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CHAPTER 8

Digestive Disorders

A wide array of digestive disorders affect rabbits. Diarrhoea, bloat, scours, mucoid enteritis, enterotoxaemia, gut stasis, wool-block, trichobezoars, enteritis, gastroenteropathy and mucoid enteropathy are among the variety of non-specific terms used to describe the diseases of the gastrointestinal tract. Many of the digestive disorders that afflict pet rabbits are related to diet and only a few are caused by enteric pathogens. There is a complex inter-relationship between the predisposing factors and causes of digestive disease. This inter-relationship is summarized in Figure 8.1. Enteric disease is manifested by a disruption in normal faecal production. The consistency and frequency of hard and/or soft faeces are altered. There may be mucus production. The term 'diarrhoea' can be confusing, both to owners and to vets, and it is necessary to discriminate between true diarrhoea and a failure to eat caecotrophs. A list of differential diagnoses of 'diarrhoea' is given in Table 8.1.

8.1 Digestive physiology

A detailed description of the rabbit's digestive physiology is given in Section 1.3.1. Briefly, the rabbit is a strict herbivore whose digestive system is adapted for the ingestion of a fibrous diet. Digestion in the stomach and small intestine is similar to monogastric animals and food that reaches the hindgut is mainly composed of fibre that cannot be broken down by the digestive enzymes of the stomach and small intestine. The rabbit has the ability to separate large fibre particles from small fibre particles in the proximal colon. The small particles and the large undigested particles are simultaneously sent in opposite directions. Large particles of undigested fibre pass distally and are excreted in hard faecal pellets. Small fibre particles are sent in a retrograde direction into the caecum where they undergo bacterial fermentation. Bacterial fermentation within the caecum releases volatile fatty acids that are absorbed as an energy source. The result of bacterial fermentation within the caecum is a fine paste containing amino acids, vitamins, enzymes, micro-organisms and volatile fatty acids.

Therefore, the rabbit's colon has a dual function. For most of the day, it mixes and separates ingesta, simultaneously sending indigestible particles towards the anus, and fermentable particles towards the caecum. Periodically, the motility of the proximal colon alters completely, and pasty caecal contents are directed along the colon to be expelled as soft faecal pellets or caecotrophs. Caecotroph production follows a diurnal rhythm. Most rabbits produce soft faeces during the morning and evening approximately 4 h after feeding. These caecotrophs are re-ingested directly from the anus to be digested in the stomach and small intestine as an additional source of nutrients for the rabbit. The nature of the intestinal contents, muscular activity, transit time and exchange of water and electrolytes alter according to the type of faeces passing through the colon. Therefore, digestion and colonic motility can be in either the 'hard faeces phase' or the 'soft faeces phase' (see Figure 1.4). The amount of ingesta and gas in the various sections of the digestive tract alters according to the phase of excretion. The size and shape of the caecum also follows a diurnal rhythm, which is an important consideration during abdominal palpation or radiography of rabbits.

Separation of ingesta in the proximal colon is accomplished by a combination of functional

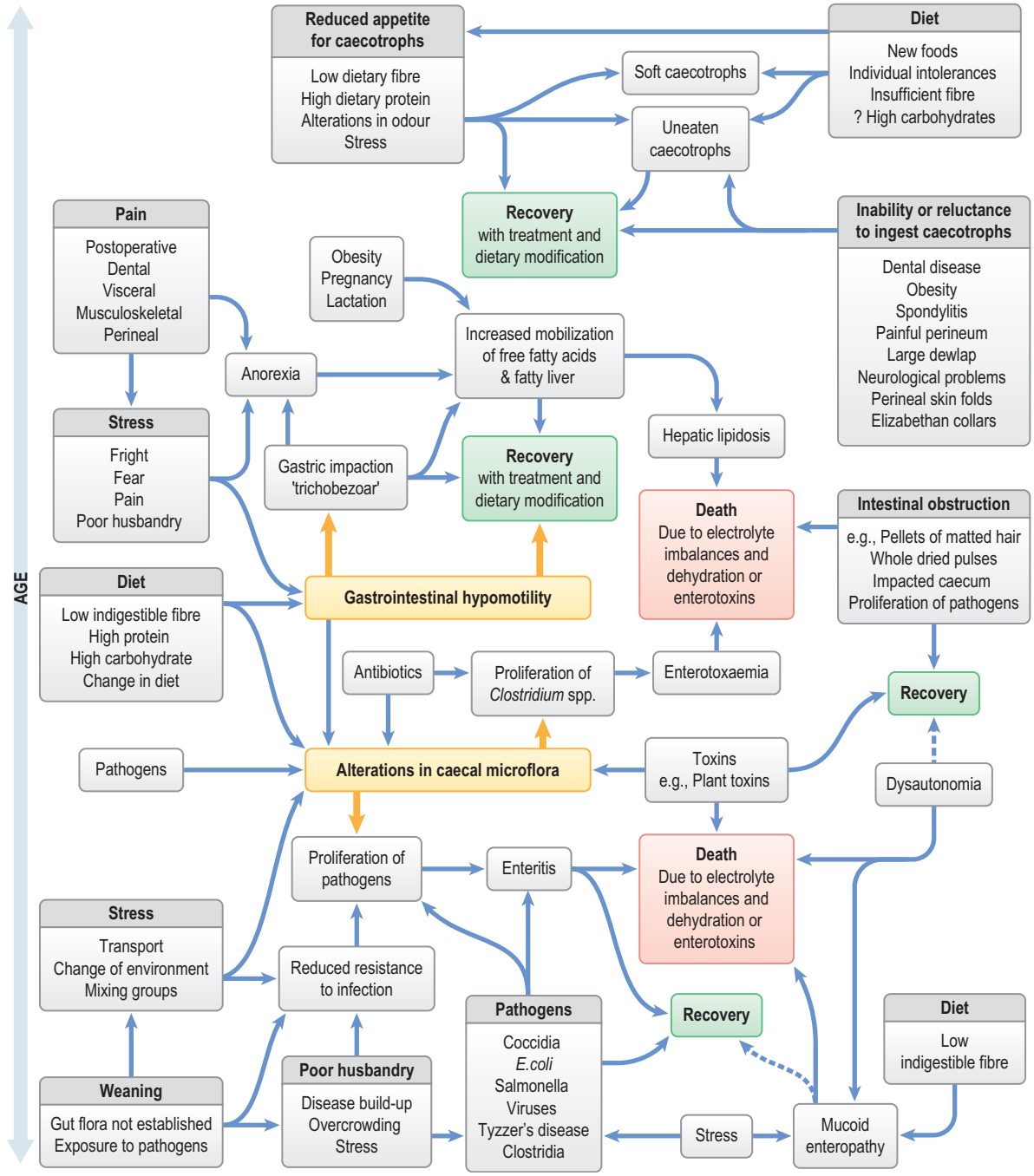


Figure 8.1 Inter-relationship of predisposing factors and causes of gastrointestinal disease in rabbits.

Table 8.1 Differential diagnosis of 'diarrhoea' in rabbits

Syndrome	Incidence in pet rabbits	Hard faeces	Caecotrophs	Condition of rabbit	Causes
Uneaten normal caecotrophs (soft odorous faecal material that looks like diarrhoea to the owner)	Common	Copious quantities of hard faecal pellets	Normal consistency	Well Appetite good	Obesity Dental disease Spondylosis Arthritis Perineal dermatitis etc.
Uneaten soft caecotrophs	Common	Copious quantities of hard faecal pellets	Soft, liquid consistency	Well	Change of diet Lack of dietary fibre Succulent foods Stress + same causes as uneaten normal caecotrophs
Coccidiosis	Rare in adult Common in juvenile	Diarrhoea can range from haemorrhagic liquid faeces to bulky soft faeces	Indistinguishable from hard faeces	Depends on severity of condition	*Eimeria* spp.
Mucoid enteropathy	Rare in adult Associated with stress Sporadic outbreaks in juveniles	Normal hard faeces are absent Mixed or interspersed mucus and diarrhoea No faecal output in later stages	Abnormal soft caecotrophs may be intermittently interspersed with mucus and diarrhoea	May be eating in early stages Bloated appearance Progresses to inappetence and tooth grinding	Still unclear Dysautonomia has been found in some cases
Caecal impaction	Sporadic incidence	Absence of hard faeces Can produce mucus, which owners mistake for diarrhoea	None in later stages	May pick at food in early stages	Appears to be associated with pain or stress Caecal impaction is also part of mucoid enteropathy complex Can be caused by ingestion of materials that are moved into the caecum, absorb water and are not broken down by caecal microflora. Examples include clay litter, methylcellulose or other bulk laxatives

Continued

Table 8.1 Differential diagnosis of 'diarrhoea' in rabbits—cont'd

Syndrome	Incidence in pet rabbits	Hard faeces	Caecotrophs	Condition of rabbit	Causes
Enteritis	Rare in adults Enteritis caused by bacterial overgrowth/ imbalances is more common in the suckling or growing rabbit	Normal hard faeces are absent Liquid diarrhoea	Not seen	Unwell Anorexic May crave fibre	Bacterial or viral pathogens such as *E. coli*, clostridia, rotaviruses Can be induced by antibiotics Plant toxins
Enterotoxaemia	Sporadic cases in adult rabbits More common in juveniles	Liquid faeces that may be tarry Rabbit may die before diarrhoea develops	Not seen	Unwell Rapidly progressive May be collapsed	Clostridial species Can be induced by antibiotics
Chronic inflammatory disease	Rare Only adults	Large amounts of bulky soft faeces	Indistinguishable from hard faeces	Thin, bloated Periods of ravenous appetite interspersed with periods of anorexia	Not known ? immune mediated Sometimes associated with adhesions? post spay

In other species, diarrhoea is manifested by the frequent evacuation of watery droppings (Blood and Studdert, 1999). Rabbits produce two types of droppings, i.e. hard faeces and caecotrophs. Normal caecotrophs are soft in consistency and are often mistaken for diarrhoea. The nature and frequency of both types of faeces are an important consideration. In some conditions, there is also excessive mucus production that can be mistaken for diarrhoea.

anatomy and colonic motility. Sacculations in the wall of the proximal colon (*haustra*) retain small particles while the larger particles accumulate in the lumen. Haustral activity directs small particles towards the caecum, while segmental activity directs large particles towards the anus. Lagomorphs have a specially adapted muscular segment of the colon known as the *fusus coli* that contains a large number of mucus glands (see Figure 1.5). The fusus coli acts as pacemaker for colonic motility. It is highly innervated and vascular and it is not only controlled by the autonomic nervous system but also subject to the effects of metabolites and hormones such as aldosterone and prostaglandins. During the excretion of caecotrophs, haustral activity ceases and caecal material is moved swiftly along the large colon. In the fusus coli, the material is formed into pellets that become encapsulated in mucus (see Figure 1.5). The transit time for soft faeces through the colon is 1.5–2.5 times faster than that for hard faeces (Fioramonti and Ruckesbusch, 1976).

Within the caecum lies a complex ecosystem of microflora nourished by water and digesta that arrive from the small intestine via the proximal colon. Water is secreted into the proximal colon during the process of mixing and separating and is sent into the caecum with the small particles. Water is absorbed from the caecum across the caecal wall into

the circulation. The retention time of digesta within the caecum is affected by both caecocolonic motility and the nature of ingesta that reaches it. Conditions within the caecum are affected by the type and amount of nutrients that supply the microflora and the products of bacterial fermentation. The balance of micro-organisms in the caecum is of paramount importance to the health of the animal. A healthy microflora digests food efficiently. Any factor that upsets the balance of caecal microflora has the potential to result in the proliferation of pathogenic bacteria and cause disease.

8.2 Inter-relating factors in digestive disease

8.2.1 Intestinal microflora

The caecum is a finely balanced ecosystem composed of a variety of micro-organisms nourished by a constant supply of water and nutrients from the small intestine. Changes in the amount and content of the ingesta that reaches the caecum have an effect on the balance of micro-organisms, which are therefore dependent on diet and intestinal motility. *Bacteroides* spp. predominate in a microflora composed of aerobic and anaerobic Gram-positive and -negative rods, cocci, filaments, coccobacilli and spirochaetes. In addition to the aerobic flora, over 74 strains of anaerobic bacteria have been isolated from the caecal mucosa and many of these species have not been cultivated (Straw, 1988). The microbial flora can contain small numbers of potential pathogens such as *Clostridium* spp. Stress has an effect on caecal microflora. Increased glucocorticoid levels increase coliform counts and narrow the aerobic-to-anaerobic bacteria ratio in the gut (Straw, 1988). Changes in the caecal microflora can be seen in Gram-stained smears of caecal contents. In the healthy rabbit, high numbers of large anaerobic metachromatic bacteria (LAMB) and protozoa are present. In rabbits suffering from mucoid enteropathy, a drop in the number of LAMB and protozoa and an increase in coliforms are found (Lelkes and Chang, 1987).

The caecal microflora synthesize volatile fatty acids that are absorbed across the caecal wall into the circulation. Anaerobic *Bacteroides* are the principal source of butyrate that is used as an energy source for the caecal epithelium. The caecal epithelium is adapted for the efficient absorption of water and electrolytes. Butyrate is also important in the regulation of caecal pH, which has an optimum of 5.7–6.1. Changes in caecal pH alter the caecal microflora and can result in the proliferation of pathogens. The proportions of volatile fatty acids in the caecum influence appetite and gut motility. In healthy rabbits, acetates predominate, followed by butyrates and propionates. Low fibre diets result in decreased acetates and increased propionates and butyrates. An increase in caecal butyrate inhibits normal peristalsis of the gut (Lang, 1981).

The microflora of the rabbit's digestive tract changes according to the age and diet of the animal. In wild rabbits and those pet rabbits that eat a natural diet of grass and hay, a healthy gut flora that is resilient to any minor dietary changes that occur as the result of eating novel foods becomes established. In contrast, in intensive situations where large numbers of rabbits are kept in a small space and fed on artificial diets containing products that rabbits would not normally eat, alterations in the intestinal microflora can rapidly result in the proliferation of pathogens and the development of enteritis. Large numbers of pathogenic bacteria are most likely to be present in intensive situations. Commercial rabbits are young, growing animals, in which a healthy caecal microflora has not become established. Because of the financial importance of losses due to enteric disease in commercial units, extensive research has been carried out into the effects of varying dietary protein, carbohydrate and fibre levels on caecal microflora and volatile fatty acid production. These considerations are beyond the remit of this book, which is mainly concerned with the individual pet rabbit and not commercial rabbit production. The nutrition of the commercial rabbit is described in detail in P. R. Cheeke's *Rabbit Feeding and Nutrition* (Academic Press, Orlando, 1987) and reviewed in *The Nutrition of the Rabbit* (C. De Blas and J. Wiseman, eds) (CAB Publishing, Wallingford, Oxford, 1998).

8.2.2 Diet

It is not possible to consider any digestive problem in rabbits without examining the diet. The role of fibre and its 'digestibility' or 'indigestibility' is an important concept in the understanding of digestive disease in rabbits. Fibre digestion depends upon the presence of cellulolytic bacteria within the digestive tract. In rabbits the term 'digestibility' includes bacterial degradation or fermentation within the caecum, and not just digestion in the stomach and small intestine. For this reason, the term 'fermentable fibre' may be less confusing than 'digestible fibre'. Bacterial fermentation of fibre within the caecum varies according to the chemical structure and particle size (see Figure 1.6). For example, hemicellulose is more digestible than lignin. Small particles enter the caecum where their digestibility is affected by their size. Smaller particles of fermentable fibre have a relatively greater surface area for bacteria to adhere to and are digested more quickly than the larger particles. Very large particles (> 0.5 mm) do not enter the caecum and are expelled, undigested, in the hard faeces. Although it has no nutritive value, indigestible fibre is an essential part of the diet because it stimulates gut motility, which sends nutrients and fluids into the caecum for bacterial fermentation. Insufficient indigestible fibre results in slow gut motility and retention of hair and ingesta in the stomach. Reduced motility in the proximal colon affects the separation of intestinal contents and reduces the supply of digesta and fluid to the caecum. Lack of both fermentable and indigestible fibre results in changes in caecal pH, volatile fatty acid distribution and the balance of microbial flora. Alterations in the populations of micro-organisms can allow enteric pathogens to proliferate. Therefore, although a low level of dietary fibre may not actually cause disease, it is a major predisposing factor. Additional factors such as coccidiosis or treatment with ampicillin are needed to cause pathological disease in commercial rabbits fed on a low fibre diet (Licois and Mongin, 1980). The caecal appendix is larger in rabbits on a low fibre diet, suggesting either an increased demand for the buffering effects of bicarbonate or an increase in lymphoid activity in response to greater production of bacterial toxins (Cheeke *et al.*, 1986).

The amount of indigestible (non-fermentable) fibre in the diet has an effect on appetite, both for food and for caecotrophs. High levels of indigestible fibre promote caecotroph ingestion, whereas high protein levels reduce it. More food is consumed by rabbits on a diet high in indigestible fibre, i.e. large particles of lignified plant material. However, processing the food to reduce the indigestible fibre down to particles small enough to enter the caecum will suppress appetite. Lignin is not digested by the caecal bacteria, whereas cellulose, hemicellulose and pectin are. Excessive amounts of ground lignified material in the caecum increase retention time and decrease digestibility (Chiou *et al.*, 1998). Caecal impaction can be the result.

8.2.3 Age and husbandry considerations

The digestive disorders of the young rabbit, especially around the time of weaning, are very different from the adult pet. The stomach pH of suckling rabbits is approximately 5–6.5. Adult rabbits have a stomach pH of 1–2, except during digestion of caecotrophs, when the pH rises. The high pH of suckling rabbits not only permits healthy bacteria to pass through the digestive tract and colonize the hindgut but also permits the passage of pathogens, such as pathogenic strains of *Escherichia coli*. Susceptibility to pathogenic strains of *E. coli* varies with age; rabbits of 3 weeks are more susceptible than rabbits of 6 weeks of age (Licois *et al.*, 1992). Weaning is a stressful period for rabbits when healthy caecal microflora is not yet established and juvenile rabbits are susceptible to disease. Ingestion of maternal caecotrophs aids the population of the caecum with a healthy gut flora and early weaning and separation from the dam increase susceptibility to bacterial enteritis.

After weaning, ammonia levels in the caecum decrease as the diet changes. Caecal pH becomes more acidic as volatile fatty acid concentrations increase. The proportions of individual volatile fatty acids alter with the change of diet from milk to solids. Propionate, valerate and branched chain fatty acids predominate until the rabbit starts to eat solid food.

The microbial flora changes in association with alterations in volatile acid production (Padilha *et al.*, 1995). Pathogenic strains of *E. coli*, *Clostridium* spp., coccidiosis or rotaviruses are likely to be present in the environment of newly weaned rabbits. Several animals sharing a small space increase faecal contamination and the risk of cross-infection. After weaning, rabbits are often stressed by change of housing and diet, transport and mixing with different individuals. Intercurrent disease such as pasteurellosis can be present. Minimizing stress and a diet containing sufficient indigestible fibre is especially important at this age to prevent enteric disease.

In the adult pet rabbit, infectious causes of enteritis are rare in comparison with the young commercial rabbit. Instead, it is far more common to see diet-related problems. Dietary changes can result in the production of soft caecotrophs that are left uneaten. Instead, the caecotrophs are deposited in the bedding or are found stuck to the fur under the tail. The smelly faecal mass is often mistaken for 'diarrhoea' by the owner, although it is not caused by infection (see Section 8.6).

8.2.4 Effect of digestive disease on water and electrolyte exchange

The effects of gastrointestinal disease on the water, electrolyte and acid–base balance of rabbits are complex. Disturbances in water, electrolyte and acid–base balance have a rapid and profound effect on health. Water and electrolytes are continually exchanged along the digestive tract and, in rabbits, any condition that affects this cycle of secretion and absorption also affects fluid and electrolyte balance (see Figure 1.4). Saliva is constantly produced by rabbits and, during the hard faeces phase, water is secreted into the stomach and proximal colon. It is then reabsorbed from the caecum and distal colon. Dehydration develops rapidly during intestinal disease, despite no obvious fluid loss in vomit or diarrhoea. Conditions that cause intestinal obstruction result in the accumulation of large amounts of fluid proximal to the site of obstruction. Conversely, gastrointestinal hypomotility reduces the secretion of water into the stomach and results in impaction of the contents. Dehydration is associated with gastrointestinal hypomotility, presumably due to decreased absorption of water from the stomach, caecum and distal colon.

Mucus is rich in potassium (Riley and Cornelius, 1989) and a feature of enteropathy in rabbits is the production of large amounts of mucus. Diarrhoea can result in hypokalaemia (Licois et al., 1978).

Key Points 8.1 The inter-relationship between internal and external factors leading to gastrointestinal disease

- There is a complex inter-relationship between stress, diet, gut motility and infectious agents in the aetiopathogenesis of digestive disorders in rabbits.
- Enteritis is more commonly encountered in the young, commercial rabbit kept under intensive conditions than in the adult, individual pet with an established gut flora.
- Adult animals, particularly those kept alone, are more likely to suffer from non-infectious digestive disease.
- Water and electrolytes are continually absorbed and secreted along the digestive tract. Dehydration and electrolyte imbalances occur readily as a result of intestinal disease.
- The role of digestible (fermentable) and indigestible (non-fermentable) fibre in the digestive physiology is an important concept in the understanding of digestive disease. Fibre is composed of constituents of plant cell walls and includes cellulose, hemicellulose and lignin.
- Indigestible fibre consists of large particles of lignified material that are directed into the colon and do not enter the caecum. It has no nutritive value but stimulates gut motility.
- Fermentable fibre is composed of small particles directed into the caecum to act as a substrate for the caecal microflora. It is mainly composed of hemicellulose and cellulose. Fermentable fibre has no direct effect on gut motility.

Continued

Key Points 8.1 The inter-relationship between internal and external factors leading to gastrointestinal disease—cont'd

- The rabbit's caecum is an ecosystem containing a microflora that is essential to the health of the rabbit. A healthy caecal microflora requires a constant supply of nutrients and fluid. Alterations in the balance of micro-organisms within the caecum can result in proliferation of pathogenic bacteria.
- Optimal gut motility is important to maintain absorption and secretion of water and electrolytes along the digestive tract and to transport nutrients and fluid to the caecum.
- The limited ability of the rabbit kidney to regulate acid–base disturbances makes this species vulnerable to acidosis and electrolyte imbalances. Fluid therapy is an essential part of treatment of many digestive disorders.

The absorption and secretion of electrolytes along the digestive tract is also affected by changes in acid–base status. In a study by Charney *et al.* (1983), alkalosis in rabbits decreased the absorption of water, sodium and chloride, whereas acidosis had the opposite effect and reduced bicarbonate secretion. Anorexia in rabbits can quickly lead to metabolic acidosis (see Section 8.3.2) and the limited ability of the rabbit kidney to correct acid–base disorders makes the species vulnerable to the effects of acidosis or alkalosis (see Section 1.13.12). Changes in acid–base status can affect the contractility of the proximal colon (Lofqvist and Nilsson, 1981), which, in turn, will affect the secretion of water and its absorption from the caecum.

Therefore, effective fluid therapy is a vital part of the treatment of many gastrointestinal diseases in rabbits (see Section 3.11). Decisions on what fluid to administer should be based on electrolyte status determined by blood sampling. Intravenous or intraosseous fluid therapy is necessary for most cases. Although subcutaneous fluids can be used, they are not suitable for ill, dehydrated or hypotensive patients as absorption of fluids from under the skin is poor when peripheral tissue perfusion is reduced by shock or hypovolaemia.

8.3 Gastrointestinal hypomotility

8.3.1 Gastrointestinal hypomotility and formation of trichobezoars (hairballs)

Optimum gastrointestinal motility is important for digestion of food, absorption of water and electrolytes and maintenance of a healthy gut flora. Many factors influence gastrointestinal motility in rabbits (see Box 8.1). Reduced gastrointestinal motility leads to impacted food in the stomach or caecum, impaired glucose absorption and a reduction in the supply of nutrients and fluids to the caecal microflora.

For many years, the presence of impacted hair and food material in the stomach ('trichobezoars' or 'hairballs') was believed to be the cause of disease in rabbits. It was thought that the trichobezoar caused a pyloric obstruction. Anorexia, weight loss, reduced faecal output, depression and death due to starvation were attributed to the presence of a trichobezoar. Many theories were put forward about the cause of trichobezoar formation. Handbooks and leaflets on rabbit care suggest that regular grooming is required to prevent excessive amounts of hair being swallowed and becoming impacted in the stomach. Some breeders still recommend one day a week without food for rabbits in order to 'clear the system' of ingested hair. Boredom, magnesium or copper deficiency, inadequate protein, individual caging and the presence of air filtration barriers have all been put forward as potential causes of trichobezoar formation (Ojerio and Ladiges, 1981). The rabbit's inability to vomit has also been cited as a contributory factor (Gillett *et al.*, 1983). Treatment was usually unsuccessful. The administration of liquid paraffin to lubricate the gastric contents and that of pineapple juice to dissolve the hair enzymatically with bromelain were suggested as therapies. Surgical removal of the trichobezoar was a last resort and carried a poor prognosis. The association between trichobezoars and fatty liver was noted by many authors (Gillett *et al.*, 1983; Ojerio and Ladiges, 1981). An association with pregnancy toxaemia was made by Patton *et al.* (1983). It is only in recent years that trichobezoars have been recognized as the

Box 8.1 Factors that affect gut motility

- **Phase of faecal excretion**: the nature and direction of the peristaltic waves alters with the excretion of hard or soft faeces. The *fusus coli* is a specially adapted area of the colon that acts as a differential pacemaker for the initiation of peristaltic waves in the proximal and distal colon. The *fusus coli* is under autonomic control. It is highly innervated and is influenced by hormones such as aldosterone and prostaglandins. Prostaglandin stimulates the excretion of soft faeces.
- **Indigestible fibre**: the passage of large particles of indigestible fibre through the colon stimulates intestinal motility as a result of intestinal distension.
- **Volatile fatty acids in the caecum**: an increase in caecal butyrate inhibits normal peristalsis of the gut. Low fibre diets result in decreased acetates and increased propionates and butyrates.
- **Motilin**: this is a polypeptide hormone secreted by enterochromaffin cells of the duodenum and jejunum. Motilin stimulates gastrointestinal smooth muscle. Fat stimulates and carbohydrate inhibits its release. In the small intestine, motilin activity is decreased aborally. It disappears in the caecum and reappears in the colon and rectum.
- **Pain and stress**: cause adrenergic stimulation and inhibit gut motility.
- **Disease**: e.g. dysautonomia, coccidiosis, *E. coli*, rotavirus, enterotoxins, plant toxins can affect gut motility in different ways. For example, in rabbits with diarrhoea experimentally induced by coccidiosis, the motility of the caecum is increased and the motility of the ileum and jejunum is reduced (Fioramonti *et al.*, 1981).
- **Pharmacological agents**: e.g. prokinetics (improve gut motility), opioids (reduce gut motility), NSAIDs (can reduce prostaglandin stimulation of caecotroph production).

result of anorexia rather than the cause. On post-mortem examination, the rabbit's stomach is never found to be empty (Okerman, 1988) and the presence of a small amount of fibrous food is normal. The presence of hair entangled in the food is also a normal finding because rabbits are continually grooming and ingesting large amounts of hair.

In 1984, Leary *et al.* attempted to induce the clinical syndrome associated with the presence of trichobezoars by the orogastric infusion of latex to reproduce a gastric foreign body. Monthly radiographs were taken and the rabbits monitored closely for food intake and faecal output for 24 weeks after infusion. Gastrotomies were then performed to remove the foreign material and the rabbits monitored closely for a further 4 weeks prior to euthanasia and post-mortem examination. The presence of a latex bezoar did not have any adverse effect on appetite and weight gain of any of the 12 rabbits that were infused. In the same study, the stomach contents of 208 clinically healthy commercial rabbits were examined after slaughter and well-defined trichobezoars were found in 23% of them. This study cast doubt on the concept that trichobezoars cause anorexia. In 1986, Fekete and Bokori found elevated cortisol levels in rabbits with trichobezoars, although they concluded that the elevation was associated with the stress of having a trichobezoar rather than the trichobezoar being the result of stress. In 1987, Buckwell described the successful medical treatment of 'gut stasis' in rabbits exhibiting anorexia, reduced water intake, depression, weight loss and absence of faecal pellets. He described the presence of a palpable impacted mass in the region of the stomach. Treatment consisted of the administration of a motility stimulant, corticosteroid, oral fluid and the provision of hay. Since that time, trichobezoars have increasingly become recognized as the result, rather than the cause, of reduced gastrointestinal motility and are secondary to many other conditions.

Pain, stress and fright can all reduce gastrointestinal motility and lead to the accumulation of hair in the stomach and the formation of trichobezoars. In one study by Jackson (1991), intestinal stasis occurred more frequently in a group of laboratory rabbits that were restrained without the use of a towel. Once towel

wrapping was introduced for the restraint of all rabbits, the incidence of the trichobezoars fell dramatically and the author concluded that stress played a significant role in the cause of the disease. Stimulation of the sympathetic nervous system causes adrenal hormones to be released into the circulation. One of the effects of adrenaline and noradrenaline is the inhibition of gastrointestinal motility. If gastrointestinal motility is reduced, water secretion into the stomach is also reduced and hair and ingesta accumulate and become impacted. The rabbit appears to be particularly susceptible to the effects of catecholamines on gut motility. In healthy rabbits with an uninterrupted daily routine, the passage of soft and hard faeces follows a circadian rhythm, with an average day-to-day variation of approximately 30 minutes. Stress or even alterations in routine can have a significant effect on the caecotrophic rhythm. Simply switching a light on during the normal period of darkness caused one rabbit to stop producing faeces for 10 days in a study of caecotrophic rhythm by Jilge (1980). Thunderstorms, bonfire night, predator attacks, pain and surgery can all slow gut motility and, if left untreated, result in impacted stomach contents and trichobezoar formation.

Gut motility is affected by the indigestible fibre component of the diet. The provision of a high fibre diet has long been recognized as a preventative measure for the formation of hairballs (Sandford, 1996). Rabbits fed on a low fibre diet are at greater risk of developing gastric stasis and trichobezoar formation. Rabbits with slow gut motility crave fibre and will often eat hay or grass in preference to other foods. The provision of palatable indigestible fibre for rabbits that are at risk of gut stasis, e.g. postoperatively, is important. Fresh grass is the most acceptable form of fibre for rabbits, although good-quality hay is acceptable.

Slow gut motility not only results in the development of trichobezoars. Gas accumulates in the stagnant stomach and caecum. Visceral distension causes pain that stimulates catecholamine release and exacerbates inhibition of gut motility. Gastric ulceration can occur. Alterations in the secretion and absorption of water and electrolytes cause dehydration and electrolyte imbalances. Reduced food intake leads to an energy deficit that stimulates mobilization of free fatty acids from adipose tissue and fatty infiltration of the liver. Ketoacidosis and hepatic lipidosis are the result. Liver failure from hepatic lipidosis is the usual end-point of untreated gastrointestinal stasis.

Reduced food intake and hypomotility of the proximal colon also reduce the amount of ingesta available as substrate for caecal microflora. Alterations in the caecal fermentation patterns can lead to changes in caecal pH and volatile fatty acid production. The balance of caecal microflora changes with the possibility of the proliferation of pathogenic bacteria such as *Clostridium* spp.

8.3.2 Anorexia and development of hepatic lipidosis

Anorexia, whatever the cause, can trigger a chain of events that can result in death of a rabbit from hepatic lipidosis and liver failure. Rabbits are obligate herbivores and their carbohydrate metabolism differs from carnivorous species such as the dog or cat. The endocrine control of the storage and mobilization of food are not as important in herbivorous species as in carnivores that eat periodically and need to regulate a fluctuating supply of nutrients from the digestive tract. Herbivorous animals withstand the absence of insulin far more readily than carnivorous ones (Bentley, 1998).

In rabbits, glucose and lactates are produced in the caecotrophs during the period of fermentation in the stomach and are absorbed during digestion of caecotrophs in the small intestine. Amylase is synthesized by the caecal flora and is present in caecotrophs to act on the carbohydrates that are present. Volatile fatty acids are a major energy source and represent about 40% of the maintenance energy requirement of rabbits (Marty and Vernay, 1984). They are absorbed from the digestive tract during digestion of caecotrophs and from the caecum where volatile fatty acids are produced by bacterial fermentation. Concentrations of volatile fatty acids in arterial blood are kept constant by the liver, despite fluctuations in absorption from the digestive tract. Volatile fatty acid absorption from the gut varies with the hard or soft

phase of faecal excretion (Vernay, 1987) and is affected by gut motility. Lipids are absorbed from the diet or are derived from endogenous synthesis of free fatty acids in the liver (Madry *et al.*, 1976).

During periods of anorexia, glucose absorption from the gut falls and there is a reduction in volatile fatty acid production by the caecal microflora. The resultant drop in glucose and glucogenic volatile fatty acid absorption results in hypoglycaemia, which stimulates lipolysis and the mobilization of free fatty acids from adipose tissue. The free fatty acids are transported to the liver to be metabolized as an energy source. The major pathway for their degradation is that of β-oxidation and ketone body production. Ketoacidosis occurs when ketone body production exceeds tissue metabolism. Rabbits do not have effective metabolic pathways for correcting acidosis (see Section 1.3.12) and are particularly susceptible to the effects of ketoacidosis. Also, during periods of increased mobilization of free fatty acids, a 'bottleneck' develops in the liver, which impairs the metabolic pathways that result in lipid transport to other tissues. Fat accumulates in the hepatocytes, causing cholestasis and eventual liver failure and death. Hepatic lipidosis occurs most readily in obese rabbits because they have already accumulated triglycerides in the hepatocytes.

8.3.3 Obesity, pregnancy toxaemia and hepatic lipidosis

Any condition that causes prolonged anorexia in rabbits can result in fatty infiltration of the liver. Stress alone alters the fat metabolism of rabbits, especially in those that are already overweight. In a study by Lafontan and Agid (1979), minor stressful stimuli such as saline injections or venepuncture induced a prompt increase in plasma free fatty acid and glycerol concentrations in naturally obese rabbits. This increase did not occur in younger, lighter rabbits. α-Adrenergic responsiveness is increased in the large fat cells of obese rabbits in comparison with the small fat cells of underfed rabbits (Lafontan, 1981). High fat diets greatly increase the risk of hepatic lipidosis. In a study by Jean-Blain and Durix (1985), rabbits fed on a high fat diet showed a twofold increase in ketonaemia during a period of fasting and were more hypoglycaemic than rabbits fed on a low fat diet. Obesity is a major problem in pet rabbits and animals that already have fatty livers can rapidly develop hepatic lipidosis if they become anorexic. Any surgical procedure in an obese rabbit carries a risk of hepatic lipidosis associated with pain, stress and withholding food.

It is well known among rabbit breeders that female rabbits should not be too fat if they are to breed successfully. Rabbits with fatty livers readily develop ketosis (pregnancy toxaemia) in late pregnancy or during early lactation when glucose requirements are high. Healthy pregnant rabbits show a period of insulin resistance between days 24 and 30 of gestation, during which high levels of insulin do not stimulate muscle glucose uptake (McLaughlin and Fish, 1994). Hepatic uptake of glucose and free fatty acids is also reduced in pregnant rabbits and brings about an arterial hyperglycaemia so more glucose is available to the uterus (Pere *et al.*, 1992). Insulin resistance results in increased hormone sensitive lipase (HSL) activity, with increased amounts of triglyceride being hydrolysed from adipose tissue and transported to the liver.

Pregnant does are susceptible to the effects of anorexia and a drop in blood glucose rapidly stimulates fatty acid mobilization from adipose tissue to a liver already being compromised by fatty infiltration. An association between hairballs and pregnancy toxaemia was made by Patton *et al.* (1983), illustrating the complex inter-relationship between anorexia, fibre, gastrointestinal motility, energy demand and fatty infiltration of the liver. Treatment of pregnancy toxaemia is unlikely to be successful, but follows the same principles as the treatment of hepatic lipidosis, apart from the complication of the fetuses. Pregnancy toxaemia can be prevented by keeping breeding does slim and feeding them a high fibre diet.

8.3.4 Diagnosis and treatment of gastrointestinal hypomotility and prevention of hepatic lipidosis

Hepatic lipidosis can be prevented in anorexic rabbits by maintaining a positive energy balance with nutritional support and prompt treatment. It is important that rabbit owners are made aware that

anorexia, in conjunction with lack of faecal output, is a potentially fatal condition and that rabbits that are not eating must be treated promptly. Hospitalization and intensive nursing are often needed.

There are many differential diagnoses for the underlying causes of anorexia and gastrointestinal hypomotility, including dental disease and recent surgery (see Table 1.7). Recognition and treatment of the underlying cause is an essential part of treatment. The onset of gastrointestinal hypomotility can be insidious and anorexic rabbits are often reasonably alert in the early stages. A reduced appetite and a reduction in faecal output are the early warning signs (Table 1.6). As the disease progresses, the rabbit becomes totally inappetent and depressed. It adopts a hunched appearance and may sit for hours, immobile in the corner of the cage or hutch. Affected rabbits do not groom and appear to be oblivious to their surroundings. They are no longer inquisitive and do not respond to being spoken to or the offer of an interesting titbit. The rabbit becomes clinically dehydrated. There are no specific clinical signs associated with the development of hepatic lipidosis but affected animals are depressed and unresponsive. In the terminal stages, they become totally inappetent and are often disorientated and ataxic. Hyperglycaemia occurs. Death is due to liver and kidney failure.

Diagnosis of gastrointestinal hypomotility can be made on clinical history and examination. It can be confirmed by radiography (see Box 8.2 and Figures 8.3, 8.4 and 8.5). Faecal output ceases completely and the impacted stomach can often be palpated as a hard mass behind the ribs, especially in the later stages of the disease. A blood sample can aid differential diagnosis, assist with choice of fluid therapy and offer prognostic indicators. A lipaemic sample or the presence of hyperglycaemia in conjunction with ataxia is a poor prognostic sign. In the early stages, hypoglycaemia may be found. This is treated by oral, subcutaneous or intravenous glucose therapy. In contrast, some rabbits show hyperglycaemia in the early stages of the disease associated with stress or pain. A blood glucose value within the normal reference range is reassuring. A PCV in excess of 40–45% indicates dehydration. Prerenal azotaemia is common in rabbits with gastrointestinal stasis. It is found in conjunction with dehydration. Blood urea and creatinine levels can be markedly elevated. If the analytical equipment is available, electrolyte status is invaluable. Once hepatic lipidosis is established, fatty infiltration of the kidneys occurs and the rabbit goes into liver and kidney failure. There can be a range of bizarre biochemistry results at this stage.

Treatment of gastrointestinal hypomotility is aimed at restoring appetite, correcting electrolyte imbalances, correcting dehydration, stimulating gastric emptying, promoting normal gastrointestinal motility and softening and lubricating impacted food and hair. The medical treatment of gastrointestinal hypomotility and the properties of therapeutic agents are summarized in Tables 8.2 and 8.3. The general treatment of digestive disorders is given in Box 8.3. Nutritional support is important to prevent the development of hepatic lipidosis. Analgesics are always indicated, as gas accumulates in stagnant sections of the gastrointestinal tract, causing distension and pain, which compound the situation further.

Diet is a key part of the treatment of gastrointestinal hypomotility, and nutritional support will prevent the development of hepatic lipidosis. All anorexic rabbits must be encouraged to eat, and assist fed if they will not or are unable. Hepatic lipidosis can develop in any rabbit that becomes anorexic, although the risk is greater in obese, pregnant or lactating animals. Tempting foods such as fresh grass, dandelions and appetizing vegetables such as curly kale, spring greens, carrots and apples should be offered. Good-quality hay is important, both to stimulate appetite and to provide a sense of security to reduce stress levels. A bed of hay smells familiar. Grass and hay provide long particles of indigestible fibre that are important to stimulate gut motility. A quiet environment away from predators and barking dogs is important. In the initial stages (less than 24 h), analgesia and the provision of palatable fibre can be sufficient to stimulate gut motility and prevent progression of the disease. In the later stages (more than 24 h without food), syringe feeding is required to provide calories and fluid to soften and lubricate impacted stomach contents and provide water and electrolytes. Several

Box 8.2 Interpretation of abdominal radiographs

The rabbit's digestive processes follow a natural circadian rhythm that affects the appearance of abdominal radiographs. It is important to consider the time of day that an X-ray was taken, and whether the rabbit had recently ingested food.

Hard faeces phase

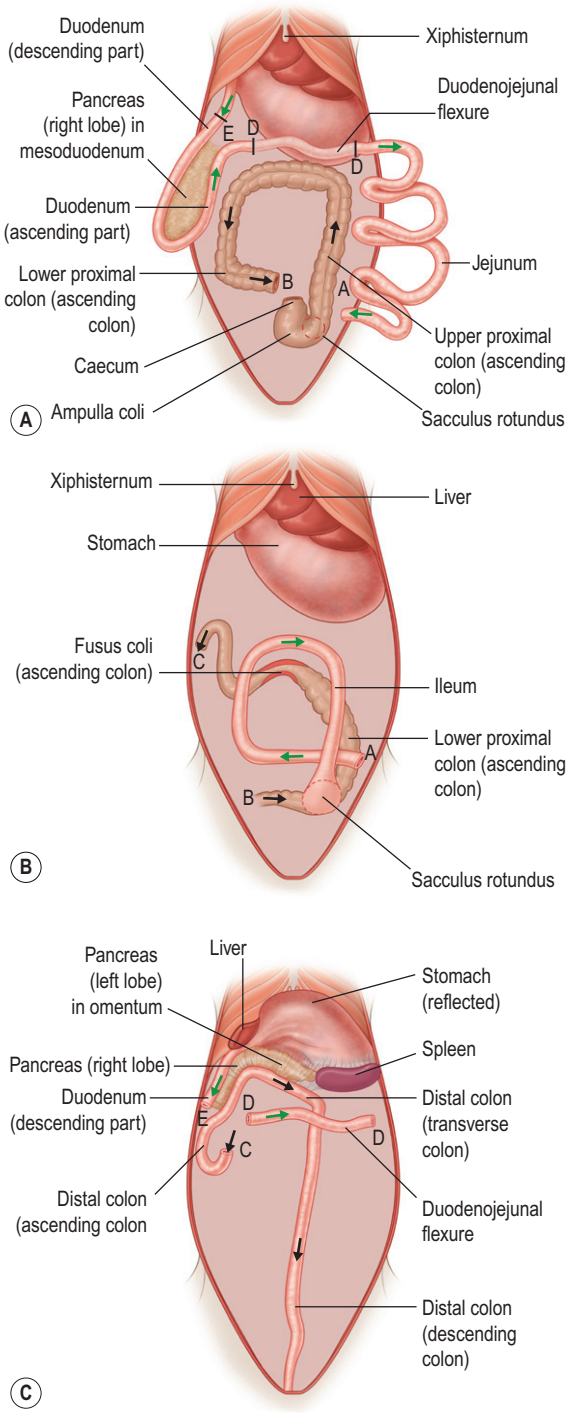
During the phase of hard faeces formation and excretion, the stomach can contain large quantities of fibrous food. The caecum becomes progressively distended as ingested food passes down the small intestine and through the ileocolic junction. A full caecum and proximal colon gives the ventral abdomen a general mottled appearance. The outline of the caecum is sometimes visible. Hard faecal pellets are often seen in the distal colon. Small amounts of intestinal gas may be seen.

Soft faeces phase

The soft faeces phase is much shorter than the hard faeces phase and usually occurs during the morning. A small amount of food may be seen in the stomach. The caecal contents are expelled into the proximal colon so the caecum is reduced in size. The caecum may contain small quantities of gas. Hard faecal pellets are absent from the distal colon and rectum.

Radiographic findings

- The stomach is situated within the costal arch and normally contains some food, which gives the organ a mottled appearance.
- The main body of the stomach lies on the left on the ventrodorsal view.
- The liver can be seen in the anterior abdomen, although the ventral border is not always clearly demarcated on the lateral view.
- The spleen cannot be seen radiographically.
- The small intestine cannot be distinguished from the long distal colon in the normal rabbit. Small pockets of gas may be seen in the intestines of normal rabbits.
- Obstruction or slowing of gut motility results in the accumulation of gas in parts of the digestive tract. Distended loops of bowel can be identified by their anatomical position (see Figure 8.2).
- The ileocaecocolic segment occupies most of the ventral abdomen. The appearance of the ileocaecocolic segment varies with the phase of digestion.
- Extraneous radiopaque material is sometimes seen in the digestive tract of rabbits that eat food that contains particles of soil or grit. Small particles are moved in a retrograde fashion into the caecum. Accumulations of sand or grit in the caecum should be differentiated from calcification in abscesses in organs such as the ovaries.
- Radiopaque deposits in the bladders are due to the presence of calcium carbonate in the urine. This is a normal finding. A solid radiopaque bladder suggests the presence of 'sludgy urine' (see Figure 12.2).
- The left kidney is usually clearly visible in the dorsal abdomen in the region of L_3–L_5. The right kidney may be less obvious and is situated cranially in the region of T_{13}–L_1. Renal length is approximately 1.25–1.75 times the length of the second lumbar vertebra (Hinton and Gibbs, 1982).
- The presence of intra-abdominal fat enhances the radiographic image of abdominal organs. The area cranial to the bladder is filled with fat deposited in the broad ligament in female rabbits and may be seen as a homogeneous grey area, especially in obese individuals.
- The uterus is not normally visible in the non-pregnant doe but may be seen if it is enlarged by pregnancy or disease.
- Nipples can be seen superimposed on the abdominal contents of some female rabbits. Nipples are rudimentary in males.
- Sometimes mineralization of ovaries, uterine tumours or intra-abdominal abscesses may be seen.
- Areas of calcification may be seen in association with soft tissue mineralization, chronic abscesses or in areas of fat necrosis. Hard areas of necrotic fat in the mesometrium can be a sequel to ovariohysterectomy.



proprietary brands of support feed are available for herbivores, and these should be fed as per the manufacturer's instructions. Puréed vegetables or baby foods provide an easily assimilated digestible energy source that can be given through a syringe, although these are not sufficiently high in fibre. A source of fermentable fibre is important to provide nutrients for caecal bacteria. Indigestible fibre is difficult to administer through a syringe because the large particles clog the nozzle; however, purpose-made support foods do contain some. There is no point in attempting to grind indigestible fibre down for syringe feeding in an attempt to stimulate gut motility. Grinding fibre to a particle size where it no longer clogs a syringe means that the particles are small enough to be moved into the caecum instead of the colon and the stimulatory action on the gut is lost. Nasogastric tube feeding may be necessary as a last resort for intractable cases, but nasogastric tubes can be counterproductive. They clog up easily and an Elizabethan collar is required. Elizabethan collars have been proven to be stressful to rabbits (Knudtzon, 1988). Pharyngostomy tubes are somewhat more practical and are placed in much the same way as they are in cats. They have the advantage that being wider bore they are less likely to block; however, it is still difficult to get sufficiently fibrous food through. Pharyngostomy tubes also carry the risk of causing abscessation at the site of entry. The use of PEG tubes has been reported; however, this is not commonly done due to the risk of abscessation at the entrance site and the difficulty of inserting these in the rabbit. All three types of feeding tubes carry common disadvantages: they are unable to

Figure 8.2 Three-dimensional topographical anatomy of the abdominal contents of the rabbit with the caecum removed. The topographical relationship of the liver, spleen, pancreas, small intestine and colon at three levels from superficial (ventral, **A**) to deep (dorsal, **C**. The mid-abdomen is illustrated in **B**) is illustrated. The diagrams were drawn from fresh dissections after removal of the caecum. Each of the three drawings shows the small intestine in green and the large intestine in black. Dotted lines show structures that are deeper (more dorsal) than the illustrated layer. The progression through the bowel from stomach to anus is shown by arrows. The intestines are held firmly in place by their mesenteric attachments.

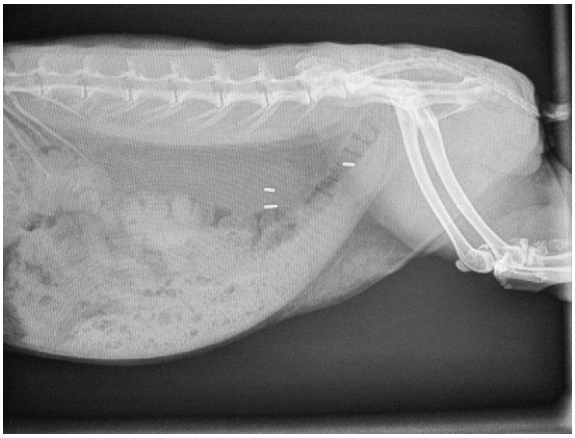


Figure 8.3 Radiographic anatomy of lateral view of normal abdomen. Interpretation of abdominal radiographs is summarized in Box 8.2. A lateral radiograph of a healthy 2-year-old neutered female rabbit is shown. Three surgical clips are visible in the caudal abdomen, used during ovariohysterectomy. The radiograph was taken during the hard faeces phase, and hard pellets are visible in the rectum. The ileocaecocolic complex is visible in the caudoventral abdomen; it is moderate in size and its contents are amorphous. Both kidneys, the stomach, liver and bladder can be visualized.

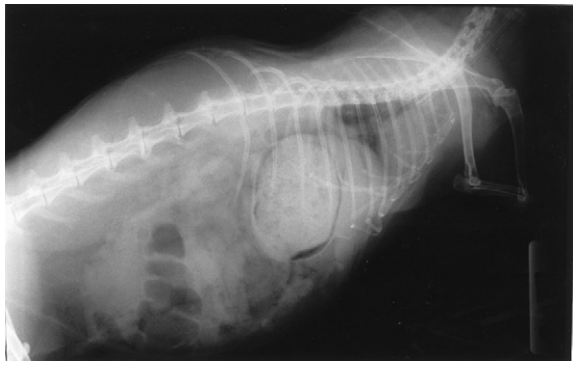


Figure 8.4 Oblique view of a rabbit with gastrointestinal hypomotility showing presence of a trichobezoar (hairball). An oblique view of a 3-year-old, obese female rabbit with gastrointestinal hypomotility is shown. Gas shadows are evident in the stagnant caecum and stomach. The stomach contains a mass of impacted food and hair that has resulted from a decrease in gastrointestinal motility (see Section 8.3.1). The initiating cause was unknown; the rabbit was presented in a moribund state and subsequently died. Post-mortem examination confirmed the presence of hepatic lipidosis. There was also fatty degeneration of the kidneys.

deliver food that will promote gut motility; they do not promote tooth attrition; and they have risks associated with their insertion. They are, however, a means to an end where otherwise a patient may die. Total parenteral nutrition has also been reported occasionally in rabbits; however, this is unlikely to be available outside of large referral institutions and is associated with the risks of sepsis, anaphylaxis, cholestasis and inflammation of the gut lining.

Pineapple juice or proteolytic enzymes have been recommended as remedies for hairballs because they are reputed to dissolve hair. Miller (1983) conducted an experiment in which they incubated rabbit hair for up to 3 days in papaya, proteolytic enzymes or pineapple juice. The pH of the solution was adjusted to 2 with hydrochloric acid to mimic conditions in the rabbit stomach. They found no difference between the treated and untreated control samples and the authors concluded that none of the enzyme treatments exhibited any ability to dissolve hair. The success of pineapple juice as a remedy for gastric stasis might be due to the introduction of liquid into the stomach that softens the hairball and aids its passage out of the stomach. Liquid paraffin can be used to soften and lubricate impacted stomach contents.

Motility stimulants are effective in promoting gastrointestinal motility. Cisapride is a very effective remedy for gastrointestinal hypomotility (see Section 3.7.1); however, because of adverse drug interactions in humans, it was withdrawn from many countries in 2004 and has been used much less in the treatment of gut stasis in the past 10 years. Many clinicians have not felt that treatment was less successful without cisapride, and have not reverted to its use now that it can be legally obtained once more. Metoclopramide is an alternative therapy but appears to be less effective than cisapride. Atropine and opioid analgesics can antagonize the effects of metoclopramide. There is *in vitro* evidence that metoclopramide is only effective in adult rabbits; however, anecdotally this does not appear to be the case (see Section 3.7.2).

Fluid therapy is always indicated in rabbits in the later stages of gastrointestinal hypomotility. Oral or subcutaneous fluids might be sufficient if the rabbit is not clinically dehydrated but intravenous therapy or intraosseous fluid therapy is essential once dehydration becomes evident.

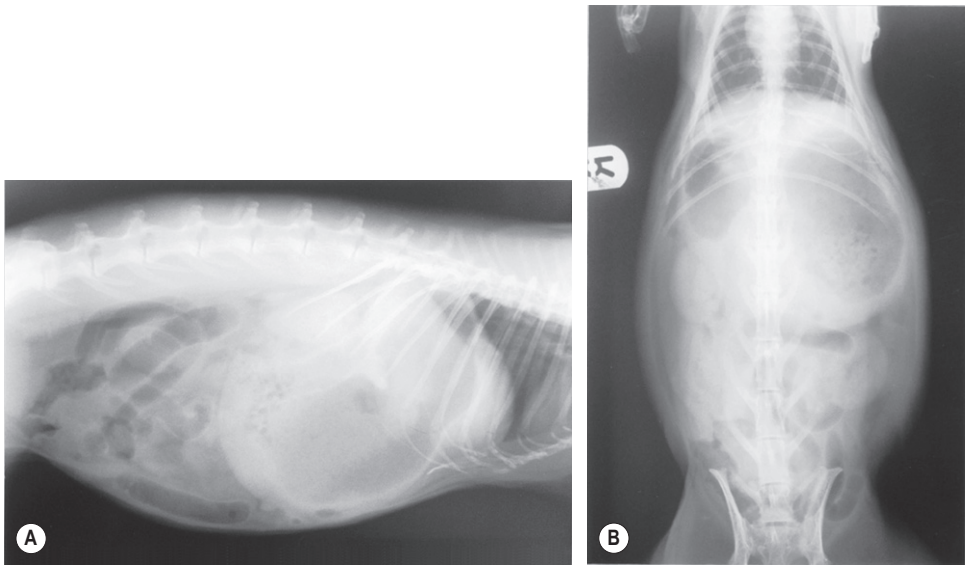


Figure 8.5 (A) Lateral view of a rabbit with an intestinal obstruction. A lateral view of a 2-year-old dwarf lop male rabbit with an acute intestinal obstruction caused by a felt of ingested hair is shown. The radiograph shows a grossly distended stomach containing fluid and gas. There is gas distension of the small intestine proximal to the site of obstruction that was in the ileum. This is a characteristic radiograph. The foreign body was surgically removed promptly (see Section 8.5.1) and the rabbit made an uneventful recovery. A differential diagnosis of intestinal obstruction is mucoid enteropathy, in which gastric dilatation may be seen in the terminal stages. An impacted caecum that can be palpated or seen radiographically is generally associated with mucoid enteropathy (see Figure 8.9). **(B) Dorsoventral view of a rabbit with an intestinal obstruction**. Figure 8.4 shows the same rabbit as Figure 8.5. Knowledge of the topographical anatomy of the intestines aids diagnosis and location of a foreign body (see Figure 8.2). The radiographs here in (A) and (B) were taken after sedating the rabbit with 0.2 mL/kg fentanyl/fluanisone (see Box 4.6). It is possible to obtain a diagnostic radiograph by placing a conscious rabbit in ventral recumbency on an X-ray plate, although positioning will be poor because the hind legs cannot be extended. Hypnosis and non-manual restraint with sandbags can be used to obtain a lateral view. A quiet room, gentle handling and patience are needed. The rabbit can be kept calm by covering its head with a towel.

8.4 Gastric ulceration

Gastric ulcers are a common post-mortem finding in rabbits, especially in those that have been anorexic prior to death. In a survey of 1000 post-mortem examinations by Hinton (1980), 7.3% were found to have ulceration of the gastric mucosa. The majority of the ulcers were found in the fundic area of the stomach and did not exhibit significant tissue reaction, suggesting that the lesions had developed rapidly and were associated with the stress of the associated illness. In 2% of the rabbits, the ulcers were in the pyloric area and the majority of these had perforated the mucosa. Many of the pyloric ulcers were found in female rabbits that had died in the perinatal period. Experimental stress ulcers can be induced in the gastric mucosa of laboratory rabbits by administering intraperitoneal injections of adrenaline (Behara *et al.*, 1980).

Rabbits are unable to vomit and therefore gastritis is more difficult to recognize than in the dog or cat. There are no specific clinical signs associated with gastric ulceration and inappetent rabbits are often already in pain from other causes. Anthropomorphically, it seems likely that gastric ulceration would add to the pain already being experienced. The clinical role of anti-ulcer preparations in the treatment of anorexic rabbits has not been evaluated but the possibility of gastric ulceration is a consideration when treating anorexic rabbits, especially when non-steroidal preparations have been administered. Several human preparations may be of use. Rabbits secrete high levels of gastric acid and pepsin in comparison with dogs, cats, rats and guinea pigs and the effects of anti-ulcer medications on gastric pH have

Table 8.2 Therapeutic agents used in the treatment of enteric disorders

Enteric disorder	Prokinetics	Narcotic analgesics	NSAIDs	Anti-ulcer drugs	Antibiotics	Cholestyramine	Liquid paraffin	Probiotics	Fluid therapy	Nutritional support
Gastrointestinal hypomotility 'hairballs'	√ Essential	√ Except in mild cases	√	In long-standing cases	X	X	In advanced cases to lubricate impacted stomach contents	May be useful adjunct to treatment	Oral fluids to soften stomach contents and to provide water and electrolytes Intravenous fluids in later stages	Provide indigestible fibre Provide tempting foods Syringe feed if necessary: carbohydrate to supply energy and prevent hepatic lipidosis Nasogastric tube as a last resort
Uneaten caecotrophs	X	May need sedation to clean perineum	If perineal skin is inflamed	X	If perineal skin is inflamed	X	X	May be useful adjunct to treatment	X	Increase indigestible fibre, i.e., lots hay/grass
Intestinal obstruction/ gastric dilatation	X **Contra-indicated**	√ **Essential**	√ Postop	√	√ Postop	√ Postop	X	May be useful adjunct to treatment	√ Intravenous (or intraosseous) fluids are essential	Tempting foods required postoperatively

Continued

Table 8.2 Therapeutic agents used in the treatment of enteric disorders—cont'd

Enteric disorder	Prokinetics	Narcotic analgesics	NSAIDs	Anti-ulcer drugs	Antibiotics	Cholestyramine	Liquid paraffin	Probiotics	Fluid therapy	Nutritional support
Caecal impaction	√	√ Buprenorphine	Use carprofen if NSAID is required Less likely to interfere with caecotroph production	√	X	X	√	May be useful adjunct to treatment	√	Tempting foods Easily digested foods, e.g., baby foods No small fibre particles that cannot easily be digested by caecal bacteria
Enteritis	X	√	√	√	√	√	X	May be useful adjunct to treatment	Essential. Oral or subcutaneous In early stages Intravenous in later stages	Hay/grass Excel
Enterotoxaemia	X	√	√	X	Metronidazole	√	X	May be useful adjunct to treatment	Essential Intravenous or intraosseous	Hay/grass Excel
Mucoid enteropathy	√	√	√	√	√	√	√	May be useful	√	Hay/grass Tempting foods

Table 8.3 Properties and dosages of therapeutic agents used in the treatment of enteric disorders of rabbits

Agent	Dose	Comments
Prokinetics		
Metaclopramide	0.5 mg/kg SC bid	Stimulates gastric emptying and GI motility.
Cisapride	0.5 mg/kg PO bid	Very effective product in rabbits. Unfortunately, the product has been withdrawn due to adverse drug interactions in humans. A veterinary tablet formulation is now available
Ranitidine	PO tid	
Domperidine	PO tid	
Narcotic analgesics		
Fentanyl/fluanisone	0.2–0.3 ml/kg IM (single dose)	Provides analgesia to treat abdominal pain that accompanies digestive disorders and gas distension of the viscera. Fentanyl/fluanisone is a good sedative to clean uneaten caecotrophs from the perineum
Buprenorphine	0.03 mg/kg SC bid	Buprenorphine provides analgesia without marked sedation. It is less potent but longer acting than fentanyl/fluanisone
NSAIDs		
Carprofen Meloxicam (ketoprofen or flunixin can also be used)	3 mg/kg 100 μg (1 drop)/kg sid	NSAIDs are used to treat abdominal pain. Carprofen is a weak cyclo-oxygenase inhibitor and does not interfere with prostaglandin synthesis as much as other NSAIDs. Prostaglandins stimulate soft faeces production
Anti-ulcer drugs		
Ranitidine	2 mg/kg IV or 5 mg/kg PO	In rabbits, gastric ulceration occurs in conjunction with stress and GI hypomotility In other species gastric ulceration can be associated with NSAID therapy
Antibiotics		
Trimethoprim/sulpha	40 mg/kg PO bid	Safe antibiotic orally. It can be used against enteric pathogens such as *E. coli.* Also effective against coccidia
Metronidazole	40 mg/kg PO bid	Metronidazole is effective against *Clostridium* spp. and has been cited as a treatment of choice for enterotoxaemia
Cholestyramine 'Questran'	0.5 g/kg bid	Binds with enterotoxins Can be used to treat enterotoxaemia Can be used prophylactically in situations where enterotoxaemia may develop
Liquid paraffin	1–2 mL/kg bid	Softens impacted gastric or caecal contents. Administer with care (preferably mixed with food) as is easily aspirated
Probiotics	As directed	May be useful either prophylactically or therapeutically to encourage a healthy gut flora and to reduce risk of spread of infection from the gut to the liver Inactivated by concurrent oral antibiotic therapy

Continued

Table 8.3 Properties and dosages of therapeutic agents used in the treatment of enteric disorders of rabbits—cont'd

Agent	Dose	Comments
Fluid therapy		
Oral (Lectade)	Approximately 10 mL/kg every 2–3 h	Oral fluids help to soften impacted stomach contents in addition to providing water and electrolytes
Subcutaneous (5% glucose or Hartmann's solution)	10 mL/kg	Subcutaneous fluids can be used in animals that are not dehydrated, although intravenous therapy is preferable for dehydrated patients with poor tissue perfusion
Intravenous	10–15 mL/kg/h	Immediate PCV, glucose, urea and electrolyte assay is advantageous. An I-stat analyser (Heska) is a very useful piece of equipment Stress can cause oliguria in rabbits 0.2–0.3 mL/kg IM fentanyl/fluanisone (Hypnorm, Jannsen) provides sedation and analgesia that reduce stress levels and facilitates intravenous fluid therapy
Nutritional support • Hay • Grass • Tempting food • Proprietary nutritional support foods (Supreme Recovery formula, and Recovery Plus, Oxbow Critical Care Formula)	Good-quality hay, fresh grass and palatable foods should be available ad lib. 20 mL/kg four times daily, dependent on the tolerance of the individual. Smaller amounts more frequently if needed	Hay/grass provides indigestible fibre that stimulates gut motility Dandelions, curly kale, spring greens and grated carrot will tempt most rabbits These diets contain varying amounts of fibre, both digestible and indigestible. They are a good alternative while a rabbit is inappetent. Many rabbits will lap these diets from a bowl once they are beginning to recover. Supreme Recovery plus contains probiotics and vitamin C
• Baby foods (only fruit and vegetable flavours are suitable, meat or dairy-based products are not)	10 mL/kg liquidized food every 2–3 h	Liquidized or cereal baby foods supply carbohydrates that are absorbed from the small intestine as an instant energy source that prevents mobilization of free fatty acids from adipose tissue and development of hepatic lipidosis. These should be used as a short-term method of support only
• Extruded complete food (Supreme Selective, Burgess Suparabbit Excel)	Can be ground up or mashed ad lib	Ground-up fibre (i.e. small enough to go through a syringe) provides substrate for caecal bacteria but does not affect gut motility
Vitamin C	50–100 mg/kg	Vitamin C reserves are depleted in times of stress

Table 8.3 Properties and dosages of therapeutic agents used in the treatment of enteric disorders of rabbits—cont'd

Agent	Dose	Comments
Anabolic steroids	2 mg/kg (nandrolone)	Anabolic steroids may stimulate appetite
Corticosteroids		
Prednisolone	0.5–2 mg/kg PO, IM, SC	Long-term use may be indicated in chronic diarrhoea (not uneaten caecotrophs) that could be immune mediated. It is preferable to base the use of steroids on a robust diagnosis
Dexamethasone Betamethasone	1–3 mg/kg IM, IV 0.1 mg/kg IV	Single injections may be of use to counteract shock in cases of acute enterotoxaemia

Abbreviations: sid, once daily; bid, twice daily; IM, intramuscular injection; IV, intravenous injection; PO, orally; SC, subcutaneous injection.

Box 8.3 General principles of treatment of digestive disorders in rabbits

Treatment of digestive disease in rabbits is aimed at identifying, treating and removing the underlying cause, preventing dehydration and electrolyte imbalances, maintaining or restoring gut motility, protecting normal gut flora and preventing hepatic lipidosis. The dosages and properties of therapeutic agents are summarized in Table 8.3.

- Hospitalization is often necessary to permit observation of appetite and faecal output. Many rabbits with digestive disorders require fluid therapy, syringe feeding and medication by injection.
- A healthy rabbit passes copious quantities of hard faecal pellets. Up to 180 pellets a day can be passed by a rabbit that is eating well and on a high fibrous diet. Hard faeces are always passed overnight by a healthy rabbit. The absence of hard faeces is a significant finding.
- Small faeces, diarrhoea, uneaten or abnormal caecotrophs are easier to monitor in the hospitalized rabbit.
- Rabbits with diarrhoea should not be fasted like a dog or cat.
- Indigestible fibre is always required by all rabbits at all times and can be provided by a bed of good-quality, palatable hay.
- Fresh grass will tempt many rabbits to eat and is a good source of both indigestible and digestible (fermentable) fibre.
- Tempting fibrous vegetables can be offered to rabbits with diarrhoea, although fruit, lettuce and other salad items should be avoided.
- Anorexic rabbits can be offered a selection of fresh, appetizing leafy green foods. Even rabbits that do not normally eat greens can safely be offered freshly picked grass, dandelions, spring greens, cabbage, kale, carrots or apple.
- Syringe feeding is necessary for rabbits that have not eaten for more than 12 h.
- Fluid therapy is an essential part of treatment for anorexic or diarrhoeic patients. Oral or subcutaneous fluids can be given to rabbits that are not dehydrated but intravenous or intraosseous therapy is essential in advances cases. Fluid therapy is described in Chapter 3. The safest choice of fluid for most conditions in rabbits is lactated Ringer's or Hartmann's solution.
- Oral, subcutaneous or intravenous glucose is indicated in rabbits known to be hypoglycaemic from blood glucose measurements.

Continued

Box 8.3 General principles of treatment of digestive disorders in rabbits—cont'd

- Analgesia is essential for treating the pain associated with colic or gas distension of the bowel.
- There is a risk of gastric ulceration in anorexic rabbits and anti-ulcer therapy is indicated, especially in rabbits that have been anorexic for more than 48 h.
- Motility stimulants are indicated in the treatment of motility disorders. They are an essential part of treatment for gastric stasis and can also be used to treat caecal impaction and mucoid enteropathy.
- Antibiotics may be indicated for the treatment of enterotoxaemia and in some types of diarrhoea. Enrofloxacin, trimethoprim preparations and metronidazole are the least likely to cause disturbances in the gut flora. Metronidazole has been cited as a treatment of choice for enterotoxaemia caused by *Clostridium spiroforme* (Carman, 1994). Trimethoprim combinations can be used to treat coccidiosis.
- Some rabbits may be malnourished due to poor diet or dental disease and the inclusion of a vitamin supplement in the treatment protocol can be beneficial. Although rabbits synthesize vitamin C, there is evidence that vitamin C requirements of rabbits increase during periods of stress when plasma ascorbic acid has been shown to decrease significantly (Verde and Piquer, 1986).
- Anabolic steroids can be effective as an appetite stimulant for rabbits and have some beneficial effect in the retention of electrolytes. There appear to be no adverse effects at low doses.
- A probiotic can be used to introduce beneficial bacteria to the hindgut. There are many anecdotal reports of the efficacy of commercial probiotic preparations although they contain lactobacillus that is not a normal inhabitant of the rabbit gut. Alternatively, caecotrophs collected from a healthy rabbit can be used to introduce normal bacterial flora.
- Rabbits with digestive disorders are at risk of developing enterotoxaemia. Cholestyramine (Questran), an ion exchange resin, can be given to absorb enterotoxins.

been investigated (Redfern *et al.*, 1991). Although omeprazole (Losec, AstraZeneca) is theoretically more effective than ranitidine (Zantac, GlaxoWellcome) in decreasing acid secretion and increasing postprandial pH, both preparations have a significant effect and appear safe as an adjunct to treatment of anorexia. Omeprazole is available in intravenous and capsule form for humans; ranitidine is available as an oral syrup. Ranitidine has the added advantage that it can also act as a prokinetic.

Key Points 8.2 Causes and effects of hypomotility

- For many years, the presence of impacted food material and hair within the stomach was believed to be a cause of anorexia and weight loss. Now, it is recognized that gastrointestinal hypomotility is the cause of impacted stomach contents (trichobezoars or 'hairballs') and anorexia and weight loss are the result.
- Stimulation of the sympathetic nervous system inhibits intestinal motility. Gastrointestinal hypomotility is associated with any stressful situation or condition that stimulates the sympathetic nervous system, including pain, surgery, stress or fright.
- A diet high in indigestible fibre stimulates gut motility and reduces the risk of gastrointestinal hypomotility.
- Gastrointestinal hypomotility results in gas formation in stagnant organs such as the stomach or caecum. Gas distension of the viscera is painful and abdominal pain stimulates the sympathetic nervous system and compounds the situation.
- Gastrointestinal hypomotility results in anorexia and a fall in glucose absorption from the stomach and small intestine. Volatile fatty acid production from the caecum is also reduced.

Key Points 8.2 Causes and effects of hypomotility—cont'd

- Hypoglycaemia stimulates lipolysis and mobilization of free fatty acids from adipose tissue. Free fatty acids are metabolized as an energy source. Oxidation of free fatty acids releases ketone bodies that can cause ketoacidosis.
- Accumulation of free fatty acids in the liver results in the development of hepatic lipidosis. Fatty infiltration of other organs, such as the kidney, occurs and, ultimately, liver and kidney failure result in death of the rabbit.
- Obese rabbits that already have a fatty liver are especially prone to the development of hepatic lipidosis.
- Increased glucose demand during pregnancy and lactation increases susceptibility to hepatic lipidosis during periods of anorexia.
- Stimulating gut motility and maintaining a positive energy balance to prevent oxidation of fatty acids, ketoacidosis and hepatic lipidosis are essential parts of the treatment protocol for many digestive disorders in rabbits.
- Gastric ulceration is a common post-mortem finding in anorexic rabbits. Anti-ulcer treatment, such as ranitidine, can be used in rabbits.

8.5 Gastric dilatation and intestinal obstruction

In pet rabbits, gastric dilatation is caused by some type of gastrointestinal obstruction. Rabbits continually secrete saliva and cannot vomit, so fluid collects in the stomach, which distends rapidly with fluid if ingesta cannot pass through and down the digestive tract. Gas is produced, which causes further distension. The stomach and intestine proximal to the obstruction becomes dilated with fluid and gas, giving a typical radiological picture (see Figure 8.5). Typical foreign bodies include pellets of impacted 'felts' of hair, whole dried pulses, pieces of carpet fibre or other small objects. The small intestine is the usual site of obstruction although pyloric obstructions can occur. Rabbits normally ingest large amounts of hair during grooming, which passes through the digestive tract with no problem. It is felts of impacted, matted hair that cause obstructions. During moulting, large felts of hair can accumulate, especially on the plantar aspect of the metatarsus, and can be ingested by the rabbit during grooming. These felts of hair are found more frequently on angora rabbits and fluffy dwarf lops, although any breed can be affected. Rabbits with dental problems appear to be especially prone to intestinal obstruction. Rabbits with incisor problems cannot pull hair out effectively and large mats can build up before the rabbit can remove them. Owners of rabbits with grooming difficulties should be advised to watch for these felts and remove them promptly.

Dried pulses such as locust bean seeds or dried peas or sweet corn can also be exactly the right diameter to occlude the small intestine. This type of ingredient should not be included in rabbit food. Again, rabbits with dental problems appear to be prone to swallowing such ingredients whole (Harcourt-Brown and Friggens, 1999).

Inflammatory lesions or tumours in the wall of the intestine can cause obstructive disease at any site along the digestive tract, including the colon. Extramural lesions such as tumours, adhesions, abscesses and tapeworm cysts in the omentum can cause an obstruction (see Figure 14.4). A cystic calculus has been reported as a cause of intestinal blockage (Talbot and Ireton, 1975). The severity of symptoms and the course of the disease are related to the site of the obstruction. Complete occlusion of the small intestine is rapid in onset and fatal unless the obstruction is removed promptly. Sometimes the foreign body can move through the small intestine, intermittently obstructing the intestine and causing abdominal pain and anorexia that passes off when the object passes through into the colon. The progress of the obstruction can be monitored radiographically from the gas shadows in the small intestine. The ileocaecal valve is a potential site of intestinal obstruction. Intestinal lymphoma has been found at this site in

two cases (Harcourt-Brown, unpublished data), one of which developed an intussusception of the colon into the caecum. Occlusion of the colon shows a more protracted course that lasts for days rather than hours. Obstructions of the large intestine are not caused by ingested foreign bodies, as the lumen of the small intestine is much smaller than that of the colon. Instead, tumours, adhesions and impacted caecal contents can obstruct the colon.

The typical history of a rabbit with an acute proximal intestinal obstruction is that the rabbit was well one minute and moribund the next (see Box 1.8). A feature of the condition is severe gastric dilatation with fluid and gas, which gives the rabbit a bloated appearance. Affected rabbits are totally inappetent, depressed and often collapsed. Dehydration and an unusual feeling abdomen are evident. A distended stomach may be palpable in the cranial abdomen, especially on the left side. Alternatively, the abdomen may be distended and tympanic, or feel doughy if intestinal rupture has occurred. Electrolyte imbalances cause a variety of symptoms. Twitching, blindness and convulsions can occur in the terminal stages. Abdominal radiography is usually diagnostic. The hugely distended stomach can be seen occupying the anterior half of the abdomen, compromising respiratory and circulatory function. Gas shadows can be seen in the small intestine proximal to the obstruction (see Figure 8.2).

Prompt treatment is required for this painful and stressful condition. Analgesia and prompt decompression of the stomach are essential. The stomach can be decompressed by passing a stomach tube to release the gas and liquid. Frequently the stomach tube blocks with hair and has to be emptied and repositioned. In most cases, the intestinal condition is rapidly fatal, with death occurring within 12 h. There is a small chance of a moving foreign body passing through the small intestine and into the colon. Motility stimulants may aid this process but can also cause intestinal rupture if the gut is completely obstructed. Surgery is straightforward and successful if the case is presented early and surgery is performed rapidly. However, there are many potential life-threatening problems associated with enterotomy in rabbits; high-risk anaesthesia, narrow intestinal lumen, soft friable tissue, small omentum, propensity to develop adhesions, water and electrolyte imbalances, postoperative ileus, infection and risk of recurrence due to stenosis of gut. Long-haired rabbits or those with dental problems will still have the predisposing cause, even if they survive the surgery. Therefore, euthanasia is the most humane option unless the owners are keen for surgery, and accept all the risks and expense that are incurred.

Key Points 8.3 How to discriminate between gut stasis and obstructive disease

- In pet rabbits, gastric dilatation is usually associated with an intestinal obstruction. Mucoid enteropathy can also cause gastric dilatation.
- Rabbits with intestinal obstruction are depressed, inappetent and shocked. The onset is sudden and the severity of symptoms depends on the site of the obstruction. The nearer the obstruction is to the mouth, the more rapid the onset and the more severe the clinical signs.
- Felts of hair, carpet fibre, dried pulses, such as peas or beans, tumours, tapeworm cysts, abdominal abscesses, intussusceptions and adhesions are among the causes of intestinal obstruction.
- Motility stimulants and assist feeding are contraindicated in cases of gastric dilatation.
- Intestinal obstruction usually requires surgery that can be successful if performed promptly.
- Occasionally, moving foreign bodies will pass through the ileocolic valve into the large intestine. Radiography can be used to monitor the progress of moving foreign bodies by the gas shadows in the intestines.

Gastric dilatation is also a feature of mucoid enteropathy. The onset is usually more gradual than dilatation due to an intestinal obstruction. A palpably, impacted caecum in association with gastric dilatation is suggestive of mucoid enteropathy. Radiology can be used to differentiate the two conditions (see Figures 8.4 and 8.9), although exploratory laparotomy may be indicated to confirm the diagnosis.

8.5.1 Surgical removal of intestinal foreign bodies

Basic surgical principles in rabbits are described in Chapter 15. If the rabbit has been premedicated with low-dose (0.2 mL/kg) fentanyl/fluanisone to obtain the abdominal radiographs, it can subsequently be masked down with isoflurane to induce anaesthesia (see Box 4.6). Prior to surgery, blood samples should be taken to assess PCV, glucose and electrolyte status before commencing fluid therapy. The passage of a stomach tube is required to decompress the stomach and remove as much fluid and gas as possible. The stomach tube can remain in place throughout surgery. Endotracheal intubation is advisable. If the anaesthetic induction agent does not contain an analgesic such as fentanyl/fluanisone, pre-emptive analgesia with butorphanol or buprenorphine is also required.

The abdomen is opened with a midline incision in the region of the umbilicus. In many cases, the small intestine lies just beneath the incision and is easily recognized. It is visibly distended with gas and fluid cranial to the obstruction. The topographical anatomy of the small intestine and its relationship to other abdominal organs is illustrated in Figure 8.5. Once the obstruction is located, the intestinal loop can be exteriorized and the surrounding tissues protected by sterile absorbent material. The intestinal contents are milked away from the obstruction before applying bowel clamps or asking an assistant to occlude the intestine with digital pressure. The enterotomy incision is made along the antimesenteric edge of the intestine distal to the foreign body to avoid placing sutures in devitalized tissue. The foreign body is removed and any everted mucosa trimmed off before suturing the wound with a single layer of appositional interrupted sutures, making sure that they include the submucosa (see Figure 13.1). A fine inert, absorbable monofilament suture material with a high tensile strength is required, such as 5/0 poliglecaprone (Monocryl) or polydioxanone (PDS II, Ethicon). The repair of an intestinal incision is difficult due to the small diameter of the organ and the friability of the tissue. It is important to avoid stenosis as much as possible as it increases the possibility of re-obstruction at a later date. If enterectomy is indicated, the intestine should be sectioned at a slight angle to preserve its antimesenteric vascularity. Although techniques such as side-to-side or side-to-end anastomosis can be performed, they have no advantage over an end-to-end anastomosis, which is technically simpler (Bouvy and Dupré, 1997). A good seal to prevent leakage of intestinal contents is necessary as omentalization is difficult in rabbits due to the small omentum. Post-surgical adhesions to other organs form readily.

Withholding food postoperatively is not an option in rabbits. Small meals of soft digestible food can be fed for the first few days postoperatively to allow the intestine to heal. Postoperative analgesia and motility stimulants are essential.

8.6 Disorders of caecotrophy

8.6.1 Normal caecotrophy

Caecotrophy refers to the ingestion of soft faeces (caecotrophs) that are clusters of mucus-encapsulated pellets of pasty, odorous material that originates from the caecum. Caecotrophs contain bacteria, protozoa, yeasts and their fermentation products, which are amino acids, volatile fatty acids, vitamins and enzymes such as amylase and lysozyme. Caecotrophs are a valuable source of nutrients to the rabbit. Caecotrophy starts at about 3 weeks of age and is established by 6 weeks (Lang, 1981).

Caecotrophs are produced approximately 4 h after the last meal during quiet periods of the day or night when the rabbits are at rest. A period without disturbance is required for ingestion (Lang, 1981). Many pet rabbits produce caecotrophs during the morning and if their routine is disturbed, they may deposit a pile of caecotrophs that are left uneaten. This phenomenon is sometimes observed in rabbits that have been admitted for an anaesthetic or some other procedure. Soft faeces may be found in the bottom of their cage or carrier and are not necessarily a cause for concern.

The ingestion of caecotrophs from the anus is triggered by stimulation of rectal mechanoreceptors and

the perception of the specific odour of the soft faeces. The odour of the caecotrophs is influenced by the volatile fatty acids they contain. Germ-free rabbits do not eat their caecotrophs (Lang, 1981). Metabolites and hormones affect the rabbit's appetite for caecotrophs (Fekete, 1989). When food is scarce, all caecotrophs are consumed. When food is available *ad libitum*, the amount of caecotrophs consumed is influenced by the protein and fibre content of the diet. Increased levels of fibre increase caecotrophy, whereas high protein levels reduce it. Increasing the indigestible fibre component of the diet not only stimulates the rabbit to eat the caecotrophs but also makes the pellets firmer and less sticky. Healthy rabbits that eat a high fibre diet will consume all their caecotroph, whereas rabbits that are fed *ad libitum* on low fibre cereal diets will often leave caecotrophs uneaten. On some diets, particularly where certain herbs or legumes are included, the soft faeces appear less attractive than usual and are not ingested (Lang, 1981). Many diseases alter normal caecotrophic function, either by altering the consistency and composition of the caecotrophs or by interfering with the ingestion of caecotrophs from the anus (see Figure 8.6).

Rabbits that do not eat their caecotrophs are deprived of certain vitamins and amino acids that are synthesized by the caecal microflora. The effect of caecotrophy on protein and amino acid metabolism is greater in rabbits on a poor diet that is deficient in amino acids than in rabbits on a diet with a higher protein content (Jécsai *et al.*, 1985).

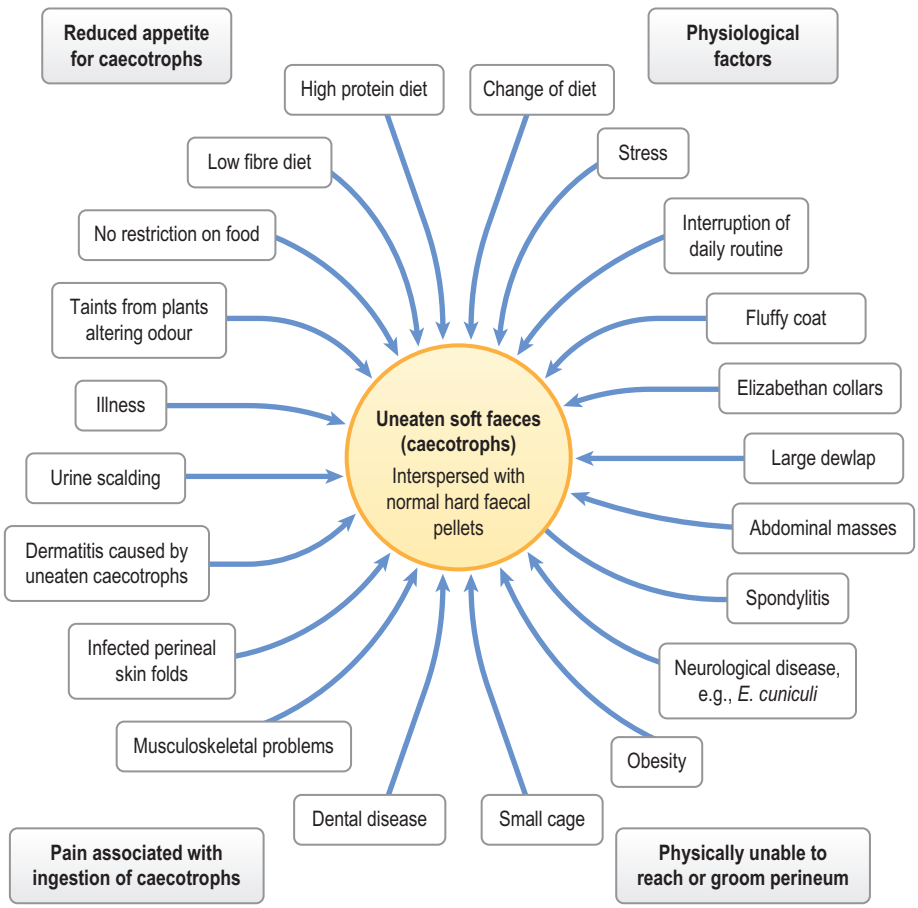


Figure 8.6 Causes of uneaten caecotrophs that may adhere to fur around anus.

8.6.2 Differentiation between uneaten caecotrophs and diarrhoea

A healthy rabbit on a balanced diet ingests caecotrophs straight from the anus without the owner ever seeing the caecotrophs or being aware of their existence. Many conditions interfere with the ingestion of caecotrophs (see Figure 8.6). Abnormalities in caecotrophy result in quantities of uneaten faecal material being deposited on the floor of the hutch or becoming entangled in the fur around the anus. The strong characteristic odour of uneaten caecotrophs and their soft, pasty consistency often misleads owners into believing their rabbit has diarrhoea. So, at the outset of the consultation, it is important to differentiate between uneaten soft faeces and true diarrhoea. Uneaten soft faeces is an unpleasant condition for both the owners and the rabbit but is not life threatening. Diarrhoea results in major disturbances in water and electrolyte metabolism and can be rapidly fatal. Caecotrophs are produced intermittently, usually once or twice every 24 h, when the animal is at rest. Copious amounts of hard faecal pellets are produced between episodes of soft faeces production and can be seen interspersed with any uneaten soft faeces in the bedding or on the floor of the hutch. Rabbits with enteritis and true diarrhoea do not produce hard faecal pellets. Instead, they produce soft faecal material that may be mixed with mucus. Rabbits suffering from caecotrophic disorders continue to eat well and produce large numbers of hard faecal pellets. Rabbits with diarrhoea are usually anorexic and depressed.

Although uneaten caecotrophs are not directly life threatening, the implications for the welfare of the individual rabbit are far reaching. The condition is difficult to treat successfully in the short term and tends to recur. Owners become disillusioned and are deterred by the smell and inconvenience of bathing and cleaning their pet's perineum. The constant smell and presence of the faecal mass can result in owners abandoning their pet, either by releasing it into the wild or by leaving it permanently confined to its hutch. The strong smell of uneaten caecotrophs attracts bluebottles during the summer months and affected rabbits are high-risk candidates for fly strike.

8.6.3 Physical conditions that interfere with caecotrophy

Many conditions can stop a rabbit consuming caecotrophs. Any skin condition that makes the perineal area sore and painful has the potential to prevent caecotrophy. The volatile fatty acid content of caecotrophs not only gives the characteristic odour but also scalds the skin under the mass of caked faecal material. The perineum of a rabbit is a very sensitive area and if the skin is sore, the rabbit may be reluctant to groom the area and ingest caecotrophs as they arrive at the anus. A vicious circle is formed, which results in sore, inflamed infected perineal skin (see Figure 7.3). Rabbits with fast-growing, soft, fluffy coats can develop large mats of fur around the anus and under the tail. This fluffy coat texture is impossible for these rabbits to groom themselves. Soft faeces become entangled in the fur and can provide a physical barrier to the anus.

In order to reach the anus and ingest caecotrophs, the rabbit must position itself correctly. Any condition that reduces flexibility, affects balance or causes immobility can result in uneaten caecotrophs. This includes restriction in a small cage or carrier. Obese rabbits are often too fat to turn round and reach their perineum, both to groom or to ingest caecotrophs. Loose-skinned individuals often develop large perineal skin folds, especially if they are overweight. These skin folds can become infected and sore, which makes grooming painful. Faecal material can become entrapped in the folds of skin and exacerbate the problem. Some obese females or even castrated males develop huge dewlaps that pose an additional physical barrier to the perineum. Rabbits that are fed *ad libitum* on low fibre diets are not only more likely to leave caecotrophs uneaten but are also likely to become fat and lazy. Musculoskeletal conditions that either affect the rabbit's flexibility or cause pain when it turns round to reach its anus also interfere with caecotrophy. Spinal deformities such as kyphosis or vertebral spondylitis are a common radiological finding. Arthritic joints or painful infected hocks can make a rabbit reluctant to change position to clean and groom properly. Affected rabbits may not eat caecotrophs from the anus but will deposit

them in the bedding and consume them later or not eat them at all.

Dental disease is a common reason for rabbits to leave caecotrophs uneaten and not to groom their perineal area. Sometimes caecotrophy abruptly ceases when sharp hooks develop on the cheek teeth and lacerate the tongue as the rabbit attempts to lick and groom. In other cases, incisor malocclusion prevents the rabbit from picking up and consuming caecotrophs.

Any condition that reduces appetite also reduces the appetite for caecotrophs, so almost any condition that makes a rabbit unwell can result in uneaten caecotrophs. Neurological diseases that affect either the sense of smell or the neural pathways that supply the rectal mechanoreceptors may interfere with caecotrophy. Degenerative disc disease, lumbosacral dislocations or fractures, and granulomatous lesions in the central nervous system caused by *E. cuniculi* are possible causes of such deficits.

8.6.4 Consistency of caecotrophs

Although softer than hard faeces, caecotrophs should have a firm pasty consistency. Uneaten caecotrophs that are soft in consistency are more likely to become entangled in the fur under the tail, rather than drop into the bedding. Therefore, changing the texture of the caecotrophs so that they are firmer is beneficial for both the rabbit and its owner.

Key Points 8.4 Discriminating between failure to eat caecotrophs and diarrhoea

- Caecotrophs have a soft pasty consistency and a strong odour. Many owners mistake uneaten caecotrophs for diarrhoea, especially when they adhere to the fur around the anus.
- It is important to make the distinction between uneaten caecotrophs and diarrhoea. Diarrhoea is a life-threatening condition in rabbits due to its effects on water and electrolyte metabolism. Uneaten caecotrophs are not life threatening.
- Rabbits that are not ingesting caecotrophs do not have a reduced appetite and pass normal hard faeces in addition to uneaten caecotrophs.
- Rabbits with enteritis do not pass hard faecal pellets. They are usually unwell and inappetent.
- The consistency of caecotrophs can be soft or liquid and can mimic diarrhoea. Change in routine or dietary change such as the introduction of salad items or soft fruit can result in production of soft caecotrophs.
- Several clinical conditions can either reduce a rabbit's appetite for caecotrophs or prevent a rabbit from consuming caecotrophs from the anus.
- Uneaten caecotrophs can become entangled in the fur around the anus and cause a superficial pyoderma in the skin beneath.
- Treatment of uneaten caecotrophs is aimed at identifying and treating the underlying cause, clearing up any skin infection, improving the rabbit's appetite for caecotrophs and improving their consistency so they are not so sticky.
- Decreasing dietary protein and increasing dietary fibre increase the rabbit's appetite for caecotrophs.
- Increasing dietary fibre also results in caecotrophs of a firmer consistency.
- True diarrhoea should be viewed as an emergency, as electrolyte and fluid balance disturbances can be rapid and significant. Aggressive treatment, including fluid therapy, support feeding and diagnosis and treatment of the cause, is required.

Caecotrophs have a higher protein and water content and lower fibre content than hard faecal pellets. The amount and consistency of caecotrophs is affected by the fibre content of the diet. The type of fibre is important. Increasing the amount of indigestible fibre in the diet does not affect the volume or consistency of soft faeces because long fibre particles do not enter the caecum (Fraga *et al.*, 1991; Garcia *et al.*, 1995). Increasing the fermentable fibre content of the diet does have an effect on caecotroph consistency because small fibre particles are moved into the caecum. Most sources of fibre are a mixture of

fermentable and indigestible fibre, so increasing the overall fibre content of the diet is likely to increase the amount of fermentable fibre that reaches the caecum. Increasing dietary fibre also increases appetite for caecotrophs and the amount of soft faeces produced (Carabaño and Piquer, 1998).

The consistency of soft faeces is also influenced by the water content. Water is absorbed from soft faeces during their passage through the colon and variations in transit time can lead to changes in consistency in soft faeces. The introduction of novel foods, especially succulent items such as lettuce or fruit, can alter the consistency of caecotrophs so they are more liquid. This transitory change could be due to alterations in the transit time or changes in the caecal microflora. Dietary starch levels have no effect on the chemical composition of caecal contents or on the composition of hard or soft faeces (Carabaño *et al.*, 1988). The approach to treatment of uneaten caecotrophs is summarized in Box 8.4. In the short term, treatment is directed at clipping and cleaning the perineum and identifying the cause of uneaten caecotrophs. In the long term, dietary modification and weight reduction are required.

8.7 Caecal impaction

The cause of caecal impaction in rabbits is not always clear. Dry, impacted caecal contents in conjunction with mucus production in the colon is a feature of mucoid enteropathy, which is more often encountered in the juvenile rabbit than in the adult. In the adult pet rabbit, caecal impaction occurs sporadically. Like gastric stasis, there is often a history of a stressful situation (see Figure 8.7). Dehydration may play a part in the aetiopathogenesis. It is known that feeding small fibre particles that absorb water can cause caecal impaction. Bulk laxatives, such as methylcellulose or psyllium, are examples. Ground-up lignified material can have a similar effect. Small particles, such as clay cat litter, can also become impacted as they are moved into the caecum during mixing and separation of ingesta in the proximal colon.

The onset of caecal impaction can be insidious. In the initial stages, the rabbit may not look particularly unwell, but is inappetent and loses weight. The condition may be mistaken for dental disease as the rabbits may pick at food, eat a little and then drop it uneaten. Affected rabbits adopt a hunched stance. Faecal output is reduced or absent. There is often mucus production. The impacted organ can usually be palpated as a hard sausage-shaped structure in the ventral abdomen that can be seen on abdominal radiographs. On post-mortem examination, the caecal contents are solid and dry. Occasionally, a large lump of hard, dry caecal contents can move into the colon and cause an obstruction. Caecal dilatation may be the result (see Figure 8.8).

Caecal impaction is difficult to treat. Surgery is unlikely to be successful. Medical treatment is directed at providing nutrition, relieving pain, promoting gastrointestinal motility, softening the caecal contents and promoting caecal evacuation. Fluid therapy by all routes, intravenous, subcutaneous and oral, is indicated, plus liquid paraffin. All those foods reputed to cause 'diarrhoea' such as lettuce or fruit may tempt an inappetent rabbit to eat and provide additional fluid in addition to stimulating intestinal motility. As in all gastroenteric conditions in rabbits, good-quality hay or fresh grass must be constantly available as a source of indigestible fibre. Motility stimulants such as cisapride and metaclopramide can be useful in stimulating motility, although their effect on caecal motility in rabbits is not clear. Sometimes, motility stimulants appear to cause stomach cramps, perhaps due to their effects on the impacted organ. Analgesics are indicated, although, theoretically, interference with prostaglandin production by non-steroidal analgesics could have an inhibitory effect on the fusus coli. Carprofen is a weak cyclo-oxygenase inhibitor and therefore has less effect on prostaglandin production than some other NSAIDs. Non-steroidal analgesic therapy could contribute to gastric ulceration, which is often a post-mortem feature of anorexic rabbits, and anti-ulcer treatment with ranitidine or omeprazole is indicated.

Experimentally, prostaglandin administration is followed by the passage of soft faeces (Pairet *et al.*, 1986). The original author (FHB) has used prostaglandin therapy (0.2 mg/kg dinoprost) as a last resort

Box 8.4 Treatment of uneaten caecotrophs and perineal soiling

Rabbits with 'sticky bottoms' can be a challenge to treat successfully. The first step is to clean and treat the soiled perineum. The next step is to identify and treat the underlying cause (see Figure 8.6).

In the short term

- Soiled fur should be carefully clipped away from the perineum. Simply bathing the area can be counterproductive, as it leaves the fur soiled and damp and leads to infection of the underlying skin.
- If the skin is inflamed, analgesia is indicated. Analgesics can also bring about a temporary respite from caecotroph production that is beneficial. Non-steroidal analgesics reduce caecotroph production by inhibiting endogenous prostaglandin synthesis (Pairet *et al.*, 1986). Meloxicam or ketoprofen has a greater influence on prostaglandin production than carprofen. Soft faeces production also appears to be temporarily reduced after sedation with narcotic analgesics, especially fentanyl/fluanisone (Hypnorm, Janssen).
- Analgesics also alleviate pain from spinal problems or arthritis, which may be preventing a rabbit from grooming and cleaning the perineal region.
- Systemic antibiotics do not improve the consistency or reduce the production of soft faeces, although they may be beneficial in treating the perineal dermatitis. A 'safe' antibiotic such as enrofloxacin or trimethoprim that is unlikely to cause antibiotic-associated diarrhoea should be selected.
- In the early stages, plenty of good-quality hay or grass is required. Grass is ideal as it contains a mixture of fermentable and indigestible fibre and is palatable to most rabbits. A gradual dietary change will be required in the long term.
- Probiotics may play a part in establishing a healthy caecal microflora.

In the long term

- Dietary modification is of paramount importance in altering the consistency of the caecotrophs and stimulating the rabbit's appetite for them.
- Increasing the amount of fibre in the diet and reducing the amount of high calorie treats and cereals increases the rabbit's appetite for caecotrophs and makes them more fibrous and less sticky.
- Cereal mixtures should be reduced or withdrawn and substituted with small amounts of complete rations. Treat foods such as chocolate should be cut out altogether. Vegetables, but not fruit, may be offered, introducing one new item every few days, starting with the more fibrous varieties such as spring cabbage or broccoli. Apples, carrots and garden weeds such as dandelions can be introduced later. Soft fruit and salad items such as cucumber, lettuce and tomatoes are not necessary and should be avoided altogether in rabbits that have a tendency to not to eat soft caecotrophs.
- The introduction of fibrous green foods and vegetables is beneficial in increasing the fibre content and reducing the calorie content of the diet. In the short term, the introduction of new foods can unbalance the caecal flora, alter the consistency of the soft faeces and compound the problem. Therefore, dietary modification should take place gradually.
- Obesity is one of the main causes of perineal soiling, and weight reduction is an essential part of the treatment (see Chapter 2). Exercise is also important.
- Weight reduction and dietary modification may only be partially effective in resolving the problem in rabbits that have deep perineal folds. In obese animals, the skin folds often persist after the rabbit has lost weight. Surgical removal of the skin folds is a simple and effective remedy.

Long-term management of incurable cases of perineal soiling

In some cases of perineal soiling, the underlying cause cannot be removed and the owner will have to manage the problem for the lifetime of the rabbit. Other steps may be needed, in addition to modifying the diet to alter the consistency of caecotrophs.

- Fluffy-coated breeds require constant grooming and clipping in the area around the tail and genitalia to prevent the hair becoming long and forming mats. Rabbits with maloccluded or no incisors require regular grooming in that area.
- Enough space is required for the rabbit to move away from soiled bedding and decrease the likelihood of caecotrophs sticking to the fur.
- Caecotroph production follows a circadian rhythm. Caecotrophs are usually produced during the morning. Observation of the individual rabbit's excretion pattern and changing the bedding accordingly can minimize soiling of the fur.
- Long-term NSAID analgesic therapy may be helpful in the treatment of underlying spondylitic or arthritic conditions.

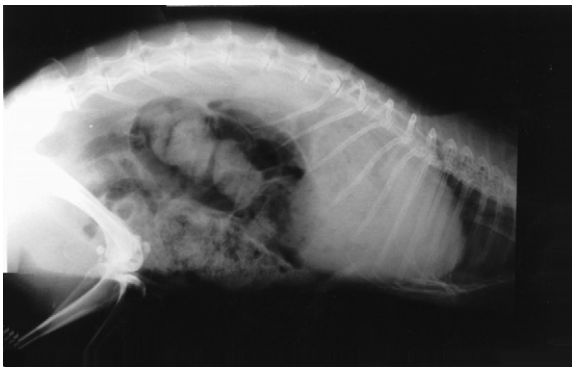


Figure 8.7 Lateral view of the abdomen of a rabbit with an impacted caecum. This radiograph was taken with the rabbit conscious. Gas has collected within the caecum and outlines several large pieces of impacted caecal material. Further impacted material can be seen in the caudoventral abdomen. In some cases, hard pieces of impacted material (caecoliths) can obstruct the colon as they are moved into the large intestine (see Figure 8.8). Like gastric impaction, impaction of the caecum can be the result of stress. The rabbit had recently been abandoned and, as a result, was subjected to the additional stresses of transport and rehoming. In this case, treatment was successful (see Section 8.7).

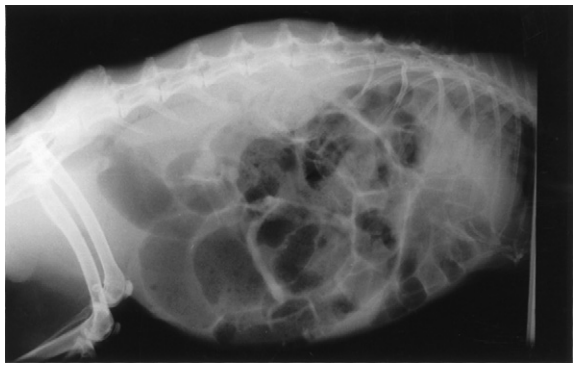


Figure 8.8 Lateral radiograph of a rabbit with caecal and intestinal tympany in association with chronic diarrhoea. A lateral view of the abdomen of a 4-year-old neutered male rabbit that suffered from periodic bouts of anorexia and abdominal distension is shown. In the interim, the rabbit had a good appetite but suffered from chronic diarrhoea. The stools were voluminous and contained a mixture of indigestible fibre particles and bacteria. Hard and soft faeces were indistinguishable. The rabbit was fed on a high fibre diet consisting of mainly grass hay with a small amount of good-quality mixed ration. Vegetables appeared to exacerbate the problem. Blood samples showed a mild anaemia and hypoproteinaemia. Bouts of tympany responded to treatment with analgesics and oral trimethoprim/sulpha combinations. The rabbit was eventually euthanized. Post-mortem examination revealed a large (2–3 times normal size) flaccid caecum. Histopathological examination of the caecum and intestines showed lymphoplasmacytic enterotyphlocolitis suggestive of an immune-mediated aetiology. The author has seen several similar cases in which dietary modification and oral prednisolone has been prescribed, in addition to other treatment, with a limited degree of success. A similar radiological picture can be seen in cases of caecal obstruction, which results in gas distension of the caecum. The cause of the obstruction is usually a large impacted lump of caecal material (caecolith) or a neoplasm such as a lymphoma. The cause of the obstruction can sometimes be seen radiographically or ultrasonographically. In cases of caecal obstruction, there is not the history of large loose voluminous faeces in association with a good appetite.

on a small number (3) of rabbits with impacted caeca. The caecal contents had been softened by orally administered liquid paraffin for 24–36 h prior to prostaglandin treatment. In all cases, the impacted caecal contents were evacuated 24–48 h after prostaglandin administration. All the rabbits went on to make a full recovery although they appeared to be in some abdominal discomfort for a few hours after the injection. However, prostaglandins have a number of systemic effects and the decision to use them should not be taken lightly. Concurrent oral and parenteral fluid therapy and analgesia are necessary. There might be adverse effects associated with the use of prostaglandins in rabbits.

8.8 Dysautonomia

Dysautonomia is a dysfunction of the autonomic nervous system that results in loss of sympathetic and parasympathetic function. Dysautonomias have been described in dogs, hares, horses (grass sickness) and cats (Key–Gaskell syndrome). The disease mainly affects the digestive tract and is characterized by reduced gut motility, although other signs associated with loss of autonomic function, such as mydriasis, urine retention or dry mucous membranes, may also be evident. Histopathological changes are seen in the autonomic ganglia. Chromatolysis-like degenerative changes take place in the neurons. Dysautonomic disease is well documented in the dog, cat

and horse in which loss of autonomic function carries a poor prognosis although the occasional mild case can survive with careful nursing. In recent years, dysautonomia has been described in rabbits suffering from mucoid enteropathy.

Cheeke (1987) observed that a strain of non-albino white rabbits with pigmented eyes were particularly susceptible to diarrhoea and that evidence of 'insufficient nerve ganglia in the intestine' was seen. An analogy with grass sickness in the horse was made. The discovery of degenerative changes in ganglionic neurons in rabbits suffering from mucoid enteritis had been made as early as 1967, but was not investigated further, although a syndrome of caecal impaction in conjunction with pulmonary oedema and urine retention was described by several authors (Van der Hage and Dorrestein, 1996). In 1991, post-mortem examination of two sick hares found on an English estate where horses had died from grass sickness revealed changes in the ganglia and alimentary tract that were remarkably similar to those seen in grass sickness (Griffiths and Whitwell, 1993; Whitwell, 1991). Van der Hage and Dorrestein (1996) described the clinical findings, pathological lesions and microscopic and transmission electron microscopic features of the coeliac ganglia of 19 rabbits with mucoid enteropathy. Typical cases were selected that had died following a disease characterized by emaciation, respiratory distress, distended abdomen with a palpable obstipated caecum or a distended bladder. Degenerative changes, manifested as chromatolysis, were found in the coeliac ganglia. No viruses, infectious agents, aflatoxins or other causative agents were discovered on food analysis or on extensive examination of the liver and intestinal contents of affected animals. An analogy was again made with grass sickness in horses, which is thought to be caused by a neurotoxin.

Dysautonomia was first confirmed in rabbits in the UK in 1996 in a colony of Belgian hares (which are actually rabbits) suffering from mucoid enteropathy (Whitwell and Needham, 1996). Histology of the ganglia showed chromatolysis-like degenerative changes in many neurons and some neuronal vacuolation. Boucher and Nouvelle (1997), in an outbreak of mucoid enteropathy, described clinical signs similar to those found in dysautonomic disease in horses and cats, i.e. mydriasis, dry mucous membranes, reduced tear production, bradycardia (less than 100 bpm), urine retention and intestinal impaction. They described an age predisposition of 6–8 weeks and the presence of opportunistic pathogens such as coccidia, *Clostridium spiroforme* and *Clostridium perfringens*. Histological examination of the coeliac and mesenteric ganglia revealed characteristic lesions similar to dysautonomia in other species.

The incidence of dysautonomia or its importance in the syndrome of mucoid enteropathy is not clear at the present time. Mucoid enteropathy is not invariably linked with chromatolysis-like degenerative changes in the neurons. Detailed post-mortem examination is required to confirm the diagnosis of dysautonomia, which can be expensive. Most cases of mucoid enteropathy are not presented to veterinary surgeons for treatment and there is a great deal of confusion among rabbit breeders about the condition. 'Mucoid enteropathy' is a term used in a non-specific manner to describe a number of inter-related enteric diseases that occur in rabbits, especially around the time of weaning. It should perhaps be viewed as a non-specific response of the rabbit gut to various challenges. Rabbit breeders will often cull and dispose of ill animals themselves. Caecal impaction in connection with pneumonia, and perhaps other autonomic signs such as bradycardia, dilated pupils or urine retention, is suggestive of dysautonomic disease. A feature of confirmed cases in the UK has been the presence of an inhalation pneumonia, as affected rabbits have problems swallowing and may have uneaten food in the mouth and pharynx (Whitwell, personal communication).

Treatment for rabbits with dysautonomia follows the same principles as the treatment of mucoid enteropathy or an impacted caecum. In horses, some mild cases of grass sickness can survive with careful nursing and supportive care (Milne, 1997).

The diagnosis of dysautonomia can be confirmed at post-mortem examination, including histopathology of the autonomic ganglia and gut wall. The site of the mesenteric ganglia is illustrated in Figure 14.1, and a technique for removing autonomic ganglia is described in Section 15.3.

8.9 Mucoid enteropathy

Mucoid enteropathy is a confusing condition both in its terminology and in its aetiopathogenesis. Many lay people and rabbit breeders use the terms 'mucoid enteropathy', 'ME', 'mucoid enteritis', 'mucoid enteritis complex' interchangeably to describe any enteric condition of rabbits characterized by diarrhoea, mucus production, constipation or death. These signs are non-specific and can be caused by several diseases. 'Mucoid enteritis' has been the cause of significant losses in commercial breeding units, with reported mortality rates of approximately 5–10% but rising to over 60% (McLeod and Katz, 1986). Colibacillosis, enterotoxaemia, Tyzzer's disease, coccidiosis and viral enteritis can all occur concurrently with mucoid enteropathy, and can obscure the classical signs. The syndrome often affects young rabbits especially around the time of weaning, although adult animals can be affected. 'Mucoid enteropathy' is characterized by the presence of large amounts of mucus in the colon and is usually associated with impaction of the caecum (see Figure 8.9). Inflammatory changes are minimal. The term 'constipative mucoid enteropathy' or CME can also be used to describe this syndrome. At post-mortem examination, the caecum is often impacted with dried contents and gas (see Figure 8.10). The colon is distended with gelatinous mucus. The stomach and small intestine may be distended with fluid and gas.

The aetiopathogenesis of mucoid enteropathy is far from clear. It is not known what role diet, stress, pathogens, caecal microflora or dysautonomia have in the disease, although it seems likely that all these factors could be implicated. Mucoid enteropathy is a disease of intensively reared domestic rabbits rather than wild ones (Lelkes and Chang, 1987). The disease is occasionally encountered in adult pet rabbits, especially after a stressful incident such as transport or parturition. It is known that increasing the amount of indigestible fibre in the diet of newly weaned rabbits significantly reduces the incidence of mucoid enteropathy. Stress appears to play a major role in the development of the disease. Enzyme deficiencies, infectious agents and enterotoxins have all been cited as other possible causes. Inflammation is not a feature of the disease and intestinal hypomotility or changes in the acidity of the caecum have been proposed as aetiological factors (Lelkes and Chang, 1987). Investigations are often hampered by the presence of concurrent infections such as coccidiosis, Tyzzer's disease or opportunist pathogens such as *Clostridium* spp. or *E. coli*.

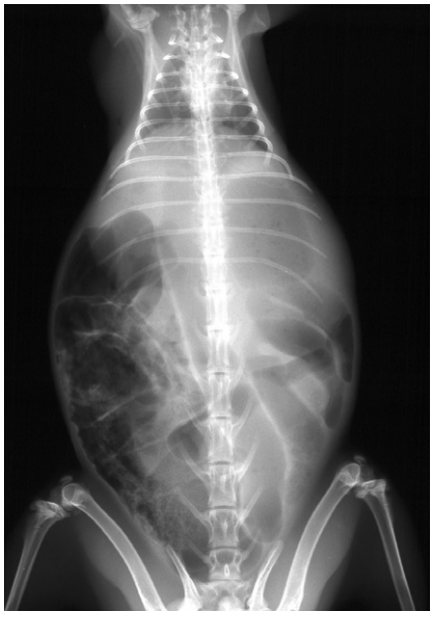


Figure 8.9 Ventrodorsal view of a rabbit with mucoid enteropathy. A ventrodorsal view of a 4-month-old, mixed breed, male rabbit suffering from mucoid enteropathy is shown. The stomach is dilated and filled with fluid. There is gas distension of the duodenum and jejunum. There is impacted material within the caecum that also contains gas. The rabbit died shortly after this radiograph was taken. Evidence of dysautonomia was not found on histopathological examination of the autonomic ganglia and other organs. Note the normal small volume of the thoracic cavity in comparison with the abdomen.

A feature of mucoid enteropathy is the presence of large amounts of mucus in the colon. At post-mortem examination, a large plug of mucus is often found obstructing the colon. In rabbits, mucus production is a response of the hindgut to untoward stimuli (Bergdall and Dysko, 1994) and is not necessarily specific to mucoid enteropathy. Experimentally, ligation of the caecum results in a mucoid

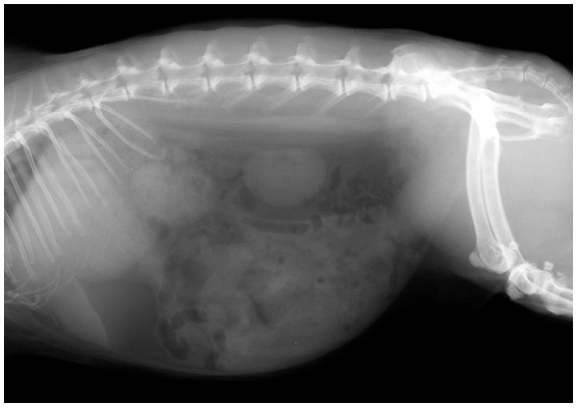


Figure 8.10 Mucoid enteropathy. The abdominal contents of a 14-week-old dwarf lop male rabbit that was euthanized is shown. He had passed no faeces for 3 days and had become bloated. He was inappetent and could be seen grinding his teeth. A hard impacted caecum was palpable. On post-mortem examination, the caecum was found to be filled with hard impacted material. The colon was distended and quantities of gelatinous mucus spilled out when it was incised.

enteropathy-like syndrome in some rabbits, with large amounts of mucus production in the colon. Incorporating the nerves and blood vessels in the ligature increases the likelihood of inducing a mucus hypersecretion 3–5 days after surgery (Hotchkiss and Merritt, 1996a). Surgical removal of the caecum does not result in mucus production, whereas filtrates from the ligated caecum administered to *in vitro* sections of colon do stimulate mucus secretion. Injection of oxytetracycline into the ligated caecum prevents colonic mucus secretion, suggesting that a bacterial secretory product is the stimulus for excessive goblet cell secretion characteristic of mucoid enteropathy. Hotchkiss and Merritt (1996b) postulated a blood-borne factor (termed mucus-stimulating substance or MSS) is present that binds to receptors on goblet cells causing mucus release. Serum from rabbits suffering from ME causes increased mucus secretion when applied to *Sipunculus nudus*, a mucus-secreting coelomate. Mucus secretion is also stimulated in the respiratory tract. Injections of cholestyramine into the ligated caecum can prevent the development of mucoid enteropathy-like symptoms, suggesting the presence of some type of toxin (Toofanian and Targowski, 1983).

The caecal microflora of rabbits with experimental mucoid enteropathy induced by caecal ligation is different from that of healthy rabbits. There is a decline in the number of Gram-positive bacteria, protozoa and large anaerobic metachromatic bacilli and an increase in Gram-negative organisms. The production of volatile fatty acids also alters after caecal ligation. In healthy rabbits, acetate predominates, followed by butyrate and propionate. In experimental mucoid enteropathy, caecal acetate and butyrate concentrations are reduced, with an increase in propionate, isobutyrate, valerate and isovalerate production (Toofanian and Hamar, 1986).

Typically, growing rabbits are affected by mucoid enteropathy but the disease is occasionally seen in adults, especially breeding does. Clinical signs include abdominal distension, subnormal body temperatures, depression, crouched stance and 'sloshy' sounding guts. There is a disruption of normal faeces production. Hard faecal pellets are not produced. Diarrhoea can be present in the early stages. In the later stages, large amounts of mucus, either on its own or mixed with faecal material, are excreted. Faecal production may cease completely. Appetite is reduced, sometimes to the point of complete anorexia. Some rabbits are polydypsic, whereas others may have a reduced water intake. A feature of the disease is tooth grinding, presumably due to abdominal pain. A solid impacted caecum may be palpable and seen radiographically. Some acute cases present with gastric dilatation rather than caecal impaction. Gas shadows may be seen in the caecum and small intestine. In the terminal stages, there is gastric distension with large amounts of fluid and/or gas in the stomach. There may be lung changes. Some rabbits are presented with respiratory signs. The disease is progressive and usually fatal.

In the live animal, differential diagnosis includes hepatic coccidiosis and enteritis caused by the variety of diseases that affect weanling and juvenile rabbits. Intercurrent disease is common. Confirmation of the diagnosis is usually made at post-mortem by the presence of large amounts of mucus in the colon.

Most rabbit breeders do not present cases of mucoid enteropathy to veterinary surgeons for diagnosis and treatment. Affected animals are culled or treated with a variety of home remedies. As a result,

there is much confusion about the disease and there are claims of success with many different treatments, including antibiotics. In most cases, it is not clear whether the treatments were effective against other diseases, such as respiratory or enteric pathogens or coccidiosis rather than mucoid enteropathy. In commercial units, affected rabbits are often not treated, although antibiotic therapy can be instigated, either prophylactically or therapeutically. Mucoid enteropathy is not common in pet rabbits. It may be seen in the newly acquired baby rabbits from the pet shop or breeder, or in an adult stressed by parturition, transport or a change of home. In these circumstances, the individual rabbit is valuable to the new owner and treatment is often requested. However, the prognosis is poor and most cases die despite aggressive treatment. Treatment is non-specific and follows the same principles as for other digestive disorders (see Tables 8.2 and 8.3 and Box 8.3). Frequent enemas have been recommended (Breitweiser, 1997). The role of antibiotics is unclear, although many breeders believe that antibiotics are effective. In advanced cases, euthanasia is the most humane choice.

Key Points 8.5 Caecal impaction

- Onset is often insidious.
- The caecum may be palpated as a firm sausage-shaped mass in the ventral abdomen.
- The condition is painful and analgesia is indicated. Opiates do not block prostaglandin production; this is important because prostaglandins stimulate caecal emptying. These should be used in preference to NSAIDs.
- If NSAIDs are used, those drugs which are weak cyclo-oxygenase inhibitors such as carprofen may be preferable.
- Occasionally caecal impactions can move and cause colonic obstruction. This leads to the caecum distending with gas (this may be visible radiographically) and the rabbit becoming rapidly depressed and anorexic.
- Treatment involves pain relief, fluid therapy and prokinetic medications. In the 2002 edition of this book, Frances Harcourt-Brown stated that some success was achieved using synthetic prostaglandins in treating this condition.
- Caecal impactions can be caused by feeding small-particle fibre that absorbs water, such as bulk laxatives.
- Caecal impaction may be part of a larger spectrum of signs in diseases such as dysautonomia or mucoid enteropathy.

Key Points 8.6 Dysautonomia

- Dysautonomia, similar to equine grass sickness or Key–Gaskell syndrome in cats, has been identified in rabbits.
- There is loss of both sympathetic and parasympathetic nerve function. This results in reduced gut motility, particularly in the caecum.
- In the terminal stages, gastric dilatation and aspiration pneumonia can occur.
- The diagnosis may be confirmed at post-mortem histopathological examination of autonomic ganglia.
- There is no known treatment, although some cases may respond to supportive care and long-term management.

Key Points 8.7 Mucoid enteropathy

- The aetiology of this disease is unknown, although faecal-oral transmission has been suspected and either a bacterial toxin or other agent found in the serum of affected rabbits is postulated to cause the signs displayed.
- The hallmark of this disease is massive mucus secretion into the colon, without notable associated inflammation. The mucus secreted can be enough to plug the colon with a gelatinous mass.
- The caecal contents become inspissated and solid, adhere to the caecal wall and may obstruct the ileocaecal junction.

Continued

Key Points 8.7 Mucoid enteropathy—cont'd

- Clinical signs include abdominal distension, depression, crouched stance and 'sloshy' sounding guts. Tooth grinding is common.
- Disruption of normal faecal output is one of the first signs of mucoid enteropathy. Diarrhoea and/or mucus may be seen in the early stages, followed by cessation of faecal output and abdominal distension.
- Mucoid enteropathy can occur concurrently with other enteric diseases such as Tyzzer's disease or colibacillosis.
- The prognosis is poor; however, some rabbits respond to intensive therapy that includes antibiosis, pain relief, fluid therapy and prokinetic drugs.

8.10 Enteric diseases caused by specific pathogens

8.10.1 Coccidiosis

Coccidiosis is a disease of animals kept under crowded conditions and occurs in many breeding establishments. Intensive, damp, dirty conditions predispose to coccidiosis and the environment can become heavily contaminated. The disease is caused by a protozoan parasite with a complex life cycle. Coccidia strains are highly host-specific. Infection is by ingestion of sporulated oocysts passed in the faeces of infected rabbits. The oocysts require 48–70 h outside the host in which to sporulate. The oocysts are very resistant in the environment and can be spread through feed, soil and fomites. Wild rabbits can be affected and, theoretically, are a potential source of infection to pet rabbits that are fed on grass. Long grass picked by hand is less likely to be contaminated than short grass grazed by large numbers of wild rabbits.

The protozoan parasites that cause coccidiosis are Sporozoa belonging to the suborder Eimeriorina. *Eimeria* are parasites of epithelial cells. They invade the mucosa of the intestine, colon and caecum and the epithelium of various ducts. Infected rabbits void oocysts that require oxygen and a period of a several days to become infective. Ingestion of the oocyst releases sporozoites into the duodenum after the oocyst has been broken down by digestive enzymes. The sporozoites invade cells and cause tissue damage as they complete their complex life cycle, ultimately to release oocysts into the lumen of the gut. *Eimeria* spp. are host- and site-specific. Oocysts can survive for many years in the environment but are susceptible to dry conditions. Recovered rabbits become immune to infection. As many as 14 species of *Eimeria* have been described in the rabbit. All but one species are found in the small intestine, caecum or colon and cause 'intestinal coccidiosis'. One species, *Eimeria stiedae*, inhabits the epithelial cells of the bile ducts and causes 'hepatic coccidiosis'. There is no cross-immunity between the different *Eimeria* spp.

8.10.1.1 Intestinal coccidiosis

Eimeria magna and *Eimeria irresidua* are the two most pathogenic coccidial species that affect the intestine of rabbits. Other less pathogenic intestinal species include *Eimeria perforans*, *Eimeria media*, *Eimeria elongata*, *Eimeria neoloporis*, *Eimeria intestinalis*, *Eimeria caecicola* and *Eimeria piriformis*. The developmental stages are restricted to the ileum and jejunum but, in heavy infestations, overspill into the caecum has been observed (Owen, 1992). There are two asexual stages and oocysts appear in the faeces 7–8 days post-infection. Mixed infections can occur and coccidia are often found in conjunction with other pathogenic agents such as *E. coli*. It is not always clear how important intestinal coccidiosis is during an outbreak of enteritis, although the introduction of a pathogenic species into a susceptible population can prove fatal, especially in young rabbits around the time of weaning. Acute infection causes inappetence, weight loss, depression and diarrhoea that can be haemorrhagic. Intussusceptions may be associated with chronic infections. Subclinical coccidiosis results in reduced feed conversion.

On post-mortem examination, the parasite can be found on microscopic examination of scrapings of the intestinal lining. Lesions occur primarily in the ileum and jejunum and are immediately identifiable by inflammation and oedema at the site of infection. Mucosal ulcerations and haemorrhages may be seen. Characteristic changes can be seen histologically in the gut wall. During life, oocysts are found in the faeces. Sulpha drugs are used to treat coccidiosis. Groups of rabbits can be medicated in the food or drinking water. Oral trimethoprim preparations or toltrazuril can be used to treat individual pets. Dose rates are given in Table 3.1. Single oral doses of toltrazuril (2.5–5 mg/kg) or a single oral dose of 50 mg/kg sulphadimethazine followed by its inclusion in the drinking water at 1 g/L for 9 days were found to reduce faecal egg count by 73–90% (Redrobe *et al.*, 2010).

8.10.1.2 Hepatic coccidiosis

Hepatic coccidiosis is a serious disease of rabbits caused by the species-specific *E. stiedae*. Wild rabbits can be infected and transmission occurs by the ingestion of sporulated oocysts in food that has been contaminated by faeces. Sporulation of the oocysts is required for infectivity and requires at least 2 days outside the host. Oocysts are extremely resistant and can remain viable in soil, on vegetation and fomites for long periods of time (Harkness and Wagner, 1995). Recently, voided faeces do not contain oocysts that are infective (Harkness, 1997) as a prepatent period in the presence of oxygen is required for development. *Eimeria stiedae* has a slightly different life cycle to the intestinal *Eimeria* spp. Ingested oocysts hatch in the duodenum and sporozoites penetrate the intestinal mucosa before being transported to the liver, either in the bloodstream or in macrophages in the lymphatic system. Replication takes place in the mesenteric lymph nodes before transport via the hepatic portal circulation to the liver where they enter bile duct epithelial cells. Here the life cycle is completed with the ultimate release of oocysts into the bile duct. The prepatent period lasts for 15–16 days and oocysts are found in the faeces for at least 10–14 days after this (Owen, 1992).

Clinical symptoms of hepatic coccidiosis depend on the severity of infection (numbers of oocysts taken in) and on the immune status of the individual. Three- to 4-week-old rabbits may have oocysts in their faeces; however, clinical signs tend to be more severe in slightly older rabbits (5–8 weeks) at the time of weaning. Signs are associated with the lesions in the liver and bile ducts, and include weight loss, ascites, jaundice, diarrhoea and hepatomegaly. Weanling rabbits are most commonly affected.

Diagnosis can be made on finding oocysts on faecal flotation (concentration methods may be required). The oocysts of *E. stiedae* are elliptical in shape and are larger than intestinal coccidian oocysts. They can be differentiated on the basis of size and shape. Histological examination of the liver demonstrates coccidial stages within the bile duct epithelium.

Post-mortem signs relate to the predilection of the parasite for the bile ducts. There are pale yellow foci or cords in the liver. These foci may exude yellowish fluid when cut. The gall bladder and bile ducts may be thickened and distended. The liver is enlarged (possibly several times its normal size) and fibrotic. The gall bladder is enlarged, distended and packed with oocysts that can be seen in wet smears of the bile. Impression smears of the cut surface of the mesenteric lymph nodes or liver can reveal all stages of the parasite, which is reputed to have nine different schizont stages (Owen, 1992). Remnants of the disease may be evident in the liver for life and can occasionally be discovered many years later, during post-mortem examination.

Newly weaned animals are most susceptible and those that recover have a solid lifelong immunity. The best method for prevention or control of this disease is good hygiene. In an individual rabbit, hepatic coccidiosis can be treated with sulpha drugs (Schmidt, 1995); however, the changes in the liver are irreversible, and some authors (Harkness *et al.*, 2010) feel the disease is essentially untreatable. Commercial pellets often contain a coccidiostat to

prevent clinical disease in rabbit colonies while allowing an immunological response to confer immunity. Treatment of established disease can be problematic, as rabbits that are not eating well will not receive the medication in the feed. Medical treatment must be combined with suitable cleaning and disinfection procedures in order to be successful. In a comparative study of the response of rabbits infected with *E. stiedae* to treatment with sulphaquinoxaline, robenidine, methyl benzoquate, clopidol and a mixture of methyl benzoquate and clopidol, only sulphaquinoxaline and the combination of methyl benzoquate and clopidol gave satisfactory control of the parasite (Joyner *et al.*, 1983). Toltrazuril (Baycox, Bayer) in the drinking water is highly effective in reducing oocyst output of intestinal and hepatic *Eimeria* spp. A regimen of 2 days' treatment repeated after 5 days reduces clinical signs and allows the development of immunity (Peeters and Geeroms, 1986; Redrobe *et al.*, 2010).

8.10.1.3 Coccidiosis in pet rabbits

In pet rabbits, coccidiosis is sometimes encountered in the newly acquired young rabbit. Intestinal coccidiosis causes inappetence, weight loss and chronic diarrhoea, which can be blood tinged. Animals affected with hepatic coccidiosis are often thin, pot-bellied and small for their age. Occasionally icterus is seen. Mixed infections occur. Raised bilirubin values in rabbits of this age are virtually pathognomonic for hepatic coccidiosis, especially in conjunction with other biochemical evidence of liver damage such as a raised AST, ALT, gamma GT and alkaline phosphatase values. Coccidial oocysts may be evident in the faeces. By the time the animals are presented for treatment they are often recovering from infection. If the rabbit is active and eating well, the prognosis is usually good with administration of sulpha drugs. Paediatric suspension of trimethoprim/sulfamethoxazole can be used to treat the individual patient (see Table 8.3). A well-balanced diet is also required as the hepatic coccidiosis interferes with vitamin metabolism.

Key Points 8.8 Intestinal and hepatic coccidiosis

- Several species of *Eimeria* can cause intestinal coccidiosis. *Eimeria magna* and *E. irresidua* are the most pathogenic.
- Hepatic coccidiosis is caused by *E. stiedae*.
- Intestinal coccidiosis presents as an outbreak of diarrhoea, particularly in weanlings of 1–3 months of age. Clinical signs include inappetence, weight loss, fluid/mucoid faeces (sometimes containing blood), reduced body temperature and increased thirst. Rabbits may die without clinical signs if infection is acute.
- Hepatic coccidiosis presents as anorexia, failure to thrive, reduced weight gain, icterus, diarrhoea and death (up to 50% mortality in young naïve rabbits). Weanling rabbits (5–8 weeks old) are most susceptible.
- Diagnosis of both types of coccidiosis is based on identification of coccidian oocysts in the faeces, in conjunction with histological examination of post-mortem specimens.
- Treatment of coccidiosis relies on improved cleaning and disinfection of premises, reduction of stocking density, in addition to the use of sulpha drugs or toltrazuril. In commercial rabbitries coccidiostats may be added to feed.

8.10.2 Clostridial enterotoxaemia

Enterotoxaemia occurs in rabbits kept in colonies and occasionally in the individual pet rabbit. The disease is caused by *Clostridium* spp. that are anaerobic Gram-positive bacilli capable of producing powerful enterotoxins. The organisms can reside in the gut without causing disease but under certain conditions will rapidly proliferate and cause a severe enteritis. *Clostridium spiroforme* is a major pathogen in rabbit enterotoxaemia, although *Clostridium difficile* and *Clostridium perfringens* may also be involved (Perkins *et al.*, 1995). Pathogenic rabbit strains of *C. spiroforme* are different from non-pathogenic strains in other species. A similar pathogenic strain has been isolated from humans affected with

diarrhoea (Carman, 1993). Rabbit isolates of *C. spiroforme* produce a toxin that is neutralized by antiserum to *C. perfringens* type E iota toxin. Virtually all rabbit isolates of *C. spiroforme* are toxigenic, although this is not the case in other species. *Clostridium difficile* produces two exotoxins, toxin A and toxin B. Toxin A is a lethal enterotoxin that binds to specific enteroreceptors and induces fluid secretion, mucosal damage and intestinal inflammation. Toxin B is a potent cytotoxin that interacts synergistically with toxin A (Perkins *et al.*, 1995).

In intensive situations, the mortality rate from enterotoxaemia can be high due to the prevalence of pathogen in the environment. Low fibre, high carbohydrate diets are associated with enterotoxaemia in commercial units. Recently weaned rabbits are most susceptible. Young rabbits do not digest and absorb starch as efficiently as adults (Blas and Gidenne, 1998) and carry a greater risk of unabsorbed carbohydrate reaching the caecum to act as a bacterial substrate. Substantial amounts of glucose are required by *C. spiroforme* for toxin production. There is a marked difference in starch digestibility between adult and growing rabbits. In adult rabbits, carbohydrate is hydrolysed and absorbed before it reaches the caecum. Enterotoxaemia in adult pet rabbits is not associated with a high carbohydrate diet but usually follows a disruption of the gut flora by antibiotics, other pathogens, toxins or stress. Experimentally, enterotoxaemia can be induced by oral administration of clindamycin. The accidental inclusion of lincomycin in the diet of commercial rabbits has resulted in clinical outbreaks.

Enterotoxaemia is manifested by brown, watery diarrhoea, collapse or sudden death. It is an acute disease although it is sometimes preceded by a short period of anorexia. In most cases, enterotoxaemia is rapidly fatal due to toxaemia, dehydration and electrolyte loss, although the occasional case can recover. Peracute cases may be found dead with no prior evidence of disease. Others are found moribund, often with liquid tarry brown diarrhoea. Chronic cases are manifested by anorexia and weight loss and intermittent diarrhoea (Carman and Evans, 1984). A typical time course is 6–48 h, with individuals showing clinical signs, including anorexia, polydipsia, reduced body temperature, profound diarrhoea (watery to haemorrhagic), cyanosis, tooth grinding, recumbency and possibly convulsions (Harkness *et al.*, 2010).

At post-mortem examination, the rabbits are often in good bodily condition but may have liquid faeces oozing from the anus and staining the perineum and hind legs. Typical post-mortem findings include inflammation and hypereamia of the caecum. The small intestine or proximal colon can also be affected. Extensive petechial or ecchymotic haemorrhages on the serosal surface of the caecum are characteristic of enterotoxaemia. The caecal contents are very liquid and may contain gas. Haemorrhages or ulcers may be seen on the mucosal surface of the caecum. The submucosa can be thickened and oedematous. To be certain that enterotoxaemia was the cause of death, prompt post-mortem examination is required to differentiate the lesions from post-mortem changes.

Sometimes, enterotoxaemia can be confirmed by detection of the organism in caecal contents. Comma-shaped organisms may be seen on Gram-stained caecal smears. Anaerobic culture for 24–48 h on blood agar is required to grow the organism. Anaerobic conditions can be preserved by tying off a section of caecum or small intestine at each end before it is removed and submitted to the laboratory. Alternatively, a swab of intestinal contents can be immediately plunged to the bottom of the transport medium where conditions remain anaerobic. *Clostridium* spp. concentrate at the interface of the deposit and supernatant after centrifugation of caecal contents and may be seen on a Gram stain from material taken from this area. Toxin is also present in the supernatant but requires specialized tests such as the guinea pig dermonecrosis or the mouse lethality assay for detection (Delong and Manning, 1994). DNA PCR tests for detecting clostridial endotoxins in other species are now available.

Treatment of enterotoxaemia is not usually successful. Most cases are presented dead or dying. Prompt, intravenous fluid therapy and supportive care are necessary. Antibiotics and short-acting corticosteroids might be of value. Metronidazole is indicated to kill anaerobic *Clostridium* spp. Antibiotics

such as ampicillin, clindamycin, lincomycin, amoxycillin, penicillin and erythromycin that are known to precipitate enterotoxaemia should be avoided. There is evidence that the ion exchange resin cholestyramine absorbs the enterotoxin and improves survival rate if it is given in the early stages (see Section 3.9.2). This preparation is safe enough to give to rabbits in any situations where enterotoxaemia could develop. Probiotics can also be administered, although it is not known if they are effective.

Vaccination protects sheep from clostridial enterotoxaemia and there are anecdotal reports from breeders that vaccinating rabbits with sheep vaccine reduces mortality rates in colonies of rabbits that have experienced losses from clostridial infections. Clostridial enterotoxaemia in sheep is caused by *C. perfringens* not *C. spiroforme*, which is the usual pathogen involved in enterotoxaemia. Experimentally, the protective value of toxoids prepared from *C. spiroforme* have been evaluated in laboratory- and farm-bred rabbits (Ellis *et al.*, 1991). The trials showed that a single vaccination at 4 weeks of age was protective, especially if a second dose was administered 14 days later. Maternal immunity was not passed from vaccinated dams to their offspring. Clostridial vaccines are now produced commercially for protection against *C. perfringens* enterotoxaemia in rabbits, although these are not available directly in the UK (vaccines are produced in the USA and China).

Key Points 8.9 Clostridial enterotoxaemia

- It is a potentially fatal condition caused by enterotoxins produced by *C. spiroforme*, *C. difficile* and *C. perfringens*.
- It is associated with a high carbohydrate diet, particularly in weanlings.
- Clinical signs include death without premonitory signs, diarrhoea (profuse, watery to bloody), anorexia, polydipsia, cyanosis, tooth grinding, hypothermia, recumbency and seizures.
- Diagnosis is based on identification of organism on direct faecal smear, culture (anaerobic), cytotoxicity testing and post-mortem findings.
- Treatment is often unsuccessful. Aggressive fluid therapy (based on clinical pathological results ideally) must be instituted; supportive feeding with a high fibre diet, antibiotics (metronidazole) to kill anaerobic bacteria and cholestyramine resin (to adsorb enterotoxins) may be successful in isolated cases.

8.10.3 Coliform enteritis

Pathogenic strains of *E. coli* can be a major cause of enteritis and losses in colonies of commercial rabbits or laboratories. *Escherichia coli* is normally absent from the intestinal flora of rabbits or is only present in small numbers. In some circumstances pathogenic strains of the organism proliferate and cause diarrhoea. There are seven groups of pathogenic *E. coli* (Harkness *et al.*, 2010):

- Enteropathogenic *E. coli* (EPEC)
- Enterohaemorrhagic *E. coli* (EHEC)
- Enteroinvasive *E. coli* (EIEC)
- Enterotoxigenic *E. coli* (ETEC)
- Enteroaggregative *E. coli* (EAEC)
- Diarrhoea-associated *E. coli* (DHEC)
- Cytolethal descending toxin (CDT-) producing *E. coli*.

Most pathogenic *E. coli* produce very stable toxins. These are secreted directly into the cytoplasm of infected cells, leading to cell death. Clinical signs include profuse watery to haemorrhagic diarrhoea, anorexia and significant weight loss. Concurrent infection such as coccidiosis or rotavirus and dietary factors (low fibre diet or dietary change) predispose to disease. Antibiotics can be effective in treating some of the less virulent strains. There appears to be age susceptibility associated with *E. coil* with suckling rabbits being most susceptible. At post-mortem examination, the small intestine may appear normal but there is inflammation of the caecum and large intestine. In neonates, Gram-stained smears from the small intestine may show large numbers of Gram-negative rods (Okerman, 1988). In older animals, differential diagnosis from coccidiosis,

enterotoxaemia, Tyzzer's disease and viral enteropathies depends on gross and microscopic changes and isolation of the pathogen.

Diagnosis of colibacillosis depends on compatible clinical signs and culture and speciation of pathogenic coliforms. Mild cases can be treated symptomatically, with fluid therapy, supportive feeding and antibiosis. In a colony situation strict hygiene protocols and vigorous culling may be a better solution.

8.10.4 Tyzzer's disease

Tyzzer's disease is an inflammation of the caecum caused by a sporulating, obligate intracellular bacterium, which has recently been reclassified as *C. piliforme* rather than *Bacillus piliformis* based on molecular studies of the genome (Besch-Williford, 1997). The disease usually occurs in weanling rabbits 6–8 weeks old and is predisposed by poor husbandry, overcrowding, immunosuppression (including immunosuppressive medication) and incorrect diet. Serological testing of pet rabbits by the University of Missouri, USA, reported an incidence of 47%, although the majority of rabbits were asymptomatic (Besch-Williford, 1997).

Spores from *C. piliforme* are shed in the faeces and can remain viable in the environment for over a year. Oral ingestion of spores from contaminated material results in bacterial invasion of the epithelium of the lower small intestine and caecum. The presence of antibodies in apparently healthy animals suggests that the organism can reside latently in the gastrointestinal tract. Overt disease is precipitated by stress or immunosuppression. Experimentally, corticosteroid administration is required to reproduce the disease (Delong and Manning, 1994). The organism penetrates the intestinal mucosa and disseminates throughout the liver and eventually the myocardium via the lymphatics.

Tyzzer's disease causes necrosis of the caecum, intestine, liver and heart. Peracute cases may show intestinal lesions only. Myocardial lesions occur later in the course of the disease, and lesions are principally found in the left ventricle and septum.

Clinical signs include diarrhoea, faecal soiling of the perineum, dehydration and death within 48–72 h, and are therefore non-specific. Weanling rabbits 6–12 weeks old are primarily affected, although the disease can affect rabbits of any age. In common with many of the infectious agents that cause diarrhoea in rabbits, Tyzzer's disease is predisposed by stress, low fibre diets, intensive husbandry and intercurrent disease.

Chronic infection can occur with intestinal stenosis and fibrosis occurring at the sites of necrosis. There is little information about the clinical syndromes associated with intestinal stenosis or myocardial necrosis. Diagnosis is usually made at post-mortem examination and is confirmed by histological examination of the liver where the organism can be seen in hepatocytes. It is not known whether Tyzzer's disease is a significant cause of disease in adult pet rabbits in the UK. Serological and PCR tests which would facilitate the screening of stock for carriers and aid diagnosis in the live animal may become available.

Treatment is affected by the acute course of the disease and the location of the organism (intracellular). These factors reduce effectiveness. Oral antibiotics (tetracyclines) can be administered via the drinking water. Cephalosporins, penicillins and chloramphenicol may also be effective. While antibiotics may suppress infection, asymptomatic carriers may develop.

8.10.5 Salmonellosis

In common with most animals, rabbits can suffer from salmonellosis, although the disease is uncommon, especially in the individual pet. *Salmonella typhimurium* or *Salmonella enteritidis* can cause diarrhoea, septicaemia and rapid death.

8.10.6 Viral causes of enteritis

8.10.6.1 Rotavirus

Rotaviuses are enveloped RNA viruses that are particularly associated with diarrhoea in young animals. They are host-specific. Rotavirus has been associated with outbreaks of enteritis, usually in rabbits under 6 weeks of age. In most cases, diarrhoea is mild (Thouless *et al.*, 1996). Rotavirus was originally isolated from weanling rabbits with diarrhoea, although it has also been recovered from unaffected animals

(Bryden *et al.*, 1976). Serological tests have revealed that rotavirus infection is widespread in colonies of domestic rabbits. The disease has been reported in many parts of the world, including Japan, Europe, Canada and the USA (DiGiacomo and Mare, 1994). In infected colonies, adult animals are seropositive and confer maternal immunity on their offspring. The young rabbits become infected when maternal immunity wears off, which coincides with weaning. Infected rabbits shed virus in faeces, which is probably the main route of transmission, although there is evidence for airborne spread. Severity of clinical signs depends on virus strain, intercurrent disease, immune status and all the other factors involved in enteric disease in weanling rabbits. In a study by Thouless *et al.* (1996), it was found that concurrent infection with rotavirus and *E. coli* resulted in increased mortality and morbidity due to diarrhoeal disease compared with infection with *E. coli* alone.

Diagnosis is achieved using a combination of clinical signs, serology (where available) and histopathological findings. Control measures include improved hygiene and reduced stocking density. Individual rabbits can be given supportive care, including fluid therapy and supportive feeding. Any concurrent disease should be addressed.

8.10.6.2 Coronavirus

Rabbit enteric coronavirus (RECV) has been reported in association with enteritis in rabbits. The virus has also been associated with pleural effusion and cardiomyopathy and an analogy has been made with feline infectious peritonitis (Deeb *et al.*, 1993). RECV has been implicated in outbreaks of enteric disease in a barrier-maintained rabbit colony (DiGiacomo and Mare, 1994). RECV is unlikely to be a cause of disease in the pet rabbit.

8.11 Poisoning

8.11.1 Plant toxicity

Plant toxicity is a cause of concern to owners who give their rabbits the freedom of the garden or pick plants to feed to their pets. Actual proven cases of plant toxicity in rabbits are rare in the veterinary literature although there are some anecdotal reports and an abundance of myths (see Section 1.3.19.1). Rabbits are known to be resistant to the toxic components of deadly nightshade and ragwort. However, it is wise to avoid exposure to plants known to be toxic in other species (see Table 1.5).

8.11.2 Lead poisoning

Rabbits are susceptible to lead poisoning by chewing wood covered in lead-based paint, pipes or vinyl floor covering. The primary presenting signs are lethargy and reduced appetite, which can progress to other symptoms (Swartout and Gerken, 1987). Typical haematological changes of anaemia and basophilic stippling may be seen in chronic cases. Reduced appetite appears to be linked with slow gut motility. Radiographically, radiopaque material may be seen in the stomach and unevacuated hard faeces may be seen in the large intestine. Treatment with motility agents such as cisapride or metaclopramide in addition to a chelating agent, such as sodium calcium edetate or D-penicillamine, facilitates excretion of the lead from the gut. An advantage of the rabbit's rapid elimination of large particles is that flakes of lead paint will be quickly passed out in the hard faeces rather than moved into the caecum and retained in the body for longer periods before being re-ingested.

8.11.3 Liver disease

The rabbit liver is divided into six lobes, two on the left- (anterior and posterior) and four on the right-hand side (anterior, posterior, caudate and quadrate). The caudate lobe is susceptible to torsion. Rabbits secrete large volumes of bile daily, and this enters the duodenum through the common bile duct just caudal to the pylorus. The bile and pancreatic ducts are separate in the rabbit. The primary bile pigment produced by rabbits is biliverdin rather than bilirubin, meaning that jaundice is less common.

Liver disease in rabbits is well recognized; however, the clinical signs can be very non-specific, making diagnosis challenging.

Common clinical sign scan include:

- Weight loss
- Anorexia
- Abdominal pain
- Ascites
- Jaundice.

Liver disease can be categorized by aetiological cause:

- Bacterial: tularaemia, toxoplasmosis (see Section 14.4.3)
- Viral: rabbit haemorrhagic disease (see Section 14.6.2), herpes simplex
- Protozoal: encephalitozoonosis (see Section 14.4.2), coccidiosis
- Toxic: lead (see Section 14.4.2.4), alfatoxicosis
- Neoplastic: bile duct adenoma/adenocarcinoma
- Metabolic: fatty liver disease (see Section 8.3 and Key Points 8.2)
- Physical liver lobe torsion.

Many of these diseases have been covered either earlier in this chapter or elsewhere within this book.

Diagnosis proceeds in the same manner as in other species, with clinical examination, blood parameters (it should be noted that some enzymes commonly linked with hepatic inflammation and cholestasis in other species are less specific in the rabbit) and imaging such as radiology and ultrasonography forming the basis. The gold standard for definitive diagnosis is histopathology.

8.11.4 Liver lobe torsion

Liver lobe torsion is one of the less frequently encountered causes of anorexia and gastrointestinal stasis.

Rabbits with liver lobe torsion present with:

- Anorexia
- Lethargy
- Jaundice
- Abdominal pain.

A liver lobe has rotated about its axis causing venous congestion and eventually diffuse necrosis of the lobe.

Biochemical abnormalities include:

- Anaemia
- Increased alanine aminotransferase
- Increased aspartate aminotransferase
- Increased γ-glutamyl transferase.

Definitive diagnosis is by radiography (signs of hepatomegaly and gastrointestinal stasis) or ultrasonography (heterogeneous liver parenchyma, increased free fluid in the abdomen, reduced bowel motility).

Treatment is surgical, with removal of the affected liver lobe being indicated. Lobectomy is undertaken in a similar way to other species. Rabbits with this condition require very good supportive care perioperatively.

8.12 Approach to an outbreak of enteric disease in a breeding colony

Many rabbit breeders keep a small number of animals that they use as exhibition animals and sell young stock into the pet trade. In many cases, diseases are treated with home remedies or by culling affected stock. Half-truths, myths and legends abound, although some traditional remedies have a grain of truth or some sound common sense in them. Professional veterinary advice is seldom sought except when a disease threatens all the stock, a prize-winning bloodline or perhaps a particularly valuable individual. Expense is always an issue. Cases of enteritis can be difficult and expensive to investigate and treat. Prompt, detailed post-mortem examinations and laboratory investigations are required. The causes are often multifactorial and home visits to examine the stock and assess the husbandry may be needed. Successful treatment of individual rabbits with enteric conditions is difficult and usually expensive. Intensive therapy, including intravenous fluids, hospitalization and nursing, is required despite the breeder's expectation that some 'wonder drug' will provide an instant cure. Therefore compromises must be made and general principles applied to prevent further losses. Post-mortem examination is extremely valuable and *all* dead rabbits should be examined,

not just one or two, as soon after death as possible. Microscopic examination of impression smears, gut contents and faeces can be a cheap way of obtaining information. A provisional diagnosis of mucoid enteropathy, coccidiosis or enterotoxaemia can be made from post-mortem examination, although concurrent infections can be present. Histology or specialized laboratory techniques are required to confirm the diagnosis or detect viral infections.

In general, it is often easier to prevent further losses than it is to treat existing outbreaks. It may be advisable for breeders to take a break in their breeding programme and reduce stocking density so they have no young susceptible rabbits on the premises for a few weeks. A break gives the opportunity to clean and disinfect the premises thoroughly, and reduce the number of pathogens in the environment. Simply washing cages and hutches thoroughly in hot water and detergent to remove organic debris is beneficial and can be followed by the use of a disinfectant that kills viruses and bacteria. Povidone–iodine compounds such as Tamodine (Vetark) or non-irritant Virkon can be used. Coccidial oocysts are particularly resistant to disinfection but are susceptible to desiccation. The use of a blowtorch to flame hutches is a simple method of killing oocysts or a 10% solution of ammonia is effective (Pakes and Gerrity, 1994). Ammonia is unpleasant and potentially hazardous to handle. Soil may need to be removed and replaced in outdoor enclosures. The introduction of a feed containing a coccidiostat can be required in the long term.

Key Points 8.10 Investigating and controlling disease outbreaks

- Many disease outbreaks have multifactorial causes, so robust investigation is required.
- Many instances of disease within a colony do not reflect a single pathogen; concurrent infections can be significant.
- Questions to ask include:
  1. What clinical signs are being exhibited?
  2. What age range of rabbits is affected?
  3. What percentage/number of rabbits are affected?
  4. What medications have already been administered?
  5. What is the policy regarding moving individuals in/out of the colony? (quarantine protocols)
  6. What is the cleaning/disinfection protocol?
- Site visits are very useful for assessing hygiene and stocking levels.
- Diagnostics will be required: post-mortem examination (including scrapes of gut lining, and histopathology), faecal examination, bacterial culture and serology. The diagnostics chosen should reflect a logical diagnostic plan in order to get the most relevant information.
- Basic strategies for controlling infectious disease should include:
  1. Stop stock moving in and out of the colony, and maintain as a closed community.
  2. Reduce stocking density and consider removing all vulnerable age classes for a period of time to allow disinfection.
  3. Maximize nutrition and ensure that sufficient fibre is being fed.
  4. Comprehensive cleaning and disinfection should be undertaken. This must include removal of organic debris as well as use of a suitable disinfection agent. The disinfectant must contact the clean surfaces for the effective amount of time in order to kill the organism in question. Using a blowtorch to burn the inside of wooden hutches can be a good option, as liquid disinfectants are less effective on porous surfaces.
  5. Advise staff on fomite transmission, and institute appropriate measures to avoid this: i.e. foot baths, hand-washing, changing clothes, not mixing utensils between groups, ordering which animals are attended to and when. Healthy animals should be first, proceeding to the sickest last. Different staff for each group could be considered.
- Preventing disease outbreaks is often easier than controlling them. Put a long-term plan in place including preventive medicine, surveillance diagnostics, stock control, hygiene and optimizing nutrition.

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