Clostridial diseases in cattle and sheep

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Abstract

A brief summary of common *Clostridium* sp. affecting cattle and sheep is provided. New insights and unusual presentations of disease entities caused by *C. botulinum*, *C. chauvoei*, *C. sordellii*, *C. difficile* and *C. perfringens*, such as fatal abomasitis in calves and lambs, are highlighted.

Introduction

A wide variety of clostridia pathogens may affect cattle and sheep. An overview of the common disease entities is given in Table 1 and further details may be found in contemporary textbooks on large animal veterinary medicine, such as Radostits and others (2006). This paper will highlight some more unusual presentations, potentially novel disease entities, and aspects of clinical management, including diagnosis.

Clostridial diseases have several features in common: pathogenesis caused by toxins; a necrotising, and often haemorrhagic, pathology; rapid progression and death; and although potentially ubiquitous, typically confined to small regional areas or individual farms where soil or feed has become contaminated with pathogen spores. Risk factors include processes that reduce oxygen tension in, or trauma to, tissues (bruising, injections, dystocia, surgical tissue trauma, liver fluke). Most *Clostridium* species can be found in small numbers in the intestine of healthy ruminants (and other mammals), and some are post-mortem invaders. Definite diagnosis, therefore, relies on evidence of toxins or immune-system reaction (e.g. fluorescent antibody test). In cases of *C. perfringens* enterotoxaemia, studies have looked at the diagnostic value of localised overgrowth (colony forming units per millilitre of intestinal contents), with ambiguous results (Lebrun and others, 2010; Uzal, 2004; Valgaeren and others, 2013).

Treatment of individual cases is often unrewarding. There is little antimicrobial resistance and so, in theory, any product with an anaerobe spectrum is suitable, (e.g. procaine penicillin at above label dose of 25,000 – 40,000 IU per kg BW, or ceftiofur). However, the rapid disease process limits the usefulness of antibiosis, because it will not reverse the effect of toxins once bound. The often per-acute nature also limits the use of serotherapy. However, both treatment modalities may be useful in cohort animals not yet showing overt clinical signs. Antimicrobials must be used with care in botulism cases, as several potentiate the neuro-muscular block (e.g. penicillin, oxytetracyline). Botulism cases may benefit from intravenous administration of transmitter release enhancers (e.g. guanidine hydrochloride), if licensed. Antitoxins are effective against bound toxins but, currently, only tetanus antitoxin is available. Force-feeding is often necessary in patients affected by clostridial diseases with neurotoxic effects (e.g. botulism, tetanus), and the creation of a rumen fistula aids this. Further nursing care should include a low-stimulant environment.

Vaccines for cattle and sheep are available in the UK, varying in the species of *Clostridium* included, as well as the *C. perfringens* toxoids.

New aspects and unusual presentations to highlight with regard to selected species of *Clostridium* include:

Clostridium botulinum

- Substantially more incidents of botulism were observed in cattle and sheep by AHVLA between 2003 – 2009 than in the 1990's (187 incidents from 2003 – 2009 compared to 22 between 1990-2000; Payne and others, 2011). In addition, type D toxin was involved in a much higher proportion of cases than previously observed.

- Typical outbreaks involve a relatively small number of animals (up to 10% of group). However, high losses can occur. In one such example, in spring 2014 AHVLA dealt with an outbreak of botulism in a Welsh dairy herd that resulted in the death of a large number of animals (around 175 cattle out of 1200 over one week). The cause was suspected to be ingestion of toxin from a decomposing animal carcass that was accidentally incorporated in the silage clamp. Possibly contributing factor was that the clamp was opened after only three weeks of ensiling.

  Periodic reviews on the public health risk posed by botulism toxin C and D have so far concluded that there is no need for compulsory restriction of meat or milk from affected cattle herds entering the food chain (ACMSF, 2006). A follow-on report in 2007 came to the same conclusion with regard to sheep and goat milk and meat. However, a voluntary restriction of clinically affected cattle is usually followed, remaining in place for 18 days after recovery.

- Field reports from Denmark describe a clinical picture that may reflect early or mild infection with *C. botulinum* (J. Erri, 2014, personal communication). Cows demonstrate altered drinking behaviour, raising their heads after every sip, possibly suggesting a swallowing inability. In the herds observed, water intake is markedly reduced (60-70 litres per head, daily milk yield of about 30 litres), with clinical signs of dehydration. Other clinical signs in these herds include flaccid tails (resulting in injury in herds using automatic scrapers), recumbency in cows two to three months in milk, and sudden death. After vaccinating against *C. botulinum*, water consumption was observed to rise by 30-40%.

- Visceral botulism has been postulated as a new clinical presentation in cattle by German colleagues (Böhnel and others, 2001). Especially cattle in the peri-partum period are affected, with the most prominent sign being disturbances of the digestive tract (indigestion, with constipation alternating with diarrhoea). Other signs include paralysis, acute laminitis, udder, limb and ventral oedema, increased respiratory effort, and venous engorgement and pulsation. Effects of the botulinum toxin on the autonomous nervous system are recognised in humans, and *C. botulinum* type C is suspected in equine grass sickness.

- Diagnostic advancements: Field diagnosis relies on the presence of clinical signs, with several animals affected and exclusion of differential diagnoses. Mouse inoculation is the traditional laboratory test to confirm. Because not all cases are positive on the mouse test, and with a drive to reduce the number of laboratory animals in testing, alternative confirmatory tests have been explored. Performing a single antibody ELISA was found unhelpful in the diagnosis of type D botulism in both clinically affected and in-contact cattle (Mawhinney and others, 2012).

Clostridium chauvoei

- The most common, and best known, manifestation of this pathogen is a necrotising myositis with haemorrhages into muscle and connective tissue. The colloquial name 'blackleg' is somewhat misleading, as any skeletal muscle group may be involved. *C. chauvoei* may occasionally cause meningeal lesions, as well as present as cardiac form with heart muscle myositis and fibrinous pericarditis. A large proportion of reports of the cardiac form involve suckling calves. A more unusual presentation involves necrotising lesions of the tongue and intestine (Harwood and others, 2007)

- A report of a large-scale outbreak in Norwegian beef animals highlights that the disease is not confined to animals at pasture (Groseth and others, 2011). Substantial soil contamination of silage was the suggested source of the clostridia spores in this outbreak.

- Vaccination is a commonly-used tool to control blackleg. A recent evidence-based review of vaccination against *C. chauvoei* found only few studies investigating the efficacy of vaccination to prevent disease and mortality (Uzal, 2012). However, protection appeared to be close to 100% in the three studies using experimental challenge. Only one paper studied the length of protection, finding that full protection lasted six months, reducing to 50% by twelve months after vaccination. The review found no publications comparing efficacy based on age at vaccination, number of doses, or monovalent versus polyvalent vaccines.

C. sordellii

Compared to some other clostridia species, *C. sordellii* relatively rarely causes substantial disease problems, but it must be remembered that only the 10-in-1 vaccines cover this pathogen.

- A fatal abomasitis is recognised in young lambs and calves caused by this pathogen (SAC 2012). Typically, just two to three animals out of a larger group are affected. Unsanitary milk feeding and high exposure to faecel material are risk factors. *Sarcina sp.* can cause a similar abomasitis with similar risk factors (Edwards and others, 2008), as can *C. perfringens* in calves (Van Kruiningen and others, 2009).
- *C. sordellii* may also be involved in cases of malignant oedema, on its own or in combination with other clostridial pathogens (including *C. septicum, C. chauvoei, C. novyi, C. perfringens* type A). When associated with unhygienic injection techniques (or contamination of the product used), fatalities in a substantial number of treated animals may result, such as in the case report by Costa and others (2007), where several dozen sheep out of a flock of 1000 developed malignant oedema around the injection site of a clostridial vaccine. The same needle had been used for the entire flock.

C. difficile

- *C. difficile* causes a serious infection in humans and the number of cases is increasing. Traditional risk factors have been antibiotic treatment and a stay in hospital, but infections originating in the community are now recognised more frequently. This has prompted a closer look at farm animals as potential source of the infection in humans.
  Studies from Switzerland (cattle and goats; Romano and others, 2012) and Australia (sheep; Knight and Riley, 2013) come to the similar conclusion that the overall carriage of this pathogen is low in live animals, with prevalence of positive faecal samples in adults of 0.5 % (sheep) and 1.5 % (cattle), with higher levels in youngstock of 6.5% (lambs) to 12.7 % (calves). Samples taken in the farm environment had a prevalence of 21 %. While the pathogen was found, the researchers conclude that these levels are unlikely to be a major risk for human infections.

C. perfringens

- This pathogen continues to receive attention because of the potent toxins it is capable of producing and its role in food poisoning. It remains a serious pathogen in ruminants. Advances in understanding toxin actions, diagnosis, clinical veterinary presentation and prophylaxis are summarised in recent reviews (Lebrun and others, 2010; Uzal, 2004 and 2014).
- *C. perfringens* Type A is implicated in necrotic enteritis of calves and haemorrhagic bowel syndrome in dairy cattle (also referred to as Jejunal haemorrhagic syndrome; Elhanafy, 2013). Just as with other *Clostridium* sp., this pathogen is commonly present in small numbers in the intestine of healthy animals. The history of patients often reveals potentially predisposing factors that may favour overgrowth of the pathogen, such as concurrent other GI-tract infections (e.g. *E. coli* in calves), carbohydrate-rich / fibre-poor diets, or recent stress events. Affected dairy cows initially show rather non-specific clinical signs, such as reduced food intake, depression, and reduced rumen motility and faecal production, common to a range of differential diagnosis affecting early-lactation animals.
- In small ruminants, *C. perfringens* Type B, C and D are regarded as main pathogens. However, Type A is being recognised as a potential cause of mortality in lambs and kids and some case reports suggest that the toxin beta-2 may be responsible, protection against which is currently not afforded by the commercially available vaccines (Greco and others, 2005). Type A should be considered especially in cases of apparent vaccine failure.
- Type E is regarded as an infrequent cause of fatal enterotoxaemia in calves (Songer and Miskimmins, 2004) and lambs, and has now also been described in adult beef cows in Argentina (Redondo and others, 2013). Current vaccines do not afford meaningful protection against Type E.
- *C.perfringens* may cause gangrenous mastitis in ewes, although is far less common than *Staphylococcus aureus* in such cases (Mork and others, 2007).

Table 1: Overview of clostridial infections recognised in cattle and sheep.

Pathogen	Disease name	Aetiology	Main clinical features	Control
C. botulinum	Botulism	1) Ingestion of pre-formed toxin, e.g. ensiled animal carcasses, particularly where chicken litter applied to fields. Also carcass decomposing in water troughs 2) Gastro-intestinal infection with pathogen. Decaying plant material (e.g. big-bale silage), brewer's / high moisture grains are a risk. 3) Type C and D toxin most commonly involved in cattle and sheep disease.	Neurotoxin causes flaccid paralysis, progressive; leading to recumbency and death after several days. In sheep, staggering gait, stiffness and head bobbing may be seen prior to flaccid paralysis.	Avoid chicken litter on pasture land, or other direct or close proximity contact. Check fields for animal carcasses prior to cutting. Ensile for at least one month to ensure sufficient fermentation. Vaccination only under VMD Special Treatment Licence. Antitoxin not available in the UK. Antibiotics of limited use once the toxin is bound, and may enhance the neuro-muscular block (see main text: introduction)
C. chauvoei	Blackleg	1) Trauma to affected area. 2) Iatrogenic: injection site related 3) Ingestion of spores	Myositis affecting skeletal muscles, with soft tissue swelling and severe lameness. Later on cold extremities with reduced sensation. Cases also show lethargy, anorexia and sometimes pyrexia. Rapid deterioration and death. May also affect heart, meninges, tongue and intestine, with acute haemorrhage and necrosis.	High-dose penicillin in acute cases or prophylactic to cohorts. Vaccination available. Spores may be brought onto farm with top soil or conserved forages.
C. haemolyticum	Bacillary haemoglobinuria	Ingestion of infected material. Summer and autumn months, on irrigated (natural or artificial) or previously flooded pastures. May be present on hay.	Pyrexia, abdominal pain, inappetence, rumen stasis, toxaemia, haemoglobinuria. Abortion in surviving females is common.	Treatment with antimicrobials, fluid therapy, blood transfusion. Vaccination, timed for risk period.
C. novyi Type B	Black disease	Associated with cereal-rich diets and liver fluke. Localised areas, more common in sheep than cattle, and typically adults in good condition.	Seasonal in line migration of immature fluke. Infectious necrotising hepatitis. Pyrexia; blood clots rapidly; dull, depressed, reluctant to move. Reduced bowel sounds, abdominal pain over liver	High-dose antibiotics. Vaccination and liver fluke control.
C. perfringens Type A	1) HBS[1] 2) Enterotoxaemia in cattle 3) Malignant oedema	1) & 2): intensively managed cattle; Enterotoxaemia typically affects young and well-performing animals; fibre-poor diets and stress are risk factors 3) usually in combination with other Clostridium spp.	Sudden death, signs of toxaemia with multiple organ failure, haemorrhagic enteritis (small intestine)	Vaccine: must contain alpha-, beta- and epsilon toxoid. Antibiosis or serotherapy: often disease too acute Probiotics: empirical suggestion at times of stress or diet change

[1] Haemorrhagic bowel syndrome, also referred to as Jejunal haemorrhagic syndrome

Type B	Lamb dysentery, Calf enterotoxaemia	Lambs are affected at few days old. Proliferation of pathogen in gut, toxin release leads to enterotoxaemia.	Haemorrhagic enteritis with diarrhoea Abdominal pain, tenesmus, lack of suckling. Occasionally causes brain oedema, with neurological signs.	
Type C	Struck (sheep), Calf enterotoxaemia	Proliferation of pathogen in gut, toxin release leads to enterotoxaemia	Necrotising enteritis with abdominal pain, bloody diarrhoea; particularly young animals	
Type D	Pulpy kidney disease	Vascular permeability increases, leading to oedema and excess free fluid; sheep more susceptible than cattle. Up to and shortly after weaning. Typically in good condition, on good nutritional plane.	Oedema of brain, lung, hydropericardium; dyspnoea, neurological signs with opisthotonus, paddling, blindness, convulsions. Hyperglycaemia and glycosuria.	Vaccination, feed restriction. Disease progression typically too fast for treatment.
Type E	Enterotoxaemia	Lambs and calves		
C. piliforme	Tyzzer's Disease	Entero-hepatic infection. Only occasionally reported in cattle (young calves) and sheep.	Necrotising hepatitis. Lethargy, diarrhoea, illthrift, pyrexia, jaundice, shock.	Antibiosis and supportive therapy.
C. septicum	1) Malignant oedema 2) Braxy	1) Often in association with other *Clostridium* species (e.g. *C novyi, C. sordellii, C. chauvoei*). Pathogen or spores typically enter at site of tissue injury, including injection / blood sampling sites 2) Cold weather (frost and snow). Typically young / yearling sheep.	1) Initially hot, painful swelling and oedema at site of injury. Later cold and desensitised. Crepitus due to subcutaneous emphysema. 2) Abomasitis	1) High-dose antibiotics. Debate whether opening affected area to increase oxygen exposure is helpful. Observing injection hygiene, including drug bottles. 2) None valuable.
C. sordellii		Environmental pathogen, commonly found in cereal or soil. Hardy, e.g. tolerates very low pH (>1)	1) Fatal abomasitis in young lambs, with haemorrhage oedema, congestion, emphysema. 2) Malignant oedema, often in combination with other clostridial pathogens (e.g. *C. septicum*)	Abomasitis: Risk factors appear to include supplementary milk feeding and unhygienic conditions with exposure to faecal material
C. tetani	Tetanus	1) Entry through wounds (incl. surgical) or mucous membranes (e.g. at parturition). 2) Contaminated injectable solutions Neurotoxin advances via nerve trunks to CNS.	Muscle stiffness and rigidity, with failure of respiratory muscles eventually causing death. Signs advance from point of entry. Rumen tympany, raised tailhead, immobile ears, lock jaw, hyperaesthesia (light, noise) and lateral recumbency with opisthotonus and extended limbs are commonly observed.	Tetanus antitoxin, high-dose penicillin or ceftiofur, muscle relaxant (e.g. opoids; if licensed), force feeding, dark and quiet environment. Vaccination prior to routine procedures (castration, docking, ear tagging), antibiosis at time of procedure. Good hygiene during routine procedures and in parturition environment.

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