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Gastrointestinal Diseases of Rabbits

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OUTLINE

GASTROINTESTINAL MOTILITY DISORDERS

Gastrointestinal Stasis Syndrome

Gastrointestinal (GI) stasis is the common term used to describe a syndrome of reduced or absent GI motility and its consequences in rabbits. It is by far one of the most common disorders seen in pet rabbits. Very often, it is caused by an inappropriate diet. However, stress is a common initiator of decreased GI motility, so any illness, painful condition, or stressful event can trigger an episode. Rabbits with GI stasis will eventually stop eating, and a lack of food in the intestinal tract will exacerbate GI stasis. Left untreated, GI stasis can rapidly become life-threatening.

The Role of Fiber

To understand the pathogenesis of GI diseases of the rabbit, the normal anatomic and physiologic aspects of rabbit digestion must be appreciated. Details of this are discussed in Chapter 13. In rabbits, the main driving force for normal intestinal motility is the presence of large quantities of indigestible fiber. Lack of this fiber, caused by either dietary inadequacies or conditions that cause anorexia, is a major cause of GI stasis.[18] Fiber stimulates cecocolic motility, either by a distention effect of the bulk or directly. Diets high in fiber promote the production of specific volatile fatty acids in the cecum that promote peristalsis.[18] Inadequate ingestion of coarse fiber will inhibit normal GI peristalsis. Rabbits ingest hair routinely in the process of grooming.

However, they 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, hair and ingesta accumulate in the stomach. Fluid is absorbed from the stomach, further compacting the contents. Compacted ingesta causes discomfort, 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 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 a complex milieu of microorganisms, including anaerobic organisms, such as *Bacteroides* species, large anaerobic metachromatic staining bacteria, and many as-yet unidentified species of bacteria.[14,23,40] Other bacteria normally present are gram-negative oval and fusiform rods, as well as yeast and several nonpathogenic species of protozoa and amoebas.[40] This combined microflora is responsible for processing fiber 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* and coliform species such as *Escherichia coli,* are normally present in small numbers in the cecum.[14,23] 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 cause an increase in these pathogens as the populations of normal organisms decrease. Overgrowth of these pathogens can cause a range of pathologic changes, from intestinal gas distention to death from enterotoxemia. Gas and toxin formation cause pain and stress, further decreasing appetite, and a cycle of pain, inappetence, and hypomotility ensues. Without intervention, all motility can be lost, leading to end-stage ileus. 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 by-product of carbohydrate digestion, is necessary to produce iota toxin by *Clostridium* species. Thus diarrhea and enterotoxemia in pet rabbits are often caused by this disruption in microflora, commonly referred to as *dysbiosis*.

History and Clinical Signs

During physical examination, obtain a complete dietary history, including the type and amount of commercial pellets, hay, leafy greens, and treats. Rabbits with a regular diet consisting primarily of pellets without adequate fresh hay supplementation are at increased risk for development of GI stasis. The risk is even higher in rabbits fed rations consisting of a mix of dried fruits, vegetables, seeds, nuts, grains, and pellets. Acute episodes of GI stasis and dysbiosis are common in rabbits after ingesting a large volume of high-carbohydrate, high-fat treats. Rabbits at low risk are those fed diets of unlimited, good-quality, high-fiber grass or timothy hay, a moderate amount of fresh leafy greens, minimal pellets, and no or only occasional treats.

Stress alone, including stress caused by pain or concurrent disease, can cause GI stasis. Question the owner about recent potentially stressful events such as changes in housing, introduction of new rabbits or other pets, recent illness, trauma, or surgery, or any underlying disease processes. Common underlying disorders that may cause anorexia are dental disease, chronic upper respiratory tract disease, neurologic disorders, lower urinary tract disease, and renal or hepatic disorders. Many rabbits with stasis will have a history of little or no routine exercise.

In rabbits with GI stasis, the most common presenting complaint is a gradual decrease in appetite over 2 to 7 days and subsequent decrease in fecal production. Left untreated, rabbits will eventually stop eating entirely. Water consumption also is often decreased. Feces become scant, dark, dry, and small, eventually ceasing altogether. Owners may report a corresponding decrease in activity, due to 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.

Physical Examination Findings

Rabbits with stasis generally appear alert and quiet, exhibiting little or no sign of lethargy. In suspect cases, palpate the abdomen with careful attention to the stomach contents, intestines, and cecum. The size and consistency of the stomach are key in differentiating GI stasis from obstructive disorders. With GI stasis, stomach size may vary with the duration of disease, but it always contains ingesta, as opposed to fluid and gas seen in rabbits with obstructive disorders. In GI stasis, fluid is pulled from the stomach, eventually leading to stomach contents that feel firm, doughy, and remain pitted on compression. Occasionally, stomach contents are very dehydrated and solid. No fluid and little or no gas is palpable in the stomach, whereas the intestines and cecum frequently contain variable amounts of gas. Little or no feces are palpable in the colon. Auscultate the abdomen, listening for borborygmus, because the character and frequency of gut sounds also will distinguish GI stasis from obstructive disorders. Rabbits with intestinal hypomotility have decreased or absent gut sounds. The remainder of the physical examination is usually unremarkable except for those findings related to any underlying disorder.

Diagnostic Testing

Other than evidence of dehydration, results of the complete blood count and biochemical profile will not change because of GI stasis. Radiographs are very helpful in the diagnosis and essential to differentiate GI stasis from obstructive disorders. Radiographic changes vary with the severity of illness, but in

all cases, the stomach will contain ingesta. Presence of an ingesta-filled stomach in a rabbit that has been inappetent for several days is suggestive. As fluid is pulled from the stomach, ingesta will become compact and dense and may be surrounded by a small halo of gas (Fig. 14.1A–B). This appearance contrasts sharply with the dilated, fluid-filled stomach observed radiographically in rabbits with obstructive disorders (Fig. 14.2A–B). Moderate to severe gas distention of the cecum and scant fecal pellets are commonly seen.

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 stasis is mild or treated early, many rabbits respond well to oral and subcutaneous fluid administration and are less stressed when treated on an outpatient basis. If anorectic for more than

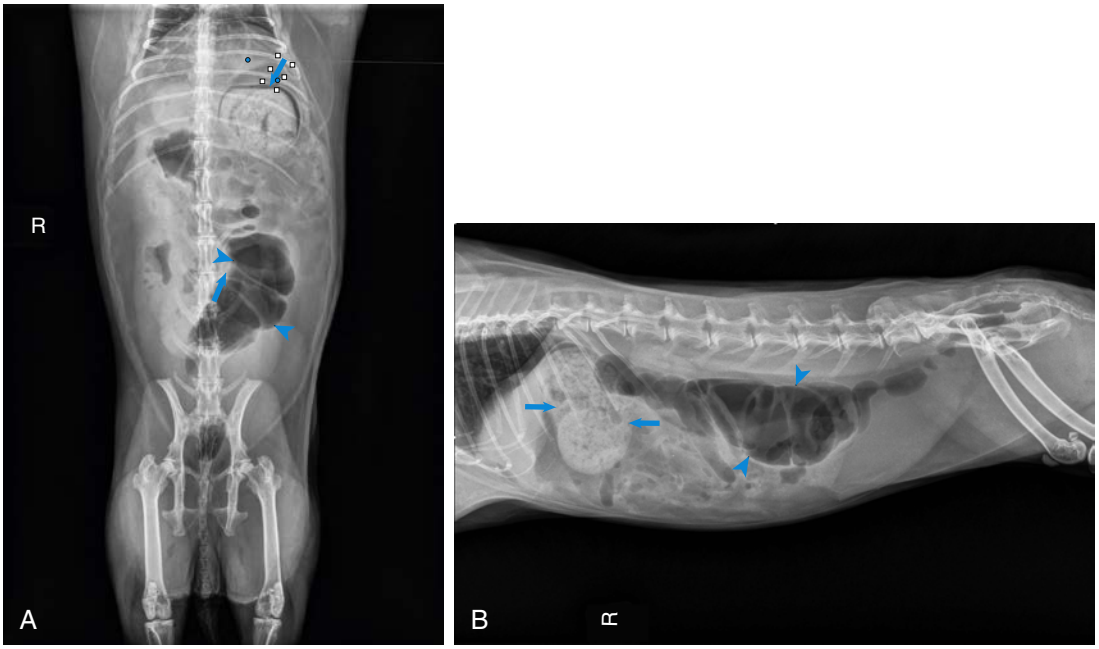

Fig. 14.1 Survey lateral (A) and ventrodorsal (B) radiographs of a rabbit with gastrointestinal stasis. Note the increased density of firm ingesta *(arrows)* and large amounts of gas within the in cecum *(arrowheads)*, characteristic of gastrointestinal stasis.

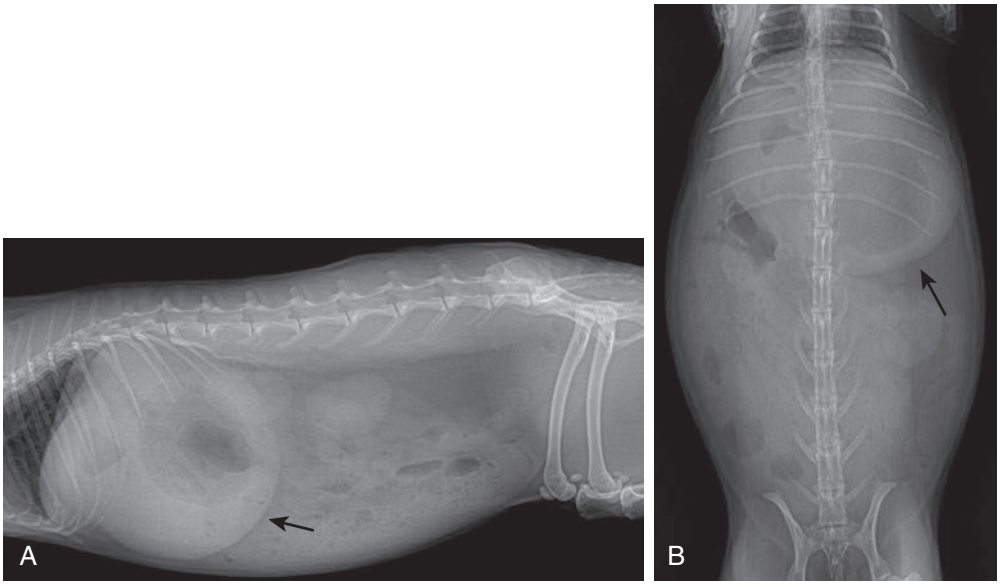

Fig. 14.2 Survey lateral (A) and ventrodorsal (B) radiographs of a rabbit with a proximal acute gastrointestinal obstruction. Note the severely distended, fluid-filled stomach with central gas cap ("fried-egg" appearance) and the lack of gas within the gastrointestinal tract distal to the stomach. This is consistent with an acute proximal small intestinal obstruction.

1 to 2 days, rabbits are usually severely dehydrated and generally require hospitalization for intravenous fluid therapy. Rehydrate the stomach contents by assisted feeding with a syringe or by placing a nasogastric feeding tube (see Chapter 12) if the rabbit will not accept syringe feeding. Ensuring that the patient continues to eat during and after treatment is important. Continued anorexia will exacerbate GI hypomotility and cause further derangement of the gastrointestinal microflora. The act of eating itself stimulates gut motility. Maintaining caloric needs will prevent secondary hepatic lipidosis, which progresses quickly in anorectic rabbits. Several commercial nutritional products for rabbits are available for this purpose, and most rabbits will readily accept them when offered by syringe. Base the volume and consistency of the feeding formula on your palpation of the stomach and radiographic findings. For example, if the stomach is small with radiographically dense ingesta, feed a diluted formula. If the stomach is very full or even dilated with ingesta, withhold assist feeding until the stomach contents begin to move out of the stomach. Do not feed pineapple, pineapple juice, or papaya, because these are ineffective and can be detrimental (see below). Offer rabbits free-choice water in a bowl, fresh hay, and a variety of greens to provide every opportunity to self-feed. Ingestion of fibrous food is critical to reestablish GI motility.

Rabbits with GI stasis have moderate 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 painful (reluctant to move, hunched posture), administer an opioid such as buprenorphine (0.03–0.05 mg/kg subcutaneously [SC] or intravenously [IV] every 6–12 hours) or a nonsteroidal antiinflammatory drug (NSAID) such as meloxicam (0.5–1.0 mg/kg SC every 24 hours) or carprofen (1.0–2.2 mg/kg by mouth [PO] every 12 hours). Less painful rabbits may respond well to NSAIDs alone, but a combination of opioids and NSAIDS can be used in very painful rabbits. Before administering NSAIDs, be certain that the rabbit is fully hydrated and that no underlying renal disorders are present. Initially, always use a parenteral route for medications, because intestinal absorption is limited with ileus. A recent study compared the effects of IV buprenorphine and IV lidocaine continuous rate infusion (CRI) on gastrointestinal motility and evidence of pain in New Zealand white rabbits after ovariohysterectomy.[59a] Rabbits that received a lidocaine CRI (2 mg/kg loading dose, then 100 µg/kg/min CRI for 2 days) had higher gastrointestinal motility, food intake, fecal output, and normal behaviors and lower blood glucose levels than rabbits treated with buprenorphine (0.06 mg/kg IV q8h for 2 days). Therefore, a CRI of lidocaine may be useful in treating or preventing pain and associated stasis in rabbits.

Intestinal prokinetic agents are usually beneficial. Metoclopramide (0.2–1.0 mg/kg PO, SC, or Intravenously (IV) every 8–12 hours) should initially be administered parenterally. If IV fluid therapy is being administered, metoclopramide also can be administered as a constant rate infusion (2 mg/kg per day). Ranitidine (2–5 mg/kg PO, SC, or IV every 12–24 hours) has intestinal prokinetic effects in addition to protecting against gastric ulceration. If GI motility is sufficient to allow oral administration of medications, administer cisapride (0.5 mg/kg PO every 8 hours, available through compounding pharmacies). Antibiotics are only indicated if evidence of severe dysbiosis is present. Encourage movement to stimulate gut motility further by making the rabbit hop around on the floor one to two times daily.

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 be abnormal in shape, size, and consistency and may contain mucus or hair. If a rabbit is not responding to treatment, reevaluate the animal to identify underlying disorders contributing to anorexia.

Other remedies such as lubricants (e.g., petroleum laxatives), protein-digesting enzymes (e.g., pineapple for bromelain and papain), and simethicone have no beneficial effect because 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, because these can be irritating to oral and potentially gastric mucosa. The risk of gastric ulceration is increased in anorectic rabbits, and use of these enzymes may exacerbate this.

Gastrointestinal Obstructive Disorders: Acute Gastrointestinal Obstruction and Moving Obstructions

Gastrointestinal obstructive disorders can be divided into two major categories: acute obstructions and moving obstructions. Acute GI obstruction (also referred to as GI dilation or "bloat") is an acute, life-threatening condition. The pathogenesis, history, and clinical findings differ considerably from those of GI stasis. Both acute and moving intestinal obstructions are usually caused by a compact mat or "felt" of hair, approximately 3 × 1 cm (size of an almond). Where these mats of hair are formed is not clear, but possibly they are compacted in the cecum, then ingested and swallowed whole with other cecal contents during normal cecotrophy.[31,32] Other foreign objects reported to acutely obstruct the intestinal tract include carpet or other cloth fibers, locust beans, and plastic.[31,32] Extraluminal compression of the intestinal tract by neoplasia, postsurgical adhesions, tapeworm cysts, abscesses, and hernias may also occur.[29,31,32,54]

The most common cause of death from an acute intestinal obstruction is hypovolemic shock, caused by a sudden loss of fluid into the lumen of the GI tract proximal to the obstruction. In studies of intestinal obstruction with rabbits used as models, ligating the intestinal tract results in rapid, active secretion of sodium, followed by water into the intestinal lumen proximal to the obstruction.[10,11,47,68] Within hours, as much as 200 to 250 mL of fluid accumulates first in the obstructed intestinal segments and then in the stomach.[10,11,47,68] Sodium and fluid secretion is most active in the first 25 to 30 cm of the duodenum, proximal to the entrance of the pancreatic duct.[10] Fluid resorption is impaired in obstructed segments, and this rapid loss of fluid leads to hypovolemic shock. Gas formation also contributes to GI tract distension proximal to the obstruction. Within 1 hour of ligation, gut pH and bacterial flora begin to shift. Eventually, bacterial flora completely reverses, with an overgrowth of Enterobacteriaceae and gas-forming clostridia, adding to gastrointestinal dilation.[9,14,68] Accumulated fluid in obstructed intestines and eventually stomach results in stretching of the intestines, compromise of venous outflow, and pressure necrosis

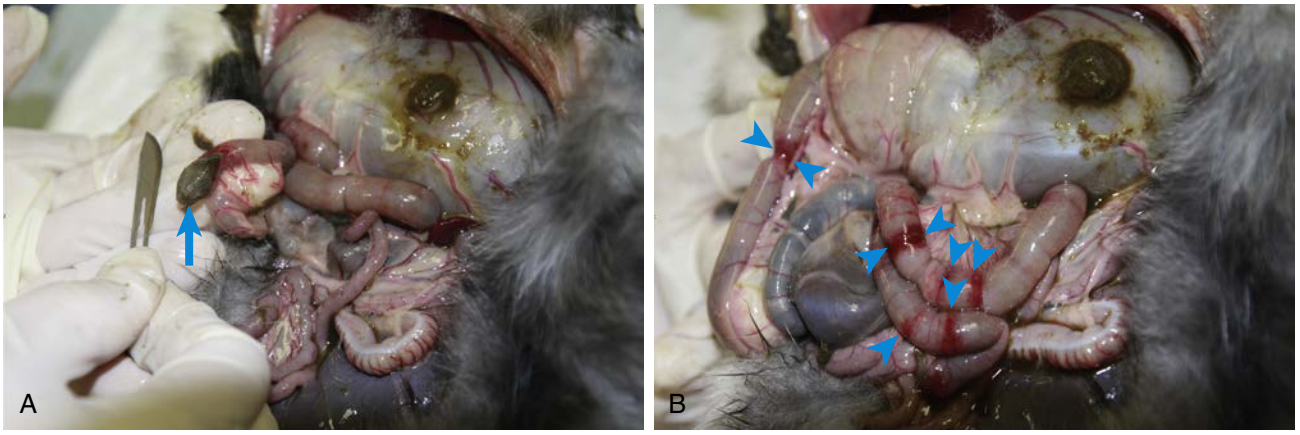

Fig. 14.3 Postmortem examination of a rabbit that died from gastric rupture due to an untreated, moving obstruction. (A) Note the typical appearance of acute gastrointestinal obstruction caused by a hair pellet *(arrow)*. (B) Note the hyperemic appearance of the intestinal serosa at multiple locations at which the hair pellet had previously lodged *(arrowheads)*.

of the affected segments.[47,68] In some cases, the stomach will acutely rupture. If the obstruction is not relieved, the affected intestinal loops will begin to necrose.[47,68] As this occurs, motility declines and secondary GI stasis develops.

The location of the obstruction determines the rapidity of the course of disease. The most common location is the proximal duodenum, approximately 2 to 5 cm from the pylorus where the lumen narrows. With a proximal obstruction, shock begins within hours and, if untreated, death occurs within 6 to 8 hours. If the obstruction is more distal, in the jejunum or ileocecocolonic junction, obstructed loops become progressively fluid or gas filled over a longer time. Experimental ligation in rabbits at the level of the jejunum results in death in 12 to 24 hours and at the ileum within an average of 21 hours.[11]

In contrast to GI stasis, the intestinal tract proximal to the obstruction becomes hypermotile. Studies of electrical activity in obstructed horses and rabbits demonstrate intense, irregular activity proximal to the obstruction.[11,17,35] This intestinal hyperactivity will often be successful in moving the obstruction distally. These "moving obstructions" are common (Fig 14.3A–B). The obstruction may pass with appropriate treatment, and small mats of hair may pass without treatment. Clinical signs of moving obstructions often resemble those of GI stasis.

History and Physical Examination Findings

A sudden onset of anorexia and depression is the hallmark feature of GI obstructive disorders. Some rabbits with proximal obstructions are found acutely moribund or dead with no premonitory signs. Affected rabbits suddenly refuse all food and abruptly stop producing feces. This contrasts with a gradual decline in appetite and production of small, dry fecal pellets with GI stasis. With moving obstructions, gut sounds may be audible from a distance, and the rabbit may stretch out and change positions frequently to get comfortable. With complete obstruction, they demonstrate signs of severe pain, such as reluctance to move and a hunched posture. As shock develops, 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, the stomach will palpate as large, fluid-filled, or tympanic, in contrast to the firm, ingesta-filled stomach found with GI stasis. Rabbits may appear painful on palpation. Early on, before the affected segments become necrotic, gut sounds are increased, and sometimes gut motility is visible through the abdominal wall. Initially, affected animals are alert but quiet, tachypneic, and tachycardic. With the onset of shock, they become hypothermic, bradycardic, and hypotensive.

Always obtain body temperature in suspect cases. With the onset of shock, body temperature will decline. Rabbits with a body temperature of 98°–99°F (36.7°–37.2°C) are in early stages of shock. Temperatures below 98°F (36.7°C) indicate severe, life-threatening shock.[19]

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 a normal rabbit. The most prominent feature is that the stomach is distended with fluid as opposed to ingesta seen in rabbits with GI stasis. The degree of distension depends on the location of the obstruction and the time interval between presentation and the onset of obstruction. With proximal (duodenal) or late-stage distal obstructions, the stomach will appear severely distended with fluid and may have a gas cap, giving it a characteristic "fried-egg" appearance (Fig. 14.2A–B). If the obstruction is proximal, only the stomach is distended, and no organized gas is seen in intestinal loops. With distal obstructions, gas distention of intestinal loops from the point of obstruction proximal to the stomach are usually are noted (Fig 14.4).

Obtain a blood sample for a complete blood count and biochemical profile. Blood glucose concentration can be helpful in differentiating obstructive disorders from GI stasis.[30] Obstructed rabbits, especially at the onset of shock, often have blood glucose concentrations >300 mg/dL (15 mmol/L). This is in part due to stress, but glucose concentrations also will increase to maintain serum osmolality in the face of sodium loss into the GI tract.[8] Most rabbits with acute obstruction will have increased renal values, and some develop acute renal failure. If renal values are increased,

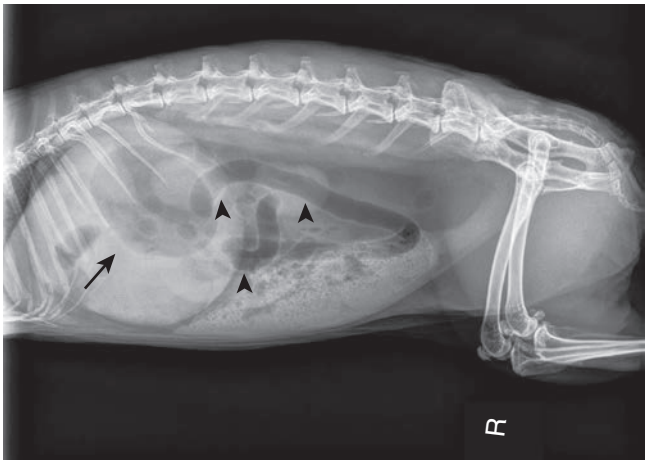

Fig. 14.4 Survey lateral radiograph of a rabbit with a distal intestinal obstruction. Note the severely distended, fluid-filled stomach (*arrow*) with central gas cap and gas distention of intestinal loops (*arrowheads*) leading to the point of obstruction.

monitor values after treatment. The biochemical profile will also help to rule out liver torsion, which may have a similar presentation.

Initial Medical Treatment

Begin treatment immediately, because this is a life-threatening disorder. Initial treatment goals are to warm the patient (if hypothermic), treat shock, decompress the stomach, correct any fluid and electrolyte imbalances, and control pain. If hypothermic, immediately begin external heat support. Place an intravenous catheter and begin treatment with a shock dose (60–90 mL/kg per hour for the first hour) of warmed, isotonic crystalloid fluids. When shock is controlled, reduce administration to a maintenance rate. If shock is severe and a response to crystalloid fluid therapy is not seen, administration of 7.5% NaCl or hetastarch (3 mL/kg over 5 minutes) may be effective (see Chapter 41). (Hetastarch is not available in the UK or Europe. In 2018, the European drug regulators announced the suspension of marketing authorizations for all hydroxyethyl starch [HES] plasma volume replacement solutions across the European Union and the UK.) Correct any electrolyte imbalances. To control pain, administer buprenorphine (0.02–0.05 mg/kg SC or IV every 6–12 hours), butorphanol (0.2–0.4 mg/kg SC or IV), or hydromorphone (0.1 mg/kg IV). Avoid NSAIDs until renal status is known.

Sedation is necessary to decompress the stomach in most cases. Sedation with midazolam (0.5–1.0 mg/kg IM, IV) or dexmedetomidine (0.03–0.05 mg/kg IM) or both, in addition to pain medications, may be sufficient if the patient is depressed, although the addition of gas anesthesia is often needed. A well-lubricated 18-Fr red-rubber catheter works well as an orogastric tube in most medium-sized rabbits; a smaller size may be needed in small breeds. 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. With the head held in ventroflexion, pass the well-lubricated tube gently by mouth into the stomach. If the tube becomes clogged, remove the tube and flush, then repass the tube to remove as much fluid and air as possible from the stomach. Percutaneous trocharization of the stomach is contraindicated as a method of decompression, because this will likely cause rupture of the stomach. The color and odor of the fluid are a prognostic indicator. The fluid should be brown to green and smell of food. If the fluid is odiferous and dark brown to red or black, the stomach is likely necrotic, and the prognosis is grave.

In many cases, the obstruction will pass after medical treatment and decompression. Palpate the abdomen frequently, monitor for signs of pain, and repeat radiographs to determine whether the obstruction is passing. 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, usually within 24 hours. If the patient does not improve, and the stomach begins to fill with fluid, decompression should be repeated. If no improvement is seen after a second orogastric decompression, the obstruction is either not moving or is caused by extraluminal intestinal compression. Surgical treatment is indicated, because the intestines will begin to necrose if the obstruction is not relieved.

Surgical Treatment

Exploratory laparotomy allows for diagnosis and possible treatment of intestinal obstructions caused by extraluminal compression (e.g., tumor, adhesions, hernia) and removal of complete, immobile intraluminal obstructions. Indications for surgery are a lack of response to medical treatment, an inability to decompress the stomach, or declining GI tract motility. These indicate that the obstruction is either extraluminal or is not moving. Surgery may also be indicated to quickly remove the obstruction if close monitoring of the patient is not possible after initial medical treatment. When possible, decompress the stomach and stabilize the patient for shock before attempting surgery. Because intraoperative gastric reflux may occur, always place an endotracheal tube for anesthesia. Provide IV fluids and heat support during surgery. A lidocaine CRI (loading dose 2 to 3 mg/kg, then 33–100 ug/kg/min) provides additional pain control, is antiinflammatory, and may help to prevent postoperative ileus.[59a,62]

Most acute intraluminal obstructions are in the proximal duodenum, 3 to 5 cm from the pylorus. When possible, avoid enterotomy by manipulating the foreign body into the cecum. If this is not possible, move it 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. Assess the viability of the obstructed portion of the intestine. If the portion of intestine surrounding the foreign body appears necrotic, an intestinal resection and anastomosis may be indicated. If large sections of obstructed intestinal loops have become ischemic, the prognosis is grave, and euthanasia may be warranted. 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 and pain management. If GI motility has declined, provide promotility agents and assist feeding. With prompt removal of the foreign body, the prognosis is good. If intestinal viability is compromised, the prognosis is guarded to poor.

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* (see Chapter 13). Because they are swallowed whole directly from the anus, most owners rarely see normal cecotrophs. If intact, cecotrophs appear as multiple, soft fecal pellets stuck together, resembling a blackberry, and have a strong odor. If cecotrophs are not eaten, they often stick to the fur around the perineum or are found smeared on the fur and flooring. This is often confused with 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 cecotrophs are abnormally formed. Obesity is a common cause of inability to consume cecotrophs because the rabbit cannot reach the anal region. Other causes are musculoskeletal disorders, vestibular disease, 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 may be soft, malformed, pasty, or odiferous and are not eaten. 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. Correcting the underlying disorder will allow a return to normal cecotrophy.

If the rabbit can reach the perineum and the cecotrophs are soft, fluid, or malformed, question the owner about the diet. Insufficient fiber (hay) or excessive carbohydrate intake is a common cause. In this case, correcting the diet will usually correct the problem. Feed only hay (preferably first-cut, high fiber) until uneaten cecotrophs are no longer seen. This can take days to weeks depending on the severity of cecal dysbiosis. Once no uneaten cecotrophs are seen for several days, gradually add back pellets, then greens to the diet. For some rabbits, the addition of greens will consistently cause abnormal cecotrophs and will need to be withheld permanently.

Cecoliths

Altered motility of the cecum, rate of transit in the colon, or abnormal diet (e.g., very short 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. Rabbits that form cecoliths often have a chronic history of large, malformed feces, recurrent cecal impaction, abdominal pain, and anorexia. Because these rabbits are unable to form normal cecotrophs, they are often underweight and lack normal muscle mass. A congenital progressive and eventually fatal disorder of sodium transport into the cecum is found in homozygous spotted (English Spot) and Checkered Giant breeds.[6] This is commonly referred to as "megacolon-syndrome" but involves primarily the cecum, not the colon. A presumptive diagnosis of cecolith formation can be made by palpation of doughy to very firm material in the cecum. Radiographs or ultrasound examination can confirm the presence of cecoliths. If the intestine is completely obstructed, gas will accumulate in the sacculated large intestine. Rabbits with cecal obstipation are in severe pain and may present moribund.

Treatment of cecoliths requires rehydration of inspissated cecal and colonic contents. Administer fluid therapy by the intravenous or subcutaneous route, depending on the degree of dehydration. Long-term administration of SC fluids may be helpful. Feed foods with a high water content (assist feeding slurries, wetted leafy vegetables) along with an appropriate fiber source, such as grass hay, to stimulate normal cecal motility and function. Intestinal promotility agents may also be of benefit. Provide analgesia, because these patients are often painful. The long-term prognosis is generally guarded to poor.

Rabbits with complete cecal obstipation are critically ill and in pain and require immediate treatment. Begin intravenous fluid therapy and pain medications. Occasionally, the obstructing cecolith can be softened and moved with a gentle enema. Take great care in administering enemas, because the colon may be necrotic at the point of obstruction. If the obstruction does not resolve with medical therapy, surgical removal will be required once the patient is stable.

DYSBIOSIS, ENTERITIS COMPLEX, AND ENTEROTOXEMIA

In clinical practice, the enteritis complex—with signs ranging from soft stool and diarrhea to enterotoxemia, sepsis, and death—is common in rabbits. Factors that allow pathogenic bacteria to proliferate are the usual causes. These factors involve stress, diet, antibiotics, and genetic predisposition to gut dysfunction. Epinephrine-mediated inhibition of gut motility is believed to cause stress-induced enteritis. Simple 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. Correcting the diet, adding fiber in the form of hay, and decreasing stress will often correct the problem.

Enterotoxemia

Enterotoxemia in rabbits, which is characterized by more significant dysbiosis than with enteritis, is caused by the iota-like toxin from *Clostridium spiroforme*.[51] Newly weaned animals (3–6 weeks of age) are most often affected, and they have the highest mortality rate. These rabbits may develop enterotoxemia from simple exposure to *C. spiroforme*, likely because young rabbits have an undeveloped population of normal GI flora and a high gastric pH, which allows *C. spiroforme* to proliferate. Adult rabbits are more resistant and generally require some dietary, environmental, or other stress for dysbiosis to be induced and growth of the bacteria to occur. Rapidly multiplying *C. spiroforme* significantly alters the rabbit's normal cecal flora. Nursing does can develop "milk enterotoxemia" that is believed to be caused by *Clostridium* endotoxin produced in the does' cecum and passed to the bunnies in the milk.

In acute disease, rabbits stop eating and become markedly depressed. Brown, watery diarrhea soils the perineum and rear legs, and it may contain blood or mucus. As the disease progresses, rabbits become hypothermic and moribund and die after 24 to 48 hours. Postmortem findings include petechial and ecchymotic hemorrhages on the serosal surface of the cecum; lesions can also involve the appendix and proximal colon. Various amounts of gas throughout the intestinal tract, cecum, and colon result from ileus. Hemorrhage, pseudomembranes, or mucus may be present in the mucosa of the cecum and proximal colon.

Mucoid Enteritis

Mucoid enteritis is a major cause of morbidity and death 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.[40] 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.

Antibiotic-Induced Dysbiosis

Antibiotic administration can cause enteritis. Certain 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.

Treatment and Prevention of Dysbiosis and Enterotoxemia

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. Antimicrobial drugs have limited value in the treatment of the disease and are used primarily as supportive therapy. *Clostridium spiroforme* has been shown to be sensitive to metronidazole and penicillin G.[13] The use of metronidazole (20 mg/kg PO or IV every 12 hours) has been reported to reduce the number of deaths from enterotoxemia. Administration of cholestyramine (2 g in 20 mL water every 24 hours by gavage), an ion-exchange resin capable of binding bacterial toxins, has been reported to prevent death in rabbits with clindamycin-induced enterotoxemia.[41] Correcting dehydration and maintaining 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. Cecal transfaunation by means of retention enema with cecotrophs or feces from a healthy rabbit has been anecdotally reported and may be helpful.

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.

Primary Bacterial Enteritis

Bacterial enteritis may be seen occasionally in the adult pet rabbit. It is a common cause of mortality in commercial rabbit industry, where mortality rates ranging between 50% to 100% have occurred. Typically, however, enteritis is seen in neonates or rabbits under 16 weeks of age that are stressed by weaning, transport, or overcrowding.

Escherichia coli

Enterohemorrhagic *Escherichia coli*, a potential zoonotic pathogen, produces shiga toxins that cause hemorrhagic colitis with hemorrhagic diarrhea. Rabbits are susceptible to this common water- and food-borne pathogen by oral ingestion. Naturally infected rabbits develop thrombotic microangiopathy, the hallmark of shiga toxin, and this is believed to be the cause of the less frequently seen acute renal failure.[50] From the seven groups of pathogenic *E.coli,* enteropathogenic *E. coli* is a major cause of economic loss in the commercial rabbit industry. Rabbit enteropathogenic *E. coli* is an attaching and effacing *E.coli* strain, where bacterial adherence, via a fimbrial adhesin, results in destruction of the brush border and rearrangement of the enterocyte structure. Diarrhea, caused by the resultant villus atrophy and malabsorption, varies in severity depending on the age of rabbit and specific serogroup involved.

In infected does, subsequent litters 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 research tool only.

Treat individual rabbits with antibiotics, guided by the results of culture and sensitivity testing, and supportive care including fluid therapy, assist feeding, and maintaining normothermia. Use trimethoprim-sulfamethoxazole (30 mg/kg PO every 12 hours) or enrofloxacin (15–20 mg/kg PO every 12 hours) until culture and sensitivity test results are obtained. The role of probiotics in the prevention and treatment of these cases is still unproven.

Proliferative Enteritis, Proliferative Enteropathy, Proliferative Enterocolitis

The obligate intracellular bacterium *Lawsonia intracellularis* has been reported as a cause of enterocolitis in rabbits both as a single pathogen and in association with an enteropathogenic strain of *E. coli* distinct from the prototypical rabbit diarrhea *E. coli* strain.[34,59] 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 or enteropathy is most reported in in swine and hamsters but also occurs in many species.[59] Histologic findings often show proliferative ileitis, with or without proliferative colitis, characterized by epithelial hyperplasia and mucosal inflammation. Similar disease in pigs and ferrets is caused by a different bacterium, *Desulfovibrio desulfuricans*.[26,44] 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) that are not recommended for use in rabbits. Chloramphenicol (30 to 50 mg/kg PO or SC every 12 hours for 7–14 days) is generally efficacious. Florfenicol (20–30 mg/kg PO, IM or IV) has shown good efficacy, although more-frequent doses may be required to maintain plasma antibiotic levels above the minimum inhibitory concentration for longer than 6 hours.[22]

Tyzzer's Disease

Tyzzer's disease is caused by *Clostridium piliforme* (formerly *Bacillus piliformis*), a motile gram-variable, spore-forming, obligate intracellular bacterium.[21] Stress (produced by overcrowding, unsanitary conditions, high temperatures, or breeding) is an important component of this disease. Clinical signs of Tyzzer's disease are watery diarrhea, depression, and death. Morbidity and mortality rates may be especially high in weanling rabbits, whereas older rabbits can develop a more chronic form of the disease that results in chronic weight loss. Necropsy 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 treatment. If exposed animals are treated early with preventative measures (isolation, good hygiene, supportive care, and a high-fiber diet), they may not develop the disease. Prevention depends on good husbandry. Clostridial spores are killed with a 0.3% sodium hypochlorite (bleach) solution, some disinfectants, or with heating to 173°F (80°C) for 30 minutes.

Other Causes of Bacterial Enteritis

Campylobacter species (*C. cuniculorum, C. jejuni, C.coli*) have been found in healthy and diarrheic rabbits. Although a pathogenic role of *C. cuniculorum* is not known, it has shown antibiotic resistance to fluoroquinolones and macrolides but is sensitive to chloramphenicol.[53]

Other causes of bacterial enteritis are *Salmonella* species, *Klebsiella pneumoniae, Klebsiella oxytoca,* and *Pseudomonas aeruginosa*. Because these are water-borne pathogens, outbreaks of disease can be seen when the watering system becomes contaminated. Salmonellosis is not common but can cause disease with high rates of both morbidity and mortality. *Salmonella typhimurium* is most often associated with salmonellosis in rabbits; however, other species and serovars have been reported.[7] Disease transmission 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.

Mycobacteriosis, including *Mycobacterium bovis* and *Mycobacterium avium* subspecies *paratuberculosis,* can cause diarrhea and emaciation in rabbits. *Mycobacterium bovis* is zoonotic, whereas *M. a. paratuberculosis* has zoonotic capacity. Natural infections of *M. a. paratuberculosis* have been reported in wild rabbits examined from farms with a high prevalence of ruminant paratuberculosis (Johne's disease) in Scotland.[4] Fecal cytology and tissue biopsy can be useful to confirm the presence of acid-fast bacteria in suspect cases. Mycobacterial culture or polymerase chain reaction analyses are required for a definitive diagnosis. Speciation of the mycobacteria involved requires molecular diagnostic methods. Treatment is challenging and can be controversial.

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.[45,60] Lesions consist of small white growths on the ventral surface of the tongue but only rarely occur elsewhere in the mouth. Early lesions are sessile, later becoming rugose or pedunculated and ultimately ulcerated. Papillomas can exceed 4 to 5 mm at their greatest dimension but are typically smaller (1–3 mm). Lesions may persist up to 145 days, but they usually disappear within weeks.

Rabbit Hemorrhagic Disease Virus

Viruses of the *Lagovirus* genus within the family Caliciviridae that affect rabbits include rabbit hemorrhagic disease virus (RHDV), European brown hare syndrome virus, and the nonpathogenic rabbit calicivirus.[28] Although European brown hare syndrome virus affects European hares of the *Lepus* genus, RHDV specifically afflicts domestic rabbits worldwide but does not cause disease in wild cottontail rabbits, jackrabbits, or hares. Although RHDV is endemic in Europe, Cuba, Australia, and New Zealand, limited outbreaks have occurred in the Middle East, South America, Mexico, and the United States. 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. In 2010, a new variant, hemorrhagic disease virus 2 (RHDV2), was identified in mainland Europe and has been reported in the United Kingdom and Australia since 2015.[2] This variant affects both domestic and wild rabbits, and disease has been seen in rabbits vaccinated against the classic RHDV strain.

Clinical disease occurs in rabbits older than 2 months of age; younger rabbits appear unaffected, although this is not absolute.[3,24,43,58] Virus is shed in urine, feces, and respiratory secretions. Transmission of RHDV is by direct contact, contact with carcasses or fur from affected rabbits, or contact with fomites such as water, feed, utensils, clothing, or cages. Flies and other insects may serve as vectors, and virus can be found in

feces from predators that have eaten infected rabbits. The disease 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 incubation period is 1 to 3 days. During outbreaks, the number of rabbits affected peaks in 2 to 3 days, and the disease course may last 7 to 13 days. The variant RHDV2 is less virulent, with lower observed mortality rates than RHDV, and clinical signs tend to be more chronic.

Virus replicates in the liver, resulting in severe hepatic necrosis and death from disseminated intravascular coagulation.[12,42,43] In peracute disease, rabbits die with no premonitory signs, or they become febrile and lethargic and die within 12 to 36 hours of infection. In acute disease, rabbits are febrile and exhibit depression, lethargy, anorexia, constipation, or diarrhea. Some may show neurologic signs such as ataxia, opisthotonos, excitement, or seizures. At end-stage disease, tachypnea, cyanosis, and a blood-tinged, foamy nasal discharge are often seen. In some rabbits, the disease course is slower, with 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.[2,24]

Hematologic testing often shows a lymphopenia and a gradual thrombocytopenia. In moribund rabbits, prothrombin and thrombin times are prolonged, and fibrin degradation products can be detected.[55] The most consistent postmortem changes are hepatic necrosis, splenomegaly, and evidence of disseminated intravascular coagulation. Congestion and hemorrhage may be seen in most organs but are 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.[20,55] Presumptive diagnosis is based on history, clinical signs, and pathologic findings. Definitive diagnosis requires identifying the virus by a variety of diagnostic tests, such as electron microscopy, reverse transcription polymerase chain reaction, Western blot, and enzyme-linked immunosorbent assay. The variant RHDV2 has been deciphered based on the major capsid protein (VP60) sequence. [58] In North America, on suspicion of disease, immediately contact state or federal regulatory agencies to report this disease, and send diagnostic samples only to authorized laboratories under secure conditions.

Several vaccines are available, including heat-killed liver extracts, VP60 protein, and a recombinant myxoma-RHD live virus. These vaccines do not provide protection against RHDV2.[58] Specific vaccines for RHDV-2 or combined RHDV-1/RHDV-2 are commercially available in mainland Europe and the United Kingdom. The virus can be inactivated by 0.5% sodium hypochlorite or 1% formalin.

Rabbit Enteric Coronavirus

In 1980, a coronavirus was found as a cause of diarrhea in laboratory rabbits.[39] This virus affects rabbits 3 to 10 weeks of age, but it is also found in clinically normal adult rabbits. In naturally occurring outbreaks, clinical signs are lethargy, diarrhea, abdominal swelling, and death. Pleural effusion and cardiomyopathy in rabbits have also been associated with coronavirus-like particles.[48] Morbidity and mortality rates can be high; in one described outbreak, 40% to 60% of rabbits were affected, and almost 100% died within 24 hours of the onset of clinical signs.[20] At necropsy, cecal contents are fluid, and histopathologic examination shows atrophy of intestinal villi. Tentative diagnosis is based on 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 demonstrating the virus in feces or cecal contents.

Rotavirus

Rotavirus infection causes diarrhea in rabbits. Serosurveys have revealed that it is endemic within domestic rabbits, as well in wild *Sylvilagus* and *Lepus* lagomorphs in Europe, Asia, and the United States. Infant rabbits are most susceptible, because the virus targets terminally differentiated enterocytes lining the tips of villi of the jejunum and ileum.[3] Transplacentally derived maternal antibodies are protective, and some protection continues past 45 days, when antibody levels decline, so less severe or subclinical infections may be seen in weaned rabbits. Morbidity and mortality rates vary with age, host immunity, and environmental stressors. Coinfection with other pathogens, such as *E. coli,* can have an additive effect and greatly increase morbidity and mortality rates.[3] Diarrhea, dehydration, and sudden death are the main clinical signs. Necropsy findings include mild to severe villus blunting, villus fusion, and submucosal edema of the small intestines, and fluid cecal contents. The lamina propria is usually infiltrated with lymphocytes and occasionally with neutrophils. Definitive diagnosis is based on results of histopathologic examination of the intestine. Isolation of the virus or demonstration of antibodies is suggestive. Clinical signs and gross pathologic findings alone are not diagnostic.[20] Human enzyme-linked immunosorbent assay test kits will detect rotavirus group A in rabbits.[3] Preventing and controlling rotavirus infection is complicated by its highly infectious nature. Reducing stress (reducing crowding, stopping breeding, removing socially dominant animals, and adding fiber to the diet) along with appropriate treatment of concurrent disease and improved hygiene should reduce mortality rates.

Other Viral Causes of Enteritis

Adenovirus and astroviruses have been found in young rabbits with diarrhea and enteritis. Co-pathogens are often also present. Prevention and control is like that used for rotavirus. A novel bocaparvovirus, a parvovirus, was recently described in both healthy rabbits and rabbits with enteritis.[38] The prevalence and pathogenesis of this virus is unknown.

PARASITIC DISORDERS OF THE GASTROINTESTINAL TRACT

Coccidia

Coccidia are the most common parasites of the rabbit GI tract and are a frequent cause of illness in young rabbits less than 6 months old. Adult rabbits are rarely clinically ill, and identifying oocytes on fecal examination does not equate to disease. Twelve

species, all members of the genus *Eimeria,* infect rabbits.[49] Only one species, *Eimeria stiedae,* which infects the liver, is found outside the intestinal tract. Two or more species of coccidia often are present in diseased rabbits; the exact role of different species as pathogens therefore is not clear.

Hepatic Coccidia

Eimeria stiedae, the coccidium responsible for hepatic coccidiosis, is ubiquitous in open rabbitries in which rabbits are not treated preventatively with coccidiostats. Infection results from ingesting sporulated oocysts that undergo excystation in the duodenum. Sporozoites then 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.[36] Many infections are asymptomatic; however, the disease can be fatal, especially in young rabbits. Heavily infected rabbits show signs related to decreased hepatic function and bile duct obstruction. These rabbits become anorectic and debilitated; diarrhea or constipation can occur in the terminal stages of the disease. The abdomen is occasionally enlarged, and the animal may be icteric. Serum biochemical testing reveals increased levels of alanine aminotransferase, aspartate aminotransferase, bile acids, and total bilirubin. On radiographs, hepatomegaly and ascites may be present. At necropsy, 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 by identifying 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, the 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. 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. At necropsy, lesions are seen in the small or large intestine, depending on the agent involved, and intestinal epithelium may be ulcerated. The presence of organisms in fecal samples or intestinal scrapings in symptomatic animals supports a presumptive diagnosis. Definitive diagnosis is based on histologic findings.

Numerous drugs have been used to prevent and treat intestinal and hepatic coccidiosis. 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.[49] Amprolium 9.6% in drinking water (0.5 mL per 500 mL) also is effective. Treat individual pet rabbits with a single dose of toltrazuril (2.5 mg/kg PO)[56] sulfadimethoxine (15 mg/kg PO every 12 hours for 10 days) or trimethoprim-sulfamethoxazole (30 mg/kg every 12 hours 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.[49]

Cryptosporidia

Cryptosporidium parvum can cause a discrete and transitory diarrhea in young rabbits, peaking at 30 to 40 days, which may lead to growth retardation. Adult rabbits are unaffected. Clinical signs are diarrhea lasting 3 to 5 days, decreased appetite, depression, lethargy, exhaustion, and dehydration. The organism infects the intestinal tract, especially the ileum and the jejunum. Atrophy of villi of the ileum in young rabbits has been observed histologically.[46] 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. *Monocercomonas cuniculi* and *Retortamonas cuniculi* are flagellates found in the cecum, as well as large ciliated protozoa such as those of the genus *Isotricha* in ruminants. *Entamoeba cuniculi* is commonly found in the cecum and colon of rabbits.[49]

Helminths

Nematodes

Passalurus ambiguus is the common pinworm of domestic rabbits, although *Passalurus nonanulatus* also is reported.[33] 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 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 identifying adult worms or by demonstrating 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 are 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. In farmed rabbits raised for slaughter, nematodes are more prevalent and include *Obeliscoides cuniculi, Graphidium strigosum*, *P. ambiguus*, *Trichuris leporis,* and *Trichostrongylus* and *Strongyloides* species.[61]

Cestodes and Trematodes

Clinical disease as the result of intestinal cestode or trematode infection has not been reported in pet rabbits. However, these parasites are present in wild rabbit species and are possible in laboratory animal populations.[1,5,33] The rabbit's GI tract can host several species of cestodes*: Cittotaenia variabilis, Mosgovoyia pectinata americana, Mosgovoyia perplexa, Monoecocestus americana,* and *Ctenotaenia ctenoide*s. Adult parasites are found in the small intestine. The life cycles of some species are not well known; however, oribatid mites or ants are believed to act as intermediary hosts. Rabbits are the intermediate host for several tapeworms that affect dogs and foxes, including *Cysticercus pisiformis,* the larval stage of *Taenia pisiformis*; *Coenurus serialis*, the larval stage of *Taenia serialis;* and *Echinococcus granulosus*.[57] Oral ingestion of the eggs, shed in carnivore feces, and then larval migration from the intestines leads to formation of cysts in various tissues, depending on their predilection site. Treatment of cestode parasites consists of the administration of a single dose of praziquantel (5–10 mg/kg PO). Prevent infestation of pet rabbits by avoiding feeding of wet grass clippings from areas where feces from possible natural hosts may be present.

NEOPLASIA

Neoplasms of the GI tract are uncommon and 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, can involve 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) are benign and are not related to the papillomas of skin or the oral cavity. Removal of these lesions is 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 ultrasonography. Surgical removal is often not practical. Metastatic disease is most often miliary and carries a grave prognosis.[64]

LIVER LOBE TORSION

Liver lobe torsion has been recognized as a problem in rabbits for some time, with published reports dating back to 1958 and occasional reports after.[16,26,65–67] 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.[27,52,66,67] Both acute and chronic forms of liver lobe torsion are observed. With acute torsion, hemorrhage at the base of the torsed lobe is common, rapidly resulting in hemoabdomen and death if untreated.

Signs of acute liver lobe torsion generally progress rapidly. History resembles acute GI tract obsrtruction, as affected rabbits become acutely anorectic, demonstrate cranial abdominal discomfort, and become weak and depressed.[27,52] The stomach usually contains food and a small amount of gas, suggesting gastric stasis syndrome. An abnormal liver is sometimes palpable. Affected rabbits deteriorate over a short time; if not treated, they become obtunded and hyporthermic, with pale mucous membranes if hemoabdomen is present. Death may occur 12 to 72 hours from the onset of signs. The most common hematologic and biochemical abnormalities are anemia (packed cell volume, 16%–17%) and mild to severe increases in the liver enzymes alanine aminotransferase, aspartate aminotransferase, and gamma glutamyl transferase (GGT).[26,27,52,63,66] However, these values may be normal initially. On radiographs, rounded liver margins, hepatomegaly, increased density of the liver, or free abdominal fluid are sometimes visible. Ultrasonographic examination is diagnostic and demonstrates a heterogeneous appearance and lack of blood flow on color doppler in the affected liver lobe.[27,52] With hemoabdomen, free fluid is visible in the peritoneum, and fresh blood is obtained on abdominocentesis. Treatment of acutely ill rabbits initially is supportive care, including intravenous fluids, analgesia, and thermal support. Prompt surgical removal of the affected liver lobe in these rabbits is the treatment of choice.[27,52] However, if this is not feasible for the owner and hemoabdomen is not present, some affected rabbits will survive with supportive care alone.[27]

Signs of chronic liver lobe torsion are often nonspecific. These rabbits are often described as "poor doers" with a history of recurrent GI stasis. Liver lobe torsion has also been diagnosed as an incidental finding at necropsy in previously asymptomatic rabbits.[65,67] 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.[63]

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.[15] In one described outbreak, affected animals

showed anorexia, dullness, and weight loss followed by jaundice in terminal stages, and rabbits died within 3 to 4 days.[37] At necropsy, livers were congested and icteric, and gallbladders were distended and had inspissated bile. Liver sections showed degenerative changes of hepatic cells and dilatation and engorgement of sinusoids. Bile ducts had mild to severe periportal fibrosis. The level of aflatoxin B_1 in tested feed samples varied from 90 to 540 mg/kg of feed. Withdrawal of feed and supportive care resulted in gradual disappearance of signs and deaths.[37]

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