CPD article

Clostridial disease in cattle

Clostridial disease affects cattle across the UK throughout the year but particularly in the grazing season. All clostridial disease occurs when conditions in the muscles or organs become anaerobic allowing for bacterial proliferation and toxin production. The most common pathogenic clostridium is *Clostridium chauvoei* which causes blackleg and has both skeletal and cardiac forms. *Clostridium perfringens* is the second most commonly identified clostridia with type A causing enterotoxaemia and type D causing pulpy kidney. *Clostridium novyi* is the third most common clostridia — type B causes black disease and type D causes bacillary haemoglobinuria. Cattle are most at risk during the grazing season meaning that control and prevention of disease should be particularly targeted at this time of year. The cost of vaccination is so low compared with the cost of losing even one animal that an appropriate protocol should be implemented on all farms.

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Clostridial organisms are found across the UK in soil, vegetation and surface water as well as often being present as commensals in the guts of healthy cattle. There are around 100 species of these anaerobic Gram-positive bacilli that can produce spores in the environment (Harwood, 2007; Radostits et al, 2007) or in their hosts, but only a handful are pathogenic (Radostits et al, 2007). Clostridial disease is caused by a change in conditions on, or in, the host leading to a low oxygen environment and the subsequent proliferation of bacteria (Harwood, 2007). Hosts will be more susceptible to disease if they are suffering from concurrent disease, have sustained bruising from rough handling or have experienced a dietary change such as an increase in concentrates (Harwood, 2007).

The prevalence of the different clostridial diseases from 2010–2018 is shown in *Figure 1* (Animal and Plant Health Agency (APHA), 2019). These data are based on the Veterinary Investigation Diagnosis Analysis (VIDA) database diagnoses so the apparent reduction in disease may be linked to the decrease in the number of APHA Veterinary Investigation Centres rather than a genuine reduction. The most commonly diagnosed *Clostridium*

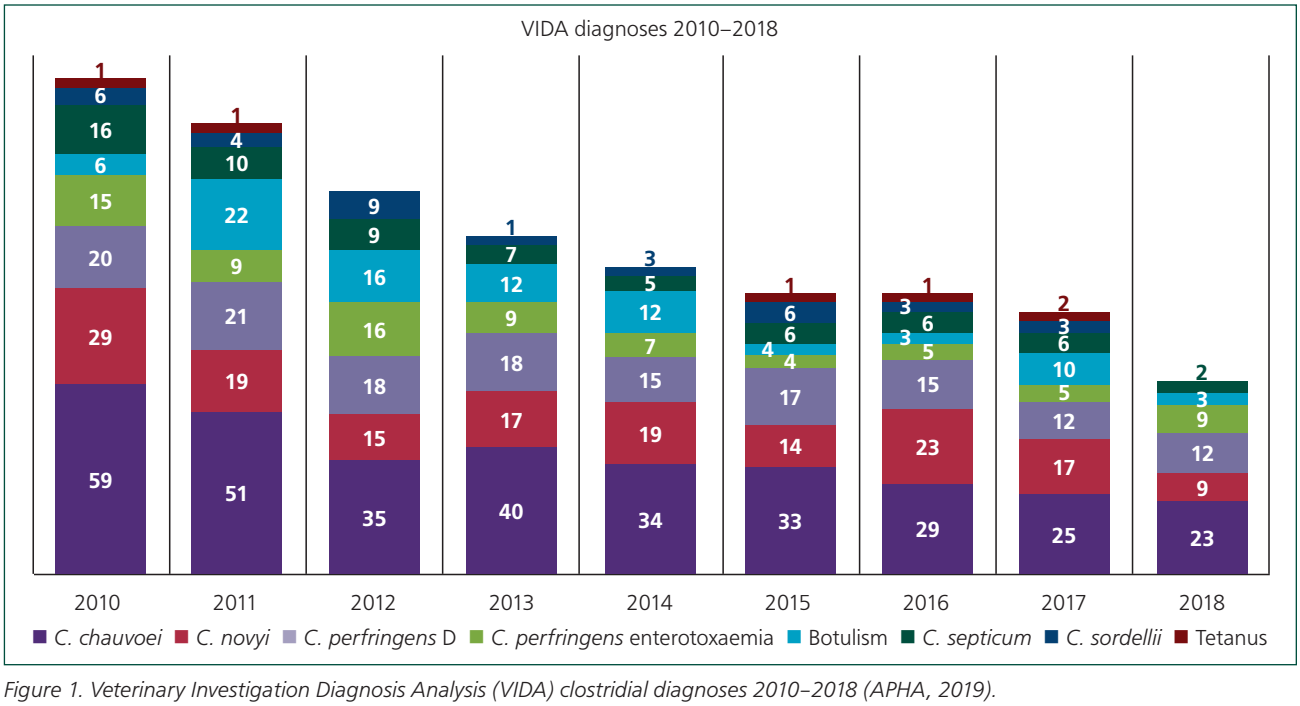

Figure 1. Veterinary Investigation Diagnosis Analysis (VIDA) clostridial diagnoses 2010–2018 (APHA, 2019).

spp. in cattle over this period of time are *Clostridium chauvoei* (36%), *Clostridium novyi* (18%) and *Clostridium perfringens* D (16%) (APHA, 2019). These remain the main pathogens today with the diagnoses for 2018 showing *C. chauvoei* (39%), both types of *C. perfringens* (34%) and *C. novyi* (15%) as the principal disease causing clostridial species (*Figure 2*) (APHA, 2019).

There is an increased incidence in deaths associated with clostridial disease during the summer grazing period, but as clostridia are associated with decaying plant or animal material or contaminated feed they can affect cattle all year around (*Figure 3*) (APHA, 2019). In 2018 clostridial disease was associated with 0.7% of investigated cattle deaths in the UK (APHA, 2019). The key clostridial diseases in the UK are shown in *Table 1* in decreasing prevalence and these will be discussed in detail throughout the article.

C. chauvoei

C. chauvoei infection predominately causes clostridial myositis or 'blackleg' which accounts for around a third of all clostridial diagnoses each year (APHA, 2019). Blackleg was first reported 250 years ago (Armstrong and MacNamee, 1950), and despite a vaccine being available for almost 100 years sporadic cases do still arise (Useh, 2007). *C. chauvoei* spores enter muscles via skin wounds or can be absorbed via the gut and lie dormant in the liver or spleen and become activated by trauma or injury. Disease occurs 2 to 5 days after the initial disease causing event (Useh et al, 2006).

Younger beef animals (between 6 months and 2 years old) are most likely to be affected (Radostits et al, 2007) and tend to be found dead without showing clinical signs. If cattle are still alive they can have difficulty moving or be lame or stiff on an identifiable limb. The affected muscles may have subcutaneous emphysema evident over them as a result of bacterial gas production. Less common forms include lesions in the heart or the meninges (Malone et al, 1986) and certainly in recent years cardiac lesions have been detected more than skeletal muscle lesions. While this may be because the skeletal muscle form is more identifiable in the field, and so the cases investigated by the APHA have some bias, it still indicates that blackleg should not be ruled out based on a lack of limb involvement (APHA, 2018). Rarer forms have also been identified in practice including an outbreak affecting tongue and intestines with seemingly no skeletal muscle involvement (Harwood et al, 2007).

Regardless of the bacterial location, the gross pathology involves dry, darkened skeletal muscle in the limbs, lumbar muscles, diaphragm and heart combined with emphysema and a dark exudate — in the cardiac form this is pericardial. The liver and spleen can also show similar pathology; diagnosis can be confirmed with fluorescent antibody test (FAT) or anaerobic culture on the affected muscle (Otter, 2017). If cattle are identified sufficiently early in the course of the disease via FAT or anaerobic culture of aspirated fluid then penicillin-based treatment can be successful (Radostits et al, 2007).

C. perfringens

C. perfringens is split into *C. perfringens* type D and *C. perfringens* enterotoxaemia by VIDA, but when these diagnoses are combined they accounted for 24% of clostridial disease between 2010 and 2017. *C. perfringens* is one of the most widespread anaerobic pathogens in the world and is a normal intestinal component of healthy mammals including people (Rood and Cole, 1991). Type A and Type D are the common disease-causing types; type B and C rarely cause disease and are associated with necrotic or haemorrhagic enteritis (Lebrun et al, 2010). Type A is associated with diarrhoea and enterotoxaemia due to α toxin in a variety of domesticated species. Type D is implicated in pulpy kidney enterotoxaemia caused by ε toxin release (Radostits et al, 2007; Lebrun et al, 2010).

Cattle enterotoxaemia is associated with an overproduction of locally and systemically acting clostridial toxins causing sudden death, at an almost 100% fatality rate, within minutes to hours (Manteca et al, 2001). While cattle of any age can be affected, well-conditioned suckling or veal calves reared in intensive conditions are most susceptible to the disease (Manteca et al, 2000). Cases occur sporadically and are associated with stressful conditions, particularly dietary change, the day before death (Lebrun et al, 2010). If animals do show clinical signs these are typically non-specific in-

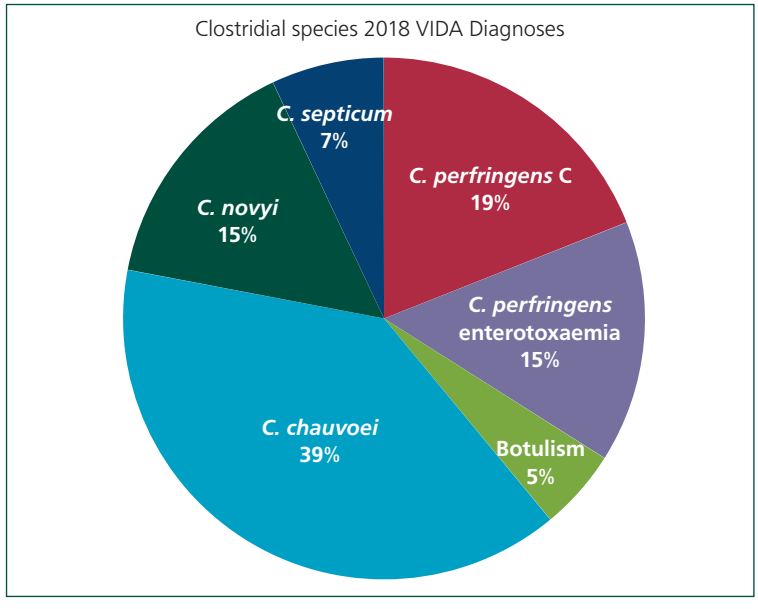

Figure 2. Veterinary Investigation Diagnosis Analysis (VIDA) clostridial diagnoses 2018 (APHA, 2019).

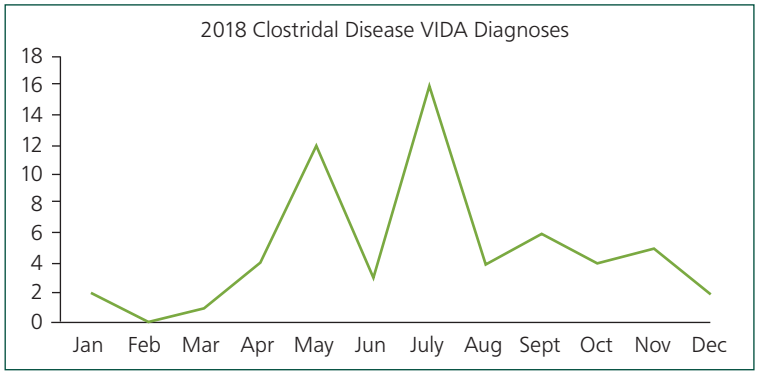

Figure 3. Veterinary Investigation Diagnosis Analysis (VIDA) clostridial disease diagnoses 2018 by month (APHA, 2019).

Table 1. Common clostridial diseases

Disease	Causative pathogen
Blackleg	*Clostridium chauvoei*
Black disease	*Clostridium novyi* type B
Bacillary haemoglobinuria	*Clostridium novyi* type D (previously *C. haemolyticum)*
Pulpy kidney	*Clostridium perfringens* type D
Enterotoxaemia	*Clostridium perfringens* type A *Clostridium perfringens* type D
False blackleg	*Clostridium novyi* *Clostridium septicum* *Clostridium sordellii*
Botulism	*Clostridium botulinum*
Gas gangrene (malignant oedema)	*Clostridium septicum* *Clostridium sordellii* *Clostridium chauvoei* *Clostridium novyi* *Clostridium perfringens* type A
Abomasitis	*Clostridium sordellii*
Tetanus	*Clostridium tetani*

cluding: depression, diarrhoea, abdominal pain or colic (Radostits et al, 2007), while type D can be also associated with neurological signs such as head pressing (APHA, 2017). For type A, penicillin therapy may be attempted, but as the disease for all strains is predominately per-acute, treatment is usually impossible.

Field cases of enterotoxaemia are difficult to confirm due to the commensal nature of *C. perfringens*, but small intestinal colony counts will be high (Manteca et al, 2001). *C. perfringens* type A is associated with haemorrhagic and segmental enteritis as well as mucosal ulceration (Manteca et al, 2001). Despite *C. perfringens* type D being referred to as 'pulpy kidney', friable nephrotic lesions are not always present. Lungs and intestines are frequently oedematous, while prominent haemorrhages including those surrounding the brainstem are present in some cases (APHA, 2017). Epsilon toxin is not identified in all cases meaning that brain histopathology showing focal symmetrical encephalomalacia is often required (APHA, 2010; 2017).

C. novyi

C. novyi accounts for one fifth of clostridial diagnoses and is implicated in a number of disease syndromes, most notably *C. novyi* type B in necrotic hepatitis (black disease) and *C. novyi* type D in bacillary haemoglobinuria. Both diseases are associated with liver damage which can often be caused by a *Fasciola hepatica* burden (Radostits et al, 2007; Navarro et al, 2016). Post-mortem research finds no evidence of fluke infestation or other causes of liver damage such as ruminitis or liver biopsies (Olander et al, 1966; Janzen et al, 1981; Navarro et al, 2017) suggesting another mechanism may also be involved. The likely route of infection involves ingestion of spores that remain latent in the liver until anaerobic conditions occur.

Black disease is often seen during the late summer and into the winter as is expected for a disease associated with the migration of immature fluke. Alpha toxin appears to be the pathogenic factor which causes liver necrosis (Navarro and Uzal, 2016). Cattle are mostly found dead with no warning, but clinical signs are non-specific and include constipation, recumbency, lethargy, inappetence, tachycardia and tachypnoea (Navarro and Uzal, 2016). Penicillin treatment is rarely effective due to the advanced toxin damage to the liver.

Bacillary haemoglobinuria is commonly seen in the same time period as black disease due to also being associated with liver damage. Large quantities of beta toxin are released on *C. novyi* type D proliferation in the anaerobic areas left by trematode migration which causes haemolysis (Navarro et al, 2016). As with black disease cattle are often found dead but may also show inappetence, reduced rumination, dark red urine and recumbency. Death will occur rapidly unless penicillin treatment starts prior to excessive liver damage — case reports suggest recovery can occur even if animals show severe anaemia (Shinozuka et al, 2011).

Post-mortem examination shows liver necrosis for both presentations along with thickened bile ducts or the presence of trematodes (APHA, 2010). Black disease is associated with dark peritoneal and pleural fluids that pool ventrally and give the disease its name (Navarro and Uzal, 2016) as well as rapid autolysis. Bacillary haemoglobinuria is associated with the pathological changes associated with haemolysis such as jaundice, dark kidneys and petechiation throughout the body (Navarro et al, 2016). Identification of *C. novyi* in the liver does not guarantee definitive diagnosis as spores can be present in low numbers in healthy animals meaning that positive culture, FAT, polymerase chain reaction (PCR) or immunohistochemistry (IHC) must be associated with clinical signs or pathological findings (Navarro et al, 2016).

C. botulinum

Botulism in cattle is associated with the ingestion of botulinum neurotoxins which are found in standing water and rotting or contaminated feed, particularly with avian carcasses or poultry litter (Le Maréchal et al, 2016). Cattle may be found dead but more commonly a progressive flaccid paralysis is observed (Mayhew, 2009). This starts with a reluctance to move while the animal remains bright, followed by hindlimb and forelimb weakness, difficulty breathing, recumbency, hypersalivation and protrusion of the tongue (Guizelini et al, 2019) — animals are frequently euthanased on welfare grounds. Unlike the previously discussed clostridial diseases botulism may be associated with large outbreaks with morbidity rates of around 65% and mortality rates of 99.1% (Guizelini et al, 2019).

Diagnosis using post mortem examination is challenging as no gross or histopathological findings are pathognomic and the definitive test involves a mouse bioassay (Sebald and Petit, 1994) despite having a low sensitivity — in one study only three of 60 (5%) samples were positive (Guizelini et al, 2019) — which may be linked to the high susceptibility of cattle to botulinum toxin (Galey et al, 2000). Treatment requires botulinum antitoxin during initial infection as treatment will be ineffective once the toxin binds to the neuromuscular junction (Le Maréchal et al, 2016). The author has experience of treating an outbreak of presumed botulism in a dairy herd with high doses of penicillin (Ultrapen LA, Norbrook)

with only three out of 40 recumbent animals recovering (*Figure 4*) — self-resolution will rarely occur, so it is difficult to determine the impact of penicillin in these cows.

Clostridium septicum

Gas gangrene (or malignant oedema) is caused by several clostridial agents (see *Table 1*), particularly *C. septicum* (Silva et al, 2016). This generally enters through a skin wound such as those caused by castration, contaminated needles or traumatic calvings, although as the most aero-tolerant clostridial species it does not require tissue trauma (Stevens et al, 1990). Clinical signs include pyrexia, swelling, subcutaneous emphysema and oedema of the affected area (*Figure 5*) that generally progresses to the area becoming cold and pain free with death occurring within 24 hours (Odani et al, 2009; Silva et al, 2016). The common gross pathological findings are diffuse haemorrhagic and gelatinous sub-cutaneous oedema and emphysema. If the muscles are affected they will appear dark red, grey or blue (Silva et al, 2016). For cases such as gangrenous mastitis a clearly marked line will separate the mastitic area from healthy skin (Silva et al, 2016). If cases are detected early then treatment with penicillin combined with supportive therapy can be considered, but mortality rates of over 50% have been reported even with treatment (Silva et al, 2016).

Clostridium sordellii

Abomasitis is most frequently associated with *C. perfringens* type A (see above), but *C. sordellii* may also be identified as a cause of this poorly understood disease (Prescott et al, 2016). Risk factors include ingestion of large amounts of fermentable carbohydrates, poor hygiene, feeding large amounts of milk at incorrect temperatures or other practices that may affect abomasal function (APHA, 2018). Clinical signs include abomasal bloat, severe pain and ulceration, as well as depression and diarrhoea. Disease can occur concurrently with clostridial enteritis or, if the ulcers erode, with peritonitis (Glenn Songer and Miskimins, 2005; Prescott et al, 2016). Affected calves may simply be found dead, especially where *C. sordellii* is implicated. At post-mortem examination the abomasum will be distended and may contain clotted milk, the walls will be oedematous and emphysematous and the mucosa is also haemorrhagic (Glenn Songer and Miskimins, 2005; Prescott et al, 2016). Penicillin is indicated for calves demonstrating early signs but is frequently unrewarding (Marshall, 2009).

Clostridium tetani

Tetanus is the least diagnosed clostridial disease of cattle; it is mainly associated with puncture wounds but has also been identified after tail docking, ring or surgical castration or ear tagging (Das et al, 2011; Pugh and Baird, 2012). Unlike *C. chauvoei* or *C. septicum* there is a long incubation period of up to a fortnight after which the neurotoxins will cause muscle rigidity and spastic paralysis (Wright, 2016). Clinical signs include hyperaesthesia, convulsions, inability to eat, progressive tetany of skeletal muscles and death due to asphyxia within a week if the animal is not euthanased before this point (Wright, 2016; Lotfollahzadeh et al, 2019). Post-mortem examination is generally unrewarding meaning that diagnosis is based on history and clinical signs; if the wound is

Figure 4. Treated botulism cattle.

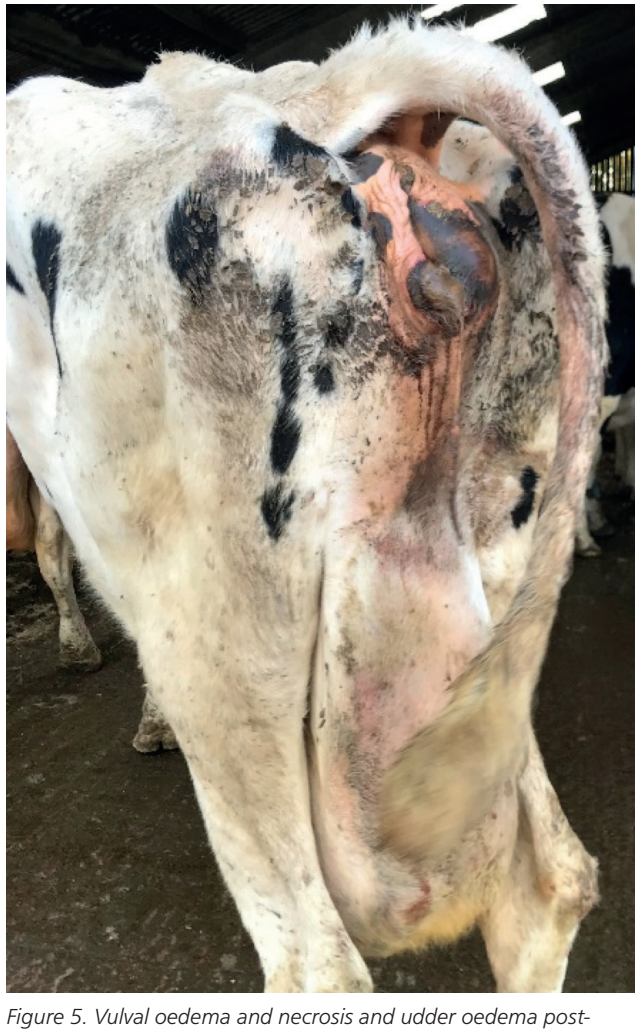

Figure 5. Vulval oedema and necrosis and udder oedema post-calving.

Table 2. Clostridial vaccines

Vaccine	*C. chauvoei*	*C. novyi* type B toxoid	*C. novyi* type D (haemolyticum) toxoid	*C. perfringens* A toxoid	*C. perfringens* D toxoid	*C. perfringens* B and C toxoid	*C. botulinum* type C and D toxoid	*C. septicum* toxoid	*C. sordellii* toxoid	*C. tetani* toxoid
Blackleg (Zoetis)	√	x	x	x	x	x	X	x	x	x
Bravoxin 10 (MSD)	√	√	√	√	√	√	X	√	√	√
Covexin 8 (Zoetis)	√	√	√	x	√	√	X	√	x	√
Covexin 10 (Zoetis)	√	√	√	√	√	√	X	√	√	√
Tribovax T (MSD)	√	√	√	x	x	x	X	√	x	√
Available under 'special treatment certification' by application to the VMD										
Longrange Botulinum (Zoetis)	x	x	x	x	x	x	√	x	x	x
Singvac (Virbac)	x	x	x	x	x	x	√	x	x	x

present a swab should be taken to attempt to culture Gram-positive rods with terminal spores, drumstick or tennis racquet appearance (Popoff, 2016). Treatment with anti-toxin and penicillin along with supportive therapy can be effective if started early or even prophylactically; cattle should be kept in the dark during treatment to reduce hyperaesthesia (Wright, 2016).

Control and prevention

Given that treating clostridial disease is often hopeless, or impossible, preventing infection from occurring is the key to control. The cost of animal losses or even prolonged illness can be high while vaccination is cheap — typically less than £1 per injection for multivalent vaccines or around £0.40 for blackleg vaccine. Licensed vaccines are outlined in *Table 2*; there are no licensed botulism vaccines in the UK so options for import are described. It is important that farmers do not simply vaccinate without also considering management changes. Botulism risk can be mitigated by not spreading poultry litter on pasture intended for cattle grazing; abomasitis risk can be reduced by feeding milk correctly, while blackleg and gas gangrene risk can be lessened by using clean needles and otherwise reducing the chances of trauma and tissue damage. Farmer education is also important as treatment will be most successful if disease is identified quickly. All sudden deaths should be reported and, after anthrax has been ruled out, post-mortem examination is advisable to determine the cause and consider strategies for preventing further losses such as removal of cattle from affected fields.

Conclusion

Clostridial disease is a not insignificant cause of morbidity and mortality in cattle. *C. chauvoei* and *C. perfringens* are the main clostridial causes of death and can be diagnosed on post-mortem examination. Definitive identification of toxins in the rarer forms can be challenging so better diagnosis of botulism and tetanus should be a focus of clostridial research in the future. Additionally, methods should be considered to improve detection of *C. perfringens* ε toxin in pulpy kidney, as should finding the inciting cause of black disease and bacillary haemoglobinuria where fasciolosis is not found. Due to the ubiquitous nature of clostridia cattle are most at risk during the grazing season, meaning that control and prevention of disease should be particularly targeted at this time of year. LS

KEY POINTS

- Around 100 species of clostridia are found in soil and vegetation as well as being present as commensals in the guts of healthy cattle with a handful indicated in disease.
- Disease is often associated with a change in conditions such as rough handling, trauma or dietary changes allowing proliferation of bacteria and release of toxins.
- The most commonly diagnosed clostridium in cattle are *Clostridium chauvoei* (36%), *Clostridium novyi* (18%) and *Clostridium perfringens* D (16%) with an increase in disease in the summer grazing period.
- Blackleg is the most common clostridial disease, it affects younger beef animals causing sudden death or lameness on a specific limb although cardiac lesions can also be present.
- *C. novyi* diseases are associated with liver damage and necrosis, typically cattle are found dead due to hepatitis (black disease) or haemolysis (bacillary haemoglobinuria).
- *C. perfringens* type A and D cause enterotoxaemia and pulpy kidney enterotoxaemia which have a 100% fatality rate and are associated with stressful conditions such as dietary change.
- A number of cost effective clostridial vaccines are available for cattle and should be considered in conjunction with good pasture management.

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