Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

CHAPTER 11

Cardiorespiratory Disease

11.1 Anatomy and physiology of the respiratory system

Rabbits have sensitive nostrils and a good sense of smell. There are 20–25 vibrissae in each upper lip. In healthy rabbits, the nostrils constantly twitch at a rate of 2–120 times per minute, unless the rabbit is at rest (Brewer and Cruise, 1994) or is unwell. The nasal cavity is lined with a protective layer of mucus that entraps foreign particles and bacteria. The mucus also prevents water loss and enhances the sense of smell. The nasal glands secrete serous fluid into the nasal cavity. In the rabbit, there is glandular tissue along the nasal septum and a cluster of glands, collectively known as the lateral nasal gland, occupy the entire wall between the nasal cavity and maxillary sinus (Bojsen-Moller, 1964). The function of these nasal glands is to moisten inspired air, which has a role in thermoregulation. The position of the conchal and maxillary sinuses and the structures of the nasal cavity are illustrated in Figures 1.18 and 5.1. There is no frontal sinus.

The oropharynx is narrow and the base of the tongue is large in rabbits. The glottis is small. Breathing takes place through the nostrils; the epiglottis is engaged with the soft palate, making the rabbit an obligate nasal breather. Mouth breathing only occurs during severe respiratory distress.

Each lung is divided into cranial, middle and caudal lobes and there is an accessory lobe on the right lung. Respiratory movement in rabbits is mainly diaphragmatic rather than due to the action of the intercostal muscles. This means that respiration can be restricted when there is increased intra-abdominal pressure. The thoracic cavity is small and the thymus, which in contrast with other species does not regress, but remains large throughout life, occupies the anterior ventral thoracic cavity (see Figure 11.7).

11.2 Respiratory diseases

11.2.1 Pasteurellosis

Pasteurella multocida is associated with a number of diseases of rabbits (see Section 14.5.1). Pasteurellosis is not a recognized problem in wild rabbits but is a serious disease in colonies of commercial or laboratory rabbits. In pet rabbits, although *P. multocida* is found as an opportunist pathogen in many secondary infections, primary pasteurellosis is uncommon. It is usually encountered in situations where there has been increased stress and an increased number of interactions with other rabbits: for example, the newly acquired rabbit that has recently been bought from a breeder or pet shop. Respiratory disease is the most common manifestation. Acute infections and septicaemia occur, especially in young animals, but chronic, insidious recurrent infections are more common in the adult pet rabbit. Rhinitis, conjunctivitis, nasolacrimal duct infections, otitis media, tracheitis and bronchopneumonia can all be caused by *P. multocida*; however, it is wise to remember that other organisms can be involved. The bacteria can spread to other sites from the nasal cavity where it can reside as a commensal organism. Infection often persists despite mucosal and humoral antibody responses in addition to effusive neutrophilic exudation. The deleterious effect of pasteurellosis on laboratory colonies of rabbits and interference with

experimental procedures has resulted in the evolution of expensive 'pasteurella-free' rabbits for use in research. The epidemiology of pasteurellosis is discussed in Section 14.5.1. See Figure 11.1 for the many predisposing factors that trigger disease.

11.2.2 Respiratory disease due to pasteurellosis

Pet rabbits are often already infected with *P. multocida* when they are purchased from a pet shop or breeder. Lu *et al.* (1983) surveyed the capsular and somatic serotypes of *P. multocida* found in healthy and diseased rabbits and concluded that while several major serotypes can be differentiated, one (serotype 12A) was predominant in both healthy and diseased individuals. The development of rhinitis and other respiratory tract problems in the newly acquired young rabbit is likely to be due to pasteurellosis. In the older animal, stress or poor husbandry can result in a flare-up of a latent infection. The possibility of disease being due to pasteurellosis does not replace the need for diagnostic evaluation. Poor air quality, caused by high ammonia levels or dusty hay, irritates the respiratory tract and predisposes secondary infection. Ventilation and good air quality are important in disease prevention. Pasteurellosis can be spread between animals and the disease is endemic in most breeding establishments. It often causes problems in premises such as sanctuaries, where several animals are housed in close proximity. A distance of greater than 1.8 m (6 feet) or 'sneezing distance' is needed to control the spread of infection between individuals (Whittaker, 1989).

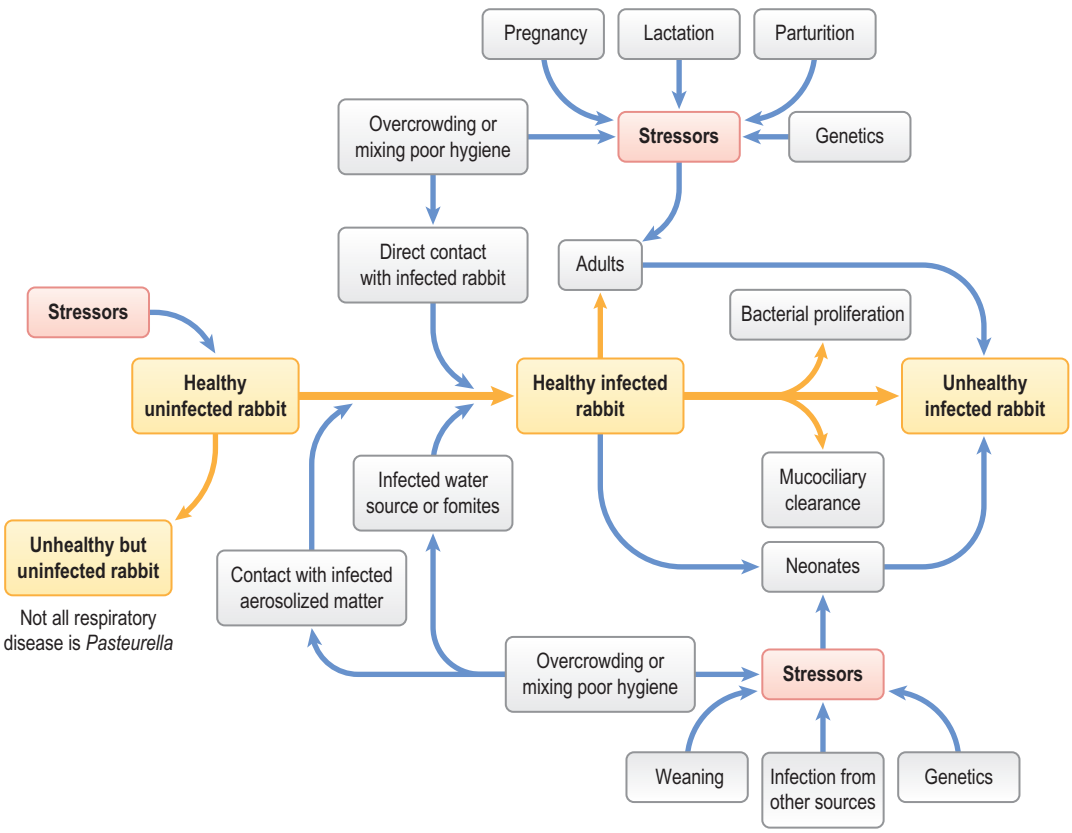

Figure 11.1 The inter-relationship of various factors that affect the expression of *Pasteurella* infection in rabbits.

11.2.3 Rhinitis ('snuffles')

Repetitive sneezing and upper respiratory tract noise is a feature of rhinitis. Rhinitis and sinusitis can be manifestations of pasteurellosis, although other organisms such as staphylococci or *Bordetella* can also be involved. The differential diagnosis of upper respiratory tract disease in rabbits includes nasal foreign bodies and periapical abscesses of the maxillary incisors or premolars. Both these conditions are common in the pet rabbit, so it cannot be assumed that all rabbits with a purulent nasal discharge are suffering from pasteurellosis or that all cases of 'snuffles' are due to infectious agents.

In the initial stages of pasteurellosis, the nasal discharge is serous and the condition is responsive to antibiotic therapy. In advanced cases, the nasal discharge is thick, yellow and viscid. Copious amounts of mucopurulent material can be discharged from the nostrils and form crusts on the surrounding skin. Affected rabbits wipe the purulent discharges from their nose with their forepaws, which become matted and discoloured. Coughing is not as common as sneezing and snorting. Respiratory noises may be audible to the owner who may think their rabbit is 'wheezing'. Anorexia can occur, perhaps due to a reduced sense of smell or because it is difficult to chew and breathe at the same time. Grooming difficulties occur because the rabbit finds it difficult to breathe and groom simultaneously. Response to antibiotic therapy is poor in advanced cases and relapse is common. Post-mortem examination of the sinuses and nasal passages of rabbits with chronic rhinitis shows why these cases are so difficult to treat. The nasal cavity is filled with pus, which can spread into the paranasal sinuses (see Figure 5.1 and Figure 11.2). The pus becomes thick and inspissated. There is ulceration of the mucous membranes and osteomyelitis of the turbinates, causing severe atrophy and erosion (Deeb, 1997). The presence of pus in the nasal cavity impedes gas exchange and causes physical discomfort and irritation.

11.2.3.1 Differential diagnosis of rhinitis

The clinical history can be very suggestive of pasteurellosis. Young rabbits that have recently been stressed by weaning, change in routine and transport are often exposed to infection at the breeding establishment where they originated. Rabbits housed with several others in sheds and outhouses are susceptible. In older, individual pet rabbits, bacterial infection is less likely to be a cause of rhinitis than dental disease, which is common. Nasal foreign bodies can cause rhinitis (see Section 11.3). Myxomatosis is another possible cause of rhinitis. Myxomatosis in rabbit colonies can present as rhinitis in association with ocular discharge. Aerosol infection is more likely to give respiratory tract signs than insect spread (see Section 14.6.1). Myxomatosis is progressive and almost invariably fatal.

Bacteriology can be used to identify bacteria present in the nasal passages of rabbits with rhinitis and to ascertain antibiotic sensitivity. The rabbit's nose is sensitive and it can be difficult to insert the swab deep into the nasal passages in the conscious animal. Sedation or anaesthesia is usually required to take a deep nasal swab for culture. Culture results do not necessarily illustrate the organism causing the clinical signs; it merely gives an overview of the organisms present. Caution is therefore necessary in their interpretation. Depending on the method of collection of swab samples for culture, contaminants can be present, presenting a false result. Common causes of inaccurate results are failure to clean the external nares prior to sample collection, and failure to insert the swab deeply enough into to nasal cavity. False-positive and -negative results can occur on bacterial culture due to inaccuracies in various laboratory methods of bacterial strain identification.

Underlying dental problems can be diagnosed by visual examination and by radiography (see Section 5.6 and Figure 11.2B). The structures of the nose and teeth can be assessed on skull radiographs. The paranasal sinuses can be identified (see Figures 5.10 and 11.2) and abnormalities may be detected radiologically. Opacity of the conchal sinus indicates the presence of exudate (see Figure 11.2B). Erosion of the ethmoturbinates can be seen on a well-exposed radiograph. However, the presence of *P. multocida* or other bacterial infection and erosion of the turbinates does not rule out the possibility of an underlying foreign body or perapical abscess. Large abscesses or rhinoliths can form in the nasal passages because of tooth root infection (see Figure 5.12).

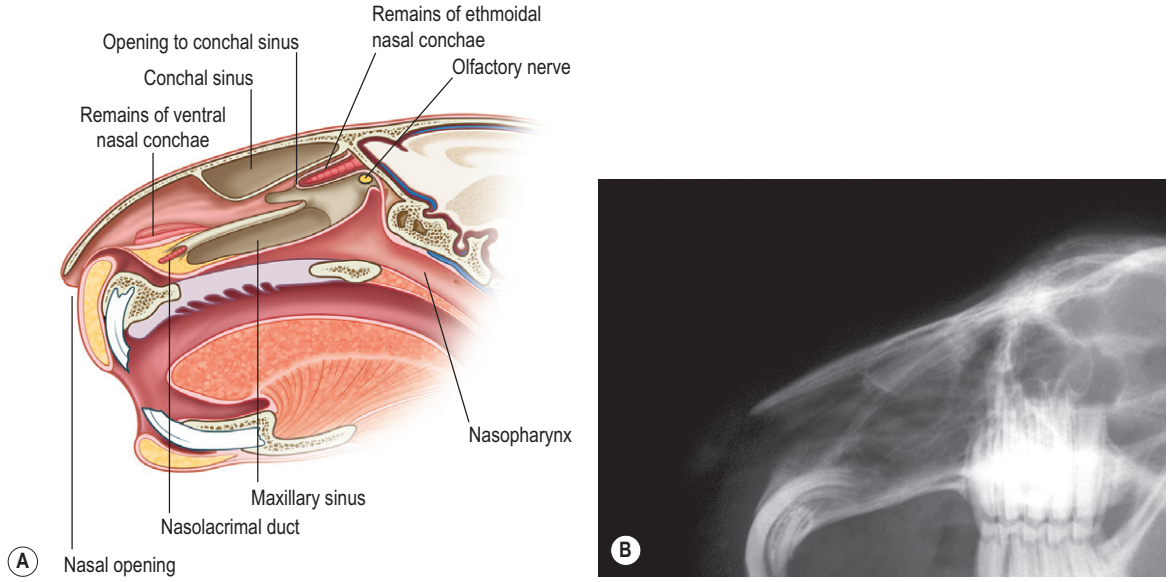

Figure 11.2 (A) Sagittal section through the head to show the position of the paranasal sinuses. This figure was drawn from a post-mortem specimen of a sagittal section through a decalcified head. The nasal conchae have been removed. There are two paranasal sinuses in rabbits: the conchal sinus and the maxillary sinus (sometimes called the maxillary recess). There is no frontal sinus. Both the conchal and the maxillary sinus form blind cavities. At the cranial end of each sinus there is a single opening into the nasal passage. The structures of the nasal cavity are illustrated in Figure 1.20. The position of the paranasal sinuses is also illustrated in Figure 5.1. **(B) Chronic infection of the conchal sinus**. This figure is a lateral view of the nasal cavity of an 18-month-old dwarf lop female rabbit with chronic rhinitis. The rabbit had started sneezing and developed a nasal discharge shortly after she was purchased at 10 weeks of age. Antibiotic therapy and mucolytic therapy failed to cure the condition although the symptoms were temporarily alleviated. Radiology shows increased radiopacity of the conchal sinus, indicating the presence of infection. There is erosion of the turbinates. The conchae and ethmoturbinates are not visible on the radiograph. Rhinitis was due to infection and not related to dental disease.

11.2.4 Otitis media

Pasteurella multocida primarily resides in the nasal cavity but can spread via the eustachian tube to the tympanic bulla and affect the middle ear (see Figure 11.3). Infection can spread further to affect the inner ear and vestibular apparatus or track through the acoustic meatus and along the vestibulocochlear nerve. On post-mortem examination abscesses can be found in the cranial cavity.

It is not easy to diagnose otitis media in the live rabbit and in many cases clinical examination and routine imaging are not sufficient. Hammond *et al.* (2010) demonstrated that plain radiography of the rabbit skull had a specificity and sensitivity for finding fluids similar to that of cat and dog radiography, and confirmed that the dorsoventral view was the most consistently useful one. The presence of exudate in the external ear canal does not signify the presence of otitis media. In many pet rabbits, especially lop-eared breeds, it is difficult to visualize the tympanic membrane due to the presence of waxy ear secretion. Post-mortem examination of the ear canal of pet rabbits often reveals the presence of inspissated pus that occludes the external ear canal. The presence of purulent material in the external ear canal does not necessarily signify the presence of pus in the tympanic bulla. Neither does pus in the tympanic bulla always cause otitis interna and vestibular symptoms (see Section 10.4.3). Radiological changes can often be seen as an incidental finding on skull radiographs (see Figure 11.4). It seems likely that rabbits with pus in the external ear canal and/or the tympanic bulla will have impaired hearing, although they may

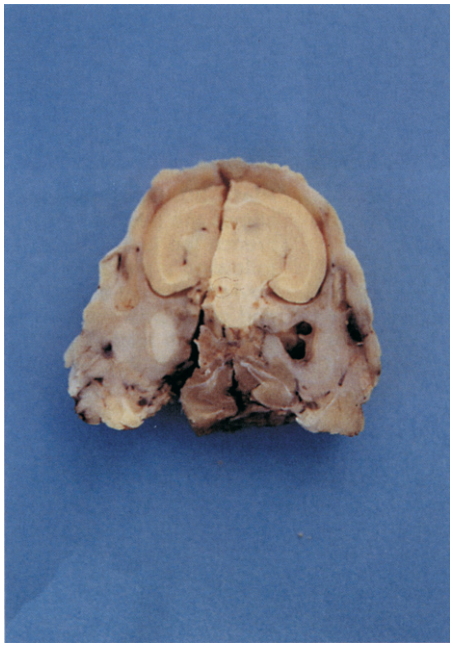

Figure 11.3 Pus in tympanic bulla. A cross-section of a decalcified head is shown. There is also a sagittal section through the specimen. The skull is from a Netherland dwarf male rabbit that developed a head tilt. Despite an initial response to antibiotic therapy, the rabbit relapsed and was euthanized. The skull has been sectioned at the level of the tympanic bullae. The left tympanic bulla is filled with pus.

appear clinically normal. Some observant owners can detect hearing deficits in their pets and aggression in rabbits has been attributed to deafness when rabbits have been startled by the unheard approach of their owners. Computed tomography scanning or ultrasonographical examination of the area (King *et al.*, 2007) will give more useful and sensitive information.

In a study by Flatt *et al.* (1977), otitis media was found in 4% of 2001 young rabbits and 32% of adults slaughtered for human consumption. The animals appeared clinically healthy on ante-mortem inspection. Gross lesions included the presence of white tenacious exudate filling the tympanic bulla. The mucous membrane lining the bulla was thickened, translucent and discoloured. The eustachian tube was dilated and filled with pus. Microscopic lesions consisted of an accumulation of heterophils

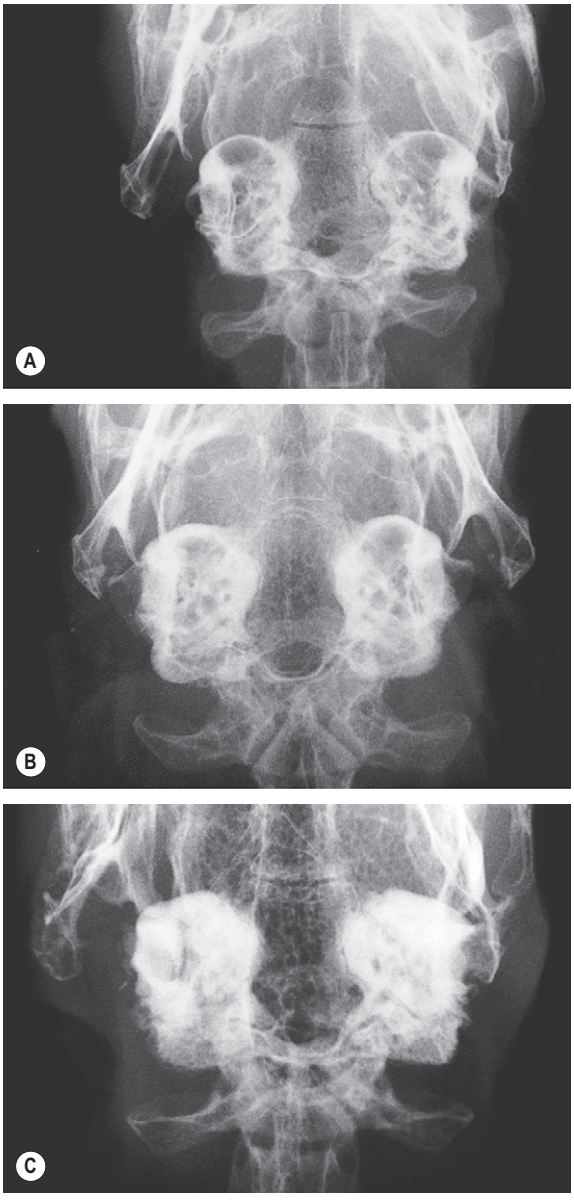

Figure 11.4 Radiographic changes of the tympanic bulla. **(A)–(C)** are dorsoventral views of the caudal area of the skull to show progressive changes of the tympanic bullae from normal **(A)** to severe **(C)**; **(B)** is an incidental finding on a rabbit that was radiographed to investigate his dental disease; and **(C)** is of a 3-year-old French lop male that was rescued by the RSPCA from a small shed containing between 20 and 30 rabbits. Upper respiratory problems were endemic. The rabbit appeared totally deaf and was ataxic. He was quiet and subdued. He was euthanized due to dental problems. Post-mortem examination showed pus in both tympanic bullae.

in the lumen of the tympanic bulla and in the mucosa and underlying periosteum. In some of the affected ears, the simple squamous epithelium over the tympanic membrane and auditory ossicles had undergone squamous metaplasia with necrosis of the mucosa in severe cases. In the rabbits with periosteal changes, the thickened periosteum was infiltrated by a variable number of heterophils, plasma cells and lymphocytes. Occasionally, granulation tissue was present. In some cases, the tympanic membrane was ruptured and a suppurative exudate was present in the tympanic cavity and the external auditory canal.

11.2.5 Pneumonia

Septicaemia and acute suppurative pneumonia can be caused by *P. multocida*. Infection can be peracute and cause rapid death (see Figure 11.5). Chronic pneumonia and abscesses in the thoracic cavity also occur. Poor exercise tolerance and increased respiratory rate may not be obvious to owners of pet rabbits that are confined to hutches or small runs with no opportunity to exercise. These individuals pose a poor anaesthetic risk due to poor gaseous exchange in consolidated lungs.

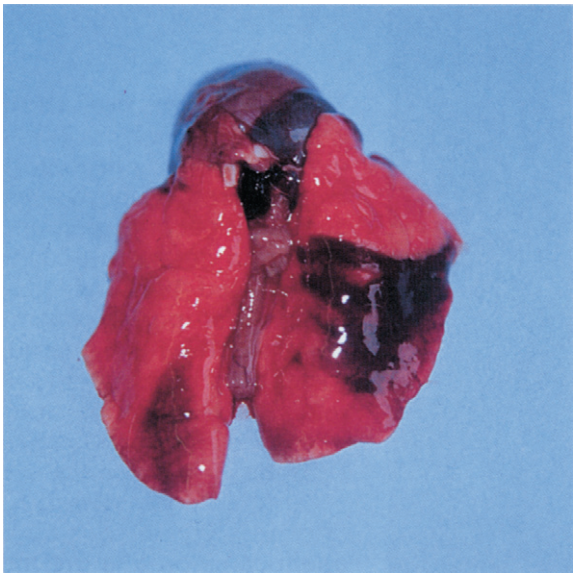

Figure 11.5 Pneumonia. The lungs of a juvenile mixed breed male rabbit found dead after not eating for 24 h are shown. The lungs showed evidence of acute pneumonia typical of *Pasteurella multocida* infection.

11.2.6 Treatment of pasteurellosis

Pasteurellosis is a difficult condition to cure. Acute upper or lower respiratory infections can be responsive to prompt antibiotic and non-steroidal anti-inflammatory medication. An antibiotic that is unlikely to cause diarrhoea but is effective against *P. multocida* should be selected. Examples include enrofloxacin, trimethoprim sulpha combinations, tetracyclines, parenteral cephalexin or penicillin. *In vitro*, most rabbit isolates of *P. multocida* are susceptible to penicillin, chloramphenicol, tetracycline, erythromycin, novobiocin and nitrofurans with a variable susceptibility to streptomycin, kanamycin, neomycin and sulphonamides. *Pasteurella multocida* is usually resistant to clindamycin and lincomycin (Manning *et al.*, 1989). More recently Sellyei *et al.* (2009) demonstrated the increasing resistance of *P. multocida* isolates from swine and poultry to certain antibiotics (namely, sulphonamides, tetracyclines and aminoglycosides); however, they found third-generation quinolones such as enrofloxacin to be effective. The tendency for the fluoroquinolones to concentrate in the mucosa of the maxillary sinus at levels greater than that found in the blood (Dan *et al.*, 1989) makes this drug a good first choice for treating *Pasteurella*. Penicillin has been used widely to treat rhinitis in laboratory rabbits (Gaertner, 1991). Concurrent infection with other pathogens such as *Bordetella bronchiseptica* can affect the response to therapy. Tilmicosin is an effective antibiotic in the treatment of acute pasteurellosis in sheep and has been used to treat rabbits despite the possibility of a fatal adverse reaction to the drug.

Long-term or periodic courses of antibiotic can be given to control long-standing infections although they are unlikely to be curative. Antibiotics can also be introduced directly into the nose. Some rabbits will tolerate this procedure. Gentamicin is available as an ophthalmic preparation (Tiacil, Virbac) that

can be used as nose drops. Purulent exudate needs to be removed before the drops are instilled.

Chronic pasteurellosis is manifested by the presence of copious quantities of thick, viscid, mucopurulent material that presents a physical barrier to medication. The pus is often in inaccessible sites such as the nasal passages, paranasal sinuses, tympanic bullae or even the brain. Surgery, such as trephination, to remove the pus, provide drainage and create a route for local medication, is possible. Bulla osteotomy has been suggested as a treatment for rabbits with severe, refractory, chronic otitis media in association with vestibular signs such as head tilt and anorexia (Redrobe, 2000). Two surgical techniques have been described (Redrobe, 2000; Swindle and Shealy, 1996). Chow *et al.* (2009) and Chow (2011) describe in detail the technique for ventral bulla osteotomy in the rabbit and include a period of follow-up, with encouraging results. This experience has been replicated by the staff of the Exotics Service at the University of Edinburgh. Trephination of sinuses has been widely described in rabbits (Gilbert *et al.*, 2004; Scharf *et al.*, 1994; Watanabe *et al.*, 1999) as they are used as models of maxillary sinusitis in humans; however, clinical reports are less common but the procedure appears to be well tolerated (Kelleher, 2008). Trephination rarely provides freedom from clinical signs of chronic sinusitis in cats.

The chances of successful treatment of pasteurellosis are greater in sites where the pus can be removed, e.g., by flushing an infected nasolacrimal duct or removing an abscess or infected organ such as a uterus or testicle. Dacryocystitis, facial abscesses or purulent nasal discharges are often associated with underlying dental disease that needs to be addressed if there is to be any hope of success in treating the secondary *Pasteurella* infection (see Sections 5.5.1 and 6.1).

In cases of rhinitis, it is important to establish adequate systemic hydration by ensuring adequate fluid intake. Dehydration leads to dry airways, resulting in increased viscosity of secretions, decreased ciliary function, inflammation and degeneration of the mucosa. The inclusion of fresh leafy vegetables in the diet can increase a rabbit's fluid intake, particularly if they are fed wet (water is left on the vegetables after washing). Water can be added to inspired gases by the use of humidifiers or placing the rabbit in a steamed-up room such as a bathroom, although care must be taken to ensure the rabbit does not overheat. Nebulization is sometimes used as a method of introducing antibiotic, decongestants and other agents directly into the respiratory tract and to loosen secretions and bring relief. Nebulization introduces charged particles into the respiratory tract as an aerosol. In other species, nebulization is used to treat lower respiratory tract disease. Medication introduced by nebulization is unlikely to reach the tympanic bullae or paranasal sinuses or to penetrate thick mucopurulent exudate in rabbits. Mucolytic agents such as bromhexine or *N*-acetyl-cysteine have been recommended for nebulization in rabbits with rhinitis (Meredith, 2000). In other species, *N*-acetylcysteine is irritating to mucosal surfaces and can inactivate certain antibiotics when it is mixed with them (McKiernan, 1983). Systemic bromhexine (Bisolvon, Boehringer Ingelheim) can be used as a mucolytic in rabbits. In cattle and pigs, when bromhexine is administered simultaneously with oxytetracycline, the antibiotic in the bronchial mucus is considerably increased (product datasheet).

Occasionally, owners administer human decongestants to their rabbits. There is no proven efficacy in the use of such products in the treatment of 'snuffles'. Oxymetazoline is a common topical nasal decongestant that has been investigated in experimentally induced infections of the maxillary sinus in rabbits (Bende *et al.*, 1996). Paradoxically, a higher degree of inflammation was found in the oxymetazoline-treated sinuses. The authors concluded that oxymetazoline nose drops interfere with the normal defence mechanisms, possibly by a decrease in mucosal blood flow.

Topical application of fluoroquinolones to the surface of the eye has been shown to result in concentrations of drug greater than the MIC_{90} for most ocular pathogens for 6 or more hours (Dan *et al.*, 1989; Green *et al.*, 1996; Hendrix and Cox, 2008). The use of ciprofloxacin eye drops has been suggested for adjunctive treatment of rhinitis and sinusitis in rabbits (Carpenter, 2007), because the tear film drains

into the nasal sinuses. The current author (MJV) has found this very useful clinically as part of a multi-therapeutic approach.

11.2.7 Other infectious causes of respiratory disease

11.2.7.1 Fungal

Rabbits can suffer from fungal respiratory diseases such as nasal and disseminated aspergillosis (Schoppler, 1919, and Höppli, 1923, recorded cases of spontaneous aspergillosis in rabbits, while Thjøtta, 1933, reported similar condition in free living hares) and pneumocystis pneumonia (Dei-Cas *et al.*, 2006). Rabbits have often been used as experimental models for human respiratory aspergillosis (Chakrabarti *et al.*, 1997; Francis *et al.*, 1994).

Aspergillosis in mammals is a primary pulmonary disease, which, although infectious, is not contagious. It is due to inhalation of spores from hay, for example, and related to poor ventilation and hygiene, all of which may be encountered in situations where many rabbits are kept in close proximity. *Pneumocystis* spp. are a ubiquitous group of fungal organisms that can cause pneumonia and pneumonitis in immunosuppressed individuals. *Pneumocystis oryctolagi* causes pneumonia in rabbit kits at weaning age (Dei-Cas *et al.*, 2006).

There have been sporadic reports of respiratory mycobacteriosis, typically caused by *Mycobacterium avium* in rabbits, with clinical signs varying from nasal discharge and upper respiratory obstruction, to disseminated disease and pneumonia.

Key Points 11.1 Dealing with a dyspnoeic rabbit

- Rabbits are obligate nasal breathers, so open mouth breathing is always abnormal.
- Upper respiratory dyspnoea usually presents with inspiratory effort.
- Lower respiratory dyspnoea usually presents with expiratory effort.
- Stertorous breathing may be noted.
- Clinical baseline should include RR, HR, auscultation, colour and CRT, as well as examination for any discharges. An oral examination is mandatory.
- Oxygenation can be achieved using an oxygen tent (even an improvised one such as a pet carrier in a bin bag will work well), but beware of the rabbit overheating.
- Diagnostic testing (once the patient is stable) should include radiography of the skull and chest, blood work, culture and sensitivity and cytology of any abnormal discharges.
- Be aware that some conditions with extra-respiratory causes can mimic dyspnoea, for example heat stroke or metabolic acidosis.

11.3 Nasal foreign bodies

Pieces of hay, grass seeds or shafts of hair can enter and become lodged in the nasal cavity. Repetitive sneezing, nose rubbing and a unilateral discharge (this may be bloody, mucoid or mucopurulent) are indicative of a nasal foreign body. If the foreign material has penetrated deep into the nasopharynx, snorting and dyspnoea can occur, which can be mistaken for pneumonia. The patency of the nasal passages can be assessed by occluding each nostril in turn and listening to the respiratory noises. Sometimes the end of a blade of hay or hair shaft can be seen protruding from the nostril (see Figure 11.6). The foreign body can be gently pulled out. In other cases, endoscopy is required. Dislodging or removing a nasal foreign body often results in a complete recovery.

11.3.1 Endoscopic examination of the nasal passages

The nasal passages can be examined endoscopically. They require flushing to clear away discharges and exudate prior to endoscopic examination. Foreign material can also be flushed out during the procedure. Nasal flushing in rabbits poses problems due to the small nasopharynx and inaccessible larynx. Great care is required to prevent purulent material

Figure 11.6 Nasal foreign body. The nostrils of a mature dwarf lop male rabbit that was presented because he was sneezing are shown. In this case, a blade of hay could clearly be seen protruding from the nostril and the foreign body was easy to remove. Seeds and stems of hay can make their way into a number of sites and cause disease in rabbits. Nasal foreign bodies are relatively common. Sometimes stems of hay can lodge in or around the larynx and cause choking. Foreign bodies can become wedged in the periodontal space. Both these conditions are linked with dental disease. Grass seeds can also lodge in the inguinal skin folds situated on either side of the genital orifice.

entering the larynx and trachea. Endotracheal intubation is mandatory and the rabbit should be positioned so fluid drains out of the mouth. This is best achieved by placing a small sandbag or similar underneath the rabbit's neck, allowing the nose to point downwards. This avoids having increased pressure being placed on the thorax by the weight of the abdominal contents as would occur were the rabbit just tilted head downwards. The nasal passages are examined using a rigid endoscope such as a 1.9-mm needlescope (Stortz) and irrigation sheath. The endoscope can go from the nostril to the nasopharynx via the ventral meatus and can also be used to explore the turbinate area.

11.4 Dyspnoea

Key Points 11.2 Differential diagnoses of dyspnoea

- Diseases affecting upper respiratory airway patency, e.g., rhinitis due to *P. multocida*, nasal foreign bodies, dental apical abscessation.
- Diseases affecting lower airway patency, e.g., pneumonia from any cause, viral haemorrhagic disease, tracheal or bronchial foreign body, pulmonary oedema, traumatic lung contusion.
- Diseases affecting the available space for the lungs to expand, e.g., cardiomegaly, pleural effusion, fractured ribs, increased abdominal pressure affecting diaphragmatic excursion, space-occupying lesions, for example abscesses or metastatic neoplasia.
- Diseases external to the respiratory system that can cause increased respiratory rate, e.g., heat stroke or metabolic acidosis.

Metastatic tumours can cause dyspnoea. Uterine adenocarcinomas can metastasize to the lungs where they are seen as multiple spherical opacities (Rübel *et al.*, 1991). Some rabbits with upper respiratory tract disease are dyspnoeic because they cannot breathe through their nose. As in other species, external trauma can cause chest injuries and respiratory problems. Bite wounds from predators can penetrate the chest wall, causing serious internal injury and introducing infection. A small external wound can easily be overlooked. Abscesses can develop within the thoracic cavity as result of haematogenous spread from other sites. Auscultation and radiology are useful adjuncts to clinical examination. Radiographic features of the normal chest are illustrated in Figure 11.7. Chronic pneumonia is illustrated in Figure 11.8.

11.5 Heat stroke

Rabbits are tolerant of low temperatures and can withstand sub-zero environmental temperatures

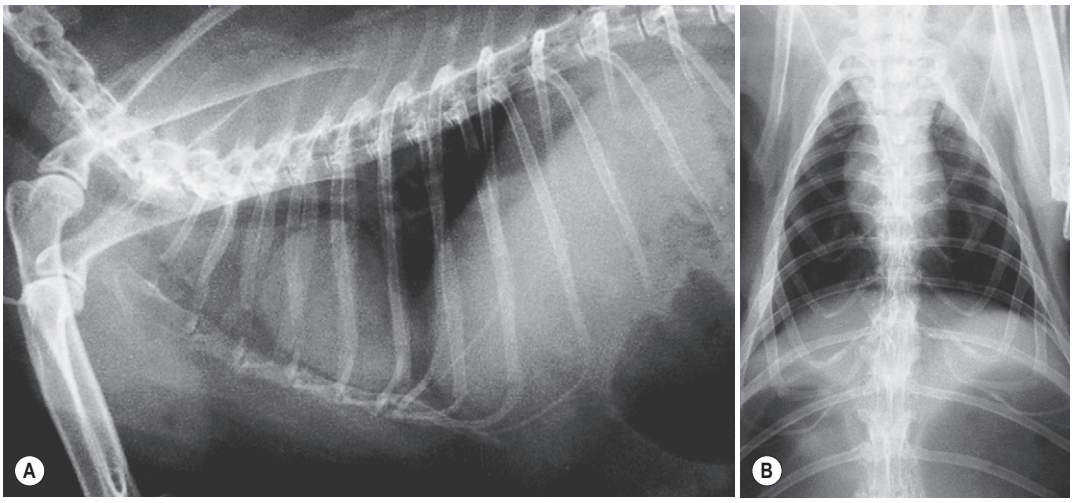

Figure 11.7 Radiographic anatomy of the thoracic cavity. Sedation or general anaesthesia is required to position a rabbit for thoracic radiography. The forelegs need to be retracted cranially to prevent superimposition of the scapulae on the cranial portion of the thoracic cavity. Normal findings are as follows:

- The thoracic cavity is small in comparison with the abdominal cavity.
- The heart occupies a relatively large volume of the thoracic cavity.
- The small cranial lung lobes are not seen in as much detail as the caudal lobes.
- The thymus remains large throughout life.
- The aorta and caudal vena cava should be visible.
- In obese animals, intrathoracic fat deposits can sometimes be seen (Rübel *et al.*, 1991).
- Cartilage rings are often visible within the tracheal wall.
- The carina lies at the 4th or 5th intercostal space.
- The pulmonary vessels can be seen within the lungs.

(A) shows a normal lateral view of the thoracic cavity, and **(B)** shows the dorsoventral view.

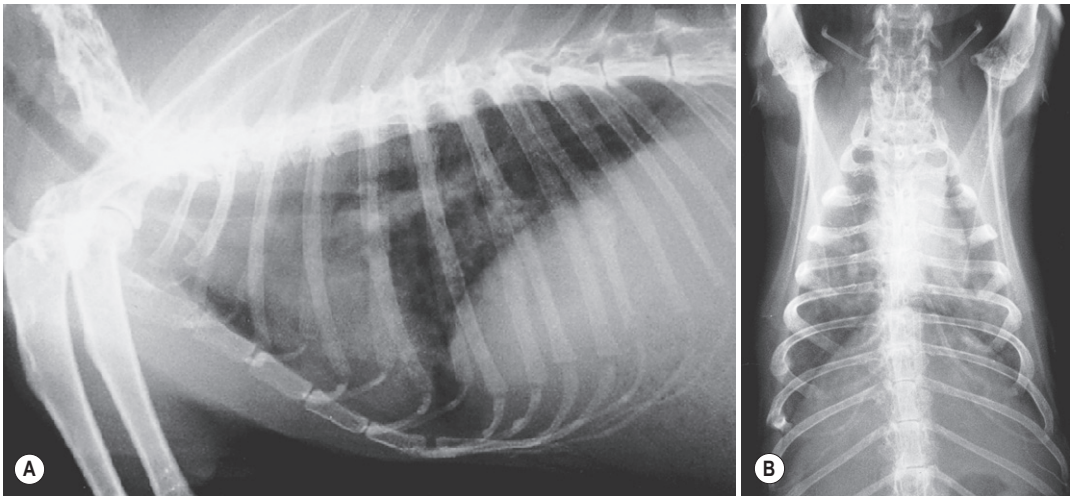

Figure 11.8 Pneumonia. (A) and **(B)** show a lateral and dorsoventral view, respectively, of a 4-year-old Himalayan neutered male rabbit that was thin, anorexic and dyspnoeic. An alveolar pattern can be seen on both views. At post-mortem examination, pneumonic changes were found throughout the lung tissue.

without discomfort, provided they are acclimatized and healthy, and have shelter with plenty of bedding. Their dense fur insulates them from the effects of cold weather but can be a liability in hot weather. In the wild, rabbits respond to extremes of temperature by retreating down their burrows, where the temperature remains more steady.

Rabbits do not sweat and cannot pant effectively. Their ears play an important part in thermoregulation. Signs of heat stroke are similar to other species: anorexia, increased respiratory rate, prostration, pulmonary oedema, cyanosis and death. Some cases can have blood-tinged fluid from the nose and mouth. A high rectal temperature (in excess of 40°C) is suggestive of heat stroke, and temperatures of 42–45°C are associated with a fatal outcome (Adolph, 1947). The pathological changes in heat stroke include a reduction in blood pressure (secondary to vasodilation), which can result in reduced cerebral perfusion, cerebral ischaemia and oedema (Shih *et al.*, 1984). Reduced perfusion can also affect renal and hepatic function. A metabolic acidosis and electrolyte abnormalities also occur. Treatment is aimed at reducing body temperature, e.g., bathing in cold water, wetting the ears and blowing them with a cold hair-drier and administration of intravenous fluids. The administration of a vasodilator such as acepromazine may be helpful. Close monitoring of acid–base and electrolyte parameters may help guide treatment. In human medicine, the use of an interleukin-1 receptor antagonist has shown promise in the treatment of heat stroke (Shen *et al.*, 2008).

11.6 Cardiovascular disease

Most recorded information about cardiac diseases relates to infectious, toxin-induced or diet-related diseases of laboratory rabbits. Heart disease also occurs in pet rabbits and more information has become available as rabbits live longer and more diagnostic and therapeutic procedures are adopted for the individual animal. Congenital abnormalities (see Figure 11.9) such as ventricular septal defects occur as do age-related cardiac problems such as valvular disease. Commonly noted clinical signs include exercise intolerance and dyspnoea; however, they may be very non-specific such as anorexia or weight loss.

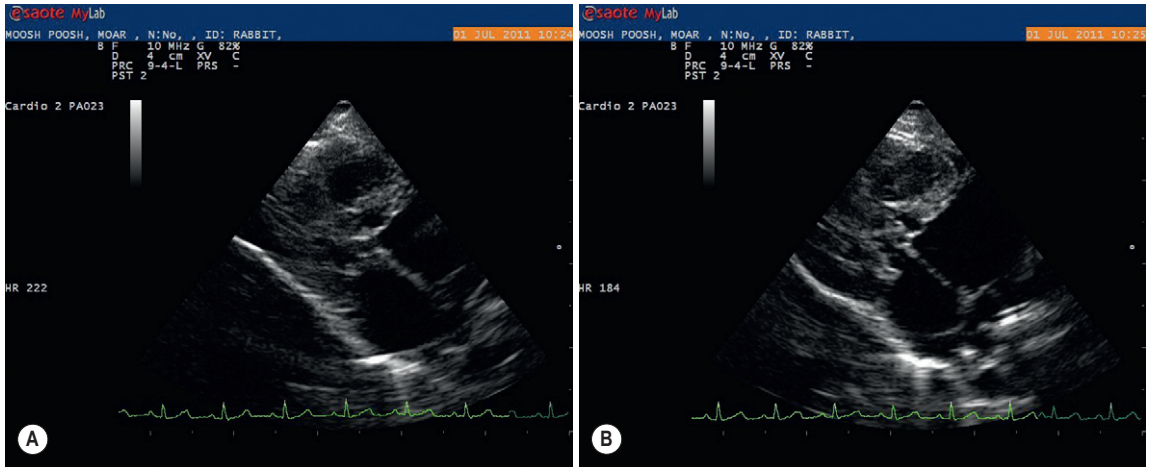

Figure 11.9 Echocardiographic images of a congenital malformation in the heart of a 7-month-old dwarf lop rabbit. These echocardiographic images show a rabbit with suspected cor triatriatum dexter. The right atrium is abnormally divided and is three times the size of the left one. This is a malformation resulting from lack of normal regression of the embryonic right valve of the sinus venosus. In this situation, the right atrium is divided by a membrane into two chambers. This rabbit suffered from episodic weakness and cyanosis. Initial treatment with benazepril and furosemide was successful and the patient improved clinically. However the condition worsened progressively and the patient died 6 months after diagnosis. Images courtesy of M. Holgate.

On examination it may be possible to detect cyanosis of the mucous membranes, or appreciate a heart murmur or arrhythmia. Diagnosis and treatment follow the same lines as for dogs and cats (see Box 11.1). Clinical examination, auscultation, electrocardiography and chest radiography should form part of the minimum database. Most cases will be positively diagnosed by echocardiography. Some reference values for normal parameters determined in laboratory rabbits are given in Box 11.2. Most cardiac disease is diagnosed in pet rabbits over the age of four years, and the larger breeds such as New Zealand whites and French lops are over-represented. See Table 3.1 for details of commonly used cardiac drugs.

Box 11.2 Circulatory data

Electrocardiography (from Kozma *et al.*, 1974)

P wave:	0.1–0.15 mV and 0.03–0.04 s Low or negative in lead I Always positive in leads II–III
P-R:	0.05–0.1 s
QRS:	0.015–0.04 s

Arterial blood pressure

Systolic:	90–130 mmHg
Diastolic:	80–90 mmHg

Arterial blood pH

7.2–7.5

11.6.1 Cardiomyopathy

Cardiomyopathy occurs in pet rabbits. Giant breeds appear most susceptible (see Figure 11.10) but the aetiology is unknown at the present time. Hypertrophic, restrictive and dilated forms have all been reported. Histopathological findings indicate the presence of myocardial fibrosis.

Box 11.1 Treating cardiac arrhythmias and congestive heart failure

Cardiac arrhythmias should be characterized using electrocardiography and heart structure and function assessed echocardiographically.

- Tachyarrhythmias: Prolonged rapid heartbeat over a period of weeks to months can lead to congestive heart failure. Short episodes may contribute to syncope.
  1. Supraventricular tachycardias: these can be treated using digoxin (0.005 mg/kg sid-bid); however, there is a significant risk of toxicity with this drug. Ideally, blood digoxin levels should be monitored after the first few days of treatment. The levels are usually checked 6–7 h post-dosing. Alternatively, the rabbit can be watched carefully and the drug dose reduced/stopped if signs of anorexia or gastrointestinal stasis occur. Diltiazem, a calcium channel blocker, can also be used to treat tachycardia by slowing atrioventricular conduction (0.5–1 mg/kg sid-tid). The downside to this medication is that it reduces myocardial contractility and may cause a drop in blood pressure.
  2. In emergency situations, rapid ventricular tachycardias may respond to boluses of intravenous lidocaine (1–2 mg/kg IV prn).
  3. Sotalol and mexiletine have also been used anecdotally in rabbits at dog doses.
- Bradyarrhythmias: Severe bradycardia may lead to episodic weakness or syncope.
  1. Bradycardia during anaesthesia (not in the case of α_2-agonists) should be treated with glycopyrrolate (0.01 mg/kg).
  2. Severe atrioventricular block may respond to oral theophylline (10–20 mg/kg); however, mechanical pacing may be required.

Emergency treatment of congestive heart failure

- Oxygen
- Percutaneous nitroglycerin approximately 1 cm on the internal pinna
- Furosemide 1–2 mg/kg intravenously
- ACE inhibitors: enalapril 0.25–0.5 mg/kg once daily
- Pimobendan: 0.1–0.3 mg/kg sid-bid

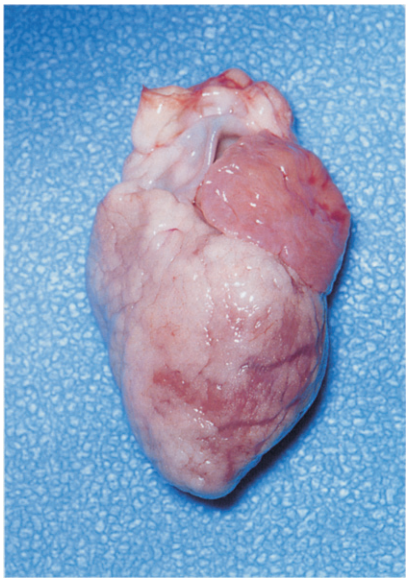

Figure 11.10 Cardiomyopathy. The heart of an adult neutered male French lop (> 6 kg) that died suddenly following a period of lethargy but no other obvious clinical signs is shown. Histopathological and gross post-mortem examination showed no lesions in other organs apart from congestion. Sections of heart muscle showed myocardial fibrosis.

The rabbit myocardium can be affected by several diseases. Vitamin E deficiency, coronavirus infection and some bacterial infections such as salmonellosis and pasteurellosis have been recorded as causes of cardiomyopathy in laboratory rabbits (Marini *et al.*, 1999). Tyzzer's disease not only causes intestinal and hepatic lesions but can also cause a myocarditis resulting in myocardial fibrosis in those animals that survive (Percy and Barthold, 1993). *Encephalitozoon cuniculi* has been reported as a cause of myocarditis in rabbits (Pakes and Gerrity, 1994). Stress and catecholamines are proven causes of cardiomyopathy and experimental models of the human disease can be provided by keeping rabbits in overcrowded conditions (Weber and Van der Walt, 1975). Myocardial necrosis and fibrosis have been recorded in rabbits anaesthetized with ketamine/xylazine combinations by continuous infusion. Marini *et al.* (1999) postulated that hypoxaemia and coronary vasoconstriction result in cell death and necrosis. The rabbit has limited collateral coronary circulation and is therefore predisposed to ischaemia induced by coronary vasoconstriction. The authors draw an analogy with rabbits used as models of catecholamine-induced cardiomyopathy in which α-adrenergic-mediated coronary vasoconstriction occurs. Hypotension and hypoxaemia are further contributory factors.

Key Points 11.3 Cardiac disease in rabbits

- Rabbits can suffer from both congenital and acquired heart disease.
- Clinical signs can include dyspnoea, exercise intolerance, weight loss and anorexia.
- Diagnostic evaluation should include a full physical examination, auscultation, ECG, chest radiography and echocardiography.
- Treatment recommendations follow those for other species; please see Table 3.1 for additional information.
- In an emergency decompensation situation, oxygenation, and application of 3 mm of isosorbide mononitrate paste to the inner pinna can be lifesaving.

11.6.2 Arteriosclerosis

Arteriosclerosis is a thickening and hardening of the arteriolar walls resulting from proliferative or degenerative changes. Aortic arteriosclerosis occurs in rabbits and can cause seizures or vague symptoms such as inactivity and weight loss. Mineralization of the aorta occurs in hypercalcaemic rabbits, usually in association with renal disease that impairs calcium excretion. Mineralization of the aorta is seen radiologically (Shell and Saunders, 1989) and on post-mortem examination. Calcification of the aorta is often associated with calcification of the kidney (see Section 12.5.2). Calcification of soft tissues can be caused by excessive intestinal absorption of calcium, such as in cases of vitamin D toxicity.

11.6.3 Coronavirus

Coronavirus infection in rabbits can result in cardiomyopathy and pleural effusion. Experimentally, coronavirus-infected rabbits are used as laboratory models to study virus-induced cardiomyopathy. The disease was first discovered in Sweden in the 1960s in rabbits inoculated with emulsified testicular tissue containing *Treponema pallidum* (human syphilis). Coronavirus was found in the testicular tissue. An analogy has been made between rabbit coronavirus and feline infectious peritonitis. Clinical signs vary, but infected rabbits are generally pyrexic and many die within 5 days of infection. Pulmonary oedema, pleural effusion and dilation of the right ventricle are found at post-mortem. As in feline infectious peritonitis, hypergammaglobulinaemia is a feature of chronic infection that can be manifested by myocardial degeneration, ascites and uveitis. An enteric form has also been described. At the present time, coronavirus-induced pleural effusion and cardiomyopathy have only been reported in experimentally inoculated rabbits (DiGiacomo and Mare, 1994). It has not been described in pet rabbits.

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