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CHAPTER 3

Gastrointestinal Diseases

Heidi L. Hoefer, DVM, Diplomate ABVP (Avian), James G. Fox, DVM, MS, Diplomate ACLAM, and Judith A. Bell, DVM, PhD

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Salivary Mucocele
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GENERAL GASTROINTESTINAL DISORDERS

Disease of the gastrointestinal (GI) tract is common in ferrets. Clinicians should be familiar with the more common GI disorders in ferrets and be able to recognize clinical signs and differentiate among potential diagnoses.

DENTAL DISEASE

Ferrets are obligate carnivores with specialized tooth form and function designed to consume animal tissue. Compared with New Zealand feral ferrets, North American pet ferrets have a much greater amount of dental pathology. This is speculated to be a result of dental trauma from inappropriate chewing behavior and kibble-mediated disease.[14]

Dry kibble, the mainstay of most pet ferret diets, may be responsible for structural changes to the teeth. These low-moisture, hard crunchy diets appear to be quite abrasive to ferret teeth and result in significant wear to the cheek teeth and molars.[14] Although moist or semimoist diets have been associated with the formation of dental calculi and periodontal disease in experimental cases,[40] most ferrets on a dry kibble diet develop tartar and gingivitis that progresses with age (Fig. 3-1). Periodontal disease is considered pervasive in pet ferrets (see Chapter 32).

Chewing inappropriate objects (cage bars and toys) can lead to damage. Biting and gnawing habits often result in discoloration, wearing, and breaking of the tips of the canine teeth. Broken canine teeth do not usually result in obvious discomfort or pain unless the dental pulp is exposed. Root canal restoration or surgical removal of the affected teeth may be necessary in some ferrets.[44] Tooth root abscesses are uncommon in ferrets. Although dysphagia and drooling are sometimes seen, dental disease is often an incidental finding during physical examination. Dental extractions and scaling can be performed with the animal under anesthesia. Follow the basic principles for dental disease management that apply in the care of the dog or cat. Offering a natural prey diet or moistening the dry kibble may decrease dental abrasions.

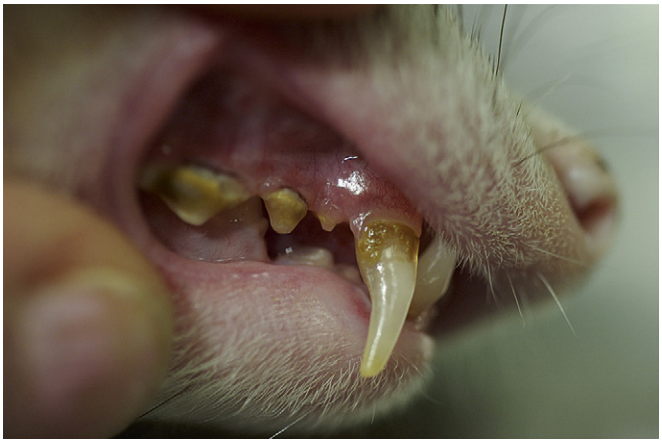

Fig. 3-1 Broken canine teeth and dental tartar are common in ferrets.

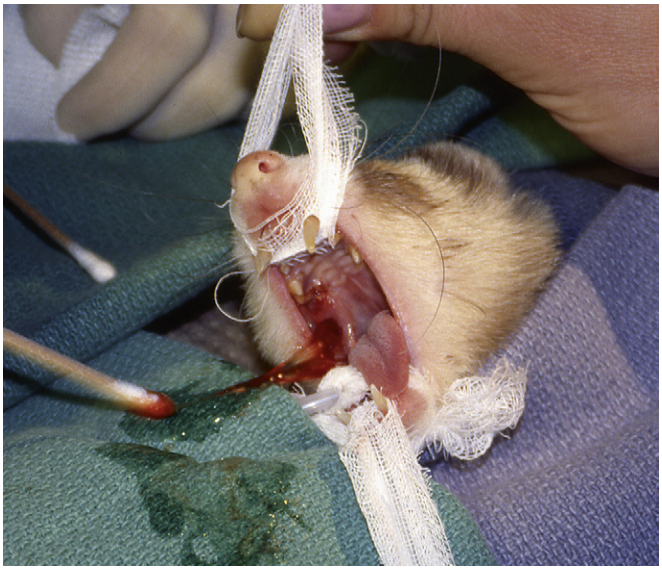

Fig. 3-2 Surgical correction of a salivary mucocele. The medial aspect of the mucocele is marsupialized into the mouth.

SALIVARY MUCOCELE

Ferrets have five major pairs of salivary glands: the parotid, submandibular, sublingual, molar, and zygomatic.[66] Trauma to a gland can result in extravasation of saliva and salivary mucocele formation. Although this lesion is uncommon in ferrets, mucocele diagnosis and treatment have been described.[5,57]

Diagnosis of a mucocele is relatively straightforward. Facial swellings are often seen in the commissures of the mouth or in the orbital area in the case of a zygomatic mucocele. Other locations also are possible. Aspirate the mass to obtain samples for cytologic analysis. The fluid is viscous or mucinous and clear or blood-tinged. Cytologic examination reveals amorphous debris and occasional red blood cells.

Treatment for salivary mucoceles is usually surgery. In one reported case, scalpel blade lancing of the medial wall of the mucocele resulted in drainage and no recurrence.[5] Marsupialization into the mouth with the use of a wide circular incision in the medial wall of the mucocele may be effective for mucoceles that bulge into the oral cavity (Fig. 3-2). Surgical excision of the affected salivary gland is ideal for avoiding recurrence (see Chapter 11). It may be possible to inject contrast medium into the mucocele in an effort to trace the origin of the saliva. Before attempting surgical excision of a salivary gland, review the superficial anatomy of the head and neck region of the ferret.[66] Recurrence is possible.

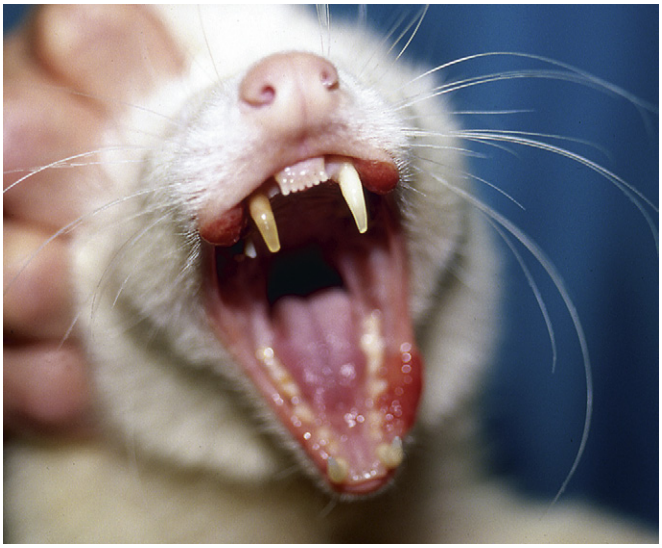

Fig. 3-3 Oral squamous cell carcinoma in situ, multiple sites, in the mouth of a ferret.

ORAL NEOPLASIA

The oral cavity is an uncommon site of neoplasia in ferrets. Squamous cell carcinoma is the most commonly reported oral tumor in ferrets and typically manifests as a firm swelling of the upper or lower mandible.[36,38,47] These masses are usually solitary but can appear in situ, in multiple sites (Fig. 3-3).

Treat squamous cell carcinoma with wide surgical excision, including maxillectomy or mandibulectomy as required. In one report, surgical resection of the mass was followed with radiation therapy.[36]

ESOPHAGEAL DISEASE

Diseases of the esophagus are rare in ferrets. Acquired megaesophagus has been reported in ferrets[8,39] and is occasionally seen in practice. *Megaesophagus* describes an esophagus that is enlarged (dilated) on radiographic examination and that lacks normal motility. Recognizing this disease is important because the prognosis in ferrets with megaesophagus is poor. Clinical signs include lethargy, inappetence or anorexia, dysphagia, and weight loss. Regurgitation is common. Coughing or choking motions are sometimes described, and some ferrets have labored breathing. Differential diagnoses includes the presence of an esophageal or GI foreign body, gastritis, influenza, and respiratory diseases.

Diagnosis of megaesophagus is based on clinical signs and radiographic evidence. On radiographs, the esophagus is often dilated in both the cervical and thoracic segments (Fig. 3-4). Food may be visualized in the esophagus. Aspiration pneumonia and gastric gas are sometimes evident in addition to esophageal dilation. In suspect cases, always take radiographs of the abdomen to exclude lower GI disease. Administer barium

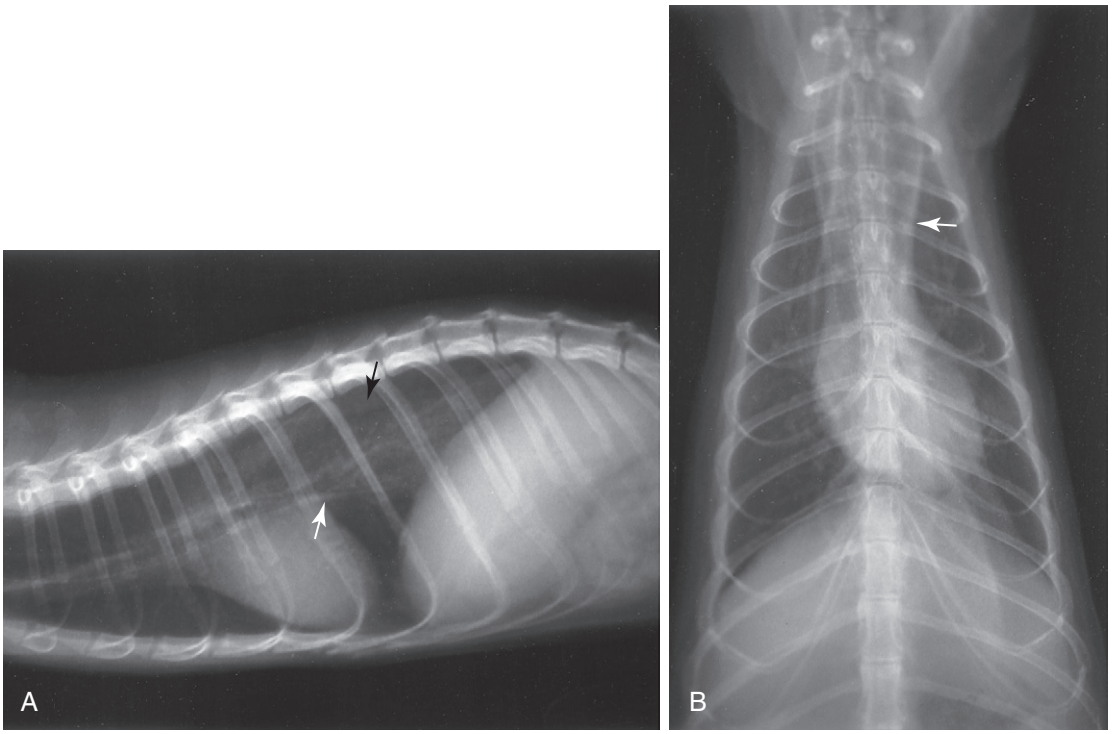

Fig. 3-4 **A,** Lateral thoracic radiograph of a ferret with megaesophagus. Note the subtle dilation of the thoracic esophagus *(arrows)*. **B,** Ventrodorsal radiograph of the same ferret in **A.** The cranial thoracic esophagus is dilated *(arrow)* and is much easier to visualize in this view than in the lateral view.

(10 mL/kg by mouth [PO]) to delineate the esophagus and to evaluate mural lesions, strictures, or obstructions (Fig. 3-5). An endoscope can also be used to evaluate the esophagus. Use fluoroscopy, if available, to determine the motility of the esophagus after a barium swallow.

The cause of megaesophagus in ferrets is unknown. Consider possibilities in the differential diagnosis as for dogs, and tailor the diagnostic workup accordingly. To test for myasthenia gravis, serum acetylcholinesterase antibody testing can be performed (Comparative Neuromuscular Laboratory, University of California San Diego, La Jolla, CA; http://vetneuromuscular.ucsd.edu/) and edrophonium chloride (Tensilon) testing is possible, albeit difficult to administer and interpret. Myasthenia gravis has been documented in a young ferret, but an association between megaesophagus and myasthenia was not reported.[43]

The management of ferrets with megaesophagus is similar to that of canine patients but is less successful. Supportive care and antibiotics are palliative at best. Administration of a GI motility enhancer such as metoclopramide (0.2 to 1 mg/kg PO or subcutaneously [SC] q6-8h) may be helpful. Cisapride, which until recently was marketed for gastroesophageal reflux and gastroparesis in humans, reduces the frequency of regurgitation in dogs with megaesophagus when given at 0.5 mg/kg PO q8-24h.[80] This drug has been removed from the market for human use in the United States because of adverse cardiac effects in some people but is available through veterinary compounding pharmacies. Its use in ferrets has not been evaluated. If esophagitis is suspected, add an H_2-receptor blocker, such as cimetidine, ranitidine, or famotidine.

The prognosis for ferrets with megaesophagus is poor; generally, they die or are euthanized within days of diagnosis. Affected ferrets are debilitated and may suffer from malnutrition, hepatic lipidosis, and aspiration pneumonia.

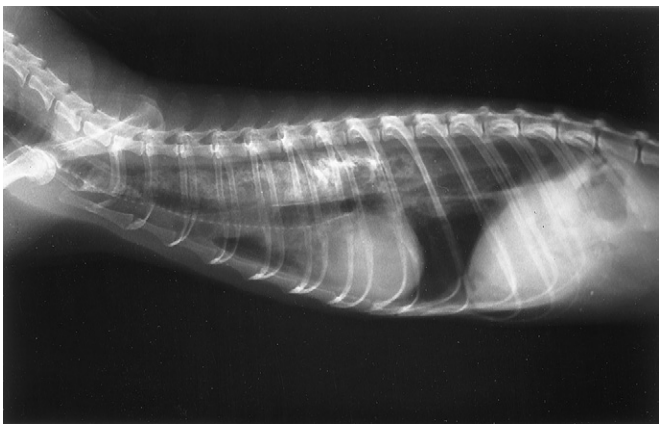

Fig. 3-5 Lateral radiograph of a ferret with megaesophagus. Orally administered barium sulfate delineates the esophagus.

Other causes of esophageal disease in ferrets are rare. Esophageal foreign body has been reported in a ferret and was successfully managed surgically.[12] One of the authors (HH) has seen a ferret with a sponge foreign body lodged in its distal esophagus; the sponge was broken into smaller pieces by using a 2.7-mm rigid endoscope. The foreign material then passed through the gastrointestinal tract without incident.

GASTRITIS AND ULCERATION

Gastric and duodenal ulcers have been reported in laboratory ferrets and are relatively common in pet ferrets (Fig. 3-6). Causes of GI ulceration are foreign body or toxin ingestion, *Helicobacter mustelae* infection, neoplasia of the intestinal tract, treatment

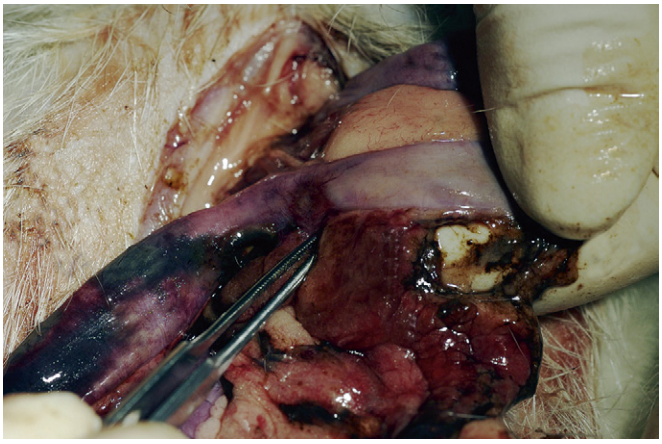

Fig. 3-6 Ruptured duodenal ulcer with marked inflammation and hemorrhage in a ferret.

with nonsteroidal anti-inflammatory drugs (NSAIDs), and azotemia caused by renal disease.

The laboratory ferret is used as an animal model for the study of *H. pylori* infection in humans. *Helicobacter mustelae* isolated from the gastric mucosa of ferrets shares many molecular and biochemical features of *H. pylori*. Infection with *H. mustelae* in ferrets is associated with varying degrees of gastritis, with or without duodenitis, and can result in ulcer formation (see discussion later in this chapter).[26]

Ulcerogenic drugs such as nonsteroidal and steroidal anti-inflammatory agents can be associated with ulcer formation in many species. It is rare, however, for ferrets to have GI bleeding with corticosteroids, even at dosages as high as 2 to 3 mg/kg/day. Be careful with NSAIDs in ferrets; overdose of anti-inflammatory agents such as ibuprofen (see Chapter 5) can cause ulceration with prolonged or inappropriate use. Severe uremia and associated melena can develop in ferrets with primary renal disease, but this is uncommon.

Gastritis in ferrets may be acute or chronic, or subclinical in some cases. Affected ferrets may hypersalivate, paw at the roof of the mouth, or display teeth-grinding, all of which indicate nausea and abdominal pain. Vomiting is not always reported, but owners sometimes describe "coughing" or gagging episodes that may actually represent gastric reflux. Some ferrets may not display obvious clinical signs, or signs may be missed if the ferret is part of a multi-ferret cage setup. Significant weight loss may be the only indication of a problem. Gastric or duodenal ulceration results in melena, anorexia, lethargy, and weight loss.

Basic diagnostic testing includes whole-body radiography and screening blood tests. Fast the ferret for a short time (4 to 6 hours) to facilitate visualization of a gastric foreign body or hairball. The stomach should be empty, and any residual food-like material may represent ingested hair or other material. The diagnosis of *H. mustelae* gastritis may be a diagnosis of exclusion of other common disorders, such as the presence of a GI foreign body. Treatment for *H. mustelae* gastritis is often based on a presumptive diagnosis. Treat gastritis and gastric ulceration with both specific therapy (according to the diagnosis) and supportive care. Hospitalize sick and anorexic ferrets for fluid therapy and parenteral treatment. Antibiotics are indicated for sick ferrets; consider choosing a combination that will target *Helicobacter* (e.g., amoxicillin and metronidazole in combination with bismuth or proton-pump inhibitor—see *Helicobacter* treatment later in this chapter). For ferrets that are not vomiting, offer multiple small feedings of a bland, moist diet such as a/d Canine/Feline (Hill's Pet Nutrition, Inc., Topeka, KS) or a recovery diet formulated for carnivores such as Carnivore Care (Oxbow Pet Products, Murdock, NE) or Emeraid Carnivore (LafeberVet.com, Cornell, IL). Avoid dry, high-fiber foods. For vomiting animals, withhold food for 6 to 8 hours while closely monitoring for any signs of hypoglycemia (older ferrets often have subclinical insulinomas); then, if vomiting has resolved, introduce small, frequent feedings.

Bismuth compounds have action against pepsin, a proteolytic enzyme believed to be an important factor in the development of peptic ulcers. Administer bismuth subsalicylate at a dose of 1 mL/kg PO q8h. Sucralfate is a cytoprotective agent that binds to the erosion site and helps to form a protective barrier. It is a safe and useful adjunct to ulcer treatment and can be given orally in suspension form (100 mg/kg) every 6 hours.

Systemic H_2-receptor antagonists, such as ranitidine or famotidine, are often used to treat gastric ulcers because they block the histamine receptor on the gastric parietal cell and reduce gastric acid secretion. Famotidine is convenient to use because it is available for parenteral administration and has long dosing intervals (0.5 mg/kg PO, intravenously [IV], or SC q24h). The proton pump inhibitors, such as omeprazole, are occasionally used in ferrets. One quarter of the contents of a 10-mg capsule can be mixed with soft food and given orally.

HELICOBACTER MUSTELAE GASTRITIS

Helicobacter mustelae is a gram-negative rod morphologically similar to *Campylobacter* species that requires a microaerobic environment for growth on artificial media. It is antigenically related and biochemically similar to *H. pylori*, a human pathogen associated with gastritis and ulcers.[26] Virtually all North American ferrets are likely to be exposed to *H. mustelae* as kits, becoming persistently infected at weaning and developing some degree of gastritis.[22] Colonization of the antral area of the stomach and pyloric area of the duodenum with *H. mustelae* is common in domestic ferrets, unless they are specifically treated or hand reared in isolation.[17,22] Colonization is accompanied by a specific immune response, but infection persists despite high serum antibody titers.[22] Although infection is common, clinical gastritis and ulcers occur relatively infrequently. Severe gastritis may be evident in gastric biopsy samples from ferrets showing no signs of clinical disease.[22]

The histopathologic lesions of *H. mustelae*–associated gastritis in ferrets, like *H. pylori* gastritis in humans, consist of mucus depletion, loss of glands, epithelial hyperplasia, foci of dysplasia, and leukocyte infiltration. The organism can be observed in silver-stained histologic sections of gastric mucosa.[26] Severely affected ferrets that die usually have a single large pyloric ulcer or many small ones, and the stomach and intestinal tract contain digested blood and mucus, causing the ingesta to appear very dark. Cultures of *H. mustelae* from fecal samples are usually difficult to obtain, even when the organism is readily identified histologically or by culture in gastric biopsy samples.

In humans, chronic infection with *H. pylori* leads to varying clinical and pathologic outcomes, including chronic gastritis, peptic ulcer disease, and gastric adenocarcinoma or mucosa-associated lymphoid tissue (MALT) lymphoma.[61] The severity and distribution of the *H. pylori*–induced inflammation are

key determinants of these outcomes.[60] Gastritis involving the antrum is associated with excessive acid secretion and a high risk of duodenal ulcer. Gastritis involving the acid-secreting corpus region of the stomach is associated with hypochlorhydria, gastric atrophy, gastric ulcers, and increased risk of gastric cancer.[32]

As in humans infected with *H. pylori*, transient hypochlorhydria develops in ferrets approximately 4 weeks after experimental infection.[53] This condition probably facilitates fecal-oral transmission as well as recovery of *H. mustelae* from feces.[55] Infection is associated with urease produced in abundance by *H. mustelae*, which is detectable in gastric biopsy samples and can be used for presumptive diagnosis. Urease production correlates with the degree of colonization and the occurrence of gastritis in biopsy results.[22] A urease breath test is available for humans to aid in diagnosis, and a similar test has been used in ferrets under research conditions but is not practical for clinical use.[55] Gastric atrophy and hypochlorhydria are associated with the ability of *H. mustelae* to persistently colonize the stomach; hypochlorhydria due to loss of parietal cells allows non–urease-producing bacteria to colonize the stomach as well.[22] *Helicobacter* species inhibit secretion of acid by parietal cells in vitro, and this mechanism may also contribute to hypochlorhydria.[26] In humans, chronic infection with *H. pylori* is associated with release of cytokines that impair function of enterochromaffin cells, which are neuroendocrine cells in the gastric mucosa that control acid secretion by releasing histamine. The impaired secretory function of these cells may predispose to hypochlorhydria and gastric carcinogenesis. Loss of parietal cells due to chronic inflammation is, however, the primary cause of achlorhydria in humans and ferrets colonized with their respective *Helicobacter* species.[67]

Gastrin is a hormone that stimulates gastric acid secretion and is secreted by the G-cells of the gastric antrum. In humans and probably in ferrets, high levels of gastrin may initiate GI mucosal damage and ulceration. Hypergastrinemia is probably a response to the presence of *H. mustelae* in the antrum or to its associated inflammation. Hypergastrinemia is abolished after antibiotic therapy eradicates the *Helicobacter* infection.[22]

In humans, *Helicobacter pylori*–associated gastritis is a risk factor for gastric adenocarcinoma and gastric lymphoma, and *H. pylori* has been classified as a Class I carcinogen by the World Health Organization (WHO).[22] There is some evidence that this is also the case in ferrets. As *H. pylori* does in humans,[41] infection with *H. mustelae* in ferrets stimulates cell proliferation in the gastric mucosa.[27] Under research conditions, gastric adenocarcinoma developed in aged ferrets that were naturally infected with *H. mustelae* and treated with a known gastric carcinogen.[22] Spontaneously occurring gastric adenocarcinoma has been reported in pet ferrets. Although in some cases *H. mustelae* was neither cultured from the lesions nor identified histologically,[69,76,78] in other cases, silver-stained organisms that were morphologically compatible with *H. mustelae* were present in the neoplastic tissues.[27]

Lymphoid follicles are observed in the gastric mucosa of humans colonized with *H. pylori*[91] and in that of ferrets colonized with *H. mustelae*[26] but not in uninfected individuals. In humans this condition may progress to MALT lymphoma. Eradicating *H. pylori* usually causes early tumors to regress, implicating the infection as the cause of neoplasia.[90,91] Gastric MALT lymphoma associated with *H. mustelae* infection has also been reported in adult ferrets[17] (Fig. 3-7). None of the affected ferrets were treated with antibiotics to eradicate *H. mustelae* either before or during the illness associated with neoplasia.

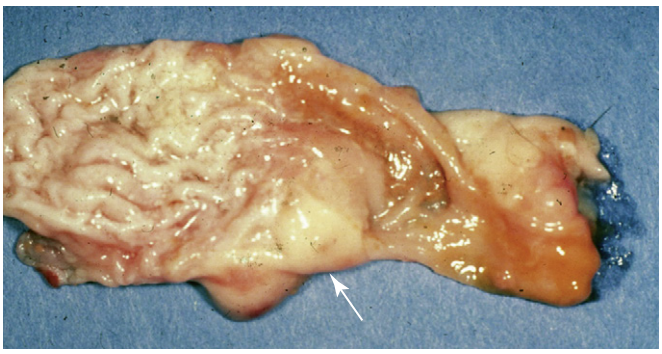

Fig. 3-7 MALT lymphoma in the stomach of a ferret infected with *Helicobacter mustelae.*

Fig. 3-8 Melena in a ferret with upper gastrointestinal bleeding from gastric ulcers.

Clinical Signs and Diagnosis of *H. Mustelae* Gastritis with Ulcers

Illness may develop in ferrets 12 to 20 weeks of age under conditions of stress caused by a combination of factors, such as rapid growth, dietary changes or inadequacy, and concurrent diseases. Infection is lifelong in untreated ferrets, and the severity of chronic gastritis increases with age.[29] In mature ferrets, the disease may become clinically apparent in animals that are stressed by concurrent disease or by surgery for other conditions such as adrenal disease or insulinoma. Ferrets with severe *H. mustelae* gastritis and ulcers are lethargic and anorexic, and they rapidly become emaciated. Chronic vomiting may occur. Excessive salivation and pawing at the mouth, which are signs of nausea in ferrets, may be evident. Affected ferrets are often moderately to severely dehydrated and may have mild anemia and melena (Fig. 3-8). Black, tarry feces often stains the fur of the tail and perineal region.

Definitive diagnosis of *Helicobacter* infection is confirmed by histopathologic examination of a gastric mucosal sample obtained by endoscopic or surgical biopsy. Gastric mucosa or fecal samples can be submitted for polymerase chain reaction (PCR)-based analysis (Taconic Rockville, Rockville, MD, www.taconic.com; Veterinary

Table 3-1 Summary of Suggested Treatment Regimens for *Helicobacter mustelae* Gastritis, Inflammatory Bowel Disease, Proliferative Bowel Disease, and Eosinophilic Gastroenteritis

Disease	Drug	Dosage
Helicobacter mustelae gastritis		
Original triple therapy[a]	Amoxicillin	10 mg/kg PO q12h
	Metronidazole	20 mg/kg PO q12h
	Bismuth subsalicylate	17 mg/kg (1 mL/kg) PO q12h
Alternative therapy[a]	Clarithromycin	12.5 mg/kg PO q8h[36]
	Ranitidine bismuth citrate	24 mg/kg PO q8h[36]
	or	
	Clarithromycin	50 mg/kg PO q24h[1]
	Omeprazole	4 mg/kg PO q24h[1]
	Metronidazole	75 mg/kg PO q24h[1]
H_2 receptor blocker	Famotidine	0.5-1 mg/kg PO, SC q24h
Inflammatory bowel disease	Azathioprine	0.9 mg/kg PO q24-72h
	Prednisone	1 mg/kg PO q24h
	Sucralfate	100 mg/kg PO q6h
	Hypoallergenic diet	
Proliferative bowel disease	Chloramphenicol	50 mg/kg PO, IM, SC q12h
Eosinophilic gastroenteritis	Prednisone	1.25-2.5 mg/kg PO q24h
	Ivermectin	0.4 mg/kg SC, PO once; repeat in 14 days

IM, Intramuscular; *PO,* per os; *SC,* subcutaneous.
Chloramphenicol, ranitidine bismuth citrate, azathioprine, and metronidazole can be prepared as suspensions by compounding pharmacists.
[a]Treat for a minimum of 14 days.

Molecular Diagnostics, Milford, OH, www.vmdlabs.com). Specialized techniques are necessary for culturing the organism, which is not shed consistently in feces of infected ferrets.[31]

Treatment of *H. Mustelae*–Associated Gastritis with Ulcers

Treatment for *Helicobacter* infection in humans usually consists of "triple therapy" consisting of two antibiotics from different classes, such as amoxicillin or metronidazole and clarithromycin, and a proton pump inhibitor. Differing combinations of antibiotics and proton pump inhibitors are used, with varying success. In humans with resistant *Helicobacter* infections, "quadruple therapy" with an added bismuth compound is often used. Bismuth interferes with the colonization of *H. pylori* in humans and suppresses colonization of *H. mustelae* in ferrets.[77] Bismuth also has direct antimicrobial actions against *Helicobacter*.[64]

In ferrets, the initial treatment for *Helicobacter* species in ferrets is commonly a triple-therapy combination of amoxicillin, metronidazole, and bismuth subsalicylate, administered q12h for at least 2 weeks (Table 3-1). Oral veterinary or pediatric amoxicillin suspensions are palatable and well accepted by most ferrets; metronidazole can be compounded into a suspension for oral administration. Although *H. mustelae* is sensitive to either amoxicillin or metronidazole, treatment with one of these antibiotics alone or single treatment with other antibiotics is ineffective for eradication therapy. Other drug combinations have been used in ferrets to eradicate *H. mustelae,* with advantages of improved palatability and convenience of dosing. Clarithromycin (Biaxin, Abbott Laboratories, North Chicago, IL) (12.5 mg/kg PO q8h) in combination with ranitidine bismuth (24 mg/kg q8h) has been shown to eradicate *H. mustelae* in ferrets.[53] Ranitidine bismuth citrate tablets (not available in the United States) may be crushed and mixed with a palatable liquid or compounded, and clarithromycin is available as a pediatric suspension. Both drugs are administered for 14 to 21 days (dosages are given in Table 3-1). A combination of clarithromycin, metronidazole, and omeprazole or clarithromycin and omeprazole proved more effective than triple therapy with amoxicillin, metronidazole, and omeprazole in eradicating *H. mustelae* in research ferrets.[2] Resistance to clarithromycin has not yet been reported in ferrets but does occur in humans.[53] To prevent development of macrolide-resistant strains, clarithromycin should be combined with a second antibiotic not in the macrolide class.[2] Chloramphenicol has no effect on *H. mustelae*.[61] Colloidal bismuth subcitrate (8 mg/kg PO q8h) may be substituted for bismuth subsalicylate.

Antacid therapy may not be helpful in the early treatment of *Helicobacter* infection because affected ferrets usually develop transient hypochlorhydria.[31] However, once affected with gastritis and inappetence, antacids can decrease discomfort, improve appetite, and reduce effects of acid reflux on esophageal mucosa. Famotidine (0.50-1.0 mg/kg PO q24h) or other H_2-receptor blockers, sucralfate suspension (25 to 100 mg/kg PO q8h), or a proton-pump inhibitor such as omeprazole (4 mg/kg PO q24h) (if not used in triple therapy) may be helpful in very sick animals that are bleeding from extensive gastric ulcers.

Although eradication of *H. mustelae* is accompanied by decreasing antibody titers, lesions may take longer to resolve.[53] Successfully treated ferrets can be reinfected with *H. mustelae* through contact with infected ferrets.[4] For treated ferrets to

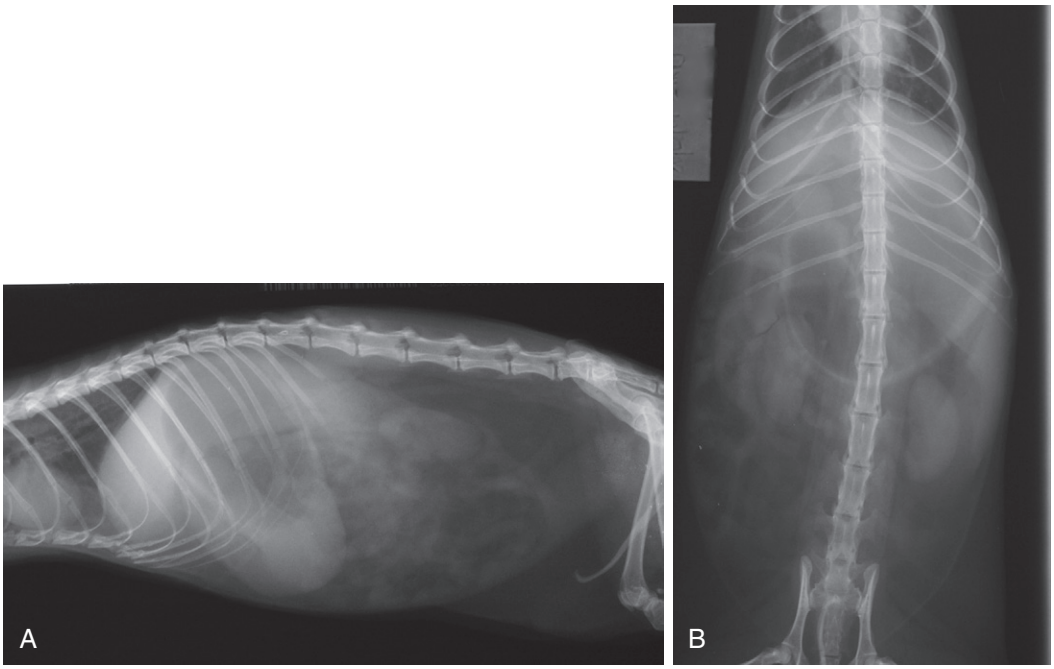

Fig. 3-9 Lateral **(A)** and ventrodorsal **(B)** radiographic views of a ferret with a pyloric outflow obstruction from a foreign body. The stomach is greatly distended with fluid and gas.

remain free of *H. mustelae*, they should not be exposed to ferrets of unknown *Helicobacter* infection status until the newly introduced ferrets have also been treated.

GASTROINTESTINAL POLYPS

Two ferrets with GI polyps have been seen at the Animal Medical Center (New York, NY). Both ferrets showed lethargy, inappetence, melena, and weakness from anemia. Abdominal radiographs suggested GI abnormalities. On surgical abdominal exploration, one ferret had a gastric polyp and the other had a small intestinal polyp. Both ferrets did well after surgical resection of the polyps, which were histologically benign.

GASTRIC DISTENTION (BLOAT)

Pet ferrets occasionally are seen with an acute gastric or small intestinal foreign body blockage that results in a distended, fluid-filled stomach. These ferrets are acutely very weak, reluctant to ambulate, and anorexic. To confirm the diagnosis, take full-body radiographs (Fig. 3-9). These animals are in shock and need immediate aggressive therapy that includes intravenous fluids and decompression. Relieve gastric pressure by placing an orogastric tube (8- or 10-French red rubber feeding tube), treat the hypovolemic shock, and prepare these cases for surgery when stable.

Pyloric stenosis and gastric outflow obstruction can manifest as an acute bloat in the ferret. Pyloric adenocarcinoma in ferrets and in humans has been associated with infection with *H. mustelae*.[69,76] Pyloric stenosis caused by muscular hypertrophy of the pylorus has been seen clinically by one author (HH), with one case occurring in a 4-month-old ferret. Pyloromyotomy and dilation of the pyloric outflow is the recommended treatment, especially where *Helicobacter* and cancer are not present.

Other than associated with foreign body disease, gastric bloat is rarely seen in pet ferrets, but it has been reported on domestic ferret farms and in black-footed ferrets *(Mustela nigripes)*.[21,73] Clinical signs are usually observed in weanling ferrets and include acute gastric distention, dyspnea, and cyanosis. Sudden death can occur. The cause is unknown but is thought to be related to an overgrowth of *Clostridium perfringens* (previously called *C. welchii*). Certain conditions may predispose to clostridial overgrowth, including increased concentration of carbohydrates in the GI tract from overeating, dietary changes, and intestinal hypomotility. *Clostridium perfringens* multiplies rapidly, producing enterotoxins that attack the villous epithelial cells of the gut. Gas production by the bacteria results in abdominal distention.

GASTROINTESTINAL FOREIGN BODIES

Gastrointestinal foreign bodies are common in ferrets.[58,84] Ferrets are naturally inquisitive and like to chew on miscellaneous environmental objects, particularly rubber or sponge products. Rubber or foam foreign bodies are most commonly ingested by young ferrets (younger than 2 years of age); in contrast, trichobezoars (hair balls) are more common in older ferrets (Fig. 3-10). Linear foreign bodies, commonly ingested by cats, are very rare in ferrets.

The most common clinical signs of a GI foreign body in ferrets are lethargy, inappetence or anorexia, and diarrhea. Vomiting is sometimes *not* reported by the owner. However, if vomiting is observed, consider a GI foreign body (Table 3-2). Some ferrets display signs of nausea, including bruxism, ptyalism, and face rubbing. Weakness can be profound in acutely obstructed animals; some of these ferrets are recumbent and reluctant to ambulate. Trichobezoars can manifest as chronic, intermittent gastric problems: bruxism, weight loss, inappetence, and melena may be reported. Some of these cases can become acute outflow obstructions, whereas in other cases, a more subtle, chronic history can be seen, depending on where the hairball is located in the stomach.

If a GI foreign body is suspected, palpate the abdomen carefully. Foreign bodies in the small intestine often are associated with localized discomfort or pain and can usually be palpated, especially under sedation. Gastric foreign bodies are more difficult to palpate because the stomach is under the ribcage. Hold the sedated ferret vertically from the axillae to allow the spleen with the attached stomach to drop down for easier palpation. Hairballs tend to be firm, tubular structures (see Fig. 3-10) and can often be palpated in the stomach through the gastric wall.

Fig. 3-10 Trichobezoars surgically removed from a ferret stomach.

If a foreign body is suspected, take whole-body survey radiographs. Make sure to include the thorax to evaluate the esophagus. Abnormal abdominal radiographic findings are segmental ileus, gaseous distention of the stomach, and, occasionally, a visible foreign object or trichobezoar (Fig. 3-11). Contrast (barium or negative gastrogram with air) studies can be done if needed and can be helpful to determine the presence of hairballs[84] (Fig. 3-12). Base the diagnosis on history, clinical signs, palpation, and the radiographic results. At a minimum, submit a blood sample for a complete blood count (CBC) and plasma biochemical analysis in a ferret that is sick for longer than 24 hours.

Ferrets rarely pass GI foreign bodies unassisted. Occasionally, a small, partially obstructing object may pass after treatment with intestinal lubricants (hairball laxatives) q8h and replacement fluids. However, most GI foreign bodies must be removed surgically (see Chapter 11). Stabilize debilitated ferrets before surgery. Parenteral fluids are essential because these ferrets are usually dehydrated. If the ferret is stable, alert, and ambulatory, fluids can be given subcutaneously until prepping for surgery; then, place an IV catheter and administer fluids intravenously. Perform an exploratory laparotomy as soon as possible. Collect biopsy specimens as needed from the stomach or intestines if ulcerated or abnormal in appearance. Some ferrets also may have *H. mustelae*–associated gastritis or GI lymphoma. Check the adrenal glands and the pancreas in older ferrets; discovery of concurrent abdominal disease is not unusual during surgery. In

Table 3-2 Differentiation of Common Gastrointestinal Diseases That Cause Weight Loss and Diarrhea in Ferrets by Typical History, Clinical Findings, and Laboratory and Radiographic Results[a]

Disease	Typical Diarrhea	Vomiting/ Bruxism	Prolapsed Rectum/ Tenesmus	Physical Findings	Laboratory/ Radiographic Results	Comments
Eosinophilic gastroenteritis	Mucoid, green	Possible	No	± Thickened intestinal loops	Eosinophilia ± Reactive hepatitis	Rare; multiple tissue involvement (visceral lymph nodes, spleen)
Ferret enteric coronavirus/ (Epizootic catarrhal enteritis)	Acute: profuse, green Chronic: grainy ("bird seed")	Possible	No	Thickened or fluid-filled intestines	± Reactive hepatitis	Acute onset, can become chronic; exposure to new or young ferrets
Foreign body	Black, tarry or mucoid, green	Yes	No	Palpable gastric or intestinal gas Painful abdominal palpation	± Reactive hepatitis Anemia (chronic) Gas in stomach or intestinal loops	Acute or chronic Young ferrets—rubber objects, toys Older ferrets—hairballs more common
Helicobacter mustelae gastritis	Black, tarry or mucoid, green	Yes	No	Enlarged mesenteric lymph nodes	± Reactive hepatitis ± Anemia Gas in stomach	Recent stress (i.e., surgery); can increase in severity with age
Inflammatory bowel disease	Mucoid, green	Possible	No	± Enlarged mesenteric lymph nodes	Reactive hepatitis ± High globulins ± High lipase	May develop secondary to other GI disease
Proliferative bowel disease	Mucoid, green	Rare	Yes	Palpably thickened large bowel; proliferative rectal mucosa	± Globulins	Primarily affects young ferrets

[a]Although typical findings are listed, clinical signs and physical findings are variable in any of the described diseases.

most cases, recovery is rapid after GI foreign body removal, and ferrets are able to eat soft foods within 12 hours after surgery. Most ferrets can be discharged within 48 hours after surgery.

Prevention of foreign body obstructions includes recommending the regular use of a hairball laxative preparation during active shedding seasons and "ferret-proofing" the household. Ferrets should not be left uncaged or unsupervised. Advise owners to avoid giving small rubber "squeak" toys to pet ferrets and remove soft rubber objects (e.g., rubber-soled shoes and earphones) from the ferret's accessible environment.

LIVER DISEASE

Lymphoma is the most common hepatic neoplasm seen in ferrets. Other reported hepatic neoplasms include hemangiosarcoma, adenocarcinoma, hepatoma, biliary cystadenomas, and

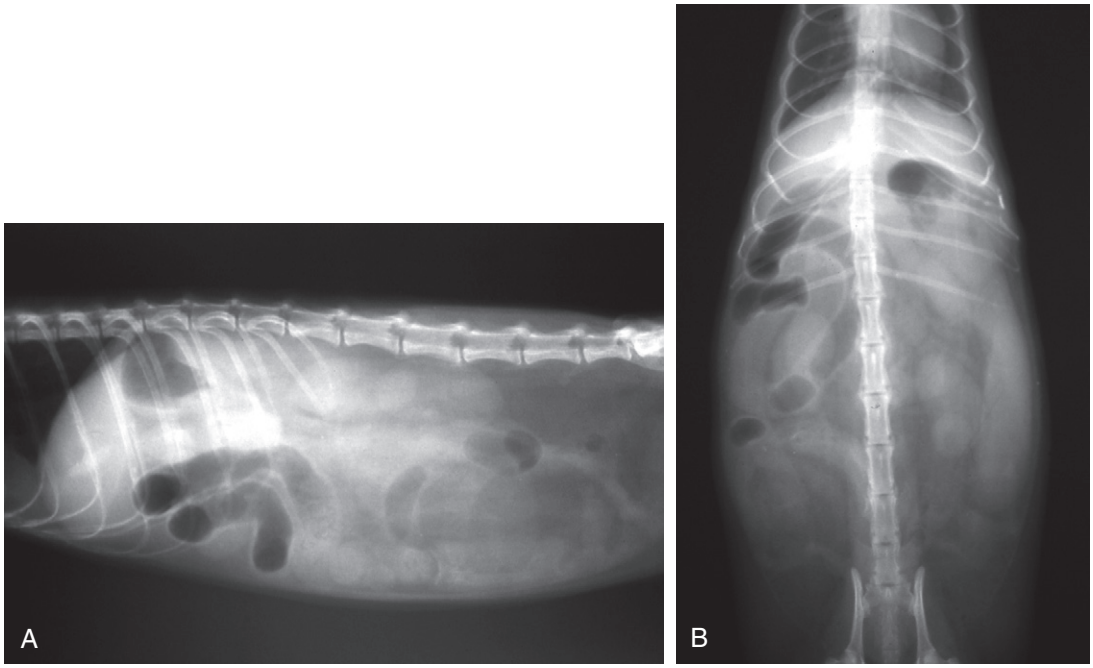

Fig. 3-11 Lateral **(A)** and ventrodorsal **(B)** radiographic views of a ferret with a gastrointestinal foreign body. The proximal small intestine is markedly dilated with fluid and gas, compatible with segmental ileus. The foreign body is not visualized.

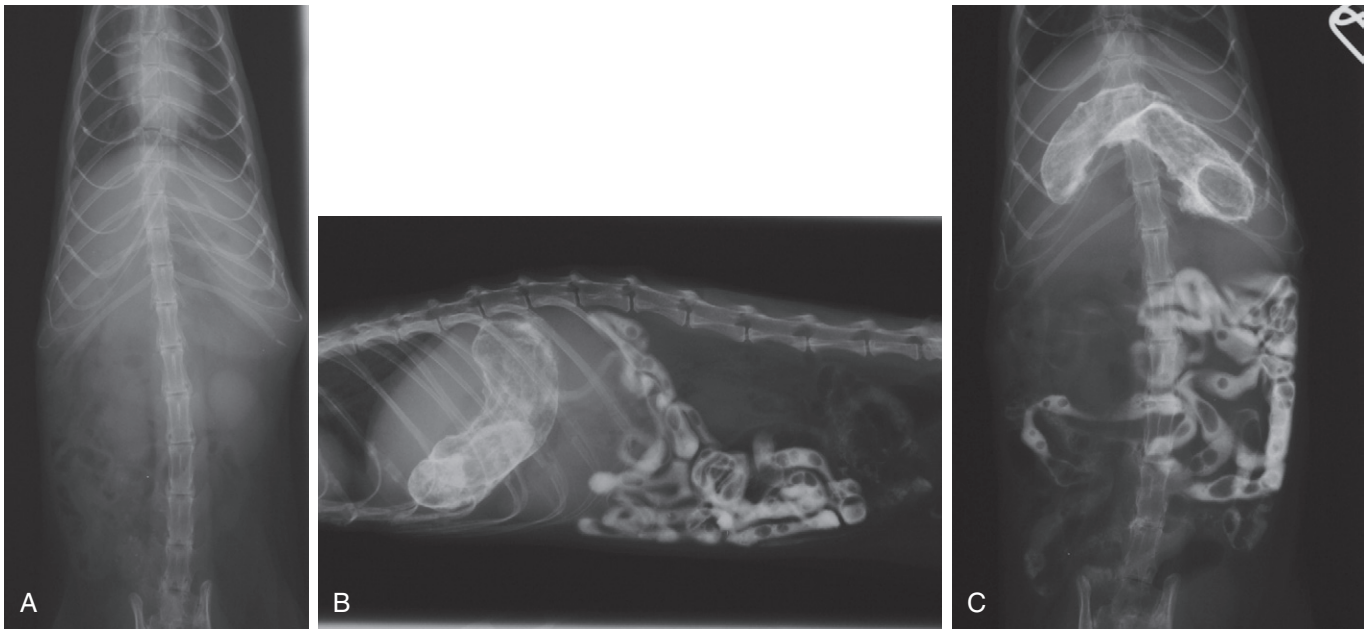

Fig. 3-12 **A,** Ventrodorsal radiograph of a ferret with a gastric trichobezoar. The trichobezoar appears as a tubular soft tissue density poorly delineated in the stomach. Contrast studies were performed. **B,** lateral and **C,** ventrodorsal radiographic views of the same ferret 30 minutes after administration of barium sulfate. Note the delineation of at least two trichobezoars.

hepatocellular adenoma.[16,37,47] Pancreatic islet cell tumors can metastasize to the liver. Prognosis is guarded regardless of tumor type.

Other than neoplastic diseases, primary hepatopathies are uncommon in ferrets. Vascular shunts have not been reported. Cholelithiasis and cholestasis have been described in ferrets and may be underdiagnosed in clinical practice.[37a,40a] Hepatic lipidosis can be found in association with long-term anorexia. Chronic GI diseases (e.g., trichobezoar formation) can lead to hepatic lipidosis. Foreign bodies in the proximal duodenum can obstruct the bile ducts as they enter the small intestine and cause increased liver enzyme and bilirubin levels. Steroid hepatopathy is rare in ferrets, even with long-term steroid administration or hyperadrenocorticism.

Chronic-lymphocytic portal hepatitis has been found on histologic examination of hepatic biopsy samples. The cause is unknown but may be related to chronic visceral inflammation such as inflammatory bowel disease. Chronic cholangiohepatitis with biliary hyperplasia of variable intensity was reported in 8 of 34 cohabitating ferrets.[34] Three ferrets had neoplastic lesions in the liver. Spiral-shaped bacteria were identified in the livers of three ferrets, and bacteria with 97% similarity to *Helicobacter* species were identified by PCR in the feces of one ferret. Because of the clustering of cases and the pathologic findings, a possible infectious cause was suggested.

Copper toxicosis was diagnosed in two sibling ferrets on the basis of high hepatic copper concentrations and histologic changes in hepatic tissue.[33] Clinical signs in these two ferrets were mostly nonspecific and included severe central nervous system depression with hypothermia and hyperthermia, respectively. One ferret was icteric. Both ferrets died within a few days of clinical evaluation despite supportive care. A genetic predisposition to copper toxicosis in these two ferrets was proposed because they were siblings with the same phenotypic coat color and because no environmental source of copper could be identified.

In most ferrets with liver disease, a high concentration of alanine aminotransferase (ALT greater than 275 IU/L) is present on plasma biochemical analysis. Alkaline phosphatase concentration is sometimes increased. High total bilirubin levels are uncommon, and ferrets are rarely icteric. Be careful in diagnosing liver disease in ferrets with high enzyme concentrations; these laboratory findings are also common in ferrets with intestinal disease. Base the diagnosis of liver disease on the presence of persistently high liver enzyme concentrations, radiographic and ultrasound findings, and, for definitive diagnosis, analysis of liver biopsy samples. Ultrasound-guided needle biopsy of the liver is possible, but a full abdominal exploratory is often recommended because of the likelihood of concomitant disease in ferrets.

GASTROINTESTINAL PARASITISM

Intestinal parasites are uncommon in ferrets. However, in any ferret with diarrhea, perform a complete fecal parasite check, including a direct fresh wet mount and fecal flotation. In juvenile ferrets, nematodiasis is rare, but coccidiosis and giardiasis are occasionally seen. Coccidiosis can be subclinical in ferrets or it may be associated with diarrhea, lethargy, and dehydration.[9] Rectal prolapse is possible. Diagnose coccidiosis by results of fecal testing, either direct wet mount and microscopic examination or fecal flotation. Follow the same treatment protocols as for canine and feline patients with coccidiosis.

Cryptosporidiosis is described in ferrets but may not result in clinical disease.[1,68] Young ferrets can have a subclinical infection with *Crytosporidium parvum* that can persist for several weeks. The oocysts can be shed in the feces of clinically normal ferrets. Histologically, the organism may be associated with an eosinophilic infiltrate in the lamina propria of the small intestine. The zoonotic potential of the ferret genotype of *C. parvum* to infect humans is unknown[1]; however, if oocysts are detected, discuss the potential of transmission to immunocompromised owners.

ENTERITIS AND DIARRHEA

SALMONELLOSIS

Salmonellosis is a contagious disease characterized by fever, bloody diarrhea, and lethargy. Conjunctivitis and anemia also may be present. *Salmonella newport*, *S. typhimurium*, and *S. choleraesuis* may be involved.[52] The incidence of salmonellosis in pet ferrets is very low and the infection may be associated with feeding of raw or undercooked meat, poultry, and meat by-products. Isolation of *Salmonella* organisms usually requires collecting multiple fecal samples and the use of selective media. Treatment consists of aggressive supportive care, antimicrobials, and treatment for shock as needed.

MYCOBACTERIOSIS

Ferrets can be naturally or experimentally infected by several species of mycobacteria.[10,20,74] *Mycobacterium bovis* and *M. avium* infections have been recognized in research, farm, and feral ferrets in England, Europe, and New Zealand. These infections have been associated with the feeding of raw meat and poultry and unpasteurized dairy products, or, in feral ferrets, feeding on carrion infected with *M. bovis*.[50] Infections with *M. avium*, *M. genavense*, *M. abscesses*, and *M. celatum* have been reported in domestic ferrets.[48,49,65,71,74,82]

Ferrets with mycobacterial infections can have a variety of clinical symptoms, which may include weight loss, lymph node enlargement, conjunctival lesions, splenomegaly, and pneumonia. At necropsy, granulomas with acid-fast organisms can be found in the liver, lungs, lymph nodes, intestines, stomach, and trachea.

Mycobacteriosis is diagnosed by results of tissue biopsy, including histopathologic examination with acid-fast staining, polymerase chain reaction (PCR) testing, and culture. In several reported cases, treatment regimens usually involving rifampicin alone or in combination with enrofloxacin and azithromycin have been used with variable success. The zoonotic potential of infection is unknown but should be discussed with owners before beginning treatment in any ferret diagnosed with mycobacteriosis.

CAMPYLOBACTERIOSIS

Campylobacter jejuni is a bacterial enteric pathogen that is associated with diarrhea and enterocolitis in humans and many animal species, including dogs, cats, calves, and sheep. *Campylobacter jejuni* can be isolated from the feces of normal ferrets, and during the 1980s, it was suspected to be the cause of proliferative colitis, or proliferative bowel disease (PBD), in ferrets.[24,25] However, inoculation of *C. jejuni* into 54 conventionally reared

Fig. 3-13 Grainy loose feces in a ferret with chronic diarrhea, consistent with infection ferret enteric coronavirus (epizootic catarrhal enteritis).

and 2 gnotobiotic ferrets caused diarrhea but not the full spectrum of clinical signs and histopathologic lesions seen in PBD (see later discussion).[6] The *Campylobacter*-like organism that causes of PBD was subsequently thought to be a *Desulfovibrio* species,[28] but is now known to be *Lawsonia intracellularis*, the agent that causes porcine proliferative enteropathy (see later discussion).[20] The importance of *C. jejuni* as a primary pathogen in pet ferrets is not known.

VIRAL DIARRHEA

Coronavirus

Epizootic catarrhal enteritis (ECE) is a highly transmissible diarrheal disease of ferrets that first appeared in 1993 in several rescue and breeder operations in the eastern United States. The causative agent of ECE is now attributed to a coronavirus.[86,88] In intestinal biopsy samples of ferrets infected with ferret enteric coronovirus (FECV), histologic findings include lymphocytic enteritis, villous atrophy, and blunting or degeneration of apical epithelium. Ferrets infected with FECV initially develop a profuse, green mucoid diarrhea that may progress to a loose, grainy stool resembling birdseed (Fig. 3-13).

Adult ferrets are most susceptible to ECE, and the typical history includes recent exposure to a new, young ferret that acts as an asymptomatic carrier. The incubation period is 48 to 72 hours, and affected ferrets are anorexic and lethargic. Coronavirus may be detected by PCR testing of fecal or intestinal tissue (jejunum and ileum) samples of affected ferrets (Diagnostic Center for Population and Animal Health, Michigan State University, Lansing, MI, www.dcpah.msu.edu; Veterinary Molecular Diagnostics, Milford, OH, www.vmdlabs.com). Treat sick ferrets with signs of ECE with aggressive fluid therapy, antibiotics, and supportive care, and isolate these ferrets from asymptomatic or unexposed ferrets. Although the morbidity rate can be high, the mortality rate is low in ferrets that are treated appropriately. After recovering from ECE, some adult ferrets develop a persistent, intermittent malabsorption syndrome with diarrhea. The clinical course can be prolonged in these ferrets, lasting weeks to months. Treatment with a short course of steroids (prednisone 1 mg/kg q12h for 14 days) and changing the diet to an easily absorbed food may speed recovery.

More recently, a ferret systemic coronavirus (FSCV) has been identified as the causative agent of a progressive systemic pyogranulomatous disease in ferrets that resembles the dry form of feline infectious peritonitis (FIP).[35,54,63] Affected ferrets exhibit weight loss, palpable abdominal mass or masses, diarrhea, hypergammaglobulinemia, anemia, and sometimes central nervous system signs. The disease is progressive and carries a high mortality rate, with the duration of clinical illness averaging 67 days.[35] Partial gene sequencing indicates that the ferret systemic and enteric coronaviruses are closely related but not identical, and that FSCV is more closely related to FECV than to other group 1 coronaviurses.[35,87] There is no treatment for this form of coronavirus in ferrets. Similar to FIP in cats, this disease carries a poor prognosis.

Rotavirus

Infection with rotavirus causes diarrhea in very young ferrets. Farm outbreaks of diarrhea are associated with high morbidity and mortality rates in neonatal kits from 2 to 6 weeks of age.[7,81] In a report of an outbreak of diarrhea in 1-week-old ferrets, a group C rotavirus was identified and appears to be highly prevalent.[89] The morbidity is low in adult ferrets, but infection may result in a transient, green, mucoid diarrhea. The virus is shed in the stool, and transmission is by contact with infected animals or the environment. Diagnosis is by PCR testing of fecal or tissue samples (jejunum or ileum) (Diagnostic Center for Population and Animal Health, Michigan State University, Lansing, MI; www.animalhealth.msu.edu). Treatment is supportive with fluids and antibiotics.

Canine Distemper Virus

Distemper is caused by a highly contagious paramyxovirus that causes fatal disease in unvaccinated ferrets. Clinical signs can vary but often include diarrhea in conjunction with nasal and ocular discharges and a generalized orange-tinged dermatitis (see Chapter 6). Diarrhea may be acute or intermittent. The widespread practice of vaccinating ferrets against canine distemper virus has greatly limited the occurrence of distemper and it is now a rare disease in ferrets. Cold-like symptoms and diarrhea in newly purchased, unvaccinated ferrets should arouse suspicion. Distemper virus is generally considered incurable and fatal in ferrets, although vitamin A has been shown to have promising antiviral properties when administered as a supplement (30 mg) to experimentally infected ferrets.[70]

Influenza Virus

Ferrets infected with influenza (an orthomyxovirus) sometimes have transient diarrhea. The virus also causes upper respiratory disease associated with coughing, sneezing, inappetence, and lethargy. Affected ferrets are often febrile (see Chapter 6).

INFLAMMATORY BOWEL DISEASE AND EOSINOPHILIC GASTROENTERITIS

Inflammatory bowel disease (IBD) is a relatively common cause of gastroenteritis in ferrets.[11] The cause is unknown but may be related to dietary intolerance, hypersensitivity reaction, or another aberrant immune response. The inflammation typically is lymphoplasmacytic and should be distinguished from eosinophilic gastroenteritis, which often involves multiple tissues.

This condition is easily overlooked in ferrets because it resembles viral diarrhea (ECE), dietary indiscretion, and *Helicobacter*-associated gastroenteritis.

Affected ferrets can have loose grainy stools, intermittent nausea, occasional vomiting, and weight loss. Clinical signs can be subtle and chronic, or some ferrets can have acute vomiting and lethargy. Ferrets with IBD are usually young or middle-aged adults and in multiple-ferret households; typically only one ferret in the household is affected. Results of blood tests may reveal an increase in liver enzyme activities and plasma globulin concentrations, and lymphocytosis is occasionally present. In some ferrets, laboratory results are unremarkable.

Diagnosis is based on clinical signs, a detailed clinical history that eliminates the possibility of exposure to coronavirus, and results of diagnostic tests such as radiographs and routine blood tests. Diseases such as *Helicobacter* gastroenteritis and intestinal lymphoma should be ruled out. Definitive diagnosis can only be made by histologic examination of full-thickness gastric and intestinal biopsy samples. Treating without a histologic diagnosis is common because of the risks and costs of an abdominal exploratory procedure to collect biopsy samples.

Therapy is aimed at suppressing the immune response and dietary management. Corticosteroids such as prednisone (1 mg/kg PO q12–24h) are often used, but some ferrets with inflammatory bowel disease respond poorly to long-term treatment with steroids. Azathioprine (Imuran, Prometheus Laboratories, San Diego, CA) (0.9 mg/kg PO q24–72h) is another treatment option and seems to be well tolerated in ferrets.[11] Hypoallergenic diets made for cats (z/d feline; Hill's Pet Nutrition, Topeka, KS) can be tried, but ferrets are often reluctant to make dietary conversions. A chicken-free diet formulated for ferrets is available (Totally Ferret Turkey-Venison-Lamb Meal Formula, Performance Foods, Broomfield, CO; www.totallyferret.com) but efficacy for IBD is unknown. A grain-free ferret diet is also available (ZuPreem, Shawnee, KS; www.zupreem.com).

Eosinophilic gastroenteritis is a rare type of inflammatory bowel disease that occurs in ferrets and has also been reported in dogs, cats, horses, and humans.[3,83,92] In all reported cases in ferrets, animals were older than 6 months of age; however, because of the small number of reports, the incidence of disease in young animals is not known. No specific causative agent has been found in ferrets,[13,18,62] dogs,[75] or humans,[79] but food allergy is implicated in most humans and in some dogs. In specific cases in humans and in other species, clinical signs were relieved when appropriate treatment for food allergies or parasitism was instituted. Peripheral eosinophilia is a common but not a constant finding in affected dogs and humans,[75] but it has been reported in most of the relatively few ferrets diagnosed with this disease.[62] Eosinophilia in ferrets, however, is highly suggestive of the disease. No reports of food elimination tests in affected ferrets have been published.

The lesion of eosinophilic gastritis in ferrets, as in other animals and humans, is a mild to extensive infiltration of the mucosa, submucosa, and muscularis of the stomach and small intestine with eosinophils. Focal eosinophilic granulomas may be found in the mesenteric lymph nodes or abdominal organs of affected ferrets.[62] No pathogens have been observed in or isolated from the lesions of affected ferrets. In humans and other affected species, granulomas may cause partial bowel obstruction. Affected animals typically have chronic diarrhea, with or without mucus and blood, and severe weight loss. Granulomas and a thickened lower bowel may be palpable. Vomiting, anorexia, and dehydration are variable signs. Signs may be clinically indistinguishable from those of gastritis, persistent ECE, or GI obstruction by a foreign body.

Humans, dogs, and cats with eosinophilic gastroenteritis usually respond to steroid treatment. Because the disease in ferrets resembles that in other species, prednisone administration has been the treatment of choice.[62] Remission has occurred in ferrets treated with prednisone (1.25 to 2.5 mg/kg PO q24h for 7 days and q48h thereafter) until the ferret is clinically normal. Immediate recovery also followed removal of an enlarged mesenteric lymph node in one ferret and treatment with ivermectin (0.4 mg/kg SC) in another.[62] When eosinophilic gastroenteritis is a response to the presence of parasites, eliminating the parasites is preferable to prolonged treatment with corticosteroids to relieve clinical signs. In a recent report of a case series of dogs with gastrointestinal masses composed primarily of eosinophilic infiltrates, an underlying cause was not ascertained. Interestingly however, most dogs that were treated with corticosteroids and ivermectin improved clinically, with resolution of the eosinophilic infiltrates and prolonged survival. In contrast, all dogs treated surgically to remove the eosinophilic masses died of complications of their disease.[51]

PROLIFERATIVE BOWEL DISEASE

Proliferative bowel disease, which has been recognized for decades in pigs and hamsters, was first diagnosed in ferrets in 1982. The cause in swine is a bacterium classified as *Lawsonia intracellularis*.[56] This same agent causes PBD in hamsters and in ferrets[23] and has more recently been implicated in proliferative enteropathies of other species, including rabbits,[72] white-tailed deer, ratite birds, and domestic foals.[15] *Lawsonia intracellularis* is an obligate intracellular organism that cannot be propagated on artificial media but can be grown in embryonated chicken eggs. Two tests that detect this organism have been developed and are used in ferret tissues under research conditions: a PCR test specific for the swine isolate, and an indirect fluorescent antibody test that identifies the omega antigen common to organisms found in PBD lesions of swine, hamsters, and ferrets.[23] However, diagnosis of clinical cases usually depends on observing clinical signs and gross or histopathologic lesions.

Areas of intestine affected by PBD can be palpated, appear grossly thickened, and are often discolored on the serosal surface. The colon and less commonly the small intestine may be involved. Ridges of proliferative tissue, distinct from adjacent normal tissue, are obvious on the mucosal surface (Fig. 3-14). Occasionally the affected bowel perforates and causes fatal peritonitis. On histologic examination, epithelial proliferation with hypertrophy of the muscularis and infiltration of the bowel wall with either monocytic or granulocytic inflammatory cells, or both, are present.[30] In silver-stained sections, comma-shaped organisms can be found inside enterocytes lining crypts or glands. The normal architectural pattern of the mucosa is lost. Normally, straight tubular glands are covered evenly with enterocytes and numerous goblet cells. In PBD, the irregular, branching, proliferative glands lack goblet cells, and necrotic debris accumulates in the crypts. Severe glandular hyperplasia resembles neoplasia and may translocate to liver and regional lymph nodes.[23]

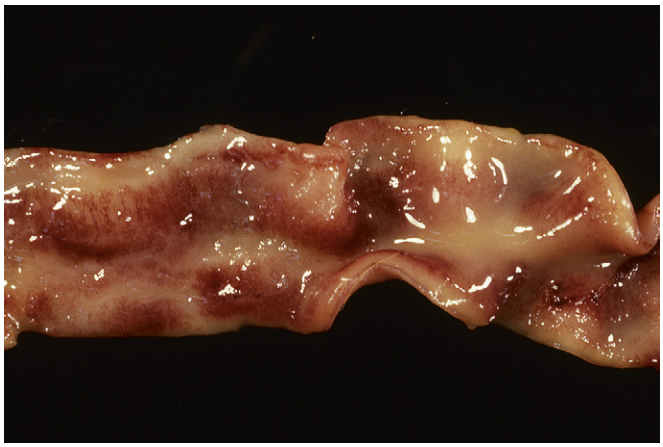

Fig. 3-14 Mucosal surface of a ferret with proliferative bowel disease. The mucosa appears thickened and hemorrhagic.

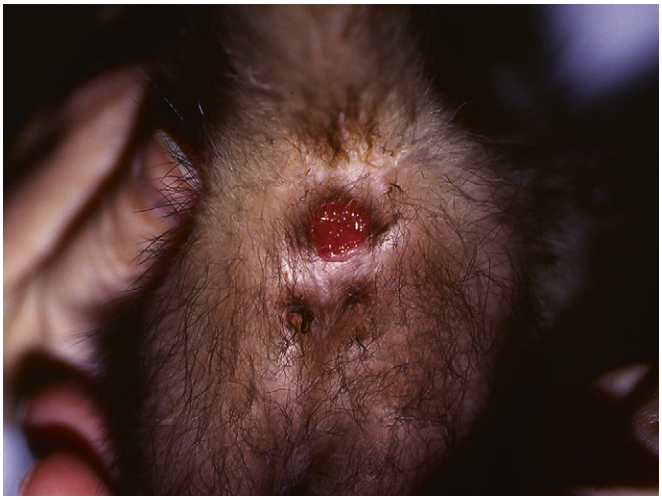

Fig. 3-15 Prolapsed rectum in a young ferret.

CLINICAL SIGNS AND DIAGNOSIS OF PROLIFERATIVE BOWEL DISEASE

Proliferative bowel disease occurs most frequently in rapidly growing juveniles, 10 to 16 weeks of age. Environmental and nutritional stress factors appear to play a role in resistance of infected animals to clinical disease. *Lawsonia intracellularis* is probably transmitted by the oral-fecal route,[23] and all ferrets that are housed in groups presumably will be equally exposed to the agent. However, clinical disease develops in only a small percentage (usually 1% to 3%) of group-housed juvenile ferrets. Improvements in the quality of care and nutrition of pet ferrets may be responsible for the apparently decreasing incidence of PBD in recent years.

Affected ferrets have chronic diarrhea that may vary from dark, liquid feces streaked with bright red blood to scant, mucoid stool, often with bright green mucus. The fur of the tail and perineal area may be stained and wet with fecal material, and the preputial area of males is often wet with urine. Rectal tissue may continuously or intermittently prolapse (Fig. 3-15). Affected animals moan or cry while straining. Some continue to eat but lose weight at an alarming rate. If not appropriately treated, a ferret weighing 800 g may lose 400 g in less than 2 weeks. These animals are moderately to severely dehydrated and may be hypoalbuminemic. They are weak and sleep most of the time.

Because of their general debility, ferrets with PBD are more susceptible to other infectious diseases. They may have upper respiratory tract infections that do not affect other healthy ferrets housed with them and often develop clinical gastritis or ulcers. Severely affected animals will die if not treated appropriately, and most of those that die despite treatment have proliferative ileitis alone or in combination with colitis.

Diagnosis is based on clinical signs, history, and response to treatment. A PCR assay is available for fecal, rectal swab, or ileal biopsy tissue samples (Zoologix, Inc., Chatsworth, CA; www.zoologix.com).

TREATMENT OF PROLIFERATIVE BOWEL DISEASE

Lawsonia intracellularis is sensitive to chloramphenicol. No other antibiotic consistently resolves PBD in ferrets. Chloramphenicol is administered at a dose of 50 mg/kg q12h IM or SC (chloramphenicol sodium succinate) or orally (chloramphenicol palmitate oral suspension) for at least 10 days.[45] A ferret with colitis of recent onset improves quickly with this treatment and gains 50 to 100 g/day within a few days of the first dose. Although the organism is also sensitive to tylosin, tetracyclines, tiamulin, and several other antimicrobials that are used to treat PBD in pigs,[56] and to erythromycin, which is commonly used in affected foals,[46] treatment of ferrets with any of these drugs is disappointing. Treatment of infected but clinically normal 6- to 9-week-old ferrets with oral tylosin (5 mg/kg mixed in soft food once daily) appears to reduce the incidence of clinical PBD in a colony, but only chloramphenicol produces a dramatic improvement in sick ferrets.

Repair of rectal prolapse with a purse-string suture is rarely necessary because as the colon heals, the prolapse usually disappears spontaneously. It may appear intermittently for weeks but causes no apparent distress. If a purse-string suture is used, the owner must closely monitor the ferret to make sure that it can defecate, especially when the stool regains its normal consistency. Sutures should be removed in 2 to 3 days.

RECTAL DISEASE

Rectal prolapse can occur in ferrets. It is most often associated with diarrhea and is usually a disease of young ferrets. Possible causes include coccidiosis, PBD, colitis, and neoplasia. Some young ferrets protrude the rectal mucosa from poor surgical analsacculectomy technique. Straining from adrenal-associated prostatic disease, urinary outflow obstruction, or an enlarged sublumbar lymph node (lymphosarcoma) may result in protrusion of the rectum. Anal gland impactions or abscesses are rare in ferrets that have been surgically descented.

Neoplasia is rare in the rectal area, with one recent report of anal sac apocrine adenocarcinoma.[59] One author (HH) has seen a descented ferret with leiomyosarcoma that surrounded the rectal opening. The ferret presented for a rectal prolapse, and a tumor was found on palpation. Treatment of rectal neoplasia involves surgical debulking, possible rectoplasty, and possible localized radiation therapy. Prognosis is poor.

Include a careful rectal examination (visualization and palpation) in all physical examinations in ferrets. Undescented ferrets may develop anal gland disease, including impactions and

abscessation. Palpation of the anal area may reveal either unilateral or 360-degree perianal swelling. Manage anal gland disease as in dogs. Be forewarned: anal gland odor is quite noxious. Anal gland removal is described in Chapter 11.

Diagnostic tests should include radiographs in the ferrets that present for straining, and a fecal wet mount and flotation to check for parasites. Other than coccidiosis, GI parasitism is uncommon.

Rectal prolapse often resolves with treatment of the causative condition. Treat with antibiotics and antiparasitic agents, as indicated. Although rarely needed, rectal purse-string sutures can be placed if the prolapse is extensive; these sutures can be left in place for 2 to 3 days.

NEOPLASIA

The GI tract is not an uncommon site of primary neoplasia in ferrets. Squamous cell carcinoma of the oral cavity manifests as locally aggressive tumors usually involving the jaw bone.[36,85] Wide surgical resection is the only treatment, and radiation therapy has been applied. Pyloric adenocarcinoma has been reported,[69,76] and may be related to chronic gastritis induced by *Helicobacter* infection. Intestinal adenocarcinoma has been seen clinically in several ferrets by one author (HH). Clinically, these cases presented for nonresponsive diarrhea and signs of intestinal obstruction or rupture. In all cases, adenocarcinoma was rapidly progressive and fatal.

Lymphoma frequently affects the GI tract of ferrets. Visceral and mesenteric lymph nodes, liver, and spleen are common sites for lymphoma; intestinal lymphoma is less common. Intestinal lymphoma results in chronic weight loss and diarrhea and is often overlooked because it resembles other more common causes of chronic diarrhea such as ECE and inflammatory bowel disease. Intestinal rupture from an affected segment of bowel can be seen in some cases of intestinal lymphoma. These ferrets usually have an acute abdomen and septic peritonitis. Diagnosis can only be made by exploratory laparotomy and intestinal biopsy, although if other organs such as the liver or spleen are involved, needle aspirate or biopsy of these organs can be performed. Treatment for intestinal lymphoma carries a poor prognosis. Chemotherapy for lymphoma is described in Chapter 8.

GENERAL APPROACH TO VOMITING

Owners may describe "vomiting" in their ferrets, but some of these animals may actually be regurgitating. In light of this, the differential diagnoses for emesis in ferrets include both esophageal diseases and gastroenteric disorders. In the clinical history, vomiting is not as frequently described in ferrets as it is in dogs or cats. For example, ferrets rarely vomit hairballs, and often vomiting is not part of the history associated with foreign body ingestion. The reason for this is unclear. No anatomic feature prevents emesis in ferrets; in fact, ferrets have long been laboratory animal models for human emesis studies because vomiting can be induced readily in ferrets in a laboratory setting.[19]

The major differential diagnoses for vomiting or regurgitation in ferrets include the presence of a GI foreign body, *H. mustelae* gastritis, gastroenteritis, and, rarely, megaesophagus. It is uncommon for ferrets with metabolic problems such as azotemia or hepatic disease to vomit. Although definitive diagnosis is not always possible, recognizing whether medical or surgical treatment is required is important. For example, most obstructions caused by a foreign body require surgery, whereas gastroenteritis is a medical disease. However, differentiating these two diagnoses is often quite challenging (see Table 3-2).

Diagnosis begins with the history. Pointedly question the owner regarding the chewing habits of the ferret: Does the ferret have a squeak toy? Is it unsupervised in the household or usually caged? Has vomiting been observed? The description of any vomiting behavior is significant. Also question the owner regarding the animal's appetite and obtain a description of the feces. Ferrets that live in groups will need to be separated for observation.

On physical examination, some foreign bodies in the small intestine can be distinctly palpated. However, enlarged mesenteric lymph nodes can feel like foreign objects. Also remember that foreign bodies in the stomach are difficult to detect on palpation. Proliferative bowel disease may result in palpably thickened intestines in the ferret; however, vomiting is not usually a feature of this disease.

Radiography is the most important diagnostic test in the workup of a vomiting ferret. Always include the whole body in a survey radiograph. Radiographic signs of megaesophagus can be subtle. The heart may appear small because of hypovolemia from dehydration. Varying amounts of gas can be seen with a foreign body–related obstruction, and sometimes the incriminating object is visible. Segmental ileus or a dilated and gas- or fluid-filled stomach is a typical radiographic sign of obstruction (see Fig. 3-11). Not all cases of GI foreign body are obvious on radiographs. If evidence of foreign body obstruction is not well defined, consider medical therapy and repeat radiographs in 24 hours. Alternatively, give barium sulfate (8 to 10 mL/kg PO) for a series of contrast-enhanced films. Ferrets will readily take barium force-fed from a syringe.

If there is a strong indication of the presence of a foreign body, perform abdominal exploratory surgery as soon as possible, preferably after parenteral fluid therapy has been started (see Chapter 11). Obtain tissue biopsy samples as needed (e.g., the liver or gastric mucosa), and save any foreign object to show to the owner. Always check the entire intestinal tract for lesions, and examine the pancreas and adrenal glands, especially in older ferrets. If a foreign body is not found, collect gastric and duodenal mucosal biopsy samples to submit for special staining or PCR testing for *H. mustelae*. Infection is associated with gastritis, especially in the antral region and the proximal duodenum (see earlier discussion). Although results of exploratory surgery may be negative for a foreign object, histologic examination of biopsy samples may or may not reveal a diagnosis. The possibility of negative findings should be discussed with the owner before surgery.

If surgery is not an option or is not recommended, consider treatment for *H. mustelae*–associated gastritis (see earlier discussion) and administer fluid therapy as needed. If obstruction is still a possibility, administer a petrolatum hairball preparation at 1 mL q8–12h. Carefully examine all feces passed in the hospital; foreign objects or matter may sometimes be found in the stool.

GENERAL APPROACH TO DIARRHEA

Normal ferrets nibble on food all day. Their GI transit time is short (3 hours), so defecation is frequent in the healthy state. The normal stool is slightly soft and formed. Diarrhea can range from mucoid and green to hemorrhagic. Anorexic ferrets may

produce a very dark green (bile) stool that can resemble melena. Some owners describe a "birdseed" type of diarrhea that may be caused by malabsorption and is often associated with ECE or inflammatory bowel disease (see Fig. 3-13). Unlike canine patients, diarrhea in ferrets is difficult to classify as originating in the small intestine or the large intestine. More important are the onset, duration, and severity of the diarrhea, as well as concurrent clinical signs.

Causes of diarrhea can be separated into diseases of young or older ferrets, as well as infectious or noninfectious causes. The most common noninfectious causes of diarrhea include stress, dietary indiscretion, foreign body ingestion, lymphosarcoma, and inflammatory bowel disease. Occasionally, severe metabolic disease can result in a green (bile-tinged), mucoid diarrhea. Eosinophilic gastroenteritis typically affects mature ferrets but is uncommon (see Table 3-2 and earlier discussion).

Infectious agents are rare causes of diarrhea in closed groups or isolated ferrets, such as those kept as individual household pets. Ferrets do not usually have GI parasites, but coccidia can be present in young, newly purchased ferrets. Rotavirus can cause outbreaks of severe diarrhea, but most reports of this are in very young, unweaned ferrets. Ferrets that have been exposed to unfamiliar ferrets, such as show ferrets, may be susceptible to ferret enteric coronavirus. Newly acquired young ferrets can also act as asymptomatic carriers of coronavirus and expose naïve, older ferrets in a household group. Proliferative bowel disease is usually seen in young ferrets. *Helicobacter*-associated gastritis may also be present. Canine distemper virus in the epitheliotropic form can cause diarrhea in conjunction with respiratory and integumentary disease in unvaccinated ferrets.

The clinical approach to the diagnosis of diarrhea depends on the severity and duration of clinical signs. Obtain a vaccination and dietary history and perform a direct fecal wet mount and centrifugation to check for GI parasites. Sick ferrets need a more comprehensive workup that includes radiographs to check for obstructive lesions and a CBC and a plasma biochemical analysis to assess metabolic conditions. If simple diagnostic tests do not reveal a cause and therapy is unsuccessful, consider exploratory surgery to evaluate the GI tract and obtain biopsy samples. Endoscopy can be difficult in ferrets because of their small size but may be an alternative to surgery. Consider culture of the feces for *Salmonella* species, especially if the ferret is febrile or the feces are hemorrhagic.

Treat ferrets with mild diarrhea, without anorexia or vomiting, on an outpatient basis with an antibiotic such as amoxicillin or chloramphenicol. Metronidazole is a good enteric antibiotic, especially when paired with amoxicillin for *Helicobacter* therapy. Ferrets find metronidazole strongly distasteful, even when it is compounded into a suspension with fruit or chicken flavor. Hospitalize sick or dehydrated ferrets for supportive care and a diagnostic workup. Give fluids subcutaneously if a ferret is stable or intravenously if it is weak and dehydrated. Administer antibiotics parenterally if possible. A short course of a kaolin/pectin suspension (1 to 2 mL/kg PO q2–6h as required [prn]) or bismuth subsalicylate can be administered as a GI protectant until a more definitive diagnosis is established. Drugs that affect the motility of the GI tract should not be administered without an initial diagnosis, although in ferrets with severe diarrhea, loperamide can be administered (0.2 mg/kg q12h). Ferrets with chronic diarrhea may have diminished levels of cobalamin from intestinal malabsorption.[42] Cobalamin administration can be given following the feline protocol:

250 µg SC every 7 days for 6 weeks, then 250 µg SC every 14 days for 6 weeks, then monthly.[42]

DIFFERENTIATION OF EMACIATION ("WASTING DISEASE") WITH DIARRHEA

Helicobacter mustelae–associated gastritis and PBD may occur independently, sequentially, or concurrently in the same animal. Proliferative bowel disease is a sufficient stressor to induce clinical gastritis in a ferret colonized with *H. mustelae*. Although these two diseases are most common in ferrets 12 to 16 weeks of age, sufficiently stressed mature ferrets may also be affected. However, clinical disease in adult animals is more often associated with *Helicobacter*-associated gastritis than with PBD. Although eosinophilic gastroenteritis has been confirmed only in adults, it also may occur in young animals. Any of the wasting diseases can be diagnosed by gastric and intestinal biopsy. However, a presumptive diagnosis may be based on the clinical examination, an accurate history, and results of routine diagnostic tests, which may include radiographs, CBC, plasma biochemical analysis, and fecal examination. Diagnosis may be "confirmed" by the response to appropriate treatment. Characteristics of GI diseases that cause diarrhea and weight loss are summarized in Table 3-2. Other important differential diagnoses for diarrhea and weight loss in domestic ferrets are chronic GI foreign bodies, lymphoma, coronavirus, Aleutian disease, and rarely, mycobacteriosis.

STEPS IN DIAGNOSIS OF WASTING DISEASE

History

Question the owner of a lethargic, anorexic ferret with diarrhea and sudden weight loss about changes in the ferret's diet, feeding schedule, and access to water. The stress factor most commonly associated with wasting diseases is restriction of food for any reason, including the following.

Self-Denial of Food. Ferrets resist changing to a food that differs in flavor and texture from the one to which they are accustomed and may fast for several days rather than eat the new food. Fasting depletes fat stores, which should not be confused with the loss of muscle mass associated with wasting diseases.

Restricted Access to Water. Ferrets consume about three times as much water as dry food pellets and cannot meet their nutritional requirements if water is restricted.

Restricted Access to Food. Food hoppers used with some types of ferret cages may be easily blocked by large food pellets or pellets with unusual shapes, and the owner may not realize that the ferret is unable to get its food. Children caring for ferrets are less likely than adults to understand the significance of an unchanging level of food in the hopper for several days. In addition, some ferrets habitually dig their food out of the container and refuse to eat food that becomes wet or contaminated on the cage floor.

Inappropriate or Nutritionally Deficient Diet. Occasionally, new owners provide ferrets with inappropriate foods, such as dog food or poor-quality cat food, or offer them excessive amounts of sweet treats, especially raisins, which are palatable

but contain almost 100% sugar and no protein. Rapidly growing young animals with nutritional deficiencies are much more susceptible to infectious diseases.

Environmental Stress. Exposure to extremes of temperature, particularly heat, is very stressful to ferrets. Animals may be stressed during inclement weather if they are housed outdoors without adequate protection from wind and rain, especially if their food is of poor quality or subject to wetting, caking, and molding. Ask the owner if the affected pet is his or her first ferret. You may identify stressors that the owner would not have taken into consideration.

Physical Examination

Palpate the abdomen of an emaciated ferret. Grossly thickened areas of bowel in ferrets with PBD and eosinophilic gastroenteritis are sometimes palpable. A focal area of pain in the abdomen is more typical of the presence of a GI foreign body. Splenomegaly is common in ferrets in association with many diseases, and mesenteric lymph nodes are likely to be enlarged in ferrets with any of the wasting diseases. Projectile vomiting has been reported in one ferret with eosinophilic gastroenteritis.[18] Although rectal prolapse is not pathognomonic for PBD, this diagnosis is highly probable in a ferret with prolapse associated with diarrhea and weight loss. In young ferrets (younger than 16 weeks of age and usually younger than 10 weeks), coccidiosis may be associated with diarrhea and rectal prolapse but is rarely associated with significant weight loss. Both Aleutian disease and lymphosarcoma are insidious; thin ferrets will have lost condition over a period of weeks or months and may not have diarrhea.

Radiography is the most useful tool for detecting a GI foreign body (see earlier discussion). Contrast radiographs are sometimes helpful in identifying obstruction with a radiolucent foreign body, but radiographs may also suggest areas of gastric ulceration or intestinal mucosal proliferation in ferrets with either PBD or eosinophilic gastroenteritis.

To help rule out the possibility of lymphosarcoma or eosinophilic gastroenteritis, obtain a blood sample for a CBC. Ferrets with eosinophilic gastroenteritis usually have dramatic eosinophilia (10% to 35% eosinophils compared with 3% to 5% in normal ferrets). Ferrets with lymphosarcoma may not be leukemic, and further tests, such as peripheral lymph node biopsy or a splenic aspirate, are necessary for diagnosis. Inflammation associated with PBD often causes leukocytosis with neutrophilia and a left shift. Ferrets with bleeding ulcers are usually anemic (normal hematocrit is 40% to 55% in spayed or neutered pets, lower in jills in estrus). Dehydration may mask mild anemia and hypoproteinemia in emaciated animals; therefore repeat the CBC after rehydration. Aleutian disease may cause diarrhea, anemia, leukocytosis, and wasting. Serologic tests for Aleutian disease virus are available (see Chapter 5), but many ferrets with positive test results are asymptomatic for Aleutian disease. Clinicians should not assume that illness in ferrets that are seropositive for Aleutian disease virus is caused by the virus.

TREATMENT OF FERRETS WITH WASTING AND DIARRHEA

Debilitated ferrets with diarrhea need rehydration with either intravenously (preferred) or subcutaneously administered balanced electrolyte solutions. These ferrets are often very weak and usually allow a saphenous or cephalic catheter to be inserted with little resistance. However, if a catheter cannot be placed, fluids administered subcutaneously usually are well and rapidly absorbed. Alternatively, an intraosseous catheter can be used until hydration is improved and an intravenous catheter can be placed. Hospitalize an emaciated, dehydrated ferret until fluid and electrolyte balances are reestablished.

Most cachectic ferrets with diarrhea that do not have a GI foreign body or eosinophilia presumably have both ileitis/colitis and *H. mustelae–associated* gastritis with ulcers. While waiting for results of diagnostic tests, if the ferret is treated for only one disease, the time required for recognizing treatment failure may be the factor that ultimately decides if the ferret will survive. Unfortunately, the effective drugs used for treating the diseases associated with wasting are different, and therapy necessitates multiple daily doses of several drugs for at least 2 weeks. Because the gut flora of ferrets is very simple and plays no vital role in digestion, long-term administration of broad-spectrum antibiotics does not cause dysbiosis and diarrhea in ferrets as it does in many species. Emaciated ferrets that die despite proper treatment usually have either very extensive gastric ulcers or severe ileitis, each of which drastically reduces the absorption of essential nutrients. The age of the animal may sometimes help in the differential diagnosis; young ferrets are more likely to develop PBD, whereas older ferrets develop inflammatory bowel disease or severe, chronic gastritis associated with *H. mustelae* infection.[29] Also, *H. mustelae*–associated disease is more often associated with stress factors common in mature pet ferrets, such as concurrent disease or surgery (see Table 3-2).

Emaciated animals have no energy reserve and should receive intensive care. Offering a variety of premium ferret foods and high-calorie, easily absorbed foods is important. Some animals refuse to eat their regular diet of dry pellets but do accept the same food mixed with water and heated in a microwave until it develops a porridge-like consistency. Supplemental foods formulated specifically for carnivores such as Carnivore Care (Oxbow Animal Health) or Emeraid Carnivore (Lafebervet.com) are readily accepted by most ferrets when fed by syringe. Alternatively, offer nutritional recovery foods formulated for dogs and cats such as Maximum-Calorie (The Iams Company, Dayton, OH) or Canine a/d (Hill's Pet Nutrition); most sick ferrets accept these foods readily. Nutritional recovery diets such as these can be used as the sole source of nutrition for several weeks if necessary. When using these diets, calculate a minimum daily intake of 400 kcal per kilogram of body weight. Sick ferrets may not make the effort to get up and drink from a water bottle but do usually drink from a dish. Offer fresh food and water by hand several times daily during hospitalization and home care; ferrets often take a few mouthfuls of every new offering but never go back for more. The first 2 days are critical for an animal that has lost 40% to 50% of its body weight, and intensive supportive care is essential.

When ferrets regain their appetites, often within 48 hours of the first doses of medication, and diarrhea has subsided, owners may be tempted to stop treatment. However, ferrets treated for less than 2 weeks often relapse, and some ferrets need antibiotic therapy and supportive care for an additional 2 to 3 weeks if they are to recover completely. Many ferrets with wasting diseases will survive with aggressive and continued treatment.

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