), and presence of dental disease (29).[2] The case–fatality rate was 58%.

PATHOGENESIS

Development of impaction of the large colon is frequently attributed to abnormal colonic motility. Other factors, including mild dehydration as a result of limited water intake or ingestion of poorly digestible material, can cause impaction. Stabling is associated with decreases in large-intestinal motility, fecal water content, and volume of feces compared with horses on pasture and could predispose to development of impaction colic.[4,5] The end result of abnormal motility, intestinal contents, or both is accumulation of a large mass of inspissated feed material in the large colon. Material usually accumulates first at the pelvic flexure or right dorsal colon, presumably because of the reduction in lumen diameter at those points. **Accumulation of inspissated material** causes distension of the colon and prevents aboral passage of ingesta. **Distension** causes pain and changes in colonic motility that exacerbate or perpetuate the impaction. Changes in motility can lead to displacement of the colon, such as right dorsal displacement. If the distension is sufficiently severe or prolonged the colon can become ischemic and necrotic with subsequent rupture, peracute diffuse peritonitis, and death.

CLINICAL FINDINGS

Moderate abdominal pain is the typical sign in horses with SCOD; pulse rate and respiration are relatively normal, and gastrointestinal sounds are reduced.[1] There is no reflux on nasogastric intubation. This often continues for 3 to 4 days and sometimes for as long as 2 weeks. The horse is not violent, the principal manifestation of pain is stretching out and lying down, and the bouts of pain are of moderate severity occurring at intervals of up to a half-hour. There is anorexia and the feces are passed in small amounts and are hard and covered with thick, sticky mucus. More severe clinical signs including elevated heart rate, signs of severe or unremitting abdominal pain, discolored mucous membranes, and absences of normal gut sounds are associated with vascular compromise of the colon, impending rupture, or displacement of the colon.

On **rectal examination** impaction of the pelvic flexure of the large colon is the most common site, and the distended, solid loop of the intestine often extends to the pelvic brim or even to the right of the midline. Lying on the floor of the abdomen, it is easily palpated; the fecal mass can be indented with the fingers, and the curvature and groove between the dorsal and ventral loops of the left colon can be easily discerned. Careful attention should be paid to identifying caudal abdominal structures because impaction of the large colon can lead to displacement of the colon, such as right dorsal displacement, which necessitates surgical correction of the displacement. Impaction of the right dorsal colon cannot usually be palpated per rectum, and the only abnormality can be distension of the colon with soft ingesta that has accumulated behind the obstruction.

CLINICAL PATHOLOGY

Hemogram, blood chemistry, and peritoneal fluid are normal until the colon becomes ischemic, at which time there is a leukopenia with a left shift and an increase in the white blood cell count and protein concentration in peritoneal fluid.

NECROPSY FINDINGS

Necropsy findings include large intestine is packed full of firm, dry fecal material, and rupture may have occurred.

DIFFERENTIAL DIAGNOSIS

See Table 7-19.
- Impaction of the pelvic flexure is readily diagnosed on rectal examination.
- A clinical similar syndrome is produced by strictures of the large colon.

TREATMENT

The principles of treatment are pain control, correction of fluid and electrolyte abnormalities, and softening of ingesta to facilitate its passage. Pain control is discussed in Table 7-15. Fluid therapy is discussed in Chapter 5.

Softening of ingesta is achieved by rehydrating the inspissated material and providing lubrication to hasten its passage. **Fecal softeners** (see Table 7-16) such as magnesium sulfate or sodium sulfate can be given to increase the fecal water content and soften the impacted, inspissated ingesta. Magnesium sulfate is associated with a small risk of hypermagnesemia and neurologic signs, whereas sodium sulfate causes a mild hypernatremia and hypokalemia. Oral administration of a balanced, polyionic electrolyte solution is associated with the greatest increase in colonic water content and no change in serum electrolyte concentrations. Enteral administration of 10 L/h (to a 500-kg horse) of a balanced, isotonic, polyionic electrolyte solution is more effective than intravenous administration of the same quantity of water in combination with oral administration of MgO_4 in hydrating colonic contents in normal horses. Oral administration of plain water (100 mL/kg/day) is effective at increasing fecal water content in healthy horses dehydrated by withholding of water. Oral administration of water resulted in equivalent increases in fecal water content as did intravenous administration of polyionic isotonic fluids, but with less urine output and less sodium loss.[6]

Mineral oil (see Table 7-17) is a lubricant that might not penetrate the impacted ingesta sufficiently to soften the material, although it is frequently given to horses with colon impaction.

Softening of colonic contents is ideally achieved by enteral administration of water or polyionic, isotonic fluids. Water can be given by nasogastric tube at a rate of 4 to 10 L for a 450-kg horse every 1 to 2 hours until the impaction softens. Use of this regimen results in resolution of the impaction in 20 hours (standard deviation 5 hours) in almost all horses with colon displacement and in ~80% of horses with nonstrangulating displacement.[7] However, some horses develop decreased small-intestinal motility or ileus with the disease and have delayed gastric emptying and reflux of fluid through the nasogastric tube. Such horses should not be administered any medication or water through the nasogastric tube until reflux has resolved. Alternatively, isotonic fluids can be given intravenously at 100 mL/kg/day until the impaction is passed.

Promotility agents such as neostigmine are usually contraindicated because of the risk of rupture of the distended colon when vigorous contractions are induced pharmacologically.

Horses may need to be treated for 1 to 6 days until the impaction resolves and should **not be fed** during this time. When feed is again provided it should be easily digestible and initially be of limited volume. Horses recovered from impaction of the large intestine have a higher than expected rate of recurrence of colic (30%).

Surgical treatment may be needed for refractory cases (about 15%) but is associated with a poor prognosis because of the risk of iatrogenic rupture of the colon during attempts to exteriorize it from the abdomen during surgery. Impaction of the right dorsal colon is more likely to require surgical treatment.

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ENTEROLITHS AND FECALITHS

ETIOLOGY

Enteroliths are rock-like concretions, which are either spherical or tetrahedral, that form in the large colon of horses, usually around

a foreign body and which can cause disease evident as **obstructive enterolithiasis**. Most enteroliths in the colon of horses are of two major types: magnesium phosphates/struvite and magnesium vivianite. There is wide variability in macrotexture and ionic concentrations between and within enteroliths of ammonium magnesium phosphate (struvite). Affected horses often have more than one enterolith and the enteroliths can weigh up to 12 kg.

Fecaliths are aggregations of indigestible material such as fencing, plastic, or rope that often have an irregular shape.

EPIDEMIOLOGY

Enteroliths occur sporadically in horses in most regions of the world, but the disease is endemic with greater than expected incidence in certain areas, such as California. Equids with enterolithiasis represented 15.1% of horses admitted for treatment colic, and 27.5% of patients undergoing celiotomy for treatment of colic in a study from California, but less than 2% of horses with colic examined at a referral center in Texas. Of 1105 horses subjected to exploratory laparotomy because of colic over a 16-year period, 21% had obstructive enterolithiasis of which 41% had an enterolith in the descending colon and 59% in the ascending (large) colon.[1] Of 97 horses with obstructive enterolithiasis of the descending colon, 49 also had enteroliths in the large colon. Of the 139 horses with obstructive enterolithiasis of the large colon, 32 had multiple enteroliths detected.[1]

Arabians and Arabian crosses, Morgans, American Saddlebreds, and donkeys are overrepresented, and Thoroughbreds, Standardbreds, warmbloods, and stallions are underrepresented in some studies, suggesting a predilection of these breeds for the disease.[1] The disease is reported in American Miniature horses.

Female horses are overrepresented among surgical cases of obstructive enterolithiasis, and horses with disease of the small colon are younger on average than those with disease of the large colon (13.2 versus 15.4 years).[1] Enteroliths rarely occur in horses less than 4 years of age and are more common in older horses (>11 years). Fecaliths associated with ingestion of foreign bodies occur more commonly in young or adolescent horses.

Feeding >50% of the diet as alfalfa hay, <50% as oat hay, and lack of daily access to pasture (stabling) are associated with increased risk of enterolithiasis in horses in California (OR of 4.7, 0.2, 0.2, and 2.8, respectively).[2] The mean pH of colonic contents from horses with enterolithiasis is significantly higher than for control horses, and horses with enterolithiasis have a significantly lower percentage of dry matter in colonic fecal samples and higher mean mineral concentrations than controls.

About 15% of cases examined at referral institutions that see large numbers of cases develop a ruptured viscus caused by the enterolith and die. The long-term survival rate of horses treated surgically is approximately 80% to 90% and does not differ for disease of the small or large colon.[1]

Fecaliths occur sporadically and appear to be more common in younger horses, perhaps because of their propensity to dietary exploration and ingestion of foreign materials.

PATHOGENESIS

The mechanism underlying enterolith formation is not known. Enteroliths are formed in the large colon and, rarely, the cecum. They are clinically inapparent, even if quite large, until they cause obstruction of aboral passage of ingesta, usually by occluding the right dorsal or transverse colon. Occasional enteroliths pass into the small colon. Obstruction of the colon causes mild to moderate, often intermittent, colic, presumably when the enterolith or fecalith obstructs the colon, with the pain resolving when the enterolith moves and the obstruction clears. Complete obstruction results in obstruction of aboral movement of ingesta, accumulation of gas and ingesta proximal to the obstruction, and distension of the large colon. There is no loss of integrity of the colon early in the disease but with time and distension there is ischemia and necrosis of the colon, with subsequent perforation, development of acute peritonitis, and death.

CLINICAL FINDINGS

Clinical signs of horses with obstructive enterolithiasis of the small (descending) colon differs somewhat from that of horses with disease of the large colon. Horses with disease of the small colon have shorter duration of clinical signs and more severe disease than do horses with obstructive enterolithiasis of the large colon. The most common historic manifestation of enterolithiasis of the large colon in horses is recurrent, intermittent colic (about one-third of cases), often with passage of enteroliths in feces (about 10% of cases).

A higher proportion of horses undergoing surgery for obstructive disease of the small colon were tachycardic (56% versus 12%) and/or had a low white cell count (16% versus 5%) than did horses treated for disease of the large colon. Horses with enterolithiasis of the small colon had a shorter duration of clinical signs (median 5 hours, range 5–72 hours) than did horses with enterolithiasis of the large colon (median 2 days, range 12 hours to 3 months).[1]

Horses with acute obstruction have signs typical of obstructive, nonstrangulating disease of the large colon, including mild to moderate colic with failure to pass feces. The heart rate is 50 to 70 beats/min, borborygmi are decreased but not absent, and there is mild abdominal distension. **Rectal examination** can reveal a mildly distended large colon but the offending enterolith is never palpable, except on the rare occasion that the enterolith or fecalith is lodged in the distal small colon. In horses with complete obstruction of the small colon the severity of pain increases over the next 24 hours and there is readily apparent distension of the large colon. There is usually no reflux through a nasogastric tube. The terminal phase, which can take 72 hours to occur and is caused by rupture of a viscus, is marked by moderate to severe pain, abdominal distension, tachycardia (>80 beats/min), decreased capillary refill time, discolored mucous membranes, sweating, muscle fasciculations, and death. Rupture of a viscus and acute peritonitis occurs in approximately 15% of cases.

Radiography of the abdomen is useful in identifying enteroliths in horses with colic (Fig. 7-6) and is more accurate for detection of enteroliths in the large colon than the small colon.[1,3,4] The accuracy of the diagnosis is approximately 80% for enteroliths in the large colon and 40% for those in the small colon, with sensitivity and specificity of 84% and 96% respectively.[4] Sensitivity is lower for enteroliths in the small colon (62%) because visualization is impeded by gas distension of the gastrointestinal tract.[4] Observation of an enterolith on radiographic examination of an equid with compatible clinical signs is very highly suggestive of the diagnosis of obstructive enterolithiasis. Failure to detect an enterolith does not rule out this disease, particularly for small-colon enterolithiasis (sensitivity of 62%). The most common reason for not detecting an enterolith is poor imaging of the abdomen because of inadequate penetration by the x-ray beam, emphasizing the need for appropriate radiographic equipment.

CLINICAL PATHOLOGY

There are no diagnostic changes in the hemogram, serum biochemical profile, or examination of peritoneal fluid. Horses with enteroliths have higher serum bilirubin concentrations on examination at referral centers, but this change is not sufficiently large to be useful as a diagnostic aid. Similarly, horses with enteroliths have higher protein and white cell counts in peritoneal fluid than do horses with other forms of colic, but again these differences are too small to be of diagnostic significance. Changes in hematological and biochemical variables during the terminal phases of the disease are characteristic of acute, diffuse peritonitis and include leukopenia with left shift, hemoconcentration, and azotemia.

NECROPSY FINDINGS

Enteroliths are frequent incidental findings at necropsy examination of mature horses, and their presence should not be overinterpreted. Obstructive disease caused by an enterolith is characterized by colon distension, presence of an enterolith in the right
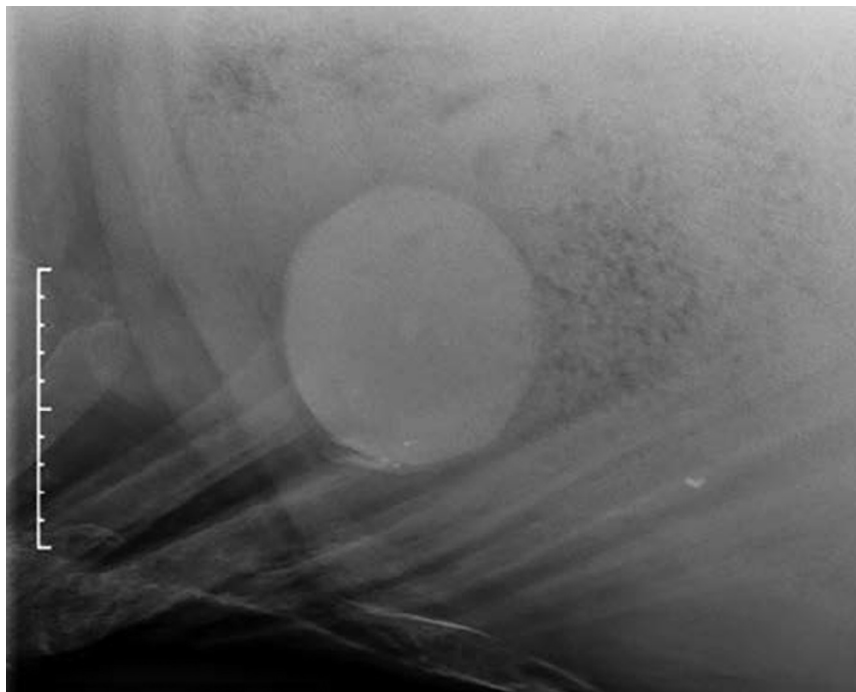
Fig. 7-6 Enterolith in the large colon of a horse with colic. The scale marker is 10 cm. (Reproduced with permission from Kelleher ME, et al. *JAVMA*. 2014;245:126.[4])

dorsal, transverse, or small colon and, in cases dying of the disease, acute diffuse peritonitis resulting from colon rupture or perforation at the site of the enterolith. Tetrahedral enteroliths with sharp points are believed to be more dangerous than are spherical enteroliths.

DIFFERENTIAL DIAGNOSIS

See Table 7-19.
The main differential diagnosis is colon impaction, which can be difficult to differentiate from enterolith obstruction in the absence of radiographic examination of the abdomen.

TREATMENT

The definitive treatment is surgical removal of the enterolith. Supportive care including analgesia and fluid therapy should be provided (see section Equine Colic).

CONTROL

Prevention of ingestion of foreign bodies, such as small pieces of metal, can decrease the incidence of the disease. Strategies that decrease fecal pH and mineral content of feces might also decrease the incidence of the disease.

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SAND COLIC

Ingestion of sand with its accumulation in the large colon causes mild to severe colic, which can be recurrent, and cause acute or chronic diarrhea and weight loss in equids.[1] Sand colic is a disease of horses grazing sandy fields with short pasture, fed on sandy ground, or provided with feed contaminated with sand. It is often associated with underfeeding. Horses of all ages are affected, including foals that acquire the sand while eating dirt. The **case–fatality rate** for horses treated by surgical removal of sand is 20% to 40%, whereas the survival rate for horses treated medically is approximately 90%.[1] The disease is attributable to sand accumulation in the right dorsal or transverse colon or pelvic flexure causing mucosal irritation, luminal obstruction, and abnormal motility. Sand in the ventral colon does not cause obstruction but is associated with colon volvulus or displacement. Sand does not accumulate in the small intestine.

Clinical signs are of mild to severe colic that is often recurrent and can be associated with diarrhea (20%), abdominal distension (80%), and anorexia (10%).[1,2] The colic is often mild unless there is colon torsion or volvulus, in which case the signs are typical of that disease. Equids with signs of severe or persistent colic have an increased likelihood of having additional abnormalities such as colon volvulus or displacement.[1] The diarrhea is watery but not profuse or malodorous. Affected equids are frequently tachycardic and are sometimes mildly pyrexic.[1,2] **Auscultation** over the cranial ventral abdomen just caudal to the xiphoid reveals sounds similar to those made when a paper bag is partially filled with sand and rotated. This sound is diagnostic of sand accumulation in the ventral colon.

Rectal palpation can reveal sand impaction in the ventral colon in approximately one-quarter of cases, but more frequently (50%) the colon, cecum, or both are distended with gas.[2] Rectal palpation will not detect sand accumulation in the right dorsal or transverse colon because they are beyond reach. Feces collected during rectal examination can be examined for sand by mixing it with water in a rectal sleeve, agitating the mixture of water and feces to suspend the sand, and allowing the mixture to sediment. Sand is evident in the dependent part of the glove and is detected in this way in approximately 50% to 80% of affected equids.[1,2]

Radiography will demonstrate sand in the ventral and dorsal colons (Fig. 7-7) and can be used to monitor the efficacy of treatment. The severity of sand accumulation can be assessed radiographically and assigned a grade:[3]

---

0 = No sand

1 = A small amount of sand (largest accumulation <5 × 5 cm), not ventrally

2 = A small or moderate amount (largest accumulation ~15 × 5 cm, or ~5 × 15 cm) of sand, relatively ventrally or only a small part of the sand close to the ventral abdominal wall

3 = A moderate amount of sand ventrally (largest accumulation ~15 × 5 cm, or ~5 × 15 cm)

4 = A large (>10 × >10 cm) sand accumulation ventrally

Horses with sand impaction colic have sand accumulations of grade 2 to 4, with most having grade 4, and unaffected horses having grades 0 to 2.[4,5] Clinically normal equids can have small amounts of radiographically detectable sand in the colon. Additional information obtained radiographically and associated with a diagnosis of sand colic is, in addition to the presence of sand, the number of sand accumulations, opacity of the accumulation, location, and standardized height of the accumulation.[5]

Ultrasonography has good sensitivity (88%) and specificity (88%) compared with a gold standard of radiography for detection of sand in the ventral colon. Ultrasonography is not as effective at detecting sand in the right dorsal or transverse colon. Ultrasonography can enable detection of associated abnormalities including evidence of colonic displacement or mural thickening and small-intestinal distension.

Abnormalities in the hemogram and serum biochemistry profile are consistent with inflammation and dehydration and
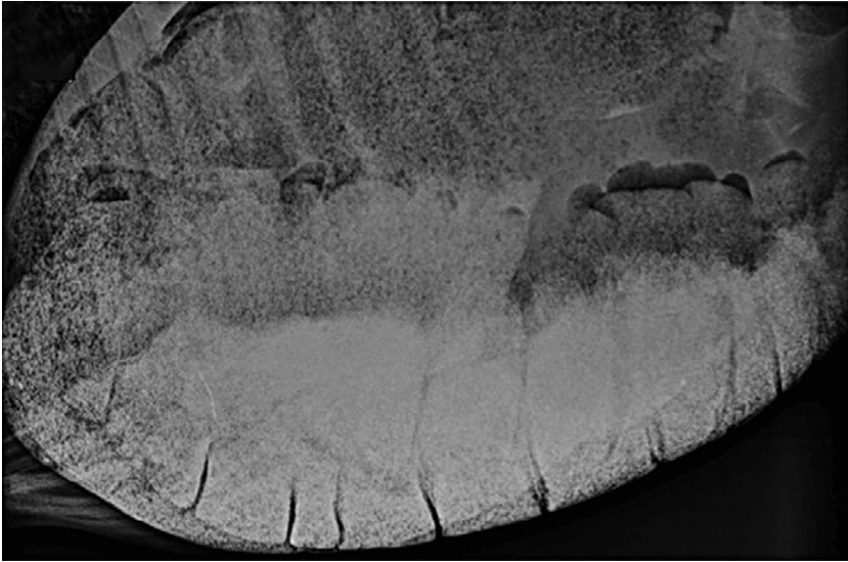
Fig. 7-7 Lateral abdominal radiograph of a Miniature horse with severe sand accumulation. (Reproduced with permission from Hart KA, et al. *Equine Vet J.* 2013;45:465.[1])

include a left shift in the leukogram, neutrophilia, hyperfibrinogenemia, and mild azotemia.[1,2] Peritoneal fluid can be normal in mildly affected horses or indicative of inflammation and compromised intestine in severely ill equids.[1]

Treatment consists of pain relief, correction of fluid and electrolyte abnormalities, prevention of continued ingestion of sand, and removal of the sand. In horses with severe colic consistent acute obstruction of the right dorsal or transverse colon by sand, volvulus, or displacement, surgical removal is indicated. Equids that require surgical correction of sand colic and associated gastrointestinal abnormalities have a worse prognosis than do equids requiring solely medical treatment.[1]

Medical treatment to effect sand removal is indicated in less acute cases. A widely used medical treatment is administration of **psyllium mucilloid** (0.5–1 g/kg orally every 12 hours for 4–8 weeks) administered via a nasogastric tube or as a dressing on feed. However, in an experimental model of the disease this treatment was no more effective than no specific treatment in removal of sand from the cecum and colons. In contrast, administration of a combination of psyllium (0.5 kg orally twice daily) and mineral oil (2 L orally once daily) effectively removed 51% of the administered sand load, whereas treatment with mineral oil resulted in the passage of 26% of the sand. The largest amount of sand was excreted after 24 hours of treatment with psyllium and oil and after 5 days of treatment with oil only.[6] Mineral oil (1 mL/kg) or MgSO4 (1 g/kg) orally may hasten sand removal. Administration of a combination of psyllium (1 g/kg BW) and MgSO4 (1 g/kg BW) resulted in elimination of sand in 9/12 horses with naturally occurring sand accumulation, whereas MgSO4 alone resulted in elimination in 2/12 and psyllium alone in 3/12.[7] Pasturing of horses with sand accumulation that are otherwise housed in stables aids removal of the sand.

Control of the disease is done by preventing ingestion of sand by feeding horses hay and grain from clean feeding bins, providing adequate roughage in the diet, pasturing horses in fields with adequate grass cover, and perhaps, in areas where sand ingestion is unavoidable, daily administration of psyllium mucilloid. The recommendation for daily administration of psyllium is based on studies in healthy horses, anecdote, and extrapolation from treatment of affected horses.[8]

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RIGHT DORSAL COLITIS

This is a chronic disease caused by ulcerative colitis of the right dorsal colon. The disease is associated with prolonged administration of NSAIDs in most, but not all, cases. Ulcerative colitis occurs after administration of phenylbutazone.[1,2] The case–fatality rate is greater than 50%, although descriptions of large numbers of affected horses are not available.

The **pathogenesis** involves inhibition of mucosal prostaglandin synthesis and consequent decreases in water, chloride, and bicarbonate secretion by mucosa of the right dorsal colon and apoptosis (programmed cell death) of mucosal cells. Loss of secretion of bicarbonate might be associated with failure of alkalinization of right dorsal colon contents and subsequent development of mucosal lesions. The right dorsal colon is the only section of the colon with net water secretion, and this unique activity may predispose this section of colon to disease.[3] Exposure of mucosal cells to phenylbutazone can occur both from the lumen and from blood. Luminal exposure may be related to release of phenylbutazone from ingesta in the right dorsal colon. Ulceration of the colonic mucosa allows leakage of plasma constituents into the colonic lumen, resulting in hypoalbuminemia and loss of electrolytes,[2-4] and entry of colonic substances such as endotoxin into the systemic circulation, with consequent signs of endotoxemia and systemic inflammatory response (leukopenia, hyperfibrinogenemia, and fever). Chronic and extensive mucosal ulceration causes growth of granulation tissue and fibrosis of the right dorsal colon with subsequent loss of secretory function, stricture, and partial obstruction.

Clinical signs include depression, anorexia, mild fever (38.6–39.5°C [101.5–103°F]), mild intermittent colic, ventral edema, weight loss, and occasionally mild diarrhea. There is almost always a history of administration of an NSAID. The disease can persist for weeks and often prompts inappropriate administration of NSAIDs. Rectal examination is unremarkable. **Ultrasonography** is useful in the diagnosis of right dorsal colitis by detecting the presence of a hypoechogenic submucosal layer and permitting measurement of the wall thickness of the right dorsal colon. The hypoechogenic layer in the wall of the right dorsal colon corresponds with edema and cellular infiltrates observed histologically. The right dorsal colon in adult horses has a maximal thickness of 6 mm, whereas that in horses with right dorsal colitis is greater than 8 mm and can be as great as 16 mm. Additionally, the ratio of right dorsal colon to right ventral colon wall thickness is up to 1.6 in normal horses and greater than 2.0 in affected horses. **Scintigraphic** detection of right dorsal colitis is achieved by the administration of 99m technetium hexamethylpropyleneamine oxime-labeled white blood cells. Images obtained 20 hours after administration of labeled white cells demonstrated uptake of cells into the right dorsal colon (right cranioventral abdomen).

There is often mild **peritonitis** (neutrophilia in peritoneal fluid). Leukopenia with a left shift and hypoproteinemia are characteristic.[4] **Serum biochemical abnormalities** include hypoalbuminemia, hyponatremia

(<135 mEq/L), hypochloremia (<90 mEq/L), and azotemia (serum creatinine >2 mg/dL, 170 μmol/L).

Necropsy examination reveals ulcerative colitis of the right dorsal colon. In chronic cases there may be stricture of the right colon with subsequent impaction of ingesta and colon rupture.

Treatment is often unrewarding, although successful treatment by feeding of a low residue diet, such as a complete pelleted ration fed 4 to 6 times daily, is reported. Psyllium (120 g once daily) for 3 to 6 weeks might enhance healing of the colon. Administration of misoprostol (see Table 7-20) has been suggested but has no demonstrated efficacy. Surgical excision of the lesion is difficult because of its location in the abdomen, but bypass of the right dorsal colon can be beneficial.[5] **Control** involves minimizing the amount of NSAIDs administered to horses.

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SMALL COLON OBSTRUCTION

- Small colon impaction[1]
- Obstruction by enterolith or fecalith (see section Enteroliths and Fecaliths)
- Meconium retention (see section Foal Colic)
- Atresia coli (see section Foal Colic)
- Strangulation by pedunculated lipoma, volvulus, intussusception, and herniation through mesenteric rents including the mesocolon or gastrosplenic ligament, ovarian pedicle,[2] or enlarged ovary
- Neoplasia (intramural), including lymphoma[3]
- Hematoma
- Rectal prolapse
- Rupture of mesocolon
- Colonic lipomatosis
- Perirectal abscess

The likelihood of any particular cause of the obstruction is related to a number of factors including age, diet, and use. A review of 84 cases of small-colon obstruction that underwent laparotomy revealed that the most common causes were impaction (37%), strangulation by a pedunculated lipoma (27%), focal eosinophilic colitis (6%), and adhesions of the small colon (6%).[4]

EPIDEMIOLOGY

Small colon disease is present in approximately 2.5% to 5% of horses treated for colic at referral institutions, and small-colon impaction represents approximately 2% of horses with colic. Aged female horses are most commonly affected, although the conditions can occur in horses of any age. Arabians, ponies, and Miniature horses are reported to be at increased risk of small-colon disease, although others have not detected this apparent predilection. Rupture of the mesocolon occurs during parturition. Small colon impaction can occur as limited outbreaks in a number of horses on a single farm over a period of days to weeks, without obvious predisposing causes or inciting events. The **case–fatality rate** depends on the condition and is 10% to 40% for impaction of the small colon.[1] The survival rates at discharge from hospital and 1 year and 2 years after surgical correction of small-colon disease in horses that survived the surgery were 91, 81, and 74%. Approximately 80% of horses survived surgery in the short term.[4]

PATHOGENESIS

Obstruction of the small colon causes accumulation of ingesta and gas in the small colon aboral to the obstruction and in the large colon, with subsequent distension, pain, and reduced motility. Distension of the small colon may impair blood flow with subsequent ischemia, necrosis, and rupture or perforation of the small colon. Incarceration of the small colon results in ischemia of the entrapped segment and restriction of flow of ingesta. Subsequent signs are characteristic of toxemia and intestinal obstruction. The high proportion of affected horses from which *Salmonella* spp. are isolated suggests a role for colitis in the pathogenesis of small-colon impaction.

CLINICAL FINDINGS
Nonstrangulating Lesions

Nonstrangulating lesions manifest as mild to moderate colic that may persist without a change in severity for up to 36 hours. The heart rate depends on the severity of the colic but averages 60 beats/min with a range of 30 to 110 beats/min. There is mild dehydration. **Abdominal distension** is usually mild initially but increases as the disease progresses. Borborygmi are reduced and tympanitic sounds may develop as the large colon and cecum become distended. **Rectal examination** reveals the presence of distended large colon but no evidence of colon displacement.

Small colon impaction is palpable as a tubular column of material in the small colon, although it might not be detected if the impaction is in the cranial section of the small colon. Approximately 40% of cases have diarrhea and 13% strain to defecate.[1] Fever is present in about one-third of cases.[1] Rectal examination reveals impaction of the small colon, evident as a tubular mass in the caudal abdomen, in approximately 40% of cases, although complete examination per rectum can be difficult because of large-colon distension and accumulation of feces in the distal small colon. There is reflux through the nasogastric tube in approximately 30% of cases.

Strangulating Lesions

Strangulating lesions that interfere with small-colon blood supply usually present as an acute colic of moderate to severe intensity. There is tachycardia and evidence of toxemia. Abdominal distension is usually marked and there is an absence of borborygmi. Rectal examination reveals distension of the large colon and occasionally soft, compressible distension of the small colon.

Avulsion of the mesocolon occurs during parturition and is often evident as a **rectal prolapse** in the mare. Avulsion results in ischemia of the distal colon. Initially the mare does not display signs of pain but, as the section of the colon from which the mesocolon has avulsed becomes necrotic, signs of toxemia develop.

CLINICAL PATHOLOGY

There are no characteristic changes in the hemogram or serum biochemical profile. Peritoneal fluid is normal until the viability of the small colon is compromised, at which time the protein concentration and white blood cell count increase. *Salmonella* spp. are isolated from approximately 20% of cases of small-colon impaction, suggesting a role for colitis in the pathogenesis of the disease.

NECROPSY FINDINGS

Small colon impaction is evident as a tubular column of firm ingesta in the small colon with large-colon distension. Small colon accidents, such as rupture of the mesocolon at parturition and intussusception, are readily apparent.

DIFFERENTIAL DIAGNOSIS
See Table 7-19.

TREATMENT
Small-Colon Impaction

The principles of treatment of small-colon impaction are relief of pain and of the impaction. Horses with signs of mild to moderate colic easily controlled with analgesics should be treated medically. Horses with intractable pain or progressively worsening pain, abdominal distension, or abnormal peritoneal fluid should be treated surgically. Horses treated surgically have a worse prognosis than do horses treated medically, probably because the former group has more severe disease.

Medical treatment of small-colon impaction involves administration of analgesics (see Table 7-15); correction of fluid, electrolyte, and acid-base abnormalities; and

administration of fecal softeners (see Table 7-16). Treatments to hasten softening and passage of the impaction include overhydration, administration of sodium or magnesium sulfate and a lubricant such as mineral oil, and occasionally administration of an enema to the standing horse. Overhydration should be achieved by either intravenous or oral administration of polyionic fluids at three to five times maintenance (10 mL/kg/h). Administration of enemas to standing horses is controversial and should be done with care so as not to rupture the small colon. Trocarization of the large colon or cecum might be necessary in horses with severe abdominal distension. Trocarization can be associated with adverse outcomes including peritonitis and hemorrhage.[5,6]

Small-colon accidents including strangulation and intussusception require surgical correction including in some instance a parainguinal approach.[7-10] Surgical correction of rupture of the mesocolon is not available because of limited surgical access to the site of the lesion.

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SPASMODIC COLIC

ETIOLOGY
Spasmodic colic occurs sporadically and causative factors are not usually identified. Suggested causes include excitement, such as occurs during thunderstorms, preparations for showing or racing, and drinks of cold water when hot and sweating after work, although epidemiologic evidence of these associations is lacking. Presence of a heavy burden of tapeworms is associated with a high incidence of spasmodic (undiagnosed) colic. Mucosal penetration and submucosal migration of *Strongylus vulgaris* larvae are known to cause changes in ileal myoelectrical activity that could lead to the development of colic in horses. Psychogenic colic occurs rarely in horses.

EPIDEMIOLOGY
The condition is sporadic. It affects horses of all ages but is not recognized in young foals. No apparent breed or gender predisposition is noted.

PATHOGENESIS
The hypermotility of spasmodic colic in horses is thought to arise by an increase in parasympathetic tone under the influence of the causative factors mentioned earlier.

CLINICAL FINDINGS
Spasmodic colic of horses is characterized by **brief attacks of abdominal pain**. The pain is intermittent, with the horse rolling, pawing, and kicking for a few minutes, then shaking and standing normally for a few minutes until the next bout of pain occurs. Intestinal sounds are often audible some distance from the horse and loud, rumbling borborygmi are heard on auscultation. The pulse is elevated moderately to about 60 beats/min, and there may be some patchy sweating, but rectal findings are negative and there is no diarrhea. Rectal examination is usually unremarkable. The signs usually disappear spontaneously within a few hours.

CLINICAL PATHOLOGY AND NECROPSY FINDINGS
Laboratory examinations are not used in diagnosis and the disease is not fatal.

DIFFERENTIAL DIAGNOSIS
See Table 7-19.

TREATMENT
Acute hypermotility as manifested by spasmodic colic is usually transient, and the use of specific spasmolytics is not necessary. Detomidine, xylazine, or butorphanol are effective analgesics. Administration of hyoscine is effective. Affected horses are often administered mineral oil (1 mL/kg) by nasogastric intubation.

INTESTINAL TYMPANY IN HORSES

Intestinal tympany is one of the most common causes of colic, as illustrated by it reported as occurring in approximately 64% of horses with acute abdominal disease in Japan.[1]

ETIOLOGY
The cause of most cases of idiopathic intestinal tympany is unknown, although the ingestion of highly fermentable green feed is considered to be a risk factor. Feeding of rations rich in grains is associated with changes in colonic contents that might predispose to tympany. Intestinal tympany occurs secondary to obstructive diseases that prevent aboral passage of ingesta and gas.

PATHOGENESIS
The excessive production of gas or its retention in a segment of bowel causes distension and acute abdominal pain. Intestinal distension reduces intestinal motility and may contribute to the course of the disease. Severe tympany can interfere with normal respiration and cardiovascular function (see section Pathogenesis of Equine Colic).

CLINICAL FINDINGS
Abdominal distension is evident and pain is acute and severe. Peristaltic sounds are reduced, but fluid may be heard moving in gas-filled intestinal loops, producing a tinkling, metallic sound. Pinging sounds consistent with tightly distended viscus may be heard on simultaneous flicking and auscultation of the abdomen. On rectal examination, gas-filled loops of intestine fill the abdominal cavity and make proper examination of its contents impossible. In primary tympany much flatus is passed. It is important to differentiate primary tympany from that occurring secondary to obstructive diseases such as enterolithiasis and displacement of the colon.

CLINICAL PATHOLOGY
Laboratory examinations are of no value in diagnosis.

NECROPSY FINDINGS
In cases of secondary tympany, the causative obstruction is evident. In primary cases, the intestines are filled with gas and the feces are usually pasty and loose.

DIFFERENTIAL DIAGNOSIS
See Table 7-19.

TREATMENT
The principles of treatment are the relief of pain and distension, maintenance of hydration, and reduction of gas production. In secondary tympany the primary disease should be identified and treated.

Pain should be relieved by administration of xylazine, detomidine, or butorphanol, or similar agents (see Table 7-21). Distension of the bowel should be relieved by trocarization, which should only be performed if there is no or minimal response to analgesic medication and no return of normal peristaltic activity because of the risk of peritonitis, hemorrhage, or infection.[2] Trocarization can be performed percutaneously or per rectum.[3] Normal hydration should be restored by intravenous administration of polyionic fluids. Intestinal gas production should be minimized by the administration of mineral oil or a similar laxative (see Table 7-16).

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VERMINOUS MESENTERIC ARTERITIS (VERMINOUS ANEURYSM AND THROMBOEMBOLIC COLIC)

ETIOLOGY

The etiology is unknown, although it is presumed to result from thromboemboli originating at sites of verminous arteritis in the cranial mesenteric artery.

EPIDEMIOLOGY

The disease is assumed to be more prevalent among horses on poor parasite control programs; however, except in extreme cases that die and have a necropsy examination or exploratory laparotomy, the diagnosis is not confirmed. Therefore accurate measures of its incidence are not available. Cases can occur in foals as young as 3 to 6 months. The incidence of the disease has decreased remarkably with the advent of effective broad-spectrum anthelmintics and almost complete prevention of *Strongylus* spp. infection in horses in developed countries. Postmortem examination of 46 horses in Sardinia that were recorded as having been treated with broad-spectrum anthelmintics identified gross lesions of the cranial mesenteric artery in all horses and *S. vulgaris* larvae in 39% of the horses.[1]

PATHOGENESIS

Migration of the larvae of *Strongylus vulgaris* into the wall of the **cranial mesenteric artery** and its branches occurs in horses. The presence of larvae causes chronic-active inflammatory lesions and thickening of the tunica intima and adventitial tunic of the ileocecal and colic arteries.[1] These lesions can cause thromboemboli that restrict blood supply to the intestines, with subsequent ischemia and dysfunction. The recurrent colic of verminous arteritis is possibly caused by impairment of the vascular and nerve supply to the intestine. The disease is basically an infarction of bowel wall without displacement of the bowel. The small intestine, colon, and cecum can be affected. The disease has also been associated with larval cyathostomiosis.

CLINICAL FINDINGS

Signs vary depending on the severity of the disease. It is assumed that **mild, intermittent colics** that respond to analgesics in the short term and anthelmintics in the long term are caused by verminous arteritis. Affected horses are often depressed and spend long periods recumbent. Weight loss and inappetence are features of the disease in some horses. The disease can have a course of weeks to months.

Acute, severe cases of the disease are caused by infarction of parts or all of the small intestine, cecum, or colon. Affected horses have an acute onset of severe abdominal pain, tachycardia (>100 beats/min), and sweating. Auscultation reveals decreased borborygmi.

There is mild distension of small intestine or large colon, depending on the segment of bowel affected, on rectal examination. There are rarely signs of intestinal obstruction. Palpation of the cranial mesenteric artery can reveal thickening and pain but is not a useful diagnostic sign for the acute disease. **Death** is caused by peritonitis secondary to devitalization of the intestine,[2] usually within 24 hours of the onset of signs.

CLINICAL PATHOLOGY

There are no diagnostic changes in the hemogram or serum biochemical profile. Horses with mesenteric artery lesions have higher mean corpuscular volume, mean corpuscular hemoglobin, concentrations of -α-2 globulins, -β-globulins, and -γ-globulins than in healthy horses.[1] Peritoneal fluid in mild cases can have mild elevations in protein concentration and white blood cell count. In severe cases, peritoneal fluid protein concentration is increased (>25 g/L, 2.5 g/dL) as is white blood cell count (9000–100,000 cells/μL, 9–100 × 10³ cells/L).

NECROPSY FINDINGS

Infarction of the colon and cecum is most common and evident as either gangrene of large sections of the organ or multifocal mottled lesions that are red and edematous. Histologic examination rarely reveals the presence of thrombi. There is often verminous arteritis of the cranial mesenteric artery, evident as thickening of the intima and narrowing of the lumen.[1,3]

DIFFERENTIAL DIAGNOSIS

See Table 7-19.

TREATMENT

Mild, recurrent cases are treated with analgesics such as flunixin meglumine (see Table 7-15), laxatives such as mineral oil (see Table 7-16), and anthelmintics (ivermectin 200 μg/kg orally once; or fenbendazole 50 mg/kg orally every 24 hours for 3 days).

Severe cases are treated with analgesics (see Table 7-15), intravenous administration of fluids (see Chapter 5), and supportive care. Usually the severity of the colic prompts surgical exploration of the abdomen with resection of small lesions. Most severe cases do not survive.

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RETROPERITONEAL ABSCESS (INTERNAL ABDOMINAL ABSCESS, CHRONIC PERITONITIS, AND OMENTAL BURSITIS)

A recognized form of recurrent or intermittent colic is associated with an abscess in the abdominal cavity. The abscesses are usually **retroperitoneal**, sometimes involving the omental bursa, and chronic leakage from them into the peritoneal cavity causes chronic or recurrent peritonitis. Complete recovery is difficult to effect, and there is a high failure rate in treatment. These abscesses result from any of the following:

- Infection of a **verminous aneurysm,** especially in young horses
- **Metastatic *S. equi* infection** (metastatic strangles)
- **Minor perforations of intestinal wall** allowing minimal leakage of intestinal contents so that omental containment of the leak occurs
- Erosion through a **gastric granuloma** associated with *Habronema* sp. or a squamous cell carcinoma of stomach wall
- In **mares,** development of an abscess in the pelvic fascia results after **tearing of the rectal wall during pregnancy diagnosis.**
  - Abscesses caused by *R. equi* in foals

Clinical findings suggestive of the disease include persistent or intermittent chronic colic and weight loss. A **fever** is common and **varying degrees of anorexia** are typical. In cases with a concurrent chronic peritonitis or an omental bursitis, the amount of inflammatory exudate may be large enough to cause abdominal distension. When the abscess is perirectal and in the pelvic fascia there may be straining and constipation caused by voluntary retention of feces.

On **rectal examination** it can be possible to feel an abscess or adhesions to one. They are often multiple and quite large and adherent to one another, so that tight bands of mesentery can be felt that will lead the hand to the site of the abscess. Pain is usually elicited by rectal palpation of the infected sites and by firm palpation of the external abdominal wall. Ultrasonography through the abdominal wall has been used to locate large retroperitoneal abscesses in a foal.

The **hemogram**, especially in acute cases, is characterized by a neutrophilia, which may be as high as 30,000/μL with a left shift. **Chronic anemia** caused by bone marrow depression may occur as well as increased **plasma fibrinogen** and **hypoalbuminemia**. Abdominocentesis may yield turbid fluid with a protein content greater than 2.5 g/dL and an increase in leukocytes. If culture is possible the causative bacteria are usually *S. equi, S. zooepidemicus, Corynebacterium*

equi, C. pseudotuberculosis, or mixed infections if there has been intestinal leakage. It is common, even when there is an active infection in a retroperitoneal abscess, to fail to grow bacteria from a peritoneal effusion.

Intraabdominal abscesses must be differentiated from **abdominal neoplasms** in the horse. Anorexia, weight loss, fever, colic, and depression are common to both syndromes. The laboratory findings in both groups are similar, but cytologic examination of the peritoneal fluid may yield an accurate diagnosis in the case of neoplasms.

Compromised or perforated stomach wall can result in adhesions to the spleen and development of splenic abscesses in horses.[1] In these animals a sharp pain response can be elicited on firm palpation of the abdomen in the left flank just behind the last rib. Abscesses in liver are not so easily located. Abscesses in pelvic fascia are usually not very discrete but are instantly noticeable on inserting the hand into the rectum.

TREATMENT

Treatment with broad-spectrum antimicrobials is indicated and the initial response is good but often transitory if the usual course of treatment is only 3 to 5 days' duration. The prognosis is usually tentative because of the difficulty of completely eliminating the infection. Treatment must be continued for at least 2 weeks and in some cases for a period of 2 to even 4 to 5 months. Surgical treatment might be possible, but is usually ineffectual because of the deformity of the area by adhesions, and the usual outcome of tearing the intestine and spillage into the peritoneal cavity while attempting to exteriorize the lesion.

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RECTAL TEARS

Iatrogenic tears of the equine rectum are a serious problem in equine practice. They are a leading cause of malpractice suits for the veterinarian, comprising approximately 7% of insurance claims against veterinarians in equine practice in the United States and can be a large economic loss for the owner. The occurrence of rectal tears is often an emotionally charged event because they are unexpected and they usually occur in otherwise healthy horses being subjected to routine rectal examination. Prompt diagnosis and vigorous treatment, along with frank disclosure of the event to the horse's owner or handler, is essential in increasing the likelihood of a good outcome both for the horse and for the veterinarian–client relationship.

Rectal tears also occur in **cattle and sheep** during reproductive procedures including manual pregnancy diagnosis in cattle and during insertion of ultrasound probes per rectum in sheep. The frequencies and risk factors are not recorded.

ETIOLOGY

The etiology of rectal tears is usually readily apparent, with the vast majority of rectal tears in horses being iatrogenic. Iatrogenic rupture occurs during rectal examination by veterinarians or laypersons for reproductive management (broodmare), or examination of other intraabdominal structures, for example, during evaluation of a horse with colic.[1] Spontaneous or noniatrogenic rupture can occur associated with infarctive lesions of the distal small colon or rectum, injuries during parturition or coitus, and malicious trauma caused by insertion of foreign objects by attendants.[2] It is important that rectal tears should not be assumed to be iatrogenic until a thorough evaluation of the animal and the history has been performed.

EPIDEMIOLOGY

Risk factors for rectal tears in horses have not been quantified. Reports of the *frequency* of occurrence do not provide information about the *relative risk* of occurrence in an individual animal. For example, rectal tears occur more frequently in mares, but the risk of a rectal tear occurring in a mare expressed as either the risk per examination or the risk per year might be less than that of a stallion. The less frequent occurrence in stallions (i.e., number of cases) might be because stallions are much less seldom subject to rectal examination. Given this caveat, identified associations with rectal tears include:

- Age: Contrary to earlier speculation, increasing age is likely a risk factor for rectal tears in horses and it is more frequent in animals >9 years of age.[1]
- Gender: The condition is more common in mares,[1] likely because they are more frequently subject to rectal examination as part of routine reproductive management. The relative risk of mares versus stallions and geldings is unknown.
- Breed: Arabian and American Miniature horses appear to be at increased risk of iatrogenic rectal tears.[1]
- Size: Smaller animals can be at increased risk.
- Inadequate restraint: Horses must be adequately restrained for rectal examination (see section Prevention).
- Inadequate preparation of the rectum: The rectum and distal small colon should be emptied of feces before an examination of the reproductive organs or gastrointestinal tract is performed.
- The experience of the examiner is not a factor in the risk of rectal tears in horses.
- The use of ultrasonographic probes per rectum does not appear to increase the risk of rectal tears.

PATHOGENESIS

Rectal tears occur in horses because the rectum of the horse is relatively sensitive and fragile and powerful contractions occur during rectal palpation. In contrast, the bovine rectum is relatively durable and, while often traumatized, is rarely ruptured. Tears occur because of excessive tension on the rectal wall. This usually occurs in horses by peristalsis and contraction of the rectum over the examiner's hand, with splitting of the rectum often occurring over the back (knuckles) of the hand.

Complete rupture of the peritoneal portion of the rectum results in fecal contamination of the abdomen and rapid onset of septic peritonitis and death. Tears in the nonperitoneal portion of the rectum (that is, caudal to the peritoneal reflection) cause perirectal cellulitis and abscessation.

CLINICAL SIGNS

The prominent clinical sign of the occurrence of a rectal tear is the presence of blood on the rectal sleeve of the examiner. Slight bloodstaining of mucus or lubricant is usually not associated with rectal tears (although this should be verified by repeat examination), whereas the presence of frank hemorrhage on the sleeve is usually indicative of a rectal tear. The rectum in an adult, 450-kg horse, is approximately 30 cm long and is partially within the abdomen, where it is covered by peritoneum, and partially in the pelvic canal, where it is not surrounded by peritoneum but is supported by thick connective tissue and muscle. The peritoneal portion of the rectum is supported dorsally by the mesorectum (mesocolon). Most iatrogenic rectal tears in horses occur within 25 to 30 cm of the anus, but can occur up to 60 cm from the anus, in the peritoneal portion of the rectum. The tears are almost always in the dorsal or dorsolateral wall and are longitudinal (parallel to the long axis of the rectum). It is speculated that the dorsal wall of the rectum is weaker than other segments because it is not covered by serosa, and blood vessels perforate the muscularis layers, weakening it.

Rectal tears in the horse have been classified according to the layers of the rectal wall disrupted. The classification is also a useful guide to the clinical signs to be expected and the treatment that is indicated (see the following section Treatment for management of each grade of tear):

- *Grade I:* Disruption of the mucosa only, or the mucosa and submucosa. There are usually no clinical signs other than some blood on the examiner's sleeve. Most of these injuries occur to the mucosa of the ventral aspect of the rectum.
- *Grade II:* Disruption of the muscular layer of the rectal wall with the mucosal and serosal surfaces intact. This is a

rarely recognized form of tear. There are minimal clinical signs.

- *Grade IIIa:* Tear includes mucosa, submucosa, and muscularis, but the serosal surface is intact. This degree of tear usually causes septic peritonitis. If the tear is caudal to the peritoneal reflection the pelvic fascia becomes infected, but the infection may remain contained within it for 7 to 10 days, forming a local cellulitis or abscess. During this period, the horse is likely to be affected by mild chronic peritonitis, with mild abdominal pain, fever, and mild toxemia. At the end of this time, the infection can erode through the peritoneum and cause an acute, severe, diffuse peritonitis or rupture through the perianal tissue causing a fistula.
- *Grade IIIb:* Tear is on the dorsal wall and includes the mucosa, submucosa, and muscularis. Because there is no serosa at this position, the tear extends into the mesocolon. There is usually septic peritonitis.
- *Grade IV:* Complete rupture with leakage of fecal material into the peritoneal space. Clinical signs of septic peritonitis are severe and death is almost inevitable.

Horses with a rectal tear will not display any immediate signs of discomfort. However, if there is a grade III or grade IV tear, the horse will have signs of septic peritonitis, including elevated heart and respiratory rates, sweating, colic, increased capillary refill time, and discolored mucous membranes within 1 to 2 hours.

CLINICAL PATHOLOGY

Hematological and serum biochemical changes in horses with grade III and grade IV tears are consistent with acute septic peritonitis. These changes include leukopenia and neutropenia, increased band cell count, elevated hematocrit, and total protein concentration initially, after which serum total protein concentration can decline as protein leaks into the abdomen. Peritoneal fluid has a high white blood cell count and protein concentration. Cytologic examination reveals the presence of degenerate neutrophils, intracellular and extracellular bacteria, and plant material. Lipid material can be detected in the peritoneal fluid if there has been leakage of mineral oil through the tear.[3]

PROGNOSIS

The **case–fatality rate** varies depending on the type of tear (see later section Clinical Signs). Horses with grade I or II tears almost all survive, whereas the survival rate for horses with grade III tears treated appropriately is 60% to 70%. Almost all horses with grade IV rectal tears die. Survival rates for grades I, II, III, and IV rectal tears are 100, 100, 38, and 2% for horses treated at a referral center.[1]

TREATMENT

If the person doing the rectal examination feels the mucosa tear, if there is blood on the rectal sleeve, or if a horse that has had a rectal examination up to 2 hours previously starts to sweat and manifest abdominal pain, a rectal tear should be suspected. A thorough examination should be conducted immediately but great care is necessary to avoid damaging the rectum further. The principles of care are to verify the presence of a tear, determine its severity, prevent leakage of fecal material into the peritoneum or tissues surrounding the tear, treat for septic peritonitis, prevent extension of the tear, and provide pain relief.

Immediate Care

If a rectal tear is suspected the horse should be appropriately restrained and examined immediately. There should be no delay in conducting this examination. The client should be informed of the concern about a rectal tear. First-aid measures taken at the time of a grade III or IV tear can have a marked influence on the outcome. Horses with grade III or IV rectal tears should receive first-aid treatment and then be referred for further evaluation and treatment.[4]

The existence of a tear should be determined and its severity assessed. This is best achieved by sedating the horse, providing local analgesia of the rectal mucosa and anus, and careful manual and visual examination of the rectal mucosa. Sedation can be achieved by administration of adrenergic agonists (xylazine, romifidine, and detomidine) with or without a narcotic drug (butorphanol, meperidine, pethidine, and morphine). Analgesia of the rectum and anus can be induced by epidural anesthesia (lidocaine or xylazine) or local application of lidocaine gel or lidocaine enema (10–15 mL of 2% lidocaine in 50–60 mL of water infused into the rectum). Peristalsis can be reduced by administration of hyoscine (*N*-butylscopolammonium bromide, 0.3 mg/kg intravenously).

Manual or visual examination of the rectum can then be performed. Manual examination is performed after generous lubrication of the anus and examiner's hand and arm. Some authorities prefer to use bare hands, rather than gloves or a rectal sleeve, for this examination because of the decreased sensitivity when wearing gloves. However, one should be aware of the health risks to the examiner of not using barrier protection (gloves) during a rectal examination. The rectum should be evacuated of feces and a careful and thorough digital examination should be performed. If a tear is detected, the position, distance from the anus, and length and depth of the tear should be determined. Gentle digital examination should be used to determine the number of layers involved and if there is rupture of the rectum and communication with the peritoneal space.

Alternatively, the rectum can be examined visually through a mare vaginal speculum, or using an endoscope. Both of these approaches are likely to minimize the risk of further damage to the rectum. These examinations can be impaired by the presence of fecal material.

If a grade III or IV rectal tear is detected, then the horse should be administered broad-spectrum antibiotics (penicillin, aminoglycoside, and possibly metronidazole) and NSAIDs, and referred for further evaluation. Some, but not all, authorities recommend placement of a rectal pack to prevent further contamination of the rectal tear. This is formed from a 7.5-cm (3-inch) stockinette into which is inserted a roll of cotton (approximately 250 g). The roll is moistened with povidone iodine solution, lubricated, and inserted into the rectum in the region of the tear. Epidural anesthesia will prevent expulsion of the roll in the short term.

Prompt referral and care is essential for maximizing the likelihood of a good outcome in horses with grade III and IV tears.

Grade I and II Tears

Treatment of these tears is medical. Horses should be administered broad-spectrum antibiotics and feces should be softened by the administration of mineral oil. These wounds heal in 7 to 10 days.

Grade III Tears

Both medical and surgical treatments are effective in approximately 60% to 70% of cases of grade III tears. The choice of treatment depends on the expertise and experience of the attending clinician and financial constraints imposed by the horse's owner. Surgical treatment includes direct repair of the tear (for those lesions that can be readily exposed via the anus), placement of a rectal sheath by ventral laparotomy, and placement of a loop colostomy. Various techniques are described.[5,6] Surgical repair is in addition to aggressive treatment of peritonitis.

Medical treatment includes administration of broad-spectrum antibiotics (such as penicillin, aminoglycoside, and metronidazole), antiendotoxin drugs (such as hyperimmune serum or polymyxin sulfate), NSAIDs, crystalloid fluids, colloidal fluids (hetastarch and plasma), and heparin, as well as other care. Peritoneal lavage might be indicated. Manual evacuation of the rectum at frequent intervals (every 1–2 hours for 72 hours and then 4–6 times daily for a further 7 days) was suggested to improve the prognosis, although others caution against manual evacuation of the rectum because of the risk of worsening the tear.

Grade IV Tears

Tears of this severity require immediate surgical intervention to minimize fecal contamination of the peritoneum. However, the grave prognosis and high cost of treatment, and poor success of surgical intervention in these cases, means that most horses are

euthanized. If surgical care is attempted, there should also be aggressive medical treatment of the peritonitis.

PREVENTION

As noted earlier, rectal tears can occur during examination by even the most experienced operators. Ideally, the owner should be informed of the risks of rectal palpation and explicit consent to perform the examination should be obtained. This is especially important for animals that are at increased risk of rectal tears.

The examination should be performed only when there is a clear clinical reason for performing a rectal examination, when the animal is a suitable candidate for rectal examination, and when the animal can be adequately restrained to permit a thorough examination to be performed in relative safety for both the examiner and the animal.

The examiner should proceed cautiously with the examination. The gloved hand and arm of the examiner should be well lubricated with a water-based lubricant. The anus should be gently dilated by using fingers shaped into a cone. Feces should be evacuated from the rectum such that the rectum is empty to the most cranial extent of the region to be examined. If the horse is anxious and straining, or if there is excessive peristalsis, then the animal should be sedated and antiperistaltic drugs (such as hyoscine) should be administered. The examination should be halted if the horse begins to struggle or resist the examination excessively. Application of a nose twitch often facilitates the examination.

During the examination care should be exercised not to resist peristaltic waves; the hand should be withdrawn in front of these advancing waves and reinserted as peristalsis passes. The fingers should not be opened widely during the examination and care should be taken not to put excessive pressure on a small region of rectum, such as might occur when trying to grasp an ovary or loop of distended intestine.

A rectal tear in a horse is a common cause of a malpractice suit and the veterinarian involved with the case is advised to recommend to the owner that a second opinion be solicited from another veterinarian to minimize any misunderstanding.

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ACUTE DIARRHEA OF SUCKLING FOALS

ETIOLOGY

The causes of diarrhea in suckling foals are listed in Table 7-22. In a large proportion of foals the cause of diarrhea is not determined, in part because the disease is usually sporadic, mild, and transient. The more common identified infectious causes of diarrhea in foals on breeding farms in Britain include rotavirus, *C. perfringens, Salmonella, Cryptosporidium* sp., and *Strongyloides westeri,* although the relative importance of various pathogens varies from year to year, from farm to farm, and from region to region.[1] Potential pathogens can be isolated from both foals with diarrhea and healthy foals,[2] making etiologic diagnosis of the cause of diarrhea challenging. Of over 1000 foals examined at studs in the UK the most common disease was diarrhea with systemic disease (fever, tachycardia, depression, dehydration, or combinations thereof) affecting 5.9% of foals <30 days of age. Approximately one-half of these foals tested positive for rotavirus.[1]

Etiologic infectious organisms were isolated from 55% of 223 foals hospitalized in the United States for treatment of diarrhea, with 78% of the 122 positive foals having only one organism isolated.[3] Foals were tested for the presence of rotavirus, *Salmonella* spp., *C. perfringens, C. difficile,* coronavirus, helminthes, and cryptosporidium. Rotavirus was the most commonly detected organism and was identified in 20% of the foals.

C. perfringens causes diarrhea in young foals. There are five major types of *C. perfringens* and, while the organism is clearly associated with disease, a definitive role for each of these types in causing disease has not been established, partly because toxin production for strains isolated from foals with diarrhea has not been routinely documented. However, there is clear evidence that *C. perfringens* type C causes diarrhea in foals. *C. perfringens* types A, B, D, and E might be associated with disease in foals, but definitive proof is lacking. β-2 toxigenic *C. perfringens* type A has been described as a cause of colitis in a foal.[4] *C. difficile,* alone or in coinfection with *C. perfringens,* is a cause of diarrhea in foals.[5,6]

E coli, an important cause of disease in neonates of other livestock species, does not appear to be an important cause of diarrhea in foals, although some strains are pathogenic. Similarly, although there are reports of coronavirus causing severe disease in foals, this does not appear to be a common cause of diarrhea in foals. *Candida* spp. can cause diarrhea in critically ill foals and those administered antibiotics, but yeasts are apparently not causally associated with diarrhea in foals.[7] *Yersinia* spp. have been associated with diarrhea in foals but do not appear to be a common cause of disease. *Bacteroides fragilis* is an uncommon cause of diarrheal disease in foals. *C. parvum* or a specific horse-related cryptosporidium causes diarrheal disease in foals and can be isolated from broodmares.[8-10] The role of *Campylobacter* spp. in foal diarrhea, if there is any, is unclear, although it has been isolated from foals with enteritis.[11]

Strongyloides westeri infection, although usually regarded as causing only mild disease, if any, can cause severe disease in a foals and an outbreak of diarrhea.[12]

Group A rotaviruses are an important cause of diarrhea in foals and are discussed separately.[13,14]

Most foals develop transient, clinically unimportant mild diarrhea in the first 2 weeks of life. Colloquially referred to as **foal heat** diarrhea because of its temporal association with postpartum estrus in the dam, the occurrence of diarrhea is not associated with estrus in the dam but rather changes in intestinal flora as the foal ages.[15]

Noninfectious causes of diarrhea in foals include foal heat diarrhea, overfeeding of orphan foals or feeding of incorrect milk replacers, primary or secondary lactose intolerance, and pica (allotriophagia), including eating of sand or dirt. Primary lactose intolerance, the congenital absence of lactase in foals, is reportedly rare.[16] Secondary lactase deficiency occurs in foals recovering from enteritis and responds to feeding of lactose-free milk or administration of exogenous lactase. Acute pancreatitis causes diarrhea in foals, along with signs of abdominal pain and increases in lipase activity in blood and peritoneal fluid.[17]

Diarrhea is common in foals with systemic sepsis (septicemia) in which it can be attributable to the agent causing septicemia also causing colitis/enteritis (for example *Salmonella* spp.) or as a result of systemic organ dysfunction.[18] Approximately 50% of foals with diarrhea treated at a referral institution were bacteremic, although bacteremia was not associated with risk of death.[18]

EPIDEMIOLOGY

Diarrhea is common in suckling foals worldwide although studies of its incidence, risk factors, and outcome are exiguous. Diarrhea affects 21% of foals annually in Texas, being second only to respiratory disease (22%) as a cause of disease. The frequency of disease varies with age: 25% of foals 0 to 7 days of age have diarrhea, compared with 40% and 8% of foals aged 8 to 31 days and 32 to 180 days, respectively. Although a common disease syndrome, diarrhea is not associated with a high death rate (2.6%). Results of the Texas study might not be applicable to foals in other regions as indicated by the finding of 5.9% of foals affected by diarrhea with systemic signs and an additional 2.9% with undiagnosed diarrhea without systemic signs on horse studs in the UK.[1]

Among the common causes of diarrhea the highest death rates are associated with diarrhea associated with *C. perfringens, Salmonella* sp., and *Cryptosporidium* sp.[2]

Risk factors for development of the diarrhea vary depending on its etiology, but generally the disease is less common in foals born on pasture and at low stocking density.[11]

Table 7-22 Epidemiological and clinical features of suckling foals with diarrhea

Etiological agent or disease	Important epidemiological factors	Major clinical findings; *diagnostic criteria*
Idiopathic		
Foal heat diarrhea	Foals <2 weeks of age	No systemic signs of disease; diarrhea is mild and pasty
		No specific diagnostic criteria
Bacterial causes		
Septicemia (coliforms, *Actinobacillus* sp., *Salmonella* sp., *Klebsiella* sp., and others)	Newborn foal to <2 weeks of age; failure of transfer of passive immunity	Signs of systemic sepsis in addition to diarrhea; fever, depression, recumbency, failure to nurse, swollen joints, pneumonia, omphalitis, or omphalophlebitis; *blood culture*
Salmonella sp.	Outbreaks in newborn foals, even those with adequate passive immunity; mare is the likely carrier	Acute onset diarrhea, depression, fever, and toxemia; *culture of blood and feces*
	Hygiene at parturition may prevent disease	
Escherichia coli	Not a well-documented disease in foals (cf. calves and piglets)	Nonfetid diarrhea; *culture of feces yields heavy growth of mucoid E. coli (circumstantial evidence only)*
Enterococcus (*Streptococcus*)	Young foals; disease is rarely reported	Diarrhea; *demonstration of S. durans in feces*
Rhodococcus equi	Foals 2–5 months of age, some with history of respiratory disease	Diarrhea associated with *R. equi* pneumonia; *culture respiratory tract*
Clostridium difficile	<2 weeks of age	Colic, fever, ileus, hematochezia, toxemia, and depression; *fecal culture and demonstration of toxin in feces*
C. perfringens type C	Neonatal foals; sporadic disease to annual outbreaks on breeding farms; most foals excrete *C. perfringens* type A, which rarely causes diseases in foals	Colic, fever, ileus, hematochezia, toxemia, depression *Culture of C. perfringens type C in feces, demonstration of toxin in feces*
Lawsonia *intracellularis*	Older suckling foals and weanlings; sporadic or outbreaks on farms	Weight loss, mild to moderate diarrhea, ventral edema, depression, hypoproteinemia; *serology and polymerase chain reaction on feces*
Yersinia pseudotuberculosis	Suckling foals; outbreaks on breeding farms	Watery diarrhea and suppurative pneumonia; *culture of feces and lesions*
Aeromonas hydrophila	Reports of disease are uncommon; uncertain importance	Diarrhea; *culture of feces*
Viral causes		
Rotavirus	<3 months of age; occurs as outbreaks or endemic disease on farm; highly contagious	Profuse watery diarrhea with variable hypovolemia and depression; *detection of virus in feces by EM, IFA, ELISA*
Adenovirus	Immunodeficient foals (Arabians with severe combined immunodeficiency)	Diarrhea, depression; may be associated with other diseases including pneumonia; *detection of virus in feces by EM*
Coronavirus	Young foals (age range not well defined)	Diarrhea; *detection of virus in feces by EM*
	Apparently rare cause of diarrhea in foals	
Parasites		
Cryptosporidium sp.	Foals of any age; may be spread from other species, including calves and crias	Inapparent infection to fulminant disease with diarrhea, hypovolemia, and collapse; chronic diarrhea
		Detection of oocysts in feces, IFA
Strongyloides westeri	Individual foals; uncertain importance as a cause of diarrhea	Acute to chronic diarrhea; *patent infections evident by fecal examination for parasite eggs*
Other		
Nutritional	Sporadic; orphan foals fed inappropriate or poor-quality milk replacers; nursing foals fed inappropriate supplements	Mild to moderate chronic diarrhea; failure to thrive; *feed diet intended for foals (not plant-, protein-, or bovine-milk–based)*
Lactose intolerance	Nursing foals	Moderate to profuse diarrhea; *historical confirmation of administration of compounds*
Overdosing of cathartics (DSS, MgSO₄, NaSO₄, castor oil)	Sporadic; secondary to viral diarrhea; occurs only in milk-fed foals	Moderate to severe watery, acidic diarrhea; *oral lactose tolerance test or trial administration of lactase with milk feedings*
Enema	History of administration; diarrhea short lived	Bright alert and responsive foal with mild to moderate diarrhea; no specific diagnostic tests
Antibiotic induced	Administration of antibiotics	Mild to moderate diarrhea; may be associated with *Candida* sp. or *C. difficile*; *culture of feces, examination for C. difficile toxin*

DSS, dioctyl sodium sulfosuccinate; ELISA, enzyme-linked immunosorbent assay; EM, electron microscopy; IFA, indirect fluorescent antibody.

Rotavirus diarrhea is often endemic on farms, and the disease occurs as outbreaks on successive years. Affected foals range in age from less than 7 days to more than 3 months.

Diarrhea caused by **R. equi** occurs in foals with *R. equi* pneumonia, and the disease is endemic on some farms. Not all foals with *R. equi* pneumonia develop diarrhea. The disease occurs in foals 2 to 5 months of age.

Salmonellosis also occurs as outbreaks of disease among foals less than 8 days of age on breeding farms and is associated with a carrier status in mares.[12]

Diarrhea associated with **C. perfringens** type C occurs in foals less than 10 days of age with most foals being less than 6 days old,[4] and can occur as a farm problem with multiple foals affected on each of several successive years.[13] Farm risk factors include presence of other livestock, stock-horse–type foals, foals born on dirt, and stall or drylot confinement for the first few days of life.[14] *C. perfringens* type A is excreted in feces of most normal foals, whereas *C. perfringens* type C is rarely isolated from feces of normal foals.[15] **C. difficile** causes diarrhea in foals not administered antibiotics,[16] in contrast to the situation in adult horses, and usually affects foals less than 14 days of age, although foals up to 120 days of age can be affected.[17] FTPI is not a risk factor for *C. perfringens* or *C. difficile* enteritis in foals.

L. intracellularis causes mild to moderate diarrhea in older suckling or weaned foals. The disease occurs as outbreaks on breeding farms. There are no recognized foal or farm risk factors.

PATHOGENESIS

The pathogenesis of diarrhea varies somewhat depending on the inciting cause (see appropriate sections of this text for discussion of pathogenesis), although if sufficiently severe all cause excessive loss of fluid and electrolytes in feces and subsequent hypovolemia, electrolyte abnormalities, metabolic acidosis, and weakness. Although not demonstrated in foals, diarrhea in calves causes metabolic acidosis through loss of sodium and other cations in feces, which results in a decrease in the strong ion difference in blood, causing acidosis. Bicarbonate loss, per se, is not a cause of the metabolic acidosis, at least in calves. Infectious agents generally cause enteritis, although rotavirus infection is associated with loss of villous cells and subsequent loss of enzyme activity derived from the mature epithelial cell. The loss of enzyme activity, including that of disaccharidases, causes malabsorption of nutrients in milk and other feed. Failure to absorb nutrients in the small intestine causes them to be delivered to the cecum and large intestine where they are fermented. Subsequent reductions in colonic pH and increases in osmotic activity of the colon contents result in excretion of large quantities of fluid and electrolytes. *C. difficile* and *C. perfringens* produce enterotoxins that cause damage to intestinal cells and accumulation of hemorrhagic fluid in the intestine.[16] *L. intracellularis* causes an infiltrative and proliferative enteropathy with subsequent protein loss and malabsorption of nutrients.[19]

CLINICAL SIGNS

Clinical signs vary from mild, pasty diarrhea that adheres to the perineum and causes no detectable systemic signs of disease to profuse watery diarrhea with rapid development of loss of suckling, depressed mentation, tachycardia, increased skin tent, ileus, and recumbency.

Signs of systemic disease include failure to nurse, increased frequency or prolonged duration of recumbency, foals on pasture failing to follow the mare, fatigue, less frequent urination or production of concentrated urine (urine from normal foals is normally dilute), and weakness. Affected foals often have depressed mentation, tachycardia, fever (depending on the cause of the diarrhea), decreased capillary refill time, dry mucous membranes, increased skin tent, and eyes that are retracted into the orbit (consistent with dehydration). Depending on the cause of the diarrhea, foals can have signs of colic, which can range from mild with intermittent flank watching or biting and restlessness, through profound agitation, rolling, and dorsal recumbency. Severely affected foals can have seizures as a result of profound hyponatremia.[18]

Chronic diarrhea and that caused by nutritional imbalance or lactose intolerance causes rapid weight loss, failure to thrive, poor hair coat, and lethargy. Chronic fecal contamination of the perineum and escutcheon causes excoriation and loss of hair.

Diarrhea associated with foal heat is usually mild and transient and not associated with systemic signs of disease. However, diarrhea caused by infectious agents is often severe and accompanied by systemic signs of disease.

Diseases associated with *Clostridium* sp. are often severe with rapid onset of signs of toxemia, colic, hypovolemia, and death. Diarrhea is usually present and is often bloody, although it can be watery and profuse. Severely affected foals usually have signs of colic, toxemia, and ileus and may not develop diarrhea before dying. Salmonellosis can present as septicemia, with subsequent development of diarrhea, although in older foals diarrhea is a common presenting sign.

CLINICAL PATHOLOGY

Diarrhea with systemic signs of disease in foals can cause hyponatremia, hyperkalemia, hypochloremia, metabolic acidosis, hypoproteinemia, and azotemia. The magnitude of abnormalities varies with the cause of disease and its severity. Hyponatremia can be profound (<100 mEq/L). Hypoproteinemia can be a result of loss of protein from the inflamed intestine, a reflection of FTPI, or a combination of both. All young foals with diarrhea should have serum or plasma immunoglobulin concentrations measured or some other test for transfer of passive immunity performed.

Viral causes of diarrhea can be diagnosed by examination of feces by electron microscopy (EM). However, more rapid and sufficiently sensitive and specific tests exist for diagnosis of rotaviral disease (enzyme-linked immunosorbent assay [ELISA] and indirect fluorescent antibody [IFA]). Culture of feces will demonstrate *Salmonella* spp. in most cases if they are the cause of disease. Fecal culture yielding *C. perfringens* or *C. difficile* is insufficient for diagnosis of clostridial enterocolitis because these organisms can be recovered from normal foals. Confirmation of the diagnosis is achieved by demonstration of clostridial toxins in feces, which can be problematic given that the toxins are very labile.[4,6,20]

DIAGNOSTIC CONFIRMATION

For diagnostic criteria for specific diseases, see the appropriate sections in this text.

LESIONS

Lesions associated with diarrhea in foals depend on the inciting cause. Characteristically in severe cases there is enteritis and colitis with ulceration of intestinal mucosa. Foals with rotavirus diarrhea, most of which survive, have flattening of small-intestinal epithelium.

TREATMENT

The principles of treatment are
- Correction and maintenance of hydration, acid-base, and electrolyte status
- Ensuring adequate transfer of passive immunity
- Ensuring adequate nutrition
- Preventing complications of disease, including bacteremia

Correction of hypovolemia and electrolyte abnormalities should follow the general guidelines presented elsewhere in this text. Mildly affected foals, such as those with no systemic signs of disease, might not require administration of fluids orally or parenterally and care involves watchful waiting and intervention as indicated by deterioration in the foal's clinical status. More severely affected foals might require oral supplementation with balanced, isotonic electrolyte rehydration solutions, such as those marketed for use in calves. The amount and frequency will depend on the size of the foal, severity of disease, and response to treatment. Foals that have clear signs of hypovolemia should be administered fluids intravenously. These fluids should ideally be selected based on the foal's serum electrolyte concentrations, but in most instances a balanced, polyionic isotonic fluid such as lactated Ringer's solution is

appropriate. Correction of hyponatremia in some but not all foals requires administration of hypertonic (7%) sodium chloride intravenously. However, rapid correction of hyponatremia, especially if it is long-standing (more than 24 hours) might be associated with an increased risk of cerebral demyelination.[21,22] Correction of hyponatremia will resolve seizure activity.

Correction of acid-base usually occurs with correction of fluid and electrolyte abnormalities. Provision of fluids that are sodium rich and have a high strong ion gap, for instance, lactated Ringer's solution, will usually correct the metabolic acidosis common in foals with diarrhea. However, in some foals the rate of fecal loss of cations including sodium and potassium prevents resolution of metabolic acidosis without administration of sodium bicarbonate. Sodium bicarbonate can be administered intravenously or orally. Oral administration has the advantages that it is convenient and does not require administration of large amounts of fluid or of hypertonic solutions. The dose of sodium bicarbonate can be calculated from the foal's BW and base deficit. As a guideline, a 40-kg foal that is not hypovolemic but has continued profuse watery diarrhea and metabolic acidosis should receive 30 g of sodium bicarbonate orally every 6 hours. Serum sodium and bicarbonate concentrations should be measured at least daily and doses of sodium bicarbonate should be adjusted on the basis of these values. Overdosing, or continued dosing when diarrhea has resolved, results in hypernatremia and metabolic alkalosis.

Foals with diarrhea should have serum immunoglobulin concentrations measured. Hypogammaglobulinemic foals should be administered plasma intravenously (20–40 mL/kg BW).

Ensuring that foals affected by diarrhea continue to ingest sufficient calories is critical to the foal's survival. Foals require up to 150 (kcal/kg)/day for growth but can maintain weight on as little as 50 (kcal/kg)/day, especially if the nutrients are provided intravenously. Foals with mild to moderate diarrhea should be permitted to nurse at will. If there is concern that the foal is not nursing sufficiently, a feeding tube can be placed and the foal's diet supplemented with mare's milk substitute lactose-free milk. Lactase is sometimes added to the milk on the assumption that enteritis causes lactase deficiency (see section Tests of Absorptive Function for details of lactose tolerance testing in foals).

Foals with severe diarrhea can benefit from parenteral administration of nutrition and gastrointestinal rest. Feed withholding results in a marked reduction in fecal volume and the extent of electrolyte and acid-base abnormalities. However, it is critical for foal recovery that complete feed withholding is accompanied by partial parenteral nutrition.

Antibiotics are usually administered to foals with severe diarrhea because approximately 50% of such foals have bacteremia.[18] Although there is no evidence that parenteral administration of antibiotics reduces morbidity or case–fatality rate, the precaution has merit, as it does in calves. Oral administration of antimicrobials to foals with diarrhea is common but is not recommended because of the risk of exacerbating the disease, and unknown efficacy. Foals with suspected clostridial enterocolitis should be administered metronidazole (15–20 mg/kg, intravenously or orally, every 6–12 hours).

Drugs that affect gastrointestinal motility, such as loperamide, parasympatholytics, and narcotics, have no demonstrated efficacy in reducing morbidity or case–fatality rate and their use is not recommended.

CONTROL

Control of foal diarrhea is problematic because it is very common, many cases are mild and transient, a definitive diagnosis is frequently not available in a timely fashion, and it can be associated with a wide variety of infectious and noninfectious agents. Basic principles include ensuring adequate transfer of passive immunity, reducing exposure to pathogens, and minimizing the effect of other risk factors.[23]

Of the important causes of disease, in terms of morbidity and case–fatality rate, control of diarrhea associated with rotavirus and clostridial species is most important. Control of rotaviral diarrhea is discussed elsewhere. Control of clostridial diarrhea on farms with an endemic problems includes vaccinating of mares, administration of metronidazole to at-risk foals, and supplementation of passive immunity with antitoxins to clostridial toxins. Vaccination of mares with toxoids (*C. perfringens* type C and D toxoid) prepared for use in other species has been practiced, but there are no reports of safety or efficacy. Administration of antitoxin raised against *C. perfringens* C, D, and E might provide protection against the α-, β-, and ε-toxins that have the potential to affect foals. The antiserum, which is intended for use in ruminants, is administered orally (50–100 mL per foal) soon after birth. The efficacy of this practice has not been determined. Foals at risk may also be administered metronidazole (10 mg/kg every 12 hours) for the first 4 to 5 days of life. Again, the efficacy of this practice has not been determined. Vaccination of mares with recombinant protein of *C. difficile* toxin resulted in production of specific antibodies, although the efficacy of the vaccine in protecting foals was not tested.[24]

Administration of a probiotic containing *Lactobacillus pentosus* WE7 did not confer any protection against development of diarrhea in foals, and was associated with an increased risk of clinical disease, including diarrhea.

FURTHER READING

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ACUTE DIARRHEA OF ADULT (NONSUCKLING) HORSES

SYNOPSIS

Etiology *Salmonella* spp., *Strongylus* spp., cyathostomes, *Neorickettsia risticii*, *Clostridium difficile*, antibiotic administration, coronavirus, idiopathic

Epidemiology Usually a sporadic disease of young horses, often temporally associated with mild respiratory disease or a stressful event such as transport. Helminthiasis has a seasonal distribution and can occur as a herd problem. *N. risticii* has a defined geographical distribution.

Clinical signs Vary from acute and transient diarrhea with minimal changes in vital signs to acute onset of profuse watery diarrhea with rapid development of severe clinical disease. Depression, fever, dehydration, and anorexia are common. Laminitis occurs as a sequela.

Clinical pathology Leukopenia, hemoconcentration, hyponatremia, hypokalemia, or hyperkalemia, and metabolic acidosis. IFA or PCR for *N. risticii*, fecal culture or PCR of *Salmonella* spp. Fecal culture for *Clostridium* spp. and ELISA to demonstrate toxin in feces

Lesions Colitis with or without enteritis

Diagnostic confirmation Cause is frequently not confirmed.

Treatment Maintenance of hydration and correction of acid-base and electrolyte abnormalities. Severe cases require more intensive care. Oxytetracycline for equine neorickettsiosis (monocytic ehrlichiosis). Metronidazole for *C. difficile*-associated diarrhea. Administration of anthelmintics

Control None

IFA, indirect fluorescent antibody; PCR, polymerase chain reaction.

ETIOLOGY

Causes are as follows:

- **Salmonellosis:** Various *Salmonella* spp.
- **Helminthiasis:** *Strongylus* sp., cyathostomes
- **Equine neorickettsiosis** (Potomac horse fever): *Neorickettsia risticii*
- **Antibiotic administration:** macrolides (lincomycin, tylosin, and erythromycin), tetracyclines, ciprofloxacin, trimethoprim-sulfonamide combination, penicillin, aminoglycosides, ceftiofur, and others[1-3]
- **Intestinal clostridiosis:** *C. perfringens* (types A and C[4]), toxigenic strains of *C. difficile,*[5-8] and possibly *C. cadaveris*
- *Aeromonas* **spp.:** Sometimes isolated from horses with diarrhea but definitive role as a causative agent has not been demonstrated[9]
- **Coronavirus**[10,11]
- **Idiopathic**
  - Intestinal hyperammonemia[12,13]
  - Excessive concentration of sulfate in drinking water[14]
  - Administration of imidocarb for treatment of equine piroplasmosis[15]
  - Intoxication with inorganic arsenic, cantharidin, or purgatives such as castor oil

Unlike other species, *E. coli* does not appear to be an important cause of diarrhea in adult horses.

In most cases (65%) of acute diarrhea in horses the cause is not determined, or if the cause is determined it is frequently at necropsy examination or as a result of serologic or microbiological testing after the horse has recovered.

EPIDEMIOLOGY
Occurrence

The syndrome of acute diarrhea occurs **worldwide** in adult horses of all breeds and both genders. The pattern of occurrence of the syndrome is dependent on the causative factors, with equine neorickettsiosis, associated with *N. risticii,* having a geographic distribution and **acute cyathostomiosis** having a seasonal distribution. Salmonellosis can occur sporadically or as outbreaks in stables, barns, and veterinary hospitals. *C. difficile* enterocolitis is often associated with hospitalization, antibiotic administration, or both to adult horses.

Colitis X refers to an idiopathic peracute to acute enterocolitis with a high case–fatality rate. It is usually a sporadic disease, but multiple cases can occur in a barn or racing stable over a period of weeks and cause considerable economic hardship.

Estimates of incidence, morbidity and mortality, and case–fatality rate are not available for all diseases and are discussed in greater detail in those sections of this text dealing with those diseases.

The **case–fatality rate** for the spontaneous disease can be 25% to 50% even in intensively treated horses, although these estimates are based on horses treated at referral practices. The recovery rate for acute but transient diarrhea in adult horses examined in primary practice is much higher. The case–fatality rate is higher for horses with *C. difficile*-induced diarrhea than for horses with acute diarrhea of other causes and for horses with antibiotic-induced diarrhea. The prognosis is worse in horses with tachycardia, severe dehydration (PCV > 45% [0.45 L/L]), azotemia, metabolic acidosis, low serum albumin concentration, or higher immature neutrophil (band cell) count in peripheral blood.

Risk Factors

The risk factors for salmonellosis, equine neorickettsiosis, and strongylosis/cyathostomiosis are addressed under those topics.

Stress

Stressful episodes, such as shipping or racing, hospitalization, surgery, administration of antibiotics, or mild respiratory disease, frequently precede the onset of diarrhea.

Celiotomy

Celiotomy for colic is associated with an incidence of severe diarrhea of up to 27% in surviving horses. The risk of diarrhea is greatest in horses with large-colon disease or with enterotomy, but is not influenced by the type of antibiotic administered after surgery.

Antibiotic Administration

Antibiotic administration is associated with acute diarrhea in horses, and almost all antimicrobials can cause the disease although some are apparently associated with greater risk or more severe disease. For example, administration of macrolide antibiotics including lincomycin, clindamycin, and erythromycin are consistently associated with higher risk of diarrhea in adult horses. Diarrhea occurs in horses administered antimicrobials, but such horses frequently have other risk factors for development of diarrhea, and the link to antimicrobial administration is unclear.[1] The prevalence of antimicrobial-induced diarrhea in 5300 adult horses in three referral hospitals over 1 year was 0.6% and had an 18% case–fatality rate.[3] However, 6.3% of horses administered antimicrobials developed diarrhea within 7 days of arthroscopic surgery compared with none of 44 horses after arthroscopic surgery and not administered antimicrobials.[16]

The macrolide antibiotic **lincomycin** causes acute, often fatal, disease of horses even when administered at relatively low doses, such as that resulting from horses ingesting medicated pig feed. Erythromycin is associated with diarrhea in adult horses and in mares of foals administered the combination of erythromycin and rifampin. **Tetracyclines** have been associated with the development of acute diarrhea but, when given intravenously at therapeutic doses (6.6 mg/kg every 12–24 hours) are probably no more likely to cause diarrhea than other broad-spectrum antibiotics. Tetracycline contamination of feed causes outbreaks of diarrhea on horse farms. Enrofloxacin can be a cause of diarrhea in horses.[3] The combination of **trimethoprim and sulfadiazine** given orally caused diarrhea in 7% of hospitalized horses, whereas pivampicillin, a prodrug of ampicillin, caused diarrhea in 3%, although this difference was not statistically significant. The risk of diarrhea was greatest in hospitalized horses administered enrofloxacin or combinations of drugs including gentamicin. However, the number of horses with diarrhea was small and important associations might have not been detected.[3]

PATHOGENESIS

Diarrhea is the result of abnormalities in colonic water and electrolyte metabolism. Approximately 90 L of isotonic fluid enters the colon of an adult (450-kg) horse every 24 hours, and any disruption to the normal absorption of this fluid results in increased fecal water and electrolyte excretion. Horses with colitis have markedly different fecal microbiota compared with healthy horses, with loss of predominance of clostridia normally present in healthy horses and reduced diversity of microorganisms.[17] There appears to be a general dysbiosis of fecal microbiota in horses with colitis.

The pathogenesis of **antimicrobial-associated diarrhea** is unclear but could involve one or more of altered gastrointestinal motility (e.g., erythromycin), disturbed enteric flora allowing overgrowth of pathogens and subsequent enteritis or colitis, or altered microbial digestion of ingesta with abnormalities in water and electrolyte balance.[1] Antimicrobial administration markedly alters the flora of healthy horses.[18] Oral administration of trimethoprim-sulfadiazine or intramuscular administration of ceftiofur to healthy horses for 1 week caused a >99% decrease in the number of viable cellulolytic bacteria in feces for at least 1 week after cessation of administration.[18] Ceftiofur resulted in a marked reduction in the number of viable lactobacilli in feces. Antibiotic-treated horses shed more *Salmonella* in feces and

horses only had *C. difficile* during and after administration of antimicrobials.[18] Potential, or identified, pathogens identified in horses with suspect antimicrobial diarrhea include *C. difficile, C. perfringens, Salmonella* sp., and coliforms. Almost all adult horses with diarrhea from which *C. difficile* or its toxin can be isolated were administered antibiotics before onset of diarrhea.

Colitis results from physical, chemical, or infectious causes that induce inflammation in the colon. The proximate causes vary with the etiology of the disease. For example, colitis caused by infection from toxigenic strains of *C. perfringens* type C is attributable to binding of β-2 toxin to colonic mucosa, whereas colitis caused by salmonellosis is associated with invasion of the organism and loss of colonic mucosa. Colitis is associated with increased production of inflammatory cytokines, including tumor necrosis factor, in the colon, and with impaired mucosal absorptive function. Additionally, bacterial toxins and inflammation result in an increase in mucosal permeability with loss of plasma proteins into the colonic lumen and systemic absorption of toxins, including endotoxin. Loss of plasma proteins causes a reduction in plasma colloidal oncotic pressure with subsequent extravasation of water and electrolytes and development of edema and decreased effective intravascular volume (hypovolemia). The effect of the decrease in oncotic pressure becomes most apparent in horses that are treated aggressively with fluids. These horses, which often inadvertently receive excessive amounts of sodium as part of their treatment, rapidly develop edema of the ventral body wall and colon, among other tissues. Loss of other plasma proteins, including antithrombin III, and absorption from the gut of activators of coagulation, fibrinolysis, or inflammation, can contribute to the disseminated intravascular coagulation often observed in horses with enterocolitis.

The large volume of diarrhea in horses causes a reduction in body water and electrolyte content. Hypovolemia, hyponatremia, hypochloremia, and hypoproteinemia develop. Derangements in acid-base and electrolyte status impair gastrointestinal motility. Hypovolemia impairs perfusion of peripheral tissues, which, combined with absorption of endotoxin through the damaged colonic mucosa, results in toxemia, lactic acidosis, and death.

CLINICAL SIGNS

The onset of clinical signs is usually abrupt, although in some horses diarrhea can be presaged for up to several days by inappetence, mild depression, and a mild fever. The disease varies in severity from short-lived with mild to moderate diarrhea and minimal systemic signs of disease to a fulminant disease with death in hours. The description here is of the more severe forms of the disease. Once diarrhea occurs there is often **rapid progression**, with some horses

dying within 12 hours of initial clinical signs, although most survive at least 24 hours. In a peracute form of the disease horses die, often within 6 hours, before developing diarrhea.

Typically horses are often severely depressed and stand with their heads down. They may play in water, but rarely eat or drink. Horses are usually mildly pyrexic (101.5–103°F [38.6–39.5°C]) but markedly tachycardic (80–100 beats/min), tachypneic (30–40 beats/min), and dehydrated (8%–12%). There is slow capillary refill of mucous membranes, which are usually bright red initially and then become bluish-purple as toxemia and dehydration become severe. The development of a purple line at the gingival margins is a sign of a poor prognosis. Most horses are oliguric.

The diarrhea is profuse and watery. **Abdominal pain** is usually present but mild; the onset of severe abdominal pain is often associated with necrosis of the large colon or cecum and impending death. **Rectal examination** reveals large amounts of fluid feces with minimal distension of the large colon.

Complications of acute, severe enterocolitis include laminitis, thrombophlebitis of the jugular veins, **thrombosis** of vessels including arteries in the limbs, renal failure, pulmonary aspergillosis, and necrotizing enterocolitis. Laminitis develops within 1 to 3 days of onset of diarrhea in approximately 10% of cases and can occur in any horse with enterocolitis, but is most common in horses with Potomac horse fever (equine neorickettsiosis). Thrombophlebitis, which may or may not be septic, usually affects veins, usually the jugular, that have or have had catheters placed or are the site of frequent intravenous injections. Thrombosis of the vein can occur several days to a week after removal of the catheter, although most occur while the catheter is in place. Renal failure occurs as a result of the combined insults of hypovolemia, endotoxemia, and administration of nephrotoxic drugs, including aminoglycosides and NSAIDs. Pulmonary aspergillosis is usually clinically inapparent. Clinically affected horses have rapidly progressive toxemia; respiratory distress; hypoxemia; and blood-tinged, frothy nasal exudates. Fatal necrotizing enterocolitis of horses is characterized by a brief course, with most horses dying within 48 hours of onset of diarrhea, profound dehydration, electrolyte derangements, severe metabolic acidosis and, terminally, severe abdominal pain.

Most horses that survive have resolution of diarrhea in about 7 days, although a small but clinically important proportion develop chronic diarrhea.

CLINICAL PATHOLOGY

Hematological examination reveals an increased hematocrit (45%–60%), variable changes in plasma protein concentration, and neutropenia with a marked left shift. As the disease progresses and horses are

treated by intravenous administration of fluids, plasma protein concentrations and plasma oncotic pressure decline. Plasma or serum albumin concentration may be as low as 1.2 g/dL (12 g/L). Changes in **coagulation and fibrinolysis** are evident as increases in one or more of the following occur: one-stage prothrombin time, activated partial thromboplastin time, and concentration of fibrin degradation products, variable changes in plasma fibrinogen concentration, and a reduction in blood platelet concentration. Approximately one-third of horses hospitalized for treatment of severe diarrhea have subclinical evidence of disseminated intravascular coagulation, which carries a reduced likelihood of recovery.

Serum biochemical analysis usually reveals hyponatremia, hypochloremia, variable changes in serum potassium concentration, hypocalcemia (both concentrations of ionized and total calcium), azotemia (increased serum urea nitrogen and creatinine concentrations), hyperphosphatemia, and increased activities of enzymes indicative of muscle (creatine kinase) or intestinal damage (aspartate aminotransferase and alkaline phosphatase).

Blood gas analysis often reveals a severe metabolic acidosis, and the more negative the base excess the worse the prognosis. Interpretation of acid-base status in horses with severe enterocolitis is difficult because of the opposing effects of hypoproteinemia and combination of lactic acidosis and electrolyte loss on blood pH. Hypoproteinemia causes a metabolic alkalosis, whereas increases in plasma lactate concentration and hyponatremia cause metabolic acidosis. The presence of hypoproteinemia therefore tends to diminish the effect of lactic acidosis on blood pH, which underestimates the severity of the acidosis. Acid-base status in horses with severe abnormalities in plasma protein concentration should be ascertained by examination of base excess, strong ion gap, or strong ion difference.

Plasma endothelin concentrations are higher in horses with enterocolitis than in normal horses, although the clinical significance of this finding is unclear.

Abdominal fluid is usually normal initially but becomes bloody and has an increased white blood cell count and protein concentration if intestinal necrosis occurs.

DIAGNOSTIC CONFIRMATION

This depends on the results of fecal culture for *Salmonella* sp., fecal examination for helminth eggs or larvae, and IFA or PCR tests for *N. risticii*. Demonstration of large numbers of salmonellas in feces on multiple fecal samples, or in lymph nodes of horses dying of the disease, is persuasive evidence that the horse had **salmonellosis**. However, demonstration of low numbers of salmonellas in a single fecal culture is not definitive evidence that *Salmonella* sp. infection was the cause of the horse's diarrhea.

Fecal examinations for helminth eggs may be negative in cases of **acute cyathostomiosis**, although large numbers of fourth-stage larvae may be present in the feces. Diagnosis of *N. risticii* infection is based on a positive IFA test. Isolation of *Clostridium* sp. *and* demonstration of **clostridial enterotoxin** in feces of horses with acute diarrhea supports a diagnosis of intestinal clostridiosis, although demonstration of toxin alone is usually considered sufficient evidence for diagnosis. **Latex agglutination tests** are available for the detection of *C. perfringens* type A and *C. difficile* toxins.

NECROPSY

There are extensive lesions at necropsy examination, the most dramatic being in the large intestine, especially the cecum and ventral colon. These include hyperemia, extensive petechiation, and edema of the gut wall in the early stages, and later an intense, greenish-black, hemorrhagic necrosis. The contents are fluid, often foamy and foul smelling, and may be bloodstained.

Histologic examination demonstrates mucosal necrosis with a fibrinohemorrhagic exudate and extensive inflammation of the mucosa and submucosa.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis list:
- Salmonellosis
- Equine neorickettsiasis (Potomac horse fever)
- Cyathostomiosis
- Antibiotic-induced diarrhea
- *Clostridium* sp. infection (*C. difficile*)
- Colitis X
- Intoxication with inorganic arsenic, cantharidin, or purgatives such as castor oil
- The incipient disease in horses before onset of diarrhea can resemble colon torsion or ischemia of the large colon secondary to verminous arteritis.

TREATMENT

Horses with mild disease, those that do not manifest systemic signs of disease, usually recover with symptomatic treatment. However, horses with severe disease require more specific treatment and supportive care, which is often intensive and expensive.

The **principles of treatment** for horses with acute diarrhea are

- Restoration and maintenance of normal hydration
- Correction of electrolyte and acid-base abnormalities
- Provision of analgesia
- Prophylaxis and treatment of the effects of endotoxemia/toxemia including management of systemic inflammatory response syndrome
- Prevention of absorption of toxins
- Correction and prevention of disseminated intravascular coagulation

Restoration of Hydration

Restoration of hydration should be considered an **emergency procedure** in severely affected horses. Fluids should be administered intravenously until hydration is restored, after which hydration can be maintained by either oral (via nasogastric tube) or intravenous administration of fluids. Suitable fluids for restoration of hydration are sodium-rich, isotonic, preferably polyionic, electrolyte solutions such as **lactated Ringer's** or Ringer's solution. **Isotonic sodium chloride** is also suitable. Isotonic dextrose solutions are not suitable because they do not contain any electrolytes. After correction of dehydration, attention should be paid to sodium balance because the administration of excessive quantities of sodium, especially to horses with plasma oncotic pressure that is lower than normal, may cause expansion of the extracellular fluid volume and edema.

Fluid therapy is discussed elsewhere. **Maintenance of hydration** in severely affected horses can be challenging and is best accomplished by intravenous administration of fluids. **Oral administration** of fluids to horses with diarrhea, although not providing ideal rehydration or maintenance of hydration, can be effective and less costly than intravenous administration.

Horses that become **hypoproteinemic** can require transfusions of plasma or administration of synthetic colloids such as hetastarch or pentastarch. Clinical signs indicating the need for transfusion include a persistently elevated heart rate and poor peripheral perfusion in spite of the administration of large quantities of fluids. Ventral edema and edema of the head and legs can develop in hypoproteinemic horses. Sufficient plasma should be administered to restore the plasma protein concentration to at least 40 g/L. Hetastarch or pentastarch provide none of the complex proteins present in plasma and essential for maintenance of normal clot formation and fibrinolysis and do not increase plasma protein concentration. Additionally, synthetic colloids can impair platelet function. Efficacy of administration of synthetic colloids should be assessed by examination of clinical signs or by measurement of plasma oncotic pressure.

Electrolyte and Acid-Base Status

Hyponatremia and hypochloremia will usually be corrected by administration of isotonic, sodium-rich electrolyte solutions such as lactated Ringer's solution. If this does not occur, then sodium chloride or sodium bicarbonate can be added to the intravenous fluids, or given orally. **Hypocalcemia** can be corrected by the addition of calcium gluconate (20 mL of 23% calcium gluconate per liter of fluids) to the fluids, provided that the fluids do not contain sodium bicarbonate. The mixture of sodium bicarbonate and calcium gluconate causes calcium to precipitate out of solution. Affected horses have **total body potassium depletion**, even though serum potassium concentrations may be normal or elevated, and maintenance fluids should contain potassium at up to 25 mEq/L. Fluids with high potassium concentration should be administered slowly. Alternatively, potassium chloride can be given orally (50–100 g per 450 kg every 12 hours).

The **metabolic acidosis** in horses with acute diarrhea often resolves either partially or completely when hydration is restored. However, severe acidosis can be treated with intravenous **sodium bicarbonate**. Oral administration of sodium bicarbonate (100 g per 450 kg every 8–12 hours) is often adequate in restoring and maintaining normal acid-base status. The serum sodium concentration should be monitored if large quantities of sodium bicarbonate are administered.

Antimicrobial Therapy

Approximately one-third of adult horses with acute diarrhea requiring hospitalization have positive blood cultures within the first day.[19] Bacteria detected include *Corynebacterium* spp., *Streptococcus* spp., *Pantoea agglomerans,* gram-negative rod, *Bacillus* spp., and yeast. Horses with positive blood cultures were sicker and 13 times more likely to die,[19] which could be a reflection of the lethality of bacteremia or that horses that were sicker and more likely to die were at greater risk of developing bacteremia. Administration of antimicrobials was not associated with outcome (lived versus died, risk of complications).

Administration of tetracycline to horses with acute diarrhea associated with *N. risticii* is clearly indicated and is often curative. However, the administration of antimicrobial drugs to horses with acute diarrhea other than that associated with *N. risticii* is controversial.

There is no evidence that administration of antimicrobials improves the prognosis of horses with acute diarrhea. The concern with antimicrobial administration is that antimicrobials can exacerbate the diarrhea in some cases. Conversely, withholding antimicrobials from severely ill horses with damaged colonic mucosa, and therefore presumably increased risk of bacteremia, is problematic. Regardless, many clinicians choose to treat horses with acute diarrhea with broad-spectrum antibiotics such as the combination of potassium penicillin (20,000 IU/kg, intravenously every 6 hours) and gentamicin (7 mg/kg intravenously or intramuscularly every 24 hours) or trimethoprim and sulfadiazine (30 mg/kg intravenously or orally every 12 hours). Metronidazole (15–20 mg/kg orally every 6–12 hours) or vancomycin has been recommended for horses with intestinal clostridiosis, although the wisdom of veterinary use of vancomycin, a drug used for the treatment of methicillin-resistant staphylococci in humans, could be questioned. In areas in which equine neorickettsiasis is endemic, all suspected cases should be treated with tetracycline (6.6 mg/kg intravenously every 12

hours for 3 days), or another effective antibiotic, pending confirmation of the disease. Isolates of toxigenic *C. difficile* from horses with diarrhea are almost always susceptible to metronidazole (15–29 mg/kg orally every 6–12 hours).

Prophylaxis and Treatment of Endotoxemia/Toxemia and Systemic Inflammatory Response

Treatment of endotoxemia is covered elsewhere in this text. Administration of plasma from horses **hyperimmunized** with *S. typhimurium* or *E. coli* reduces the severity of clinical signs and shortens the duration of disease in horses with endotoxemia secondary to enterocolitis or colic. **Polymyxin** (5000 IU/kg intravenously every 12 hours) attenuates the effect of endotoxin in experimental disease and is used for the prevention and treatment of endotoxemia in hospitalized horses. Its efficacy in clinical settings has not been determined in appropriate clinical trials. **Aspirin** (10 mg/kg orally every 48 hours) is administered to diminish platelet aggregation around intravenous catheters. **Flunixin meglumine** (1 mg/kg intravenously every 8–12 hours) or **phenylbutazone** (2.2 mg/kg intravenously every 12 hours) is given for analgesia and to prevent endotoxin-induced increases in plasma prostaglandins. **Pentoxifylline** (8 mg/kg orally every 8 hours) is administered for its putative effective in attenuating the effects of endotoxemia. The efficacy of these treatments in a clinical setting and their effect on measures of outcome of disease, such as duration of illness, case–fatality rate, and incidence of complications, has not been determined, with the exception of hyperimmune plasma or serum.

Binding of Toxins

Smectite or activated charcoal is sometimes administered to horses with acute enterocolitis in an attempt to adsorb toxins, such as those produced by *Clostridium* spp., and prevent systemic absorption. There is in vitro evidence that smectite can bind clostridial toxins and endotoxin, but evidence of efficacy in vivo is lacking.

Disseminated Intravascular Coagulation

Prevention and treatment of disseminated intravascular coagulation includes monitoring for changes in variables indicative of coagulation and fibrinolysis including D-dimer concentration; antithrombin III activity; one-stage prothrombin; and activated partial thromboplastin times, platelet count, and fibrinogen concentration. Plasma can be administered to increase blood antithrombin III activity, often in conjunction with heparin or low molecular weight heparin (dalteparin or enoxaparin). Doses of 50 U of dalteparin or 0.5 mg/kg of enoxaparin per kilogram subcutaneously every 24 hours seem to be adequate for prophylactic anticoagulation treatment of

horses. For treatment of coagulation disorders or for ill horses that are considered to be at high risk of developing thrombotic disease, dosages may need to be increased to 100 U of dalteparin or 1 mg/kg of enoxaparin per kilogram subcutaneously every 24 hours.

CONTROL

Specific control measures for *Salmonella* spp. infection, equine neorickettsiasis, and cyathostomiosis (strongylosis) are discussed under their respective headings. The incidence of antibiotic-induced colitis can be reduced by minimizing the frequency with which antibiotics are administered to horses. Administration of smectite to horses undergoing colic surgery reduced the proportion of horses with postoperative diarrhea from 41% to 11%.[20] There is no evidence that probiotics reduce the severity of disease or shorten its duration, although most are regarded as safe and easy to administer.[21]

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CHRONIC UNDIFFERENTIATED DIARRHEA OF HORSES

SYNOPSIS

Etiology Common sign of many enteric and nonenteric diseases

Epidemiology Sporadic disease of adult horses, except for cyathostomiosis and salmonellosis, which are discussed under those headings

Clinical signs Passage of unformed or liquid feces, either in increased or normal quantities. Weight loss, increased appetite. Otherwise normal physical examination. Rectal examination is usually normal.

Lesions Colitis in most cases

Diagnostic confirmation Examination of feces for cyathostome larvae, rectal biopsy demonstrating lymphoma or granulomatous enteritis, and *Salmonella* spp. in rectal mucosal biopsy or feces. Sand in feces or evident on abdominal radiography

Treatment Supportive: anthelmintics, corticosteroids, antidiarrheal preparations

Control As for cyathostomiosis and salmonellosis

ETIOLOGY

Chronic diarrhea is the **final common sign** of a number of causes of colonic dysfunction in horses. Diseases that cause chronic (more than 2 weeks' duration) diarrhea in horses include: cyathostomiosis, chronic idiopathic colitis, salmonellosis, alimentary lymphosarcoma,[1,2] granulomatous colitis, eosinophilic colitis, ingestion of sand, chronic liver disease, peritonitis, lymphangiectasia, and as a sequela to acute diarrhea. Immune deficiency, including variable adult-onset B-cell deficiency, can predispose a horse to the disease. *Brachyspira* sp. have been implicated as a cause of chronic diarrhea in horses.[3,4] *Campylobacter fetus* subsp. *fetus* has been isolated from feces and rectal biopsy of a 2-year-old Quarter Horse with chronic diarrhea and weight loss. Administration of enrofloxacin was temporally associated with passage of formed feces, although this change did not persist.[5]

There are many causes and their relative importance varies between locations. Even with concerted effort, a definitive antemortem diagnosis is achieved in fewer than 30% of cases.

EPIDEMIOLOGY

The occurrence is sporadic, with only single cases occurring in a group. Other horses in contact are not affected. The case–fatality rate is 35% to 65%. There appears to be no age-related, gender-related, or breed-related variation in incidence. Older horses do not appear to be at increased risk of having chronic diarrhea. The epidemiology of cyathostomiosis (strongyloidosis) and salmonellosis are discussed under their respective headings.

PATHOGENESIS

Diarrhea is attributable to colonic dysfunction, which can result in excessive loss of electrolytes in feces and diminished absorption of nutrients from the large colon. Disease of exclusively the small intestine does not cause diarrhea in horses. Protein-losing enteropathy might be present in addition to the diarrhea. Colonic dysfunction

can be associated with inflammatory or infiltrative lesions of the colon but in many cases an anatomic lesion is not detected. However, the colonic contents of affected horses have a greater fermentative capacity than those of normal horses, suggesting that in some horses the disease is essentially one of abnormal colonic digestion and absorption.

CLINICAL FINDINGS

The characteristic finding is chronic diarrhea. The feces vary in consistency from thick porridge (oatmeal), through undigested fibers in liquid, to liquid without fiber. The consistency of the feces in an individual horse can vary widely from one day to the next. The duration of the diarrhea is variable but might be lifelong. Death or euthanasia usually results from progressive weight loss. The onset of diarrhea is usually abrupt and can be associated with signs of toxemia and dehydration, as described earlier. However, often there is no toxemia or other systemic sign apart from weight loss, and affected horses are bright and alert and have a normal or increased appetite.

Rectal examination usually fails to reveal any abnormalities, although horses with granulomatous enteritis or alimentary lymphosarcoma can have enlarged mesenteric lymph nodes.

Abdominal radiography will reveal the presence of excessive amounts of sand in the large colon in horses with that disease.

CLINICAL PATHOLOGY

- Hematological examination can reveal a mild **neutrophilia** and **anemia**, but these changes are of little use in determining the etiology of the diarrhea.
- Serum biochemical examination typically demonstrates a mild **hypoalbuminemia**, **hypoglobulinemia**, **hyponatremia,** and **hypokalemia**, but again these changes are not specific for any particular disease.
- Hypoalbuminemia is consistent with the presence of protein-losing enteropathies such as chronic colitis, alimentary lymphosarcoma, cyathostomiosis, or granulomatous colitis.
- **Hyperbilirubinemia** and elevated serum concentrations of **serum bile acids** are suggestive of liver disease.
- Increases in **serum alkaline phosphatase** activity, while common, are of no diagnostic utility.
- Horses with cyathostomiosis usually have increased concentrations of β-globulins, although the sensitivity of this test is low.

Peritoneal fluid has a neutrophilic leukocytosis and increased (>25 g/L) protein concentration in horses with peritonitis but is normal in most horses with chronic diarrhea, including those with alimentary lymphosarcoma or granulomatous colitis.

Fecal examination of horses with cyathostomiosis can reveal strongyle-type ova or fourth-stage cyathostome larvae. The presence of **sand** in feces, demonstrated by allowing feces to settle in a transparent rectal glove or similar container, suggests sand accumulation in the colon as a cause of the diarrhea. The presence of **protozoa** in feces has no diagnostic significance. *Giardia* **spp.** are commonly found in feces of normal horses of all ages and, despite earlier reports of their presence in feces of horses with diarrhea, they are not associated with disease. **Coccidiosis** is very uncommon in horses, and *Eimeria leuckarti* is probably not pathogenic.

Demonstration of *Salmonella* spp. in feces or rectal mucosal biopsy, either by culture or PCR, is suggestive but not diagnostic of salmonellosis, given the high proportion of normal horses that shed *Salmonella* spp. in feces. Isolation of *R. equi* from feces of young horses with diarrhea is suggestive of enteric disease associated with that organism.

An abnormal **D-xylose**, **glucose,** or **starch absorption test** indicates small-intestinal disease and is suggestive of granulomatous enteritis, although most horses with this disease do not have diarrhea.

Exploratory laparotomy, either ventral midline under general anesthesia or through the left flank under local anesthesia, and **intestinal biopsy** can demonstrate alimentary lymphosarcoma, granulomatous enteritis, eosinophilic enteritis, chronic colitis, and other abdominal disease. **Rectal biopsy** is less expensive and invasive but has a relatively poor sensitivity, although good specificity for granulomatous enteritis, eosinophilic enteritis, and alimentary lymphosarcoma.

NECROPSY FINDINGS

Necropsy findings are consistent with the underlying disease, although in many cases gross lesions are not evident. The histologic changes in some cases are restricted to a mild inflammatory response and can be difficult to correlate with the severity of clinical disease. In some of these cases the diarrhea probably reflects an imbalance in the microflora of the large bowel, and demonstration of a specific etiologic agent is an unrealistic goal. Conversely, isolation of *Salmonella* spp. from the gastrointestinal tract or mesenteric lymph nodes should be interpreted with caution in the absence of histologic evidence of salmonellosis.

Because of the wide variety of potential causes of chronic diarrhea of horses it is not possible to list all the samples required to a "confirm" a diagnosis. In most instances, formalin-fixed samples from the liver, mesenteric lymph nodes, and numerous levels of the gastrointestinal tract comprise the minimum diagnostic material required. Regardless of what other testing is performed, it is prudent to hold back frozen segments of both large and small bowel (with content) in case other tests are deemed necessary.

TREATMENT

The **principles of treatment** are to deal with the underlying disease, correct fluid and electrolyte disturbances, give symptomatic treatment of diarrhea, and provide supportive care. Except in cases of cyathostomiosis or sand accumulation, treatment of horses with chronic diarrhea is frequently unrewarding.

Specific Treatments

Cyathostomiosis should be treated with larvicidal doses of anthelmintics such as fenbendazole (50 mg/kg once, or 7.5 mg/kg daily for 3 days), moxidectin (400 µg/kg), or ivermectin (200 µg/kg). Treatment can be unrewarding if there is severe damage to the large colon.

Diarrhea secondary to **sand accumulation** in the gastrointestinal tract should be treated by preventing the horse from ingesting sand and, although the efficacy is debatable, with psyllium mucilloid (1–2 g/kg orally once daily for 4–5 weeks; see section Sand Colic).

Chronic idiopathic colitis can be treated with corticosteroids (dexamethasone 0.2–0.4 mg/kg once daily) or prednisolone (0.5–1.0 mg/kg once daily) for 3 to 4 weeks and the dose reduced as clinical signs permit.

Chronic salmonellosis has been treated with enrofloxacin (2.5–5 mg/kg orally every 12 hours for 3–4 weeks), sometimes in combination with metronidazole (15–20 mg/kg orally every 6–12 hours), but one should be aware of the risk of articular cartilage damage in horses treated with enrofloxacin.

Many diseases commonly associated with chronic diarrhea are not treatable.

Symptomatic and Supportive Treatments

Symptomatic treatments include **metronidazole** (7.5–20 mg/kg orally every 6–12 hours) or **iodochlorhydroxyquin** (10–20 mg/kg orally once daily). Although some horses have resolution of diarrhea while being treated with these compounds, there is no clear demonstration of their efficacy. **Antibiotic** administration, other than as described previously, does not usually alter the course of the disease. **Antidiarrheal** preparations

such as codeine phosphate, **loperamide,** and **bismuth subsalicylate** often provide temporary improvement in fecal consistency. Some horses with chronic diarrhea respond to **transfaunation**, in which 5 to 10 L of colonic fluid collected immediately after death from a horse without enteric disease is administered via nasogastric intubation.

Supportive treatment includes provision of supplemental electrolytes, principally sodium, potassium, and bicarbonate, as a feed additive. Suitable supplements include some commercial products designed for fluid replacement in diarrhetic calves, or a mixture of potassium chloride (300 g), sodium chloride (400 g), and sodium bicarbonate (300 g). This mixture is isotonic when dissolved at the rate of 90 g/12 L, or can be given orally at the rate of 30 to 90 g per 400-kg horse every 24 hours. Unsupplemented water should be supplied without restriction and serum electrolyte concentrations should be monitored. **Severely affected** horses can require intravenous administration of polyionic isotonic electrolyte solutions or plasma.

Nutritional support should include provision of a diet of high-quality roughage and grain. Some trials can be needed to determine the diet that is best for individual horses, but care should be taken that the diet contains adequate energy and is nutritionally balanced. Horses should be fed to attain, and then maintain, an ideal BW.

Spontaneous recovery does occur, particularly in young horses, and this, and the often lengthy duration (6–12 months) of the illness, make it difficult to decide accurately the value of the treatment.

CONTROL

Control of cyathostomiosis and salmonellosis is discussed under their respective headings. Diarrhea caused by sand accumulation in the colon should be prevented by not feeding horses on the ground and by avoiding grazing of short pastures on sandy soil.

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IDIOPATHIC CHRONIC INFLAMMATORY BOWEL DISEASES OF HORSES

A syndrome of combinations of weight loss, ill-thrift, diarrhea, recurrent low-grade colic, intestinal malabsorption, and hypoproteinemia attributable to chronic inflammatory disease of the small and/or large intestine of horses is described.

The causes of idiopathic inflammatory bowel disease in horses are not well described, and the syndrome has been subdivided into granulomatous enteritis, eosinophilic enteritis, lymphocytic-plasmacytic enterocolitis, basophilic enterocolitis, and multisystemic eosinophilic epitheliotropic disease. Other causes of chronic inflammatory bowel disease in horses include parasitism, alimentary lymphosarcoma and other gastrointestinal neoplasms,[1] tuberculosis, pythiosis, and histoplasmosis.[2] Intolerance to gluten, a protein found in wheat and similar grains, is a well-recognized cause of inflammatory bowel disease in humans. Although most horses with inflammatory bowel disease do not have evidence of gluten hypersensitivity, a horse with high concentrations of antibodies to gluten and which responded to a gluten-free diet is reported.[3]

Empirical treatment of 20 horses with a presumptive diagnosis of inflammatory bowel disease, based on a combination of hypoproteinemia, hypoalbuminemia, malabsorption, increased intestinal wall thickness on ultrasonographic examination or characteristic changes in rectal mucosal biopsy with a larvicidal anthelmintic, and >3 weeks' administration of corticosteroids resulted in a good response to treatment in 15 of the horses with 13 surviving for at least 3 years.[4] Peak xylose absorption was higher (1.36 ± 0.44 mmol/L) in survivors than in nonsurvivors (0.94 ± 0.36).[4]

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GRANULOMATOUS ENTERITIS OF HORSES

Granulomatous enteritis is one of several inflammatory bowel diseases of horses. It is characterized by gradual onset of weight loss and ill-thrift.

The etiology of granulomatous enteritis is unknown. Infection with *Mycobacterium* spp. is suggested as a cause but demonstration of acid-fast bacteria in tissue sections or by culture of gut or mesenteric lymph nodes of affected horses is rare and inconsistent.

The disease occurs with greatest incidence in **Standardbred horses** between 1 and 6 years of age, although it does affect other breeds of horses. The disease is usually sporadic, although it has been recorded in siblings raised on the same farm. Estimates of incidence are not available. The disease has a case–fatality rate of almost 100%, although recovery is documented for a small number of horses.

Accumulation of lymphocytes and multinucleated giant cells in the lamina propria is associated with villous blunting in the small intestine. There is malabsorption of carbohydrates and fats and excessive loss of protein in feces with subsequent hypoalbuminemia, edema, and weight loss.

Weight loss and anorexia are the most common presenting signs. Fever is uncommon. Approximately one-third of horses have diarrhea or a history of abdominal pain. Affected horses can have a diffuse, scaling alopecia and excoriations, especially of the coronary band. Rectal examination can reveal enlarged, soft mesenteric lymph nodes. Colic is an unusual manifestation.

Hematological and serum biochemical examination reveals a mild, macrocytic **anemia** (hemoglobin < 100 g/L, hematocrit < 30%) with a normal leukogram. Hypoalbuminemia is a consistent finding (<25 g/L, <2.5 g/dL) whereas the globulin concentration can be normal, low or, more commonly, high (>50 g/L, >5.0 g/dL). Plasma fibrinogen concentration is usually increased (>4 g/L, 400 mg/dL), and there are no characteristic changes on serum biochemical analysis. Peritoneal fluid is normal.

Absorption tests using D(+)-xylose, glucose, or starch indicate diminished absorption of carbohydrate by the small intestine in many affected horses. The D(+)-xylose absorption test is performed by administering D(+)-xylose at a dose of 0.5 or 1 g/kg as a 10% solution by nasogastric intubation after an overnight fast. The concentration of D(+)-xylose in blood samples collected at 0, 1, 2, 3, 4, and 5 hours after dosing is determined. An abnormal test is one in which there is not an obvious peak in the D(+)-xylose curve and in which the peak concentration is lower than expected for a normal horse on a similar diet. In horses with a normal small intestine, administration of a 10% glucose solution orally at a dose of 1 g/kg BW results in an increase in the plasma glucose concentration of >85% of the baseline values. An increase of <15% over baseline is found in horses with small-intestinal disease that impairs glucose absorption. Intermediate values are found in both normal and diseased horses.

Differential diagnoses include other causes of malabsorption syndrome in horses such as parasitism, chronic inflammatory disease (abdominal abscess), neoplasia,[1] multisystem eosinophilic epitheliotropic disease, and malnutrition.[2] **Diagnostic confirmation** is achieved by histologic examination of a biopsy of the rectum or small intestine. Rectal biopsy has a low sensitivity (less than 50%) but high specificity for diagnosis of granulomatous enteritis. Biopsy of small intestine and mesenteric lymph nodes has a much higher sensitivity than rectal biopsy and is the recommended test. Endoscopic duodenal biopsy might be useful in providing a diagnosis.[3]

Necropsy examination reveals that the intestinal wall is thickened uniformly, especially in the jejunum and ileum. Mesenteric lymph nodes may be enlarged. There is villous atrophy with a diffuse and patchy granulomatous infiltration of the lamina propria of the small intestine. Crypt abscesses are common. Granulomas are also present

in the liver, spleen, kidney, and bone marrow of many cases. The predominant cell types are macrophages and epithelioid cells with occasional giant cells. The disease may be difficult to distinguish from alimentary lymphosarcoma.

Attempts at **treatment** with a variety of antiinflammatory and antimicrobial drugs, including prednisone and sulfasalazine, have been almost university unsuccessful. Resolution of the disease occurred for up to 7 months, whereas a horse was treated with a decreasing dose of dexamethasone, beginning at 40 mg (0.1 mg/kg) intramuscularly every 4 days for 4 weeks, and then slowly decreasing. Surgical resection of defined, solitary lesions is reported, but this is an unusual manifestation of the disease.

There are no effective control measures.

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LYMPHOCYTIC-PLASMACYTIC ENTEROCOLITIS

This is an uncommon disease of horses, in contrast to dogs, which affects horses of any age and without discernible breed or gender predilection. The etiology is unknown. Presenting signs include weight loss, diarrhea, and lethargy. Clinicopathologic abnormalities include hypoproteinemia and hypoalbuminemia in approximately one-half and three-quarters of cases, respectively. Results of an oral glucose tolerance test are abnormal in approximately 75% of cases. Histologic examination of a rectal mucosal biopsy reveals abnormal tissue suggestive of the disease in about one-half of cases. The diagnosis is confirmed by biopsy of ileum or necropsy examination. Differential diagnoses are similar to those for granulomatous enteritis. There is marked infiltration of the lamina propria with lymphocytes and plasma cells in the absence of granulomatous changes. Administration of dexamethasone improves clinical signs of disease in a small proportion of horses. Control measures are not available.

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IDIOPATHIC FOCAL EOSINOPHILIC ENTERITIS

Focal, idiopathic eosinophilic enteritis is an uncommon disease of horses characterized by intestinal obstruction secondary to constrictions of primarily the small intestine caused by an eosinophil-dominated chronic inflammatory reaction.[1,2] The cause of the disease is unknown, although hypersensitivity or immune-mediated mechanisms are likely important in the pathogenesis of the disease. The disease is recognized with increasing frequency in the UK.[3]

Idiopathic focal eosinophilic enteritis occurs without any apparent gender or breed predisposition. Younger horses (<5 years) are at increased risk.[3] The disease is more common during the July to November period in the Northern Hemisphere.[3] The disease is reported in the northern United States, UK, Ireland, and the Netherlands.[4-6]

Clinical signs are usually caused by an acute intestinal obstruction and manifest as colic.[4,5] Affected horses rarely have weight loss or diarrhea. The common form of the disease is one in which the infiltration is segmental and associated with acute colic caused by obstruction of the small intestine or large colon by mural lesions.[4,5] The disease must be differentiated from other causes of colic.

Histologically, the disease is characterized by the presence of eosinophilic infiltrates in a chronic active inflammatory reaction affecting the small or large intestines. The infiltrates are restricted to the intestinal tract. There are activated endothelial cells, eosinophils and neutrophils, and components indicating a duration of inflammation of greater than 3 days.[2] Macrophages and eosinophils are the predominant cell type in the lesions.[2]

Antemortem diagnostic confirmation is achieved by small-intestinal biopsy. *Pythium insidiosum* infection can induce a similar focal enteritis.

The **prognosis** for affected horses is good. The lesion is usually amenable to surgical resection, but this does not appear to be necessary for recovery unless there is acute luminal obstruction of the intestine.[1,4,5] Control measures are not reported.

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EQUINE GRASS SICKNESS (EQUINE DYSAUTONOMIA, GRASS DISEASE, AND MAL SECCO)

SYNOPSIS

Etiology Unknown

Epidemiology Horses of all breeds and both sexes in the UK, Europe, and southern South America. Greatest incidence in spring/ early summer

Clinical signs
  Acute grass sickness Colic, nasogastric reflux, absent gut sounds, depression, dysphagia, and small intestinal distension of <2 days' duration at time of death
  Subacute grass sickness Tachycardia with or without signs of colic, reduced intestinal sounds, impaction of the colon, and clinical course of 2–7 days
  Chronic grass sickness Insidious onset weight loss, intermittent colic, decreased appetite, rhinitis sicca, patchy sweating, and mild dysphagia

Clinical pathology None is specific or diagnostic.

Lesions Both forms of the disease have degeneration of neurons of the autonomic nervous system, especially of the myenteric and submucosal plexuses.

Diagnostic confirmation Examination of ileal biopsy. Rectal biopsy is not reliable.

Treatment
  Acute grass sickness/subacute grass sickness Supportive. None effective
  Chronic grass sickness Nursing care

Control Nonspecific. Vaccination is not currently available.

Equine grass sickness is a noncontagious acute, subacute, or chronic disease with a high case–fatality rate affecting equids in predominantly the UK and northwestern Europe.

ETIOLOGY

There is increasing confidence that equine grass sickness is a toxicoinfectious form of botulism caused by exposure of susceptible equids to *C. botulinum* type C toxin (BoNT/C and/or C2 binary toxin).[1,2] However, the hypothesis of a role for toxicoinfectious botulism in grass sickness of horses does not completely explain the geographic distribution of the disease. The presence of IgG antibodies to BoNT/C in serum of 30.8% (61 of 198) of horses in Israel, where the disease is not recognized, suggests that factors other than simply exposure to BoNT/C are required for induction of the disease.[3] It is speculated that dietary factors (hence "grass sickness") alter gastrointestinal biota of horses and allow proliferation of *C. botulinum* type C or D, or promote increased production or absorption of neurotoxin, and initiate development of the disease.[4] Interestingly, horses with grass sickness have a higher prevalence of *C. perfringens* in feces (7/9 detected by culture and 15/37 by ELISA) and ileal contents than do horses with colic (1/16) of other cause or grazing healthy horses (0/60 by culture and 1/74 by ELISA).[5] This is interpreted as indicative of altered gastrointestinal biota rather than as

indicating a causative role for *C. perfringens* in equine grass sickness.[5]

Evidence supporting a role for *C. botulinum toxins* in the etiology of the disease included the isolation of toxin (BoNT/c) producing strains of *C. botulinum* type C from the ileum of 45% of horses with grass sickness and 4% of clinically normal control horses, the presence of higher concentrations of IgA antibodies to BoNT/C and BoNT/D in the ileum of horses with acute grass sickness than of unaffected controls,[6] and higher risk of the disease in horses with low serum concentrations of anti-BoNT/C IgG antibodies. Vaccination of horses with a botulinum toxoid markedly reduced the mortality rate among vaccinated, compared with unvaccinated, horses providing evidence of a role for immunity to *C. botulinum* toxins in resistance to the disease.[1] Remarkably, this study was conducted in 1922 and 1923. There are plans to conduct further vaccine trials.[7]

EPIDEMIOLOGY
Occurrence
Grass sickness is locally common in its restricted distribution to all parts of Great Britain (including possibly Ireland), the Czech Republic, Sweden, Switzerland, Hungary, Cyprus, and the northern and western coasts of Europe.[2,8-10] A clinically and histologically indistinguishable disease, *mal secco*, occurs in the Patagonia region of Argentina, southern Chile, and in the Falkland (Malvinas) Islands. Dysautonomia, with clinical signs and histologic changes consistent with equine grass sickness, is reported in a mule from Kansas in the United States.[11]

Horses, ponies, donkeys, zebras, Przewalski's horses, rabbits, and hares are affected. The **incidence** on farms with a history of the disease ranges between 0.4% and 16% per year or 2.1 grass sickness cases per 100 horses per year. Approximately 47% of cases are acute, 20% subacute, and 33% have the chronic form of the disease.[12]

The **case–fatality rate** for acute grass sickness is 100%, whereas that for the chronic form of the disease in horses overall is 49%,[12] and 60% to 70% for those treated at a referral hospital. Horses diagnosed in June are 2.7 times (95% CI 1.4–5.4) more likely to survive than those diagnosed in May.[12]

Horses that survive the initial phases of the chronic form of the disease are often destroyed because of weakness and emaciation, although they can make complete recoveries.

Risk Factors
Animal Risk Factors
The risk and prevalence of disease is greatest in 4- to 5-year-old horses (adjusted OR of 1.9 compared with 0–3 year olds) and then declines such that the risk of disease is lowest in horses >12 years old (OR 0.02 compared with that of 0–3 year olds).[12] Similarly, horses 11 to 20 years of age are at

reduced risk compared with horses 2 to 10 years of age (OR 0.32) when only horses in Scotland are considered.[13] The median age at diagnosis is 6 years (mode 5 years) and cases are recorded in horses 2 months to >30 years of age.[12] Foals born of affected mares are clinically normal. There is no apparent breed predilection beyond that attributable to higher numbers of particular breeds of horses in at risk areas,[12] although native Scottish breeds are at increased risk compared with other breeds (OR 3.56) when only horses in Scotland are considered.[13] There is no clear association with gender of the horse when age distribution of genders is considered.[13]

Horses on pasture are at increased risk (hence the colloquial name of the disease), and the disease rarely, if ever, occurs in horses that are denied access to pasture and grazing. A recent (<14 day) change of pasture carries an increased risk (OR 24) of development of the disease. Horses that have been on the farm for less than 2 months are at increased risk of developing the disease. Horses on farms with previous cases of the disease are at increased risk (OR 2.2–45) of the disease, although horses that have been in contact with animals with the disease are at reduced risk (OR 0.1). Horses with lower serum concentrations of antibodies to BoNT/C are at increased risk for the disease.

Environmental Risk Factors
The risk of disease in horses in Scotland increases with increasing latitude (northing) at a rate of OR 1.08 per 10 km.[13] The disease occurs year round with a marked seasonal distribution peaking with 61% of cases occurring in April, May, and June in the UK.[12] Outbreaks of the disease are associated with the occurrence of cooler and drier weather than normal during the 2 weeks preceding the outbreak. There is increased risk associated with more sun hours (OR 1.44–2.48 per additional hour per month, after correction for latitude, as previously mentioned) and more frost days (OR 1.13–1.18 per day per month) and decreased risk with higher average temperature (0.82–0.76/°C).[13]

Pasture and Soil Risk Factors
Access to grazing is an acknowledged risk factor. Examination of pasture and soil reveals that sites that have had horses with grass sickness have significantly higher concentrations of soil nitrogen and herbage iron, lead arsenic, and chromium.[14] *Ranunculus* sp. (buttercup) was common at sites with affected horses.[14] The role, if any, for *Ranunculus* sp. or the heavy metals in pathogenesis of the disease is unclear.

Horses with grass sickness have plasma amino acid profiles expected of those with subacute or chronic cyanide intoxication. This has led to investigation of the cyanide concentration of common pasture plants

in areas with affected horses. The concentration of cyanogenic glycosides in white clover (*Trifolium repens*) is higher in pasture associated with cases of equine grass sickness (497 mg cyanide/kg dry matter) than in white clover from control pasture (<300 mg/kg).[4] Although white clover is a common pasture plant in many parts of the world, including areas with cases of equine grass sickness, a role for it in the pathogenesis of grass sickness is speculative. The amount of cyanide ingested by horses on pasture with a high cyanide concentration is predicted to be insufficient to induce toxicosis, but there might be other roles for the plant in predisposing the development of the disease.[4] Alternatively, the changes in pasture cyanogen content could be simply coincidental.

Farm or Premise Risk Factors
Farms with a history of horses with the disease are at increased risk of having further cases.[12] For premises with previous cases of grass sickness there is an increased risk of the disease developing as the number of horses on the farm increases, with the presence of young horses, on stud farms and livery/riding schools, on farms having sandy or loamy soil, and those rearing domestic birds and using mechanical fecal removal. The risk of recurrence of disease on a farm decreased with the presence of chalk soil, cograzing ruminants, grass cutting of pastures, and manual removal of feces. There is no association between the disease and the type of pasture or with provision of supplementary feeds. Feeding hay or haylage is associated with a decreased risk of the disease. Any disturbance of the soil, such as when plowing, increases the risk of disease.

Transmission
The disease is not contagious. Injection of normal horses with serum of affected horses causes lesions, but not clinical signs, consistent with the disease.

PATHOGENESIS
The clinical signs are attributable to widespread damage to the autonomic nervous system, including the sympathetic neurons in prevertebral and paravertebral ganglia,[15] resulting in sympathetic and parasympathetic dysautonomia that is most clinically evident in the gastrointestinal tract. Coincident with damage to the autonomic nervous system are increases in plasma concentrations of dihydroxyphenylalanine, epinephrine, norepinephrine, and dopamine, possibly because of increased secretion of these compounds from affected sympathetic ganglia and neurons. Lesions in the cranial nerves and brainstem are probably responsible for dysphagia and drooling evident in most cases. Rhinitis is associated with diminished noradrenergic, noncholinergic innervation, greatest in neurons positive for substance P

or calcitonin gene-related peptide, of the nasal mucosa in subacute and chronic cases.

Electrocardiographic examination of affected horses reveals evidence of loss of parasympathetic innervation of the heart, which is consistent with lesions in the terminal cardiac ganglia. Splanchnic lesions are most severe in the myenteric and submucosal plexuses of the ileum, with less severe changes in the large colon and celiacomesenteric ganglion. There is also a reduction in interstitial cells of Cajal (cells involved in pacemaker activity and autonomic transmission within the gut). These neuronal changes are associated with a marked impairment of cholinergic activity in ileal tissue of affected horses. Because of the altered autonomic activity, peristalsis decreases (in chronic cases) or ceases (in acute cases) with subsequent accumulation of ingesta in the small intestine, stomach, and large colon. Death is caused by emaciation in chronic cases or rupture of the stomach or intestine in acute cases.

CLINICAL FINDINGS

The clinical signs of grass sickness are varied, and accurate antemortem diagnosis on clinical signs alone is difficult. The diagnosis is usually made based on clinical signs, elimination of disease with similar presentation, and consideration of the horse's provenance.[16] The incubation period of the disease is approximately 10 to 14 days.

Acute, subacute, and chronic forms of the disease are recognized, although some authorities use a designation of acute and chronic. In all cases, there is some dysphagia, resulting in drooling of saliva and trickling of ingesta from the nose. Dried food is impacted between the cheeks and the teeth and the animal plays at drinking. These signs are attributable to lesions in the cranial nerves. Most animals are depressed.

Acute Cases

The onset is sudden and the course of the disease is 1 to 4 days. Abdominal pain may be severe but also may be absent even in the presence of severe tachycardia. There is tachycardia (80–90 beats/min may be >100), decreased to absent gut sounds, lack of defecation, and abdominal distension. On rectal examination, the small intestine is distended with fluid and readily palpable in the caudal abdomen. Nasogastric intubation yields a large (20 L) quantity of fluid. Urination is frequent and may be accompanied by tenesmus. Affected horses may wander about in a restless manner and a fine muscle tremor occurs constantly, especially in the upper forelimb. Periodic attacks of patchy sweating are common. There is noticeable salivation. Esophageal endoscopy reveals linear ulcerations resulting from reflux esophagitis.

Subacute Cases

These cases have signs of mild colic, or may not have any signs of colic, in the presence of tachycardia, depression, reduced gastrointestinal sounds, and impaction of the large colon with characteristic corrugated appearance. The clinical course is 2 to 7 days and death is inevitable. Esophageal endoscopy reveals the presence of linear erosions in many affected horses.

Chronic Cases

The course is usually >7 days and is characterized by weight loss, patchy sweating, and intermittent colic. Horses stand with all four feet close together under them ("elephant on a tub stance") and have a tucked up abdomen. Dysphagia is evident and the gut is empty except for the colon and rectum, which contain dry, hard feces. In the late stages the horse snores, the penis droops, and attempts are made to eat abnormal materials. Most cases of the chronic form have rhinitis, characterized by crusting of mucopurulent material on the turbinates and this is considered, in the presence of appropriate history and other clinical signs, almost pathognomonic for grass sickness. There can be esophageal obstruction with secondary inhalation pneumonia.

Application of phenylephrine (0.5 mL of a 0.5% solution) into one eye causes a dorsal deviation of the eyelashes of the upper eyelid in horses with grass sickness, but not in normal horses.

There is a radiologic discernible defect in esophageal motility in horses with grass sickness.

Horses with acute, subacute, or chronic grass sickness usually (12 of 14 examined) have abnormalities on electromyography including excessive spontaneous activity; fibrillation potentials; doublets, triplets, or quadruplets; neuromyotonic discharges; and complex repetitive discharges.[17]

Recurrence of the disease in a horse is exceedingly rare.

Antemortem diagnostic confirmation can only be achieved by examination of biopsy specimens of the ileum, although biopsy of nasal mucosa has been suggested as an alternative. Examination of rectal biopsy is specific (estimated 100% based on detection of at least three chromatolytic neurons), but not sufficiently sensitive (70%), for diagnosis of the disease based on a study of 14 cases and 10 controls.[18] Antemortem rectal biopsy is not reliable for diagnosis of the disease compared with ileal biopsy, which has a high sensitivity.[19,20] Ileal biopsies can be collected via conventional laparotomy or by laparoscopy.[20] The use of formalin-fixed ileum has both sensitivity and specificity of 100%.[21] Immunohistochemical staining for synaptophysin does not aid in the differentiation between autolytic tissue and tissue from horses with grass sickness.[22]

CLINICAL PATHOLOGY

Serum biochemical profiles and hematological examinations do not demonstrate pathognomonic changes. Serum amyloid A and plasma fibrinogen concentrations are significantly higher in horses with grass sickness than in healthy horses or horses with colic not caused by inflammatory disease, but similar to those in horses with enteritis, colitis. or peritonitis.[23] Signs of dehydration, electrolyte imbalances, hyperbilirubinemia, and elevations of serum activity of liver-derived enzymes are all secondary to the disease. Urine from horses with grass sickness has higher specific gravity, protein and creatinine concentrations, and lower pH than that from unaffected horses, consistent with dehydration and electrolyte imbalances that occur with the disease. Peritoneal fluid is often abnormal, with an increased protein concentration and leukocyte count but, because of the considerable overlap with values in horses with lesions of the gastrointestinal tract requiring surgery, is of limited diagnostic value.

NECROPSY FINDINGS

In cases of short duration, the stomach and small intestines are distended with an excess of fluid and gas, and the colon is often impacted with corrugated ingesta coated with black material. In chronic cases, the alimentary tract is empty.

Histologically there is extensive degeneration of neurons of the autonomic nervous system without evidence of inflammation. These neurons include those of the ganglia (cranial cervical, stellate, celiacomesenteric, etc.) and those of the myenteric and submucosal plexuses of the intestines. Degenerative neuronal changes may also be observed in the CNS, including the oculomotor, facial, lateral vestibular, hypoglossal, and vagal nuclei; the ventral horns of the spinal cord; and the dorsal root ganglia. This neuropathy is difficult to confirm unless fresh, well-fixed samples are submitted for histologic examination. Immunohistochemical staining for synaptophysin does not aid in the differentiation between autolytic tissue and tissue from horses with grass sickness.[22]

Samples for Postmortem Confirmation of Diagnosis

Samples for light microscopic examination include formalin-fixed sympathetic ganglia, brainstem, spinal cord with dorsal root ganglia, gastric fundus, duodenum, jejunum, distal ileum, ventral colon, and dorsal colon.

DIFFERENTIAL DIAGNOSIS

Differential diagnosis list:

Acute grass sickness
- Small intestinal strangulation or volvulus
  - Esophageal obstruction
- Large colon displacement or torsion
- Anterior enteritis
- Peritonitis

Continued

- Terminal ileal impaction
- Ileocecal intussusception
  - Hemoperitoneum
  - Hypocalcemia (lactation tetany and exhaustion)

Subacute or chronic grass sickness
- Impaction of the large or small colon
- Helminthiasis
- Mesenteric abscessation or other chronic inflammatory disease
- Gastric squamous cell carcinoma
- Botulism
- Equine motor neuron disease
- Alimentary lymphosarcoma or other neoplasia
- Inadequate diet
- Poor dentition
- Equine motor neuron disease

TREATMENT

Acute cases respond transiently to gastric decompression and intravenous fluid administration, but death is inevitable. Selected chronic cases benefit from careful nursing care with provision of high energy, high-protein diet, and access to grazing. Administration of the promotility, indirect acting cholinergic agent, cisapride (0.5–0.8 mg/kg orally every 8 hours for 7 days) has been recommended but is not rewarding.[16] Administration of brotizolam (a putative appetite stimulant), acetylcysteine (antioxidant and neuroprotectant), and aloe vera gel (antioxidant, antiinflammatory, and laxative) was without beneficial effect in 29 cases.

CONTROL

Successful measures have not been satisfactorily established and no definitive recommendation can be made. However, consideration should be given to the factors identified as increasing the risk of disease, such as pasturing and movement to new properties, especially those on which previous cases of this disease have occurred, and the disturbance of soil. Feeding of hay and haylage is associated with a reduced risk of developing the disease. Although administration of ivermectin is associated with an increased risk of the disease, appropriate parasite control should not be ignored in horses in areas in which grass sickness is endemic.

There is no commercially available vaccine, although trials are planned.[7]

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INTESTINAL HYPERAMMONEMIA

Intestinal hyperammonemia is a syndrome recently recognized in horses and characterized by abnormally high concentrations of ammonium ion (NH_4^+) in blood combined with signs of neurologic and gastrointestinal disease but in the absence of clinical or clinicopathologic evidence of liver disease.[1-6] The syndrome is associated with gastrointestinal dysfunction that results in increased production of ammonium (NH_4^+), possibly as a result of altered gut microbiota, or increased absorption of ammonia (NH_3) caused by altered mucosal permeability. The disease is not a hepatic encephalopathy in which increased blood ammonium concentrations are secondary to liver disease and reduced clearance of ammonium.

Ammonium is produced in the hind gut by urease-positive bacteria and in the small intestine by a glutaminase located in the enterocytes. Under normal circumstances ammonia is absorbed and transported as ammonium in the blood to the liver, where it is converted to urea or incorporated into amino acids. A decrease in liver function or absorption from the gut of excessive amounts of ammonium can result in hyperammonemia. Increases in blood ammonium concentration adversely affect neuron and astrocyte function leading to depolarization, activation of N-methyl-D-aspartate receptors and cell swelling. There is only a poor correlation between blood ammonium concentrations and signs of neurologic disease, although systemic inflammation combined with hyperammonemia results in more severe signs than hyperammonemia alone.[1]

The epidemiology of the syndrome is not well described. The disease is reported in the UK and the eastern and southeastern United States. Equids of any age can be affected including foals less than 1 day of age.[4] Risk factors include gastrointestinal disease (colitis, enterocolitis, colic, and meconium impaction).[4] Case–fatality rate in equids treated at a referral hospital was 60% (22 of 36 cases). Ingestion of black locust roots (*Robinia pseudoacacia*) caused the disease in two ponies.[7] Infection with *C. sordellii* is a suspected cause in adult horses.[8]

The clinical signs include those of colitis, enterocolitis, or colic and can include diarrhea and depressed mentation. Horses are usually tachycardic and tachypneic but not usually pyrexic. Signs of neurologic dysfunction can be present at the initial examination, with signs of gastrointestinal disease, or can develop over the next 24 to 72 hours. Signs of neurologic disease include profound depression, head pressing, ataxia, central blindness, recumbency, personality changes, aggression, abnormal mentation, compulsive walking, circling, lip smacking, and seizures (petite mal or grand mal).[4]

Hyperammonemia (normal is less than ~55 µmol/L) is present and an essential component of the diagnosis. Blood ammonium concentrations are usually over 100 µmol/L and can exceed 1000 µmol/L, although horses with severe systemic inflammation can have signs of neurologic disease with blood ammonium concentrations as low as 60 µmol/L.[4] Affected horses have hematological signs consistent with inflammation (leukocytosis), hypovolemia (increased hematocrit, and serum total protein concentration), and some have mild increases in serum activity of liver-derived enzymes (GGT).[4]

Treatment is largely supportive, including correction of hypovolemia, protection from self-harm, control of seizures, efforts to reduce blood ammonium concentration, and reduction of systemic inflammation. The underlying disease should be treated as appropriate. Reduction of blood ammonium concentration can involve the administration of oral neomycin, lactulose, or both. The efficacy of these treatments has not been determined. Lactulose (~300 mg/kg orally every 8 hours) is used, but the decrement in blood ammonium concentration in affected horses is undetermined and in healthy horses is modest (3 µmol/L).[4] Lactulose is proposed to act by acidifying the colon contents, favoring conversion of the freely absorbable ammonia (NH_3) to ammonium. Activated charcoal or mineral oil can be given to reduce absorption and increase excretion of ingested toxic materials.[7] Sedatives might need to be administered to control abnormal ambulation or behavior.

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Abdominal Diseases of the Pig Including Diarrhea

ACUTE GASTRIC DILATATION IN PIGS

This occurs in pigs as a result of excessive intake of finely ground meal (grain) and water resulting in excessive fermentation and gaseous distension. In the pig, simple gastric distension is usually readily relieved by vomiting.

ACUTE GASTRIC VOLVULUS IN SOWS

This is a much more serious problem. It is most common with once-a-day feeding and is caused by the rapid intake of a large quantity of food followed by physical activity. Volvulus is thought to occur because the sow eats a large, sloppy meal very quickly. The occurrence is specifically related to intense excitement and activity at feeding time. Death occurs 6 to 24 hours after the pig's last meal. At necropsy the stomach is enormous (50–60-cm diameter), with engorgement of vessels and hemorrhagic effusion into the stomach, which contains a large amount of gas, fluid, and usually a great deal of food. Rotation varies in degree from 90° to 360° around the mesenteric axis and can occur in both directions but is usually clockwise. The spleen is markedly displaced, the liver is bloodless, and the diaphragm encroaches deeply into the chest. It is easily prevented by twice daily feeding, especially if automatic feeding is implemented.

GASTRIC ULCERS AND HYPERKERATOSIS OF SWINE

Ulcers can occur in the fundic part of the stomach or in the PE (nonglandular part) of the stomach. The former are uncommon and occur usually as part of other diseases such as salmonellosis, *H. rubidus* infestation in sows, or transmissable gastroenteritis, and their significance in pig medicine is as yet not completely understood. The latter are far more important as a cause of economic loss and clinical importance. They are single or multiple bleeding ulcers often associated with varying degrees of hyperkeratosis. Experimental lesions in the stomach are usually produced in the glandular part of the stomach as a model for the condition in humans.

SYNOPSIS

Etiology Fine particles and pelleted feed. Certain bacterial species and other factors contribute.

Epidemiology Highly variable incidence but is increased with greater intensification of swine industry, emphasis on improving digestibility and feed efficiency and use of fine particle and pelleted feed. Growing and finishing pigs, adult sows, and boars

Signs Sudden death from peracute gastric hemorrhage. Subacute form causes anemia, pallor, unthriftiness, and black tarry feces.

Clinical pathology Hemorrhagic anemia

Lesions Hyperkeratosis, erosions, ulcers of pars esophagea, gastric hemorrhage, and anemia

Diagnostic confirmation Lesions at necropsy

Differential diagnosis list
- Proliferative enteritis of swine
- Enteric salmonellosis
- Swine dysentery

Treatment None that is effective

Control Use of diets prepared through hammer mill screen of at least 6 mm. Incorporate S-methylmethionine-sulfonium chloride in diet and reduce stress.

ETIOLOGY

The etiology of ulceration of the PE is multifactorial. Finely ground and pelleted feed are the important causes of ulceration of the PE. Certain environmental stressors may also be contributing factors.

EPIDEMIOLOGY
Occurrence

There may be a genetic susceptibility which may be related to fastness of growth. Ulceration is not mediated by glucocorticoids.

The disease can occur in all ages but it is most common in pigs of 45 to 90 kg BW but may occur in pigs after weaning and in adults. All breeds are susceptible. Prevalence in groups of pigs may vary anywhere in the world from 1% to 90% depending on husbandry practices and feeding regimes.

Examination of the stomachs of pigs at abattoirs in various countries has revealed a high proportion of pigs with varying degrees of hyperkeratosis, erosions, and ulcers of the PE. Extensive erosions of the PE may be present in up to 63% of sows and 36% of finishing pigs. In pigs at slaughter, a range from 4% to 57% has been seen. The ulcers were mild in 9.5% and severe in 13.4% of cases. The incidence is variable between countries, which may reflect differences in feeding or husbandry methods. The disease has assumed increased economic importance with increased intensification of the swine industry.

The feed manufacturing industry is faced with the dilemma of finely ground pelleted feed providing high digestibility and feed efficiency in growing and finishing pigs but with a high incidence of lesions of the PE, which may affect performance. Pelleting swine feed is also advantageous because it flows more easily and effectively in automated distribution systems in swine farms compared with finely ground meal, which may bridge and clog in distribution systems, decrease dustiness and segregation of ingredients, and increase bulk density. Meal is less damaging than pellets.

The incidence of clinical disease is low, but the case–fatality rate is high when severe hemorrhage occurs. The effects of the lesions on performance may vary considerably. In one study, pigs with extensive lesions gained 50 to 75 g/day less than pigs with no lesions but another showed no effects.

The disease has increased in significance with the occurrence of postweaning multisystemic wasting syndrome and PDNS associated with porcine circovirus type 2 (PCV2). There is also an increased occurrence where there is a problem with porcine respiratory disease complex (PRDC) particularly during summer months.

Risk Factors

Many of the risk factors affect the speed of the passage of the ingesta through the stomach whether or not the stomach contains food. Generally, anything that increases the consistency of the stomach contents reduces ulceration and vice versa. For example, finely ground feed decreases the consistency.[1]

Anything that causes an empty stomach will potentially increase the acidity in the PE region of the stomach is a risk factor. Back in the 1960s all that was needed to produce an esophageal ulcer in a pig was to keep the pig restricted in a feeding or farrowing crate and deprive it of water and food for 24 hours. This would therefore include intermittent feeding and watering, respiratory disease, and hot weather.

Dietary Risk Factors

Generally, ulceration is influenced by grain component, milling procedures, and processing. A hammer mill increases the ulceration risk and in this type of milling wheat shatters more than when it is subjected to a rolling meal. The rolling mill squashes rather than shatters the grains; therefore is not so ulcerogenic. A rolling meal producing a diet based on barley or oats is the least ulcerogenic.

The disease occurs primarily in penned pigs receiving a grain diet and growing rapidly. It has also occurred in pigs fed large quantities of cheese whey or skimmed milk. Too much copper and not enough zinc may also be a factor. The incidence is highest in pigs receiving diets containing a higher proportion of corn (maize) than other grains. The incidence is even greater if the corn is finely ground or is gelatinized or expanded.

Finely Ground Feed

This is the most important risk factor. One of the explanations of this may be the rapid emptying of the stomach when fine particles are used as the food in the stomach becomes more fluid and empties more quickly. There is normally a gradation of ascending pH from the cardia to the esophagus, but with

rapid emptying there is the possibility of the low pH reaching the esophageal region.

Feeding a diet based on finely ground barley to pigs beginning at 10 to 11 weeks results in lesions as early as 1 month later, and the incidence and severity of lesions increased progressively over the next 2 months. Diets high in wheat or corn starch may be worse than diets based on barley or oats.

The particle size and the physical form of the feed are important risk factors. The size of particles in feed is significant whatever feed is used. Finely ground diets (particularly wheat and maize) have detrimental effects on the gastric mucosa of finishing pigs. Grinding through a 4.68-mm screen approximates the screen size used most frequently for grinding barley for pigs in practice and is associated with a low incidence of ulcers. Reducing particle size and pelleting improves growth performance of finishing pigs. For every 100 μm of decrease in size of the article size there is an approximately 1.3% increase in gain efficiency but each time the level of ulcers increases. Fine diets have the effect of increasing pepsin levels as do pelleted diets.

A pelleted diet uses grain that is finely ground before it is compressed into a pellet, but on reaching the stomach it reverts back to the fine particles that were compressed into the pellet. A diet finely ground through a 3-mm screen in a hammer mill and then pelleted will be associated with a 75% incidence of pigs with hyperkeratosis of the PE, and 11% of the pigs may have severe erosions and ulceration of the PE. The incidence of lesions decreases when the diet is ground through a 6-mm screen. Even straw (coarsely ground barley straw at 5%–10% of the ration) gives almost complete protection. In growing pigs, dietary fiber rich in structural polysaccharides has been shown to be important in preventing the development of parakeratotic lesions in the PE. An increase in the crude fiber content of a diet that is finely ground does not affect the occurrence of severe erosions and/or ulcers of the PE.

The processes have additive effects on digestibilities of dry matter, nitrogen, and energy, with maximum nutrient digestibility in pelleted diets with corn milled to a particle diameter size of 400 μm. Reducing the particle size to below 400 μm causes practical problems with milling and an increased incidence of gastric lesions, and it is suggested that a particle size of 600 μm, or slightly less, is optimal for corn in either meal or pelleted diets for finishing pigs.

Using endoscopic examination of the stomachs of pigs fed a fine-particle diet (geometric mean size of 578 μm) it was found that as ulcer severity increases, the growth performance of individually fed pig decreases. Feeding a coarse particle diet (geometric mean size of 937 μm) for 3 weeks resulted in a decrease in the severity of the ulcers.

High levels of unsaturated dietary fat are not helpful, especially if they are accompanied by low levels of vitamin E. Similarly, pigs fed waste food had more severe gastric lesions.

Environmental and Management Risk Factors

It has been suggested that confinement, crowding, transportation, changes in environment, and exposure to other pigs are important in the etiopathogenesis of gastric ulcers of pigs. Method of feeding may also be important. Interruption of feeding may also increase dietary stress. All of these are stresses and many others including anxiety, fear, pain, fatigue, fasting, etc., will be associated with an increase of ulcers. There is an even greater occurrence in summer when water demands are higher. Males are always more affected in prevalence and severity, but they may be more easily stressed. One of the most important factors is time in the lairage. Premortem handling is extremely important. Pigs kept overnight in the lairage have more ulcers than pigs killed on the day of arrival.

Larger herds always show more of the problem, and it is probably a reflection of the different diets that they use (based on wheat and pelleted). The larger farms also have more infection pressure, more selection pressure, and more feed-related factors.

Pigs that receive porcine somatotropin may have an increased level of ulcers possibly caused by the elevated circulating gastrin.

There are a variety of foreign bodies reported from the pigs' stomach including stones, which outside sows chew all the time, and also sand. The majority of the stones are probably passed in the feces, but may accumulate in and stretch the stomach. The stomach capacity is normally about 3 to 6 L. This may lead to reduced appetite and gastritis but is not believed to be a contributor to ulceration. Similarly, hairballs are a common finding, reaching 10 to 15 cm in size in the stomach. The occurrence of rubbish indicates pica or a depraved appetite, which is often an indicator of inadequate feeding. One of the other substances found in outdoor pigs stomachs is the flakes of bitumen that remain from clay pigeon shooting, which are toxic.

Pathogen Risk Factors
Gastric Bacteria

Ulcers in the fundic part of the stomach are often associated with gastritis. *Helicobacter heilmannii* and *Gastrospillium suis* (now called *H. suis,*[2] have been found in gastric ulcers, but not ulcers of the PE of pigs and are unlikely to be the primary cause of the lesion. *Helicobacters* and *Arcobacters* are uncommon before weaning and increase with age; thus over 80% of market hogs may be infected [3] and 90% of adults have them in their stomachs. They are capable of causing ulcers in experimental challenges.[4] They have been found in some studies but not in others. They are normally found in the antrum of the stomach in close proximity to the acid-producing cells in the fundus, and

the gastritis they produce may be related to parietal cell stimulation which leads to further hyperacidity and then the damage will extend to the PE. They may extend into the PE if there is gastritis. Experimental inoculation of these *Helicobacter* agents in a carbohydrate-enriched liquid diet has failed to produce ulcers of the PE, but inoculation of *Lactobacilli* spp. and *Bacillus* spp. did produce ulcers when they were given in the same substrate. This may all be related to the degree of fermentation produced, the production of short chain fatty acids, and then the acidity generated.

The spiral-shaped *H. suis* has been found in 84% of the stomach of pigs with frank gastric ulcers of the PE. The organisms were mainly in the mucous layer and in gastric foveolae of the antral and oxyntic mucosa and only occasionally in the cardiac-PE region. The presence of the organism is now thought to be associated with lesions of the pyloric mucosa and gastritis in pigs.[2]

H. heilmannii type 1 has been found more frequently in the stomachs of pigs with ulcers (100%) and in those with preulcer lesions (90%) than in stomachs with macroscopically normal PE (35%).

PATHOGENESIS

In pigs, nearly all naturally occurring gastroduodenal ulcers are localized in the PE of the stomach. Excessive gastric acid production, depletion of the gastric buffering system resulting in prolonged activation of pepsinogens, and changes in mucous composition are suggested as important factors related to gastric ulceration in swine. The physical texture of the feed can influence pepsin and acid secretion, and the fluidity of the stomach contents induced by ulcerogenic diets may alter the normal pH gradient within the stomach. This allows greater pepsin and acid contact to the esophagogastric area.

The concentrations of short chain fatty acids are high in the proximal gastric contents of pigs and associated with intakes high in readily fermentable carbohydrates, like ground corn. These products of bacterial metabolism, principally acetate and lactate, reach high concentrations within 4 hours after feeding because of high pH in the proximal gastric contents, which may allow some types of bacteria to proliferate. These weak acids are lipid soluble in their undissociated form and could penetrate and acidify underlying tissue more readily than free hydrogen ions. In this way, rapid production of short chain fatty acids, followed by their absorption and tissue acidification, may be similar to ruminal acidosis and rumenitis in ruminants following the ingestion of large quantities of readily fermentable carbohydrates.

The rumen epithelium, also a stratified squamous mucosa, is easily injured by short chain fatty acids at pH ≤5.0. The breaking of the barrier by short chain fatty acids could result in underlying inflammation and widespread tissue destruction.

Experimentally, exposing undissociated short chain fatty acids to swine gastric mucosa results in rapid penetration of the outer barrier and acidification of the underlying viable tissue. This results in cell swelling and vesicle formation, followed by sloughing of the outer barrier, erosion into deeper zones, and finally, ulceration.

Weak organic acids, at pH ≤2.5, induce a greater degree of functional and histologic injury in three stomach zones (squamous, cardiac, and oxyntic) than does hydrochloric acid. The predilection for the squamous mucosa in naturally occurring ulcers may be attributed to the lack of defense or repair mechanisms that are present in the cardiac and oxyntic mucosa, which are capable of HCO_3^- and mucous secretion, which may raise the pH adjacent to these epithelial layers. Thus the increased digestibility associated with decreased particle size of the diet may promote rapid fermentation following eating resulting in the production of increased concentrations of short chain fatty acids. Any increase in fluid content will also contribute to the changes in pH gradient that exist in the stomach. Excessive gastrin is then stimulated and more acid secretion follows.

Normally, the PE is white, smooth, and glistening and may be bile stained. The first stage in ulceration is hyperkeratosis. This is followed by erosions, ulcerations, and hemorrhage. The erosions may heal, resulting in a fibrous contraction. Chronic ulceration may occur with the development of several ulcers in combination with fibrous tissue involving all of the squamous mucosa. Advanced hyperkeratosis may cause partial stenosis of the terminal esophagus.

The erosion of a blood vessel within the ulcer will result in acute to subacute gastric hemorrhage. These cases are usually sporadic, causing deaths of individuals within a group, with cases occurring over a period of several weeks. Clinical signs are often not observed, and affected pigs are found dead from acute hemorrhage into the stomach.

The regurgitation of bile into the stomach and the intensity of bile staining of esophagogastric tissue have been linked to the pathogenesis of esophagogastric ulcers in pigs. Almost all stomachs of pigs contain bile and bile staining of the PE; there is no evidence for the hypothesis that the regurgitation of bile into the stomach is associated with esophagogastric lesions in finishing pigs. There is no evidence of an association between gastritis and ulcer.

CLINICAL FINDINGS

The clinical signs reflect the rate of blood loss, but an animal can go from perfectly healthy to ulceration within 24 hours. It is therefore possible to have sudden death (hyperacute) acute, subacute, and chronic stages of the condition. Usually there is no fever. Mortality may be in the range of 1% to 2%, but in some cases where there is a group outbreak it may be higher.

Most cases are subclinical but sows will die of blood loss. Pigs frequently die of ulcers during concurrent disease such as respiratory disease and in this case anorexia may disturb the gastric contents and allow material of high acidity to reach the cardia. Similarly, where there is a reduced consumption of water the integrity of the mucus may be broken into plaques or flakes by desiccation of the mucosal surfaces.

Gastric ulceration is most common in pigs over 6 weeks of age and occurs in adult sows and boars; the clinical findings are dependent on the severity of the ulcers. The effects of ulceration on production may be highly variable. Most pigs with esophagogastric ulcers are clinically normal, and growth rate and feed intake appear unaffected. Some observations suggest that there is no effect of ulceration on growth rate, whereas others indicate that the presence of esophagogastric ulcers results in a marked decrease in growth rate and an increase in the length of time required for the pig to reach market weight. Some affected pigs also eat slowly and regurgitate frequently. Endoscopic monitoring of the stomachs of pigs fed ulcerogenic diets found that as the severity of the ulcer increased growth performance was decreased. The greatest economic losses were associated with sudden deaths caused by hemorrhage and marked decreases in performance associated with fine particle size.

The erosion of a blood vessel within the ulcer will result in acute to subacute gastric hemorrhage. These cases are usually sporadic, causing deaths of individuals within a group, with cases occurring over a period of several weeks. Clinical signs are often not observed, and affected pigs are found dead from acute hemorrhage into the stomach. When pigs are found dead from peracute hemorrhage, inspection of the in-contact pigs may reveal other animals with pallor and black tarry feces (melena), which represent those with subacute hemorrhage.

Cases with subacute gastric hemorrhage may survive for a few days and there is evidence of marked pallor, weakness, anorexia, and black pasty feces changing to mucous-covered pellets in small amounts. The weakness may be sufficient to cause recumbency. Vomiting frothy bile-stained fluid and grinding of the teeth may occur. Abdominal pain may be elicited by deep palpation over the xiphisternum and there may be a reluctance to walk along with a rigid back indicative of pain. Animals that survive are often unthrifty, which is usually caused by anemia from chronic blood loss, and a few cases are affected by chronic peritonitis. When the disease is occurring careful observation may detect early cases. Suggestive signs are a darkening of the feces and the development of pallor. Sows at parturition are also at risk. In cull sow surveys 60% may have stomach lesions and 10% to 15% may have ulcers. It is a common cause of sow mortality or the most common cause. Many sows have scars that indicate previous healed ulcers.

CLINICAL PATHOLOGY

Laboratory testing is not indicated. Animals with gastric ulceration generally have lower than normal hematocrit values, hemoglobin concentrations, and erythrocyte counts. The black tarry feces can be examined for the presence of blood.

NECROPSY FINDINGS

At postmortem animals are usually in very good condition. Ascarids have been found in the stomach, but these are not a factor in the field. If bleeding has been extensive then the carcass may be very pale.

At necropsy, the ulcers are confined to the esophageal region of the stomach, although hyperkeratosis may block the exit from the esophagus and cause increase in the muscular layers of that organ to force through the cardia. In this case pigs often vomit and then start eating again immediately as they have voided the food. Affected stomachs consistently have more fluid contents than unaffected ones. If severe blood loss from the ulcer has been the cause of death, then the carcass is pale and fresh blood is usually present in the stomach (there may be large blood clots) and intestines. The colonic contents may also appear melenic. Early lesions in clinically unaffected animals include hyperkeratinization of the mucosa (usually pale raised areas without bile staining initially), which progresses to epithelial erosion without actual ulceration. Ulcers usually initially occur along the junction of the PE with the glandular stomach but may enlarge to efface the entire squamous portion of the stomach. These more diffuse ulcers are easily missed on cursory examination because of their uniform appearance. Chronic gastric ulcers develop thickened, raised edges caused by ongoing fibrosis, occasionally resulting in a gastroesophageal stricture. The histologic appearance varies with the stage of lesion development, but in fatalities there is typically complete loss of the epithelial layer, with exudation of neutrophils from a bed of mature granulation tissue. In one survey of apparently normal stomachs it was found that 32% had histologic parakeratosis, 38% had mild erosions, and 23% had severe ulcerations. Recent studies have demonstrated *Helicobacter*-like bacteria in porcine stomachs, but further research is required to determine whether this infection plays a significant role in ulcer formation. Small clusters of *H. heilmannii* have been seen in the gastric crypts, but they are not associated with histologic changes. A recent survey suggested no correlation between infection in the cardiac mucosa and the severity of the lesions shown by the esophagogastric region. The macroscopic findings are usually sufficient for the confirmation of a diagnosis

of esophagogastric ulceration. The initial lesion of hyperkeratosis (often stained green by bile) leads to parakeratosis with fissures and the lamina propria is then exposed. The epithelium sloughs off and then ulcers of the epithelium develop with hemorrhage from the vessels. Chronic lesions may be seen as craters floored by smooth muscle. Histologically, the lesions are thickened, with parakeratosis, and there are nucleated cells on the mucosal surface, the papillae are elongated, and there are infiltrations of neutrophils and eosinophils. Usually only the mucosa is ulcerated, but occasionally the submucosa is affected and then the muscularis and very rarely the serosa.

Severity and extent of esophagogastric lesions can be graded according to the following scheme

0 Intact epithelium

1 Small degree of hyperkeratosis (<50% of total surface)

2 Distinct hyperkeratosis (=50% of the total surface)

3 Hyperkeratosis and less than five erosions smaller than 2.5 cm in size

4 Hyperkeratosis and more than five erosions or erosions larger than 2.5 cm in size

5 Hyperkeratosis and more than 10 erosions or erosions larger than 5 cm in size, and/or an ulcer (with or without bleeding) or stenosis of the esophagus toward the stomach

No difference in lesion score was found between Duroc, Landrace, and Iberian pigs.

DIFFERENTIAL DIAGNOSIS

The occurrence of sudden death with a carcass that shows extreme pallor and marble white skin suggests the possibility of peracute hemorrhage from an esophagogastric ulcer. The disease must be differentiated at necropsy from proliferative hemorrhagic enteropathy, swine dysentery, and salmonellosis. Black tarry feces in growing and finishing pigs are characteristically caused by subacute hemorrhage associated with esophagogastric ulceration. There may be anemia and raised plasma pepsinogen levels.

It is possible to detect stomachs with helicobacters by covering the stomach with urea gel containing an indicator sensitive to pH change. If there are large numbers of these urease-positive bacteria then the pH changes.

Severe infestation with whipworms is a differential. The clinical diagnosis can be confirmed by endoscopy, which requires an empty stomach (may cause ulceration in itself) and anesthesia.

TREATMENT

In extremely valuable animals blood transfusions and intravenous fluid injections have been used. Ranitidine syrup at 300 mg per sow per day has been tried. Vitamin K and hematinics have been tried with little success. Bovine serum concentrate given as a 1% solution is supposed to have reduced the extent and severity of signs associated with ulcers in growing pigs, but generally medication does not help. If a diagnosis is made euthanasia is advised.

CONTROL

Attention to social factors such as overcrowding, proper ventilation, slowing growth rate, and reducing stress is important. Administration of melatonin at 5 ppm (5 mg/kg feed) has been used. Methionine has been used but is not really proven as a treatment.

Control of esophagogastric lesions of growing and finishing pigs is dependent on using diets with a particle size and physical form that will provide the most economical performance in terms of digestibility and feed efficiency and minimize the incidence of lesions. A diet based on barley and oats may be more beneficial than one based on wheat or maize. Meal may be better than pellets. Increasing fiber levels is important (oats and sugarbeet pulp). The use of a diet ground through a 6-mm screen instead of 3-mm screen using a roller rather than a hammer mill is recommended. However, screen size is not the only factor affecting particle size. Other factors include the condition of the screen and hammer, the type and variety of grain and its moisture content, the speed of the mill, the 3-week pelleting process, and the flow rate in the distribution of the feed to the pigs. A particle size of 600 µm, or slightly less, is suggested as optimal for corn in either meal or pelleted diets for finishing pigs. Increasing the particle size to 750 µm, using meal instead of pellets for 3 weeks, and using straw as bedding have been shown to produce improvements when an outbreak occurs.

The incorporation of *S*-methylmethionine sulfonium chloride often sold as vitamin U, a nutritional component of many vegetables such as cabbage and carrots, has antigastric ulcer properties. Addition to the diet of this substance, ground through a 3-mm screen, and fed to grower pigs from 45 kg to 107 kg live weight, at 400 parts per million (ppm) decreased the incidence of severe erosions or ulcers by about 50%. The addition of lucerne meal to increase the crude fiber content of one of the experimental diets did not have an effect on the incidence or severity of the lesions. Others have reported the beneficial effects of alfalfa (high in the antioxidants vitamins E and K), but not when somatotropin was used and it produced ulcers. Sunflower hulls in the diet have also been used to reduce the speed of feed transition from the stomach.

Incorporation of zinc in the diet may help. The diet should contain adequate amounts of vitamin E and selenium. The reduction of environmental and managemental stressors with attention to stocking rates may be of value.

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Noninfectious Intestinal Disease of Swine

INTESTINAL REFLUX

Acute dilatation also occurs in pigs secondary to acute obstruction of the small intestine. The obstruction may be as far down as the ileocecal valve. The oral segment of intestine dilates and fills with fluid, and refluxes into the stomach, filling it. In the pig, vomiting follows. The outcome depends on whether sufficient gastric motility returns to evacuate the stomach.

DIAGNOSIS

The vomiting in gastric dilatation is more profuse and projectile than that of gastritis or enteritis, but may be simulated by that of obstruction of the upper part of the small intestine.

INTESTINAL OBSTRUCTION IN PIGS

ETIOLOGY

Some causes of intestinal obstruction include the following:
- Torsion of the coiled colon about its mesentery occurs in adult pigs.
- Obstruction of the terminal small colon in young piglets causes very hard fecal balls, or barley chaff used as bedding may be implicated in obstruction. The use of wood shavings or peat as a bedding may cause piglets to become impacted as a result of large consumption of the material.
- Heavy feeding on lactose causes a dilatation and atony of the intestine in the same way as grain feeding does in ruminants.

Sometimes the presence of ascarid worms will block the intestine. Genetic and environmental factors may contribute to the incarceration of the intestine in a patent umbilicus.

CLINICAL FINDINGS

In pigs, distension of the abdomen, absence of feces, and complete anorexia are evident. The distension may be extreme in young pigs when the terminal colon is obstructed. Death usually occurs in 3 to 6 days.

IMPACTION OF THE LARGE INTESTINE OF PIGS

ETIOLOGY

- In pigs, impaction of the colon and rectum occurs sporadically, usually in adult sows that get little exercise and are fed wholly on grain. The disease also occurs in pigs that are overcrowded in sandy or gravelly outdoor yards.
- In young weaned pigs there may be obstruction of the spiral colon.
- A presumed inherited megacolon of fattening pigs is reported as a cause of abdominal distension, constipation, and wasting. There is no anal stricture.

Torsion of the long axis of the mesentery is a common condition in pigs and leads to impaction and rapid death. It can involve the small intestine or the large intestine, or both.

CLINICAL FINDINGS

In impaction of the large intestine the effects appear to be caused largely by autointoxication, although the commonly occurring posterior paresis seems more likely to be caused by pressure from inspissated fecal material.

Retention of the meconium has no specific signs. There is anorexia and dullness and the pig is recumbent much of the time. Feces passed are scanty, very hard, and covered with mucus. Weakness to the point of inability to rise occurs in some cases. Hard balls of feces in the rectum are usually detected when a thermometer is inserted.

In paralysis of the rectum there is inability to defecate and usually some straining. The anus and rectum are ballooned and manual removal of the feces does not result in contraction of the rectum. Spontaneous recovery usually occurs 3 to 4 days after parturition.

INTESTINAL TYMPANY IN PIGS

This is usually an incidental finding at slaughter.

ETIOLOGY

- Primary tympany occurs with ingestion of excess whey. It has been recorded in adult dry sows. Distension of the proximal colon causes rupture with death from endotoxic shock.
- Secondary large bowel tympany is usually secondary to acute intestinal obstruction.

OSSEUS METAPLASIA

The finding of metastatic plates of bone in the mesentery or wall of the small intestine is not an uncommon occurrence and probably results from an attempt to repair local damage by calcification. It does not seem to cause problems and is found at slaughter.

INTESTINAL HEMORRHAGE SYNDROME

This is a sporadic occurrence but occasionally may involve all the finishing pigs in one batch, causing a significant economic loss through sudden death or enforced casualty slaughter. It has had a variety of other names including hemorrhagic bowel syndrome, porcine intestinal distension syndrome, "bloody gut," or "whey bloat." It is similar to intestinal distension. Large pigs are affected usually from 35 kg to adults. They become pale, have a distended abdomen, and die suddenly.

ETIOLOGY

The cause is raised intraabdominal pressure from +3.5 mm Hg or −15 mm to >30 mm Hg.[1] The most pronounced cause is whey bloat, in which where there is excess fermentation of carbohydrate in the large intestine. This causes an anticlockwise torsion of the whole of the intestines so that the cecum is directed cranially. A twist of the mesentery does not usually involve the large intestine. Other possible etiologic factors include allergy because there are large numbers of eosinophils in the gut wall, skim milk not whey and dry meal, and Lawsonia infections.

EPIDEMIOLOGY

On whey-fed units the deaths occur more frequently because the level of whey feeding increases.

CLINICAL SIGNS

The pigs are usually found dead or have abdominal colic. They occasionally appear pallid. There may be a distended abdomen.

PATHOLOGY

The small intestine is almost always autolytic, but there is an underlying loss of epithelium, villous loss, and inflammatory cell infiltration with large numbers of clostridia in the gut. The small intestine is filled with bloodstained fluid and there may be volvulus with gross distension of the colon and bloodstained fluid in the abdomen.

TREATMENT

Usually there is no time for treatment.

CONTROL

The only possible control is to change the diet, particularly to reduce the whey concentrations, but be aware that this may reduce the growth rate and the diet needs to be adjusted to compensate.

REFERENCE

1. Thomson JR, et al. *Pig J*. 2007;59:152.

DIVERTICULITIS AND ILEITIS OF PIGS

In this disease there is thickening of the wall of the ileum, particularly in the terminal portion, so that the intestine becomes thick and rigid. There is a close clinical similarity to Crohn's disease in humans, and the etiology of both conditions is obscure. Familial predisposition is probable in humans and has been suggested in pigs.

The signs are those of acute peritonitis caused by ulceration and, sometimes, perforation of the affected ileum. Illness occurs suddenly with loss of appetite, excessive thirst, dullness, and disinclination to rise. The temperature is subnormal, the respiration is distressed, and there is a bluish discoloration of the skin. Death occurs in 24 to 36 hours. Acute cases occur in young pigs up to 3 months of age, and chronic cases, caused by ulceration and chronic peritonitis, occur in the 7- to 8-month age group.

At necropsy there may be diffuse peritonitis caused by leakage of alimentary tract contents through perforating ileal ulcers. Gross thickening of the ileal wall with nodular proliferation of the ileal mucosa and enlargement of the mesenteric lymph nodes are common accompaniments. Although the macroscopic findings are similar to those of Crohn's disease in man, the histopathological findings differ markedly. There is an obvious and significant protein loss through the intestinal lesion and a marked hypoproteinemia.

RECTAL PROLAPSE

Prolapse of the rectum is an occasional occurrence in cattle and is rarely seen in other species. Common causes include enteritis with profuse diarrhea, violent straining such as occurs in coccidiosis in young cattle, in rabies sometimes, in spinal cord abscess, and also when the pelvic organs are engorged.

RECTAL PROLAPSE IN PIGS

Rectal prolapse is quite a common condition in pigs. It is a welfare issue often requiring casualty slaughter.

ETIOLOGY

It seems likely that any event producing an increase in intraabdominal pressure to an average of 29 mm Hg may cause prolapse. Such a happening occurs when sows are tethered and strain against the tethers while sitting.

EPIDEMIOLOGY

In a prospective study of rectal prolapse in a commercial swine herd, 1% of the pigs prolapsed between 12 and 28 weeks of age, with a peak incidence occurring at 14 to 16 weeks of age. Prolapse rates were highest during the winter and autumn months.

Other risk factors included:

- Male: Relative risk 2.3
- Birth weight less than 1000 g: Relative risk 3.4
- A particular Yorkshire boar: Relative risk 2.8

- Dams of litter number: 1, relative risk 14.9; 2, relative risk 8.2; 3, relative risk 9.8

There was no evidence to support the hypothesis that diarrhea and coughing are factors associated with a risk of prolapse.

It has been suggested that low birth weight pigs may be particularly susceptible in that they have poor pelvic muscle development, which leaves a weakness at the point in the pelvis where perineal hernia is possible, and there is no firm ligamentous attachment of the rectum to the pelvic wall. In the same context excessive anal nuzzling in very young pigs has been suggested as weakening these intrapelvic structures.

Feeding rations with lysine concentrations in excess of the requirements is considered a risk factor for rectal prolapse in swine. Other practitioners have suggested that it occurs when pigs are transported at high stocking densities. It may follow impaction of phosphate crystals in the urethra. Administration of tylosin and lincomycin has also been suggested as a cause, but these effects disappear after 72 hours of treatment.

The use of estrogens as a growth stimulant and access to estrogenic fungal toxins (zearalenone) predispose to rectal prolapse. It has been suggested that mycotoxins in swine rations are a cause of rectal prolapse, but there is insufficient evidence to prove such a claim.

CLINICAL FINDINGS

There is severe abdominal distension, which may be accompanied by coughing and the production of soft feces. Straining may or may not be present. The prolapse may reduce naturally. It may become strangulated, necrotic, drop off, or be bitten off by other pigs.

PATHOLOGY

There may be severe loss of blood and peritonitis.

TREATMENT

Mild cases should be hospitalized individually and severe cases euthanized immediately. Treatment is surgical by reduction under anesthesia.

CONTROL

One possible control is to place weaners in a straw yard for 3 weeks between rearing in a cage system and transferring to slatted floors.

RECTAL STRICTURE

The most common occurrence is as an acquired condition in pigs simply called rectal stricture. Rectal stricture occurs in feeder pigs of 2 to 3 months of age. Rectovaginal constriction occurs as an inherited defect in Jersey cattle.

ETIOLOGY

The cause of rectal structure is unknown, but there a number of associations. A strong genetic component suggests it may be a developmental weakness in the structure of the rectum, which facilitates nonhealing at that particular point just proximal to the anal ring. This may be the inherited component. This point has a poor collateral blood supply as it is the point where the rectum is supplied from the caudal hemorrhoidal artery rostrally (caudal mesenteric originally) and caudally from the perineal arteries from the internal pudendal artery originally from within the pelvis.

EPIDEMIOLOGY

- It may be a sequel to enteric salmonellosis, particularly *S. enterica Typhimurium* or possibly other infections such as *Candida, Selenomonas, Chlamydia,* or *Lawsonia,* but these may move in after the problem and not be an etiologic factor.
- It may develop from a prolapse.
- It may follow the use of tylosin.
- Quite often it follows 10 days after dietary change.

PATHOGENESIS

The presumed pathogenesis is that a prolonged enterocolitis with ulcerative proctitis results in an annular cicatrization of the rectal wall 2 to 5 cm anterior to the anorectal junction. This results in colonic dilatation and compression atrophy of the abdominal and thoracic viscera. The disease can be reproduced experimentally with *S. Typhimurium* or the surgical manipulation of the rectal arterial blood supply, resulting in ischemic ulcerative proctitis.

CLINICAL SIGNS

In a particular group it may affect up to 10% of the feeder pigs. The pigs are dull, depressed, and fail to grow. There is progressive abdominal distension, inappetence, emaciation, dehydration, and watery to pasty feces. The stricture of the rectum can be palpated on digital examination of the rectum. Some pigs with incomplete strictures are unaffected clinically.

PATHOLOGY

At necropsy there is a low-grade peritonitis and gross dilatation of the colon, and sometimes the terminal ileum also. A stricture is present 2 to 5 cm from the anus, and may be so severe that it exists as a scirrhous cord with or without a narrow luminal remnant in the center. There may be abscessation at the site. Histologically, there is necrotic debris and granulation tissue at the site of the stricture.

TREATMENT

Most affected pigs die or are destroyed on humane grounds. Surgical treatment of the condition is described but it is rarely cost-effective.

Bacterial and Viral Diseases of the Alimentary Tract

SALMONELLOSIS IN SWINE (PARATYPHOID)

Salmonella infections of pigs are important as a cause of salmonellosis in pigs and many serotypes in the pig may act as a potential source of infection for humans.

SYNOPSIS

Etiology *Salmonella* Typhimurium, *Salmonella* Choleraesuis, *S.* Derby, and rarely others.

Epidemiology Worldwide. Important zoonosis and food-borne illness. Prevalence of infection in healthy animals varies according to species and country. Incidence of clinical disease much lower than prevalence; outbreaks occur precipitated by stressors. Spread by direct or indirect means; infected animal is source and this contaminates feed and water supplies.

Disease may become endemic on farm. Carrier animals shed the organism and may introduce infection into herd. Deprivation of feed and water, transportation, drought, intensive grazing and housing, and mixing animals from different sources contribute to the onset of disease. Antimicrobial resistance is a major public health problem with subclinical infection in pigs a potential zoonosis.

Signs Septicemia in pigs up to 4 months of age with high case–fatality rate. Acute diarrhea and dysentery, fibrinous fecal casts, fever, marked dehydration, and toxemia; chronic enteritis; abortion; dry gangrene of extremities; and arthritis and foci of osteomyelitis

Clinical pathology Culture organism from feces. Detect organism with special tests; use hematology for changes in leukocyte picture and clinical chemistry for electrolyte changes.

Lesions Septicemic hemorrhages Mucoenteritis to marked fibrinohemorrhagic necrotic enteritis and enlarged mesenteric lymph nodes. Kidney petechiation, foci of necrosis and thickened intestinal wall in chronic enteritis. Culture organism from blood, spleen, liver, and lymph nodes.

Differential diagnosis list
- Septicemia of neonates
- Coliform septicemia in piglets
- Septicemia in growing pigs
- Hog cholera
- Erysipelas
- Pasteurellosis
- Swine dysentery

Treatment Antimicrobials

Control Prevent introduction of infection into herd. Limit spread of infection within herd by identification of carrier animals,

prophylactic antimicrobials, restricting movement of animals, clean water supply, hygiene, and disinfection of buildings. Dispose of infective materials. Vaccines for immunization are available but not effective.

ETIOLOGY

Serovars of *S. enterica* subsp. I are associated mainly with warm-blooded vertebrates and are responsible for most *Salmonella* infections in humans and domesticated animals. *Salmonella* serovars differ in the range of hosts they can infect and in the nature of disease that may result: this difference is referred to as **serovar–host specificity**. Some *Salmonella* serovars, for example, Typhimurium (STM) and Enteritidis, can infect a wide range of hosts and are termed ubiquitous. They are usually associated with a relatively mild enteric disease, although in some hosts, such as mice, the disease can be systemic and severe.

Other serovars are very restricted in their host range, causing severe systemic disease in only one host, for example, *S.* Choleraesuis (SCS).

A third group of serovars is associated predominantly with disease in one species but may also infect a limited number of other hosts for example, *S.* Dublin (SD). The nature of disease associated with this third group of serovars is variable and usually systemic.

The molecular methods are now available for epidemiologic investigation of *S. enterica* subsp. *enterica* infections. Of recent concern is the emergence of multiple-resistance isolates of SCS and also STM.[1] STM is the most common isolate from pigs in North America[2] and most other parts of the world. Occasionally, other species are found in pigs such as *S.* Heidelberg, which may be associated with PWD, and SD has also been found in pigs.

Localized epidemics of *S.* Typhisuis also occur, and recently it has been shown that it can exist on antibiotics alone.[3] Other serotypes are usually transient and may be associated with special factors. Salmonellas have been recovered from wild boar in Portugal, Spain, and Northern Italy, and STM is one of the serovars recovered.

EPIDEMIOLOGY

Salmonellas are marvelous at surviving because they have the ability to persist in reservoir hosts, have the ability to be shed from carriers, persist within the environment, and use transmission vectors effectively.

Salmonellosis outbreaks are usually in intensively reared weaned pigs, but infection can also be in neonates (protected by colostral antibodies) and adults.

In a survey of *Salmonella* in slurry tanks, in fresh pooled feces from finishers, sows, and weaners it was found that Salmonellas were not so easy to recover in winter and more likely to be recovered from slurry tanks than fresh pooled samples. The four most common types were STM var Copenhagen (31%), SD (12.4%), STM (10.6%), and *S.* Agona (10.6%).[4]

In an interesting study of environmental samples, it was found that certain areas in the indirect environment (compartment aisles, driving boards, central aisle of the barn—areas which are often forgotten) had residual *Salmonella.*[5]

In a study in Germany, it was found that the main risk factors for the spread of salmonellosis were the moving of animals during the finishing period, not having a separate transporter for different age groups of pigs, and pigs having contact with other animals.[6]

In the United States, a study was made of *Salmonella* isolates in 2003 and 2008 from the Iowa State University diagnostic Laboratory.[7] Group C, SCS var. Kunzendorf decreased but Group B strains increased, *S.* Typhimurium var 5 (formerly, Copenhagen), *S.* Agona, *S.* Derby, *S.* Heidelberg, and STM all increased.

Prevalence and Occurrence of Infection

The majority of *Salmonella* infections are subclinical, associated with a large number of serotypes. Factors influencing the prevalence of *Salmonella* spp. in swine farms using a meta-analysis approach have been described in an attempt to explain the variation between various estimates.[8] STM has a worldwide distribution and causes enterocolitis in young pigs.

The incidence has been increasing in some geographic areas. It is usually manifested as a septicemia. On the other hand, there is difficulty in isolating this organism at all in the UK. SCS is frequently isolated from clinically ill pigs but rarely from pig feeds or nonporcine hosts. The major sources are shedding pigs and contaminated environments. Both vertical and horizontal transmissions occur. The presence of other Enterobacteriaceae and the composition of these were not found to be useful indicators of subclinical *Salmonella* infections.[9]

Belgium

In a study in Belgium[10] 7.8% of the pigs were seropositive (12 farms). Open farms (buying in) had twice as many seropositive pigs as closed farms. The results were also twice as high at slaughter age than halfway through finishing. STM was found in 65% of the cases, and 65% of these had a tetra-resistant antimicrobial resistance (AMR) profile.

Canada

In Canada a study of *Salmonella* serovars found that sows had 43% of the isolates, 29% were in the nursery pigs, and 28% were in grow-finish units. There were 19 different serovars and SD (28.5%) and STM var Copenhagen (19.15) were the most common.[11] In a study of approximately 90 Alberta finishing farms it was found that the sample prevalence was 13.2% (most farms were below 20% seroprevalence) and the on-farm prevalence was 83.3%.[12] In addition, the status changed frequently over the visits. Meal feeding and antibiotics given in water were associated with lower seroprevalence.

Czechoslovakia

In Czechoslovakia, STM dominates in pigs but *S.* Enteritidis (SE) is also quite frequent because it is in several countries in Central Europe.[13] SE colonizes the intestinal tract in higher quantities but was shed in the feces in lower quantities.

Denmark

In Danish pig herds, *Salmonella* infections are usually subclinical. A survey from 1993 to 1994 found that 22% of 1368 larger herds were infected with *Salmonella*. The most prevalent serotypes were STM (62% of infected herds), *S.* Infantis (10%), *Salmonella* 4.12:b (8%), and *S.* Panama (5%). Phage typing of isolates of STM from pigs and humans reveals that pigs are probably a major source of the infection in humans in Denmark. A more recent survey in Denmark showed that STM (mostly DT12 and DT120) was most common in finishers (7.4% + ve in lymph nodes and 3.2% + ve in carcasses) and SD in breeding herds (40.9% were + ve in at least one sample). An AMR to one or more antibiotics was found in 35.2% and to four or more in 19.3%.[14] The prevalence of *Salmonella* in Danish pork decreased from 3.5% in 1993 to 0.7% in 2000 following the introduction of a national program to reduce the prevalence of salmonellas in pork.

In Danish pig abattoirs it was found that by keeping the number of seropositive pigs below 50 it was possible to keep carcass prevalence below 1%, and that improved hygiene practice would reduce the carcass contamination further.[15]

Italy

A similar distribution was found in Italy.[16]

Japan

SCS is also an important pathogen of pigs in Japan.[17]

The Netherlands

In the Netherlands, the infection rate is 25% in healthy pigs at abattoirs, but similar investigations elsewhere record a 10% (New Zealand) and 6% (UK) infection rate.

The serotype and phage-type distribution of *Salmonella* strains isolated from pigs, in the Netherlands from 1984 to 2001, showed that in pig serovars Typhimurium and Dublin were the most common. Monitoring of the population and herd for *Salmonella* seroprevalence in finishing pigs and sows provided a baseline for the success of future intervention and control strategies for *Salmonella* in pork. The seroprevalence of *Salmonella* in sows and finishing pigs in the Netherlands

was determined using indirect ELISAs on blood samples collected at the abattoirs. The population prevalence for finishing pigs in 1996 and 1999 was 23.7% and 24.5%, respectively, and for sows 40.5% and 60.4%, respectively. The prevalence in free-ranging finishing pigs was higher, at 44.6%, than in intensively housed finishing pigs. In 46 multiplying sow herds, the average herd prevalences were 54, 44, and 19%, respectively.

Spain
In Spain, it was found that swine farms are a reservoir of *Salmonella* serovars, particularly STM and also Rissen and Derby.[18] A study in Spain of free-range pigs[19] showed that 33% of the herds had *Salmonella,* and the prevalence was 3.3% and *S.* Anatum and STM were the most commonly isolated.

Sweden
In Sweden the prevalence of salmonellosis in food-producing animals is low because of the *Salmonella* control programs.

Switzerland
In Switzerland, there is a low rate of positivity for *Salmonella* in meat juice ELISA from diaphragm samples (4%).[20]

Thailand
In a study in Thailand[21] it was found that there was fecal prevalence of 63% and a seroprevalence of 72%, and the results were not significantly different. *S.* Rissen was found in 49% and STM in 19% of farms.

United Kingdom
In the UK advisory visits were made to farms with *Salmonella*; 15,790 samples were collected from 296 farms and *Salmonella* was isolated from 28% of the samples. STM accounted for 64% of the samples (phage types U288 and DT193) and SD for 16%.[22]

Salmonella infections (seropositive pigs) on farrow to finish farms decreased from 21 to 65 days and then increased from 65 to 165 days of age.[23] A study in the UK[24] has shown that between 1994 and 2010 the number of *Salmonella* cases has greatly decreased (360–172) and STM has been the most common over the period, although the relative proportions have decreased. Today most cases are DT193 or U288. The numbers of DT104 are much reduced and now are less than 5%. The percentage of monophasic STM has increased over the period and now reaches 25%. The percentage showing AMR to six or more antibiotics has increased from 27.3% in 1994 to 58.3% in 2010. Only 3.3% were fully sensitive to all antibiotics in 2010.

United States
American figures indicate a 10% to 13% infection rate. Salmonellas were isolated from the mesenteric lymph nodes and cecal contents of 84% of slaughtered sows in a Minnesota abattoir. These data are based on abattoir material and should be viewed with caution because of the very rapid increase in infection rate that occurs when animals are held over in yards for several days.

The cecal carriage rate was 23.0%, although carcasses were only moderately contaminated at 5.3%. The meat juice ELISA results indicated that 15.2% of tissue fluid samples were positive at the 40% cutoff level and 35.7% at the 10% experimental cutoff level. This indicates that pigs are exposed to a relatively high level of *Salmonella* during the weeks before slaughter. A national U.S. survey for fecal *Salmonella* shedding by pigs most frequently found *S. enterica* serotypes Derby, Agona, Typhimurium, Brandenburg, Mbendaka, and Heidelberg. STM is most commonly isolated from clinically ill pigs in the United States.[25] In the Midwestern United States, salmonellosis associated with the host-adapted facultative intracellular SCS is an important cause of economic loss in pig herds because of death and reduced productivity. It is the most frequent serotype recovered from pigs and is isolated from more than 95% of porcine salmonellosis outbreaks in Iowa. In a study from the United States, it was found that *Salmonella* increased from the first to the second pull by 9.2% in bacteriologic prevalence and 31.3% in serologic prevalence.[26]

Morbidity and Case–Fatality Rate
The morbidity rate in outbreaks of salmonellosis in pigs is usually high, often reaching 50% or more. The case–fatality rate in septicemia cases can be 100%.

Methods of Transmission and Sources of Infection
Salmonellas are spread by direct or indirect means. Infected animals are the source of the organisms; they excrete them and infect other animals, directly or indirectly, by contamination of the environment, primarily feed, and water supplies. The farm animal may be infected in different ways: by animal-to-animal transmission, especially of host-adapted serovars; by contaminated animal feed; and by a contaminated environment (soil, birds, rodents, insects, and water supplies). In most cases transmission is over short distances, i.e., within the same pen or room, with some transmission between rooms and buildings on the same site but with limited transmission between sites.[27] Usually infection spreads from pen to pen, but it may be over some distances caused by fomites or vectors. Transmission of *Salmonella* between swine farms by the housefly has been shown.[28] Liquid wastes from infected animals may contaminate the environment directly. Bacteria may also be disseminated during the transport of infected animals and during the holding of animals in a lairage before slaughter. In both situations, the excretion of salmonellas is exacerbated by the stress imposed.

When all animals become ill at the same time it is likely that a common source is involved such as water, feed, bedding, or contamination from one source. It is always higher in continuous flow systems in which there is no all-in/all-out systems with cleaning and disinfection. Slatted floors are much better than simple drainage gutters.

Salmonellas can be isolated from piggery wastewater, and the recirculation of contaminated water through the piggery serves as a constant source of the organism. Housing of finishing-age pigs in barns with open-flush gutters may contribute to increased shedding of *Salmonella* compared with pigs housed on partially slatted floors. Methanogenic fermentation in waste ponds does not eliminate *Salmonella* from piggery waste; acidogenic fermentation with the production of free acid can destroy salmonellas and other potential pathogens.

During slaughter, fecal contamination of the carcass commonly occurs and can be carried through all slaughter procedures up to the processing of the raw products. Airborne transmission can be a primary mode of infection of STM. Studies have shown that the organism can survive in air long enough to present a significant hazard of airborne spread.

In a study in Germany of 50 finishing herds with *Campylobacter* spp., *Yersinia enterocolitica* (YE)*,* and *S. enterica,*[29] the sampling of feces, the direct environment, indirect environment, and flies and pests revealed the information shown in Table 7-23.

Respectively, for the three groups, 22 herds (80%), 12 herds (48%), and 7 herds (12%) were positive for both *Campylobacter* and YE*,* for both *Campylobacter* and *S. enterica,* and for both *Y. enterocolitica* and *S. enterica,* respectively. *Campylobacter* and YE were found more often in the low S risk group.

This study provided evidence that the pigs' environment should be studied when implementing control studies.

Shedding and the Carrier State
In experimental infections with SD it was found that all pigs shed bacteria constantly for 2 weeks and then intermittently for several weeks.[30] Pigs given a high dose of

Table 7-23 Proportion of samples testing positive for one of the listed organisms

	Fecal	Direct environment	Indirect environment	Flies/pests
Campylobacter	38.1%	32.7	5.3	4.6
Yersinia enterocolitica	17.1	8.1	1.2	3.1
Salmonella enterica	11.2	7.1	4.1	1.5

bacteria also seroconverted, whereas those given a low dose did not. Shedding was reduced when pigs were given oral sodium chlorate, topical disinfection, and weaned younger.[31] Sows are more likely to be shedding virus than nursery or grow-finishers.[11] The shedding can be increased by a long list of stressors including mixing of groups, transport, concurrent disease, antibiotic therapy, and food deprivation.

A longitudinal study of *Salmonella* shedding in naturally infected finishing pigs has been studied, and it was discovered that most pigs shed intermittently and there are differences in pigs and within the cohorts.[32] Feeding egg yolk containing anti-*Salmonella* immunoglobulin Y may not be effective in controlling shedding of *Salmonella* in pigs.[33] In many ways shedding is more of a problem for contamination of the food chain for humans than a source of infection for other pigs. Pigs carry low numbers of *Salmonella*, but excretion will occur when there is overcrowding, and isolation for 24 hours will cause excretion. Feed withdrawal increases cortisone production and encourages shedding.

Because salmonellas are facultative intracellular organisms that survive in the phagolysosome of macrophages, they can evade the bactericidal effects of antibody and complement. Thus persistence of infection in animals and in the environment is an important epidemiologic feature of salmonellosis.

For STM the donor can be any domestic animal species, including humans, or any wild animal or bird. Although all infected adults become carriers, it is rarely for any length of time.

The carrier pig is a source of infection in the lairage at the abattoir, especially in the absence of cleaning and disinfection. STM was the most common serotype. At the start of the week following cleaning and disinfection 6% of the swabs were positive, but by the end of the week 44% were positive.[34]

Experimental infection of pigs at 7 to 8 weeks of age with a single oral dose of STM can persist continually, at least until market age. Regardless of the route of infection, SCS can persist in the tonsil and ileocolic lymph nodes, ileocolic junction and colon, and can be excreted in the feces of experimentally infected pigs for at least 12 weeks. The amount of shedding and persistence of infection is dose dependent. Low doses of SCS can be easily cleared, moderate doses can persist for at least 2 months, and high doses result in long-term carrier states. After intranasal inoculation of STM the organism rapidly appears in the intestines, suggesting that the tonsils and lungs may be important sites for invasion and dissemination of *Salmonella* species. Experimental infection with a zoonotic strain of *S.* Newport can also be established in pigs at 7 weeks of age to persist until market age (28 weeks). Long-term persistence of infection is limited generally to the palatine tonsils, the intestinal tract caudal to the midjejunum, and their lymph nodes. The prevalence of the organism in pigs creates a reservoir of infection for animals and humans. The transmission of salmonellosis in pigs can occur in a few days. Exposure to relatively low levels of SCS may result in high morbidity and initiate a severe outbreak in naive pigs within several days of being exposed to infected pigs. Only a small fraction of carrier pigs are responsible for the maintenance of the pathogen in a pig population. SCS may persist for at least 3 months in wet feces and 6 months in dried feces.

Risk Factors Predisposing to Clinical Disease

The clinical characteristics of salmonellosis in large animals vary depending on the various management systems used, the intensity of stocking, whether or not the animals are housed, and the epidemiologic characteristics of the different *Salmonella* species.

Animal Risk Factors

The response to infection varies depending on the challenge dose and the immunologic status of the animal, itself dependent on colostrum intake in neonates, previous exposure to infection, and exposure to stressors, particularly in older animals. It is generally accepted that the intervention of some precipitating factor such as transport, intercurrent disease, dosing with antimicrobials, acute deprivation of food, or other stress is usually necessary to cause the disease Salmonellosis, which is distinct from infection with *Salmonella* spp.

Infection is almost always via the mouth; thus the severity of the disease in an individual, or of an outbreak in a group, depends on the degree of contamination and the environmental conditions of temperature and dryness that determine the survival time of the salmonellas. Just as important is the influence of the host on the outcome of the infection. Many animals become infected naturally and are passive carriers; they shed *Salmonella* in their feces without clinical disease but only for the duration of their cohabitation with other infected animals. It is also possible to reproduce salmonellosis experimentally in most animals using a sufficiently large dose of a virulent strain of the organism. There still remains the common occurrence of the animal that is a subclinical carrier of the infection but develops clinical salmonellosis when exposed to stressors such as long transportation, hospitalization, severe feed deprivation, or parturition. Oropharyngeal secretions may contain salmonellas because the tonsils are rapidly colonized.

Genetic Resistance to Salmonellosis in Domestic Animals

There is evidence of a strong genetic association with resistance to salmonellosis. However, as yet, selective breeding for resistance traits is not used in control of diseases or the carriage of *Salmonella*. The control of *Salmonella* colonization of the gastrointestinal tract of food animals, particularly where intensive rearing occurs such as in pig units, would appear to be a particularly useful objective with enormous potential public health benefits. There may be a role for several inherited immunologic traits, including polymorphonuclear leukocyte function and lecithin-induced mitogenic proliferation.

Salmonella *Choleraesuis*

The epidemiology of SCS infection in pigs is well documented and has changed remarkably since the mid-1960s, when explosive outbreaks occurred that could easily be mistaken for classical swine fever. The morbidity and mortality rates were high and the disease spread rapidly through commercial pig-finishing units. These outbreaks are now rare and small in scope, largely because of the restriction of garbage feeding, much less movement and mixing of pigs through public auction marts, and disease-prevention strategies such as the use of specific pathogen-free (SPF) pigs, an all-in/all-out policy in commercial finishing units, and the vertical integration of pig-producing enterprises. This ensures a constant supply of disease-free growing hogs to finishing units and the assumption of a pyramid-type responsibility at all levels of the enterprise. The marked decline in the prevalence of swine salmonellosis coincided with the decline in and eradication of classical swine fever. However, modern methods of raising pigs in multisite production systems, using all-in/all-out management of finishing pigs, appear to have no benefit in reducing the prevalence of *Salmonella* compared with conventional farrow–finish systems.

Subclinical Infections

S. enterica does not normally cause clinical disease in pigs, but subclinical infections constitute an important food safety problem throughout the world. Comprehensive longitudinal studies of two multisite pig production systems in the United States revealed considerable temporal variability in *Salmonella* prevalence between cohorts of pigs. Cohorts of sows and individually identified growing pigs from their litters were serially sampled to determine the prevalence and serotypes of salmonellas in each stage of production based on fecal culture and feed and environmental samples. A total of 15 different serotypes were isolated from the two systems. Pig prevalence estimates ranged from 0 to 48.1%. Environmental contamination was frequently encountered despite cleaning and disinfection. Feed was only rarely contaminated. The prevalence of infection within and among cohorts of pigs was highly variable, which indicates that point estimates of *Salmonella* prevalence and serotypes are not reliable indicators of the *Salmonella* status on farms, and that uncontrolled studies of interventions to control *Salmonella* on pig farms may yield misleading results.

In the United States, new regulations regarding the safety of meat products have been implemented in response to public concerns about food-borne disease outbreaks. The salient features of the regulations are requirements for approved systems of microbiological monitoring of *S. enterica, E. coli* O157:H7, and generic *E. coli* as an indicator of contamination by gastrointestinal contents. From the perspectives of public health, regulatory compliance, and international competitiveness, *S. enterica* is the most important food-borne pathogen for the U.S. pig industry. This has resulted in longitudinal epidemiologic studies of fecal shedding of *S. enterica* in both breeding and growing pig populations.

The relationship between subclinical infections at the levels of the herd, the individual pig, and at slaughter is complex. The onset and duration of *Salmonella* shedding and the patterns of transmission between individual pigs and between different age groups during the growing period all have influence. Bacteriology and serology can be used to assess this relationship, but repeated sampling in different cohorts of animals is required to correctly assess the infection dynamics.

Longitudinal studies of STM infection in farrow–finish pig herds in Denmark reveal that the *Salmonella* occurrence varies between and within age groups within herds, even in herds with an apparent moderate-to-high infection level. *Salmonella* was predominant in weaners, growers, and finishers, and was only occasionally detected in sows and gilts. This is contrary to the results of studies in the United States, in which *Salmonella* was found to be common in sows. In the Danish study, there was a rapid increase in *Salmonella* prevalence in the nursery, which may be associated with the stressors of weaning such as change in feed, commingling of litters, and piglets being deprived of the antibodies in sow's milk before activation of their own immune response. The observation that no piglets were shedding *Salmonella* just before weaning, but 3 to 4 weeks later in the nursery between 5% and 50% of the piglets were shedding, suggests that horizontal transmission occurred in the nursery. During the finishing period *Salmonella* shedding decreased, but with considerable variation. Some pigs cleared themselves of the infection, whereas others continued shedding. Average shedding time was estimated to be 18 to 26 days. Seroprevalence peaked approximately 60 days after peak prevalence in culture. At slaughter there is a marked increase in the prevalence of *Salmonella* infection. This increase may be caused by rapid cross-contamination during transport and lairage. Rapid infection during transport, and particularly during holding, is a major reason for increased *Salmonella* prevalence in pigs. A high degree of carcass contamination occurs at slaughter from the delivery of *Salmonella*-positive pigs and cross-contamination from the slaughterhouse environment. Contaminated feed trucks also may serve as a potential source of *Salmonella* contamination. The withdrawal of feed from pigs before slaughter does not increase the prevalence of *Salmonella* colonization or the risk of carcass contamination. Over time in a swine production unit it was found that a particular genotype of *Salmonella,* if introduced into a breeding-gestation unit of a farm, would evolve only slowly over short time intervals; its spatial distribution would be limited primarily to adjacent or nearby pens.[35]

Risk factors associated with serologic *Salmonella* prevalence in finishing pig herds in the Netherlands have been examined. Feeding a complete liquid feed containing fermented by-products and the omission of disinfection after pressure washing a compartment as part of an all-in/all-out procedure were both associated with a lower *Salmonella* seroprevalence. A small to moderate herd size (<800 finishing pigs), a previous diagnosis of clinical *Salmonella* infection in the herd, the use of tylosin as an antimicrobial growth promoter in finishing feed, and herds that have more than 16% of their pigs' livers condemned at slaughter because of white spots were associated with a higher *Salmonella* seroprevalence. There was no effect on experimental *Salmonella* infection of the use of tylosin as an antimicrobial growth promoter.

In those herds in which the disease does occur, introduction is usually associated with the importation of infected carrier pigs. However, it is possible for the infection to be spread by flies and the movement of inanimate objects such as cleaning equipment and utensils. Feedstuffs do not provide a favorable environment for SCS, so food-borne infection is not common. Survival in soil and water is approximately 6 months and in slurry up to 5 weeks. Persistence in streams fouled by piggery effluent is unlikely. Susceptibility to salmonellosis in pigs is thought to be increased by intercurrent disease, especially hog cholera, nutritional deficiency of nicotinic acid, and other nutritional stress such as a sudden change in diet.

Immune Mechanisms
Early immune responses have been described,[36] and there is a higher expression of proinflammatory cytokines and T-helper type 1 cells.

In an experimental STM study, along the intestinal tract (jejunum, ileum, and colon) it was shown that there were different changes in gene expression along the tract.[37] All chemoattractant cytokines were upregulated in the ileum and jejunum and IL-8 was overexpressed in the colon.

Most information on the mechanisms of immunity to *Salmonella*, including the safety and immunogenicity of most *Salmonella* vaccines, has been done experimentally in mice. In primary infections in mice, early bacterial growth in the reticuloendothelial system is controlled by the contribution of both macrophages and polymorphonuclear cells and is affected by the virulence of the strain. In lethal infections, the early growth of the bacterins the tissues results in high bacterial numbers that lead to death of the animal. Following natural infection with *Salmonella* antibody, responses to lipopolysaccharides (LPS) and protein determinants can be detected. Anti-*Salmonella* IgM appears in serum early after infection followed by IgG. T-cells have a critical role in the later stages of primary infection. The presence of STM in mesenteric lymph nodes was examined, and it was found that there was an immune response marked by a substantial infiltration of phagocytes and an upregulation of proinflammatory genes. This resulted in a reduction of STM but not the total elimination. It might be that STM interferes with dendritic cell–T-cell interactions.[38,39]

Environmental and Management Risk Factors
Farming Practice in General
There are a wide variety of contributing factors to *Salmonella* infections. These include other livestock on the farm, herd size, previous clinical cases, bowl-type drinkers, dry feeding, pelleted feed, *Salmonella*-positive breeding herds, solid or partially slatted floors, reduced floor space allowance, persistent floor contamination, reduced floor space allowance, coinfections, porcine reproductive and respiratory syndrome (PRRS) infections, lack of hygiene and biosecurity practices, contact between pigs in adjacent pens, continuous flow systems, multiple pig suppliers, environmental temperature fluctuations, and *Salmonella*-contaminated feed. In a study of split marketing it was found that a significant increase in *Salmonella* prevalence occurs between the first and last groups to leave the finishing lots with the close-out groups posing a higher risk for *Salmonella* contaminations.

Longitudinal Dutch studies have shown that 25% of herds are never infected, 24% are constantly infected, and 50% are infected most of the time. There appear to be infection cycles when infection reaches a peak over the 2 to 4 weeks following the arrival of an infection, and between 5% and 30% may still be excreting by the end of the finishing period.

Intensification of husbandry in all species is recognized as a factor contributing significantly to an increase in the new infection rate. A typical example is the carrier rate of 54% observed in intensive piggeries in New Guinea compared with the 9% in village pigs. Any significant change in management of the herd or a group of animals can precipitate the onset of clinical salmonellosis if the infection preexists in those animals. Pelleted feed is associated with increased *Salmonella* prevalence.[40]

The association between biosecurity and *Salmonella* species prevalence on English pig farms was suggested.[41] Farms practicing biosecurity had a lower muscle tissue ELISA score than those that did not. Effective implementation of biosecurity in large herds may be the reason they have a shorter high serology period compared with smaller herds.[15]

Temperature and wetness are most important, because salmonellas are susceptible to drying and sunlight. STM can remain viable on pasture and in soil, still water, and feces for up to 7 months. Survival times of the bacteria in soil are influenced by too many variables to make any overall statement meaningful.

The survival time of *Salmonella* spp. in cold liquid manure depends on several factors, including pH of the slurry and the serotype of the organism, and can be as long as 28 weeks. Drinking water can remain infected for long periods (up to 9 months). Thus infection can be introduced by infected domestic animal carriers.

Housed Animals

In housed animals the premixing of food into a liquid form for pumping to feeding stations in piggeries is an effective way of spreading salmonellosis if infection is present in the feedstuffs and the mix is allowed to stand before feeding. Nose-to-nose contact through pens is also associated with a raised prevalence.[40]

In a longitudinal study of nucleus breeder and multiplier units in England there was an association between the *Salmonella* serovar and the immediate environment of the pens.[42] Pens holding breeding stock designed for production units were frequently positive, and herds under common ownership frequently had the same serovar combinations. Serovars from the wildlife were similar to those found on the associated premises.

Contaminated Feedstuffs

Housed animals are generally more susceptible to infection from purchased feeds. Organic feedstuffs, including bonemeal, are being increasingly incriminated in the spread of salmonellosis and although the usual figure, for example, in the UK, is 23% of consignments being infected, the figure may be as high as 70%. Most of the contamination of meat and bonemeal occurs after heat sterilization, especially if the material is left in digester tanks. Fishmeal is one of the most frequently and badly contaminated feedstuffs. For example, most of a recent increase in reported isolations of salmonellas in the United States was from *S.* Agona introduced in Peruvian fishmeal. These feed meals need to be heated at 82°C (180°F) for an hour to be sterilized. The infection of these materials may derive from antemortem infections in the animals used to make the by-product, but soiling of the material at the preparation plant or abattoir or during storage may also occur. Stored feed not of animal origin, especially grain, is also commonly contaminated by the droppings of rodents or birds that infest it, and this can lead to sharp outbreaks of salmonellosis caused by STM. All feed stores should be protected from birds and rodents. Dried milk products appear to be relatively safe. Vegetable material can also be a source of infection.

Some serotypes such as STM have been isolated from 2.8% of pig feed and feed ingredient samples and from 46% of farm feed samples tested. SCS was not isolated from pig feed.

The risk of culturing *Salmonella* with or without AMR was higher if pelleted feed was used compared with mash or liquid feed. Fecal samples from farrow to finish farms had a lower chance of testing positive than grow-finisher farms.[43]

Commercial feed is potentially a vehicle for *Salmonella* transmission.[44] In a study in the UK it was found that cereals could become contaminated, particularly with STM, and the most likely reason was the storage of grains on cattle farms with access for birds and wildlife.[45] The effect of carbohydrate composition in barley and oat cultivars was studied in vitro, and it was shown that the population of salmonellas decreased with hull-less barley cultivars and increased with oat cell cultivars.[46]

Introduction of the Infection to a Farm

Contaminated feedstuffs, carrier animals, and infected clothing of visitors and casual workers are the most common methods of introducing infection. Less common methods include free-flying birds, such as the herring gull, and nematode larvae that are already infected with salmonellas. Salmonellas have been isolated from a wide variety of wild animals, which could act as reservoirs for infection of domestic animals under certain conditions.

Pathogen Risk Factors

Salmonellas are facultative intracellular organisms that survive in the phagolysosome of macrophages and can therefore evade the bactericidal effect of an antibody. Compared with other organisms of the same family, salmonellas are relatively resistant to various environmental factors. They multiply at temperatures between 8°C and 45°C, at water activities above 0.94, and in a pH range of 4 to 8. They are also able to multiply in an environment with a low level of or no oxygen. The bacterium is sensitive to heat and will not survive temperatures above 70°C. It is sensitive to pasteurization. Salmonellas have been shown to be resistant to drying, even for years, especially in dried feces, dust, and other dry materials such as feeds and certain foods. Prolonged survival in water and soil has also been described. They are quite sensitive to beta and gamma irradiation. The O-antigen LPS of salmonellas is toxic and an important virulence factor, and immunity directed against the LPS is thought to be of major importance in the host defense against salmonellosis.

Fimbrial antigens of some *Salmonella* species have been described and characterized. The fimbriae mediate a variety of virulence factors important for the maintenance and survival of the organisms in the host and environment, including initiation and stabilization of the organism to epithelial cells, colonization of the organism to receptor sites, maintenance of persistent infection in the host by mediating selective bacterial trapping by phagocytic cells, and evasion of the host's specific immunologic defense mechanisms. The fimbriae are also useful in diagnostic tests.

Naturally occurring strains with varying virulence factors and antimicrobial susceptibility patterns can be identified in herds with endemic infection.

Antimicrobial Resistance of Salmonella

Strains of *Salmonella* spp. with resistance to antimicrobials are now widespread. Since 1990 there have been dramatic increases in the occurrence of multiresistant strains of *Salmonella* spp. in many developed countries. Of particular note has been the epidemic spread of STM DT104, which now has a worldwide distribution. AMR in zoonotically transmitted salmonellas is an undesirable but almost inevitable consequence of the use of antimicrobials in food animals. Generally, such use is legitimate. Recommendations have been made that new antimicrobials with cross-resistance to those used in human medicine should not be used for prophylaxis in food-animal production. For example, it is argued that the use of antimicrobials in food animals has been a major factor in the development of decreased susceptibility to antibiotics such as ciprofloxacin in zoonotically transmitted salmonellas. Multidrug resistant strains that also carry specific virulence factors are more likely to be of clinical significance.[47]

AMR of *Salmonella* has been a major controversial concern in veterinary medicine and human public health. Antimicrobials are used in food-producing animals for the treatment of infectious diseases and for growth-promoting effects. Their continued use has long been incriminated as a major cause of selective pressure that leads to the appearance and persistence of resistant strains. The resistance is usually to multiple antimicrobials and its existence is considered as a potential risk factor. The significance of AMR is most obvious in its impact on the treatment of human infections. If the frequency of drug resistance increases, the choice of antimicrobials for the treatment of systemic salmonellosis in humans becomes more limited. There

is also an association between drug-resistant salmonellas and the routine clinical use of antimicrobials for infections other than salmonellosis. The AMR *Salmonella* infections can complicate antimicrobial therapy of other infections; prior antimicrobial therapy allows fewer numbers of AMR *Salmonella* to cause symptomatic infections, and an increase in the proportion of *Salmonella* species that are AMR will increase the overall frequency of salmonellosis.

Infections in humans associated with AMR *Salmonella* are increasing and have become a cause for public health concern. Prospective studies in the United States claim to show that human infections with AMR *Salmonella* are increasing, and that these resistant strains can be traced to foods of animal origin. There are wide variations from country to country in the percentage of *Salmonella* isolates that are AMR. Generally, AMR among *Salmonella* is much higher in the United States than in other countries. In the UK, over a period of about 20 years, little change has occurred in the AMR patterns of salmonellas isolated from animals. Most of the resistance in STM is associated with phage-type DT204C. Serotypes other than SD and STM show low levels of resistance to most antimicrobials, with the exception of sulfonamides and tetracyclines, to which resistance is increasing.

AMR in *Salmonella* in the UK has been monitored since 1970 using disk diffusion tests. A total of 76% of all *Salmonella* isolates are still sensitive to all 16 antimicrobials used for testing.

In the Netherlands, from 1984 to 2001, monitored resistance was most common in STM. Among the strains from humans, pigs, and chickens, the level of resistance to tetracycline, ampicillin, chloramphenicol, and trimethoprim-sulfamethoxazole increased over the 17 years.

Since their introduction into veterinary medicine in Europe in the late 1980s and early 1990s, the susceptibility of several bacterial species to fluoroquinolones has increasingly been reported to be decreasing and their resistance to quinolones has been reported to be increasing. The incidence of quinolone resistance in strains of *Salmonella*-isolated pigs in Germany between 1998 and 2001 has increased.

In Canada, resistance in STM isolated from animals, animal food products, and the environment of animals to each of seven antibiotics (ampicillin, chloramphenicol, kanamycin, neomycin, streptomycin, sulfisoxazole, and tetracycline) increased persistently during each of the years from 1994 to 1997, and none of the isolates showed decreased sensitivity to ciprofloxacin.

The prevalence of STM and SCS isolates from pigs and humans that are fluoroquinolone and multidrug resistant has increased in Taiwan, and the isolates have become widespread across the country. The SCS isolates from humans and pigs were closely related genotypically, suggesting the nationwide dissemination of the organism from pigs to humans.

In Japan, Taiwan, and Thailand there is SCS resistance to many antibiotics and many are multiresistant, including fluoroquinolone and cephalosporins.[17]

AMR to an antibiotic was more common in fecal samples (98%) than environmental samples (65%),[48] and multidrug resistance followed a similar pattern (35.7% from the barns versus 56.4% in the feces).

In the UK AMR was seen in 92% of isolates tested.[22] The highest frequencies were seen with tetracyclines (T), sulfonamide compounds (SU), ampicillin (AM), sulfamethoxazole/trimethoprim (SXT), streptomycin (S), and chloramphenicol (C). Fifty-nine AMR patterns were observed with the one listed previously in 33% of cases.

In a study in the United States between 2003 and 2008, it was shown that SD had increased resistance to spectinomycin and sulfadimethoxine, as did *S.* Heidelberg (and also with florfenicol). Other species had increased resistance to spectinomycin,[7] but only two or three isolates were resistant to enrofloxacin.

In Korea, there was also a catalog of increased resistance in STM. All the isolates were resistant to 4+ antibiotics, particularly streptomycin (94.1%), tetracycline 90.1%, and ampicillin (64.7%).[49]

In a study in Belgium,[10] 7.8% of the pigs were seropositive (12 farms). STM was found in 65% and of these 65% had a tetra-resistant AMR profile.

A study in Spain of free-range pigs[19] showed that multidrug resistance (four or more) was found in 36% of the pigs. Streptomycin (46%) and tetracyclines (30%) were commonly resistant.

In a study of AMR in the United States, comparing the years 2000 and 2006, it was found that 6.2% and 7.2% of the samples (2000) and 34.2% and 52.6% (2006) of the farms were positive. STM, SD, and *S.* Agona were the most common serotypes. The most common AMR pattern was streptomycin, sulfisoxazole, and streptomycin. The proportion susceptible to all antibiotics was 38.1% in 2000 and 20.4% in 2006. The proportion resistant to three or more antibiotics was similar in both years (52.8% and 52.7%).[50] A later study at Purdue University in the United States showed similar results in AMR but they also noted that STM and others possessed multiple AMR to amoxicillin/clavulanic acid, ampicillin, ceftiofur, and cephalothin.[51]

In a study of AMR in Korea,[52] it was found that STM, *S.* Rissen, and *S.* Schwarzengrund were most commonly isolated in normal pigs, but STM was the most commonly isolated in diarrheic pigs (89.7%). The most common were PT194 and PT203. Only 3% were DT104. The most common resistance in *Salmonella* was to streptomycin,

sulfamethoxazole, and tetracycline. Nearly all STMs were resistant to more than four antibiotics.

The genetic diversity and AMR profiles of *S.* Derby in pigs in France have been described.[53] The patterns were very similar among pigs, pork, and humans. Only 15.5% *S.* Derby had no AMR. The majority (over 70%) had AMR to more than three antimicrobials. Only a few isolates had resistance to β-lactams. The pig reservoir is the second largest contributor to human salmonellosis in the EU.

A longitudinal study of salmonellas in a unit that did not use antibiotics and a conventional production unit showed a 4% AMR in the conventional unit pigs and 11.7% in their environment and 0.2% in the pigs in the antibiotic-free unit and 0.6% in their environment. There were 42 serotypes (particularly Anatum, SD, STM, and Infantis) and they were resistant to tetracycline, streptomycin, and sulfisoxazole. Multidrug resistance was found in 27% of the pigs on the conventional unit.[54]

Zoonotic Implications From Pigs

The disease has assumed increasing importance in recent years because of the much more frequent occurrence of human salmonellosis, with animal salmonellosis as the principal reservoir.[2,25] *Salmonella* is the second most important zoonosis to *Campylobacter.*

Human infection is usually through food and four are commonly isolated from swine (Typhimurium, Heidelberg, Agona, and Infantis), but there is also the possibility of direct contact as a source of human salmonellosis.[55] The important pathway today is pigs and poultry, and in Denmark this was an important source of human salmonellosis until control measures were instituted. In most instances the increase in human infections is with *exotic* serotypes other than STM that come by animal feedstuffs to pigs and chickens and then to humans through pork and chicken products. The most serious risk is that the transmitted bacteria will have acquired resistance to specific antibiotics because the animals from which they originate have been treated with the particular antibiotics repeatedly or over a long period. It is usually enteritis in humans with the exception of SCS, which often produces a septicemia.

Infected pigs leaving the farm are the major source of infection for the abattoir in which the spreading of salmonellas occurs. The longer the length of time in the lairage the greater is the chance of spread of infection.

The *Salmonella* status in lairages in Ireland in relation to the slaughter process has been assessed and it was found that the lairage, evisceration operatives, conveyor belts, and equipment in the boning hall were significant sources of contamination.[56] Cross-contamination within the plant

accounted for up to 69% of the *Salmonella* carcass contamination.

A study of the small abattoirs in Wisconsin suggested that contamination could be reduced by chilling carcasses 2 days before fabrication and by improving carcass-handling hygiene.[57]

Salmonella Serovar Typhimurium DT104

The increasingly common isolation of STM DT104 (definitive phage type) is of major concern for public health officials. STM DT104 was first reported in the UK in 1984 and emerged in the 1990s as an increasing cause of *Salmonella* infections in humans and animals in the UK and other European countries such as Germany, France, Austria, and Denmark, as well as Canada. A wide range of potential reservoirs is associated with this infectious strain, from humans to the traditional food animals such as poultry, cattle, sheep, and pigs. Over a 1-year period in Scotland it was the predominant *Salmonella* isolated from nine species of animal (cattle, pigs, sheep, chickens, pigeons, horses, cats, dogs, and rabbits). All isolates were resistant to at least one antimicrobial and 98% were resistant to multiple antimicrobials.

The organism has been found in a variety of human foods, including salami and sausages. Human infections may result from contact with farm animals and from consumption of contaminated foods such as pork, sausages, and meat pastes.

Clinical signs in humans infected with DT104 include diarrhea, fever, headache, nausea, and vomiting. Septicemia may develop in a small percentage of cases with potential complications of meningitis and foci of infection in bones and joints.

The AMR factor of DT104 is a major concern. Resistance to ampicillin, chloramphenicol, streptomycin, tetracyclines, and sulfisoxazole is characteristic of the organism. There is now evidence that DT104 is developing resistance to trimethoprim and fluoroquinolones such as ciprofloxacin, the drug of choice for treating human adult *Salmonella* infections.

Control and prevention of infection with DT104 will depend on increasing surveillance activities, investigating outbreaks, and identifying vehicles and risks of infections.

Various clinical forms of salmonellosis (gastroenteritis, bacteremia, and other systemic abnormalities) can occur in veterinarians working with *Salmonella*-infected animals.

Economic Importance

Salmonellosis is a significant cause of economic loss in farm animals because of the costs of clinical disease, which include deaths, diagnosis and treatment of clinical cases, diagnostic laboratory costs, the costs of cleaning and disinfection, and the costs of control and prevention. In addition, when the disease is diagnosed in a herd it can create considerable apprehension in the producer because of the difficulty in identifying infected animals. The veterinarian is also often in a difficult position because the diagnosis, treatment, and control of the disease are less than reliable and it is difficult to provide advice with confidence. The losses incurred by livestock producers include reduced feed efficiency and reduced weight gains or deaths because of salmonellosis.

PATHOGENESIS

Infection is much more common than clinical disease. The development of disease is very variable. Severity is influenced by serotype, virulence, host resistance, route, and quantity of the infective dose. Over 200 virulence factors have been identified. The establishment of experimental infections requires large numbers of organisms (10^8–10^{11}). The initial infective dose in the field is probably much less than that required experimentally.

The ability to invade is a requirement for pathogenesis and is encoded by a serotype-specific plasmid. STM resides as an extracellular pathogen in the tonsils independently of biofilm mechanisms.[58]

There are many virulence factors but two of the most important are genes encoding for two different type III secretion systems (T3SS) localized on the two major pathogenetic islands 1 and 2.[59] Island 1 gets into the cell and it encourages the cell to take up *Salmonella*. It is found in the tonsil (SPI-1) and SPI-2 is important for intracellular survival. The T3SS of SCS is important for the invasion of the intestine and causes enteropathy,[60] and one of its effector proteins, SipB, induces capsase-1–dependent apoptosis in macrophages and plays an essential role in *Salmonella* pathogenesis. STM SPI-1 genes promote intestinal but not tonsillar colonization in pigs[61] and start the initial influx of neutrophils.

The replication of SCS and STM is associated with their differential virulence.[62] Enteric virulence of STM is associated with rapid replication in the intestinal wall and with rapid induction of proinflammatory cytokines (tumor necrosis factor [TNF]-α, IL-8, and IL-18), whereas the systemic virulence of SCS is associated with enhanced persistence in mesenteric lymph nodes which may help it to evade host innate immunity. The induction of seroconversion and persistence of STM in pigs is strain dependent.[63]

The suppression of cytokine signaling in the palatine tonsils may facilitate the initial colonization of the palatine tonsils.[13] Septicemic isolates may have a particular pattern of invasion.[64]

The pathogenesis of salmonellosis is a complex and multifactorial phenomenon. The nature of the disease that occurs following infection is dependent on the specific combination of serovar and host known as serovar–host specificity. A range of infections is included in the term *salmonellosis*. The most common type of infection is known as "the carrier state," in which carriage of the organism is not accompanied by clinical abnormalities or clinical disease. In production animals, these carriers are of importance because they may serve as reservoirs for further spread of infection through shedding and may be present as contaminated food products.

The infected oral secretions may lead to the possibility of aerosolized secretions, feces, or contaminated dust particles.

The evolution of host-specific *Salmonella* serovars is considered to be associated with an increase in pathogenicity for the specific host. The hypothesis is based on the fact that broad-range serovars (Typhimurium and Enteritidis) are generally associated with severe disease only in young animals, whereas host-restricted serovars cause high mortality in both young and adult hosts.

The mycotoxin deoxynivalenol promotes uptake of STM in porcine macrophages coinciding with cytoskeleton reorganization.[65]

Infection

Salmonella infects animals and humans by the oral route. Following ingestion, a proportion of the organisms resists the low pH of the stomach, reach the distal ileum and the cecum, invade the mucosa, and replicate in the submucosa and Peyer's patches.

In young animals, and in adults whose resistance has been lowered, spread beyond the mesenteric lymph nodes occurs and the infection is established in the reticuloendothelial cells of the liver; from there it invades the bloodstream. These steps in the infection process can occur very rapidly. Once systemic infection has been established, salmonellosis as a disease can develop. Its principal manifestations are as septicemia, enteritis, abortion, and a group of localizations in various tissues as a result of bacteremia. It is likely that stress increases the effects of the salmonellas, as the catecholamines released will result in decreased gastric acid production and increased intestinal motility, aiding the passage of the salmonellas through the stomach and into the intestine and colon.

During the invasion process there is induction of synthesis of new proteins that enhance intracellular survival. Many epithelial types may be infected, but the Peyer's patches may be a major site of invasion.

SCS localizes in the colon on the luminal surface of the ileal M-cells of Peyer's patches. Attachment of epithelial receptors triggers microfilament-controlled uptake, vacuole formation, vacuole transport through the cell, and entry into the lamina propria via exostosis through the basement membrane. They cause mild and transient enterocyte damage. Salmonellas can synthesize over 30 proteins, which in practice can make the bacteria virtually intracellular parasites. Spread

to local lymph nodes can take place rapidly because of transport by CD18+ phagocytes to the spleen and the liver and then the macrophages and dendritic cells. At the same time there is an acute macrophagic inflammatory reaction and microvascular damage. Neither STM or SCS in a refeeding experiment produced changes in systemic TNF-α or Il-1β, although SCS reduced the growth rate by 25%.[66] Part of the first line of defense against invading pathogens is the innate immune system, and part of this is the release of antimicrobial peptides into the lumen of the intestinal tract, and a group of these are the defensins. Thus far in the pig 12 peptides have been identified, and the expressions of pBD-1 and pBD-2 have been described in the small intestine of the pig.[67,68] The porcine ileal cell line expressed increased levels of both when exposed to viable STM but not to SCS.[69]

STM does not spread effectively beyond the intestinal tract and draining lymph nodes in weaned pigs.[70] The lower cytokine signaling but higher toxicity of STM for macrophages correlates with the higher virulence for pigs of this serotype compared with SD or *S.* Infantis.[71]

Septicemia, Bacteremia, and the Carrier State

After invasion of the bloodstream a febrile reaction follows in 24 to 48 hours, and the acute phase of the disease, similar to that seen in natural cases, is present 3 to 9 days later. The early septicemia may rapidly be fatal. If the systemic invasion is sufficient to cause only a bacteremia, acute enteritis may develop, and abortion is a common final sequel in sheep and cattle. Many animals survive this stage of the disease, but localization of the salmonellas occurs in mesenteric lymph nodes, liver, spleen, and particularly the gallbladder. In experimental STM infection in pigs, the organism can persist from 6 to 8 weeks of age until market age with long-term persistence in the palatine tonsils, gastrointestinal tract, and adjacent lymph nodes. In healthy adults there may be no clinical illness when infection first occurs, but there may be localization in abdominal viscera. In either instance the animals become chronic carriers and discharge salmonellas intermittently from the gallbladder and foci of infection in the intestinal wall into the feces and occasionally into the milk. For this reason they are important sources of infection for other animals and for humans. Carrier animals may also develop an acute septicemia or enteritis if their resistance is lowered by environmental stresses or intercurrent infection. Salmonellas can reside intracellularly where they are able to escape antibody-mediated killing, and the numbers of organisms are controlled by cellular defense mechanisms involving the macrophages in which they reside.

Septicemia in pigs associated with SCS can cause pneumonia in pigs similar to the pneumonia in pasteurellosis and infection with *Actinobacillus pleuropneumoniae,* hepatitis, enterocolitis, and encephalitis.

Enteritis

Enteritis may develop at the time of first infection or at some other time in carrier animals. The best information available on the pathogenesis of enteritis is derived from the experimentally produced disease. In most instances the disease is produced by the administration of massive doses of bacteria, and this may result in the production of a different syndrome from that which occurs naturally. The pathogenesis of enteric salmonellosis is much more complex than cholera, involving an increase in mucosal cell cyclic AMP content and prostaglandin concentration, as well as an inflammatory response to the invading bacteria. Intestinal invasion is a characteristic feature of *Salmonella* pathogenesis. The organism must invade the intestinal mucosal epithelium to cause disease. Neutrophil recruitment and transmigration across the epithelium is important in the enteritis. Host-derived caspase-1 can act as a proinflammatory agent by cleaving IL-1-β and IL-18 into active molecules. SipA is a protein that *Salmonella* injects into the host cells, which has also been shown to contribute to the inflammatory response by activation of phosphokinase C. This activates the transepithelial migration of neutrophils into the intestinal lumen. Diarrhea is a result of decreased sodium absorption and increased chloride secretion caused by cholera-like and Shiga-like enterotoxins. Certain *Salmonella* outer membrane proteins also mediate cell damage. Survival within the phagocyte (O side chains, smooth LPS, and an LPS core are important) is also an important attribute of virulent salmonellas.

STM requires a functional type III secretion system encoded by SPI-1 to cause diarrhea. The SPI-1 secretion system mediates the translocation of secreted effector proteins into target epithelial cells. These effector proteins are key virulence factors required for *Salmonella* intestinal invasion and the induction of fluid secretion and inflammatory responses.

Although there is sufficient obvious enteritis to account for the diarrhea that characterizes the disease, there appear to be other factors involved. For example, it has been shown experimentally that in *Salmonella* enteritis there is stimulation of active chloride secretion combined with inhibition of sodium absorption, but invasion of the mucosa is not essential for these changes to occur. These observations are of interest in light of the known hyponatremia that characterizes the disease. In pigs, ulcerative lesions may develop in the intestinal mucosa and may be of sufficient size to cause chronic intermittent diarrhea. In pigs it has also been observed that villous atrophy is a sequel to infection with SCS.

In pigs, most clinical cases of salmonellosis are associated with SCS or STM. SCS is host-adapted to pigs, causing a systemic, typhoid-like disease. STM is not host-adapted to pigs, and infection results in a localized enterocolitis.

In the **pig** the development of enteritis associated with SCS begins 36 hours after infection with the appearance of erosions and edema of the cecal mucosa. At 64 hours the wall is thickened and there is diffuse caseation overlying the erosions. Microvascular thrombosis and endothelial necrosis in the submucosa and lamina propria, probably caused by endotoxins, are important early lesions in porcine salmonellosis. This then facilitates the ischemia that results in the mucosa mediated via IL-1. They have direct effects on the tissues or have effects on a variety of cytokine mediators. The necrotic membrane sloughs at 96 hours, and at 128 hours all function is lost, and the entire intestinal wall is involved in the inflammatory process with the muscular coat obliterated by 176 hours. The colon is usually the major organ affected in STM infections in pigs, causing either focal or diffuse necrotizing colitis. The organisms proliferate in the intestine, invade the intestinal epithelium, stimulate fluid secretion, and disseminate from the intestine to mesenteric lymph nodes and other organs. SCS invades enterocytes by penetration of the brush border, resulting in focal loss of microvilli, and the bacteria are endocytosed into membrane-bound vacuoles. Experimental infection of ileal–gut loops of pigs with *S. enterica* results in preferential bacterial adherence to M-cells within 5 minutes, and by 10 minutes, bacterial invasion of the apical membrane occurs in M-cells, goblet cells, and enterocytes. Experimental perfusion of porcine livers with polysaccharide or live SCS results in the release of mediators that mediate biological activities that have an important role in reducing the severity of bacterial infections.

CLINICAL FINDINGS

The disease is most satisfactorily described as three syndromes, classified arbitrarily according to severity as **septicemia, acute enteritis, and chronic enteritis.** These are described first, but the differences between the animal species are sufficiently significant to justify describing the disease separately in each of them. There are no significant differences between infections associated with the different *Salmonella* species.

Porcine Salmonellosis

In pigs, the disease varies widely and, although all forms occur in this species, there is often a tendency for one form to be more common in any particular outbreak. In the septicemic form in pigs affected by SCS a dark red to purple discoloration of the skin is evident, especially on the abdomen and ears, and subcutaneous petechial hemorrhages may also be visible. Nervous

signs, including tremor, weakness, paralysis, and convulsions, may be prominent and occur in a large proportion of affected pigs. The case–fatality rate in this form is usually 100%.

A semispecific entity occurring in pigs up to 4 weeks old is manifested by meningitis and clinical signs of prostration and clonic convulsions.

In the acute form there is also a tendency for pulmonary involvement to occur, but the main feature of the disease is enteritis, with pneumonia and occasionally encephalitis present as only secondary signs. In some situations, pigs dying of septicemia more commonly yield SCS, whereas those with acute enteritis are usually infected with STM. Acute pneumonia is a common accompaniment of this form of the disease in pigs, and nervous signs and cutaneous discoloration as described in the septicemic form may also be present. Meningitis caused by STM DT104 in 1-week-old piglets has been reported. Incoordination, paralysis, opisthotonus, paddling, and polyarthritis resulting in runts and deaths were common. Bronchopneumonia resembling pasteurellosis, and pleuropneumonia resembling *A. pleuropneumoniae* infection can be associated with SCS.

A syndrome of rectal stricture occurs in feeder pigs as a sequel to enteric salmonellosis associated with STM and is described under that heading.

Septicemia

This is the characteristic form of the disease in young pigs up to 4 months old. Commonly, there is profound depression, dullness, prostration, high fever (40.5–42°C; 105–107°F), and death within 24 to 48 hours. There is often a soft, moist cough with dyspnea. There may be cyanosis of the extremities. Diarrhea is not a feature until 3 to 4 days. Rarely nervous signs may be seen. Pregnant sows may abort. Morbidity is usually low (<10%), but case mortality rates may be high.

Acute Enteritis

This is the common form in adult animals of all species. It is most commonly associated with STM. There is a high fever (40–41°C; 104–106°F) with severe, fluid diarrhea; sometimes dysentery; and occasionally tenesmus. The fever often subsides precipitously with the onset of diarrhea. The feces are often a watery yellow without mucus or blood initially; have a putrid smell and contain mucus, and sometimes blood; have fibrinous casts, which may appear as complete tubular casts of intestine; and have intestinal mucosa in sheets or casts. There is complete anorexia and in some cases increased thirst. The heart rate is rapid, the respirations are rapid and shallow, and the mucosae are congested. Pregnant animals commonly abort. The case–fatality rate without early treatment may reach 75%. In all species, severe dehydration and toxemia occur and the animal loses

weight, becomes weak and recumbent, and dies in 2 to 5 days. Newborn animals that survive the septicemic state usually develop severe enteritis, with diarrhea becoming evident at 12 to 24 hours after the illness commences. If they survive this stage of the illness, residual polyarthritis or pneumonia may complicate the recovery phase.

Chronic Enteritis

This is a common form in pigs following a severe outbreak. Although chronic enteritis may occur initially, it usually succeeds an acute episode. Episodes may occur at regular intervals. Affected pigs may have pyrexia, decreased feed intake, and are dehydrated.

CLINICAL PATHOLOGY

There is heterogeneity in diagnostic accuracy revealed by using a review/metaregression approach.[72]

A definitive etiologic diagnosis of salmonellosis depends on culture of the organism from feces, blood, and other body fluids or tissues. Feed and water samples may also be cultured to determine the source of the organism. Numerous serologic tests are available but lack sensitivity and specificity.

Clinicopathologic support helps:
- Diagnosis in the individual animal, when its treatment and prognosis depend on a definitive diagnosis
- Diagnosis of a herd problem to ensure that expensive herdwide control measures are not implemented unnecessarily

The diagnostic techniques available are as discussed in the following sections.

Bacterial Culture and Detection

This is the only way of making a definitive etiologic diagnosis of salmonellosis and of exactly determining the serotype. However, culturing the organism may be unreliable for various reasons, including the method used to collect samples, the amount of sample submitted, variation in the shedding of the organism, and the bacteriologic method used. A major complicating factor is the occurrence of apparently healthy carriers, which shed the organism intermittently in the feces, and silent carriers, which do not shed but harbor the organism in mesenteric lymph nodes or in the mucosa of the cecum and colon. The difficulty varies according to genotype. The conventional drag swab method probably gives a better recovery than the Swiffer wipe method.[48]

A discussion of enrichment media suggests that the modified semisolid Rappaport–Vassiliadis medium (MRSV) is beneficial in isolating *Salmonella*.[73] In a study in Japan it was shown that this method of culture was as good as flow-through immunocapture PCR.[74]

Fecal Culture

The culturing of salmonellas from feces is common but can be unreliable. This difficulty is noticeable with SCS infections in

pigs. The difficulties relate to dilution by diarrhea and the heavily contaminated nature of the sample; a sample of fluid feces collected in a container is superior to a fecal swab. Clinical laboratories generally require at least 48 hours for presumptive diagnosis of *Salmonella* spp. in feces. Biochemical and serologic confirmation of the genotype and the antibiogram may require an additional 24 to 48 hours. The use of extended enrichment of fecal samples with tetrathionate broth is superior to primary enrichment for detection of salmonellas from cattle.

Multiple Fecal Cultures

An antigen-capture ELISA with enrichment culture for detection of salmonellas from fecal samples is more rapid than routine culture techniques, with a test sensitivity of 69% and specificity of 97%.

DNA Probes

The use of the DNA probe encoding a well-conserved VG of the *Salmonella* virulence plasmid is a sensitive method for screening large numbers of samples to detect potentially virulent *Salmonella* spp.

A reverse transcriptase-polymerase chain reaction (RT-PCR) may be a useful alternative to culture for screening large numbers of samples particularly when *Salmonella* prevalence is low.[75]

Serology

In a study of pulsed-field gel electrophoresis (PFGE) subtypes there was a correlation of serotype to PFGE subtype. PFGE using XbaI restriction provided a possible method for screening and identifying swine *Salmonella* serotypes.[76]

Serum Enzyme-Linked Immunosorbent Assay

The Danish mix-ELISA (DME) is a combination of LPS extractions of SCS (O antigens 6 and 7) and STM (O antigens 1, 4, 5, and 12), used to assay serum samples collected from live animals on the farm or from meat juice (collected when a meat sample from the carcass is frozen and thawed). The DME was designed for surveillance and is recommended for monitoring herds and detecting high levels of *Salmonella* infection. The test has been the basis for national *Salmonella* control programs in Denmark (SALINPORK), Germany, and the UK and is being considered in the Netherlands and Belgium. In a series of studies using pigs experimentally infected with either STM or *S. infantis*, the sensitivity of the DME was more than 95% and the specificity 100% compared with culture used to determine the positive or negative status of the pigs. There is a strong association between herd serology and the prevalence of *Salmonella* measured at three sampling sites: cecal content, pharynx, and carcass surface. A comparison of three commercial ELISAs showed that the results from the three different tests were very different.[77]

The meat juice ELISA results are always lower than the serum ELISA results.[78]

Indirect Tests

These include a total and differential white cell count. A leukopenia, neutropenia, and severe degenerative left shift are highly suggestive. There is also a marked hyponatremia and a mild hypokalemia.

A positive diagnosis depends on culture of the organism, usually from feces but possibly from blood in the septicemic stage. If serologic diagnosis is available a serum sample should also be submitted. Indirect tests are very valuable and, if laboratory availability is good, a total white cell count and estimation of serum sodium levels should be undertaken urgently. A presumptive diagnosis is often all that can be stated, and this may be supported by a herd diagnosis—a diagnosis that the disease or infection is present in the herd and that it is presumed that the subject case is one of the group.

Herd Diagnosis

A serologic examination of a sample of animals is a first step. A completely negative serologic test would indicate that the infection is not present. Positive results indicate a need for further examination, and periodic fecal cultures at 15-day intervals using enriching media should be undertaken. When STM is the causative bacteria, the feces of other species of animals on the farm should be examined, because ducks, dogs, horses, pigs, sheep, and cattle may be sources of infection for each other. It is always advisable to examine the drinking water and feed for evidence of infection.

Detection of Clinically Normal Carrier Animals

The most difficult diagnostic problem in salmonellosis is the detection of the clinically normal carrier animal.

The reliability of diagnosis based solely on culture of fecal swabs is not high and represents the major difficulty in detecting carriers. A combination of fecal culture and serologic tests offers some improvement in accuracy, but even with the agglutination or complement fixation (CF) tests, accuracy is insufficient.

Determination of Prevalence of Infection in Population of Animals

It is particularly important to determine the prevalence of *Salmonella* infection in a population of pigs. Pork and pork products are important sources of nontyphoidal *Salmonella* for humans consuming these products if they are not handled with care. Pigs entering the abattoir that are carriers of *Salmonella* are the most important source of carcass and product contamination. To be able to estimate the number of infected animals entering the abattoir and estimate the size of the *Salmonella* problem in pig herds, the population and herd level prevalence of *Salmonella* have to be investigated. An estimation of the prevalence of *S. enterica* infection in finishing pigs in Iowa was done using on-farm fecal cultures, culture of on-farm necropsy and abattoir-collected samples, and serum ELISA using serum exudate (meat juice). Fecal samples collected on the farm detected only 13.3% of all positive pigs necropsied on the farm. Abattoir and on-farm results combined, the fecal sample detected 57.4% of positive pigs. Abattoir-collected samples provided prevalence estimates much higher than on-farm collected samples (39.9% versus 5.3%). Thus fecal samples have a low sensitivity for detecting infected pigs, and abattoir-collected samples overestimate the on-farm *S. enterica* prevalence. A study of subiliac lymph nodes at slaughter showed that they had a low rate of detection compared with the on-farm incidence.[79] Pigs can become infected during routine testing or holding periods during marketing when exposed to relatively low numbers of *Salmonella* in the preslaughter environment. Intervention at this step on the production process may have a major impact on the safety of pork products.

The probability of detecting *Salmonella* in seropositive pig herds with a correlation between serologic and fecal culture results was examined in pig herds as part of an international research program sponsored by the European Commission, Salmonella on Pork. Samples were examined from herds in Denmark, the Netherlands, Greece, and Germany. The serologic herd status was determined by blood sampling 50 finishing pigs. There was an increased probability of recovering *Salmonella* with increasing within-herd seroprevalence, but the correlation was only moderate.

NECROPSY FINDINGS

Septicemia

There may be no gross lesions in animals that have died peracutely, but extensive submucosal and subserosal petechial hemorrhages are usually evident. The petechiae are very prominent and may give the kidney the "turkey-egg" appearance usually associated with hog cholera. A rhomboidal area of gastric mucosal infarction is usually present in pigs sometimes with frank hemorrhage. Congestion and hepatization of lung tissue may also be present with bronchopneumonia. Skin discoloration is marked and, depending on the severity of the case, this varies from extreme erythema with hemorrhage, to plaques and circumscribed scabby lesions similar to those of swine pox. There may be infarction of the tips of the ears, which may slough completely. The lymph nodes are often enlarged, moist, congested, and hemorrhagic. The liver may have focal areas of necrosis and the wall of the gallbladder may be thickened and edematous. In some cases the necropsy findings may include splenomegaly and pinpoint white foci in the liver (paratyphoid nodules). The histologic lesions are extensive, but none specific with the exception of the somewhat granulomatous character of the older paratyphoid nodules. There are areas of coagulative necrosis, with neutrophils and histiocytes. There may be fibrinoid thrombi in the venules of the gastric mucosa, in cyanotic skin, glomerular capillaries, and pulmonary vessels. The spleen and lymph nodes show reticular cell hypoplasia and histiocytosis.

Acute Enteritis

The most common lesion is an enterotyphlocolitis usually involving the ileum, cecum. and spiral colon. In the past, in the UK, infection with SCS has been associated with significant "button ulcers" in the affected segments, particularly near the ileocecal-colic junction. The mesenteric lymph nodes are consistently markedly enlarged and moist. The stomach contents are usually scant and bile-stained. Often cecal or colonic contents are black or are sand-like and gritty.

Some of the changes associated with the septicemic form are often present, but the most consistent damage is found in the large and small intestines. The character of the inflammation here varies from a mucoenteritis with submucosal petechiation to diffuse hemorrhagic enteritis. Congestion and infarction of the gastric mucosa is often seen. Infections with STM are characterized by severe necrotic enteritis in the ileum and large intestine. The intestinal contents are watery, have a putrid odor, and may contain mucus or whole blood. In cases that have survived for longer periods, superficial necrosis and fibrin exudation may proceed to the development of an extensive diphtheritic pseudomembrane and fibrin casts. The mesenteric lymph nodes are enlarged, edematous, and hemorrhagic. The wall of the gallbladder may be thickened and inflamed.

Histologic lesions are most common in the cecum and spinal colon but may be found elsewhere. The *lamina propria* and the submucosa are typically infiltrated by neutrophils and then macrophages and a few lymphocytes. Fibrin thrombi are frequently observed in the capillaries. There may be a fibrinonecrotic crust on the surface of the mucosa often containing other bacteria and *Balantidium coli.*

Survivors of the septicemic and acute enteric forms of salmonellosis may develop rectal strictures. Lesions in pigs with *S.* Heidelberg are mild or nonexistent.

Chronic Enteritis

In pigs the lesions in chronic enteritis are diffuse. Less commonly the lesions are discrete in the form of button ulcers, occurring most frequently in the cecum around the ileocecal valve. The mesenteric lymph nodes and the spleen are swollen. In all species,

chronic pneumonia and a variety of other localized inflammatory processes such as polyarthritis and osteomyelitis may be found.

DIAGNOSIS

Clinical signs and lesions may lead to a presumptive diagnosis of salmonellosis, but all porcine septicemias are superficially similar.

Salmonellas are present in the heart, blood, spleen, liver, bile, mesenteric lymph nodes, and intestinal contents in both septicemic and acute enteric forms. In the chronic form, the bacteria may be isolated from the intestinal lesions and less commonly from other viscera. Culture is more successful if enrichment media such as tetrathionate broth are used. In pigs experimentally infected with STM and SCS the organisms can be detected with peroxidase–antiperoxidase immunoenzymetric labeling and Immunogold techniques. Surveys that set out to determine the percentage of carriers in animal populations by examining abattoir material show that by far the largest number of isolations are made from the lymph nodes draining the cecum and lower small intestine.

Samples for Confirmation of Diagnosis

- *Bacteriology:* Ileocecal lymph node, ileum, colon, spleen, lung, liver, culture swab from gallbladder (CULT). It requires brilliant green bismuth sulfite, blood agar, or MacConkey agar. Enrichment is not required unless there is fecal contamination or mishandling. In these cases, tetrathionate broth at 42°C to 43°C is the enrichment medium of choice. Selenite broth is inhibitory for SCS. Ileum is not good for septicemia confirmation.
- *Histology:* Formalin-fixed samples from these tissues plus kidney, stomach, brain Other tests are not used routinely. PCR has a high cost and lacks sensitivity without preenrichment.

Serology (ELISAs) is used for herd diagnosis. Mixed ELISA meat juice is most important for assessing infection at slaughter.

Note the zoonotic potential of these organisms when handling carcasses and submitting specimens.

DIFFERENTIAL DIAGNOSIS

The clinical diagnosis of salmonellosis is difficult because of the number of diseases that resemble each form of the disease. Salmonellosis is characterized by septicemia in young animals and acute and chronic enteritis in adults, although acute enteritis can occur in neonates. Thus the septicemic form of the disease must be differentiated from all other causes of septicemia and the enteric forms from all other causes of diarrhea in both young and adult animals. At necropsy the isolation of salmonellas from tissues and intestinal contents, although suggestive of the presence of salmonellosis, does not of itself confirm the diagnosis, and care must be taken to ascertain whether other disease is present.

Pigs

Septicemic salmonellosis occurs in pigs 1–4 months of age and is characterized by fever, depression, skin color changes, diarrhea, and rapid death.

- **Hog cholera**, **African swine fever, coliform gastroenteritis of recently weaned pigs**, and **pasteurellosis** may resemble septicemic salmonellosis very closely and laboratory examination is usually necessary for identification.
- **Acute erysipelas** is characterized by typical skin lesions, fever, swollen joints, and typical lesions at necropsy.
- **Swine dysentery** is characterized by mucoid feces with dysentery and typical lesions of the large intestine.

Acute enteritis

The differential diagnosis of diarrhea includes:

Swine dysentery

Proliferative enteropathy

Coronaviruses

Circovirus

Colibacillosis

Coccidiosis

Trichuriasis

TREATMENT
Primary Treatment: Antimicrobial Therapy

The choice of antibiotic should depend on the use of an antibiogram and the practitioner's previous knowledge and experience. In most salmonellas AMR is plasmid mediated.

The DT104 is especially worrying because it has a chromosomally integrated multiple AMR.

The use of antimicrobials for the treatment of clinical salmonellosis is controversial and different approaches to the problem exist among veterinarians. The controversy centers on two parts of the response to treatment and which view is taken depends to a large extent on the experience one has with respect to them.

The first issue is that of the success of treatment in saving the lives of clinically affected animals. It is the author's experience that early treatment with broad-spectrum antimicrobials is highly effective in reducing mortality and returning animals to normal function. It is generally agreed that treatment must be early, because delay means loss of the integrity of intestinal mucosa. A common pattern of response to treatment in a herd is that the first one or two cases are regarded lightly by the owner and they are treated 24 to 48 hours after diarrhea begins. When these cases die, a more prompt regimen is instituted in which the farmer has the approved drug on hand and begins treatment as soon as diarrhea with fever is observed. The cure rate is then likely to be around 100%.

The second issue in the controversy about antimicrobial therapy for salmonellosis is the risk of inducing "carrier" animals. In humans and in animals there is some evidence that antimicrobials can prolong the duration of the period after clinical recovery during which the causative bacteria can be isolated from the intestine. It is accepted that this can occur and that the use of antimicrobials can theoretically contribute to the spread of disease. However, because of the way in which animals are kept, and because they constantly ingest contaminated pasture or other feed, there is an almost universal carrier segment in animal populations, and to regard another survivor from salmonellosis as a significant contributor to the carrier frequency seems an exaggeration. In many situations this appears to be the correct view, but in other situations an animal can become infected, for example, in a veterinary hospital or at an exhibition or show, recover clinically with treatment and, after returning to its parent herd, initiate an outbreak of fatal and debilitating salmonellosis. Both epidemiologic patterns occur, and they seem to occur in different places, so that the most appropriate attitude to take seems to be the one that fits local circumstances. In an area in which only sporadic cases of the disease occur in herds, it would be professionally negligent not to treat infected animals with appropriate antimicrobials. In endemic areas, recovered animals should not be sent into herds until they are known not to be carriers.

Other related issues are the creation of drug-resistant strains of the bacteria and the effect on the normal intestinal flora that results from oral medication. The problem with resistant strains would not have become significant if only individual animals had been treated, but mass medication of in-contact animals and prophylactic treatments have generally resulted in a large population of resistant strains.

Oral treatment in pigs is recognized as a satisfactory treatment. In summary, antimicrobials are recommended for all clinically affected animals (see later). The choice of antimicrobials depends on a test of drug sensitivity in each case or outbreak, but failing this the following generalizations can be applied.

For pigs with septicemic salmonellosis, trimethoprim-sulfadoxine is recommended, along with a combination of mass medication of the water supply with chlortetracycline and sulfamethazine (75 mg of each per liter of water). Where large numbers of pigs are affected, mass medication via the feed or drinking water is usually practiced. Because sick pigs do not eat, water treatment is necessary, and if drugs are unpalatable individual treatment is the last recourse. Drugs that dissolve readily and are palatable are therefore

in demand. Experimental disease of pigs with *S. typhisuis* can be controlled by the inclusion of low concentrations of chlortetracycline, penicillin, and sulfamethazine in the feed.

CONTROL

It has become clear that successful interventions must be based on a range of preventive approaches.[80] Although in theory increased hygiene and establishing all-in/all-out production should reduce the level of *Salmonella* in practice, it is not easy to do so.[81]

Control of *Salmonella* in pigs can be divided into three main areas. Herd interventions are not sufficient to reduce *Salmonella* to <1% the desired target of the Danish schemes.[82] The cost-effectiveness of abattoir interventions varies with the size of the plant, and the most likely to succeed are steam vacuum and steam ultrasound. As yet these have not been tested for effectiveness.

Preventing Infection From Entering the Herd (Biosecurity)

In a simulation study in France, it was found that if the movement of animals was based on the level of prevalence, and movement was not allowed from herds with high herd prevalence to those of low herd prevalence, then *Salmonella* could be significantly reduced.[83]

Avoidance of infection is the major objective but is not easily achieved. The principal sources of infection are carrier animals and contaminated feeds containing foodstuffs of animal origin.

Breeding stock should only be bought from herds that are certified free if the receiving herd is free from salmonellas. Buying in gilts or sows is a much greater risk than buying in boars.

For the pig finishers the following rules apply:

- Introduce the animals directly from the farm of origin. Avoid auction marts, saleyards, and public transport, all of which are likely to be sources of infection. Ensure that the farm of origin is free of salmonellosis. Finishers receiving growers that were positive had a much higher level of seroprevalence in the finishers than those that did not.
- If possible, purchase animals when they are older to provide an opportunity for specific and nonspecific immunity to develop. Animals from vaccinated herds are desirable but not always available.
- The premises of dealers, saleyards, and transport vehicles must be under close surveillance, and the need for frequent vigorous disinfection must be stressed. With decreasing levels of infection it is important that the infections in transport systems and the lairage are managed.[84] Introduce only those animals likely not to be carriers. Unfortunately the detection of carriers is inaccurate and expensive. To have any

confidence in the results, fecal samples for culture must be submitted on at least three occasions. Even then, occasional carriers with lesions in the gallbladder or tonsils will escape the net and be capable of reviving the disease on the farm or transferring it to another one. Rodent and bird control is essential. Control of access to potential human fomites is also important, and they should be provided with clean protective clothing and boots before entering the herd. The significance of various environmental sources is often neglected and should be studied more intensely, such as lairages and truck-washing facilities.[85]

Increased Hygiene to Prevent Intraherd Spread

Possibly the most effective method for the control of *Salmonella* infection in weaners appears to be segregated early weaning (no extra benefit before 3 weeks) into clean accommodations.[86]

When an outbreak occurs, procedures for limiting spread, as set out next, need to be strictly enforced, and medication of affected groups, and of susceptible groups at high risk, must be performed. The drugs to be used are those listed under treatment as well as the choice of the individual drug depending on its efficiency and cost.

- **Identify carrier animals and either cull them or isolate and treat them vigorously.** Treated animals should be resampled subsequently to determine whether a "clean" status has been achieved.
- **The prophylactic use of antimicrobials** such as oxytetracycline in the feed at the rate of 10 g/tonne, or chlortetracycline in the drinking water at the rate of 55 mg/L, is used but not recommended, because results are poor and there is a risk of developing resistant strains.
- **Restrict the movement of animals around the farm** and limit the infection to the smallest group. Pasture and permanent buildings are both important, although the major source of infection in most cases is the drinking water.
- **The water supply should be provided in troughs that are not susceptible to fecal contamination.** Static drinking water or pasture may remain infected for as long as 7 months.
- **Rigorous disinfection of buildings is important.** An all-in/all-out policy should be adopted and steam cleaning and chemical sterilization performed after each batch of animals. Piglets can be reared free of *Salmonella* infections up to 6 weeks of age by removing the piglets from infected herds to isolation facilities when they are weaned at 10 to 21 days of age. The movement of pigs either at weaning, from the nursery, or from the grower unit to newly built or rigorously cleaned and disinfected

finishing units with a known history of *Salmonella* infection is highly successful. If economics permit, individual pens for calves are beneficial. Where calves are reared indoors these pens are common and economical. Pig houses need especially careful treatment. Dirt yards present a problem, especially those used for sheep and calves, but, provided they can be kept dry and empty, two sprayings, 1 month apart, with 5% formalin are recommended. Disinfection greatly reduces the numbers but does not eliminate the organism,[48] irrespective of which disinfectant is used.

- **Suitable construction of housing is important.** Impervious walls to stop spread from pen to pen, pen design to permit feeding without entering the pen, avoidance of any communal activity, and slatted floors to provide escape routes for manure all assist in limiting the spread of enteric diseases. Deep litter systems are satisfactory provided they are kept dry and plenty of bedding is available. With pigs the opportunity for oral–fecal cycling of the organism and buildup and spread of infection within and between groups must be kept to a minimum. Pen design and the environment should encourage proper eliminative behavior and good pen hygiene. Drinkers should be sited at one end of the pen, preferably on a narrow end with oblong pens, to encourage defecation in this area. Wet or damp areas of the floor in other parts of the pen will encourage defecation and urination there and should be eliminated. Drinkers of the nipple type rather than bowls are preferable for hygienic reasons. Communal dunging alleys increase the possibility of spread, especially during the cleaning procedure, and the trend is toward slatted or meshed areas over a channel. A totally slatted or mesh floor for pigs from weaning until 10 to 12 weeks of age will markedly reduce the opportunity of oral–fecal cycling of organisms in this age group, which is especially susceptible to enteric disease. Feeders should allow the ingress of the pig's head and should be constructed to avoid fecal and other contamination of feed. Pigs need to be grouped according to size, and overcrowding, which may result in improper pen hygiene, must be avoided. Space requirements vary according to pen and housing design but generally fall in the region of 0.3 m^2 for recently weaned piglets to 0.6 to 1 m^2 for market-size pigs. In conventionally floored or partially slatted floored pens, approximately $\frac{2}{7}$ of the area should be available for the dunging area. The construction of the pen should allow for easy and efficient cleaning. In problem herds an especial vigilance for the

occurrence of enteric disease is needed following the breakdown of pen hygiene on very hot days.

- **Disposal of infective material should be done with care.** Carcasses should be burned or, better still, sent to an institution for diagnosis, rather than to a rendering plant to be converted into still more contaminated bonemeal. Slurry decreasing the storage time and manure for disposal should be placed on crops rather than on pasture. Slurry does not constitute a danger via hay, and salmonellas do not survive silage making. When slurry is used on pasture it should be stored for at least a month beforehand and even longer if silo effluent is included. Slurried pasture should not be grazed for 1 month, and for young animals a 6-month delay is recommended. Pig slurry is most dangerous and should always be avoided. Urea and to a lesser extent ammonia may be used to disinfect *Salmonella*-contaminated slurry, decreasing the storage time required while increasing its fertilizer value.[87]
- **All persons working on infected premises should be warned of the hazards to their own health.** Other peripatetic species, especially dogs, should be kept under close restraint. Restrictions on staff movements within the unit may also prevent cross-infection.
- No moving back of animals from pen to pen is essential.

Reducing Exposure to Pathogens
- Promoting appropriate personal hygiene
- Using effective methods for cleaning and disinfection
- Controlling the flow of human and animal traffic
- Implementing protocols for prompt identification of patients with signs of contagious disease
- Controlling birds, rodents, and flies

Avoiding Increasing Susceptibility to Pathogens
- Controlling ambient temperature
- Using antimicrobials appropriately
- Aiding in establishing normal intestinal or rumen flora
- Controlling endotoxemia

Monitoring Effectiveness of the Infectious Disease Control Program
- Bacterial culture of fecal samples of animals admitted to the hospital
- Regular culture of environmental samples

Feed Interventions to Aid the Pigs' Defenses
Physical Form of the Feed
Herds that use pelleted feed have on average three times the seroprevalence of herds that mix their own feed. This is surprising because most pelleted feed follows stringent rules for production and home-mixed diets use nonheat-treated soya. Home-mixed feed and coarse ground feed protect pigs against *Salmonella*, although there is a loss of productivity.

The addition of 25% of nonheat-treated, nonpelleted wheat or barley does have a beneficial effect in those herds with a high seroprevalence. Meal feeding increased the viscosity of the stomach contents compared with pelleted feed and a higher content of organic acid producing lactobacilli were found in the stomach. Increasing the amount of barley also has a protective effect.

The use of organic acids in dry pelleted feed could reduce the seroprevalence in finishers, and 0.8% of formic acid or lactic acid could also reduce *Salmonella* prevalence.[88] The same can be achieved by placing organic acids in drinking water. They seem to be more beneficial in weaner diets than in finisher diets. These effects are probably much reduced in sows. In a study of direct-fed microbials or organic acids, there was no effect on the treatments except for the in-feed antibiotic.[89]

The effect of organic acids on *Salmonella* colonization and shedding in weaner pigs in a seeder model has shown that the organic acids could reduce fecal shedding and numbers of coliforms and salmonellas in cecal digesta. Colonization of tonsils and ileocecal colic lymph nodes by salmonellas was not affected.[90]

Liquid feed for finishers seems to reduce the level of seroprevalence by two-thirds compared with herds using dry feed. The key seems to be to keep the pH of the feed below 5.5 so that the piped feed is also acidic by encouraging fermentation or by the addition of formic acid.

Oxygenated drinking water enhances the immune activity and response of pigs exposed to STM.[91]

Organic Acids
In a study of the effects of a mixture of formic acid and lactic acid (both 0.4% w/v) or 1.0% lactulose influenced the numbers of *Salmonella* in the ileum and cecum of experimentally challenged pigs.[92]

The administration of organic acids to drinking water during the last 2 weeks before slaughter on *Salmonella* shedding by slaughter pigs and the contamination of carcasses was shown to be ineffective in reducing the levels of bacteria.[93] The effect of the addition of organic acids in drinking water or feed during part of the finishing period on the prevalence of *Salmonella* in finishing pigs has been described.[94] Pigs received a mixture of acids (lactic, formic, and propionic) or potassium diformate. At the end of the trial the proportion of seropositive pigs was less with either treatment than in the controls. The frequency of fecal shedding was also lower.

Heat treatment of feed is an effective procedure for pigs. Heating during pelleting greatly reduces the bacterial content of feed, and the special treatment is worthwhile because of the very high proportion of animal-derived feeds that are infected. The availability of such feeds guaranteed to be *Salmonella*-free would be an advantage.

Feed Withdrawal
As feed withdrawal times increased before slaughter, so the numbers of salmonellas increased as the numbers of lactobacilli decreased.[95]

Other Options
In the future there is the potential use of bacteriophages to reduce the populations of salmonellas,[96] but this study showed that they were at very low levels in the commercial swine population. Experimental phage cocktail therapy of slaughter pigs significantly reduced the cecal STM concentrations and reduced numerically the ileal *Salmonella*.[97]

It may be possible to use 2-nitro-1-propanol and 2-nitroethanol with added chlorine as feed additives to control *Salmonella*.[98]

Immunization
Salmonella Vaccinology
A successful vaccine should prevent colonization of the host, shedding of the organism to the environment, the development of the carrier state, and the development of the clinical state.[80] At present no vaccine fulfills all these criteria, but vaccines can reduce the on-farm pressure.[99-103] An attenuated vaccine reduced STM numbers in a model simulating preslaughter stress.[104]

A live attenuated STM expressing swine interferon (IFN)-α has antiviral activity and alleviates clinical signs of TGE. The result indicates the value of attenuated *Salmonella* vaccines as delivery systems of cytokines.[105]

An inactivated STM bacterin was shown to reduce the shedding and horizontal transmission of STM as well as the proportion of shedders or carriers at slaughter.[94]

Immunization of pregnant sows with a novel virulence gene (VG) deleted live *Salmonella* vaccine, and protection of their suckling piglets against salmonellosis has been successful. The systemic and mucosal immune responses were highly induced by the vaccine candidate, especially when this was administered by both routes of intramuscular prime and oral booster and oral prime and booster.[106]

The literature on *Salmonella* vaccines has been reviewed. Host resistance to *Salmonella* relies initially on the production of inflammatory cytokines leading to the infiltration of activated inflammatory cells in the tissues. Thereafter, T-cell– and B-cell–dependent specific immunity develops, allowing the clearance of *Salmonella* from the tissues and

the establishment of long-lasting acquired immunity to reinfection. The increased resistance that develops after primary infection or vaccination requires T-cell cytokines such as IFN-γ, TNF-α, and IL-2, in addition to opsonizing antibody. Seroconversion and/or the presence of detectable T-cell memory do not always correlate with the development of acquired resistance to infection.

Immunization with live salmonellas induces early resistance rechallenge with virulent organisms that appear 1 day after infection or vaccination with live but not killed organisms. Early protection is nonspecific and effective against different *Salmonella* serotypes. Long-term immunity using live attenuated vaccines is serotype specific and involves the recall of immunologic immunity. Killed vaccines induce strong antibody responses but trigger insufficient T-helper-1 (Th1)-cell responses.

Vaccines have been developed and tested in pigs. If vaccination is combined with the hygienic precautions described, the vaccines are an aid to management. Killed bacterins and live attenuated vaccines are available. Either can be used as a prenatal vaccine to provide passive immunization of the newborn. It is now generally accepted that live *Salmonella* vaccines are more effective immunogens in calves than are killed vaccines. Experimentally, a live STM vaccine delivering recombinant *E. coli*, K88ab, K88c, Fed A, and Fed F has been shown to be highly immunogenic.[106]

A commercial vaccine containing living, attenuated SCS has also been shown to protect neonatal pigs after vaccination of sows and weaned pigs. Because of the early age at which pigs need to be immune, it is recommended that sows be vaccinated three times at 7- to 14-day intervals. The young pigs are vaccinated at 3 weeks of age. A live avirulent SCS vaccine has been developed and evaluated for protection against experimental challenge. Vaccinated pigs were able to maintain normal BW gains during a 4-week observation period following challenge inoculation with a high dose of a virulent strain. It has consistently been safe and efficacious in pigs as young as 3 weeks and provides protection for at least 20 weeks. An STM live negative-marker (OmpD) vaccine has been constructed and given to pigs that will not interfere with meat juice ELISA diagnosis[107] and this holds hope for the future. A sophisticated plasmid-cured and CRP gene-deleted SCS live vaccine has been described, and the mutant may form the basis for a new vaccine.[108]

Most cases of salmonellosis in pigs are subclinical and caused by *S.* Typhimurium. The ideal vaccine against STM would prevent colonization, shedding of the organism in the environment, development of carriers and clinical salmonellosis, and promote elimination of the organism from infected animals. Live vaccine strains are considered to provide superior protection compared with inactivated vaccines.

Monitoring

Statistical methods to categorize pig herds based on serologic data have been described[109,110] as well as descriptive spatial epidemiology.[111]

Herds can be classified quite differently according to the test used[112] when three ELISAs were compared and their results examined.

Nationwide Surveillance and Control Programs

In 1993, the Ministry of Food, Agriculture, and Fisheries of Denmark and the Danish Bacon and Meat Council initiated an ambitious program to eliminate pork as an important source of human salmonellosis. In the early 1990s pork had become recognized as an increasingly important source of human salmonellosis in Denmark. In Denmark, the proportion of human salmonellosis attributable to pork was estimated to be 10% to 15% in 1997 and 1998. In the Netherlands, it was estimated that approximately 15% of human cases of salmonellosis were associated with the consumption of contaminated pork.

The Danish Salmonella Surveillance and Control Program for pigs operates at all stages of the production chain and has been applied nationally since 1995. As a result of the program the level of *Salmonella* in Danish pork declined from 3.5% in 1993 to 0.7% in 2000. Simultaneously, the number of human cases of salmonellosis caused by pork declined from approximately 1444 in 1993 to 166 in 2000. Quality control has been described.[113]

The control program is integrated from "feed to food." It is based on routine testing and classification of slaughter pig herds and the subsequent slaughter of pigs according to the inherent risk, as measured by the continual test program. In a study of culture and ELISA testing, it was found that results cannot be compared easily, because some seronegative pigs were + ve on culture and some culture – ve pigs were + ve on serology, so the test has to be selected to answer a specific question.[114] Methodological problems related to the optical density data obtained from meat juice ELISAs have been shown to require recalculation; otherwise there would be an underestimation of actual seroprevalence.[115]

The Danish Control system and a description of an extended preharvest surveillance and control program has been described.[116] Only hot-water decontamination was socio-economically profitable in a comparison with the control plan as it operated in 2006.[117]

Basically, the level of *Salmonella* is controlled at various stages. The UK plan has been described.[118] The barriers to the adoption of measures to control *Salmonella* in pigs in the UK has been reviewed[119] and one of the most important measures was the failure of farmers to recognize the importance of *Salmonella* control. Other factors are the low awareness of pork as a risk for *Salmonella,* the low incidence of *Salmonella* associated with pork, and the food chain members do not want to raise the problems. It is important to recognize that pooled sampling is highly efficient compared with individual sampling and that clustering at pen level influences the results; thus it is important to take this into account in the estimation of appropriate sample sizes and the estimation of prevalence from pooled sample data.[120] These data can be used to study spatial disease epidemiology.[121]

Feedstuffs

Compounded feeds are heat treated at 81°C to eliminate *Salmonella.* The national program requires mandatory *Salmonella* testing in all plants producing animal feeds. In 2000 the level of *Salmonella* spp. in final products was only 0.3%.

Low-level nitrate or nitroethane preconditioning enhances the bactericidal effect of chlorate treatments, and this may offer opportunities to control *Salmonella* in the future.[122] The supplementation of meal diets with potassium dichromate significantly reduced the duration of survival and increased the rates of decline in *Salmonella.*[123]

The direct feeding of microencapsulated bacteriophages has been shown experimentally to reduce colonization and shedding.[124]

A probiotic strain of *E. faecium* fed to pigs resulted in an enhanced infection but also an increased level of specific antibodies to STM DT104.[125] High-dosage dietary zinc oxide had no protective effects on weaned pigs with DT104.[126] Caprylate in the form of encapsulated beads or as an oil might be a *Salmonella*-reducing additive in pig feed.[127]

Breeder and Multiplier Herds

Each month all herds are blood sampled and examined for *Salmonella* antibodies. Based on the level of antibodies, a *Salmonella* index is calculated. If the index exceeds 5, pen fecal samples must be taken and examined for the presence of *Salmonella* spp. When the index exceeds 15, a sales ban on breeding pigs is imposed until the index has declined below 15 again.

Weaner Producers

If a sow herd sells weaners to a *Salmonella* level 2 or 3 finishing herd, pen fecal samples must be taken and examined for *Salmonella.*

Slaughter Pigs

In a study of slaughter pigs, ileal contents were 18.7% + ve, the lymph nodes 17.8%, 7.2% in the rectal contents, and 3.6% in the carcass swabs.[93]

Slaughter herd pigs are monitored continuously by serologic testing of meat juice.

Meat samples are frozen, and meat juice (harvested after thawing) is examined for specific antibodies against *S. enterica* using an ELISA. The ELISA combines several *S. enterica* O antigens and allows detection of antibody response after a variety of serovar infections. The meat samples for testing are collected at the slaughter line, and the number of samples and frequency of sampling are determined by the size of the herd. Herds sending fewer than 200 pigs to slaughter per year are not examined, which amounts to about 1.6% of slaughter pigs. The herds are categorized in four levels based on the proportion of seropositive meat juice samples during the previous 3 months. Based on the optical density percent of the ELISA test, the herds are classified into the following levels:

Level 0: Herds having only seronegative over 3 months or more
Level 1: Herds with acceptable low *Salmonella* prevalence
Level 2: Herds with moderate *Salmonella* prevalence
Level 3: Herds with unacceptable high *Salmonella* prevalence

The herd information as to status can be used to direct the risk-based approaches to surveillance.[128-130]

A herd categorized as level 2 or 3 must receive an advisory visit by a practicing veterinarian and a local extension specialist, and certain management precautions must be adopted. In a level 3 herd, the finishing pigs must be slaughtered under special hygiene conditions. In a study in the UK, an increased risk of carriage at slaughter was associated with >12 hours in the lairage, pigs transported from northeast UK, and not feeding when there was no bedding available.[131]

The proportion of serologically positive meat juice samples collected during 1995 ranged from a mean of 2.9% in small herds to 6.1% in large herds.

Segregated transport to the abattoir has additional costs but may reduce contamination.[132] Costs were governed by the percentage of changed shipments and the additional distance of a changed shipment.

In a study of hog carcasses in Canada it was shown that the cleanliness of the hogs and the status of the scald water were the two most important factors involved in the *Salmonella* carriage at the end of the slaughter process.[133] Decontamination of pork carcasses can be achieved using hot water and acidified sodium chlorite.[134]

The use of lactic acid sprays as a decontamination measure when used with good manufacturing processes during processing will significantly reduce *Salmonella* contamination of pork variety meats (liver, heart, intestines, and stomachs).[135]

Cleaning and disinfection in the slaughterhouse, particularly the lairage area, is an area that can influence the presence of *Salmonella* on the carcass.[34]

Enumeration of *Salmonella* in feces of naturally infected pigs has been described.[136] Most exposures to *Salmonella* of swine are at doses below the infectious dose. Doses >10^3 CFU increase the probability of infection in swine.[137] Only a few high concentrations of *Salmonella* in feces were clustered within the pig and the pen. Identification and removal of high shedders may be very effective to reduce carcass condemnation. The robustness and rapidity of the direct q-PCR assay can be a very useful screening tool for removal of the high shedder at the lairage. In an experimental evaluation of on-farm interventions, five activities were ranked feeding meal > inclusion of acids in ration > feeder pen disinfection or > *Salmonella* spp. vaccination > in-feed tetracyclines.[138]

Slurry

The addition of urea to pig slurry will add additional antimicrobial ammonia and carbonate anions. It could greatly reduce the time needed to eliminate *Salmonella in slurry* and reduces the pathogen recycling risks associated with using porcine waste as a fertilizer.[139]

At Abattoir

Lesion profiling at processing can be used to predict *Salmonella* contamination of swine carcasses.[140]

The roles of slaughtering in *Salmonella* spreading and control in pork production has been reviewed,[141] and they have indicated that there is a continuous source of infection from the farm. At the slaughterhouse there are some dressing activities that can reduce the carcass contamination but others may jeopardize carcass hygiene.

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INTESTINAL CLOSTRIDIOSIS IN THE PIG

There are three Clostridia involved in intestinal clostridiosis in the pig.

- *C. perfringens* type C (CPC) affects pigs of 1 to 14 days, usually less than 7 (rarely older) and produces hemorrhagic, watery diarrhea and sudden death.
- *C. perfringens* type A (CPA) affects pigs of 2 to 10 days (rarely older) and produces creamy, watery mild diarrhea and decreased growth rate.
- *C. difficile* (CD) affects pigs of 1 to 5 days of age (rarely older) and produces creamy diarrhea, dehydration, and death.

CD is an important cause of diarrhea in humans associated with antibiotic usage. It may also present as a colitis, or fulminant colitis followed by ileus, toxic megacolon, and bowel perforation. It may also cause diarrhea in antibiotic treated foals, hamsters, and guinea pigs. Some authors highlight the high level of relatedness of CD ribotypes found in human and porcine isolates.[1,2] It was originally associated with hospital infections but now approximately 40% may be community-associated CD infections.[3,4] The ribotype O78 is an emerging strain in humans and pigs.[5] There is still confusion as to whether this is a potential zoonotic or food-borne disease.[6] It is likely that there is little food-borne risk because the level of infection in slaughter pigs is greatly reduced.[7] It has been suggested that humans and pigs may be exposed to the same environmental sources of CD. The comparative pathology of CD-associated disease has been described.[8] It may be the most important uncontrolled cause of neonatal diarrhea in the pig.[9]

ETIOLOGY

CPC is a primary pathogen but can colonize other lesions. It is a large, gram-positive rod that only occasionally forms spores and produces the α- and β-toxins (CPA and CPB toxins). The β-toxin is more important and is sensitive to protease/trypsin. A second toxin, the β-2 toxin, has been found in necrotic enteritis, and the function of this is not yet clear. Variable amounts of α-, β- and δ-toxin are produced. *C. perfringens* type B is found occasionally.

CPA is a normal inhabitant of the intestinal microflora of the newborn piglet but can also cause severe disease via the α-toxin, which it produces. Immediately after birth, there are large numbers in the stomach of piglets and later large numbers in the colon. Quite often, there are greater numbers in the healthy piglets than diarrheic piglets. The *cpb2* gene and its expressed protein a 27.6-kD toxin (CPB2) was first described in an isolate from necrotic enteritis. It was subsequently demonstrated by PCR in a variety of animals with diarrhea and necrotic enteritis.[10] The

CPB2 toxin is encoded by either a "consensus gene" or by an "atypical gene" with 80.4% similarity between the two proteins.[11] In a study of cpb2 encoding CPA and diarrhea it was shown that the consensus cpb2 was present in 93% of the isolates in healthy and diarrheic piglets and the atypical gene was shown in only 56% healthy and 32% diarrheic piglets.[12] The presence of CPB2 toxin in the intestinal contents of normal and diarrheic piglets did not differ significantly. There is a role for β-2 toxin, and nearly all of the strains of type A also produce this toxin. There are also some strains that produce enterotoxin.

CD can be asymptomatic or can cause diarrhea in piglets. Spores germinate in the ileum, cecum, and colon. It has emerged as a cause of enteritis in pigs. It is classified by ribotype (O) and toxin types, e.g., O76 toxin type V. It produces two major toxins, A (lyses epithelial cells) and B (damages underlying tissues), both of which are involved in the pathogenicity, as well as a third binary toxin. Ribotype O78 was found in 83% of pig isolates from North America.[13]

EPIDEMIOLOGY

The prevalence and diversity of toxigenic CPC and CD among the swine herds of the Midwest United States was studied.[14] CPC was isolated from 89.8% of the pigs and CD from 57.7% of the pigs. Most of the CD isolates were toxinotype V, but there was considerable diversity in the CD isolates.

In a study from Poland, CPC was found in 92% of feces samples and all the isolates belonged to type A and 48.7% of them contained the *cpb2* gene. Type A subtype β-2 isolates showed expression of *cpa* genes in 100% of strains and *cpb2* gene in 71% of the analyzed strains. The isolate from 1-day-old piglets demonstrated both *cpa* and *cpb2*.[15]

CPC occurs in most pig-producing countries; necrotic enteritis has even been seen in isolated communities in Switzerland.[16] In Switzerland it occurs on breeding farms that do not vaccinate for CPC.[17,18]

It may be transmitted from piglet to piglet but the source is usually sows' feces. It often follows the introduction of new stock to a farm and then may occur for a few months. If regular imports are made it may last for 15 months. They are usually present in small numbers in the feces of sows but are capable of outgrowing the other flora in the neonatal pig gut and eventually multiply in huge numbers.

The organism persists in the environment as spores that are resistant to heat, disinfectants, and ultraviolet light.

The epidemiology of CPA has been studied on Ontario farms with special reference to cpb2-positive isolates.[19] The conclusion was that if type A strains were involved in neonatal enteritis then there might be strains that were not identified by the existing genotyping system. In this study the

cpb2-positive and expressing CPB2 population was clonal, and this lineage appeared to be adapted to the young piglet. This was the first time this was established at the farm level.

CPA infections usually occur in the first week of life and sows are the source of infection. It is ubiquitous in the gut and the soil, and there are some strains that cause disease and others that do not, but at the moment it is not possible to tell them apart unless CBP2 positivity is shown on PCR. There are likely to be spores formed and the organism can be found in feed.

CD has appeared worldwide but particularly in Canada, the United States, France, and recently the Netherlands. Nearly two-thirds of piglets in major swine-producing areas in the United States have CD with some herds having 100% infection. It may reflect the routine use of antibiotics and also bad husbandry and hygiene. In a study in Spain,[20] the bacteria were recovered from newborn piglets (25.9%) and were not recovered from 1- to 2-month-old pigs. Genes for the production of both toxins were found in most of the isolates, and only a few had neither of the toxin genes. In this study there was no clear link between bacterial isolation and neonatal porcine diarrhea. A longitudinal study comparing CD in conventional and antimicrobial-free pigs at farm and slaughter[21] showed that CD was at its highest in both systems in the farrowing house and decreased with age. At slaughter it was very low in both carcasses and equipment. Toxinotype V was the most common type isolated at about 90% and the others were type XIII. The authors found antibiotic resistance regardless of antibiotic use on the farm.

In a study of acquisition of CD by piglets in the Netherlands a group of six sows, their crates, and their litters were studied.[22] Within 48 hours of birth all 71 piglets were positive for CD. One was positive within 1 hour. All six sows were positive within 113 hours, and the crates were intermittently positive. CD was found in the air and on the sow's teats. All were O78 and as in most of the Netherlands the same clonal spread except one isolate. This study showed that O78 spreads easily through the sows, piglets, and the environment. Vertical transmission was not found and is not likely to be a factor.

Piglets may be infected within 1 hour of birth, but there is no vertical transmission. The high prevalence of CD ribotype O78 in Iberian wild pigs has been demonstrated[23] as well as its occurrence in feral pigs.[24]

In a study in Switzerland,[25] no CD was found in pigs or ground meat.

In a study of slaughter pigs in the Netherlands, a higher incidence of CD was found than was expected.[26] The prevalence was 8.6%, and 16 different ribotypes were identified with O78 the most common. No specific farm factors were identified associated with the prevalence of CD.

A similar study in 2011 showed a high prevalence of CD ribotypes in pigs arriving at the slaughterhouse.[27] The results showed that pigs had CD ribotypes after they were stunned and bled in a slaughterhouse. Pigs from 9/10 different farms were positive with seven different PCR ribotypes, and O15 was the predominant ribotype.

In a recent study in the United States,[28] 88% of the pigs had a single strain of CD (196/223 pigs) but 12% carried multiple strains. This was the first report of multiple strains in one pig. Overall this study showed that a significant percentage of strains were toxigenic and often are associated with AMR genes, although they are not resistant to drugs that are used to treat CD infections.

C. difficile genotypes in piglet populations in Germany have been described.[29] The organism was isolated from 73% of rectal swabs from piglets. The rate of isolation was at 68% postpartum, 94% in animals from 2 to 14 days of age, and declined to 0% after 49 days of age. There was no link between isolation and antibiotic treatment. This study demonstrated that the human pathogenic PCR ribotypes 078 and 126 are dominant in piglets in Germany. The presence of CD in pigs is correlated with animal age but not with antibiotic treatment or clinical disease.

PATHOGENESIS

The type C organisms colonize the neonatal bowel within 24 hours of birth. They can multiply very rapidly in the absence of colostral immunity and attach to the jejunal epithelial cells at the tips of the villi. These then slough off and the organisms proliferate along the basement membrane. Necrosis is extensive and hemorrhage follows. The necrosis may extend through the gut wall to the muscular layers. Then there may be perforation and peritonitis. The lethal and necrotizing β-toxin is the key factor.[30] The β-toxin binds to the endothelial lining of vessels showing early signs of thrombosis. Initially, it binds to small-intestinal mucosal endothelial cells in the early stages of experimentally induced CPC.[31] It disrupts the actin cytoskeleton of the cell and causes cell border retraction and cell shrinkage followed by cell death.[32]

Trypsin secretion deficiencies and colostral protease inhibitors probably account for the susceptibility of piglets less than 4 days old.

The toxin has been found in the intestinal contents and the peritoneal fluid. This suggests that death may be caused by the effects of intestinal damage and toxemia.

Type A pathogenesis is not understood but it is likely to be similar to type C without the attachment of organisms to the epithelium. Attachment and invasion do not occur in experimental infections, but epithelial necrosis does occur in these, although less obviously than in natural cases. There is a minimum of lesions, which suggests this is a secretory diarrhea. CPB2 is likely to be a marker of virulence because it occurs in >90% of natural enteritis cases but is rarely found in normal pigs. The role of the toxins is still uncertain, and the association of neonatal diarrhea requires the isolation of large numbers of cpb2-positive bacteria and the exclusion of other causes. In swine the CPB2 is nearly always the consensus type and is almost invariably expressed. The CPA nearly always belongs to a clonal type. Diarrhea disease isolates nearly all carry the CPB2 compared with a smaller proportion of CPB2-positive isolates from healthy pigs.

CD is likely to possess pili, capsule, and degradative enzymes but toxins are essential to produce the clinical picture. The two toxins produced by CD are the largest known bacterial toxins. A type of enterotoxemia is associated with the presence of monomeric CD toxin A (TcdA; 308 kDa). It causes fluid production in the intestine. Toxin B ((TcdB; 270kDa) does not appear to bind to any tissue nor does it produce lesions in explants,[34] but it appears to be a cytotoxin that is extremely toxic to cultured cells. Both toxins are internalized by target cells and disrupt the cytoskeleton. There is cessation of enzyme production and cell division. Degranulation of mucosal mast cells and release of inflammatory mediators follows with resultant tissue damage. The key event appears to be the receptor-mediated endocytosis in intestinal epithelial cells.[35]

A pore-forming toxin has been identified in necrotic enteritis strains of *C. perfringens*.[36]

A large survey of AMR and toxin genes in commercial swine was undertaken.[37] In young pigs, sampled at farrowing time, 73% had CD, and it was isolated from 47% of sows. Only one pig was positive in the nursery and no finishing pigs were positive. Resistance to ciprofloxacin was found in 91.3% in young pigs and in 94% of sows. The profile ciprofloxacin–erythromycin–tetracycline was detected in 21.4% of the piglets and 11.75 of the sows. Most had TcdA (65%), TcdB was found in 84%, and the binary toxin CdtB was found in 77%. The presence of CD spores in the feces of food-producing animals represents a risk for contamination of meat products.[38] In colon explants, toxin A produces cell swelling, swelling of mitochondria and other organelles, distension of cytoplasmic vesicles, expansion of paracellular spaces, apoptosis, and necrosis.[35]

C. perfringens type E rarely causes damage in the pig gut but it can in weaned pigs and does so when maternal antibodies have disappeared.

CLINICAL SIGNS

In all three forms of intestinal clostridiosis it is likely that the picture varies with immune status and age of the pig.

In CPC the pigs are normal at birth, and in peracute cases there is often sudden death

without other clinical signs. There may also be hemorrhagic diarrhea with perineal staining. Affected pigs are weak, reluctant to move, and become rapidly moribund. They may then be crushed or starve to death. Many pigs are found dead within 12 to 36 hours.

In acute cases, the piglets may survive 1 to 2 days after the onset of clinical signs. The feces may be reddish brown (bloodstained) with tissue debris and perineal staining, and they rapidly become dehydrated, weak, and die.

In subacute cases there is yellow diarrhea without blood, but they become progressively emaciated, may pass tissue flakes, and become very thin, dehydrated, and then die usually at about 5 to 7 days of age.

Chronic cases may have intermittent diarrhea for more than 1 week. The feces are yellowish gray and mucoid, and the tail and perineum may be fecal stained. Lesions are not visible through the serosa.

In CPA cases the condition may occur over 10 to 21 days, but there is often a creamy diarrhea within 2 days of birth, the piglets have a rough hair coat, and there is perineal fecal staining. Diarrhea may last up to 5 days and may become mucoid and pink. Most piglets recover but some may be growth retarded.

In CD cases the piglets are affected between 1 and 7 days of age and quite often they are born to gilts. The prevalence decreases with age and is uncommon after 60 days of age. They present with a history of early onset scours, and occasionally with respiratory distress. The piglets develop dyspnea, emaciation, abdominal distension, and scrotal edema. Diarrhea occurs and animals rapidly dehydrate with sunken eyes and perineal staining. It can cause preweaning losses up to 90% but 50% is the norm. There is a suggestion that piglets born to sows that have been treated with fluoroquinolones are more susceptible to CD.

PATHOLOGY

The pathology of hyperacute CPC is characterized by severely hemorrhagic small intestines full of bloodstained pasty feces and bloodstained fluid in the peritoneal cavity. Lesions are usually in the jejunum (may be only a part) and ileum but can almost reach forward to the pylorus. Mesenteric lymph nodes may be congested.

Histologically, there may be necrotic villi with a surface pack of gram-positive organisms on the epithelial surface. The crypts may be necrotic and there may be significant hemorrhage.

The pathology of acute CPC is less severe. The lesions are usually localized and there may be emphysema. Often these lesions are segmental. There may be a fibrinous peritonitis, and the intestinal wall may be thickened with blood and necrotic debris. In the subacute cases, there may be a thickened intestinal wall. The chronic cases may have a diphtheritic membrane over the jejunum, and the contents are more watery.

Histologically, there is severe villous necrosis with an overlying carpet of necrotic debris, blood, and fibrin with large numbers of gram-positive bacteria.

The pathology of CPA is much less severe. The intestine is usually thin-walled, gas-filled with watery contents, and without blood. The small intestine is often congested. The necrotic areas may be seen on the intestinal surface. The inflammation is mild occasionally with adherent debris. The large intestine does not usually have lesions but may be full of pasty contents. Usually there is nothing to see outside of these gut lesions.

Microscopically, there may be villous tip necrosis. There may be large numbers of organisms on the surface or in the lumen. There is no hemorrhage. The stomach usually has no lesions.

Enterotoxigenic strains may produce superficial mucosal necrosis and villous atrophy. Experimentally, these cases have creamy diarrhea and emaciation with low mortality to profuse bloodstained diarrhea, enteritis, and death.

In CD infections, there is sometimes mesocolonic edema, and the intestines are filled with pasty to watery yellow feces. Many piglets are toxin positive in an infected barn and piglets without signs may be toxin positive.[39-41] Focal suppuration in the colonic lamina propria is the key lesion, and colonic and serosal edema is common. There is frequently an inflammatory infiltrate. There is frequently segmental erosion of colonic mucosal epithelium, and exudation of neutrophils and fibrin into the lumen also occurs. The association of CD toxins and gross and microscopic lesions was evaluated.[42] There was no significant correlation between CD toxins and mesocolonic edema. There was a significant correlation between toxins and colitis and typhlitis. The toxins were isolated in a significant proportion of the healthy pigs, which may represent a significant subclinical reservoir in swine.

DIFFERENTIAL DIAGNOSIS

A presumed diagnosis of type C is formed when the clinical signs, pattern of mortality, and gross and microscopic lesions are evaluated.

A more chronic form may require detection of type C organisms in the lesions. Although it may be confused with coccidiosis, rotavirus, TGE, porcine epidemic diarrhea (PED), it is most likely to be confused with CPA, especially in the less severe forms. This requires bacteriologic culture, toxin detection, or genotyping.

Diagnosis of type A is more difficult because the clinical signs and epidemiology are more equivocal. You can find large numbers of gram-positive organisms particularly in the stomach but also the small intestine and from feces. Genotyping reveals type A organisms with CBP2 toxin (β-toxin). In a summary of a recent study,[12] it was said that it was impossible to separate healthy and diarrheic piglets on the basis of bacterial numbers in the intestine, the presence of consensus CPB2 in CPA isolates, the expression of CPB in the intestine of pigs, and between diarrheic piglets with known or unknown causes of diarrhea. There was also no association between histologic findings and the presence of CPB2. The exclusion of other agents is not an adequate diagnostic criterion,[12] and the large numbers of cpb2-positive type A CP should be regarded as normal.

A very interesting document was sent to swine practitioners and veterinary pathologists to see how they diagnosed CPA infections.[43] Most practitioners diagnosed it based on the age of the pig affected (1–7 days), and 41% of pathologists were not certain of the diagnosis even based on the isolation of the organism, genotyping, or detection of the toxins and ruling out other pathogens through histopathology.

Diagnosis of CD is by finding the lesions in the colon and by finding TcdA and TcdB in the feces or colonic contents using commercially available enzyme immunoassays.

LABORATORY DIAGNOSIS
Bacteriology

It is possible to smear the intestinal contents and the mucosal lesions. Large gram-positive rods are visible. In culture the organisms are 3 to 5 mm in diameter, gray, and circular after 24 hours on horse or bovine blood agar. The CPC produces an inner zone of hemolysis associated with theta toxin (perfringolysin O) and an outer less complete area caused by the β-toxin. A large gram-positive rod that grows anaerobically and has a double layer of hemolysis is *C. perfringens*.

Toxin testing is then essential. The β-toxin is demonstrated in the intestinal contents or peritoneal fluid. Clonal relationships can be detected by multilocus sequence typing (MLST).[33]

Enzyme immunoassays are now in use to detect the genes for the toxins. An RT-PCR can be used for the detection of CP toxin genes in animal isolates.[43]

The presence of enterotoxin in fecal infiltrates can be confirmed using commercial reversed passive latex agglutination tests, counter electrophoresis, ELISA, and Vero cells. An antigen-capture ELISA for CP β-2-toxin has been developed.[45] PCRs for the genes are also in use. The detection of toxigenic CD in pig feces has been described.[46] The authors developed three different sequences: the triose phosphate isomerase gene *tpi*, specific for CD, and the *TcdA* and *TcdB* genes, which code for the A and B toxins of CD, respectively.

Four different diagnostic tests were used to detect CD in piglets.[47] It was concluded

that all four tests had a low performance as a test for CD in pigs. The RT-PCR was the most appropriate test to screen for negativity in a herd as a first step, followed by toxigenic culture as the second part of the two-step algorithm.

HISTOLOGY

Large gram-positive rods can be seen in sections. The hemorrhagic lesions can be almost diagnostic.

In many instances the clostridia are found in association with other agents causing diarrhea in the neonate (e.g., rotavirus, TGE, PED, coccidia, cryptosporidiosis).

TREATMENT

Treatment is of little use in type C cases and prophylaxis is the most important. Protection against type C can be achieved by the use of equine antitoxin in nonimmune sows, or given to the piglets parenterally immediately after birth, when it will usually protect for about 3 weeks.

Treatment is of more use in type A infections and antimicrobials will work.

Treatment of CD may be successful using tylosin. A North American study showed 99% resistance to ciprofloxacin, while 1% showed resistance to tetracycline and 6% to erythromycin.[21]

CONTROL

For type C infections oral antibiotics such as ampicillin or amoxicillin should be given immediately after birth and continued daily for 3 days. There may be resistance and tetracycline-resistant plasmids have been identified.

Sows should be vaccinated with type C toxoid at breeding or midgestation and 2 to 3 weeks before farrowing. The disease is usually eradicated after one farrowing cycle. Booster injections should be given 3 weeks before the next farrowing. Even after repeated vaccinations and the absence of clinical necrotic enteritis on the farm, CPC can still be detected.[18]

To prevent type A infections autogenous vaccines can be made and toxoids for α-toxin and β-2-toxin have been used in sows for protecting piglets or some other products used off license. In addition, avoparcin and salinomycin have been used in feed.

For CD there is a limited approach with Bacitracin methylene disalicylate, which can be used in the sows to protect the piglets. It is given at 250 g/tonne for 2 weeks in the feed prefarrowing and in the lactation ration at the same level for 3 weeks.

In a recent study the use of recombinant *C. perfringens* toxoids α and β produced in *E. coli* elevated antepartum and passive humoral immunity and could possibly be used for the development of a commercial vaccine.[48]

There has also been a suggestion that competitive exclusion with nontoxigenic organisms can also inhibit CD toxigenic strains.[49] Spores were given to the dams or sprayed on the teats or given orally to the piglets.

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ESCHERICHIA COLI INFECTIONS IN WEANED PIGS

Diarrhea is most frequent when pigs are exposed to pathogenic *E. coli* strains. The effect of weaning is to produce a marked decrease in the diversity of coliforms in the individual piglet. Different strains of *E. coli* were predominant in different animals, which may in turn facilitate the spread of pathogenic strains.

Many strains are nonpathogenic. Nonpathogenic *E. coli* supports the physiologic intestinal balance of the host. Pathogenic *E. coli* with VG profiles can cause outbreaks of diarrhea. It was concluded that VG carrying *E. coli* are a normal part of the intestinal bacterial population.[1] Pathogenic *E. coli* can be divided into a variety of pathotypes, but there are three major types. These are ETEC, verotoxin-producing *E. coli* (VPEC), and attaching and effacing *E. coli* (AEEC).

There are two major complicating factors in pigs: one of these is that the intestine has different distributions of receptors with changing age. The other is that nearly all isolates (94.8%) that carry the enterotoxin genes also carry genes for one of the fimbrial adhesins. The two most prominent genotypes are K88, LT1, STb and F18, STa, STb, and SLT.

Enterotoxigenic *Escherichia coli*

ETEC have two major virulence factors: (1) adhesins or fimbriae and (2) enterotoxins. The adhesins promote or control the adherence to small-intestinal epithelial cells and include K88, K99, F41, 987P, and F18. Only F18 and K88 are frequently associated with disease in weaned pigs. Only young pigs are susceptible to K99 or 987P. Age-related susceptibility is related to the presence or absence of the appropriate receptors in the small intestine. The enterotoxins belong to two groups; heat-labile enterotoxin (LT) and the heat-stable enterotoxins STa or STb. Only weaned pigs are susceptible to F18, and resistance develops by 8 weeks of age, because the binding appears to be blocked. The receptor for F18 has not yet been identified, but it is a glycoconjugate in which the attached carbohydrate acts as a target for the fimbriae. The F18 adhesin occurs in two forms: ab found in VTEC and ac found in ETEC.

There is also an F4 fimbrial antigen that is on a different chromosome from F18. F4 ETEC cause problems in the first week after weaning, but F18 VTEC cause problems 1 to 2 weeks after weaning.

Verotoxin-Producing *Escherichia coli*

These strains produce Shiga toxin or Shiga-like toxins (verocytotoxins) and cause edema disease (ED). Swine VTEC colonize the intestine via the F18 pilus, as do some swine ETEC. It is not uncommon to find F18-positive strains that produce enterotoxins and verotoxins and can cause both diarrhea and ED.

Attaching and Effacing *Escherichia coli*

These bacteria possess the *eae* gene, which encodes for intimin. This is an adhesin factor that facilitates the attachment of bacteria to intestinal epithelial cells. It is on a plasmid that is distinct from the K88-encoding plasmid in ETEC and ETEC strains that produce attaching and effacing lesions.

The following strains are found:

- K88 ab, ac, and ad
- F18ab (more associated with ED) and F18ac
- F41, usually associated with K99 fimbriae
- Strains containing LT, STa, STb, Shiga-like toxin 2e (Stx2e), and possibly enteroaggregative *E. coli*

Twenty years ago most of the pig strains were 987 or K99 positive. The genes for Stx2e and F18 were rare then, but are much more common now.

O157 in Pigs

In a recent survey in Sweden only two O157:H7-positive and four O157:H7-negative strains were found. Pathogenicity is indicated by genes encoding for one or more of the Shiga toxins, but several other factors may also be necessary. Most strains do not possess Shiga toxins but do carry the F4 or F18 fimbrial adhesins. A third of the strains examined produced STa or STb, but less than a third produced STx and half the *eae* gene.

Postweaning diarrhea (PWD) and **ED** are two common *E. coli* infections of weaned pigs. In PWD, there is diarrhea, dehydration, and often death. In ED or enterotoxemia there is subcutaneous edema of the forehead and eyelids, and neurologic clinical signs such as ataxia, convulsions, recumbency, and death. ETEC strains isolated from cases of PWD mainly belong to O Groups O8, O141, O147, O149, and O157. Strains associated with ED predominantly have O Groups O138, O139, or O141. PWD is a significant cause of mortality between weaning and slaughter in some herds. Although the clinical signs in these two diseases are different, they occur in similar age groups, and the same type of management change may precede their occurrence. Weaning and weaning age are both associated with significant effects on the microbial populations. In PWD the bacteria disappear more quickly, usually by about 7 days postinfection (DPI), but in ED they may still be there 9 DPI but with a slower buildup to a peak within 3 to 5 DPI. A typical scenario would be 4 to 5 days PWD followed by clinical ED with mortality reaching as high as 50%. Both are associated with the proliferation of predominantly hemolytic serotypes of *E. coli* within the small intestine. However, it is rare to encounter both diseases concurrently on the same farm. In PWD the serotypes are ETEC and the major manifestation is diarrhea resulting from enterotoxin activity at the time of proliferation. In ED nonenterotoxigenic strains produce a verotoxin that, after a period of time, indirectly produces the neurologic syndrome characteristic of this disease.

One of the features of virulence in *E. coli* is the presence of mobile genetic elements such as plasmids, bacteriophages, and pathogenicity islands. A pathogenicity island coding for F18-positive fimbriae has been found. Cytolethal distending toxins have also been described. In many countries the prevalence of ED has decreased, whereas coliform gastroenteritis has increased. It is possible that this change reflects the trend toward earlier weaning of pigs, although the emergence and spread of new ETEC strains may also be a factor. More recently a third disease, cerebrospinal angiopathy, has been attributed to the effects of infection with *E. coli*. Although there are some similarities in the etiology and epidemiology of these diseases, they are sufficiently different to warrant a separate description.

One of the major features in common is the process of weaning, which is probably the most serious disturbance a young piglet may face. This change of diet from liquid to solid is also accompanied by a multitude of other changes such as moving, mixing, environmental, and managemental. It also alters immune functions and produces stress and profoundly alters the intestinal microflora, particularly the coliform flora. Some strains may increase but others may decrease.

It is also important to realize that some *E. coli* may also cause fatal shock. They are usually F4 (K88-positive) ETEC (O149, O157, or O8) or ED causing *E. coli* (Stxe). Death occurs before either the diarrhea or the edema is produced. It is probably caused by the rapid release of large amounts of LPS by colonizing ETEC, which then produce a cytochrome storm (TNF-α, IL-1, and IL-6). There are usually no clinical signs and minimal lesions including congestion and blood-tinged enteritis.

Systemic *E. coli* infections also occur in pigs of any age but often in the very young when there is little colostral protection. Usually, the infections are ETEC. The clinical signs are quite variable and develop within 12 hours, with as little as distended abdomens on or piglets are found dead within 48 hours on the other.

EDEMA DISEASE (GUT EDEMA, *ESCHERICHIA COLI* ENTEROTOXEMIA)

ED occurs in weaner and grower pigs and is characterized by subcutaneous and subserosal edema, progressive ataxia, recumbency, and death. Although isolated strains from pigs are unlikely to be associated with severe human disease, healthy pigs cannot be excluded as a potential source of human infection with Stx2e-producing STEC (Shiga toxin producers).[2]

SYNOPSIS

Etiology *Escherichia coli* strains producing verocytotoxin and Shiga-like toxin

Epidemiology In rapidly growing weaner pigs between 4 and 12 weeks of age following change in diet or feeding practices and waning of maternal antibody

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Sign Sudden death. Incoordination, falling, edema of eyelids and face; piglets die in 6–36 h.

Clinical pathology Culture *E. coli* from feces.

Lesions Facial edema, full stomach, and mesenteric edema

Diagnostic confirmation Culture specific organism

Differential diagnosis list
- Pseudorabies
- Viral encephalomyelitis of pigs
- Encephalomyocarditis
- Streptococcal meningitis
- Salt poisoning
- Organic arsenic poisoning
- Mulberry heart disease

Treatment None

Control Avoid drastic changes in diet.

ETIOLOGY

ED is associated with *E. coli* strains producing a Stx,Stx2e toxin, which enters the bloodstream and damages vessel walls. Three serogroups cause ED: O138, O139, and O141 and sometimes O147. They are called EDEC and are nearly all α-hemolytic. The strains have adhesins that enable the bacteria to colonize the intestine and elaborate protein exotoxins. The biochemical phenotypes were studied in Sweden and O138, O139, and O141 are dominated by one phenotypic type, even though others do occur within the serotype. The entire pathogenicity island known as ETT2 is necessary for the ED virulence factors in O138, O139, or O141. Isolates of *E. coli* have been found in which the toxin or F18 fimbrial types were not related to selected electrophoretic types. This suggests that toxin and F18 genes in the isolates from pigs with PWD or ED occur in a variety of chromosomal backgrounds. The bacteria colonize the small intestine without causing significant changes by means of the adherence factor F18 (F107), usually F18ab or occasionally F18ac, as the fimbrial adhesin. The *E. coli* strains with the highest mucin-binding capacity belonged to potential ST toxin producers, whereas strains without genes encoding for toxin production displayed a much weaker binding to mucin capacity. In a recent outbreak in Denmark, in which ED had not previously been observed, most isolates were O139, but a few were untypeable. All the isolates from the Danish pigs with ED were in one cluster in contrast to isolates from other countries, which did not form any clusters. In the Denmark study, 563 isolates were serotyped and O149 was found in 49.9% of the isolates, O138 in 14.9%, O139 in 6.9%, O141 in 4.1%, and O8 in 3.7%. The VGs were examined and they fell into six pathotypes that covered 65.7% of all isolates. The F107 fimbriae are a major colonization factor in *E. coli* that causes ED.

Inheritance of Susceptibility to ED

Inheritance of resistance to intestinal colonization with *E. coli* causing ED is thought to be under the control of one locus consisting of two alleles with susceptibility (S)-dominating resistance(s). Genetic susceptibility to ED is caused by the ability of F107-expressing *E. coli* to adhere to and colonize intestinal brush border cells and not toxin susceptibility. There is a high correlation between intestinal F18 receptor genotype and susceptibility to disease, but pigs with resistant F18 receptor genotypes were not entirely protected against colonization by *E. coli*.

EPIDEMIOLOGY

Possibly the most significant factor in the development of ED is the loss of milk antibodies at weaning. The environment of the weaner unit is the most likely source of the *E. coli*, either from other weaned pigs or from a dirty environment. Not all infected pigs develop the disease.

The specific serotypes of *E. coli* that may cause disease are introduced into a piggery and become part of the normal intestinal flora. They may not cause disease until a particular set of environmental conditions arises, such as when they proliferate excessively within the intestine to produce toxin. The disease occurs predominantly in pigs between 4 and 12 weeks of age. It may occur sporadically but more commonly occurs as an outbreak affecting up to 50% of the pigs within the group. Characteristically, the larger and faster growing pigs within the group are affected. The disease is not common in runt or poorly thriving pigs. Age at weaning, diet, overcrowding, chilling, transportation, and other factors influence the susceptibility of pigs to *E. coli*-producing SLTIIe, and could determine whether subclinical or clinical ED occurs following infection. Piglets fed high-protein diets are more susceptible to experimental clinical ED than piglets fed low-protein diets. The disease frequently occurs within 1 week following a change in diet or ad libitum feeding but may also follow such factors as weaning, vaccination, pen change, and regrouping. A study even found VPEC O139 in water storage tanks and drinking water.

F18 fimbriae have increased greatly since 1997 from 10% to 70%, and this may be tied into the genetic selection of the stress gene.

The outbreak is sudden in onset but short-lived, averaging 8 days and seldom exceeding 15 days. The epidemiology of the disease in affected herds is not characteristic of a highly contagious disease, and it does not usually spread to involve other pens of pigs on the same farm.

The disease follows proliferation of the relevant serotypes within the intestine. Serotypes of *E. coli* associated with gut edema may be isolated from the feces of healthy pigs. The factors initiating proliferation are unknown, but changes in the composition or amount of diet commonly precipitate the onset. Management factors that potentiate oral–fecal cycling of these organisms are likely to be important to spread within the group.

PATHOGENESIS

A number of F18ab or F18ac strains produce both enterotoxins and Stx2e, and in these cases PWD is usually more common than ED. There may also be mixed infections of both ETEC and EDEC strains in which diarrhea usually predominates.

The F18 receptors important in ED are not fully expressed in pigs under 20 days of age. The F18-positive strains cause ED about 5 to 14 days after weaning. The fimbrial receptors can be moderated by lectins in the diet, and this may be the reason that the F18 colonization is reduced after weaning. Toxemia resulting in severe edema in specific sites that have absorbed Stx2. Colonization by EDEC develops on the tips and sides of the villi in the distal jejunum and ileum. The Stxe is absorbed into the circulation and causes vascular damage to the target organs. It is not normally absorbed, but is under the influence of unknown factors that may include bile. Absorption causes a degenerative angiopathy of small arteries and arterioles. In the brain the changes may be exacerbated by the anoxia that results from the slow blood flow.

It is a simple progression. The intestine of a susceptible pig, which is usually fast-growing and without maternal antibody, has receptors for F18 pili. This appears to be the major factor, and then colonization by *E. coli* occurs with toxin production, absorption of toxin, and damage to vascular epithelium. The endothelium appears to have a specific toxin receptor for Stx2e, and finally edema develops in target tissues. Epithelial receptors for pathogenic ED are not found in all pigs. The receptors for both F14 are on one chromosome (13) and for F18 on another.[3,4] The numbers of *E. coli* rapidly proliferate when infected to levels of 10^9/g feces.

Nutritional factors and gastrointestinal stasis result in proliferation of the *E. coli* strains in the small intestine and toxin production. There is generally a delay between the initial period of maximal intestinal proliferation and the onset of clinical signs. In the experimental disease, clinical signs occur 5 to 7 days following initial oral challenge with bacteria and up to 36 hours following intravenous inoculation with toxin. The delay appears to be related to the development of vascular lesions, with increased vascular permeability leading to edema formation and encephalomalacia. The experimental oral inoculation of the ED-producing *E. coli* results in colonization of the small intestine, and lesions of the vessels of the intestinal mucosa are detectable as early as 2 days after infection. An experimental model for subclinical ED in weaned pigs has been described. Microscopic vascular lesions were found in pigs 14 days after oral inoculation with a SLT2-positive strain of *E. coli*. Once PWD occurs there is an increased intestinal permeability that predisposes to ED, and once developed the influx of SLT toxin into the bloodstream is facilitated further, precipitating the disease. ED is associated with metabolic acidosis, which might be explained by endogenous acid production and small-intestinal acidosis. Intestinal acidosis is known to cause mucosal hyperexcitability.

CLINICAL FINDINGS

PWD and ED can occur simultaneously. The case mortality rate varies from 50% to 90%. It may appear suddenly and disappear suddenly. Recurrence on premises is not unusual. It usually occurs after weaning but can occur at any time.

The diseases occur sporadically and unexpectedly in a group, often affecting a number of pigs within a few hours, and show no tendency to spread from group to group. The thriftiest pigs are most likely to be affected and, once the diagnosis is made, all pigs in the pen should be examined in an attempt to detect other animals in the early stages of the disease. The incidence in a litter will vary up to 50% or more.

Quite often pigs may become inappetent, with swelling of the eyelids and forehead. The earliest and most obvious sign is incoordination of the hindlimbs, although this may be preceded by an attack of diarrhea. The pig has difficulty in standing and sways and sags in the hindquarters. There is difficulty in getting up and in getting the legs past each other when walking because of a stiff, stringhalt-like action affecting either the forelegs or hindlegs. In some cases there are obvious signs of nervous irritation manifested by muscle tremor, aimless wandering, and clonic convulsions. Complete flaccid paralysis follows. A peculiar squeal may also be heard. There is usually no diarrhea or fever. There may be pruritus. In the terminal stages there may be a watery diarrhea.

Subclinical disease may occur when pigs are clinically normal and may then develop vascular lesions and have a slow growth rate.

On close examination, edema of the eyelids and conjunctiva may be visible. This may also involve the front of the face and ears but cannot usually be seen until necropsy. The voice is often hoarse and may become almost inaudible. Blindness may be apparent. The feces are usually firm, and rectal temperatures are almost always below normal. The course of the disease may be very short, with some pigs being found dead without signs having been observed. In most cases, illness is observed for 6 to 36 hours, with a few cases being more prolonged. Recovery does sometimes occur,

but some degree of incoordination may persist.

CLINICAL PATHOLOGY

As an aid to diagnosis, while affected animals are still alive, fecal samples should be cultured to determine the presence of hemolytic *E. coli.* Knowledge of the drug sensitivity of the organism may be important in prescribing control measures. The ED principle is cytotoxic to Vero cells and may be useful in an assay system for diagnosis. The toxin Stx2e has been detected in the peripheral blood of pigs with clinical disease, which not only shows that toxin is transported but may eventually lead to a technique for the detection of early cases.

NECROPSY FINDINGS

The pig is well grown for its age, the stomach is full of feed, and the feces are usually normal. Edema is variable. Edema of the eyelids, forehead, belly, elbow and hock joints, throat, and ears is accompanied by edema of the stomach wall and mesocolon in classical cases. The gelatinous edema may be very thick around the stomach and mesentery. The mesocolon is also edematous and edema of the gallbladder is sometimes observed. The lymph nodes may be swollen and edematous. Quite often the stomach is full of dry food. Colonic contents may be reduced. There may be pulmonary edema and petechial hemorrhages in the epicardium and pericardium. Excess pleural, peritoneal, and pericardial fluid is also characteristic, and the skeletal muscles are pale. The edema may often be slight and quite localized, so examination of suspected areas should be performed carefully, using multiple incisions, especially along the greater curvature of the stomach near the cardia. Hemolytic *E. coli* can be recovered in almost pure culture from the intestine, particularly the colon and the rectum, and in some cases from the mesenteric lymph nodes. Polyclonal antisera directed against serotypes of *E. coli* associated with ED are used to confirm the diagnosis via an agglutination test.

In some cases, an atypical hemorrhagic gastroenteritis has been described with marked edema, but the mucosae of the small and large intestine show extensive hemorrhage and there is a watery diarrhea, followed by death.

There may be multifocal encephalomalacia in the brainstem together with typical lesions in small arteries and arterioles.

Histologically, the important lesions are mural edema, hyaline degeneration, and fibrinoid necrosis in arteries and arterioles. Sometimes the lesions are minimal and difficult to recognize. In subacute to chronic cases this angiopathy may result in focal brain hemorrhages and encephalomalacia. Patchy layers of bacteria are adherent to distal jejunal and ileal mucosa but have often disappeared by the time the pig dies.

Samples for Confirmation of Diagnosis

- *Bacteriology:* Ileum and colon (CULT); culture of the types of *E. coli* and confirmation of serotype and virulence factors is essential. In ED a large number of the *E. coli* may have disappeared. The presence of hemolytic *E. coli* is not diagnostic for ED because there are some strains of EPEC that can cause ED but are nonhemolytic. There are more cases of mixed infections with *E. coli* now than before. The differentiation of pathogenic and nonpathogenic *E. coli* can be achieved through PCR. A multiplex PCR has been developed for STa, STb, K99, 987P, and F41.[5] A multiplex PCR assay for nine different virulence factors associated with *E. coli* that cause ED in swine is available.[6] The tests tell you that the gene is present but not whether it is actually encoding for the proteins.
- *Histology:* Formalin-fixed colon, ileum, jejunum, gastric fundus, brain, and mesenteric lymph node (LM).

DIFFERENTIAL DIAGNOSIS

The appearance 2 weeks postweaning is suggestive, as are visible edema and nervous signs. Although there are a number of diseases of pigs in the susceptible age group in which nervous signs predominate, gut edema is usually easy to diagnose because of the rapidity with which the disease strikes, the number of pigs affected at one time, the short duration of the outbreak, and the obvious edema of tissues. Affected pigs are usually in prime condition. The ataxia and recumbency must be differentiated from diseases of the nervous system of pigs that cause ataxia and recumbency. These include pseudorabies, viral encephalomyelitis (Teschen disease), encephalomyocarditis, streptococcal meningitis, salt poisoning, and organic arsenic poisoning. Mulberry heart disease and encephalomyocarditis can produce similar signs, and differentiation on necropsy findings and histopathology is necessary. In poisoning by *Amaranthus* spp. and *Chenopodium album* the signs may be roughly similar, but the edema is limited to the perirenal tissues.

TREATMENT

Sick pigs should be treated initially with antimicrobials and electrolytes parenterally because they do not eat or drink. Administration in water may then follow. Treatment is ineffective. Elimination of the toxin-producing bacteria may be attempted by use of antimicrobials in the feed or water supplies. The choice of antimicrobial will vary depending on area variations of the drug sensitivities of *E. coli.* The drug should be highly active in the lumen of the gut (possibly fluoroquinolones, cephalosporins, apramycin, ceftiofur, neomycin, or trimethoprim),

depending on the prescribing rules in each country. The feed consumption of the unaffected pigs in the group should be reduced immediately and then gradually returned to previous levels over a period of a few days. Recovered pigs have protective antibodies to Stx2e.

CONTROL

Nurseries should be managed as all-in/all-out facilities and properly cleaned, disinfected and dried, and rested before the next arrivals. Correct temperatures for weaning and the avoidance of cooling drafts are especially significant.

The strains of PWD and ED of all the *E. coli* are the ones that are likely to show the most antibiotic resistance.

Pigs should be kept on the same creep feed for at least 2 weeks after weaning, and the change in feed should be made gradually over a 3- to 5-day period. Feed restriction through the critical period is frequently practiced and may reduce the occurrence of ED. Similarly, an increase in crude fiber and decrease in nutrient quality of the diet through this period may reduce the incidence. However, it is evident that a severe restriction and marked decrease in nutrient quality is required to fully achieve this effect, and this is not compatible with the purpose of growing pigs. It is essential that pigs on restricted intakes be provided with adequate trough space to allow an even intake of food among the group. For similar reasons, litters of pigs that are batched at or after weaning should be divided into groups of approximately equal BW.

The strategic incorporation of an antimicrobial into the feed during the risk period may be necessary on some farms. A reduction in the potential for oral–fecal cycling of organisms in the group may reduce the incidence of ED. A reduction in the age of weaning may also reduce the incidence. Both organic acids and medication with 50 ppm of enrofloxacin are useful in controlling and/or preventing PWD or ED.

Treatment with anti-VT2E serum can provide protective immunity against ED in pigs.

Spray dried porcine plasma has helped because it contains specific anti-ETEC antibodies. The use of eggs from previously vaccinated hens has also been used.

No successful vaccine is available to produce the increased levels of IgA required to neutralize the attached *E. coli.* A new recombinant vaccine has been developed for a Stx22e subunit vaccine.[7] Only vaccines with the preformed fimbriae induce protection, and this is limited to the homologous variant but, experimentally, vaccination of piglets with a genetically modified Shiga-like toxin 2e prevents ED following challenge with the Shiga-like toxin after weaning. The concentration of protein in the diet also influenced susceptibility to ED. Pigs fed a

low-protein diet and not vaccinated developed subclinical ED. Pigs fed a high-protein diet and not vaccinated developed clinical ED. Pigs fed a high-protein diet and vaccinated had a reduction in the incidence of subclinical edema and did not develop clinical ED.

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POSTWEANING DIARRHEA OF PIGS (COLIFORM GASTROENTERITIS)

PWD is common within several days after weaning and is characterized by a reduced growth rate associated with alterations in the mucosa of the small intestine and, in some pigs, by acute coliform gastroenteritis characterized by sudden death, or severe diarrhea, dehydration, and toxemia. It is a major cause of economic loss from both mortality and inferior growth rates for several days to 2 weeks following weaning. The etiology, epidemiology, and pathogenesis are multifactorial and complex because of the several weaning-associated factors that may interact. In some instances the PWD may be followed by ED.

SYNOPSIS

Etiology Specific serotype of enterotoxigenic *Escherichia coli*

Epidemiology Three to 10 days postweaning; high morbidity and case–fatality rates. Stressors of weaning are risk factors (change of feed, loss of maternal contact and maternal antibody, mixing litters, and environmental changes)

Sign Some pigs found dead. Outbreaks of severe diarrhea a few days postweaning. Fever, dehydration, anorexia, loss of weight, and death in a few days

Clinical pathology Culture organism from feces and intestinal contents.

Lesions Dehydration, serofibrinous peritonitis, fluid-filled intestines, and mesenteric edema

Diagnostic confirmation Isolate specific serotypes of *E. coli.*

Differential diagnosis list
- Gut edema
- Swine dysentery
- Salmonellosis
- Erysipelas
- Pasteurellosis

Treatment Antimicrobials in water supply

Control Minimize stress at weaning. Antimicrobials in feed and water postweaning. Intestinal acidification. Zinc oxide in diet postweaning

ETIOLOGY

Some strains of *E. coli* can cause both ED and PWD. The key feature is the disappearance after weaning of antibodies to *E. coli* previously provided by milk. The disease is associated with ETEC that produce adhesion factors that allow colonization of the intestine and mediated by enterotoxins that induce the intact intestinal mucosa to secrete fluid. It can also be caused by EPEC that do not possess any of the virulence factors of PWD or ED. A summary would be that PWD is associated with fimbrial types F4 (K88) and F18 variants (F18ac or F18ab as fimbrial adhesins)[1,2] and carrying the genes for the Shiga-like toxin 2(SLT-2E), LT, and/or Shiga toxin A and B (STa or STb). Toxin and F18 fimbrial genes in *E. coli* isolated from pigs with PWD or ED occur in a variety of chromosomal backgrounds. The three F4 receptors (F4ab, F4ac, and F4ad) are encoded on distinct loci.[3] Nearly all are α-hemolytic and belong to a limited number of serotypes.

The presence of the F4 receptor was associated strongly with pigs being high shedders of *E. coli.*[4] Most commonly, F4 is serotype O149, and F18 is serotype O 139, O138, O141, O149, and O157, which are associated with the disease. Most serotypes appear to be O149:STaSTbLT:F4 (K88). The strains of O149 isolated in recent years from weaned pigs with diarrhea possess the gene for an additional enterotoxin STa, which older strains lack. Of the new strains that correspond to O149 H10, 92% code for this gene. This enteroaggregative *E. coli* heat-stable enterotoxin 1 (*EAST 1*) gene is found in isolates from weaned pigs that have diarrhea or ED. The F107 fimbriae can be found in association with PWD isolates, and other adhesive fimbriae such as Av24 and 2134P have been described. Many ETEC isolates colonize the small intestine of weaned pigs but lack known colonization factors. The serogroups of *E. coli* isolated from pigs with PWD in piggeries in Spain include strains that produce the ETEC and VTEC *E. coli* and cytotoxic necrotizing factor toxins. The disease can be reproduced consistently in weaned pigs, provided the pig's epithelial cell brush borders are susceptible to the adhesin of strains of *E. coli* with fimbrial antigen F4 (K88). The DNA sequences coding for the F18 fimbrial antigens and AIDA adhesin are on the same plasmid in *E. coli* isolated from the cecum. Usually they were LTSTb or STb (13%) and 12% were hemolytic and F18-positive. The remainder were nonhemolytic, belonging to the K48 serogroup.

Although there is an etiologic similarity between PWD and neonatal enteric colibacillosis in suckling piglets, the relationship is not exact. Strains associated with neonatal enteric colibacillosis may not have the ability to produce PWD, and many strains isolated from coliform gastroenteritis lack K88+ antigen.

Cytotoxic necrotizing factor strains of *E. coli* have been isolated from weaner pigs with necrotic enteritis in South Africa.

Some nonenterotoxigenic O45 isolates of *E. coli* associated with PWD produce AEEC, and their proliferation may be associated with diet. Dual infection with AEEC may also be associated with PWD.

Infection with rotavirus may be an etiologic factor. The rotavirus may infect and destroy villous epithelial cells of the small intestine, which may allow colonization of the *E. coli*. Experimentally, a high nutrient intake fed three times daily to piglets weaned at 3 weeks of age produced the most prolonged diarrhea, colonization of the intestine by hemolytic ETEC, and persistent shedding of rotavirus. However, other observations cast doubt on the importance of rotaviruses as a cause of the diarrhea, because rotaviruses may be found in the feces of pigs without diarrhea a few days after weaning. The acute disease can be reproduced using K88 *E. coli* strains without concomitant infection with rotavirus.

A number of F18ab-positive or F18ac-positive strains produce enterotoxins and Stxe, and in these strains it is more likely that PWD will occur rather than ED.

EPIDEMIOLOGY

It is found worldwide and in a single geographic area a serotype may predominate.[46] Occasionally different serogroups may be involved in an outbreak.

PWD occurs predominantly in pigs 3 to 10 days after they are weaned. There is considerable variation in the morbidity and mortality between groups, rooms of pigs, and buildings. The age group clinically affected varies with pig age and diet. F4 receptors are expressed in pigs of all ages, but F18 is not fully expressed until pigs are 2 to 3 weeks of age. The diet may push back the time of PWD to as far as 6 to 8 weeks after weaning if substances such as zinc or acidifying agents are added to the diet.

Most outbreaks are in early weaned pigs. Infections are usually picked up from the environment. Most commonly, pigs are first observed sick or dead on the fourth or fifth day. The spread within affected groups is rapid and a morbidity rate of 80% to 90% of the group within 2 to 3 days is not uncommon. Frequently, other pens of susceptible pigs within the same area will also develop the disease within a short period of the initial outbreak. The problem may persist within a herd, affecting successive groups of weaned pigs over a period of weeks or months. The

onset of the problem may be associated with the introduction of a different batch or formulation of the creep feed. The case–fatality rate may be as high as 30%, and survivors may subsequently show a reduced growth rate. The weaning of piglets at 3 weeks of age is commonly followed in a few days by a postweaning reduction in growth rate, variations in total dietary intake, and the development of diarrhea. Piglets weaned at 3 to 4 weeks of age into an uncomfortable dirty environment appear especially susceptible.

The proliferation of *E. coli* in the intestine following weaning appears secondary to some underlying gastrointestinal disturbance. After weaning there is a progressive increase in viscosity of the intestinal contents, which alters the intestinal structure and growth and stimulates the proliferation of ETEC in newly weaned pigs. In all groups of pigs examined the number of serotypes or diversity of intestinal flora was reduced in the first week after weaning. The disease is associated with an earlier, more prolonged and greater proliferation of ETEC in the small intestines than occurs in healthy pigs after weaning. Some studies have shown that susceptibility to adhesion with K88+ ETEC is a requirement for the production of the disease. Experimentally, pigs that did not have the adhesin receptor did not develop diarrhea when challenged with K88+ *E. coli* and when in the same environment as the adhesin-positive pigs.

It is believed that several factors commonly associated with weaning predispose pigs to PWD associated with ETEC. Some of these risk factors include:

- Stress from loss of maternal contact
- Introduction to strange pens and penmates
- Inadequate ventilation in the weaning pens
- Reduction in ambient temperature
- Change in diet
- Cessation of lactation immunoglobulins
- Decreased gastric bactericidal activity attributable to a temporary increase in gastric pH
- Preweaning exposure (creep feeding) to the dietary antigens fed after weaning

Hand-washing and donning clean outerwear did not prevent the transmission of *E. coli*, but showering and donning clean outerwear did.

Experimentally, there is some evidence that the stress of cold ambient temperature (15°C) can result in a greater incidence of diarrhea in weaned pigs than in those housed at 30°C.

The nature and the amount of the diet that the piglet consumes before and after weaning may be a predisposing factor. One hypothesis suggests that a transient hypersensitivity of the intestine may occur if piglets are primed by small amounts of dietary antigen before weaning (creep feeding), followed by ingestion of greater quantities of the diet after weaning. Pigs that develop diarrhea tend to be those that consume more food after weaning than their contemporaries.

Generally, weaning at 3 weeks of age is associated with alterations in the villous epithelium of the small intestine that result in varying degrees of malabsorption and a reduction in daily growth rate that may last for 2 weeks. There are large rapid reductions in intestinal lactase activity that coincide with reductions in growth rate and a reduced ability to absorb xylose. There is a reduction in villous height and an increase in crypt depth in the small intestine, but these alterations are not necessarily associated with the consumption of creep feed before weaning, which does not support the hypothesis that hypersensitivity to a dietary antigen caused by priming before weaning is a factor. There is now considerable doubt about the validity of the intestinal hypersensitivity hypothesis. Recent experimental work indicates that creep feeding is not required for the production of the diarrhea and does not induce morphologic changes characteristic of an allergic reaction in the small intestine. The presence of nondigested food in the gut lumen favors proliferation of ETEC. Proteins of animal origin may provide some protection.

Dietary manipulation can modify several changes that normally occur in the small intestine of the piglet after weaning. Feeding a sow milk replacer or a diet based on hydrolyzed casein reduces the increases in crypt depth and the reductions in brush border enzymes. The use of an antibiotic to suppress the microbial activity does not alter the changes in the mucosa after weaning.

The ecology of *E. coli* and rotavirus in the stomach and intestines of healthy unweaned pigs and pigs after weaning has been examined. Gastric pH is higher in weaned pigs and may not reach a level sufficient to prevent significant numbers gaining access to the small intestine. This factor can be of importance in pigs weaned in pens where oral–fecal cycling of *E. coli* may provide a massive challenge. After weaning, the hemolytic ETEC serotype O149:K91, K88ac (Abbotstown strain), commonly colonizes the rostral small intestine from lower down the intestinal tract. This serotype has never been found in the gastric contents of weaned pigs. When this serotype is present it tends to dominate the *E. coli* flora at all levels of the intestine. Although rotaviruses are common in the intestinal contents of weaned pigs, the presence of the virus is not necessary for production of PWD.

The loss of lactogenic immunity at weaning may be a risk factor. Milk from sows whose progeny develop PWD contain antibodies capable of neutralizing the enterotoxigenic effect of the homologous *E. coli*. This suggests that the presence of antibody-mediated activity against ETEC may be important in preventing the disease during the nursing period. At weaning this protection is removed and the piglet is unable to produce its own antibodies rapidly enough to prevent the disease. The stress of weaning does not appear to affect the immune mechanisms of the pig.

The weaning of piglets at birth or at 1 day old is associated with a high mortality rate caused by diarrhea and septicemia. The high mortality rate is associated with a lack of colostral antibodies and the strict hygienic conditions required for the artificial rearing of pigs weaned at birth.

PATHOGENESIS

Different parts of the porcine intestinal tract may harbor different strains of *E. coli*, and it may be that these strains have different characteristics.[5]

The colonization and proliferation of *E. coli* in the small intestine originates from organisms in the lower part of the intestinal tract. There is a rapid increase in numbers of the organisms in the small intestine epithelium or the mucus covering from the midjejunum to the ileum serotypes of *E. coli* associated with PWD, which may be found in the feces of healthy pigs. The virulence factors for PWD are associated with the F4 and F18 fimbrial antigens that carry the genes for the production of toxins (STa, STb, LT, SLT2a, and SLX2e). The receptor for the F4 adhesin is not found in all pigs. There are five phenotypes based on the susceptibility of brush borders of different pigs to adherence of isolates producing variants F14ab (K88ab), F4ac (K88ac), and F4ad (K88ad). Pigs with at least one copy of the dominant allele for the receptor are susceptible to epithelial cell adherence and therefore colonization. The F18ab variant is expressed by the *E. coli* O139 strain producing Shiga-like toxin and causing ED. The F18ac fimbrial *E. coli* strains often relating to O141 or O157 cause diarrhea by expressing enterotoxins (STa or STb) either together or with or without Shiga-like toxins. STb binds to a particular receptor.[6] The PWD strains also produce LT, which lead to hypersecretion of electrolytes and water.[7,8] Following weaning, their numbers in feces normally increase markedly, even in pigs that remain healthy. The *E. coli* proliferate in the small intestine and produce an enterotoxin that appears to attach to the receptors. This triggers the uptake of calcium into the cell, which results in the excretion of water and electrolytes into the lumen. This causes a net loss of fluid and electrolytes to the lumen and subsequent diarrhea. After weaning, the net absorption of fluid and electrolytes in the small intestine of pigs is temporarily decreased.

In porcine EPEC the intimin binds to its receptor on the apical surface of the cells of the small and large intestine[9,10] with most in the colon and the duodenum. How they produce diarrhea is not really understood.

Heat-labile enterotoxins type IIa and type IIb are involved in the pathogenesis of ETEC for neonatal pigs.[48]

The number of hemolytic *E. coli* present in the proximal portion of the jejunum may be 10^3 to 10^5 times higher in affected pigs than healthy weaned pigs of the same age. The susceptibility of the small intestine to the enterotoxin varies according to area; the upper small intestine is highly susceptible, and susceptibility decreases down through the more distal portions. Unlike many other species, the weanling pig depends largely on its large intestine for absorption of fluid and electrolytes with only small changes in net fluid movement occurring along the jejunal and ileal segments. In fatal cases, death results from the combined effects of dehydration and acidosis resulting from fluid and electrolyte losses. In the peracute and acute forms of the disease, there is a shock-like syndrome with marked gastric and enteric congestion, hemorrhagic enteritis, and death.

The experimental model of the disease is characterized by the three syndromes:
- Peracute fatal diarrhea
- Moderate diarrhea of 3 to 4 days' duration, accompanied by fecal shedding of the inoculated organism and reduced BW gain
- Fecal shedding of the organism with reduced weight gain but without diarrhea

The role of the rotavirus in the pathogenesis of PWD is uncertain. It can be found in the feces of healthy unweaned and weaned pigs. The virus is capable of infecting and destroying villous epithelial cells that could contribute to the partial villous atrophy, loss of digestive enzyme activity, malabsorption, and reduced growth rate. Experimental inoculation of an ETEC and the rotavirus causes a more severe disease than either agent does alone.

Changes in the mucosa of the small intestine of recently weaned pigs have been observed and are the subject of much controversy. There is a reduction in the length of the villi, a marked reduction in intestinal disaccharidase activity, and an increase in the depth and activity of the intestinal crypts. These changes are maximal at 3 to 7 days following weaning, persisting until the second week and coinciding with the reduced growth rate.

CLINICAL FINDINGS

PWD and ED can occur simultaneously. Usually in PWD mortality is 1.5% to 2.0% but in prolonged outbreaks may reach 25%. The mortality is similar to the neonatal disease but is less severe, and there is a lower mortality. Morbidity may reach 100%. The postweaning reduction in growth rate may affect 50% to 100% of the pigs within a few days after weaning and persist for up to 2 weeks. In some situations diarrhea may not develop in any of the pigs in the group or may be delayed for 6 to 8 weeks. A reduction in feed intake, gaunt abdomens, and lusterless hair coats are characteristic findings of piglets with postweaning "check." They may appear unthrifty for 10 days to 2 weeks, by which time they will improve remarkably.

It is common for one or two pigs, in good nutritional condition, to be found dead with little seen in the way of premonitory signs. At this time the others within the group may appear normal, but closer examination will reveal several pigs showing mild depression and moderate pyrexia. A postmortem examination of dead pigs should be conducted early in the examination. A proportion of the group will develop diarrhea within 6 to 24 hours, and by 3 days after the initial onset the morbidity may approach 100%. Feed consumption falls precipitously at the early stages of the outbreak, but affected pigs will still drink. Affected pigs may show a pink discoloration of the skin of the ears, ventral neck, and belly in the terminal stages. Diarrhea is the cardinal sign—the feces are very watery and yellow in color but may be passed without staining of the buttocks and tail. Pyrexia is not a feature in individual pigs once diarrhea is evident. Affected pigs show a dramatic loss of condition and luster and become progressively dehydrated. Voice changes and staggering, incoordinated movements may be observed in the terminal stage in some pigs. The course of an outbreak within a group is generally 7 to 10 days, and the majority of pigs that die do so within the initial 5 days. Surviving pigs show poor growth rate for a further 2 to 3 weeks, and some individuals show permanent retardation in growth. In outbreaks in early weaned pigs diarrhea is usually evident before death occurs. There is some evidence to show that PWD may be activated by PRRS.

CLINICAL PATHOLOGY

Culture of the feces and intestinal contents for ETEC strains of *E. coli* is indicated.

NECROPSY FINDINGS

Pigs dying early in the course of the outbreak are in good nutritional condition, but those dying later show weight loss and dehydration and occasionally cyanosis. Mild skin discoloration of the ears and ventral areas of the head, neck, and abdomen is usually present. In acute cases there is a moderate increase in peritoneal fluid, and barely perceptible fibrinous tags between loops of the small intestine may be present. The vessels of the mesentery are congested and occasionally petechial hemorrhages and edema are present. The stomach may be distended with dry food, and the small intestine may be dilated with slight edema and hyperemia. The gastric mucosa is congested, and an infarct (ulceration) may be present along the greater curvature. The small intestines are dilated and contain yellow mucoid liquid or occasionally bloodstained material. The mucosa of the small intestine is congested and sometimes there are hemorrhagic areas. The content of the large intestine is fluid to porridge like in consistency, and the mucosa may be congested. Pigs dying later may be emaciated and smell of ammonia. In some cases mild mesocolonic edema is visible. Hemolytic *E. coli* can be isolated in large numbers from the small intestine and mesenteric lymph nodes. Polyclonal antisera directed against known pathogenic serotypes are usually used to test the isolate, but a negative result does not preclude the strain from being an enteropathogenic organism.

Microscopically, there may be no lesions, but there is usually bacterial adherence to intestinal villi. This is at its worst in the duodenum and the colon. There may be bacteria in the cells in enterocytes, and sometimes these cells disintegrate and lead to sloughing. Other changes are those commonly associated with endotoxemia, especially microvascular thrombosis in a variety of organs.

Samples for Confirmation of Diagnosis

- *Bacteriology*: Mesenteric lymph node, segment of ileum, colon (CULT); in PWD cases the culture usually yields of hemolytic (ETEC) and nonhemolytic (EPEC) *E. coli*. An RT-PCR assay for the detection of *E. coli* F14 in pig fecal samples by targeting part of the *rfb* sequence specific for this group has been used.[11] A multiplex PCR for nine different virulence factors associated with *E. coli* that cause diarrhea and ED in swine has been described.[12] An RT-PCR for the differentiation of F4 (K88) variants (F4ab, F4ac, and F4ad) of ETEC from diarrheic piglets has been described.[47]
- *Histology*: Formalin-fixed stomach, several segments of small intestine, colon, liver, lung, spleen (LM); colonization of the epithelium can be seen by light microscopy, and confirmed using immunohistochemistry (IHC) or in situ hybridization (ISH).

DIFFERENTIAL DIAGNOSIS

Postweaning diarrhea is the prime consideration in pigs that are scouring or dying within a 3- to 10-day period after a feed or management change with marked dehydration and low to moderate mortality. The gross lesions and the associated smell are helpful.

Swine dysentery and salmonellosis are manifested by diarrhea and death but they are not necessarily related to weaning or feed change, and both are more common in older growing pigs. Salmonellosis poses the greatest difficulty in initial diagnosis from coliform gastroenteritis. In salmonellosis, the feces are generally more fetid with more mucus, mucosal shreds, and occasionally blood, and the skin discoloration is more dramatic. On necropsy examination enlarged hemorrhagic

peripheral and abdominal lymph nodes and an enlarged pulpy spleen are more suggestive of salmonellosis; however, cultural differentiation is frequently required. If there is doubt, the pigs should be treated to cover both conditions until a final decision is obtained. The onset of swine dysentery is comparatively more insidious than that of postweaning diarrhea; the characteristic feces, clinical and epidemiological pattern, and postmortem lesions differentiate these two conditions.

Swine fever should always be a consideration in outbreaks in pigs manifested by diarrhea and death. However, the epidemiological and postmortem features are different.

Other common causes of acute death in growing pigs such as erysipelas, pasteurellosis, and *Actinobacillus pleuropneumoniae* infection are easily differentiated on necropsy examination.

Edema disease occurs under similar circumstances to coliform gastroenteritis, but the clinical manifestation and postmortem findings are entirely different.

TREATMENT
Antimicrobial Resistance and *E. Coli*

In a study in Spain,[13] it was shown that *E. coli* in the pig fecal microbiome were highly dynamic and show a high level of diversity. The finishing pigs showed the lowest levels of AMR. On-farm AMR did not select for the VGs in *E. coli* carried by a population of healthy pigs.[14]

In a study of pigs fed antibiotics it was shown that bacterial biotypes shifted after 14 days of treatment, with the medicated pigs showing an increase in Proteobacteria (1%–11%) compared with the nonmedicated pigs. Antibiotic resistance genes increased in diarrhea and diversity. Some of the new genes conferred resistance to antibiotics that had not been given.[15]

The *E. coli* stored in a storage tank was more diverse than that in fresh feces. The detection of resistance to specific antibiotics was not significantly different.[16]

There may a horizontal exchange of AMR genes. Almost half (47%) of *E. coli* and *Salmonella* isolated from the same fecal samples showed the AMR genes at the same level.[17,18]

Significant space-time clusters of resistant *E. coli* were found in parts of Denmark.[19] In a study of *E. coli* isolated from pigs in China it was found that most isolates were genetically unrelated. AMR was found in 89% of *E. coli* strains. Most prevalent VG was *East 1*, followed by Stx2e and *eae*. The authors stressed that there was a great need to monitor changes as a result of the high incidence of VG and AMR.[20] The pharmacodynamics of antimicrobials at different levels of the intestinal tract of pigs and their relationship to *E. coli* resistance patterns in the pig have been described.[21] A study of AMR and

virulence profile genes in multidrug-resistant ETEC isolated from pigs with PWD in Australia[22] has shown that nine serogroups were identified, particularly O149. None showed resistance to ceftiofur or enrofloxacin, and 9.4% were resistant to florfenicol. O141 had a higher AMR index than other serogroups. There were few associations between AMR and VGs. The multidrug-resistant ETEC ARG/VG profiles suggested that there was a considerable strain and plasmid diversity reflecting various selection pressures at the individual farm level rather than emergence and lateral spread of multidrug-resistant clones.

A Swedish study showed that, except for resistance to tetracyclines, sulfamethoxazole, and streptomycin, antibiotic resistance is not equally spread across *E. coli* isolates. Tetracyclines should not be the first choice of treatment because of the rapid acquisition of resistance. Nearly all isolates are highly susceptible to enrofloxacin, gentamicin, and neomycin.

It is imperative that treatment of all pigs within the group is instigated at the initial signs of the onset of PWD, even though at that time the majority of pigs may appear clinically normal. Delay will result in high mortality rates. Any pig within the group that shows fever, depression, or diarrhea should be initially hospitalized, treated individually, both parenterally and orally, and the whole group should then be placed on oral antibacterial medication. Water medication is preferable to medication, although the feed is easier to institute, but affected pigs will generally drink (less than usual if sick) even if they do not eat. Neomycin, tetracyclines, sulfonamides, or trimethoprim-potentiated sulfonamides and ampicillin are the usual drugs of choice. Danofloxacin is safe and highly effective. Experimental infection with K88-positive *E. coli* was controlled by ceftiofur sodium given intramuscularly daily for three consecutive days. When pulse dosing is used there appears to be less resistance. In herds with PWD problems, prior sensitivity testing will guide the choice of the antibacterial to be used. Antibiotic medication should be continued for a further 2 days after diarrhea is no longer evident and is generally required for a period of 5 to 7 days.

Consideration should be given to the medication of at-risk equivalent groups of pigs within the same environment. Intraperitoneal fluid and electrolyte replacement for severely dehydrated pigs and electrolytes in the drinking water should also be considered.

CONTROL

Recommendations for effective and economical control of postweaning reduced growth rate and PWD in pigs weaned at 3 weeks of age are difficult because the etiology and pathogenesis of this complex disease are not well understood. Epidemiologically, the

disease is associated with weaning and the effects of the diet consumed before and after weaning. In all cases the piglet should be 4.5 kg (10 lb) and preferably 5.5 kg (12 lb) at weaning. Protective antibodies are produced in recovered animals.

A whole variety of techniques, including intestinal acidification; antimicrobial medication in water or feed; environmental modifications; competitive exclusion; feeding probiotics; binding agents such as eggs, milk, or bacterial by-products (most of these studies show they do not work); zinc oxide; or vaccination of sows and piglets with toxoids have been tried. The use of dietary egg yolk antibodies may or may not be effective.

Spray dried plasma powder obtained from pigs immunized with a vaccine containing ETEC fimbrial subunit F4 and LT can reduce diarrhea because of spontaneous antibodies against ETEC.[23] This study showed that the combination of anti-LT and anti-F4 antibodies is most effective.

Intestinal acidification reduces the binding of the *E. coli* to the epithelial surface, and a pH of 3.5 to 4.0 at the trough or nipple drinker is best. Citric acid, formic acid, propionic acid, or a citric acid/copper sulfate mixture can be used.

Zinc oxide in particular stabilizes the intestinal flora. It impacts both host cell and pathogen metabolism and may provide insight into the mechanisms for diarrhea reduction.[24] Piglets given lactose and fiber were least affected, and the next least affected were animals that received zinc oxide. Pigs fed dietary antibiotic growth promoters and zinc oxide had lower counts of anaerobic bacteria in their feces than control piglets. The removal of these ingredients from the diet will increase days to slaughter. In a study of the effect of feeding kaolin on ETEC infections in weaned pigs,[25] it was found that there was a protective effect on the course of ETEC. Colonization and shedding of ETEC by piglets fed the kaolin were milder and of shorter duration.

It has been traditionally accepted, without reliable evidence, that the sudden transition in diet at weaning is the major predisposing factor, but the experimental observations are conflicting. One set of observations indicates that, if pigs eat a small quantity of creep feed before weaning, they are then "primed" and develop an intestinal hypersensitivity that, following the ingestion of the same diet after weaning, results in PWD. On the other hand, it has been suggested that piglets should consume at least 600 g of creep feed before weaning to develop a mature digestive system. Another set of observations indicates that those pigs that consumed an excessive quantity of feed after weaning developed the disease.

The complete withholding of creep feed followed by abrupt weaning at 3 weeks of age seemed to have a protective effect, possibly

associated with a low dietary intake. Farms with lower rates of PWD used their first piglet ration (phase 1 feeding) for much longer and also changed over to the second ration over a much longer period. Competitive exclusion has been shown to be beneficial.

The recommendations set out here are based on the hypothesis that the consumption of adequate quantities of creep feed before weaning is the most effective and economical practice. Every effort should be made to minimize the stress associated with weaning. Stressors influence the fecal shedding of ETEC by young piglets by a mechanism that may not involve modulation of the immune response. To avoid a sudden transition in diet at weaning, creep feed should be introduced to the suckling piglets by at least 10 days of age. It is important that the creep feed and feeder area be kept fresh to maintain palatability. The same feed should be fed for at least 2 weeks following weaning, and all subsequent feed changes should be made gradually over a 3- to 5-day period. Feed restriction in the immediate 2-week period following weaning may reduce the incidence but generally is not successful. It is a common field observation that the incidence of diarrhea varies with different sources of feed, but experimental studies to confirm this relationship are not available.

The addition of fiber to the diet may be beneficial but leads to a reduced growth rate. In a study[26] of the role of fiber in the control of PWD it was found that there were two major means of reducing enteric disorders: (1) by minimizing the use of nonstarch polysaccharides (NSPs) such as pearl barley and guar gum, which lead to increased digesta viscosity and (2) by including moderate levels of NSPs that do not increase digesta viscosity, such as oats and inulin, especially where there are levels of high crude protein. NSP fractions affect the taxonomic composition and metabolic features of the fecal microbiota.[27]

The use of low-protein diets may reduce the toxic products and reduce PWD. A diet with decreased protein content reduces protein fermentation and the incidence of PWD challenged with ETEC.[28] The development of greater digestibility or stimulation of higher feed intake may also be responsible for reduction of PWD.[29] Zinc oxide in the diets at 300 to 4000 ppm may stop PWD by preventing colonization of the epithelial lining of the intestine. A variety of feedstuffs reduced the adhesion of ETEC to a porcine intestinal cell line and reduced the inflammatory response.[30]

A symbiotic preparation of starch and anti-ETEC K88 probiotic in the presence of raw potato starch is an effective method for reducing the negative effects of ETEC in the piglet model.[31]

Organic acid administration in drinking water to reduce the pH to 4.0 has shown that there was a reduction in the excretion of fecal E. coli, but there was also a significantly decreased water intake.[32]

β-Glucans also reduce susceptibility to ETEC,[33] and in this study there was a reduced excretion of F4 + E. coli and a reduced F4-specific serum antibody response.

Colicin also reduced PWD,[34] as did prebiotics.[35] One study of a probiotic has shown promise.[36]

A tryptophan-enriched diet improved feed intake and growth performance of ETEC-challenged (K88 +) pigs[37] and E. coli F4.[38]

Where possible, at weaning, the sow should be removed and the pigs should be kept as single litters in the same pen for the immediate postweaning period. If grouping of litters is practiced at this time, or later, the pigs should be grouped in equivalent sizes. Multiple suckling in the preweaning period may reduce stress associated with groupings of part-weaned pigs. With all pigs, but especially those weaned earlier than 6 weeks, the pen construction should encourage proper eliminative patterns by the pigs and good pen hygiene to minimize oral–fecal cycling of hemolytic E. coli. The environment also appears especially important in this group, and draft-free pen construction should encourage proper ventilation. It is preferable to wean pigs on weight rather than age, and in many piggeries a weaning weight of less than 6 kg is associated with a high incidence of PWD.

There is a development of bacterial resistance against a wide range of antibiotics. This means that the susceptibility of microorganisms should be tested before their use.

The inclusion of an antimicrobial in the feed or water to cover the critical period of susceptibility (generally for 7–10 days after weaning) can be used as a preventive measure. Apramycin at the rate of 150 g/tonne of feed for 2 weeks after weaning may be associated with improved growth rates and a reduction in mortality. The high incidence of drug resistance in isolates of E. coli makes prior sensitivity testing mandatory, and the antibiotic may need to be changed if new strains gain access to the herd. The routine use of prophylactic antibiotics for this purpose needs to be considered in relation to the problem of genetically transmitted drug resistance; however, it is currently often necessary for short-term control of a problem.

Vaccination may offer an alternative method of control. Injectable vaccines for sows are designed to produce an improved colostral provision of antibodies but do not increase suitable IgA antibodies in the weaned pig intestine.

However, currently there are no vaccines available for the control of colibacillosis in weaned pigs. Oral inoculation with 5×10^8 to 10^9 of nontoxigenic strains can be followed with K88 at day 1 of move, K88/F18ab at day 7, and F18 at days 13 to 15. Only the oral vaccines with the preformed fimbriae appear to produce any protection from the homologous fimbrial variant. The results vary, and some authors think that the prolonged transit time in the stomach after weaning may deactivate the F4 fimbriae when this has been used as a fimbrial vaccine. Microencapsulated ETEC and detached fimbriae have been used for peroral vaccination in pigs. Parenteral vaccination for the control of coliform gastroenteritis has proved of variable value, probably because parenterally administered antigens do not usually stimulate the production of IgA antibodies and intestinal immunity. Oral immunization by the incorporation of E. coli antigens into creep feed has been shown to reduce the incidence and severity of PWD. A live avirulent experimental E. coli vaccine with K88+, LT+ ETEC in weaned pigs provided protection. Rearing early-weaned piglets artificially for the purpose of increasing the efficiency of the sow is an attractive management concept. However, high death losses from diarrhea have slowed progress in this new development. The incorporation of antibodies in the diet of such piglets as a prophylactic measure should be possible and is being explored.

Bacteriophages can be used to prevent and treat diarrhea caused by experimental ETEC O149 infection.[39]

A vaccine candidate expressing ETEC adhesins (K88ab, K88ac, K99, FasA, and F41fimbrial genes) inserted into a plasmid and transferred to Salmonella produced a significantly increased antibody response.[40] The study showed that the candidate vaccine can effectively protect their young pigs against colibacillosis.

A commercial vaccine of F4 fimbrial origin has shown to be useful in preventing a virulent F4 ETEC challenge.[41,42] An F18 fimbrial vaccine did not induce protective immunity.[43]

Chitosan-alginate microcapsules for oral delivery of egg yolk immunoglobulin (IgY) has been evaluated in a pig model of enteric colibacillosis,[44] and it has been shown that it is useful and may be a future method for preventing E. coli disease.

The ultimate control of PWD is to remove the receptor gene in the population. Although this has been done experimentally, these animals are not yet available in large numbers commercially. The MUC13 gene may provide potential markers for the selection of ETEC F14ab/ac (K88ab/ac)-resistant animals.[45]

Oral antimicrobials increase AMR in porcine E. coli.[46]

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CAMPYLOBACTERIOSIS IN PIGS

Several species of the genus *Campylobacter* are known to cause disease in farm animals; some are potentially zoonotic and the role of some is uncertain. The organisms are a cause of diarrhea, often with mucus, in 3-day-old to 3-week-old pigs and in nonimmune pigs in older age groups. They are often not diagnosed because they are not suspected.

ETIOLOGY

There are two main species in the pig, *C. coli* (CC) and *C. jejuni* (CJ). Both are gram-negative, microaerophilic rods that are catalase positive and cause disease naturally and in experimental infections.[1] Other species have been given experimentally to pigs and have caused disease (*C. hyointestinalis, C. sputorum*) and some have been found naturally, often in high numbers, in the pig and have been sometimes associated with disease (*C. hyointestinalis* subsp. *hyointestinalis, C. hyointestinalis* subsp. *lawsonii, C. mucosalis, C. hyoilei, C. lari*, and *C. lanienae*). They also have been found in wild boar and feral pigs. Virulence factors include motility, secreted toxins,[2] flagella, virulence proteins,[3] inflammation, and invasion.[4,5] Six species of *Campylobacter* were isolated from feral swine in California.[6]

EPIDEMIOLOGY
Prevalence of Infection

The prevalence of *Campylobacter* infections in both diarrheic and nondiarrheic piglets may average around 50%, but there is no correlation between the occurrence of the organism in the feces and the presence of diarrhea. However, the presence of these organisms constitutes a potential zoonosis among animal handlers.

CJ, CC, and *C. lari* can be isolated from pigs in commercial swine herds. The organisms are present worldwide. CC is isolated from the intestinal contents of 99% of pigs at slaughter. Approximately 60% of the specimens of healthy slaughter pigs may yield *C. jejuni* (CJ).

The prevalence of CC may be 100% in young pigs and others such CJ may be under 10% in young pigs. Both can be isolated from the intestines of healthy pigs. Carriage of the organism is in the gallbladder, ileal mucosa, and large-intestinal mucosa.

Risk Factors

Possible risk factors for CJ were application of manure with broadcast spreaders, feeding of whole cottonseed or hulls, and accessibility of feed to birds.

Transmission

The organisms are spread by the fecal/oral route from the dam, infected feces, or water. Piglets have the same genotypes of CC as their dams[7] at the start of their lives, but these are then partially replaced by strains from elsewhere so that by 66 days of age 33% of piglet isolates were from other sources. Infected animals may secrete organisms at a high level (10^3–10^4/g feces) for months. It will survive at 4°C for 24 hours and at 22°C for 6 days. Parturition enhances fecal shedding by the sow and accounts for the piglet infection.[8] Piglets are infected when young and the infection then spreads. Management factors are correlated with herd size with the smaller farms having a higher prevalence of campylobacters.[9]

Pathogen Risk Factors

Wild birds probably constitute the main natural reservoir of infection but possibly also other farm livestock and rodents.

The distribution and diversity of *Campylobacter* in a large-scale farming environment in the UK was determined by systematic sampling of feces, soil, and water. Warmer months, large farms, and individual housing were identified as risk factors for shedding by sows.[10] The annual increase in *Campylobacter* infections in England and Wales begins in early May and reaches a peak in early June, and this seasonal incidence may be associated with transmission of the organism by flies.

There is an unprecedented level of heterogeneity in the CC in the United States.[11]

CJ is adapted to the intestinal tract of warm-blooded animals and does not normally replicate outside this environmental niche. The single polar flagellum and corkscrew shape facilitates motility in the viscous intestinal mucus. The bacterium gradually dies outside the host's intestinal tract. CJ strains could not be isolated from water after 3 weeks but may survive for up to 60 days in unstirred water.[12]

CC was widespread, with low levels of antibiotic resistance, high genetic diversity, and a strain of CC*i*, which may have become adapted to survival or persistence in water. The pig farm may become a reservoir for CC for transmission to poultry.

Antimicrobial Resistance

Increasing AMR in *Campylobacter* is being recognized worldwide, and resistance to the quinolones is most common in isolates of both CJ and CC from food-producing animals, especially poultry. In Switzerland, there were many novel sequence types in pigs with macrolide resistance,[13] and the use of tylosin selects for resistance.[14] In Canada, a study showed a high level of resistance to macrolides, lincomycin, and tetracyclines but not to fluoroquinolones.[15] In a study in eight states in the Midwest United States where there was no antibiotic usage on a pig farm there were fewer resistant organisms.[16] A high prevalence of CC in the stomach of pigs at slaughter in France was recorded, and a high proportion of the strains were resistant to tetracyclines and erythromycin.

In Japan, AMR was associated with the resistance in CC both within and between classes of antimicrobials.[17] Tetracyclines are most often used to treat pig diseases, followed by β-lactams and macrolides.[18] Most CC were resistant to one or more antibiotics in some form.[19] In Australia, pigs are more resistant to oxytetracycline than poultry. A dose–response relationship between macrolide use and macrolide resistance has been shown.[20] The use of fluoroquinolones was the most important factor associated with the emergence of fluoroquinolone-resistant CC.[21] The resistant strains are persisting environmental isolates that have been acquired by the different livestock species.

Zoonotic Implications

Campylobacter is the leading bacterial cause of diarrhea in humans in many industrialized countries. The most important cause of indigenous food-borne disease is contaminated chicken. Red meats (beef, lamb, and pork) also contribute to illness despite the lower risk.

There is a strong association of *Campylobacter* infection in humans living on farms, and contact with diarrheic animals is a major risk for *Campylobacter* enteritis in humans. Fecal contamination is the main cause in retail raw meats (chicken, turkey, pork, and beef) sampled in supermarket chain stores at levels of 1% to 10%.[22] Both of the main organisms have been identified in pig meat[23] and in livers at abattoirs,[24] but the pig is not a significant contributor to human disease,[25] although it can pose a threat to human health through the food chain.[26,27] In addition, antibiotic treatment of farm animals may have increased resistance in CC isolated from food.[28]

There is good evidence that isolates of CJ from human disease and farm animals are very similar. The use of MLST is being used to compare the genotypes of CJ from farm animals and the environment with those from retail food and human disease. The risk of a meat product being contaminated is associated with pigs that shed higher concentrations of *Campylobacter* before slaughter.[29]

PATHOGENESIS

The role of CJ as primary pathogens in farm animals is uncertain. The organism is not normally pathogenic in farm animals. In humans, the infectious dose is considered to be <1000 *Campylobacter* organisms.

The flagellated motile organisms are more invasive than the nonflagellated nonmotile ones. They can survive for long periods of time inside both phagocytes and epithelial cells. The attachment, invasion, and translocation of CJ in pig small-intestinal cells have been described.[30]

Following infection the organism rapidly multiplies, particularly in the ileum in close contact with the mucosa, but it does not appear to invade the mucosa in large numbers. They may then spread to the gut-associated lymphoid tissues, tonsils, spleen, and gallbladder.[1] It may, however, produce a cytotoxin. The organism then spreads to the large intestine.

It has been shown recently that the secretion of IL-4 damages the paracellular junctions and allows the increased invasion of CJ into cells.[31]

CLINICAL FINDINGS

The disease may be so mild as to be unapparent, without fever, and may be manifested only by mild depression and soft feces with occasional strands of mucus. The incubation period may be 1 to 3 days.

Maternal immunity usually protects against clinical disease but not infection, and most piglets have antibody by 5 to 7 weeks of age.

The clinical signs include a mild fever for 2 to 3 days and a watery or creamy diarrhea with mucus and occasional flecks of blood for a few days. In older pigs with CC there may be a chronic mucoid diarrhea with weight loss.

CLINICAL PATHOLOGY

The information on the various methods used for the detection and identification of *Campylobacter* in laboratory samples has been reviewed. Because of the unique growth characteristics of *Campylobacter,* isolation of these organisms from field samples requires the use of special media and culture conditions and is generally laborious and time-consuming. However, isolation of *Campylobacter* from feces is possible with high success rates. Recovery of *Campylobacter* from environmental samples can be difficult because the organism does not propagate in the environment. The use of molecular detection methods has greatly facilitated the specific and rapid detection and identification of *Campylobacter,* but has not replaced the gold standard of traditional culture methods. Detection and quantification of CJ in the feces of naturally infected cattle is possible using real-time quantitative PCR.

NECROPSY FINDINGS

At necropsy, lesions are restricted to the small intestine; there may be diffuse catarrhal to severe hemorrhagic enteritis of the jejunum and particularly the terminal ileum. The lymph nodes may be enlarged, and the terminal ileum may be thickened. There may be ileal villi loss, and the mucosa may be slightly inflamed. Histologically, the most important finding is proliferation of the lymphoid tissue in the terminal ileum. Large numbers of *Campylobacters* may be seen on smears from the mucosa and isolated in culture.

DIAGNOSIS

If there is a mucoid diarrhea with some mucus and perhaps a little blood in young piglets with no great morbidity and no mortality, then campylobacteriosis should be suspected.

Culture is sufficient but can be supplemented by DNA probes and PCR and improved by using RT-PCR.[32] Discrimination of the major capsular types of CJ is possible using multiplex PCR.[33] It is possible in some laboratories to use ELISA for serum antibody, but this has limited commercial availability.

TREATMENT

Treatment is rarely performed, which is good as a high proportion of CC are resistant to erythromycin (5%–62%) and streptomycin (70% in Canada).[34] Potential macrolide resistance is associated with farms that use tylosin for the treatment of diarrhea in young pigs.[26] A high resistance was also reported for pig CC for ciprofloxacin.[25]

CONTROL

Control depends on sanitation and hygiene in livestock barns to reduce the bacterial populations in the environment of the animals. A high dosage of zinc oxide dietary supplement has an inhibitory effect on CC excretion in weaned piglets.[35]

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PORCINE PROLIFERATIVE ENTEROPATHY

SYNOPSIS

Etiology Lawsonia *intracellularis* (ileal symbiont intracellularis)

Epidemiology Four to 8 weeks after weaning; feeder pigs, and young gilts, sows, and boars. Risk factors not known

Signs Diarrhea, weight loss, inappetence, and may recover. Outbreaks of bloody diarrhea and rapid death may occur in feeder pigs, young gilts, and boars.

Clinical pathology Demonstrate organism.

Lesions Proliferative ileitis. Proliferative hemorrhagic enteropathy, fibrinous casts, and blood clots

Diagnostic confirmation Demonstrate organism in tissues.

Differential diagnosis list
- Esophagogastric ulceration
- Intestinal hemorrhage syndrome
- *Clostridium perfringens* type C hemorrhagic enteritis

Treatment Antimicrobials in feed

Control No reliable strategies. Medication of feed

Porcine proliferative enteropathy (PPE) has been called a variety of names in the past, including **ileitis regional ileitis, porcine proliferative enteritis complex, porcine intestinal adenomatosis (PIA), PPE, necrotic enteritis, regional enteritis, and proliferative hemorrhagic enteropathy (PHE) of pigs**. All of these terms are a reflection of the lesions caused by LI.

PPE causes considerable economic loss. There is a close relationship to the *Desulfovibrio* species, and it is closely related to *Bilophila wadsworthii*, which is a known inhabitant of the human colon and associated with appendicitis. It is widely found in pigs in Australia. There are no known associations with human disease.[1] It does cause disease in young horses and can be isolated from laboratory animals.[2] There may be two biovars, one for pigs and one for the other species.[3] The pig LI are >99% similar worldwide in 16S rDNA and outer membrane proteins. Most work has been performed using a mucosal homogenate challenge model.[4]

ETIOLOGY

The causative agent, first described in Iowa in the 1930s, is LI, which was isolated and Koch's postulates fulfilled in 1993. It is a gram-negative, curved rod (vibrioid shaped) obligate intracellular bacterium in the cytoplasm of intestinal epithelial cells. Molecular typing of the organism and sequencing of the genome and the three small plasmids have been described. The isolates worldwide are similar.

Both pure cultures and mucosal homogenates of LI will produce clinical signs, lesions, and shedding. It is best cultivated in cell-free media and also in a rat enterocyte cell line.[5]

The disease is complex, often just called ileitis, and occurs in two forms. There is an acute form called porcine hemorrhagic enteropathy or regional ileitis that occurs from 4 to 12 weeks and a chronic form usually referred to as PIA or necrotic enteritis, which occurs from 6 to 20 weeks.

EPIDEMIOLOGY

Occurrence

There is a worldwide occurrence. The PPE complex affects pigs from weaning age to feeder pigs and also young gilts, sows, and boars. It is characterized clinically by diarrhea, loss of BW and inappetence in recently weaned pigs, and sudden death in feeder pigs, young gilts, and boars. The essential lesions are proliferative, and there seems to be an etiologic and pathologic relationship between PIA, necrotic enteritis, regional enteritis, and hemorrhagic enteropathy. Nonhemorrhagic proliferative enteritis occurred most often in pigs 6 to 24 weeks of age.

PHE usually affects pigs over 16 weeks of age but occurs in pigs as young as 6 weeks and as old as 4 years of age. PHE is one form and appears to occur in most countries. It probably has a worldwide distribution with 30% to 60% of herds affected depending on the country. In Germany, 82.7% of finishing herds had seroconversion. It is especially common in hysterectomy-derived or SPF herds and has a higher prevalence in the hot summer period. In some countries its prevalence is increasing, and it is emerging as a major syndrome in SPF herds.

The disease in all ages is frequently associated with the concurrent occurrence of PIA, but it is unknown whether the hemorrhagic syndrome results from some insult to the intestine that also predisposes to a proliferative enteropathy or whether it is simply an acute manifestation of this disease. The related syndromes of necrotic enteritis and regional ileitis can be found in apparently healthy pigs examined at slaughter. Because the disease is common in pigs, suboptimal growth of pigs in nutritional studies may be caused by the disease complex.

It has been suggested that it can live extracellularly within the environment for 2 weeks at 5 to 15°C. It appears highly resistant to a lot of cleaning agents such as povidone iodine or potassium permanganate, but may be susceptible to 3% cetrimide. In one study transmission occurred despite cleaning, use of footbaths, dedicated boots, etc.

It has been suggested that it normally lives in organic matter in weaner units awaiting the arrival of batches of susceptible pigs, with the resultant sudden increase in shedding 4 to 12 weeks after weaning. The recent finding of LI in the tonsil may be a coincidental finding, as they may have just been trapped in the crypts after licking infected material, because they were only found in this site in 2/32 pigs. Mixed infections are found in 10% of growers, and there is a strong association between diarrhea and prevalence of *Brachyspira hyodysenteriae* and *B. pilosicoli*.

Prevalence of Infection

A study in Belgium suggested that 24% of slaughtered pigs had a thickened ileum with a range in farm batches from 10% to 49%. In Denmark 94% of herds were infected with a mean within herd prevalence of 30%. In Canada, there is a widespread distribution between 50% and 100% of herds in the provinces with 5% to 89% of pigs affected. In the United States it was found using the immunoperoxidase monolayer (IPMA) test to study antibodies that 75% of growing herds had antibodies, and within the herd the prevalence was 11% to 91%. Of the breeding herds 78% had antibodies with two peaks at the time of infection and 9 to 18 weeks later and with an overall prevalence of 5% to 61%.

In Canada, studying 96 cases of PPE, it was found that 15% were in weaners (8–10 weeks), 36% in growers from 10 to 18 weeks, and 14% among finishers of 18 to 26 weeks. A further 16% were in mature pigs of >26 weeks.

Estimation of the incidence of disease is complicated by the difficulties in making an accurate clinical and pathologic diagnosis. Surveys of pig farms in Australia indicated that 56% had either observed the disease or the veterinarian had made the diagnosis.

Surveys of fecal samples from swine herds in Taiwan revealed an overall prevalence of infection of LI in 30% of herds and 5.5% of pigs.

Morbidity and Case Fatality

The disease can occur in all ages of postweaned pigs, but it has a high incidence in young replacement gilts and boars at 6 to 9 months of age and in pigs approximately 4 to 8 weeks after weaning. The high incidence in replacement gilts may be caused by suppression of the disease by low-level feeding of antibacterial agents during the growing period, but frequently the syndrome appears first in gilts and some time later in the growing pigs. In gilts, outbreaks may be explosive, but generally are short lived with

morbidity rates of up to 50% of the group occurring within a 2- to 3-week period. The case–fatality rate does not usually exceed 10%. In large herds with continual addition to the replacement gilt herd and in herds where the disease occurs in grower pigs, outbreaks may be more prolonged. The disease in growers generally has equivalent morbidity and case–fatality rates. It is more severe in that runting of surviving and contemporary pigs may occur, necessitating further economic loss through culling.

When given experimentally at a high level of 10^9 to 10^{10} LI per pig, mortality in the untreated groups varied from 10% to 50%, which is considered much higher than in the natural outbreak.

Risk Factors

There may be two patterns of infection. One is an early infection and the second is a delayed infection, which is seen in farms that separate pigs at weaning and have all-in/all-out methods of production.

Very little is known about the risk factors of PPE. A gene has been discovered that encodes for a surface antigen (LsaA) that is believed to be associated with attachment to and entry into cells and that is synthesized during infections. A study of recorded outbreaks of PHE indicated the disease often occurred within 12 months after repopulation of the herd and following withdrawal of antimicrobials from the feed. It has been proposed that the introduction of breeding stock from herds in which the disease is endemic may be a risk factor, but this is not documented. In a study in the UK showed there seemed to be a higher risk when there were more than 500 sows. An older parity structure in the sow population seemed to reduce infection. There seemed to be a higher risk if buying in boars. Fully slatted or fully meshed floors also carried a higher risk of infection compared with solid floors or straw. A higher risk was seen in those herds in which large numbers of pigs entered the finishing units simultaneously. Pigs on concrete slats may also be predisposed. Intensive systems were more severely affected than outdoor systems. There was a reduced risk if there was thorough cleaning and disinfection (all-in/all-out) before the next group of pigs arrived. Seroconversion usually occurred as the pigs entered the finishing site suggesting that the exposure takes place in the nursery. There may be five major types of risk factor: comingling, temperature fluctuations (overheating/ chilling), transportation, depopulation, and new buildings. Sows may have low levels of antibody and are capable of passing on colostral protection to the piglets. Maternal antibodies have usually declined by 3 to 5 weeks of age but may be extended to 42 days by repeated sow vaccination, by which time exposure may have occurred and there may be both active and passive antibodies.

Methods of Transmission

The organism is found in hamsters, ferrets, foxes, hares, deer, emus, ostriches, and primates. Colonization of rodents and wild rodents has been described.[6] The significance of these alternative hosts has not yet been ascertained. The role of vectors is not clear, but the main source of infection is the incoming pig (both growing pigs and adults). Gilts can be shedders and carriers, and the organism can probably survive in the extracellular world for 1 to 2 weeks at 5°C to 15°C. It may be transmitted on boots, other fomites, and by insects and flies.[7] The method of transmission between pigs is assumed to be the fecal–oral route.[8]

PATHOGENESIS

Contact-dependent excretion systems, such as the type III secretion system (T3SS), play an important role in the pathogenicity of many gram-negative organisms.[9,10] This system transfers bacterial proteins (effectors) into the cell where they disrupt the various cellular processes[11] and promote bacterial pathogenicity. They have shown that the system is operative in LI.[9]

The infection is by oral means and enters the epithelial cells of the crypts of the small intestine. The process appears to go ileum first then colon, to cecum, and finally rectum.[4] The infection process appears to take about 3 weeks to peak with the organisms appearing in the feces about 1 week after experimental infection. The histologic lesions may have cleared from the ileum by day 29 following inoculation. Considerable progress has been made using porcine ileal models.[12]

Proliferative enteropathy is characterized by the hyperplasia of the epithelial cells of the intestinal crypts, particularly in the ileum and colon. The presence of non-membrane bound, curved bacteria free in the cytoplasm of the affected enterocytes is a consistent feature of the disease. The bacteria associate with the enterocyte and enter through an entry vacuole, which then breaks down and the LI live freely in the cell. The organisms infect the immature cells of the mucosal glands and stop them from maturing.[13] The goblet cells decrease and then disappear. The cells lose protein and fail to absorb nutrients, which then contributes to the weight loss that occurs.[14] This causes them to multiply without leaving the gland, and the cells then degenerate probably by apoptosis and the glands continue to proliferate.[15]

Gross and microscopic lesions typical of acute proliferative enteritis can be reproduced by inoculation of cell-cultured LI into pigs 3 or 7 weeks of age. The incubation period is about 7 to 14 days with the early lesions appearing in the terminal ileum. Fecal shedding usually occurs about 7 days postchallenge and the animals seroconvert about 14 days postchallenge. The disease

peak is about 21 days postinfection. The clinical signs decrease, and the lesions begin to resolve after 28 days. The disease process results in a 2-week delay in marketing. Inoculation of gnotobiotic pigs does not cause the disease. It now seems certain that LI is the causative agent of the disease complex. Infection of intestinal epithelial cells is causally linked to marked hyperplastic proliferation of affected tissue.

The organism internalizes and multiplies within the cells, and it is proposed that the organism is capable of affecting, directly or indirectly, the cell cycle within the intestinal epithelium. This may or may not be concerned with the role of cyclin kinase p27, which regulates differentiation of immature crypt cells into the differentiated form. The changes in the experimental disease are similar to those in the natural disease. Following experimental infection there is almost complete replacement of normal ileal mucosa by adenomatous mucosa. Affected crypts are enlarged and branched, with loss of goblet cells and marked proliferation of crypt epithelial cells. Hyperplastic lesions may develop 2 to 3 weeks after challenge and persist for several weeks. In older animals, the lesions may be complicated by acute mucosal hemorrhage or necrosis. In the progressive stage of the disease, 3 weeks after infection, numerous organisms are consistently present within affected intestinal epithelial cells but not elsewhere. In the developed and recovering stage of the disease, 7 to 9 weeks after infection, ultrastructural features in affected intestinal tissues consist of pale, swollen, protruding epithelial cells and shrunken epithelial cells. This is followed by the appearance of apoptotic bodies in both epithelial cells and macrophages, the reappearance of normal goblet cells, and reduced numbers of organisms within the lesions. Bacteria are released from cells via cytoplasmic and cellular protrusions into the intestinal lumen and can be found in fecal samples.

In the experimental disease in pigs, seroconversion to the organism does not occur, confirming the weak response characteristic of the natural disease.

The proliferative lesion may result in suboptimal performance in otherwise normal pigs or unthriftiness, or be manifested as acute intestinal hemorrhage during the recovery stages of intestinal adenomatosis. The hemorrhagic lesions are more difficult to explain, but there may be direct or indirect toxic damage to the endothelium of the blood vessels.

It has been suggested that there is a close association between the presence of LI and reduced T-cell and B-cell numbers. This provides evidence of an immunosuppressive effect operating in this disease. It seems also that macrophages have an important function with activated macrophages accumulating in the infected hyperplastic glands. At day 14 postinfection there were a few

pinpoint lesions, and the percentage of infected crypts was minimal. At the same time the number of CD3+ cells was reduced and the number of intraepithelial CD3+ cells was also reduced, while the CD8 and CD4 cells showed no changes. Apparently there is an induction of an immunosuppressive phenotype with downregulation of an adaptive immune response through the reduction in the CD8+ T- and B-cells.

CLINICAL FINDINGS

The disease can occur in pigs from a few weeks of age to adults and lasts about 6 weeks on average. It is most common in the newly weaned. Morbidity may reach 12% and the mortality rarely exceeds 6%, even when the hemorrhagic form is very severe.

This disease is one of the common causes of failure to grow, weight variation in batches of pigs, and delay to market. In many cases, the clinical signs are not obvious as they are growth effects. Pigs may appear gaunt and may pass watery stools.

Between 6 and 20 weeks the endemic form is called porcine intestinal adenomatous with wasting and ill-thrift. In vaccination studies the improvement has been of the order of 5% for average daily gain or feed conversion ratio.[16] A 56 g/day reduction in average daily gain for each log 10 unit increase in LI excretion has been found. In a German study, LI PCR positivity had a significant negative effect on average daily gain.[17]

Regional ileitis is the most common differential diagnosis of the granulomatous enteritis that is seen in PCV2-associated enteric disease. In many cases both PCV2 and LI have been seen in the same case as both target the ileum.

PPE or ileitis occurs in pigs 6 to 16 weeks of age. In the chronic form, a reduction in growth rate and failure to thrive are common. Affected pigs are afebrile and diarrhea occurs but is unremarkable. Most cases recover spontaneously within 6 weeks of the onset of signs. When inflammation and necrosis have resulted in necrotic enteritis and regional ileitis, diarrhea and severe weight loss occur followed by death, often by ileal perforation in the case of regional ileitis.

PHE occurs in older pigs, such as young gilts and boars, and is manifested primarily by bloody diarrhea and sudden death. Others within the group may show skin pallor and hemorrhagic feces with fibrin casts but otherwise appear clinically normal. In some pigs there is continual blood loss, and death occurs within 48 hours of the onset of hemorrhage, but in the majority of pigs the hemorrhage is transient. In outbreaks, up to 70% of pigs affected with dysentery may die within 24 hours after the onset of signs. Fever is not a feature and the majority of pigs suffer only a minor setback for a 2-week period. A small percentage will develop chronic ill-thrift.

In grower pigs the disease is economically more severe. As in gilts, acute death with marked skin pallor and without premonitory signs can occur, but survivors show ill-thrift, and as the outbreak progresses contemporary pigs may show a chronic syndrome of ill-thrift with the periodic passage of bloody feces.

When sows are affected in early pregnancy they may abort. Usually about 6 days after the onset of clinical signs and in late pregnancy they can infect their newborn litter.[18]

Pigs that have been experimentally infected are resistant to later reinfection.[19]

CLINICAL PATHOLOGY

Many affected pigs are pale and anemic and the packed cell blood volume may be only 20% of normal. In these instances there may be black feces (melena) from the digested blood.

The organism can be detected in the feces of healthy 10- to 25-week-old growing/finishing pigs, which is probably the age group of pigs serving as the main source of infection for younger nursery pigs.

A PCR assay is highly reliable for the detection of the organism in feces and intestinal tissues. It may detect as few as 2×10^2 bacterial cells per gram of feces, but it is more likely that the PCR detects shedding of 10^3 or greater per gram of feces.

Positive results with the PCR are only present in animals with active lesions of proliferative enteropathy. Shedding as detected by PCR may start as early as 6 to 8 weeks and continue to 28 weeks. From seroconversion to first shedding was 2 to 8 weeks.

A fluorescent ISH technique targeting 16S ribosomal RNA using an oligonucleotide probe successfully identified LI. The indirect IF test works as soon as 2 weeks postshedding of LI.

Seroconversion may commence between 12 and 27 weeks. The range for positivity from first detection was 7 to 23 weeks. Maternal antibody appears not to prevent infection of piglets. ELISAs detect antibodies 21 to 28 days postinfection.

NECROPSY FINDINGS

The immediate impact of PPE is a thickened ileum and cecum and less frequently a spiral colon. Not all cases have lesions. Some may be so mild they are overlooked. Obvious gross lesions occur in severe cases, but in the less severe cases histology is needed. The pathology is related to the dose. As long as you remember these facts you can monitor LI in the abattoir.

A complex gross, histologic, and immunohistochemical study of LI has been made in which the pigs showed complete recovery and were IHC −ve by 35 days postinfection. The antigen was detected in the intestine, lymph node (macrophages), and tonsils (free

living in the crypts). They were found in the rectum and in several portions of the large intestine. The first site of colonization was the jejunum and ileum and then the lower intestinal segments. On day 29 there was nothing in the small intestine, but the LI were still observed in the cecum, proximal colon, and rectum. Mucosal IgA was first detected on day 15 and was still detectable on day 29, but in all cases the titers varied from only 1:4 to 1:16.

The macroscopic lesions of proliferative enteropathy were first detected at 11 days postinfection, which is the same time as histologic identification with enterocyte hyperplasia and reduced goblet cells. Immunohistochemical identification can be seen at 5 days postinfection and continues until day 29.

In PIA, the prominent lesions are in the terminal ileum and proximal portion of the large intestine. There is gross thickening of the mucosa and submucosa of the terminal ileum, and the colonic mucosa may also appear congested and slightly thickened.

In both forms of the disease the mucosal surface may be eroded and may look granular with abundant adherent material in the form of fibrinonecrotic debris. There may also be a fibrinonecrotic core filling the lumen. In PHE the only difference may be that the surface of the mucosa may be covered by large undigested blood clots.

Histologically, the mucosal change consists of marked proliferation of immature epithelial cells and a suppurative cryptitis. In many cases the affected crypts are 5 to 10 or more cells thick with numerous mitotic figures.

In **necrotic enteritis** the lining of the intestine may be covered in yellow or gray masses of necrotic material.

In regional ileitis (called hosepipe gut) the distal ileum is rigid from thickening of the intestinal wall caused by muscular hypertrophy and granulation tissue formation. The initiating mucosal damage is often somewhat masked because of colonization of the ulcerated mucosa by secondary bacterial invaders.

In PHE, the carcass is usually very pale, and massive amounts of blood are often present within the intestinal tract. The mucosa and submucosa of the ileum are thickened and may be coated in fibrin. Fibrin casts are also sometimes present. Although the intestinal wall is dark red and hemorrhagic, there may be no obvious points of hemorrhage. Histologically, there is evidence of vascular congestion, fibrin thrombi, increased permeability of blood vessels, and necrosis of the intestinal mucosa. The character of the vascular lesion resembles an acute bacterial infection and type I hypersensitivity reaction. Again, the key microscopic feature is the presence of proliferating immature epithelial cells with basophilic nuclei,

which line the greatly elongated crypts. There are no goblet cells in this site. In an analysis of histologic lesions crypt abscesses were seen in 20% of pigs, decreased goblet cells in 90%, hypertrophy and hyperplasia in 3%, hypertrophy of both muscle coats in 78%, increased eosinophils in 34%, and lymphoid hyperplasia in 90%.

In chronic cases the lesions described previously are nearly all replaced by fibrous connective tissue, and the diagnosis may rely on seeing just isolated pieces of mucosa.

Lawsonia are also a common cause of colitis. In 70% of cases of colitis LI are also found in the colonic mucosa. In three cases, LI were found only in the colon, and in these infected large bowels there was an excess of mucus on the surface.

Staining of smears of ileal mucosa with modified acid-fast stains may reveal typical curved bacterial rods in the apical cytoplasm of the infected proliferating enterocytes, permitting a presumptive diagnosis. It is not always specific for *Lawsonia.* They are not always present in necrotic debris or autolyzed tissue. IHC or silver stains (Warthin–Starry) of formalin-fixed gut are usually sufficient to detect the intracellular organisms in all forms of proliferative enteritis. LI can also be identified using a PCR assay. It is possible to find bacterial antigen in the lamina propria and draining lymph nodes of the ileum. This is a result of the natural process of infection clearance.

There has been a considerable interest in the relationship between PCV2 and LI and the difficulties in separating the two.[20,21]

Samples for Confirmation of Diagnosis

- **Bacteriology:** Distal ileum, proximal colon (direct smear and PCR); the organism needs to grow on tissue cell lines at oxygen and CO_2 concentrations that mimic the small intestine. It is not really an option because these techniques are difficult and the organism is an obligate intracellular organism. A simple staining with **Ziehl–Neelsen** or a modified Gimenez stain will show up the organisms.

There has been a considerable development in PCR techniques for feces as an antemortem technique. This is a variable sensitivity that is affected by sample quality and the presence of inhibitory factors in feces, but the specificity is around 97%. It appears to be very useful in the clinically ill but not so reliable in the subclinically affected. The PCR is more specific when applied to the ileal mucosa rather than to feces. It has been reported that fecal samples are more likely to be PCR-positive in herds with PHE rather than in PIA herds. It is more sensitive than either WS staining or immunofluorescence antibody test (IFAT). Shedding commences around 7 weeks and is observed most between

13 and 16 weeks. A one tube–nested PCR has been developed that is very sensitive and less prone to false positives compared with a standard nested PCR. A 5′ nuclease assay has been developed with a detection limit of one LI cell per PCR tube. A real-time PCR has been designed as a high-throughput test for use on feces. It is as specific as a conventional PCR but is more sensitive. It can be quantified and performed with pure cultures, tissue homogenate, or bacteria shed in feces.

A multiplex PCR has also been described for *B. hyodysenteriae, B. pilosicoli,* and LI.[22] It has a 100% specificity for the three species and does not generate false positives. The PCR can detect 10^2 to 10^5 LI per gram feces. A TaqMan quantitative PCR for use on feces and tissue samples[23] was shown to be more sensitive and more specific than conventional PCR on tissues.

There is also an indirect fluorescent technique, but this requires expertise and a reliable *Lawsoniana*-specific antibody, and again is not 100% for subclinically affected animals. The percentage of agreement between IFAT and IPMA was 98.6%. It has been suggested that IFAT is more sensitive than PCR in antemortem testing.

- **Histology:** Distal ileum, proximal colon (LM, IHC); IHC was described.[24]
- **Serology:** Serum antibody response in pigs to LI is specific and involves both IgM and IgG.

Methods utilize LI grown in enterocytes or LI prepared on slides as the antigen. These assays are specific because cell cultures or slides are examined microscopically, and specifically stained bacteria can be distinguished from any background. Staining of bacteria is either by fluorescent (IFA), which detects antibodies 28 days after infection, or peroxidase-labeled IPMA. The IPMA test is highly specific (100%) and fairly sensitive (90%) in experimentally infected animals. It is an appropriate diagnostic test for herd screening but not for diagnosing PPE on an individual animal basis. The IgG antibodies may be only short lived and found only between 18 to 24 weeks. These have proved useful for routine PPE diagnosis, although the humoral response is often weak and short lived. Titers of 1 : 30 to LI appear about 2 weeks after infection, and 90% become positive by about 3 weeks after challenge with 5% having titers of 1 : 480 or above. They are, however, already decaying by about 4 weeks after challenge. Antibody was not detected until 16 weeks of age and often not until 19 to 22 weeks. Today there are ELISAs for herd diagnosis.

A cell-mediated response can be detected in the research laboratory using an enzyme-linked immunospot assay (Elispot-T-cell assay) that measures the LI-specific secretion of IFN-γ by lymphocytes. It appears to follow the same pattern as the humoral response, and it also starts to decay from about 3 weeks although more slowly.

Both humoral and cell-mediated responses can still be detected 13 weeks after challenge or vaccination.

DIAGNOSIS

In a comparative review of diagnostic methods in 2009, it was suggested in that gross and histopathological examinations including the use of Warthin-Starry staining (34% sensitive but 100% specific) of tissue sections were of limited value.[24] The authors suggested that PCR examination of feces was the most useful in terms of sensitivity but less specific (95%) than either IHC (99%) or ISH (100%).

DIFFERENTIAL DIAGNOSIS

Porcine intestinal adenomatosis
Characteristic clinical findings are inappetence, loss of weight, and mild diarrhea in recently weaned pigs. Must be differentiated from postweaning coliform gastroenteritis, which is clinically much more severe, and death rapidly occurs. The postweaning drop in average daily gain (postweaning check) occurs within several days after weaning, and recovery occurs within several days following consumption of a normal daily intake of feed.

Proliferative hemorrhagic enteropathy
Occurs in feeder pigs, young gilts, and boars and is characterized by sudden death and extreme pallor of the skin. Must be differentiated from fatal hemorrhagic esophagogastric ulceration, acute swine dysentery, and intestinal hemorrhage syndrome

Esophagogastric ulceration
Occurs in all ages of pigs but especially in growers. The necropsy finding of ulceration in the nonglandular portion of the stomach at the esophageal entrance along with hemorrhage into the stomach with passage into the intestines provides easy differentiation. Acute death with intestinal hemorrhage occurs occasionally in swine dysentery. More common in adults affected with the disease and at the onset of an outbreak. Skin pallor is not as marked, and hemorrhage is restricted to the large intestine and associated with the characteristic lesions of swine dysentery in this area. Contemporary pigs show clinical and necropsy findings typical for this disease, and the diagnosis can be confirmed with laboratory studies.

Intestinal hemorrhage syndrome
More difficult to differentiate from the proliferative hemorrhagic enteropathy. Occurs most commonly in 3- to 6-month-old pigs that are well nourished, and many but not all outbreaks have been associated with whey feeding. Typically associated with abdominal distension and evidence of abdominal pain preceding death and the presence of marked intestinal tympany on postmortem examination. In many cases, hemorrhage in

Continued

the intestine appears to result from torsion, which occludes the mesenteric veins. It occurs in all areas of the intestine except the proximal duodenum and stomach, which have separate drainage. Because of intestinal distension the torsion may be easily missed, but it is best determined by the abnormal cranial direction of the blind end of the cecum and palpation of the mesentery. This distribution of hemorrhage may occur without the occurrence of torsion, and the etiology in these cases is unknown.

Other diseases
Infectious necrotic enteritis associated with *Clostridium perfringens* type C may cause hemorrhage into the intestine but it is easily differentiated on clinical, epidemiologic, and laboratory findings. **Mild *brachyspiral* enteritis, salmonellosis, porcine circovirus type 2, and nutritional diarrheas are alternative diagnoses.**

TREATMENT AND CONTROL

Treatment is via antimicrobials, and control relies on biosecurity, antimicrobial therapy, and biosecurity and resolute hygiene, particularly between buildings, is also important. Strict rodent control and fly control is advisable.

Biosecurity to prevent the entry of infection is the key to control. Quarternary ammonium compounds are very effective disinfectants,[25] and iodine and Virkon S also are effective. Beware of carrier pigs; isolate for 30 to 60 days, use preventive antibiotics as outlined later, use laboratory diagnostics, and vaccinate using the new water vaccine.

A program for the monitoring of LI in breeding herd gilts has been described[18] in which gilts were tested at regular intervals before sale in an infected herd and on arrival at the recipient herd. In addition, the growing pigs in the recipient herd were also tested. It was found that it was possible to establish herd profiles and to prevent transmission from herd to herd.

Eradication using early weaning is not a possibility, but using medication and vaccination is a possibility. It has been said that pigs between 30 to 50 kg shed fewer LI in the feces when they are fed nonpelleted and non-heated (home-mixed) feed. An eradication scheme for LI used in Denmark following the use of antimicrobials (tiamulin, lincomycin, and tylosin) failed. A control program was tried in the UK using PCR to identify affected animals and medication with chlortetracycline and tiamulin for control. The number of PCR-positive animals declined from 50% to 70% to 0%. In pigs over 14 weeks there were some PCR positives derived from treated groups. Another farm used tylosin phosphate and these remained clean.

Antimicrobials

It is likely that administration of antibiotics is necessary in the early stages in water or in feed. This is usually around 8 to 11 weeks of age. A preferred treatment would be tiamulin 120 ppm or tylosin 100 ppm for 14 days.

In acute disease, water medication and particularly individual medications are more effective than treatment through in-feed medication.

Continuous medication for LI can prevent infection but is frowned upon because it can prevent the development of immunity and extend susceptibility to infection. In fact, the timing of any medication can affect the immune response, subsequent fecal shedding, and the development of lesions.

There is no published information available on the treatment of individually affected pigs. The disease is usually treated on a herd basis by medication of the feed.

There appears to have been no changes in the in vitro minimum inhibitory concentrations (MICs) since the 1980s and 1990s. There are probably four reasons why medication does not work: (1) underdosing; (2) concurrent infections; (3) some other disease or nutrition problem, i.e., misdiagnosis; and (4) antibiotics given too late to be effective.

If antimicrobials are going to be used, it is a good idea to start at least 3 weeks before the anticipated acquisition of the infection.

In a study of 10 North American and European LI isolates it was found that for extracellular activity valnemulin was the most active with intermediate activity from chlortetracycline, tylosin, and tiamulin, but lincomycin showed the least activity.[26] For intracellular activity carbadox, tiamulin, and valnemulin were the most effective. Tylosin and chlortetracycline showed intermediate activity, and lincomycin was the least effective.

The antimicrobial susceptibility of the organism isolated from pigs with proliferative enteropathy was determined in a tissue culture system. Penicillin, erythromycin, difloxacin, virginiamycin, and chlortetracycline were the most active compounds tested. Tiamulin and tilmicosin were the next most active, and the aminoglycosides had the highest minimum inhibitory concentrations. Both lincomycin and tylosin were relatively inactive against the strains of the organism tested.

In the field Bacitracin, virginiamycin, and salinomycin are useless as are penicillins and fluoroquinolones.

Oral chlortetracycline, one of the oldest drugs, is still used; at 300 ppm or 600 ppm it can prevent challenged pigs from developing clinical disease. Chlortetracycline at 300 ppm and tylosin at 600 ppm have prevented the clinical signs of PPE.

Tylosin is ideal for treatment by injection, in feed, or through water and was successfully used for treating PPE at 100 ppm. For effectiveness, the antimicrobial would have to accumulate in the cytoplasm of the intestinal cell and block bacterial protein synthesis. The macrolides, tetracyclines, and virginiamycin act by selectively blocking protein synthesis in ribosomes. The oral administration of tylosin phosphate at a dose of 100 ppm or 40 ppm in the feed to pigs for 4 days before experimental challenge and continued for 16 days when the dose was reduced to 40 and 20 ppm was effective in preventing the clinical signs and lesions of proliferative enteropathy. It does not appear to block the pattern of seroconversion to LI. Tylosin at 110 ppm significantly reduced fecal shedding of LI and histologic lesions consistent with PPE. Injection of tylosin produced an improved diarrhea score and clinical impression score, which improved weight gain. Tylosin tartrate in drinking water for the treatment of ileitis was effective in reducing clinical signs, lesions, and reduction in growth rate.

Lincomycin is ideal for injection, water treatment, and in-feed treatment. Linco-Spectin at 80 ppm used consecutively was shown to be useful for treatment of PPE. Lincomycin at 44 and 110 ppm for 21 consecutive days was effective in controlling the clinical signs of PPE and at 110 ppm also reduced the mortality associated with PPE. Lincomycin water-soluble powder at 250 mL/gal is also effective.

Aivlosin was found to be useful at concentrations 25% less than those used for tylosin.[27] Valnemulin was also shown to be effective at 75 ppm in the feed. Tiamulin is useful for in-feed medication and water administration. Tiamulin given 50 ppm, 2 days before experimental challenge and kept for 3 weeks prevented clinical disease. In addition, pigs given 150-ppm tiamulin 7 days after challenge remained clinically normal and had no specific lesions of proliferative enteropathy at necropsy. Tiamulin in water is very useful, but a study showed that in water it interfered with seroconversion, whereas administration in feed did not.

The use of Bacitracin Zinc in the feed of growing/finishing pigs at 300 ppm or 200 ppm from weaning up to 100 days of age, or 200 ppm or 100 ppm from 100 to 125 days of age, and 100 ppm or 50 ppm from 125 to 156 days of age was effective in controlling the effects of proliferative enteropathy in pigs on a farm with a previous history of the disease.[7]

Carbadox and zinc oxide might have some effect against LI. It has been shown to be useful if fed in the final 2 weeks in the nursery. It reduces fecal shedding, clinical signs, and no IHC + ve or PCR + ve animals were found in one study.

Hyperimmune chicken eggs fed to the swine have been suggested for controlling LI infection in growing swine.

Vaccines

The main difference between respiratory and alimentary diseases in the last few years has been the development of vaccines for the former but not the latter. The recent development of an ileitis vaccine is the first of these for the enteric diseases.[28,29] This vaccination[30] may increase daily gain by as much as 46 g/day,

increase the carcass weight, and shorten the finishing period. It is given orally from 3 weeks of age or in clean drinking water. Be careful with the use of antimicrobials before vaccination because this may reduce the response to the vaccine. In a recent study in Denmark,[29] the use of oxytetracycline for treatment of LI was reduced by 79% with a significantly lower number of pigs being treated.

Vaccinating pigs through the administration of drinking water using the water pro-portioner is a safe, labor-saving, efficient, and easy method of vaccination. In the presence of feed medication, vaccinated pigs per-formed better than the nonvaccinated pigs when exposed to an LI challenge. The per-centage morbidity was reduced, the feed con-version better, and the average daily gain increased by about 6%. There was also a 23% reduction in culls. It is best given in a 7-day antibiotic-free period. The present vaccine is given in water to 70- to 90-lb (30–40 kg) gilts. It can be dispensed with antimicrobials and produce protective immunity. There is a reduction in gross and microscopic lesions in the complete absence of antimicrobials when the gilts are vaccinated as finishers and the animals receive a booster vaccination every 6 months.

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BRACHYSPIRAL COLITIS (SWINE DYSENTERY, PORCINE SPIROCHETAL COLITIS) AND NONSPECIFIC COLITIS

The postweaned pig is susceptible to several severe enteric bacterial diseases causing considerable economic loss. *Brachyspira hyodysenteriae* (BH) (swine dysentery), *Lawsoniana* and *Campylobacter* infections, post-weaning *E. coli* infections including bowel edema and *B. pilosicoli* (BP; porcine spiro-chetal colitis [PCS]) are the main contenders. In addition ulcers, torsion, rectal stricture, and rectal prolapse add to the gamut of gut disorders of the older pig.

SWINE DYSENTERY

Swine dysentery is a highly fatal disease characterized by mucohemorrhagic diarrhea and death if untreated for a few days. It causes economic loss (circa $10–$15 per pig) from mortality, morbidity, slow growth and poor feed utilization, and high costs of medi-cation and biosecurity. It is of no public health significance. Human intestinal spiro-chetes are distinct.

SYNOPSIS

Etiology *Brachyspira hyodysenteriae*

Epidemiology Probably the most economically important enteric disease in growing pigs, 8–16 weeks of age. Transmitted by fecal–oral route. Crowding and high stocking density are risk factors. High morbidity and moderate mortality if not treated

Signs Mucohemorrhagic diarrhea, and weight loss that are commonly persistent if not treated

Lesions Colitis and typhlitis

Diagnostic confirmation Detection of organism, in intestine. Serological diagnosis in herd

Treatment Tiamulin, valnemulin, tylosin, and lincomycin by injection and in water and in feed. Organic arsenicals in feed and water supplies and carbadox and monensin in feed and water in some countries

Control Eliminate infection with treatment in the feed and water supplies. Prevent reinfection and avoidance of introduction of carrier animals into herd. Eradicate by depopulation and repopulation, medication, and biosecurity measures.

ETIOLOGY

The genus *Brachyspira* contains seven species including others not yet officially named. They are gram-negative, filamentous, snake-like organisms. The seven species that are known to occur in swine are listed in Table 7-24. The species characterization has recently been described.[1]

These species can be distinguished by their zones of β-hemolysis, ability to produce indole, and enzymic profiles. They all have subtypes with unusual phenotypes and geno-types. All are distinct from B. hyodysenteriae on ultrastructure, gene sequences, biochemi-cal tests, and antigenic grounds. B. hyo-dysenteriae has two specific antigens, the 36-kDa protein and the 46-kDa periplasmic

Table 7-24 Biochemical characteristics of species of Brachyspira isolated from pigs

Species	Main features
Brachyspira hyodysenteriae (swine dysentery)	Strongly hemolytic, indole +ve, some –ve
B. pilosicoli (porcine spirochetal colitis)	Weakly hemolytic, some +ve
B. suanatina (pigs and mallard)[2]	Strongly hemolytic, indole weakly +ve
B. murdochii (rarely, mild colitis in pigs)	Weakly hemolytic, indole –ve
B. intermedia (rarely diarrhea and colitis)[3,4]	Weakly hemolytic, indole –ve
B. innocens (rarely diarrhea, commensal?)	Weakly hemolytic, indole –ve
B. hampsonii (new species, colitis)	Strongly β-hemolytic

flagellar protein. There is much antigenic heterogeneity among isolates of B. hyodysen-teriae. There are 11 serogroups with subdivi-sions into serovars. Serotyping of isolates of the organism is important in terms of diag-nosis and epidemiologic evaluation. The range of serologically distinct strains of the organism is much wider than previously realized. B. hyodysenteriae has heteroge-neous antigens in the LPS portion of the outer membrane, and several serotypes of B. hyodysenteriae have been described on the basis of agar gel double immunodiffusion precipitation. Some serotypes predominate in certain geographic areas.

B. hyodysenteriae (formerly *Serpulina* and before that *Treponema*), a large strongly β-hemolytic spirochete, is the principal caus-ative agent. It is supposedly indole positive, but in a study in Belgium half were indole negative. It will cause typhlocolitis in captive rheas. Rats and mice may act as reservoirs. They are all anaerobic organisms, but they are oxygen tolerant and will grow in the presence of 1% oxygen. The genomes have been studied.[5-8] The diversity of isolates has been shown by MLST[2,9] and multilocus variable number tandem-report analysis.[10] B. hyo-dysenteriae can be confirmed using random amplified polymorphic DNA analysis.[11] It seems that they have the ability to acquire genes from each other and other enteric bac-teria. They can be differentiated by pulsed field electrophoresis and multilocus electro-phoresis, and the former is particularly good at differentiating strains that are genetically 53% to 100% similar. Strains of B. hyodysen-teriae possess several antigens, some of which are shared by both B. hyodysenteriae and BP species. Organisms have been described that are phenotypically characteristic of B. hyodysenteriae, but their 23s RNA genetic

signature and sequence are consistent with B. innocens. Within the genus of B. hyodysenteriae there are some strains that are apparently nonvirulent or of reduced virulence potential. In some cases there may be clonal groups of B. hyodysenteriae.[12] The comparative virulence of *Brachyspira* isolates has recently been compared[13] and it was suggested that the phenotypic cultural characteristics results may be a more sensitive indicator of potential to induce dysentery-like disease than molecular identification alone based on current PCR assays. The virulence factors of B. hyodysenteriae have also been examined,[14] and although several factors were isolated only the *nox* gene was found in all the isolates and *tly*A and *hly*A/ACP were restricted to some B. hyodysenteriae isolates only. In this study a high degree of heterogeneity was seen.

EPIDEMIOLOGY
Occurrence
A Swedish study showed that brachyspirae species were isolated from 58.5% of all samples. Of these 25.4% were B. hyodysenteriae, 16.4% were BP, and 58.2% were *B. intermedia, B. innocens,* or *B. murdochii.*

Swine dysentery occurs worldwide and is an important disease of pigs in South America, South East Asia, and Europe. The disease had until recently declined in North America, probably because of strict biosecurity and the use of carbadox. It is most common in the 7- to 16-week-old age group but may affect older pigs to 6 months. Adult pigs and suckling pigs are seldom affected. The overall occurrence is probably around 10% with control through drugs, particularly growth-promoting antibiotics. Once a farm is affected the organism will remain, evolve, or acquire new antibiotic resistance unless there is depopulation, disinfection, and restocking or whole herd medication.

Risk Factors
In a recent study of an outbreak in East Anglia, UK, that began on one farm following the movement of 400 pigs to an outdoor unit in mid-2006, it was found that by early 2009 it had spread to 29 units by a variety of methods (Table 7-25).

Table 7-25 Importance of fomites and animals in spread of Brachyspira sp. on one farm

Method of spread	Out of 29 (%)
Pig movement	13 (44.8)
Local spread	3 (10.4)
Management	4 (13.9)
Contractor	1 (3.4)
Pig transport	3 (10.4)
Birds	2 (6.9)
Feed truck	1 (3.4)
Unknown	1 (3.4)

Animal Risk Factors
Pigs from 8 to 16 weeks of age are most susceptible to swine dysentery. Most outbreaks occur after purchasing infected animals from herds known to have the disease or where the disease is not acknowledged (sold as weaners) and trading continues. Infection is spread within and between swine herds by carrier pigs. It has been found in feral pigs and wild boar and occasionally affects birds, mice, rats, and dogs on infected farms. Mice are capable of carrying the organism for up to 180 days after inoculation.

Pathogen Factors
There are many latent infections without clinical signs. There is some evidence that the organism destabilizes the microbial community in the large intestine. Experimentally, the oral inoculation of gnotobiotic pigs with a combination of B. hyodysenteriae and *B. vulgatus* or *F. necrophorum* will result in the development of the characteristic clinical signs and lesions of swine dysentery. The disease has been reproduced with pure cultures of B. hyodysenteriae in conventional and SPF pigs. Challenge of gnotobiotic pigs with pure cultures results in colonization, but disease does not occur until other intestinal organisms are given, which suggests that the disease is the result of a mixed synergistic infection of the spirochete and other intestinal anaerobic organisms. These results and others are consistent with the concept that B. hyodysenteriae is the primary causative agent of swine dysentery and that the presence of one or more other anaerobes is a prerequisite for expression of pathogenicity of B. hyodysenteriae. This prerequisite can be met by a variety of anaerobes. There is considerable variation in virulence among strains of different serotypes of B. hyodysenteriae when given orally to SPF piglets or mice. A virulent B. hyodysenteriae has been isolated from a herd free of clinical swine dysentery, which indicates that the organism can still be present in herds considered to be free of the disease.

The major polypeptides of B. hyodysenteriae are strong immunogens and present in the various serotypes, but there is considerable diversity in the antigenicity of LPS between those same serotypes. A PCR-based DNA fingerprinting technique can analyze genetic profiles of isolates of the organism from cases of swine dysentery in different herds, which could be important epidemiologically.

Potentially pathogenic weakly β-hemolytic intestinal spirochetes may be present in swine herds with a high incidence of diarrhea and can be distinguished from nonpathogenic strains by the hippurate hydrolysis test. The prevalence of these strains is reduced in herds medicated with olaquindox.

Environmental and Management Risk Factors
The usual source of infection is through the import of pigs. It is, however, difficult to control these because of asymptomatic carriers. Investigation has shown that it may be the dirty truck that is important. In other words, biosecurity has failed.

Overcrowding and the buildup of fecal wastes in pens contribute to an increased incidence of swine dysentery. The failure to clean solid floor pens on a regular basis results in an accumulation of fecal wastes, which increases the infection pressure. The contamination of pens with fecal effluent from adjacent pens or by open flush gutter systems allows pigs access to the flush water and can provide sources of infection and reinfection. The continuous introduction of young pigs into pens that have not been previously cleaned out and washed provides sources of infection. The mixing of weaner pigs from different sources is often a source of infection for susceptible pigs.

Several factors affect the survival of the organism from the feces of infected pigs. It can survive 10 days in soil at 10°C and up to 78 days if there is 10% pig feces in the soil. The organism can survive for up to 48 days in dysenteric feces at 0 to 10°C (32–50°F); survival is reduced to 7 days at 25°C (77°F) and to less than 24 hours at 37°C (98.6°F). Dilution of dysenteric feces with tap water (1 : 10) enhances survival to 61 days at 5°C (41°F). It has been found in feces after 112 days. Drying and disinfection rapidly eliminates the organism from the environment. Phenolic and sodium hypochlorite disinfectants are most effective. The organism can survive in lagoons for up to 60 days. In swine herd facilities with an open gutter-flush system that has housed dysentery-infected swine, the lagoon water is used to expel feces from the building, allowing the pigs to drink the effluent as it flows through the gutter. Under these conditions the organism may survive for 5 to 6 days after the removal of infected shedders. The organism has been isolated from the lagoon of a waste-handling system of a swine farm, which could be partially responsible for maintenance of swine dysentery within a herd.

The effects of dietary constituents on the commensal bacterial flora of the large intestine are not well understood. It was thought that nonstarch polysaccharide was drawn into the distal parts of the colon and was then available for fermentation. The inclusion of wheat and soybean and/or the addition of exogenous enzymes to pig diets might influence the large intestine microflora, but did not prevent swine dysentery. The colonization of the gut by spirochetes was highly related to soluble nonstarch polysaccharide, and the development of swine dysentery was influenced by the resistant starch content of the diet. Feed containing large amounts of soya bean meal and group housing of pigs were considered to be the major contributing factors in the experimental production of swine dysentery. Feed containing high levels of soluble nonstarch polysaccharides results in an increase in viscosity of gut contents, an

increased amount of gut fluid, a low pH, and an increased number of coliforms in the intestines. A recent experiment with feeding and swine dysentery showed no effect of feeding rice in the diet. The feeding of rice was not able to prevent swine dysentery, and the increase of nonstarch polysaccharide or resistant starch was not able to reduce the incidence or prevalence of swine dysentery; in fact the clinical signs were worse.

Methods of Transmission

B. hyodysenteriae is present in the feces of affected pigs. Infection is by ingestion, and transmission is enhanced by conditions leading to fecal–oral cycling. Spread of infection within a group is slow, taking up to 7 to 14 days, and it may spread to other pens of pigs over a 2- to 3-week period. Pigs that have recovered from clinical disease with or without treatment may become carriers and still have the ability to shed the organism and infect in-contact animals for 50 to 90 days. Clinical disease may initially be precipitated by stress, but infection subsequently spreads by direct contract. The frequency of shedding varies with time, and only a small proportion of a convalescent population may be expected to be carriers. Every method of fecal transmission is a likely source (trucks, people, clothing, boots, etc.).

PATHOGENESIS

B. hyodysenteriae survives gastric acid and reaches the large intestine. In viscous environments B. hyodysenteriae has an improved movement. The agent possesses several outer membrane proteins including a 29.7-kDa lipoprotein (B. hyodysenteriaelp29.7) and a 39-kDa variable surface protein.[15] It also has an LPS in the outer envelope that may help it to disrupt the colonic epithelial barrier. In addition, NADH oxidase activity protects it from oxygen toxicity. Hemolytic activity is an essential virulence factor possibly controlled by four genes, tly A, B, and C and $LlyA$.

A hemolysin with cytotoxic activity extracted from a virulent strain of the organism causes severe epithelial damage when injected into ligated loops of the ileum and colon of germ-free pigs and is a virulence factor in swine dysentery. The organism can adhere to a culture of intestinal cells in vitro, which may be one of its virulence factors. The organism is also highly motile, which provides it with the ability to move through mucus and facilitates penetration into the mucosa. This may be a very important virulence factor. A wide variety of other virulence factors may be important. The organism probably does not attach to the epithelial surface of cells; instead it colonizes the overlying mucous layer. Chemotactic attraction of the organism to sites containing mucus is also a potentially important factor. It penetrates the mucus and moves down into the crypts and disrupts the colonic epithelium, causing mucohemorrhagic colitis while resisting oxygen toxicity. The organism

colonizes the intestinal mucosa by association with intestinal mucus in both the mucous gel covering the epithelium and the mucous-filled crypts (on the other hand, the weakly β-hemolytic B. pilosicoli [BP] attaches by one cell end to the luminal surface of the colonic epithelium to form a dense carpet of adherent spirochetes).

It is still not known if invasion is a necessary feature of infection for swine dysentery. Where it lives normally is unknown, but in the intestine it can obviously breed more quickly than it is evacuated. The pattern of colonization appears to be random. The hemolysin lyses the intestinal mucosal cells, which then supply the brachyspirae with the vital sterols from the membranes. Several genes may be involved in virulence including tlyA and $LlyA$. For infection to become established, it seems that a gene for the production of NADH oxidase is required because it protects against the effects of oxygen toxicity. Similarly, there may be a *Brachyspira* iron transport system, and the presence of this may correlate with the pathogenicity of B. hyodysenteriae. Another gene of interest is the mglB gene, which may eventually be shown to be of great importance. Lipooligosaccharide production may also be a virulence factor.

Chemotactic- or motility-regulated mucous association appears to be the predominant mechanism of mucosal association. There is progressive erosion of superficial epithelium, excess mucous production, edema, and hemorrhage of the lamina propria and pseudomembrane production. When the numbers of organisms reach $10^6/cm^2$ of mucosa then lesions begin to appear. The spirochetes appear in the feces about 1 to 4 days before the diarrhea starts. The erosive colitis is the cause of the diarrhea, dysentery, and excessive quantities of mucus in the feces. Some CD8+ cells may be associated with susceptibility to experimentally induced swine dysentery, whereas monocytes and CD4+CD8+ T-cells appear to be the major responding leukocytes during the disease. Death results from chronic dehydration and bacterial toxemia. In some animals, an acute shock syndrome results in rapid and sudden death. Early in the disease it activates IL-1 and IL-6 and stimulates macrophages. In the later stages T-cells play an important part in defense.

The diet has a major effect on the outcome of B. hyodysenteriae infections. Colonization can be controlled by feeding diets high in digestibility, which alter the colonic microbiota and encourage species that inhibit spirochetes to flourish.[16,17] Diets rich in inulin will do the same.[18,19]

CLINICAL FINDINGS

The disease usually affects growers and finishers a few weeks after moving from the nursery, and rarely weaners. Occasionally it affects sows at farrowing or in midlactation. It usually affects 6- to 12-week-old pigs, but

can be of any age. The incubation period in the field may be 7 to 60 days but experimentally is usually 4 to 14 days.

Morbidity within a group of pigs can range from 10% to 75%, mortality from 5% to 25%, and if untreated the case–fatality rate can be as high as 50%. Most often, initially, only a few pigs are affected within a group, but spread occurs over a period of a few days to 2 weeks to involve the majority. Affected pigs are slightly depressed, have a reduced appetite, and a moderate fever (40.0–40.5°C). The feces are only partially formed, usually of a porridge-like consistency, and are passed without apparent conscious effort and splatter on contact with the pen floor. Affected pigs commonly defecate almost anywhere and on anything in the pen. The feces are light gray to black and on close inspection a great deal of mucus is present and flecks of blood and epithelial casts may be seen. In some pigs, the presence of larger amounts of blood will discolor the feces accordingly. The occurrence of blood in the feces generally occurs 2 to 3 days after the initial onset of diarrhea. Affected pigs become progressively dehydrated and their abdomens appear gaunt and sunken. Death usually occurs some days to weeks after the initial onset of signs and results primarily from dehydration and toxemia. Pigs with a severe hemorrhagic diarrhea die more quickly. Skin discoloration is not a feature except in the terminal stages.

In untreated pigs the disease may persist for 3 to 4 weeks before clinical recovery. Less commonly an outbreak may start with the sudden death of one or two pigs with no evidence of premonitory signs or a terminal hemorrhagic diarrhea. This occurs more often in market-age pigs and adults in herds in which swine dysentery has been introduced for the first time. It also is a rare cause of sporadic death of gilts and sows in conventional herds.

The disease responds well to treatment, but following withdrawal of treatment the disease may recur within the same group of pigs. It can also recycle on farms at 3- to 4-week intervals and reappear after the cessation of antibiotic therapy. A chronic form of the disease with persistent diarrhea and failure to grow occurs in some pigs with irreversible lesions of the colonic mucosa.

Immunity

Maternal antibody must be present to protect the young pigs. Clinical disease is associated with development of specific IgG, IgA, and IgM antibodies in serum and local production of IgA in gut mucosal tissues. The IgG levels correlate with detection of clinical signs. IgA in the large intestine indicates recent infection. Treated and untreated convalescent pigs develop elevated titers that are maintained as long as 150 days after infection. The relationship between the magnitude of the agglutinin titers and protective immunity is not clear. Carrier pigs shed B.

hyodysenteriae while elevated agglutination titers against the organism are present.

Untreated pigs that recover from swine dysentery are resistant to experimental challenge for up to 16 to 17 weeks postinfection, and these are partially species specific. In herds affected with swine dysentery, the disease may reappear at 3- to 4-week intervals following treatment, and the more efficacious drugs may inhibit the development of immunity.

CLINICAL PATHOLOGY

Hematology may well show an elevation of the leukocytes with a shift to the left. The acute phase proteins may increase. There is an early increase in the erythrocyte sedimentation rate and fibrinogen levels. Total plasma proteins may be elevated. The blood levels of sodium, chloride, and bicarbonate decrease. A marked metabolic acidosis and terminal hyperkalemia may follow. In experimental swine dysentery, neither blood glucose nor lactate showed any changes, but the serum concentrations of glucogenic nonessential amino acids such as serine, alanine, glutamine, and tyrosine decreased.[20] Lysine increased during the swine dysentery and leucine increased during the recovery.

Detection and Culture of Organism

The organism may be detected in the feces of affected pigs by dark-field microscopy as highly motile organisms with a characteristic serpentine motility or in dried smears with Giemsa or Victoria blue 4R staining. The best diagnosis is achieved by taking samples from the upper colon. Fecal samples submitted for laboratory examination should be diluted (1:10) in phosphate-buffered saline or rectal swabs placed in Amies medium to avoid death of the organisms, which will occur when the samples are stored at room temperature or sent in the mail. Microagglutination tests (MATs), slide agglutination tests, and indirect and direct FATs are also used to detect the organisms.

The organism can be cultured on Trypticase soy agar containing 5% defibrinated bovine blood under specific atmospheric conditions.

Florescent antibody staining aids considerably in its demonstration, but may not distinguish nonpathogenic strains and false-positive and false-negative results are common. The presumptive diagnosis from the fluorescent antibody test (FAT) can be supplemented with a variety of laboratory tests that serve to identify the spirochetes as pathogenic. The **slide agglutination test** is a useful and specific means of identifying an organism but requires an appreciable amount of growth of spirochetes on the surface of the agar to perform the test. The **microscopic agglutination test** is a rapid test for the definitive laboratory identification of B. hyodysenteriae, but it cannot distinguish the avirulent strains of the organism.

A major diagnostic problem has been the identification of carrier pigs that are infected with the organism and are a potential source of infection to other pigs. Indirect and direct FATs used to examine feces and colonic material from pigs for B. hyodysenteriae have not been sensitive or specific enough to identify individual infected pigs.

Any diagnostic test must be able to distinguish between the different *Brachyspira* spp. Some are harmless commensals, whereas others are potentially pathogenic. *B. innocens,* a nonpathogenic inhabitant of the porcine large intestine, is very similar to B. hyodysenteriae in both morphology and growth characteristics and shares many of the same surface antigens. Numerous serologic tests with sera from pigs that have recovered from B. hyodysenteriae infection have demonstrated the presence of cross-reactive antibodies between B. hyodysenteriae and *B. innocens,* which makes differentiation difficult.

Antigen detection methods based on the use of DNA probes or PCR have recently been developed and show considerable promise. They use portions of the 16sRNA and 23sRNA gene or the *nox* gene or *tyl*A gene. The PCR is usually performed on the primary isolation plate (3–5 days), which can also be used for antimicrobial sensitivity.

A PCR was developed that could detect 10^3 to 10^4 organisms, and this was more rapid and detected more positive samples than did fecal culture and isolation.

The duplex PCR developed was also more sensitive than the culture and biochemical tests, which were shown to detect 10^2 bacteria per gram of tissue and would be used to differentiate B. hyodysenteriae from BP.

A multiplex PCR has been developed that will differentiate B. hyodysenteriae, BP, and *L. intracellularis.*[21,22] RT-PCR enables detection of the numbers of the bacteria. ISH will also work for B. hyodysenteriae.

The most definitive method for differentiating B. hyodysenteriae, *B. innocens,* and BP is the DNA–DNA relative reassociation method.

Serologic Tests

Monoclonal antibodies against the serotype-specific LPS antigens of B. hyodysenteriae can be used in ELISA,[23] indirect immunofluorescence, and immunoblot assays to differentiate between B. hyodysenteriae and *B. innocens.*

Serologic tests such as microtiter agglutination tests and ELISAs can be used on a herd basis to identify infected herds. It is 100% sensitive and specific but cannot confirm individual infected animals. The ELISAs will detect 10^2 organisms per milliliter of feces.

A variety of serologic tests have been used, and typically these tests have used whole cultures or LPS as the antigen.[9] The former tends to increase false positives, and the latter increases false negatives but gives fewer false

positives. Generally, these techniques are useful for detecting infected herds but are unable to detect individual infected pigs that may be acting as carrier animals. Recently a 30-kDa outer membrane lipoprotein (BMPB), which is specific to B. hyodysenteriae and is recognized in both experimentally and naturally infected pigs, was identified, the gene cloned and sequenced, and specific epitopes on BMPB are being identified.

Serologic tests can assist in the identification of carrier pigs. An evaluation of several serologic tests for detection of antibodies against B. hyodysenteriae concluded that only the MAT detected antibodies to the organism. The ELISA has been used to detect antibodies in individual pigs, but cross-reactions between B. hyodysenteriae and *B. innocens* are common. An ELISA using serotype 2 B. hyodysenteriae as antigen could not differentiate between stages of infection but could indicate if the pig had been infected.

NECROPSY FINDINGS

Lesions are restricted to the cecum and colon and occasionally the rectum,[24] and these can be found in healthy pigs. Sometimes the lesions extend over the whole large intestine or are localized. There may be hyperemia and edema of the large-intestinal walls and mesentery. The mesenteric lymph nodes may be swollen with edema fluid. The mucosal lesions vary from catarrhal to fibrinonecrotic to hemorrhagic typhlocolitis. They are often covered by mucus and fibrin and flecks of blood. Colonic contents are soft to watery. With progression the edema and mucosal lesions become more severe with increased fibrin exudation and the formation of a thick mucinous pseudomembrane containing blood. Goblet cell hyperplasia is very prevalent. The cells at the base of the crypts may be elongated and hyperchromic. There may be spirochetes in the goblet cells and in disrupted epithelial cells. Some spirochetes may be found around blood vessels.

The carcasses of pigs that have died from swine dysentery usually show weight loss, dehydration, and a microscopically visible typhlitis and colitis. The colitis is initially present in the apex of the spiral colon but subsequently spreads to involve the whole colon and the cecum. In the early stages, there is inflammation and necrosis with varying degrees of hemorrhage into the lumen. The submucosal glands are enlarged and frequently visible through the serosa of the colon as opaque spots. In advanced cases a fibrinonecrotic exudate is adherent to a reddened and granular mucosal surface. Intestinal contents may also adhere to the mucosa. The crypts are often thickened with edema. The draining lymph nodes are enlarged and congested. The small intestine is spared except for involvement of the terminal ileum in advanced cases. Spirochetes may be demonstrated in large numbers using Warthin/Starry stains in smears from the mucosal

surface of these lesions, especially in early cases, but there is no systemic invasion.

Electron microscopic examination of the colon of pigs with swine dysentery reveals changes indicative of stasis in the microcirculatory vessels of the lamina propria. The earliest colonic lesion consists of superficial vascular congestion and dilatation, edema of the lamina propria, and intercellular separation of the epithelial cells at the crypt shoulders. This lesion progresses to epithelial cell necrosis and extrusion with extravasation of red blood cells into the lumen. Degeneration, necrosis, and extrusion of superficial colonic enterocytes follows progressively. Large spirochetes are present in the crypts, in the cytoplasm of damaged epithelial cells, and in cavities around vessels of the lamina propria. The characteristic lesion of swine dysentery is necrosis of the superficial colonic epithelium. This feature may be difficult to appreciate in partially autolyzed tissues, or if the animals sampled are recovering from the infection or being treated with antibiotics. In subacute lesions the crypt hyperplasia and goblet cell hyperplasia is more pronounced, and the extensive mucous production distends all the crypts.

B. hyodysenteriae is difficult to culture, requiring anaerobic conditions and selective media. This has promoted the development of alternative diagnostic techniques such as PCR and immunohistochemical stains. Wet mount preparations from the colonic mucosa are often used to make a presumptive diagnosis and an FAT is available to confirm.

A consecutive study was made of the pathology of lesions by repeated endoscopy and biopsy samplings was made.[24] On the third day, endoscopy showed a hyperemic reactive mucosa and excessive amounts of mucus. Histologically, there was crypt hyperplasia, depletion of goblet cell mucus, and epithelial erosions. At the same time there were elevations of acute phase proteins, circulating monocytes, and decreased numbers of CD3+ cells. After 5 days the pigs returned to normal.

DIAGNOSIS

The history and clinical signs indicate either B. hyodysenteriae or *B. hampsonii* and are more severe than those of BP. Confirmation can be started by smears of feces or mucosal smears and finding typical spirochetes. The rest of the confirmation requires laboratory testing using the methods described earlier, particularly culture on selective media. Spirochetes can be confirmed by growth inhibition tests and by specific antisera, and enzyme analysis using the API ZYM system is useful because B. hyodysenteriae lacks α-galactosidase.

Samples for Confirmation of Diagnosis

- **Bacteriology:** Colon culture (culture has special requirements such as an agar gel plate with added spectinomycin, colistin, and vancomycin media or BJ medium). Direct smear (modified acid-fast stains), FAT, PCR
- **Histology:** Formalin-fixed colon, several sites (LM, IHC). ISH and an IFA can be used on fixed tissue.

DIFFERENTIAL DIAGNOSIS

Swine dysentery must be differentiated from other diseases in which there is diarrhea in growing pigs. Pigs with swine dysentery are usually emaciated, dehydrated, have a rough hair coat and fecal staining of the perineum, and have mucohemorrhagic colitis. Identification of the new species *Brachyspira hampsonii* also requires laboratory identification.

Porcine colonic spirochetosis: This is the most difficult differential diagnosis of swine dysentery and is associated with a mild diarrhea in weanlings and growing pigs. It requires laboratory confirmation.

Coliform gastroenteritis, salmonellosis, and **hog cholera:** Characterized by more rapid onset and spread within a group than with swine dysentery and death occurs earlier. In coliform gastroenteritis and salmonellosis, the initial sign may be sudden death or severely depressed and weak pigs with fever, skin discoloration, anorexia, and a profuse watery diarrhea. Coliform gastroenteritis occurs within a few days after weaning, whereas hog cholera occurs in all ages of pig with a high mortality. Swine dysentery is more insidious at onset, the appetite is rarely completely lost, and the feces are soft and mucohemorrhagic. At necropsy the lesions of swine dysentery are confined to the large intestine, whereas in coliform gastroenteritis, salmonellosis, and hog cholera lesions are also present in the small intestine. Salmonellosis has deep hemorrhagic, necrotic lesions with coagulative necrosis. Other diseases may result in the passage of bloody feces. *Trichuris suis* is usually grossly visible in large numbers.

Intestinal hemorrhage syndrome: Generally persists as a severe hemorrhagic diarrhea with rapid death rather than as a chronic syndrome, but pathological differentiation may be necessary. It is usually associated with whey feeding. Swine dysentery does not affect the small intestine. Chronic hemorrhage caused by **esophagogastric ulcer** results in melena; the epidemiological findings are different, and the necropsy findings are characteristic in the intestine and other organs.

TREATMENT

Affected pigs may need supportive therapy.

Antimicrobial Therapy

Some authorities have suggested that the recurrence of B. hyodysenteriae in the United States may be caused by increasing antibiotic resistance as has happened in Europe and Asia. In a recent study, the MICs against lincomycin and gentamicin were high, as were the patterns shown by *B. murdochii* and *Brachyspira* species rather than B. hyodysenteriae. The other antibiotics had MICs at the low end of the range.

Antimicrobials are usually administered by mass medication to all pigs within the affected group. Treatment by water medication rather than feed medication is preferable, because it is generally easier and quicker to put into place, and affected pigs usually continue to drink (but perhaps not in the same quantities as when unaffected) while they are anorexic. Pigs with severe hemorrhagic diarrhea and toxemia may not drink sufficient medicated water and must be treated initially by parenteral injection.

Medication of feed is most suitable for subsequent prophylaxis. When outbreaks occur, all severely affected pigs should be treated individually, and the drinking water medicated for several days at therapeutic levels, followed by possible medication of the feed for up to 3 weeks or longer at prophylactic levels.

Choice of Antimicrobials

Several antimicrobials are suitable for the treatment and control of swine dysentery, and the choice is largely dependent on availability, cost, efficacy, and the regional withdrawal regulations. The antimicrobials and their dosages given here are used in treatment and control.

Currently, tiamulin, lincomycin, and the nitroimidazoles (dimetridazole, ronidazole, and ipronidazole) are the most effective antimicrobials for treatment by water medication. In some countries, certain antimicrobials may not be approved for use in pigs. The most efficacious antimicrobials for use in the feed are carbadox, the nitroimidazoles, tiamulin, and lincomycin.

A macrobroth dilution in vitro technique determined the antimicrobial sensitivity of a group of isolates of B. hyodysenteriae from Australia, the United States, and Canada. Dimetridazole and tiamulin were effective against most of the isolates. Lincomycin inhibited the growth of some isolates, and tylosin failed to inhibit most of the isolates tested. A group of isolates of B. hyodysenteriae from the UK were all sensitive to tiamulin, and there was no evidence that the organism was developing resistance to the drug. A large number of strains of B. hyodysenteriae isolated in Hungary between 1978 and 1992 were tested against seven chemotherapeutic agents commonly used for the treatment of swine dysentery, and the changes in patterns of resistance were also monitored. All strains remained sensitive to carbadox. The sensitivity to dimetridazole gradually decreased with about 50% of strains still sensitive. Most strains were

resistant to tylosin. Resistance to lincomycin gradually increased but about 50% remained sensitive. Tiamulin was most effective but some resistant strains have emerged. Monensin was effective for prevention but resistance may evolve quickly. Sedecamycin, a macrolide antimicrobial, was effective but the MICs were much higher than expected. Isolates of B. hyodysenteriae in Denmark were sensitive in vitro to virginiamycin, but medication of the feed at 20 ppm was ineffective for control. A combination of tiamulin and salinomycin, and salinomycin alone in the feed for 105 days in diminishing doses is effective in controlling naturally occurring disease and in the first 30 days (60 ppm salinomycin and 30 ppm tiamulin), in the next 60 days (30 ppm each), and the next 15 days (30 ppm salinomycin). For salinomycin alone the diminishing dose is the first 30 days (60 ppm), the next 60 days (30 ppm), and the next 15 days (30 ppm; Table 7-26).

Organic arsenicals are the least expensive and are recommended as the first drug of choice when available in the country. When given in either the feed or water, there is a risk of toxicity. The general recommendation is to administer the medication for a 7-day period and then withdraw it for a 7-day period before reintroduction. However, this is frequently impractical, and continuous medication at 250 ppm in the feed is often used as follow-up therapy. Toxicity does not usually occur below levels of 500 ppm, but it has occurred at levels as low as 200 ppm where continuous medication is practiced, and constant surveillance for signs of toxicity is necessary. Although resistance to organic arsenicals has been suspected, it has not been documented. There has been a marked decline in the use of arsenicals for the clinical management of swine dysentery.

It is essential to use agar or broth dilution methods to reach MICs for the various antibacterials, because there is a need to standardize at this time of decreasing sensitivity[26] and increasing transfer of resistance genes.[27]

Failure to Respond to Therapy

For elimination of B. hyodysenteriae the selection of an effective drug is necessary. The major problems with the treatment of swine dysentery are the failure of some outbreaks of the disease to respond favorably to treatment, and relapses or new cases that may occur following withdrawal of medication of the feed or water. Several drug-related problems have been postulated to explain these problems.

Drug-delayed swine dysentery occurs several days after withdrawal of medicated feed. It may be caused by either an ineffective drug or inadequate dosage of an effective drug and failure to eliminate the causative organism from the colon. However, reinfection from other swine must also be considered. The nitroimidazoles at high levels will apparently prevent the delay or recurrence of dysentery.

Table 7-26 Antibiotic therapy in use for swine dysentery	
Antibiotic	**Dosages**
Tiamulin	10 mg/kg BW IM for 3 days
	8 mg/kg for 5–7 days in water
	(60 mg/L for 5 days in water)
	106–120 ppm (30–40 g/tonne) for 7 days in feed
	Followed by 30–40 mg/tonne for 2–4 weeks
	Recovery often occurs in 24 h
Valnemulin	3–4 mg/kg BW/day for 3–4 weeks in feed
	For prevention 25 ppm (1.0–1.5 mg/kg) for 7–28 days
	Both valnemulin and tiamulin cross-react with ionophores (salinomycin, narasin, and monensin) and they should not be given together.
Carbadox	50 mg/kg of feed for 30 days to 35 kg only or combined with sulfamethazine at 100 mg/kg of feed
Lincomycin	11 mg/kg BW IM daily for 3 days, <10 days
	In water at 44 ppm (8 mg/kg BW) in water for <10 days
	In feed at 100 g/tonne for 3 weeks or until signs disappear
	Followed by 40 g/tonne
	Not suitable for animals over 110 kg
	Resistance occurs at an MIC of 30 mg/L.
Lincomycin/spectinomycin	66 ppm of both in the feed for 8 days
	Followed by 44 ppm for 20 days
Tylosin	10 mg/kg BW IM twice daily for 3–5 days
	5–10 mg/kg BW in water for 5–7 days
	Then next 100 g/tonne for 3 weeks in feed
	Followed by 40 g/tonne in feed
	Widespread resistance, but where sensitive it works
Aivlosin	Can be used when there is tylosin resistance[25]
Imidazoles	
Nitroimidazole	(Not in the United States or Europe) 260 ppm in water for 7–14 days
Dimetridazole	200 g/tonne in feed
Ronidazole	60 ppm in water for 3–5 days, 120 ppm (60 mg/tonne) in feed. Resistant strains will develop.
Monensin	100 ppm in feed for 56 days
	Followed by 50 ppm from 56–84 days, and 25 ppm until 112 days
	Toxicity if used with pleuromutilins
Arsenicals (formerly in common use)	
Sodium arsanilate	In water at 175 ppm for 6 days
Arsanilic acid	500 g/tonne for 21 days in feed (monitor for signs of toxicity)
BW, body weight; IM, intramuscularly; MIC, minimum inhibitory concentration; ppm, parts per million.	

In experimentally induced swine dysentery using colon from affected pigs, oral inoculums such as tiamulin in the drinking water at 45 mg/L or 60 mg/L for 5 days were also effective in treating clinical disease. However, diarrhea commonly recurred 2 to 10 days after withdrawal of the drug and repeated medication of the water with tiamulin was necessary to reduce the severity of diarrhea and prevent deaths. After one to three retreatments, the pigs were immune to experimental exposure and there was a significant increase in their serum anti-B. hyodysenteriae antibodies. This supports the observation that when certain antimicrobial agents such as dimetridazole, which are

highly effective in preventing the development of diarrhea, are withdrawn, the affected pigs do not become immune.

Drug-diminished swine dysentery occurs when suboptimal levels of the drug are used. The severity of the diarrhea is reduced and deaths do not occur, but the disease is not eliminated. However, severe disease may follow withdrawal of medication.

The feeding of ronidazole at 60 ppm for 10 weeks, or carbadox at 55 ppm or lincomycin at 110 ppm for 6 weeks eliminated an experimental infection, and swine dysentery did not recur during a 9-week period after withdrawal of the medication. The feeding of sodium arsanilate at a level of 220 ppm for 3

weeks to pigs, which had been fed ronidazole for only 6 weeks, did cause the development of swine dysentery.

In both drug-delayed and drug-diminished swine dysentery, there are chronic lesions in the colon. In drug-resistant swine dysentery, medication of the feed is not effective and diarrhea and deaths occur. Certain outbreaks of the disease may be resistant to both tylosin and sodium arsanilate. The sensitivity of B. hyodysenteriae to dimetridazole has not decreased significantly following use of the drug over several years.

Drug-augmented swine dysentery is a more severe form of the drug-resistant disease in which affected pigs are more severely affected than nonmedicated controls. The cause is unknown. The disease occurs in a severe form several days or weeks following withdrawal of successful medication for a previous outbreak of the disease. This form appears to occur most commonly in pigs that did not have clinical disease during an earlier outbreak but received medication. The concentration of the drug administered was sufficient to prevent diarrhea, but not sufficient to eliminate the spirochetes from the colon. During the delay of the initial diarrhea by the drug, there may have been intraglandular recolonization of spirochetes throughout the colon. After withdrawal of medication, rapid intraglandular multiplication of the large spirochetes may occur and result in clinical disease. Drug-delayed augmented dysentery usually occurs only in those pigs that have been infected but did not develop clinical disease, which usually results in immunity. The occurrence of diarrhea is necessary for its development, which occurs 4 to 13 weeks after infection. Treatment of swine dysentery with the more efficacious drugs has been shown to inhibit the development of this immunity and serum antibody to B. hyodysenteriae. However, the clinical significance of this is undermined, and at present it is suggested that outbreaks of swine dysentery be treated vigorously.

It should be possible to minimize these drug-related problems of swine dysentery by the use of therapeutic levels of effective drugs in the drinking water for short periods followed by prophylactic levels in the feed for 3 weeks or more. This must be combined with proper management techniques and waste disposal systems that minimize or prevent reexposure.

Regardless of the drug used, many pigs are reinfected following withdrawal of medication because of the continual presence of the organism in the environment. The sources of the organism include in-contact carrier pigs shedding the organism and survival of the organism in waste materials (see the section Epidemiology).

Cleaning and Disinfection
After the institution of treatment, thorough cleansing of the contaminated pens is necessary to prevent reinfection or the transmission of infection to new groups of pigs. This is usually done after 3 to 6 days, when all diarrhea has ceased. The decision to continue with prophylactic medication depends on the hygiene and a knowledge of past patterns of the disease on the farm. It is generally recommended to continue prophylaxis for at least 2 weeks. Swine housing units with open gutter-flush systems in which swine dysentery-infected pigs have been maintained should remain idle for a longer period than 5 or 6 days to eliminate B. hyodysenteriae.

CONTROL
Experimentally, a highly digestible diet can protect pigs from swine dysentery. Diet cannot influence the colonization of B. hyodysenteriae.[28] Diets containing inulin but not lupins helped to prevent swine dysentery in experimentally challenged pigs.[18]

Effective control of swine dysentery is dependent on the control of infection in the herd and the limitation of reinfection, eradication by depopulation, and repopulation or mass medication without depopulation.

Control of Infection/Limitation of Reinfection
Control of the clinical disease can be achieved by early treatment with adequate levels of antimicrobials for a sufficient length of time. This must be combined with adequate removal of fecal wastes to prevent reinfection. Pigs destined for market should be moved out as a group and their pens cleaned, disinfected, and allowed to dry for a few days before pigs are restocked. Where possible the purchase of feeder pigs should be restricted to private sales from herds with no history of the disease. Communal trucks should not be used for transport. Where this is not possible pigs should be placed in isolation pens for 3 weeks and provided with medicated feed or water to eliminate the carrier state in infected pigs. Every effort should be made to avoid potential fecal–oral cycles and contamination by feces between pens. Preventing the buildup of fecal wastes is also of paramount importance. Pigs from different source farms should not be grouped in the same pen. It is also necessary to reduce the stress of transportation and overcrowding on the pigs.

In farrowing-to-market enterprises where the disease is always a threat, routine prophylactic medication may also be necessary. This is commonly performed following weaning and during the early growing phase. In countries where withdrawal periods are in force, the use of certain microbials is precluded for this purpose.

The feeding of tiamulin at a dose of 20 mg/kg BW to pregnant sows, beginning 10 days before farrowing and continuing until 5 days after farrowing when the piglets are weaned and transferred to an isolation unit, has been successful in the prevention of infection of newborn piglets. This is known as the "barrier method," which can be an efficient method of eradicating endemic infections. To reduce the risk of postnatal infection of the progeny, the piglets should stay with the latently infected sows for the shortest time possible. Furthermore, early weaning is necessary, and strict isolation is an important condition to success. The disease is spread primarily by carrier pigs, and contact between infected and uninfected pigs must be avoided.

The administration of tiamulin at 10 mg/kg BW IM daily for 5 days to all animals in a large herd, combined with cleaning, disinfection, and rodent control, was effective in controlling the disease, and no further clinical signs occurred in the subsequent 2.5 years.

Mass Medication and Sanitation Program Without Depopulation
With the strategic use of antimicrobials, effective sanitation, serial depopulation of possible carrier animals, and the introduction of infected animals, it is possible to virtually eradicate the infection from a herd.

Elimination of infection from closed swine herds is possible using antimicrobials (see the section Treatment), and there are various options.

Dietary Modification
Experimentally, modification of the diet can assist in the control of swine dysentery. Feeding a highly digestible diet reduces fermentation in the large intestine and is associated with a failure of colonization by B. hyodysenteriae when challenged orally. Pigs fed on a diet based on steam-flaked maize and steam-flaked sorghum had a decreased incidence of disease. Pigs fed on a diet based on cooked white rice were fully protected from experimental infection with B. hyodysenteriae.

Depopulation and Repopulation
The infection can be eradicated by depopulation of the entire herd and repopulation with breeding stock free of infection. However, this can be uneconomical unless it is part of the long-term plans for the herd and the producer.

The disease can be eradicated through the use of minimal disease or high-health–status herds that are free of several infectious diseases and maintain disease-free status. In such herds, diseases such as swine dysentery occur only rarely and almost never over a period of several years.

Biosecurity
Strict biosecurity measures are necessary to prevent introduction of infected carrier pigs. This requires knowledge of the infection status of the herd of origin. It also requires a highly reliable test to detect the infected pig. Particular attention should be paid to the state of vehicles visiting the farm. The farm staff and the truck drivers should not cross over the gate at the loading point. The

loading gate should be at the perimeter of the unit.

Monitoring of the herd for continuous freedom is essential. This includes clinical observations, examination of colons at abattoir, culture of feces, ELISA monitoring,[23] and PCR examination of feces.

Vaccines

Pigs that have recovered from clinical swine dysentery may be protected against subsequent challenge, but attempts to immunize pigs with B. hyodysenteriae have been proven to provide incomplete protection and involve complex procedures that may have limited practical value. The development of effective vaccines will require attention to serospecificity of the organisms used to formulate the vaccines.

Effective vaccines are not widely available as yet. A commercial vaccine using a protein-digested bacterin has shown efficacy in the reduction of disease caused by B. hyodysenteriae. It produced both a systemic and mucosal immunity. Both IFN-γ and lymphocyte blastogenesis responses were stimulated. A recombinant outer membrane lipoprotein has also been shown to be a hopeful vaccine.

An inactivated, adjuvant, whole-cell vaccine against B. hyodysenteriae has been tested experimentally. The vaccine provided significant protection in two small trials, but some of the vaccinated and unvaccinated pigs developed late-onset swine dysentery, which is unexplainable. Field trials to test the vaccine are required. An experimentally inactivated B. hyodysenteriae vaccine with mineral oil adjuvant resulted in exacerbation of the clinical disease following challenge; a majority of the vaccinated pigs developed the disease earlier and to a more severe degree than the unvaccinated pigs.

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BRACHYSPIRA HAMPSONII

In every respect B. hampsonii produces the same clinical and pathologic syndrome as B. hyodysenteriae. It is possible that several unrecognized *Brachyspira* species play an important role in clinically relevant swine intestinal disease. Recently a novel strongly hemolytic *Brachyspira* species was encountered in North America in cases similar to those caused by B. hyodysenteriae[1] and subsequently found in Spain. In other words, swine dysentery was caused by an entirely different agent. The isolates were found to be different from all known *Brachyspira* spp. on the basis of the *nox* gene, 16S ribosomal RNA sequencing, and biochemical testing. The organism is called *B. hampsonii* after David Hampson, who contributed so much to the study of *Brachyspira.* To identify the organism, the duplex PCR was first used to differentiate or eliminate B. hyodysenteriae and BP, and then PCR was used to identify the *nox* gene. The PCR products were then sequenced and then multilocus typing was used.[2,3] The results of this typing grouped the isolates into two clades (I and II), which formed a cluster independent of each other. Most of clade I was positive for β-glucosidase and clade II negative for this enzyme. This organism is strongly β-hemolytic but is indole negative, which distinguishes it from B. hyodysenteriae and *B. suanatina,* which are the other β-hemolytic *Brachyspira.*

The disease has been almost absent from the United States until quite recently, but a number of recent outbreaks of severe bloody diarrhea have been seen in the United States and Canada.[4] Since 2008, more than 50% of isolates from query swine dysentery cases have been nontypeable at the Minnesota laboratory,[1] and only 36% at the Iowa laboratory[4] in the first 9 months of 2010 were typeable to the species level. The others may turn out to all be *B. hampsonii*. All the isolates were associated with severe bloody diarrhea in the field.

In October 2009, two herds in Saskatchewan in Canada had a disease indistinguishable from swine dysentery. All pigs had characteristic lesions in the large bowel, and abundant spirochetes were seen in smears from the colonic mucosa of affected pigs but not from the nonaffected pigs. They were unable to identify B. hyodysenteriae. A quantitative (q)RT-PCR was developed, and it showed that 10^5 to 10^6 organisms per gram of tissue or cecal contents were found.[5] In 2011 a similar condition was reported in Iowa and Minnesota.[6] Recently the organism was found in Spain and isolated from geese and ducks, which suggests that wildfowl may transmit the organism around the world to pigs.

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NONSPECIFIC COLITIS IN PIGS

This condition is found worldwide and as yet has no known definitive causes. It can be found in all ages from weaning to slaughter but particularly from weaning to 40 kg. Nonspecific colitis was first seen in the UK in intensive management systems.

ETIOLOGY

At the moment the role of the various possible players is not clear. It might involve feed ingredients, feeding practices, predisposing viral enteritis, poor management, poor hygiene, or even sudden changes in husbandry.

The condition is ill defined but nutrition and infection are thought to be important. Undigested food ingredients reach the colon as a result of poor digestion of feed. This undigested feed allows fermentation in the colon, and all these factors may not allow the colon to absorb water. Sometimes the condition is found on feeding pellets but not on meal. The pelleting has the capacity to caramelize carbohydrates, alter particle size, and destroy micronutrients.

It may be associated with variations in a wide variety of factors including feed ingredients, feed formulations, feed availability, absence of fiber, or high salt in the water.[1]

EPIDEMIOLOGY

The epidemiology may be individual farms, breeding stock suppliers, unhygienic conditions, and different suppliers of feed involved in the spread of the condition.

PATHOGENESIS

Many infections may contribute to disorders of the colon, particularly brachyspirae and *Lawsoniana* and those organisms that contribute to villous atrophy in the small intestine.

Any abnormalities of the small intestine will further increase the amount of undigested and harmful food entering the large intestine. It has now been shown that some diets induce a colonic acidosis and enhance colonization by spirochetes. Many of these cases have no involvement of any of the brachyspirae, and the possibility exists that there may be a syndrome of colonic dysfunction without direct spirochetal involvement.

It is possible that any event that leads to the disturbance of colonic microflora may lead to colonic lactic acidosis and damage to the colonic mucosa and then a reduction in colonic fluid absorption, resulting in diarrhea.

CLINICAL SIGNS

The clinical signs of nonspecific colitis are mild and characterized by mild persistent diarrhea in pigs 5 to 14 weeks of age. Growth retardation and partial anorexia are common. Morbidity and mortality data are not available.

Pigs showed a sporadic diarrhea with soft, wet feces, which may bubble on passing, occasional mucus in the stools, growth depression, and hollow flanks in 18- to 35-kg pigs and with a morbidity of 20% to 30%. Pigs may be ill for up to 3 weeks. Most pigs continued to thrive but some grew poorly.

PATHOLOGY

Pigs had enlarged colons with frothy contents and most had a reddened mucosa. In a study of nonspecific colitis there was increased crypt depth in the colon of weaned pigs with diarrhea.[2] There was no association with any of the common infectious causes of colitis, but there was an association with a diet high in protein and wheat. The total level and digestibility of protein is believed to affect the intestinal microbiota. The further fermentation of the undigested protein in the colon may then result in the production of toxic by-products, and this may be the explanation for protein-associated diarrhea. The increased crypt depth in the colon may result from the protein degradation in the colon as well as the more usual diet rich in dietary fiber and coarsely ground cereals. In this study[2] it is possible that the increased crypt depth may be associated with the feed particle size. Microscopically, they have a mild erosive colitis. A grossly distended large intestine is sometimes seen. The contents are fluid, contain bubbles, and sometimes seem oily. An increased crypt depth was discovered in these colitis cases.[1] Sometimes there may be colonic lesions.

DIAGNOSIS

Clinical signs may indicate nonspecific colitis, and the absence of any positive diagnostics on laboratory testing may further suggest this.

TREATMENT

Identify any specific causes and treat these, and provide general antibiotic treatment such as oxytetracycline.

CONTROL

Control coincident infections such as PCV2 and porcine reproductive and respiratory syndrome virus (PRRSV) through vaccination.

Introduce a general cleanup of the hygiene and in particular use all-in/all-out by age and then thorough cleaning, disinfection, and drying. Examine the nutrition and in general change from pelleted feed to meal. Also eliminate or reduce the antitryptic factors in the food (reducing trypticase in soya meal) and reduce indigestible carbohydrates. Some varieties of wheat and peas should be avoided, and wheat can be replaced by barley. Enzymes can also be used to reduce nonstarch polysaccharides entering the colon.

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PORCINE INTESTINAL SPIROCHETOSIS (SPIROCHETAL COLITIS, PORCINE COLITIS, AND PORCINE COLONIC SPIROCHETOSIS) AND NONSPECIFIC COLITIS

INTRODUCTION

Porcine intestinal spirochetosis is a nonfatal, colonic disease of recently weaned, grower and finisher pigs. The causative organism, BP, was first recognized in 1980 and is a gram-negative, anaerobic, but oxygen-tolerant spirochete found in the colon.

It is found in a wide variety of hosts including immunocompromised humans, primates, dogs, opossums, commercial chicken production, and various species of birds. There appears to be no risk to pig workers. The human strains can cause colitis in pigs, and the wide species occurrence may cause concern for zoonotic risk but this has not yet been confirmed. A cause of special concern is that in some parts of the world the level of infection in humans is quite high, and this may be an indicator that spread is possible from some of the other species to humans.

Porcine colonic spirochetosis (PCS) and nonspecific colitis may be two different syndromes, or the former may contribute to the latter with other organisms and nutritional contributions. Even now the effect of various intestinal combinations of flora and fauna to the pathogenicity of various organisms is unknown. As yet, there is no way to introduce a known intestinal microbiota that encourages well-being. The interrelationship between what goes on in the small intestine and the results in the large intestine in pigs is still largely unknown.

A nonspecific colitis can be part of *Brachyspira, Salmonella, Lawsoniana, Trichuris,* or *Balantidium* infections. PCS is certainly associated with BP, formerly known as *Serpulina pilosicoli.* B. hyodysenteriae and BP are the only two confirmed pathogens of the brachyspirae group together with the newly described *B. hampsonii, B. innocens, B. intermedia,*[1] *B. suanatina,*[2] and *B. murdochii,*[3,4] which are still considered nonpathogenic for the most part.

Large, anaerobic weakly β-hemolytic non-B. hyodysenteriae spirochetes have been associated with porcine colitis and are capable of inducing disease in gnotobiotic pigs, but their role as primary or opportunistic pathogens in colitis in conventional pigs is uncertain.

ETIOLOGY

BP is the cause of PCS. It is a weakly β-hemolytic spirochete usually typed by PFGE. It has 4 to 7 flagella and no plasmids.[5] The outer membrane has LPS, which are serologically heterogeneous. There are a number of outer membrane proteins. The organism is more tolerant of oxidative stress than B. hyodysenteriae.

Swedish workers grouped the intestinal spirochetes isolated from pigs into four groups based on phylogenetic studies, although they are closely related. Groups I and II were isolated only from pigs with dysentery or diarrhea. Group II was differentiated from Group I only by weak β-hemolysis. In Sweden, members of Group II are often isolated from young weaned pigs up to 25 kg in herds where a nonspecific diarrhea, which is clinically distinct from swine dysentery, occurs frequently. These strains seem to be absent or rare in herds without such diarrheic pigs. Group III included the type strain for *B. innocens.* Group IV (detected by PCR) included the pathogenic, weakly β-hemolytic strain P43 (BP) shown to cause spirochetal diarrhea in pigs. Most farms have distinct *BP* genotypes, and common genotypes between and among herds are rare.

A complex investigation of 20- to 40-kg pigs (8–16 weeks of age) on 85 pig units in Scotland from 1992 to 1996 showing diarrhea and slow growth provided much needed information on the occurrence of mixed infections. BP was found on 25% of the units; atypical brachyspirae on 7%; B. hyodysenteriae on 6%; with *S. typhimurium* on 4%, *Y. pseudotuberculosis* (YP) on 4%, and LI on a mere 3%. Mixed infections of BP with *Yersinia, Salmonella,* other combinations, and B. hyodysenteriae were found on 27%. On 6 of the 85 units no pathogens were detected.

Occurrence

PCS probably has a worldwide occurrence. Herds using carbadox had a lower prevalence of *Brachyspira* species than the ones using olaquindox. It has been seen in minimal disease herds in which no antibiotics are used, and it is also seen in herds where no growth promoters are used. There may be multiple strains on a farm or a farm with just one strain.

Risk Factors
Transmission
PCS is usually introduced into herds by other pigs. The shedding may be continuous over

several weeks or intermittent. It is likely that the common route of transmission is fecal–oral but there may be a role for mice and birds. It has been recorded in a wide range of species that may be naturally infected (pigs, dogs, and birds), but rodents are probably not a long-term host.[6] It is possible that feral water birds may be a reservoir.

Managemental and Environmental Factors

The organism has a greater environmental survival than B. hyodysenteriae, particularly in slurry lagoons and manure heaps and the soil itself. It will survive in lake water at 40°C for 66 days and remains viable at 10°C for 119 days in soil and 210 days in soil with 10% pig feces added. It is susceptible to most disinfectants, but not when there is organic matter present.

There may be a close association between this agent and other nonspecific factors in the gut. Changes in colonic microenvironment may predispose to colonization and damage associated with BP. There is a lower incidence if antibiotics are fed compared with no antibiotics.

Feed

Consumption of a rice-based diet significantly reduced the onset of excretion of BP after experimental challenge. In a recent set of experiments five diets were used in conjunction with BP. They included pelleted feed, nonpelleted standard food, standard diet plus lactic acid, formulated liquid diet, and a diet based on cooked rice. The group of pigs that were fed rice did indeed excrete BP for less time in their feces and in fewer numbers than the other groups. The pigs on the pelleted diet were worst. Nonpelleted and home-mixed diets were better.

PATHOGENESIS

The initial colonization of the colon appears to be mediated by the motility-regulated mucin association in which there is a positive chemotaxis toward mucin. Galactosamine and glucosamine are important constituents of intestinal mucin, and BP uses both of these substrates when it is grown in vitro. The organisms penetrate the mucus. This is followed by the multiplication of the spirochetes in close proximity to the mucosal surface and inside the lumen of the crypts. Intimate attachment of BP to the apical membrane of the colonic enterocytes occurs and causes destruction of the enterocyte microvilli. The cell junctions are the target. No receptors have been found as yet. These lesions are only seen in the first three weeks postinoculation in the experiments that have been performed. There may be a specific spirochete ligand and host cell membrane receptor interaction. BP can invade between the enterocytes and reach the lamina propria, where it may remain extracellularly or be seen in macrophages. BP can virtually eat its way through from the lumen to the lamina propria. They spread extracellularly in the underlying lamina propria and are phagocytosed by the macrophages and also enter the capillary blood vessels. They are taken up by a novel mechanism called coiling phagocytosis in which the BP are localized and replicate in the endoplasmic reticulum (ER) of the infected cells, which suggests intracellular trafficking.

Penetration of the epithelium may involve disassociation of the intercellular junctional areas by the action of a subtilisin-like serine protease present in the outer membrane of the spirochete. The proliferation of the organism raises the levels of IL-1β and IL-8.

CLINICAL FINDINGS

Porcine colonic spirochetosis is characterized by mild persistent diarrhea in pigs and loss in weight and increased days to slaughter. It affects mostly young weaned animals of 20 to 40 kg but can occur in finishers and sows. There is believed to be an incubation period of 5 to 20 days. It occurs often after a change in diet. There may a slight fever (40°C), and growth retardation and partial anorexia occur commonly.

The clinical signs of porcine intestinal spirochetosis (PIS) are difficult to distinguish from nonspecific colitis (NSC) and are similar to those seen in other forms of colitis, including early swine dysentery. In one study, prevalence was found to be 5% to 15% and the mortality <1% in affected batches.

Typically, PIS occurs 7 to 14 days after weaning or after they have been mixed. Morbidity is in the region of 5% to 30%, and the signs last for 2 to 6 weeks. It is distinct clinically and pathologically from swine dysentery. Clinical findings include a mucoid nonbloody diarrhea, which is greenish or gray, often soft and wet to start, forming puddles like "wet cement," and then becoming watery. It is usually self-limiting and lasts 2 to 14 days. There may be a stained perineum. During recovery and in chronic cases there may be large amounts of mucus. Affected pigs are usually alert and active but may become depressed, gaunt, and found with starry, rough coats. Affected pigs rarely die and eventually recover. Chronic infection and relapses are sometimes recorded. Mixed infections took longer to recover and had a more profound effect on growth rates and often persisted unless there was medication.

PATHOLOGY

Gross lesions are usually subtle or not recognized. They are restricted to the cecum and colon in all species. The spiral colon is flaccid and full of watery contents with a variable amount of mucus. The large bowel is usually full of content. Mucosal lesions are most obvious in the midregion of the spiral colon followed by the proximal spiral colon. The cecal mucosa is usually not involved or only mildly. The mucosa is reddened or thickened by edema, and it may even form ridges. There are a variable number of erosions. If there are a few erosions, then there appears to be nothing visible, but if they are many erosions then the surface appears granular, and it may be necessary to gently wash the mucosa with water to see these erosions. Fibrin may be mixed with mucus or blood, and there may be variable amounts of either loose in the lumen of the colon. In mixed infections with BP the lesions were more extensive and sometimes affected the cecum as well as the colon.

Microscopically, with time the surface epithelium becomes eroded and attenuated, but these changes are not specific to BP. There is a mild to moderately severe erosive colitis that can be multifocal or diffuse. The extent and severity of this is probably a function of the colonic microflora. The lesions may extend to the muscularis. There are often adherent fibrinonecrotic exudates and feed particles. Goblet cell hyperplasia with distended mucous-filled crypts, mucosal edema, and lymphoplasmacytic infiltrates are also found. Crypt abscesses are not uncommon.

The characteristic histologic feature is a dense mat or false brush border of spirochetes that are closely packed parallel to one another and are attached by one end to the colonic epithelium resembling a brush border. This may be a feature only in the first 2 to 3 weeks of infection. With time the spirochetes persist in the lumen of the colonic glands, which are dilated and filled with mucus. In chronic infections there may be a large increase in chronic inflammatory cells. On EM spirochetes can be seen in the epithelial cells.

IMMUNOLOGY

Immunity to BP is not understood. There is a low level of IgG produced after 2 to 3 weeks. BP may be able to evade the immune system. Recovered pigs may have serum immunoglobulins, but in experimental infections there seems to be a lack of a systemic response.

LABORATORY DIAGNOSIS

The laboratory diagnosis of PCS is similar to that for swine dysentery. The identification of spirochetes in fresh wet smears of feces viewed by phase contrast microscopy may provide evidence of spirochetal infection, but this method alone is not reliable and cannot differentiate between the various groups of pathogenic and nonpathogenic spirochetes. It can be improved with fluorescent-labeled antibodies.

Primary isolation is the technique of choice for confirmation of the disease, and it is then necessary to show BP in the mucosa or feces by culture or PCR. The weakly β-hemolytic BP organisms can then be demonstrated and provisional identification is done by hippurate hydrolysis, although there are organisms that are hippurate negative, but have been confirmed as BP by

16S ribosomal DNA analysis. Most have the hippurate cleaving capacity. It is safer to remember that biochemical analysis is not definite as they can be both hippurate negative or positive. For this reason, it is worth checking on their reaction with β-glucuronidase because they should be negative if they are true BP.

Microscopic lesions are not diagnostic because they may be confused with salmonellosis or swine dysentery but the organisms in the hematoxylin and eosin sections can be seen, and they may be confirmed in **Warthin–Starry** silver-stained sections. Specific identification requires IHC staining with BP-specific mouse monoclonal antibodies. Fluorescent ribosomal RNA can also be detected in ISH. Scanning EM shows degenerating epithelial cells and spirochetal colonization of the epithelium with BP but nothing with *B. intermedia*. The presence of *B. intermedia* can then be detected by PCR using 23S rDNA genes. Specific PCRs targeting 16S RNA or 23S RNA or *nox* genes[7] are available. The duplex and multiple PCRs have been designed to differentiate BP from B. hyodysenteriae and *Lawsoniana*. RT-PCR is available, and restriction fragment length polymorphism analysis can be used to identify the BP isolates. There are no antibody detection systems as yet.

TREATMENT
Treatment and control uses the same principles as those used for swine dysentery. In an old study in the United States, all isolates were susceptible to tiamulin and carbadox; over 50% were resistant to gentamicin; and 42% were susceptible to lincomycin, 15.8% resistant, and 42% had an intermediate susceptibility. Few strains are susceptible to tylosin. In all time-related studies of resistance there seems to be an increasing resistance. In those countries where olaquindox can be used 100 ppm is useful.

In experimental infections when given after challenge valnemulin significantly reduced diarrhea and colonization by spirochetes. More recently in-feed valnemulin has also been shown to be useful at 25 ppm for 14 to 27 days giving lower lesion scores and less widespread colitis.

CONTROL
An effective rodent control policy and prevention of bird entry is probably essential for the control of PSC. Treatment and control of PIS and PSC are achieved using the same principles as those used for swine dysentery. Control can produce significant savings where there is all-in/all-out management and multiple site production. Improving hygiene and reducing contact with feces are the essential ingredients for successful control. If there is a lot of contamination then it is always better to allow exposure for about a week before giving antibiotics because this allows at least some immunity to be produced. Because other species may be a source of infection it is necessary to control mice and birds. Rational use of antibiotics may be useful. Rotation of antibiotic usage may make the occurrence of resistance less likely. The three most likely successful treatments are valnemulin, carbadox, and tiamulin, although carbadox cannot be used in many countries.

- Rations shown to contain 33 and 110 ppm of lincomycin provided an effective control.
- In Finland the use of tiamulin at 200 ppm for 18 to 30 days combined with thorough cleaning removed PCS from a 60 farrow-to-finish operation.
- Valnemulin at 25 ppm (1.25 mg/kg) was shown to be effective in controlling spontaneous PCS.

Vaccination
Vaccination seems to induce a primary and secondary serologic response to BP, but an experimental whole-cell bacterin was not protective when administered parenterally. There is no vaccine in widespread use.

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YERSINIOSIS IN PIGS

The principal disease of pigs is caused by *Y. enterocolitica* (YE) as well as YP. It causes enteritis and typhlocolitis in pigs and similar conditions occur in man. Contamination of carcasses during the slaughtering process may lead to carcass contamination and problems in the food chain (biotypes 4, 2:O9, and 1:O3), and may pose a threat to abattoir workers. *Yersinia* also has significance in that cross-reactions of O9 with *Brucella* are a frequent cause of problems in *Brucella* testing.

ETIOLOGY
The organisms are gram-negative coccobacilli. There are biotypes and serotypes and some of the human food-poisoning types have virulence factors.

EPIDEMIOLOGY
Both species are widespread in pigs[1] and carriage may persist for a long time in both tonsils and feces. Shedding is low in weaners (30%), increases in growers, reaches a peak in finishers (70%), declines in gilts (20%), and is usually absent in sows and boars. Antibody has a similar trend, and is low in neonates and weaners and increases so that usually 100% of sows have antibodies. It can survive in the environment and infects other species including rats, mice, flies, and humans.

PATHOGENESIS
Infection is carried in the tonsils where it sometimes may lodge, and multiplication occurs in the ileum and large intestine. Shedding occurs between 5 and 21 days post infection (DPI) and may continue for up to 10 weeks. Antibodies appear after about 18 days and may also last about 10 weeks. Septicemia may occur with YP, and in these cases there may be abscesses in the liver, spleen, lymph nodes, and guts, as well as the enteritis.

CLINICAL SIGNS
There may be mild fever, watery diarrhea (3–5 days), dark-colored feces, and blood-stained mucosa and soft feces in YE cases. Rectal stricture may also be seen. In YP cases there may be dullness, inappetence, edema, and bloodstained diarrhea, and it has also been isolated from rectal stricture cases.

PATHOLOGY
In former clinical cases at necropsy there may be a catarrhal enteritis. In YP cases the lesions are perhaps more severe with button ulcers in the colon, gut, mesenteric lymph nodes, and liver.

DIAGNOSIS
Clinical signs do not make a provisional diagnosis of yersiniosis likely, but the organism is usually found at postmortem or on bacteriologic testing. They can be isolated on culture from enrichment media or broths. DNA probes or PCR will also detect both organisms, and YE can also be detected in feces by PCR in feces at 5 CFU/mL feces. Diagnosis usually depends on the pathology associated with demonstration of the organism by culture or PCR. Serology (ELISAs) can be useful for detecting herd infection from 2 weeks after infection to a peak at around 30 to 35 days and disappearance at around 70 days.

TREATMENT
If there is a problem it will usually respond to antimicrobial treatment in water or feed, particularly tetracyclines, synthetic penicillins, fluoroquinolones, and furazolidone (not in the EU).

CONTROL
Hygiene and biosecurity are the best controls, aided by rodent and fly control.

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VIRAL DIARRHEA IN NEONATAL PIGS

Neonatal diarrhea in the pig involves principally viruses such as PED, rotaviruses, and the TGE virus, probably in that order of

importance, since 2013. In addition, there are several other viruses of lesser or unknown importance.

Additional major groups in neonatal pigs include the bacterial diseases and principally clostridial infections (*C. perfringens* type A and C and *C. difficile*). In addition, there are the protozoal conditions of coccidiosis and cryptosporidiosis to further complicate the situation. Multiple infections are probably more common than realized because there is a temptation to not look for a further diagnosis once the initial culprit is found.

OVERVIEW OF VIRAL DIARRHEA

Emerging and reemerging swine viruses have been reviewed.[1] The etiologic agents of diarrhea are varied but the predominant group are the viruses. These include TGE and PED, which are the most severe infections causing considerable mortality. The latter is a cause of much recent disease in Asia (China, Thailand, Vietnam, and Korea) in which 50% of the cases may be caused by this agent[2-5] and the mortality approached 100% and now, since May 2013, a large epizootic has occurred in North America.

The most common agent is porcine rotavirus. In addition there are several newly emerging agents including porcine kobuvirus and porcine bocavirus.[6-9]

A systematic study was made in China of these viruses.[10] In finishing pigs, 5% to 10% had diarrhea and usually recovered within 1 week. Sows had diarrhea in 15% to 20% of cases when pregnant and were usually well within 1 to 3 days. Piglets were ill within 1 week of farrowing. These outbreaks spread rapidly within 3 to 5 days. Clinical signs included yellow, watery diarrhea, vomiting, depression, anorexia, and death from dehydration from within 2 to 3 days. The stomach contained a mass of curdled and undigested milk. The small intestine was thin walled and almost transparent. Mortality often reached 80% to 100% but supportive therapy might reduce this to 20% to 30%. If piglets were infected at >14 days then mortality was low. The pathologic changes were mostly in the jejunum and the ileum with little change in the duodenum. There was often villous atrophy.

The pathogens causing diarrhea are diverse with over 96% of the cases having at least one cause in Korea,[4] in Italy,[8] and in Thailand.[11]

In this Chinese study from 2013,[10] not surprisingly 82% had PED. Kobuvirus was frequently detected in single infections but more importantly in mixed infections. Bocavirus and rotavirus were also often detected in mixed infections and only occasionally in single infections. Over 75% in this study were mixed infections. Dual infections were 43.9%, triple 26.1%, and quadruple 2.3% of cases.

Various viruses may coexist with PED. Different infection patterns are observed in different age groups. The viral load of PED tended to be higher in the infected pigs than in the healthy. TGE and rotavirus were not detected in healthy pigs. The viability of enteric viruses after waste treatments has been examined.[12]

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PORCINE ROTAVIRUSES

This virus is a major cause of diarrhea in the pig. The zoonotic potential is unknown, although pig and human strains do reassort.[1] In a recent case in an infant in China it was shown that the rotavirus responsible was a pig–cattle reassortant.[2]

ETIOLOGY

The virus has 11 segments of double-stranded RNA (dsRNA), and each segment encodes for a viral structural protein (VSP) or a nonstructural protein except segment 11, which encodes for both.[3] The virus is a triple-layered particle, and if the outer proteins are removed (VP4 and VP7) by a disinfectant then there is a double-layered particle remaining; in an EM picture both particles can be seen. Only the triple-layered are infectious.[4] There are seven groups that are morphologically similar but antigenically different based on the VP6. Of these Group A is the most important in the pig,[4] but Group C has become more of a problem recently[5-7] and Group E was detected in the UK many years ago. The classification of rotaviruses has been the subject of much discussion.[8,9] In the United States, there has been a substantial diversity.[10]

The Group A rotaviruses are a common cause of diarrhea in nursing pigs from 1 to 5 weeks of age with peak occurrence from 1 to 3 weeks of age, and weanling pigs at 3 to 5 weeks of age and within 3 to 5 days of weaning. Groups A, B, and C occur in diagnostic surveys with about 90% belonging to Group A. Substantial diversity of Group B viruses has recently been described in the United States.[10] Group C rotavirus has also been found to be the cause of enzootic neonatal diarrhea in a minimal disease herd. They are divided into two serotypes, G (15 +) and P (25), and different types predominate in different outbreaks.

Multiple rotavirus G serotypes and P types have been detected in swine. In a recent survey in Europe 14% of the pig samples were positive for rotavirus and the number of G–P combinations was high and confirms the high diversity of genetic diversity.[11] New combinations are being discovered all the time, for example, the discovery of a G2-like virus with a novel VP4 type P32 in Ireland[12] and the G9 P[13] in Ohio in nursing piglets. There is little or no cross-protection between porcine rotaviruses with distinct G and P types, but viruses that share common G and P types induce at least partial cross-protection in experimental studies. This is why it is sometimes essential to know which types are present on the farm. The most common are G3, G4, G5, and G11.

In some countries a certain genotype may be more common, e.g., P23 in Thailand.[14] Variant serotypes of porcine rotavirus such as G3 may cause severe outbreaks of diarrhea in piglets. Subclinical infections are common, and age resistance to rotavirus infection may not occur.

EPIDEMIOLOGY

The serotypes are present worldwide, and up to 100% of adult pigs may be serologically positive for Groups A, B, C, and E, and multiple serogroups and serotypes have been found in the pig.[15-18]

Fecal–oral transmission is common and possibly by aerosol, although this is not confirmed. In the past most infections were Group A, but recently in the United States[6] and Brazil[19] Group C has flared up. The infection dynamics on farms have been described.[20] Reassortants have occurred between pigs on one hand and cattle, horses, and humans on the other.[9,21-23]

In an infected herd, piglets become infected between 7 and 35 days of age, and the virus cannot be detected usually in piglets under 10 days of age, presumably as a result of protection by lactogenic antibody. Virus shedding can occur from 1 to 14 days for the Group A viruses and rather less for the Group B viruses. It is suggested that in an intensive piggery, with a constant shedding of viruses in feces of sows before and after farrowing leads to a continuing cycle of rotavirus infection, with a buildup of host immunity against a circulating strain in the pig population. A virus such as CRW-8 probably could undergo changes through mutations over a period of time, leading to antigenic drift.

In piglets, rotaviral diarrhea is most common in pigs weaned under intensive management conditions, and the incidence increases rapidly from birth to 3 weeks of age. There is no age-dependent resistance up to 12 weeks of age. The disease resembles milk scours, or 3-week scours of piglets. Mortality caused by rotavirus varies from 7% to 20% in nursing pigs and 3% to 50% in weaned pigs, depending on the level of

sanitation. In the United States the peak incidence occurs in February and a moderate rise occurs in from August to September.

A case-control epidemiologic study examined the relationship between Group A rotavirus and management practices in Ontario over a 5-year period. In rotavirus-positive herds, herd size was larger and weaning age was younger compared with rotavirus-negative herds. Pigs raised in all-in/all-out nurseries were three to four times more likely to have a positive Group A rotavirus diagnosis than pigs in a continuous flow system. Pigs in the all-in/all-out system were weaned at an earlier age.

The sow is the source of infection. Seropositive sows can shed rotavirus from 5 days before to 2 weeks after farrowing, when piglets are most susceptible to infection. There are increased secretory IgA and IgG antibodies to rotavirus in the milk of sows after natural rotavirus infection or following parenteral inoculation of pregnant or lactating sows with live attenuated rotaviruses. The early weaning of piglets at a few days of age or at 3 weeks of age results in the removal of the antibody supplied by the sow's milk and predisposes to infection.

Continuous transmission of the virus from one group to another is an important factor in maintaining the cycle of rotaviral infection in a piggery. The virus can be found in dust and dried feces in farrowing houses that have been cleaned and disinfected. This suggests that the environment is also an important source of infection. The porcine rotavirus can survive in original feces from infected pigs for 32 months at 10°C. Gilts and sows shed virus antigen before farrowing and during lactation, which makes it next to impossible to eliminate the infection from a herd. As sows increase in age they develop increasing levels of lactogenic IgA rotavirus antibodies but do not transfer increasing levels of protection to their piglets.

Different electrophore types of Group A rotavirus and different groups of rotaviruses may occur at the same time in a single piggery, which must be considered when developing vaccines. The subgroups of Group A porcine rotaviruses have been classified, and there are differences in virulence of isolates. Most isolates from outbreaks of diarrhea belong to Group A, whereas a small percentage are atypical rotaviruses. Some porcine rotaviruses are related antigenically to human rotavirus serotypes 1 and 2. Porcine rotaviruses displaying the typical bovine P[1], P[5], P[11], G[6], and G8 genotypes have been detected in pigs, which indicates the high frequency of rotavirus transmission between cattle and pigs. The various G and P types of the virus have been examined and compared in Poland and the United States.

Atypical rotaviruses and other enteroviruses are often present in preweaning and PWD in swine herds and should be considered as potential pathogens. Some atypical rotaviruses are associated with villous epithelial cell syncytia in piglets with enteritis. Single and mixed infections of neonatal piglets with rotaviruses and enteroviruses have been described. Combined rotavirus and K99 + E. coli infection causes an additive effect when induced experimentally in gnotobiotic pigs. The inoculation of calici-like viruses into gnotobiotic piglets can result in diarrhea and villous atrophy. Diarrhea in unweaned piglets 1 to 3 weeks of age has been associated with a combined infection of rotavirus and *Isospora suis.* There can be an important synergistic effect with other viruses such as PED.[24] The combined effect of a dietary change at weaning and rotavirus infection in gnotobiotic piglets is a temporary villous atrophy, and there is no evidence of persistent atrophy of the small intestine.

PATHOGENESIS

They replicate in enterocytes of the small intestinal villi and the cecal and colonic epithelial cells. Jejunum and ileum are the most affected. Within 12 to 48 hours of an experimental inoculation, the affected cells lyse and disruption of villous architecture follows. To some extent this is age dependent and strain and serogroup dependent. Groups A and C produce the most serious effects. Malabsorption results as a result of impaired glucose-regulated sodium transport, impaired disaccharidase production, and increased thymidine kinase activity.

CLINICAL SIGNS

The incubation period may be 18 to 96 hours. Rotaviral diarrhea may occur in nursing piglets from 1 to 4 weeks of age and in pigs 1 to 7 days following weaning. If the condition is uncomplicated by other agents then the disease is often mild. Lactogenic immunity is very protective. Direct experimental infections are always more severe than the natural infections. In older piglets it is less severe, and in pigs of 4 to 5 weeks it produces only a very slight diarrhea. The disease in nursing piglets resembles milk scours or 3-week scours. Most of the pigs in the litter are affected with a profuse liquid to soft diarrhea with varying degrees of dehydration. Recovery usually occurs in a few days unless complicated by ETEC or unsatisfactory sanitation, overcrowding, and poor management. The disease is often most severe in herds in which there is continuous farrowing with no period of vacancy for cleaning and disinfection in the farrowing barn. The disease may also occur in pigs a few days after weaning and may be a major factor in PWD of piglets weaned at 3 weeks of age, or earlier in the case of weaning pigs at 1 to 2 days of age.

PATHOLOGY

Gross lesions are most severe in 1- to 14-day-old pigs when the stomach is empty and the intestine is thin walled, flaccid, and full of watery flocculent fluid. The lacteals in the mesentery are empty and the lymph nodes are small. In pigs older than 21 days there are no gross lesions in the uncomplicated cases.

Histologically, there is loss of the villi tips within 16 to 18 hours postinoculation. Significant villous atrophy occurs within 24 hours and reaches its height at 24 to 72 hours. Then there is a flattened squamous epithelium and crypt hyperplasia.

DIAGNOSIS

Porcine rotaviruses grow in cell cultures with a characteristic rounding of the cells, and the virus can be detected in these cultures by immunofluorescence or IHC. The latter is also used directly on tissue sections from the small intestine.

A whole variety of methods are used to detect rotavirus, but many rely on the commercial ELISA kits for rotavirus A, and monoclonal antibody capture ELISAs have been developed for Groups B and C. Nucleic acid hybridization and viral RNA have been detected by RT-PCR. The latter is often used for the detection of serogroups and genotyping.[1,6,15-17,25]

Because the infection is so widespread there is little point in measuring antibodies, but a whole variety of techniques can be used to detect high levels of IgA and IgM, which will indicate recent infection.

IMMUNITY

The immune response appears to be specific for either the P or G type. There appears to be little cross-protection between the groups. The presence of a neutralizing IgA antibody in the small intestine appears to be the most important feature in the immune response. This is the reason the pig is most prone to infection when the level of maternal antibody has decreased.

DIFFERENTIAL DIAGNOSIS

Transmissible gastroenteritis is most common in piglets under 1 week of age and explosive outbreaks are common. There is acute profuse diarrhea and vomiting. Affected piglets may continue to nurse for several hours after the onset of the diarrhea. The case–fatality rate is high in piglets under 7 days of age; older pigs usually survive.

Porcine epidemic diarrhea type I affects piglets under 4–5 weeks of age and is characterized by profuse watery diarrhea, high morbidity, and low mortality.

Porcine epidemic diarrhea type II causes a profuse fluid diarrhea in pigs of all ages, including nursing piglets. Explosive outbreaks may occur and the morbidity may reach 100%. Mortality is usually restricted to piglets under 3 weeks of age.

Enteric colibacillosis usually occurs in piglets under 3 days of age. There is acute diarrhea, dehydration, and rapid death. Pigs with coliform septicemia may die without

obvious diarrhea and usually appear cyanotic. Entire litters may be affected and the case–fatality rate may be 100%. Early treatment with antibiotics and subcutaneous fluids will result in recovery. Coccidiosis occurs in piglets from 5 to 10 days of age and is characterized by an acute diarrhea in which the feces are foul smelling and vary in consistency from cottage cheese–like to liquid, and gray or yellow and frothy. The diarrhea is persistent for several days and nonresponsive to antibiotics. Some pigs recover spontaneously, whereas others die in 2 to 4 days. Coccidial oocysts can be detected in the feces. The morbidity rate varies from 50% to 75% and the case–fatality rate from 10% to 20%.

Hemorrhagic enterotoxaemia caused by *Clostridium perfringens* type C affects entire litters of pigs under 1 week of age; is characterized clinically by severe toxemia, dysentery, and rapid death; and at necropsy there is a hemorrhagic enteritis.

Coccidiosis

C. perfringens type A

C. difficile

Other pig diarrhea viruses (calicivirus, sapovirus, norovirus, adenovirus, etc.)

TREATMENT

Diarrhea causes dehydration and electrolyte imbalance, so rehydration and energy provision is essential using oral electrolytes. The younger the pig is, the worse the effect, because in these animals reserves of energy and cold tolerance are largely reduced. It is therefore essential to maintain a warm environment and to provide the correct creep feeds for young piglets to encourage food consumption. Regular cleaning and disinfection will reduce the level of virus challenge.

CONTROL

A variety of disinfectants including phenols, formalin, and chlorine have been used to deal with a virus that is resistant to a variety of environments. It can survive for 9 months at the temperatures normally found in a farrowing house. As yet there is no good porcine rotavirus vaccine.[26]

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PORCINE HEMAGGLUTINATING ENCEPHALOMYELITIS VIRUS

Porcine hemagglutinating encephalomyelitis virus (HEV) is also known as vomiting and wasting disease. It is also a disease of neonatal pigs. It can be seen as different manifestations, and there is no public health significance.

ETIOLOGY

The cause is a Betacoronavirus of the *Coronaviridae,* and the natural host of the virus is the pig. It was originally described in the UK and Canada, and there is only one serotype. There are mostly inapparent infections with occasional outbreaks in nonimmune herds,[1,2] and it has a tropism for neural tissues.

EPIDEMIOLOGY

The condition occurs worldwide. The condition affects neonates and is maintained by the infection of piglets from sows. Because most sows are protected there are few outbreaks. A new herd of 6000 sows with 55% gilts and first or second litter sows was severely affected.[2] The piglet is affected before 3 to 4 weeks of age if born to nonimmune sows. It is transmitted in nasal secretions probably resulting in nose-to-nose transmission and possibly aerosols. Excretion of the virus following infection probably lasts 8 to 10 days. The presence of maternal antibody, which lasts up to 15 weeks, protects the piglet against neural damage. Pigs over 3 to 4 weeks do not get nervous signs.

The virus will also spread rapidly among newly weaned finishing pigs, and immunity develops within 8 to 16 weeks. The virus is rapidly destroyed by ultraviolet light.

PATHOGENESIS

After oronasal infection signs begin within 3 to 5 days. These signs are affected by age at infection and possibly also by any strain differences in the virus. Replication is widespread in the respiratory tract, particularly lungs, tonsils, and small intestine. It may spread to the CNS via the peripheral nervous system, particularly the trigeminal, vagus, and intestinal plexuses to the spinal cord. On reaching the brain it particularly affects the vomiting and appetite centers to produce wasting. Virus replication in the gastric nerve plexi causes damage and disturbs gastric emptying and starvation. Viremia is of no importance.

CLINICAL SIGNS

Piglets between 5 days and 3 weeks are affected. They will often try to suckle, then stop and vomit. The first signs are vomiting and huddling together, which indicates a raised temperature that may last 1 to 2 days. Anorexia, dehydration, and constipation follow, and the vomiting increases in frequency and is usually followed by death or wasting. Nervous signs may follow in some pigs with hindleg weakness, difficulty in swallowing, and persistent retching and vomiting. Older pigs nearer 3 weeks may just lose their appetite and become emaciated, and may require euthanasia. Morbidity may be 100% if totally susceptible, and mortality may also be high under similar circumstances. Pigs in outbreaks of the so-called motor encephalomyelitic form may huddle, sneeze, cough, and vomit as early as 7 days after birth. They may then huddle, show tremors, hyperesthesia, jerky gait, walk backward, or adopt a dog-sitting posture. Blindness, opisthotonus, nystagmus, and paddling on the side in lateral recumbency, followed by coma and death, are also seen.

PATHOLOGY

There are usually no gross lesions. The abdomen may be swollen. The intestinal tract and particularly the stomach are usually empty. There may be intestinal dilatation.

Histologically, there may be nonsuppurative inflammation in the tonsils or lungs. In the V and W form there may be degeneration of the ganglia in the stomach and perivascular cuffing in the stomach. If there is an encephalitic form, a nonsuppurative encephalitis is found that is most pronounced in the pons, medulla, and the dorsal horns of the spinal cord with perivascular cuffing, gliosis, and neuronal degeneration.

DIAGNOSIS

The clinical signs in young pigs less than 3 weeks of age are highly suggestive. Virus isolation in the first 2 to 3 days of an acute infection is possible using PK cells and then using hemadsorption, immunofluorescence, neutralization or hemagglutination, or the presence of syncytia to confirm. IHC on tonsils, brainstem, and lungs will also confirm the diagnosis.

RT-PCR on tonsils, brainstem, and lungs will also demonstrate the agent. An antibody that arises 7 to 10 DPI can be detected by plaque reduction, virus-neutralization (VN), or hemagglutination inhibition tests. Antibody concentrations increase rapidly after infection but there presence does not indicate active disease.

DIFFERENTIAL DIAGNOSIS

The most likely differential diagnoses are pseudorabies or Teschen–Talfan.

TREATMENT AND CONTROL

There is no treatment or control. If you know the herd is free, keep it so by biosecurity, purchase new stock from a known-free source and quarantine on arrival, and then adapt to the unit to encourage immunity to the strains present on the farm; otherwise maintain a high herd immunity by mixing ages of sows to encourage circulation of the virus, increasing colostral immunity.

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PORCINE ADENOVIRUSES

Porcine adenoviruses cause mild diarrhea and pneumonia in pigs.

ETIOLOGY

Porcine adenoviruses are DNA viruses and can be cultured in cells to show cytopathic effects and intranuclear inclusions. They are resistant to the environment and may live up to 1 year at 4°C but are susceptible to most disinfectants. Seven types have been found in pigs and types 1 and 4 are the most common.

EPIDEMIOLOGY

Porcine adenoviruses are found worldwide; for example, antibodies have been found in 80% of slaughter pigs in the UK and similarly in Japan. Antibody positivity increases with age. Virus has been isolated from nasal discharges, abortions, and from stillborn piglets following transplacental infection, and from normal animals. In one herd 24% of piglets to 8 weeks were positive as well as 60% of finishers and 90%+ of the sows.

PATHOGENESIS

Intestinal strains colonize the tonsils and the intestines and infect the intestinal cells of the villi of the lower jejunum and the ileum. Intranuclear inclusions can be seen in the cells that have nuclear swelling and lose microvilli, and then villous shortening follows. The affected cells migrate to the tips of the villi.

Type 4 also has a predilection for the respiratory tract, where it causes interstitial pneumonia and occasionally encephalitis.

CLINICAL SIGNS

Pigs less than 3 weeks of age are affected in the main, but there can be infection from 5 days to 24 weeks. The incubation period is 3 to 5 days, and the diarrhea lasts for 3 to 6 days. It is yellow, intermittent, and of variable consistency. Dehydration does occur but death is rare.

PATHOLOGY

There is thinning of the intestinal wall in the jejunum and ileum. Histologically, there are intranuclear inclusions in the enterocytes, particularly over the Peyer's patches, and these are of the Cowdry type (eosinophilic or amphophilic surrounded by a clear halo).

DIAGNOSIS

Diagnosis is based on the detection of virus particles in the gut contents by EM, demonstration of inclusions in histologic sections, and the detection of the virus by PCR and qPCR.

PORCINE CALCIVIRUSES

Porcine enteric caliciviruses[1,2] have been found in Europe,[3] Korea,[4] and Japan.[5,6] They are common and of unknown pathogenicity. It is not known if they are zoonotic, but they are of no public health concern at the moment.[7,8] They are RNA-containing viruses. Infection of gnotobiotic piglets causes diarrhea lasting 3 to 7 days. The viruses are found in the usual place on the sides and base of the villi and caused significant villous atrophy.

The family Caliciviridae is divided into four genera: *Norovirus, Sapvirus, Lagovirus,* and *Vesivirus.* An unassigned fifth genera[9] and both the sapoviruses and noroviruses are of uncertain pathogenicity in the pig.[8] The pig viruses are called porcine sapoviruses (PoSaVs) and the porcine noroviruses (PoNoVs). The prevalence and molecular characteristics of these viruses has been studied in the United States.[9]

No clear relationship between diarrhea and infection has been demonstrated,[10] and they are often recovered from normal pigs.[11,12,13]

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PORCINE SAPOVIRUSES

The first of the PoSaVs was isolated in 1980 in a diarrheic piglet using EM. The prototype was known as the Cowden virus, and most of the ones studied since are similar to this virus. It was originally known as the porcine enteric calicivirus. Experimental infections with this virus produced severe diarrhea, anorexia, and intestinal lesions.

They are found in all age groups of pigs including those with diarrhea and those without clinical signs. It is suggested that sapoviruses play a part in enteritis in piglets.[1] A Korean-like sapovirus was recently identi-fied in the United States.[2] Sapovirus characterization has been described.[3]

A survey of pigs with diarrhea showed that 32.5% had sapoviruses, but there was no proof that these were the cause of the problem.[4] They have evolved by recombination.[5]

Both sapoviruses and noroviruses are resistant to environmental conditions. At least six sapovirus genotypes have been identified and they are widespread on European farms.[3] They also have been identified in Japan.[6] They are highly diverse, but PoSaVs belong to genotypes GIII, GVI, GVII, GVIII, and GIX, and GX and GIII are the most common in pigs. Double infections with two or more sapoviruses are common.

In experimental infections sapoviruses do produce diarrhea. The virus produces lesions in the small intestine and replicates in the enterocytes. When given orally to piglets the virus is shed for up to 9 days.

In histologic examination it produces shortening, blunting, and fusion or destruction of the villi in the duodenum and the jejunum. There is crypt cell hyperplasia and reduction of the villus:crypt ratio (villous atrophy).

The incubation period with the original Cowden virus was 2 to 4 days after oral inoculation, and diarrhea and anorexia persisted for 3 to 7 days.

In another study, the viruses were homogenously distributed among the different age groups of pigs and were not associated with disease.[4]

In a serologic survey in Spain,[6] 85 samples from pigs of 8 to 34 weeks were examined and 62% were positive.

A high maternal antibody is probably developed in the first few weeks of life, which then falls, and by 3 months has risen again (active immunity).

No human sapoviruses were detected in pigs by the authors who analyzed sapoviruses across Europe.[3] They detected the virus in 80/1050 samples (7.6%) collected from 39 farms in 6 countries. The highest prevalence was in 2- to 8-week-old pigs, and there was no difference in prevalence between healthy and diseased piglets. Six old genotypes and two new types were discovered.

Diagnostic tests are available in research laboratories (e.g., EM PCR, RT-PCR).[7,8]

Little is known about immunity, although it is assumed that sows produce colostral antibodies.

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PORCINE NOROVIRUS

It is not certain whether the pig and human noroviruses are antigenically distinct or related. These viruses have not been detected in nursery or postweaning pigs but have been found in healthy finishing pigs.[1,2]

A PoNoV was found in asymptomatic finishers and adult pigs.[1] It has positive sense single-stranded (ss)RNA viruses with three ORFs. Genetically diverse, they have five genotypes[3] and G11 is the one found in pigs and humans. There are three separate genotypes (11, 18, and 19) in pigs, and they have a worldwide distribution.[4-11] Epidemiologically, it will survive waste treatments. Little is known about their pathogenicity.

In an experiment with human norovirus in gnotobiotic pigs, a mild diarrhea was produced with lesions in the proximal small intestine.[12] It replicated in some pigs and produced antibody in some pigs. No diagnostic tests are available commercially, but a variety have been used in research laboratories (e.g., EM, RT-PCR, and PCR).[9]

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PORCINE ASTROVIRUSES

Porcine astroviruses, although isolated from pigs, are of unknown importance. They are not zoonotic, and they were first isolated from pigs in the 1980s.

ETIOLOGY

The viruses from the different species are probably antigenically different, and five types have been recognized.[1-5] All five types have been found in the United States,[6] and in some cases more than one type was found in a pig. The porcine strains are different from the human strains.[7] They are members of the family Astroviridae and of the genera *Mamastrovirus*; are positive sense, ssRNA viruses; and are highly diverse. They have partially clustered genomes[4,8] and are of two different lineages (PAST-1 and PAST-2).

EPIDEMIOLOGY

Porcine astroviruses have a worldwide distribution. A recent survey[9] suggested that perhaps 62% of pigs had astrovirus (260 pigs with diarrhea were studied). The transmission is presumed to be the usual fecal–oral route such as for most enteric pathogens.

PATHOGENESIS

The viruses are only known to cause disease in association with other agents. In an experimental infection given with PAST-1, only mild diarrhea was produced, which occurred within 1 day and continued for 5 to 6 days.

CLINICAL SIGNS

The association between these viruses and clinical disease is obscure because they are found in pigs with diarrhea and in healthy pigs. The clinical signs are more likely to be found in association with simultaneous infection with rotavirus, coronavirus, or calicivirus.[9]

DIAGNOSIS

EM, cell culture, and RT-PCR have been used to detect the antigen. VN and IFA techniques have been used to detect antibodies.[10]

TREATMENT AND CONTROL

Treatment and control are probably not possible, and if affected then supportive therapy may be instituted.

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PORCINE TOROVIRUS

The link between these viruses and clinical disease is obscure. They are probably found worldwide and most recently have been found in Spain.[1,2] These kidney-shaped viruses are members of one of the four species within the *Torovirus* genus of the Toroviridae subfamily of the Coronaviridae[3] and have been identified in a variety of pigs with diarrhea including the following:

- A 3-week-old pig with diarrhea
- Four-week-old pigs from Italy had greenish-yellow diarrhea and 30% morbidity and 8% to 10% mortality.
- Korean torovirus strains cause sporadic infections.
- In South Africa, 6- to 8-week-old pigs showed a sudden increase in mortality with piglets showing a reduction in appetite, weakness, tremors, recumbency, and death.

Generally, they are probably endemic in most pig herds and probably occur in closely related clusters in an area. Most pigs are affected postweaning. There is a high prevalence in subclinically infected weaned pigs.[4,5] There is probably endemic subclinical infection in neonates and young pigs and possibly there is a low incidence in adults.[4] In Korea, they are genetically diverse.[5]

Toroviruses can be demonstrated by PCR, RT-PCR, and qRT-PCR for antigen, and ELISA and VN for antibodies.

Antibodies can be demonstrated using ELISAs using recombinant viral proteins.

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PORCINE ORBIVIRUSES

Porcine orbiviruses have been found in porcine feces and seem to have no clinical significance.

PORCINE PICOBIRNAVIRUSES

Porcine picobirnaviruses have been found in the UK, Argentina, Venezuela, and Hungary. Their clinical significance is unknown, but on one farm 11% of the samples from 15- to 35-day-old pigs were positive. Excretion has been followed from birth to slaughter.[1]

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PORCINE KOBUVIRUSES

The virus was first identified in Hungary in 2008.[1] These viruses are also Picornaviridae and belong to the genus *Kobuvirus*, and the virus is found in pigs with diarrhea and in healthy pigs.[1,2] No significance has as yet been attributed to them. They have been found worldwide by RT-PCR, and infection rates seem to vary from 45% to 99%. It has been reported that as many as 84.5% of pigs have the virus.[3] These infections are most commonly observed in nursery pigs and also as single infections. The viral load in healthy and infected pigs is also similar. They have been found in Brazil and the Netherlands,[4] Thailand,[5] Japan,[6] Korea,[3] and China.[7,8] They have also been found in the Czech Republic[9] and in 2013 found in the United States.[10]

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PORCINE NEW VIRUS

A new circular ssDNA virus was isolated from porcine feces,[1] and these viruses can affect a wide range of species including pigs.[2]

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PORCINE BOCAVIRUS

Studies have indicated that Bocavirus,[1] which has a close relationship with enteric disease in domestic animals, had a high prevalence in stool samples of pigs.[2,3] It is commonly found in grower pigs,[4] and the level of virus load is not different between healthy and infected pigs. It can be detected using Taq-Man-based RT-PCR.[5] A bocavirus causing respiratory tract signs has been found in China.[6] It has been found in pigs in Sweden,[7,8] China,[9,10] and in Northern Ireland.[11]

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A NEW NEONATAL DIARRHEA SYNDROME

A French study[1] has suggested that there is a new neonatal diarrhea syndrome (NNDS) in France and Denmark characterized by a mortality rate of up to 40% in suckling pigs, of unknown cause, with 15% to 20% of French herds supposedly having experienced this outbreak and with over 80% of submissions to Danish laboratories having been associated with this outbreak. It has been suggested that the herds are mainly the high-yielding well-managed herds. There is considerable variability between the litters; particularly the gilts and second litter sows may be affected. The length of parturition in the affected litters was longer than in the unaffected herds. The proportion of piglets born late was higher. Levels of antibodies in colostrum varied, but there was no evidence of differences in quality of colostrum. No consistent pattern emerged in the herds, and no consistent pattern of microbiological observations has been found. Piglet serum IgG is a reflection of the rate of absorption from the gut, which depends on the level of IgG in the colostrum and in turn depends on the level of maternal antibody in the sow. There were normal amounts of milk in the stomach of affected pigs; there were no obvious gross lesions; they were not dehydrated; the small intestines were contracted, or atonic, and dilated; hyperemia was rare, and intestinal contents were yellowish and aqueous. The intestinal mucosa was not inflamed and the lymph nodes were reactive. The colon had no changes, and the contents were creamy or watery. In the Danish laboratories 55% of the cases had nonhemolytic *E. coli* and 7% hemolytic *E. coli* that was mostly O7, 16% had ETEC, *C. perfringens* type A was found in 80%, *C. difficile* was found in 12%, and rotavirus was also found in 12%. Only 1/220 samples had *C. perfringens* type C.

Four Danish pig herds with NNDS were investigated.[2] This has occurred since 2008 and is characterized by a nonresponse to treatment or to management therapies. No pathogens have been detected in the past, and in this investigation no pathogens were detected either. Macroscopically, these pigs had filled stomachs and flaccid intestines without mucosal changes. The predominant histologic changes were villous atrophy in the jejunum and ileum. Epithelial lesions were seen in the colon in one-third of the cases. In the Danish cases it was found that (1) microbiological testing was not sufficient to explain the problem, (2) histopathology was generally inconclusive, (3) *E. coli* and *C. perfringens* type A are found in normal pigs and are therefore not considered to be important, and (4) the role of *C. difficile* under Danish conditions has not been elucidated.

A suggested case definition was nonhemorrhagic diarrhea during the first week of life without detection of known infectious pathogens characterized by milk-filled stomachs and flaccid intestines at necropsy.

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TRANSMISSIBLE GASTROENTERITIS IN PIGS

SYNOPSIS

Etiology Transmissible gastroenteritis virus, member of the Family Coronaviridae

Epidemiology Highly contagious disease of newborn piglets but may affect pigs of all ages in susceptible herds. High morbidity and high case-fatality rate in piglets under 10 days of age. Over 5 weeks of age, mortality is low. Large economic losses. Epidemics of disease occur in susceptible herds. Transmission by oral and aerosol routes. Recrudescence of infection and endemic disease commonly follows epidemics. Infection of pregnant sows results in protection of piglets by secretory IgA in milk. Porcine respiratory coronavirus mutant of transmissible gastroenteritis (TGE) virus has reduced the incidence of TGE.

Signs *Epidemic disease*: Acute diarrhea, vomiting, dehydration, and death in piglets under 10 days of age. Less severe diarrhea in older pigs of all ages.

Endemic disease: Diarrhea in young pigs 6 days of age and older, including weaned pigs.

Clinical pathology Detection of virus in tissues. Serology.

Lesions Fluid-filled intestines. Villous atrophy.

Diagnostic confirmation Detection of virus in mucosal scrapings of intestine.

Differential diagnosis list

- Enteric colibacillosis
- Coccidiosis
- *Clostridium perfringens* types A and C; *Clostridium difficile*
- Rotavirus enteritis
- Porcine epidemic diarrhea, especially new strains
- Vomiting and wasting disease
- Diarrhea of adult sows, gilts, and boars

Treatment Supportive therapy. Fluids and electrolytes. No specific treatment.

Control Isolation of sows due to farrow. Planned exposure to virus. Biosecurity and acquisition of virus-free replacement stock. All-in, all-out management system. Vaccination.

ETIOLOGY

Gastroenteritis is associated with the transmissible gastroenteritis (TGE) virus, an alphacoronavirus 1 and member of the Family Coronaviridae[1] belonging to the Order Nidovirales. The nucleotide sequences from 20 TGE virus isolates obtained from eight countries between 1946 and 1996 have been compared. The virion is an enveloped, large, single-stranded RNA genome with positive polarity. It has three major structural polypeptides: 200-Kda spike protein (S protein), 30-Kda membrane protein (M), and a minor 10-Kda protein (E). These are produced by open reading frames (ORFs) 2, 5 and 6. The function of ORF products from 3a and 3b are not known, but they have been postulated as an important determinant of virulence.

In Europe, TGE-like strains of coronavirus have recently emerged.[2] These might be novel recombinants and are associated with the winter season, possibly occur in nonporcine hosts (cats, dogs, and foxes), and can be spread by starlings and houseflies.[3]

EPIDEMIOLOGY
Occurrence and Prevalence of Infection

The disease occurs in pig-producing areas of North America, Europe, and many parts of Asia, principally in the northern hemisphere. During the past three decades, TGE has changed from a sporadic disease that historically occurred in the midwestern United States to an endemic disease in most countries of the northern hemisphere. It can cause severe disease even in seronegative herds, especially if the protection of porcine respiratory coronavirus (PRCV) is missing. In Asia, TGE and porcine epidemic diarrhea

(PED) often cocirculate. In densely swine-populated areas, such as the midwestern United States, the disease is one of the major causes of morbidity and mortality in young pigs. The disease has not been diagnosed in Australia and New Zealand. In 1990, the prevalence of infection in the United Kingdom was low, with 0.6% of sows sampled being seropositive compared with 3% in 1984. No major epidemics have occurred since 1981. In 1984, a seroconversion to the TGE virus occurred in a closed herd in the absence of any clinical disease. The TGE virus was not isolated, and it is possible that the seroconversion resulted from the emergence of PRCV throughout Europe and the United Kingdom beginning in 1986. PRCV is a deletion mutant of the TGE virus, and its high rate of prevalence has markedly reduced the number of TGE outbreaks in European swine herds. The TGE virus probably coexists in these herds together with PRCV. In 1999, a single case was diagnosed in East Yorkshire as a one-off. Other isolated outbreaks in herds that were seropositive for PRCV were also reported. An outbreak of TGE occurred in the United Kingdom in 1996 in which the virus was a variant with an intact spike gene but with a large deletion in ORF 3a, which therefore may not be necessary for enteric virulence.

The **prevalence of infection** with the TGE virus based on serological surveys of swine herds varies with the size of the herd, the distance between herds, and the purchase of breeding stock from nonspecific pathogen-free herds. Depending on the geographical location, up to 50% of herds may be seronegative, and in 45% of herds, the prevalence of infection in sows will vary from 10% to 80%. In the United States in 1990, a national survey of swine herds found that 36% of herds were positive for the TGE virus, and 24% of the producers' herds were vaccinated for the virus. By 1997, up to 100% of surveyed herds and 91% of the sampled sera were positive for both the TGE virus and PRCV, which indicates a marked increase, probably as a result of subclinical infections.

The disease is highly contagious and affects piglets primarily under 10 days to 2 weeks of age. Pigs over 5 weeks of age often have milder clinical signs. **Epidemic TGE** occurs when the virus is first introduced into a susceptible herd and is usually of short duration and no longer clinically evident after herd immunity develops. Epidemics of the disease occur most commonly during the winter months. **Endemic TGE** occurs when the virus persists in a partially immune herd into which susceptible swine are introduced or if the epidemic form is not well managed. Endemic TGE is a common sequela to a primary epidemic in herds of more than 300 sows in which diarrhea occurs in piglets from 6 days of age to approximately 2 to 3 weeks after weaning. Recurrence of clinical TGE often occurs in endemically infected herds approximately 9 months after the first outbreak as the piglets of susceptible sows are exposed to the virus. Recurrence has been associated with the following factors:

- Breeding herd sizes of over 100 sows
- Presence of finishing pigs in large herds
- Introduction of purchased gilts

Morbidity and Case Fatality

Typically, an epidemic in a herd is explosive and dramatic. Rapid spread and high morbidity occur in pigs of all ages within 2 to 3 days, but major clinical disease is restricted to pigs prior to weaning and lactating sows. Case-fatality rates can approach 100% in pigs under 10 to 14 days of age but are much lower with increasing age, and mortality is low in postweaned and adult pigs. The epidemic commonly terminates in 3 to 5 weeks with the loss of young, susceptible pigs and the development of herd immunity, and, generally, the disease does not recur again for a 3- to 6-year period.

Risk Factors
Animal Risk Factors

Level of Herd Immunity. Epidemics of clinical disease occur following the introduction of the virus into a **susceptible herd with no previous exposure** to the virus. All age groups will become infected, and most pigs will be affected clinically to variable degrees. Nursing piglets under 2 to 3 weeks of age are most susceptible to clinical disease and experience the highest case-fatality rate. Clinical disease disappears when the herd becomes immune. Endemic TGE develops when the virus and clinical disease persist within partially immune herds, as a result of continual or periodic introduction of susceptible pigs. In endemic situations, diarrhea is generally observed in pigs from the age of approximately 6 days until approximately 14 days after weaning. Overall pig mortality is lower and generally occurs in recrudescent episodes. After weaning, piglets no longer have the protection provided by TGE-specific secretory IgA antibody in milk and are susceptible to infection and clinical disease if the infection rate in the weanlings is high. Thus, weanling pigs serve as a major reservoir of infection.

Sow parity may be a risk factor. Parity-1 sows with no previous exposure to the virus may be a risk factor on some farms. On other farms, parity-3 sows were at increased risk for unknown reasons. A single boar may be a high-risk animal on some farms.

Herd Size. There is a higher likelihood that sows will be seropositive if the herd size exceeds 500 sows and if more than 25 replacement breeding animals are purchased from nonspecific pathogen-free herds. A mathematical model of the detection and dynamics of the disease in Australia indicates that the disease is likely to be established in breeding and finishing swine herds of average size. The threshold number of susceptible pigs for establishment of the infection is 90 to 160. Swine herds most at risk are those with large numbers of susceptible pigs, continuous breeding of susceptible pigs, high numbers of purchased pigs, and close contact between feral pigs and susceptible domestic pigs. The risk is highest in herds that do not receive a rapid diagnosis, such as when there is little or no veterinary involvement in health and disease management. In small farms (containing 15-40 sows), outbreaks of TGF are characterized by rapid spread of infection to most animals of all ages but a duration of only 3 to 5 weeks.

Environmental and Management Risk Factors

Climatic factors appear to be important in the occurrence and establishment of the disease. Climate does not yet have significance in the tropics or southern hemisphere, and there is evidence that spread of the disease is limited in hot climates. In areas where the disease is endemic, it has a distinct seasonal occurrence, with the majority of outbreaks occurring from midwinter to spring, and cyclic occurrence has been recorded. The virus is labile above 21° C and is very sensitive to sunlight. It is also killed by most disinfectants. The disease tends to occur in area outbreaks in which herds in close proximity are affected within several weeks. Within swine barns, the location of the farrowing crates may be a risk factor if the cold-air inlets are directly above the crates.

The use of a continuous-flow system of production in a herd is a major risk factor. The constant overlap of farrowing sows in farrowing rooms, overlap of weaned pigs in nursery rooms, and a continuous flow of finishing pigs without adequate cleaning and disinfection between each group of pigs are major risk factors and perpetuate persistent infection and the endemic form of the disease. An all-in, all-out system for each group of pigs reduces the risk of infection between pigs.

Lack of adequate biosecurity is a major management risk factor. Infection can be introduced into herds by the importation of infected breeding stock, by contaminated trucks and other vehicles, or on workers' clothing and boots.

Pathogen Risk Factors

The virus has a long survival in slurry, water, and sewage. It is readily destroyed by standard solutions of phenol and formalin, by boiling, and by drying but not by freezing. The virus is highly photosensitive, which may account for the more frequent occurrence of the disease during the winter and spring months. The virus survives freezing, and infected pork scraps or offal may provide

a source of infection either directly through feeding of uncooked garbage or possibly indirectly via dogs. Purposeful infection by the feeding of frozen infected piglet intestine to sows to induce immunity can also be a significant source of continued infection of a herd or area.

The genome and the genetic basis for the pathogenesis of the virus have been described. Antigenic differences between TGE viruses have been examined, and the nucleotide sequences of isolates from various countries have been compared.

The TGE virus is not antigenically related to the two other porcine coronaviruses, hemagglutinating encephalomyelitis virus and porcine epidemic diarrhea virus, but it is related to PRCV.

Porcine Respiratory Coronaviruses

PRCV is a deletion mutant of the TGE virus with altered tissue tropism to the respiratory tract, first recognized in Belgium in 1984. It has a partially deleted receptor binding protein. The virus closely resembles the TGE virus antigenically, and pigs infected with PRCV develop a serological response that cannot be distinguished by virus-neutralization tests from the response of pigs infected with the TGE virus. In other words, it provides cross-protection. Infection with PRCV produces high levels of interferon and nitric oxide in the lungs.[4,5] Despite the antigenic relation of PRCV and the TGE virus, they can be differentiated with monoclonal antibodies. All PRCV strains have around 600 to 700 nucleotide (nt) deletions within the amino-terminal S gene, resulting in the loss of hemagglutination activity and two antigenic sites. European PRCVs have an identical deletion of 672 nt at the same position, whereas U.S. strains have 621 to 681 nt deletions located at different positions, which suggests that they arose separately. Natural infection of the sow with PRCV induces natural antibodies that neutralize classic TGE. The virus has spread throughout Europe and has been identified in the United States and Canada. Spread of the virus has been explained in part by airborne transmission, and infection shows a seasonal pattern, affecting farms during winter and spring. Seroprevalence studies in Belgium indicate that 95% of sows are PRCV positive. Nearly all piglets are infected by 10 to 15 days of age. The infection is widespread in swine herds in Spain. The risk factors associated with seropositivity in Danish swine herds include (a) increasing herd size, (b) certain geographical locations, (c) presence of a slurry system with slatted floors, and (d) purchase of pigs. The serological status of neighboring herds is also a risk factor; closeness of a seropositive herd has been associated with an increased risk of a herd becoming serologically positive.

PRCV replicates in the respiratory tract of pigs and to a very limited extent in the intestines.[6,7] Its pathogenicity is controversial. Some studies indicate that the virus causes only subclinical respiratory infections, whereas others have linked the virus with field outbreaks of respiratory disease. Experimentally, inoculation of the virus intratracheally into 8-week-old piglets resulted in clinical respiratory disease and bronchointerstitial pneumonia, and the virus was recovered from the respiratory tract. Some isolates of the virus produce interstitial pneumonia in neonatal piglets with no recognizable clinical respiratory disease. The administration of dexamethasone will produce severe lung lesions,[8] as will concurrent infection with porcine reproductive and respiratory syndrome virus (PRRS). In a recent study in Japan, it was shown that most pigs are seropositive for PRCV, but TGE is present on some of the farms.[9]

Methods of Transmission

The exact mode of transmission of the TGE virus is uncertain. Virus shedding in the feces of infected pigs usually ends at or within a few weeks of recovery, although recovered pigs may harbor the virus in pulmonary or intestinal tissue for periods of more than 100 days. The shedding period is thought to be 14 days. After weaning, the pig is no longer protected by specific secretory IgA antibody of the sow's milk and is highly susceptible to infection if the rate of infection is high in the weanling population. The weanling pig is a major reservoir of infection for continuous infection in the herd. Feeder pigs with no clinical signs can be an important reservoir of the virus. The virus has also been isolated from pharyngeal swabs taken from farm-raised sows sent to slaughter.

Epidemics commonly follow the introduction of pigs into a herd, and the carrier pig is a major source of infection. Frequently, the disease first appears in older pigs in the herd and then subsequently spreads to newborn pigs and sows in the farrowing area. **Spread is much more rapid in a continuous-flow system of production compared with an all-in, all-out system, whereby groups of pigs of the same age or production stage are handled as groups and their housing facilities are cleaned and disinfected before and after being occupied.** Visitors and their boots, transport vehicles, equipment, and starlings have also been incriminated in the transfer of infection to new locations. Starlings may act as vectors in spreading the disease to adjacent farms. The virus can also multiply in houseflies (*Musca domestica*), and they may be a vector. Feral pigs are not a significant reservoir for the TGE virus in the southern United States but are capable of becoming infected and developing virus-neutralizing antibodies against the virus. Subpopulations of infected pigs may exist within the herd, and although shedding normally lasts for 14 days, it is possible for animals to be infected for 100 days.

Once the infection has gained access to a herd, transmission occurs by both oral and respiratory routes. The speed of spread without direct contact indicates that the virus can be spread by aerosol. Respiratory transmission appears significant in adults, and replication in the respiratory tract is followed by excretion in nasal secretions and milk within 1 day of infection and also in feces. Excretion in milk results in rapid transmission to suckling piglets, which in turn may excrete large quantities of the virus within 2 days of infection.

Immune Mechanisms

Immunity to clinical disease in newborn piglets is dependent on the level of TGE-specific secretory IgA antibody in the colostrum of the sow and is known as **lactogenic immunity**. When pregnant sows are infected orally with the virulent TGE virus, specific IgA precursor cells are sensitized in the intestine. These sensitized cells migrate to the mammary glands and differentiate into plasma cells that secrete IgA-class TGE virus antibody in colostrum and milk. This immune mechanism to induce protective antibody for suckling pigs is termed the *gut–mammary gland link* or the *gut-associated lymphoid tissue* (GALT) system. Following natural infection with TGE during pregnancy, the recovered sow or gilt is capable of protecting her litter against the disease. After farrowing, the colostrum contains antibodies of the IgG, IgM, and IgA isotypes derived from serum. After the third day, milk is produced, and the only antibody it contains is the IgA antibody, which is synthesized in the mammary gland. The IgA antibodies of immune sows are the most critical in the protection of mucosal surfaces such as the gastrointestinal tract, and this immunoglobulin is the most abundant isotype in porcine milk. These IgA antibodies are not induced after the parenteral administration of viral antigens, which explains the relative ineffectiveness of parenteral vaccines. Serum antibody induced by vaccination of the pregnant sow does not provide protection of piglets through colostrum or milk.

Secretory IgA is the predominant antibody class in milk and is responsible for lactogenic protection of pigs and active protection of the intestine. It is stimulated by oral inoculation with nonattenuated TGE virus, but it is not associated with attenuated TGE virus. Although high concentrations of IgA and IgG originating from the serum are present in colostrum, IgG does not persist in the milk, whereas IgA does persist because of local mammary secretion. After the first week of lactation, secretory IgA constitutes 50% to 60% of the total immunoglobulin concentration in swine milk, and IgG makes up 20% to 30%.

Suckling pigs are protected from infection by continued ingestion of antibody of the IgA class secreted in milk. The level of

serum IgA antibody as an indicator of immunity to transmissible gastroenteritis can be measured using the indirect immunoperoxidase antibody test. Young pigs of 6 weeks of age that are exposed to experimental infection with the virus develop both a humoral and cellular immunity, which reach peaks at 21 and 28 days, respectively.

In recent years, less typical forms of the disease have been observed. With continuous farrowing and the continual introduction of susceptible pigs into an infective environment, outbreaks may be considerably prolonged, and prolongation or recrudescence is more likely than when pregnant sows are kept in relative isolation on pasture or elsewhere. Atypical endemic forms of the disease with a low morbidity and mortality and frequently with the onset of clinical disease delayed until piglets are 2 to 4 weeks of age have been observed and may go unrecognized because of the atypical clinical findings. They are more likely to occur in large continuous-farrowing units and may be associated with partial herd immunity and low-virulence strains. Some sows do not develop a significant immunity following a single infection, and in large herds, there may be a sufficient number of these to allow the disease to perpetuate in a low-incidence, endemic form.

A recrudescence of the disease may occur after a period of several months and is thought to result from inadequate exposure and immunity of some pigs, particularly dry stock during the initial outbreak followed by reinfection from a carrier pig. Recrudescence of clinical disease is usually of much shorter duration than the primary outbreak and commonly lasts only 6 to 10 days. The periods of recrudescence are commonly precipitated by the simultaneous farrowing of several susceptible gilts in the same farrowing room. Of greater long-term concern is that approximately 50% of some large herds continue to experience clinical recrudescences for almost 2 years or more. The endemic form of the disease appears to be correlated with herds of more than 100 sows and herds in which finishing pigs were kept. In large herds, the virus may spread more slowly, and replacement gilts entering the herd may take several months to become infected and to seroconvert. In large herds, the rapid turnover of breeding stock, continuous farrowing, and early weaning also contribute to the perpetuation of an endemic infection, and thus TGE can maintain itself through the slow and incomplete spread of the virus among adult pigs, particularly herd replacements. Joint infection with PRRS and TGE does not appear to affect the clinical effects, shedding, or persistence of either virus.

Economic Losses

A herd epidemic of TGE causes economic losses through the following routes:
- Death of pigs
- Increased downtime of the swine enterprise
- Increased labor
- Disturbance of the breeding program
- Subsequent reduced growth of young pigs destined for slaughter
- Curtailed performance of older pigs

The economic losses can be very large. Simulation of the economic losses resulting from an outbreak of disease in Australia, where the disease is exotic, estimated a reduction in net revenue of 70% in the 6 months after a moderate outbreak (50% mortality of piglets under 1 week of age) and 100% for a severe outbreak (95% mortality of piglets under 1 week of age). An analysis of the economic losses resulting from the disease in swine farms in some areas in the United States over a 2-year period estimated the average loss to be between 13% and 18% of the average return earned above total production costs. It has been assumed that the growth of surviving pigs was depressed by 10% and their feed conversion by 18%, but pigs surviving or born shortly after an epidemic of TGE are profitable to raise.

PATHOGENESIS

The S protein of the viral membrane of the TGE virus (TGEv) has four major antigenic sites and is the major inducer of neutralizing antibodies. The protein mediates the binding of the virus to the cell surface and the subsequent fusion of the viral and cellular membranes.[3] High titers of serum IgG and virus-neutralizing antibody to TGEv probably reflect the amount of S protein the pig has received. Two different ligands have been shown to interact with the S protein, and binding to the porcine aminopeptidase N, the cellular receptor for TGEv, is essential for infection of the cells. TGEv is also able to recognize sialic acid residues and attach to sialylated macromolecules. A second binding site on the N-terminal division of the S protein allows TGEv to interact with terminal sialic acid residues on glycoproteins or glycolipids and to agglutinate red blood cells (RBCs). TGEv also recognizes a porcine intestinal brush-border protein called mucin-type glycoprotein (MEP), and TGEv binds to this mucin produced by goblet cells. A mutant virus that has lost its sialic acid binding capability is not pathogenic because it is unable to attach to goblet cells. Sialic acid binding activity is a pathogenicity factor for TGEv, and it is important to note that the sialic acid binding sites for TGEv and *Escherichia coli* are different.

The virus infects the upper respiratory tract and the intestines, but the major clinical effects result from intestinal infection. Following oral challenge of susceptible piglets, the incubation period may be as short as 24 hours. After 12 to 24 hours, there is massive necrosis, and no enzyme activity in the epithelium remains. The virus infects mature differentiated columnar epithelial cells of the intestinal villi but not the undifferentiated cells of the crypts. Replication occurs within 4 to 5 hours, with sloughing of the infected cells and release of the virus, and after several replication cycles, there is a marked reduction in villous size with villous atrophy. The loss of epithelial cells results in increased migration of undifferentiated cells from the crypts to line the shortened villi. With virulent virus, epithelial cells at all levels of the small intestine are infected, with major lesions occurring at the proximal jejunum and, to a lesser extent, at the ileum. In most cases, the duodenum is not affected. The lesser virulence of attenuated strains of the virus may be associated with their inability to infect and produce lesions in the villi of the more cranial portions of the jejunum. Gnotobiotic pigs inoculated orally with a TGE vaccine will develop lesions similar to those in the naturally occurring disease.

Diarrhea results from a combination of malabsorption, the osmotic effects subsequent to the loss of intestinal surface area and disaccharidase activity, and impaired lumen-to-extracellular fluid flux of sodium caused by the occurrence of undifferentiated cells lining the stunted villi. The virus invades the villus, but not the crypt epithelium of the small intestine, within hours after experimental administration. The infected villus cells are quickly shed and replaced by relatively undifferentiated enterocytes. As infected cells are shed, the epithelium proliferates, and migration of cells from the crypts accelerates. There are marked abnormalities in ion transport function in the jejunum and ileum at the peak of the diarrhea. There is a failure of the intestine to actively transport sodium and chloride, and there is a defect of glucose-mediated sodium ion transport. Macromolecular hyperpermeability of the small intestine also occurs, but its significance is uncertain. Experimentally induced infection of 3-week-old pigs results in villous atrophy, crypt hyperplasia, and a marked decrease in the secretory response of the villous epithelium to *E. coli* enterotoxins. The disease is more severe in gnotobiotic pigs that are infected with *E. coli* in addition to the TGE virus, suggesting that bacterial factors also influence the severity of the diarrhea.

In the experimental disease in 2-day-old pigs, vomiting and diarrhea occur 12 to 24 hours after oral inoculation of the virus, and affected piglets are moribund 1 or 2 days later. Before becoming moribund, most piglets become lethargic and comatose. In addition to dehydration and metabolic acidosis, there is a severe hypoglycemia resulting from a combination of inadequate glucose metabolism inherent to neonatal piglets and the acute maldigestion and malabsorption from the diffuse and severe villous atrophy. The high death rate is attributable to a combination of dehydration, acidosis, and severe hypoglycemia.

The age-dependent resistance to TGE can be explained in part by a decreased susceptibility of the epithelial cells of older pigs to infection and by an increased proliferative capacity of crypt cells with much more rapid

regeneration of atrophic villi in pigs over 2 weeks of age. It may be that the virus has developed strategies to evade apoptosis in intestinal enterocytes by producing huge amounts of the virus.

A recent experiment comparing a Korean strain with two U.S. strains showed that the progression of the Korean virus was much slower (i.e., much less virulent), possibly because there was only replication in the ileum and jejunum, whereas the U.S. strains also replicated in the duodenum. The more virulent strains attack a wider area of enterocytes. Most only attack the villous rather than the crypt enterocytes. An outbreak of reduced-virulence TGEv was associated with the presence on the farm of three strains of PRCV that had variable-sequence changes in ORF 3, 3a, and 3b.

CLINICAL FINDINGS

In a primary or epidemic outbreak, the clinical findings of typical acute TGE are characteristic. The appearance of the disease is not significantly altered by a concurrent infection with PRRS. Sows may become ill when lactating and may develop anorexia and agalactia, further contributing to piglet mortality.

Piglets

After an incubation period of 18 to 72 hours, there is a sudden onset of vomiting and diarrhea. The diarrhea is profuse and frequent; the feces are watery and usually yellow-green in color. The feces may contain clots of white undigested milk and have an offensive odor. The vomitus is yellow, foamy, and slimy. There may be a transitory fever, but in most cases the temperature is normal. Depression and dehydration are pronounced, the hair coat is ruffled, and weakness and emaciation progress to death on days 2 to 5. Some piglets may continue to suck to within a few hours of death; those that survive are severely emaciated and gain weight slowly. The illness may commence as soon as 24 hours after birth. It is not uncommon on an individual farm for the disease to become less severe (endemic), and in these cases, it resembles rotavirus infection and spreads more slowly with the passage of time.

Older Pigs

In older pigs, there may be signs similar to those that occur in piglets, but many animals become infected without clinical abnormalities. Diarrhea may occur first in the dry sows. In older pigs, recovery is much more likely to occur, with the illness lasting for up to 10 days. Lactating sows may or may not be affected clinically. Fever and inappetence occur, with or without diarrhea, and agalactia is a common complication in sows. In endemically affected herds with continuous farrowing and partial sow immunity, the disease is milder, with diarrhea affecting piglets approximately 6 days of age or older and diarrhea in weaned pigs. Brief periods of clinical disease occur in some parts of the herd, mortality is low, and affected pigs subsequently grow poorly.

CLINICAL PATHOLOGY
Serum Biochemistry

Severe dehydration with metabolic acidosis and marked hypoglycemia is common.

Detection of the Virus

TGE virus can be grown in pig kidney (PK) cells and PRCV in PK cells and swine testicle cells.

The virus can be detected in the mucosal scrapings and feces using an enzyme-linked immunosorbent assay (ELISA), immune electron microscopy, fluorescent antibody staining, or the immunoperoxidase test. A capture-enzyme immunoassay has also been developed. A reversed passive hemagglutination test for detection of the virus in feces is also available. A solid-phase immune electron microscopic technique for detection of the virus in feces is also useful for diagnosis in living animals. PRCV can be isolated by tissue culture.

DNA Probe

DNA probes can differentiate PRCV from TGEv. Polymerase chain reactions (PCRs) were described quite early on for identifying TGE. The real-time PCR (RT-PCR), a rapid RT-TaqMan, has been shown to be a very good sensitive test for TGEv in pig fecal samples.[10] Tests are now available to differentiate PRCV from TGEv.

In situ hybridization (ISH) has been described, and a nested RT-PCR has been developed that is very sensitive. A multiplex RT-PCR for differentiating the PED virus (PEDv) from TGEv in clinical samples has been described. It has also proved possible to use formalin-fixed tissue for multiplex PCR, nested-PCR, and ISH with 100% conformity.

A multiplex RT-PCR has been developed for the simultaneous detection of both TGEv and PEDv.[11] A multiplex microassay can be used for the rapid differential diagnosis of eight viruses, including TGEv.[12]

Serology

Several serological tests can detect and measure antibody to the virus in live animals. The serum neutralization test is sensitive and reliable, but it is time-consuming and requires facilities for cell culture techniques. Neutralizing antibodies appear in the serum 7 to 8 days after infection and persist for at least 18 months. An ELISA is more sensitive than the virus neutralization test, and a competitive ELISA differentiates between TGEv and PRCV. A blocking ELISA to differentiate TGEv and PRCV has also been described.[13,14]

NECROPSY FINDINGS

The lesions are confined to the intestine and stomach, although he changes may be minor in many field outbreaks and in the experimental disease. The intestinal wall is thin and translucent, and the intestine is distended with fluid ingesta. Despite the presence of milk in the intestine, there is little evidence of fat absorption in the draining lymphatics. The important histopathological change is atrophy of villi with failure of epithelial cell differentiation in the small intestine. The atrophy is evident 24 hours after infection, and regeneration occurs 5 to 7 days later. The marked reduction in the size of intestinal villi may even be detected at low magnification with a stereomicroscope. In the stomach, there may be engorgement of vessels and necrosis of the epithelium deep in mucosal crypts. No inclusion bodies are detectable. When secondary pathogens contribute to the disease, there may be inflammatory lesions in the intestines. In chronic cases, a thickening of the intestinal wall identical to that seen in terminal (regional) ileitis has been described.

In Europe, the disease is characterized by more severe mucosal lesions, often including fibrin exudation. There is also degeneration of the heart muscle and, in some cases, of the skeletal muscle.

A simple test for the presence of intestinal lactase in intestinal washings may assist in the laboratory diagnosis. Examination of frozen sections of jejunum from acutely ill piglets by the fluorescent antibody technique is a rapid and effective method for the detection of virus in tissues. The intestine may be segmentally affected, so multiple areas must be sampled. Viral antigen is detectable for only 24 to 36 hours when utilizing most fluorescent antibody (FA) conjugates. This makes the selection of acute cases critical. Electron microscopy is often utilized to identify the presence of coronavirus, but this method is not specific for TGEv. PCR methods for TGEv detection are being developed, and immunohistochemical techniques are available for use in formalin-fixed tissues.

The use of apoptotic markers shows that most of the cells are undergoing apoptosis but are not infected with TGEv; they are termed *bystander cells*. It has been previously suggested that apoptosis does not occur in the enterocytes of piglets infected with TGEv. An accumulation of interferon-alpha-producing cells occurs in the GALT of TGEv-infected piglets. It has been suggested that these are the mucosal counterparts of the dendritic cells recently shown to produce interferon (IFN) alpha after in vitro viral induction. The TGEv challenge of pigs produces an increase in CD4+/CD8+ cells, an increase in natural killer cells and cytotoxic T cells, an increase in the expression of IL-2 receptors, and a decrease in null cell phenotypes.

Samples for Confirmation of Diagnosis
- **Histology**—several segments of jejunum and ileum, stomach (LM, IHC)
- **Virology**—several segments of jejunum and ileum (FAT), feces (EM)

The epidemiological and clinical characteristics of transmissible gastroenteritis (TGE) should make possible a presumptive diagnosis, but confirmation must depend on the finding of compatible histological lesions, the detection of antigen, transmission experiments, and evidence of seroconversion. It is unusual to encounter outbreaks of diarrhea in piglets that appear to be typical of TGE where there is porcine respiratory coronavirus (PRCV) on the same farm. Either the virus can be demonstrated in the tissues by fluorescent antibody test (FAT), but serum antibodies cannot be detected in the breeding animals; or serum antibodies can be detected in the adults, but the virus cannot be demonstrated in the tissues by either immunofluorescence or tissue culture.

Villous atrophy is not pathognomonic for the disease because it occurs in 3-week-old piglets affected with diarrhea and steatorrhea, in rotavirus infections of piglets, in coccidiosis, and in some herds for undetermined causes immediately following weaning. In some instances, diagnosis in suckling or recently weaned pigs is difficult.

In piglets, TGE must be differentiated from the following:

- **Enteric colibacillosis** A common disease of piglets under 10 days of age with profuse diarrhea, no vomiting, dehydration, and a good response to therapy if treated early.
- *Clostridium perfringens* **type C** Enterotoxemia occurs in piglets under a few days of age and causes marked depression, diarrhea, dysentery, reddening of the anus, and rapid death. Lesions at necropsy are characteristic.
- *Clostridium perfringens* **type A**
- *Clostridium difficile*
- **Coccidiosis** Affects newborn piglets 5 to 15 days of age, causing profuse diarrhea, depression, dehydration, and unthriftiness. Affected piglets may continue to suck. There is high morbidity, low mortality, and oocysts in the feces.
- **Rotavirus enteritis** Rotavirus causes diarrhea in suckling and weaned piglets, with a high morbidity and low mortality. Most affected piglets recover in a few days, and epidemics are commonly associated with continuous farrowing.
- **Porcine epidemic diarrhea** A coronavirus-like virus causes diarrhea in pigs similar to that in TGE, except much less severe and with reduced mortality. **Porcine epidemic diarrhea type I** causes diarrhea only in pigs up to 4 to 5 weeks; whereas porcine epidemic diarrhea type II causes diarrhea in pigs of all ages. The morbidity may reach 100%, but mortality is low. The disease may start in the finishing pigs and spread rapidly to pregnant sows and their nursing piglets. The diarrhea may persist in the 6- to 10-week-old pigs, and seronegative gilts introduced into the herd may become infected and develop profuse diarrhea

lasting a few days. The recent strains appearing in Korea, Vietnam, China, and now the United States are much more similar to TGE.
- **Vomiting and wasting disease** Affects piglets under 10 days of age in epidemics similar to TGE. However, vomiting is characteristic, diarrhea is not a feature, and laboratory differentiation is necessary.

In adults (gilts, sows, and boars), TGE must be differentiated from diarrhea resulting from the following diseases:
- Swine dysentery
- Salmonellosis
- Porcine proliferative enteritis

TREATMENT

There is no specific treatment, but good husbandry in the form of warm, dry, draught-free conditions with ad lib water and nutrient provision helps. Treatment aims at alleviating starvation, dehydration, and metabolic acidosis, which result in hypoglycemia. Treatment with fluids and electrolytes containing glucose is indicated. Because there is loss of intestinal villi and the enzyme lactase, the ideal treatment would be to reduce the intake of milk for up to 5 days and administer a glucose–glycine–electrolyte solution orally every few hours to maintain hydration. However, removal of affected piglets from the sow is impractical and not recommended. Oral fluid therapy should improve the survival rate, with affected piglets recovering in a few days following treatment. In experimentally induced TGE, removal of the milk diet and the use of an oral glucose–glycine–electrolyte solution plus a 5% dextrose solution given intraperitoneally at the rate of 25 mL/kg body weight (BW) once daily decreased the severity of the diarrhea, dehydration, and metabolic acidosis but did not prevent or significantly improve the renal failure and severe hypoglycemia. A newborn piglet weighing 1.25 kg has an energy expenditure of approximately 170 kcal/d (711 kJ) if maintained at 30°C (86°F); 30 mL of a 5% dextrose solution supplies 1.5 g of glucose for a total of approximately 5.6 kcal/d (the gross energy of glucose is 3.74 kcal/g). Because the volume of 5% dextrose solution injected daily into piglets should not exceed 8% of their body weight, it is unlikely that the hypoglycemia can be prevented or treated.

The use of natural human interferon given orally to piglets 1 to 12 days of age affected with the disease increased survival rates compared with placebo-treated piglets.

CONTROL

Endemic infection will persist as long as susceptible or partially immune sows are exposed to the virus.

Control of the disease is complex because it is so highly contagious and because of the dynamics of infection between the different age groups of animals within large swine herds. Although there is considerable

information available about the biology of the virus and the nature of the disease, there is little documented reliable information about the control in a swine-breeding herd. Most of the recommendations for control are empirical and based on clinical experience without any controlled field trials to evaluate the different strategies. The following guidelines for the control of TGE are based on the characteristics of the virus and the disease:

- The disease is highly contagious and spreads rapidly between groups of pigs in a herd. Most epidemics last 6 weeks.
- Newborn piglets are highly susceptible to disease if the sow's milk does not contain specific TGE secretory IgA antibody.
- Infection of pregnant sows with the virulent virus results in protective immunity for their piglets. Recovered sows are immune, usually do not harbor or shed the virus, and need not necessarily be culled.
- Weaned pigs are a major reservoir of infection in farrow-finish herds.
- Vaccination of pregnant sows with any of the available vaccines is not as effective as natural infection in providing protection for piglets.
- The disease is controlled either by elimination of the virus from the herd or by controlled natural immunization and use of the all-in, all-out system of production.

Control During and After an Outbreak

The highly contagious nature of the disease makes the immediate control of an outbreak in a herd virtually impossible. Epidemics usually last approximately 6 weeks, during which time many piglets die, and the herd eventually becomes immune. Successful control depends on planning and implementation of certain strategies, which must be understood and implemented by the producer and monitored by the veterinarian. Failure of the producer to fully understand or accept the diagnosis and apply the principles of control will result in failure to control the disease and the persistence of an endemic form of the disease in the herd. Several strategies are used to control the infection pressure and to enhance immunity where possible.

Isolation of Sows Due to Farrow

To avoid further new infections of newborn piglets, sows due to farrow within 2 to 3 weeks should be isolated under strict hygienic conditions. However, this is usually impractical in most intensive swine production enterprises, where isolation facilities are usually not available. The disease is so highly contagious that isolation is ineffective. There should be no movement of pigs between the farrowing or nursery rooms. An all-in, all-out system for movement of pigs,

especially in the farrowing rooms and nurseries, with complete cleaning and disinfection between groups should be established (see later discussion of all-in, all-out practices).

Discontinuation of Breeding Stock Sales and Purchases

Once a diagnosis of TGE has been confirmed in a breeding herd that sells breeding stock, all sales should be discontinued. Likewise, all purchases of breeding stock from other herds should be discontinued for a few months until the epidemic has subsided and the future production plans of the herd, including disease control, are reviewed.

Partial Depopulation and Culling

If possible and feasible, all weaned pigs ready for finishing units should be moved off the farm to contract finishing units. This allows for a general cleanup of facilities, a break in the production cycle, and an intensive all-in, all-out system. All culled pigs should be destroyed to prevent a reservoir of pigs actively shedding the virus.

Planned Exposure to Virulent Virus

To minimize the duration and severity of the outbreak, all pregnant sows due to farrow more than 3 to 4 weeks ahead should be given an inoculum of virulent TGEv obtained from virus-infected intestines, ideally from piglets in which the disease began within the last 12 to 24 hours. The piglets should be submitted for necropsy and TGE confirmed by a diagnostic laboratory. It cannot be assumed that all piglets that die in an epidemic of TGE will be infected with the virus. The intestines of the confirmed cases should be homogenized in special media and centrifuged, and supernatants should be poured into capsules and frozen for storage. The contents of the capsules are then thawed and poured onto the feed of the sows. The inoculum is given daily for 3 days. Preparation and use of the inoculum will ensure adequate uniform inoculation of sows, compared with earlier recommendations to feed feces and intestines of piglets that died of the disease to the other pigs. More inoculum can be prepared by inoculating weaned piglets in isolation and collecting their small intestines 1 to 2 hours after onset of diarrhea, which is usually 16 to 21 hours after inoculation. The boars are also fed the inoculum. An alternative to the inoculum is to mix the intestines from two affected piglets in 25 L of water and feed 50 mL of the solution daily for 3 days.

If there is sufficient time for immunity to develop, the piglets born 3 to 4 weeks later will be protected through the colostrum and milk, which will contain the TGEv-specific IgA antibodies. Piglets sucking such sows are resistant to infection while sucking, but they become fully susceptible if transferred to a nonimmune sow. Natural infection by mouth produces a high level of secretory antibody, particularly IgA, in the colostrum and milk,

whereas vaccination produces a good IgG response but a much lower IgA response. The newer recombinant vaccines have also been shown to be immunogenic but are still not able to produce lactogenic immunity.

An alternative to the feeding of infectious material to pregnant gilts and sows is vaccination using the available vaccines. The gilts, sows, replacement stock, boars, and newborn piglets are vaccinated according to the indications of the vaccines used. However, the efficacy of the vaccines is questionable. Over the last two decades, the aim has been to produce TGEv protein subunit vaccines. The most novel approach has been to feed recombinant immunoproteins (capable of neutralizing TGEv in vitro) to confer protective immunity.[15]

Biosecurity and Acquisition of Replacement Breeding Stock

Following recovery from an epidemic in a herd, replacement breeding stock should be introduced as a group at one time and exposed to animals in the herd, monitored for clinical disease, and tested. Serological testing using paired sera at 30 and 60 days after entry will indicate seroconversion to the virus. The usual precautions to prevent transmission of infection between units of the herd and between herds are necessary, including the following:

- Washing of boots
- Sanitation of trucks
- Use of separate clothing for each unit of large herds
- Showering of personnel moving between units

Washing hands and changing into clean outerwear or showering and changing into clean outerwear after being in contact with TGEv-infected pigs was found to be sufficient to prevent mechanical transmission of TGEv to susceptible pigs.

All-in, All-out Management System

The all-in, all-out management and production system is based on the principle of handling, feeding, and housing pigs in small subgroups as they move through the various stages of production. These subgroups either remain free of certain infectious agents, if absent, or all animals in the group become infected and immune to the infectious agents that are present in some pigs and transmitted to others in the subgroup but not to other subgroups. With this system, breeding gilts and sows are handled and bred as subgroups, kept in the gestation units as subgroups, farrowed as subgroups, and nurse their pigs as subgroups. The pigs are weaned as subgroups at the same time, the weaned pigs are placed in the nursery facilities as a subgroup at the same time, and all of the pigs are moved out of the nursery to the finishing facilities at the same time. The pigs are handled in finishing units as subgroups, and all pigs are marketed as a subgroup. At each stage of production,

the housing facilities should be cleaned and disinfected following removal of the pigs and left vacant for a few days before a new subgroup of pigs is introduced into the previously cleaned rooms. This system avoids the mixing of pigs back and forth between groups and ages, which is often done to maintain uniformity of size and age of pigs. During an epidemic, the use of a strict all-in, all-out system in the farrowing and nursery units will aid in the control of clinical disease. Approximately 2 months after the epidemic and the absence of clinical disease, sentinel seronegative pigs of 2 to 4 months of age can be introduced to each part of the herd and monitored serologically for evidence of viral activity.

Complete Depopulation and Repopulation or Establishment of New Herd

In some situations where the disease cannot be controlled, complete depopulation of the herd is the best option. This should be followed by repopulation with breeding stock derived from specific pathogen-free herds or minimal disease-free herds that are known to be free of the virus. Serological testing can be used to test the animals before they are moved into the facilities. The establishment of new swine herds now commonly depends on the acquisition of breeding stock from disease-free herds.

TGEv Vaccines and Vaccination

In many instances, TGEv vaccines do not provide reliable, complete protection for suckling pigs against a challenge exposure. However, priming piglets with PRCV was shown to be very beneficial in providing resistance to TGEv and also resulted in a much better maternal antibody response.

Vaccination of Pregnant Sows

Because of the effectiveness of acquired immunity following natural infection, vaccination of the pregnant sow would appear to be the method of choice for control of the disease. However, the available vaccines have not been efficacious enough to be a reliable control strategy. Circulating virus-neutralizing (VN) antibodies, acquired actively or passively, provide insufficient protection against clinical disease, and parenteral vaccines have been relatively ineffective. Protection against the disease requires the presence of secretory IgA antibody, either actively or passively acquired, in the intestine (see "Immune Mechanisms").

TGE Vaccines

Several live-attenuated and inactivated virus vaccines are available for use in pregnant sows and neonatal pigs. Vaccines for oral and intranasal administration were developed on the basis that vaccination by the oral or intranasal route would induce the production of secretory IgA antibody. However, these vaccines have not been efficacious.

The vaccination of pregnant sows with attenuated strains of TGEv by either the parenteral or oral route does not provide sufficient lactogenic immunity to protect their piglets against virulent strains of TGEv. Some litters sucking vaccinated sows may achieve partial protection in which the onset of diarrhea is delayed, the diarrhea is less severe, and the case-fatality rate is decreased. Villous atrophy is inhibited to varying degrees in pigs sucking immunized sows, depending in part on the antibody titer in the colostrum and milk.

The severity of the losses in a vaccinated herd after exposure to the virus will vary, depending on the following factors:

- Herd management
- Environmental conditions
- History of previous exposure
- Severity of viral exposure

After natural infection or experimental oral infection of pregnant sows with a virulent strain of TGEv, lactogenic immunity is highly protective for piglets, and neutralizing antibodies in milk are mainly associated with the IgA fraction. Vaccination of sows orally with a nonattenuated vaccine provides greater levels of lactogenic protection than does orally or parenterally administered attenuated-virus vaccine. In vaccinated sows, the levels of colostral antibody correlate with the percentage of survivability of their piglets when challenge-exposed at 3 to 5 days, whereas the serum antibody to TGEv does not. There is also a significant relationship between milk antibody and percentage survivability when pigs are challenge-exposed at 5 days of age but not at 3 days of age. There is a need to develop an attenuated virus strain that is completely avirulent for pigs but that also replicates sufficiently in the small intestine of sows after oral administration and induces secretory IgA antibody. It appears that no strains of the virus have been identified that are sufficiently attenuated and safe for pigs while still being able to provide a sufficient immune stimulus in the intestine of the sow. The Nouzilly strain, which is a mutant type of TGEv resistant to acidity and the proteases of the digestive tracts of adult pigs, is being evaluated as a vaccine.

Vaccine Schedule

If vaccines are used, it is generally recommended that the two vaccinations, 14 days apart, be given during the last trimester of pregnancy. Vaccines are available for vaccination of neonatal piglets, weaner pigs, and finishing pigs, but there is insufficient published information available on the efficacy of the vaccines based on randomized clinical trials using controls under field conditions.

Subunit TGEv Vaccine

Experimentally, a recombinant TGE virus S glycoprotein subunit vaccine given subcutaneously or intramammarily to pregnant sows induced colostral and milk IgG, but not IgA, antibodies to the virus. Piglets born from vaccinated sows were challenged at 4 to 5days of age with the virulent virus, and the morbidity was 100%, with mortality ranging from 20% to 80%. The same vaccine given subcutaneously to 11-day-old piglets induced VN antibodies. This is consistent with the well-known observation that secretory IgA antibody in the milk is necessary for protection in piglets. Compared to VN antibodies, antibodies of the secretory IgA class are more effective at neutralizing TGEv because they are at higher titers in milk, are more resistant to proteolytic enzymes, and bind to gastrointestinal enterocytes. Protective immunity to transmissible gastroenteritis correlates with milk whey secretory IgA antibody titer to the TGE virus when pigs are challenge-exposed with the virulent virus at 3 to 5 days of age.

Immunity to PRCV

There is considerable cross-protection between TGEv and PRCV. There is indirect evidence that a bronchial-associated lymphoid tissue (BALT)–mammary gland link similar to the gut-associated lymphoid tissue (GALT)–mammary gland link described for TGEv may exist in pregnant, multiple-PRCV-exposed sows. In herds infected with PRCV, multiple exposures of pregnant sows are associated with higher IgA and IgG antibody titers to TGEv in milk, and these titers contribute to protection against TGEv. The immunization of pregnant gilts with PRCV induces lactogenic immunity and partial protection of piglets from challenge with TGEv. An overall survival rate of 70% was found for piglets nursing PRCV-infected gilts compared with a 16% survival rate for piglets nursing control gilts. The highest degree of protection occurs in sows primed with PRCV, then given a booster vaccination with TGEv 2 weeks later. Infection of pigs with PRCV primes the systemic and mucosal humoral immune system against TGEv, and subsequent challenge with TGEv results in a secondary antibody response and decreased duration of excretion of the virus. Protective immunity to TGEv infection can also be induced in piglets exposed to PRCV at 2 to 6 days of age.

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PORCINE EPIDEMIC DIARRHEA

PED was first described in Britain in 1977, although it probably first appeared in 1971, and spread globally and rarely occurred after the 1970s and 1980s. It is a highly contagious disease in pigs of all ages but particularly young pigs. It was thought to be similar but not as severe as TGE. Before 2012 in Asia and 2013 in the United States and then Canada, the disease was sporadic in Asia and Europe. It was not found in the Western Hemisphere before May 2013.

Recently in a new wave of severe infections it was mostly associated with Asia, particularly China,[1,2] Vietnam,[3] Thailand,[4] and Korea (originally but has recently reappeared in Europe[5]).

It was detected for the first time in U.S. swine in May 2013[6] and by November 9, 2013, 1069 PED virus (PEDV) cases had been found in over 19 states (www.aasv.org/pedv).

The 2013 outbreak in the United States of this Chinese strain is particularly severe because within 3 to 4 months of the start of the outbreak there may have been 250,000 to 300,000 deaths in Oklahoma, Indiana, and Iowa. The total number of deaths between April 2013 and June 2014 may have been 7 million.

ETIOLOGY

There are several porcine coronaviruses: TGE was described in 1946, HEV in 1962, PEDV in 1977, PRDC in 1984, and the newly discovered Deltacoronavirus described in Hong Kong in 2012. They are the largest RNA viruses. All of the coronaviruses are very closely related. They are subject to deletions and insertions of their genetic material, and two of these may have occurred in the new PEDV in the United States.

PEDV is a positive-sense RNA virus of the family Coronaviridae and subfamily Coronavirinae and the genus *Alphacoronavirus*, which contains PEDV, TGE, and PRCV.

It is a coronavirus with three major nonstructural protein antigens. The virus genome is similar to that of TGE and is composed of seven ORFs that encode four structural proteins. It can be cultured in Vero cells. Chinese and Korean isolates form clusters distinct from European isolates.[7-10] Recent Chinese strains[2] differ from Korean isolates. It has also been found in India and reemerged in Thailand,[5] where it is now endemic. It caused massive losses in Vietnam in 2009. Recent Korean strains differ from European and vaccine strains.

The complete genome sequence of the virus been described from a pig infected with the PEDV strain USA/Colorado/2013.[11] It has 96.5% to 99.5% homology with other PEDV in the gene bank and 99.5% homology with a recent Chinese strain. Thus far, the initial cases in Colorado, Oklahoma, and

Kansas have similar S gene sequences (99.8–100%).

The genetic properties of endemic Chinese strains of PEDV have been described.[12] The study showed that 10 post-2010 isolates shared high homology with each other and were clustered together with the virulent DR13 strains from South Korea and one earlier Chinese strain.

This virus has been observed in various parts of China since December 2010. Ten post-2010 isolates showed homology with one another.[12] They were all clustered close to the Korean strain and to an earlier strain from China. It is suggested that the current strains are derived by similar genetic changes from the Korean strains or earlier Chinese strains.

Viruses recently isolated in Iowa (five cases) have a different gene sequence from those investigated from April 2013 showing greater similarity to strains isolated from China between 2004 to 2012. The first isolate has been described.[11] They show only 93.9 to 94.6% nucleotide identities to those previously found since April 2013 but are 99.5% to 100% similar to each other.

The virus causes a distinct cytopathic effect with characteristic cell fusion, syncytia formation, and eventual cell death. The U.S. isolates are closely related to one another and are 96.3% to 99.5% related at the nucleotide level to the 23 non-U.S. PEDV strains, and are closest to the Chinese 2011 to 2012 strains.[16]

Recent studies suggest that there are two distinctly different groups of PEDV circulating in the United States. The first group has a 99.1% to 100% identity with the initial Chinese strains. The second group has a 99.6% to 100% identity with each other but only 93.4% to 94.4% nucleotide identity with the original U.S. strain, showing that mutation has already started to occur.

A new virus, porcine Deltacoronavirus, closely related to avian coronaviruses, was discovered in Hong Kong in 2012.[19] It causes severe diarrhea and vomiting in mature pigs but is not so severe in suckling pigs. Recovery seems to follow. It is not cross-protective. It was found in the United States in August 2013.[20,21]

EPIDEMIOLOGY

The severity and outcome of the disease depend on age, challenge dose, immunity, and other on-farm conditions. Under experimental conditions 4-week-old pigs inoculated with PEDV did not gain much weight for 7 to 10 days after challenge.

The virus is usually introduced by carrier pigs, which is usually new stock coming onto the farm. Pig movements through sale or purchase of pigs are an important source of infection. It is easily spread in markets. Contaminated transport trucks, boots, and other fomites are also a possibility for spread. There is no semen transmission.

The recommendation to use feedback in Asia has probably contributed to it becoming endemic in Asia.

In studies in the United States, in the recent outbreak, larger herds are more likely to be affected, positive sites had more feed truck deliveries, half the frequency of the visits of company service persons were found on the positive sites, and trucks removing pigs (×2) and trucks removing trash were also associated with positivity (×5). Staff or family workers working off the site were also associated with positivity.

Recent studies of the partial S gene have shown that the Thai and Vietnamese strains originated from the original Chinese strain JS-2004-2.

Transmission is by the fecal–oral route, and shedding of the virus begins at the time of the development of the diarrhea. There is a high concentration of the virus in feces and the virus is very stable, so fomites, equipment, and people are easily contaminated. Truck transport of infected feces is a considerable risk.

The virus excretion may be 10,000 to 1,000,000 times more in PEDV compared with a TGE case, and the virus is much more infectious.

The recent epidemic in the United States began in Colorado and Ohio in April 2013 and has rapidly spread to at least 16 states by July 2013, with possibly over 400 cases. The virus is 99.4% similar to the 2012 Chinese virus when sequenced. It has been difficult to find out the origin because it seemed to occur separately in several sites.

A recent study of the original Chinese virus has already suggested that new variants are appearing.

The fecal and nasal shedding was first observed 24 hours postinfection. Some studies have suggested that the greatest virus shedding is greatest at 12 to 18 hours of the onset of diarrhea. Peak fecal shedding occurs 5 to 6 DPI and was much greater than nasal shedding. Some pigs still shed 21 and 28 DPI and even 35 DPI without clinical signs.[17] Pigs remain PCR positive for up to 6 weeks. Only tissues from the gastrointestinal tract appear to be positive. No aerosol transmission was detected but virus was found in the walls, pens, and food bins. The virus is highly infectious and is highly stable in the environment (>28 days in fecal slurry at −20°C, >28 days in wet feed mixture, <2 weeks in dry feed at room temperature, >14 days and <28 days in fecal slurry at room temperature, and 28 days at 40°C in fecal slurry at room temperature). There was no effect of relative humidity on virus survival.

During acute infections in a boar stud the virus has been detected in feces, blood, and semen.[18] There is also evidence for area spread of the virus and it may travel through the area on dust particles and not as a true aerosol. Virus has been detected by PCR in

air samples collected up to 10 miles from an infected farm.

In the United States, there has been considerable discussion of how it spreads: air, people, feeds, or fomites. At the moment it seems most likely that it reached the United States either in feeds or in processed plasma. The PCRs are not designed to find the virus in feeds, but spiked feeds have been shown to be capable of infecting pigs in experimental studies. Samples from feed bins have proved positive for live virus. Live virus has also been found in air samples and in bird feces.

Recent studies have suggested that plasma proteins, particularly those that are imported, are a possible means of infection. A statement by the Canadian Food Inspection Agency on February 18, 2014, stated that testing with a swine bioassay has determined that the plasma ingredients contain PEDV capable of causing disease in pigs. The epidemiology clearly links the live PEDV-contaminated plasma shipment to the 18 infected herds in Ontario. These infected imports originated in the United States. As of March 5, 2014, there were 25 pig sites in Ontario with PED. At this date only 6% of the 1063 trailers tested for PED had turned up positive. An assembly yard also tested positive. The Ontario authorities suggested that the virus would not be as easily transmitted in the warmer months as it is in March. The Canadian authorities said that plasma products, spray dried plasma, and feed were PCR positive.

OCCURRENCE

In April 2013 in west central Iowa piglets were described with fetid, watery diarrhea and mortality in 90% of the pigs. It then spread rapidly to sites in northwest and northeast Iowa and then Indiana with a piglet mortality greater than 90%. There was no connection between the production systems, there were no known relationships and no common trucking or feed service. In May, confirmation occurred through EM of the presence of a coronavirus. The virus was then confirmed as being similar to the Chinese 2012 PEDV strain, and PCR and sequencing at the National Veterinary Services Laboratories in the United States confirmed this. On June 13, 2013, it had reached 12 states; by September[15] five more states; by December[15] another nine states; and by July 5, 2014, 29 states had reported infected pigs.

After occurring widely in the United States it has now spread to Canada. In March 2014 there were 25 cases in Ontario and one each in Quebec, Prince Edward Island, and Manitoba.

PATHOGENESIS

The virus appears to need trypsin for its replication to open up the Spike protein, which is why it is particularly attached to the intestinal enterocytes, which are a source of trypsin.

The virus resembles TGE in its behavior but does not replicate in the respiratory tract.

The major structural gene of the 28-kb PEDV genome encodes the multifunctional virulence factor, Spike (S), which is responsible for viral receptor binding, induction of neutralizing antibody and host cell fusion. These S gene sequences are a distinguishing feature of the PEDV strains, which affect virulence and evolution. The new strain began life in China in 2010.

The virus localizes in the porcine intestinal epithelial cells via receptors particularly on the sides and tips of the villi. Porcine amino-peptidase N is a functional receptor for the PEDV coronavirus. The PEDV N protein then localizes in the ER of the cell and inhibits intestinal epithelial cell growth and prolongs the S-phase of the cell cycle. It then causes the expression of IL-8, which further induces ER stress. The N protein also binds to the virion RNA and provides a structural basis for the helical nucleocapsid giving stability to the virus. The level of production of the digestive enzymes is rapidly reduced and malnutrition results in starvation very quickly followed by dehydration. In partially immune pigs only a small portion of the intestine is affected.

IMMUNITY

PEDV antibodies have been reported to persist for at least 1 year. Colostral protection may last for up to 2 weeks in the piglet (specific IgG antibodies). Lactogenic immunity is said to be poor. The length of protection depends on the titer in the dam. Colostral IgA is a better method of assessing protection than serum levels. It is more resistant to enzyme degradation in the gut and therefore better at neutralizing gut infections. It also has greater activity than IgM and IgG. One of the characteristics of the recent Chinese strains is that there is poor herd immunity, with recurrent outbreaks every 6 months.

CLINICAL SIGNS

In the 1970s, when it first occurred in Europe, there were two types described. Epidemic virus diarrhea type 1 occurred in mature pigs and not suckling pigs and was similar to a mild form of TGE. The more severe type, which occurred in suckling pigs and was associated with a much higher mortality, was called epidemic virus diarrhea type 2.

It is exactly the same as a severe TGE outbreak because it spreads very rapidly to affect all nursery pigs. Sows may have anorexia and diarrhea but the picture is more variable in adults. Now with the new strains preweaning mortality will be 100% over a 3.5- to 5-week period. In the nursery, there will be diarrhea with a slight increase in mortality and a reduction of growth rate.

It affects pigs of all ages with an incubation period of 1 to 3 days. Most sows are ill within 12 to 36 hours with diarrhea and sometimes with vomiting. Affected pigs are unwell, dull, and unwilling to rise, but pyrexia is rare. The piglets then produce an extremely watery diarrhea, may vomit, and are inappetent. In the old style PED the morbidity was often 100% but the mortality was low, which distinguished the condition from TGE. It also rarely occurred if there was access to water. The clinical signs may then last 2 to 3 days before death or recovery of the damaged piglets. This recovery may take 7 to 8 days. In older stock there may just be 100% inappetence without other signs. Only 20% to 80% of older stock may have vomiting or diarrhea. Sometimes the piglets under about 30 kg are not affected and this may be because of maternal antibodies, which may last 5 to 13 weeks.

In the United States, the new cases in 2013 have had severe diarrhea and vomiting. The death rate in many cases has been 100% below 7 days of age, and up to 3 weeks of age the morbidity is 90% but falls as the piglets become older.

There is severe watery diarrhea, dehydration, and milk curd in the stomach in all affected naive piglets. Death is caused by dehydration and loss of electrolytes.

In the new outbreaks in Vietnam the morbidity reached 100% and the mortality ranged from 65% to 91%, and the disease appeared milder in Vietnam than in Thailand. In Asia, there appears to be poor herd immunity with outbreaks recurring at 6-month intervals.

In the new outbreaks in the United States the clinical signs are characterized by acute vomiting, anorexia, watery diarrhea, and heavy mortality in pigs less than 10 days old. It is highly contagious and can be seen in all ages of pigs. It took nearly 6 weeks to return to baseline production after an outbreak. (Villous cells are replaced about three times more quickly in 3-week-old pigs than in 1-week-old pigs.)

There was also an effect on the sows with a 12% decrease in farrowing rate if infected in the first 30 days of pregnancy. A 2.2 piglet decrease in born-alive to gilt litters if affected at a similar time and a severe effect on subsequent reproduction in gilts more than sows.

PATHOLOGY

The stomach is usually empty or may be full of undigested milk curd. The intestines are thin walled and pale with watery contents. There is a severe atrophic enteritis with shortened blunted villi (villous atrophy) and fused villi within 24 hours of the onset of clinical signs. The atrophy is as severe as those seen in TGE. The villous height/crypt ratio falls from 7 : 1-9 : 1 to 3 : 1. Under experimental conditions, in weaned pigs, there was severe villous atrophy occurring by 3 DPI and remained until 7 days but was repairing by 14 days. In neonatal pigs the villous atrophy was visible within 12 hours postinfection and was significant at 24 hours.

The pathology is milder than TGE except in the new post-2010 Chinese type outbreaks in which the pathology was as severe as TGE. A study of the U.S. outbreak in 2013 shows that the disease is exactly the same as TGE. Degenerate tips and sides of villi with swollen epithelial cells full of eosinophilic cytoplasm were described. Some cells were loose from their surrounding cells, and sometimes there were syncytia. Initial investigations showed a coronavirus on EM, but the tissues were negative for TGE and rotavirus A on RT-PCR. Subsequent testing by sequencing showed that all the PCR products were PEDV and 99+% similar to the Chinese strains.

DIAGNOSIS

The clinical signs suggest either TGE virus or PEDV and in the past PEDV was mild and differentiated by the lack of mortality. The new strains of PEDV are identical to TGE. TGE and PED have the same morphology under EM, so immunoelectron microscopy is necessary to differentiate the strain, using intestinal contents or feces. Fecal samples from clinically affected pigs are considered the gold standard. The virus is difficult to grow, which is why PCR technology was developed. The virus can be demonstrated by ELISAs; RT-PCR; multiplex RT-PCR,[13] which is rapid, cost-effective, and sensitive; and qRT-PCR.[14] The new multiplex PCRs with specific primers are useful for simultaneous detection of TGE, PED, and rotavirus type A in field samples. Immunoperoxidase techniques can be used to detect virus in the intestinal epithelium. The PCR targets the conserved portion of the N gene.

Most diagnostic labs in the United States now offer a PEDV/TGE differential PCR. It is very sensitive and can be performed on intestinal tissue, feces, or oral fluid samples.

Specific antibodies can be detected by immunofluorescence, and there are ELISAs for the detection of specific antibody in pig sera and milk from recovered pigs.

Very recently, Iowa State University validated an IFA test that measures exposure to the virus, and the best time to test is 3 to 4 weeks after the onset. It is labor intensive and the antibody titers fall very quickly but will rise erratically on reexposure.

There is now a differential multiplex PCR that can be used to differentiate the two groups of virus in the United States.

Oral fluids were as good as fecal samples in a study from the United States.[17] According to PCR results on both oral fluids and fecal swabs, viral shedding began on day one and reached its peak during 3 to 4 DPI. There were no clinical signs of virus infection present 10 DPI. In oral fluids and fecal swabs, viral nucleic acid continued to be found at the limits of detection from 10 to 35 DPI. A slight increase in viral shedding was seen in days 14

to 17 in oral fluids. It was surprising to find that viral shedding occurred for nearly 30 days after the clinical signs ceased.[17] Where the virus is endemic there may be no clinical disease and the PCR may be positive.

TREATMENT

There is no real treatment. You can make sure there is adequate water provision, give milk substitute, and provide glucose : glycine electrolyte solutions for the old style PEDV infection. The new Chinese strains now in the rest of Asia, Europe, and the United States are usually too quickly fatal to necessitate early treatment. Euthanasia is often required for the very badly affected animals and for the lesser affected hospitalization is necessary.

There is no cross-immunity with TGE or PRCV. On a breeding unit the old style PED was self-limiting. Serum antibody titer levels become detectable 2 weeks after infection and rise to levels of 1 : 1000 and then decline to 1 : 20 to 1 : 640. Passive antibody levels from a previously exposed sow may protect piglets for 5 to 13 weeks, but antibody in the sow does not always mean that the piglet is protected.

Immunity from previous natural infections and the previously used Asian vaccines do not appear to give any protection to this recent strain. In China, a bivalent live vaccine has been used for protection against TGE and PED since 1977, but there is little evidence that this works for the new virulent strains of PED.

CONTROL

Disinfectants used for TGE work effectively for PEDV. Heating at 160°F for 10 minutes for trailers will kill the virus as will exposure to 68°F for 7 days.

The key thing for producers to realize is that after the disappearance of clinical signs, the virus may be shed for up to 35 days, and therefore there has to be care when moving pigs (which are then stressed and may well reexcrete the PEDV).

The only control is very tight biosecurity and strict sanitation measures including isolation before integration for new incoming stock.

Authors in the United States have drawn attention to the risk that may be associated with pig diets and their ingredients. Some producers are choosing not to use any porcine products in pig diets and many choose to remove any porcine plasma from the diet and replace it with bovine plasma. Other suitable products would be fermented soybean meal, soy protein concentrate, whey protein concentrate, skim milk powder, and poultry meal among others. Specific use of feedback may be applied with sows when efforts to control sporadic outbreaks of PEDV fail. The material to be used in feedback occurs within 24 hours of the onset of diarrhea when the virus count is very high. Exposure of pregnant sows to

virus using feces from infected piglets will stimulate rapid lactogenic immunity and shorten the outbreak on the farm.

The old method for the control of TGE may work for pigs with PEDV. The methods used for the control of TGE are as follows:
- Addition of 4 to 6 months of replacements and then close the herd.
- Feedback (forced exposure) of the entire herd, feces, intestines, and intestinal contents from acute farrowing/nursery cases is used.
- Strict all-in/all-out and one-directional flows should be practiced until after the clinical signs have disappeared.
- Introduction of sentinels about 30 days after the clinical signs have disappeared to confirm there is no circulation of virus
- Strict control of unidirectional flow of pigs and people to allow the PEDV to be walked out of the premises

In another study Dufresne[18] suggested:
- That all piglets down to 10 days of age be weaned off the farm
- Expose all gilts and sows 2 to 5 weeks prefarrow with scours wiped from the heat lamps in the farrowing areas with tissues. This can then saturated in water and placed in the water trough daily for 3 days.
- Delay feedback until they have sufficient intestines from scouring piglets. Ideal material appears to be intestines from euthanized piglets 24 hours after the outbreak has started.
- The author repeats the feedback three times in 2 weeks using one intestine for 10 sows.

This sort of approach seems to lead to a stabilization at around 18 to 20 weeks after commencement of the protocol. The process is more difficult than for PRRSV because there is greater transmission of virus, a greater virus stability, and sow immunity is lower. On the other hand, the persistence of viral infection in the host is much shorter.

Most herds return to normal mortality 5 weeks after exposure. In the experience of one veterinarian,[18] about 70% of herds' prewean mortality remains normal for an extended period but the remainder has varying degrees of clinical relapse. It is believed that the relapse is not just an example of failure of exposure, but it is possible that the relapse occurs because of waning herd immunity. They have seen relapses in herds with little or no closure time, in very large sow farms (5000+), and where there is pen gestation rather than crate gestation.

Control relies only on biosecurity and making sure that all blood products are properly heat treated to 80°F followed by storage at room temperature for 6 weeks. In 2014 the disease was made reportable in the United States so that a record of its spread is possible.

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SWINE VESICULAR DISEASE

SYNOPSIS

Etiology Enterovirus of family Picornaviridae

Epidemiology Important because it resembles foot-and-mouth disease. No outbreaks since 2011 in Europe and in Asia since 2000. Transmitted by direct contact, movement of pigs, and feeding uncooked garbage containing pork products

Signs Fever, lameness, vesicles on coronary bands, and recovery in 2–3 weeks

Clinical pathology Demonstrate antigen in tissues.

Lesions Vesicles

Diagnostic confirmation Demonstrate virus in tissues. Isolate virus. RT-PCR

Differential diagnosis
- Foot rot of pigs
- Differentiate from other vesicular diseases by laboratory examination and virus identification.

Treatment None needed

Control Control of garbage feeding and movement of infected pigs

The importance of swine vesicular disease is that the clinical signs of this economically unimportant disease are indistinguishable from those of FMD, which is an economic disaster if it occurs in your country. It can mask FMD as was the case in Taiwan in 1997,

although diagnosis is now easier and possible on farm.[1]

ETIOLOGY

The disease is associated with an enterovirus (family Picornaviridae) related to human coxsackie B5 virus. A variant of this virus may have become adapted to swine. It was once regarded as porcine coxsackie (75%–85% homogeneity with the human virus) virus. Human isolates of coxsackie B5 virus do not cause disease in pigs, although swine vesicular disease virus once infected humans, but this is not considered likely with the current strains. The disease is restricted to pigs, although experimental challenge of sheep has produced subclinical infection.

EPIDEMIOLOGY
Occurrence and Prevalence of Infection

The disease was first recognized as a limited outbreak in Italy in 1966 and was eradicated by slaughter. It then appeared in a variety of countries in Asia (last was in Chinese Taipei in 2000) and in Europe but recently only in Portugal (2007)[2] and Italy (2011). This latter outbreak was associated with the rapid rise in pig numbers in Lombardia and the increase in animal movements combined with weak biosecurity methods.[3] North and South America and Australasia remain free from infection.

Eradication programs based on a slaughter policy were instituted and in most cases were effective. There has been some variation in virulence, which is determined by two amino acids in the capsid, and there may be seven antigenic strains, although there is no wide genetic variation. The epidemiologic pattern of the disease in the various outbreaks is presumably caused by different strains of the virus.

Methods of Transmission

Infection generally occurs through minor abrasions on the feet but may occur through other routes. The incubation period is 2 to 14 days, and the virus may be excreted before the onset of clinical signs. During and for a short period following the viremic phase, the virus is excreted in oral and nasal secretions. It is excreted in feces for periods up to 3 weeks, and vesicular fluid and shed vesicular epithelium are potent sources of infection. A chronic infection with shedding of virus for periods up to 3 months has been described. Contact within a contaminated environment may lead to viremia within 1 day and clinical signs within 2 days.

Large amounts of virus are shed in the immediate vicinity of infected pigs. Transmission occurs by direct contact or contact with infected food or water or infected feces, and the disease spreads rapidly between pigs within the same group. Airborne transmission of the virus is not a feature, and the spread between groups of pigs is less rapid

than that which occurs with FMD. The resistance of the virus and its persistence within the environment allows spread by mechanical methods such as trucks and contaminated boots. Areas that have housed infected pigs may remain infective for a considerable period of time. The potential for contaminated communal livestock trucks and markets to spread infection is considerable because of the occurrence of minor foot abrasions that occur during the movement of pigs and the presence of persistently infected organic matter.

In the UK epidemic in the 1970s, the major methods of spread were movement of pigs (48%), contaminated vehicles (21%), feeding contaminated waste (15%), and contact at markets (11%). Other methods included movement of equipment or personnel, local spread, and recrudescence of previous infection. The outbreaks were fewer in the summer when less pork was consumed, and this resulted in much reduced pig movements.

The disease may be sufficiently mild to escape clinical detection. This, plus the occurrence of subclinical infection, and the reluctance of farmers to report suspicions of its occurrence, facilitates spread by the movement of infected pigs to other farms or through markets. Vertical transmission has not been demonstrated.

The disease may also be spread by the feeding of uncooked garbage, but it is believed that more of the virus is needed to infect pigs via this route. Pigs killed during the incubation period of the disease or with subclinical infection possess a considerable amount of virus in body tissues. There is little reduction in infectivity with cold storage, and the virus can persist in pork and pork products indefinitely.

Risk Factors
Pathogen Factors

There are minor antigenic differences and variation in virulence between some isolates of swine vesicular disease virus from different countries and two genetically and antigenically distinct variants exist in Europe. Swine vesicular disease virus can be grown in tissue culture and has characteristics distinguishing it from the viruses associated with FMD, VS, and vesicular exanthema. The virus is extremely resistant to chemical and physical influences, which has made control of the disease very difficult. It is inactivated only at extremes of pH (it can survive at pH 2–12) and temperatures. It may remain infective in the environment and in manure for periods of at least 6 months. It is resistant to the action of many disinfectants, and recommendations for disinfectants include 2% sodium hydroxide, 8% formaldehyde, and 0.04% sodium hypochlorite if organic material is not present. It is easily transmitted in infected meat. The virus survives the processing of pork and pork products, especially

salami, except when heated at greater than 68°C (154°F). It can persist in these products indefinitely (salami, 40 days).

Infected carcasses can be held in cold storage for months and then released at neutral pH and 40°C and the virus can still be found after 160 days. It is very stable and therefore difficult to decontaminate the environment, particularly where swine are housed on the soil. The virus can be found in earthworms from above the burial pits.

Economic Importance

Although the economic effects of the primary disease are minor, the cost of the slaughter method for eradication is high. Although the morbidity rate with most strains is high, the disease generally runs its course in 2 to 3 weeks and produces a negligible mortality and only a minor setback to production. The major importance of the disease is its close clinical similarity to other vesicular diseases and the effects of a ban on export animals to other countries. The necessity for immediate differentiation of an outbreak from FMD and the problem of having such a similar clinical entity present in the pig population has made eradication of the disease desirable. In most countries this has proved extremely expensive.

PATHOGENESIS

There is variation in the susceptibility of different sites of the body to invasion by swine vesicular disease virus, and in natural outbreaks initial infection is most likely through damaged skin, particularly damaged feet. It has been suggested that 90% of the infection may be through the tonsil. A large amount of virus is in the tissues before the clinical signs develop. Once infection is established in a pig, virus excretion is so massive it results in infection of others in the group through the tonsil and gastrointestinal tract as well as through skin abrasions. Massive amounts of the virus are excreted in the feces. Experimentally, the disease can be reproduced by intravenous, intramuscular, subcutaneous, and intradermal inoculation of virus. Virus spreads at the site of infection and enters the bloodstream through the lymphatics. It is followed by viremia, which may last 2 to 3 days. Recent research has suggested that the virus can persist for a longer length of time for up to 63 days, but at 119 DPI the virus was again found in feces when two groups of pigs were mixed. This suggests that the virus and RNA can persist for a long time and possibly suggests a carrier state, but the same authors also suggest that persistent infection is rare. Most virus is produced during the first week, but lesions are infective for a long time. The virus has a special affinity for epithelium of the coronary band, tongue, lip, and snout, and for myocardium. Lesions in the brain, especially the brainstem, are seen histologically, but nervous signs are not a common clinical finding.

CLINICAL FINDINGS

The incubation period varies from 2 to 14 days. The disease is usually mild or even inapparent. It may be seen initially just as lame pigs. The morbidity rate varies from 25% to 65% and up to 100% of pigs within a pen may be affected. A transient fever (40–41°C; 104–105°F) and temporary mild inappetence may be seen. Lameness, arching of the back, and other signs of foot discomfort are evident but are less severe than with FMD. Very occasionally they walk on the knees or scream. The incidence of lameness and of foot lesions are influenced by management and are less severe on bedding or with soft conditions underfoot. Characteristic vesicles occur at predilection sites frequently associated with trauma. They are most common on the coronary band of the claws, especially at the heel, and of the supernumerary digits. They start as areas of blanching and swelling and progress in 1 to 2 days to thick-walled vesicles that rupture, giving the appearance of an ulcer. Sometimes pigs may have a retracted recovery. In severely affected pigs, the lesions will encircle the coronary band and the horn may be shed as in FMD. Lesions also occur on the tongue, lips, and snout and the skin of the legs and belly. They are much less frequent in these areas and frequently do not progress to typical vesicles. An examination of the feet of other apparently normal pigs within the group will often reveal the presence of minor lesions, and the extent of involvement of pigs within the group may be underestimated without careful examination. In some outbreaks, the incidence of clinical lesions has been minimal and even a single vesicle on the pig's foot should be treated as suspect. Some pigs show no clinical signs but develop significant titers of neutralizing antibody. The course of the disease within a group is generally 2 to 3 weeks, mortality is very uncommon, and there is only a minor setback to production unless complete separation of the horny foot occurs. Nervous signs with ataxia, circling, head pressing and convulsions, and paralysis have been observed rarely. Recovered pigs have immunity that protects against reinfection.

CLINICAL PATHOLOGY

Tests for the identification of swine vesicular disease include the demonstration of antigen in tissue and the detection of antibody. Vesicular epithelium provides the best material for direct antigen demonstration, and it may be present even in the remnants of 10-day-old lesions. The virus can also be grown on tissue culture and identified. An RT-PCR has been developed, and PCR and PCR-ELISA have been described including those to differentiate between the various vesicular diseases.[4,5] A lateral flow device for the detection of swine vesicular disease and differentiation from FMD in clinical samples has also been developed.[6] It has potential for being used next to the animal in providing a rapid support to clinical diagnosis as a rapid pen-side test.

Specific antibody is produced within 4 to 6 days and may be demonstrable before clinical disease is evident. With FA or direct CF, a result may be obtained within 8 to 12 hours. Antibody may be detected by VN or ELISA for the diagnosis and surveillance of the disease. Isotype-specific ELISAs have been described. The direct liquid-phase blocking ELISA (LP-ELISA) correlates well with the neutralization test, which is used by the European Community authorities. Monoclonal antibody trapping ELISA was used in Canada, Italy, and England to test results against other tests, and it was found that VN should be used as a definitive test. Virus isolation and RT-PCR are the first choices for detection of swine vesicular disease virus in feces or organs.

NECROPSY FINDINGS

There are no gross or histologic findings that differentiate swine vesicular disease from FMD. Lesions in the skin consist of areas of coagulative necrosis with intraepithelial vesicle formation. Additional necrotic foci are present in the tonsils, renal pelvis, bladder, salivary glands, pancreas, and myocardium. There is also nonpurulent meningoencephalitis. Intranuclear inclusions are present in the ganglion amphicytes. An ELISA used on vesicular fluid or epithelium can give a result in 4 to 24 hours. It grows well in culture in swine kidney cells and may show effects within 6 hours. The intracerebral infection of mice causes paralysis and death.

DIFFERENTIAL DIAGNOSIS

The occurrence of vesicles differentiates this disease from other nonvesicular diseases of pigs. So-called foot rot in pigs is associated with lesions on the sole and horn of the claw rather than the epithelial area of the coronary band. The differentiation of swine vesicular disease from other vesicular diseases relies on laboratory examination and virus identification as detailed previously.

TREATMENT AND CONTROL

No treatment is described and none is warranted. In most countries where outbreaks have occurred, control has been attempted or achieved by slaughter eradication. Depopulation is followed by thorough cleansing and disinfection and limited repopulation effected after a period of 2 to 3 months. The disposal of infected carcasses can be important because the disposal site may remain infective.

The detection of infected herds can be a problem. The mild nature of the disease means that it can easily escape detection, especially in darkened pig houses or where conditions underfoot obscure observation of the feet. Mild infections may produce little clinical disease and any vesicular lesions should be treated with suspicion. The reluctance of some farmers to report suspicious lesions can also be important, and it is essential to institute educational programs that emphasize the necessity for early detection and diagnosis of outbreaks. Serologic surveys to identify present or past infections have proved of value in aiding detection of the disease. Serologic single reactors cause a lot of trouble in trade. Piglets receive maternal antibodies from the sow and these may last for 30 to 50 days.

The three most important methods of spread are
1. Feeding of garbage containing infected pig meat
2. Movement of pigs from infected farms either directly from farm to farm or indirectly through markets
3. Movement of pigs in contaminated transport vehicles

Control of these methods of spread must include:
- Strict enforcement of garbage-cooking regulations
- Closing of markets, except perhaps for holding areas for pigs going directly to slaughter
- Strict control of movement and sale of pigs
- Adequate cleansing and sanitation of infected areas and transport vehicles

Transmission through feeding of infected meat in garbage appears the most difficult to control, and the latent period of this cycle means that outbreaks can recur at a time when eradication was thought to be complete. Disinfection of slurry is also difficult but can be attempted by treatment with sodium hydroxide.

In the UK, the most crucial item for control was the introduction of a 21-day movement prevention after the initial movement. Sentinels are put in after 8 weeks after the initial disinfection and are observed for about 3 weeks. If they are free after this time they are allowed to restock.

Vaccination has not been used for control in most countries, although experimental vaccines are available but not commercially.

FURTHER READING

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VESICULAR EXANTHEMA OF SWINE

VES is an acute, febrile, infectious disease of swine associated with a calicivirus. At least 34 types of calicivirus have been recognized in the ocean and new outbreaks continue to occur. The relationship between these viruses and VES is a continual source of speculation. The virus isolated in 2000 from sea lions was shown to be infectious for swine. It is indistinguishable clinically from FMD in swine, VS, and swine vesicular disease. It has not been a problem for the pig industry for over 50 years.

ETIOLOGY

The causative virus is a calicivirus, and 13 antigenic strains have been isolated with some variation in virulence between strains. Even in one herd the virus isolated may have been antigenically different from others. At least 17 antigenic types have been isolated since 1972. Only pigs are susceptible, although experimental transmission to horses can be effected with some strains. All ages and breeds of pigs are susceptible to infection. The initial outbreak in pigs was traced to the feeding of meat from sea mammals.

EPIDEMIOLOGY
Occurrence

VES was first diagnosed in Southern California in 1932. In 1952 it was diagnosed outside California and by 1953 had occurred in 42 states. However, rigid control eradicated it by 1956 with particular importance being paid to garbage-feeding control.

Except for isolated outbreaks in Hawaii and Iceland, the disease has occurred only in the United States. This is important because of its direct effect and because of its resemblance to FMD. Although VES is a mild disease with a low mortality rate (usually less than 5% and there may be many deaths in unweaned pigs), affected animals may suffer a severe loss of BW and convalescence may require several weeks. Pregnant sows may abort and lactating sows may go dry with resultant heavy losses in baby pigs. The disease was eradicated from the United States in 1959, 27 years after its initial appearance.

Methods of Transmission

The sources of infection are infected live pigs and infective pork. Infected pigs excrete the virus in saliva and feces but not in the urine for 12 hours before vesicles develop and for 1 to 5 days afterward. Raw garbage containing infective pork scraps is the most common medium of spread from farm to farm. On infected premises the disease is spread by direct contact and, although the virus is resistant to environmental influences, spread by indirect means does not occur readily. Pigs frequently become infected, as evidenced by the development of immunity, without evidence of clinical disease. Ingestion of infected material is sufficient to produce infection.

The isolation from marine animals of an identical virus, which is capable of producing a disease identical to vesicular exanthema when inoculated into pigs, has led to the hypothesis that the primary reservoir for vesicular exanthema is in marine animals. Epizootics in pigs may have been initiated by the feeding of marine meat or garbage containing marine animal products.

Risk Factors
Pathogen Risk Factors

The virus is resistant to environmental influences and persists in frozen and chilled meats. It is readily destroyed by several different commonly used disinfectants including sodium hypochlorite, sodium hydroxide, and phenol. A good immunity develops after an attack and persists for about 20 months. There is no appreciable cross-immunity between the strains of the virus, and a series of outbreaks, each associated with a different strain of the virus, may occur in the one herd of pigs.

A similar if not identical virus, San Miguel sea lion virus, has been isolated from sea lions and fur seals off the coast of California in the United States. It is physically, chemically, and morphologically identical to the vesicular exanthema virus, although the same antigenic types have not been found. The virus produces an identical disease to vesicular exanthema when inoculated into pigs and appears to have a similar host range. The VES virus is infective for the harp seal, but the disease is inapparent and self-limiting. The intradermal inoculation of VES into otrariid (fur) seal pups will result in plaque-like lesions. Feeding swine the seal tissues from the inoculation experiments resulted in seroconversion in swine that were fed tissues from seals infected with VES virus but not in those fed tissues from seals infected with the San Miguel sea lion virus. Antibody to this virus has also been detected in California gray whales and in feral swine inhabiting coastal areas.

PATHOGENESIS

As in other vesicular diseases there is a viremia, lasting for 72 to 84 hours and commencing 48 hours before vesication, with localization occurring in the buccal mucosa and the skin above the hooves. The intradermal inoculation of the VES virus and the San Miguel sea lion virus into swine results in fluid-filled vesicles at the sites of inoculation in the snout, coronary band, and tongue. Lesions are usually limited to the nonhaired portions of the integument and tongue. A mild viral encephalitis occurs in pigs inoculated with the swine virus, and the sea lion virus can be recovered from the brain tissue of pigs infected with the virus.

CLINICAL FINDINGS

The incubation period varies with the virulence of the causative strain of virus but is usually 1 to 3 days. Morbidity is always high but mortality is low. There is an initial high fever (40.5–41°C; 105–106°F) followed by the development of vesicles in the mouth, on the snout, on the teats and udder, as well as on the coronary skin, the sole, the heel bulbs, and between the claws. This is accompanied by extreme lassitude and complete anorexia. The initial lesion is a blanched area that soon develops into a vesicle full of clear fluid. The vesicles rupture easily leaving raw, eroded areas. This usually occurs about 24 to 48 hours after they appear and is accompanied by a rapid fall of temperature. Secondary crops of vesicles often follow and may cause local swelling of the face and tongue. Lesions on the feet may predominate in some outbreaks, whereas in others they may be of little significance. The affected feet are very sensitive and there is severe lameness. Healing of the oral vesicles occurs rapidly, although secondary bacterial infection often exacerbates the lesions on the feet. Recovery in uncomplicated cases is usually complete in 1 to 2 weeks. It may occasionally cause encephalitis, myocarditis, and diarrhea as well as failure to thrive. When sows become infected late in pregnancy, abortion frequently occurs and lactating sows may go dry.

CLINICAL PATHOLOGY

Fluid from the vesicles is used in transmission experiments and for tissue culture. Blood serum is used for the CF, viral neutralization in cell culture, and gel diffusion precipitin tests.

NECROPSY FINDINGS

Postmortem examinations are not of much value in the diagnosis of vesicular exanthema, but the pathology of the disease has been defined. The lesions are limited to epithelial lesions in which there are vesicles, necrosis, sloughing, and rapid healing with mild scarring. Diagnosis involves virus isolation in cell culture, with EM as a possibility and various serologic tests including FATs for the antigen. PCR tests have also been developed.

DIFFERENTIAL DIAGNOSIS

Because of its case-for-case similarity to foot-and-mouth disease (FMD), prompt and accurate diagnosis of the disease is essential. In most countries the **disease is notifiable**.

All species
- FMD and other vesicular diseases

Cattle
- Bovine virus diarrhea
- Bovine malignant catarrh
- Pseudocowpox

Horses
- Blister beetle toxicosis
- Bullous pemphigoid
- Phenylbutazone toxicity
- Grass seed awns

TREATMENT

There is no effective treatment. The immunity is solid following infection, but heterologous infection is possible.

CONTROL

Eradication of the disease should be attempted whenever practicable. In most instances it is essential to report to the regulatory authorities. The first step is to quarantine infected premises and restrict movement of pigs in the area. Infected animals should be slaughtered, but the carcasses may be salvaged for human consumption provided the meat undergoes special treatment to ensure destruction of the virus. Normal freezing and chilling procedures are not sufficient to destroy it. All garbage fed to pigs must be boiled. Infected premises should be thoroughly cleaned and disinfected with a 2% sodium hydroxide solution before restocking. The implementation of these measures was eminently successful in eradicating the disease from the United States.

In view of the reservoir of virus in marine animals and apparent infection in feral swine in the coastal areas of California, it is possible that the disease could recur in domestic swine in the United States. Possible methods of reintroduction that need to be guarded against have been described.

Active immunization may be practicable if the disease reappears and other control measures fail. A formalin-killed virus preparation produces an immunity lasting for at least 6 months. Multivalent vaccines may be required if more than one strain of the virus is involved.

Recently the pathogenic class of VES virus–like caliciviruses (genus *Vesivirus*) endemic in certain ocean species and U.S. livestock has possibly caused vesicular disease on the hands and feet of humans.

SALMONELLOSIS IN RUMINANTS AND HORSES

SYNOPSIS

Etiology *Salmonella* spp. Cattle: *S.* Typhimurium, *S.* Dublin, and *S.* Newport. Sheep and goats: *S.* Typhimurium, *S.* Dublin, *S.* Abortusovis, and *S. enterica* subsp. *diarizonae*. Horses: *S.* Typhimurium and *S.* Enteritidis. Differentiation between host-specific, host-restrictive, and ubiquitous serovars

Epidemiology Worldwide occurrence. Important zoonosis and food-borne illness. Prevalence of infection in healthy animals varies according to species and country. Incidence of clinical disease lower than prevalence, and outbreaks occur precipitated by stressors. Spread by direct or indirect means; the infected animal is the source of organism, which contaminates feed and water supplies.

Disease may become endemic on farm. Carrier animals shed organism and may introduce infection into herd. Deprivation of feed and water, transportation, drought, intensive grazing and housing, and mixing animals from different sources contribute to onset of disease. Antimicrobial resistance is a major public health issue and is more common in isolated sick animals than from healthy carriers.

Signs Septicemia in neonatal ruminants and foals with a high case–fatality rate. Acute diarrhea and dysentery, fibrinous fecal casts, fever, marked dehydration, and toxemia; chronic enteritis; abortion; dry gangrene of extremities; and arthritis and foci of osteomyelitis. Severe diarrhea and dehydration characteristic in the horse

Clinical pathology Culture of organism from feces, repeated culture of feces required to identify carrier animals, serology in blood or milk, use hematology for changes in leukon and clinical chemistry for electrolyte changes

Lesions Septicemic hemorrhages. Mucoenteritis to marked fibrinohemorrhagic necrotic enteritis; enlarged mesenteric lymph nodes. Foci of necrosis and thickened intestinal wall in chronic enteritis

Diagnostic confirmation Culture of organism from feces, tissue, or body fluids; polymerase chain reaction and antigen-ELISA to detect specific DNA

Treatment Antimicrobials in cases of bacteremia, antiinflammatory therapy, and supportive fluid and electrolyte therapy

Control Prevent introduction of infection into herd. Limit spread of infection within the herd by identification of carrier animals, prophylactic antimicrobials, restricting movement of animals, clean water supply, hygiene, and disinfection of buildings. Avoid spread of infection in veterinary clinics and dispose of infective materials. Vaccines for immunization are available but not effective.

ETIOLOGY

Salmonella are gram-negative, rod-shaped bacilli belonging to the family Enterobacteriaceae. *Salmonella* spp. belong to the most important food-borne pathogens causing human infection. The bacterium is a facultative intracellular organism with worldwide occurrence in all mammal species. The genus *Salmonella* consists of only two species,

S. enterica and *S. bongori*. Based on molecular characteristics *S. enterica* is further divided into six subspecies that are subsp. *enterica* (formerly subgenus I), subsp. *salamae* (formerly subgenus II), subsp. *arizonae* (subgenus IIIa), subsp. *diarizonae* (subgenus IIIb), subsp. *houtenae* (subgenus IV), and subsp. *indica* (subgenus VI). Subgenus V is now assigned to *S. bongori* to avoid confusion with serovar names of *S. enterica* subsp. *enterica.*[1] Within each subspecies different strains are classified into serovars (or serotypes) based on their LPS antigen (O) and flagellar antigen (H) characteristics according to the Kauffmann–White scheme. Currently over 2600 serovars are recognized, of which most of the ones causing infection in people and mammals belong to *S. enterica* subsp. *enterica.*[2] In practice for *S. enterica* subsp. *enterica,* the subspecies name does not need to be indicated as only serovars of this subspecies bear names. Serovars of the other subspecies are designated by their antigenic formula. The name of the serovar is no longer italicized but is capitalized.[1]

Before this novel taxonomy and nomenclature for the genus *Salmonella* was introduced in 1986, subspecies were treated as subgenera and serovars were considered species. This change in taxonomy has caused and will be causing confusion as long as both terminologies appear in the medical literature. The way former *Salmonella* species and now serovars were designated changed with time. Initially the serovar name denoted a syndrome (e.g., *S. typhi*) or host-syndrome combinations (e.g., *S. abortus-ovis, S. abortus-equi*). Later serovars were designated by the geographic origin of the first identified strain of the serovar in question (e.g., *S. dublin,* S. *london*). When the new nomenclature was introduced names were retained for serovars of subspecies *enterica,* which comprises the great majority of isolated serovars, because these names were so familiar. In contrast, serovars of other subspecies are now designated by their antigenic formula.[1]

Salmonella serovars differ in the range of hosts they can infect and in the nature of disease that may result: this difference is referred to as **serovar–host specificity**. So-called **ubiquitous serovars** such as *S.* Typhimurium or *S.* Enteritidis can affect a wide range of hosts and produce acute but self-limiting illness. **Host-specific serovars**, such as *S.* Typhi in humans or *S.* Gallinarum in poultry affect only a single species, and are associated with severe illness that does not necessarily include diarrhea. **Host-restricted serovars** primarily affect one specific species, but can also cause illness in a limited number of other species. Such serovars are, for example, SD, primarily affecting cattle or SCS, primarily affecting pigs.[3] The serovars that most commonly cause salmonellosis in farm animal species are as follows:

- **Cattle**: *S.* Typhimurium, SD, *S.* Newport, *S.* Enteritidis

- **Sheep and goats**: S. Typhimurium, SD, *S. enterica* subsp. *diarizonae, S.* Abortusovis
- **Horses**: S. Typhimurium, *S.* Abortusequi, *S.* Newport, *S.* Enteritidis

EPIDEMIOLOGY

The epidemiology of salmonellosis is complex, which often makes control of the disease difficult. The epidemiologic patterns of prevalence of infection and incidence of disease differ greatly between geographic areas depending on climate, population density, land use, farming practices, food harvesting and processing technologies, and consumer habits. In addition, the biology of the serovars differs so widely that consideration of salmonellosis, *Salmonella* infection, or *Salmonella* contamination are inevitably complex.

Prevalence of Infection

Surveys investigating the prevalence of fecal shedding indicate considerable variation between countries and animal species. In the following section the literature of the prevalence of infection or fecal shedding in healthy animals is reviewed by species.

Cattle

The prevalence of positive culture results in feces from dairy cattle in the United States has been studied in three comparable studies conducted in 1996, 2002, and 2007 and including over 90 operations from at least 17 states.[4] In the most recent study, 39.7% of participating herds and 13.7% of tested animals were culture positive for *Salmonella* spp., which is double the herd and animal prevalence reported in the first study of 1996.[4] Overall larger herds with more than 500 cows were found to be more likely to have culture-positive fecal samples (61.0%) than smaller herds with less than 500 cows (41.5%). The most common serovars isolated in the 2007 study were, in descending order, *S.* Cerro, *S.* Kentucky, *S.* Montevideo, *S.* Muenster, *S.* Meleagridis, *S.* Mbandaka, and *S.* Newport.

A study conducted in one large U.S. feedlot receiving calves from the Midwest and High Plains found a prevalence of culture-positive environmental samples in cohorts at the time of feedlot entry of 64.7%.[5] The predominantly isolated serotypes in this study were *S.* Anatum, *S.* Montevideo, *S.* Orion, *S.* Kentucky, *S.* Mbandaka, and *S.* Newport. The geographic distribution of the serotypes differs: *S.* Typhimurium has a universal distribution and SD has a patchier habitat. In the United States, up until 1948, it was limited to California and as recently as 1971 it had not been reported in cattle east of the Rocky Mountains. In 1980 the first case of SD occurred in Indiana. The movement of infected adult cattle and calves is responsible for the introduction of infection to areas in which it had not previously been diagnosed. In a California survey of 60 dairy herds, milk

samples and serum samples tested with an ELISA for antibodies against *Salmonella* serogroups B, C1, and D1 antigens found that 75% of dairy herds surveyed had cows with serologic evidence of recent exposure to salmonellas, especially *S.* Typhimurium and SD.

Data from bacteriologic monitoring of *Salmonella* in cattle herds were reported by several member states of the European Union (EU) in 2009.[6] Finland and the Netherlands reported a herd prevalence of 0% and 5.5% of culture-positive fecal samples, respectively. Animal prevalence levels determined either at the farm or at the time of slaughter between 0% and 3.4% were reported from 8 European member states and Norway. The results of microbiological examinations of bovine meat conducted in Denmark, Germany, Ireland, Italy, and the Netherlands indicate that the most prevalent serovars, in descending order, were *S.* Typhimurium, SD, *S.* Infantis, *S.* Derby, and *S.* Enterididis.[6]

An Australian study investigating the prevalence of culture-positive fecal samples in slaughter age cattle reported an estimated animal level prevalence of 1.7% for dairy, 0.8% for feedlot beef, and 0.5% for pasture beef cattle.[7] The determined herd level prevalence for non-Dublin *Salmonella* spp. positive fecal samples in this study was 17% for dairy, 13% for feedlot beef, and 5.5% for pasture beef herds.[7] The most prevalent serovars in cattle were SD, *S.* Typhimurium, and *S.* Anatum.

The prevalence of culture-positive fecal samples from cattle and calves hospitalized in a veterinary teaching hospital in the United States that were cultured as part of a *Salmonella* surveillance program but were not clinical *Salmonella* suspects was 3.2% for calves and 2.3% for adult cattle.[8] The most prevalent serotypes in these non–*Salmonella*-suspect patients were, in the order of occurrence, *S.* Newport, *S.* Typhimurium, and *S.* Agona.[8]

Sheep

The literature on infection prevalence in sheep is scant. The recent U.S. Department of Agriculture-Animal and Plant Health Inspection Service (USDA-APHIS) "Sheep 2011" study included 247 sheep operations from 22 states to investigate the prevalence of enteric pathogens and commensal organisms in the U.S. sheep population.[9] In this study a herd prevalence of culture-positive fecal samples of 66.4% was determined. The proportion of positive composite fecal samples stratified by sheep type was 38.2% for ewes nursing lambs; 30.9% for the group of nursing lambs, market lambs, and replacement ewes; and 29.1% for pregnant ewes and others.[9] By far the most prevalent serovar was *S. enterica* subsp. *diarizonae* IIIb:61 -:1,5,7 accounting for 94.6% of all isolates. *S.* Enteritidis and *S.* Newport combined accounted for only 4% of all isolates, whereas *S.* Typhimurium was not isolated.[9]

Abattoir studies conducted in different countries reported prevalences of culture-positive samples of sheep between 0.1% in the UK and 40% in Australia.[10] In a recent Australian abattoir study, *Salmonella* spp. were isolated from 20% of fecal samples and 13% of fleeces in slaughtered sheep.[11] Another Australian study used a multiplex qPCR to determine the prevalence of *S. enterica* in fecal samples collected from lambs at weaning, postweaning, and preslaughter from eight farms across four states. The overall prevalence of *Salmonella*-positive fecal samples was 5.0%, but wide variations among states were found. Highest prevalence rates were determined in New South Wales in lambs at weaning (18.1%) and postweaning (23.8%).[10]

S. Abortusovis is an ovine-restricted serovar that represents a common cause of abortion and mortality in newborn lambs in Western Asia.[12] Infections have been reported from France, Spain, Germany, Cyprus, Italy, Switzerland, Russia, and Bulgaria, but few infection prevalence studies are available. A recent Swiss study determined the seroprevalence of *S.* Abortusovis infection in sheep flocks in 2007 after a series of abortion storms that had occurred between 2003 and 2007 throughout the country. Before 2003 abortion caused by *S.* Abortusovis had not been reported for several decades in this country. Overall an animal seroprevalence of 1.7% and a flock prevalence of 16.3% were found.[13]

Horses

Few infection prevalence studies conducted in nonclinical horses have been conducted. The National Animal Health Monitoring System Equine 1998 study that included over 8000 horses on nearly 1000 operations across the country reported prevalence of culture-positive fecal samples of 0.8%. At least one horse on 1.8% of operations was estimated to shed salmonellas in feces.[14] A total of 14 different serotypes were isolated with the most common serotype being *S.* Muenchen.

Four percent of specimens of equine origin submitted to a diagnostic laboratory in the United Arab Emirates were found to be *Salmonella* positive. The two predominant *Salmonella* serovars were *S.* Typhimurium and *S.* Kentucky, followed by *S.* Anatum and *S.* Agona.[15]

Occurrence

Salmonellosis occurs universally in all species.

Cattle

The disease has assumed major importance, particularly for the dairy industry. Apart from having implications for health and productivity on an individual animal and on a herd level, infections and outbreaks in dairy cattle present an important risk of zoonotic transmission. Remarkably the prevalences of

the different *Salmonella* serovars isolated in samples in clinically healthy animals differ considerably from the prevalence rates of serovars isolated in fecal samples from sick animals.

A recent U.S. field study conducted in 831 dairy herds from New York, Pennsylvania, Vermont, Massachusetts, and Connecticut that agreed to submit fecal samples of *Salmonella*-suspect clinical animals to a diagnostic laboratory reported culture-positive results in 22.5% of over 2500 cultured samples.[16] The herd level incidence rate was 8.6 positive herds per 100 herd years, and the animal-level incidence rates for preweaned heifers, postweaned heifers, and adult cows was 8.1, 0.04, and 1.8 cases per 1000 animal years, respectively.[16] In this study *S.* Newport was the most prevalent serovar with 41%, followed by *S.* Typhimurium (including var. Copenhagen) with 19.1%, *S.* Infantis (8.2%), 4,5,12:i:- (6.1%), *S.* Agona (5.2%), and *S.* Muenster (4.2%).[16]

Among 768 *Salmonella* suspect clinical cases of a veterinary teaching hospital in New York State 6.5% were identified as fecal shedders based on culture results.[8] The prevalence of culture-positive fecal samples of clinical cases was 9.1% in calves and 3.6% in adult cows with highest proportions of positive samples in the fall and lowest during spring.[8] The most common serovars were *S.* Typhimurium, *S.* Typhimurium var. Copenhagen, and *S.* Newport with similar numbers of isolates.[8]

In the UK, with a cattle population of 8.26 million in 2013, a total of 52.922 samples from clinical cases have been submitted for diagnostic purposes; salmonellas were isolated from 604 samples. The most prevalent serovars isolated in cattle were SD (72.5%), *S.* Mbandaka (7.5%), *S.* Typhimurium (5.0%), and *S.* Montevideo (3.3%).[17] SD was the most common serovar isolated from cattle with clinical disease for the past 15 years in the UK. The prevalence of *S.* Typhimurium, which was the most prevalent serovar with over 60% at the end of the 1990s in the UK and other countries, has continuously declined over the past years, and in particular *S.* Typhimurium definitive type (DT)104 that was associated with outbreaks of salmonellosis in dairy cattle and humans in the UK and the United States subsided.

In Germany the number of outbreaks of bovine salmonellosis has decreased over the past years from 258 outbreaks in 2002 to 81 outbreaks in 2009. From 2009 to 2011 this number had increased again to 109 outbreaks of bovine salmonellosis in 2011.[18] *S.* Typhimurium (including var. Copenhagen) was the most common serovar associated with approximately 40% of all outbreaks between 2009 and 2011, followed by SD (22%), *S.* Enteritidis (6.4%), and *S.* Abony (5.5%).[18]

A recent study investigated the prevalence of different serovars of culture-positive

fecal samples from diarrheic calves in Australia including a total of 597 samples from 84 herds.[19] The most common serovars in these diarrheic calves were SD (27.4%), *S.* Typhimurium (14.5%), *S.* Zanzibar (11.3%), and *S.* Bovismorbificans (9.7%).

S. Montevideo has been the cause of large economic losses from abortion and cow mortality in an outwintered beef herd in Scotland. Up to 25% of the cows aborted and the overall herd mortality was 7%. The organism had been the cause of abortion in a neighboring sheep flock.

Sheep

Salmonellosis is commonly encountered when sheep are assembled at high stocking rates. In the UK, with a sheep population of 30.95 million, approximately 9500 ovine samples from *Salmonella*-suspect clinical cases have been processed by official diagnostic laboratories in 2013.[20] The most common serovars were *Salmonella enterica* subsp. *diarizonae* 61:k:1,5,(7) and variants (36.6%), followed by *S.* Montevideo (32.1%), SD (11.6%), and *S.* Agama (8.9%).[20] There were no *S.* Typhimurium or *S.* Abortusovis cases in sheep in the UK in 2013.

Serovar Dublin can cause both enteritis and abortion in adult sheep, and the disease is often associated with metritis, anorexia, and loss of wool. Newborn lambs may develop diarrhea with a high mortality rate. Serovar Typhimurium is associated with acute disease, enteritis but not usually abortion. *S.* Brandenburg has affected livestock and humans in the South Island of New Zealand. The strain has caused abortions in sheep and cattle as well as gastroenteritis in calves and adult cattle. The same strain also caused disease in horses, goats, deer, pigs, and humans. Spread of the disease on farms was strongly associated with aborting ewes, which resulted in considerable environmental contamination. During the abortion season, black-backed gulls appeared to spread the disease to other farms. Other potential sources of infection were carrier sheep, contaminated water sources, and contaminated sheep dust.

Outbreaks of *S.* Abortusovis infections causing abortion storms in sheep have occurred in different European and West Asian countries. Most recently such outbreaks occurred in Switzerland during the lambing seasons of 2003/2004 to 2007/2008 with up to 70% fetal losses in affected flocks.[13]

Horses

The incidence of salmonellosis has been increasing in the horse population, particularly where horses are assembled at large clinical centers and breeding farms. Nosocomial salmonellosis is an important problem for horses in veterinary hospitals.[21] It is also possible that many of the unidentified enteritides of horses may have been associated with *Salmonella* spp.

In the UK 44 isolations of *Salmonella* spp. from clinical cases were reported in 2013. Unlike previous years *Salmonella* 4,5,12:i:-, and not *S.* Typhimurium was the most commonly isolated serovar (25%).[22]

Morbidity and Case Fatality

The morbidity rate in outbreaks of salmonellosis in calves and sheep is usually high, often reaching 50% or more. Morbidity and mortality are usually highest in calves under 12 weeks of age. In all species the case–fatality rate often reaches 100% if treatment is not provided. In outbreaks in outwintered suckler cattle herds, the morbidity varied from 14% to 60% and mortality in adult cattle from 0% to 14%. In a review of 40 cases of clinical salmonellosis in horses that were diagnosed in one clinic, the case–fatality rate was 60%. Epidemics of salmonellosis affecting up to 40% of foals under 8 days of age on one Thoroughbred horse farm have been reported.

Methods of Transmission

Salmonellas are spread by direct or indirect means. Infected animals are the source of the organisms; they excrete bacteria and infect other animals, directly or indirectly, by contamination of the environment, primarily feed and water supplies. The farm animal may be infected in different ways: by animal-to-animal transmission, especially of host-adapted serovars; by contaminated animal feed; and by a contaminated environment (soil, birds, rodents, insects, and water supplies). Liquid wastes from infected animals may contaminate the environment directly, including streams, rivers, and pastures. Bacteria may also be disseminated during the transport of infected animals and during the holding of animals in a lairage before slaughter. In these situations, the excretion of salmonellas is exacerbated by the stress imposed.

The mixing of young susceptible calves and their subsequent transportation is an efficient mechanism for the rapid dissemination of *Salmonella*. Saleyards and dealers' premises can serve as reservoirs of infection despite cleaning and disinfection. Many vehicles and markets are contaminated with *Salmonella*. The introduction of infected carrier animals into a herd is a common cause of outbreaks of clinical salmonellosis in dairy herds that are expanding in size.

The organism can persist for an average of 14 months in the environment where calves are reared. *Salmonella* spp. do not survive for more than 5 days in bovine urine not mixed with feces but will survive in dried bovine feces for up to 6 years. After a clinical outbreak of salmonellosis, for example, in a dairy herd raising its own replacements, the premises cannot be declared to be *Salmonella* free solely on the basis of freedom from clinical cases over the next few years or on the basis of comparatively high herd

performance. In large dairy herds with modern free stalls that recycle water in their manure flush systems, it may be possible to isolate *Salmonella* serovars for several years following an outbreak of clinical salmonellosis. The organisms may be found in recycled water samples, bulk tank milk filters, and the feces of calves and adult cows.

During slaughter, fecal contamination of the carcass commonly occurs and can be carried through all slaughter procedures up to the processing of the raw products. Milk can be contaminated directly by cows that excrete the organism in the udder, especially those cattle infected with SD and *S. Muenster*, both of which have adapted to colonize the bovine mammary gland. Although *S. Typhimurium* is not usually excreted in milk, except during the febrile stage of clinical disease, it has been reported to have been persistently isolated from the milk of a healthy cow. *S. Enteritidis* has been isolated from milking filters, milk from a bulk tank, and milk from one-quarter of a 5-year-old dairy cow that persistently shed the organism in the milk for several months. Milk is most likely to become contaminated by feces, either from an animal with clinical salmonellosis or from a healthy carrier animal, during the milking process. Additional sources of contamination during milking are use of polluted water or contaminated equipment. Workers who lack personal hygiene skills and have clinical salmonellosis or are chronic shedders of the organism may also contaminate milk supplies.

Airborne transmission can be a primary mode of infection of *S. Typhimurium*. Studies have shown that the organism can survive in air sufficiently long to present a significant hazard of airborne spread.

Carrier State
Because salmonellas are facultative intracellular organisms that survive in the phagolysosome of macrophages and other cells, they can evade the bactericidal effects of antibody and complement. Thus persistence of infection in animals and in the environment is an important epidemiologic feature of salmonellosis. A cow infected with SD may become a clinical case or an **active carrier,** shedding organisms constantly or intermittently in the feces. It may alternatively become a **latent carrier** with infection persisting in lymph nodes or tonsils but no salmonellas in the feces, or even a **passive carrier,** which is constantly acquiring infection from pasture or the calf-pen floor. In passive carriers invasion of tissues does not occur, and when the animal is removed from the environment the infection disappears. However, passive carriers probably multiply the salmonellas, contributing to the epidemiology of the pathogen. Latent carriers can become active carriers or even clinical cases under stress, especially at calving time or during illness. A major problem with the

control of SD infection is that latent carriers of the organism, unlike persistent excreters, cannot be readily identified by fecal culture or serologic methods. In a 3-year study of one dairy herd, the organism was isolated occasionally from the feces of adult cattle, from some cattle after parturition, and from some calves within 24 hours after birth. In some dairy herds, the organism may persist for many years with a low incidence rate of clinical disease.

For *S. Typhimurium*, which is one of the most common serovars associated with human disease, the donor can be any domestic animal species, including humans, or any wild animal or bird. Although all infected adults become carriers, it is rarely for any length of time, and calves rarely become carriers. In sheep and cattle the carrier state may persist for as long as 10 weeks, and in horses up to 14 months.

Risk Factors Predisposing to Clinical Disease
The clinical characteristics of salmonellosis in large animals vary depending on the various management systems used, the intensity of stocking, whether or not the animals are housed, and the epidemiologic characteristics of the different *Salmonella* species. Thus salmonellosis in cattle is a very serious and persistent disease in areas where it is caused principally by the host-adapted serovar SD. In contrast bovine salmonellosis associated with *S. Typhimurium* is sporadic and, even though it is fatal to individual animals, it is not a serious disease. Although there are probably similar differences with the other species, they are not particularly well defined. The difference between the diseases associated with SD and *S. Typhimurium* is the marked tendency for SD to persist in adult cattle and create a significant reservoir of carrier animals. *S. Typhimurium* does not do so as much, so that the disease is likely to subside after an initial exposure and to recur only when the source of infection, from rodents or feedstuffs, or sewage or slurry, reappears. This does not preclude the disease from persisting in a flock or herd for long periods. *S. Typhimurium* infection persisted in a large dairy herd for 3.5 years. Although the incidence rate of clinical disease declined over the study period, the organism could still be cultured from the bulk tank milk filters, which may have been associated with one cow identified as a milk excretor. Several incidents of human illness associated with *S. Typhimurium* infection following the consumption of raw milk are documented.

In hospitalized horses several studies determined an increase of developing a nosocomial *Salmonella* infection following treatment with antimicrobial drugs or nasogastric intubation as well as in horses presenting with colic at the time of admission.[21] Other studies reported an increasing risk of

developing salmonellosis with prolonged duration of parenteral treatment with penicillin G potassium.[21]

Animal Risk Factors
Except in the newborn, especially foals, infection with a *Salmonella* sp. is usually not sufficient to cause clinical salmonellosis. The response to infection with a *Salmonella* sp. varies depending on the size of the challenge dose and the immunologic status of the animal, itself dependent on colostrum intake in neonates, as well as previous exposure to infection and exposure to stressors, particularly in older animals. It is generally accepted that the intervention of some precipitating factor such as transport, intercurrent disease, anesthesia and surgery, dosing with antimicrobials or anthelmintics, acute deprivation of food, or parturition is usually necessary to cause clinical disease distinct from infection with *Salmonella* spp.

The portal of infection in salmonellosis is almost always the mouth, so that the severity of the disease in an individual, or of an outbreak in a group, depends on the degree of contamination and the environmental conditions of temperature and dryness that determine the survival time of salmonellas. Just as important is the influence of the host on the outcome of the infection. Many animals become infected naturally and are passive carriers; they shed salmonellas in their feces without clinical disease but only for the duration of their cohabitation with other infected animals. It is possible to reproduce salmonellosis experimentally in most animals using a sufficiently large dose of a virulent strain of the organism. There still remains the common occurrence of the animal that is a subclinical carrier of the infection but develops clinical salmonellosis when exposed to stressors such as long transportation, hospitalization, severe feed deprivation, or parturition.

Genetic Resistance to Salmonellosis in Domestic Animals
There is evidence of a strong genetic association with resistance to salmonellosis in several economically important domestic animal species. However, selective breeding for resistance traits is not used in control of diseases or the carriage of *Salmonella* in any of these species. The value of a particular resistance trait in reduction of disease must be balanced against other factors, such as productivity of meat and milk. The control of *Salmonella* colonization of the gastrointestinal tract of food animals would appear to be a particularly useful objective with enormous potential public health benefits. There may be a role for several inherited immunologic traits, including polymorphonuclear leukocyte function and lecithin-induced mitogenic proliferation.

The interrelationships between the risk factors of the host, the environment, and the

pathogen are described here according to species differences.

Dairy Cattle

In calves, the disease is usually endemic on a particular farm, although outbreaks can occur.

S. Typhimurium is commonly associated with enteritis or septicemia in calves younger than 2 months, whereas serovar Dublin is identified with similar frequency in young (>2 months) and adult cattle.[23] Spread between calves of a group is by the fecal–oral route. Infection of the newborn calf may be from the dam because many cows that are latent shedders become active shedders at parturition. The calves are not infected at birth but become infected from the environment.

In adult cattle, SD is the common infection and occurs sporadically, but as outbreaks when stressors occur. Spread is usually by the oral route and in cattle at pasture is greatly enhanced by persistently wet conditions. Wild mice are potential reservoirs of SD in dairy herds.

Beef Cattle Herds and Feedlots

Although salmonellosis can cause significant economic losses in beef herds and feedlots, it is not as important as in dairy cattle. Low numbers of beef cattle are found to shed Salmonella at the time of slaughter, and beef cattle do not appear to be a major risk of carcass contamination.

Sheep

Salmonellosis in sheep may occur with a range of different syndromes of variable severity, depending mainly on the particular serovar involved. Salmonella enterica subsp. diarizonae are most commonly found in sheep. Serovars of Salmonella enterica subsp. enterica commonly found in sheep include S. Montevideo, SD, S. Typhimurium, and S. Agama.

Horses

Horses are frequently passive carriers, hosting Salmonella in internal organs such as lymph nodes but not or only intermittently shedding them in feces. Accordingly the search for a carrier can be laborious and even fruitless. At least five negative cultural examinations of feces should be made before acquitting a suspected donor.[21]

As in other species age is an important risk factor for developing clinical diseases, with foals at increased risk of developing severe clinical disease and septicemia. Risk factors in foals include a history of dystocia, immaturity or prematurity, FTPI, an unsanitary environment, infection with a concomitant pathogen, or other debilitating disease and poor health of the dam.

The occurrence of salmonellosis in horses hospitalized for another disease has become a major problem and can at least in part be attributed to increased stress and immune suppression caused by illness and debilitating procedures such as anesthesia or surgery.

Immune Mechanisms

Most information on the mechanisms of immunity to Salmonella, including the safety and immunogenicity of most Salmonella vaccines, has been found experimentally in mice. In primary infections in mice, early bacterial growth in the reticuloendothelial system is controlled by the contribution of both macrophages and polymorphonuclear cells and is affected by the virulence of the strain. In lethal infections, the early growth of the bacteria in the tissues results in high bacterial numbers that lead to death of the animal. Following natural infection with Salmonella antibody, responses to LPS and protein determinants can be detected. Anti-Salmonella IgM appear in serum early after infection followed by IgG. T-cells have a critical role in the later stages of primary infection.

Environmental and Management Risk Factors

Cattle

Intensification of husbandry in all species is recognized as a factor contributing significantly to an increase in the new infection rate. Any significant change in management of the herd or a group of animals can precipitate the onset of clinical salmonellosis if the infection preexists in those animals. The risk factors for fecal shedding of Salmonella and clinical salmonellosis in dairy herds were herd size, rodent activity in housing and feed areas, use of flush water systems, and feeding brewers' products to lactating cows. Large herd size and intensive management are likely to provide an environment conducive to Salmonella shedding and chronic dairy herd infection.

Nutritional stress caused by transition diets and heat stress was associated with outbreaks in some herds. Feed withdrawal, transport stress, and the commingling of animals before slaughter can affect the number of cattle that are contaminated with bacterial pathogens such as Salmonella. However, none of the risk factors evaluated before or throughout the transport process had an impact on fecal shedding and hide or carcass contamination. The pH of rumen contents has been shown to affect the number of salmonellas surviving passage through the rumen. A high volatile fatty acid content and a low pH, such as prevails when a ruminant is on full feed, is unfavorable to salmonellas passing through the forestomachs. Feed intake depression as a result of transportation or around calving may further contribute to the risk of clinical or subclinical infection. In some herds there are sporadic cases in periparturient cows, usually within 1 week of calving.

Pastures contaminated by the feces of infected animals present an important source of infection for grazing animals. In grazing cattle there is a distinct seasonal incidence in late summer, fall, and early winter, probably because of greater exposure to infection at pasture. Temperature and wetness are most important, as salmonellas are susceptible to drying and sunlight. S. Typhimurium can remain viable on pasture and in soil, still water, and feces for up to 7 months. The use of "slurry" as a means of disposal of animal manure from cow housing is a highly efficient means of spreading Salmonella infections. The chance of cows becoming infected increases considerably if they are grazed soon after the slurry is applied, and is less likely during dry, sunny periods and when there is sufficient pasture growth to avoid it being eaten right down to the ground surface. The survival time of Salmonella spp. in cold liquid manure depends on several factors, including pH of the slurry and the serotype of the organism. It can be as long as 28 weeks.

Salmonella contamination of water supplies of calves and cows was identified as a potential source of exposure. Water offered to weaned dairy calves in a continuous water-tank–filling method was a risk factor compared with a valve on demand and a water pH of more than 8. Drinking water can remain infected for long periods, as long as 9 months, and in cattle at extensive pasture infected drinking water in stagnant ponds is a significant source of infection. Feedlot playas (temporary shallow lakes) are frequently contaminated with many Salmonella serotypes. Using playas as a source of water for feedlots can be a source of Salmonella, and they should not be used to cool cattle in the summer months, or for dust abatement, or for irrigation of crops. Wildlife, birds, and migratory waterfowl have access to these bodies of water and, because of their size and number, there is little that can be done to prevent them from becoming contaminated.

Infection can be introduced by infected domestic animal carriers. For example, in large-scale calf-rearing units many of the calves are infected when they are picked up from their home farms and, if they are penned in groups, all calves in the group are soon infected. The infection can spread among calves penned individually, which suggests that aerosol spread may occur. S. Typhimurium can survive for several months in calf-rearing premises despite depopulation, cleansing, and disinfection. However, because of the failure of most calves to continue as carriers, they are usually free of infection within 6 weeks of arrival.

Contaminated feedstuffs, carrier animals, and infected clothing of visitors and casual workers are the most common methods of introducing infection. Less common methods include free-flying birds and nematode larvae that are already infected with salmonellas. Salmonellas have been isolated from a wide variety of wild animals that

could act as reservoirs for infection of domestic animals under certain conditions.

Previous antimicrobial treatment of cattle or calves with laboratory-confirmed *Salmonella* infections increases the probability of isolating salmonellas. Vaccination with a modified-live vaccine producing a systemic reaction, treatment with irritant compounds such as carbon tetrachloride for fluke, and fluke infestation can also precipitate clinical disease.

Sheep

In range sheep, the most common occurrence of the disease is during a drought when sheep are concentrated in small areas of surviving grass heavily contaminated by feces. Sheep held in holding yards or transport vehicles previously occupied by sheep for long periods are also susceptible to clinical disease. This is most likely to occur when they drink from puddles of water, especially in heavily contaminated yards, or when they are exposed to recycled dip wash. In sheep, the disease is commonly associated with deprivation of feed when animals are assembled for vaccination, anthelmintic administration, or shipment over long distances. Lambs in feedlots are susceptible to salmonellosis within a few weeks after arrival in the lot.

The modern development of pen lambing, in which ewes about to lamb are brought into small pens, is also a means of potentiating spread from a chronic shedder. In all these situations feed stress by deprivation is likely to contribute to susceptibility. Field outbreaks in range sheep have been recorded. In some instances they have been caused by the use of unsterilized bonemeal as a phosphorus supplement. Outbreaks occurring in sheep on a number of farms in the same area at the same time have been ascribed to contamination of drinking water by birds eating carrion. Heavy dosing with zinc oxide as a prophylaxis against facial eczema is also credited with precipitating outbreaks of salmonellosis in young sheep.

Horses

In adult horses, most clinical salmonellosis occurs after the stress of transport and mostly in horses that are overfed before shipment, receive little or no food or water for the duration of a protracted journey, and are fed excessively on arrival. Cases can appear 1 to 4 days later. Groups of horses that have been exposed to a contaminated environment, such as saleyards or railroad yards, may experience outbreaks in which up to 50% are affected. Multiple serotypes of *S*. Enteritidis have been isolated from the mesenteric lymph nodes of 71% of healthy horses examined at an abattoir, which indicates that extraintestinal infection occurs in the horse as it does in other species. In the light of the high carrier rate in this species, it is surprising that there are not more outbreaks.

The occurrence of salmonellosis in horses hospitalized for another disease has become a major problem for veterinary teaching hospitals and private equine practices that provide surgical veterinary care. In these circumstances there is a constant reintroduction of carriers of the disease, a persisting contamination of the environment, and a large population of horses, all of which are under stress because of anesthesia, surgical invasion, or intercurrent disease and many of which are exposed to oral and parenteral treatment with antimicrobials, which appears to greatly increase their chances of acquiring salmonellosis. Horses in which nasogastric tubes were passed were at 2.9 times greater risk of having salmonellas isolated than horses that did not undergo this procedure. Horses treated with antibiotics parenterally were at 6.4 times greater risk, and those treated with antimicrobials orally and parenterally were at 40 times greater risk of developing salmonellosis, compared with horses not receiving such treatment. In hospitalized horses, the factors found to be associated with fecal shedding of salmonellas included diarrhea at the time of admission as well as fever and a change of diet while hospitalized.

Outbreaks of nosocomial salmonellosis among horses in a veterinary teaching hospital have been described. Case–fatality rates may be high, necessitating closure of the hospital for complete disinfection and systematic sampling of the environment to detect the presence of persistent *Salmonella*. Strict isolation of hospitalized horses that have been shedding *Salmonella* and the planning and implementation of infectious disease control (IDC) throughout the hospital are necessary. Bleach is an effective disinfectant on the largest number of surfaces. The factors potentially associated with *Salmonella* shedding among horses hospitalized for colic at a veterinary teaching hospital were examined. *Salmonella* spp. were detected in the feces of 9% of patients at least once during hospitalization. They were more likely to shed *Salmonella* if diarrhea was evident 6 hours or less after hospitalization and the duration of hospitalization exceeded 8 days (OR 20.3), laminitis developed during hospitalization (OR 12.0), results of nasogastric intubation were abnormal (OR 4.9), leukopenia was evident 6 hours or less after hospitalization (OR 4.6), or travel time to the teaching hospital exceeded 1 hour (OR 3.5). Horses treated with a probiotic did not differ from control horses in likelihood of fecal shedding of *Salmonella* (OR 1.5) or prevalence of clinical signs.

Salmonellosis is also one of the common causes of neonatal septicemias of foals, and the disease may occur as endemic on particular studs, or there may be outbreaks with many foals being affected at one time. The common management strategy on "visiting stud-farms" of bringing mares and newborn foals to communal studs and then bringing

them daily to a central point for observation and teasing is also likely to facilitate spread of an infection through a group of foals.

Contaminated Feedstuffs

Housed animals are generally more susceptible to infection from purchased feeds containing animal by-products than are pastured animals, which are again more susceptible to animal-product–based fertilizers. Organic feedstuffs, including bonemeal, are being increasingly incriminated in the spread of salmonellosis. Most of the contamination of meat and bonemeal occurs after heat sterilization, especially if the material is left in digester tanks. Fishmeal is one of the most frequently and badly contaminated feedstuffs. These feed meals need to be heated at 82°C (180°F) for an hour to be sterilized. The contamination of these materials may derive from antemortem infections in the animals used to make the by-product, but soiling of the material at the preparation plant or abattoir or during storage may also occur. Stored feed not of animal origin, especially grain, is also commonly contaminated by the droppings of rodents that infest it and this can lead to sharp outbreaks of salmonellosis caused by *S*. Typhimurium. Of special importance is colostrum stored without refrigeration. If the colostrum is contaminated initially, multiplication of salmonellas may occur and transmission of the infection is likely. Dried milk products appear to be relatively safe.

Pathogen Risk Factors

Salmonellas are facultative intracellular organisms that survive in the phagolysosome of macrophages and other cells and can therefore evade the bactericidal effect of antibodies. Compared with other organisms of the same family, salmonellas are relatively resistant to various environmental factors. They multiply at temperatures between 8°C and 45°C, at water activities above 0.94, and in a pH range of 4 to 8. They are also able to multiply in an environment with a low level of or no oxygen. The bacterium is sensitive to heat and will not survive temperatures above 70°C. It is sensitive to pasteurization. Salmonellas have been shown to be resistant to drying, even for years, especially in dried feces, dust, and other dry materials such as feeds and certain foods. Prolonged survival in water and soil has also been described. They are quite sensitive to beta- and gamma-irradiation.

Salmonella spp. have 13 predicted fimbrial loci, of which most are deployed in vivo. **Fimbriae** are required for the attachment onto host cells, colonization, and biofilm formation, but not specifically for intracellular survival.[24]

Flagella have been implicated as virulence factors because they may enhance motility and the invasiveness of the bacterium. This view, however, remains controversial because flagella that consist of flagellin

monomers are potent inducers of innate immunity. In the intestinal epithelium flagellin induces inflammation while inhibiting apoptosis.[24]

Like in other gram-negative bacteria, the cell membrane of salmonellas contain LPS (endotoxins), which on release, can induce shock in the host organism, contributing to its virulence. The O-antigen LPS of salmonellas is toxic and an important virulence factor, and immunity directed against the :LPS is thought to be of major importance in the host defense against salmonellosis.

Salmonellas possess a **type three secretion system (TTSS)** that is required for invasion of epithelial cells of the intestine. The TTSS functions like a needle allowing the bacterium to inject its outer proteins, the so-called effector proteins, into the host cell to which it is attached. Effector proteins signal the host cell to take up the bacterium, which consequently is engulfed into the host cell encased in a vesicle called the *Salmonella*-containing vacuole.[25]

Salmonellas have acquired at least five **SPIs** through horizontal gene transfer. SPI-1 and SP-2 in particular are important determinants of the pathogen's virulence.

The capacity to produce **superoxide dismutase** is another virulence factor that protects salmonellas from reactive oxygen species produced by the host cells to kill intracellular pathogens.[24]

In states of iron deprivation salmonellas have the capacity to produce two potent siderophores, **enterobactin** and salmochelin, allowing them to overcome this limitation.[24]

Antimicrobial Resistance of *Salmonella*

Strains of *Salmonella* spp. with resistance to antimicrobials are now widespread in both developed and developing countries. Since 1990 there have been considerable increases in the occurrence of multiply-resistant strains of *Salmonella* spp. in many developed countries.

AMR of salmonellas has been and is a major point of concern and controversy in veterinary medicine and human public health. The continued use of antimicrobials in veterinary medicine, and in food animals in particular, is believed to be a major cause of selective pressure that leads to the appearance and persistence of resistant strains. The resistance is usually to multiple antimicrobials and its existence is considered as a potential risk factor. The significance of AMR is most obvious in its impact on the treatment of human infections. AMR of *Salmonella* spp. causing clinical disease leads to increased morbidity, mortality, and treatment costs and limits the choice of antimicrobials for the treatment of systemic salmonellosis in humans.[26] Antimicrobial-resistant *Salmonella* infections can further complicate antimicrobial therapy of other infections; prior antimicrobial therapy allows fewer numbers

of antimicrobial-resistant salmonellas to cause symptomatic infections, and an increase in the proportion of salmonellas that are antimicrobial resistant will increase the overall frequency of salmonellosis. Infections in humans associated with antimicrobial-resistant salmonellas are increasing and have become a cause for public health concern. Resistance to third- and fourth-generation cephalosporins and fluoroquinolones is considered of greatest public health importance, because these are the antimicrobials of particular relevance for the treatment of human salmonellosis.[27]

The prevalence of *Salmonella* isolates that are antimicrobial-resistant varies widely between countries, animal species, and serovars. National and species-specific differences have been attributed to differences in the practice of antimicrobial use between animal species, production systems, and countries. Generally, AMR among salmonellas is higher in the United States than in other countries, is more common in isolates from swine than from other species, and is more common in serovar Typhimurium than in other *Salmonella* serovars. The comparison of AMR levels in different studies consistently showed that AMR is much less common in isolates from healthy individuals than in isolates from diseased animals.

During the 1990s AMR of *Salmonella* became an important issue because of a global epidemic of the *S.* Typhimurium DT104 in animals and humans that was frequently resistant to a wide range of commonly used antimicrobials for the treatment of salmonellosis in humans. Multidrug-resistant *S.* Newport has been spreading on an epidemic scale in both animals and humans throughout the United States. In addition to the resistance to five drugs found in *S.* Typhimurium DT104, *S.* Newport, called Newport MDR-AmpC, is also resistant to amoxicillin–clavulanic acid, cephalothin, cefoxitin, and ceftiofur and exhibits decreased susceptibility to ceftriaxone. The emergence of Newport MDR-AmpC strains in humans has coincided with the emergence of Newport MDR-AmpC infections in cattle. Although the role of farm animals as a primary source of *Salmonella* infection in humans is not undisputed, it should be noted that transfer of AMR between species does not necessarily require pathogen transfer.[28] Resistance genes can be carried on plasmids or integrons, which are potentially independently mobile DNA elements encoding a site-specific integration system responsible for the acquisition of multiple small mobile elements called gene cassettes which, in turn, encode antibiotic resistance genes. Integrons have also been described on plasmid DNA in *S.* Enteritidis. Plasmids and integrons can be transferred between animal-associated *Salmonella* and *E. coli,* and identical *CMY-2* genes carried by similar plasmids have been identified in humans, suggesting that the *CMY-2* plasmid

has undergone transfer between different bacterial species and may have been transmitted between food animals and humans.

A survey including 380 *Salmonella*-positive samples from diseased animals submitted to different diagnostic labs in the United States revealed that 82% of the samples were resistant to at least one antimicrobial and 70% to at least three antimicrobials.[29] When stratified by animal species the highest prevalence rates of resistance to at least one antimicrobial were found for swine (92%), followed by cattle (77%), chickens (68%), and horses (29%).[29] Approximately 35% of cattle isolates and 10% of equine isolates were resistant to over 9 antimicrobials. The serovars showing resistance to 5 to 8 antimicrobials were *S.* Typhimurium (71%), SD (69%), and SCS (40%). In this study resistance was most often observed to tetracyclines (78%), streptomycin (73%), sulfamethoxazole (68%), and ampicillin (54%).[29] Worryingly, 36% of cattle isolates exhibited resistance to ceftiofur, a third-generation cephalosporin extensively used in cattle practice in the United States. Resistance to nalidixic acid, a compound used to detect emerging resistance to fluoroquinolones, was observed in isolates from chicken (9%), cattle (8%), and turkeys (6%).

The annual UK survey of 2013, including a total 2886 isolates from submissions of clinical cases to diagnostic laboratories, reported resistance to at least one antimicrobial in 35.8% but 87.1% of swine isolates.[27] When stratified by serovar 69.7% of *S.* Typhimurium but only 5.1% of SD isolates were resistant to at least one antimicrobial. Of the serovars other than *S.* Typhimurium and SD 38.8% were resistant to at least one antimicrobial substance.[27] AMR was most often observed to tetracyclines (26.1%), sulfonamide compounds (24.8%), streptomycin (18.8%), and ampicillin (13.2%). Resistance to nalidixic acid was observed in 5% of all isolates and was most common in turkeys (20.2%), other avian species (14.6%), chickens (8.0%), and dogs (6.0%). Isolates from cattle were resistant to this compound in 1.4%. Resistance to ceftazidime occurred in 0.03% of all samples.[27]

A smaller study from Australia including 76 *Salmonella*-positive fecal samples from diarrheic calves reported resistance to at least one antimicrobial in 27.6% of all isolates. Resistance to over four antimicrobials occurred in 14.3%.[19] Most common resistance was to streptomycin (25.5%), a combination of sulfonamides (21.1%), and ampicillin (18.4%). Resistance to nalidixic acid was not observed in this study.

Zoonotic Implications

Salmonellosis, a common human intestinal disorder primarily associated with *Salmonella*-contaminated meats and poultry, causes over 90 million human cases every year. Annual costs of human salmonellosis

have been estimated to be approximately €3 billion in the EU and $2.7 billion in the United States.[30] The Centers for Disease Control estimate approximately 1 million illnesses per year, 19,000 hospitalizations, and 380 annual deaths.[31] In the EU approximately 109,000 confirmed cases of human salmonellosis have been reported in 2009, corresponding to 23.7 cases per 100,000 population.[30]

The disease has assumed increasing importance in recent years because of the much more frequent occurrence of human salmonellosis, with animal salmonellosis as the principal reservoir. *S.* Enteritidis and *S.* Typhimurium are the serovars most commonly associated with human illness. Human *S.* Enteritidis cases are most commonly associated with the consumption of contaminated eggs and poultry meat, whereas infection with *S.* Typhimurium is typically associated with the consumption of pig, poultry, or bovine meat.[30] The most serious risk is that the transmitted bacteria will have acquired resistance to specific antibiotics because the animals from which they originate have been treated with the particular antibiotics repeatedly or over a long period.

Various clinical forms of salmonellosis can occur in veterinarians working with *Salmonella*-infected animals. Gastroenteritis, bacteremia, and other systemic abnormalities can occur. Cutaneous salmonellosis has been reported in veterinarians attending to infected cattle at the time of parturition. The disease was characterized by pustular dermatitis from which *S.* Virchow and SD were isolated. Veterinarians may develop skin lesions after obstetric deliveries, even after hygienic precautions and the use of abundant amounts of disinfectant creams and careful washing of the arms and hands.

Salmonella Typhimurium DT104

Throughout the 1990s there was a global epidemic of multidrug-resistant *S.* Typhimurium DT104 (DT stands for definitive phage type) in animals and humans. It was important because of its widespread prevalence, its presumed zoonotic nature, and the high frequency of multiple AMR. *S.* Typhimurium DT104 was first reported in the UK in 1984 and emerged in the 1990s as an increasing cause of *Salmonella* infections in humans and animals in England, Wales, and Scotland, as well as other European countries such as Germany, France, Austria, and Denmark and Canada. A wide range of potential reservoirs is associated with this infectious strain, from humans to the traditional food animals such as poultry, cattle, sheep, and pigs. Over a 1-year period in Scotland it was the predominant *Salmonella* isolated from nine species of animal (cattle, pigs, sheep, chickens, pigeons, horses, cats, dogs, and rabbits). A large outbreak of salmonellosis caused by multiply-resistant (mr) DT104 occurred in people in England who had consumed milk from a dairy that received raw milk supplied by two farms. The DT104 was isolated from the milk filter, and failure of on-farm pasteurization was thought to be the cause. Strains of the organism from humans, the dairy cattle, and the milk filter showed decreased susceptibility to ciprofloxacin.

All isolates were resistant to at least one antimicrobial and 98% were resistant to multiple antimicrobials, with R-type ACTSp being the predominant resistance pattern. In the UK, a clonal strain of mrDT104 resistant to at least five antimicrobials (ampicillin, chloramphenicol, streptomycin, sulfonamides, and tetracycline; R-type ACSSu T) was detected in humans in 1984 and cattle in 1988. The organism has emerged as an important cause of diarrhea in horses in Ontario.

The organism has been found in a variety of human foods, including salami, sausages, chicken, burgers, oysters, and vegetables. Human infections have been associated with contact with farm animals and from consumption of contaminated foods such as chicken, pork, sausages, meat pastes, and beef. The organism's ecology, its precise reservoirs, and its distribution in the human food chain are unclear. Clinical signs in humans infected with DT104 include diarrhea, fever, headache, nausea, and vomiting. Septicemia may develop in a small percentage of cases with potential complications of meningitis and foci of infection in bones and joints.

Economic Importance

Salmonellosis is a significant cause of economic loss in farm animals because of the costs of clinical disease, which include deaths, diagnosis, and treatment of clinical cases, diagnostic laboratory costs, the costs of cleaning and disinfection, and the costs of control and prevention. In addition, when the disease is diagnosed in a herd it can create considerable apprehension in the producer because of the difficulty in identifying infected animals. The veterinarian is also often in a difficult position because the diagnosis, treatment, and control of the disease are less than reliable, and it is difficult to provide advice with confidence. An estimation of the economic impact of an outbreak of SD infection in a calf-rearing unit indicated that the cost of disease represented a substantial proportion of the gross margin of rearing calves. The losses incurred by livestock producers include reduced feed efficiency and reduced weight gains or deaths because of salmonellosis.

PATHOGENESIS

The pathogenesis of salmonellosis is a complex and multifactorial phenomenon. The nature of the disease that occurs following infection is dependent on the specific combination of serovar and host known as serovar–host specificity. A range of infections is included in the term *salmonellosis*.

The most common type of infection is known as "the carrier state," in which carriage of the organism is not accompanied by clinical abnormalities or clinical disease. In production animals, these carriers are of importance because they may serve as reservoirs for further spread of infection through shedding and may be present as contaminated food products.

The evolution of host-specific *Salmonella* serovars is considered to be associated with an increase in pathogenicity for the specific host. The hypothesis is based on the fact that broad-range serovars (Typhimurium and Enteritidis) are generally associated with severe disease only in young animals, whereas host-restricted serovars cause high mortality in both young and adult hosts.

The pathogenesis of different *Salmonella* serovars possessing different degrees of host restriction have been studied in young lambs to evaluate the basis of the serovar–host specificity in sheep. Infection with *S.* Abortusovis resulted in clinical signs of salmonellosis, including a fever and bacterial dissemination to systemic tissues. This confirms the virulence of the strain with sheep. *S.* Gallinarum caused relatively mild disease but is virulent in chickens. SD was virulent in sheep, confirming its association with ovine salmonellosis. The apparent specificity of a serovar for a particular host or range of hosts as defined by epidemiologic data is influenced not only by bacterial virulence but also by the ability of the serovar to circulate within the population of the host.

Infection

Salmonella infects animals and humans by the oral route. Following ingestion, a proportion of the organisms resists the low pH of the stomach, reach the distal ileum and the cecum, invade the mucosa, and replicate in the submucosa and Peyer's patches.

In young animals, and in adults whose resistance has been lowered, spread beyond the mesenteric lymph nodes occurs, and the infection is established in the reticuloendothelial cells of the liver, and from there it invades the bloodstream. These steps in the infection process can occur very rapidly. For example, in newborn calves, SD when taken by mouth can be found in the bloodstream 15 minutes later. In older calves bacteria can be isolated from the intestinal lymph nodes 18 hours after their oral administration. Provided a sufficient number of a sufficiently pathogenic serotype is used, the disease is reproducible with pure cultures, for example, of *S.* Typhimurium in lambs, SCS in pigs, SD, *S.* Typhimurium, and *S.* Enteritidis in calves, and *S.* Typhimurium in horses. Once systemic infection has been established, salmonellosis as a disease can develop. Its principal manifestations are as septicemia, enteritis, abortion, and a group of localizations in various tissues as a result of bacteremia.

Septicemia, Bacteremia, and the Carrier State

After invasion of the bloodstream occurs, a febrile reaction follows in 24 to 48 hours, and the acute phase of the disease, similar to that seen in natural cases, is present 3 to 9 days later. The early septicemia may be rapidly fatal. If the systemic invasion is sufficient to cause only a bacteremia, acute enteritis may develop, and abortion is a common final sequel in sheep and cattle. Many animals survive this stage of the disease, but localization of the salmonellas occurs in mesenteric lymph nodes, liver, spleen, and particularly the gallbladder. In healthy adults there may be no clinical illness when infection first occurs, but there may be localization in abdominal viscera. In either instance the animals become chronic carriers and discharge salmonellas intermittently from the gallbladder and foci of infection in the intestinal wall into the feces and occasionally into the milk. For this reason, they are important sources of infection for other animals and for humans. Carrier animals may also develop an acute septicemia or enteritis if their resistance is lowered by environmental stresses or intercurrent infection. Salmonellas can reside intracellularly where they are able to escape antibody-mediated killing, and the numbers of organisms are controlled by cellular defense mechanisms involving the macrophages in which they reside.

Enteritis

Enteritis may develop at the time of first infection or at some other time in carrier animals. The best information available on the pathogenesis of enteritis is derived from the experimentally produced disease. In most instances the disease is produced by the administration of massive doses of bacteria, and this may result in the production of a different syndrome from that which occurs naturally. The pathogenesis of enteric salmonellosis is much more complex than cholera, involving an increase in mucosal cell cyclic AMP content and prostaglandin concentration as well as an inflammatory response to the invading bacteria. Intestinal invasion is a characteristic feature of *Salmonella* pathogenesis. Within minutes of injecting ileal loops in calves, *Salmonella* can be seen to invade both M-cells and enterocytes that overlie domed villi associated with lymphoid follicles and absorptive villi. The organism must invade the intestinal mucosal epithelium to cause disease.

After oral infection with SD, invasion occurs through the intestinal wall in the terminal ileum and cecum and progresses only as far as the mesenteric lymph nodes. Progress beyond this point, and the development of salmonellosis, is determined by factors such as immune status and age of the animal, whether or not it is exposed to stress, and the virulence of the strains. A number of characteristics of the bacteria influence their virulence, including the presence of adhesin pili and flagella, cytotoxin, enterotoxin, LPS, and the inflammatory response that they initiate in the intestinal wall. The effects of some of these factors are not limited to the intestinal tract and also contribute to the systemic complications of salmonellosis. The SD virulence plasmid mediates systemic infection in cattle by causing macrophage dysfunction.

SD infections in calves have been used to create the disease experimentally. In calves 6 to 7 weeks of age, an oral dose of the organisms is fatal within 24 hours, with the animals dying of septicemia and an acute necrotizing panenteritis. Calves 12 to 14 weeks of age developed a progressive fatal diarrhea within 1 week following infection. Experimental infection of ligated ileal loops from calves with *S.* Typhimurium results in an acute neutrophilic inflammatory response associated with invasion of Peyer's patches.

In calves, infection is initiated by bacterial invasion of the mucosal epithelium of the distal ileum or proximal colon causing extensive local tissue damage that leads to shortening of the villi and degeneration of the enterocyte layer. *Salmonella* invasion induces potent inflammatory response characterized by a massive infiltrate of polymorphonuclear cells into the lamina propria and submucosa and secretion of fluid into the intestinal lumen. Damage to the enterocyte layer and the secretion of fluid into the intestinal lumen results in diarrhea, and the fever is caused by circulating inflammatory cytokines.

Experimentally induced *Salmonella* infection in calves results in an increase in serum haptoglobin levels within 3 days of challenge. By day 3 after experimental infection the serum haptoglobin levels increased to a median level of 212 μg/mL, whereas placebo controls had median levels of 0 μg/mL. The increased levels closely reflected the clinical findings of infection and are considered useful markers of infection severity in salmonellosis in calves.

In **sheep**, the experimental disease produced by oral dosing with *S.* Typhimurium includes an early acute enteritis of the small intestine at 24 hours. At 5 to 8 days there is hemorrhagic and necrotic typhlitis and the infection is established in mesenteric lymph nodes and the liver. Experimental SD infection of the mammary gland of dairy cattle results in a persistent infection associated with a chronic active mastitis similar to carriers with naturally acquired SD infection.

In ponies with experimental infection with *S.* Typhimurium orally, there is much variation in the time after infection that the various signs appear. Pyrexia, neutropenia, and high fecal *Salmonella* counts coincided on the second and fourth days, but diarrhea occurred in only some ponies and then on the third to eleventh days after inoculation. Positive agglutination tests were recorded from day 1 but were mostly during the period 6 to 12 days postinoculation. The neutropenia of the early stages of the disease is transient, and neutrophilia occurs when diarrhea commences.

The characteristic **fever** and **leukopenia** of **equine salmonellosis** have been attributed to the release of endotoxin from the bacteria during invasion of, and replication within, the intestinal epithelium. The equine colonic mucosa can respond to cholera toxin, which causes an increased secretion of chloride, sodium, and water into the intestinal lumen. The enterotoxin activity of *S.* Typhimurium of equine origin has been compared with cholera enterotoxin.

Although there is sufficient obvious enteritis to account for the diarrhea that characterizes the disease, there appear to be other factors involved. For example, it has been shown experimentally that in *Salmonella* enteritis there is stimulation of active chloride secretion combined with inhibition of sodium absorption, but invasion of the mucosa is not essential for these changes to occur. These observations are of interest in light of the known hyponatremia that characterizes the disease. Studies of calves with salmonellosis have shown that the fluid loss associated with the diarrhea of this disease is much greater than in other calf diarrheas. This, together with a large solid matter output, contributes to the significant weight loss occurring in salmonellosis.

Abomasitis

S. Typhimurium DT104 has been associated with some independent outbreaks of abomasitis in veal calves. Abomasitis was reproduced experimentally by oral infection of calves.

Abortion

Abortion is a common manifestation of salmonellosis in cattle between days 124 and 270 of gestation. When infection is associated with SD, the organism multiplies in the placenta, having been seeded there from a primary lesion in other maternal tissues. Fetal death has already occurred in many cases, because of its invasion by bacteria, but live calves also occur, suggesting that the placental lesion is the critical one. *S.* Montevideo, *S. enterica* subsp. *diarizonae*, and *S.* Abortusovis all are frequently associated with a significant number of outbreaks of abortion in ewes.[13,20] Abortion caused by *S.* Abortusovis infection typically occurs during the second half or last third of pregnancy. In horses *S.* Abortusequi is typically associated with late abortion (7–8 months of gestation).

Terminal Dry Gangrene, Osteitis, and Polyarthritis

Terminal dry gangrene caused by endarteritis of the extremities of the limbs, ears, and tail may occur in calves with SD infection. Epiphyseal osteomyelitis affecting the metaphyses, and polysynovitis and arthritis are also possible sequelae.

CLINICAL FINDINGS

The most common clinical manifestation of salmonellosis is enteritis, but a variety of other conditions including acute septicemia, abortion, arthritis, and respiratory disease are frequently observed.

The disease is most satisfactorily described as three syndromes classified arbitrarily according to severity as **septicemia, acute enteritis, and chronic enteritis.** These are described first, but the differences between the animal species are sufficiently significant to justify describing the disease separately in each of them.

Septicemia

This is the characteristic form of the disease in newborn foals, calves, and lambs. Commonly, there is profound depression, dullness, prostration, high fever (40.5–42°C, 105–107°F), and death within 24 to 48 hours.

Acute Enteritis

This is the common form in adult animals of all species. There is a high fever (40–41°C, 104–106°F) with severe, fluid diarrhea, sometimes dysentery, and occasionally tenesmus. The fever often subsides precipitously with the onset of diarrhea. The feces have a putrid smell and contain mucus, sometimes blood, and fibrinous casts, which may appear as complete tubular casts of intestine, and intestinal mucosa in sheets or casts. There is complete anorexia but in some cases increased thirst. The heart rate is rapid, the respirations are rapid and shallow, and the mucosae are congested. Pregnant animals commonly abort. The case–fatality rate without early treatment may reach 75%. In all species, severe dehydration and toxemia occur and the animal loses weight, becomes weak and recumbent, and dies in 2 to 5 days. Newborn animals that survive the septicemic state usually develop severe enteritis, with diarrhea becoming evident at 12 to 24 hours after the illness commences. If they survive this stage of the illness, residual polyarthritis or pneumonia may complicate the recovery phase.

Chronic Enteritis

This is a common form in pigs following a severe outbreak, and occurs occasionally in cattle and adult horses. In calves there is intermittent or persistent diarrhea, with the occasional passage of spots of blood, mucus, and firm fibrinous casts; intermittent moderate fever (39°C, 102°F); and loss of weight leading to emaciation. Although chronic enteritis may occur initially, it usually succeeds an acute episode.

Bovine Salmonellosis

The disease associated with SD is usually endemic on a particular farm, with sporadic cases occurring when individual animals are exposed to stress. Severe outbreaks are rare but do occur when there is severe stress, usually acute nutritional deprivation, applied to the entire herd.

When S. Typhimurium is the cause, it is usual to have a single animal or a small number of animals affected at one time. When the disease is in the calf population it is usual for it to be much more severe, with many affected, either as a point outbreak or, when there is a succession of calves, a continuing occurrence of the disease. The emphasis therefore is generally on the occurrence of individual, sporadic cases in newborn calves and recently calved cows. Depending on the geographic region other less commonly occurring serovars that have been associated with clinical disease in cattle and calves include S. Newport, S. Agona, S. Infantis, S. Enteritidis, S. Mbandaka, S. Muenster, and S. Bovismorbificans.[16-19] S. Muenster in a dairy herd has been associated with abortions, diarrhea in adults and calves, and shedding of the organism in the milk of about 8% of the cows.

Septicemia is the common form of the disease in newborn calves under a few weeks of age. There is depression, toxemia, fever, dyspnea, and weakness, and nervous signs, including incoordination and nystagmus, may occur. Diarrhea and dysentery may occur but are not common.

Calves older than a week and adults are usually affected by **acute enteritis**, followed in survivors by abortion in pregnant cows and polyarthritis in calves. In severe cases of enteritis, there is often dysentery, with whole blood passed in large clots, and complete agalactia in lactating cows. Abdominal pain, with kicking at the abdomen; rolling; crouching; groaning; and looking at the flanks, may occur in adult cattle. Rectal examination at this stage usually causes severe distress.

Chronic enteritis with inappetence, reduced weight gain, and unthriftiness may follow an attack of acute enteritis or be the only manifestation of the disease. Abortion is a common sequel in pregnant cows that survive an attack of acute enteritis. However, infection with SD is also a significant cause of abortion in cattle without there having been any clinical signs other than retained placenta. A sequel to some cases of apparent enteric salmonellosis is the development of terminal dry gangrene caused by endarteritis of the extremities, including ear tips, tail tips, and the limbs from the fetlock down.

Terminal dry gangrene of the extremities of calves is characterized by lameness, swelling of the hindlimbs below the fetlocks, and separation of the skin above the fetlock. The distal portion of the limb is cool, not painful, and the skin is dry or moist. There is a clear line of demarcation of the skin at the level of the fetlock joints between the normal proximal skin and the distal necrotic tissue. The phalanges may be separated from the metatarsus. The tips of the ears may be indurated and deviated medially, and the distal aspect of the tail may be dry and shriveled.

Abortion caused by SD may occur spontaneously without any previous clinical evidence of salmonellosis in the herd and occurs from days 124 to 270 of gestation. Cows that abort may be ill with a fever, anorexia, and hypogalactia, and some will retain fetal membranes. In a number of cases, calves may be born shortly before term and die in the perinatal period. S. Muenster has also been implicated in abortions in a dairy herd.

The experimental disease produced by infecting adult cattle with SD by mouth varies from no clinical illness to fatal dysentery. Abortion occurs in some pregnant females. Many suffer pyrexia, anorexia, and mild diarrhea. Experimental infection of calves with S. Typhimurium has the same general effect, with more severe syndromes occurring in younger calves. Chronic cases may develop bone lesions, including osteoperiostitis and osteomyelitis, sometimes with epiphyseal separation. Experimental infection with S. Enteritidis causes profuse yellow diarrhea, fever, dehydration, frequent cough, and a mucopurulent nasal discharge.

Ovine and Caprine Salmonellosis

Depending on the geographic region the serovars most commonly associated with clinical disease in sheep include S. Typhimurium, S. enterica subsp. diarizonae, S. Montevideo, SD, S. Abortusovis, and S. Enterididis.[13,20,32] Salmonellosis in sheep may occur as acute enteritis or abortion on a flock scale. However, in the early stages of the outbreak and young lambs the infection may present as septicemic form. After experimental infection of sheep with SD, fever and diarrhea are followed in pregnant ewes by abortion. Abortion is also common in the naturally occurring disease associated with all serovars causing clinical disease, not just S. Abortusovis. Some ewes die after abortion, and many of the lambs born alive die subsequently. Fever and diarrhea, followed by abortion, have also been produced experimentally in sheep by the administration of SD.

In goats, naturally occurring cases are not often reported. SD is the usual pathogen in those countries where it is a resident, but S. Typhimurium is also recorded as a cause. Peracute septicemia, in newborn animals, and acute enteritis occur with signs and lesions similar to those in cattle.

Equine Salmonellosis

Salmonellosis is one of the common causes of infectious diarrhea in horses, and S. Typhimurium and S. Agona are the most commonly isolated serovars from clinical cases. The disease in horses usually occurs in a single animal and is sporadic. However, outbreaks do occur in newborn foals, in groups of horses recently transported, and in horses hospitalized in veterinary clinics. Analysis of spatial and temporal clustering of horses with salmonellosis in an intensive

care unit of a veterinary teaching hospital suggested that affected horses were grouped in time. Experimental infection of horses by oral administration of *S.* Typhimurium produces a disease similar to the natural disease. The incubation period may be as short as 24 hours. The following four syndromes occur:

- **Asymptomatic shedding** of *S.* Typhimurium in feces intermittently or continuously for short periods of 4 to 6 days
- A **subacute enteric form in adult horses** on farms in which the disease is endemic, with fever, depression, and anorexia but without severe diarrhea, although the feces may have the consistency of soft bovine feces. There is no other obvious intestinal abnormality. There may be a neutropenia with a left shift.
- Severe, acute fulminating enteritis with diarrhea, fever, dehydration, and neutropenia occurs. There is abdominal pain, which may be sufficiently severe to stimulate violent actions. This is the common form of the disease, occurring commonly in adults that are exposed to stress in one form or another. Newborn and young foals up to 8 days of age also often have this form of the disease, characterized by depression, anorexia, and diarrhea.
- **In foals up to about 2 days of age there is a highly fatal septicemia.** Localization in survivors includes lesions in the brain, causing meningoencephalitis and polyarthritis. Fatal meningoencephalomyelitis caused by *S.* Agona has been described in a 7-day-old foal. Clinical findings included head tilt, seizures, and diarrhea.

S. Abortusequi has become a rare, only occurring in few countries worldwide. Infection with this serovar is associated with abortion in the last third of gestation, followed by retained placenta and metritis. Foals born alive may develop acute septicemia in the first week of life or polyarthritis in the second week of life. In stallions orchitis, pneumonia, arthritis, and more rarely tendovaginitis have been described.

CLINICAL PATHOLOGY

A definitive etiologic diagnosis of salmonellosis depends on the isolation of the organism from tissue aseptically collected at necropsy and from feces, blood, milk, and other body fluids. In the case of abortion suitable material for culture include placenta, vaginal swabs, and fetal stomach contents.[33] Feed, water, and environmental samples may be cultured to confirm the presence of the pathogen in a herd or flock or to determine the source of the organism. The type of sample required and frequency of sampling will largely depend on the objective of the

testing strategy, the clinical presentation (if any), and the degree of precision of prevalence estimates that is required. Samples from individual animals should be obtained as aseptically as possible to prevent cross-contamination. Clinical cases are best sampled during the acute phase of the disease and before initiating antimicrobial therapy. In the case of herd/flocks testing environmental samples, such as pooled feces or swabs from floor swabs or boots, may be most cost effective.[33] Identifying subclinical infection may require repeated sampling and a larger sample size because so-called carrier animals may shed the bacterium only intermittently and in low numbers.

The diagnostic techniques available are as follows.

Bacterial Culture

Bacterial culture is the only way to make a definitive etiologic diagnosis of salmonellosis and to exactly determine the serotype. However, culturing the organism, particularly from feces, is unreliable for various factors including the method used to collect samples, the amount of material submitted, variation in the fecal shedding of the organism, and the bacteriologic method used. A major complicating factor is the occurrence of apparently healthy carriers, which shed the organism intermittently and in low numbers, and silent carriers, which do not shed *Salmonella* in feces but harbor the organism in mesenteric lymph nodes or in the mucosa of the cecum and colon. The difficulty varies according to genotype. Host-adapted serovars (e.g., SD in cattle or *S.* Abortusovis in sheep) are more difficult to isolate from feces than serovars with a broader host range such as *S.* Typhimurium. In cattle with SD infection, the bacteria are present in the blood and milk for a very brief period during the bacteremic phase and before diarrhea commences. Cows near calving are most likely to be shedding *Salmonella* in the feces. Multiple cultures at 24-hour intervals were found to be superior to single fecal cultures for the diagnosis of clinical salmonellosis in horses; currently at least five consecutive fecal samples are recommended to rule out the carrier state in an individual animal with over 95% confidence.[21]

The organism can be cultured from tissue, body fluids, fecal samples, bulk tank milk, milk filters, water, feed, and environmental sites. When sampling dairy farms weekly for 7 to 8 weeks, the prevalence of fecal shedding from different groups of cattle may vary widely among herds, indicating that herds with infected cattle may be classified incorrectly if only one group is tested.

Clinical laboratories generally require at least 48 hours for presumptive diagnosis of *Salmonella* spp. in feces because of required preenrichment and enrichment steps. Biochemical and serologic confirmation of the genotype and the following susceptibility

testing may require an additional 24 to 48 hours.

There are numerous methods to culture *Salmonella*, and the choice of the appropriate method depends on the suspected serovars, the source and type of the sample, and the affected animal species.

Preenrichment Media

The use of preenrichment media, such as buffered peptone water or preenrichment broth, can increase the sensitivity of the fecal culture by resuscitating severely damaged salmonellas that may otherwise not grow on selective culture media. The use of preenrichment media may, however, not be ideal to isolate host-specific serovars that are less vigorous and may suffer from overgrowth of competing bacteria during this nonselective enrichment process.[33]

Enrichment Media

Enrichment media contain additives that selectively stimulate growth of *Salmonella* while inhibiting the growth of competing organisms. Examples of selective growth media include sodium tetrathionate, selenite cysteine, or brilliant green broth. Some of these specific enrichment media are, however, toxic to the certain *Salmonella* serovars; for example, brilliant green is toxic to many SD strains.[33]

Selective Plating Media

Selective media are solid agars inhibiting growth of bacteria other than *Salmonella* spp. while giving information on some of the principal biochemical characteristics, such as nonlactose fermentation and hydrogen sulfide production of *Salmonella* spp.[33] Selective agars are usually incubated for 24 to 48 hours at 37°C and *Salmonella* are present as characteristic colonies on these agars that can be differentiated from colonies of other bacteria. There are, however, certain organisms such as *Proteus, Pseudomonas,* or *Citrobacter,* which may be difficult to differentiate from *Salmonella* on selective agars. In positive samples additional biochemical tests are required to identify specific serovar variants.

DNA Recognition and Immunologic Methods

A variety of rapid *Salmonella* detection methods such as electrical conductance/impedance immunomagnetic separation, ELISA, and DNA probe PCR methods are available. Many of these methods have been developed for the use in human foodstuffs but have not been fully validated for environmental or fecal samples. Samples containing fecal material present a problem for PCR-based methods because of the presence of inhibitors of the PCR reaction in the test sample matrix.[33] In most cases selective or nonselective enrichment stages and DNA extraction techniques are required when using DNA-based methods, resulting in

more steps and operator time for the isolation procedure.

Serology

Serum Enzyme-Linked Immunosorbent Assay

Serologic testing using ELISA tests on serum or milk can be used in herds to identify *S.* Typhimurium or *S.* Enteritidis infections in farm animals and has also been used as a diagnostic aid to identify SD carriers. The test is based on immunoglobulins to the O antigens of the LPS of the organism and is usually designed to detect a limited range of *Salmonella* serovars or serogroups.[33]

Salmonella antibody ELISAs are now in routine use and are widely available commercially. The tests can be run on individual blood or milk samples to identify potentially infected individuals or to determine a vaccine response; it can also be used to identify infected herds or flocks by determining the presence or absence of antibody in bulk milk samples.[33] Bulk tank milk testing for antibodies to SD is used as a national screening diagnostic aid in some countries. Using a variety of ELISA tests, muscle fluid samples from cattle taken at slaughter can be used as an alternative to serum to detect antibodies to *Salmonella* polysaccharide.

Serologic results of individual animals should be interpreted cautiously because serologically positive animals may no longer be infected with *Salmonella*. On the other hand, infected and shedding individuals may not have seroconverted. Particularly in regions with low prevalence of *Salmonella* infection the specificity issue means that most positive results will be false.[33] Repeated positive serology in individual animals may, however, be used as a diagnostic aid to selective culling of chronic carrier animals.

Laboratory Diagnosis in a Suspected Sick Animal

A positive diagnosis depends on culture of the organism, usually from feces but possibly from blood in the septicemic stage. In case of abortion fetal material and placenta should be submitted for culture. If serologic diagnosis is available a serum sample should also be submitted. Indirect tests are very valuable and, if laboratory availability is good, a total white cell count and estimation of serum sodium levels should be undertaken. A presumptive diagnosis is often all that can be stated, and this may be supported by a herd diagnosis.

Herd Diagnosis

A serologic examination of a sample of animals is a first step. A completely negative serologic test would indicate that the infection is not present. Positive results indicate a need for further examination, and periodic fecal cultures at 15-day intervals should be undertaken. When *S.* Typhimurium is the causative bacteria, the feces of other species

of animals on the farm should be examined, because ducks, dogs, horses, pigs, sheep, and cattle may be sources of infection for each other. It is always advisable to examine the drinking water and feed for evidence of infection.

Detection of Clinically Normal Carrier Animals

The most difficult diagnostic problem in salmonellosis is the detection of the clinically normal carrier animal. The recommended procedure is to do fecal cultures on all cows at 14-day intervals for three examinations and repeat the examination on the day of calving. At that time, swabs are taken from feces and the vagina of the cow and the feces of the calf. The sampling should preferably be done when the cows are tied in stanchions and not grazing pasture, because of the large number of passive carriers of the infection in the latter circumstance. In horses at least five samples should be submitted for fecal culture as a diagnostic procedure to identify carrier horses to have over 95% confidence that the tested animal is negative for *Salmonella* spp.[21]

The reliability of diagnosis based solely on culture of fecal swabs is not high and represents the major difficulty in detecting carriers. A combination of fecal culture and serologic tests offers some improvement in accuracy, but even with the agglutination or CF tests accuracy is insufficient.

Determination of Prevalence of Infection in Population of Animals

In food-producing animals it is particularly important to determine the prevalence of *Salmonella* infection in a population of cattle.

NECROPSY FINDINGS

Septicemia

There may be no gross lesions in animals that have died peracutely but extensive submucosal and subserosal petechial hemorrhages are usually evident. In some cases the necropsy findings may include splenomegaly and pinpoint white foci in the liver (paratyphoid nodules). The histologic lesions are nonspecific, with the exception of the somewhat granulomatous character of the older paratyphoid nodules. The placentas of cattle and sheep aborting because of *Salmonella* spp. often contain very large numbers of intravascular bacteria.

Acute Enteritis

Some of the changes associated with the septicemic form are often present, but the most consistent damage is found in the large and small intestines. The character of the inflammation here varies from a mucoenteritis with submucosal petechiation to diffuse hemorrhagic enteritis. Similar lesions may be present in the abomasum, and in SD infections in calves multiple mucosal erosions and petechiation of the abomasal wall are common. Infections with *S.* Typhimurium

are characterized by severe necrotic enteritis in the ileum and large intestine. The intestinal contents are watery, have a putrid odor, and may contain mucus or whole blood. In cases that have survived for longer periods, superficial necrosis and fibrin exudation may proceed to the development of an extensive diphtheritic pseudomembrane and fibrin casts. The mesenteric lymph nodes are enlarged, edematous, and hemorrhagic. The wall of the gallbladder may be thickened and inflamed.

Chronic Enteritis

In cattle, the chronic form is usually manifested by discrete areas of necrosis of the wall of the cecum and colon. The wall is thickened and covered with a yellow-gray necrotic material overlying a red, granular mucosal surface. Less commonly the lesions are discrete in the form of button ulcers, occurring most frequently in the cecum around the ileocecal valve. The mesenteric lymph nodes and the spleen are swollen. In all species, chronic pneumonia and a variety of other localized inflammatory processes such as polyarthritis and osteomyelitis may be found.

*Salmonella*s are present in the heart, blood, spleen, liver, bile, mesenteric lymph nodes, and intestinal contents in both septicemic and acute enteric forms. In the chronic form, the bacteria may be isolated from the intestinal lesions and less commonly from other viscera. Culture is more successful if enrichment media such as tetrathionate broth are used. Surveys that set out to determine the percentage of carriers in animal populations by examining abattoir material show that by far the largest number of isolations are made from the lymph nodes draining the cecum and lower small intestine.

Samples for Confirmation of Diagnosis

- Bacteriology: Ileocecal lymph node, ileum, colon, spleen, lung, liver, and culture swab from gall bladder (CULT)
- Histology: Formalin-fixed samples from these tissues plus kidney, stomach, and brain (LM)

Note the zoonotic potential of these organisms when handling carcasses and submitting specimens.

DIFFERENTIAL DIAGNOSIS

The clinical diagnosis of salmonellosis is difficult because of the number of other diseases that resemble each form of the disease. Salmonellosis is characterized by septicemia in young animals and acute and chronic enteritis in adults, although acute enteritis can occur in neonates. Thus the septicemic form of the disease must be differentiated from all other causes of septicemia, and the enteric forms

differentiated from all other causes of diarrhea in both young and adult animals. At necropsy the isolation of salmonellas from tissues and intestinal contents, although suggestive of the presence of salmonellosis, does not of itself confirm the diagnosis, and care must be taken to ascertain whether other disease is present.

Cattle
Septicemia
The septicemic form of salmonellosis in calves resembles coliform septicemia, and differentiation is possible only by bacteriological examination of blood, feces, and tissues. Salmonellosis occurs most often during the second and third weeks of life in contrast to coliform septicemia, which occurs most often in the first few days of life. Both are characterized by weakness, depression, polypnea, tachycardia, fever or hypothermia, scleral injection and hemorrhages, diarrhea, and rapid death.

Acute enteritis
Acute enteric salmonellosis in adult cattle or calves is characterized by fever, anorexia, toxemia, abdominal pain, diarrhea and dysentery, excessive mucus and fibrinous casts and strands in the feces, and dehydration.
- **Coccidiosis** is most common in young cattle 2–8 months of age and is characterized by diarrhea with frank blood in the feces, tenesmus, only occasionally systemic signs of dehydration and anemia, and spontaneous recovery in a few days; rarely there are nervous signs and death.
- **Acute intestinal obstruction** is characterized by abdominal pain, scant or absent feces, bloodstained feces, tenesmus, anorexia, and palpable abnormalities on rectal examination.
- **Hemorrhagic bowel syndrome** is characterized by acute onset and pronounced abdominal pain associated with signs of systemic disease but no fever. Feces contain large amounts of dark red, partially or entirely clotted blood resembling blackberry jam. The condition typically affects individual adult midlactating cows.
- **Winter dysentery** occurs in explosive outbreaks in housed adult cattle; the feces are gray with flecks of blood, there is no toxemia, no dehydration, and the disease is self-limiting in 24–48 h.
- **Mucosal disease** is characterized by typical oral erosions, anorexia, fever, persistent diarrhea, dehydration, lesions in the interdigital clefts, and a high case–fatality rate.
- **Bracken fern poisoning** is characterized by dysentery, scleral hemorrhages, and a history of access to the bracken plant.
- **Other poisonings**, especially arsenic and to a lesser extent lead and a number of miscellaneous weeds, may cause a similar acute enteritis.

Chronic enteritis
Chronic enteric salmonellosis may resemble **paratuberculosis (Johne's disease)** or **chronic molybdenum poisoning**, but

dysentery and epithelial casts do not occur in these diseases. Massive **stomach fluke infestations** may also cause diarrhea and dysentery.

Abortion
Abortion caused by salmonellosis requires laboratory examination of the fetus, fetal fluids, vaginal mucus, feces, and milk of the aborting animals.

Sheep
Diarrhea associated with infections with coccidia or *Campylobacter* spp. or by parasitic infestation may resemble enteric salmonellosis in sheep, but the latter is usually more acute with a higher fatality rate. *Salmonella*-related abortion requires laboratory examination of the fetus, fetal fluids, vaginal mucus, feces, of the aborting animals.

Horses
Septicemia
Septicemic salmonellosis in foals may resemble the septicemias associated with *Escherichia coli* and *Actinobacillus equuli*.

Acute enteritis
Acute enteric salmonellosis in adult horses causes profuse diarrhea, dehydration, severe depression, and weakness. A history of recent transportation often helps in suggesting the diagnosis of salmonellosis in adult horses, in which colitis X is the important differential diagnosis.

Idiopathic equine colitis X is a severe enterocolitis of adult horses characterized by profuse diarrhea, marked dehydration, and a high case–fatality rate in spite of intensive fluid therapy. Many cases are considered to be enteric salmonellosis, but the definitive etiological diagnosis is often not obtained.

Other diagnoses that must be considered include:
- **Clostridiosis** caused by *C. perfringens* type A and *C. difficile* may result in peracute hemorrhagic diarrhea, marked dehydration, and rapid death.

Chronic enteritis
Chronic diarrhea caused by salmonellosis may resemble **parasitism**, **granulomatous enteritis**, or **lymphosarcoma.**

TREATMENT
Primary Treatment: Antimicrobial Therapy
The use of antimicrobials for the treatment of clinical salmonellosis is controversial. Concerns with this treatment approach include the risk of creating so-called carrier animals and the selection for AMR particularly when using antimicrobials not only on clinically affected individuals but metaphylactically on a group of exposed animals. Issues are in part derived from experience in human medicine where invasive infection with *Salmonella* is uncommon and antimicrobial therapy is discouraged.[23] However, bacteremia is frequently encountered in cattle with acute enteritis, and septicemia is

a feature of clinical salmonellosis in foals, calves, and lambs. In acute cases of clinical salmonellosis with suspected or confirmed bacteremia it would be professionally negligent not to treat affected animals with appropriate antimicrobials. There is indeed evidence that antimicrobials can prolong the duration of the period after clinical recovery from acute and in particular from chronic enteritis in humans and animals during which the causative bacteria can be isolated from the intestine. It is accepted that this can occur and that the use of antimicrobials may contribute to the spread of disease.

Another related issue is the creation of drug-resistant strains. The problem with resistant strains would not have become a significant one if only individual animals had been treated, but mass medication of in-contact animals and prophylactic treatments have generally resulted in a large population of resistant strains.

Oral treatment in cattle and pigs is recognized as a satisfactory treatment, but it is not recommended in horses in which an immediate worsening of the diarrhea, or its prolongation as a persisting chronic diarrhea, may be encountered. It is thought that both sequelae result from an alteration of the normal population of intestinal microflora resulting from the 8 to 10 times greater concentration of drug that occurs in the intestine after oral treatment, compared with the concentration resulting from parenteral injection.

If antimicrobial therapy is considered, the choice of antimicrobials should be based on antimicrobial susceptibility testing whenever this is possible. Because salmonellas are facultative intracellular pathogens, it is critical to choose an antimicrobial with good tissue penetration that attains adequate intracellular concentrations.

Ruminants
Currently many countries lack antimicrobials labeled for treatment of bovine salmonellosis. In cases of acute and severe disease in which antimicrobial therapy is most appropriate and treatment cannot be delayed, broad-spectrum antibiotics are often used because of the considerable turnaround time of bacterial culture and susceptibility testing in the case of *Salmonella*. As a result, treatment of salmonellosis in cattle is largely empirical, and extralabel use of certain antimicrobials is common in veterinary practice.

Salmonella spp. are gram-negative bacteria that are generally resistant to penicillin, erythromycin, and tylosin. Resistance to other antimicrobials such as ampicillin, amoxicillin, ceftiofur, florfenicol, sulfonamides, ceftiofur, trimethoprim-sulfas, and tetracyclines is variable.[16,23] Multidrug resistance is encountered more often in strains isolated from calves than from adult cows.[16]

Historically ampicillin, chloramphenicol, and trimethoprim-sulfas have been widely

used for the treatment of salmonellosis in cattle, but with resistance to these compounds becoming increasingly common and food safety concerns with the use of chloramphenicol in food-producing animals the use of ceftiofur has become more common, particularly in the United States. Chloramphenicol is now banned for use in food-producing animals in many countries. Nitrofurazone given orally to calves and adult cattle was commonly used for the treatment of salmonellosis but is now similarly banned. In countries where it is permitted fluoroquinolones are widely used for the treatment of clinical cases. The use of third- and fourth-generation cephalosporins and fluoroquinolones that are considered critically important antimicrobial agents in human and veterinary medicine for veterinary use is, however, discouraged by the World Organization of Animal Health (OIE); the use of these compounds should be limited to cases in which resistance to other antimicrobials is confirmed or at least must be assumed.

Horses

As in other species antimicrobial therapy in horses infected with *Salmonella* is controversial. Although antimicrobials are indicated in cases of bacteremia or septicemia as it occurs in foals, their efficacy for the treatment of enterocolitis or healthy shedders is questionable. In any case the choice of an antibiotic should be based on drug sensitivity of the organisms isolated whenever possible. Based on some studies of isolates from horses, gentamicin at 3 mg/kg BW combined with ampicillin at 20 mg/kg BW given intravenously at 8- to 12-hour intervals has been recommended. An alternative is trimethoprim-sulfonamide given twice daily intravenously at a combined dose of 30 mg/kg BW or ceftiofur at 2 to 4 mg/kg BW, twice daily. Sulfadiazine, sulfadoxine, and sulfamethoxazole are the best sulfonamides to combine with trimethoprim for salmonellosis in the horse. Care needs to be exercised when treating adult horses for salmonellosis because of the tendency for antimicrobials, especially tetracyclines, to precipitate attacks of diarrhea.

Foals with septicemic salmonellosis are usually treated both systemically and orally with antimicrobials, sometimes a different one by each route. Treatment must be given at least at 6-hour intervals and accompanied by a supportive fluid therapy. Antimicrobials recommended include gentamicin, ampicillin, sulfonamide combinations, and chloramphenicol.

Supportive Therapy

Supportive therapy includes the use of oral electrolyte solutions and polyionic ion fluids administered intravenously to replace fluid and correct electrolyte and acid-base imbalances (see Chapter 5).

NSAIDs have been recommended to alleviate endotoxin-related symptoms, control pain, and possibly prevent the risk of laminitis in horses. Maintaining adequate hydration is particularly important when using NSAIDs that decrease renal perfusion and may become nephrotoxic in dehydrated individuals. Prolonged use of NSAIDs has been associated with gastric/abomasal ulceration in different species and colonic ulceration in horses. Their use should therefore be limited in time and at the lowest possible dose.

TREATMENT

Antimicrobial therapy in cases of suspected/confirmed bacteremia

The use of antimicrobials for the treatment of chronic enteritis or healthy shedders is highly controversial.

Cattle/calves

Trimethoprim-sulfonamide (20 mg combined/kg) IV/IM every 12–24 h) (R2)

Amoxicillin (10 mg/kg IM every 12 h) (R2)

Amoxicillin-clavulanate (12 mg combined/kg IM every 12 h) (R2)

Ampicillin (10 mg/kg PO/IM every 12 h) (R2)

Enrofloxacin* (2.5–5.0 mg/kg SC/IM every 24 h) (R2)

Ceftiofur* (1.1–2.2 mg/kg BW every 24 h SC/IM for 3 days) (R2)

Horses/foals

Trimethoprim-sulfonamide (30 mg combined/kg IV/IM/PO every 12 h) (R2)

Ampicillin (20 mg/kg IV/IM every 8–12 h) (R2)

Amoxicillin trihydrate (20 mg/kg IM every 12 h) (R2)

Ceftiofur* (2–4 mg/kg every 24 h SC) (R2)

Fluoroquinolones* (R3)

Foals

Gentamicin 6.6 mg/kg IV every 24 h or 4.4 mg/kg IV every 12 h, ensure adequate hydration (R2)

Chloramphenicol (50 mg/kg IV every 6–8 h) (R2)

Antiinflammatory therapy

Flunixin meglumine (2.2 mg/kg IV as a single dose) (R2)

Meloxicam (0.5 mg/kg SC/IV as a single dose) (R2)

Fluid therapy

Oral and parenteral fluid therapy to substitute water and correct acid-base and electrolyte imbalances†

IM, intramuscularly; IV, intravenously; PO, orally; SC, subcutaneously.

*Are classified as critically important antimicrobials in human and veterinary medicine. Use as first line treatment is discouraged.

CONTROL
Prevention of Introduction of Infection (Biosecurity)

Avoidance of infection is the major objective but is not easily achieved. The principal sources of infection are carrier animals and contaminated feeds containing foodstuffs of animal origin. There is a critical need to develop methods to control the spread of *Salmonella* infections on dairy farms by instituting biosecurity and biocontainment practices in addition to enhanced farm management. This would result in a reduction in the use of excessive antibiotic treatment of individual animals or herds.

A closed herd minimizes the risk of infection but is not a practicable procedure for the types of animal producer (the calf-rearer and the commercial pig fattener) for which salmonellosis is a major problem. For such producers the following rules apply:

- Introduce the animals directly from the farm of origin. Avoid auction marts, saleyards, and public transport, all of which are likely to be sources of infection. Ensure that the farm of origin is free of salmonellosis.
- If possible, purchase animals when they are older, such as 6 weeks of age for calves, to provide an opportunity for specific and nonspecific immunity to develop. Animals from vaccinated herds are desirable.
- The premises of dealers, saleyards, and transport vehicles must be under close surveillance and the need for frequent vigorous disinfection must be stressed. The infection rate in calves delivered to calf-dealers' yards in the UK was less than 1%, but the infection rate increased to 36% if the calves were kept on the premises over the weekend.
- Introduce only those animals likely not to be carriers. Unfortunately the detection of carriers is inaccurate and expensive. To have any confidence in the results, fecal samples for culture must be submitted on at least three occasions. Even then, occasional carriers with lesions in the gallbladder or tonsils will escape the net and be capable of reviving the disease on the farm or transferring it to another one.

Management practices to reduce the risk of *S. Brandenburg* on a sheep farm include reducing stocking density; avoiding strip grazing; maintaining adequate nutrition; minimizing yarding of ewes and the time spent in yards; dampening down yards before yarding; providing stock with a fresh clean source of drinking water; avoiding the purchase and/or grazing of stock from known affected farms, as they may contain carrier animals; preventing dogs from scavenging; and preventing scavenging by black-backed gulls by removing and burying aborted fetuses frequently during the lambing season.

Limitation of Spread Within a Herd

When an outbreak occurs, procedures for limiting spread, as set out next, need to be strictly enforced, and medication of affected groups, and of susceptible groups at high risk, must be performed.

- **Identify carrier animals and either cull them or isolate and treat them vigorously.** Treated animals should be resampled subsequently to determine whether a "clean" status has been achieved.
- **The prophylactic use of antimicrobials** is used but **not recommended** because results are poor and there is a risk of developing resistant strains. Probiotics intended for the prevention of shedding of *Salmonella* in the postoperative period in horses with colic have been evaluated and found to be ineffective.
- **Restrict the movement of animals around the farm** and limit the infection to the smallest group. Pasture and permanent buildings are both important, although the major source of infection in most cases is the drinking water.
- **The water supply should be provided in troughs that are not susceptible to fecal contamination.** Static drinking water or pasture may remain infected for as long as 7 months.
- **Rigorous disinfection of buildings is important.** An all-in/all-out policy should be adopted and steam cleaning and disinfection performed after each batch of animals. If economics permit, individual pens for calves are beneficial. Where calves are reared indoors they are common and economical. Dirt yards present a problem, especially those used for sheep and calves, but, provided they can be kept dry and empty, two sprayings, 1 month apart, with 5% formalin is recommended.
- **The control of salmonellosis in veterinary clinics and veterinary teaching hospitals** requires special attention to the possible sources of infection and containing and preventing the spread of infection. Following the diagnosis of the disease in a clinic, an environmental survey should be performed using bacteriologic culturing of stalls, wall padding, stomach pumps, nasogastric tubes, alleyways, water drains, and other equipment used routinely. This is followed by a thorough cleaning and disinfection of the entire animal-holding premises. The surfaces are then recultured to determine the presence of residual contamination. Medical and surgical equipment are cleaned and sterilized. Traffic flow patterns in the clinic are reviewed and modified accordingly. Use of disposable gloves and thorough washing of hands after handling suspect animals are recommended. Stalls in which horses with salmonellosis were housed should only be used to accommodate newly hospitalized horses after samples (collected after two cycles of cleaning and disinfection) from stall drains, cracks, and corners yield negative results

on bacteriologic culture. Using PCR assay for *Salmonella* DNA, samples from floor drains and drainpipes yield the greatest proportion of positive results. The PCR results should be confirmed by bacteriologic culture, because a positive PCR in itself is not considered to pose a risk of salmonellosis to hospitalized horses. When a hospitalized horse leaves its stall permanently, it should be cleaned of organic matter using a cold water hose and scrubbed with a steel wool mop. This is followed by an application of generic bleach solution. This is then followed 24 hours later by another cleaning and disinfection with a peroxygen solution (Virkon) and allowed to dry. Virkon is a balanced stabilized blend of peroxygen compounds, surfactants, organic acids, and inorganic buffer system. Active ingredients are potassium peroxymonosulfate, sodium chloride, and other ingredients. It is effective against a wide range of bacteria, virus, and fungi, including: *S. pyogenes, C. pyloridis, Klebsiella pneumoniae, E. coli,* and *S.* Typhimurium.

- **Suitable construction of housing is important.** Impervious walls to stop spread from pen to pen, pen design to permit feeding without entering the pen, avoidance of any communal activity, and slatted floors to provide escape routes for manure all assist in limiting the spread of enteric diseases. Pen design and the environment should be such as to encourage proper eliminative behavior and good pen hygiene. Drinkers should be sited at one end of the pen, preferably on a narrow end with oblong pens, to encourage defecation in this area. Wet or damp areas of the floor in other parts of the pen will encourage defecation and urination there and should be eliminated. Drinkers of the nipple type rather than bowls are preferable for hygienic reasons. Communal dunging alleys increase the possibility of spread, especially during the cleaning procedure, and the trend is toward slatted or meshed areas over a channel.
- **Disposal of infective material should be done with care.** Carcasses should be burned or, better still, sent to an institution for diagnosis, rather than to a rendering plant to be converted into still more contaminated bonemeal. Slurry and manure for disposal should be placed on crops rather than on pasture. Slurry does not constitute a danger via hay, and salmonellas do not survive silage making. When slurry is used on pasture it should be stored for at least a month beforehand and even longer if silo effluent is included. Slurried pasture should not be grazed for 1 month, and

for young animals a 6-month delay is recommended. Pig slurry is most dangerous and should always be avoided.
- **All persons working on infected premises should be warned of the hazards to their own health.** Other peripatetic species, especially dogs, should be kept under close restraint.

Principles of Infectious Disease Control for Prevention of Nosocomial Gastrointestinal and Respiratory Diseases in Large-Animal Hospitals

The principles of an IDC program for the prevention of gastrointestinal and respiratory diseases in a large-animal hospital have been described and are applicable to the control of salmonellosis. The three basic strategies are reducing exposure to pathogens, avoiding increasing susceptibility to pathogens, and monitoring effectiveness of the IDC program. The major procedures are summarized here.

Reducing Exposure to Pathogens
- Promoting appropriate personal hygiene
- Using effective methods for cleaning and disinfection
- Controlling the flow of human and animal traffic
- Implementing protocols for prompt identification of patients with signs of contagious disease
- Controlling birds, rodents, and flies

Avoiding Increasing Susceptibility to Pathogens
- Controlling ambient temperature
- Using antimicrobials appropriately
- Aiding in establishing normal intestinal or rumen flora
- Controlling endotoxemia

Monitoring Effectiveness of the Infectious Disease Control Program
- Bacterial culture of fecal samples of animals admitted to the hospital
- Regular culture of environmental samples.

Recommended Steps in Developing an Effective Infectious Disease Control Program for a Large-Animal Hospital

An effective IDC program is necessary for all large-animal veterinary teaching hospitals and private veterinary clinics. The recommended steps are outlined here.
- Have all clinicians work together to develop and approve the IDC program, because grassroots buy-in is vital.
- Develop a specific, written IDC program and disseminate it widely among staff members.
- Identify a veterinarian who is active in the large-animal hospital to serve as the IDC officer; this individual will oversee

- the IDC program and should report to the hospital director and practice partners.
- Provide the resources, both human and monetary, needed for the IDC officer to effectively perform the approved IDC program; prevention costs less than the alternatives.
- Make students, residents, and staff aware of the key points of the IDC program and the importance that clinicians place on compliance.
- Teach the barn crew, particularly those actually responsible for cleaning, disinfecting, and feeding, about the goals of the IDC program and the methods to be used.
- Monitor the effectiveness of cleaning and sanitation by means of bacterial culture of environmental samples and give regular feedback to the barn crew, staff, students, and clinicians.
- Hold a seminar at least yearly to distribute written information about the IDC program and results of monitoring.

Animals Being Transported
Animals being transported are a special case. They should be unloaded or exercised at least once every 24 hours and given water and feed, with the feed provided first and at least 2 hours before watering. Hay or chopped hay is preferred to succulent feeds. All railroad cars and feeding and watering troughs should be properly cleaned and disinfected between shipments. Horses that are to be transported should be yarded and hand-fed on hard feed for 4 to 5 days beforehand. If the disease is likely to occur, prophylactic feeding with sulfonamides or antimicrobials has been shown to decrease the incidence in all species. Apart from the risk that this practice will produce resistant bacteria, there has been a suggestion that it may so change the normal bacterial flora of the gut as to encourage the proliferation of salmonellas and lead to the development of the clinical disease.

Immunization
Salmonella Vaccinology
Host resistance to *Salmonella* relies initially on the production of inflammatory cytokines leading to the infiltration of activated inflammatory cells in the tissues. Thereafter, T- and B-cell–dependent specific immunity develops, allowing the clearance of *Salmonella* from the tissues and the establishment of long-lasting acquired immunity to reinfection. The increased resistance that develops after primary infection or vaccination requires T-cells, cytokines such as IFN-γ, TNF, and IL-2, in addition to opsonizing antibody. Seroconversion and/or the presence of detectable T-cell memory do not always correlate with the development of acquired resistance to infection.

Long-term immunity using live attenuated vaccines is serotype specific and involves the recall of immunologic immunity. Killed vaccines induce strong antibody responses but trigger insufficient Th1-cell responses.

Vaccination can decrease the number of bacteria shed in feces and the number of blood-culture–positive calves, thus decreasing the number of carriers and reducing environmental contamination. Many types of vaccines have been developed and tested in cattle and pigs. If vaccination is combined with the hygienic precautions described, the vaccines are an aid to management. Killed bacterins and live attenuated vaccines are available. Either can be used as a prenatal vaccine to provide passive immunization of the newborn. It is now generally accepted that live *Salmonella* vaccines are more effective immunogens in calves than are killed vaccines.

Cattle
In cattle, SD is the infection likely to be endemic in a herd and a commercial vaccine, to be effective, must have a strong SD component. Live organisms are better able to stimulate anti-LPS antibodies and to stimulate cell-mediated immunity. Calves vaccinated at 1 to 3 weeks of age with a modified-live aromatic-dependent SD bacterin have detectable anti-LPS immunoglobulins after immunization. Safe live oral vaccines against *S.* Typhimurium and SD have been constructed and shown to confer protection against experimental infection with virulent wild-type strains of the organism. Vaccination of calves orally with a genetically altered stable nonreverting aro-SD as a modified-live vaccine provided a measurable systemic immune response, but the vaccine volume makes it unlikely to be practical for field use. Vaccinated calves responded with increases in humoral-mediated and cell-mediated immunity, as measured by ELISA and skin testing. It is claimed that the combination of humoral immunity and cell-mediated immunity stimulated by live-organism vaccines provides superior protection. Other genetically altered vaccines consisting of hybrid strains derived from SD and *S.* Typhimurium are being evaluated. An avirulent live SCS vaccine is efficacious experimentally against salmonellosis caused by SD infection in calves.

The vaccine strain 51, produced in the UK from a rough variant strain of this organism, has been found to be efficient and safe and provides good protection against *S.* Typhimurium as well as SD. It has the disadvantages of a living vaccine, but calves can be vaccinated successfully at 2 to 4 weeks of age. In limited experiments other living, attenuated, and killed, adjuvanted vaccines have given calves protection, and a comprehensive program of vaccination, hygiene, and adoption of a closed herd policy has been successful in controlling the disease. Reports on

killed *S.* Typhimurium vaccines used in calves indicated good results provided the antigenic mass in the vaccine is kept high, but commercial killed vaccines are of doubtful value.

Attenuated *S.* Typhimurium (strain SL1479) given orally or intramuscularly has shown good efficiency, and attenuated SD (strain SL1438) has been similarly effective. The *S.* Typhimurium vaccine also gives some protection against SD.

The autogenous bacterin, which must be precipitated on aluminum hydroxide to have any significant effect, is given as two injections 2 weeks apart. Good immunity is produced but calves and pigs less than 6 weeks of age are refractory, and anaphylactic reactions may cause the loss of a significant number of animals. To protect young calves the best program is to vaccinate the cows during late pregnancy. This will give passive protection to the calves for 6 weeks, provided they take sufficient colostrum, and the calves can be vaccinated at that time if danger still exists. Vaccination of pregnant cattle with a formalin-killed *S.* Typhimurium vaccine approximately 7 weeks and then 2 weeks before parturition protected their calves against experimental infection. Reports of results have not been enthusiastic, but if proper attention is given to the detail of the program it has been sufficient, in the author's hands, to provide almost complete protection. A similar observation has been made with respect to vaccination of calves against *S.* Typhimurium.

Horses
In horses, a similar regimen with a booster dose for all mares in late pregnancy appears to be effective. In foals, an autogenous *S.* Typhimurium bacterin has been used in several bad field situations and has been credited with preventing further clinical cases and with reducing environmental contamination, in spite of continued poor hygiene and management practices.

Sheep
Results in sheep have been unconvincing. Some live *S.* Typhimurium vaccines are being evaluated for their efficacy against salmonellosis in sheep.

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ACUTE UNDIFFERENTIATED DIARRHEA OF NEWBORN FARM ANIMALS (PARTICULARLY CALVES AND PIGLETS)

Diarrhea in newborn farm animals, particularly calves under 30 days of age and piglets in the first week of life, is one of the most common disease complexes that the large-animal clinician encounters in practice. It is a significant cause of economic loss in cattle and pig herds and continues to assume major importance as livestock production becomes more intensified. Considerable progress has been made in the treatment of the effects of diarrhea, such as dehydration and acidemia, but less so in the control of these disease complexes.

The causes of calf and piglet diarrhea are complex and usually involve an interaction between enteropathogenic bacteria, viruses, protozoa, the colostral immunity of the animal, and the effects of the environment (Table 7-27). Thus the term **acute undifferentiated diarrhea of newborn calves** is used to describe the type of acute diarrhea that occurs in newborn calves under 30 days of age, characterized clinically by acute profuse watery diarrhea, progressive dehydration, acidemia, and death within days, or earlier if not treated. Based on clinical findings alone, it is not usually possible to differentiate between the common known causes of diarrhea in newborn calves, which include ETEC, enteropathogenic (attaching and effacing) *E. coli* (EPEC), necrotoxigenic *E. coli*, rotavirus, coronavirus, bovine torovirus (Breda virus), norovirus, *Cryptosporidium* spp., *Giardia* spp., and *Salmonella* spp. The common necropsy findings are dehydration, emaciation, and a fluid-filled intestinal tract, with no other obvious gross lesions. The exceptions are enteritis associated with *Salmonella* spp., *C. perfringens* types B and C, *Eimeria* spp., and EPEC, in which there are usually typical gross lesions at necropsy.

Thus the disease is considered to be a complex syndrome because one or any combination of more than one of the specific etiologic agents is isolated in clinical cases. **Animal and environmental risk factors** play an important predisposing role in the development of clinical disease, and disease may not occur or may occur with lower incidence and/or severity in absence of such predisposing factors.

RISK FACTORS

Many interrelated risk factors have been associated with increased incidence of calf diarrhea and have added to the difficulty of understanding the complexity of the disease and controlling it. The identification and modification or removal of these risk factors can be very effective in the clinical management and control of epidemics of the disease.

Animal Risk Factors

The host risk factors, some of which are interrelated, include the following:
- Primiparous dam (higher risk of dystocia, lower quality of colostrum …)
- Immaturity/low birth weight of the neonate
- Difficult birth (mechanical trauma, asphyxia, acidemia, and impaired vigor)
- FTPI

Table 7-27 Differential diarrhea: Most likely causes of acute neonatal diarrhea in farm animals

Calves	Piglets	Lambs and kids	Foals
Acute neonatal diarrhea			
Enteropathogenic and enterotoxigenic *Escherichia coli*	Enteropathogenic *E. coli*	*C. perfringens* type C	Foal-heat diarrhea
Rotavirus	*Salmonella* spp.	*C. perfringens* type B	Rotavirus
Coronavirus	Transmissible gastroenteritis virus	(lamb dysentery)	*C. perfringens* type B
Bovine torovirus (Breda virus)		Rotavirus	
Bovine calicivirus	*C. perfringens* type C (rarely A)	Caprine herpesvirus	
Bovine norovirus			
Cryptosporidium spp.	*C. difficile*		
Giardia spp.	Rotavirus		
Salmonella spp.	PRRSV		
Eimeria spp. (calves at least 3 weeks old)	*Isospora* spp.		
Clostridium perfringens type C			

PRRSV, porcine reproductive and respiratory syndrome virus.

- Nutrition of the pregnant dam (reduced quantity and altered nutrient content of colostrum)
- Litter size (increased morbidity and mortality with increasing litter size in piglets)
- Disease of the dam around or after parturition (e.g., mastitis–metritis complex in sows)

Colostrum

The role of colostrum in protecting the newborn calf from infectious disease in early life cannot be overemphasized. The failure of the neonate to ingest an adequate quantity of colostrum containing a high level of colostral immunoglobulin within a few hours after birth is a major risk factor contributing to development of diarrhea and other infectious diseases. Complete or partial FTPI occurs with an incidence of between 5% and over 20% in different farm animal species, with highest incidence rates in dairy calves (see also Failure of transfer of colostral immunoglobulins (transfer of passive immunity) in Chapter 19).

Causes for FTPI can be various and include impaired vigor of the calf with low drive to suck (e.g., immaturity, acidemia, asphyxia, birth-related trauma), inadequate immunoglobulin content of colostrum (e.g., colostrum leaking before calving, colostrum collected later than 6 hours after calving), inadequate volume of colostrum available to the calf (e.g., agalactia, mastitis, poor mothering skills of the dam), or delayed ingestion of colostrum.

Cases of diarrhea caused by specific **nutritional deficiencies** are reported rarely and not well documented. However, field observations indicate that outbreaks of diarrhea in suckling beef calves may have been associated with specific nutrient deficiencies such as copper or selenium. These are not documented but should be considered in certain situations in which these deficiencies are known to be present in the herd. An epidemic of intractable diarrhea in 2-month-old beef calves was associated with deficient tissue and plasma levels of vitamin E in the affected calves, which also had lesions of skeletal and myocardial muscular dystrophy with adequate levels of selenium. An inadequate supply of vitamin E and β-carotene to the neonate though colostrum from dams that were vitamin E and β-carotene deficient during late gestating has been incriminated as a predisposing factor for neonatal diarrhea in dairy calves.[1] A combination of low vitamin E status and low immunoglobulin status may contribute to neonatal diarrhea by impairing the immune cell function of calves, but this is not well documented.

Environmental and Management Risk Factors

A number of environmental and management risk factors have been identified as predisposing diarrhea in different farm animal species and different production systems.

Table 7-28 Calf diarrhea risk factors: Risk factors and their role in acute undifferentiated diarrhea of newborn calves

Risk factor	Role of risk factor
Colostral immunity of calf	Low levels of serum immunoglobulins render calves highly susceptible to death from diarrhea.
Dystocia	Calves born at a difficult calving were at increased risk of developing and dying of diarrhea.
Parity of dam	Calves born from heifers may not acquire sufficient levels of colostral immunoglobulins.
Residence time in maternity pen (dairy)	Dairy calves remaining in the maternity pen with their dam for longer than 24 h were found to be at increased risk of developing diarrhea, presumably caused by longer exposure to pathogens and/or lower amounts of ingested colostrum.
Group housing (versus hutches)	Calves housed in groups were at higher risk of developing diarrhea, presumably because of facilitated fecal–oral transmission of pathogen.
Overcrowding	Increased population density increases infection rate and high morbidity and mortality.
Preventive antimicrobial use	Calves with adequate colostrum supply were at higher risk of developing diarrhea when treated preventively with medicated milk replacer.[12]
Meteorological	Changes in weather; wet, windy, and cold weather commonly precedes outbreaks of diarrhea in beef calves; higher mortality in dairy calves exposed to hot environmental temperatures; high environmental temperatures precipitate outbreaks
Quality of diet	Heat denatured skim milk used in milk replacers is less digestible than whole milk and precipitates diarrhea.
Calf rearer	The concern and care provided by the calf rearer will have a direct effect on morbidity and mortality associated with diarrhea.
Herd size	Conflicting reports over the effect of herd size on the incidence rate of calf diarrhea and calf mortality have been published.

Calves

A wide range of management practices from housing and feeding of the pregnant dam, to over calving management, to calf housing and feeding have been associated with an increased risk of enteric disease in dairy calves (Table 7-28).

Nutrition of the Dam in the Preparturient Period

Nutrient deficiencies in cows during the late trimester of pregnancy have been associated with decreased birth weights and impaired efficiency of intestinal IgG absorption of the calves born to cows fed a protein deficient diet.[2,3] Although little effect of the dam's nutrition on the colostral immunoglobulin content has been reported, β-carotene and tocopherol deficiency of the dam during late gestation was associated with deficiency of these substances in their calves. Because deficiencies in β-carotene and tocopherol were more common in herds with high incidence rates of neonatal diarrhea, this has been incriminated as a potential predisposing factor.[1,4]

Calving Management: Dairy

The calving management has a great impact on the calf's health and development during the neonatal period and beyond. Calves born in a separate maternity facility are at decreased risk of developing neonatal diarrhea compared with calves born in regular stalls (either stanchion or free stalls),[5] and calves born in individual maternity pens had a lower risk of diarrhea than animals born in a group maternity pen.[6] Prolonged residence time of the neonate in the maternity pen (over 24 hours) was associated with increased risk of diarrhea and calf mortality. These effects have been attributed to differences in exposure to pathogens and differences in colostrum intake associated with the different management systems.

The degree of calving supervision and quality of obstetric care also affects the disease incidence in neonatal calves. Lack of calving supervision can lead to prolonged calvings resulting in more severe acidemia and asphyxia, which will impair the calf's vigor in early life. Good obstetric technique will reduce stress and reduce the risk of birth-related trauma in dams and calves.[5]

Calving Management: Beef

Crowding of maternity or wintering lots and calving cows and heifers on the same grounds is considered an important risk factor for calf diarrhea in cow–calf operations. A decrease in the surface of the effective calving yard per cow is generally associated with poor drainage and wetness and results in increased pathogen exposure. Similarly, the odds of diarrhea occurring in calves born toward the end of the calving season are twice that of

calves born in the first part of the calving season. This also may be because of increased pathogen exposure as the calving season progresses.

Colostrum Management: Dairy

Although in most farm-animal species adequate colostrum intake can be anticipated in the large majority of spontaneously delivered healthy neonates, this is not the case in dairy calves. Numerous studies have demonstrated that a considerable number of calves allowed to voluntary nurse from their dam after birth suffer from FTPI, which is the major risk factor for diarrhea and other neonatal infectious diseases (see also Failure of transfer of passive immunity).[4,6] Assuring adequate colostrum intake in a timely manner by separating the calf from its dam and hand-feeding colostrum is associated with significantly lower rates of FTPI and a significantly lower risk of neonatal diarrhea.

Other colostrum management practices that can affect the occurrence of disease are avoiding fecal contamination during collection, pasteurization of colostrum, and proper storage.

Calf Housing and Feeding: Dairy

Group housing of calves during their first month of life is associated with higher diarrhea incidence than housing calves in individual hutches, and the overall morbidity rate of neonatal calves is higher when calves are housed in groups of 6 to 30 calves compared with small groups of up to 6 calves.[7] Similarly indoor housing was associated with higher morbidity and mortality rates in neonatal dairy calves than housing calves in outdoor hutches.

Overall disease occurrence and mortality of neonatal calves has been shown to be influenced by feeding practices. Adequate energy and nutrient supply are critically important for proper immune function. In the dairy industry it is customary to limit the daily feed supply of unweaned calves to 10% to 15% BW, a procedure also known as "restricted feeding." The objective of restricted feeding is to facilitate early weaning and to decrease the risk of diarrhea. Notwithstanding the voluntary intake of calves fed whole milk ad libitum can easily exceed double this amount, and it was shown that calves can safely ingest milk equivalent to 20% of their BW and achieve markedly higher daily weight gains than calves on restricted feeding.[8] The effect of feeding larger amounts of milk on the incidence of diarrhea was studied with inconsistent results; some studies have reported higher diarrhea incidence when feeding larger volumes while others did not.[8]

Feeding milk replacer instead of whole milk also presents a form of undernutrition, particularly during the cold season of the year, when the energetic requirements of the calf are increased. The energy density and the digestibility of proteins contained in commercial milk replacers are generally speaking lower than in whole milk, which has been proposed to predispose to impaired immune function and thus to disease. A study comparing calves fed the same amount of whole milk or milk replacer in a commercial dairy farm found that mortality rates in both groups were similar during summer but differed dramatically during winter between calves fed whole milk (2.8%) and milk replacer (21.0%).[9]

Some studies have shown that the major contributing factor to dairy calf mortality is the care provided by the calf attendant.

Calf Housing and Feeding: Beef

In beef herds veterinarians have commonly observed a relationship between adverse climatic conditions and epidemics of diarrhea in calves. During inclement weather, such as a snowstorm, a common practice in beef herds is to confine the calving cows in a small area where they can be fed and watered and observed more easily. The overcrowding may be followed by an outbreak of calf diarrhea.

Disease Control and Management: Dairy

Antibiotics are widely used for the control and treatment of diarrhea and other diseases, particularly in dairy and veal calves. A common practice is feeding medicated milk or milk replacer during the first weeks of life, which is a practice that has been associated with reduced calf morbidity and mortality and increased daily weight gains particularly in herds with a high prevalence of FTPI and high infectious pressure.[10] In contrast, this effect was much less pronounced over even the opposite in a well-managed herd with low FTPI prevalences. In well-managed herds calves fed a medicated milk replacer had over 30% more days with diarrhea than herd mates receiving nonmedicated milk replacer.[10]

Although antimicrobial therapy is clearly indicated in diarrheic calves with signs of systemic disease, antibiotics may be counterproductive in scouring calves without systemic illness.[11] Scouring calves without systemic illness that were treated with antibiotics in addition to oral rehydration had 70% more days with diarrhea than calves without systemic disease that received oral rehydration without antibiotics.[12]

Other Environmental and Management Factors

Cold, wet, and windy weather during the winter months in temperate climates and hot humid weather during the summer months may be associated with an increased incidence of dairy calf mortality caused by diarrhea. Changes in weather and wet, windy, and cold weather are commonly associated with subsequent outbreaks of the disease in beef calves raised outdoors. Increases in population density in calf barns, and on calving grounds, resulting in highly contaminated calving grounds, are important risk factors.

Increasing the percentage of heifers calving in the herd is associated with an increased risk of diarrhea because calves born to heifers may be about four times greater than in calves born to cows.

Large herd size was found to be associated with increased diarrhea incidence and overall calf morbidity and mortality in some studies but not in others.[7]

Piglets

Epidemics of diarrhea in piglets are commonly associated with inadequate sanitation and hygiene in the farrowing facility, which may be under continuous use without sufficient time for cleaning and disinfection between farrowings. Producers that managed their farrowing barns as all-in/all-out facilities had lower diarrhea-related morbidity and mortality rates.[13] Herd size was found to have a positive association with piglet morbidity but not mortality related to diarrhea.[13]

Piglets in litters receiving milk replacer as feed supplement were at increased risk of developing diarrhea (OR 1.9) compared with piglets that did not. Although the explanation for this observation is not evident, it was suggested that feed supplementation might either be associated with increased occurrence of hypogalactia or agalactia in sows, or the provision of milk replacers reduces the voluntary intake of sow's milk.[13]

Other management practices that were associated with reduced diarrhea incidence in piglets were the parenteral administration of iron to piglets and vaccination of the sow herd against *E.coli*.[13] Increasing the percentage of gilts among the sow population was associated with increasing diarrhea incidence in the herd.[14]

Seasonal effects have also been reported with highest diarrhea incidence rates in piglets occurring during the cold season of the year.[15]

Lambs

Management factors associated with diarrhea in neonatal lambs were animal density in pens, cleaning frequency of lambing pens, and the use of anthelminthic drugs.[16,17]

Conflicting results regarding the effect of the flock size on diarrhea incidence in lambs have been published. Although some authors reported an increased risk of diarrhea with increasing flock size, this was not confirmed by others.[17]

Pathogen Risk Factors
Calves

The distribution and occurrence of enteropathogens in the feces of diarrheic and normal healthy calves vary depending on the geographic location, the farm, the age and type of calves being examined, and the extent

to which the diagnostic laboratory is capable of isolating or demonstrating the pathogens. Rotavirus, *Cryptosporidium* spp., coronavirus, and ETEC, collectively, are responsible for 75% to 95% of infections in neonatal calves worldwide. The relative frequencies of each of the four differ between locations and between seasons and years. Any one of the common pathogens may predominate or be absent in a certain group of animals. Mixed infections are common. Rotavirus will be most common in some groups, especially housed calves. Coronavirus may predominate in beef calves in some countries, and *Cryptosporidium* spp. may occur in 30% to 50% of diarrheic calves on a worldwide basis. *Cryptosporidium* spp., rotavirus, and coronavirus are the most commonly identified enteropathogens in intensively reared veal calves. In dairy calves, the prevalence of giardiasis and cryptosporidiosis may be high and both parasites may be associated with diarrhea. *C. parvum* is an important pathogen in calves under 1 month of age, but *Giardia duodenalis* may be more important in older calves. Calves may clear *C. parvum* infections within 2 weeks, whereas *G. duodenalis* infection may become chronic in the same calves. The combination of *Cryptosporidium* spp. and rotavirus may predominate in some situations. *Cryptosporidium* spp. were the second most commonly detected pathogens next to rotavirus, and case–control studies indicated a highly significant association with diarrhea. Enteropathogens may not be detectable in up to 30% of diarrheic calves. *Eimeria* spp. can cause coccidiosis in calves any time after about 21 days after birth, but the disease is more common in calves several months old.

In some countries, enterotoxigenic F5 (K99$^+$) *E. coli* may occur in 30% to 40% of diarrheic calves, whereas in others the incidence may be as low as 3% to 6%. AEEC that causes hemorrhagic colitis and blood in the feces of diarrheic calves about 2 weeks of age is being recognized with increasing frequency. It may occur concurrently with other enteropathogens (cryptosporidia, rotavirus, coronavirus, ETEC, bovine viral diarrhea virus [BVDV], and coccidia).

The age occurrence of the common enteropathogens associated with diarrhea in calves is shown in Table 7-29. Case–control studies of diarrheic and healthy calves from the same groups indicate that the enteropathogens commonly found in diarrheic calves can also be found in healthy calves but at a lower frequency, with the exception of rotavirus, which may be excreted by up to 50% of healthy calves. It appears that healthy calves may be infected more often with ETEC, *Cryptosporidium* spp., coronavirus, and rotavirus in herds in which some calves have or recently have had enteric disease than in herds free from major enteric disease.

Campylobacter spp. and *Yersinia* spp. are well adapted to the bovine host and can be

Table 7-29 Calf enteropathogens: Age occurrence of the common enteropathogens in calves	
Enteropathogen	**Age (days)**
Enterotoxigenic *Escherichia coli*	<3
Attaching and effacing *E. coli*	20–30
Rotavirus	5–15
Coronavirus	5–21
Other viruses (Breda virus, parvovirus, bovine virus, diarrhea virus)	14–30 (and older, up to several weeks)

found in the feces of diarrheic and healthy calves at a similar prevalence. Their significance as pathogens in newborn calves is uncertain. They are probably part of the normal enteric flora of ruminants. However, as they represent a source of gastrointestinal infections in humans, management factors limiting intestinal colonization of these bacteria should be considered in beef cow/calf herds.

Rotavirus and coronavirus occur with almost equal frequency in the intestinal tracts of normal and diarrheic calves of some studies. Intestinal lesions compatible with the viral infection are found in about 70% of diarrheic calves. Thus these viruses are widespread in the bovine population and only under some predisposing circumstances will the infection be severe enough to cause clinical disease. Other viruses, such as parvovirus, astrovirus, Breda virus, and norovirus, have been isolated from the feces of diarrheic calves, but their role in the etiology is yet to be defined.

A necrotizing enteritis of suckled beef calves 7 to 10 weeks of age on pasture in Scotland has been reported. Fever, acute diarrhea and dysentery, and a case–fatality rate of 25% are characteristic. No etiologic agent has been identified.

Lambs and Goat Kids
The *E. coli* strains isolated from diarrheic lambs and goat kids on Spanish farms are not generally toxigenic and belong to a large number of O serogroups.

Piglets
In outbreaks of diarrhea in neonatal piglets during the first 5 days of life, the enteropathogens that are commonly present in the feces include the TGE virus, ETEC, *Isospora* spp., rotavirus, *C. perfringens,* and adenovirus. *C. difficile* has emerged as an important pathogen causing enteritis in suckling piglets. The TGE virus causes diarrhea in piglets under 15 days of age, *Isospora* sp. between 5 and 15 days of age, and rotavirus in piglets over 10 days of age. ETEC was found to

be preferentially shed by weaned diarrheic piglets. Suckling diarrheic piglets had a low prevalence of ETEC shedding that decreased from the first to third week of life.[18] During the second and third weeks of life, *I. suis* is the most common pathogen in outbreaks of diarrhea in litters of piglets. Although individual piglets may be infected by a single pathogen, it is common for more than one pathogen to be present in the litter.

A seasonal occurrence of the common enteropathogens has also been observed. The prevalence of the TGE virus may be highest during the fall, winter, and spring months, and coccidia and *E. coli* are more common during the summer, fall, and early winter, with the lowest prevalence in the spring.

Foals
Diarrhea in foals is common but most cases are mild, transient, and not associated with infectious agents. Diarrhea is the most commonly reported disease in foals under 7 days of age. The most common occurrence is associated with "foal heat" in the mare. Diarrhea is a common clinical finding in septic foals and is presumably the result of mucosal hypoperfusion and sepsis-related inflammatory mediators rather than bacterial or viral enteritis.

Rotavirus group A (RVA) is the most common cause of epidemics of diarrhea in foals and most commonly occurs in foals under 30 days of age.[19] Clostridial infection associated with diarrhea is most commonly caused by *C. perfringens* type C or *C. difficile*.[19] *Salmonella* spp. have been associated with diarrhea in foals but can cause diarrhea in horses of any age. A variety of other pathogens have occasionally been isolated from diarrheic foals, such as *E. coli, B. fragilis, Enterococcus* spp., and *Aeromonas* spp.

CLINICAL MANAGEMENT OF EPIDEMICS
When faced with an outbreak of acute diarrhea in neonatal calves (less than 30 days old) in which there is profuse watery diarrhea, progressive dehydration, and death within a few days or earlier, the following steps are suggested:
1. Visit the herd and do an epidemiologic investigation to identify the risk factors that may be responsible for the outbreak. Most outbreaks are multifactorial and an interaction among the environment, management, feeding, and the pathogens is probable. The investigation of the underlying causes of the outbreak should involve an examination of the following:
   - Dry cow management (including vaccination protocols)
   - Calving management
   - Colostrum management
   - Calf management (housing, prophylactic treatments, vaccinations …)

- Calf feeding (whole milk or milk replacer, type of milk replacer, amount fed, feeding frequency, feeding hygiene …)
- History of the present outbreak
- Farm history of previous disease outbreaks (not only affecting neonatal calves)
- The affected calves (which calves are affected?, age, vigor, housing type …)
- Results of necropsy, clinical pathology, and microbiology if available
- Treatments used in the current outbreak and their efficacy
- Recent changes in management and environment or changes of the herd that may be associated with the outbreak

2. Each of the commonly recognized risk factors must be examined for its possible role in the particular outbreak:
- Overcrowding of calving yards in beef herds
- Recent changes in incidence rate of dystocia and perinatal mortality in calves and periparturient disease in cows
- Recent changes in climate and recent stress of any kind on the herd
- In dairy herds feeding milk replacer, the feeding plan should be investigated.
- Any recent introductions of replacement calves into the herd should be considered as possible sources of pathogens.
- Prevalence of FTPI can be crudely assessed by checking 10 to 12 healthy calves between 24 hours and 7 days of age for the serum protein or preferably the serum IgG concentration (see Failure of transfer of passive immunity); the prevalence of FTPI should certainly not exceed 20%.

3. Affected calves should be examined clinically, dead ones by necropsy, and a case definition should be determined to ensure that diarrhea is the major problem.

4. All affected calves should be identified, isolated, and treated immediately with oral and parenteral fluid therapy as indicated. The use of oral fluid and electrolyte therapy for the treatment of dehydration and acidemia as soon as the calves are seen to be diarrheic must be emphasized.

5. Antimicrobial therapy should be considered for diarrheic calves with systemic illness but not for alert calves with diarrhea as the only clinical sign.

6. Fecal samples (30–50 g) should be collected from diarrheic calves at the first sign of diarrhea and from normal calves and submitted to a laboratory for the attempted isolation and characterization of ETEC as well as rotavirus and coronaviruses, *Salmonella* spp., and *Cryptosporidium* spp. A rapid ELISA test is available for the simultaneous detection of *E. coli* F5 (K99+) antigen, bovine coronavirus (BCoV), and rotavirus in the feces of diarrheic calves during the acute phase of the infection. Commercial test kits that can be used calf-side for the detection of BCoV, RVA, F5 (K99+) *E. coli,* and *Cryptosporidium spp.* antigen have become available in recent years.

7. Pregnant cows that are due to calve shortly should be moved to a new calving area. In a dairy herd this means a different, clean calving stall, preferably in another barn not previously occupied by cattle; in beef herds it may mean moving a large number of cows to a new, uncontaminated calving pasture.

8. The control of the disease in future calf crops will depend on application of the principles of control, which are described under Acute undifferentiated diarrhea of newborn farm animals and Viral diarrhea of calves, lambs, kids, piglets and foals. If a significant number of cows are due to calve in more than 3 to 6 weeks, vaccination with the calf diarrhea vaccines can be considered.

9. A report should be submitted to the owner that records the observations made at the farm visit and outlines specific recommendations for clinical management of affected calves and for control of the disease in the future.

CONTROL

The principles of control are presented in detail in the sections on colibacillosis of newborn calves, piglets, lambs, kids, and foals, and viral diarrhea in calves, lambs, kids, piglets, and foals, using the following principles:

- Reduction of the degree of exposure of the newborn to the infectious agents
- Provision of maximum nonspecific resistance with adequate colostrum and optimum animal management
- Increasing the specific resistance of the newborn by vaccination of the dam or the newborn

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ENTEROCOLITIS ASSOCIATED WITH *CLOSTRIDIUM DIFFICILE*

SYNOPSIS

Etiology Toxigenic strains of *Clostridium difficile.* Common bacterial etiology in antibiotic-associated diarrhea. Fecal–oral spread

Epidemiology Horses: occurs in foals and adults. Commonly precipitated by therapy with antimicrobial agents and/or hospitalization. Pigs: diarrhea and death in piglets in first week of life

Clinical findings Profuse watery diarrhea, tachypnea, dehydration, and metabolic acidosis. High case fatality, especially in very young foals

Necropsy findings Fibrinous to necrotic enterocolitis. Edema of mesocolon in pigs

Diagnostic confirmation Demonstration of organism and toxins

Treatment Fluids and electrolytes. Horses: metronidazole, if sensitive, or vancomycin (noting public health concern)

Control Isolation and barrier protection and prophylactic metronidazole

ETIOLOGY

C. difficile is a gram-positive, spore-forming, anaerobic bacterium. It is a recognized cause of antibiotic-associated diarrhea and pseudomembranous colitis in humans suffering perturbation of the bowel flora from antibiotic therapy or other causes. *C. difficile* causes enterocolitis in horses of any age and is associated with diarrhea in neonatal pigs.

Strains of *C. difficile* pathogenic to horses produce two toxins, A and B, and the degree of pathogenicity is related to the capacity for toxin production.[1] There are numerous strains of *C. difficile* (>50 ribotypes by one estimate), although a much smaller number (~4) constitutes the predominant isolates in animals.[2] Ribotype 078 is the most commonly reported in animals, especially in pigs and cattle,[3] although common human ribotypes (014/020 and 002) also occur in animals. *C. difficile* is isolated commonly from cattle. All *C. difficile* isolates from pigs, cattle, and poultry in the Netherlands were toxinogenic.[3]

EPIDEMIOLOGY
Occurrence
Horses
The disease can occur as outbreaks or, more commonly, is sporadic and associated with the risk factors of antimicrobial administration, hospitalization, or both.[1] It appears to occur worldwide. In young foals within the first 2 weeks of life it may occur without apparent predisposing causes but in adult horses it commonly follows the use of antimicrobial agents.[4] Case–fatality rates are highest in very young foals, in which the disease can be complicated by other existing neonatal diseases.

The microbiota of horses is complex and clostridial species are common in the feces of healthy horses, although *C. difficile* (mostly nontoxinogenic) is isolated from <10% of horses on single sampling.[5-7] However, monthly sampling of 25 healthy horses for 1 year detected toxinogenic *C. difficile* in 40% of horses at least once,[8] and toxinogenic *C. difficile* was detected in 7 of 55 healthy race horses examined once during summer in Ohio, suggesting that asymptomatic carriage of toxinogenic strains by some populations of healthy horses is relatively common.[9] Detection of toxigenic *C. difficile* is often, but not always, associated with disease in horses of any age, as demonstrated by the disproportionate representation of this organism in feces of horses with diarrhea.[6-8,10-14] Seven of 14 foals with diarrhea had *C. difficile* toxin (A/B) identified in feces, whereas none of 139 healthy foals were positive.[15] *C. difficile* was detected only in foals with gastrointestinal disease, and not in healthy foals (OR 5.4), in central Kentucky.[14] *C. difficile* toxin(s) is detected in approximately 5% of hospitalized foals with diarrhea,[10] and *C. difficile* was isolated from 10 of 73 hospitalized horses, 7 of which were positive for toxin A and/or B.[16] There was no association of *C. difficile* with a particular disease in this study.[16] One or both animals in mare–foal pairs can be subclinically infected with *C. difficile* and are potentially a source of infection for the other.[11] This is exemplified by the development of acute *C. difficile* enterocolitis in mares of foals treated with erythromycin and rifampin. Both *C. perfringens* (type A) and *C. difficile* can simultaneously infect foals with severe enterocolitis not associated with administration of antimicrobials, suggesting the potential for an interaction resulting in more severe disease.[4]

There is a strong anecdotal association of *C. difficile*-associated enterocolitis in horses with the administration of antimicrobials. Although most clinicians would agree that this association exists, there is no evidence that quantifies the increase in risk of a horse developing *C. difficile*-associated disease with the administration of antimicrobials or particular antimicrobials. Antimicrobial administration was not significantly more likely in horses with *C. difficile*-associated

diarrhea than in horses with diarrhea from which *C. difficile* was not identified, and only 26% of hospitalized horses with *C. difficile*-associated diarrhea had been administered antimicrobials.[17] Thirty-two of 33 (97%) horses and all adult horses with *C. difficile*-associated diarrhea had been administered antimicrobials before onset of diarrhea compared with 48% to 79% of horses with diarrhea of other causes.[18]

Horses with longer duration of hospitalization before onset of diarrhea are more likely to develop *C. difficile*-associated diarrhea.[18]

Pigs
C. difficile has increasing reportage, or recognition, and occurs predominantly in young piglets but also is recorded as a major cause of disease and mortality in sows.[19] The disease occurs worldwide and is an important cause of loss of young piglets.[20,21] The disease in piglets occurs predominantly in the first week of life, when the majority of the litter can be affected, and the case fatality can approach 50% but is usually lower. Stunting is a common sequel. Outbreaks occur with or without a history of processing with antibiotics.

The disease has not been effectively reproduced with simple challenge of conventional animals, suggesting that *C. difficile* in itself is not a sufficient cause. Challenge of adult horses with *C. difficile* with and without pretreatment with penicillin did not result in clinical disease in any of the horses, but *C. difficile* was subsequently isolated at greater frequency from the feces of the horses pretreated with penicillin. Challenge of newborn foals with *C. difficile* has resulted in enteric disease and diarrhea, but only in foals not receiving adequate transfer of colostral antibodies. *C. difficile* has been reproduced in gnotobiotic but not conventional pigs.

Routine prophylactic antimicrobial treatment of periparturient sows for diseases such as mastitis–metritis–agalactia has resulted in outbreaks of enterocolitis.

Pathogen Risk Factors
Pathogenic strains of *C. difficile* produce an enterotoxin (toxin A) and a cytotoxin (toxin B). There are degrees of virulence between strains, but nontoxigenic strains are considered nonpathogenic. Other virulence factors, including an actin-specific adenosine diphosphate-ribosylating toxin and an outer cell surface coat S layer, have been proposed as additional virulence factors.

The organism can be isolated from a number of environmental samples, including soil and the environment of veterinary hospitals. Although it appears that the organism is not commonly present in the feces of normal horses, it can be isolated from those of other animal species and has high prevalence in the feces of dogs and cats. The organism can survive in feces for at least 4

years. Spores are resistant to common disinfectants, but a 5% bleach solution is stated to be effective for disinfection.

Zoonotic Implications
C. difficile is a cause of diarrhea in humans and most commonly occurs following the administration of antibiotics, although sporadic cases without these risk factors also occur. The disease in humans may be mild and self-limiting or develop to severe pseudomembranous colitis with risk of intestinal perforation. In one study using molecular typing, 25% of isolates from humans were indistinguishable from isolates from animals. The risk for zoonotic infection should be considered, but barrier protection and attention to personal hygiene when handling animal cases should limit the risk for infection. Veterinarians and animal handlers undergoing antimicrobial therapy are particularly at risk.

PATHOGENESIS
The disease is associated with severe watery diarrhea and a hemorrhagic necrotizing enterocolitis. The enterotoxin A damages villous tip and brush border membranes and causes necrosis and increased intestinal permeability. The cytotoxin B is lethal to cells once the gut wall has been damaged. Complete erosion of the mucosa may result. Both toxins induce the production of TFN and proinflammatory interleukins, with a resultant inflammatory response and pseudomembrane formation. Lactose intolerance may develop secondary to infection.

CLINICAL FINDINGS
Horses
C. difficile occurs in horses of any age. In foals, it is part of the complex of diseases causing diarrhea and with a variety of clinical severity characteristic of these diseases.[10,14] In adults, infection causes hemorrhagic or necrotizing enterocolitis with classical signs of that syndrome.[22]

The disease in foals ranges from mild, self-limiting diarrhea to acute, rapidly fatal enterocolitis. Disease occurring with onset in the first 2 weeks of life is initially manifested with a decreased interest in suckling, often with signs of colic with increasingly prolonged and severe episodes of rolling and kicking at the abdomen and the occurrence of profuse watery and occasionally hemorrhagic diarrhea. Rectal temperatures are within the normal range but there is severe dehydration, an elevation of heart rate and respiratory rate, acidemia attributable to metabolic acidosis, and the development of septic shock. There is progressive enlargement of the abdomen, and transcutaneous ultrasound shows thickened, fluid-filled loops of intestine and fluid in the ventral abdomen.

In adult horses the disease is manifested with acute and often fatal colitis with profuse

diarrhea, toxemia, hypovolemia, and metabolic acidosis and is reported in individuals and as outbreaks in horses hospitalized and treated for various diseases.[13,17,18] The clinical signs of horses with *C. difficile*-associated disease are not distinguishable from those with non–*C. difficile*-associated disease,[17] although horses with *C. difficile*-associated diarrhea have higher rectal temperatures, band neutrophil counts, hematocrit, and hemoglobin concentration than do horses with diarrhea not associated with toxinogenic *C. difficile*. Horses with *C. difficile*-associated diarrhea have longer duration of hospitalization after onset of diarrhea than do horses with diarrhea of other causes.[18] The case–fatality rate for adult horses is approximately 25%.[18]

Pigs

Affected piglets are depressed and have a yellow, mucoid diarrhea with occasional piglets passing feces with specks of blood. As the condition progresses, affected pigs show abdominal distension and tachypnea, and some have scrotal edema. There is progressive dehydration and hypoglycemia.

CLINICAL PATHOLOGY

There is a leukopenia, a toxic left shift, a high hematocrit, and hyperfibrinogenemia. Plasma protein may be normal to low and there are high bilirubin and elevated liver enzyme values. Metabolic acidosis, as evidenced by an increase in anion gap and decrease in total CO_2 concentration, hyponatremia, and azotemia are present.[17,18] Blood IgG concentrations of affected foals are commonly within the normal range.

Classic methods of diagnosis are by examination of feces by culture of the organism and demonstration of toxins A and B by cytotoxin assays and enzyme immunoassays, some of which have been validated for use in horses with acute diarrhea and in foals.[12,23] Cycloserine–cefoxitin–fructose agar is commonly used to isolate *C. difficile* from feces, and detection is improved by use of PCR technology.[24] The isolation of *C. difficile,* in itself, is generally not considered to be diagnostic and should be accompanied by demonstration of toxin A in the feces by ELISA, or by tissue culture cytotoxin assays, to allow a putative diagnosis. Fecal toxin testing in live animals is an effective method of diagnostic conformation and correlates highly with toxin tests on intestinal contents at postmortem.

The organism, but not the toxins, is labile when kept aerobically at 4°C, with a significant decrease in recovery after 24 hours. Consequently, samples for culture should be taken in anaerobic transport media and shipped on ice.

PCR can provide a more reliable method of detection of genes encoding toxin A and toxin B.[11,13,15] Feces, or isolates, can be tested for genes encoding toxins A and B by PCR, and PCR can also be used retrospectively following postmortem for diagnosis in formalin-fixed tissues.

Human assays are not all suitable for diagnosis of the disease in piglets, with performance of molecular tests designed for humans being inadequate for diagnosis of disease in pigs.[25]

NECROPSY FINDINGS
Horses

Gross findings are of necrotizing or hemorrhagic enterocolitis with histologic findings that vary from a superficial fibrinous colitis with hemorrhage and edema to a severe hemorrhagic multifocal necrosuppurative and ulcerative enterocolitis.[22]

Pigs

The contents of the small intestine are scant and those of the large intestine yellow to dark yellow in color. Edema of the mesocolon is a common finding, along with increased fluid in the peritoneal and pleural cavities. Histologic findings vary from necrosis and exfoliation of the intestinal mucosa to segmental transmural necrosis in the large intestine.[11,15]

DIFFERENTIAL DIAGNOSIS

- Horses: See Table 7-5.
- Swine: See Table 7-6.

TREATMENT

Horses should be aggressively treated with fluids, plasma, and pressors to correct the fluid and electrolyte imbalance, correct the metabolic acidosis, and control pain. Antimicrobial therapy should be based on sensitivity testing if possible, but most isolates of *C. difficile* are susceptible to commonly used antimicrobials.[26] Isolates are usually resistant to trimethoprim-sulfamethoxazole and bacitracin, variably resistant to rifampicin, and susceptible to vancomycin. Metronidazole, 10 mg/kg intravenously four times daily or 15 mg/kg orally four times daily, has been commonly used for therapy, but there is geographic variation in sensitivity and there are reports of clinically important resistant strains.[27] Metronidazole and vancomycin are not approved for use in food animal species in most countries, and use of vancomycin is not prudent on public health grounds. Pharmacokinetics of metronidazole in foals are highly age dependent, and dosing should be adjusted in foals by increasing the period between administration of the drug from every 6 hours to every 12 hours until foals are 2 to 3 weeks of age.[28]

In vitro studies have shown that di-tri-octahedral (DTO) smectite can bind *C. difficile* toxins A and B, and that this can occur without inhibiting the antibacterial action of metronidazole. Clinical trials of efficacy have not been conducted but pharmacologic considerations indicate that an initial dose of 1.4 kg of DTO smectite, administered by stomach tube, followed by 454 g every 6 to 8 hours, could be of therapeutic value. Experimental studies in hamsters indicate promise for the use of immune sera and vaccines, but these are not currently available in agricultural animals.

CONTROL

There is no definitive control procedure. The organism is commonly present in veterinary environments and equine environments where there are foals. Foaling areas should be clean and disinfected with a sporicidal disinfectant. Metronidazole, 500 mg administered orally twice a day for 2 weeks, may be indicated for at-risk horses. Clinical cases should be isolated and, in a veterinary environment, strict barrier protection established between them and other animals under antimicrobial therapy. Orally administered probiotics and lactic-acid–producing bacteria are in use as an aid to prevention, but there are data indicating lack of efficacy.[29]

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PROLIFERATIVE ENTEROPATHY IN HORSES

ETIOLOGY

Proliferative enteropathy is associated with LI, an obligate intracellular gram-negative

bacterium associated with proliferative enteropathy in pigs, horses, hamsters, dogs, deer, rabbits, rats, camels,[1] and ratites. The disease in foals can be reproduced by experimental oral infection of foals with a virulent organism.[2] The organism can be isolated from feces of a large number of mammalian species including striped skunks, Virginia opossums, jackrabbits, and coyotes.[3] There is close similarity in DNA among isolates from a variety of species, although strains of the organism isolated from one species vary in their capacity to produce disease in other species. Infection of foals with an organism derived from clinically affected foals, foals with an organism derived from pigs, pigs with an organism derived from foals, and pigs infected with an organism derived from pigs demonstrated more severe disease in species-specific isolates. Such isolates resulted in the development of clinical signs, longer fecal shedding of the organism, and high serologic response than non–species-specific isolates.[4] There is also evidence of varying infectivity and pathogenicity in laboratory animals (hamsters and New Zealand rabbits) of equine or porcine isolates from clinically affected foals or piglets.[5]

EPIDEMIOLOGY

The disease was initially reported from North America and has subsequently been detected in most, if not all, areas of the world with commercial horse studs, including Japan, Europe, South America, Australia, and Israel.[6-11] Prevalence of serum antibodies against the organism increases with increasing age, for instance, 15% of foals before weaning, 23% in weanlings, 89% in yearlings, and 99% in horses >2 years of age.[8] Serum antibodies are detected, by ELISA, in 14% to 100% of horses on individual farms in Kentucky, with seroprevalence positively related to occurrence of the disease. Farms without evidence of endemic clinical disease had lower mean titers and lower maximal titers in individual horses than did farms on which the disease was endemic. Whether this finding is a reflection of prevalence of the disease (i.e., a consequence of high disease prevalence on some farms) or reflects greater exposure of horses that subsequently develop disease is unclear.[12] Approximately 50% of mares on farms with endemic disease are seropositive and ~50% of foals acquire passive immunity (become seropositive after nursing) from mares, and these maternally derived antibodies persist for 1 to 3 months.[13] Thirty percent of foals have evidence of infection, but not disease.[13]

The organism was not detected in foals with signs of gastrointestinal disease in Kentucky in one study,[9] although the disease is endemic in the area.[14] The disease occurs almost exclusively during late summer and early winter in Kentucky.[14]

Affected foals are usually 3 to 13 months of age and disease in adults is rare.[15] There is insufficient information to determine whether there is a breed predisposition to the disease. The disease is presumably transmitted by the fecal–oral route, with mares a potential, but unproven, source of infection.[16]

Proliferative enteropathy in foals occurs as isolated cases and as outbreaks on breeding farms. There is evidence that outbreaks begin after introduction of foals or weanlings to farms with no history of the disease, although whether this is coincidence or represents the mechanism of introduction of infection to the farm is unknown. Morbidity among foals and weanlings on affected farms is 20% to 25%, although this is based on disease outbreaks on only two farms. Case–fatality rate is as low as 7% in treated foals.[14]

PATHOGENESIS

The pathogenesis of the disease in foals has not been determined, but it is probably similar to that of the disease in pigs. Infection results in development of an enteropathy characterized by proliferation of intestinal crypt epithelial cells and infiltration of the lamina propria with mononuclear inflammatory cells. Subsequent malabsorption of small-intestinal contents and protein loss from diseased intestine cause weight loss and hypoproteinemia characteristic of the disease in foals. There is decreased or absent absorption of glucose in foals that can persist, with decreasing severity, for >2 months.[17] Colic and diarrhea result from intestinal dysfunction and malabsorption. Hypoproteinemia and the subsequent decrease in plasma oncotic pressure result in edema and signs of hypovolemia. Death is associated with severe hypoproteinemia, inanition, and colic.

CLINICAL SIGNS

The disease may present as one with a short course characterized by rapid weight loss, colic, and death within 2 to 3 days of onset of clinical signs or as a more chronic disease characterized by gradual development of weight loss and depression. Weight loss and poor body condition are consistent findings among foals affected by the chronic disease. Most affected foals have diarrhea that ranges in severity from acute profuse watery diarrhea to, more commonly, excessively soft feces. Foals are often depressed although they continue to nurse. Edema of the ventral abdomen and intermandibular space is common.[14] Fever is not a consistent feature of the disease.

An acute form of the disease results from ulcerative and necrotizing hemorrhagic enteritis.[18,19] Affected foals might be found dead or die after a brief illness (usually <8 hours) characterized by mild fever and rapid development of mild to severe colic and signs of sepsis.

Ultrasonographic examination of the abdomen reveals multiple loops of mildly distended small intestine with thickened walls. Loops of intestine can have walls of 5 to 8 mm thick (normal <3 mm; Fig. 7-8).

Many affected foals, and especially those that die of the disease, have concurrent diseases including parasitism and pneumonia.

The incubation period in pigs is 2 to 3 weeks but that in horses is unknown. Foals that recover from the disease may take several weeks to regain normal BW. Recovered foals that recover sell for approximately 70% of the sale price of unaffected siblings and peers.[14]

CLINICAL PATHOLOGY

Hypoproteinemia with moderate to severe hypoalbuminemia is present in most affected foals. Serum albumin concentrations can be as low as 0.6 g/dL (6 g/L). Hyperfibrinogenemia and mild anemia are common but not consistent findings. White cell count is elevated ($>14 \times 10$ cells/L) in most foals. Serum sodium and chloride concentrations are lower than normal and serum creatinine concentrations higher than normal in about 50% of affected foals.

Detection of exposure can be by detection of antibodies in serum (IPMA or ELISA) or detection of LI DNA in feces or rectal swabs.[12-14,20,21] PCR examination of feces for LI is specific for detection of the organism in affected foals. Examination of feces detects LI in approximately 80% of samples, of rectal swabs approximately 75%, and of both combined approximately 90% of samples from affected foals.[21] An indirect immunofluorescent assay detects serum IgG antibody to LI in foals, although the specificity of this finding for detection of the disease in foals is unknown. Foals with proliferative enteropathy have titers of 1:30 or greater.

NECROPSY

Gross lesions are mainly thickening and irregular corrugation of the small intestine. There is proliferation of intestinal crypt epithelium with projection of crypt cells into the intestinal lumen. The lamina propria is infiltrated by mononuclear inflammatory cells. Silver staining of intestinal sections reveals numerous short, curved bacteria in apical cytoplasm of crypt epithelial cells.

Samples for Confirmation of Diagnosis

- **Histopathology** of small intestine
- **Silver staining** of small intestine to demonstrate intracellular bacteria associated with hyperplastic cryptic cell
- **Bacteriology** is culture (which can be difficult as it requires cell cultures) and PCR examination of small-intestinal tissue
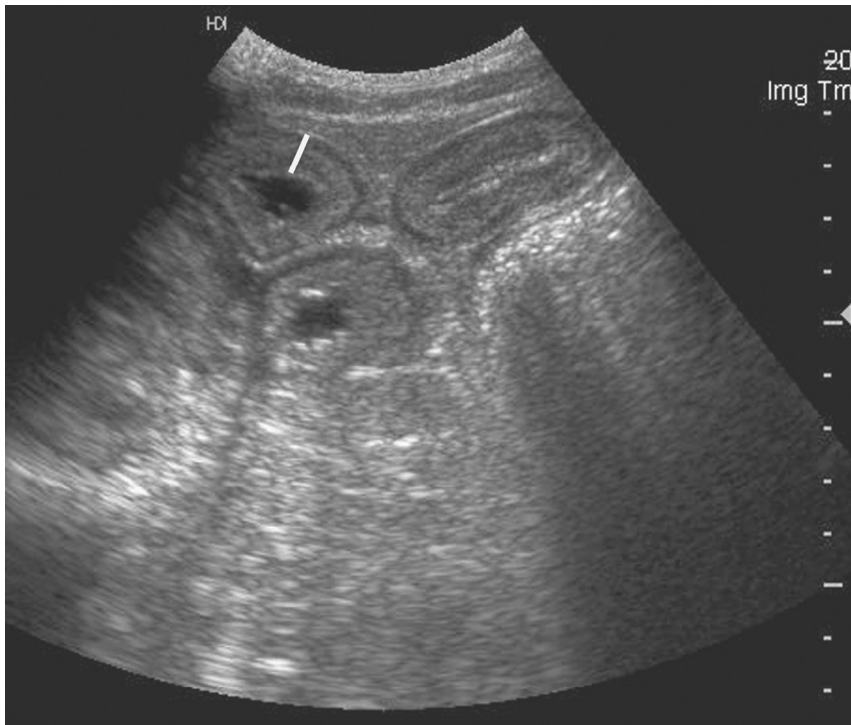
Fig. 7-8 Percutaneous ultrasonographic image of an 8-month-old filly with enteritis caused by Lawsonia *intracellularis* and demonstrating markedly thickened small-intestinal wall (9 mm; normal <3 mm). (Reproduced with permission. Arroyo LG, et al. *Can Vet J.* 2013;54:853.[18])

DIFFERENTIAL DIAGNOSIS

Antemortem diagnosis of proliferative enteropathy in foals should be based on the presence of characteristic clinical, hematologic, and biochemical signs; positive serology; and detection of Lawsonia *intracellularis* DNA in feces by polymerase chain reaction.

The primary differential diagnosis is **parasitism** by *Parascaris equorum*, cyathostomes, and large strongyles (in older foals). Examination of feces for helminth ova is diagnostic in cases with patent infections, but parasite infestations are often not patent in young foals. A history of an adequate parasite control program makes parasitism less likely but does not rule it out. **Malnutrition** caused by inappropriate or inadequate feeding practices or agalactia should be ruled out as a cause of failure to thrive.

Protein-losing enteropathy secondary to **enteritis and colitis** may be associated with *Salmonella* sp., *Rhodococcus equi,* or *Cryptosporidium* sp. Other intestinal diseases that cause enteritis but less often cause protein loss include the intestinal clostridioses, equine granulocytic anaplasmosis, and *Bacteroides* sp. infection. Intraabdominal abscesses associated with *R. equi* or *Streptococcus* sp. can cause chronic weight loss and hematological signs similar to proliferative enteropathy.

Hypoproteinemia can occur secondary to gastrointestinal ulceration. Neoplasia is rare in foals of this age, but intestinal lymphosarcoma can cause hypoproteinemia and weight loss.

Intoxication by **nonsteroidal antiinflammatory** drugs can cause a protein-losing enteropathy.

Diarrhea and ill-thrift caused by colitis and typhlitis associated with *Brachyspira* sp. (a spirochete) are reported from Japan.

TREATMENT AND CONTROL

Principles of treatment are eradication of infection and correction of hypoproteinemia. Administration of **antibiotics** is curative in many foals, and response to treatment does not appear to vary markedly with administration of oxytetracycline, chloramphenicol, or clarithromycin.[14] Isolates of the organism from pigs are sensitive in vitro to a wide range of antimicrobials including penicillin, erythromycin, difloxacin, virginiamycin, and chlortetracycline. Antibiotics used to treat LI infection in foals include oxytetracycline (6.6 mg/kg every 12 hours intravenously), doxycycline (10 mg/kg every 12 hours orally), chloramphenicol (50 mg/kg, every 6 hours orally), clarithromycin (7.5 mg/kg orally), or erythromycin estolate or similar product (15–25 mg/kg every 6–8 hours orally), sometimes in combination with rifampin (5–10 mg/kg every 12 hours orally). Erythromycin or oxytetracycline/doxycycline appear to be effective in the treatment of affected foals. Chloramphenicol is used in place of erythromycin in foals that develop intractable or severe diarrhea when treated with erythromycin, but its use is

illegal in some countries and is not recommended because of the risk of aplastic anemia in people exposed to the drug. Enrofloxacin might be effective, based on MIC values, but should be reserved as a drug of last resort because of the arthropathy associated with its use in foals.

Mildly or moderately affected foals require only administration of antimicrobials and nursing care. More severely affected foals can require intensive supportive care including intravenous administration of plasma and/or hetastarch to restore plasma oncotic pressure and minimize edema formation, fluid and electrolyte supplementation because of hypovolemia and abnormalities in serum electrolyte concentration, calorie-enhanced diets or parenteral nutrition, and antiulcer medications if signs of gastric ulceration are present.

Specific **control measures** to prevent spread of the disease among horses have not been developed. Given the putative fecal–oral cycle of infection and association of outbreaks of the disease in pigs after introduction of new stock or mingling of groups, hygiene measures that minimize fecal contamination of the environment by potentially infected foals are sensible. The organism from pigs can survive in feces for up to 2 weeks. Foals with the disease should be isolated from healthy foals, although the duration of this isolation is not known, and should not be transported to other farms until clinical and hematological signs of the disease have resolved. The role for wildlife hosts, if any, in the disease of foals is unknown.

Administration of an avirulent, modified live vaccine intrarectally appears to protect foals from disease after experimental exposure or on farms with endemic disease.[22-24]

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EQUINE NEORICKETTSIOSIS (EQUINE MONOCYTIC EHRLICHIOSIS, EQUINE EHRLICHIAL COLITIS, AND POTOMAC HORSE FEVER)

SYNOPSIS

Etiology *Neorickettsia risticii*, which is a rickettsia. Infection occurs by ingestion of infected immature trematodes (the aquatic cercariae), trematode-infected snails, or aquatic insects (including adults capable of flight, e.g., mayflies).

Epidemiology An infectious, but not contagious, sporadic disease of horses in North and South America and parts of Europe. Localized epidemics occur. Disease is most common near large rivers, but can occur elsewhere.

Clinical signs Fever and diarrhea with colic and laminitis in severe cases. Abortion is a sequela of clinical disease in some mares.

Lesions No gross lesions, except for laminitis. Histologic evidence of typhlitis and colitis

Diagnostic confirmation Demonstration of *N. risticii* by polymerase chain reaction or cultivation, in blood or feces of sick horses. More commonly the presence of a high antibody titer in horses with appropriate clinical signs is considered diagnostic.

Treatment Oxytetracycline (6.6 mg/kg, intravenously every 12–24 h), fluids, and supportive care. Prophylaxis for laminitis

Control Vaccination, which is of questionable efficacy and not recommended

ETIOLOGY

The causative agent is *N. risticii*, a small gram-negative coccus that is closely related to the agents of human ehrlichiosis (*Ehrlichia sennetsu*) and salmon poisoning of dogs (*N. helminthoeca*).[1]

EPIDEMIOLOGY

This disease is infectious, but not contagious, and usually has a sporadic occurrence. Localized epidemics occur.

Occurrence

Equine neorickettsiosis is recorded in the United States, Canada, Europe, Uruguay, and southern Brazil. Although it might have wider occurrence, evidence of infection based on the commonly used indirect FAT should be interpreted with caution because of the high rate of false-positive results. The highest prevalence of disease is near large rivers, apparently related to the infection of horses by ingestion of infected aquatic insects, although the disease can occur elsewhere, for instance, when strong winds carry infected insects (mayflies, *Hexagenia* spp.) from water sources.[2]

Clinical disease is sporadic and seasonal, with the predominance of cases occurring during the summer and the autumn periods in areas with cool to cold winters. In warmer areas, such as Florida and Texas, cases occur year round. The prevalence of horses in the Midwest and East Coast of the United States with antibodies to *N. risticii* varies with geographic region, but can be as high as 86% of horses tested, although the overall rate appears to be closer to 25%. The prevalence of horses with serologic evidence of exposure is much less in California. There is a marked seasonal variation in the prevalence of seropositive horses, with the highest prevalence in the summer months (July and August) and the lowest prevalence in the winter.

Animal Risk Factors

Clinical disease is believed to be uncommon in horses under 1 year of age (14% in one case series),[3] although peracute disease can occur in foals, and there is no age difference in prevalence of disease in adult horses. Similarly, there is no evidence that breed and sex influence susceptibility to disease. The risk for disease is greater in horses housed on premises with a history of previous infection or those that have other livestock.

The clinical attack rate varies considerably, but estimates range between 0.44 and 19 cases per year per 1000 horses at risk. During epidemics, the clinical attack rate may be as high as 20% to 50% of horses on affected farms. **Case–fatality** rates range from 7% to 30%.[3]

The risk of horses being seropositive in some areas is related to breed (Thoroughbreds are three times more likely to be seropositive than are non-Thoroughbreds and non-Standardbreds), sex (females are 2.7 times more likely to be exposed than are stallions and geldings), and age (increasing risk up to 12 years of age). Horses that have had clinical signs compatible with neorickettsiosis are more likely to be seropositive than are horses with no such history.

Transmission

The disease is infectious but not contagious. Horses develop infection and disease after ingestion of aquatic insects including caddisflies (*Dicosmoecus gilvipes*) or mayflies (*Hexagenia* spp.).[1,2] The disease can be transmitted experimentally to horses by parenteral administration of *N. risticii* or blood from infected horses. Studies of a tick (*Dermacentor variabilis*), black flies (*Simulium* spp.), fleas, flies (*Tabanus* spp., *Hybomitra* spp., *Stomoxys* spp., *Haematobia* spp.), and mosquitoes have failed to demonstrate transmission of infection.

N. risticii infects trematodes stages (cercariae and xiphidiocercariae) found in freshwater snails (*Juga yrekaensis* and *Planorbella subcrenata* in California and northwestern United States and *Elimia* sp. including *E. livescens* and *E. virginica* in the eastern United

States).[4] *N. risticii* infects metacercariae found in adults and juveniles of aquatic insects including caddisflies (Trichoptera), mayflies (Ephemeroptera), damselflies (Odonata, Zygoptera), dragonflies (Odonata, Anisoptera), and stoneflies (Plecoptera). *N. risticii* DNA has been detected in trematodes (Lecithodendriidae) infecting bats and swallows. *N. risticii* DNA is present in eggs of the trematodes (*Acanthatrium oregonense*) found in bats demonstrating vertical (adult to egg) transmission of infection in trematodes. Furthermore, *N. risticii* DNA was detected in the blood, liver, or spleen of bats infected with the trematode, suggesting that *N. risticii* can also be transmitted horizontally from trematode to bat. These results indicate that the trematode *A. oregonense* is a natural reservoir and probably a vector of *N. risticii*. This information suggests that insectivorous bats and birds are the definitive hosts of trematodes that maintain the natural reservoir of *N. risticii*. Briefly, it appears that horses are accidentally infected by *N. risticii* that normally cycles between trematode life stages in bats, freshwater snails, and aquatic insects. Infection by horses occurs when they ingest *N. risticii*-infected immature trematodes (the aquatic cercariae) directly while drinking from waterways or trematode-infected snails or aquatic insects while drinking or feeding.

Infected horses develop a sterile immunity and so are unlikely to be a source of subsequent infection.

PATHOGENESIS

Infection is followed by monocyte-associated bacteremia and the organism is present in monocytes, macrophages, and the glandular epithelial cells of the intestinal tract. The number of *N. risticii* in blood is greatest before the development of clinical signs, which in experimentally infected horses and ponies occurs approximately 19 days after infection by ingestion of infected aquatic insects. The prominent clinical sign of diarrhea is caused by colitis and typhlitis and is associated with a neorickettsia-induced disruption of sodium and chloride absorption by the large colon. Fluid and electrolyte losses associated with diarrhea cause dehydration, hyponatremia, and acidosis.

Transplacental infection with *N. risticii* occurs and causes abortion, which can be weeks to months after resolution of clinical disease in the dam.[5]

CLINICAL FINDINGS

The classic manifestation of *N. risticii* infection in horses is fever, depression, anorexia, diarrhea, colic, and laminitis. A retrospective review identified diarrhea (66% of 44 horses), fever (50%), anorexia (45%), depression (39%), colic (39%), and lameness (18%) as the most common clinical signs of the disease in horses at each of two referral clinics.[3] However, infection can result in a variety of clinical abnormalities ranging

from inapparent infection, through transient fever and depression, to the severe signs described earlier. Equine neorickettsiosis should be considered in any horse living in an endemic area that demonstrates fever and depression.

In naturally occurring cases of severe clinical disease there is typically an acute onset with depression, anorexia, tachycardia, congested mucous membranes, and fever. There are decreased intestinal sounds on abdominal auscultation in the early stages of the syndrome and subsequently tinkling sounds before the onset of diarrhea, which usually occurs 24 to 72 hours later. The severity of the diarrhea varies, but it is usually profuse and projectile. It persists for up to 10 days and there can be sufficient fluid loss resulting in severe and rapid dehydration and hypovolemic shock. Colic is a presenting sign in some horses and may be mild or present as an acute abdomen. There can also be subcutaneous edema in the ventral abdomen and limbs. Less severe clinical manifestations of infection include the occurrence of fever and anorexia without other signs or the occurrence of mild colic or subcutaneous edema.

Laminitis occurs in up to 40% of horses and is usually apparent within 3 days of initial signs of disease.[3] One retrospective review of 44 cases identified laminitis present on admission (12 hours to 5 days after first developing clinical signs of equine neorickettsiosis) in 18% of cases with a further 18% developing laminitis during hospitalization (0–4 days after admission, median of 24 hours).[3] Laminitis is often severe, involving all four feet in most horses (88% of those with laminitis) and with rotation of the distal phalanx in 60% of cases that had radiographic examination of the feet (likely the most severely affected horses).[3]

Abortion occurs as a result of N. risticii infection and, in experimental and natural infections, occurs 65–111 days after infection of the dam.[5] The dams that aborted all became clinically ill after infection, but clinical signs of disease had resolved at the time they aborted. Abortion was presaged by ventral edema and enlargement of the udder in experimental disease, and placenta was retained in some cases including that with natural infection.

CLINICAL PATHOLOGY

Hematological examination usually reveals leukopenia (<5000 leukocytes per microliter) with neutropenia (74% of cases) and a marked left shift, mild thrombocytopenia, and hemoconcentration (hematocrit 50%–60%, 0.5–0.6 L/L) in 38% of cases.[3] **Serum biochemical analysis** often reveals hypocalcemia (76% of 32 horses), hyponatremia (64%), hyperglycemia (59%), hypochloremia (53%), azotemia (50%), hyperbilirubinemia (50%), and hypoalbuminemia (34%).[3] Hyperlactatemia and metabolic acidosis are common. **Peritoneal fluid** is usually normal.

Horses with hemoconcentration are less likely to survive.[3]

Diagnostic confirmation is achieved by demonstration of N. risticii in blood or feces, or serologic evidence of infection, in horses with clinical signs compatible with the disease. Routine diagnosis is based on demonstration of a high serum antibody titer on the IFA test. Most horses with disease caused by N. risticii have titers ≥1:80 at the onset of clinical signs, whereas horses with titers ≤1:40 probably do not have the disease. The presence of a high titer at the time of onset of clinical signs is a result of the 8- to 12-day incubation period during which there is a high level of neorickettsemia and the production of a strong IgM antibody response. The IgM antibody response wanes rapidly and can be undetectable by 60 days after infection, although a prominent IgG response occurs. Therefore by the time clinical signs are apparent the horse has a high titer that might decline, making the use of acute and convalescent (2 weeks after clinical signs resolve) serum titers potentially misleading. A rising titer in samples collected several days apart soon after the onset of disease is indicative of the disease, but a declining titer does not rule it out. The IFA test performed in some laboratories has a high rate of false-positive reactions and should be interpreted with caution. The preferred diagnostic test is a demonstration of antigen or DNA of N. risticii.

Detection of the organism in white blood cells by microscopic examination of stained blood smears is usually not possible because of the low level of infection of blood monocytes. The organism can be cultivated, but this is time-consuming and expensive. However, nest PCR detects the presence of N. risticii nucleic acid with a sensitivity similar to that of blood culture in experimental infection. PCR testing depends on the presence of the organism in the blood and could lack sensitivity because of variables levels of the organism in blood.[3] The specificity of the test, in the presence of compatible clinical signs, is assumed to be high.

Similarly, N. risticii can be detected by a PCR test in feces of horses. The sensitivity is not reported, but specificity is assumed to be high in the presence of compatible clinical signs.

NECROPSY FINDINGS

The gross changes in horses dying of equine neorickettsiosis usually include subcutaneous edema of the ventral body wall and a very fluid consistency to the contents of the large bowel. Congestion, hemorrhage, and mucosal erosions can occur throughout the alimentary tract but are concentrated in the cecum and colon. The mesenteric lymph nodes are often swollen and edematous. There may be lesions of laminitis. Histologic examination confirms the alimentary mucosal erosion and ulceration, which is

accompanied by an infiltrate of a mixed population of leukocytes within the lamina propria and submucosa. The causative organisms can be demonstrated in tissue sections using Steiner's silver stain. Detection using EM or PCR techniques are other options.

Fetuses that are aborted as a result of N. risticii infection of the dam have gross lesions consisting of enlarged liver, spleen, and mesenteric lymph nodes and histologic evidence of enterocolitis, hepatitis, myocarditis, and lymphoid hyperplasia with necrosis of mesenteric lymph nodes.[5]

Samples for Postmortem Confirmation of Diagnosis

The parasite can be demonstrated in cecum, colon, and mesenteric lymph node by a polymerase reaction test or EM. Formalin-fixed tissue for light microscopy should include cecum, colon, liver, and mesenteric lymph node.

DIFFERENTIAL DIAGNOSIS

The main differentials are as follows (Table 7-5):
- Diarrhea caused by salmonellosis, Clostridium difficile colitis, massive emergence of hypobiotic cyathostomes, colitis X, and antibiotic-induced colitis
- Abortion caused by equine herpesvirus-1, leptospirosis, congenital anomalies, and Salmonella abortusequi

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TREATMENT

TREATMENT AND PROPHYLAXIS

Treatment of equine neorickettsiosis
- Oxytetracycline 6.6 mg/kg intravenously every 12–24 h for 5 days (R1)

Prophylaxis
- Vaccination (R3)

The specific treatment of equine neorickettsiosis is oxytetracycline (6.6 mg/kg BW intravenously every 12–24 hours for 5 days), and horses treated early in the disease respond well. Administration of oxytetracycline increases the likelihood of survival by nine times (OR 95% CI 1.2–70), with 6/14 horses not treated with oxytetracycline (usually treated with another antibiotic) surviving compared with 26/30 oxytetracycline-treated horses.[3] Administration of metronidazole with oxytetracycline offers no clear survival advantage.[3]

Given the effectiveness of oxytetracycline in the treatment of the disease and the lack of clear evidence that oxytetracycline at the recommended dose induces or exacerbates diarrhea, this drug should be administered to all horses that live in an endemic area and that develop signs consistent with equine neorickettsiosis. Treatment does not

interfere with the development of immunity. Other antibiotics that have been used include combinations of a sulfonamide and trimethoprim or rifampin and erythromycin. Doxycycline has been used, but intravenous administration is associated with cardiovascular abnormalities and sudden death.

Treatment of horses with acute diarrhea is discussed in Chapter 7. Prophylaxis for laminitis is indicated in Chapter 15.

CONTROL

Control centers on vaccination, although this is inadequate in controlling disease in field situations.[6] The apparent lack of efficacy of vaccination in the United States might be caused by the inclusion of only one strain of *N. risticii* in the vaccine, and this strain is immunologically distinct (based on the P51 surface protein) from most strains from the eastern or midwestern United States and from most strains isolated after 2000.[6] There are a number of strains of the organism, with associated variation in surface-expressed proteins and in particular P51, and the vaccine might not confer immunity to all these strains.[1,6] P51 is strongly recognized by sera from horses with IFA titers of 1:80 and above, and it could be useful for inclusion in vaccines or diagnostic tests.[6]

Infection is followed by the development of a neutralizing antibody response that is associated with clearance of *N. risticii* and the presence of a sterile immunity to the homologous strain, which persists for at least 20 months. An inactivated whole-cell adjuvanted vaccine is available, and vaccinated animals have resistance to experimental challenge. However, protection from vaccination is not complete and wanes within 6 months. Survival rate of horses with clinical equine neorickettsiosis is not different among horses that were vaccinated (7 of 9, 78%) before development of the disease from that of all horses studied (n = 44, 79% survival rate).[3] In an area with a low attack rate of the disease (0.44–1.7 horses/1000 per year) the risk of neorickettsiosis in horses vaccinated once per year is almost identical (OR 0.93) to that of unvaccinated horses, and there is no difference in the severity of the disease in vaccinated and unvaccinated horses. Furthermore, it is more economical *not* to vaccinate horses in areas with a low attack rate. In areas with a high attack rate it may be appropriate to provide an initial vaccination of two doses 3 weeks apart, with revaccination at 4-month intervals during the disease season.

Current recommendations from the American Association of Equine Practitioners included details on vaccination of horses against equine neorickettsiosis.[7] Because of evidence demonstrating the limited, or lack of, efficacy of vaccination with the currently available product, routine vaccination of horses is not recommended at this time.

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EQUINE CORONAVIRUS INFECTION

Coronavirus infection is associated with diarrhea in foals, although rarely,[1] and is also incriminated as a cause of acute lethargy, fever, and signs of gastrointestinal dysfunction in adult horses. The putative causative agent is equine coronavirus (ECoV), and the strains identified in Japan, France, and the United States are virtually identical to the strain initially isolated from foals in North Carolina.[1-4] There is some variation in the virus, principally within p4.7 and the noncoding region following the p4.7 gene.[5] ECoV is of the genus *Betacoronavirus* and the species *Betacoronavirus-1*, which includes BCoV, porcine HEV, and canine respiratory coronavirus.[6] Experimental inoculation of adult horses reproduces the disease.[7]

The association between coronavirus infection and clinical disease in adult horses is reported in Japan, North America, and Europe.[1-5,8] Animal risk factors have not been identified, and the disease occurs in horses from 1 to 29 years of age.[2,5,8] The disease in adult horses is most commonly reported as an outbreak in stables affecting 15% to 60% of horses.[2,4,5] The case–fatality rate is approximately 0% to 7% with deaths caused by acute, profuse diarrhea; septicemia; or signs of neurologic disease.[2,5,8] A case–fatality rate of 27% is reported in two outbreaks of disease in Miniature horses and Miniature donkeys.[8]

Transmission is assumed to be fecal–oral, but the importance of fomites is spread within a stable, and longevity of the virus in the environment is not reported. The virus can be detected in feces for at least 12 to 14 days after oral inoculation of horses,[7] although the median shedding time from onset of clinical signs in horses with spontaneous disease is 4 days.[8]

The incubation period for horses experimentally infected with ECoV is 2 to 4 days before development of fever or anorexia.[7] The main clinical signs are anorexia, lethargy, and fever (43). Approximately 10% of affected horses have diarrhea and colic in approximately 2% of horses.[2,5] Horses that die do so with rapid progression of the disease including profuse diarrhea, septicemia, or neurologic disease. Depression, ataxia, and recumbency with abnormally high blood ammonia concentrations are suggestive of intestinal hyperammonemia.[8] Clinical signs generally resolved within 1 to 4 days with supportive care. Outbreaks last approximately 3 weeks.[2,5]

Affected horses are leukopenic (neutropenic).[2,5] Serum amyloid A concentrations increase in experimentally infected horses 2 to 4 days after inoculation with the virus.[7] Serology is useful for demonstrating seroconversion to ECoV or high titers in recovered horses.[3-5] The virus can be detected in feces and blood, but not nasal discharges, in nonexperimental cases using PCR technology.[2,3] Reverse transcription and loop-mediated isothermal amplification (LAMP) assay are less sensitive but cheaper than RT-PCR technology for detection of the virus.[9] The virus is more frequently recovered from feces of clinically affected horses during outbreaks, and viral load in feces is associated with severity of disease.[2,3,8]

Treatment is supportive. There is no vaccine. Control is facilitated by implementation of measures to reduce viral spread, such as strict limitations on movement of horses within the facility, use of sanitary procedures including disinfectants, and cessation of racing or competition until the outbreak has abated. Most commonly used disinfectants are efficacious in reducing infectivity of coronavirus on surfaces, including benzalkonium and glutaraldehyde as well as alcohol-based hand disinfectants.

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VIRAL DIARRHEA IN CALVES, LAMBS, KIDS, PIGLETS, AND FOALS

SYNOPSIS

Etiology Rotaviruses, coronaviruses, toroviruses, and parvoviruses

Epidemiology Common cause of diarrhea in newborn farm animals, usually in calves but also in lambs, kids, piglets, and foals. Rotaviruses ubiquitous in environment and 50%–100% of adults seropositive. Spread by feces. Protection dependent on specific antibody in colostrum in intestinal lumen. Bovine coronavirus is also pneumotropic and causes respiratory disease.

Signs
Calves Outbreaks of diarrhea at 5–14 days of age and older up to 3–4 weeks. Recovery occurs in a few days.

Piglets Outbreaks of diarrhea at 1–4 weeks of age and following weaning. Porcine epidemic diarrhea type I at 4 to 5 weeks of age; type II at all ages. Recovery occurs in a few days.

Foals Profuse diarrhea, slight fever, and dehydration. Recovery occurs in a few days.

Lesions Fluid-filled intestine and dehydration. Villous and crypt atrophy. Diagnostic confirmation. Many diagnostic tests to identify viruses in fecal samples

Treatment Oral and parenteral fluid and electrolyte therapy; correction of acid-base disturbances

Control Reduce infection pressure, ensure adequate transfer of passive immunity, and vaccination of dam to provide specific colostral antibody.

ETIOLOGY

Several families of viruses cause diarrhea in neonatal farm animals, and occasionally in adults. These include Reoviridae, Coronaviridae, Toroviridae, Parvoviridae.

Rotaviruses

Rotaviruses are nonenveloped, dsRNA viruses pertaining to the family Reoviridae and are a primary cause of diarrhea in humans, calves, lambs, kids, piglets, and foals. All members of the group of viruses share a common morphology and were previously designated as reovirus-like viruses. Rotaviruses of human infants, calves, pigs, and foals are morphologically indistinguishable from each other and from the virus of infant mice; the lamb rotavirus is similar to both calf and pig viruses.

Rotaviruses are assigned to serogroups with group members sharing distinctive common antigens. Currently, seven serogroups (A through G) are recognized, which are antigenically and electrophoretically distinct. Rotaviruses belonging to groups A–C are associated with clinical disease in humans and animals, whereas groups D–G have only been isolated from diarrheic animals. **RVA is by far the most prevalent group in humans and animals.**

Rotavirus serogroups are further classified into serotypes based on specificity of the outer capsid proteins VP7 (G type, for glycoprotein) and VP4 (P type, for protease sensitive protein). At least 27 G serotypes and 35 P serotypes of Group A rotavirus are recognized.[1]

Coronaviruses

Coronaviruses are ssRNA viruses pertaining to the family Coronaviridae. They are associated with acute enteritis in neonatal calves and piglets and possibly also in foals. In ruminants coronavirus infection can be associated with calf diarrhea, calf respiratory disease, diarrhea in adult cattle (winter dysentery), and respiratory disease in adult cattle.[2]

The coronavirus-like virus of pigs is similar to, but distinct from, the virus of TGE and is the cause of PED type II.

Toroviruses

The family Toroviridae includes the Berne virus of horses and the Breda virus, which has been isolated from cattle.

Parvovirus

Parvoviruses have been associated with diarrhea in calves but are not significant pathogens in cattle.

Other Viruses and Mixed Infections

Although the rotavirus and coronavirus are the most common causes of viral diarrhea in newborn farm animals (other than TGE of piglets), the adenovirus and small viruses resembling astroviruses and caliciviruses have been isolated from diarrheic calves and foals, but their etiologic significance is uncertain.[3]

Multiple mixed viral infections are being recognized more frequently as diagnostic techniques are improved. Both rotavirus and coronavirus may occur in the same diarrheic calf with or without the presence of ETEC.

EPIDEMIOLOGY

The general aspects of the epidemiology of viral diarrheas of newborn farm animals are described here, followed by the specific epidemiologic features in calves, lambs and kids, piglets, and foals. The rotavirus is used as a model.

Occurrence

The rotavirus is ubiquitous in the environment of domestic animals, and serologic surveys indicate that 50% to 100% of adult cattle, sheep, horses, and pigs have antiviral antibody. Although different animal species commonly host different coronavirus genotypes there is evidence for interspecies transmission not only between animal species but also between animals and humans. Two routes for interspecies transmission have been proposed, direct interspecies transmission and transmission coupled with reassortment.[4] However, the significance of interspecies infection under field conditions has not been evaluated. Cross-infection between species is not a property shared by all rotaviruses.

Methods of Transmission

The intestinal tract is the site of multiplication of the rotavirus and the virus is excreted only in the feces. Infected feces may contain as many as 10^{10} virus particles per gram. **Rotaviruses** are considered to be **highly contagious**; studies in pigs showed infection can be achieved with as little as 90 virus particles. **Because rotaviruses are stable in feces and relatively resistant to commonly used disinfectants, it is extremely difficult to prevent gross contamination of animal housing once infection has been introduced.** The adult animal is the primary source of infection for the neonate. The survival of the bovine rotavirus in air and on surfaces is directly influenced by the level of relative humidity. The rotaviruses generally survive well in an aerosol state, and medium-range of relative humidity and air may be one of the vehicles for dissemination of the virus.

Immune Mechanisms

An important epidemiologic characteristic of rotavirus and coronavirus infections in newborn farm animals is that protection against disease is dependent on the presence of specific colostral antibody in the lumen of the intestine of the newborn. Colostral antibody in serum does not directly protect but contributes to mucosal immunity through re-secretion into the gut lumen. Protection against clinical disease depends on the amount of immunoglobulin in the lumen of the intestine. The daily oral administration of colostrum containing specific antibody or hyperimmune serum to neonates beyond the time of "gut closure" (intestinal absorption of colostral antibody) will improve resistance to clinical rotavirus enteritis.

The protection is against clinical disease but not necessarily against infection, which means that calves, lambs, and piglets can shed virus in feces while being protected from clinical disease. The protection lasts only as long as colostral antibody is present within the lumen of the intestine, which explains why rotaviral diarrhea occurs commonly after 5 to 7 days of age. Survival from rotavirus diarrhea in calves may be dependent on a high level of serum colostral immunoglobulin.

Calves: Bovine Rotavirus

Many of the epidemiologic characteristics of neonatal calf diarrhea associated with the rotavirus and coronavirus must be considered in the context of "acute undifferentiated diarrhea of newborn calves," because mixed infections are more common than single infections.

Occurrence and Prevalence of Infection

Worldwide prevalence rates for bovine rotavirus infection range from 7% to 94% depending on the geographic region, although most studies report prevalences in the range of 30% to 40%.[5] RVA is by far the most prevalent group and is the group most commonly associated with clinical disease, although serogroups B and C have also been isolated from diarrheic calves. Diarrhea caused by RVA occurs in calves from 1 to 2 weeks of age.

In cattle RVA strains belonging to at least 12 G types (G1–G3, G5, G6, G8, G10, G11, G15, G17, G21 and G24) and 11 P types (P[1], P[3], P[5–7], P[11], P[14], P[17], P[21], P[29], and P[33]) have been identified. Most common strains belong to G6, G8, and G10 in association with P[1], P[5], and P[11].[1] Serotypes G6 and G10 are the most

prevalent RVA serotypes in dairy and beef calves with diarrhea in the United States. Rotavirus strains belonging to G10 P[11] constitute the largest proportion of bovine rotaviruses in cattle throughout India. This has major zoonotic implications because this strain is related to those found in newborn children in India.

The prevalence of subclinical infection may be greater than that indicated by isolation of the virus from feces. Rotavirus–immunoglobulin and coronavirus–immunoglobulin complexes may be present in the feces of 44% and 70% of adult cattle, respectively, whereas the free rotavirus and coronavirus may be absent or present in only 6% of fecal samples, respectively. Clinically normal cows can shed the virus for several weeks in the presence of fecal and serum antibody. Repeated bovine rotavirus infection and reexcretion can occur in calves several months of age, even in the presence of serum antibodies. Clinically normal calves may also shed the virus and there may be histologic evidence of lesions of the small intestine caused by rotavirus infection.

Concurrent Infections
Rotavirus was detected in the feces of 43% of neonatal diarrheic dairy calves in Spain. A concurrent infection was detected in 58% of the rotavirus-infected calves, and the most common mixed infection was rotavirus-*Cryptosporidium.* The detection rates of the other enteropathogens with rotavirus infection were 20% for coronavirus, 85% for *Cryptosporidium* spp., 17% for F5 (K99) *E. coli*, and 2% for *Salmonella* spp. As the age of the calf increased, the detection rates of other enteropathogens decreased. Similar results were recently reported from dairy calves in the Netherlands.[6]

Risk Factors
Animal Risk Factors
The factors that influence rotavirus infection and its clinical severity include the following:
- Age of the animal
- Immune status of the dam and absorption of colostral antibody
- Ambient temperature
- Degree of viral exposure
- Occurrence of weaning
- Presence of other enteropathogens

Calves are most susceptible to rotavirus diarrhea between 1 to 3 weeks of age. This age occurrence is related in part to the rapid decline in specific colostral antibody to rotavirus.

The mortality is highest in the youngest animals that have received insufficient colostrum and are subjected to severe weather conditions.

Environmental Risk Factors
Although the rotavirus has been most commonly associated with outbreaks of diarrhea in beef calves raised in groups outdoors, it has also been recovered from dairy calves raised together in large groups in large dairy herds. The morbidity rate in beef herds varies from herd to herd and from one year to another.

The survival of the bovine rotavirus in air and on surfaces is directly influenced by the level of relative humidity. Rotaviruses generally survive well in an aerosol state and medium range of relative humidity, and air may be one of the vehicles for dissemination of the virus.

Pathogen Risk Factors
There are differences in virulence among the bovine rotaviruses, which may explain the variability in the severity of disease in natural outbreaks and must be considered when developing vaccines.

Rotaviruses possess two outer capsid proteins, VP4 and VP7. The neutralization specificity related to VP7 is the G (for glycoprotein) serotype and that associated with VP4 is referred to as the P (for protease sensitive protein) serotype. Specific G and P types have been associated with specific animal species. As more rotaviruses have been characterized from diverse locations worldwide, the host species specificity of P and G types has become less distinct. G types 6, 8, and 10, once thought to be specific to cattle, have been found in humans.

In contrast to natural recovery from infection, which results in high titers of P-specific neutralizing antibodies, parenteral administration elicits primarily G-specific neutralizing antibodies. Thus failure in passive protection with a monovalent vaccine for prevention of rotavirus-associated diarrhea in neonatal calves may be less than optimal because of the diversity of P and G types occurring in nature.

Natural subclinical infections are common in calves in the second week of life, which raises doubts about rotavirus pathogenicity. Experimentally, the clinical outcome of infection is dependent on both age and rotavirus isolate. Age-dependent resistance to infection was not found. Bovine rotaviruses differ in virulence for calves in the second week of life, and older calves are susceptible to rotavirus infection and disease.

The calf rotavirus can be experimentally transmitted to piglets and has been isolated from natural outbreaks of diarrhea in piglets. The isolation of a rotavirus from neonatal deer affected with diarrhea in a zoo in Australia raises some interesting epidemiologic possibilities.

Morbidity and Case Fatality
In some herds the disease starts at a low rate of 5% to 10% in the first year, increases to 20% to 50% in the second, and to 50% to 80% in the third year. In other herds, explosive outbreaks affecting 80% of the calves have occurred in the first year. The case–fatality rate has also been variable (in some herds as low as 5%), whereas in other herds it has been as high as 60%. The mortality rate probably depends on the level of colostral immunity in the calves, the incidence of enteric colibacillosis, and the level of animal husbandry and clinical management provided in the herd.

Method of Transmission
The virus is excreted by both calves and adult cattle in large numbers (up to 10^{10}/g of feces) and excretion may last for several weeks. Transmission is by the fecal–oral route via contaminated feces or fomites. The minimal infectious dose in cattle does not appear to have been determined, but as few as 90 virus particles were found to be sufficient to induce infection in piglets, making this a highly infectious pathogen.

Even under open-range conditions, there is a rapid spread of the virus throughout calves that come into frequent contact with each other, particularly during the calving season. Calves are infected after birth from the dam's feces or from other infected diarrheic calves. Pregnant cows excrete the rotavirus intermittently throughout pregnancy, from one calving to the next, and provide a direct source of infection for the newborn calf. Both subclinically infected and diarrheic calves infected by rotavirus can be a source of infection for other in-contact calves.

Immune Mechanisms
Newborn calves are protected from the rotavirus only during the first few days after birth, when colostrum contains a specific rotavirus antibody that is active in the lumen of the intestine. This correlates well with the peak incidence of rotavirus diarrhea, which is at 5 to 7 days of age, and coincides with a marked drop in colostral immunoglobulin by the third day after parturition and an incubation period of 18 to 24 hours for the disease to occur. The serum colostral immunoglobulin of the calf may also be re-secreted from the serum into the intestine and complement the role of colostral and milk antibodies in the lumen of the intestine.

Bovine Coronavirus (Calf Diarrhea)
BCoV is associated with diarrhea in adults (winter dysentery) and calves (calf diarrhea). Diarrhea in both dairy and beef calves associated with BCoV has a worldwide prevalence and occurs from 1 day to 3 months of age but mostly between 1 and 2 weeks of age. Disease is more common during the winter months, which may reflect enhanced survival of the virus in a cool, moist environment. The virus is ubiquitous in cattle populations, and the majority of adult cattle are seropositive. The coronavirus may be present in both diarrheic and healthy calves; the incidence rates range from 8% to 69% and 0% to 24% for diarrheic calves and healthy calves, respectively.

The virus can be shed by up to 70% of adult cows despite the presence of specific antibodies in their serum and feces. The peaks of shedding are during the winter months and at parturition. Calves born to carrier cows are at a higher risk of diarrhea. Subclinical persistence and recurrent infections are also common in both neonatal and older calves, and virus excretion from these animals may maintain a reservoir of infection.

Vaccination of the cows with a modified-live rotavirus–coronavirus–*E. coli* combination vaccine does not influence seasonal shedding, but in vaccinated cows the incidence of shedding does not increase at parturition as it does in nonvaccinated cows. The BCoV isolates all belong to a single serotype as polyclonal sera have detected only minor antigenic variations.

The **BCoV is also a pneumotropic virus** that can replicate in epithelium of the upper respiratory tract. In dairy calves, initial infections occur when the calves are 1 to 3 weeks of age, but there are multiple episodes of shedding of viral antigens or seroconversion when the calves are several weeks of age. Clinical signs of respiratory disease occur between 2 and 16 weeks of age but are mild. A more severe lower respiratory tract infection causing minor lung lesions has been reported but is also not severe enough to warrant treatment. Such infections are probably common in closed herds with recurrent subclinical infections occurring in older calves. Persistence of infection or reinfection of the upper respiratory tract with the virus is also common. The amount and specificity of BCoV maternal antibodies in calves at the time of infection with the virus may interfere with the development of an active antibody response in serum and mucosal secretions. The fecal–oral route is the presumed method of transmission, but aerosol transmission may also occur.

The BCoV has been isolated from wild ruminants with diarrhea. Feces from diarrheic sambar deer, one waterbuck, and one white-tailed deer in wild animal habitats contained coronavirus particles identified as BCoV. Gnotobiotic and colostrum-deprived calves inoculated with the isolates developed diarrhea and shed coronavirus in their feces and nasal discharge. Thus wild ruminants may harbor coronavirus strains transmissible to cattle.

The BCoV of winter dysentery in adult cattle is closely related to the BCoV causing diarrhea in young calves.[2] There is no evidence for serologic or in vivo antigenic differences between these two BCOVs.

Parvovirus

The parvovirus has been associated with outbreaks of PWD in beef calves, but its pathogenicity is uncertain. Seroprevalence studies found 49% to 83% of adult cattle seropositive to the virus over a 2-year period.

Bovine Torovirus (Breda Virus)

Breda virus, a member of the genus *Torovirus,* has been isolated from the feces of neonatal calves with diarrhea in Iowa, Ohio, several areas in Europe, and in Canada. In Ohio, the virus was detected in 9.7% of fecal samples from cattle with diarrhea; it occurred in 26% of the total calf samples. It is a common virus in the feces of calves with diarrhea on farms in Ontario. In veal calf operations in Ohio, 24% of calves shed the virus during the first 35 days after arrival, which was associated with diarrhea. Calves shedding additional pathogens were more likely to have diarrhea than those shedding less than one pathogen. Calves that were seronegative or had low antibody titer to the Breda virus on arrival were more likely to shed the virus than those calves that were seropositive on arrival.

More than 88% of adult cattle are seropositive for the Breda virus. More than 90% of newborn calves have high maternal antibodies to the virus that wane at a few months of age, followed by active seroconversion between 7 and 24 months of age.

Bovine Norovirus

Noroviruses, formerly known as Norwalk-like viruses, are ssRNA viruses belonging to the family Caliciviridae and have been recognized as the most common pathogens involved in outbreaks of acute nonbacterial gastroenteritis in humans. Noroviruses can be genetically classified into five genogroups, GI-GV. Genogroups I, II, and IV are considered as human pathogens, whereas genogroup III is isolated from bovines. The prototype strains identified in cattle are the Newbury-2 strain (formerly Newbury agent 2) and the Jena virus. The seroepidemiologic prevalence of the Jena virus, a bovine enteric calicivirus, is 99% in some selected cattle populations in Germany. In the Netherlands Norovirus is endemic in veal calf operations and in a selected dairy herd. The highest number of norovirus-positive veal calf farms was found in the regions with the highest number of veal calf farms. The virus is endemic in cattle populations and genetically distinct from human norovirus.[7] Norovirus genotype III strains were isolated from healthy and diarrheic calves in Hungary, Italy, and recently in France.[7-9] Although the clinical significance of the presence of norovirus in diarrheic calves remains unclear, a significant quantitative difference in the amount of virus particles shed in feces between healthy and diarrheic calves has been demonstrated in a recent case–control study.[10]

Lambs and Kids
Rotavirus

Rotavirus has been associated with diarrhea in lambs 7 to 30 days of age.[11] Rotavirus infection associated with diarrhea in lambs has been reported from several countries including the UK, United States, Australia, Japan, Spain, Egypt, Morocco, and India. Rotavirus groups A and B have been isolated from diarrheic lambs, but there appear to be geographic differences in the occurrence between groups A and B. Although group B has predominantly been isolated in the United States and the UK, RVA is most common in India.[12]

The prevalence of rotavirus infection in diarrheic lambs was recently assessed in India by screening 500 fecal samples from diarrheic lambs collected over a period of 3 years. RVA was isolated from 13.2% of all samples.[13] A similar study from Egypt reported a prevalence of rotavirus infection among diarrheic lambs of 12.3%.[14]

Atypical rotaviruses, possibly group B, have been isolated from the feces of diarrheic goat kids. Affected kids were 2 to 3 days of age, and the disease was severe with marked dehydration, anorexia, and prostration.

The prevalence of rotavirus infection in lambs appears to be influenced by the season of the year, because an increase in the number of outbreaks with high morbidity and mortality has been reported in the early spring months.[11]

The experimental disease in lambs is mild and characterized by mild diarrhea, abdominal discomfort, and recovery in a few days. The mortality in lambs is much higher when both the rotavirus and EPEC are used.

Piglets
Porcine Rotavirus

Rotavirus is recognized as an important etiologic agent of diarrhea in weaned and unweaned piglets. At least four of the rotavirus groups (A–E) have been associated with diarrhea in piglets, but RVA is by far the most prevalent. Within the RVA the genotypes G3–G5, G9, and G11 in combination with P[6], P[7], P[13], and [P19] are most prevalent in pigs and there are differences in virulence of isolates.[4] Different genotypes of RVA and even different groups of rotaviruses may occur at the same time in a single piggery. Some porcine rotaviruses are related antigenically to human rotavirus serotypes. Porcine rotaviruses that display the typical bovine P[1], P[5], P[11], G6, and G8 genotypes have been detected in pigs, which indicates the high frequency of rotavirus transmission between cattle and pigs.

There is little or no cross-protection between porcine rotaviruses with distinct G and P types, but viruses that share common G and P types induce at least partial cross-protection in experimental studies. Variant serotypes of porcine rotavirus such as G3 may cause severe outbreaks of diarrhea in piglets. Subclinical infections are common, and age resistance to rotavirus infection may not occur.

Rotaviruses have a worldwide occurrence and are highly prevalent in the swine population. Infected gilts and sows shed the virus

before farrowing and during lactation, which makes it next to impossible to eliminate the infection from a herd. Continuous transmission of the virus from one group to another is an important factor in maintaining the cycle of rotaviral infection in a piggery. The virus can be found in dust and dried feces in farrowing houses that have been cleaned and disinfected. This suggests that the environment is also an important source of infection. The porcine rotavirus can survive in original feces from infected pigs for 32 months at 10°C (50°F).

In an infected herd, piglets become infected between 19 and 35 days of age, and the virus cannot be detected in piglets under 10 days of age, presumably as a result of protection by lactogenic antibody. There are increased secretory IgA and IgG antibodies to rotavirus in the milk of sows after natural rotavirus infection or following parenteral inoculation of pregnant or lactating sows with live attenuated rotaviruses. Early weaning of piglets at 3 weeks of age results in the removal of the antibody supplied by the sow's milk.

In piglets, rotaviral diarrhea is most common in pigs weaned under intensive management conditions, and the incidence increases rapidly from birth to 3 weeks of age. There is no age-dependent resistance up to 12 weeks of age. The disease resembles milk scours or the 3-week scours of piglets. Mortality caused by rotavirus varies from 7% to 20% in nursing pigs and 3% to 50% in weaned pigs depending on the level of sanitation. In the United States the peak incidence occurs in February, and a moderate rise occurs from August to September.

A case-control epidemiologic study examined the relationship between RVA and management practices in Ontario over a 5-year period. In rotavirus-positive herds, herd size was larger and weaning age was younger compared with rotavirus-negative herds. Pigs raised in all-in/all-out nurseries were 3.4 times more likely to have a positive RVA diagnosis than in pigs in a continuous flow system. Pigs in the all-in/all-out system were weaned at an earlier age.

Concurrent infection of rotavirus with other enteric pathogens such as ETEC, *Salmonella* spp., or TGE virus is common and causes an additive effect resulting in more severe clinical disease and higher mortality rates.

Porcine Coronavirus

The **PEDV** is a corona-like virus that causes diarrhea in pigs. This is similar to TGE except much less severe and with less mortality. Two clinical forms of the disease have been described: PED types I and II. **PED type I** causes diarrhea only in pigs up to 4 to 5 weeks of age. **PED type II** causes diarrhea in pigs of all ages. The morbidity may reach 100% but mortality is low. The disease may start in the finishing pigs and spread rapidly to pregnant sows and their nursing piglets.

The diarrhea may persist in the 6- to 10-week-old pigs, and seronegative gilts introduced into the herd may become infected and develop a profuse diarrhea that lasts a few days.

A PRCV with close antigenic relationship to the TGE virus has been identified as enzootic in the UK and in some European countries. A Canadian isolate of the virus inoculated into 8-week-old piglets caused polypnea and dyspnea and diffuse bronchioloalveolar lesions. Seroprevalence studies in Spain revealed that 100% of large herds and 91% of small herds had animals with antibodies. Only mild or inapparent respiratory signs occur and the growth of finishing pigs may be temporarily affected.

Foals

Equine Rotavirus

Rotavirus is the most common viral cause of diarrhea and is endemic in most if not all horse populations, as has been concluded from high seroprevalence rates in unvaccinated adult horses.[15,16] RVA is the group most commonly associated with diarrhea in foals up to 3 months of age. Most equine rotaviruses are distinct from those of other species with a distinctive electropherotype and subgroup reaction. Six G types and six P types have been described among equine rotaviruses thus far; however, the majority of circulating equine rotaviruses are G3 P[12] and G14 P[12].[17]

The virus can be isolated from the feces of healthy foals and from diarrheic foals in outbreaks of diarrhea. Outbreaks of the disease occur on horse farms with a large number of young foals in which the population density is high. A case-control study of foal diarrhea in the UK over a 3-year period revealed rotavirus was a significant pathogen associated with diarrhea in foals. The other common pathogens were *C. perfringens, S. westeri,* and *Cryptosporidium* spp. A survey of the enteric pathogens in diarrheic Thoroughbred foals in the UK and Ireland revealed a prevalence of 37% rotaviruses and 8% in normal foals.

Dual infection with different rotavirus strains as well coinfection with other enteropathogens including *Salmonella* spp., *Cryptosporidium* spp., and ECoV have been reported, but their clinical significance remains to be determined.[15]

PATHOGENESIS

Rotavirus

The rotavirus infects mature brush border villous epithelial cells in the small intestine and to a lesser extent in the large intestine. The infected cells are sloughed, leading to partial villous atrophy, and the atrophic villi are rapidly recovered with relatively undifferentiated crypt cells that mature over a few days and result in the healing of the lesion. The activity of the mucosal β-galactosidase (lactase) in the brush border of the villous epithelium is less than that found in normal

animals, which results in decreased utilization of lactose. This reduction in enzymes is associated with immature enterocytes on the villi during rotavirus infection. In vitro studies have suggested that lactase may be the receptor and uncoating enzyme for rotavirus, which may explain the high degree of susceptibility of the newborn with high levels of lactase. The net effect of the morphologic and functional changes in the intestine is malabsorption resulting in diarrhea, dehydration, loss of electrolytes, and acidemia.

The pathogenesis is similar in calves, lambs, pigs, and foals. Lesions occur within 24 hours after infection, villous epithelial cells of the small intestine are infected and become detached, and regeneration occurs within 4 to 6 days after the onset of the diarrhea. The intestinal villi usually return to near normal within about 7 days after recovery from the diarrhea. However, calves and pigs may require 10 to 21 days to fully recover to a normal growth rate following rotavirus infection. Experimental rotaviral infection in 3-week-old piglets results in diarrhea, anorexia, and vomiting. Villous atrophy of the small intestine is the most severe lesion but returns to normal in 6 days. Infection and clinical disease developed in the presence of serum-neutralizing antibody obtained from seropositive sows.

Although it has been generally accepted that lactose malabsorption is an important factor in the pathogenesis of diarrhea, the experimental infection of gnotobiotic lambs with rotavirus did not result in lactose intolerance, as assessed by the measurement of reducing substances in the feces or by the clinical effects and blood glucose levels after a lactose load. Lactose intolerance could be demonstrated by using extremely high doses of lactose, three to four times the normal dietary intake. Thus lactose-containing feeds such as milk are not necessarily contraindicated in rotavirus diarrhea.

A combined infection with rotavirus ETEC may result in a more severe disease than produced by rotavirus infection alone, particularly in calves several days of age when the rotavirus normally produces a mild disease and when calves are resistant to enterotoxigenic colibacillosis. The intestinal lesions of villous atrophy are also more severe and extend into the colon in dual infections. Naturally occurring cases of the dual infection in calves are considered to be more severe than single infections. Under field conditions more than one enteropathogen is likely to be involved in the pathogenesis of the diarrhea.[6,12,15]

Experimentally, in gnotobiotic 1-day-old calves, concurrent infection with BVDV and bovine rotavirus results in a more severe enteric disease than that associated with either virus alone. The BVDV potentiated the effect of the rotavirus. Severe lymphoid depletion was associated with BVDV infection regardless of the concurrent rotavirus infection. The clinical findings of induced

combined BVDV and rotavirus infections in neonatal calves at 8 to 9 days of age are much more severe and the duration of diarrhea much longer than in rotavirus infection alone.

Coronavirus

The pathogenesis of coronaviral enteritis in calves is similar to the rotavirus infection. The villous epithelial cells of the small and large intestines are commonly affected. The crypt epithelium is also affected, which makes regeneration of villous epithelial cells much longer, which in turn results in persistent diarrhea for several days and death from dehydration and malnutrition. Experimental infection of calves with virulent BCoV results in depletion of lymphocytes in the mesenteric lymph nodes and Peyer's patches, low levels of immunoglobulin, and generalized immune suppression. Experimental infection with the attenuated virus results in lower levels of intestinal immunoglobulin titers than with the virulent virus. Experimentally, newborn calves are capable of mounting an intestinal immune response to BCoV and vaccine failures may be the result of overattenuation of the virus. The pathophysiological changes caused by coronavirus-induced diarrhea in the calf have been described and are similar to the changes that occur in acute diarrheal disease in the calf associated with other enteropathogens.

Porcine Coronavirus

This virus replicates in the villous epithelial cells of both the small and large intestine and clinically resembles TGE of piglets. There is no evidence that rotavirus infection in piglets is accompanied by increased permeability of the intestine to macromolecules.

Calicivirus-Like (Norovirus) Agent

Norovirus causes degeneration of the villous epithelial cells of the proximal part of the small intestine leading to villous atrophy, a reduction in disaccharidase activity, and xylose malabsorption. In gnotobiotic calves experimentally infected with the Breda virus, the villous epithelial cells of the ileum and colon are affected, including the dome epithelial cells.

Parvovirus

Experimental infection of calves with the parvovirus results in lymphopenia and viremia and damage to the small-intestinal crypt epithelium and the associated mitotically active lymphoid tissues. Villous atrophy occurs because of failure of replacement of villous epithelial cells. By 5 days after inoculation there was evidence of repair of the intestinal lesions. Following experimental challenge, the tonsillar tissues, intestinal mucosa, and mesenteric lymph nodes all become infected. Subsequent spread also results in greater involvement in the large intestine and the upper jejunum, Peyer's patches, and mesenteric lymph nodes.

CLINICAL FINDINGS
Calves

The naturally occurring disease usually occurs in calves over 4 days of age and is characterized by a sudden onset of a profuse liquid diarrhea. The feces are pale yellow, mucoid, and may contain flecks of blood. Recovery usually occurs in a few days. Explosive outbreaks occur, and up to 50% of calves from 5 to 14 days of age in the affected population may develop the disease. If ETEC are present, the disease may be acute; dehydration is severe and deaths may occur. Multiple mixed infection with *E. coli,* coronavirus, and *Cryptosporidium* spp. are common in calves over 4 days of age; thus it may be impossible to describe a typical case of uncomplicated naturally occurring rotavirus or coronavirus-like diarrhea. There is a tendency for viral diarrhea in newborn calves to occur in explosive outbreaks; the calves are usually not toxemic, but the character of the diarrhea cannot be differentiated clinically from that associated with the other common enteric pathogens of newborn calves.

A coronaviral enteritis affecting calves from 1 to 7 days of age has been described, but there are no distinguishing clinical characteristics. The diarrhea may be persistent for several days, followed by death in spite of fluid therapy and careful realimentation with milk. The feces are voluminous, mucoid and slimy, and may be dark-green or light-brown in color.

Lambs

Experimentally, newborn gnotobiotic lambs develop diarrhea 15 to 20 hours following oral inoculation and show dullness and mild abdominal discomfort. There are only a few documented descriptions of naturally occurring rotaviral diarrhea in newborn lambs. Affected lambs under 3 weeks of age develop a profuse diarrhea, and the case–fatality rate is high. It is not clear if outbreaks of uncomplicated rotaviral diarrhea occur in newborn lambs.

Piglets

Rotaviral diarrhea may occur in nursing piglets from 1 to 4 weeks of age and in pigs following weaning. The disease in nursing piglets resembles milk scours or 3-week scours. Most of the pigs in the litter are affected with a profuse liquid to soft diarrhea with varying degrees of dehydration. Recovery usually occurs in a few days unless complicated by ETEC or unsatisfactory sanitation, overcrowding, and poor management. The disease is often most severe in herds in which there is continuous farrowing with no period of vacancy for cleaning and disinfection in the farrowing barn. The disease may also occur in pigs a few days after weaning and may be a major factor in PWD of piglets weaned at 3 weeks of age or earlier in the case of weaning pigs at 1 to 2 days of age.

PED type I affects piglets only up to 4 to 5 weeks of age and is characterized by profuse watery diarrhea, high morbidity, and low mortality.

PED type II causes a profuse fluid diarrhea in pigs of all ages, including nursing piglets. Explosive outbreaks may occur and the morbidity may reach 100%. Mortality is usually restricted to piglets under 3 weeks of age.

Foals

Affected foals—usually from 3 days to 5 months of age—appear depressed, fail to suck, and become recumbent. The temperature ranges from 39.5 to 41.0°C (103–106°F) and respirations may be rapid and shallow. There is a profuse, watery, nonfetid diarrhea that results in severe dehydration and electrolyte imbalances. Recovery following treatment usually occurs within 2 to 4 days. Death may occur within 24 hours after the onset of diarrhea.

CLINICAL PATHOLOGY
Detection of Virus

Fecal samples (20–30 g) should be collected from affected animals as soon possible after the onset of diarrhea and submitted to the laboratory in a chilled state. Samples of intestinal mucosa from several sections of the small and large intestine should be submitted chilled for virus detection and possible isolation.

Because multiple mixed viral and bacterial infections are common, the request for a laboratory diagnosis must include consideration of all of the common pathogens. The viruses are much more difficult to detect than bacterial enteropathogens. In herd outbreaks, fecal samples from several affected animals and some normal animals should be submitted. The rotavirus will usually be present in both normal and diarrheic animals, which presents problems in interpretation and requires evaluation of the clinical and epidemiologic findings.

Several laboratory tests are available for detection of rotaviruses and coronaviruses in the feces and intestinal contents and tissues. The particular test used will depend on the facilities and equipment available.

Electron Microscopy

Demonstration of the virus in feces using EM has been a standard diagnostic technique. It is easier to see the virus if it has been concentrated by ultracentrifugation or clumped by immunoelectron microscopy using specific antiserum. With EM, the virus can be detected for up to 6 to 10 days after the onset of diarrhea. Protein A-gold immunoelectron microscopy is a valuable test to detect BCoV in the feces and nasal secretions of infected calves. However, because the equipment and expertise necessary for EM are not available in many laboratories, alternative diagnostic techniques have been developed.

Immunofluorescence

Several tests are based on immunofluorescence. These include immunofluorescent

staining of fecal smears and cell culture immunofluorescence of fecal preparations. Immunofluorescent staining of a fecal smear is a more convenient test for diagnostic laboratories because a diagnosis can be made in a few hours, and an EM is not necessary. However, the immunofluorescence tests may not be as reliable as some other tests. The FA technique will only detect the virus within epithelial cells which are present in the feces for 4 to 6h after the onset of diarrhea. In some studies the FA technique detects the virus in only 20% of samples, whereas EM detected the virus in about 60% of the samples.

Immunodiffusion and Electron Microscopy

Immunodiffusion and EM are superior to the FA technique. Treatment of the feces with chymotrypsin improves the detection rate. Monoclonal antibodies to porcine Group C rotavirus can be used in an immunofluorescent test and may have wider applications in the study of Group C rotavirus diarrheas in swine, cattle, and potentially, other species.

Testing immunofluorescent sections of spiral colon is the diagnostic method of choice for the detection of coronavirus in calves; fecal samples are unreliable. Isolation of coronavirus in tracheal organ culture is the most sensitive in vitro culture technique. A hemadsorption–elution–hemagglutination assay test for the detection of coronavirus in the feces of calves is a simple and rapid procedure. A counterimmunoelectrophoresis test is available for the detection of coronavirus in calves. An immunohistochemical technique can be used to detect the virus of PED in the small intestine.

ELISAs are more sensitive and simple than immunoelectroosmophoresis, CF, immunofluorescence on inoculated cell cultures, or EM for the detection of rotavirus in calf feces. The ELISA is effective in detecting the presence of porcine rotavirus in feces and was confirmed in two-thirds of the samples tested using EM, immunofluorescence, and polyacrylamide gel electrophoresis (PAGE). A blocking-ELISA using monoclonal antibodies can detect the PEDV in feces and serum antibodies in both naturally and experimentally infected piglets and earlier than an indirect immunofluorescence test.

A competitive blocking-**ELISA** is considered most suitable for routine detection of porcine epidemic virus in the feces of pigs.

The ELISA and EM of feces are equally reliable in detecting the rotavirus and coronavirus in the feces of experimentally infected calves. The agreement between the two tests was 95% for coronavirus and 84% for rotavirus. There will always be borderline samples containing antigen in quantities near the detection limit for each test. Some samples will be positive for one test and negative for the other and vice versa. This problem can be minimized if several individual samples from a disease outbreak are examined. The morphologic identification of rotavirus is usually straightforward, but the pleomorphism of BCoV can present problems. The ELISA may also fail to detect viral antigen in feces that also contain antibody. The test can provide diagnostic results within 24 hours after collection of the fecal samples.

Reverse Passive Hemagglutination, ELISA, and Polyacrylamide Gel Electrophoresis

The three techniques for the detection of rotavirus in fecal samples from diarrheic calves have been compared. The reverse passive hemagglutination (**RPHA**) was at least as sensitive as the ELISA, and both were compared with the PAGE. The overall agreement between **RPHA** and **PAGE** was 96%; the ELISA was not as sensitive. The commercial ELISA has a slightly higher sensitivity than agglutination, **PAGE**, and concentrated **PAGE**, but the specificity of **ELISA** is lower. The latex agglutination test has a lower sensitivity than ELISA, but its specificity is higher. The latex agglutination test is easy to perform, more sensitive than EM, and more specific for detection of rotavirus. A dot hybridization assay can detect and differentiate two serotypes of porcine rotavirus.

The fast and inexpensive ELISA combined with the highly specific and sensitive RT-PCR is a practical approach in epidemiologic studies of bovine rotavirus.

PCR assays are now available for the detection of BCoV in feces. Nonradioactive PCR-derived cDNA probe assays can be used to detect rotavirus serotypes.

A rapid ELISA using monoclonal antibodies can be used for the simultaneous detection of BCoV, rotavirus serogroup A, and *E. coli* K99 antigen in the feces of calves. The specificity of all of the components was more than 90% specific and the sensitivity for BCoV, F5 (K99) *E. coli,* and rotavirus, 77, 93, and 100%, respectively.

Immunochromatography is used for the detection of RVA in the feces of calves, piglets, and foals, and has a sensitivity of 89% and specificity of 99% compared with ELISA, and its reproducibility is 100%. It is a one-step procedure, simple to use, very rapid, and can be performed on the farm.

A field enzyme immunoassay test (Rotazyme test) is highly accurate and reliable for the detection of rotavirus in the feces of horses with and without diarrhea. The test is a simple, rapid, and specific procedure that can take the place of a more expensive and slower procedure such as EM.

ImmunoCardSTAT Rotavirus is a human group A assay that can be used as an on-site diagnostic test for bovine rotavirus with a sensitivity and specificity of 87.0% and 93.6%, respectively. The assay is a 10-minute one-step test with all the necessary reagents included in the kit and with no need for any laboratory equipment.

Serology

Several serologic tests are available for the measurement of rotaviral antibody in serum and lacteal secretions. An ELISA is used to detect PED coronavirus antibodies in swine sera. The radioimmunoassay is the most sensitive test compared with the agar gel immunodiffusion, CF, hemagglutination, and hemagglutination inhibition tests.

NECROPSY FINDINGS

The pathology of experimentally induced rotavirus and coronavirus diarrhea in colostrum-deprived and gnotobiotic calves, lambs, and piglets has been described. Grossly, the changes are unremarkable and consist of dehydration, fluid-filled intestinal tract, and distension of the abomasum. The microscopic changes consist of shortening of the length of the villi and replacement of the tall columnar villous epithelial cells by cuboidal and squamous cells. Segments of the small intestine may reveal villous fusion, rounded absorptive cells, villous atrophy, and exposure of lamina propria. Crypt hyperplasia occurs in response to the loss of columnar epithelial cells from the villi. Histologic lesions caused by previous rotavirus infection may be present in the upper small intestine of clinically normal calves. The rate at which enterocytes are affected in older disease-resistant calves is caused by the slowing of the virus from entering the cells.

In coronavirus enteritis in calves, there is commonly villous atrophy of both the small and large intestines and destruction of the crypt epithelium; destruction does not occur in rotavirus enteritis. The changes are more severe in field cases of acute diarrhea in calves in which both viruses and ETEC can be isolated. Concurrent infection with BVDV has also been demonstrated to be synergistic in bovine rotaviral diarrhea.

The histologic appearance of the intestinal lesions of experimental infection of calves with Breda virus, calicivirus-like agent, and parvovirus have been described. Generally, the lesions are similar to those associated with rotavirus and coronavirus infection.

The wide array of diagnostic tests available to confirm the presence of enteric viruses has already been discussed. Because of the frequency of subclinical infection with these agents, it is important to histologically confirm concurrent atrophy of villi.

Samples for Confirmation of Diagnosis

- **Histology:** Duodenum, jejunum, ileum, colon (LM, IHC)
- **Virology:** Colonic content (EM, ELISA, latex agglutination); colon, ileum, jejunum (FAT, culture)

DIFFERENTIAL DIAGNOSIS

The cause of acute diarrhea in newborn farm animals cannot be determined clinically. All of the common bacterial and viral enteropathogens can cause an acute profuse fluid diarrhea, with progressive dehydration and death in a few days.

When outbreaks of diarrhea are encountered, a detailed examination of the possible risk factors should be made, and the appropriate fecal samples and tissues from affected animals should be submitted to the laboratory. The most reliable specimens include fecal samples obtained from animals within a few hours after the onset of diarrhea, and untreated affected animals are submitted for necropsy and microbiological examination within a few hours after the onset of diarrhea.

The clinical and epidemiological characteristics of the common acute diarrheas of neonatal farm animals are as follows:

Calves

Enterotoxic colibacillosis occurs primarily in calves under 5 days of age and is characterized clinically by an acute, profuse diarrhea. Recovery following treatment usually occurs in 2 days. Outbreaks occur in beef and dairy calves. Rotavirus and coronavirus diarrhea usually occur in calves over 5–10 days of age and up to 3 weeks of age. Explosive outbreaks occur, characterized by an acute profuse liquid diarrhea with recovery in 2–4 days. Recovery is assisted by oral fluid therapy.

Cryptosporidiosis occurs in calves from 5 to 15 days of age and is characterized by a persistent diarrhea that may last for several days. The cryptosporidia may be detected by Giemsa stain of fecal smears or by fecal flotation.

Bovine viral diarrhea virus (BVDV) Whether or not BVDV causes clinically significant diarrhea with lesions of the small intestine of calves 3–6 weeks of age is unknown. Diagnostic laboratories report the presence of intestinal lesions such as villous atrophy and crypt cell destruction in calves 3–6 weeks of age that have been affected with intractable diarrhea and from which the BVDV was isolated from the feces. However, there is no evidence of a cause-and-effect relationship.

Piglets

Transmissible gastroenteritis is most common in piglets under 1 week of age, and explosive outbreaks are common. There is acute profuse diarrhea and vomiting. Affected piglets may continue to nurse for several hours after the onset of the diarrhea. The case–fatality rate is high in piglets under 7 days of age; older pigs usually survive.

Porcine epidemic diarrhea type I affects piglets under 4–5 weeks of age and is characterized by profuse watery diarrhea, high morbidity, and low mortality.

Porcine epidemic diarrhea type II causes a profuse fluid diarrhea in pigs of all ages, including nursing piglets. Explosive outbreaks may occur and the morbidity may reach 100%. Mortality is usually restricted to piglets under 3 weeks of age.

Enterotoxic colibacillosis usually occurs in weaned and unweaned piglets. There is acute diarrhea, dehydration, and rapid death. Pigs with endotoxemia (Shiga-toxin producing *Escherichia coli*) may die without obvious diarrhea and usually appear cyanotic. Entire litters may be affected and the case–fatality rate may be 100%. Early treatment with antibiotics and subcutaneous fluids will result in recovery.

Coccidiosis occurs in piglets from 5 to 10 days of age and is characterized by an acute diarrhea in which the feces are foul smelling and vary in consistency from cottage cheese–like to liquid and gray or yellow and frothy. The diarrhea is persistent for several days and nonresponsive to antibiotics. Some pigs recover spontaneously; others die in 2–4 days. Coccidial oocysts can be detected in the feces. The morbidity rate varies from 50% to 75% and the case–fatality rate from 10% to 20%.

Hemorrhagic enterotoxemia caused by *Clostridium perfringens* type C affects entire litters of pigs under 1 week of age; is characterized clinically by severe toxemia, dysentery, and rapid death; and at necropsy there is a hemorrhagic enteritis.

Lambs

Enterotoxic colibacillosis occurs in lambs most often under 1 week of age and is characterized by dullness, failure to suck, and acute diarrhea, which responds to antibiotic and fluid therapy.

Coliform septicemia affects lambs under a few days of age and usually causes sudden death. Lamb dysentery occurs most often in lambs under 10 days of age, and there may be sudden death or acute toxemia, tucked-up abdomen, and a severe diarrhea and dysentery. At necropsy the characteristic finding is hemorrhagic enteritis.

Foals

Rotaviral diarrhea occurs in foals from 5 to 35 days of age, but is most common in foals under 2 weeks of age. There is acute profuse watery diarrhea, failure to suck, recumbency, and dehydration. Recovery is common within 1 week. A mild fever is common.

Foal heat diarrhea occurs in foals 6–10 days of age whose dams are in estrus 7–10 days after foaling.

Salmonellosis, *C. perfringens* type B, and dietary diarrhea from excessive consumption of milk are less common causes of diarrhea in newborn foals.

TREATMENT

The treatment of viral diarrheas in newborn farm animals is essentially the same as described for acute undifferentiated diarrhea of newborn calves. There is no specific therapy for viral diarrhea, but antimicrobial agents may be used both orally and parentally for the possible occurrence of secondary enteric and systemic bacterial infections. In the absence of complications, recovery from viral enteritis usually occurs without specific treatment in 2 to 5 days, which parallels the replacement of the villous epithelial cells whose complete replacement and maturation requires several days after the cessation of diarrhea.

Oral and parenteral fluid therapy as indicated is essential (Chapter 5). Affected foals may require fluid and electrolyte therapy for up to 72 hours. A glucose–glycine electrolyte formulation is an effective fluid therapy for pigs affected with experimental rotaviral diarrhea. The formula is glucose 67.53%, sodium chloride 14.34%, glycine 10.3%, citric acid 0.8%, potassium citrate 0.2%, and potassium dihydrogen phosphate 6.8%. A weight of 64 g of this formula is dissolved in 2 L of water to produce an isotonic solution.

When possible, affected animals, particularly calves and foals, should be separated from other neonates. When outbreaks of the disease occur in any species, the principles of good sanitation and hygiene should be emphasized to minimize the spread of infection.

CONTROL

The principles of control of viral diarrhea are similar to those described for acute undifferentiated diarrhea of newborn calves:
- Reduce infection pressure
- Ensure adequate transfer of passive immunity
- Vaccinate the dam to induce specific immunity in the colostrum (passive immunization of the neonate)

Management and Colostral Intake

Colostrum management strategies are discussed in detail (see the section Failure of transfer of Passive Immunity).

Vaccination

Vaccination of the dam before parturition is a common strategy to control rotavirus infection in calves, piglets, and foals.

Two major approaches are used to provide specific immunity for the control of rotavirus and coronavirus diarrhea in calves:
1. Stimulation of active immunity by vaccinating the newborn calf with an oral vaccine containing MLVs
2. Enhancement of lactogenic immunity by vaccinating the dam during pregnancy (passive immunization)

Oral Vaccines to Newborn Calves

An MLV rotavirus vaccine for oral administration to calves immediately after birth has been available commercially for many years. Initially, good results were claimed but vaccine field trials did not include contemporary controls, and the efficacy of the vaccine was uncertain. The incidence of diarrhea in herds not vaccinated in the previous year was compared with the incidence during the year of vaccination, which is inadequate to assess the efficacy of the vaccine.

Field trials using the oral vaccine indicate a failure of protection of calves against rotavirus infection and rotavirus–coronavirus infection. Effective oral vaccination of calves may be hindered by the presence of specific antibodies in the colostrum (the colostrum barrier) and may explain the failure of the vaccine under field conditions. The intestinal antibody response of young calves to an enteric viral infection is associated with the production of IgM and IgA antibodies locally in the intestine. This response is absent or diminished in calves that have ingested adequate amounts of colostrum with specific antibodies to the viruses. Most of the efficacy trials with the vaccine were performed on colostrum-deprived gnotobiotic calves that were vaccinated orally at birth and experimentally challenged a few days after birth. It is probably futile to vaccinate calves orally immediately after birth, particularly in herds in which the disease is endemic, because the colostrum will contain high levels of specific antibodies.

Fecal shedding of oral vaccine rotavirus seldom occurs after oral inoculation of gnotobiotic calves with a commercial modified-live bovine rotavirus-BCoV vaccine. Because of low shedding of virus in gnotobiotic calves that do not have the interfering effects of colostral antibodies, it seems unlikely that vaccine rotavirus will be shed in quantities from orally vaccinated conventional calves that have ingested colostrum containing antibody. Thus detection of the virus by negative stain EM in feces from orally vaccinated calves is most likely to be virulent field virus rather than vaccine virus.

Vaccination of Pregnant Dam (for Passive Immunization of the Neonate Through Colostral Immunoglobulin)

Vaccination of the pregnant dam to enhance specific colostral immunity can provide passive protection against enteric viral infection of newborn farm animals. The success of this method depends on the continuous presence of a sufficient amount of specific antibody to the rotavirus and coronavirus in the intestinal lumen. Normally, the colostral levels of antibody are high in the first few milkings after parturition. However, there is a rapid decline in colostral antibodies to below protective levels within 24 to 48 hours following parturition. Most cases of rotavirus and coronavirus diarrhea occur from 5 to 14 days after birth when the antibody levels in the postcolostral milk are too low to be protective.

The parenteral vaccination of the pregnant dam before parturition with a rotavirus and coronavirus vaccine will usually increase the level and duration of specific antibody in the colostrum. The use of a modified-live rotavirus–coronavirus vaccine stimulated a small but insignificant increase in colostral and milk antibodies. However, by 3 days after parturition, the rotavirus and coronavirus antibody titers in the milk of vaccinated heifers had declined to low or undetectable levels.

Inactivated rotavirus vaccines given to pregnant cows in the last trimester will significantly increase rotavirus antibody in colostrum and milk from vaccinated dams compared with controls, but the severity of diarrhea may be the same in calves from both groups. The increased milk antibody delays the establishment of infection but does not reduce the severity of clinical disease that was experimentally induced.

Experimental Studies of Maternal Bovine Rotavirus Vaccines

The use of an adjuvanted rotavirus vaccine given simultaneously intramuscularly and by the intramammary route significantly enhanced serum, colostrum, and milk rotavirus antibody titers, whereas intramuscular vaccination with a commercial modified-live rotavirus–coronavirus vaccine did not. Colostrum supplements, from the cows vaccinated by the intramammary and intramuscular routes, fed to rotavirus-challenged calves at a rate of 1% of the total daily intake of milk, provided protection against both diarrhea and shedding. The 30-day milk antibody titers from these experimental cows were also considered to be protective for calves by which time the calves should have developed a high degree of age-specific resistance to rotavirus infection. The use of an inactivated rotavirus vaccine in an oil adjuvant given to pregnant cows 60 to 90 days before calving and repeated on the day of calving resulted in a significant increase and prolongation of colostral antibodies up to 28 days after calving. Diarrhea in calves from vaccinated cows was less common and less serious. Similar results were obtained with a combined inactivated adjuvanted rotavirus and E. coli vaccine. Similar results have been achieved by vaccination of pregnant ewes. Vaccination of ewes can result in an elevation of specific colostral antibody and prolong the period over which the antibody is present in the lumen of the intestines of the lambs. The vaccination of cows with a monovalent vaccine results in a heterotypic response to all serotypes of rotavirus to which the animals have been previously exposed, which suggests that single serotype vaccination may be sufficient.

The lactogenic antibody responses in pregnant cows vaccinated with recombinant bovine rotavirus-like particles (VLPs) of two serotypes or inactivated bovine rotavirus vaccines have been evaluated. Bovine rotavirus antibody titers in serum, colostrum, and milk were significantly enhanced by the use of triple-layered VLPs, and inactivated vaccines but higher antibody responses occurred in VLP-vaccinated cows.

Bovine Coronavirus Vaccine

An oil-adjuvanted vaccine containing BCoV antigen to enhance lactogenic immunity in the calf by vaccinating pregnant cows and heifers between 2 and 12 weeks before calving increased serum antibody in the dams, which was reflected in a similar increase in the titer and duration of specific antibody in colostrum and milk for up to 28 days after calving. The overall response was dependent on an adequate antigen payload being incorporated within the single dose vaccine.

Commercial Bovine Rotavirus–Coronavirus and E. Coli F5 (K99) Vaccines

The original rotavirus and coronavirus vaccines for use in pregnant cows to provide passive immunization were not sufficiently efficacious because of the rapid decline in specific colostral antibodies, which renders the calves susceptible to the viral diarrhea several days after birth. The relative success of the enterotoxigenic F5 E. coli bacterins has resulted in a shift of the epidemic curve for acute diarrhea in calves under 30 days of age from a few days of age to 2 to 3 weeks of age.

More recently developed vaccines are efficacious. An inactivated combined vaccine against rotavirus, coronavirus, and E. coli F5 administered 31 days before the first expected calving date has been evaluated and compared with controls. There was a significant increase in serum antibody against all three antigens in vaccinated animals, which was accompanied by increased levels of protective antibodies to rotavirus, coronavirus, and E. coli in their colostrum and milk for at least 28 days. The levels of specific rotavirus and coronavirus antibodies in the milk of vaccinated cows were greater than the fourfold increase seen in the control cows for at least 28 days after calving.

The primary vaccination of pregnant cows with a trivalent commercial vaccine containing live attenuated bovine rotavirus and coronavirus and E. coli F5 followed by an annual booster at 6 weeks and 3 weeks before calving, or using the same protocol with an inactivated trivalent vaccine resulted in significant increase in the serum antibody of all vaccinated animals compared with controls. The antibody titers were higher in cows receiving the live vaccine compared with those receiving the inactivated vaccine.

The colostral antibodies against all three antigens increased in all live vaccinated groups, whereas inactivated vaccinated animals had only significant increases in F5 titers. The colostrum of live vaccinated cows contained much higher specific antibody titers. Thus the MLV vaccine can significantly enhance the specific response to rotavirus and coronavirus and *E. coli* F5 after a primary vaccination followed by a booster annually.

Stored Colostrum

The high levels of viral antibody in the colostrum of the first two milkings of cows can be used to advantage in hand-fed calves. The daily feeding of stored colostrum from the first milkings of cows from the affected herd will reduce the incidence of clinical disease in the calves. The colostrum must be fed daily—beyond the time of gut closure (i.e., intestinal absorption of colostral immunoglobulin)—because rotavirus antibody is not retained in the intestinal lumen for more than 2 to 3 days. In affected herds the specific antiviral antibody in the stored colostrum may be sufficient to prevent the disease if colostrum is fed daily for up to 20 to 30 days. If a large number of cows are calving over a short period of time, the colostrum from immunized cows can be pooled and fed to the calves daily. Even small amounts of colostrum from immunized cows are efficacious if mixed with cows' whole milk or milk replacer. This supplemental feeding of colostrum may be required for only 3 to 4 weeks, because older calves generally possess a high degree of age-specific resistance to rotavirus infections.

Systemic Colostral Antibody

For many years it was uncertain if circulating colostral antibody in calves was transferred back into the intestinal tract. Evidence shows that passive immunity to calf rotavirus diarrhea can be achieved by adequate calf serum colostral antibody titers. Calves fed colostrum on the first day of life had significant rotavirus-neutralizing antibody titers in their small-intestinal lumina for 5 and 10 days later. The intestinal antibody titers correlated with the serum antibody titers derived from colostrum and were predominantly of the IgG_1 isotype. Intestinal antibody titers were approximately equivalent in 5- and 10-day-old calves, suggesting that **antibody transfer to the intestinal tract is a continuing process for up to 10 days after birth.** Additional evidence that transfer of passive immunity occurs is that calves can be protected from rotavirus challenge by the administration of colostral immunoglobulin by parenteral injection. This protection was not caused by lactogenic antibody, because the calves received no source of dietary antibody. The transfer of circulating antibody into the intestinal tract may be the mechanism that results in the decreased morbidity and case fatality caused by diarrhea in calves with high concentrations of passive serum immunoglobulin.

Porcine Rotavirus Vaccines

Although oral porcine rotaviral vaccines have been unsuccessful, the use of either modified-live or inactivated rotavirus vaccines for parenteral immunization of the sow before farrowing is common practice. In pigs, as in ruminants, IgG antibodies to rotavirus are predominant in colostrum and decline 8- to 32-fold in the transition to milk. However, secretory IgA is the primary isotype of rotavirus antibody in the milk of pigs. Increased levels of IgA and IgG antibodies to rotavirus occur in the milk of sows after natural rotavirus infection of nursing piglets or following parenteral inoculation of pregnant or lactating sows with live attenuated rotaviruses. But titers decline by the end of lactation, suggesting that repeated natural rotavirus infection of sows or parenteral revaccination may be necessary to maintain high IgA antibody to rotavirus in milk. This observation may account for the higher prevalence of rotavirus infection during the first week of life in pigs born to gilts (38%) than in those born to sows (3%).

Equine Rotavirus Vaccine

Several inactivated equine rotavirus vaccines are available. These vaccines were shown to significantly increase serum antibody concentration in vaccinated mares and their foals. Notwithstanding it was shown that foals can acquire rotavirus infection despite having a high rotavirus antibody titer. The incidence of rotaviral diarrhea was lower in foals born to vaccinated mares, compared with foals born to control mares but the difference was not significant. Because most clinical trials found that foals of vaccinated mares can still contract a rotavirus infection and develop clinical disease, these vaccines can at most be considered to be partially protective.[15] Parenteral vaccination of mares with inactivated rotaviral vaccine stimulates production of high levels of specific IgG, and not IgA, in colostrum and milk.

Subunit Vaccines

Subunit rotaviral vaccines consisting of VLPs given parenterally can enhance bovine rotavirus antibody titers in serum, colostrum, and milk. These vaccines offer advantages over conventional modified-live or inactivated vaccines including:

- Exclusion of adventitious agents associated with live vaccines
- Consistent production of outer capsid proteins
- Genetic engineering to allow updating of efficacious vaccines for boosting lactogenic immunity

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VESICULAR STOMATITIS (SORE MOUTH, INDIANA FEVER)

SYNOPSIS

Etiology Vesicular stomatitis virus, genus *Vesciculovirus* in the family Rhabdoviridae

Epidemiology Disease of cattle, horses, and pigs occurring only in the Americas. Affects predominantly adult animals. Seasonal disease occurrence with clustered outbreaks in summer and autumn. Vector-borne, direct, and mediate transmission. World Organization of Animal Health List A disease (reportable in most countries). Prime importance as differential diagnosis for foot-and-mouth disease

Clinical findings Vesicular lesions or healing ulcers on oral mucosa, coronary bands, teats, and prepuce

Diagnostic confirmation Virus isolation, indirect sandwich ELISA, complement fixation, and polymerase chain reaction. Serology (paired samples) via liquid-phase blocking ELISA, virus neutralization, or complement fixation

Treatment None specifically, just supportive

Control Notifiable disease. Quarantine and movement control

ELISA, enzyme-linked immunosorbent assay.

ETIOLOGY

The causative agent of VS is the *vesicular stomatitis virus* (VSV), genus *Vesiculovirus,* pertaining to the family Rhabdoviridae. Two distinct immunologic classes of the virus have been recognized: VSV New Jersey (VSV-NJ) and VSV Indiana (VSV-IND). There are three subtypes of VSV-IND based on serologic relationships, including IND-1

(classical IND), IND-2 (cocal virus), and IND-3 (alagoas virus). The serotype NJ is the most virulent and most common.

The virus is much less resistant to environmental influences than the virus of FMD. It is readily destroyed by sunlight, boiling, and the use of common disinfectants but can survive in the environment for prolonged periods in a dark and cool environment.[1]

VS is listed on "List A" of the OIE and as such is a reportable disease to the OIE for member states. Accordingly it is a **reportable disease** in most countries of the world. The disease is of major importance because it is clinically indistinguishable from FMD in ruminants and swine. It is considered as a minor zoonosis because it can cause disease in humans.

EPIDEMIOLOGY
Occurrence
Geographic Occurrence
The disease is limited to the Americas, although historically it has been reported from South Africa (1896–1897) and France (1915 and 1917). VS is **endemic** in Mexico, Central America, northern South America, and eastern Brazil as well as in limited areas of the southeastern United States in which area outbreaks occur annually.[2] Periodic **incursions** to the north and south of the endemic area into the United States, Brazil, and Argentina produce epizootic disease. It is also enzootic in Ossabaw Island, off the shore of Georgia in the United States. Ossabaw Island is the only recognized enzootic focus of VSV-NJ. The VSV-NJ antibodies have been detected only from feral swine, cattle, horses and donkeys, deer, and raccoons. However, despite high transmission rates, clinical disease is rarely detected.

Strains of VSV-NJ are endemic in southern Mexico, Central America, Venezuela, Colombia, Ecuador, and Peru and account for more than 80% of clinical cases. Sporadic activity of these strains has been observed in northern Mexico and the western United States. Cases of the disease reported from Brazil and Argentina were related to VSV-IN2 and VSV-IN3.[1] VSV-IN2 has only been isolated in these two countries and only from horses. Cattle in close proximity to affected horses neither developed clinical disease nor antibodies against VSV.[1]

In endemic areas, outbreaks are seasonal, often associated with the transitions between rainy and dry seasons. In these regions the disease occurs seasonally every year, emerging from tropical areas to cause sporadic outbreaks in cooler climates during the summer months.

In the **United States** outbreaks occur periodically in the late summer and autumn; a major outbreak occurred in 14 western states from 1982 to 1983, one in 1995 involving six states, and another one in 2005 involving nine states, with sporadic disease in the intervening and following years. The outbreaks occur in the **southwestern and western states**, start in the south and progress northerly, and **cluster** in areas of high livestock density in irrigated and green zone areas.[3]

In the 1995 outbreak the disease occurred in Arizona, Colorado, New Mexico, and Utah. The epidemic curve suggested a propagating epidemic; the number of positive premises peaked during week 39 and then rapidly declined. As in previous outbreaks in the southwestern United States, there was a northerly progression of the disease over time. Nationwide, horses accounted for 88% of examinations done for the disease, and 97% of the premises on which species of infected animals were identified recorded horses to be positive. Cattle accounted for 10% of examinations performed, and 3% positive premises on which species were identified were cattle positive.

The first major occurrence of the disease or "sore tongue" in horses, cattle, and swine in the United States was in 1801. The disease disabled 4000 horses needed to fight the Civil War in 1862. Major epidemics in U.S. cattle and horses occurred in the southwestern states from 1889 to 2005. A major outbreak occurred in military horses in the United States during the 1914 to 1918 war but in recent years, in addition to clinical disease in horses, it has come to assume greater importance in cattle and pig herds.

Host Occurrence
VS primarily affects equids including horses, donkeys, and mules, as well as cattle and swine. Camelids and possibly sheep and goats as well as humans occasionally develop clinical signs. Domestic animals appear to be dead-end hosts in which the virus does not persist and does not return to its natural cycle. Outbreaks of the disease are **most common in horses followed by cattle** and to a lesser extent in pigs. Calves are much more resistant to infection than adult cattle. Serologic surveys have found that in endemic areas of Mexico and Central and South America in addition to domestic livestock, many species of wild animals such as deer, pronghorn antelope, bighorn sheep, bats, raccoons, opossums, bears, coyotes, foxes, dogs, monkeys, rabbits, rodents, turkeys, ducks, and humans are exposed to the infection and develop neutralizing antibodies.[2] Experimental infection is possible in guinea pigs, mice, ferrets, hamsters, and chicken. The reservoir and amplifying host of VSV has thus far not been identified.

Humans are susceptible with the infection causing an influenza-like disease, and the development of high antibody titers in humans often accompanies outbreaks in cattle.

In the 1995 outbreak in the United States, the overall seroprevalence in livestock in Colorado was lower than the seroprevalence in epidemic areas, and seroprevalence rates in epidemic areas were greater for horses than cattle. The seroprevalence results suggest that some animals had subclinical VS infection during epidemics, and that animals may be exposed to the virus between epidemics. Sentinel premises in Colorado visited quarterly during a 3-year period, when there was no clinical disease, found evidence of seroconversion to both serotypes of virus.

Morbidity and Mortality
The morbidity rate varies considerably; 5% to 10% is usual but it may be as high as 80%. There is usually no mortality in horses and dairy herds, but overall case–fatality rates ranging from 0% to 15% are recorded for beef herds. Higher mortality rates than in other species have been reported in pigs infected with VSV-NJ. Most cases occur in adult animals, whereas animals under 1 year of age are rarely affected. Outbreaks in an area are usually not extensive, but the disease closely resembles FMD and has achieved considerable importance for this reason.

Method of Transmission
The mechanisms of VSV transmission are still not entirely understood. **Vector-borne transmission** is considered the epidemiologically most relevant route, although transmission through direct skin-to-skin contact is likely to contribute to the spread of the disease within a herd.[4] There is strong epidemiologic evidence corroborating the assumption of vector-borne transmission. Apart from an obviously seasonal pattern of disease occurrence, the disease incidence was determined to be increased with an increasing population of potential insect vectors, with proximity of affected animals to running water as well as with a lack of use of shelters.[4] Biological transmission by blood-feeding insects, which have been demonstrated repeatedly to be abundant on case-positive premises, also indicates that the insect-vector hypothesis is plausible. **Biological transmission** of VSV has been verified in **blackflies** (*Simulium vittatum*), phlebotomine **sandflies** (*Lutzomyia* spp.), and **biting midges** (*Culicoides* spp.).[4] Mechanical transmission through flies (*Musca domestica,* and *M. autumnalis*) and eye gnats (*Hippelates* spp.) on which the virus has been isolated may also occur. Experimentally, VSV-NJ–infected blackflies readily transmitted the virus to domestic swine. Transmission was confirmed by seroconversion or by the presence of clinical VS.

Vector-borne virus transmission has been debated because viremia, which is considered to be essential for disease transmission by blood-sucking insects, is not commonly observed in animals infected with VSV. As in other domestic animal species in which viremia has not been detected naturally or experimentally, viremia did not occur in the pigs experimentally infected by infected blackflies. Furthermore, the natural vertebrate host required to maintain the

virus between outbreaks has not been identified. Antibody to VSV has been demonstrated in a large number of **wildlife species** in Central America, but their significance as wildlife reservoirs remains to be determined. Feral pigs are believed to be the reservoir and amplifying host on Ossabaw Island.

Another proposed hypothesis is that VSV is actually a plant virus that would be ingested with forages and then undergo an adaption process to infect its host.[1]

Mediate or immediate contagion occurs by contact or ingestion of contaminated materials, especially in large intensive dairies where there is a great deal of communal use of water and feed troughs. It also occurs by the ingestion of contaminated pasture. Spread within dairy herds also appears to be aided by milking procedures. The importation of embryos from infected areas is considered a minimal risk for introduction of infection.

Convalescent cattle have been suspect as perpetuating disease and spreading it with movement to other herds. VSV has been isolated from convalescent cattle 38 days after the disappearance of clinical signs, and disease can recur in convalescent cattle. Viral RNA can be detected in the tongue and draining lymph nodes of cattle 5 months after experimental inoculation, but there is no evidence for the long-term persistence of replication-competent virus in cattle.

Risk Factors
Host Risk Factors
Differences in susceptibility of different species are well established with horses followed by cattle and then swine, which are considered most susceptible to clinical disease.[1] Age is another well-documented risk factor predisposing to clinical disease, with foals and calves less than 1 year old being less likely to develop clinical disease, although infection and seroconversion still occur.[1] In Costa Rica, which is an endemic area for VS in dairy cattle, parity was associated with clinical disease (animals of parity 4 or 5 were 5.3 times more likely to exhibit clinical signs of VS than animals of parity 3 or lower). Animals of parity 6 and higher had an OR of 4.6 times greater than animals of parity 3 and lower. Factors associated with seropositivity at birth were also found to be breed associated (Jersey calves had an OR of 14.7 times greater than Holstein calves).[5]

Environmental Risk Factors
There is a marked **seasonal incidence** of the disease, with cases decreasing sharply with the onset of cold weather. The disease is enzootic in low-lying coastal countries with tropical climates, heavy rainfall, and high insect populations. There is also a greater incidence in geographically protected areas with heavy rainfall, such as valleys in the mountains and foothills. Areas of low incidence are protected by natural barriers to

insect migration. These observations promote the importance of biting insects in the spread of the disease both locally and from infected to clean areas. In enzootic areas there is a much higher risk for dairies in forest land, the presence of sandflies, and a higher risk for clinical disease in older cows and cows in lactation.

The management factors affecting the risk for VS in horses, cattle, and sheep during the 1997 outbreak in Colorado, New Mexico, Utah, and Arizona were examined. Animals with access to a shelter or barn had a reduced risk of developing the disease with an OR of 0.6. This was more pronounced for horses at an OR of 0.5. When horses had access to pasture, the risk of developing disease was increased with an OR of 2.01. On all premises where owners reported insect populations were greater than normal, the OR was 2.5. Premises with animals housed <0.5 miles from running water were more than twice as likely to have clinical signs of VS (OR 2.6). This suggests that rivers are a pathway or a risk factor for VS, which is consistent with outbreaks of the disease following major waterways northward during the summer.

Pathogen Risk Factors
The two major VSV serotypes, VSV-IN and VSV-NJ, are distinct viruses with only 50% similarity in the glycoprotein gene sequence. VSV-NJ is more predominant than VSV-IN in North America.

In the last 70 years, each sporadic outbreak in the southwestern United States has been associated with viral lineages distant from those causing previous outbreaks in the United States but closely related to viruses maintained in endemic areas in Mexico. This pattern of viral occurrence contrasts with that observed in endemic areas in Central and South America where viral genetic lineages are maintained in specific ecological areas over long periods of time. Thus the phylogenetic data and the geographic and temporal distribution of outbreaks indicate that VS does not have a stable endemic cycle in the western United States.

Experimental Reproduction
Livestock can be infected with VSV by injection or aerosol exposure but not by rubbing virus on intact skin. Intradermal injection causes obvious skin lesions at the inoculation site. Experimental inoculation with the virus kills neonatal mice and chick embryos, and most guinea pigs, hamsters, ferrets, and mice, and chicks.

Experimentally, VS-NJ virus-infected blackflies when exposed to the abdomen or snout of young pigs results in lesions developing postinfection day 1. The entire surface of the snout ventral to the nostrils becomes reddened and swollen with pinpoint pale raised areas. This proceeds to vesiculation on day 2, and subsequent rupture, erosion, and crusting by day 3. Erosion persists for several

days, and by day 7, the vesiculated area is almost healed. Secondary vesicles develop on the upper lips and the tip of the tongue by day 3. Virus can be recovered from tissues surrounding the snout lesions but cannot be isolated from whole blood or plasma.

Viremia has not been detected in any domestic animal species naturally or experimentally infected with the New Jersey serotype of the virus.

Economic Importance
Most cases of VS recover within days. The economic losses on large dairy farms are largely caused by decreased milk production and mastitis occurring secondary to VSV infection. There is also a great deal of inconvenience and the temporary inability to feed.

There are also losses associated with quarantine such as loss of market opportunities and pasture damage from overgrazing of pastures used for quarantine. Other economic effects result from the cancellation of animal events such as fairs and the cost of loss of international markets.

In the 1995 epidemic of VSV-NJ in the western United States, the direct costs for increased labor and veterinary expenses incurred in caring for horses with the disease were estimated at $382.00 per case. In a dairy herd, losses were estimated at $787.00 per animal from increased culling, and in beef ranches the costs were $15,565.00 per ranch. State regulations restricting the movement of animals within a zone of 10 miles around premises with confirmed cases for 30 days after the last lesion healed, and declaring a quarantine, all added to economic losses.

VS is classified by the OIE as a so-called List A disease, making it a **reportable disease** in all member countries of the OIE.[6] In the United States, all livestock with clinical signs of vesicular disease must be inspected by personnel from USDA-APHIS. Premises confirmed to have VS-positive animals remain quarantined until 30 days after all clinical signs of the disease have disappeared from livestock on the premises. Thus local and national activities involving horses and cattle may be disrupted, and international exports may be prohibited because of meat and livestock embargoes.

Zoonotic Implications
Occasional human infections give the disease some public health significance, but the disease is mild, resembling influenza, and is considered as minor zoonosis.[1]

PATHOGENESIS
Local infection of the mucous membrane of the mouth and the skin around the mouth and coronets is followed by the development of vesicles on the lips, muzzle, tongue, as well as on the teats and interdigital clefts. The frequent **absence of classical vesicles** on the oral mucosa of affected animals in field outbreaks has led to careful examination of the

pathogenesis of the mucosal lesions. Even in experimentally produced cases, only 30% of lesions develop as vesicles; the remainder dehydrate by seepage during development and terminate by eroding as a dry necrotic lesion.

Immune Mechanisms

Following infection, serum-neutralizing antibodies develop within a few days and may persist for 8 to 10 years. Reinfection can occur in the presence of a high antibody titer. In cattle, horses, and swine, high titers of virus are found at the margins of lesions and in vesicular fluids for a short period after infection. However, viremia is undetectable and there is no known carrier state in cattle, horses, or swine.

CLINICAL FINDINGS
Cattle

In cattle after an incubation period of 3 to 15 days, there is a sudden appearance of mild fever and the development of vesicles on the dorsum of the tongue, dental pad, lips, and buccal mucosa. The vesicles rupture quickly and the resultant irritation causes profuse, ropy salivation and anorexia. Confusion often arises in field outbreaks of the disease because of failure to find vesicles. In some outbreaks with thousands of cattle affected, vesicles have been almost completely absent. They are most likely to be found on the cheeks and tongue where soft tissues are abraded by the teeth. At other sites there is an erosive, necrotic lesion. In milking cows there is a marked decrease in milk yield. Lesions on the feet and udder occur only rarely except in milking cows where teat lesions may be extensive and lead to the development of mastitis. Lesions are very painful and cause a decline in feed intake and resistance to be milked in dairy cattle. Recovery is rapid, affected animals are clinically normal in 3 to 10 days, and secondary complications are relatively rare.

Horses

In horses, the signs are broadly similar. There is fever, depression, inappetence, drooling of saliva, and affected horses may rub their lips on troughs and jaw champ. Vesicles coalesce and rupture with detachment of the epithelium and the formation of shallow ulcers. The period of fever and vesicles is short lived. Not infrequently the lesions seen are limited to the dorsum of the tongue or the lips and are in the coalescing ulcer stage. Other less common sites include the udder of the mare and the prepuce of males. Lesions may occur at the coronary band and lead to lameness and deformity of the hoof wall.

Pigs

In pigs, vesicles develop on or behind the snout, the lips, or on the feet, and lameness is more frequent than in other animals.

CLINICAL PATHOLOGY

Vesicle fluid, epithelium covering unruptured vesicles, epithelial flaps of freshly ruptured vesicles, or swabs of vesicles are ideal diagnostic specimens for virus isolation. If unavailable, oropharyngeal fluid from cattle or throat swabs from pigs may be submitted. Samples should be placed in containers with Tris-buffered tryptose broth with phenol red at pH 7.6. Glycerophosphate buffer, pH 7.2–7.6, can be used for specimens intended for CF.[1] Samples need to be kept refrigerated for shipping for up to 48 hours or otherwise frozen.

The **indirect sandwich ELISA** (IS-ELISA) is currently the diagnostic method of choice for identification of viral serotypes of VSV and other causative agents of vesicular diseases. Virus isolation can also be performed by inoculation into Vero **cell cultures** and subsequent staining with anti-VSV FA conjugate. CF is less sensitive than the IS-ELISA and is affected by procomplementary or anticomplementary factors.[1] Nucleic acid recognition by PCR has been used to detect presence of viral DNA.

Serologic tests include VN, CF, and a LP-ELISA, all of which are prescribed tests for international trade. LP-ELISA is currently considered the method of choice for the detection and quantification of antibodies against different VSV serogroups. The ELISA has advantages in speed and expense and has comparable specificity and gives fewer false-negative results than VN.[1]

NECROPSY FINDINGS

Necropsy examinations are not usually undertaken for diagnostic purposes.

DIFFERENTIAL DIAGNOSIS

Because of its case-for-case similarity to foot-and-mouth disease (FMD), prompt and accurate diagnosis of the disease is essential. In most countries the **disease is notifiable**.

Cattle
- FMD
- Pseudocowpox
- Bovine papular stomatitis
- Bovine viral diarrhea/mucosal disease
- Infectious bovine rhinotracheitis
- Bovine malignant catarrh fever
- Bluetongue
- Epizootic hemorrhagic disease
- Rinderpest
- Chemical or thermal burns

Horses
- Blister beetle toxicosis
- Bullous pemphigoid
- Equine infectious arteritis
- Equine herpes virus infection
- Calicivirus infection
- Jamestown Canyon virus infection
- Phenylbutazone toxicity
- Equine exfoliative eosinophilic dermatitis and stomatitis

- Squamous cell carcinoma
- Melanoma
- Grass seed awns

Swine
- FMD
- Swine vesicular disease
- Vesicular exanthema of swine
- Foot rot
- Thermal or chemical burns

TREATMENT

Treatment is seldom undertaken, but nonsteroidal antiinflammatories may contribute to the comfort of the animal and the rapidity of recovery.

CONTROL

Hygienic and quarantine precautions to contain the infection within a herd are sufficient control, and the disease usually dies out of its own accord. Animal movement off the farm should be prohibited until 30 days after all lesions have healed. There are usually restrictions of movement of animals from infected areas to different jurisdictional areas that are free of clinical disease, and VS is an **OIE List A disease**.

Immunity after an attack appears to be of very short duration, probably not more than 6 months, but serologic titers persist much longer. An **autogenous killed vaccine** was approved for use in dairy cattle in infected or at-risk areas during the 1995 outbreak in the United States, but vaccine efficacy could not be determined.

A DNA vaccine expressing the glycoprotein gene from VS-NJ virus elicits neutralizing antibody titers in mice, cattle, and horses. The level of protection of antibody required for protection is unknown.

A recombinant VSV-IND expressing NJ and IND glycoproteins has been generated and examined as vaccine candidate. When inoculated into pigs it induced neutralizing antibodies and the pigs were protected against homologous high-dose challenge.

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Parasitic Diseases of the Alimentary Tract

CRYPTOSPORIDIOSIS

SYNOPSIS

Etiology Usually *Cryptosporidium parvum*, *C. andersoni*, and/or *C. bovis*

Epidemiology Infection common in ruminant neonates. May cause diarrhea, particularly if there is intercurrent infection with other enteropathogens and nutritional or environmental stress

Clinical findings Malabsorption-type diarrhea

Clinical pathology Oocysts in feces demonstrated by immunofluorescent or oocyst DNA detected by polymerase chain reaction

Lesions Villous atrophy

Diagnostic confirmation Demonstration of lesions and the organism

Treatment Supportive. Halofuginone in cattle, if approved

Control Hygiene and management to ensure passive transfer of colostral antibodies and minimization of infection pressure

ETIOLOGY

Cryptosporidium spp. are apicomplexan (coccidial) protozoans.[1-14] They have direct life cycles, and infections are transmitted via the fecal–oral route. Currently, based primarily on molecular data, more than 16 *Cryptosporidium* species and more than 44 genotypes have been reported to parasitize the epithelial cells (usually in the gastric or intestinal tract) of hosts representing all classes of vertebrates.[2-4] *C. parvum* is a **common infection** in young animals, including ruminants, and is found in many species of mammals, including humans. *C. parvum* is considered a significant cause of varying degrees of naturally occurring diarrhea in neonatal farm animals. This agent can act in concert with other enteropathogens to produce intestinal damage and diarrhea.

EPIDEMIOLOGY
Occurrence and Prevalence

Cryptosporidiosis has been recognized worldwide in numerous host animals, including cattle, lambs, goat kids, foals, and piglets.[4] Many studies report prevalence of infection, but this does not imply clinical disease.

Calves

Many studies have found limited association between infection and diarrhea, but there are many reports that associate infection in calves with diarrhea occurring between 5 and 15 days of age. A study of preweaned (5–60 days of age) and postweaned (3–11 months of age) calves has shown strong evidence of an age-related association between host and cryptosporidiosis. The prevalence of *Cryptosporidium* in preweaned calves has been shown to be ~50% (of 503) and can decrease to ~20% (of 468) calves following weaning. Interestingly, although most of the infections in preweaned calves relate to *C. parvum,* only a small percentage (e.g., <1%) of weaned calves have been found to be infected with this species; the dominant species in weaned calves, based on DNA studies, are *C. andersoni* and *C. bovis.* This information suggests that young calves represent a more significant zoonotic risk than older cattle. Infection of calves is often followed by the development of resistance to reinfection, and oocyst excretion is less common and intermittent in older and adult cattle, although high excretion rates can be found in adult cattle in some herds (which likely relate to species other than *C. parvum*).

Because calves are likely to be infected by *C. parvum* shortly after birth, and clinical signs of disease are typically limited to a period of intense, self-limiting diarrhea, and the high cost and limited effectiveness of chemotherapeutic and supportive treatment, there appears to have been little incentive for developing husbandry practices to limit bovine cryptosporidiosis. However, intensive farms (e.g., dairy and feedlots) can represent a significant source of human-infective oocyst contamination in the environment, which is presumably exacerbated by the presence of newborn calves.

Sheep and Goats

C. parvum is also a **common** enteric infection in **young lambs** and **goats**, and diarrhea can result from a monoinfection, but more commonly it is associated with mixed infections. The features of infection(s) and pattern of excretion of the cryptosporidial oocysts is similar to that in calves.[1] Infection can sometimes be associated with outbreaks of diarrhea, with high case fatality in lambs from 4 to 10 days of age and goat kids from 5 to 21 days of age.[1]

Pigs

Cryptosporidial infection in pigs occurs over a **wider age range** than in ruminants and has been observed in pigs from 1 week of age through to market age. Infection seems to be common between 6 and 12 weeks of age. Many cryptosporidial infections appear to be **asymptomatic**, although cryptosporidiosis might contribute to malabsorptive diarrhea after weaning.

Foals

Cryptosporidial infection in foals appears to be less prevalent. Diarrhea has been recorded in foals from 5 days to 6 weeks of age. Disease might occur in Arabian foals with inherited combined immunodeficiency.

Farmed Deer

Cryptosporidiosis is also recorded in young deer and can be a cause of diarrhea. Infection has also been recorded in red deer calves dying at 24 to 72 hours of age, following a syndrome of severe weakness and depression accompanied by a terminal uremia.[1]

Source of Infection and Transmission

Experiments have shown that a small number of oocysts are required for infection. The replicative cycle in the intestine amplifies a minor infective dose, and studies in gnotobiotic animals indicate a minimum **infectious dose** as low as one oocyst. The source of infection is **feces** that contain oocysts that are already sporulated and infective when excreted. Large numbers of oocysts are excreted during patency in calves, resulting in heavy environmental contamination. Transmission may occur directly from calf to calf, indirectly via fomite or human transmission, and from contamination in the environment or fecal contamination of the feed or water supplies. Infection in newborn animals and an increase in contamination of their immediate environment might occur as the result of a **periparturient rise** in fecal output oocysts by the dam.

Risk Factors

The factors that make animals susceptible to infection and that predispose infected animals to develop clinical disease are still not well understood.[4] Cryptosporidiosis in young agricultural animals is often associated with infection with *C. parvum.* Other enteric infections can occur concurrently with *Cryptosporidium*/cryptosporidiosis. The site of infection with *Cryptosporidium* is predominantly on the enterocyte where it results in cell damage, loss of brush border enzymes, and a reduction of villous surface area.

Pathogen Risk Factors

Oocysts are resistant to most **disinfectants** and can reportedly remain viable for ≥18 months in a cool, damp, or wet environment and can survive for several months in soil and slurry, but are susceptible to desiccation, temperatures of more than 60°C, and ultraviolet light. The infectivity of the oocysts can be destroyed by ammonia, formalin, freeze-drying, and exposure to temperatures below 0°C (32°F) and >65°C (149°F). Ammonium hydroxide, hydrogen peroxide, chlorine dioxide, 10% formol saline, and 5%

ammonia are effective in destroying the infectivity of the oocysts. The infectivity of oocysts in calf feces is reduced after 1 to 4 days of drying.

Concurrent Infections

Infections with other enteropathogens, particularly rotavirus and coronavirus, are common, and epidemiologic studies suggest that diarrhea is more severe with mixed infections with other pathogens. The rates of single and mixed infections vary among studies. Generally, mixed pathogen infections are most common, but cryptosporidial infection can be very significant in its own right. **Immunologically compromised** animals are more susceptible to cryptosporidiosis than immunocompetent animals, but the relationship between disease and failure of passive transfer of colostral immunoglobulins is not entirely clear. Disease can be reproduced in both colostrum-deprived and colostrum-fed calves and, in the field, clinical disease can occur, for example, in calves with adequate passive transfer of colostral immunoglobulins. However, the shedding of oocysts has been observed to be higher in calves with low absorptive efficiency of IgG from colostrum and low serum IgG concentrations.

Case–fatality rates in cryptosporidiosis are usually low and the disease self-limiting, unless there are other complicating factors. In addition to concurrent infections, these include deficits linked to an inadequate intake of colostrum and milk and chilling from adverse weather conditions. Age-related resistance, unrelated to prior exposure, has been observed in lambs but not calves. Infection may result in a serum antibody response, but both cell-mediated and humoral responses are important in immunity against cryptosporidia.

Zoonotic Implications

Infections in domestic animals may be a reservoir for infection to susceptible humans.[4-9] In humans, *Cryptosporidium* is recognized as a relatively common nonviral cause of self-limiting diarrhea in immunocompetent persons, particularly children. In symptomatic, immunocompetent patients, cryptosporidiosis most commonly presents with diarrhea that can lead to rapid weight loss and dehydration and require parenteral fluid therapy. The disease is usually self-limiting, with symptoms normally lasting between 3 and 12 days. In **immunologically compromised** persons, clinical disease may be severe. This is particularly serious in human patients with acquired immune deficiency syndrome or who are immunocompromised or immunosuppressed. The infection can be transmitted from person to person, but direct infection from animals and indirect water-borne infection from surface water and drinking water contaminated by domestic or wild animal feces can also be significant. Animal manures and slurry may contain *Cryptosporidium* oocysts, and there is potential for contamination of the food chain as a result of runoff into adjacent surface waters or from direct application of the untreated wastes to crops.

Direct animal contact can result in human infection where there is hand to mouth transmission and infection. Cryptosporidiosis has been recorded in veterinary students and is a concern for children at fairs, petting zoos, and sometimes during educational visits to farm settings. Cryptosporidiosis is one of a number of zoonotic infections that have recently emerged in these settings. The apparent increase in prevalence of these infections might be caused by the general movement of populations from rural to urban communities and the consequent removal from early exposure to farm animal–derived zoonotic agents. Similarly, it could result from better detection and reporting by public health authorities. Regardless, the risk of transmission of zoonotic agents associated with petting zoos, farm animal exhibits, fairs, etc., is real and veterinarians are increasingly asked for advice on this issue. This can be in association with an official capacity as a fair veterinarian or in consultation with farm owners, who desire to bridge the increasing estrangement of urban populations to farm activities. Animal handlers on cattle farms can be at high risk of diarrhea caused by cryptosporidiosis transmitted from calves infected with *Cryptosporidium,* and immunocompromised people might be restricted from access to young animals and possibly from access to farms.

PATHOGENESIS

Cryptosporidium is usually transmitted via the fecal–oral route and exhibits a monoxenous (single-host) life cyle.[4] Briefly, a sporulated oocyst (containing four infective sporozoites) is ingested by the host and exocysts usually in either the intestine or the stomach (abomasum) (depending on the species of *Cryptosporidium*). Each motile sporozoite migrates, by gliding motility, along the exterior surface of the epithelial cells of the gut (e.g., microvilli in the small intestine) and penetrates the cell, eliciting an invagination in the cell membrane (of enterocytes in the small intestine) and forming a bilayered membranous vacuole (outer layer is host derived; inner layer is parasite derived, parasitophorous vacuolar membrane [PVM]). The host-derived outer layer of the vacuole disintegrates, and the inner PVM thickens and acts as the interface between the developing parasite and the host cytoplasm, which results in the parasite being located intracellularly but external to the cell cytoplasm (i.e., extracytoplasmic). Intracytoplasmic invasions are possible in rare instances, but appear to be limited to the invasion of macrophages within the Peyer's patches.

Within the cell, the sporozoite develops into a trophozoite, which subsequently undergoes asexual reproduction (schizogony or merogony; longitudinal binary fission) to produce type 1 meronts (schizonts). Each of these type 1 meronts contains 16 merozoites, which are released from the enterocyte. Each merozoite infects a new enterocyte, then replicates and develops into new type 1 meronts to repeat the cycle, or enters into the reproductive phase to replicate and develop into a type 2 meront, each of which contains four merozoites. After entering a host cell, each type 2 merozoite initiates the sexual cycle (gametogony) and eventually develops either into a microgamont (containing 12–16 microgametes) or a macrogamont (maturing into a macrogamete). Microgametes (male) are released and fertilize macrogametes (female) to form zygotes. The zygote then develops, within the PVM into an oocyst. In another asexual reproductive phase (sporogony), the oocyst sporulates to produce, internally, four naked sporozoites. Two types of oocyst are produced and slough off the epithelial layer. The thin-walled oocysts (~20% of the overall population of oocysts) remain in the alimentary tract and have the ability to sustain an autoinfection, whereas the thick-walled oocysts (~80%) are passed in the feces. The thin-walled oocysts are of particular relevance in immunocompromised, immunodeficient, or immunosuppressed individuals, as the likely cause of chronic cryptosporidiosis. In cattle, cryptosporidia are most numerous in the small intestine or abomasum (*C. andersoni*). The prepatent periods can range from 2 to 7 days in calves, and from 2 to 5 days in lambs. Oocysts are usually passed in the feces of calves for 3 to 12 days, but there is considerable variation in both prepatency and patency.

Cryptosporidium infection usually most directly and severely impacts the intestinal tract. Cryptosporidial infection in the intestine is best characterized and is initiated when zoites infect vicinal enterocytes and endogenous forms spread to the enterocytes of both the villi and crypts. Severe diarrhea occurs mainly as a result of proximal infection of the small intestine, whereas infections confined to the distal ileum and/or the large bowel tend to be associated with intermittent diarrhea or can be asymptomatic. Endogenous forms of *Cryptosporidium* disrupt the microvillous border, which leads to the loss of mature enterocytes, a shortening and fusion of villi, and a lengthening of crypts caused by increased cell division and edema. This leads to the loss of membrane-bound digestive enzymes; diminishes the absorptive capacity of the intestine; and reduces the uptake of fluids, electrolytes, and nutrients from the intestinal lumen.

CLINICAL FINDINGS

There are no clinical findings that are pathognomonic for cryptosporidiosis in calves.[4] Affected calves are usually 5 to 15 days old and have a mild to moderate diarrhea, which persists for several days, regardless of treatment. The duration of diarrhea tends to be a few days longer than that associated with rotavirus, coronavirus, or ETEC. Feces are yellow or pale and watery and can contain mucus. Persistent diarrhea can result in a marked loss of BW and emaciation. In most cases, the diarrhea is self-limiting after several days. Varying degrees of apathy, reduced feed intake, and dehydration are common. Only rarely does severe dehydration, weakness, and collapse occur, which is in contrast to other causes of acute diarrhea in neonatal calves. Case–fatality rates can be high in herds with cryptosporidiosis when the calf feeder withholds milk and feeds only electrolyte solutions during the episode of diarrhea. The persistent nature of the diarrhea leads to a marked energy deficit in these circumstances, and the calves can die of inanition at 3 to 4 weeks of life. This syndrome may be particularly common in the winter months when cold stress can affect energy requirements.

In the experimentally induced cryptosporidiosis in calves, depression and anorexia are the earliest and most consistent clinical findings. Feed intake is reduced and, combined with the persistent diarrhea over several days, may cause emaciation. Recovery can occur between 6 and 10 days after the onset of diarrhea. In the experimentally induced cryptosporidiosis in lambs and kids, depression, diarrhea, and reduced feed intake are common, and recovery can occur within a few days. Severe clinical manifestations have been observed in the field in lambs subject to environmental cold stress and those that are energy deficient because of an inadequate intake of colostrum.

CLINICAL PATHOLOGY

Traditionally, diagnosis of cryptosporidiosis has been based on the detection of *Cryptosporidium* oocysts or DNA in host feces. Oocysts can be detected in the feces by examination of fecal smears with particular stains, by fecal flotation, and by immunologically or DNA-based methods.[4] Diagnostic techniques include the immunofluorescent assay detection of fecal oocysts. It has been suggested that, if the diarrhea is associated with cryptosporidia, the feces might contain 10^5 to 10^7 oocysts per milliliter. The oocysts are small (5–6 μm in diameter), relatively nonrefractile, and difficult to detect by light microscopy. They can be detected by phase-contrast microscopy. Oocysts can be concentrated from fecal samples by centrifugal flotation in high specific gravity salt or sugar solutions. The modified Ziehl–Neelsen is a simple and rapid staining procedure suited for large-scale routine diagnosis.[4] Immunofluorescence and other immunologic techniques are relatively widely used, as are a range of PCR-coupled DNA methods for the specific detection and genetic characterization of *Cryptosporidium* stages present in fecal samples.[4]

NECROPSY FINDINGS

Varying degrees of dehydration, emaciation, and serous atrophy are present in calves that suffer from persistent diarrhea over many days. There is atrophy of villi in the small intestine. Histologically, large numbers of different stages of the parasite, including meronts or schizonts, are at the tips of the enterocysts (microvilli). In low-grade infections, only small numbers of parasite stages are detected, with no apparent or limited histopathological changes in the intestine. The villi are shorter than normal, and crypt hyperplasia and infiltration with a mixture of inflammatory cells are common.

Samples for Confirmation of Diagnosis

- **Parasitology:** Feces (microscopic examination, ELISA, IFAT)
- **Histology:** Formalin-fixed intestine (several sites) or abomasum (e.g., *C. andersoni*)

> **DIFFERENTIAL DIAGNOSIS**
>
> The disease must be differentiated from other common infectious diarrheas in calves, which are covered in the section Acute undifferentiated diarrhea of newborn farm animals.

PREVENTION AND CONTROL

In animals, the key **components for prevention and control** of cryptosporidiosis include the maintenance of a clean environment and the introduction of effective management strategies to minimize the potential for rapid spread from animal to animal, farm to farm, and from animal to human.[4] The prevention of *Cryptosporidium* infection is challenging in intensively farmed animals, because the infective dose can be very low; thus exclusion or elimination of the parasite from the farm environment is almost impossible. Although the maintenance of "closed" herds or flocks can control the introduction of cryptosporidiosis from animals purchased from external sources (e.g., saleyards), additional external factors, such as parasite transport via "mechanical" means and parasite introduction through contaminated water or feed, can introduce infection on to a farm and are difficult, if not impossible, to control. In addition, oocysts shed by wildlife and/or introduced into water supplies from wildlife may represent another potential source of infection for herds of domestic animals. The role of wildlife as a reservoir and its involvement in transmission to and disease in livestock and humans are not yet well understood, requiring further investigation using advanced molecular methods.

Because the prevention of infection in livestock herds is not always practical, control is a critical feature of a sound management strategy. However, limiting infection of neonatal animals and minimizing the risk of spread from infected to uninfected animals is a significant challenge. Numerous scientists have studied the factors linked to the prevalence of *Cryptosporidium* and the associated impact of cryptosporidiosis. Although useful for highlighting potentially important factors either contributing to or protecting against infection and disease, such studies are usually limited to showing a statistical association between any "factor" and increased or decreased "risk" caused by unavoidable limits of the experimental designs of such surveys. Specifically, because these surveys are conducted in herds, multiple factors (e.g., housing, frequency of pen cleaning, proximity to other livestock herds, food and water sources) can vary among herds, all of which can contribute to disease prevalence. None of these factors can be specifically isolated, making the determination of the actual impact of any single factor difficult. Acknowledging this, herd management practices, which appear to be associated with protection against infection by *Cryptosporidium* and/or affliction with cryptosporidiosis, include calving in winter rather than summer, removing neonates from the dam within 1 hour of birth, ensuring the neonate receives an adequate initial dosage of colostrum (either from the dam, from another animal, or via bottle feeding from a frozen supply), and ensuring optimal housing for calves.

Environmental factors considered important in decreasing the risk of cryptosporidiosis in neonates include low population density for calves; use of concrete flooring over straw, gravel, or sand; and the routine cleaning of pens (i.e., hygiene) and feeding utensils. The regular cleaning of pens and feeding apparatus is considered to be essential to a rigorous management strategy of cryptosporidiosis; however, because of the robust nature of *Cryptosporidium* oocysts, care must be taken to ensure that such cleaning regimens are effective. Oocysts remain viable for long periods of time and are resistant to various disinfectants suitable for use in agricultural settings (e.g., bleach-based disinfectants). Ammonia-based disinfectants can kill *Cryptosporidium* oocysts, but they release irritating fumes and can only be used after destocking. Disinfectants containing hydrogen peroxide plus either

peracetic acid or silver nitrate have also been shown to have a deleterious effect on the survival of *C. parvum* oocysts and are commercially available for application in a farm setting. Steam cleaning is another supportive measure, has been shown to be effective for killing *Cryptosporidium* oocysts on instrumentation in hospitals, and may be suitable for decontaminating instrumentation used in farming for feeding or milking.

Mechanical removal of oocysts daily from concrete surfaces using a high-pressure hose appears to be an effective means of reducing the spread of *Cryptosporidium* and is preferable to sweeping, which imposes an increased risk of cross-contamination among pens via the mechanical transfer of oocysts. Importantly, the desiccation of oocysts appears to be a highly effective means of parasite control and further highlights the benefit of using concrete floors in pens instead of porous or absorptive materials to facilitate drying.

Treatment Options

Compared with the previous management strategies, immunotherapeutic or chemotherapeutic options are limited.[4,10,11] The demonstrated host age stratification of *Cryptosporidium* in many animal species suggests that passive immunity is possible and likely results from prior exposure to disease, but the effective eliciting of passive immunity via colostrum is still unclear. Passive immunotherapy using colostrum from dams immunized with native or recombinant antigens of *Cryptosporidium* has been explored and shown to be a protective infection of young calves in some studies but not in others.[4]

"Risk-factor" surveys indicate that neonate calves have a reduced probability of infection by *Cryptosporidium* following the ingestion of colostrum; however, the prevalence of infection in neonates, even after colostrum ingestion, is high before weaning, indicating that the passive transfer of immunity is limited. Overall, evidence indicates that the passive transfer of immunity via colostrum is unlikely to be effective as a single means of defense against cryptosporidiosis in young calves.

Although various avenues have been explored for the development of a vaccine against cryptosporidiosis, none are yet commercially available. Recently the use of a whole oocyst-based vaccine from an attenuated line of *C. parvum* (gamma irradiated) has been revisited and shown to show a protective response in calves. Other efforts have focused on assessing immune responses against antigens derived from oocysts or the cell surface of sporozoites.[10] The proteins CP15 and P23, involved in zoite motility and/or host cell invasion, have been expressed using recombinant methods and appear to be promising immunogens. Although overall success has been limited, the availability of the complete nuclear genome sequences

for some *Cryptosporidium* spp. and developments in molecular and computer technologies might provide opportunities for identifying novel proteins as vaccine targets.

In the absence of a vaccine, supportive and chemotherapeutic treatment options have been an area of significant research. The simplest, but at present one of the more effective, means of treating cryptosporidiosis cases in livestock is oral or intravenous rehydration of clinically affected, dehydrated animals. Chemotherapy has been explored with only limited success. Numerous organic-based antimicrobial compounds, including various quinones, aminoglycosides (e.g., paromomycin and streptomycin) and folate antagonists (e.g., sulfanitran and trimethoprim), have been evaluated with mixed success. **Halofuginone lactate** (HFL) has been used as a supportive measure to treatment of clinical cryptosporidiosis in calves. Studies have indicated that administering HFL to infected calves at a dosage of 60 to 125 μg/kg BW (e.g., for 7 days from 1 day of age) decreased the severity of clinical disease as well as oocyst numbers in feces shortly after treatment. Other studies have provided further support of these findings, indicating that HFL is an effective chemotherapy in calves for the purpose of reducing the severity of bovine cryptosporidiosis, and suggesting that HFL decreases the spread of *Cryptosporidium* from animal to animal because of decreased fecal oocyst output. However, although HFL may be useful in diminishing the severity of disease symptoms, this drug delays rather than eliminates the excretion of oocysts in feces. In spite of the use of HFL as a supportive measure, its recommended dosage must be strictly adhered to (given its limited safety index), and severely dehydrated calves should not be treated to prevent toxic effects. **Paromomycin sulfate** given orally at a dose of 100 mg/kg BW daily for 11 consecutive days from the second day of age seems to prevent disease in goat kids and to reduce, but not completely prevent, diarrhea in infected lambs.[1]

Supportive Treatment

Affected calves should be supported with **fluids and electrolytes**, both orally and parenterally, as necessary until spontaneous recovery occurs.[4,12] Cows' **whole milk** should be given in small quantities several times daily to optimize digestion and to minimize loss of BW. It is important to **continue to feed** milk to the full level of requirement despite the presence of diarrhea, because a reduction in intake may lead to death from inanition. Several days of intensive care and feeding may be required before recovery is apparent. **Parenteral nutrition** could be considered for valuable calves.

Management Strategies

In addition to treatment and control regimens to limit the impact of *Cryptosporidium*

infection on herds, **management** strategies are critical to limit the spread of infective *Cryptosporidium* oocysts to other farms, and, for *C. parvum*, to the human population.[4] Cryptosporidiosis is difficult to control. The rational approach to prevention is to **minimize transmission** between the source of the organism and neonatal farm animals and between the animals. Reducing the number of oocysts ingested may reduce the severity of infection and allow immunity to develop. Calves should be born in a clean environment, and adequate amounts of colostrum should be fed at an early age. Calves should be kept separate without calf-to-calf contact for at least the first 2 weeks of life, with strict hygiene at feeding. Disinfectants detailed earlier should be used in hygiene.

Diarrheic calves should always be **isolated** from healthy calves during the course of the diarrhea and for several days after recovery. Sick calves are commonly treated by the same person who feeds the healthy calves, and great care must be taken to avoid mechanical transmission of infection. Calf-rearing houses should be vacated and cleaned out on a regular basis; an all-in/all-out management system, with thorough cleaning and several weeks of drying between batches of calves, should be used.

Manure from animals is a major contributor of *Cryptosporidium* oocysts in the environment on farms, and measures also need to be implemented to reduce the risks of pollution to drinking water.[4,13,14] Adequately controlled storage and handling of manures and slurry (e.g., from cattle yards or dairies) or leachate from bedding will assist to reduce the risk of contamination in waterways. Runoff into water catchments presents a significant risk, particularly during and after heavy rainfall; although the risk posed by oocysts in water runoff varies depending on the soil type and the density of vegetation in the surrounding area. Generally, grazing animals should be excluded from access to water catchments and water sources through the introduction of buffer zones.

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COCCIDIOSIS

SYNOPSIS

Etiology Many different *Eimeria* spp., *Isospora* spp.

Epidemiology Mainly young calves, lambs, piglets, and kids. Infection rate can be high, clinical disease relatively common; high morbidity with low case–fatality rate. Occurs most often in crowded conditions both in barns and on pasture, particularly in calves and lambs moved from pasture to feedlot. Transmitted by fecal–oral route; oocysts shed from infected animals. Immunity develops after infection; clinical disease occurs rarely in adult cattle.

Signs Diarrhea, dysentery, tenesmus, appetite normal or inappetence, mild abdominal pain in lambs, nervous signs in calves with coccidiosis in cold climates, loss of body weight, and anemia in some cases but it is uncommon. Epidemics occur in calves and lambs, particularly in feedlot animals.

Diarrhea without blood in feces of piglets

Clinical pathology Diagnostic number of oocysts in feces

Lesions Ileitis, cecitis, and colitis

Diagnostic confirmation Oocysts in feces; asexual stages (schizonts or merozoites) in intestinal tissues

Differential diagnosis
  Calves: Rotavirus and coronavirus diarrhea; *Clostridium perfringens* type C enterotoxemia; colibacillosis caused by attaching and effacing *Escherichia coli*
  Lambs: Salmonellosis; helminthiasis; *C. perfringens* type C enterotoxemia
  Piglets: Transmissible gastroenteritis; colibacillosis; *Strongyloides ransomi*; *C. perfringens* type C enterotoxemia

Treatment Supportive therapy. Coccidiostats

Control Control population density to minimize number of oocysts ingested while immunity develops. Use of coccidiostats in feed and water supplies. Sanitize the environment if possible.

ETIOLOGY

Coccidial species are as follows:
- **Cattle:** *Eimeria zuernii, E. bovis,* and *E. ellipsoidalis*; *E. alabamensis, E. auburnensis,* and *E. wyomingensis* may also cause disease in calves
- **Sheep:** *E. arloingi A* (ovina), *E. weybridgenis* (*E. arloingi* B), *E. crandallis, E. ahsata,* and *E. ovinoidalis* (previously known as *E. ninakohlyakimovae*), and *E. gilruthi*
- **Goats:** *E. arloingi, E. faurei,* and *E. gilruthi, E. caprovina, E. ninakohlyakimovae,*[1] and *E. christenseni*
- **Pigs:** *I. suis*; numerous species of *Eimeria* (no clinical importance), including *E. debliecki, E. neodebliecki, E. polita, E. perminuta, E. scabra,* and *E. suis*
- **Horses and donkeys:** *E. leuckarti* (ubiquitous, but of no clinical significance)

EPIDEMIOLOGY
Occurrence and Prevalence of Infection

Coccidiosis is most frequently seen in livestock animals housed or confined in small areas contaminated with oocysts.[2,3] Coccidia are usually host specific, and there is no cross-immunity between species of coccidia. Clinical disease is common in cattle and sheep. Coccidiosis causing diarrhea in newborn piglets is a major problem in some swine herds.

Coccidiosis is most common in young animals, with a seasonal incidence that may be associated with the time of year young calves and lambs are brought together for weaning or moved into feedlots or fed in small areas for the winter months. The prevalence of infection and the incidence of clinical disease are also age related. In housed dairy cattle, the prevalence of infection in calves and in yearlings can be high (40%–50%).

Calves

In North America, the disease is most common in beef calves after weaning in the fall and when confined and fed in small, overcrowded areas during the winter months. Infection occurs most often when weaned calves are fed on the ground, resulting in continuous fecal contamination of the feed. The prevalence of infection in calves in the northwestern and midwestern part of the United States is highest in summer, fall, and spring compared with midwinter (January) and early summer (June). In Canada, for example, winter coccidiosis occurs in beef calves 6 to 10 months of age, most commonly following a prolonged cold period or a sudden change from a moderate winter to severely cold temperature. Cold weather may act as a stressor to precipitate clinical disease in animals previously infected. Acute coccidiosis and a marked increase in the numbers of oocysts discharged will occur following the treatment of infected calves with a corticosteroid on the 20th day after infection, when clinical signs are apparent, or from the 12th to 15th day after infection.

Occasional outbreaks occur in nursing beef calves on pasture when they mingle near water supplies. Postweaning coccidiosis occurs in beef calves grazing on pastures in the subcoastal, dry tropics (e.g., northern Queensland, Australia). It may be more severe in dry years, suggesting that oocyst challenge is less important than immunosuppressive effect of weaning and dietary stress in precipitating clinical disease. Calves are usually weaned and yarded for 3 weeks and then turned out to graze. Severe *E. zuernii* coccidiosis causing diarrhea, dysentery, weight loss, and death occurs with up to 10% of calves clinically affected. The disease is most severe in hot, dry, and sunny conditions when, despite heavy fecal contamination, the yard conditions remain dry and dusty, and oocysts are difficult to find. Coccidiosis caused by *E. alabamensis* along with other species is a common cause of diarrhea and unthriftiness in calves 2 to 4 months of age within the first few weeks after being placed on permanent pasture in the spring.

In **dairy calves**, the disease occurs under overcrowded and dirty, wet conditions, and when feed is contaminated with feces. Some surveys of dairy farms reveal that coccidiosis is one of the most common health-related problems, particularly in crowded situations. Dairy farmers quite frequently elect to treat animals, or feeding a coccidiostat, for the control of coccidiosis.

Adult Cattle

Coccidiosis is uncommon in adult cattle, but occasional cases and even epidemics can occur, sometimes in dairy cows that have calved 6 to 8 weeks earlier. Older animals can serve as a source of infection for younger calves in the herd.

Sheep and Goats

Coccidiosis can be a major problem in housed lambs. In some countries, such as Germany, the cumulative incidences of *E. ovinoidalis* and *E. weybridgensis*/*E. crandallis* have been found to increase rapidly, resulting in an incidence of almost 100% in 8-week-old lambs. Acute coccidiosis in intensively grazed lambs occurs at about 6 to 8 weeks of age when the oocyst output is very high in healthy and in clinically affected lambs. There is no periparturient rise in oocyst output in ewes. The fecal oocyst excretion rates in grazing lambs are very high compared with those of ewes. Disease can occur commonly in lambs following introduction into a feedlot situation with problems of overcrowding and other stressors. Lambs with no previous exposure to coccidia are highly susceptible to infection.

Coccidiosis is one of the most important diseases of goats kept in large numbers under intensive management conditions. The prevalence of infection may be as high as 100% in some goat farms. Kids are the major source of pasture contamination, and newly weaned kids can have high oocyst counts. More than 13 different species of *Eimeria* have been described in different parts of the world.

Pigs

Observations suggesting neonatal porcine coccidiosis include repeated episodes of diarrhea in piglets 5 to 15 days of age, no response to therapy with antimicrobials, and a failure of vaccination of the pregnant sow with *E. coli* bacterins to control neonatal piglet diarrhea. Peak incidence occurs between 7 and 10 days of age, most commonly during the warm summer months when high temperatures favor the sporulation of the oocysts. *I. suis* is a common parasite on pig farms;[1,3] it can be found in 90% of herds and 25% to 50% of litters. The prevalence may be higher when piglets and their sows are kept on solid concrete floors compared with self-cleaning floors. The morbidity rates are variable, and case–fatality rates can be up to 20%. Rotavirus infection may occur concurrently with *I. suis* infection in piglets of 1 to 3 weeks of age, which may be important causes of steatorrhea or unspecified diarrhea, known as milk scour, white scour, or 3-week diarrhea. *I. suis* infection commonly occurs in large pig-producing farming systems; the highest rate of infection occurs in litters at 3 to 4 weeks of age.

Morbidity and Case Fatality

Generally, for **most species** of farm animals, the infection rate is high, and rate of clinical disease is usually low (5–10%), although epidemics affecting up to 80% can occur. The case–fatality rate is usually low, with the exception of the high case–fatality rate in calves with winter coccidiosis accompanied by nervous signs.[1] The case–fatality rate may be high in calves or lambs with no previous exposure to coccidia. In calves, BW gains and feed consumption are commonly reduced for many weeks after acute clinical coccidiosis, and affected calves do not regain losses in BW compared with uninfected controls.

In **lambs on pasture**, subclinical infections are common but there is no documented evidence that growth rate is affected, even with high levels of infection. Although medication with a coccidiostat may lower the infection rate, there is no apparent difference in performance between medicated and nonmedicated sheep. In lambs raised under crowded conditions indoors, the acquisition of infections with multiple species of *Eimeria* does not appear to affect growth rates, but artificial infection with *E. ninakohlyakimovae* has been shown to cause severe clinical disease and a case–fatality rate of up to 50%.

Piglets infected with *I. suis* have significantly reduced BW at 7, 14, and 21 days of age. The reduction in weight at 3 weeks is economically important, because this weight is factored into the "sow productivity index," which is used as a management aid to help producers assess the potential value of gilts as replacement animals.

Methods of Transmission

The **source of infection** is the feces of clinically affected or carrier animals, and infection is acquired by ingestion of feed and water contaminated with sporulated coccidial oocysts or by licking the hair coat contaminated with such oocysts. Unsporulated oocysts are passed in the feces and require suitable environmental conditions to sporulate. **Moist, temperate, or cool conditions favor sporulation, whereas high temperatures and dryness impede it.** Depending on the species of coccidium, oocysts sporulate at a range of 12°C to 32°C (53.5°F–89.5°F) and require oxygen. They can resist freezing down to approximately −7°C to −8°C (19.5°F–17.5°F) for 2 months, but −30°C (−22°F) is usually lethal.[1] It has been suggested that oocysts might sporulate in the winter months on the hair coats of animals contaminated with feces. This may explain the continual production of several different species of coccidia during the cold winter months, when sporulation on the ground is not possible.[1] Dry conditions and high temperatures also destroy sporulated oocysts within a few weeks, but the oocysts may survive for up to

2 years under favorable conditions. Temperatures of >35°C, humidity of <25%, and sunlight for at least 4 hours are fatal for *E. zuernii*.

Ingestion of the sporulated oocysts results in infection. **Large numbers of oocysts usually arise by continual reinfection and a buildup of the degree of environmental contamination.** This is most common when calves or lambs are crowded into small pens or confined in feedlots. Lambs can become infected within a few weeks after birth from lambing grounds heavily contaminated by the ewes. Overcrowding of animals on irrigated pastures, or around surface water holes in drought conditions, may also lead to heavy infections and disease. Feeder lambs and calves brought into feedlots from sparse grazing may carry a few oocysts, which build up into heavy infections in the lots, particularly if conditions are moist. In such situations, clinical signs of the disease usually appear several weeks to a month after the animals are confined. Young calves and lambs on pasture may shed large numbers of oocysts for long periods, which results in a buildup of coccidial populations. In cow–calf herds, the prevalence and intensity of oocyst excretion can vary with time, resulting in peak values around the time of parturition (periparturient rise).

Sows do not play a significant role in the transmission of *I. suis* infection from one generation of piglets to the next through contamination of the farrowing pen. Oocysts of *I. suis* cannot usually be found in the feces of sows on swine farms where neonatal coccidiosis occurs.

Risk Factors
Animal Risk Factors

Acute coccidiosis occurs primarily in **young animals**, but may occur at any age when resistance is affected by intercurrent disease or inclement weather. The prevalence of infection is usually higher in calves than yearlings or adults in the same herd, but there is also evidence of variation in resistance against *Eimeria* species. A concurrent experimental infection of calves with the viruses and *E. bovis* can result in clinical disease and lesions that are more severe than those caused by either infection alone.

Nutritional status of the animal as a risk factor for clinical coccidiosis is well known. Early weaning of lambs at 21 days of age, followed by experimental infection, results in a failure of growth. In addition, field observations have shown that lambs that are weaned early are more susceptible to coccidiosis than those weaned at a later date. This observation might be a reflection of a lack of immunity in the younger lambs, but dietary stress in early weaned lambs can contribute to disease. Lambs kept on a low plane of nutrition have been reported to be less affected by clinical coccidiosis than those

kept on a high plane of nutrition. The planes of nutrition can also be associated with differences in the prevalence of *Eimeria* spp. Considerable numbers of oocysts can be excreted into the environment, even by well-fed sheep 14 to 16 months of age.

In many countries in Europe, for example, coccidiosis is common in **housed lambs weaned at 6 to 8 weeks of age** and reared on straw with a high stocking density, which provides an ideal environment for oocyst survival and sporulation. Often the use of coccidiostats does not affect the oocyst excretion rate, which suggests either inconsistencies in the effect of in-feed medication, or the infection may be controllable in nonmedicated flocks without the use of coccidiostats.

Environmental and Management Risk Factors

Coccidiosis occurs in livestock when environmental and managemental conditions result in **oral exposure** of large numbers of sporulated oocysts to nonimmune animals. Overcrowding, overstocking, feeding animals on the ground, or situations in which the feed and water supplies are contaminated with feces and oocysts increase coccidial infection pressure and promote transmission. The disease is common in small beef cattle herds that raise their own replacements and finish their own feedlot cattle in small pens that are overcrowded; in these situations, feed and the environment become heavily contaminated with fecal matter. Grazing calves for the first time on permanent pastures can be associated with clinical coccidiosis caused by the ingestion of oocysts that have survived over the winter.

In parts of Europe, the rare occurrence of clinical coccidiosis in housed dairy cattle appears to be associated with management practices, in which calves are individually housed during the first few weeks and subsequently housed in small groups in relatively large pens. Hygiene standards are high, and manure is frequently removed. These measures reduce the intake of high numbers of oocysts and are favorable; the intensity of coccidial infections is usually associated with the number of oocysts in the environment and ingested by animals.

The production system can influence the development of subclinical and clinical coccidiosis. Two production systems are commonly used for the fattening of lambs. In the **extensive system**, lambs are not weaned until slaughter, with little or no concentrate feeding. In the **intensive system**, the lambs receive a high level of concentrates. Even if no clinical signs of coccidiosis are observed, lambs are likely to be subclinically affected in both systems. Straw and high stocking density predispose lambs to a heavy contamination of the environment, which supports oocyst survival and rapid sporulation.

Multiinfections

Natural infections commonly involve multiple species of coccidian. A single species of coccidia might be a major pathogen, but others likely contribute to disease. In some cases, clinical coccidiosis in cattle happens only when *E. bovis* and *E. zuernii* occur together. Although *E. bovis* and *E. zuernii* are the species most commonly associated with bovine coccidiosis,[2] many more species have been described. In sheep and goats, the prevalence of multiple species can be high (> 80%). *I. suis* is a major cause of neonatal or weanling diarrhea in pigs,[3] whereas *E. debliecki* is not pathogenic. Coccidia often have a widespread distribution in livestock animals.

Immune Mechanisms

Immunity against intestinal coccidia consists of both cellular and humoral components.[1] Cellular immunity appears to be more important in "resistance" against reinfection than humoral immunity. Field observations suggest that coccidiosis in cattle is immunosuppressive, which can increase their susceptibility to other common infections. In experimental coccidiosis, neutrophil function may be inhibited, and the feeding of decoquinate may prevent this inhibition.

The administration of dexamethasone to calves suppresses the immunologic response of the animal, and allows the life cycle of the coccidia to proceed uninterrupted. Estradiol and progesterone can enhance cell-mediated immunity and can provide some protection against the often severe wasting and debilitation in calves associated with *E. bovis* infection.

Coccidiosis is an important disease in young lambs on pasture after having been raised indoors, as is also the case in European countries, for example. In this situation, lambs spend the first few weeks of their life indoors and have little exposure to infective oocysts, and little or no immunity is acquired. When the lambs are turned out on to pastures grazed by sheep in the previous grazing season, they rapidly become infected with overwintered oocysts. Coccidiosis develops in such nonimmune lambs 2 to 3 weeks later. The immunity induced by the first infection seems to protect most lambs from reinfections later in the grazing season. If lambs are treated with sulfadimidine at 200 mg/kg BW on days 12, 13, and 14 after turnout, then a marked reduction in the severity of the coccidial infections is seen.

Specific immunity to each coccidial species develops after infection, so that young animals exposed for the first time are often more susceptible to a severe infection and clinical disease than other animals. A single initial infection with as few as 50 oocysts can induce strong immunity to reinfection with the same species, and oocyst production can cease after about 10 days. Under field conditions, animals (e.g., sheep) are probably continually ingesting oocysts from pastures that become increasingly contaminated as the season progresses. Thus immunity to a range of species of coccidia is boosted by frequent reinfection or reexposure.

Very young lambs are relatively resistant to infection with a mixture of pathogenic species of coccidia, but susceptibility increases progressively up to at least 4 weeks of age.[1] Lambs inoculated at 4 to 6 weeks of age develop severe diarrhea, whereas the same inoculum given at 1 day of age causes no clinical disease. Early subclinical infection improves the resistance of lambs to later challenge. When lambs receive a relatively large inoculum of oocysts during their first week of life, they are relatively resistant to the pathogenic effects of some coccidia, are able to respond immunologically, and seem to be protected from subsequent challenges. This information suggests that early exposure or infection of lambs with coccidia, before they are susceptible to the parasites' pathogenic effects, may assist in reducing the incidence, prevalence, and severity of subsequent coccidiosis. In calves, resistance to *E. zuernii* infection can occur after chemotherapy, or experimental infection, with monensin or amprolium. Both drugs suppress the development of disease, during which time immunity can develop. An effective immunity develops in piglets following natural or experimental infection with *I. suis,* which appears to be the most immunogenic coccidial parasite of pigs. Susceptible piglets are infected by this species from infected older pigs. Piglets develop a disease that is more severe when infected with *I. suis* at 1 to 3 days of age than when infected at 2 weeks of age.[3]

PATHOGENESIS

The coccidia of livestock pass through most stages of their life cycle in the gastrointestinal tract. Individual species of coccidia have their particular predilection sites. For instance, *E. zuernii* and *E. bovis* occur primarily in the cecum, colon, and the distal ileum, whereas *E. ellipsoidalis* and *E. arloingi* affect the small intestines. *E. gilruthi* localizes in the abomasum and occasionally the duodenum.

Life Cycle

The life cycles of *Eimeria* spp. are direct. Unsporulated oocysts are passed in the feces from an infected host and develop into the infective stage (sporulated oocysts) in the environment. The original single cell of *Eimeria* divides, forming four sporoblasts, each of which develops into one sporocyst, and within each sporocyst two sporozoites develop ($1:4:2$ configuration of the oocyst for *Eimeria*). When ingested, the wall of the oocyst breaks down, and sporocysts and sporozoites are released. The sporozoites then enter epithelial cells. Once within the cells,

the sporozoites transform to merozoites, which then undergo asexual replication (schizogony or merogony) and produce **first-generation schizonts,** which contain many merozoites. After the schizont matures, the merozoites are released by rupture of the epithelial cell. New epithelial cells are again invaded, and **second-generation and third-generation schizogony** occur. The second-generation and/or third-generation schizonts (depending on *Eimeria* species) are deeper in the mucosa than first-generation schizonts and usually lead to the sloughing of the epithelium, associated hemorrhage, and tissue destruction; therefore these schizonts cause pathogenic effects and lead to enteritis (bloody in severe infections) and clinical disease, but also induce immunity. Following schizogony, the final merozoites that are released invade epithelial cells and "switch" to produce sexual stages, **called the macrogametocyte** (female) **and the microgametocyte** (male) during the phase of **gametogony**. The microgametocyte eventually produces microgametes, which fertilize macrogametes (from microgametocyte; within the mucosa) to produce zygotes. These zygotes become oocysts, which slough from the epithelium and are excreted in the feces. The sloughing of the epithelial layer during gametogony can also lead to bleeding. The prepatent period varies depending on the species of coccidian.

In cattle, *E. zuernii* and *E. bovis* are pathogenic, and their life cycles are similar. In infected calves, first-generation schizogony occurs in the lower ileum, and second-generation schizogony and gametogony occur in the cecum and proximal colon. Both phases cause pathogenic effects for these two parasites and cause rupture of the cells they invade, with consequent exfoliation of the epithelial lining of the intestine. It is notable that the oocyst count is often low when the disease is at its peak, because the oocysts have not yet formed. Exfoliation of the mucosa causes diarrhea, and in severe cases, hemorrhage into the intestinal lumen, and the resultant hemorrhagic anemia may be fatal. If the animal survives this stage, the life cycle of the coccidia terminates without further damage, and the intestinal mucosa will regenerate and return to normal. The patent periods of *E. zuernii* and *E. bovis* are 15 to 17 and 18 to 21 days, respectively. Treatment of calves with a corticosteroid can convert subclinical infection in calves to acute disease, which suggests that environmental, nutritional, and managemental factors can also act as stressors in inducing disease.

Severely affected calves surviving the acute phase of the disease do not regain losses in BW unless they are fed for an additional 3 to 4 weeks, suggesting that bovine coccidia can have a marked effect on performance. A subclinical coccidial infection superimposed on an established, low-grade, subclinical nematode infection in the small intestine may have a marked effect on the mineralization of the skeletal matrix in young adult ruminants, predisposing them to osteodystrophy.

That infections with multiple species of *Eimeria* are so common in livestock may explain the variations in oocyst discharge from infected animals, but, more importantly, in groups of animals. New cases may develop every few days for some weeks, because of the variation in length of the prepatent periods among species of coccidia.

The **pathogenesis of the neurologic signs associated with coccidiosis** in calves is unknown. Examination of a series of cases excluded possible explanations such as alterations in serum electrolytes, vitamin A and thiamin deficiencies, lead poisoning, uremia, *H. somnus* meningoencephalitis, severity of disease, and gross alteration in intestinal bacterial flora and hepatopathy.

The **pathogenesis of bovine winter coccidiosis**, which occurs during or following very cold weather in Canada and the northern United States, is not understood. In January, February, and March, the outside temperatures may reach −40°C (−40°F) with daily mean temperatures of −10°C to −15°C (14°F–5°F) for several consecutive days. Such temperatures should be too cold for sporulation of oocysts in feces on the ground. There is speculation that sporulation could occur on the moist hair coats of cattle, or the endogenous stages of *E. zuernii* may be in a latent phase and reactivated by the stress of cold weather.

In **lambs**, most natural infections are composed of multiple different species of coccidia, and there is a wide range of values in the production of oocysts from individual lambs, either in the feces from the same lamb over a period of time or in the feces from a number of lambs on any one occasion. Under field conditions, constant reinfection occurs and waves of pathogenic stages succeed each other. The occurrence of villous atrophy in the intestinal mucosa of lambs affected by coccidiosis is probably related to recurrent diarrhea. However, in lambs, there is some doubt about the effects of coccidial infection on growth rate, feed consumption, and clinical signs. There may be no obvious relationship between infective dose, the fecal oocyst production, and disease. This information suggests that, in lambs, the mere presence of large numbers of fecal oocysts does not constitute a diagnosis of coccidiosis and that a range of factors may lead to disease. In many cases, it is possible that a large number of oocysts in sheep feces, in the absence of disease, may relate to nonpathogenic species of *Eimeria*.

I. suis has at least three asexual and one sexual intraintestinal replication cycles.[3] All stages are most prominent in the distal half of the small intestine, but also occur in the proximal small intestine, cecum, and colon. The prepatent period is 5 to 7 days; patency is usually 4 to 16 days. Disease relates to diarrhea, villous atrophy, and necrosis of intestinal epithelium, and is characterized by high morbidity and low mortality. In the temperature range of 32°C to 35°C (89.5°F–95°F), the oocysts of *I. suis* can sporulate and become infective within 12 to 16 hours. Pathogenic changes are most pronounced in the small intestine and consist of villous atrophy and focal ulceration from the destruction of villous epithelial cells, principally during the peak of asexual reproduction. A fibrinonecrotic pseudomembrane may develop in severe cases. Extraintestinal stages of *I. suis* have been detected in lymph nodes, liver, and spleen, and their significance is unclear. Piglets develop more severe clinical signs of coccidiosis when inoculated with *I. suis* at 3 days of age than at 19 days of age, and affected piglets that survive develop immunity to reinfection. Rotavirus and other infections can complicate disease.

CLINICAL FINDINGS

The prepatent period depends on the causative agent(s) and the host animal. It usually ranges from 1 to 3 weeks in cattle, from 2 to 3 weeks in sheep, and can be as short as 5 days in piglets. The clinical syndromes associated with the various coccidia are similar in all animals.

Cattle and Sheep

A mild fever may occur in the early stages, but in most clinical cases body temperature is normal or subnormal. The first sign of clinical coccidiosis is the sudden onset of diarrhea with foul-smelling, fluid feces containing mucus and/or blood. Blood may appear as a dark, tarry staining of the feces or as streaks or clots, or the evacuation may consist entirely of large clots of fresh, red blood. The perineum and tail are commonly smudged with bloodstained feces. Severe straining is characteristic, often accompanied by the passage of feces, and rectal prolapse may occur. The degree of hemorrhagic anemia is variable, depending on the amount of blood lost, and in most naturally acquired cases in calves anemia is not a feature. Nonetheless, in exceptional cases, anemia can occur with pale mucosa, weakness, staggering, and dyspnea. Dehydration is common, but is not usually severe if affected animals continue to drink water.

Inappetence is common and, in exceptional cases, there may be anorexia. The course of the disease is usually 5 to 6 days, but some animals undergo a long convalescent period in which feed consumption and BW gains are reduced. Severely affected calves do not rapidly regain BW losses that occurred during the clinical phase of the disease. In mild cases of coccidiosis, diarrhea and reduced growth rate may occur. Subclinical cases may show inferior growth rates and chronic anemia only.

Clinical coccidiosis occurs only rarely in adult cattle. Young dairy cows may be affected, commonly 6 to 8 weeks after calving. Diarrhea, dysentery, tenesmus, pale mucous membrane, thickening and corrugation of the rectal wall, and rapid recovery often without treatment are common signs.

Coccidiosis With Nervous Signs

Nervous signs consisting of muscular tremors, hyperesthesia, clonic–tonic convulsions with ventroflexion of the head and neck and nystagmus, and high mortality rate (80%–90%) can occur in calves with acute clinical coccidiosis. Outbreaks of this "nervous form" have occurred, in which 30% to 50% of all susceptible calves are affected. It is most common during, or following, severely cold weather in midwinter in the northern United States and in Canada. Affected calves may die within 24 hours of the onset of dysentery and the nervous signs, or they may live for several days, commonly in a laterally recumbent position with a mild degree of opisthotonus. In spite of intensive supportive therapy, mortality is high. Nervous signs have not been described in experimentally induced coccidiosis in calves, which suggests that the nervous signs may be unrelated to the dysentery or, indeed, even to coccidiosis.

Lambs

Coccidiosis in lambs is similar to that in calves, but with much less dysentery. In groups of lambs raised and fed under intensive conditions, inferior growth rate, diarrhea (with or without blood), low-grade abdominal pain, gradual onset of weakness, inappetence, fleece damage, mild fever, recumbency, emaciation, or death with a course of 1 to 3 weeks have been described. The diarrhea may escape cursory examination, but clinical examination of affected lambs reveals a perineum smudged with feces, and soft feces in the rectum. Lambs moved directly from range pasture to a feedlot and with little or no previous exposure to coccidia often develop acute disease with a high morbidity and case–fatality rate.

Piglets

In piglets, severe outbreaks of coccidiosis occur between 5 and 15 days of age, irrespective of time of the year. Anorexia and depression are common. There is profuse diarrhea; the feces are yellow, watery, and sometimes appear foamy. The diarrhea may persist for several days when dehydration and unthriftiness are obvious. Although affected piglets continue to suck, they become dehydrated and lose weight. Vomition may occur. Entire litters may be affected, and the case–fatality rate may reach 20%. The disease may persist in a herd for several weeks or months, particularly where a continuous farrowing program is used.

CLINICAL PATHOLOGY
Fecal Oocyst Counts

Animals with acute coccidiosis will be excreting oocysts in the feces only if the infection is patent (i.e., multiple generations of schizogony have occurred and gametogony has led to the production of oocysts). In ruminants with a patent infection and/or disease, a count of more than 5000 oocysts per gram of feces is considered "significant." Although counts of <5000 oocytes per gram of feces do not usually suggest clinical disease, they indicate a source of infection and spread, depending on management and environmental conditions. Oocyst counts of >10^5/g are common in severe coccidiosis outbreaks, although similar counts may also be encountered in asymptomatic animals (e.g., sheep). The output of oocysts following an acute infection or disease can fall sharply after a peak. If oocysts are not found and the disease is suspected, fecal smears can be examined for merozoites; these zoites can also be detected upon fecal flotation. Depending on the host animal, some species of coccidia can be identified and differentiated based on the size and characteristics of the oocysts (particularly following sporulation), although there can be some size overlap among species.

Calves

Affected animals exposed to oocysts may develop severe dysentery a few days before oocysts appear in the feces. However, when the feces from several affected animals are examined, and usually within 2 to 4 days after the onset of dysentery, oocysts can be detected in the feces. The period during which oocysts are discharged in significant numbers (patent period) varies among species of coccidia, the age of the animal, and the degree of immunity; therefore it is useful to examine a number of animals in a group or herd (preferably multiple times) rather than to rely only on the results from a single animal.

Lambs

In lambs at pasture, oocysts first appear in the feces at about 2 weeks of age. The oocyst count continues to rise in lambs until about 8 to 12 weeks when the counts can reach 10^5 to 10^6/g of feces. Thereafter, the counts will decline to approximately 500/g when lambs are 6 to 12 months of age. There is also considerable variation, both among individual lambs and from day to day, in the numbers and species of oocysts present in the feces. Hence, it is useful to examine several samples over a period of several days to assess oocyst output.

Piglets

In piglets, the prepatent period varies from 5 to 7 days, and oocysts are shed in the feces for 5 to 8 days after the onset of clinical signs. Piglets may develop coccidiosis at 5 days of age, and oocysts may not be present in the feces until 3 days later. The use of a saturated sodium chloride with glucose as a flotation solution is recommended when examining piglet feces for *I. suis* oocysts.

Necropsy examination of selected, untreated clinical cases is often useful to make a diagnosis. The disease should be suspected when piglets 5 to 8 days of age develop diarrhea that responds poorly to treatment. Outbreaks of diarrhea in piglets under 5 days of age are usually associated with *E. coli* or TGE. However, mixed infections are common, and extensive laboratory investigations are often necessary to isolate the causative agents. The diagnosis often requires a combination of consideration of the history of diarrhea in piglets of 5 to 15 days of age, gross and microscopic lesions, the presence of coccidial stages in mucosal scrapings and/or histologic sections, and the identification of oocysts in intestinal contents and feces. In heavy infections, piglets may die before the sexual stages of the parasite have developed, and the diagnosis is dependent on finding lesions and, in particular, schizonts and merozoites of *I. suis* in the jejunum and ileum. These developmental stages can also be detected on fecal smears or mucosal scrapings. A rapid field diagnostic procedure consists of staining glass slide impression smears of the mucosa of the ileum and jejunum. Autofluorescence microscopy and PCR-based methods can be used as complementary tools for the detection of *I. suis* and other coccidia.

NECROPSY FINDINGS

Carcasses often have generalized tissue pallor, and there is usually fecal staining of the hindquarters. **In cattle**, congestion, hemorrhage, and thickening of the mucosa of the cecum, colon, rectum, and ileum are the characteristic gross changes seen at necropsy. The thickening may be severe enough to produce ridges in the mucosa. Small, white cyst-like bodies, formed by large schizonts, may be visible on the tips of the villi of the terminal ileum. Ulceration or sloughing of the mucosa might occur in severe cases. Infections in the small and large intestines can be characterized by a fibrinous typhlitis and colitis. Clotted blood or bloodstained feces might be present in the lumen of the large intestine. Histologically, there is a denudation of the epithelium, and merozoites might be detected in some cells. Smears of the mucosa or intestinal contents should be examined for the various developmental stages.

The necropsy findings **in sheep** are marked by more severe involvement of the small intestine than in cattle. Characteristic intestinal changes seen in sheep are hemorrhagic typhlitis and colitis (*E. ovinoidalis*), focal epithelial desquamation (*E. crandallis*), focal mucosal lesions with the formation of

polyps (*E. bakuensis*), and catarrhal enteritis (*E. ahsata* and *E. faurei*), associated with the presence of one or more stages of the parasites (schizonts = meronts and/or gamonts). In sheep affected with *E. gilruthi,* the abomasum contains numerous nodules of 1 to 2 mm in diameter, similar (superficially) in gross appearance to nodules caused by *Ostertagia*. These nodules contain the large schizonts of *E. gilruthi*.

In piglets, the small intestines are usually flaccid, but occasionally a fibrinonecrotic enteritis may be observed. Clinical signs precede the production of oocysts, such that mucosal scrapings should be examined for the presence of earlier stages of the life cycle.

Samples for Confirmation of Diagnosis

- **Parasitology:** Feces (fecal flotation); segments of jejunum, ileum, and colon (direct smear)
- **Histology:** Formalin-fixed duodenum, jejunum, ileum, cecum, and colon (LM)

DIFFERENTIAL DIAGNOSIS

Calves Clinical coccidiosis is characterized by dysentery, tenesmus, mild systemic involvement, and dehydration. The presence of large numbers of oocysts supports the diagnosis, and necropsy findings are usually characteristic. When nervous signs occur in calves appearing to have coccidiosis, differentiation from other diseases causing brain dysfunction must be made.

Sheep The diagnosis is dependent on the clinical findings of diarrhea and/or dysentery, the presence of large numbers of oocysts in the feces, and the intestinal lesions at necropsy. Large numbers (10^5/g) of oocysts may occur in the feces of asymptomatic lambs; thus the observation of large numbers of oocysts in the feces of lambs affected with diarrhea and/or dysentery may not, in itself, constitute a diagnosis of coccidiosis. In lambs that have had previous exposure to coccidia, and that may be relatively immune, other causes of diarrhea, such as helminthiasis, salmonellosis, *Clostridium perfringens* type C enterotoxemia and helminthiasis, should be considered. See Table 7.7 for epidemiological and clinical features of the diseases causing diarrhea in small ruminants.

Piglets Diarrhea caused by coccidiosis must be differentiated from enteric colibacillosis, transmissible gastroenteritis, rotavirus infection, *Strongyloides ransomi,* and

C. perfringens type C. See Table 7.6 for epidemiological and clinical features of the diseases causing diarrhea in pigs.

TREATMENT

Coccidiosis is usually a self-limiting disease, and spontaneous recovery without specific treatment is common when the schizogony (merogony) stages have passed. Many treatments have been recommended without taking this into account, and it is unlikely that any of the chemotherapeutic agents in common use for clinical coccidiosis has any effect on the late (gametogony) stages of the coccidia. Most of the coccidiostats have a depressant effect on the early, first-stage schizonts and are used for prevention or control.

In an outbreak, the clinically affected animals should be isolated and given supportive oral and parenteral fluid therapy, as necessary. The population density of animals in pens should be reduced. All feed and water supplies should be elevated from the ground to avoid fecal contamination. Mass medication of the feed and water supplies may be indicated, in an attempt to prevent new cases and to minimize the effects of an outbreak. Cattle with coccidiosis and nervous signs should be brought indoors, kept warm and on bedding, and given fluid therapy orally and parenterally. However, the case fatality of bovine coccidiosis can be high, in spite of intensive supportive therapy. Sulfonamide therapy parenterally may be indicated to control the development of secondary bacterial enteritis or pneumonia, which may occur in calves with coccidiosis during very cold weather. Corticosteroids are contraindicated.

Calves and Lambs

The chemotherapeutic agents recommended for treatment and control of coccidiosis in calves and lambs are summarized in Table 7-30. There is insufficient information available to make reliable recommendations for the specific treatment of acute clinical coccidiosis. Most of these chemotherapeutic agents have not been adequately tested in clinical trials. Sulfadimidine is used widely empirically for the treatment of acute coccidiosis in calves. **Amprolium** is also used for treatment, and there may be a beneficial effect in terms of increased BW gains and feed consumption compared with untreated controls recovering spontaneously.

Piglets

Symmetric triazinetriones are effective against the asexual and sexual stages of experimental *I. suis* infection in piglets and are most effective before the onset of clinical signs.[1]

Table 7-30 Chemotherapeutics recommended for treatment and control of coccidiosis in calves and lambs
Chemotherapeutic agent treatment prevention
Sulfadimidine (sulfamethazine) *Calves and lambs:* 140mg/kg BW orally daily for 3 days individually *Calves*: in feed 35mg/kg BW for 15 days
Lambs: daily dose 25mg/kg BW for 1 week
Amprolium *Calves*: individual dose at 10mg/kg BW daily for 5 days or 65mg/kg BW one dose *Calves*: in feed at 5mg/kg BW for 21 days
Lambs: in feed, 50mg/kg BW for 21 days
Monensin *Lambs*: 2mg/kg BW daily for 20 days beginning on 13th day following experimental inoculation Lambs: 20mg/kg feed fed continuously
Calves: 16.5 or 33g/tonne for 31 days
Lasalocid *Lambs*: 25–100mg/kg feed from weaning until market. Also, in ewe's diet from 2 weeks before and until 60 days after lambing.

CONTROL

The control of coccidiosis assumes greatest importance in calves, lambs, and pigs, and can sometimes be challenging to achieve.

Management of Environment

Successful control will depend on avoiding the overcrowding of animals while they develop a specific anticoccidial immunity. Only small numbers (50 per day) of oocysts are required for the development of solid immunity in lambs. Lambing and calving grounds should be well drained and kept as dry as possible. Lambing pens should be kept dry, cleaned out frequently, and bedding disposed of, such that oocysts do not have time to sporulate and become infective.[1] All measures that minimize the amount of fecal contamination of hair coats and fleece should be practiced. Feed and water troughs should be elevated to avoid fecal contamination. Feeding cattle on the ground should be avoided if possible, particularly when overcrowding is a problem.

Lambs at Pasture

In groups of lambs at pasture, the frequent rotation of pastures for parasite control will also assist in the control of coccidial infections. However, when lambs are exposed to infection early in life as a result of infections from ewes and a contaminated lambing ground, a solid immunity can usually develop; only when stocking density is extremely high will a problem arise.

Feedlot Cattle and Lambs

Control of coccidiosis in feeder calves and lambs brought into a crowded feedlot depends on the management of population density, or the preventative use of chemotherapeutics to suppress infections in animals while effective immunity develops. Management procedures include establishing a suitable stocking density, which can be assessed by visual inspection. When animals are overcrowded, they usually become dirty, there is excessive competition for feed supplies, and their growth rate can be affected.

Piglets

The control of coccidiosis in newborn piglets infected with *I. suis* has been unreliable. The use of coccidiostats in the feed of sows for several days or a few weeks before and following farrowing has been recommended and used in the field, but the results are variable. Amprolium and monensin have been evaluated for the prevention of experimental coccidiosis in piglets and are ineffective. An effective control program consisting of proper cleaning, disinfection, and steam cleaning of the farrowing housing to decrease oocysts in the environment has been recommended. Amprolium (25% feed grade) at the rate of 10 kg/tonne of sows' feed, beginning 1 week before farrowing and continuing until piglets are 3 weeks of age, has been recommended, but results are reported to be unsatisfactory. A single oral dose of 1.0 mL of toltrazuril, given to piglets of 3 to 6 days of age, reduces considerably the occurrence of coccidiosis and the patency period by approximately half.[1] A single treatment of toltrazuril at 20 mg/kg BW (oral) is highly effective against *I. suis* at an early stage of infection (e.g., 2 days) in suckling pigs.[1]

Coccidiostats

Coccidiostats are used for the control of naturally occurring coccidiosis, mainly in calves and lambs. The ideal coccidiostat suppresses the full development of the life cycle of the coccidia, allows immunity to develop, and does not interfere with production performance. Drugs that have been used for treatment are summarized in Table 7-30.

To be effective, coccidiostats must be given beginning early in infection. In any group of animals, there will be several different species of coccidia at different stages of the life cycle, some at the drug-susceptible stage (before 13–15 days in calves) and some beyond the drug-susceptible stage (after 16–17 days), which explains why coccidiostats appear to be effective in some epidemics and ineffective in others. In an epidemic in calves, new cases may develop for up to 12 to 15 days after the commencement of feeding of an effective coccidiostat to in-contact calves. However, precise commencement of infection is unknown and the prepatent period cannot be established; the most that can be done is to medicate the feed and water supplies with a coccidiostat of choice, treat new cases that develop, and avoid the stressors of overcrowding and nutritional disorders.

Some comments about some of the coccidiostats are made here. Routine prophylactic medication of the feed and water supplies of feeder calves and lambs with an effective coccidiostat will usually control the disease and allow the development of effective immunity, but drug resistance can develop.

Antimicrobials

Sulfonamides in the feed at a level of 25 to 35 mg/kg BW for at least 15 days are effective for the treatment of coccidiosis in calves and lambs. Sulfadimidine at 55 g/tonne is also effective in goats. A combination of chlortetracycline and a sulfonamide has provided protection in calves and lambs.

Ionophores

Monensin is an effective coccidiostat and growth promotant in cattle, sheep, and goats. The recommended doses are 16 to 33 g/tonne feed for calves and 20 g/tonne of feed for lambs. Levels of 11 g/tonne feed are not as reliable as the higher dose for calves. The recommended level for goats is 16 g/tonne of feed. A concentrated ration containing monensin at 15 g/tonne can be fed to ewes from 4 weeks before lambing until weaning, and to lambs from 4 to 20 weeks of age. Monensin can markedly reduce the oocyst output from ewes and lambs when fed before and after lambing. Withdrawal of monensin may be followed by the development of fatal coccidiosis in some animals, presumably because the drug suppressed infection and the development of immunity. Coccidiosis in beef calves after weaning has been treated with monensin from intraruminal continuous release devices. The toxic level of monensin for lambs is 4 mg/kg BW.

Lasalocid is related to monensin and is also an effective coccidiostat for use in ruminants. For maximum benefit, lasalocid should be used daily in the feed of coccidia-susceptible lambs for as long as possible. An effective method of control is to medicate the feed of the ewes beginning approximately 2 weeks before lambing and continuing the medication until the lambs are weaned. The lambs begin to receive lasalocid in their creep ration and subsequently in their rations from weaning until market. For the treatment of coccidiosis and improved feedlot performance, lasalocid should be given before and during the time that coccidia-naive lambs are first exposed to the natural occurrence of oocysts. A dose as low as 25 mg/kg of feed will control coccidiosis and improve performance when fed to lambs early in life. Improvements in feedlot performance do not usually occur in heavier lambs already passing oocysts and being fed lasalocid at 25 mg/kg feed.

Lasalocid fed at a dose rate of 40 mg/kg of starter to dairy calves beginning at 3 days of age, and up to 12 weeks of age, is effective in reducing fecal oocyst excretion rates and increasing mean daily BW gain, dry-matter intake, and improved feed efficiency. Mixing lasalocid in the milk replacer of calves beginning at 2 to 4 days of age is an effective method of preventing or controlling coccidiosis. It is also effective as a coccidiostat when fed free choice in salt at a level of 0.75% of the total salt mixture. Lasalocid at levels from 0.75 to 3 mg/kg BW are effective in preventing experimental coccidiosis in calves. The level of 1 mg/kg BW is the most effective and rapid and is recommended when outbreaks of coccidiosis are predicted or imminent in cattle. Lasalocid and decoquinate are effective in suppressing coccidial infections in young calves under conditions of apparent low exposure and good management. However, evidence shows that neither lasalocid nor decoquinate, or both, added to the feed of 16-week-old dairy calves naturally infected with subclinical coccidiosis for 56 days, have any significant effect on weight performance.[1]

Monensin, lasalocid, and decoquinate at the manufacturer's recommended levels are equally effective. A combination of monensin and lasalocid at 22 mg/kg and 100 mg/kg of diet, respectively, is an effective prophylactic against naturally occurring coccidiosis in lambs weaned early under feedlot conditions. Ionophores have been used in the feed continuously from weaning to market, and control coccidiosis and improve feedlot performance. The continuous feeding of lasalocid, decoquinate, or monensin will effectively control coccidiosis; cessation of medication might result in the appearance of oocysts in the feces and of diarrhea.

Decoquinate in the feed at a dose of 0.5 to 1.0 mg/kg BW can suppress oocyst production in experimentally induced coccidiosis of calves.[1] It is effective in preventing coccidial infections when fed continuously in dry feed at 0.5 mg/kg BW.[1] When fed to dairy calves from 9 weeks to 24 weeks of age, there appears to an improvement in growth rate. A level of 0.5 mg/kg BW is also effective in goats.

Toltrazuril is an efficacious compound.[4,5] Used at 20 mg/kg BW as a single oral dose, 10 days after being turned out to pasture, will prevent coccidiosis in cattle and sheep. In addition, medication of naturally infected lambs with toltrazuril on day 10 after turnout markedly reduces the excretion of oocysts for a prolonged period, and lessens the contamination of pasture with oocysts. A single treatment of toltrazuril can reduce the oocyst output in naturally infected lambs for a period of approximately 3 weeks after administration. Weekly oral treatment of suckling lambs with 20 mg/kg BW of toltrazuril can reduce oocyst output and increases weight gain over a 10-week period.[1]

Vaccines

Although subunit vaccines might offer theoretical advantages, limited detailed understanding of the immunobiology of coccidioses in livestock and the relatively large number of species remain obstacles to developing effective anticoccidial vaccines.

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GIARDIASIS

SYNOPSIS
Etiology *Giardia duodenalis*. Zoonotic and livestock-specific assemblages
Epidemiology High prevalence of infection in young farm animals. Fecal–oral cycle of infection from excreting young animals, the dam, and fomite contamination in environment. Cross-species and water transmission possible
Clinical findings May result in intermittent pasty feces and growth suppression. Some infections are asymptomatic.
Clinical pathology Demonstration of cysts in feces by phase microscopy or fluorescent antibody
Necropsy findings Villous atrophy
Treatment and control Benzimidazoles, metronidazole, and hygiene

ETIOLOGY

Giardia duodenalis (synonym *G. lamblia, G. intestinalis*) is a flagellate (binucleated) protozoan that infects a variety of vertebrates, particularly mammals.[1-8] It is a major cause of diarrhea in humans and has been recognized to causing diarrhea in agricultural animals. Currently, there are numerous genetic variants within *G. duodenalis,* and the genotypic assignment of members of *G. duodenalis* is evolving. Genetic variants (genotypes) are called assemblages. Cattle are susceptible to infection with the zoonotic assemblage A, which infects several different animal species, and assemblage E, which appears to be restricted to hoofed animals.

The organism develops in the small intestine, where it multiplies by longitudinal binary fission on the surface of the intestinal mucosa at the trophozoite stage, and is excreted in feces as a cyst.[2,3]

EPIDEMIOLOGY
Occurrence

Giardia infection, as opposed to disease, has been reported from most continents and has been identified in **all of the common agricultural animals**.[4] There is a wide variation in reported prevalence among regions, which probably reflects sampling strategies and methods of detection. The excretion of *Giardia* cysts may be continual but is also usually intermittent in young animals. Most prevalence studies have been in calves, and reported point prevalence infection rates of 1% to 100% in different countries, with the majority of studies showing prevalences of between 20% and 80% in calves.[1] A similar range is evident for more limited studies in lambs, kids, foals, and piglets.[1] Longitudinal studies of excretion patterns in grazing beef cattle, feedlot cattle, dairy cattle, calves, and foals sometimes show high infection rates.[1]

Source of Infection

Young animals are the primary source of infection, and infection is transmitted through the fecal–oral route. High cyst excretion rates in young animals result in the contamination of the **environment** and infection via fomites.

The **dam** is also a source of infection for young animals. Linked to a decrease in immunity in terminal pregnancy, a **periparturient rise** in *Giardia* cyst shedding has been shown in ewes, where cyst excretion increased 2 weeks prepartum, peaked at 0 to 4 weeks postpartum, and declined to low levels at 6 to 8 weeks postpartum.[1] A periparturient rise is suspected to occur also in mares. Cross-infection from other animal species and infection from contaminated water and feed are other possible sources of infection.

Pathogen Risk Factors

The infectious dose of *Giardia* is thought to be very small. *Giardia* cysts are relatively resistant to environmental influences, can survive at 4°C for 11 weeks in water, 7 weeks in soil, and 1 week in cattle feces, but do not survive freezing. They are resistant to chlorination, and extensive disinfection of the environment does not prevent reinfection.

Animal and Management Risk Factors

Age is a determinant of infection; cyst excretion rates in feces are much higher in the young livestock than in adults. Cyst excretion rates in groups of calves are usually highest between 3 and 10 weeks of age, with the number of cysts in feces being highest at 1 to 6 weeks of age. Cyst excretion falls after weaning, but may persist intermittently into adulthood. Similar patterns are seen in lambs. The influence of age on infection in pigs may be confounded by prophylactic medicants routinely used in pig operations. No effect of housing, feeding water management, or season has been observed in cattle, but hygiene in management practices can influence exposure and infection dynamics. The high and early infection rates in calves and lambs compared with other livestock species are probably a reflection of this. Pigs reared on wire floors are infected later in life than pigs reared on porous concrete floors. The prevalence of infection is higher in calves left with their dams to nurse colostrum for 3 days than in calves removed from the dam at birth to individual housing and fed colostrum by a nipple bottle.

Experimental Studies

Based on experiments in calves, *Giardia* has a prepatent period of 7 to 8 days and a patency of 60 to 112 days without evidence of giardiasis.[1] Infection of 6-week-old SPF lambs with *Giardia* trophozoites resulted in the occurrence of episodes of diarrhea and soft feces that were temporally associated with the detection of *Giardia* cysts in feces.[1] Compared with controls, infected lambs had a reduced rate of weight gain without reduction in food intake and took longer to reach market weight.

Economic Importance

Evidence for a significant economic importance for the majority of *Giardia* infections in agricultural animals is not convincing.

Zoonotic Implications

The majority of giardial infections in cattle are with the livestock-associated assemblage E, with a small proportion of infections with the zoonotic assemblage A.[2-6] Contact with farm livestock is a risk factor for disease in humans. There is considerable concern in public health circles that infection of humans could also occur via water bodies receiving agricultural effluent and pasture runoff, leading to drinking water contamination. There is also concern for fecal dispersion of *Giardia* in back-country watersheds from pack animals.

PATHOGENESIS

Ingested cysts excyst and release trophozoites, which multiply and colonize the surface of small intestine. Trophozoites adhere to the villi of the small intestine by means of a sucking disk on their ventral surface. The parasite induces an inflammatory response, villous atrophy, a reduced **villus to crypt**

ratio, and a reduction in brush border disaccharidase enzymes.[1] Disease is believed to result from increased motility in the gut (as a consequence of inflammation) and consequent diarrhea and nutrient maldigestion and malabsorption.

CLINICAL FINDINGS

There are several reports that detail the demonstration of giardial infection in individual animals with a chronic, malabsorptive type of diarrhea, and most imply an association with diarrheal disease. Most of these reports relate to young animals at an age when both undifferentiated diarrhea and *Giardia* cyst excretion are common, but the evidence for a causal association is not always entirely convincing, because other possible causes of diarrhea are not excluded. There are also various studies in animals that describe that infection is sometimes not accompanied by evidence of clinical disease.[3-5] In calves and lambs, giardial infection has been associated with a semifluid, pasty, intermittent diarrhea containing mucus, lasting 2 to 3 days but up to 6 weeks in some animals, and growth depression despite a normal appetite. Controlled experimentation demonstrating loose feces and reduced weight gain in experimentally infected lambs has indicated that *Giardia* can be pathogenic in sheep.

CLINICAL PATHOLOGY

Giardia cysts can be demonstrated in feces by phase contrast microscopy or immunofluorescent microscopy following flotation. Saturated salt or sugar solutions may disfigure the cyst, and the demonstration of infection is best conducted by sucrose gradient or zinc sulfate solution flotation. Immunofluorescence might be more sensitive than microscopy for the detection of cysts, and PCR-coupled methods are commonly used for the detection and genetic characterization of *G. duodenalis.*[7]

NECROPSY FINDINGS

Findings are in the upper small intestine. Although there is often no macroscopic change, microscopically there may be an increase in intraepithelial lymphocytes in the jejunum, with moderate to severe diffuse inflammation, villous atrophy, crypt distortion, and a reduction in the villus to crypt ratio. Trophozoites can be detected histologically on the mucosa and in stained mucosal scrapings taken from the small intestine.

TREATMENT AND CONTROL

Giardial infections in agricultural animals have been successfully treated with dimetridazole at an oral dose of 50 mg/kg BW daily for 5 days[1] and are also susceptible to furazolidone, but both drugs are illegal for use in food animals in many countries.

Oral administration of the **benzimidazoles** albendazole (20 mg/kg BW daily for 3 days) and fenbendazole (10 mg/kg BW daily for 3 days) are effective for the treatment of *Giardia* infection or giardiasis in calves.[8] The 3-day course is required for effective treatment; some calves become reinfected following treatment. The principles for the control of giardiasis are similar to those used for cryptosporidiosis, but have not really been developed specifically for livestock. Recommended procedures described to achieve a reduction of exposure (in the section Acute undifferentiated diarrhea of newborn farm animals) are appropriate.

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ASCARIASIS IN PIGS, HORSES, AND CATTLE

SYNOPSIS

Etiology Nematode worms from the ascarid family: *Ascaris suum* in pigs, *Parascaris equorum* in horses, and *Toxocara vitulorum* in buffalo and cattle

Epidemiology Transmission is by ingestion of highly resistant and long-lived larvated eggs; *T. vitulorum* is also transferred via colostrum.

Signs Heavy infestation leads to poor growth and afebrile diarrhea, sometimes with obstructive jaundice, intestinal obstruction, and respiratory signs.

Clinical pathology Characteristic eggs in feces and a marked eosinophilia

Lesions Petechial hemorrhages in lungs and fibrotic spots on the liver

Diagnostic confirmation Demonstration of characteristic eggs in feces

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Treatment
  Pigs: Ivermectin, abamectin, doramectin, flubendazole, febantel, oxibendazole, thiophanate, pyrantel tartrate, and levamisole
  Horses: Febantel, fenbendazole, mebendazole, and oxibendazole
Control
  Pigs and horses: Keep young stock away from sites in which eggs may accumulate.
  Cattle/buffalo: Prophylactic anthelmintic treatment of 10- to 16-day-old calves

ETIOLOGY

Each species has its own ascarid: *Ascaris suum* in pigs and *Parascaris equorum* in horses are cosmopolitan, whereas *Toxocara vitulorum* is an important cause of mortality in buffalo calves in India and Southeast Asia.[1] Genetic studies show that although *A. suum* of the pig is very similar to *A. lumbricoides* of man, host-specific differences do exist,[2] and cross-infections occur only infrequently.[3] There is no ascarid specific for sheep, but they may rarely become infected with *A. suum.*

LIFE CYCLE

A. suum and *P. equorum* have similar life cycles. The adult worms are long (females are 20–40 cm and males are 15–25 cm in length), cylindrical, and pointed at both ends and have a thick, glistening, yellow-white cuticle. They live in the small intestine and lay very large numbers (0.5–2 million eggs per day) of thick-shelled eggs.[4] These are not infective until a larva has developed inside. This process needs suitable warmth and humidity and takes place over a period of several weeks. When swallowed, infective eggs hatch quickly in the intestine of the host and the larvae migrate through the intestinal wall, reach the portal vein, and are transported to the liver. They cross to the hepatic venous system and travel to the lungs, are passed up the bronchi and trachea to the pharynx, and are swallowed and come to rest in the intestine where they mature. The prepatent period (time from infestation to the appearance of eggs in the feces) is 6 to 8 weeks for *A. suum* and 11 to 15 weeks for *P. equorum.*

T. vitulorum has a more complex life cycle. When eggs are ingested by cattle or buffalo more than 4 to 5 months of age, the larvae settle in somatic tissues without developing or growing instead of traveling to the intestine. Subsequently they become activated around calving and migrate to the udder. They transfer to the calf in the colostrum and grow to the adult stage in the intestine over a period of 3 to 4 weeks and produce large numbers of eggs for about 4 weeks.[1] After 8 weeks of infection, the worm counts in the infected calf decline because of strengthened host immunity.[1]

EPIDEMIOLOGY

In pigs and horses the only route of infection is by ingestion of larvated eggs. Because the eggs have very thick walls the infective stage is protected from deleterious environmental influences. Few disinfectants will harm them, and they are very resistant to cold but survive most readily in cool, moist surroundings. Periods of survival of up to 5 years have been recorded. In the UK, *A. suum* eggs shed from September to May, become infective more or less synchronously in July, and the number of eggs becoming infective then falls away rapidly. This coincides with the prevalence of damaged livers recorded at bacon factories. Transmission is therefore seasonal but as ascarid eggs are very resistant and can overwinter, pigs and horses may in the absence of good hygiene become infected at all periods of the year. Clinical ascariasis is usually associated with conditions that allow infective eggs to accumulate. This may happen where, for example, the stocking rate is high and the same paddocks are used year after year, or when indoor pens are inadequately cleaned. Although the eggs in the environment are resistant to drying and freezing, exposure to sunlight will kill them within a few weeks.[4]

Protective immunity develops and consequently only the young are seriously affected. Ascarid worms are very immunogenic and induce strong Th2 immune responses characterized by eosinophilia and high levels of antiinflammatory cytokines, resulting in worm expulsion.[5] However, this strong Th2 induction may inhibit Th1 responses against bacterial and viral infections, reducing the efficacy of vaccinations.[6,7] Under field conditions, eggs are passed by foals from 12 to 13 weeks of age and spontaneous expulsion of worms occurs 6 to 9 weeks later. Eggs are seen occasionally in the feces of very young foals, but this is thought to be from the ingestion of uninfective eggs during coprophagia. In older animals no clinical signs are observed but infested animals, particularly adult sows and yearling horses, continue to contaminate their surroundings and are an important link in the chain of infection.

T. vitulorum larvae are present in greatest numbers in the colostrum 2 to 5 days after calving, and few are present after day 9. Mature worms are present in the intestine of the calf by 10 days of age, and eggs are passed by 3 weeks. Worms are expelled by 5 months of age; thus toxocariasis is a calfhood disease.

PATHOGENESIS

Migration of larvae through the liver results in hemorrhage and fibrosis, the latter appearing as white spots under the capsule. In heavy infection diffuse fibrosis may occur. The most serious damage occurs in the lungs where the larvae provoke alveolar injury with edema and consolidation. This damage can exacerbate preexisting lung infections or provide a portal of entry into the body for pyogenic organisms. Immunity to migrating larvae is acquired and can be transferred through colostrum or immune serum.

In animals other than pigs, *A. suum* larvae migrate and develop, but the worms do not normally reach the small intestine. During this process severe clinical signs of pulmonary involvement may appear. The disease has been produced experimentally in lambs and calves and has also been observed as a field occurrence in yearling cattle.

Foals with *P. equorum* have reduced gut motility, an increase in the ratio of body water to body solids, and a lowering of the body pool of albumin.

CLINICAL FINDINGS

In pigs up to 4 to 5 months old, clinical signs associated with heavy infestation are poor growth, an afebrile diarrhea, and lowered resistance to other disease. There is some evidence that exposure to parasites during the growing phase without anthelmintic treatment causes permanent damage to growth potential. Adult worms may be vomited up and occasional cases of obstructive jaundice and intestinal obstruction or rupture occur. There may be coughing while larvae are passing through the lungs, but this is not marked, and there is seldom sufficient damage to cause a noticeable increase in respiratory rate or depth. In rare cases the infestation may be so severe that pigs manifest severe dyspnea or die of acute hepatic insufficiency. Enzootic pneumonia of pigs and swine influenza are reported to be much more serious diseases when accompanied by heavy *A. suum* infections, and breaks in hog cholera vaccination with live virus have been attributed to this cause. *A. suum* in other host species produces fever, dyspnea, and anorexia about the 8th day after infestation.

Effects in foals and calves caused by heavy infestation with *P. equorum* and *T. vitulorum* are similar to those observed in young pigs and include poor coat, diarrhea, and occasionally colic. In addition, in foals, convulsions, intestinal obstruction, and perforation may occur. Lung damage may give rise to fever, coughing, and a mucopurulent nasal discharge.[8] In calves, anemia and steatorrhea are additional signs.

CLINICAL PATHOLOGY

Characteristic eggs are usually present in large numbers in the feces of clinically affected animals. A marked eosinophilia and systemic elevated expression of IL-4[7] often accompany the early stages of infestation in pigs and in other species, with the eosinophilia shown to persist in calves for at least 1 year.

NECROPSY FINDINGS

In the early stages of a massive infestation, there are subpleural hemorrhages and edema and congestion of the lungs. The pleural cavity may contain bloodstained fluid. The liver is enlarged and congested, and there may be hemorrhages under the capsule. Microscopically, necrotic tracts and sections of larvae are observed. In species other than the pig, infestation with *A. suum* is accompanied by emphysema, alveolar wall thickening with fibrin, eosinophils and hemorrhage in the lungs, and necrotic tracts in the liver.

In chronic cases the capsule of the liver is marked with small-diameter white spots which may, in severe cases, be confluent and constitute a network of connective tissue. Histologically, the necrotic tracts have been replaced by fibrous tissue. The carcass is usually in poor condition and may be jaundiced. Large numbers of mature worms may almost fill the lumen of the small intestine.

DIAGNOSTIC CONFIRMATION

Ascarid eggs are brown and have thick walls with a pitted surface. Fecal egg counts in excess of 1000 epg (eggs per gram) are considered to be indicative of significant infection. Migrating larvae are too small to be observed by the naked eye at postmortem examination. They can be recovered from macerated lung tissue by the Baermann technique or seen microscopically in scrapings of bronchial mucus. Experimentally, for *T. vitulorum,* species-specific and highly sensitive molecular diagnostic PCR and LAMP DNA-based tests have been developed for accurate identification and diagnosis of *Toxocara* spp., overcoming the inherent limitations of the traditional approaches.[8,9]

DIFFERENTIAL DIAGNOSIS

Early stages of massive infection:
- Enzootic pneumonia in pigs
- Chronic form of *Rhodococcus equi* pneumonia in young foals
- Other forms of pneumonia in calves

Chronic infection:
- Other causes of unthriftiness including malnutrition and chronic enteritis caused by infections with *Salmonella* and *Brachyspina* spp.

TREATMENT

TREATMENT AND PROPHYLAXIS

Treatment
Pigs
Ivermectin or doramectin (0.3 mg/kg by IM) (R1)[10,11]

Abamectin (0.1 mg/kg/day for 7 days in feed) (R1)[10]

Flubendazole (5 mg/kg as a single dose or 30 g/tonne finished feed given for 5–10 days) (R2)

Fenbendazole (5 mg/kg in feed as a single dose or divided over 7–14 days) (R3)

Febantel (5 mg/kg, orally) (R3)

Oxibendazole (15 mg/kg or 1.6 mg/kg/days orally for 10 days) (R3)

Horses
Febantel (6 mg/kg, orally) (R1)
Fenbendazole (7.5 mg/kg, orally) (R1)
Mebendazole (5–10 mg/kg, orally) (R1)
Oxibendazole (10 mg/kg, orally) (R1)

Buffalo
Pyrantel (12.5 mg/kg, orally) (R2)[17]

Pigs

In pigs, ivermectin, abamectin, or doramectin and flubendazole are effective against adult and fourth-stage (intestinal) larvae of *A. suum*, whereas fenbendazole, febantel, oxibendazole, thiophanate, pyrantel tartrate, and levamisole are effective against the adult worm. Ivermectin, fenbendazole, flubendazole, thiophanate, and pyrantel may be given in feed as divided doses over several days. Ivermectin may have some activity against migrating larvae.

Horses

In horses, febantel, fenbendazole, mebendazole, and oxibendazole are all effective against adult *P. equorum.* Fenbendazole is also active against immature forms in the intestine. *P. equorum* has been shown to be resistant to ivermectin and pyrantel.[11-15]

Buffalo Calves

In buffalo calves, the limited data available suggest that pyrantel has good efficacy against both immature and adult worms.[16] Other compounds such as levamisole, febantel, oxfendazole, and even piperazine can be used for treatment but may not expel all worms.

CONTROL

Important life cycle features that must be taken into account when devising a control program for ascarid infections include the following:
- Worms are prolific egg layers
- Infective eggs are very resistant and long lived
- Young animals are most susceptible

Emphasis must be placed on preventing the environment from becoming contaminated. This is achieved by periodic treatment of the animals likely to be shedding eggs, which are asymptomatic adult carriers and the more vulnerable young stock. Exposure of young pigs and foals to contaminated soil or bedding should be avoided.

Unnecessary treatments can be avoided by regular monitoring with fecal egg counts. In intensive pig-raising systems on concrete floors, the risk of ascarid infestation can be greatly reduced, but rarely eliminated, with good standards of hygiene. In the case of straw yards, epidemiologic studies in the UK suggest that all bedding should be removed at the end of June (to remove eggs shed in preceding months before they become infective) and again at the end of August (to remove eggs deposited in the summer). If pigs are allowed access to small earthen yards, these must be kept well drained and the manure removed frequently. Control is difficult in free-range systems because the eggs become infective in 4 to 6 weeks in summer and many persist over the winter. Deep plowing of contaminated soil after use will reduce risk of *A. suum* and *Trichuris suis* eggs infecting future batches of pigs.

If farrowing pens are regularly cleaned with high-pressure water and sows are treated immediately before entry, it may be possible to control infection in piglets without anthelmintic treatment. Breakdowns may occur as ascarid eggs are adhesive and not all will be washed away by hosing. For the same reason, eggs are easily introduced from outside on boots, etc. It may therefore be necessary to treat piglets at weaning. Ascarids may be controlled in growing pigs by periodic anthelmintic treatments, but this has to be combined with rigorous hygiene to eliminate liver damage caused by migrating larvae.

Young foals present more of a problem because they often run on permanent pasture used by foals in previous years. Such pastures may become heavily contaminated with eggs. Recommendations for control include:
- Thorough cleaning and disinfection of the maternity stall after each foaling
- Use of small exercise paddocks that should preferably have been rested from occupation by horses for a year
- Weekly removal of manure from the pasture. The foals should be routinely treated at about 10 to 12 weeks of age when the worms are first becoming mature and again at bimonthly intervals. In this way heavy egg contamination of the pasture can be avoided.

Anthelmintic resistance in *P. equorum* in recent years been widely reported.[11-14,]

In buffalo calves, a single anthelmintic treatment at 10 to 16 days of age using a compound with high activity against larval stages gives good control of *T. vitulorum.*[18]

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STRONGYLOSIS (CYATHOSTOMINOSIS) IN HORSES

SYNOPSIS

Etiology Two nematode subfamilies: the Strongylinae (large strongyles) and Cyathostominae (known variously as small strongyles, small redworms, trichonemes, cyathostomes, or cyathostomins)

Epidemiology Eggs are shed by horses of all ages, the life cycle is direct, infective larvae develop seasonally on pasture, and hypobiotic cyathostomin larvae can cause severe disease when they resume development in late winter.

Signs
  General strongylosis: Ill-thrift, weight loss, poor hair coat, and impaired performance
  Verminous arteritis (associated with *Strongylus vulgaris*): Variable, including colic and diarrhea
  Larval cyathostominosis: Rapid weight loss, often with sudden onset diarrhea

Clinical pathology Strongylid eggs in feces (except disease caused by larvae); reduced hemoglobin, erythrocyte counts, and packed cell volumes; leukocytosis; eosinophilia (with migrating larvae); hyperglobulinemia, particularly IgG(T); hypoalbuminemia

Lesions
  General strongylosis: Large numbers of adult worms in cecum and colon; hemorrhagic inflammation of mucosa with multiple small ulcers, and large and small nodules
  Larval cyathostominosis: Mucosa grossly inflamed with large numbers of larvae appearing as brown specks
  Verminous arteritis: Wall of cranial mesenteric artery greatly thickened, organizing thrombi and larvae on internal surface; and ischemia or

Continued

necrosis of parts of the intestinal wall caused by emboli

Migratory larvae: Seen in various subserosal sites; some cause nodules in the liver

Diagnostic confirmation Few pathognomonic indicators; judgment made on overall appraisal of clinical history, presenting signs, and laboratory findings; arteritis of cranial mesenteric artery sometimes palpable per rectum; immature worms are sometimes in feces in larval cyathostominosis

Treatment

General strongylosis: Ivermectin, moxidectin; benzimidazoles, e.g., febantel, mebendazole, oxibendazole

Migrating strongyles: Ivermectin, moxidectin

Larval cyathostominosis: Ivermectin, moxidectin

Control Twice-weekly removal of feces from pastures, mixed or alternate grazing, and routine dosing to prevent contamination of pasture with eggs

ETIOLOGY

The redworms (strongyles) are nematodes commonly found in the large intestine of horses and other Equidae. They belong to two subfamilies: the Strongylidae (large strongyles) and Cyathostominae (known variously as small strongyles, small redworms, trichonemes, cyathostomes, or cyathostomins).[1] The large strongyles include *S. vulgaris, S. edentatus,* and *S. equinus,* which migrate extensively through the body, and *Triodontophorus* spp. and *Oesophagodontus robustus,* which do not. The cyathostomins consist of a complex of 50 species from 14 genera including *Cylicostephanus, Cyathostomum, Cylicocyclus, Cylicodontophorus, Poteriostomum, Gyalocephalus,* and *Cylindropharynx.*[1] Of these, about 10 species are common.

LIFE CYCLE

Eggs are passed in the feces, and under suitable climatic conditions produce infective third-stage larvae from 7 days onward. As in many other parasitic conditions, the survival of eggs and larvae is favored by shade, moisture, and moderate temperature. Desiccation, ultraviolet light, and repeated freezing and thawing are particularly detrimental to their development and survival.[2] Some eggs and larvae may withstand freezing temperatures, but development ceases below 7.5°C (46°F) to be resumed when temperatures increase. Optimum chances for infection of the host occur in the early morning or evening, when dew produces a moisture film on plants, or after rain, both of which give conditions that encourage larvae to migrate onto pasture.[3] The pasture's soil moisture content influenced by rainfall in the days before fecal deposition on pasture influences larval development and migration onto herbage.[4] The life cycle of all species is direct; horses become infected by ingestion of the infective larvae.

After ingestion, the larvae of nonmigratory strongyles, such as the cyathostomins, exsheath and enter the walls of the cecum and colon, where they remain in small subserous nodules for 7 to 18 weeks before breaking out into the lumen of the intestine. The time spent in the mucosa depends on the following:

- Species
- Season of the year
- Age and degree of immunity of the host

They can become arrested in their mucosal development, and their synchronous emergence some weeks later may provoke severe clinical signs. This may occur spontaneously, particularly in late winter, or may be induced by anthelmintic treatment. Expulsion of the adult worm population seems to remove an inhibitory feedback mechanism and may provoke clinical signs. Hypobiotic early third-stage larvae are present in the mucosa at all seasons of the year.

Larvae of *S. edentatus* penetrate the intestine and travel via the portal vessels to the liver, where larvae remain and produce hemorrhagic tracts for a month or so. They then migrate via the hepatorenal ligament to the connective tissue under the peritoneum and form hemorrhagic nodules. After about 3 months, they return via the root of the mesentery to the large bowel wall and again form hemorrhagic nodules, which finally rupture and release the worms into the lumen. Adult egg-laying females are present from 40 weeks. Larvae may be found in other organs, e.g., the testes, but these larvae do not return to the intestine. *S. equinus* migrates via the liver to the pancreas and peritoneal cavity but how they return to the intestine is uncertain.

Larvae of *S. vulgaris* penetrate the intestinal wall, molt to the fourth larval stage in the submucosa, and then pass into and up small arteries. By day 14, they have reached the cranial mesenteric artery, where they develop to late fourth-stage larvae. In 3 to 4 months they molt and the young adults then return to the intestine via the lumina of the arteries. Nodules are formed in the intestine wall and later rupture, releasing adults into the lumen of the intestine. The prepatent period is 6 months.

EPIDEMIOLOGY

Strongylosis is a common disease of horses throughout the world and causes death when control measures are neglected. In areas with cold winters and mild summers, egg deposition peaks in spring and remains high over summer. At this time, temperatures are suitable for larval development, and massive contamination of infective larvae may occur in late summer and early autumn, when young susceptible horses are present. *S. vulgaris* larvae can overwinter in considerable numbers in Europe. If the summers are hot and dry, only a small proportion of strongyle eggs develop to larvae and these may be short lived, but continual reinfestation keeps pasture contamination high.

In subtropical regions, eggs can hatch throughout the year, and larval availability is influenced more by rainfall than temperature. For example, in Florida fecal egg counts remain high throughout the year, and there is an autumn rise in infective larvae. Such associations between disease risk and local climate have important implications in the timing of treatments.

The onset of disease following ingestion of large numbers of larvae depends on the maturation period of the parasite in the host and whether it is the immature or adult stages that are pathogenic. Outbreaks of disease caused by the emergence of small strongyles after hypobiosis are commonly seen in Europe in late winter and early spring (winter or larval cyathostominosis), whereas arterial lesions caused by larval *S. vulgaris* are first seen in late summer and reach a maximum by midwinter.

Mares are the main source of infection for younger horses because many adults carry appreciable burdens of adult stages of strongyle worms and pass large numbers of eggs.[5] Nevertheless, horses do gain some acquired immunity to infection, so young stock are the most susceptible. Possibilities for vaccination are being investigated, but a commercial product seems an unlikely prospect in the short term.

The extensive use of anthelmintics with high efficacy at regular intervals has resulted in a marked decline in the prevalence of *S. vulgaris* in many regions. The cyathostomins, on the other hand, are becoming increasingly important. This may be caused by any of the following factors:

- Insusceptibility of mucosal cyathostomins to many drugs
- Selection for benzimidazole-resistant worms
- Selection for shorter egg reappearance periods

PATHOGENESIS

The disease processes associated with the strongyles can be divided into those produced by migrating larvae, those provoked by the mass emergence of mucosal larvae, and those associated with adult worms. Heavy intestinal infection can alter intestinal motility, permeability, and absorption.

The larvae of *S. vulgaris* are the most pathogenic, causing arteritis, thrombosis, and thickening of the wall of the cranial mesenteric artery. Emboli may break away and lodge in smaller blood vessels, leading to partial or complete ischemia in part of the intestine, thus producing colic. The result of this depends on the length of the segment of intestine affected and the ability of the collateral blood supply to become established

before necrosis and gangrene occur. It is not clear whether the ischemia is directly caused by the mechanical effects of embolism or by consequent pathophysiological events. Whatever the cause, greatly enhanced mobility proximal to the lesion follows and can cause volvulus or torsion. Intussusception is seen occasionally. Colic may also be caused by pressure of the thickened cranial mesenteric artery on the mesenteric plexus.

Other arterial lesions associated with migrating *S. vulgaris* larvae include aneurysm of the cranial mesenteric artery, but this is a relatively rare occurrence. More often, larvae aberrantly migrating beyond the cranial mesenteric artery cause migratory tracts and thrombi in other blood vessels. Multiple lesions may be seen in the cecal and colic arteries, which may completely occlude the lumen and cause gangrene in parts of the bowel. Smaller lesions are occasionally seen in iliac, renal, splenic, hepatic, and coronary arteries. Aortic and iliac thrombosis may result in hindlimb lameness. Field and experimental cases of cerebrospinal nematodosis caused by *S. vulgaris* invasion of the CNS have been reported.

Strongylus sp. larvae returning to the intestine cause large nodules in the wall of the cecum and colon. Considerable hemorrhage may follow when these rupture to release the worm into the lumen of the intestine. In very heavy burdens, bleeding sufficient enough to cause death can occur.

Developing cyathostomin larvae provoke the formation of small nodules, which may be superficial or submucosal, depending on species. In heavy infections, the emergence of large numbers of larvae over a short period causes inflammation of the cecum or ventral colon, with small ulcers where larvae have emerged; hemorrhages of varying sizes; and excess mucous production. Typically, this leads to weight loss, diarrhea, and sometimes a variety of other clinical manifestations including colic and cecocecal intussusception. Affected animals may sometimes secrete *Salmonella*.

Adult strongyles can be divided into those that cause blood losses and those that are superficial tissue feeders. *Strongylus* spp. have large buccal cavities, which they use to draw in and digest plugs of mucosa, while secreting anticoagulants to aid the ingestion of blood. Hemorrhage continues from feeding points after worms detach to find new attachment sites. *Triodontophorus* spp. and *O. robustus* feed similarly but are less harmful because they have smaller buccal capsules. An exception is *T. tenuicollis*, because this species attaches in groups in the right dorsal colon and can cause large ulcers. The small strongyles (cyathostomins) have even smaller buccal cavities and produce only superficial damage, so that even relatively large numbers (tens or hundreds of thousands) of adults often cause little apparent harm.

CLINICAL FINDINGS

In natural infestations it is often impossible to quantify the effects of individual strongyle species because the clinical picture usually represents the combined effects of a mixed infestation. Ill-thrift, poor hair coat, impaired performance, weight loss, and anemia are signs associated with a "wormy" horse. The greatest losses are probably caused by the failure of young horses to grow optimally and the less efficient performance of moderately parasitized working horses and donkeys.

Clinical syndromes caused by arteritis in the cranial mesenteric artery, aorta, and iliac artery are described in other chapters. Experimentally, the migratory phase of *S. vulgaris* infection is associated with pyrexia, inappetence, depression, leukocytosis, and intermittent or continuous colic. In more chronic cases there is a

- Persistent low-grade fever
- Poor appetite
- Intermittent colic
- Poor weight gain

Diarrhea may be present. Adult mares exposed to heavy *S. vulgaris* in late pregnancy may become very weak to the point of recumbency. On clinical examination the mucosae are pale, the heart rapid and loud, and respiration moderately increased. Intestinal sounds are increased although the feces are normal. Abortion may occur and the mare usually dies.

The simultaneous maturation of large numbers of hypobiotic larvae induces the condition known as winter or larval cyathostominosis, which is potentially life-threatening and associated with development of large numbers of immature worm stages in the wall of the large intestines, typically in horses 1 to 3 years old. This is usually characterized by severe loss of weight, weakness, acute or chronic diarrhea, subcutaneous edema, pyrexia, and colic.[6] Numerous cyathostomin larvae may be passed with the feces or may be seen adhering to the glove after rectal examination. Larval cyathostominosis can occur in horses of all ages but are most common in adults under 5 years old. Unless treated early, prognosis is guarded.

CLINICAL PATHOLOGY

Examination of feces for strongylid eggs confirms the presence of adult strongyles but does not differentiate species. To do this it is necessary to hatch the eggs and examine the infective larvae. This has to be done by an expert parasitologist and delays results by at least 10 days. Experimentally, specific amplification of ribosomal DNA in feces can be used for the detection and identification of strongyle infections and may lead to diagnostic tests.

Hematological values, particularly reduced hemoglobin levels, erythrocyte counts, and PCVs are often taken as a nonspecific indication of the degree of infestation with strongyles. Leukocytosis is a feature of heavy infection, whereas eosinophilia may reflect the presence of migrating larvae. Serum analysis reveals a marked increase in β-globulins, particularly IgG(T), and a decrease in albumin.

NECROPSY FINDINGS

Adult strongyle worms may be seen attached or close to the mucosal surface. The three *Strongylus* spp. are red in color and 2 to 5 cm long. *Triodontophorus* and *Oesophagodontus* are smaller, up to 2 cm. Less easy to see are the small strongyles (cyathostomins), which are more slender and generally under 2 cm long with smaller buccal capsules. Because most cases of strongylosis are caused by mixed infestations with all genera, necropsy findings usually include most of the lesions characteristic of each worm.

In cases of general strongylosis, very large numbers of adult worms will be found in the cecum and colon. There may be so many that they appear to form a living cover to the contents of these organs. Catarrhal, hemorrhagic, or fibrinous inflammation of the cecum and ventral colon with multiple small ulcers is associated with the emergence of cyathostomin larvae. There may be edema with excessive mucous production or numerous punctate hemorrhages. Fewer adult worms may be present in winter cyathostominosis but large numbers of larvae (several per square centimeter) can be seen as brown specks in the mucosa, especially if this is illuminated from behind. Adult *T. tenuicollis* are often found in large numbers in the right dorsal colon in association with small circular hemorrhages, and they are sometimes attached in groups at the base of deep mucosal ulcers.

Strongylus larvae occur in many subserous sites, especially in nodules in the intestinal wall, and the body cavities may contain an excess of bloodstained fluid. Verminous arteritis lesions of varying size associated with *S. vulgaris* are common at the root of the cranial mesenteric artery and occasionally in the iliac artery. The affected arterial wall is greatly thickened and contains loculi on its internal surface, many of which contain living larvae. Lamellated thrombi are also common at this site and these are sometimes infected. The thickening of the arterial wall often extends along the cecal and colic arteries and complete occlusion of these may be followed by gangrene of a segment of intestine. Similar lesions of arteritis may be present at the base of the aorta. Spontaneous rupture of the vessel occasionally occurs. A significant correlation has been reported between lesions in the proximal aorta and the presence of focal ischemic lesions in the myocardium. These are thought

to be caused by microembolization causing arteriosclerotic lesions in the myocardial arterioles.

Larvae of *S. edentatus* cause hemorrhagic tracts and nodules in the liver and adhesions and disruptions of omental architecture. Hemorrhagic nodules 1 to 3 cm in diameter are produced in the subperitoneal region, and these are reported to cause colic and anemia.

DIAGNOSTIC CONFIRMATION

A specific diagnosis is difficult to achieve in every case. Few clinical observations or laboratory results are pathognomonic for the disease syndromes associated with strongyle infection. Often a judgment has to be made on an overall appraisal of clinical history, presenting signs, and laboratory findings. For example, only 7 of 14 cases of larval cyathostominosis were diagnosed antemortem in a series of adult horses with chronic diarrhea investigated at university referral clinics.

A diagnosis of general strongylosis should be considered when poor growth, inappetence, diarrhea, and some degree of anemia are the presenting signs. It is generally accepted that strongylosis is an important cause of anemia in horses. Fecal egg counts are generally high (over 800 epg) but are difficult to interpret. They have little direct correlation with worm burden because they are influenced by immunity and species composition. Also, they do not differentiate between different strongyle genera or between these and *Trichostrongylus axei* infection of the stomach. In foals, eggs observed during the first few weeks of life are obtained by coprophagia and are not indicative of a patent infection.

The diagnosis of verminous arteritis also presents difficulty. The thickening of the cranial mesenteric artery may be palpable *per rectum;* the artery is situated below the aorta at the level of the posterior pole of the kidneys. Low serum albumin and increased β-globulins, particularly IgG(T), are the most useful laboratory tests, and arteriography may demonstrate lesions in a number of arteries. Transrectal ultrasonography may also be useful.

In larval cyathostominosis marked weight loss, diarrhea, leukocytosis, microcytosis, hyperglobulinemia, elevated serum fibrinogen, and hypoalbuminemia are usually seen.[6] Peripheral edema is present in a proportion of cases. Fecal egg counts may be low or zero because it is the immature stages that cause this disease, and owners have often wormed the animal before advice is sought. Consequently, species-specific serologic diagnostic tests using larval antigens are being investigated.[7,8] Additionally, experimental PCR assays targeting the intergenic spacer region of ribosomal DNA have been developed for the identification of cyathostomin larvae at species level.[9-11]

DIFFERENTIAL DIAGNOSIS

General strongylosis:
- Other causes of anemia in the horse, including:
  - Babesiosis
  - Equine infectious anemia
  - Dietary deficiency in stabled stock and the effect of racing for long periods
- Other causes of ill-thrift in horses, including:
  - Ascariosis in the foal
  - Gross nutritional deficiency or agalactia in the mare

Larval cyathostominosis:
- Other causes of chronic diarrhea including:
  - Other parasitic infections, particularly migratory strongyles
  - Granulomatous enteritis
  - Alimentary neoplasia
  - Salmonellosis
  - Chronic liver disease
  - Peritonitis
  - Sand enteropathy
  - Hyperlipidemia

TREATMENT

TREATMENT AND PROPHYLAXIS

Treatment and prophylaxis
Ivermectin (0.2 mg/kg, orally) (R1)

Moxidectin (0.4 mg/kg, orally) (R1)

Febantel (6 mg/kg, orally) (R3)

Mebendazole (10 mg/kg, orally) (R3)

Oxibendazole (10 mg/kg, orally) (R3)

Prophylaxis
Ivermectin (0.2 mg/kg orally every 8–10 weeks) (R3)

Moxidectin (0.4 mg/kg orally every 13–16 weeks) (R3)

Oxibendazole (10 mg/kg orally every 4–6 weeks) (R3)

Febantel (6 mg/kg orally every 4–6 weeks) (R-3)

Mebendazole (5–10 mg/kg orally every 4–6 weeks) (R3)

Treatment may be targeted against immature and adult large and small strongyle worms in the lumen of the intestine, against migrating *Strongylus* larvae, particularly *S. vulgaris,* or against cyathostomin larvae in the intestinal mucosa. The latter may be developing third- or fourth-stage, or hypobiotic early third-stage larvae. Anthelmintics vary in their efficacy against these larval stages. This influences the egg reappearance period (i.e., the time from treatment to the reappearance of eggs in the feces as new adult worm populations establish). This in turn determines the treatment interval in control programs.

For elimination of adult worms there is a wide choice of compounds and formulations for use in feed, as pastes, or by tubing.

Most of these, however, belong to just three chemical groups that are administered orally:
1. *Avermectin/milbemycins,* also known as macrocyclic lactones (ivermectin 0.2 mg/kg, moxidectin 0.4 mg/kg)
2. *Benzimidazoles* (febantel 6 mg/kg, mebendazole 5–10 mg/kg, oxibendazole 10 mg/kg)
3. *Tetrahydropyrimidines* (pyrantel 19 mg pyrantel embonate [pamoate]/kg or 6.6 mg pyrantel base/kg)

In both Europe and North America, a high prevalence of cyathostomin populations resistant to the benzimidazoles and pyrantel has been reported.[12] Cyathostomin resistance to fenbendazole is ubiquitous in many regions, and this anthelmintic is now not recommended for use to control cyathostomins.[13-17] There are also reports of emerging resistance to macrocyclic lactones (both ivermectin and moxidectin).[18,19] Where resistance to any of the three groups is a problem, the choice of effective anthelmintics can be extended by use of products containing piperazine, which may be synergized with phenothiazine. An alternative is the cautious use of selected organophosphorus compounds such as dichlorvos or haloxon (which should not be given to foals).

Mucosal cyathostomin larvae are more problematic. Publications on this topic are difficult to interpret because results may be influenced by experimental design and methodology. Moxidectin 0.4 mg/kg orally has activity against hypobiotic and developing third-stage larvae as well as the fourth stage. Consequently, this compound has a prolonged egg reappearance period allowing a treatment interval of 13 weeks for prevention of egg output onto pasture. Ivermectin seems at best to be variable in its activity against mucosal stages, and a treatment interval of 8 to 10 weeks is generally recommended. Other anthelmintics at adulticidal doses have little or no effect on mucosal cyathostomin larvae, and treatment intervals of 4 to 6 weeks are necessary during periods of heavy pasture challenge.

Migrating *S. vulgaris* and *S. edentatus* can be controlled with ivermectin 0.2 mg/kg orally or fenbendazole at 60 mg/kg orally (single dose) or, more reliably, 7.5 mg/kg orally daily for 5 days. In cases of verminous arteritis, it may take some months after removal of the parasites for the lesion to resolve.

CONTROL

Eradication of all horse strongyles is not feasible, because infections are ubiquitous and no drug currently available can completely eliminate the mucosal larvae. Adult horses can pass substantial numbers of eggs throughout their lives; stocking densities are often high and foals usually graze with their dam. Infective larvae on grass can be long lived and there are usually few opportunities for the long-term resting or reseeding of

pastures on horse farms. Consequently, the primary objective of control programs is to minimize the numbers of infective larvae accumulating on pasture. There is no pasture treatment that is economically or environmentally acceptable. The possibility of using nematophagous fungi that will destroy larvae in the feces is an exciting prospect. Options for control by grazing management are limited. Alternate or mixed grazing with ruminants can reduce pasture infectivity, as horse strongyles will not establish in these hosts. The stomach worm *T. axei,* however, is a shared parasite. Removal of all horse feces from fields twice weekly is highly effective provided heavy rainfall does not disperse the material. This approach can be cost-effective where valuable animals are at risk or labor is relatively inexpensive. Tractor-mounted mechanical devices are available for this purpose. A further benefit of fecal removal is that the area within the field grazed by the horses is enlarged, i.e., the ratio of lawn to rough increases. Harrowing is effective in hot, dry conditions when eggs and larvae are quickly desiccated, but at other times is likely to have a deleterious effect by spreading infective larvae.

Prophylactic chemotherapy is used to a greater or lesser extent at most stables because land and labor constraints often limit the effectiveness of nonchemical approaches. The latter should, nevertheless, be used wherever possible to minimize the number of treatments needed during the year, which in turn reduces the risk of development of anthelmintic resistance. The purpose of prophylactic chemotherapy in the control of strongylosis is to prevent the output of strongylid eggs onto the pasture. Under conditions of heavy pasture challenge, regular dosing at 4 to 6 weeks with benzimidazoles (other than fenbendazole), 8 to 10 weeks with ivermectin, or 13 to 16 weeks with moxidectin is necessary throughout the period of risk. Once pasture larval counts have been reduced to insignificant levels, the time between doses can be extended. Routine fecal egg counts are an important component of any control strategy because they are a direct measure of the rate at which pasture contamination is taking place. They also confirm the continuing efficacy of the drugs used and can be used to determine optimum treatment intervals.

Parasitism is a herd problem and all horses on a property should be treated simultaneously, even if they have different owners. If routine fecal examinations are performed, dosing can be restricted to those horses with significant egg counts. Untreated animals then provide parasite refugia for conserving anthelmintic efficacy. As horses and ruminants generally harbor different worm parasites, disease risk can be reduced by grazing these species together or by alternating the use of paddocks between each species. As most eggs are deposited on the pasture in spring and summer in temperate regions, concentration of treatments at this time should reduce contamination and give much lower pasture larvae counts in the following autumn and winter. Intensive treatment programs are often adopted on stud farms, where maximum reduction of contamination is required. Less frequent dosing may be necessary on properties with lower stocking intensities or where horses are run with other stock. As the mare is the main source of contamination for the foal, she should be treated about 2 months before foaling, again at foaling, and regularly thereafter. Treatment of foals should commence at 10 weeks of age to remove small strongyles before they start to lay eggs and should be repeated at intervals, depending on the choice of drug.

Delaying the onset of resistance is an important consideration in the design of any control program. The major equine anthelmintics belong to just three chemical groups and worm populations resistant to one compound are usually insusceptible to, or more tolerant of, the effects of others in that chemical group. The level of resistance in a herd can be estimated by means of the **fecal egg count reduction technique**. At least six horses with high egg counts are weighed (e.g., with a weigh band) and treated with an accurately measured dose of anthelmintic. A reduction in mean egg count after 7 to 14 days of less than 90% is suggestive of resistance. More stringent tests are required for confirmation. Recommendations for extending the useful life of existing products similar to those listed earlier for ruminants have been published for horse anthelmintics.

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OXYURIS EQUI (PINWORM)

Oxyuris equi is a nematode that provokes irritation of the perianal region of horses, causing them to rub and bite their tails. This can result in hair loss and sometimes physical damage to the tissues of the area. The parasite is ubiquitous but of greater prevalence in areas of high rainfall.

The life cycle is direct. The mature worms are gray in color and inhabit the cecum and colon. The male is 1 to 2 cm long, but the female is much longer, up to 15 cm, and has a long tapering tail. When full of eggs, the female migrates down the gut and crawls onto the perianal area, where she exudes her eggs onto the skin in yellow clusters and then shrivels up and dies. An embryo develops in about 3 days within the egg, which is then infective. Eggs may be licked off the skin and swallowed or they may eventually fall to the ground. They resist desiccation, may become airborne in dust, and remain viable in stables for long periods. Transmission then occurs via contaminated feedstuffs.

Diagnosis is by detection of operculated eggs, slightly flattened on one side, on transparent adhesive tape that has been pressed against the perianal skin and then placed on a microscope slide for examination or by the chance observation of an adult worm in the feces.

TREATMENT AND PROPHYLAXIS
Treatment
Ivermectin (0.2 mg/kg, orally) (R1)
Moxidectin (0.4 mg/kg, orally) (R1)
Pyrantel (13.2 mg/kg, orally) (R1)
Febantel (6 mg/kg, orally) (R1)
Mebendazole (10 mg/kg, orally) (R1)
Oxibendazole (10 mg/kg, orally) (R1)

Treatment comprises the application of a mild disinfectant ointment to the perianal region and the administration of ivermectin, moxidectin, pyrantel, and any of the newer broad-spectrum benzimidazoles at the standard dose rate for horses.[1] Piperazine salts are also effective. However, recent studies in Europe and the United States have found that *O. equi* resistance to ivermectin and moxidectin is emerging.[2,3]

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STRONGYLOIDES (THREADWORM)

Farm animals in many countries are exposed to infection with the nematode genus *Strongyloides*. Disease outbreaks occur in young pigs, foals, calves, and lambs, but the overall economic importance of this parasite does not appear to be very great. Different species occur in each host: *S. ransomi* in pigs, *S. westeri* in horses, and *S. papillosus* in sheep and cattle. All are parasites of the small intestine. They are threadlike and less than 1 cm in length.

Only female worms are present in the intestine, so eggs are produced by parthenogenesis. The eggs are thin shelled and contain an embryo. The larvae that hatch out may develop into infective or nonparasitic forms. The latter become free-living males and females that live in decaying organic material and produce fertilized eggs that give rise to infective larvae. Transmission occurs when infective larvae enter the host either by ingestion or by skin penetration. In older animals they accumulate in subcutaneous tissues and migrate to the mammary gland when lactation starts. Thus neonates are infected via milk, and egg-laying females may be present in the intestine from about 1 week after birth. Infective larvae penetrating the skin of young animals travel via the blood to the lungs, where they break into alveoli, ascend the air passages to the pharynx, and are then swallowed.

Diarrhea in young animals is the most common clinical sign, but the passage of massive numbers of larvae through the skin may also provoke dermatitis. Experimental infections in calves cause pallor and coughing, but cases of sudden death without previous symptoms have been ascribed to heavy burdens with many migratory larvae. In bulls, balanoposthitis may be seen. In lambs, dermatitis, pulmonary hemorrhage, and enteritis occur. Sheep may also develop lameness or be more susceptible to foot rot when subject to heavy infestations. Experimental infection of young goats produced transient diarrhea, dehydration, cachexia, gnashing of teeth, foaming at mouth, anemia, and nervous signs. Pigs may show anorexia, listlessness, and anemia but diarrhea is the principal clinical sign. Infestation in pigs has been shown to reduce intestinal enzyme activity, to increase intestinal plasma and blood loss, and to reduce protein synthesis in the liver. In foals, high egg counts may be recorded in apparently healthy animals but may coincide with the onset of diarrhea (independent of the first heat of the mare) in other individuals. Episodes of frenzy in foals

lasting approximately 30 minutes have been attributed to percutaneous larval invasion. Within 2 days skin lesions developed on the lower limbs that persisted for 2 to 3 weeks. Experimental PCR assays targeting the 18S ribosomal DNA sequence have been developed for species-specific identification of *Strongyloides* species.[1]

TREATMENT AND PROPHYLAXIS

Treatment

Pigs
Ivermectin (0.1 mg/kg, orally) (R1)[2]
Abamectin (0.1 mg/kg, orally) (R1)[2]
Moxidectin (0.4 mg/kg, orally) (R1)

Foals
Ivermectin (0.2 mg/kg, orally) (R1)
Moxidectin (0.4 mg/kg, orally) (R1)
Oxibendazole (15 mg/kg, orally) (R3)

Sheep
Combination of derquantel (2 mg/kg, orally) and abamectin (0.2 mg/kg, orally) (R1)[3]

Most broad-spectrum anthelmintics are effective in eliminating this parasite. In foals, ivermectin is used at the standard equine dose, but elevated doses of oxibendazole (15 mg/kg) are needed. The treatment of mares with ivermectin on the day of parturition did not prevent transmammary transmission but markedly reduced egg counts in the foals. Treatment of infected sows was effective in removing arrested larvae from the subventral fat. In sheep derquantel, which belongs to a new class of anthelmintics called spiroindoles, when used in combination with abamectin, has been shown to have consistently high efficacy against *Strongyloides* infections.[3]

Control depends on the elimination of warm, moist areas such as damp litter or bedding, which is suitable for parasite multiplication.

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TRICHURIS (WHIPWORM)

Three species of whipworms are found in ruminants: *Trichuris ovis, T. discolor,* and *T. globulosa,* whereas *T. suis* occurs in pigs. Whipworms in farm livestock are usually considered to be relatively innocuous. Indeed, induced *T. suis* infections are being evaluated in human medicine for amelioration of chronic inflammatory bowel disease, because whipworm-induced Th2 immune responses dampen harmful Th1 activity in some patients.[1] Heavy infestations can, nevertheless, produce serious disease with

diarrhea and dysentery, and the mortality rate can be high in recently weaned pigs. Severely affected animals are anorexic and rapidly lose weight. The feces may contain bloodstained mucus and strips of necrotic mucosa. The nematodes lie with their thin anterior end superficially embedded in the wall of the cecum, and in heavy infections the colon may also be involved. The activities of the worms produce little tissue reaction per se but enable microorganisms in the gut microflora to become invasive. This is the main cause of the severe inflammation and clinical signs associated with whipworm infestation. A synergy has also been demonstrated between *T. suis* and *C. jejuni.*

The life cycle of the whipworm is direct. The eggs are very resistant to external environmental conditions and can survive for up to 6 years in old pigsties, and for at least 2 years on pasture in the south of England. An infective larva develops inside the egg, but a relatively high temperature is required for rapid growth. In temperate climates, embryonation of *T. suis* eggs may take more than 1 year. When swallowed by a suitable host, the eggs hatch and develop to mature adults in about 12 to 20 weeks after infection in lambs and goats and 6 to 7 weeks in pigs.[2] The disease in sheep is most common after hot, dry weather, which effectively cleanses the pasture of other nematode larvae, but the resistant *Trichuris* spp. eggs survive and are ingested when the sheep eat close to the ground to obtain grain given as drought feed.

Diagnosis depends on detection in the feces of the yellow oval eggs, which have a transparent plug at each end. The eggs are heavier than many others and do not always float well in saturated salt (NaCl) solution. An alternative flotation fluid such as zinc sulfate or sugar is more reliable. At necropsy, the adult worms, which are 2 to 5 cm long, are easily recognized by their whiplike appearance—the anterior third is much thinner than the handle-like posterior end.

TREATMENT AND PROPHYLAXIS

Treatment
Ivermectin (0.1 mg/kg orally every 24 hours for 7 days) (R2)[3]
Abamectin (0.1 mg/kg orally every 24 hours for 7 days) (R2)[3]
Oxfendazole (30 mg/g orally) (R2)[4]

Chemotherapy

Low uptake of benzimidazoles by *Trichuris* worms is responsible for low pharmacologic efficacy of this class of anthelmintics against *Trichuris* infestations.[5] Therefore dosages that are five times higher than recommended are used to treat *Trichuris* infestations.[6] Similarly, high efficacy of ivermectin and

abamectin is achieved when they are administered repeatedly for seven consecutive days.[3]

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PARASITIC GASTRITIS IN PIGS

SYNOPSIS

Etiology The nematodes *Hyostrongylus rubidus*, *Ascarops*, and *Physocephalus*

Epidemiology Infections occur in outdoor husbandry systems; *H. rubidus* has a direct life cycle, but *Ascarops* and *Physocephalus* use dung beetles as intermediate hosts.

Signs Generally asymptomatic but heavy infections can produce gastritis; sows with *H. rubidus* may become thin during lactation.

Clinical pathology Eggs of *Ascarops* and *Physocephalus* in feces are characteristic; those of *H. rubidus* are similar to *Oesophagostomum*.

Lesions Excess mucus; gastritis; often ulceration of glandular part of stomach; nodular hyperplasia in hyostrongylosis

Diagnostic confirmation Demonstration of eggs of *Ascarops* or *Physocephalus*; examination of larvae from fecal culture for *H. rubidus*

Treatment
   H. rubidus: Doramectin, abamectin, ivermectin, fenbendazole, flubendazole, febantel, oxibendazole, thiophanate, levamisole, and dichlorvos
   Ascarops: Ivermectin

Control Good husbandry practices, such as rotating pastures, normally suffice.

ETIOLOGY

Three categories of nematode inhabit the stomach of the pig. The first is a trichostrongylid, *Hyostrongylus rubidus.* This is closely related to the *Ostertagia* spp. of ruminants and occurs in most countries where pigs are kept. The next group comprises members of several related genera including *Ascarops strongylina, A. dentata,* and *Physocephalus sexalatus,* which occur in the United States, Southeast Asia, and Australia, and *Simondsia paradoxa,* found in parts of Europe and India. Finally, *Ollulanus tricuspis* is a very small nematode (0.7–1.0 mm) that causes gastritis on rare occasions in pigs, cats, foxes, and dogs.

LIFE CYCLES

H. rubidus is a small (0.5–1.25 cm) thin, red worm with a life cycle very similar to that of *O. ostertagi.* Eggs develop at temperatures between 10°C and 27°C (50°F and 80°F). In the UK, eggs deposited outdoors from May to October develop into infective larvae. These larvae survive on pasture for up to 10 months but are rapidly killed by desiccation and by freezing. Transmission occurs by ingestion of the infective larvae, which spend the next 13 to 14 days in the gastric glands. They then return to the lumen, and the first eggs are passed 20 to 25 days after infection. In some circumstances larvae become hypobiotic and remain in the gastric mucosa for several months.

Ascarops and *Physocephalus* are thick, white worms 1 to 2.5 cm long. They have indirect life cycles; eggs passed in the feces of the pig are eaten by dung beetles, in which hatching and development to infective larvae occur. Infestation of the final host occurs when pigs eat infested beetles. Little is known of the biology of *Simondsia paradoxa.*

EPIDEMIOLOGY

The stomach worms of pigs are almost exclusively confined to outdoor management systems. The reason for this is different in each group. With *Ascarops* and *Physocephalus,* it is a consequence of the essential role of the dung beetle in the life cycle. With *H. rubidus,* it is because the daily output of eggs by each female is so sparse that the life cycle is unlikely to persist in pig houses practicing a reasonable standard of hygiene. Young pigs are the most susceptible to hyostrongylosis but adult sows, especially when lactating, may also be affected. Hypobiosis is seasonal, but disease outbreaks analogous to type II ostertagiosis have not been reported.

PATHOGENESIS

Developing *H. rubidus* provokes hyperplastic nodular lesions in the glandular part of the stomach. These and consequent biochemical and physiologic sequelae are similar to those described for *O. ostertagi.* *Ascarops* and *Physocephalus* lie close to the gastric mucosa where they stimulate excessive mucous production. Heavy infections cause a catarrhal gastritis.

CLINICAL FINDINGS

The effect of *H. rubidus* on young pigs is not usually clinically apparent. Heavy infestations may be associated with anemia, unthriftiness, poor growth, and diarrhea. Signs in adult sows are usually seen during lactation. Affected animals lose more weight than normal and are slow to regain condition after weaning. In severe cases, sows may become emaciated. There may be pallor caused by anemia and often a depraved appetite, but no diarrhea. Adult sows often carry heavy infestations without clinical illness, but sudden death caused by hemorrhage

from gastric ulcers or to peritonitis by ulcerative perforation has been observed on rare occasions.[1] Although *Ascarops* and *Physocephalus* are common in many areas, most infections are low grade and without clinical effect. Heavy infections can lead to inappetence and other signs of gastritis.

CLINICAL PATHOLOGY

Fecal examination is not very useful for the diagnosis of hyostrongylosis, because the eggs of *H. rubidus* are indistinguishable from those of the less pathogenic but more prolific *Oesophagostomum* spp. *Physocephalus* and *Ascarops* spp. eggs are small, thick shelled, and contain a larva when laid.

NECROPSY FINDINGS

The presence of *H. rubidus* is easily missed as the worms are slender and often lie beneath a thick layer of mucus. Adult worms are <10 mm in length and are bright red when first removed from the host. The gastric mucosa is hyperemic and nodular lesions are present. There may be one or more deep ulcers in the glandular region of the stomach. These may contain clusters of adult *H. rubidus.* In severe cases the mucosa is thickened and edematous and covered with a diphtheritic pseudomembrane.[1] In *Physocephalus* and *Ascarops* infections, adult worms are readily visible lying in mucus on the gastric mucosa. There is an obvious gastritis in heavy infections and ulceration may occur.

DIAGNOSTIC CONFIRMATION

Confirmation of infection with *H. rubidus* is made by examination of larvae from fecal cultures. Those of *H. rubidus* are longer and more vigorously motile than those of *Oesophagostomum* spp. As *H. rubidus* produces so few eggs, even small numbers of larvae may indicate a pathogenic worm burden. Elevated serum pepsinogen concentrations may also be indicative of infection.

DIFFERENTIAL DIAGNOSIS

Hyostrongylus rubidus must be differentiated from other causes of unthriftiness or emaciation such as:
- Swine dysentery
- Necrotic enteritis
- Coccidiosis
- Infestation with *Oesophagostomum* spp.
- Thin sow syndrome
- Malnutrition

TREATMENT

TREATMENT AND PROPHYLAXIS

Treatment
Doramectin (0.3 mg/kg, IM) (R1)
Abamectin (0.1 mg/kg of feed/day for 7 days) (R1)[2]

Continued

Ivermectin (0.3 mg/kg BW by SC or IM injection or 0.1 mg/kg of feed/day for 7 days) (R2)[3]

Fenbendazole (5 mg/kg BW in feed as a single dose or divided over 7–14 days) (R3)

Flubendazole (5 mg/kg BW as a single dose or 30 g/tonne finished feed given for 5–10 days) (R3)

Febantel (5 mg/kg BW) (R4)

Oxibendazole (15 mg/kg BW or 1.6 mg/kg BW/day for 10 days) (R4)

Doramectin, abamectin, ivermectin, fenbendazole, and flubendazole are active against fourth-stage and adult *H. rubidus*. Febantel, oxibendazole, and thiophanate have label claims only for the adult worms. Levamisole and dichlorvos have also been widely used in the treatment of pig nematodes. In-feed ivermectin is also effective against *A. strongylina*.

CONTROL

Standard hygienic precautions including frequent removal of manure, the provision of drainage in outside pens, and rotation of pastures will reduce environmental contamination. Control of the dung beetle intermediate hosts of *Physocephalus* and *Ascarops* is impracticable.

Hyostrongylosis is most likely to affect sows during lactation, so animals at risk should be dosed before farrowing. The behavior of *H. rubidus* larvae on pasture is similar to that described for *Oesophagostomum,* and control schemes should be effective for both parasites.

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GASTEROPHILUS SPP. INFESTATION (BOTFLY)

Infestations with larvae of *Gasterophilus* spp. have a widespread distribution. They cause a chronic gastritis and a loss of condition in infested horses, donkeys, and mules. Reduced performance is often attributed to this infestation. On rare occasions they cause perforation of the stomach and death.

SYNOPSIS

Etiology Six species of *Gasterophilus* spp. that inhabit the gastrointestinal tract of horses

Epidemiology Eggs are laid on the hair of the body or around the lips; eggs hatch spontaneously or are stimulated to hatch by oral grooming, larvae penetrate oral mucosa or external epithelium of cheek and migrate to inner regions of mouth, and congregate at epithelial surface around teeth for 6–10 weeks before migration to the stomach and intestine. Larvae attach in stomach or intestine and remain there for a number of months before being passed in the feces. One species attaches near the rectum. Larvae pupate and adults emerge after 3–5 weeks. Adults only live a few days and are mainly active in the summer, and the larvae overwinter in the stomach.

Clinical signs Adult flies frighten horses and larvae cause nonspecific signs of unthriftiness.

Clinical pathology Eggs can be seen on hairs on legs or around the lips by direct inspection.

Lesions Area of larval attachment is pitted and the gastric wall may be thickened.

Diagnostic confirmation Eggs present on hairs, and there are characteristic lesions at autopsy.

Differential diagnosis Unthriftiness usually caused by helminth infection

Treatment Ivermectin, moxidectin

Control Treatment given when fly activity has ceased and when larvae are in stomach, usually two treatments in mid and late winter. Fringes and tassels protect against worry associated with one species of fly

ETIOLOGY

Six species of flies have larvae that are known to parasitize domestic equids: *Gasterophilus nasalis, G. intestinalis, G. haemorrhoidalis, G. pecorum, G. nigricornis,* and *G. inermis.* Their larvae are the "stomach bots" of horses, donkeys, and mules. Three species, *G. intestinalis, G. nasalis,* and *G. haemorrhoidalis,* are the most important and have a worldwide distribution, although *G. pecorum* is noted as becoming more important, particularly in parts of Asia and in the UK.[1,2] The later larval stages inhabit the stomach and duodenum. These creamy pink larvae are thick, segmented, and about 5 to 15 mm long. The adult flies are golden brown, hairy, and about the size of a bee, with two wings and vestigial mouth parts.

LIFE CYCLE AND EPIDEMIOLOGY

Flies do not feed and only live a few days. They are active during the summer months and there may be overlap among the species in their periods of activity. In areas with mild winters the flies may be active throughout the year. In colder regions fly activity ceases with the first frost, and there is usually only a single generation per year. In these regions the second and third instars remain in the stomach over the winter.

Eggs are attached to hairs while the fly hovers close to the horse. Fecundity is roughly correlated to the size of the fly. *G. haemorrhoidalis* matures about 50 to 200 eggs, *G. nasalis* 300 to 500 eggs, and *G. intestinalis* up to 1000. Eggs of the various species are laid in specific locations and are attached in a specific manner, allowing identification of eggs to species. The eggs are laid on the horse's coat except for *G. pecorum,* which lays up to 2000 eggs in batches of 100 to 200 on pasture plants. The eggs of *G. pecorum* and *G. haemorrhoidalis* are dark brown; the eggs of the others are yellow and are readily visible glued to the hairs, usually one to a hair. The eggs of *G. intestinalis,* the most common fly, are laid on the front legs, particularly the lower parts; those of *G. nasalis* in the intermandibular area; and the others species' eggs are laid on the cheeks and lips.

The eggs are ready to hatch in about 2 to 10 days, and the first instars enter the mouth either by host biting or licking or by subcutaneous migration from the cheeks into the oral cavity. The eggs of *G. intestinalis* and *G. pecorum* require a stimulus, provided by licking (moisture) or rubbing (friction), before they will hatch. The larvae penetrate oral mucosa, migrate to inner surfaces, and emerge in the interdental spaces. The larvae of *G. intestinalis* penetrate the anterior end of the tongue and burrow in the buccal mucosa for about 3 to 4 weeks before invading pockets between the teeth or between the gum and molars. *G. nasalis* may also accumulate in pockets alongside the molar teeth and cause mouth irritation. *G. haemorrhoidalis* can penetrate the skin of the cheek and after wandering in the tissues of the mouth may attach in the pharynx. The second instar of *G. intestinalis* may also attach for a few days to the pharynx and the sides of the epiglottis before passing to the stomach. The first instars of *G. pecorum* burrow into the mucous membranes of the hard palate, cheek, and tongue where they develop into second instars. They then move to the pharynx where they develop into the third instar. Occasional larvae migrate to abnormal sites including the brain, the cranial sinuses, the heart, and lungs.

Third instars of *G. intestinalis* larvae are found attached to the mucosa, usually in bunches, at the junction of the glandular and nonglandular portion of the stomach, where they become attached to the mucosa. *G. nasalis* larvae are found in the pyloric region of the stomach and the duodenum. *G. pecorum* larvae may be found in the pharynx and upper part of the esophagus and in the fundus of the stomach. *G. haemorrhoidalis* larvae are found in the tongue, the pharynx, and the gastric fundus.

In the host, two molts are made and the larvae pass out in the droppings 10 to 12 months after infestation, usually in the spring and early summer. Some larvae may attach temporarily to the rectal mucosa on their way through. The larvae migrate into the ground, pupate, and adult flies emerge after 3 to 5 weeks to recommence the late summer attacks on horses.

PATHOGENESIS

The adult fly causes considerable annoyance when ovipositing. The droning noise and the sudden attacks to lay eggs cause head tossing

and running in the host. *G. nasalis* is particularly troublesome because it darts at the lips and throat.

There is some doubt as to the importance of the lesions caused by the larvae. At the sites where they adhere there is an area of thickening and inflammation, and in rare cases gastric perforation occurs. It is probable that there is some chronic gastritis and interference with digestion in most infestations. *G. intestinalis,* the most common species, attaches to the squamous epithelium, and this has a relatively slight impact on the digestion in the horse. However, the ulceration, edema, and abscessation caused by this species cannot be overlooked, and one must expect some effect from such lesions, although it is difficult in practice to separate these findings from those caused by a concurrent worm burden. Occasional perforation of the gut has been documented The larvae do not remove sufficient blood to cause anemia, feeding mostly on tissue exudate. In rare cases pleurisy may occur following perforation of the esophagus close to the cardia. In very heavy infestations with *G. pecorum* the presence of large numbers of larvae (100–500) on the soft palate and base of the tongue can cause stomatitis and some deaths. Migration of first instars in the tongue and interdental gingiva and the aggregation of larvae in periodontal pockets may produce irritation or pain and may prevent foals from eating.

A recent proteomic analysis using two-dimensional (2D) gels and other techniques has described the influence of larvae on the development of immune responses.[3] Novel antigens that were identified could be developed as a vaccination for a control option.

CLINICAL FINDINGS

A nonspecific syndrome of unthriftiness, poor coat, occasional mild colic and lack of appetite, plus bad temper and unwillingness to work is usually ascribed to bot infestations. Adult flies frighten horses by their hovering, darting flight, especially around the head of the horse, and may be a cause of shying and balking.

CLINICAL PATHOLOGY

The eggs on the hairs can be seen by direct inspection, but the presence of larvae in the stomach and intestines can only be detected after treatment with a suitable insecticide.

NECROPSY FINDINGS

A few larvae are present in the stomach of most horses at necropsy, but clinical illness is usually associated with very large numbers. The areas of larval attachment are pitted and the gastric wall thickened. There may be an adhesive peritonitis and attachment and abscessation of the spleen over such areas.

DIAGNOSIS

The syndrome produced is not sufficiently characteristic to make antemortem diagnosis

possible, and bot infestations are commonly associated with helminth infestations, which produce most of the signs observed. A tentative diagnosis of infestation of the gums can be made by signs of pain on mastication and the presence of botfly eggs on the horse at that time. A variety of serologic tests, including an ELISA, have been evaluated and found to be generally specific and sensitive. There has been no further development of a practical test. Endoscopy using an video gastroscope has been applied to the diagnosis of gasterophilosis, although its use has been confined to use in drug efficacy studies.

TREATMENT

Macrocyclic lactone-based compounds administered as a paste are the most effective products for treatment.

CONTROL

Treatment should be administered after fly activity has ceased and the larvae have reached the stomach but before gastric damage has occurred. Single treatments are usually all that is required for control. Recent combination therapies containing a macrocyclic lactone plus praziquantel are used for control of gastrointestinal worms, tapeworms, and bots in a single dose. In foals showing pain on mastication, treatment with ivermectin paste should be given as needed throughout the fly season.

Treatment Recommendations

Treatment with a macrocyclic lactone-based product is strongly advised to increase productivity and to maintain overall health of the animals.

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THORNY-HEADED WORM IN PIGS (*MACRACANTHORHYNCUS HIRUDINACEUS*)

Macracanthorhynchus hirudinaceus is included with other nematodes for convenience, but it is not a nematode. It belongs to a different phylum, the acanthocephalans. These resemble roundworms in appearance but in some ways are more similar to tapeworms because they lack, for example, a digestive tract. The name "thorny-headed worm" denotes the hook-covered proboscis they all possess.

M. hirudinaceus infestations in pigs are not usually heavy and cause relatively little loss. The worms have thick bodies (0.5–1.25 cm), are long (up to 38 cm), and are transversely wrinkled. They inhabit the small

intestine and pass eggs that are very resistant to environmental stress and survive for up to 2 years. The life cycle is indirect with a variety of beetles acting as intermediate hosts. Transmission occurs when a pig eats an infested grub or adult beetle, and eggs are passed about 2 to 3 months later. The female worm is a prolific egg layer and lives in the host for about 1 year.

Heavy infestations cause slow growth or loss of BW. The head of the worm pushes deeply into the intestinal mucosa and causes nodules that are clearly visible from the serous surface. Occasional deaths may occur because of intestinal perforation. Sedimentation techniques are better than flotation methods for detecting eggs in feces. Treatment is rarely given because the condition is usually only diagnosed at necropsy.

TREATMENT AND PROPHYLAXIS
Treatment Ivermectin (0.1 mg/kg orally every 24 hours for 5 days) (R3)

A single dose of doramectin is only partly effective. Control, if necessary, involves suitable disposal of pig manure and avoidance of contact with the intermediate hosts (beetles).

TAPEWORM INFESTATIONS

LARVAL TAPEWORM INFESTATION

Livestock may act as the intermediate hosts for the tapeworms of humans and other animals. The larval tapeworms (metacestodes) develop as fluid-filled cysts, each at a typical site in the body. They act as space-occupying lesions and cause condemnation at meat inspection. Cattle around the world may harbor the metacestode of *Taenia saginata* (the beef tapeworm of humans), also known as *Cysticercus bovis,* in their striated musculature. *T. solium* (the pork tapeworm of humans) occurs similarly in pigs (known as *C. cellulosae*), mainly in poorer regions.[1] The recently discovered *T. asiatica,* found only in East Asia, is closely related to *T. saginata* but uses pigs as its intermediate host. Cysts in the musculature of sheep (known as *C. ovis*) are the intermediate form of a dog cestode (*T. ovis*). Hydatid cysts (*Echinococcus granulosus*), which develop in the lungs and/or liver of sheep, cattle, and horses, are also acquired from tapeworm eggs excreted by infected dogs and wild canids. These metacestodes rarely cause clinical disease in veterinary species (although some are serious zoonoses), so the reader is referred to parasitology textbooks for detailed information.

Clinical disease is, however, associated with two other metacestodes. *T. (Multiceps) multiceps* metacestodes cause coenurosis ("gid") in sheep,[1] which is described later. *T. hydatigena* metacestodes are normally asymptomatic, but if a sheep or goat swallows a whole tapeworm segment, which may

contain 100,000 eggs, sudden death may occur as massive numbers of developing metacestodes (known as cysticerci) migrate through the liver parenchyma. This condition (hepatitis cysticercosis) resembles acute hepatic fasciolosis but is an individual rather than a flock problem.

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ADULT TAPEWORM INFESTATION

SYNOPSIS

Etiology Cestodes belonging to the anoplocephalid family, including *Moniezia* spp. in ruminants and *Anoplocephala* spp. in horses

Epidemiology Transmission by ingestion of infected free-living pasture (oribatid) mites

Signs Little pathogenicity but heavy infestation may cause failure to thrive and, in horses, increased risk of ileocecal colic.

Clinical pathology Demonstration of tapeworm eggs in feces

Lesions
  Horse: Mild inflammation of intestinal mucosa with small ulcers

Diagnostic confirmation Tapeworm segments around tail base or on feces; eggs in feces

Treatment
  Ruminants: Albendazole, febantel, fenbendazole, mebendazole, netobimin, oxfendazole, and praziquantel
  Horses: Pyrantel, praziquantel

Control If necessary, periodic dosing is the only feasible option.

ETIOLOGY

The common anoplocephalid tapeworms of ruminants, *Moniezia expansa, M. benedeni,* and *Thysaniezia* (syn. *Helictometra giardi* also known as *T. ovilla*) are cosmopolitan, whereas *Avitellina* spp. occur mainly in Mediterranean countries and India, *Stilesia hepatica* in Africa, and *Thysanosoma actinioides* in North America.

In horses, *Anoplocephala magna, A. perfoliata,* and Anoplocephaloides (syn. *Paranoplocephala mamillana*) are cosmopolitan in their distribution.

LIFE CYCLE

The life cycles of all the anoplocephalid tapeworms are very similar. Eggs, which are immediately infective, pass in the feces of the host, either singly or protected within a tapeworm segment. These are ingested by free-living pasture (oribatid) mites and the

intermediate stage (the metacestode) forms. Mature tapeworms develop when the primary host accidentally swallows infected mites while grazing. Most species establish in the small intestine, but *T. actinioides* also invades biliary and pancreatic ducts, whereas *A. perfoliata* is found around the ileocecal junction and *S. hepatica* lives in the bile ducts. Lengths vary with species: *A. perfoliata* grows to 4 to 8 cm and *Moniezia* may be over 2 m.

EPIDEMIOLOGY

Oribatid mites are ubiquitous but most numerous on permanent pastures in the summer months. All grazing animals are therefore potentially at risk.

PATHOGENESIS

In ruminants, anoplocephalid tapeworms have little apparent effect on health. In heavy infestations, it has been postulated that they may compete for nutrients, excrete toxic materials or, because of their length, interfere with the motility of the gut. Very heavy burdens of *M. expansa* in lambs have been associated with outbreaks of enterotoxemia. Pancreatic and biliary duct species cause little harm, but liver damage may cause rejection at meat inspection.

In horses, *A. perfoliata* causes a mild local inflammatory response around its site of attachment. Where 20 or more tapeworms are clustered, ulceration and other degenerative changes may occur. This may be accompanied by diphtheresis, granulomatosis, and occasionally polyp formation. The ileocecal valve may be thickened. Heavy infestations may interfere with gut motility and increase the risk of ileocecal colic. A recent matched case-control study indicated that 22% of a series of spasmodic colic cases were likely to have been tapeworm associated. Evidence is accumulating to implicate *A. perfoliata* as a significant risk factor in ileal impaction cases.

CLINICAL FINDINGS

In ruminants, there is disagreement over the importance of anoplocephalid tapeworms in causing disease; farmers usually overemphasize their importance and veterinarians underestimate it. Most infestations are asymptomatic but, on occasion, heavy burdens may result in unthriftiness; poor coat; vague digestive disturbances including constipation, mild diarrhea, and dysentery; and sometimes anemia. These signs are restricted chiefly to animals less than 6 months of age on an inadequate diet. With *T. actinioides,* signs may be delayed until the animal reaches a later age. Infested animals may be more susceptible to the effects of other internal parasites and to other diseases or adverse environmental conditions.

Infections in horses are usually asymptomatic[1] but, occasionally, heavy infestations may be associated with a range of abdominal conditions including colic[2]; perforation of the cecum; ileocecal, cecocolic, and ileoileal

intussusception; colonic and cecal torsion; and ileal thickening and obstruction.

CLINICAL PATHOLOGY

Shed tapeworm segments may be visible macroscopically on the skin and hair around the tail base or in the feces. Eggs may be present in feces.

NECROPSY FINDINGS

The site of attachment on the intestinal mucosa may be indicated by the presence of a small ulcer and a mild inflammatory response. In the case of infestations with *T. actinioides* and *S. hepatica,* the presence of worms in the biliary and pancreatic ducts is accompanied by fibrosis and thickening of duct walls. In horses, *A. perfoliata* can cause inflammation of the lamina propria and mucosal damage at the region of the ileocecal junction, and there is an association between the number of worms present and the severity of the histologic changes.[3,4] Significant gross thickening and fibrosis of the ileocecal junction and several changes in neuronal cells in horses have been observed where more than 20 tapeworms were present.[4]

DIAGNOSTIC CONFIRMATION

Shed segments are much wider than they are long. They can be seen to be full of characteristic eggs if broken in a drop of water on a slide and examined microscopically. Anoplocephalid eggs are roughly D shaped, thick shelled, and contain an embryo within a chitinous ring. They are not easy to find in feces. Centrifugation/flotation using a saturated sugar solution is recommended for diagnosis in horses. At best the sensitivity of such techniques is only 60% for light infections rising to 90% for heavy burdens, so repeat samples may be needed to demonstrate the presence of the parasite. Methods have been devised for detection of specific antibodies in serum or antigen in feces[5] but are not as yet generally available. Experimentally, a species-specific and highly sensitive molecular diagnostic PCR has been developed for accurate identification and diagnosis of *Moniezia* species targeting the parasites' 18S regions of the ribosomal DNA.[6-8] In equines an experimental multiplex PCR assay for simultaneous detection of various *Anoplocephala* spp. targeting the hypervariable SSUrRNA gene regions has been developed.[9]

DIFFERENTIAL DIAGNOSIS

- Other causes of unthriftiness
- In horses, other causes of colic

TREATMENT

TREATMENT AND PROPHYLAXIS

Treatment
Cattle
Praziquantel (5 mg/kg BW, orally) (R2)

Horses
Pyrantel (38 mg/kg) (R2)
Praziquantel (2.5 mg/kg BW, orally) (R2)

For ruminants, praziquantel 3.75 mg/kg is highly effective against *Moniezia*, but higher doses are required for *Thysaniezia* spp. (5 mg/kg), *Avitellina* (7.5 mg/kg), and *S. hepatica* (15 mg/kg). Some benzimidazole and probenzimidazole drugs have cestocidal activity in ruminants, including albendazole, febantel, fenbendazole, mebendazole, netobimin, and oxfendazole. The efficacy of some of these compounds against *Moniezia* may be variable. Albendazole at 7.5 mg/kg orally is effective against cestodes in the bile ducts.

For horses, pyrantel embonate at 38 mg/kg orally (i.e., double the standard dose for roundworm control) is an established treatment for *A. perfoliata* but is ineffective against *A. mammillana*. Although toxic effects have not been fully evaluated at this high dose rate, pyrantel is generally regarded as having low toxicity in herbivores when administered orally. More recently praziquantel has been shown to provide high efficacy against *A. perfoliata* at doses of 1 to 2.5 mg/kg BW orally and *A. mammillana*. Such treatment may half the estimated risk of tapeworm-associated colic.

Control

Control of the mites that act as intermediate hosts is impractical. If a potential problem is perceived in, for example, valuable horses, consideration could be given to reducing the numbers of oribatid mites by plowing permanent pasture and reseeding. Otherwise stabling or tactical dosing, in early summer and autumn, are the only options.

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Toxins Affecting the Alimentary Tract

PHOSPHORUS TOXICOSIS

Poisoning from phosphorous-containing products rarely occurs anymore. Rodenticides, once a common source of phosphorus intoxication for animals, are no longer used, and current exposure occurs primarily from ingestion of old products found in abandoned sheds and buildings. Animals may also be exposed either by grazing on pastures or drinking water contaminated with white phosphorous used for military ammunitions training.[1,2] Occasionally, animal feeds inadvertently contain an excess concentration of dietary phosphates disrupting the Ca:P balance and causing clinical signs. In ruminants, this may result in urinary or bladder calculi, and in horses, secondary hyperparathyroidism.[3]

Phosphorus has a local caustic action, and ingestion is associated with severe irritation of the gastrointestinal mucosa with signs of gastroenteritis appearing within an hour or two. Some phosphorus may be absorbed and is associated with acute hepatic necrosis, but signs do not appear for several days. Toxic effects are increased when the phosphorus is finely divided and mixed with oils or fats that facilitate absorption.

CLINICAL FINDINGS
Common signs include salivation, acute abdominal pain, intense thirst, and diarrhea. Pigs vomit violently and the vomitus is luminous with a garlic odor. The animal often dies of acute shock during this stage. Survivors show jaundice, weakness, anorexia, oliguria, and hematuria. Death may occur suddenly or be accompanied by convulsions. Phosphorus can be detected in the vomitus and feces of affected animals.

NECROPSY FINDINGS
Macroscopically there is congestion and hemorrhage of the gastrointestinal mucosa. The carcass is often jaundiced and the liver is swollen and pale. Histologically there is fatty degeneration of both the liver and kidney, sometimes accompanied by hepatic necrosis. The acute stages of phosphorus poisoning may appear similar to acute stages of inorganic arsenic, mercury, or selenium poisoning.

DIAGNOSTIC CONFIRMATION
Diagnostic confirmation requires evidence of access to the poison and the detection of large amounts of it in the gastrointestinal tract.

Samples for Analysis
- Toxicology: Use 50 g of liver, kidney, and a portion of gastrointestinal tract with content
- Histology: Formalin-fixed liver, kidney (LM)

TREATMENT
The use of emetics to remove the contents from the stomach is generally not recommended because phosphorous is caustic and can cause significant damage to the esophageal lining during emesis and because vomiting normally occurs. Gastric lavage followed by activated charcoal with a cathartic may be beneficial in solitary animals when used early after ingestion. Further treatment is supportive and includes analgesics and intravenous fluids for dehydration. Hypotension and shock as well as coagulopathy may occur and should be treated supportively as needed.

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ARSENIC TOXICOSIS

SYNOPSIS

Etiology Insecticidal dips or sprays; herbicides; wood preservatives, pharmaceuticals, and feed additives. Inorganic compounds are the most toxic, and organic arsenicals are the least toxic.

Epidemiology Outbreaks caused by accidental access; use of excessive amounts in feed, spray, or dip. Most cases result from ingestion, but percutaneous absorption is also possible.

Clinical signs Enteric form a highly fatal gastroenteritis with diarrhea; dehydration. Neurological form with incoordination and blindness or a syndrome of incoordination, restlessness, squealing, and convulsions

Clinical pathology High levels of arsenic in feces, urine, and milk for 5 days (organic arsenicals) and 10 days (inorganic arsenic). Chronic cases best assayed in hair or skin

Necropsy lesions Gastroenteritis in enteric form, and no lesions in neurological form

Diagnostic confirmation Higher than normal levels of arsenic in body fluids or tissues

Treatment Decontamination, antidotes, and supportive care

Control Remove from environment and do not exceed label directions.

ETIOLOGY
Background Information
- Inorganic arsenicals most often have a valence of +3 (trivalent; arsenite) or +5 (pentavalent; arsenate) and arsenite is more toxic than arsenate.
- Organic arsenicals most often have valences of +3 (trivalent) or +5 (pentavalent) and by definition contain at least one carbon atom.

The toxicologic profile of arsenic is complicated. The absorption and toxicity of arsenic depend on many factors other than the valence and chemical form. Absorption is dependent on particle size, solubility, and species, with other factors such as animal

health playing a role. Large, less soluble particles of an inherently toxic arsenical compound may not be well absorbed, whereas a less toxic but more soluble substance may have greater absorption.[1,2] Animals in poor health with compromised gastrointestinal systems may have far greater absorption than those in good health. Species plays an important role with humans and dogs the most susceptible to arsenic toxicity and the development of clinical signs.

Arsenic compounds likely to be encountered by large animals are numerous and varied but include the following:

Inorganic compounds used as insecticidal dips or as herbicides
- Oxide, e.g., arsenic trioxide (+3)
- Trivalent, e.g., sodium arsenite (+3), copper acetoarsenite (Paris green)
- Pentavalent, e.g., sodium arsenate (+5)

Inorganic compounds used as wood preservatives
- Chromated copper arsenate (+5)

Inorganic compounds used as medicinals
- Inorganic lead arsenate (+5)
- Potassium arsenite (+3), e.g., Fowler's solution and others

Organic compounds used as herbicides
- Monosodium and disodium methanearsonates (+5), e.g., MSMA and DSMA

Organic compounds used as medicinals
- Trivalent phenylorganic arsenicals (+3), e.g., thiacetarsamide and melarsoprol
- Pentavalent phenylorganic arsenicals (5), e.g., arsanilic acid, roxarsone (4-hydroxy-3-nitrophenylarsonic acid), and nitarsone (4-nitrophenylarsonic acid)

Relative Toxicities

The organic pharmaceuticals are least toxic, the insoluble oxides are of medium toxicity, and the trivalent inorganic compounds are associated with the most severe syndrome.[1,2,4] Toxic oral doses may range from 1 to 25 mg/kg for the arsenites, 30 to 100 mg/kg for the arsenates, 25 mg/kg daily for 8 to 10 days for cacodylic acid, and 10 to 25 mg/kg for 5 to 6 days for the methanearsonates.

Aromatic organic arsenicals are toxic when the cumulative dose is exceeded by two to four times the recommended dose, delivered by either exceeding the recommended percentage in the feed, or feeding it for too long. Seven to 10 days' feeding of arsanilic acid at 500 mg/kg diet or 3-nitro, 4,hydroxyphenylarsonic acid at 250 mg/kg diet will be associated with toxicosis in swine; approximately twice these concentrations will result in poisoning of poultry.

EPIDEMIOLOGY

Occurrence

Arsenic toxicosis usually occurs after ingestion of the toxic substance, but dermal absorption can occur especially if the skin is abraded or hyperemic. Today, arsenic is less commonly associated with generalized livestock poisoning, but poisoning still occurs in some areas of the world because of its presence in groundwater.[3] In addition, arsenic can still be found in the following products.

Dips and Sprays

Fluids used for dipping and spraying of animals to control ectoparasites are a very common source of poisoning. Animals may swallow the solution while in the dip or in the draining yards after dipping. Animals that are not allowed to drain completely as well as faulty disposal of drainage from yards and dips may contaminate the pasture. Opened containers of dipping solutions or powders may accidentally contaminate feed or be mistakenly applied as a skin dressing. Appreciable amounts of arsenic are absorbed through the skin after dipping in sodium arsenite. The absorption is increased if the animals are dipped when hot, if the fleece is long, if they are crowded too tightly in draining yards, or driven too soon after dipping. However, in most outbreaks of poisoning some ingestion appears to occur and supplements the cutaneous absorption. There is some danger in dipping rams at mating time when erythema of the skin of the thighs and scrotum is present. Dipping immediately after shearing and jetting at too high pressure or with excessively strong solutions may also be associated with increased absorption.

Herbicides

These include sodium or potassium arsenite, arsenic pentoxide, and monosodium or disodium acid methanearsonate sprays used to kill weeds. Grass clippings taken from lawn areas treated 6 months earlier with arsenical herbicides may carry 15,000 mg/kg arsenic.

Insecticidal Sprays

These are often used in orchards and pasture applied to kill Colorado beetle grubs and other pests. In most instances poisoning occurs when animals accidentally gain access to recently sprayed areas, although drifting of windblown spray may result in accidental contamination of pasture.

Leaded Gasoline

The major effects are usually ascribed to the effects of the lead, but this does not always appear to be so.

Insect Baits

Paris green (copper acetoarsenite) has historically been mixed with bran and applied to large areas of land in an attempt to control grasshopper plagues.

Wood Preservatives

Wood products such as fence boards, posts, calf hutches, and old buildings treated with a chromated copper arsenate preservative remain a source of arsenic exposure. The compound has a salty taste and arsenic concentrates in the ashes when the wood is burned.

Metal-Bearing Ore Deposits

Several natural deposits, including iron arsenic pyrites in volcanic soils as well as gold and copper ores, contain large quantities of arsenic that may be licked in situ or carried off in the fumes from smelters and contaminate surrounding pastures and drinking water supplies.

Pharmaceuticals and Growth Stimulants

These include arsanilic acid and sodium arsanilate, as well as phenylarsonic acid preparations such as roxarsone and nitarsone, which are used as feed additives, growth promotants, antidotes for selenium toxicosis, and in the control and treatment of animal dysentery. Overdosing can occur by continuing the administration for too long or when there is an error in mixing a batch of feed. The toxicity of feed containing arsanilic acid depends to a certain extent on the intake of drinking water, but moderate water restriction does not make normal dose rates dangerous.

Animal Risk Factors

Soluble salts are highly poisonous; arsenic trioxide and sodium arsenate are much less soluble and thus less toxic than sodium arsenite. The LD_{50} of sodium arsenite varies between species with pigs, horses, cattle, and sheep requiring increasing doses to be affected. Organic chemicals used as herbicides are as poisonous as the arsenite, but organic arsenicals used as growth stimulants are less toxic, although they are absorbed rapidly.

In cases in which gastroenteritis is the predominant lesion, the case–fatality rate approximates 100%.[4] In cases characterized by nervous system involvement the illness is incidental and losses minimal if access to the poison denied, but residues become a problem.

Human Risk Factors

Meat and milk residues reduce the safety of the products for human consumption.[1,5] Arsenic is excreted rapidly after absorption, chiefly in the urine, and after the ingestion of nontoxic amounts by the cow there is no detectable secretion into the milk.[6] When much larger doses are consumed arsenic may be excreted in the milk, as well as in urine and feces, but the concentration is still low. The biological half-life of arsenic taken orally in the form of arsanilate is 4.2 days in liver, 5.7 days in kidney, and 15 days in muscle. In pigs receiving arsanilic acid at 200 mg/kg in the feed the level of arsenic in muscle is still more than the admissible level of 0.1 mg/kg 18 days after withdrawal. The usual recommendation is to withdraw arsanilic acid 5 to

7 days before slaughter. This is adequate at normal dose levels.

Environmental Risk Factors

The presence of arsenic in groundwater is well documented in various parts of the world, especially in some parts of Asia.[7,8] This is associated with suboptimal milk production in cows as well as the potential for further soil and water contamination from arsenic excreted in the urine.[8]

PATHOGENESIS
Mechanism of Action

Inorganic trivalent salts and trivalent organic compounds exert their toxic effects by combining with sulfhydryl groups on proteins and inhibiting tissue enzymes such as α-keto oxidase, pyruvic acid oxidase, and α-oxyglutaric acid oxidase.[2,4,9] Trivalent arsenicals are most toxic because of their greater affinity for these sulfhydryl groups. The efficiency of sulfur-containing compounds such as dimercaptopropanol (British antilewisite or BAL) as antidotes depends on the ability of these compounds to compete with sulfur-containing compounds of enzyme systems for the available arsenic.[2,4] Pentavalent inorganic arsenates work by uncoupling oxidative phosphorylation, perhaps by substituting phosphate into the reaction. The mechanism of action for pentavalent organic compounds is unknown, but interference with the actions of pyridoxine and thiamine may be involved.[2] In ruminants, pentavalent arsenicals can be converted to trivalent arsenicals.

Tissue Susceptibility

Once absorbed into the bloodstream, arsenic is well distributed to all body organs, accumulating in the liver before distribution. Others organs such as the kidneys, lungs, and spleen also accumulate arsenic.[2,4,9] The body areas affected are primarily those with tissues rich in oxidative enzyme systems. Thus the alimentary tract wall, liver, kidney, spleen, and lung are most susceptible to the general depression of metabolic activity and development of clinical signs. Gastrointestinal tract lesions produce the most obvious clinical signs because of the extensive damage to capillaries causing increased permeability and exudation of serum into tissue spaces. The mucosa lifts from the underlying muscle coat and is shed with a resultant loss of large quantities of body fluids. Arsenic does not precipitate protein, and there is no direct local effect on alimentary tract mucosa; this is indicated by the fact that the parenteral injection of arsenic produces lesions in the gut wall, which are identical with those associated with ingestion.

Time Lag

Because arsenic does not precipitate protein it does not limit its own absorption, and there is a considerable time lag after ingestion before clinical signs appear; corrosive substances produce lesions and signs immediately.

Percutaneous Absorption

Arsenic absorbed from the skin may be associated with local necrosis without systemic signs if the peripheral circulation is poor or the concentration of arsenic is excessively high, but if the cutaneous circulation is good, the arsenic is quickly carried away and is associated with a systemic disease without skin necrosis.

Chronic Poisoning

The chronic toxicity of arsenic at low levels of intake is caused by its accumulation in particular organs, especially the skin, bone, hooves, and hair.[1,4,10]

Nervous Tissue Lesions

Pentavalent organic arsenicals cause degenerative changes in peripheral nerves. These appear as demyelination and axonal degeneration in prolonged cases.[2] Animals recumbent longer than 7 days are unlikely to recover and will remain paralyzed until death from other associated conditions. In poisoning with arsanilic acid compounds the lesions occur primarily in the optic nerves, causing blindness. In poisoning with the phenylarsonic acid group the nerves to the limbs appear to be most affected.

CLINICAL FINDINGS

The occurrence of clinical signs depends on the specific form of arsenic to which animals are exposed. As a general rule, all inorganic arsenicals and trivalent organic arsenicals affect the capillaries and gastrointestinal tract, and pentavalent organic arsenicals affect the neurologic system.

GASTROINTESTINAL SYNDROME
Peracute Cases

These animals show little except depression and prostration and generally die before signs of enteritis develop.[4,11] Death occurs minutes to a few hours after exposure and may be preceded by clonic convulsions and diarrhea.

Acute and Subacute Cases

In ruminants, the onset of signs of illness is often delayed 20 to 50 hours from ingestion of the poison, with the length of time depending on the fullness of the forestomachs.[4,11] Distress develops suddenly, beginning with severe abdominal pain, restlessness, groaning, an increased respiratory rate, salivation, grinding of the teeth, complete rumen stasis, and vomiting (even in cattle), followed by a fluid and fetid diarrhea that may be hemorrhagic. Tachycardia, rapid and weak pulse, dehydration, and oliguria are marked.

Horses show similar signs with a marked congestion of the mucous membranes and a very sudden onset of severe colic. Severe diarrhea (± blood) may be followed by a period of complete stasis of the alimentary tract with diarrhea recurring just before death.

Subacute cases give the same signs as acute cases, but the course may extend over 2 to 7 days. Nervous signs of muscle tremor, incoordination, and clonic convulsions are followed by terminal coma.

Chronic Cases

Commonly observed signs include low BW; a dry, rough coat that is easily shed; fatigue; bouts of indigestion; conjunctival and mucosal erythema; eyelid edema; and conjunctivitis. Buccal mucosal ulceration may extend to the muzzle. Milk yield is seriously reduced and abortions and stillbirths may occur. Local skin lesions include initial hyperemia followed by necrosis and sloughing, leaving indolent lesions that are extremely slow to heal.

NEUROLOGICAL SYNDROME

Chronic poisoning resulting from arsanilic acid overdose occurs primarily in pigs and lambs. It is manifested by incoordination 3 to 7 days after ingestion; blindness may or may not occur. Consciousness, body temperature, and appetite are unaffected. If feeding is continued the signs gradually worsen; if feed is changed the signs disappear within a few days. Some pigs remain permanently blind or paralyzed. In chronic poisoning with roxarsone and nitarsone the emphasis is on restlessness, frequent urination and defecation, incoordination caused by loss of balance, frequent shrill "screaming," tremor, and convulsions, all of which are stimulated by rousing the pig. If left alone in a recumbent position it may appear normal. Almost all animals have some form of gastrointestinal irritation.

CLINICAL PATHOLOGY

Arsenic can be detected in the urine, feces, and milk for periods of up to about 10 days, beginning shortly after the toxic material is ingested. The rate of excretion is faster with organic compounds than with inorganic arsenic, and urine levels may be back to normal in 5 days. The most satisfactory material for laboratory examination from a living animal is a large volume (about 1 L) of urine in which arsenic levels may be as high as 16 mg/kg. Levels in milk are low.[6] Normal levels of up to 0.25 mg/kg in cows' milk may be elevated to 0.34 to 0.47 mg/kg in cases of acute poisoning and to 0.8 to 1.5 mg/kg in the milk of normal cows that graze arsenic-contaminated pasture for long periods. Deposition in the hair occurs and arsenic persists there until the hair is shed, making possible the detection of prior arsenic ingestion in the absence of arsenic from the blood and feces. The hair of animals not exposed to arsenic should contain less than 0.5 mg/kg, and that of exposed animals may contain as much as 5 to 10 mg/kg.

NECROPSY FINDINGS

In acute and subacute cases of **inorganic arsenic poisoning** there are pronounced

hyperemic and patchy submucosal hemorrhages in the stomach, duodenum, and cecum. Hemorrhage and multifocal ulceration of the cecum and large colon have been observed in horses. In ruminants, the mucosa of the forestomachs is unaffected, but typical lesions are present in the abomasum and intestines. Renal tubular necrosis, suppurative pyelonephritis, and petechiation of bladder mucosa are found in cattle.[4] The gut contents are very fluid and contain mucus and shreds of mucosa. Profuse subendocardial hemorrhages are common, and ulceration of the gallbladder mucosa is often observed in sheep. Macroscopic lesions may be minimal in cases that die after a very short course. Histologically, most of the hemorrhages can be attributed to the necrosis of capillaries, although damage to the walls of larger vessels may sometimes be found. Severe intravascular hemolysis has been observed in sheep. Degenerative changes are common in the liver and kidney of animals suffering from arsenic toxicosis, and these changes become more pronounced if the disease course is prolonged. In some cases of chronic poisoning, loss of myelin may be observed in the peripheral nerves, with secondary neural degeneration in the CNS.

The liver is the best organ for assay of acute arsenic poisoning, whereas the kidney may contain high levels in subacute or chronic poisoning. Levels of over 10 to 15 mg/kg wet matter of arsenic trioxide in the kidney or liver are considered to be diagnostic of arsenic poisoning. However, it is probable that many animals die of arsenic poisoning when their hepatic levels are much lower than this. Maximum concentrations of arsenic in tissues occur about 8 hours after ingestion, and animals that survive for 2 to 3 days may have levels as low as 3 mg/kg. Diagnostic levels in the urine and feces are between 10 and 20 mg/kg. Conversely, normal animals that are dipped routinely in arsenical dips may have hepatic levels of the element as high as 8 mg/kg. Levels of 1 to 3 mg/kg are obtained in cattle dying from arsenic poisoning after percutaneous exposure, and levels of over 10 mg/kg are found in cattle that ingest arsenical dip. Assay of the arsenic level in hair may be useful in chronically poisoned animals.

Animals poisoned with **organic arsenicals** show no significant gross pathologic changes. Histologically, degeneration and demyelination of the optic nerves, optic tracts, and peripheral nerves are apparent. The animals maintain tissue levels of arsenic for as long as exposure continues, although the levels fall rapidly during the first 7 days after feeding of the arsenic ceases, and normal levels are not reached for another 7 days. The liver and kidney obtained from pigs dying of roxarsone toxicosis contained an average arsenic content of 2.9 and 1.8 mg/kg (wet weight), respectively.

Samples for Confirmation of Diagnosis
TOXICOLOGY:

- Liver and kidney, segment of stomach/intestine including content, sample of suspected poison, and hair (chronic)

HISTOLOGY:

- Inorganic arsenic: Formalin-fixed stomach, intestine, cecum, large colon, liver, kidney, and peripheral nerve
- Organic arsenic: Formalin-fixed optic nerve and tract and peripheral nerve

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DIFFERENTIAL DIAGNOSIS

Diagnostic confirmation in all arsenic poisoning is by detection of toxic levels of arsenic in animal tissues and fluids.
   Differential diagnosis list:
- **Acute inorganic arsenic toxicosis**
  Bovine malignant catarrhal fever (peracute, gastrointestinal form)
  Lead toxicosis
  Mushroom toxicosis (amatoxins)
  Poisonous plants (bracken, mustards, etc.)
  Salmonellosis
- **Chronic inorganic arsenic toxicosis**
  Parasitism (ostertagiasis, trichostrongylosis, and oesophagostomiasis)
  Starvation
- **Organic arsenical toxicosis**
  Encephalitis
  Mercury (organic) toxicosis
  Salt toxicosis
  Selenium toxicosis
  Tri-ortho-cresyl phosphate or other industrial chemical toxicosis

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TREATMENT

TREATMENT AND PROPHYLAXIS

Treatment and prophylaxis[2,4]
Sodium thiosulfate (20–40 mg/kg intravenously every 8 h; 80 mg/kg orally every 24 h or 30–60 mg/kg orally every 6 h for 3–4 days) (R2)

2,3-Dimercaptopropanol (1.5–5 mg/kg intramuscularly every 4–6 h for 10 days) (R2)

Thioctic acid (50 mg/kg intravenously every 8 h) (R2)

In acute cases, treatment is of little value because of the large amount ingested and the delay between ingestion and the onset of clinical signs. Affected animals are unsuitable for human consumption, so treatment is not usually undertaken. Although BAL has a general beneficial effect and is recommended as a treatment, the drug is quite toxic itself and in the doses required may be associated with death in sheep. It also is associated with a reaction at the injection site that is sometimes serious enough to warrant the animal's destruction.

The most commonly used antidotes are sodium thiosulfate, dimercaptopropanol (BAL), and thioctic acid.[2,4] There is a wide variation in results as well as recommended dose and dosage. A comparison of these antidotes used in experimentally poisoned cattle showed little benefit from sodium thiosulfate administration, and most benefit with a combination of BAL and thioctic acid. Dimercaptosuccinate, a water-soluble analog of dimercaprol, is less toxic than BAL, may be available in the United States, and should be more effective than BAL. The antioxidants zinc, methionine, and cysteine, used with chelation therapy, have been reported to enhance excretion of arsenic in experimental poisoning. Their use may be helpful as adjuncts to recommended chelation therapy.

Further therapy is supportive. Attempts should be made to adsorb the residual arsenic in the gut by administering charcoal (1–4 g/kg orally), and moved through the gastrointestinal tract with the administration of an oil demulcent or osmotic agent like magnesium sulfate. Drastic purgatives should be avoided. Severe dehydration occurs, and outcome improves when supportive treatment includes the provision of ample fluids, preferably by parenteral injection.[4] An adequate supply of drinking water containing electrolytes should be provided, and the animals should be disturbed as little as possible and provided shelter from the sun and elements. Recovering animals should receive a bland diet and high-quality protein.

CONTROL
Arsenical preparations must be handled and stored with care and contamination of feed and pasture avoided. Old products should not be left in abandoned sheds or buildings. Wood treated with chromated copper arsenate should not be used for fences, posts, or buildings inhabited by animals. When treated wood is destroyed, animals should not be allowed access to the ashes, and the ashes should not be spread on the pasture or drylots. Therapeutic preparations containing arsenic should be labeled "Poison" and strict instructions given on dosage, particularly the length of time for which administration should continue. Animals to be dipped in arsenical solutions should be allowed to cool off before dipping, drain properly afterward, and dry before being driven. They should be watered before dipping to prevent them from drinking the dip. Much mortality has occurred when instructions for mixing dip solutions were not closely followed. Dipping solutions containing more arsenic than is safe usually occur when tanks, which have lost water by evaporation, are reconstituted by guesswork. The maximum safe concentration of arsenic trioxide in a dip for cattle is 0.20%.

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MOLYBDENUM TOXICOSIS (MOLYBDENOSIS)

SYNOPSIS

Etiology Ingestion of toxic amounts of molybdenum

Clinical pathology High serum levels of molybdenum, low serum levels of copper

Necropsy lesions No significant lesions

Diagnostic confirmation High levels of molybdenum in feed and blood

Treatment
Primary: Copper salts orally
Supportive: None necessary

Control Dietary supplementation with copper

ETIOLOGY

Molybdenum is an essential element needed by humans and animals for activity of the biological enzymes xanthine oxidase, aldehyde oxidase, and sulfite oxidase.[1] It is involved in a variety of metabolic processes including protein and sulfur metabolism and iron transport. Signs of molybdenum toxicosis may be associated with inhibition of these processes and other enzymes, such as glutaminase and cytochrome oxidase, but many are linked to specific deficiencies in copper-containing enzymes.[1,2] Species variation occurs, with cattle the most susceptible to poisoning, followed by sheep and goats, pigs, and finally horses.[3] The toxic dose varies widely with the intake of sulfate, copper, and other factors.[2,3]

EPIDEMIOLOGY
Occurrence

The major occurrence of molybdenum poisoning is associated with ruminants grazing on pasture growing on molybdenum-rich soils, usually derived from particular geological formations, e.g., the "teart" pastures of Somerset (UK), the United States, and Canada; marine black shales in the UK; pastures containing excess molybdenum intake with or without a marginal deficiency of copper in New Zealand, Canada, Ireland, and Australia.[4] Soil in areas of mining operations, metallurgical industries, paint manufacturers, and refineries may be heavily contaminated with molybdenum, and animals grazing there or ingesting water or plants grown there may develop molybdenum toxicosis.[4-6]

Acute poisoning has occurred in cattle ingesting 7400 mg molybdenum/kg of diet ingested or approximately 30 mg molybdenum/kg BW per day.[2,7] Acute toxicosis occurred in sheep receiving 132 to 137 mg molybdenum/kg for 2 to 3 days.

Chronic toxicosis occurs in cattle receiving only 3 mg molybdenum/kg BW per day.[7] Diets providing less than 3 mg/kg BW are usually considered to be safe, but signs of toxicosis may occur when the diet contains as little as 1 mg/kg BW if the sulfate intake is high and the copper status low; the level of molybdenum at which the interference with the metabolism of copper may occur is 2.4 mg/kg dry matter in the diet.

Forage containing 10 mg/kg must be considered dangerous at all times and, on pasture, affected by aerial contamination levels of 10 to 200 mg/kg may be encountered. Such intakes can be provided by the following:

- The use of molybdenum in fertilizer mixtures to increase nitrogen fixation by legumes may lead to excessive amounts of molybdenum in soils.
- Contamination of pasture by motor oil containing molybdenum as an additive
- Industrial fallouts of 5 to 40 ng/m^3 of air or 2 mg/m^2 per month on pasture

Aerial contamination by fumes from aluminum and steel alloy factories and oil refineries using molybdenum is associated with secondary copper deficiency.

Drinking water may not be as toxic as the same amount in fresh forages. For calves, the minimum toxic concentration in drinking water is between 10 and 50 mg/kg when dietary copper and sulfur intake in the diet is normal.

Risk Factors
Animal Risk Factors

Cattle, sheep, and goats are clinically affected in field outbreaks of the disease and signs are most marked in young growing animals. Cattle are much more susceptible than sheep.[3] Horses and pigs are susceptible to

a lesser extent, presumably because of a decreased absorption and lack of a rumen.[3]

Environmental Risk Factors

The concentration of molybdenum in forage varies with the season; it is highest in the spring and autumn and with the plant species, legumes, and particularly alsike clover taking up molybdenum in much greater quantities than grasses. Soil and plants in pastures and other grazing areas near mining industries or using molybdenum may be contaminated.[4-6]

Transmission

Animals are primarily poisoned by ingesting plants or soil high in molybdenum, but the amount of dietary sulfur/sulfates and copper in the diet plays an integral role.

PATHOGENESIS

Molybdenum, sulfur, and copper are all intimately involved in the development of poisoning. The mechanism of action differs for ruminants and monogastrics. Sulfur or sulfate in the rumen is converted to sulfide, which combines with molybdenum to form four thiomolybdates (mono-, di-, tri-, and tetra-).[2,3,8] In the digestive tract, these thiomolybdates bind to copper forming a cupric–thiomolybdate complex that prevents copper absorption; once systemic, they bind to copper preventing further copper utilization and increasing copper excretion.[2,3,9] In addition, some free molybdenum is absorbed throughout the intestinal tract.[2] Monogastric animals, who lack a rumen, do not form thiomolybdates; instead molybdenum is absorbed beginning with the stomach and continuing throughout the intestinal tract.[9]

Once absorbed molybdenum is rapidly distributed to many body tissues, with the highest concentrations in the liver, kidney, spleen, and bone.[3,10] Excretion is rapid and occurs primarily in the urine and bile (ruminants), with milk a concentration-dependent route in lactating animals.[9,11]

Most signs of molybdenum poisoning result from some form of copper deficiency, either real or functional. The situation is exacerbated by a high intake of sulfur or a low intake of copper. The syndrome of molybdenum intoxication resembles that of copper deficiency, and treatment and prevention by the administration of copper is effective.

Not all signs of molybdenum poisoning, particularly diarrhea, are characteristic of copper deficiency and may represent a specific toxic effect of molybdenum. An identified toxic effect specific to molybdenum occurred in sheep experimentally fed molybdenum. Exostoses and hemorrhages about the long bones developed, as well as separation of the great trochanters of the femur. The lesions appear to be caused by defects in connective tissue at muscle insertion points and by defects in the epiphyseal growth plates.

CLINICAL FINDINGS
Acute Intoxication
Cattle and sheep show anorexia and inappetence, profuse salivation, weakness and progressive ataxia beginning with the hindlimbs, recumbency, and death.[9]

Chronic Intoxication
Cattle, sheep, and goats show the following signs[1,8,9,11]:
- Persistent diarrhea within 8 to 10 days of the animals having access to affected pasture
- Emaciation and a dry coat
- Profound decrease in milk production
- Depigmentation of black hair with the appearance of a red or gray tinge to hair. This may be particularly noticeable around the eyes, giving a bespectacled appearance.
- Intense craving for copper supplement has been noted.
- Young cattle (3 months to 2.5 years) show abnormalities of locomotion, including marked stiffness of the legs and back, difficulty in rising, and great reluctance to move. The gait is suggestive of laminitis but the feet appear normal. The lameness may be caused by the periosteal lesions described earlier. The appetite remains good.

Horses, although rarely affected, show diarrhea and impaction colic. The mortality rate is high.

CLINICAL PATHOLOGY
Blood copper levels are reduced from the normal of 1.0 μg/mL to 0.25 μg/mL. Seasonal variations occur depending on the intake of molybdenum.

Blood molybdenum levels in normal animals are of the order of 0.05 mg/kg and rise to about 0.10 mg/kg when excess molybdenum is ingested. Levels as high as 0.70 and 1.4 mg/kg have been recorded in cattle and horses grazing on pasture contaminated by smelter fumes. On very large intakes of molybdenum cattle, which are clinically normal, may have molybdenum levels of 1000 mg/kg in feces, 45 mg/kg in urine, 10 mg/kg in blood, and 1 mg/kg in milk.

Goats treated with ammonium molybdate orally at 20 mg/kg BW per day for 30 days developed significant declines in the mean values of hemoglobin, PCV, total leukocyte count, total erythrocyte count, and mean corpuscular hemoglobin concentration, with significant increases in neutrophil count and mean corpuscular volume.[1] These did not occur in a similar group treated with molybdenum and copper sulfate (II) pentahydrate.

NECROPSY FINDINGS
There are no gross or histologic findings that characterize the disease, and enteritis is conspicuously absent. The carcass is emaciated and dehydrated and there may be anemia if there is an accompanying copper deficiency. Tissue copper levels will be below normal.

DIFFERENTIAL DIAGNOSIS

Diagnostic diagnosis list:
- Copper toxicosis
- Internal parasitism, e.g., trichostrongylosis, ostertagiasis
- Paratuberculosis
- Acute enteritides including salmonellosis, winter dysentery, and virus diarrhea

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TREATMENT
Effective treatment depends on removing the source of molybdenum and providing copper to the affected animals. The most effective method is to treat affected animals orally with copper sulfate (2 g daily or 5 g weekly for adult cattle and 1.5 g for adult sheep). The diarrhea should stop in 2 to 3 days, and improvement in the other signs is rapid. Care should be used in sheep not to overdose and cause copper toxicoses. In monogastric animals, sulfate may enhance elimination.[9]

TREATMENT AND PROPHYLAXIS

Treatment
Copper sulfate (2 g/day orally for adult cattle; 1.5 g orally for adult sheep × 2–3 days) (R1)

Prophylaxis
Keep Cu : Mo ratio at 4 : 1 and S : Mo ratio < 100 : 1. (R2)

CONTROL
If animals cannot be removed from the source (i.e., grazing on contaminated lands), then copper sulfate should be added to their diet.[6] For long-term control, the recommended ratio of Cu : Mo is 4 : 1 to 10 : 1, and a S : Mo ratio of <100 : 1 is considered safe as opposed to copper accumulation.

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AMITRAZ TOXICOSIS
ETIOLOGY
Amitraz is a topical acaricide and insecticide widely used in most large-animal species including cattle, sheep, goats, and ostriches.[1] It is not labeled for use in horses because they are easily poisoned when amitraz is applied to their skin or accidentally ingested.[1] Most commercial products on the market contain 12.5 to 50% amitraz in a solvent such as xylene and must be diluted before use.[1,2]

PATHOGENESIS
Amitraz is a centrally acting α-2 adrenergic agonist that also inhibits monoamine oxidase and prostaglandin synthesis. It is highly soluble and rapidly absorbed through skin and mucous membranes.[3] Concentration of the dipping fluid, solvent carrier, environmental temperature, and the condition of the skin may influence absorption of the compound, clinical signs, and susceptibility of the animal.

CLINICAL FINDINGS
Clinical signs occur in horses within 12 to 48 hours and include anorexia, depression, sedation, ataxia, incoordination, and large intestine impaction. Resolution of signs may take 7 to 8 days.[1] Equine susceptibility to amitraz is likely caused by prolonged persistence in the body. Salivation, depression, anorexia, ataxia, tremors, and coma are signs attributed to amitraz in other species.

TREATMENT
Decontamination with activated charcoal and a cathartic may be used in an ingestion if clinical signs have not yet occurred. Residual topical amitraz should be removed from affected animals by bathing with soap and tepid water. Further therapy is supportive and includes oral or intravenous fluids, analgesics, and treatment of the impaction colic. The use of α-2 adrenergic antagonists such as yohimbine and atipamezole has been suggested.[1]

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PROPYLENE GLYCOL TOXICOSIS

Propylene glycol is an unlikely poison, but it is used extensively as an oral treatment for acetonemia in cattle and can be associated with poisoning if it is accidentally administered to horses, when mistaken for mineral oil. Dose rates of 3 L to horses of 500 kg BW by stomach tube is associated with an immediate but short duration episode of abdominal pain, sweating, salivation, severe ataxia and depression, and a fetid odor of the feces. Much larger doses (8 L) can be fatal. Moderate-to-severe inflammation of the lining of the gut and edema of the brain are noticeable at necropsy examination.

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PLANT MATERIALS CAUSING PHYSICAL DAMAGE

COLIC IN HORSES FROM INGESTION OF INDIGESTIBLE FIBER IS ASSOCIATED WITH

- Gastric impaction (*Senecio jacobaea*)
- Impaction of the ileocecal valve (*Sorghum* spp.)

RUMINAL IMPACTION IN CATTLE IS ASSOCIATED WITH INGESTION OF CUTTINGS FROM

- *Fraxinus excelsior* (ash tree)
- *Chrysocoma tenuifolia* (bitter weed)
- *Eriocephalus* spp.
- *Pinus taeda* (loblolly pine)
- *Prosopis juliflora* (mesquite)
- *Eremocarpus setigerus* (turkey mullein)

Gastric impaction in pigs is associated with ingestion of *Nicotiana* spp. stalks.

The tough fiber in *Romulea rosea* (onion grass, rosy sandcrocus) is associated with an enzootic problem of bovine intestinal and abomasal impaction by phytobezoar in parts of Australia.[1] Phytobezoars can be a problem wherever indigestible fiber is available to ruminants. Cocoon silk of *Gonometa* spp. (Molopo moth) can be associated with ruminal impaction in cattle that eat foliage of *Acacia erioloba* or *A. mellifera* trees, the preferred habitat for the moth larvae.

Other physical injuries associated with plant material include persistent corneal ulcers from the bristles of *Arctium lappa* (burdock seeds) and ulcers in the mouth from the spines of *Setaria lutescens* (yellow bristle grass) and the awns of *S. geniculata* (prairie foxtail) and *Triticosecale* (triticale varieties).[2] *S. lutescens* carries heavy bristles that are associated with mechanical stomatitis in cattle and horses. *S. geniculata* awns are associated with ulcerative stomatitis and glossitis and gingivitis in horses.[2] Triticale is a hybrid between wheat and rice used mainly for grain production. If it is harvested green as a crop and made into hay the dried awns are irritating to the pharynx and mouth of cattle and horses. Affected horses are slow eaters, refuse hay, and show excess salivation. Clinical signs result in about a week and include cough, mucoid nasal discharge, foul breath, hypersalivation, quidding, and loss of BW. Some horses develop submandibular edema and there are severe ulcerations at the gum–tooth margins, with many awns embedded in the ulcers. The ulcers are very painful and up to 5 cm in diameter at the labial–gingival junction, the lingual frenulum, the base of the lingual dorsum, soft palate, and the sides of the tongue. After careful cleaning, the lesions heal slowly over about 3 weeks.

Grass seed abscesses are frequent when there is a large population of *Stipa* and *Stipagrostis* spp. (spear grass), *Tagetes* spp., *Aristida arenaria* (silver or kerosene grasses), *Opuntia* spp. (prickly pear), and *Hordeum jubatum* (barley grass) in the pasture. The hairs on the plant *Dittrichia graveolens* (stinkwort) are thought to be associated with the fatal enteritis that occurs in sheep eating the plant.

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PLANT TOXINS AFFECTING THE ALIMENTARY TRACT

ANDROMEDOTOXIN

Andromedotoxin (syn. acetylandromedol, grayanotoxin, rhodotoxin) is a resinoid substance, a member of the diterpenoid group of substances, and found in plants of the Ericaceae family including:

Agarista spp.
Agauria salifolia
Clethra arborea
Kalmia spp. (laurels, lambkill)
Ledum spp. (labrador tea)
Leucothoe spp. (sierra laurel, hanahiri)
Lyonia ligustrina (staggerbush)
Menziesia ferruginea (mock azalea)
Pieris (Andromeda) spp.
Rhododendron spp. (rhododendrons and azaleas)

Andromedotoxins, or more commonly grayanotoxins, are found in the flowers, leaves, twigs, and stems of plants in the Ericaceae family.[1-4] More than 25 different grayanotoxin isoforms (e.g., grayanotoxin I, grayanotoxin II, etc.) exist depending on the species of plant.[1] Plants in this family are very poisonous to animals and humans. Cattle, horses, sheep, and goats have all become symptomatic or died shortly after exposure.[1,2] Death occurs most often when livestock or horses have access to clippings thrown into their pastures or drylots. Different grayanotoxin isoforms do not degrade in a similar manner during composting but are not expected to be a risk to animals coming into contact with the waste.[5] Humans are exposed by ingesting honey produced by bees obtaining nectar from rhododendrons (mad honey disease), herbal teas, and other natural products.[1]

The toxins interfere with the function of voltage-gated sodium channels resulting in a continuous state of cell membrane depolarization.[1,2] Clinical signs are related to the gastrointestinal, cardiovascular, nervous, and respiratory systems. Signs generally begin within 3 to 14 hours after the plant or clippings are eaten and include dullness, salivation, projectile vomiting, bloat, repeated swallowing or belching, tenesmus, abdominal pain, a staggering gait, recumbency, convulsions with opisthotonus, tremor, dyspnea, and groaning and bleating. Tachycardia, hypotension, and cardiac arrhythmias occur in some cases. Aspiration pneumonia is a common sequel and is the only common gross necropsy finding. Histopathological changes are limited to minor lesions in the gray matter of the spinal cord.

ANTHRAQUINONE

Anthraquinones are extracted commercially from plants for use as irritant cathartics. Plants growing wild that contain these compounds include:

Cassia occidentalis (syn Senna occidentalis) (coffee senna)
Senna obtusifolia (sicklepod)
C. roemieriana
C. italica
Frangula alnus (alder buckthorn)
Rhamnus spp. (buckthorn)

Horses, pigs, and cattle may be poisoned by *S. occidentalis* seeds that contaminate prepared rations.[6] All of these plants are associated with severe gastroenteritis manifested by diarrhea, often with transitory signs of abdominal pain if the dose is large. Liver damage is a common lesion in experimental and field cases and may dominate the necropsy findings.[6,7] Smaller doses of *Senna* spp. over a period of a week are associated with necrosis of striated muscle fibers characterized by limb weakness, incoordination, dragging the hind toe tips, and eventually paralysis in sternal or lateral recumbency. Necropsy lesions are cardiac and skeletal muscle necrosis, but these have not been shown to be direct effects of anthraquinones.

COLCHICINE

The alkaloid colchicine, found in *Colchicum autumnale* (autumn crocus, meadow saffron) and *Gloriosa superba* (flame or glory lily), is associated with acute fetid diarrhea ± blood), abdominal pain, tenesmus, vomiting, and salivation in sheep, cattle, and pigs.[2,8] Colchicine interferes with mitotic spindle formation, and the rapidly dividing, sensitive cells of the gastrointestinal tract are most frequently affected.[8] Consumption of 8 to 10 g of fresh leaves/kg BW has been associated with severe diarrhea. Mortalities are likely when cattle graze dense patches of *C. autumnale* in pasture or are fed hay containing the plant. Excretion is primarily through the bile with extensive enterohepatic recirculation; a small percentage (10%–30% in humans) is excreted unchanged in the urine. The toxin is excreted in the milk for an unspecified time period.[8] Confirmation of colchicine in the serum, urine, or milk can be made with several laboratory methods; liquid chromatography/mass spectrometry is the most current.[2,8] Treatment is limited as sudden death is the normal result, but would include multiple doses of activated charcoal and intravenous fluid and electrolyte therapy. In human cases, colchicine-specific antibodies (colchicine-specific Fab fragments) have been used successfully.[8] At necropsy, subserosal hemorrhages and gastroenteritis are evident.

IRRITANT DITERPENOIDS

The two important irritant diterpenoids are 12-deoxyphorbol found in *Euphorbia* spp. (spurges) and simplexin, an irritant diterpenoid daphnane ester found in *Pimelia simplex, P. trichostachya,* and others.

Poisoning by **12-deoxyphorbol** is associated with a syndrome of stomatitis and enteritis presumably related to the irritant nature of the latex sap.[9] Cattle generally avoid leafy spurge (*E. esula*), apparently because they develop a conditioned aversion to it, but sheep and goats will graze it.

Simplexin is primarily associated with a syndrome of congestive heart failure with diarrhea and anemia in cattle in eastern Australia called St. George disease or Marree disease.[10,11] The syndrome is only rarely reported in horses.[12] St. George or Marree disease is associated with ingestion of *P. trichostachya, P. simplex, P. contunua,* and *P. elongata* (desert rice flower, flaxweed, wild flax, mustard weed, broom bush) and is characterized clinically by massive edema under the jaw and down the brisket, distended jugular veins, persistent diarrhea, anemia, loss of condition, and death. Ingested simplexin is associated with constriction of pulmonary venules, pulmonary venous hypertension, and right heart failure.[12] Diarrhea is caused by direct irritation of the intestinal lining. Inhalation of the powdered plant is associated with the pulmonary–cardiac lesion only. A severe anemia caused by

a significant hemodilution of unknown pathogenesis occurs. The usual field picture is that of cattle looking for feed between old, dry flaxweed plants and inhaling it, so the pulmonary–cardiac form is most common in summer. Experimentally, it has been possible to produce two forms of the disease: the subacute with diarrhea, weakness, and anemia as the predominant signs, and the chronic form characterized by circulatory failure as evidenced by anasarca, hydrothorax, and cardiac dilatation.

Severe diarrhea and colic without other cardiac effects have occurred in cattle, sheep, and horses consuming *Pimelea* plant material.[11,12] The difference between the signs present in St. George disease and acute diarrhea/colic, among other things, is likely related to lower concentrations of simplexin in various species of *Pimelea*.[10,11]

IRRITANT OILS

Irritant oils in plants are associated with gastroenteritis, salivation, oral mucosal lesions, abdominal pain, diarrhea, and sometimes dysentery. Plants known to contain these oils include:

Actaea spicata (baneberry)
Artemisia filifolia
Barbarea vulgaris (yellow rocket)
Bryonia dioica (white bryony)
Croton spp. (croton)
Cryptocarya pleurosperma (poison walnut; contains cryptopleurine and pleurospermine)
D. graveolens (stinkwort)
Inula conyza (ploughman's spikenard)
Sambucus spp. (elders, elderberry)

Bryonin is an irritant oil found in the roots and seeds of *B. dioica* (white bryony or British mandrake) and is associated with a syndrome of depression, dyspnea, diarrhea, polyuria, stumbling gait, tremor, recumbency, and convulsions. Sweating, agalactia, and sudden death are also recorded.

LYCORINE

Lycorine, an alkaloid found in the bulbs or roots of many garden plants, e.g., *Amaryllis, Clivia, Daffodil, Lycoris, Narcissus,* and *Nerine* spp., is associated with salivation, vomiting, and diarrhea when eaten by animals.

PODOPHYLLIN POISONING

Podophyllin, a resin found in *Podophyllum peltatum,* is associated with enteritis with excessive salivation and severe, acute diarrhea.

PROTOANEMONIN POISONING

Protoanemonin exists in the plant as a glucoside ranunculin, which releases protoanemonin when the leaves are macerated. Plants containing ranunculin include:

Anemone spp.
Caltha palustris
Clematis spp.
Pulsatilla spp.
Ranunculus spp. (buttercups)
Thalictrum spp.
Trollius spp.

Ingestion of these plants may be associated with salivation, stomatitis, abdominal pain, diarrhea, dysentery, hematuria, blindness, ataxia, and convulsions.

TOXALBUMINS (LECTINS)

Plants known to be associated with toxalbumin poisoning are:

Abrus precatorius (abrin is toxin; jequirity, rosary pea, Crab's eye)[15]
Adenia spp.
Jatropha curcas (purging nut, Barbados nut)
Phaseolus vulgaris containing phytohemagglutinin (*Phaseolus* hemolytic agent)
Robinia pseudoacacia (robinin is toxin; black locust, false acacia)[2,16]
Ricinus communis (ricin is toxin; castor bean, wonder tree)[2,13,14]
Wisteria sinensis (wisteria, Chinese wisteria)

Lectins are important glycoproteins in human nutrition because of their common occurrence in foods. Many of the toxalbumins, however, are poisonous to animals. Horses appear to be the most susceptible to toxicosis followed by sheep, cattle, and pigs.[2,13,14] Toxalbumins are associated with inhibition of protein synthesis and damage to the gut epithelium, leading to defective digestion and absorption and increased permeability of the intestinal mucosa.[13,15] The toxins are present in foliage and seeds but are concentrated in the latter.[14] The clinical syndrome includes inappetence, vomiting, severe diarrhea, dehydration, dyspnea, rapid weight loss, recumbency, and death in most cases. Neurologic signs including depression, weakness, and encephalopathy may occur.[2,15,16] PCV, serum liver enzymes, and blood urea nitrogen (BUN) and creatinine levels are elevated.[14] Necropsy lesions include abomasal and intestinal hemorrhage and erosions, hepatocyte and renal tubular injury, pulmonary hemorrhage, edema, and emphysema.

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PLANTS (UNIDENTIFIED TOXINS) AFFECTING THE GASTROINTESTINAL TRACT

The following plants affect the gastrointestinal tract in some manner. Toxins are believed to be involved but have not yet been identified.

DIARRHEA: WITHOUT GASTROENTERITIS AS A LESION

Anredera cordifolia (lamb's tail)
Blechnum spp. (bungwall fern)
Bulbine bulbosa (native leek)
Cadaba rotundifolia
Centaurium spp.
Chaerophyllum sylvestre
Cichorium intybus (chicory)
Chlorozophora spp.
Datisca glomerata (Durango root)
Dichrocephalia chrysanthemifolia
Juncus inflexus (blue rush)
Linum catharticum (purging flax)
Mentha australis (native mint)
Pipturus argenteus
Philydrum languinosum (woolly water lily)
Polygala klotzchii
Salvia coccinea (red salvia)
Synadenium arborescens (African milk bush)

DIARRHEA: WITH GASTROENTERITIS AS A LESION, OFTEN WITH ABDOMINAL PAIN AND INCOORDINATION, SOMETIMES WITH DYSENTERY AND VOMITING

Azadirachta indica (neem)
Brunfelsia australis (*B. bonodora*; yesterday, today, and tomorrow)
Buxus sempervirens (common box bush)
Centaurium beyrichii (rock centaury)
Chrysocoma tenuifolia (bitter bush)
Cissus quadrangularis
Cuscuta spp. (dodder)
Datisca glomerata (Durango root)
Dichrocephalia chrysanthemifolia
Dipcadi glaucum (poison onion)
Diplocyclos palmatus
Diplolophium africanum
Drymaria spp.
Ephedra viridis
Fagus sylvatica (European beech tree)
Galanthus nivalis (snowdrop)
Gymnocladus dioica (Kentucky coffee tree)
Ligustrum vulgare (privet hedge)
Ludwigia peploides (water primrose)

Ornithogalum longibracteatum (chincherinchee)
Robinia pseudoacacia (black locust, locust tree)
Rudbeckia spp.
Sapium sebiferum (Chinese tallow wood)
Scrophularia aquatica (water betony)
Sisyrinchium spp. (scour weed)
Sium angustifolium
Tulipa spp. (tulips)
Turraea robusta

DYSPHAGIA

Buxus sempervirens (box tree)
Descurainia pinnata (tansy mustard); difficulty in swallowing caused by paralysis of the tongue and the masseter and pharyngeal muscles is accompanied by spasmodic contractions of neck muscles, causing head bobbing in sheep, and may occur after sheep ingest *D. pinnata*; there is doubt about the relationship.[3]
Prosopis juliflora

ESOPHAGEAL ULCERATION

Crotalaria aridicola (horses only)
C. medicaginea (horses only)

SALIVATION WITH OR WITHOUT STOMATITIS

Arenaris serpyllifolia (thyme-leaved sandwort)
Puccinia graminis
Scabiosa succisa (devil's bit)

VOMITING

Cephaelis ipecacuanha
Tamus communis (black bryony; plus colic, paralysis, and death)

SLAFRAMINE TOXICOSIS (SLOBBERS, BLACK PATCH DISEASE)

SYNOPSIS

Etiology Contamination of leguminous pasture plants with slaframine, a mycotoxin produced by the fungus *Rhizoctonia leguminicola*

Epidemiology Ingestion of slaframine from contaminated hay or pasture is associated with a syndrome identified as "slobbers"; the term *black patch disease* refers to the discoloration of pasture or stored hay.

Clinical pathology Nothing in particular

Lesions The primary clinical sign in horses and ruminants is profuse salivation occurring within 4–6 h of ingestion.

Diagnostic confirmation The diagnosis is made based on the clinical sign of profuse salivation after ingestion of contaminated hay or pasture. The toxin can be identified

in legumes by gas chromatography/mass spectrometry.

Treatment Treatment is generally not needed. Signs resolve 24–48 h after removal from contaminated pasture or hay.

Control Remove animals from contaminated food source, dispose of hay, and plant chemically treated seeds.

ETIOLOGY

Slaframine is an indolizidine alkaloid produced by the fungus *Rhizoctonia leguminicola* that contaminates leguminous pasture plants, in particular red clover (*Trifolium pretense*) and *Medicago sativa* (alfalfa or lucerne). Swainsonine, the phytotoxin found in *Swainsona* and *Astragalus* spp., is very similar to slaframine and has also been isolated from this fungus. Infested plants carry bronze to black spots or rings, and the hay is usually discolored by black patches on the stems and leaves.

EPIDEMIOLOGY

Occurrence

Ingestion of slaframine is associated with a syndrome, identified colloquially as "slobbers." Horses and cattle are primarily affected, although sheep, goats, llamas, and swine have also developed signs of toxicosis after ingestion.[1-3] Slaframine poisoning has been reported most often in the United States, but domestic animals in South America (Uruguay, Argentina, and Brazil), Japan, France, and the Netherlands have been affected.[2,4] The fungus *R. leguminicola* grows well in hot, humid weather and remains active in stored hay for at least 10 months and perhaps as long as 2 years.[2,4]

Risk Factors

Animal Risk Factors

There are no animal risk factors.

Environmental Risk Factors

The fungus grows well in hot, humid weather and survives growth cycles once the pasture or field is contaminated.[2]

Farm or Premise Risk Factors

Intoxication is primarily associated with ingestion of contaminated red clover or alfalfa, either in the field or stored hay, but other legumes such as white clover, alsike clover, soy beans, kudzu, cowpea, blue lupine, and black medic can become infected under the right weather conditions.[4] The fungus appears as black patches or rings in the pasture or black to brownish discolored areas on the plant stems or leaves.[1,5]

Transmission

Animals are intoxicated by grazing on pastures or eating hay infected with *R. leguminicola*. The fungus is seedborne and contaminates hay and pasture in this manner.[1]

PATHOGENESIS

Slaframine, a mycotoxin, undergoes metabolism in the liver into 6-ketoimine.[2,5] Structurally, ketoimine is very similar to acetylcholine, a parasympathetic neurotransmitter. Pharmacologically, ketoimine is a cholinergic agonist with action at the muscarinic receptors. Stimulation of muscarinic receptors by slaframine results in stimulation of exocrine glands, in particular the salivary glands and pancreas.[1,2] Swainsonine, another alkaloid produced by *R. leguminicola,* may also be involved with the production of some of the clinical signs.[1,5]

CLINICAL FINDINGS

Horses

Hypersalivation (and thus the term *slobbers*) is most frequent and often the only sign observed.[1,2,4] Other signs such as anorexia, diarrhea, polyuria, epiphora, and abortion have been reported but are uncommon.[2,4] Salivation occurs 4 to 6 hours after ingestion and lasts for 24 to 48 hours after the horses have been removed from contaminated pastures or hay.[1]

Ruminants

Hypersalivation occurs in ruminants as well but is often accompanied by decreased milk production, epiphora, and piloerection.[1,2] Other less common signs are polyuria, bloat, dyspnea, and stiffness. Occurrence and regressions of signs is similar to horses.

Swine

Vomiting, dyspnea, and stiffness have been reported.

NECROPSY FINDINGS

No necropsy lesions are recorded.

DIFFERENTIAL DIAGNOSIS

The diagnosis is generally made based on the clinical sign of hypersalivation and consumption of contaminated hay or pasture. The toxin can be identified in hay by gas chromatography/mass spectrometry.[4]

Differential diagnosis list:

Horses

Cholinesterase toxicosis (e.g., carbamates [imidocarb], organophosphorus insecticides)

Dental abnormalities

Esophageal choke

Foreign body (oral cavity, plant awns in hay)

Glossitis

Other infectious diseases (rabies, botulism, etc.)

Trauma

Vesicular stomatitis virus

Ruminants

Bluetongue virus

Caterpillar hairs (*Thaumetopoea processionea,* oak processionary caterpillar)

Cholinesterase toxicosis (e.g., carbamates [imidocarb], organophosphorus insecticides)

Food-and-mouth disease

Foreign body (oral cavity, plant awns in hay)

Vesicular stomatitis

TREATMENT

No treatment other than removing animals from the contaminated source is generally needed.[2,4] Atropine may be used to reverse hypersalivation but must be used with caution in horses and ruminants.[2]

CONTROL

The presence of the fungus *R. leguminicola* cannot be controlled once the pastures and/or hay are contaminated. Grazing animals should be removed from contaminated pasture, contaminated hay disposed, and seeds chemically treated before planting.[4]

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CANTHARIDIN TOXICOSIS (BLISTER BEETLE POISONING, CANTHARIASIS)

SYNOPSIS

Etiology Blister beetle (*Epicauta occidentalis, E. temexa,* etc.)

Epidemiology Cantharidin, the toxin present in blister beetles, is incorporated into alfalfa hay and ingested by animals

Clinical pathology Hemoconcentration, azotemia, profound hypomagnesaemia and hypocalcaemia, hematuria, hyposthenuria

Lesions Oral and gastrointestinal ulcers and erosions

Diagnostic confirmation History, presence of beetles in hay, GCMS or LCMS using urine, blood, gastrointestinal contents, and feed

Treatment Activated charcoal, intravenous fluids, electrolyte replacement as needed, analgesics, gastrointestinal protectants

Control Know beetles in area, examine hay, do not harvest infested fields.

GCMS, gas chromatography-mass spectrometry; LCMS, liquid chromatography-mass spectrometry.

ETIOLOGY

Cantharidin toxicosis has been reported in horses as well as a number of other species including emu, sheep, goats, and cattle.[1,2] Horses are more susceptible and generally poisoned by the consumption of blister beetles (*Epicauta* spp.) present in hay. Cantharidin, a potent vesicant, is found in the hemolymph and leg joints of blister beetles.[3] There are over 200 named species of the beetle, and the most common association with toxicosis in horses are the three striped blister beetles *E. occidentalis* and *E. temexa.*

EPIDEMIOLOGY

Occurrence

Blister beetles feed on flowering foliage, primarily alfalfa, and are incorporated into hay when it is harvested. Cantharidin is stable in the environment and persists for extended time periods. Toxicosis was originally confined to the Southern states, but outbreaks now occur elsewhere because of the widespread shipment of alfalfa hay, and occasionally weedy meadow hay, infested with the beetles.

Risk Factors

The greatest risk factor for horses is the ingestion of blister beetle–contaminated hay. The beetles contain cantharidin, and administration of 1 g of ground beetles by nasogastric tube is fatal to a pony. The ingested lethal amount in adult horses is 0.5 to 1 mg/kg or about 4 to 6 g of dried beetles.[2,3] The cantharidin content of the beetles varies widely (0.77%–3.31% dry weight) between species, and male beetles contain more toxin than females.

Transmission

Whole or crushed blister beetles can be incorporated into hay and fed to horses and other livestock. It is possible that cantharidin released from crushed beetles may contaminate hay without any evidence of their presence.

PATHOGENESIS

The mechanism of action of cantharidin is not well established but may include inhibition of phosphatase 2A and protein mitochondrial damage from inhibition of enzymes responsible for active transport.[1,3]

Cantharidin is rapidly absorbed across all mucous membranes and to some extent the skin. It produces a strong irritant effect on the esophagus, stomach, and intestines. Once absorbed it is transferred to several body organs in which it produces systemic effects. It is not metabolized but is excreted unchanged in the urine where the irritant effect continues in the bladder, ureters, and urethra.[3]

CLINICAL FINDINGS

Clinical signs are dose dependent. Horses ingesting large amounts may die within 4

hours of ingestion. The ingestion of smaller doses may result in gastroenteritis (anorexia, diarrhea ± blood and/or mucus, severe colic), myocarditis (tachycardia, decreased capillary refill), nephritis (polyuria, oliguria), cystitis, or urethritis.[1,3,4] Generalized systemic signs include hyperthermia, depression, dehydration, sweating, synchronous diaphragmatic flutter, dyspnea, and rales. Death occurs in approximately 50% of cases. Prognosis is good for those horses surviving 7 days or more.[3]

CLINICAL PATHOLOGY

Serum protein and PCV will be elevated, indicating hemoconcentration, dehydration, and shock. Other laboratory abnormalities include an elevation in BUN, profound hypocalcemia and hypomagnesemia, hyposthenuria, and hematuria.[1,3]

NECROPSY FINDINGS

Vesiculating gastropathy of the gastric squamous mucosa is highly diagnostic, but no necropsy findings occur in many cases. Mass spectrometric and gas or liquid chromatographic methods facilitate detection of cantharidin in field specimens of blood, urine, stomach and intestinal contents, and feed. Cantharidin is rapidly excreted and may not be present in samples taken more than 4 to 5 days after ingestion.[3]

DIFFERENTIAL DIAGNOSIS

Differential diagnosis list:
- Arsenic toxicosis
- Cyanobacteria toxicosis
- Ionophore (monensin) toxicosis
- Colic (impaction and tympanic)
- Gastrointestinal enteriditis (colitis, proximal enteritis, peritonitis)

TREATMENT

There is no antidote and treatment is symptomatic. In early cases, activated charcoal or smectite may be used to decrease absorption of cantharidin.[1,5] The use of mineral oil is not recommended because it may actually increase cantharidin absorption and worsen morbidity.[1,2] Intravenous fluid therapy should be used to correct fluid and electrolyte deficits, with specific attention to calcium and magnesium supplementation.[1,5] Analgesics and gastrointestinal protectants should be used as needed. Broad-spectrum antibiotics may be used in animals with gastrointestinal erosions; the use of nephrotoxic antibiotics is contraindicated.

TREATMENT AND PROPHYLAXIS

Activated charcoal (1–3 g/kg per nasogastric × 1) (R2)

Mineral oil (4–6 L per nasogastric tube × 1) (R4)

Furosemide (1 mg/kg intramuscularly or intravenously every 6 h) (R3)

Sucralfate (20 mg/kg orally every 6–8 h) (R1)

CONTROL

Veterinarians should be aware of the presence of blister beetles in their area, and infested fields should not be harvested. Hay purchased from unknown sources should be inspected for the beetles, although cantharidin may still be present in the absence of beetles.

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Neoplasms of the Alimentary Tract

MOUTH

Oral neoplasms in ruminants, other than viral papillomas, may be associated with heavy bracken intake. The tumors are usually squamous cell carcinomas arising from the gums and cause interference with mastication. They are most common in aged animals and probably arise from alveolar epithelium after periodontitis has caused chronic hyperplasia. Sporadic occurrences of other tumors, e.g., adenocarcinoma, cause obvious local swelling and dysphagia.

PHARYNX AND ESOPHAGUS

Papillomas sometimes involve the pharynx, esophagus, esophageal groove, and reticulum and cause chronic ruminal tympany in cattle. A high incidence of malignant neoplasia affecting the pharynx, esophagus, and rumen has been recorded in one area in South Africa. The tumors were multicentric in origin and showed evidence of malignancy on histologic examination. The clinical disease was chronic and confined to adult animals, with persistent, moderate tympany of the rumen and progressive emaciation as typical signs. A similar occurrence has been recorded in cattle in western Scotland and

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related to the long-term consumption of bracken. The tumors were squamous cell carcinoma in the pharynx and dorsal esophagus. The principal clinical abnormality was difficulty in eating and swallowing. Many of the carcinomas arise in preexisting papillomas, which are associated with a virus infection. The carcinomas occur only in cattle more than 6 years of age.

STOMACH AND RUMEN

Squamous cell carcinomas occasionally develop in the mouth and stomach of horses and the rumen of cattle. In the stomach of the horse, they occur in the cardiac portion and may cause obscure indigestion syndromes, lack of appetite, weight loss, anemia, obstruction of the lower esophagus, dysphagia, colic, and occasionally chronic diarrhea. Also, a tumor may ulcerate to terminate with perforation of the stomach wall and the development of peritonitis. Metastases may spread to abdominal and thoracic cavities with an accumulation of fluid. Subcutaneous edema is a common accompanying sign. There may also be pleural effusion caused by metastases in the pleura. Metastases in the female genital tract have also been noted. Most affected animals are euthanized because of anorexia and chronic weight loss. Large masses of metastatic tumor tissue may be palpable on rectal examination. In such cases an examination of paracentesis fluid sample cells should be valuable.

Lymphoma in horses is classified into multicentric, alimentary, mediastinal, cutaneous, and solitary tumors of extranodal sites. The alimentary form accounts for approximately 19% of the equine lymphoma cases and is often manifested by chronic diarrhea caused by massive infiltration of the intestinal wall.[1] There is severe weight loss, even in the absence of diarrhea in some cases, usually a large appetite and often severe ascites, and anasarca and sometimes colic. The same signs are recorded in a case of mesothelioma in a horse. The oral glucose absorption test is abnormal with a poor absorption response. Rectal examination may reveal large masses of hard nodular tissue, and hematological examination may be of assistance in diagnosis. Pseudodiverticula or intestinal obstruction may develop in the small intestine associated with tumor tissue.[2,3] Paracentesis and examination of cells in the fluid for the presence of mitotic figures is an essential part of an examination in suspected cases of neoplasia in the abdominal cavity. Nasal fibrogastroscopy is an obvious technique for visualizing proximally located tumors but is limited because standard instruments are usually not long enough. The course of this disease in horses is quite variable, with the period of illness lasting from 3 weeks to 3 months.

In a large case series from Brazil, the alimentary tract was the most common

location for tumor development (comprising 24% of 586 tumors), with squamous cell carcinoma of the upper gastrointestinal tract predominating.[4] Lesion locations were preferentially located at the base of the tongue, in the esophagus, and adjacent to the cardia in the ruminal wall. Lesion location was typically associated with clinical signs, including dysphagia and coughing for proximal tumors and bloating for tumors in the dital esophagus or ruminal wall.[5] Almost all affected cattle had access to bracken fern (*Pteridium aquilinum*), and it was speculated that chronic bracken fern ingestion was the cause for the tumors. Small numbers of lingual fibroma, abomasal adenoma, small-intestinal adenocarcinoma, ruminal fibrosarcoma, peritoneal mesothelioma, peritoneal fibroma, and anal squamous cell carcinoma were also reported. Ruminal tumors in cattle include papilloma/fibropapilloma, and bovine papillomavirus-1, -2, and -5 were associated with some of these lesions.[6] Squamous cell carcinoma of the reticulum with metastasis to the liver has been reported in a Simmental cow.[7] Although most ruminal tumors are small, if large enough they may obstruct the cardia and cause chronic tympany.

Small omasal and abomasal papillomas have been reported in 1-week-old calves and were associated with papillomavirus infection.[8] In lymphomatosis of cattle, there is frequently gross involvement in the abomasal wall causing persistent diarrhea. Ulceration, hemorrhage, and pyloric obstruction may also occur.

INTESTINES

A higher than normal rate of occurrence of carcinoma of the small intestine has been recorded in sheep in Iceland, Norway, and New Zealand and in cows only in New Zealand. A series of intestinal carcinomas is also recorded in Europe and another series in Australia. The tumors in the Australian series were located at abattoirs and were causing intestinal stenosis. Metastasis to regional lymph nodes occurred readily. In New Zealand there appeared to be a much higher prevalence in British-breed ewes (0.9%–0.15%) compared with Merino and Corriedale ewes (0.2%–0.4%), and a report of intestinal adenocarcinomas in three generations of sheep is suggestive of a genetic predisposition.[9] Significantly higher tumor rates were observed in sheep that had been pastured on foodstuffs sprayed recently with phenoxy or picolinic acid herbicides. The use of the herbicides 2,4-D, 2,4,5-T, MCPA, piclorum, and clopyralid has been associated with an increased incidence of these tumors. A higher prevalence in sheep kept at higher stocking rates was also suggested.

Occasional tumors of the intestine are recorded in abattoir findings, but they can cause clinical signs such as chronic bloat and intermittent diarrhea in cattle, persistent colic caused by partial intestinal obstruction in horses, and anorexia and a distended abdomen in sheep. A series of cases of lymphoma in horses was characterized by malabsorption without diarrhea but with some cases of anemia.

Occasional tumors recorded as causing colic in horses include an intramural ganglioneuroma occluding the jejunum, a jejunal myxoma that resulted in jejunoileocecal intussusception,[10] a stromal tumor in the cecum[11] or colon,[12] an intraluminal leiomyoma causing an intussusception of the small colon, a granulosa cell tumor of an ovary causing external pressure and occlusion of a small colon, and a ganglioneuroma in the small colon.[13] A juvenile granulosa cell tumor in a weanling filly caused a fatal volvulus and severe continuous colic. Anorexia, weight loss, abdominal distension, and constant chewing and swallowing movements are the prominent signs in gastric leiomyoma and squamous cell carcinoma. Leiomyoma may also be confined totally to the omentum and cause colic because of its size or excessive tension on the omentum.[14] Metastases in the peritoneal cavity are palpable in some cases. Leiomyosarcomas have caused chronic intermittent colic caused by constriction of the duodenum and partial intestinal obstruction. A colonic adenocarcinoma has caused weight loss, intermittent colic, poor appetite and scant feces, and a mass palpable in the abdomen.

Carcinoma of the stomach, small intestine, and colon are occasionally encountered in pot-bellied pigs.[15,16]

Tumors of the anus are rare; a mucoepidermoid carcinoma is recorded in a goat, but most tumors of the perineal area are anogenital papillomata. A rectal carcinoma has been reported in an aged Holstein cow.[17]

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TUMORS OF THE PERITONEUM

Primary tumors of the peritoneum are rare. Most tumors of the peritoneum occur by metastasis from adjacent organs, such as with gastric squamous cell carcinoma, or disseminated disease such as lymphosarcoma. Primary tumors include leiomyomatosis and mesothelioma.

Disseminated peritoneal leiomyomatosis has been reported to occur in a mature Quarter Horse. Clinical findings included inappetence, weight loss, intermittent fever, chronic abdominal pain, and enlargement of the abdomen. Rectal examination revealed a prominent, firm, smooth-walled mass in the ventral aspect of the abdomen. Transabdominal ultrasonography was used to detect the mass, which was a friable, polycystic structure occupying a large portion of the abdominal cavity and weighing 34 kg. The mass was removed and recovery was complete.

Mesothelioma has been reported in cattle and goats,[1] predominantly in the peritoneal cavity, but mesothelioma can also occur in the pleural cavity and the vagina of adult cattle. The cause of mesothelioma in cattle is unknown, but pleural mesothelioma in humans is associated with asbestos exposure. One report suggested that the frequency of diagnosis in cattle is increasing. All ages of cattle can be affected with peritoneal mesothelioma, but affected animals are typically young, with fetal and neonatal cases also being reported. Calves and adult cattle most frequently present with moderate abdominal distension. Other presenting signs include scrotal edema in intact males and ventral pitting edema. Occasionally, small 2- to 20-mm, well-demarcated "bumps" can be felt on all serosal surfaces during palpation per rectum in adult cattle. Peritoneal fluid is easily obtained by ventral abdominal paracentesis and has the characteristics of a modified transudate with a moderate to marked increase in phagocytically active mesothelial cells. Definitive diagnosis is made during a right-sided exploratory laparotomy, in which numerous raised, white, and well-demarcated masses are palpated on all serosal surfaces, with copious abdominal fluid present. Biopsy of these masses and microscopic examination confirms the presumptive diagnosis of mesothelioma. Extensive peritoneal mesothelioma is fatal and there is no known treatment. All cases reported have been sporadic, and there is no apparent association with asbestos or other toxic agent in cattle.

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Congenital Defects of the Alimentary Tract

HARELIP AND CLEFT PALATE

Harelip may be unilateral or bilateral and may involve only the lip or extend to the

nostril. It may be associated with cleft palate and cause dysphagia and nasal regurgitation of milk and food, and a risk of inhalation pneumonia. It may be inherited or a result from poisoning of lambs with *Veratrum californicum*. Cleft palate is difficult to correct surgically, especially in foals, in which it is a common congenital defect. Cleft palate (palatoschisis) is a common inherited defect in calves and is described later.

ATRESIA OF THE SALIVARY DUCTS

Congenital atresia of salivary ducts usually results in distension of the gland followed by atrophy. Rarely the gland may continue secreting, resulting in a gross distension of the duct.

AGNATHIA, MICROGNATHIA, AND BRACHYGNATHIA

These are variations of a developmental deficiency of the mandible, which is relatively common in sheep. The mandible and its associated structures are partially or completely absent. Single cases of a similar defect, combined with cleft palate, are recorded in calves.

Brachygnathia is an abnormal shortening of the mandible, resulting in malocclusion of the maxillary and mandibular dental arcades and creating the appearance of a maxillary overbite. It is considered to be a congenital abnormality but may be acquired within the first few months of life. The incisive malocclusion is of little consequence to the nursing foal but can affect the ability to prehend and masticate as the animal matures. It is not known to spontaneously regress, and surgical intervention is necessary to correct the malocclusion.

The cause may be genetic or environmental. Some reports indicate a genetic influence but the mode of inheritance is controversial. One report suggests that brachygnathia in Angus calves was transmitted by a single autosomal recessive gene, but such mode of inheritance has not been supported in other studies. In a series of 20 horses with brachygnathia the amount of disparity between the mandible and premaxilla varied between 0.75 and 3.0 cm. Surgical correction of the abnormality resulted in improved incisive occlusion. Complete correction of the malocclusion was more likely to occur if foals were treated before 6 months of age.

PERSISTENCE OF THE RIGHT AORTIC ARCH

Persistence of the right aortic arch as a fibrous band may occlude the esophagus and cause signs of obstruction, particularly chronic bloat in young calves.

CHOANAL ATRESIA

Failure of the bucconasal membrane to rupture during fetal life prevents the animal breathing through the nostrils. The membrane separates the alimentary tract and the nasal cavities in the pharynx. It is incompatible with life in foals, lambs, and llama and alpaca crias, the species in which it is identified. The defect is usually bilateral; a unilateral lesion is tolerable. Surgical correction is likely to be only partially effective.

CONGENITAL ATRESIA OF THE INTESTINE AND ANUS

Congenital intestinal atresia is characterized by the complete closure of some segment of the intestinal tract. Intestinal atresia has been reported in calves, lambs, foals, and piglets, and the affected newborn usually dies of autointoxication within a few days of birth. The incidence of intestinal atresia in 31 Irish dairy herds monitored over 1 year was 0.3% of all calves born.

INTESTINAL ATRESIAS

Congenital atresia of the intestine can be differentiated from retention of meconium in foals, and rarely calves, by the passage of some fecal color in the latter. Animals with intestinal atresia die at about 7 to 19 days of age unless the defect is corrected surgically. The intestine is grossly distended by then, and the abdomen is obviously swollen as a result. There is marked absence of feces.

Intestinal atresias have been classified into type I (membrane atresia caused by a diaphragm or membrane), type II (cord atresia caused by blind ends joined by a small cord of fibrous or muscular tissue or both, with or without mesentery), and type III (blind-end atresia, caused by absence of a segment of the intestine, with disconnected blind ends and a gap in the mesentery, and often a short small intestine).

Atresia of the ileum and colon is probably conditioned by inheritance in Swedish Highland cattle.

ATRESIA OF THE TERMINAL COLON

Atresia of the terminal colon occurs in foals, especially those of the Overo breed; the ileum and colon are affected in calves and the small intestine in lambs. Atresia coli has been reported in Holstein, Ayrshire, Shorthorn, Simmental, Hereford, Angus, and Maine Anjou breeds and in crossbred cattle. In one dairy herd over a 10-year period the overall incidence of atresia coli in calves was 0.76%. All the affected calves were related to one another, some were inbred, and the frequency was higher in males than females. Some affected calves were aborted or born dead at term. More calves were born with atresia coli from dams in which pregnancy was diagnosed before 41 days of gestation

than from dams diagnosed as pregnant at a later date.

It is suggested that atresia coli in calves has an inherited basis and that affected calves are homozygous recessives for the defective allele for atresia coli. This is supported by planned matings between putative carrier sires and putative carrier dams. The estimated minimum gene frequency of atresia coli in cattle is 0.026, and it is thought that the defective allele for atresia coli is at high frequency in Holstein cattle in the United States. It is also plausible that early pregnancy diagnosis by palpating the amniotic sac before 40 days of gestation may be a contributing factor, but it is not essential for all cases. Intestinal atresia can be produced experimentally by terminating the mesenteric blood supply to some parts of the intestine during development.

In atresia coli, the abdomen may be grossly distended before birth when the defect is in the small intestine, and the distension may interfere with normal parturition. In defects of the large intestine, distension usually occurs after birth. In these the anus is normal, and the part of the intestine caudal to the obstructed section may be normal or absent. The principal clinical findings are depression, anorexia, and abdominal distension. Frequently the owner has not seen the calf pass meconium or feces. Thick mucus may be passed through the anus if it is patent or through the vagina in heifers with concomitant rectovaginal fistula. In many cases the animal has not sucked since the first day, and 5- to 6-day-old animals are very weak and recumbent. The intestine may rupture and acute diffuse peritonitis develop. Intestinal segmental atresia has been produced experimentally by occluding the blood supply to the intestine in fetal lambs. In one large series of congenital defects in calves the most common site of atresia was the midportion of the spiral loop of colon. The passage of a rectal tube or the infusion of barium and radiography may assist in the detection of atresia of the intestine, but care must be exercised during this procedure or the rectum and descending colon may be perforated. There are usually large quantities of thick tenacious mucus in the rectum with no evidence of meconium or feces. In the latter case only exploratory laparotomy can reveal the extent and nature of the defect. The differential diagnosis of atresia coli in calves includes acute intestinal obstructions such as volvulus and intussusception, diffuse peritonitis, and septicemia. **The presence of feces in the rectum rules out the presence of atresia coli.**

Surgical repair appears to be a satisfactory outcome in 30% to 50% of cases, and may be better with placement of a colostomy or cecostomy rather than a colocolic anastamosis.[1-3] In a series of intestinal atresia in calves admitted to a veterinary teaching hospital over a period of 10 years, the

survival rate was influenced by the atretic segments affected. In a series of 58 cases of intestinal atresia in calves, 7 of 18 cases corrected surgically made a satisfactory recovery; the remaining 40 calves were euthanized for different reasons.

The incidence of **atresia coli in foals** has been reported at 0.44% of foals under 2 weeks of age admitted to veterinary teaching hospitals over a period of 27 years. Clinical findings included progressive abdominal distension, colic, lack of feces, and lack of response to enemas. A neutropenia may reflect the presence of toxemia. The large transverse or small colon is commonly involved. Agenesis of the mesocolon in a 1-month-old foal with colic has been described. The prognosis for most cases is grave and surgical correction is usually unsuccessful. Atresia coli has also been reported in an alpaca cria.[4]

The common causes of colic in newborn foals include ileus with or without gas distension, intussusception, diaphragmatic hernia, gastroduodenal ulcers, necrotizing enterocolitis, small and large-intestinal strangulation, large intestine displacement, intraluminal obstruction other than meconium, ruptured bladder, and congenital abnormalities of the gastrointestinal tract.

ATRESIA OF THE ANUS

This is recorded as a congenital defect in pigs, sheep, and calves. Its occurrence is usually sporadic and no genetic or management factors can be indicated as causes. When the rectal lumen is quite close to the perineum, surgical intervention is easy and the results, in terms of salvaging the animals for meat production, are good. These animals can usually be identified by the way in which the rectal distension bulges in the perineum where the anus should be; pressure on the abdomen provokes a tensing or further distension of this bulge.[1]

MULTIPLE ORGAN DEFECTS

In many animals the congenital defects of the intestine are accompanied by defects in other organs, especially the lower urinary tract, so that reparative surgery is not possible. For example, multiple gut and urogenital defects are recorded in one calf and gut defects plus defects of the pancreas and gallbladder in another.

Congenital constriction of the anus and vagina is an inherited defect of Jersey cattle and discussed later. The defect may be combined with rectovaginal fistula manifested by the passage of feces via the vulva or penile urethra.

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Inherited Defects of the Alimentary Tract

INHERITED DEFECTS OF THE MOUTH AND JAW

Harelip in cattle often has a distinct familial tendency but little work appears to have been done on the mode of inheritance. An apparently inherited harelip combined with poor growth and accompanying cryptorchidism is recorded in Holstein-Friesian cattle. Bilateral cleavage of the lip, which also involves the maxilla, is recorded in Texel sheep as being conditioned by a single recessive autosomal gene.

Cleft Palate

Cleft palate is inherited as a simple recessive character in Hereford and Charolais cattle, concurrent with arthrogryposis in the latter, and is commonly thought to be inherited in sheep and pigs. The progeny of a commercial swine herd (Landrace × Duroc) and Large White Boar contained a number of piglets with cleft palates. Chromosomal analysis of affected piglets found all had identical unbalanced karyotype with partial monosomy of chromosomes 16 and partial trisomy of chromosome 3, compared with normal piglets in the litters with balanced karyotypes.

Jaw Deformity

Shortness of the maxilla is thought to be inherited in Jersey cattle and Large White pigs, sometimes in association with chondrodysplasia. Shortness of the mandible is also inherited in cattle, and in Angus in combination with cerebellar hypoplasia and osteopetrosis.

Smooth Tongue (Epitheliogenesis Imperfecta Linguae Bovis)

Smooth tongue is a defect of Holstein-Friesian and Brown Swiss cattle, and it is inherited as an autosomal recessive factor. The filiform papillae on the tongue are small, there is hypersalivation and poor hair coat, and the calves do not fare well. The heterozygote is normal.

Tongue Aplasia

Congenital absence of the median part of the tip of the tongue occurs rarely in piglets, often in association with cleft palate and/or harelip.

Rectal Prolapse

Rectal prolapse may be inherited in piglets as a result of agenesis of the anal sphincter (see Inherited atresia of alimentary tract segments).

INHERITED RECTOVAGINAL CONSTRICTION

The rectovaginal constriction defect is inherited in Jersey cattle and is manifested as stenosis of the rectum in either sex and stenosis of the vaginal vestibule in females. The tone of both rectal and vaginal sphincters is increased, but attempts to detect heterozygotes by electromyographic measurement of these tones have been unsuccessful. The defect is regulated by an autosomal recessive gene. Affected cows are difficult to inseminate and have difficulty in calving. Their udders are small and hard and productivity is low. The condition is caused by the presence of bands of nonelastic fibrous tissue. Edema of the udder is also a common complication. Some assistance in the identification of affected animals is available by the detection of collagen type II in muscle biopsies. Fifty percent of heterozygotes also test positively as well as a small percentage of normals.

INHERITED ATRESIA OF ALIMENTARY TRACT SEGMENTS

Anal sphincter atresia occurs rarely in piglets and causes rectal prolapse. **Atresia ani** is quite common in pigs, sheep, and, to a less extent, cattle. Affected animals may survive for up to 10 days, and are identified by their depression, anorexia, colic, marked abdominal distension and lack of feces, and feces being replaced by thick white mucus. Abdominal distension in utero occasionally causes dystocia. Surgical repair is possible in some cases, but in others a large segment of rectum is missing, and creation of a colonic fistula in the inguinal region is necessary. The condition is thought to be inherited in pigs and calves, but supporting evidence is slim, and the evidence is less clear still in sheep. A suggestion that the defect may be also associated with the manipulation of the fetus during pregnancy examination has not been supported. A calf with atresia ani and diphallus and separate scrota has been described.

Inherited **atresia coli**, with complete closure of the ascending colon at the pelvic flexure, has been recorded in Percheron horses. A clinically similar defect in overo horses, described in the section on pseudoalbinism, is in fact an aganglionosis. Death occurs during the first few days of life. The defect appears to be inherited as a simple recessive character.

Inherited **atresia ilei** has been recorded in Swedish Highland cattle. Affected calves manifest marked abdominal distension causing fetal dystocia. The distension is caused by accumulation of intestinal contents. Inheritance of a single recessive gene conditions the occurrence of the defect in some species and breeds, but the prevalence may be higher than would be expected with

that form of inheritance, especially in Jersey cattle with atresia coli.

LETHAL WHITE SYNDROME IN FOALS AND LAMBS (INTESTINAL AGANGLIONOSIS)

White foals and white lambs of certain breeds or matings are affected by this syndrome, which is attributable to a mutation in the endothelin type B receptor gene (EDNRB).[1,2] Lethal white foal syndrome (OMIA #000629-9796) is an autosomal-recessively inherited condition of newborn foals born to American Paint Horse parents of the overo coat-pattern lineage.[3] In addition to foals of American Paint Horses, Quarter Horses and, rarely, Thoroughbreds are affected.[1] The overo coat-color pattern is characterized by pigment spreading down both sides from the dorsal midline, giving way to lack of pigment (i.e., white) primarily on the ventral surfaces.[3]

A mutation in the EDNRB of two nucleotides (TC > AG) in the coding EDNRB sequence results in the substitution of a single amino acid (Ile118Lys) and interference with migration of neural crest cells to the intestine causing intestinal aganglionosis, leading to a functional obstruction (megacolon) and death. Both melanocytes and myenteric ganglia cells are of neural crest origin, and their failure to migrate from the neural crest results in the absence of melanocytes in the skin and aganglionosis of the intestine.[1]

Over 94% of frame overo, highly white calico overo, and frame blend overo horse are heterozygotes, whereas fewer than 20% of tobiano, sabino, minimally blend overo, and breeding-stock solid are carriers.[1] Many solid (nonwhite coat-color pattern) horses with Paint horse bloodlines are heterozygous; therefore the genotype cannot necessarily be inferred from coat-color patterns.[1] White coat color can result from other genetic conformations and is not invariably associated with lethal white syndrome. Some affected foals may have flecks of black hair in the mane and tail or a small black body spot.[1]

Affected foals and lambs die within hours to several days of birth. Affected foals are all white or nearly all white and die of colic shortly after birth because of functional intestinal obstruction. Rectal examination reveals a lack of meconium. Radiographic examination of the abdomen reveals a distended large colon. Diagnosis is based on characteristic coat color and confirmation of megacolon. Diagnostic testing for the causative mutation is available commercially. Control is by testing and detection of heterozygotes and implementation of appropriate breeding programs.

A similar hypopigmentation syndrome occurs in Cameroon sheep and is associated with a homozygous 110-kb interstitial deletion on chromosome 10, including the entire EDNRB gene. The disease is inherited as an autosomal recessive trait.

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