Working up Gastrointestinal Disease Syndrome in the Rabbit
Angela M. Lennox, DVM, DABVP-Avian, ECM; ECZM-Small Mammal
Avian and Exotic Animal Clinic
9330 Waldemar Rd
Indianapolis, IN 46268

The Rabbit Gastrointestinal tract
(Special thank you to Micah Kohles, DVM)
Rabbits are herbivores, concentrate selectors and are classified as hindgut (Cecum and colon) fermenters. They have a complicated GI anatomy and physiology designed to handle significant amounts of low-energy density fibrous food and to effectively utilize nutrients found in a high fiber diet. In regards to surgery of the GI tract care should be taken when making ventral midline incision, as the cecum and stomach are often directly adjacent to the body wall. Additionally adhesions can be a common postoperative challenge in rabbits especially associated with gastrointestinal surgery.

The stomach is J-shaped and large compared to most monogastrics, comprises roughly 15% of the GI tract and has a transit time of 3-6 hours. The rabbit stomach has both a well-developed cardiac sphincter that prevents vomiting and a muscular pyloric area and is divided into four parts (the cardia, fundus, body, and pylorus) and contains numerous folds, called rugae. The cardia is large, thin-walled, non-glandular, and lined with stratified squamous epithelium. The stomach acts as a holding chamber and should always contain ingesta.

The small intestine, made up of the duodenum, jejunum (longest), and ileum, is short compared to other species at ~3 meters in length and comprises ~12% of the total gastrointestinal tract. Transit time through the jejunum and ileum is 10-20 and 30-60 minutes respectively. The duodenum is the largest of three segments but shortest in length (~3-5 inches in rabbits). The bile duct and pancreatic duct enter the duodenum separately, with the bile duct entering proximal to the pancreatic duct. The jejunum is less vascularized and its walls are thinner than those of the duodenum. The distal end of the ileum is thickened and referred to as the sacculus rotundus, which is unique to the rabbit
and marks the intersection of the ileum, colon, and cecum. This location signals the beginning of the large intestine and links to the ampulla coli, which forms an intersection of the distal ileum, cecum, and proximal colon. Located at the junction of the ileum and the large intestine is the ileocecal valve, which regulates the movement of material from the small intestine into the large intestine and prevents the retrograde movement of intestinal contents.

The small intestine is the site where the greater part of digestion and absorption most importantly of the cecotrophs. The stomach and small intestine in rabbits digest and absorb nutrients very similarly to monogastric animals with hydrochloric acid and pepsin as initiators of digestion. Pancreatic enzyme production, such as amylase, is minimal, with most coming from saliva or bacterial production within the cecotroph. Motilin, a polypeptide hormone secreted by enterochromaffin cells of the duodenum and jejunum, stimulates gastrointestinal smooth muscle. Motilin production is stimulated by fat and inhibited by carbohydrate ingestion. The transit time of the small intestine is rapid compared to other herbivorous species and fiber is quickly moved to the cecum and large intestine.

The rabbit hindgut is made up of the cecum and colon. The cecum is very large and has a capacity roughly ten times that of the stomach, making up around 40% of the total gastrointestinal tract. It is a thin-walled organ that folds on itself multiple times and has an internal surface made up of a long spiral fold (sometime referred to as spiral valve) that is continued into the beginning of the colon, an area known as the ampulla coli. The distal tip of the cecum is known as the vermiform appendix.

The colon is divided into three sections, the ascending, transverse, and descending colon. Because the fusus coli (located anatomically at what is referred to as the transverse colon) forms such a natural division between the morphologically and functionally distinct ascending and descending sections of the rabbit colon, some have abandoned the three sections and simply use the terms proximal and distal colon. The colon is a very functional component of the hindgut and is characterized by sacculations (haustra) and bands (taeniae). The ascending colon has four sections that contain small protrusions, approximately 0.5 mm in diameter that are commonly referred to as warzens. These wart-like protrusions are believed to be unique to rabbits. The number of taeniae and haustra
gradually taper throughout the proximal colon to the point of the fusus coli, where they are absent. The *fusus coli* has a mucosa that is four to five times thicker than the descending colon is commonly referred to as the “pacemaker” of the hind gut and controls the retrograde and normograde peristaltic activities that occur during the formation of soft and hard feces. The descending colon mucosa is smooth, and while it contains numerous goblet cells, does not contain obvious specialization and usually contains hard fecal pellets.

Rabbits do not completely ferment fiber. They instead utilize a mechanism to sort out indigestible fiber (based on size) and expel it from the body. This process occurs through the rhythmic contractions of the cecum, which constantly mix the ingesta as it undergoes fermentation by the mixed bacterial population, predominantly *Bacteriodes spp.* The mixture of fluid and nutrients is moved through vigorous peristalsis in both normo- and retrograde directions between the cecum and proximal colon. These contractions result in large indigestible fibrous particles accumulating in the center of the colon where they are rapidly transported along the colon to the rectum for defecation, usually within four hours of ingestion. Conversely, smaller, more fermentable fibrous particles accumulate at the periphery of the colon where through retrograde peristaltic contractions of the haustra, they are returned to the cecum for further fermentation. Periodically there is a dramatic change in the peristaltic activity of the cecum and colon as the retrograde movement of smaller fiber particles ceases and a large quantity of the cecal content is expelled into the colon. These contents are excreted, usually once to twice daily, as soft, mucous covered ceccotrophs. This process is controlled by the *fusus coli*. The ability of the colon to rapidly eliminate large indigestible fiber particles and retain smaller, more digestible fiber for further fermentation makes the rabbit an extremely efficient herbivore, capable of surviving on very low-quality forage.

**Rabbit Gastrointestinal Disease Syndrome (RGIS)**

Pathophysiology and Symptoms of Gastrointestinal Disease
Disruption of the normal digestive process in rabbits can result in gastrointestinal disease. For example, anorexia secondary to any painful or debilitating condition reduces the amount of fiber for the digestive tract, resulting in gastrointestinal hypomotility. Hypomotility can result in alterations in cecal microflora with proliferation of pathogens, or overgrowth of naturally occurring Clostridia spp. Worst-case situations can result in enterotoxemia and even death. Hypomotility is also produced by psychologic stress (fear, change in environment, transport, pain) and stress secondary to other disease processes. Signs and symptoms can include depression, decreased appetite to anorexia, food and gas distention of the stomach and digestive tract (bloat), discomfort, the presence of uneaten cecotrophs (often referred to as “diarrhea” by owners) and true diarrhea.

Gastrointestinal stasis is currently a vaguely defined term for decreased gastrointestinal motility. The term Gastric Stasis Syndrome was previously proposed but falls short of an accurate description, as in many cases portions of the gastrointestinal tract other than the stomach are affected. Capello has recently proposed the term Rabbit Gastrointestinal Syndrome (RGIS) to define a complex of clinical signs, symptoms and concurrent pathologic conditions affecting the digestive apparatus of the rabbit. The following pathologic conditions can be included, and often occur in combination:

- Gastric impaction
- Gastric gas accumulation
- Intestinal impaction
- Intestinal gas accumulation
- Intestinal obstruction
- Primary gastroenteritis
- Abdominal adhesions
- Neoplasia
- Pancreatitis
- Liver disease
Etiology of Gastrointestinal Disease

It should be kept in mind that RGIS is not a disease, but a range of motility disorders with multiple potential primary and secondary causes. In many causes, rabbits respond to supportive care and the underlying cause remains undetermined.

Dietary causes

Disorders of the gastrointestinal tract can be related to diet and disruption of the finely balanced digestive process. These include abrupt change in diet, inappropriate food items (grains, large amounts of fruit) and diets generally low in fiber. It should be noted, however, that the author and others are aware of many rabbits existing for years and in apparent good health on diets considered inappropriate.

Abrupt diet change is commonly implicated in gastrointestinal disease in many mammalian species; therefore, changes in diet should be made gradually. A common scenario is anorexia and diarrhea after consumption of a large amount of unfamiliar green food items. This common occurrence is often the root of the fallacious belief that greens are not good for rabbits, an opinion that is still commonly propagated among rabbit breeders and clubs.

Non-dietary causes

Primary gastrointestinal disease

A few primary etiologies have been documented in rabbits, including gastrointestinal obstruction. Primary gastrointestinal disease due to the presence of enteric pathogens is uncommon in rabbits, but can include organisms such as *E. coli* and rotavirus. Clostridial species are normal inhabitants of the rabbit gastrointestinal tract, and can proliferate under certain conditions, producing severe enteritis and in some cases enterotoxemia. Clostridial overgrowth is linked to low fiber, carbohydrate diets, and administration of certain antibiotics, in particular oral penicillins, clindamycin, lincomycin or erythromycin.

Gastrointestinal parasites uncommonly produce disease, but coccidia can be a significant pathogen in young rabbits and those housed in over-crowded, stressful conditions.
Foreign material implicated in obstruction includes bits of dried, firm hair (see trichobezoars), paper, fabric, and dried peas or beans. Other documented causes of obstruction include neoplasms, tapeworm cysts, abscesses and adhesions. Cecal impaction is another unique disease presentation, and is characterized by the presence of hard, firm material (usually food) in the cecum. It is frequently accompanied by stress and dehydration, but other underlying causes are uncertain. A rare congenital condition of rabbits is dysfunction of the autonomic nervous system of the gastrointestinal tract, or dysautonomia, and results in variable symptoms of gastrointestinal disease. Diagnosis is via histopathology of affected nerves. Other uncommonly reported diseases of the gastrointestinal tract include toxin exposure (plants, heavy metals) and coronavirus, which has been reported in a research colony.

*Secondary gastrointestinal disease*

Disease may be secondary to *any* disease producing alterations in fluid balance (dehydration/shock) and/or alterations in gastrointestinal motility, and can include things such as hepatic torsion, sepsis and toxicosis. Lichtenberger has recognized RGIS associated with non-specific hepatitis and pancreatitis confirmed histopathologically, and in some cases suspected at ultrasound. It should also be noted that psychogenic stress is well defined in terms of negative impact upon gastrointestinal motility.

*Trichobezoars*

Trichobezoars are accumulation of large amounts of hair in the stomach. Ingestion of hair is a normal part of the grooming process, and ingested hair normally passes through the digestive tract and is expelled. The presence of abnormal accumulations of hair are linked to low-fiber diets, other diseases disrupting the digestive tract, or excessive ingestion of hair during molt (especially in long-haired breeds) or due the presence of diseases of the skin. In the author’s practice, the most common cause of obstruction is small bits of compressed hair leaving the stomach and obstructing the proximal intestine.

*Complications of Gastrointestinal Disease*

Hepatic lipidosis is a common consequence of anorexia in many species, and may be a significant factor in rabbits as well Fat accumulation in the liver can result in eventual liver failure and death.
Diagnosis of Gastrointestinal Disease

Physical examination findings depend on the extent of disease and the presence of other underlying disease processes. Rabbits can present bright and alert with minimal significant findings, to moribund. Physical examination findings can include fluid imbalances (dehydration, shock), abdominal distention, including gastric and intestinal distension, and gastric tympany. Other symptoms may be related to ongoing underlying conditions. Severely ill rabbits in hypovolemic shock are often hypothermic with pale mucus membranes and decreased capillary refill time, with altered mentation (depressed to comatose). Indirect blood pressure is low or unobtainable.

Basic diagnostic testing can be useful, especially in rabbits with other underlying disease processes such as renal disease. However many rabbits with gastrointestinal disease do not present with significant alterations in complete blood count and chemistry analysis. Anorexic rabbits may demonstrate elevations in hepatic enzymes due to hepatic lipidosis. More debilitated animals show alterations in BUN and albumin consistent with dehydration.

In the author’s opinion, the most useful test for direct evaluation of the gastrointestinal tract is high quality radiographs of the abdomen in two views. Contrast studies are described infrequently in rabbits, but may be useful in some cases.

Primary bacterial gastroenteritis is uncommon in the rabbit; therefore fecal culture and sensitivity are less useful in this species. The most useful application of this test may be rabbits with true diarrhea without history of inappropriate diet, or history of exposure to potential bacterial pathogens.

Fecal floatation can be helpful in rabbits with diarrhea, especially in younger rabbits where primary coccidia is more common.

When ill rabbits present for examination it is important to determine if RGIS is present, and if so, begin treatment and a diagnostic work up to determine underlying contributing factors. Identification of underlying cause is often difficult; the authors and others have encountered many rabbits presenting with evidence of RGIS where attempts to identify an underlying cause are unfruitful. In many cases, these patients respond positively to supportive therapy including fluids, hand feeding, and motility enhancing drugs.
Treatment of Gastrointestinal Disease

Identification of any primary cause of gastrointestinal disease guides treatment decisions. It must be emphasized that the overwhelming majority of rabbits with gastrointestinal disease as a consequence of inappropriate diet, or secondary to psychologic stress, or stress of other underlying disease processes respond well to administration of fluids, analgesics, motility enhancing drugs and syringe feeding. Rabbits with diarrhea should never be fasted, as is often recommended for carnivorous.

The following clinical findings indicate a critical patient that must be managed with extreme caution: marked depression and/or failure to respond to stimuli; marked to severe accumulation of gastric and/or intestinal gas, and indications of shock, including hypotension.

Supportive treatment consists of the following elements (Table 1):

1. Hospitalization. This is beneficial to observe condition, fecal output and response to therapy
2. Fluid therapy. The aim of fluid therapy is to correct hypovolemia and hydration deficits, and to help rehydrate the gastrointestinal tract to facilitate passage of contents. In mild cases, fluids can be administered orally or subcutaneously. However, moderate to severe cases greatly benefit from aggressive intravenous fluid therapy. Fluid choice and rate is determined by patient condition.
3. Pain and anxiety management. Both contribute to stress and will exacerbate impaired motility and contribute to treatment failure. There is no clinical evidence that administration of opioids worsens RGIS by decreasing gastrointestinal motility.
4. Support feeding. Hand feeding is a critical component to therapy. The ideal product for support feeding is a balanced liquid formula able to pass through a syringe or nasogastric tube. Rabbits with suspected gastrointestinal obstruction, or gastric stasis with a full stomach should be fed with caution.
5. Motility modifying drugs. These drugs are extremely beneficial for hypomotility disorders, but should be avoided in cases of suspected gastrointestinal obstruction.

6. Antibiotics. Antibiotics are indicated for suspected cases of enterotoxemia and primary bacterial enteritis only. These drugs are of limited benefit for gastrointestinal disease secondary to other disease processes.

7. Anti-ulcer therapy. There is some evidence prolonged anorexia contributes to gastric ulceration.

Rabbits that are unable or refuse to take hand-feeding formula benefit from placement of a nasogastric tube. Placement of a tube is easier in larger rabbits. Tube size ranges from 5 to 7 Fr. Tube length is determined by measuring from the tip of the nose to the last rib. Lidocaine gel is placed in the nostril and the rabbit carefully restrained with the head ventrally flexed. The tube is placed ventrally and medially into the ventral meatus, and advanced until it enters the stomach. Correct placement can be confirmed several ways, including by aspiration of stomach contents, and radiographically. The small diameter of the nasogastric tube imposes severe limits on products that will readily pass through it. Options include strained vegetable baby food, and finely ground critical care formula (Critical Care Fine Grind, Oxbow Hay Company, www.oxbowhay.com).

Table 1. Therapeutic agents commonly used in the treatment of gastrointestinal disease in rabbits.

<table>
<thead>
<tr>
<th>Agent</th>
<th>Dosage</th>
<th>Indication</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Midazolam</td>
<td>0.25-0.50 mg/kg IV, IM</td>
<td>Anti-anxiety; may also stimulate appetite.</td>
<td></td>
</tr>
<tr>
<td>Butorphanol</td>
<td>0.40 mg/kg IV, IM SQ q4-6h</td>
<td>Analgesia</td>
<td></td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>0.01-0.05 mg/kg SQ, IM, IV q6-</td>
<td>Analgesia</td>
<td></td>
</tr>
<tr>
<td>Drug</td>
<td>Dose/Route</td>
<td>Effect</td>
<td>Notes</td>
</tr>
<tr>
<td>-----------------------</td>
<td>-----------------------------</td>
<td>-------------------------------</td>
<td>--------------------------------------------</td>
</tr>
<tr>
<td>Hydromorphone</td>
<td>0.1 mg/kg SQ, IM, IV</td>
<td>Analgesia</td>
<td></td>
</tr>
<tr>
<td>Cisapride</td>
<td>0.50 mg/kg PO</td>
<td>GI tract motility enhancer</td>
<td>Available through compounding pharmacies</td>
</tr>
<tr>
<td>Trimebutine</td>
<td>1.5 mg/kg PO</td>
<td>Author’s drugs of choice for enhancing GI motility.</td>
<td>Not available in US; oral available in Canada</td>
</tr>
<tr>
<td>Metoclopramide</td>
<td>0.50 mg/kg SQ, PO BID</td>
<td>GI tract motility enhancer</td>
<td>Anecdotally not as effective as cisapride</td>
</tr>
<tr>
<td>Ranitidine</td>
<td>2 mg/kg IV SID, 2-5 mg/kg PO BID</td>
<td>Gastric ulceration</td>
<td></td>
</tr>
<tr>
<td>Lactated Ringer’s</td>
<td>Weight (kg) x % dehydration x 1000 divided into SQ boluses or divided IV per hour over 12-24h 3-4 ml/kg/hr IV, or divided into SQ boluses</td>
<td>To correct dehydration, hypovolemia and for maintenance</td>
<td>SQ administration for mild cases only</td>
</tr>
<tr>
<td>Dehydration Maintenance</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hetastarch</td>
<td>2-5 ml/kg bolus; .3 ml/kg/hr added to crystalloid</td>
<td>Treatment of hypovolemia; with fluids in cases of</td>
<td>Current debate on use; may not be safe in cases of</td>
</tr>
<tr>
<td>Fluids</td>
<td>Hypoalbuminemia</td>
<td>Renal Insufficiency</td>
<td></td>
</tr>
<tr>
<td>-------</td>
<td>-----------------</td>
<td>---------------------</td>
<td></td>
</tr>
<tr>
<td>Metronidazole</td>
<td>10 mg/kg PO BID 5 mg/kg slow IV BID</td>
<td>For suspected clostridial overgrowth and enterotoxemia</td>
<td></td>
</tr>
<tr>
<td>Enrofloxacin</td>
<td>5-15 mg/kg PO q24h; IM single injection</td>
<td>For suspected primary bacterial enteritis</td>
<td>Primary bacterial enteritis is rare in rabbits</td>
</tr>
<tr>
<td>Oxbow Critical Care</td>
<td>See manufacturer instructions</td>
<td>Syringe feeding</td>
<td>“Fine grind” version for use with nasogastric tube</td>
</tr>
</tbody>
</table>

**Gastrointestinal Obstruction**

True gastrointestinal obstruction represents an emergency and requires accurate diagnosis and immediate therapy. Early obstruction or partial obstruction may mimic other conditions that produce RGIS signs and symptoms and may be difficult to identify. Rabbits with marked gastric distention with fluid and air accumulation, especially those that are depressed or exhibiting evidence of shock are often truly obstructed and should undergo exploratory laparotomy. Radiographs may demonstrate a pattern suggestive of obstruction such as a small bowel gas pattern that ends abruptly, often without evidence of gas accumulation distal to the suspected obstruction (it must be noted that some rabbits with confirmed obstruction also have concurrent ileus, with gas accumulation throughout the GI tract, complicating radiographic diagnosis).

The most helpful information that surgical intervention is indicated comes from careful monitoring of overall clinical condition and serial radiography. Some patients respond favorably to aggressive supportive therapy, with improving condition and radiographic findings such as decrease in the size of the stomach and dispersion of abnormal gas patterns. Any patient demonstrating worsening clinical condition and static/worsening...
radiographic findings should undergo exploratory laparotomy. Repeat radiography every 2-3 hours is indicated in these cases.

In general, rabbits tolerate surgery well, with higher rates of failure linked to poor overall condition (e.g. shock, renal insufficiency) or diagnoses that carry poor a poor prognosis, such as advanced neoplasia. Rabbits in otherwise good condition presenting for acute obstruction are usually good surgical candidates. The rabbit is a model for intestinal surgery in humans, and apparently tolerate surgeries such as resection and anastomosis relatively well.

Choose anesthetic protocols recommended for higher risk patients, utilizing surgical vascular support and careful patient support and monitoring. Guidelines for the general approach to the abdomen of the rabbit are reported elsewhere. Due to risk of adhesions, tissues should be handled as little as possible, which is often challenging when attempting to diagnose and treat an obstruction. Most obstructions are located in the small bowel, with many reported the proximal duodenum as the most likely location. Removal of the foreign body is performed as in other traditional pet species, avoiding incision over the foreign body, and using 4 to 6-0 absorbable suture.

References: