Caseous Lymphadenitis (CLA) in Sheep

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Key points

- Caseous lymphadenitis (CLA) is a chronic bacterial disease of sheep and goats, characterised by abscess development in the lymph nodes and other tissues.

- The disease is increasing in prevalence in the UK, resulting in welfare issues and economic losses due to ill thrift and carcase trimming or (in severe cases) carcass condemnation at abattoir. CLA may also increase susceptibility to other infections.

- The disease is caused by the bacterium *Corynebacterium pseudotuberculosis*; this organism is highly infectious and is able to survive for long periods of time in the environment, acting as a source of infection for other animals.

- Although not often encountered in the UK, the CLA-causing organism can also cause infections in humans. Care is required to minimise exposure to pus. Infection is caused by the bacterium gaining entry to the animal through scratches or cuts in the skin; therefore, shearing/clipping can be a risk factor for this disease.

- Abscesses in the lymph nodes often present as visible lumps around the head and neck region. If these rupture, a cheesy pus is released, containing millions of bacteria, which is the main source of infection for other sheep/goats.

- The infection can also spread to other organs of the animal (e.g. liver and lungs). In certain cases, abscesses may interfere with rumination, leading to chronic weight loss.

- According to some researchers, animals with CLA lesions in the lung may spread the infection through coughing.

- Antibiotic treatment is ineffective as the bacteria are 'protected' within the lymph node abscesses, which become surrounded by a tough fibrous capsule.

- Sheep or goats displaying chronic abscesses should be isolated and subjected to immediate veterinary and bacteriological investigation.

- Control measures should include strict biosecurity measures including: quarantining (of both animals and premises), screening of imported animals, the cull of infected animals and application of rigorous hygiene procedures. Shearing equipment should be dipped in strong disinfectant or chlorine bleach before and after use. Older animals should be handled last during routine procedures.
Introduction

Caseous lymphadenitis (CLA) is a chronic bacterial infection that results in abscess development in lymph nodes and other tissues. The disease mainly affects sheep and goats and is generally reported to have been introduced into the UK on a single occasion in the early 1990’s; however, anecdotal reports, which are supported to an extent by available scientific data, suggest that CLA may have been imported on more than one occasion. Irrespective of the ‘when’ and ‘where’, CLA is now considered to be endemic within the national flock. The economic impact of the disease is not well-defined, although, as CLA becomes more prevalent, it is believed that the impact will become more measurable.

CLA is found in most parts of the world where small ruminants are farmed, including Europe, Australasia, North and South America, Africa, and the Middle East. Prevalence of infection increases with age and is more common in sheep kept under intensive management conditions. Affected animals often have visible lumps (Fig 1) in the ‘superficial’ lymph nodes, i.e. those lymph nodes which can be assessed from the outside of the animal; although not all animals with CLA have visible signs on the outside. Most frequently in the UK, lymph node abscesses tend to be associated with the head and neck region. Abscesses in this area can press on the oesophagus preventing normal rumination, leading to weight loss. Although CLA rarely, if ever, manifests as an acute infection, it is generally held that infected animals remain infected for their entire lives, and as such sheep and goat producers must apply strict biosecurity measures to help prevent and control the disease.

Figure 1: Sheep with visible lymph node abscess
Q1. What causes CLA?

CLA is caused by an infection with the bacterium, Corynebacterium pseudotuberculosis. This bacterium can survive for months in cold and damp environments, and therefore may act as a source of infection for other livestock. C. pseudotuberculosis usually gets into host animals through cuts and abrasions to the skin, which arise as a direct result of many different management practices within the flock, such as shearing/clipping, tagging, notching, docking, castration, vaccination, or rubbing against abrasive surfaces.

Why is C. pseudotuberculosis so virulent?

Bacteria are able to produce a variety of different molecules that contribute to the ability to cause disease. It is generally thought that the presence of a waxy coat on the surface of C. pseudotuberculosis cells helps it survive in the more hostile environments outside the animal host. This outer coat is also considered to contribute to toxic effects experienced by the host animal during infection. Research at Moredun has focused on these bacterial “virulence factors” as they are very important in understanding how C. pseudotuberculosis causes infection and disease, and hence informs strategies for developing treatment options. One of these factors is the potent toxin, phospholipase D (PLD), which is important during the infection process, and therefore has been a key target in the development of new CLA diagnostics; because animals with CLA produce antibodies in their blood against PLD, this antibody can be measured and used as a means of diagnosing the disease.

Q2. How does infection cause disease?

When a bacterium gains entry to an animal through the skin, immune cells within the blood ‘capture’ the bacterial cell and transport it to a lymph node. Most bacteria are killed during this process, which often helps the animal to develop immunity against re-infection; however, C. pseudotuberculosis is able to survive this process. Therefore, when it reaches the lymph node it is still alive, and is able to establish a site of infection. In the same way, these ‘captured’ bacteria are unwittingly transported throughout the body by the immune system, leading to multiple sites of infection (Fig 2).
Figure 2: The positions of the superficial lymph nodes where CLA abscesses can be visualised or felt on the animal’s exterior

Within the infected lymph nodes, the on-going battle between the bacteria and the immune response trying to protect the animal, results in the formation of tiny pus-filled abscesses (Fig 3). These gradually get bigger and bigger, and are often visible on the exterior of the animal if the infection is within superficial lymph nodes that can be seen on the skin; the lesions may appear as areas of marked swelling, frequently accompanied by the loss of overlying hair.

Figure 3: Pus filled abscess on lymph node
Often, during the continued growth of CLA lesions, there is a further spread of the infecting organism throughout the host animal, giving rise to new areas of infection at other sites within the body.

CLA lesions occur most frequently within the lymph nodes; however, other tissues may also be affected. The disease can spread to the internal lymph nodes and other organs such as the liver, kidneys or udder, and more rarely the heart, testes, scrotum, uterus, joints, brain and spinal cord. However, the internal site most frequently affected in sheep is the lung (Fig 4).

Figure 4: Lung airway lesions

Q3. How do animals become infected?

The most significant route of transmission of *C. pseudotuberculosis* is through the rupturing of infected lymph node abscesses leading to the discharge of pus. There are millions of infectious bacteria in each gram of pus and therefore affected animals can act as a source of infection for other naïve animals and may also contaminate the immediate environment with infectious bacteria. The organism may gain entry into naïve animals through cuts or abrasions of the skin.

In some countries, particularly Australia, shearing is considered a major cause of *C. pseudotuberculosis* transmission and this is believed to be frequently caused by inappropriate disinfection of shearing equipment between sheep.

There is a suggestion that animals with CLA may be able to spread infection through coughing up of infectious material resulting from the rupture of abscesses within the lungs. However, rather than infection occurring as a result of naïve animals breathing
in the infectious material, it is more likely that, as with ruptured lymph node lesions, 
the pus causes contamination of the immediate environment. Evidence for this 
theory is based upon observations in Australia, where the incidence of CLA within 
groups of sheep increased rapidly in the absence of any obvious external lesions. 
Certainly, *C. pseudotuberculosis* has been isolated from the trachea of infected sheep, 
proving that lesions within the lungs do rupture and release live bacteria.

**Q4. How do you diagnose CLA?**

1. **Direct detection of bacteria in pus samples**

   In live animals, pus samples may be taken from affected superficial lymph node 
   lesions and identified in a diagnostic veterinary laboratory. However, this approach 
could not be used to obtain samples from internal lesions (except after slaughter).

2. **Indirect testing using blood samples to detect specific antibody responses**

   Research conducted between Moredun and SRUC led to the development of a 
blood based test which is designed to detect specific antibodies produced by infected 
animals recognising the phospholipase D (PLD) toxin. This toxin is used by the 
bacteria to help infect the host animal; because it is produced by all isolates of *C. 
pseudotuberculosis*, it is a good target for a diagnostic assay.

   This blood test enables the detection of PLD-specific antibodies which the animals 
will make following infection. Taken together with other factors such as flock history 
and veterinary examination, this diagnostic test helps farmers to get a better idea of 
disease status within their flocks.

   However, due to the nature of *C. pseudotuberculosis* infection, there are periods of 
latency when the bacteria are effectively contained within the thick walled abscesses 
in the animal, and the antibody levels in the blood may drop below detection levels. 
As a result, at any given time there is a possibility that a single animal with CLA will 
appear negative for infection using this test. Therefore, the advice is that the test is 
best to be used on a flock-basis as the infection activity will vary within and between 
animals. In addition, it is recommended to conduct further rounds of flock testing at 
specific intervals to increase the chances of identifying all infected animals within the 
flock.
The current diagnostic test (known as ELITEST CLA) is marketed by MV Diagnostics, and a testing service is provided by SRUC. The test (Fig 5) can be used to help eradicate CLA from your flock, and can also be used to boost biosecurity through screening of bought-in animals.

Figure 5: Diagnostic test - ELITEST CLA

Q5. Can CLA be treated?

Although the CLA-causing organism is susceptible to most antibiotics in laboratory tests, the situation is not the same within an infected animal. This is because during an actual infection, the organism is protected within thick-walled abscesses, and can also 'hide' within cells of the animals' immune system. In order to treat an infection of this type, prolonged administration of a specific cocktail of antibiotics would be required (similar to treatment of tuberculosis in humans).

Unfortunately, no such antibiotics are licensed for use in animals. For this reason, once an animal has been infected with *C. pseudotuberculosis*, it can usually be considered to be infected for life, unless (on rare occasions) the animal's immune system is able to overcome the infection.
Q6. How do I prevent and control CLA?

Through an understanding of how the infection is transmitted and the disease epizootiology, application of good biosecurity and flock management should help to prevent and control CLA.

- **Screening and quarantine of replacement animals**

To minimise the risk of bringing in diseased animals to your farm they should be inspected for any lumps and lesions in the superficial lymph nodes, in particular around the head and neck area. As the lesions may not be visible if they are internal, a blood test may help to determine the disease status of the animal. Try if possible to purchase animals from disease-free flocks. Experimental evidence has shown that CLA lesions may appear up to 2 months after a primary infection, therefore quarantine times should be for at least 2 months, although this is often not practical.

- **Culling of infected animals**

Animals that have been confirmed as having CLA should be culled from the flock as they will act as a reservoir of infection for other animals. Once an animal is infected with *C. pseudotuberculosis* it is considered to be infected for life.

- **Handle older animals last**

The incidence of CLA has been shown to increase with age (due to greater likelihood of exposure), so older animals should be handled last during routine procedures to minimise the risk of spreading infection.

- **De-contamination of the farm environment**

If CLA has been identified within a flock, it is worth remembering that *C. pseudotuberculosis* can persist within the environment, serving as an undetectable means of disease transmission. Pens and sheds can be effectively disinfected with 1 per cent chlorhexidine or calcium hypochlorite, and bedding and topsoil should be removed and the area treated with 20 per cent calcium hypochlorite. In addition, shearing equipment should be dipped in strong disinfectant or chlorine bleach pre- and post-use.
Q7. Is vaccination an option to prevent the disease?

Vaccination to help prevent CLA is an increasingly-attractive option for many sheep farmers. Currently in UK (and Europe), there are no routinely licensed vaccines available to help prevent this disease. “Autogenous vaccines” can be produced by specialist laboratories, and are prepared from bacteria taken from pus samples from affected animals; however, these vaccines can only be used within a specific holding, and are relatively expensive to purchase.

A CLA vaccine, known as Glanvac™ is available in Australia (sold by Zoetis), and permission for emergency use of this product in the UK can be obtained from the Veterinary Medicines Directorate. A considerable body of experimental data exists for Glanvac™; however, this vaccine, which also contains clostridial components, was developed specifically for use within the Australian sheep industry, and there are currently no plans to modify the vaccine and seek registration within the European Union.

As CLA is a relatively slow-spreading disease, the combination of a test-and-cull and vaccination approach would seem to offer the best chance of both eradicating disease from a flock and preventing further infection from outside. However, the current blood test is incompatible with the use of Glanvac™, since the vaccine produces a PLD-specific immune response which shows up as a positive result in blood tests. Producers should bear this in mind when selling on vaccinated animals, since failure to disclose vaccination status can lead to problems if blood testing is later carried out.
It is clear that a diagnostic test and vaccine suitable for concurrent use would offer the sheep farming community the greatest flexibility in dealing with CLA. To this end, scientists at Moredun have been researching innovative approaches to vaccine design and have created a vaccine which allows the differentiation between infected and vaccinated animals.

In addition, MV Diagnostics has developed a new CLA blood-test which further enhances the ability to combine blood-testing with vaccination. The diagnostic test is currently validated for use in goats, and has been adopted by the Norwegian dairy goat sector as a tool for the eradication of CLA. At the time of writing, the test is being validated for use in sheep.

**Moredun Research Focus**

Research at Moredun has determined the relationships between UK *C. pseudotuberculosis* strains and those from across the world. Significantly, all strains have been shown to be highly-related, suggesting that common control measures should be effective. The development of the CLA diagnostic blood-test in conjunction with SRUC provided a powerful tool to allow the identification of animals with CLA; however, increasing prevalence of the disease within the UK has led to a situation whereby a CLA vaccine is increasingly the preferred option. Appraisal of several experimental vaccines has been undertaken, leading to the development of the first CLA vaccine capable of concurrent use with blood-testing. The next steps are to seek a commercial partnership to help make this vaccine available to livestock producers.