GI Disease of Rabbits and Ferrets
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The Rabbit
The fusus coli acts as a pacemaker that controls the contractions for excreting the two distinct types of feces that rabbits produce: a dry, hard fecal pellet, which is discarded, and a soft fecal pellet (also known as night feces or cecotropes) which is contained in a strong mucous envelope. Large, indigestible fiber particles play a major role in the maintenance of normal cecal and colonic function and motility. Taenia (bands) move the high fiber colonic ingesta antegrade to be eliminated as hard feces, while reverse peristalsis of the haustra move fluid and nutrient particles retrograde into the cecum where microorganism assisted fermentation results in the production of B-complex vitamins, proteins, and volatile fatty acids (VFA) as well as other nutrients.

Gastrointestinal Stasis
Gastrointestinal (GI) stasis occurs when the normal physiologic contractions and microbiologic flora of the gastrointestinal tract are thrown off balance. Several factors can be involved including a dietary change or inappropriate nutritional, environmental or metabolic stressors, chronic disease, or pain from other underlying conditions such as dental disease. Chronic stress not only reduces food intake but also results in catecholamine signaling, acting on the enteric nervous system to impair intestinal motility. Diets high in carbohydrates such as grains or cereals especially when fed in conjunction with a lack of crude fiber can predispose to GI stasis. Motilin, an enzyme secreted by the enterochromaffin cells in the duodenum and jejunum, stimulates gastrointestinal smooth muscle and thereby aids in the maintenance of normal intestinal and colonic contractions. Diets high in carbohydrates suppress motilin secretion. In the absence of adequate dietary fiber gastrointestinal tract motility often diminishes with potential alteration of the cecum fermentation process and pH that results in a disruption of microbial populations. The rabbit with GI stasis will present with varying clinical signs depending on severity. The affected rabbit may be anorexic or have a reduced appetite and may produce very small stools or none at all. In response to painful GI gas formation the affected rabbit may show abdominal splinting and may be hunched-up or demonstrate bruxism. Diarrhea with mucous may or may not be present. Abdominal auscultation may reveal normal or hyperactive gut sounds early in the course of the disease with decreased to no gut sounds with disease progression. The sooner the problem is recognized and treatment initiated, the better the chance for full recovery and survival. Rabbits presented in obvious distress and with a palpably enlarged, non-compressible stomach warrant close monitoring and critical care as intestinal obstruction is occasionally seen; most commonly due to a small trichobezoar or hair filled cecotrope within the duodenum or ileoceccolic junction. These critical cases often create a diagnostic and therapeutic dilemma. Radiographically the stomach is significantly enlarged with a fluid density topped by a gas pocket, and loops of dilated intestine proximal to site of obstruction may be seen. When treating medically, serial radiographs can be used to assess treatment success; if the obstruction passes through the ileoceccolic junction gas will be identified in the cecum and gas-filled loops of intestine will move and diminish. If the obstruction is not moving, as determined by serial radiographs, then the case becomes surgical. If the rabbit is taken to surgery it is ideal to try and gently milk the obstruction into the stomach and perform a gastrotomy to remove or if in the ileum massage down through the ileocolic junction and into the hind gut instead of performing an enterotomy due to thin and friable nature of the rabbit small intestine.

Depending on the severity and degree of GI stasis and clinician discretion a variety of treatment measures may include:
- Abdominal massage. Gentle, deep massage of the abdomen to stimulate intestinal contractions and to break down impacted stomach contents. Encourage movement and exercise as a way to stimulate gut motility.
Fluid therapy in appropriate amounts and properly administered to control dehydration, rehydrate stomach contents and encourage gut motility.

Analgesics as needed; if showing signs of pain or if increased GI gas is seen radiographically or identified on palpation.

Syringe feeding an enteral nutrition product in order to provide nutritional supplementation and fiber to stimulate GI motility. Nasogastric (NG) tube placement has been advocated in the treatment of GI stasis with one paper showing that nutritional support through a 5- to 8- Fr Argyle tube (Kendall, Mansfield, MA), passed ventrally and medially into the ventral nasal meatus and advanced to the stomach, not only provided for nutritional support but also helped stimulated gastrointestinal motility and early return to function.4

Appetite stimulants: The sooner the rabbit eats the sooner the intestinal motility will return to normal. Vitamin B complex injections or 1–4 mg/rabbit PO q12–24h. Cyproheptadine (Periactin®, Merck, West Point, PA) may act to stimulate the appetite.

GI motility stimulants: Prokinetics such as cisapride (available through a compounding pharmacy) dosed at 0.5 mg/kg PO q8–12h and metoclopramide (Reglan®, Schwarz Pharm. Mequon, WI) at 0.5 mg/kg PO, SC q8–24h may be beneficial adjuncts.

**Other Causes of Rabbit GI Disease**

**Parasitism.** Coccidia (*Eimeria* spp.) more common in juvenile rabbits and can lead to diarrhea. Remains a major disease problem mostly in commercial rabbitries. *E. intestinalis* and *E. flavescens* are considered most pathologic.

**Viral.** Corona- or rotavirus enteritis usually confined to suckling and weanling animals. Secondary *E coli* infections may complicate the disease. Dx: ELISA testing, direct electron microscopy of fecal samples.5

**Dysbiosis, clostridial enteropathies, antibiotic-associated enterotoxemia.** Disruption of the normal gut flora and microbial barrier predisposes to *Clostridium* (*C difficile*, *C perfringens*, *C spiroforme*) overgrowth with subsequent diarrhea, +/- type E iota toxin production leading to enterotoxemia. Enterotoxemia related enterocyte damage often results in profuse diarrhea, depression, dehydration and death. Predisposing causes include “carbohydrate overload” with ingestion of large quantities of high-energy foods or treats that provide an available source of luminal glucose for the opportunistic *E coli* and *Clostridium* spp. Inappropriate oral antibiotic therapy (Beta lactams and macrolides) and stress have also been incriminated with clinical signs being seen within 1 to 5 days. Diagnosis is based on clinical signs, history and fecal Grams stains or cytology or PCR or ELISA-based commercial tests to identify gut clostridial, particularly *C difficile*, toxin.1,5 Treatment involves aggressive supportive care and correction of hypomotility. For enterotoxemia a dual approach of metronidazole (20 mg/kg q12h) and cholestyrine (2 g/20 ml water q24h by gavage) can be used to treat *Clostridium* infection and bind its toxin.1 Alternatively, Di-tri-octahedral smectite, has been shown to decrease the amount of *C perfringens* exotoxin in equine co-incubated samples *in vitro* and its use has been advocated in the rabbit.

**Colonic entrapment.** Partial colonic entrapment and chronic recurring colonic ileus and obstipation may result from adhesions that form secondary to an ovariohysterectomy.

**Liver lobe torsion.** Rabbits with this condition present with nonspecific signs of GI stasis and lethargy +/- cranial abdominal pain. Elevated liver enzymes are a common finding and ultrasound, which shows a lack of blood flow in the affected liver lobe on color flow Doppler, is used to make a definitive diagnosis. If the patient is stable prompt surgical removal of the affected liver lobe has met with success. Medical/supportive treatment alone resulting in the survival of 3 of 6 rabbits with liver lobe torsion has been documented.1

**The Ferret**
The ferret GI tract is designed to be excitatory and have rapid motility, and be highly secretory. Exogenous stressors, chemical and neurologic stimulations, further increase motility and secretion. During any hypoglycemic episode, whether due to inanition, GI loss or insulinoma, the clinician needs to
be aware of pancreatic and gastric physiology and treat the nausea and secretions in addition to the hypoglycemia. The ferret stomach secretes acid in response to histamine, pentagastrin, and calcium. Causes of ferret gastrointestinal disease include:

**Parasitism.** Coccidia, *Giardia*, ascarids may all be found but are uncommon.

**Gastrointestinal Obstruction /Foreign Bodies, Trichobezoars.** Ferrets, most commonly less than one year of age, have a tendency to chew and ingest soft rubber objects of any kind. In the older animal, obstruction or gastritis associated with trichobezoars becomes a more frequent cause of gastrointestinal disease. In cases of gastric foreign bodies that are not causing acute obstructive disease, the signs can be vague and may include intermittent anorexia, decreased volume of stools, tarry stools, depression, gradual weight loss with eventual severe wasting over time, teeth grinding, pawing at the mouth and hypersalivation. Vomiting does occur, but is not as frequent a finding as in dogs or cats with gastric foreign bodies. When a complete obstruction occurs, whether it is at the pylorus or in the small intestine, the signs are much more dramatic. Affected ferrets will exhibit severe depression and dehydration, vomiting is more common, stools are scant and tarry and abdominal pain/splinting is often present. The diagnosis is based primarily on history, physical examination and imaging. The ferret abdomen is easily palpated and foreign material in the stomach or intestine may be identifiable. Survey radiographs and ultrasonography are used to look for signs of gastrointestinal tract obstruction or the foreign body itself. Barium series may be necessary to Dx; barium dosage is 12–15 ml/kg, and due to the ferret’s short gastrointestinal transit time, a full barium series may be completed in three hours.

**Neoplasia.** Lymphoma, adenocarcinoma most common.

**Inflammatory Bowel Disease (IBD).** Muscle wasting, chronic diarrhea of varying character (green mucous, bird seed, melena, watery), vomiting, bruxism. Repeated trichobezoars due to decreased gastric motility resulting from underlying inflammation. Possible inciting factors include:

- Food hypersensitivity
- Carbohydrate overload or other dietary intolerance
- Bacterial (*Helicobacter, Lawsonia*) or viral (coronavirus) infection resulting in secondary
- Aberrant immune response
- Bacterial overgrowth
- Definitive diagnosis involves surgical biopsy of the stomach, duodenum, jejunum, gastric and duodenal lymph nodes and liver. Therapy aimed at long term suppression of the inflammatory response, and eliminating possible contributing factors. Food sensitivities can be addressed by changing to a hypoallergenic diet with a novel protein and carbohydrate source. This may be somewhat of a challenge in the highly carnivorous ferret. Whole prey diets may also be tried.

**Coronavirus**

- **Ferret Enteric Coronavirus (FECV).** Highly contagious; asymptomatic carriers may spread this viral enteritis resulting in a mucoid diarrhea to a naïve population of ferrets. Histopathology shows villi blunting, degeneration of villi crypt apical epithelium and concurrent plasmalymphocytic enteritis. Treatment is supportive and the disease is generally self-limiting. PCR testing of fecal or intestinal tissue available at the Diagnostic Center for Population and Animal Health, Michigan State University, E. Lansing, Michigan. www.dcpah.msu.edu or Veterinary Molecular Diagnostics, New Milford, OH, www.vmdlabs.com
Ferret Systemic Coronavirus (FSCV). Usually young ferrets < 24 mo, rapid onset, high fever, lethargy, recumbency, ataxia, posterior paresis, pain when moving, bruxism, anorexia or difficult swallowing or drinking. May present with a neutrophilic leukocytosis, anemia, thrombocytopenia, and hypergammaglobulinemia. Necropsy: whitish nodules found in numerous tissues, most frequently the mesenteric adipose tissue and lymph nodes, visceral peritoneum, liver, kidneys, spleen, and lungs. Microscopically, pyogranulomatous inflammation involved the visceral peritoneum, mesenteric adipose tissue, liver, lungs, kidneys, lymph nodes, spleen, pancreas, adrenal glands, and/or blood vessels.

*Helicobacter*. Helicobacter colonizes nearly 100 percent of ferrets shortly after weaning via the fecal-oral route. *H. mustelae* has been associated with the loss of stomach lining parietal cells with subsequent hyperacidity and hypochlorhydria leading to the development of gastric and duodenal hemorrhagic ulcers, and may cause a progressive inflammatory response over the lifetime of the ferret. The role of *H. mustelae* in gastric tumors and inflammatory bowel disease is less clear. Gastric ulceration can be difficult to detect with some ferrets showing subtle signs of lethargy and poor appetite. The stools may become soft and occasional vomiting may be seen. As the disease progresses, the ferret will start to pass dark, tarry stools indicative of upper gastrointestinal bleeding, as well as show signs of abdominal discomfort and nausea; grinding of the teeth and increased salivation. Anemia, more severe weakness, dehydration and anorexia may follow. GI biopsies may be obtained for histopathology, with Warthin-Starry and H&E stains used for assessment of colonization and mucosal histopathologic morphology respectively. Gastric lining epithelial hyperplasia, mucous depletion, and loss of glandular tissue may all be seen in varying degrees of severity. Naturally infected ferrets have a predominantly mononuclear gastritis composed of lymphocytes and plasma cells, with only occasional eosinophilic and polymorphonuclear leukocytes. A treatment regimen similar to the one employed for humans has been advocated for use in the ferret and includes antibiotics, GI protectants, and antacids.

- Amoxicillin (30 mg/kg PO q8hr) or clarithromycin (12.5 mg/kg q12h), along with metronidazole (20 mg/kg q8hr).
- A GI protectant/anti-inflammatory; bismuth subsalicylate (Pepto-Bismol, 17.5 mg/kg q8hr) is included in some regimens.
- A H2 blocker; famotidine (Pepcid, Merck 0.25–0.5 mg/kg PO, IV q 24h) or cimetidine (10 mg/kg PO q8hr) or a proton pump inhibitor; omeprazole (0.7 mg/kg q24hr) is used in conjunction for control of stomach acidity.
- An alternative regimen is ranitidine bismuth (24 mg/kg q8hr) and clarithromycin (50 mg/kg q24h or divided q12h).

Pancreatitis. A retrospective study looked at pancreatic tissues from 50 cases submitted to two exotic species pathology services. Histopathologic examination of these pancreatic tissues revealed that both acute (necrosis or neutrophilic inflammation) and chronic (lymphocytic or pyogranulomatous inflammation or fibrosis) pancreatitis was not an uncommon finding in the ferret.

REFERENCES


