

LIVER AND LARGE INTESTINE DISEASE IN RABBITS

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INTRODUCTION

Rabbits are monogastric herbivores with a hindgut fermentation system whose digestive physiology relies on caecotrophy to optimise nutrient utilisation. Their gastrointestinal system is characterised by a well-developed caecum and a particle separation mechanism in the proximal colon that allows microbial fermentation of digestible fibre, while non-digestible fibre is rapidly expelled.

This adaptation favours efficient digestion of forage-rich diets, but also makes them susceptible to nutritional disturbances and large intestine and liver dysfunction. Understanding normal digestive physiology is essential for interpreting the most common pathological processes in these regions, establishing an accurate diagnosis and designing effective therapeutic strategies for managing these diseases.

LARGE INTESTINE AND LIVER DISEASE

1) Cecotrophy and intermittent diarrhoea

Cecotropes are nutrient-rich pellets, similar in appearance to faeces, containing the products of caecal fermentation. When intact, they appear as multiple soft faecal pellets grouped together, with an intense odour, which often adhere to the fur in the perineal region or are scattered on the fur and floor (Fig. 1). This finding is often confused with diarrhoea and is a common reason for consultation.

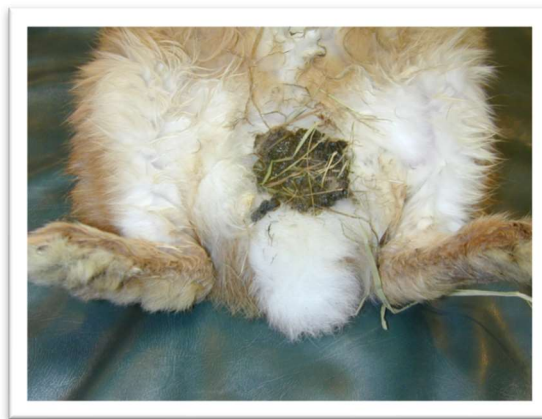


Fig 1: Rabbit presenting with uningested caecotropes in the perineal area. (Credit JRN – CHV Anicura ADVETIA)

The diagnosis is based mainly on the medical history. Soft faeces are observed stuck to the fur or staining the floor. If the rabbit cannot reach the anal region, the faeces remain stuck to the perineum, often leading to secondary dermatitis. r physical examination usually reveals obesity or signs of neuromuscular or dental disorders. Correcting the underlying disorder will allow a return to normal caecotrophy.

Microscopic examination of the faeces is important, as large amounts of the yeast *Cyniclomyces guttulatus* may be found. In such situations, treatment with nystatin may be indicated.

Insufficient fibre intake (hay) or excessive carbohydrate consumption is a common cause of soft stools. Adjusting the diet usually resolves the problem. Only hay should be offered until uningested caecotrophs are no longer observed. Once uningested caecotrophs have not been observed for several days, pellets and vegetables can be gradually reintroduced into the diet.

2) Cecoliths – Megacolon Syndrome

Impaired motility of the caecum, colonic transit speed, or an inadequate diet can cause compaction and dehydration of caecal or colonic contents, leading to the formation of abnormally hard masses of caecal contents. Rabbits that develop these caecal masses often have a chronic history of bulky, malformed faeces, recurrent caecal impaction, abdominal pain, and anorexia. These animals are often underweight and have poor muscle mass.

There is a congenital disorder of sodium transport to the caecum, described in homozygous rabbits of spotted breeds, such as the English Spot and the Checkered Giant. This condition is commonly known as "megacolon syndrome", although in reality it mainly affects the caecum, not the colon.

A presumptive diagnosis of cecolith formation can be made by palpation, identifying material with a consistency between pasty and very firm in the caecum. Radiographic or ultrasound examinations can confirm the presence of cecoliths. If the intestine is completely obstructed, gas accumulation is observed in the sacculated large intestine.

Treatment focuses on rehydrating the caecal and colonic contents through intravenous fluid therapy. It is essential to offer foods high in water and fibre to promote normal intestinal motility and caecal function. According to recent literature (Quesenberry, 2020), the use of intestinal prokinetic agents may be beneficial in these cases. Analgesia is essential, as these patients often experience significant pain; effective options include methadone or continuous lidocaine infusions, as well as combinations of fentanyl, lidocaine, and ketamine. The long-term prognosis is usually guarded or poor.

3) Dysbiosis, enteritis complex, and enterotoxemia

- Enterotoxemia

Enterotoxemia in rabbits is caused by the iota toxin produced by *Clostridium spiroforme*. Newly weaned animals are most frequently affected and have the highest mortality rate, due to their immature gastrointestinal microbiota and high gastric pH, which allows *C. spiroforme* to proliferate.

Adult rabbits are more resistant and generally require some dietary or environmental factor or some form of stress to induce dysbiosis and bacterial growth. The rapid multiplication of *C. spiroforme* significantly alters the normal caecal flora of the rabbit.

In acute disease, rabbits stop eating and appear depressed. Brown liquid diarrhoea is observed, soiling the perineum and hind legs, which may contain blood or mucus. Animals may become hypothermic and may die within the first 48 hours.

Post-mortem findings include petechial and ecchymotic haemorrhages on the serosal surface of the caecum. Different amounts of gas are also found throughout the intestinal tract, caecum and colon.

- Muroid enteritis

Muroid enteritis is a major cause of morbidity and mortality in young rabbits aged 7-14 weeks. It is characterised by anorexia, lethargy, weight loss, diarrhoea, caecal impaction and excessive mucus production by the caecum. It is believed that alterations in cecal pH, resulting from changes in the production or absorption of volatile fatty acids or vigorous fermentation of carbohydrates, can destabilise the microbial population of the caecum and stimulate mucus production in the caecum and colon. Feeding a high-fibre, low-carbohydrate diet is a preventive measure.

- Antibiotic-induced dysbiosis

Antibiotic administration can cause enteritis. Some antibiotics suppress normal flora, allowing pathogens to proliferate. Antibiotics that can induce enteritis in rabbits include clindamycin, lincomycin, ampicillin, amoxicillin-clavulanic acid, cephalosporins, many penicillins, and erythromycin.

- Treatment and prevention of dysbiosis and enterotoxemia

Treatment consists of intensive supportive care, correcting dehydration by administering fluids intravenously or intraosseously. If the rabbit is anorexic, it should be assisted with force-feeding. Increase caecal and colonic motility, prevent the growth of pathogenic bacteria and the production of toxins, and promote the growth of normal flora.

The use of metronidazole (20 mg/kg PO or IV every 12 hours) has been shown to reduce mortality from enterotoxemia. The administration of cholestyramine (2 g in 20 mL of water every 24 hours), an ion exchange resin capable of binding bacterial toxins, has been shown to prevent death in cases of clindamycin-induced enterotoxemia.

It is recommended to offer hay and control the amount of pellets in the diet. Sudden changes in diet should be avoided. In addition, it is important to make hay available to young rabbits from 3 weeks of age and to avoid early or forced weaning.

4) Primary bacterial enteritis

Bacterial enteritis is a common cause of mortality in the rabbit industry, where mortality rates ranging from 50 to 100% have been reported. However, enteritis typically occurs in newborns or rabbits under 16 weeks of age that are under stress due to weaning, transport, or overcrowding.

- *Escherichia coli*

Enterohaemorrhagic *Escherichia coli*, a potential zoonotic pathogen, produces Shiga toxins that cause haemorrhagic colitis accompanied by haemorrhagic diarrhoea. This pathogen is transmitted through contaminated water and food, via oral ingestion. Naturally infected rabbits develop thrombotic microangiopathy, characteristic of Shiga toxin, which is considered responsible for cases of acute renal failure.

In infected does, subsequent litters may acquire passive immunity. The pathological process is limited to the caecum and colon. The caecal wall may be inflamed, with longitudinal haemorrhages. In severe cases, intussusception and rectal prolapse may occur.

A presumptive diagnosis can be based on the isolation of *E. coli* from faecal samples or tissue samples from affected animals. Confirmation of the diagnosis requires histological examination of the tissues and observation of the adhesion of *E. coli* to intestinal cells.



Treatment is based on the use of antibiotics selected according to culture and antibiogram results, together with supportive care including fluid therapy, assisted feeding and maintenance of normothermia. The use of trimethoprim-sulfamethoxazole (30 mg/kg PO every 12 hours) is recommended until culture results are available.

5) Proliferative enteritis, proliferative enteropathy, proliferative enterocolitis

The obligate intracellular bacterium *Lawsonia intracellularis* has been reported to cause enterocolitis in rabbits. The disease is most often characterised as acute diarrhoea in rabbits aged 2-4 months. Histological findings usually show proliferative ileitis, with epithelial hyperplasia and mucosal inflammation.

Treatment is challenging. The antibiotics used to treat this bacterium in other species belong to the macrolide family (such as tylosin, erythromycin, and lincomycin), which are not recommended for rabbits. Chloramphenicol (30 to 50 mg/kg PO or SC every 12 hours for 7–14 days) and florfenicol (20–30 mg/kg PO, IM or IV) have been shown to be effective.

6) Tyzzer's disease

Tyzzer's disease is caused by *Clostridium piliforme*. Stress is an important component in the onset of this disease.

Clinical signs include watery diarrhoea, depression and death. Morbidity and mortality rates can be particularly high in newly weaned rabbits, while adult rabbits develop a chronic form of the disease, which manifests as progressive weight loss.

Necropsy of affected rabbits reveals foci of hepatic necrosis and degenerative lesions in the myocardium. In addition, the intestinal wall shows oedema, accompanied by areas of necrosis in the mucosa of the proximal colon.

Treatment is palliative once clinical signs have manifested. If exposed animals receive early preventive management (isolation, good hygiene practices, supportive care, and a high-fibre diet), they may not develop the disease. Prevention depends on proper health management. Clostridial spores are eliminated by 0.3% sodium hypochlorite solutions (bleach), some disinfectants, or by heating to 80°C for 30 minutes.

7) Rotavirus

Rotavirus infection causes endemic diarrhoea in rabbits, with suckling rabbits being the most susceptible.

The main clinical signs are diarrhoea, dehydration and sudden death. Necropsy findings include mild to severe villous shortening and fusion, submucosal oedema of the small intestine and liquid caecal contents.

Definitive diagnosis is based on histopathological examination of the intestine. Virus isolation or antibody demonstration are suggestive. Clinical signs and macroscopic findings alone are not diagnostic.

Preventing and controlling rotavirus infection is complex due to its high infectivity. Stress reduction, along with appropriate treatment of concomitant diseases and improved hygiene, should reduce mortality rates.

8) Parasitic disorders

Coccidia

Coccidia are a common cause of disease in young animals under 6 months of age. Adult rabbits rarely show clinical disease, and the identification of oocysts in a faecal examination does not equate to a diagnosis of disease.

Hepatic coccidia

Eimeria stiedae is the coccidian responsible for hepatic coccidiosis. Many infections are asymptomatic; however, in severe cases, especially in young rabbits, the disease can be fatal. Severe infections produce signs associated with liver dysfunction and bile duct obstruction. Affected animals often present with anorexia, progressive weakness and, in terminal stages, diarrhoea or constipation. Abdominal distension and jaundice are sometimes observed. Serum biochemical tests show increases in alanine aminotransferase, aspartate aminotransferase, bile acids and total bilirubin. Radiographically, hepatomegaly and ascites may be evident. Ultrasound findings include ascites, hepatomegaly, heterogeneous liver parenchyma, and dilation of blood vessels and hepatic bile ducts. At necropsy, the liver appears enlarged with multiple yellowish or whitish nodular lesions. The diagnosis is confirmed by the identification of oocysts in the bile, histopathological analysis, or faecal examination.

- Intestinal coccidia

The most relevant species of intestinal coccidia in rabbits are *Eimeria perforans*, *E. magna*, *E. media*, and *E. irresidua*, with *E. perforans* being the most common. Infection occurs through the ingestion of sporulated oocysts present in the environment.

The clinical presentation depends on factors such as the age of the animal, the species of *Eimeria* involved, the parasite load and individual susceptibility. Subclinical infections are common in both young and adult rabbits, and the detection of oocysts in asymptomatic animals does not in itself justify treatment. Clinical signs are usually related to poor husbandry conditions or overcrowding and are mainly seen in animals under 6 months of age. In less common cases, adult rabbits with severe immunosuppression may also develop the disease.

Clinically, signs include mild and intermittent or severe diarrhoea that may be accompanied by mucus or blood, weight loss, and dehydration. Severe and complicated cases may develop intestinal intussusception. Death usually occurs as a result of dehydration and secondary intestinal dysbiosis.

At necropsy, lesions affect the small or large intestine depending on the species of *Eimeria* involved, and the intestinal epithelium may show areas of ulceration. Detection of oocysts in faecal samples or intestinal scrapings from symptomatic animals allows a presumptive diagnosis to be made, while definitive diagnosis is confirmed by histopathological examination.

- Treatment of coccidiosis

Treatment may involve a single dose of toltrazuril (2.5 mg/kg PO), sulfadimethoxine (15 mg/kg PO every 12 hours for 10 days) or trimethoprim-sulfamethoxazole (30 mg/kg PO every 12 hours for 10 days).

Helminths

The most common nematode in domestic rabbits is *Passalurus ambiguus*. Infestations are usually asymptomatic and non-pathogenic, although adult worms can be observed macroscopically in the caecum, colon and fresh faeces. Its life cycle is direct, associated with the ingestion of eggs during caecotrophy.

Diagnosis is based on the identification of adults or eggs in faeces. Treatment is not usually required, but benzimidazoles such as fenbendazole (10–20 mg/kg PO) or thiabendazole (50 mg/kg PO) may be used.

9) Appendicitis

Appendicitis in rabbits is an underdiagnosed condition, probably due to a lack of knowledge of the specific anatomy of the species, the difficulty of identifying it using diagnostic imaging techniques, and the non-specific nature of its clinical signs, which are often confused with rabbit gastrointestinal syndrome. Rabbits have a vermiform appendix rich in lymphoid tissue, which predisposes them to inflammatory processes such as appendicitis. Clinical signs include acute anorexia, lethargy, decreased faecal production, abdominal pain and, occasionally, fever. The diagnosis is based on a combination of clinical findings, blood tests (anaemia, hypocalcaemia, hypoglycaemia), and imaging, with abdominal ultrasound being the technique of choice, where a dilated appendix with a thickened wall, loss of normal structure, and abnormal content can be observed (Fig. 2). In some cases, computed tomography can provide additional information.

Treatment may be medical or surgical, although appendectomy is considered the most effective approach in confirmed cases with abscess or in cases where there is no response to medical treatment, with good survival outcomes (Fig. 3). Medical therapy includes fluid therapy, analgesia, antibiotics, and gastrointestinal support. Early diagnosis and rapid intervention are essential to improve prognosis, especially in patients with severe signs or complications such as peritonitis.



Figure 2: Image of an abdominal ultrasound of a rabbit showing moderate to severe signs of appendicitis: marked dilation of the appendix with dense hypoechoic content, suggestive of mucoid or purulent material. (Credit JRN – CHV Anicura ADVETIA)

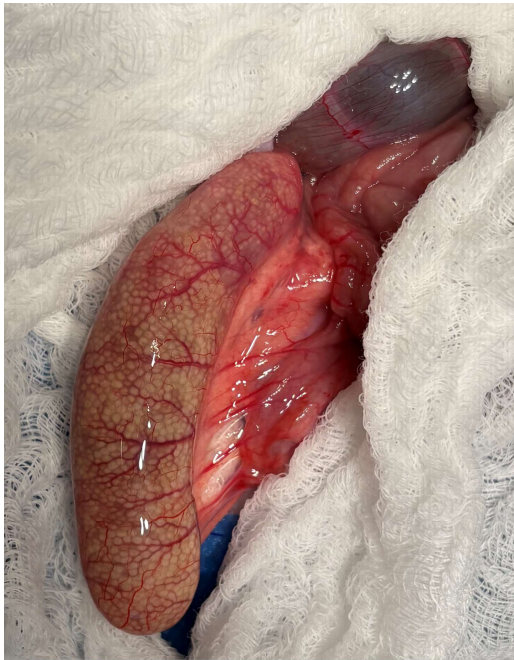


Figure 3: Images from surgery on a rabbit with appendicitis, which was treated by surgical removal of the appendix. (Credit: JRN – CHV Anicura ADVETIA)

10) Hepatic lobe torsion

The aetiology of hepatic lobe torsion in rabbits remains unclear. The caudate lobe is most frequently affected. Most cases present with non-specific clinical signs consistent with rabbit gastrointestinal syndrome, such as acute anorexia, lethargy, decreased faecal production, and cranial abdominal pain.

The diagnosis is based on a combination of imaging tests and blood tests. On radiography, findings include rounded hepatic margins, hepatomegaly, increased hepatic density, and free abdominal fluid. Abdominal ultrasound shows an enlarged hepatic lobe with rounded margins, homogeneously hypoechoic parenchyma with a "lattice" pattern, hyperechoic mesenteric fat, and absence of colour Doppler flow. Contrast-enhanced ultrasound confirms the lack of perfusion in the affected lobe. Computed tomography shows enlarged, hypoattenuating hepatic lobes without contrast uptake.

The haematological and biochemical profile usually shows moderate to severe anaemia, elevated liver enzymes (especially ALT) and azotaemia.

Treatment includes intravenous fluid therapy, multimodal analgesia (such as continuous infusion of fentanyl-lidocaine-ketamine or methadone), and thermal support. Surgical lobectomy is the treatment of choice (Fig. 5). In situations without haemoperitoneum, some rabbits may survive with conservative management.

Negative prognostic factors include moderate or severe anaemia, tachycardia on admission, several days without defecation after hospitalisation, and torsion of the right hepatic lobe.



Figure 5: Intraoperative image of a rabbit undergoing hepatic lobectomy due to torsion of the caudate lobe, complicated by haemoperitoneum. (Credit: JRN – CHV Anicura ADVETIA)

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