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CHAPTER 15

Gastrointestinal Diseases

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GASTROINTESTINAL STASIS SYNDROME

Gastrointestinal (GI) stasis is by far one of the most common disorders seen in pet rabbits. Very often, it is the consequence on an inappropriate diet. However, any illness, painful condition, or stressful event can trigger an episode of GI stasis. It is imperative that the practitioner understand the need for continued, uninterrupted intake of an appropriate diet to ensure the proper functioning of the rabbit's GI tract. Left untreated, GI stasis can rapidly become life-threatening.

THE ROLE OF FIBER

To understand the pathogenesis of diet-related and GI diseases of the rabbit, a thorough knowledge of the normal anatomic and physiologic aspects of rabbit digestion must be appreciated. Details of this are discussed in Chapter 14. In summary, rabbits have a unique digestive physiology. They are strict herbivores, but their digestive strategy differs from those of other hindgut or cecal fermenters (e.g., horses) and ruminants. Being a prey species of small size, rabbits rely on a high energy intake while at the same time having the ability to quickly eliminate fibrous waste that would otherwise have to be carried in the digestive tract. To accomplish this, the rabbit's cecum and colon have a well-developed mechanism for separating out the digestible and readily fermentable components of the diet while allowing the crude fiber components to be purged. The main driving force for this mechanism is the presence of large quantities of indigestible fiber. Lack of this fiber, either due to dietary inadequacies or conditions that cause anorexia, is the major cause of GI disease in rabbits.[12]

Digesta are separated in the colon in a process of selective retention of fluid and small particles. Normal peristaltic movements propel the larger fiber particles through the colon, while contractions of the haustra in the colon move the fluid and small particles retrograde to the cecum. Small particles and fluid are retained in the cecum, allowing for extensive fermentation.

Cecal contents are expelled at regular intervals and reflexively consumed directly from the anus. Fiber stimulates cecocolic motility, either by a distention effect of the bulk, or directly. For example, diets high in fiber promote the production of specific volatile fatty acids in the cecum that directly promote peristalsis.[12]

Inadequate ingestion of coarse, nondigestible fiber will inhibit normal GI peristalsis. Rabbits will ingest hair routinely in the process of grooming. However, unlike many other mammalian pets, rabbits cannot vomit to eliminate accumulated hair. If GI motility is normal, ingested hair moves along with food out of the stomach at regular intervals and is ultimately expelled in the feces. If GI motility is impaired, either as a result of inadequate fiber intake or ileus secondary to anorexia (stress, concurrent disease), hair and normal ingesta accumulate in the stomach. With this accumulation, fluid is absorbed from the stomach, further compacting the contents. Compacted ingesta may cause discomfort to the rabbit, contributing further to anorexia and exacerbating GI hypomotility. A vicious cycle can result, until large amounts of hair and compacted ingesta accumulate in the stomach. This accumulation is erroneously referred to as a "hairball," "wool block," or "trichobezoar." These terms imply, incorrectly, that the hair accumulation is the cause of disease in the rabbit rather than simply being the consequence or a symptom of impaired intestinal motility.

THE EFFECT OF DIET AND CECOCOLIC MOTILITY

Cecal bacteria are vital to health. The cecum acts as a fermentation chamber and contains large populations of anaerobic organisms, such as *Bacteroides* species, and large anaerobic metachromatic staining bacteria (LAMB).[9,17,31] Other bacteria normally present include gram-negative oval and fusiform rods, along with several nonpathogenic species of protozoa and amoeba.[31] A rabbit-specific ascosporogenous yeast *(Cyniclomyces guttulatus)*, in the Saccharomyces family, resides in the normal rabbit cecum.[20] Veterinarians unfamiliar with rabbit fecal flora commonly mistake this yeast for coccidia on fecal examinations. This combined microflora is responsible for the processing of food particles entering the cecum into digestible nutrients, which are then reingested as cecotrophs.

An inappropriate diet or GI stasis can disrupt the balance of this complex cecal microflora and the environment in which it grows. Diets low in fiber cause cecocolic hypomotility, prolonging the retention of digesta in the cecum and ultimately producing changes in cecal microflora. Populations of potentially pathogenic bacteria, primarily *Clostridium* species and coliform species such as *Escherichia coli*, are normally present in small numbers in the cecum.[9,17,21] A slowing of cecocolic motility leads to the production of abnormal cecal fermentation products and alterations in the cecal pH. Even mild alterations in cecal pH will cause an increase in these pathogens as the populations of normal organisms decrease. Similarly, a decrease in peristalsis in the small intestine will allow normally small populations of potentially pathogenic bacteria to proliferate. Overgrowth of these pathogens can cause a range of pathology from mild diarrhea to death from enterotoxemia. Other effects of fiber consumption are indirect. High-fiber diets have a low level of available carbohydrates and thus decrease the risk of enterotoxemia caused by carbohydrate overload of the hindgut. Carbohydrates provide an environment in which pathogens such as *E. coli* and *Clostridium* species proliferate. Glucose, a byproduct of carbohydrate digestion, is necessary for the production of iota toxin by *Clostridium* species. Thus, diarrhea and enterotoxemia in pet rabbits is often caused by this disruption in microflora, commonly referred to as dysbiosis.

Feeds high in fiber, such as long-stemmed hay, can also protect rabbits from infectious bacterial enteritis. Rabbits have highly acidic stomachs, with the normal pH of 1 to 2. This acidic environment destroys most ingested bacterial pathogens, resulting in nearly sterile gastric contents. Ingested large-particle fibers, such as hay, mix with other foodstuffs to form a lattice-like ball of food in the stomach. The lattice-like structure of this ball of food allows gastric acid to fully penetrate the ingesta and destroy bacteria. However, if a rabbit is fed primarily pelleted foods, a dense, compacted mass of food is formed in the stomach. The compacted nature of this food protects ingested bacteria from degradation by gastric acid, thus allowing potentially pathogenic bacteria to enter the small intestine. The combination of ingestion of pathogenic bacteria and slowing of intestinal motility as described above can result in clinical bacterial enteritis.

HISTORY AND CLINICAL SIGNS

Obtain a complete dietary history, including the type and amount of commercial pelleted ration, hay, fresh leafy greens, and treats. Rabbits whose regular diet consists primarily of pelleted rations are at higher risk of developing GI stasis. The pelleted diets fed exclusively to feeder rabbits are high in calories (high in digestible carbohydrates), low in fiber, high in protein, and highly digestible, designed to increase weight gain in growing rabbits raised for their meat or fur. Commercial pellet formulations available for pet rabbits vary significantly in their protein, carbohydrate, and fiber contents. Formulations that contain a mix of dried fruits, vegetables, seeds, nuts, grains, and pellets generally have the lowest fiber content and the highest content of fat and carbohydrates. As the previous discussion indicates, there is significant potential for GI complications in a rabbit fed these diets. Similarly, rabbits routinely fed large amounts of high-carbohydrate, high-fat treats such as nuts, seeds, baked goods, and fruits are also predisposed to GI stasis. Acute episodes of GI stasis and dysbiosis are common following ingestion of a large volume of these treats. Rabbits at lowest risk are fed diets of unlimited grass or timothy hay, a moderate amount of fresh leafy greens, minimal commercial pellets, and occasional treats (see Chapter 14).

Question the owner about recent potentially stressful events or underlying disease processes that may cause anorexia. Most rabbits with episodes of GI stasis have such a history, even if fed an excellent diet. Examples of stressful events include changes in housing, introduction of new rabbits or other pets, recent illness, trauma, or surgery. Common underlying disorders that may cause anorexia include dental disease, chronic upper respiratory tract disease, neurologic disorders, lower urinary tract disease, and renal or hepatic disorders. Many affected rabbits will also have a history of little or no routine exercise.

The most common presenting complaint in rabbits with GI stasis is a gradual decrease in appetite and subsequent decrease in fecal production. Appetite usually decreases over a period of 2 to 7 days. Most rabbits will first stop eating pellets, then greens, hay, and finally treats. Left untreated, they stop eating all foods. Water consumption is often decreased as well. Feces become

scant, dry, and small, eventually ceasing altogether. Owners may report a corresponding decrease in activity, usually as a result of abdominal pain. Rabbits in pain are reluctant to move, appear less social, may grind their teeth, may dig or scratch, and sit in a hunched position. Weight loss may also be noted, either due to anorexia or underlying disease.

PHYSICAL EXAMINATION FINDINGS

Affected rabbits generally appear alert and quiet, exhibiting little or no sign of depression. Palpate the abdomen, with careful attention to the stomach contents, intestines, and cecum. The size of the stomach can vary with the duration of disease, but it always contains ingesta. The stomach usually feels firm and doughy and remains pitted on compression. Occasionally, stomach contents are severely dehydrated and solid. No fluid and little or no gas is palpable within the stomach of affected rabbits. This contrasts sharply with rabbits suffering from acute GI dilation (bloat), discussed below. The intestines and cecum frequently contain large amounts of gas. Little or no feces are palpable in the colon. Auscultate the abdomen, listening for borborygmus. Rabbits with GI stasis have few or no gut sounds. The remainder of the physical examination is usually unremarkable except for those findings related to any underlying disorder. Perform a thorough oral examination in all anorectic rabbits to look for underlying dental disease.

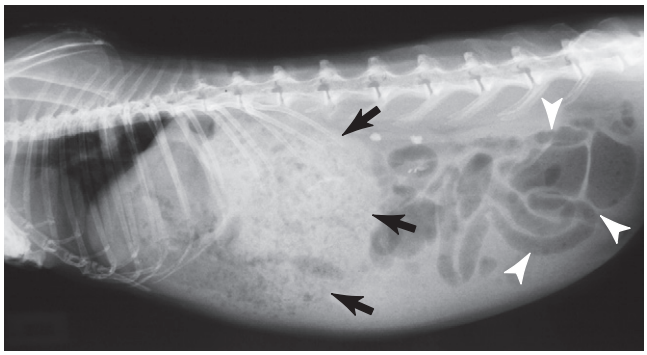

Fig. 15-1 Lateral radiograph of a rabbit with gastrointestinal stasis secondary to ureteral and renal calculi. Note the distention of the stomach with ingesta *(arrows)* and large amounts of gas within the intestines and cecum *(arrowheads)*, characteristic of gastrointestinal stasis.

DIAGNOSTIC TESTING

In many cases, the history and physical examination are sufficient for a diagnosis of GI stasis. It is very important, however, to look for an underlying cause. As discussed above, GI stasis occurs secondary to dietary or husbandry deficiencies, stress, pain, or underlying disease and will quickly recur if these are not addressed. Obtain additional diagnostics as indicated to rule out suspected underlying disorders. Radiography may or may not be helpful for diagnosis because the mass of food and hair appears similar to normal ingesta, even with contrast radiography. Visualization of a large, ingesta-filled stomach in a rabbit that has been anorexic for several days is suggestive (Fig. 15-1). This contrasts sharply with the dilated gas and/or fluid-filled stomach observed radiographically in rabbits with acute GI dilation (bloat) (Fig. 15-2) and can be helpful to differentiate the two disorders. Other common radiographic features seen in rabbits with GI stasis include moderate to severe distention of the intestines and cecum and scant fecal pellets. Radiographs may also be helpful to identify underlying causes of GI stasis.

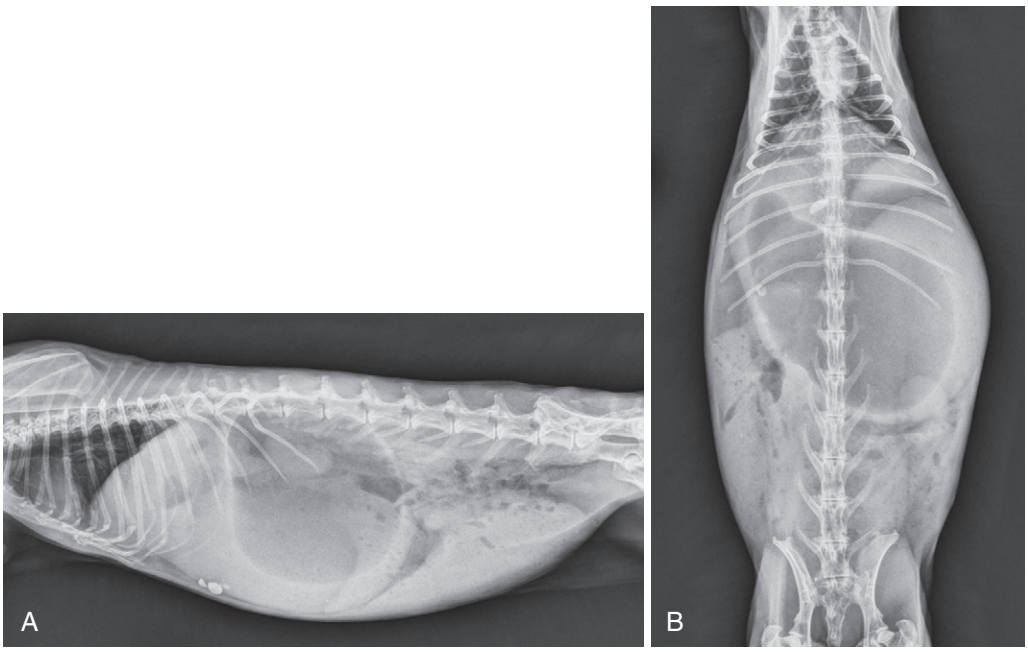

Fig. 15-2 Survey lateral **(A)** and ventrodorsal **(B)** radiographs of a rabbit with acute gastrointestinal obstruction. Note the severely distended gas- and fluid-filled stomach and the lack of gas within the gastrointestinal tract distal to the stomach. This is consistent with an acute proximal small intestinal obstruction.

TREATMENT

The key principles in the treatment of GI stasis are to rehydrate the patient and stomach contents, alleviate pain, provide nutrition, and treat any underlying disorders. Fluid therapy is essential to recovery. Administer fluids via either the intravenous or subcutaneous route, depending on the severity of dehydration. If they are anorexic for more than 1 to 2 days, affected rabbits are usually significantly dehydrated and generally require hospitalization for intravenous fluid therapy. Rehydrate the stomach contents by assisted feeding with a syringe or placing a nasogastric feeding tube (see Chapter 13) if the rabbit will not accept feeding slurries orally. A commercial product (Critical Care for Herbivores, Oxbow Pet Products, Murdock, NE) is available for this purpose, and most rabbits will readily accept this product when offered via a syringe. This formula is relatively high in fiber and will provide nutrition needed to stimulate GI motility in addition to rehydrating the stomach contents. If this formula is not available, blenderized pellets soaked with water or an oral electrolyte solution can be used. Feeding these slurries will also help to prevent hepatic lipidosis, which can develop rapidly in a rabbit with a negative energy balance. In addition to assisted feeding, offer rabbits water, plenty of fresh hay, and a variety of greens to provide every opportunity to self-feed. Ingestion of food is critical to reestablishing GI motility.

Rabbits with GI stasis have mild to severe gut pain, especially if the intestines are distended with gas. Most will not begin to eat until this pain is alleviated. If the rabbit appears to be much in pain (reluctant to move, hunched posture, bruxism), administer buprenorphine (0.01-0.05 mg/kg SC, IV q6-12h) and a nonsteroidal anti-inflammatory drug (NSAID) such as meloxicam (Boehringer Ingelheim Vetmedica, Inc., St. Joseph, MO) (0.3-0.5 mg/kg SC q12-24h) or carprofen (1.0-2.2 mg/kg PO q12h). Rabbits feeling less pain may respond well to NSAIDs alone. Be certain that the rabbit is fully hydrated and no underlying renal disorders are present prior to administering NSAIDs. If intestinal motility is severely impaired, parenteral administration is indicated.

Other treatments include GI prokinetics and antibiotics. The use of intestinal prokinetic agents is somewhat controversial; however, anecdotal evidence suggests that they may be beneficial. Cisapride (0.5 mg/kg PO q8h) is readily absorbed from the GI tract and is available through compounding pharmacies. Metoclopramide (0.2-1.0 mg/kg PO, SC, IM q6-8h) has also been used. Antibiotics may be indicated if evidence of dysbiosis is present. If an overgrowth of *Clostridium* species is suspected, administer metronidazole (20 mg/kg PO q12h). Antibiotics generally effective against other potential pathogenic bacteria include enrofloxacin (15-20 mg/kg PO q12h) and trimethoprim-sulfamethoxazole (30 mg/kg PO q12h).

Continue treatment for 3 to 5 days. Most rabbits will begin to eat and pass stool within 24 to 48 hours of treatment. Feces passed initially may look abnormal in shape, size, and consistency and may contain mucus or hair. Rabbits not responding to treatment should be reevaluated to identify underlying disorders contributing to anorexia. When treatment is successful, instruct owners to feed a diet that contains large amounts of grass or timothy hay, fresh leafy greens, and limited pellets and treats.

Other popular remedies of questionable value include the use of lubricants (e.g., petroleum laxatives), protein-digesting enzymes (e.g., pineapple for bromelain and papain), and simethicone. These treatments alone will have no beneficial effect as they do nothing to return function to the intestinal tract. Many rabbit associations and websites promote the use of simethicone, and it appears to have no ill effects. Caution owners against the use of protein-digesting enzymes, as these can be very irritating to oral mucosa and potentially gastric mucosa. The risk of gastric ulceration is increased in anorexic rabbits, and use of these enzymes may exacerbate this.

Very rarely, the mass of material in the stomach is so dehydrated that it forms a solid, immovable mass and the rabbit fails to respond to medical treatment. In this case, surgical intervention may be necessary. However, the prognosis for a successful outcome is greatly reduced in rabbits that are treated surgically. Anesthesia, pain, stress, and manipulation of the intestinal tract all exacerbate GI stasis. Complications of hepatic lipidosis are a common cause of death in these patients.

ACUTE GASTROINTESTINAL DILATION OR OBSTRUCTION

GI obstruction (also referred to as GI dilation or "bloat") is an acute, life-threatening condition. The pathogenesis, history, and clinical findings differ significantly from those of GI stasis. Confusion arises over the use of the term *trichobezoar*. As discussed above, *trichobezoar* is a common misnomer for GI stasis. In most cases of acute GI dilation, the obstruction is located in the small intestine and is a compact mat of hair (trichobezoar). It is not clear exactly where these mats of hair are formed. They may have formed while still on the coat of the animal and have been ingested whole during grooming. It has also been suggested that these trichobezoars were once large cecal pellets containing compacted hair. They may occasionally be ingested and swallowed whole with other cecal contents during normal cechotrophy.[24,25] Other foreign objects reported to acutely obstruct the intestinal tract include carpet or other cloth fibers, locust beans, and plastic.[24,25] The location of the obstruction is usually in the proximal duodenum, a short distance from the pylorus where the lumen narrows, or in the midduodenum (Fig. 15-3). The second most common location is the ileocecocolonic junction. Acute compressions of the intestinal tract by neoplasia, postsurgical adhesions, tapeworm cysts, and hernias have also been

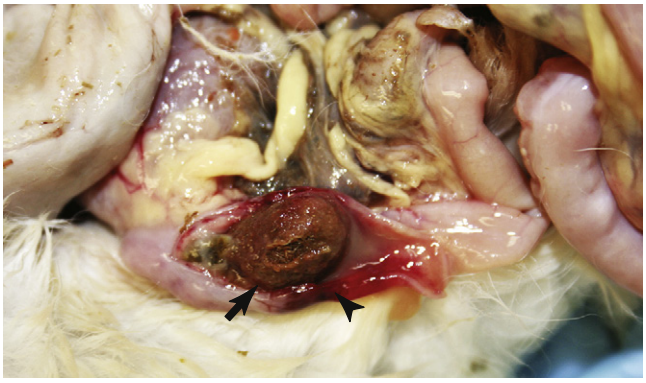

Fig. 15-3 Postmortem examination of a 4-year-old rabbit that died from acute gastric rupture. Note the typical appearance of acute gastrointestinal obstruction caused by a hair pellet *(arrow)*. The obstruction is located a few inches distal to the pylorus in the duodenum and consists of compacted hair. The location of this obstruction, along with its size and composition, are characteristic. Note the hyperemic appearance of the duodenum at the level of the obstruction *(arrowhead)*.

reported.[24,25] These all create a complete physical obstruction of the intestines and are not related to functional GI stasis. Rabbits cannot vomit and have a well-developed cardiac sphincter. When outflow from the stomach is obstructed, gastric fluid and swallowed saliva quickly accumulate. This fluid may undergo fermentation to produce large volumes of gas, resulting in a rise in intragastric pressure and a severely dilated stomach. As with gastric dilation in other species, the combination of sequestered fluid, compression of the aorta and vena cava causing hypovolemic shock, electrolyte imbalances, and acid-base disturbances can lead to death within hours of obstruction. Death can also be due to peritonitis resulting from ischemic necrosis at the site of the obstruction or rupture of the stomach.

HISTORY AND PHYSICAL EXAMINATION FINDINGS

A sudden onset of anorexia and depression is the hallmark feature of acute GI obstruction. Some rabbits are found acutely moribund or discovered dead with no premonitory signs. Unlike rabbits with GI stasis, there is no history of a recent stressful or painful event, and dietary history does not play a role. Affected rabbits suddenly refuse all food and quickly stop producing feces. Most demonstrate signs of severe pain, such as reluctance to move, hunched posture, and bruxism. As metabolic derangements and shock develop, affected rabbits become severely depressed, listless, laterally recumbent, and minimally responsive to external stimuli. With stomach rupture, they may suddenly cry out and die. On physical examination, a large, fluid-filled or tympanic stomach is palpable in the cranial abdomen. Pain is elicited on palpation of the stomach. If examined early, affected animals are alert but quiet, tachypneic, and tachycardic. Later, they become hypothermic, bradycardic, and hypotensive.

DIAGNOSTIC TESTING

Obtain radiographs to confirm the diagnosis. The radiographic appearance of a rabbit with acute GI obstruction differs sharply from that of a rabbit with GI stasis or that of a normal rabbit. The stomach will appear severely distended with gas, fluid, or both (see Fig. 15-2). Gas distention of intestinal loops proximal to the obstruction are noted, especially with obstructions occurring in the midduodenum or ileocecocolonic junction. Pneumoperitoneum indicates that the stomach has ruptured and carries a grave prognosis. Obtain blood for a complete blood count (CBC) and biochemical profile. Results may demonstrate dehydration and a variety of acid-base and electrolyte disorders.

INITIAL MEDICAL TREATMENT

Begin treatment immediately, as this is a life-threatening disorder. Initial treatment goals are to decompress the stomach, treat shock, correct any fluid and electrolyte imbalances, and control pain. To control pain, administer buprenorphine (0.02-0.05 mg/kg SC, IV q6-12h). Sedation is necessary to decompress the stomach in most cases. Sedate with midazolam (0.5-1.0 mg/kg IM, IV) and/or mask with isoflurane or sevoflurane. A well-lubricated 16- to 18-Fr red rubber catheter works well as an orogastric tube. It may be necessary to cut additional holes in the end of the tube to allow larger volumes of gas and fluid to pass. Measure the distance from the nose to the last rib (the distance to the stomach) and mark the tube. Lubricate the tube well and pass it gently per os into the stomach. Remove all gas and air from the stomach. Percutaneous trocharization of the stomach is not recommended as a method of decompression, since this will likely cause rupture of the stomach. While the stomach is being decompressed, place an intravenous catheter and begin treatment with a shock dose (90 mL/kg per hour) of isotonic crystalloid fluids. When dehydration is corrected and shock is controlled, reduce administration to a maintenance rate. Correct any electrolyte imbalances. In most instances, surgery is immediately necessary to remove the obstruction. However, in a small number of cases, the foreign object will pass following medical treatment. Monitor these rabbits closely to determine if the obstruction is passing. Palpate the abdomen frequently, monitor for signs of pain, and repeat radiographs. The gas pattern will change, and gas will be visible in the distal intestines if the rabbit is passing the obstruction. These rabbits will appear comfortable and begin eating, drinking, and defecating.

SURGICAL TREATMENT

Immediate surgery is required to remove the obstruction in the majority of cases. When possible, decompress the stomach and stabilize shock prior to attempting surgery. Most obstructions are found in the proximal or midduodenum or in the ileocecocolonic junction. When possible, manipulate proximal duodenal foreign bodies into the stomach and perform a gastrotomy rather than an enterotomy. Gastrotomies are generally better tolerated, with a lower probability of postoperative complications such as stricture, leakage, or GI stasis. If no intestinal foreign body is found, explore the abdomen for evidence of neoplasia, abscesses, or adhesions as the cause of obstruction. Provide postoperative supportive care, including fluid therapy, pain management, and antibiotic therapy. Even with prompt removal of the foreign body, the prognosis is guarded. Many patients die during surgery or within 48 hours postoperatively from peritonitis, postoperative GI stasis, endotoxemia, or acute renal failure.

CECOTROPHY AND INTERMITTENT DIARRHEA

Cecotrophs are nutrient-rich pellets resembling feces that contain the products of cecal fermentation. They are produced several times a day, usually in the morning and evening, and consumed reflexively directly from the rectum, a behavior termed cecotrophy. Cecotrophs are swallowed whole without chewing and are covered with a mucous coating that protects them from gastric degradation. This allows them to be delivered intact to the small intestines for digestion and absorption. Cecotrophs differ in appearance to rabbit fecal pellets. They are dark in color, soft and sticky in texture, have a characteristic odor, and are covered in a mucous layer. If intact, they appear as many soft fecal pellets stuck together, resembling a blackberry. If cecotrophs are not consumed, they often stick to the fur around the perineum or are found smeared on the fur and flooring. This is often confused with intermittent diarrhea and is a common presenting complaint. Rabbits that do not consume their cecotrophs are either physically unable to do so or do not eat them because they are abnormally formed. A common cause of inability to consume cecotrophs is obesity, where the rabbit cannot reach the anal region. Other causes include musculoskeletal disorders, dental disease, pain, and physical barriers such as Elizabethan collars. Changes in normal cecal motility, pH, or flora result in

the production of abnormal cecotrophs. These cecotrophs may be soft, malformed, pasty, or odiferous and are therefore not consumed. Dietary deficiencies, as discussed above, are a common cause; however, other factors such as stress, concurrent disease, or antibiotic usage may also contribute.

Diagnosis is based primarily on history. Affected rabbits produce normal fecal pellets throughout most of the day. Soft feces are found on the fur or smeared on flooring. If the rabbit cannot reach the anus, the feces are pasted to the perineum, and secondary dermatitis often results. Obesity or signs of neuromuscular, dental, or other painful disorders are present on physical examination. Correction of the underlying disorder will allow a return to normal cecotrophy. If the rabbit can reach the perineum, question the owner about the diet. Insufficient fiber in the form of hay and/or excessive carbohydrate intake is a common cause. In this case, simple correction of the diet will usually correct the problem.

CECOLITHS

Altered motility of the cecum, rate of transit in the colon, or abnormal diet (e.g., the feeding of diets consisting of very small fiber length or feeding indigestible fiber, such as psyllium) can result in compaction and dehydration of cecal or colonic material and subsequent formation of "cecoliths" or abnormally hard lumps of cecal contents. Cecoliths are the most common cause of lower bowel obstruction in the rabbit, lodging at the distal end of the sacculated portion of the large intestine, the fusus coli. Rabbits that form cecoliths often have a chronic history of cecal or large intestinal disorders including the production of large, malformed feces, recurrent cecal impaction, abdominal pain, and anorexia. Because affected rabbits are unable to form normal cecotrophs, they are often underweight and lack normal muscle mass. Many of these rabbits are serologically positive for *Encephalitozoon cuniculi*, and speculation exists that this parasite may play some role in the disorder. One of the present authors (JRJ) has also postulated that some of these rabbits may have neurologic damage associated with trauma to mesenteric nerves or spinal cord. A presumptive diagnosis of cecolith formation can be made by palpation of doughy to firm material in the cecum or colon. Radiography or ultrasound examination can be used to confirm the presence of cecoliths. If the intestine is completely obstructed, gas will accumulate in the sacculated large intestine. Obstructed patients are in severe pain and may present moribund.

Treatment of cecoliths requires rehydration of inspissated cecal and colonic contents. Administer fluid therapy via the intravenous or subcutaneous route and feed foods with a high water content (leafy vegetables, vegetable baby food). Additionally, feed an appropriate fiber source, such as grass hay, to stimulate normal cecal motility and function. Short-term administration of an intestinal promotility agent may be of benefit. In the long term, the addition of canned pumpkin (1 tbsp q12h) to the rabbit's diet may prevent recurrence.

Rabbits with complete large intestinal obstruction are critically ill, in pain, and require immediate treatment. Begin intravenous fluid therapy and administer buprenorphine (0.03-0.05 mg/kg SC, IV q6-12h). In some cases the obstructing cecolith can be softened and moved retrograde with a gentle enema. Take great care in administering enemas, as the colon may have become necrotic at the point of obstruction. If the obstruction cannot be removed via medical therapy, surgical removal will be required once the patient is stable.

ENTERITIS COMPLEX AND ENTEROTOXEMIA

In clinical practice, enteritis complex—with signs ranging from soft stool and diarrhea to enterotoxemia, sepsis, and death—is one of the most common diseases of rabbits. Pathogenic bacteria and the factors that allow them to proliferate are the usual causes. These factors involve diet, antibiotics, stress, and genetic predisposition to gut dysfunction. Simple cases of enteritis, resulting in a soft or pasty stool as the only clinical sign, may be caused by a minor disruption of cecal flora, pH, or motility. Simple correction of the diet, the addition of fiber in the form of hay, and removal of stress will often correct the problem.

Enterotoxemia in rabbits, which is characterized by more significant dysbiosis than in the case of enteritis, is caused by the iota-like toxin from *Clostridium spiroforme*.[41] Newly weaned animals (3-6 weeks of age) are most often affected, and they have the greatest mortality rate. These rabbits may develop enterotoxemia from simple exposure to *C. spiroforme*. This is likely because these young rabbits have an undeveloped population of normal GI flora and a high gastric pH, which allows the proliferation of *C. spiroforme*. Adult rabbits are more resistant and generally require some dietary, environmental, or other stress for the dysbiotic state to be induced and growth of the bacteria occur. Rapid multiplication of *C. spiroforme* results in significant alteration of the rabbit's normal cecal flora. Nursing does with enterotoxemia can develop a so-called milk enterotoxemia that is thought to be caused by *Clostridium* endotoxin produced in the does' cecum and passed to the bunnies in their milk.

In acute disease, rabbits become anorexic and markedly depressed. The diarrhea is brown and watery and soils the perineum and rear legs. It may contain blood or mucus. As the disease progresses, affected rabbits become hypothermic and, moribund and die after 24 to 48 hours. Postmortem findings in these rabbits include petechial and ecchymotic hemorrhages on the serosal surface of the cecum. The appendix and proximal colon may also be involved. Various amounts of gas throughout the intestinal tract, cecum, and colon result from ileus. Hemorrhages, pseudomembranes, or mucus may be present on the mucosa of the cecum and proximal colon.

MUCOID ENTERITIS

Mucoid enteritis is one of the major causes of morbidity and mortality in young rabbits 7 to 14 weeks of age. It is characterized by anorexia, lethargy, weight loss, diarrhea, cecal impaction, and excessive production of mucus by the cecum. Its cause is unknown; however, studies have convincingly established the relation between bacterial dysbiosis and hyperacidity of the cecum and the symptoms of mucoid enteritis.[31] Alterations in cecal pH resulting from changes in the production or absorption of volatile fatty acids or from vigorous fermentation of carbohydrates can destabilize the cecal microbial population and stimulate mucus production within the cecum and colon. Feeding a diet high in fiber and low in simple carbohydrates is preventative.

DYSBIOSIS CAUSED BY TREATMENT WITH ANTIBIOTICS

Other factors involved in the development of enteritis include antibiotic administration and stress. Some antibiotics suppress normal flora, allowing pathogens to proliferate. Clindamycin,

lincomycin, ampicillin, amoxicillin, amoxicillin-clavulanic acid, cephalosporins, many penicillins, and erythromycin can induce enteritis in rabbits. Epinephrine-mediated inhibition of gut motility is believed to be the cause of stress-induced enteritis.

TREATMENT OF ENTERITIS

The treatment of rabbits with severe enteritis, enterotoxemia and mucoid enteritis consists of aggressive supportive care and efforts aimed at increasing cecal and colonic motility, discouraging the growth of pathogenic bacteria and the production of toxins, and supporting the growth of normal flora. Administration of cholestyramine (Questran, Bristol Laboratories, Princeton, NJ), an ion-exchange resin capable of binding bacterial toxins, at a dosage of 2 g in 20 mL water q24h by gavage, has been reported to prevent death in rabbits with clindamycin-induced enterotoxemia.[33] Antimicrobial drugs have limited value in the treatment of the disease and are used primarily as supportive therapy. *C. spiroforme* has been shown to be sensitive to metronidazole and penicillin G.[7] The use of metronidazole (20 mg/kg PO, IV q12h) has been reported to reduce the number of deaths from enterotoxemia. Correction of dehydration and maintenance of normal hydration are of paramount importance, and administration of intravenous or intraosseous fluids is indicated. If the rabbit is anorectic, assist feed and provide supportive care as described for treatment of GI stasis, above.

PREVENTION OF ENTEROTOXEMIA

To prevent enterotoxemia, maintain optimal husbandry and minimize stress. Feed a good-quality grass hay and limit or remove pellets from the diet. If a pelleted diet is fed, it should contain no less than 18% to 20% fiber and should be limited to less than ⅓ cup per 5 lb (2.3 kg) of body weight. Avoid sudden changes in the diet. Make hay available to weanling rabbits from 3 weeks of age; avoid early or forced weaning.

BACTERIAL ENTERITIS

Enteropathogenic *E. coli*

Diarrhea and mortality caused by infection with enteropathogenic *E. coli* (EPEC) are major causes of economic loss in the commercial rabbit industry. Disease outbreaks have not been reported in pet rabbits. Rather than producing enterotoxins or invading intestinal mucosa, EPEC exert their virulence by attaching to enteric epithelial cells and inducing effacement of microvilli; they are thus referred to as attaching and effacing *E. coli*.[3,32,42] Diarrhea, caused by the resultant villus atrophy and malabsorption, varies in severity depending on the age of rabbit and specific serogroup involved.

E. coli-related diarrhea in postweaning commercial rabbits may be caused by a variety of different serotypes that belong to the rabbit EPEC group.[3,32] Morbidity and mortality rates vary; signs range from mild diarrhea and weight loss to death, and the mortality rate can be 50% or greater. Those animals that recover may have retarded growth. EPEC-related diarrhea in neonatal rabbits is most common between 1 and 14 days of age. The diarrhea is typically watery and stains the abdomen and perineum yellow. Morbidity and mortality rates within a litter approach 100%. Subsequent litters of the doe may have passive immunity. The disease process is limited to the cecum and colon. The cecal wall may be inflamed with longitudinal "paintbrush" hemorrhages. In severe cases, intussusception and rectal prolapse may be present. Presumptive diagnosis may be based on isolation of *E. coli* from stool or tissue samples from affected animals; however, nonpathogenic *E. coli* routinely proliferates in any rabbit with dysbiosis. Confirmation of the diagnosis requires histologic examination of tissues and observation of *E. coli* attachment to the intestinal cells. Serotyping of *E. coli* isolated from rabbits is not available to clinical veterinarians and remains a tool of research only.

Treat individual rabbits with appropriate antibiotics, guided by the results of culture and sensitivity testing. Use trimethoprim-sulfamethoxazole as a combination antibiotic (30 mg/kg PO q12h) or enrofloxacin (10 mg/kg PO q12h) until culture and sensitivity test results are obtained. Positive results may be obtained with early treatment.

Proliferative Enteritis, Proliferative Enteropathy, Proliferative Enterocolitis

The obligate intracellular bacterium *Lawsonia intracellularis*, previously referred to as an intracellular *Campylobacter*-like organism, has been reported as a cause of enterocolitis in rabbits both alone and in association with an EPEC strain of *E. coli* distinct from the prototypic rabbit diarrhea *E. coli* (RDEC-1) strain.[27,44] This intracellular bacterium is gram-negative, curved to spiral-shaped, and found free in the apical cytoplasm of intestinal epithelial cells. The disease is most often characterized as an acute diarrheal disease of rabbits 2 to 4 months of age (weanlings). Proliferative enteritis (PE) or enteropathy is an enteric disease that develops in many animals. Much of the literature focuses on the disease in swine and hamsters. In addition, PE has been reported in rats and guinea pigs; ungulates other than swine, including white-tailed deer, sheep, and horses; carnivores, including arctic foxes, dogs, and ferrets; nonhuman primates; and birds (ratites). The disease is not an important problem in these other species.[44] Histologic findings in these cases most often show a proliferative ileitis, with or without proliferative colitis, characterized by epithelial hyperplasia and mucosal inflammation. Similar disease in pigs and ferrets has been shown to be caused by a similar but distinctively different bacterium, *Desulfovibrio desulfuricans*.[21,36] Treatment of *L. intracellularis* in rabbits is challenging. Antibiotics used to treat *L. intracellularis* in other species include those of the macrolide family (e.g., tylocin, erythromycin, and lincomycin). These antibiotics are not recommended for use in rabbits. Chloramphenicol is generally efficacious and is administered at 30 to 50 mg/kg PO, SC q12h for 7 to 14 days. Florfenicol (NuFlor, Schering-Plough Animal Health Corp., Union, NJ) may be useful as an alternative antimicrobial agent in rabbits, but its efficacy and potential side effects in this species are yet to be evaluated.

Tyzzer's Disease

Tyzzer's disease is caused by *Clostridium piliforme* (formerly *Bacillus piliformis*), a motile gram-variable spore-forming obligate intracellular bacterium.[16] The disease occurs in many rodents and other mammalian species in addition to rabbits. Stress (produced by overcrowding, unsanitary conditions, high temperatures, or breeding) may be an important component of this disease. Clinical signs of Tyzzer's disease include watery diarrhea, depression, and death. Morbidity and mortality rates may be especially high in weanling rabbits. Older rabbits can develop a more chronic form of the disease that results in chronic weight loss. Postmortem examination of rabbits with Tyzzer's disease

may show characteristic foci of necrosis in the liver and degenerative lesions of the myocardium. More often, the intestinal wall is edematous, with areas of necrosis in the mucosa of the proximal colon. Treatment is palliative once clinical signs have been observed. The intracellular location of the bacteria may contribute to the difficulty in treating affected animals. If exposed animals are treated early (if they are isolated from affected animals, good hygiene is promoted; supportive care and a high-fiber diet are provided), they may not develop the disease. Once symptoms of the disease develop, treatment may be unsuccessful. Prevention of the disease depends on good husbandry. Bacterial spores are killed with a 0.3% sodium hypochlorite solution or with heating to 173°F (80°C) for 30 minutes.

Other Bacterial Enteritides

Other causes of enteritis include *Salmonella* and *Pseudomonas* species. Salmonellosis is not common but can cause disease with high rates of both morbidity and mortality. The disease is well studied in rabbits, and the rabbit is used as a model of salmonellosis in humans.[23] The species and serovar most often associated with salmonellosis in rabbits is *Salmonella typhimurium;* however, other species and serovars have been reported.[5] Transmission of the disease is most often associated with contaminated food or water. Affected rabbits usually develop sepsis, which quickly leads to death; however, diarrhea may occur as well. Postmortem findings are consistent with septicemia and include vascular congestion of organs and diffusely distributed petechial hemorrhages. Lymph nodes and gut-associated lymphoid tissue may be edematous and contain similar foci of necrosis.

One of the authors (JRJ) has seen an outbreak of lethal diarrhea in rabbits associated with *Pseudomonas aeruginosa,* which was isolated from the watering system. The morbidity rate associated with this outbreak was low to moderate, but the mortality rate in affected animals was high.

VIRAL DISEASES OF THE DIGESTIVE TRACT

PAPILLOMATOSIS

Rabbit oral papillomatosis is a benign disease caused by a papillomavirus. The disease has been reported only in colonies of laboratory rabbits, especially New Zealand white rabbits.[37,45] Lesions consist of small white growths on the ventral surface of the tongue but only rarely elsewhere in the mouth. Early lesions are sessile, later becoming rugose or pedunculated and ultimately ulcerated. The lesions can exceed 4 to 5 mm at their greatest dimension but are typically smaller (1-3 mm). Lesions may persist as long as 145 days, but they usually disappear within weeks.

RABBIT ENTERIC CORONAVIRUS

In 1980, a coronavirus was found to be the cause of diarrhea in laboratory rabbits.[30] Further research has shown that this virus affects rabbits 3 to 10 weeks of age, but it has also been found in clinically normal adult rabbits. Clinical signs in naturally occurring outbreaks include lethargy, diarrhea, abdominal swelling, and death. Pleural effusion and cardiomyopathy in rabbits have also been associated with coronavirus-like particles.[39] The disease is associated with high rates of morbidity and mortality; in one described outbreak, 40% to 60% of rabbits were affected. Death occurred in almost 100% of these animals within 24 hours of the onset of clinical signs.[13] Necropsy findings include fluid cecal contents, and histopathologic examination reveals atrophy of intestinal villi. Tentative diagnosis of this disease is based on clinical history, clinical signs, necropsy findings, and results of histopathologic analysis. The virus agglutinates red blood cells; evidence of hemagglutination activity in the feces therefore supports a tentative diagnosis. The diagnosis is confirmed by demonstration of the virus in feces or cecal contents.

ROTAVIRUS

Infections in animals caused by rotavirus alone are often only mildly pathogenic; in rabbits, however, the virus is associated with very high morbidity but variable mortality rates. Although poorly studied in pet rabbits, antibodies to rotavirus as well as the virus itself have been found in the feces of rabbits from commercial rabbitries throughout the world. Severity of diarrhea associated with rotavirus infection varies widely and is likely influenced by synergy with various microorganisms associated with the infection. Severe anorexia, dehydration, and mucoid or greenish-yellow watery diarrhea have been reported. Rabbits between 30 and 80 days of age are most often affected. The mortality rate in young rabbits with naturally occurring infections may be as high as 80%. High morbiditiy and mortality rates found in naturally occurring infections have not been well reproduced in experimental studies. In one study, rotavirus caused soft or fluid feces in some rabbits, but in most animals diarrhea did not develop at all.[8] Another study showed that a strain of rotavirus induced diarrhea, depression, anorexia, and death; however, results of the experiment were not reproducible.[14,15] The clinical signs of naturally occurring infections involving rotavirus and other agents include marked congestion and distention of the intestines and cecum and petechial hemorrhages in the small intestine and colon. Histologic lesions include moderate to severe villous atrophy, with the most severe lesions being found in the ileum. Apical enterocytes on the tips of villi are swollen, rounded, and desquamated, and the tips may be denuded. The lamina propria is usually infiltrated with lymphocytes and occasionally with neutrophils. Diagnosis is established on the basis of the results of histopathologic examination of the intestine, isolation of the virus, or demonstration of antibodies. Clinical signs and gross pathologic findings alone are not diagnostic.[13] The prevention and control of rotavirus infection is complicated by its highly infectious nature. Reduction of stress (by cessation of breeding, reduction of crowding, removal of socially dominant animals, and the addition of fiber to the diet) along with appropriate treatment of concurrent disease and improved hygiene should reduce mortality rates.

RABBIT HEMORRHAGIC DISEASE VIRUS

Viruses of the *Lagovirus* genus within the family Caliciviridae affecting rabbits include rabbit hemorrhagic disease virus (RHDV), European brown hare syndrome virus (EBHSV), and the nonpathogenic rabbit calicivirus (RCV).[22] EBHSV affects European hares of the *Lepus* genus. RHDV specifically afflicts *Oryctolagus cuniculus,* the predominant species of domestic rabbits worldwide. RHDV does not cause disease in wild cottontail rabbits, jackrabbits, or hares. Since its first emergence in China in 1984, RHDV has become endemic in Europe, Cuba, Australia, and New Zealand. Limited outbreaks have occurred in the

Middle East, South America, Mexico, and the United States. All outbreaks were traceable to the importation of live rabbits or rabbit products from China. The virus has been eradicated from Mexico. Sporadic outbreaks have taken place in the United States, the last of which occurred in Indiana in 2005. The disease was eradicated following each outbreak and as of this writing is not endemic in North America.[35]

Clinical disease is seen in rabbits older than 2 months of age; younger rabbits are clinically unaffected.[18,35] Virus is shed in urine, feces, and respiratory secretions. Transmission is via direct contact, contact with carcasses or fur from affected rabbits, or fomites such as water, feed, utensils, clothing, or cages. Flies and other insects may also serve as vectors, and the virus can be found in feces from predators that have eaten infected rabbits. RHDV is highly infectious and has traditionally been associated with high rates of both morbidity (40%-100%) and mortality (approaching 100%). Higher rates of morbidity and mortality are seen in naive populations. The number of rabbits affected during outbreaks peaks in 2 to 3 days and the disease course may last only 7 to 13 days. The incubation period is 1 to 3 days.

RHDV replicates in the liver, resulting in severe hepatic necrosis and death from disseminated intravascular coagulation.[6,34,35] In peracute disease, rabbits become febrile, lethargic, and collapse and die within 12 to 36 hours of infection; they may be found dead with no premonitory signs. With acute disease, affected rabbits are febrile and show signs of depression, lethargy, anorexia, constipation, or diarrhea. Some may show neurologic signs such as ataxia, opisthotonos, excitement, or seizures. At the end stage of the disease, tachypnea, cyanosis, and a blood-tinged foamy nasal discharge are often seen. In some rabbits, the course of the disease is slower, with the animals exhibiting jaundice, depression, anorexia, and fever, eventually dying within 1 to 2 weeks. In the subacute form, milder signs are seen and many of these rabbits live. Persistent or latent infections may occur in asymptomatic rabbits.[18,35]

Hematologic testing often shows a lymphopenia and a gradual decline in the number of thrombocytes. In most moribund rabbits, prothrombin and thrombin times are prolonged, and fibrin degradation products can be detected.[43] The most consistent gross postmortem changes are hepatic necrosis, splenomegaly, and evidence of disseminated intravascular coagulation. Congestion and hemorrhage may be seen in most organs but is most pronounced in the lungs. The liver is pale, and periportal necrosis with a fine reticular pattern is observed; the spleen is dark and thickened, and catarrhal enteritis is often identified.[13,43] A presumptive diagnosis may be made on the basis of data in the history, clinical signs, and pathologic findings. Definitive diagnosis requires identification of the virus using a variety of diagnostic tests, including electron microscopy, reverse transcription polymerase chain reaction (RT-PCR), Western blot, and enzyme-linked immunosorbent assay (ELISA). Immediately contact state or federal regulatory agencies to report this disease, and send diagnostic samples only to authorized laboratories under secure conditions.

A tissue-derived, inactivated vaccine is used to protect domestic rabbits in countries where the virus is endemic.[2,13] However, this vaccine appears to be less effective in some an antigenic variant strains, which may be responsible for the spread of disease throughout Europe despite active vaccination programs. The virus can be inactivated by 0.5% sodium hypochlorite or 1% formalin.

PARASITIC DISORDERS OF THE GASTROINTESTINAL TRACT

COCCIDIA

Coccidia are the most common parasites of the rabbit GI tract and are frequently a cause of illness in young rabbits (less than 6 months old). Adult rabbits are rarely clinically ill, and the identification of oocytes on fecal examination does not equate to disease. Twelve species, all members of the genus *Eimeria*, are reported to infect rabbits.[40] Only one species, *Eimeria stiedae*, which infects the liver, is found outside the intestinal tract. Very often, two or more species of coccidia are present in diseased rabbits; the precise role of the different species as pathogens is therefore not clearly defined.

Hepatic Coccidia

E. stiedae, the coccidium responsible for hepatic coccidiosis, is ubiquitous in open rabbitries in which rabbits are not treated preventatively with coccidiostats. Infection results from ingestion of sporulated oocysts that undergo excystation in the duodenum. Liberated sporozoites penetrate the intestinal mucosa and move to bile epithelial cells, where they undergo schizogony. Merozoites invade contiguous epithelial cells and undergo gametogeny, giving rise to microgametes and macrogametes. After being fertilized by a microgamete, the macrogamete develops into an oocyst. Oocysts rupture from the epithelial cells and are passed in the bile and eventually, in the feces.[28] Many infections are asymptomatic; however, the disease may be fatal, especially in young rabbits. Heavily infected rabbits show signs related to decreased hepatic function and bile duct obstruction. These rabbits become anorexic and debilitated; diarrhea or constipation may be noted in the terminal stages of the disease. The abdomen is occasionally enlarged and icterus is observed. Biochemical testing reveals increased alanine aminotransferase (ALT), aspartate aminotransferase (AST), bile acids, and total bilirubin. On radiographs, hepatomegaly and ascites may be present. On postmortem examination, the liver is enlarged and has yellowish-white, nodular, abscess-like lesions of varying size, some of which are within a fibrous capsule. Diagnosis is based on the identification of oocysts in a sample of bile, by histologic examination, or by fecal examination.

Intestinal Coccidia

The most important species of intestinal coccidia are *Eimeria perforans, Eimeria magna, Eimeria media,* and *Eimeria irresidua,* with *E. perforans* being the most common. Infection is by ingestion of sporulated oocysts. Although rabbits are cecotrophic, it is generally accepted that cecotrophs eaten from the anus do not contain infectious oocysts. Clinical signs vary widely depending on the age of the rabbit, the organism involved, the parasitic burden, and the relative susceptibility of the animal (determined by factors such as age, stress, and diet). Subclinical infection is common in both young and adult rabbits. The finding of oocysts in clinically normal rabbits does not warrant treatment. Clinical signs are most often associated with poor husbandry or overcrowding and generally occur in rabbits under 6 months of age. Severely immunosuppressed older rabbits may also become symptomatic. Mild intermittent to severe diarrhea that may contain mucus or blood, weight loss, and dehydration may be observed. Animals with severe diarrhea may develop intussusception. Death is most often attributed to dehydration and secondary intestinal dysbiosis. Postmortem examination reveals lesions in the

small or large intestine, depending on the agent involved. The epithelium of the intestine may be ulcerated. The presence of the organism (or organisms) in fecal samples or intestinal scrapings in symptomatic animals supports a presumptive diagnosis. Definitive diagnosis is based on histologic findings.

Numerous agents have been used to prevent and treat intestinal and hepatic coccidiosis. Sulfa drugs appear to be the most effective. The addition of sulfadimethoxine to the diet in an amount to ensure intake of 75 mg/kg for 7 days or 0.02% sulfamerazine sodium to the drinking water is efficacious for treating groups of rabbits.[40] Amprolium 9.6% in drinking water (0.5 mL per 500 mL) also is effective. Treat individual pet rabbits with sulfadimethoxine (15 mg/kg PO q12h for 10 days) or trimethoprim-sulfamethoxazole (30 mg/kg q12h PO for 10 days). The major role of antiparasitic agents is to limit multiplication until immunity develops. Instruct rabbitry, shelter, and pet store personnel in the practice of good husbandry to control outbreaks. Most healthy rabbits kept in clean, stress-free environments show no clinical signs after infection and develop immunity that may be lifelong.[40]

CRYPTOSPORIDIA

Cryptosporidium parvum may cause a discrete and transitory diarrhea in young rabbits, peaking at 30 to 40 days, which may lead to growth retardation. Clinical signs include diarrhea lasting 3 to 5 days, decreased appetite, depression, lethargy, exhaustion, and dehydration. *C. parvum* infects the intestinal tract, especially the ileum and the jejunum. The organism apparently does not cause disease in adults. Atrophy of villi of the ileum in young rabbits has been observed histologically.[38] Currently no effective treatment for cryptosporidiosis is recognized.

OTHER PROTOZOA

Several nonpathogenic flagellates may be found in the feces of rabbits. They occur more commonly in animals with diarrhea. *Giardia duodenalis* occurs rarely in the anterior region of the small intestine of rabbits and is not considered pathogenic. Other nonpathogenic protozoa found in the cecum and colon include *Monocercomonas cuniculi* and *Retortamonas cuniculi*, which are flagellates from the cecum; large ciliated protozoa found in the cecum that are similar to those of the genus *Isotricha* in ruminants; and *Entamoeba cuniculi*, which is commonly found in the cecum and colon of rabbits.[40]

HELMINTHS

Nematodes

Passalurus ambiguus is the common pinworm of domestic rabbits, although *P. nonanulatus* also is reported.[26] Occurrence is widespread in both wild and domestic rabbits; however, the presence of even relatively large numbers of pinworms is nonpathogenic. The adult parasite is found in the anterior portion of the cecum and colon. Adult worms are grossly visible in the lumen of the cecum and large intestine and when they are passed with fresh feces. The life cycle is direct, with infection through the ingestion of infected eggs during cecotrophy. Juvenile stages are found in the mucosa of the small intestine and cecum. Pinworms are commonly seen during routine surgical procedures such as ovariohysterectomy. Diagnosis is made by identification of adult worms or by demonstration of the parasite's eggs in the feces.

Pinworm infections, even those with heavy worm burdens, are usually asymptomatic and do not require treatment. However, owners may notice the worms in rabbit feces and desire treatment. Advise owners that pinworms are species-specific, and not zoonotic. The benzimidazoles are effective in greatly reducing if not eliminating pinworms. Thiabendazole (50 mg/kg PO repeated in 10-14 days) and fenbendazole (10-20 mg/kg PO repeated in 14 days) are generally effective. Piperazine (200 mg/kg PO repeated in 14 days), to treat individual rabbits, or in drinking water (100 mg/100 mL of water for 1 day repeated in 10 days), to treat large numbers of animals, may also be effective. Other helminths are extremely rare in pet rabbits.

Cestodes and Trematodes

Clinical disease as the result of intestinal cestode or trematode infection has not been reported in pet rabbits. The rabbit's GI tract can host up to five species of cestodes: *Cittotaenia variabilis*, *Mosgovoyia pectinata americana*, *Mosgovoyia perplexa*, *Monoecocestus americana*, and *Ctenotaenia ctenoide*s. Only *C. variabilis* has been found in domestic rabbits, whereas the other species are most often found in wild rabbits in North America and Europe.[1,4] Adult parasites are found in the small intestine. The life cycles of some species are not well known; however, oribatid mites or ants are thought to act as intermediary hosts. Treatment of cestode parasites consists of the administration of a single dose of praziquantel (5-10 mg/kg PO).

NEOPLASIA

Neoplasms of the GI tract include adenocarcinoma and leiomyosarcoma of the stomach, leiomyoma and leiomyosarcoma of the intestine, papilloma of the sacculus rotundus, papilloma of the rectal squamous columnar junction, and bile duct adenoma and carcinoma. Metastatic neoplasia, most commonly uterine adenocarcinoma, often involves the GI tract. Surgical resection is the treatment of choice for many of these tumors. If diagnosed early, intestinal masses can be resected with good success.

Rectal papillomas (cauliflower-like, fungating masses arising from the anorectal junction) appear to be benign and are not related to the papillomas of skin or the oral cavity. Removal of these lesions is often curative.

Bile duct adenoma and adenocarcinoma occasionally occur in pet rabbits. These tumors are often multiple and consist of interlocking cysts filled with thick, viscous, myxoid fluid. A variety of noxious stimuli, particularly infection with *E. stiedae*, may be causative factors. Antemortem diagnosis in some rabbits is based on the results of radiography and ultrasound. Surgical removal is often not practical. Metastatic disease is most often miliary and carries a grave prognosis.[47]

LIVER LOBE TORSION

Liver lobe torsion has been recognized as a problem in rabbits for some time, with published reports dating back to 1958; there have also been several reports since that time.[11,49,50] The caudate lobe is most often affected; however, torsion of the right lobe, the quadrate lobe, and the posterior lobule of the left hepatic lobe have also been reported.[49,50] Both acute and chronic forms of liver lobe torsion have been observed.

Signs of acute liver lobe torsion generally progress over a 12- to 72-hour period. Initially, affected rabbits are anorexic, weak, and depressed they demonstrate cranial abdominal discomfort.

Mucous membranes may initially appear jaundiced. The stomach may contain food and a small amount of gas, suggesting gastric stasis syndrome. However, affected rabbits deteriorate over a relatively short period of time; if not treated, they become obtunded, have decreased body temperature, dark mucous membranes, and prolonged capillary refill time. Death may occur 12 to 72 hours from the onset of signs. The most commonly reported hematologic and biochemical abnormalities include anemia (packed cell volume 16%-17%) and mild to severe elevation of the liver enzymes ALT, AST, and gamma glutamyl transferase (GGT).[19,46,49] However, these values may be normal in some cases. Hepatomegaly or an increase in density of the liver may be observed on radiographs, although this change may be difficult to appreciate. Ultrasonographic examination may be normal early in the course of disease or may demonstrate a heterogeneous appearance to the affected liver lobe, free fluid in the peritoneum, and occasionally pleural fluid. Treatment of acutely ill rabbits consists initially of supportive care, including intravenous fluids, analgesia, and thermal support. Surgical removal of the affected liver lobe in these rabbits may be lifesaving; however, the postsurgical survival rate is low.

Signs of chronic liver lobe torsion are often nonspecific. These rabbits are often described as "poor doers" with a past history of recurrent GI stasis. Liver lobe torsion has also been diagnosed as an incidental finding at necropsy in previously asymptomatic rabbits.[48,50] On physical examination, a firm, nonpainful mass is sometimes palpable in the cranial abdomen. Hematologic and biochemical abnormalities may include mild to moderate increases in liver enzyme activity, anemia, and azotemia. Diagnosis is based on ultrasonic examination of the affected lobe. Surgical lobectomy has been successfully performed in rabbits with this chronic presentation.[46] Anecdotal reports of rabbits surviving with supportive treatment alone also exist.

AFLATOXICOSIS

Aflatoxins are secondary metabolites of fungi, produced primarily by *Aspergillus flavus* and *Aspergillus parasiticus*. The LD_{50} for aflatoxins in rabbits is among the lowest for any species studied.[10] In one outbreak of aflatoxicosis in angora rabbits, affected animals had anorexia, dullness, and weight loss followed by jaundice in terminal stages. Death occurred within 3 to 4 days of the appearance of clinical signs. On postmortem examination, livers were moderately to severely congested, icteric, and hard to cut. Gallbladders were distended and had inspissated bile. Liver sections showed degenerative changes of hepatic cells along with dilatation and engorgement of sinusoids. Bile ducts had mild to severe periportal fibrosis. Focal areas of pseudolobulation and regenerative foci were also predominant. The level of aflatoxin B_1 in feed samples from various farms submitted at the time of the investigation varied from 90 to 540 mg/kg of feed. Withdrawal of feed and supplementary therapy resulted in gradual disappearance of signs and deaths.[29]

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