

# Iceberg diseases of ewes

Technical manual for vets, consultants and farmers





# Contents

- 3 Introduction
- 4 UK surveillance data on iceberg diseases
- 5 Background to the five iceberg diseases
- 8 Impact of disease
- 10 Investigation and diagnosis
- 15 Test selection
- 17 How to test for Border disease
- 19 How to test for caseous lymphadenitis
- 20 How to test for Maedi Visna
- 21 How to test for ovine Johne's disease
- 22 How to test for ovine pulmonary adenocarcinoma
- 23 Impact on trade and exports
- 24 Control options
- 37 Prevention
- 38 Summary
- 39 Glossary

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# Introduction

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This manual provides a concise reference guide to five infectious diseases of sheep that members of the sheep industry have identified as important: Border disease (BD), caseous lymphadenitis (CLA), Maedi Visna (MV), ovine paratuberculosis or ovine Johne's disease (OJD) and ovine pulmonary adenocarcinoma (OPA). However, awareness of these diseases is low, with a recent survey suggesting fewer than 5% of farmers screen for them routinely.

While the clinical presentation of these production-limiting diseases is mild, difficult to differentiate or occurs very late in the disease process, they often cause inefficiency through subclinical disease. The extent of the problem within a flock can be underestimated because visibly diseased sheep are usually just the tip of the problem, which is why these diseases are sometimes referred to as 'iceberg' diseases. These diseases also share similar issues: none are treatable with antibiotics, interpretation of the tests can be challenging and limited information is known on prevalence.

These diseases must be included in any flock investigation, particularly investigations focusing on thin sheep or poor fertility, but they should be handled carefully. The diagnosis of an iceberg disease on a farm has significant implications in terms of veterinary costs (because of the time and testing), replacement policies and the ability to trade stock. Veterinary advice may be needed to ensure the appropriate test is carried out on an appropriate sample and that results are correctly interpreted before a full diagnosis can be given.

The complex network of sheep movements between breeders in the UK means there are significant challenges in terms of knowing and maintaining health status. This applies to all diseases, but particularly for iceberg diseases because few farmers screen for them. In addition, if they do carry out testing, the tests do not always provide a clear answer.

The aim for the sheep industry is to develop appropriate health-monitoring schemes that help commercial farmers to understand the health status of their flock, while providing greater health assurance for the variety of production-limiting diseases. The responsibility starts with ram breeders and sellers of replacement ewes to ensure animals are of a known health status. However, demand also needs to come from the purchaser and, sadly, that generally only happens once they have experienced an issue.



**Lis King**  
AHDB Sheep Scientist

# UK surveillance data

In the UK, diagnoses of production-limiting and emerging diseases are recorded through subsidised submissions to regional diagnostic centres run by the Animal and Plant Health Agency (APHA) or Scotland's Rural College (SRUC) Veterinary Services. The data is not a true representation of prevalence because the cost of testing means that not all suspected cases are submitted to APHA or SRUC. Conclusions need to be drawn with caution, particularly as the submissions vary with the season, year and across the centres.

Figures 1–3 illustrate the variation in the submission and diagnosis rate of iceberg diseases over time and by region. It would appear that vets and farmers have become more willing to test for these diseases over the last decade, particularly for Border disease and Johne's, possibly in response to an increase in the number showing symptoms.

The number of ovine Johne's disease diagnoses has increased over the past decade. Johne's is potentially the most significant disease threat of the five iceberg diseases.

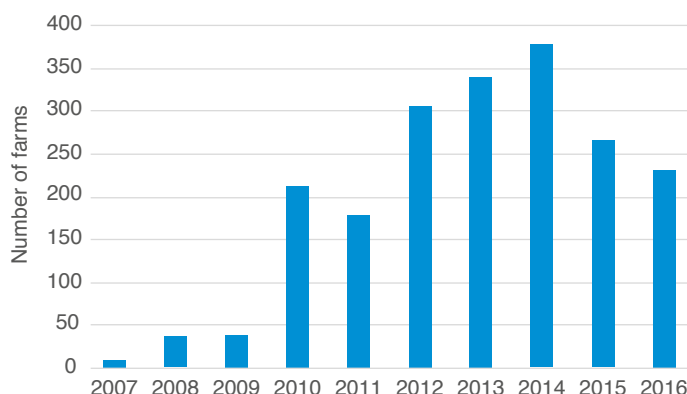


Figure 1. Total number of English and Welsh sheep flocks submitting samples for any iceberg disease, 2007–2016

Source: APHA

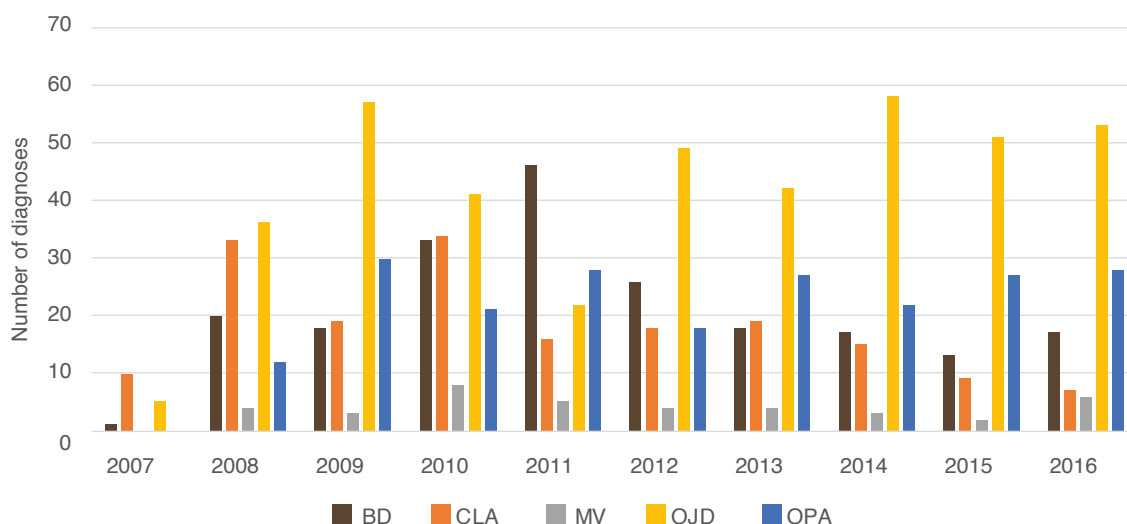


Figure 2. Number of diagnoses of iceberg diseases from England and Wales, 2007–2016

Source: APHA

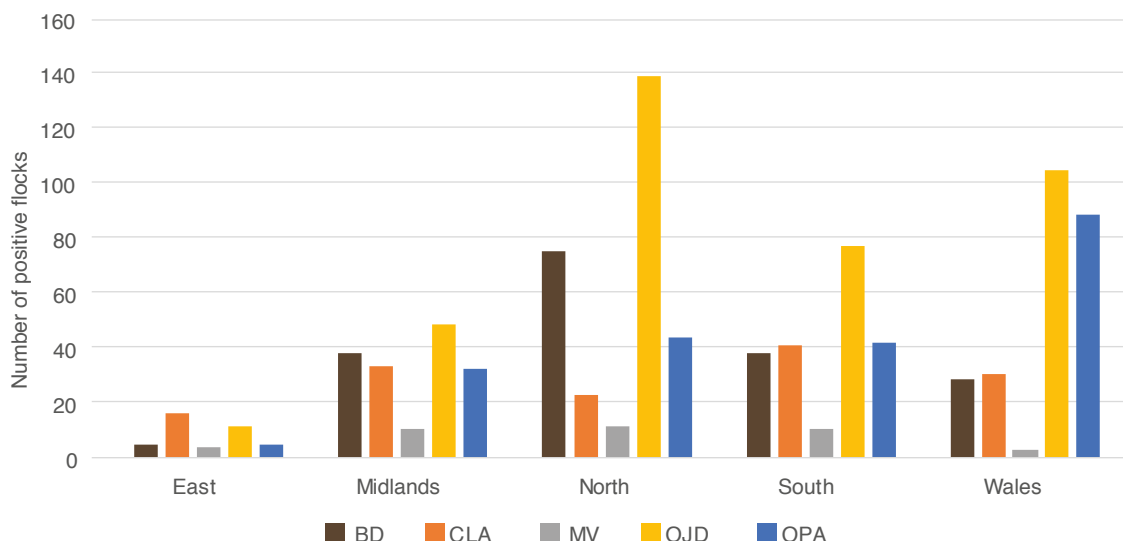


Figure 3. Number of positive flock-level diagnoses of iceberg diseases by region, 2007–2016

Source: APHA

# Background to the five iceberg diseases

## Border disease

Border disease (BD), also known as hairy shaker disease, is very closely related to bovine viral diarrhoea (BVD) virus. While the Border disease virus is known to mainly affect sheep and goats, it can also infect cattle.



Hairy shaker lamb

## Disease levels

Estimates of the proportion of UK flocks infected with BD vary from 30.4–37.4%. This is more than a threefold rise over the past 40 years. The levels of disease vary in other countries, so it is important to test any live imports.

## Transmission

Border disease may be spread in several ways: by the nose and mouth, from the dam to offspring before or immediately after birth and by highly infective semen of persistently infected (PI) rams. Typically, BD is introduced to a flock through contact with an infected animal, rather than from cross-contaminated handling equipment or livestock contractors. Once infected, the spread of disease within the flock appears to vary depending on flock management practices. Nose-to-nose contact increases the risk of disease spread, so intensive flocks will be at greater risk, whereas disease spread has been known to take years in extensively managed sheep at grass. Transmission of BD within a semi-intensively managed flock of ewes or lambs is usually only moderate. This may be partly attributed to the fact that usually, fewer infected animals live – only 0.3–0.6% of PI lambs survive – compared with BVD in cattle, where PIs typically represent 0.5–2% of the calves.

It will be important to identify any new Border viruses because the differences may influence the viruses' ability to cause disease, how infectious they are, their host preference and diagnostic test sensitivity and specificity.

## Cattle and sheep cross-infection

BVD Type 1 and BVD Type 2 are known to infect cattle, sheep, other ruminants and pigs. Outbreaks of BD have been seen in sheep in close proximity to PI cattle with BVD. Additionally, in Spain, BVD Type 2 has been found to cause abortion in sheep flocks.

## Caseous lymphadenitis (CLA)

Caseous lymphadenitis (CLA) is caused by *Corynebacterium pseudotuberculosis* and primarily affects sheep and goats worldwide. It has been the subject of attention in Australia, New Zealand and South Africa for decades, yet its importance to the UK sheep industry has not been studied in the same depth. Since its introduction to the UK in the 1990s, CLA is now classed as endemic and prevalence of infected flocks is expected to continue to rise in the absence of effective control measures.



Symptoms of CLA present depending on the location of the lymph nodes affected – in the UK, it is usually the lymph nodes around the head. Approximately 25% of affected sheep only develop internal lesions. Not all infected sheep develop abscesses and it seems to depend on the amount of exposure to bacteria. This is important because it affects the interpretation of the enzyme-linked immunosorbent assay (ELISA) test available for CLA.

CLA seropositive status indicates exposure to the pathogen and, potentially, the presence or development of lesions at some point. It might also indicate exposure but not active infection or cleared infection.

## Disease levels

In Australia, abattoir surveys to monitor CLA have driven the uptake of vaccination in ewes.

In the UK, it is suggested that more rams, specifically terminal sire breeds, are affected by CLA. In 2000, a survey of mainly terminal sires was conducted using blood samples collected as part of the Premium Sheep and Goat Health Scheme (PSGHS). Of the 745 flocks sampled, 18% had at least one seropositive ram. The high cost of diagnostic testing means that within-flock prevalence has not been studied to the same degree, but on a Scottish ram stud, up to 50% of rams were affected.

## Transmission

CLA bacteria infect sheep through abrasions on the skin, ingestion and, potentially, inhalation. The bacteria are carried to the draining lymph node, where they are able to survive and multiply within the cells. When the cells die, they release large numbers of pathogenic bacteria and the cycle is repeated. Small abscesses develop and combine within the draining lymph node, forming large lesions containing bacteria, cellular debris and white blood cells.

Infection is spread between sheep through direct contact with discharging lesions or airborne transmission. Grouping sheep for management purposes (e.g. yarding, housing, shearing, dipping or feeding) increases transmission. Consequently, skin lesions, e.g. teeth eruption, orf or fighting wounds, are likely to increase the risk of disease transmission. Similarly, infection can be spread through the use of tagging and shearing equipment without disinfection between sheep and the movement of shearers.

The primary means of transmission between flocks is the introduction of an infected animal to a naive flock, although transmission by contractors or shearers, or at live markets, are all possible routes of infection and transmission. CLA was initially thought to be an issue concerning terminal sire pedigree flocks, but it is now being seen more often in commercial UK flocks, usually introduced by infected rams. In a UK study, farmers of 20 out of 31 CLA-affected flocks could clearly identify how CLA was introduced on to their farms. In pedigree flocks, both ewes and rams appeared to introduce infection, while in commercial flocks, CLA was most commonly introduced by a new ram.

CLA bacteria can survive in faeces, shavings, hay and straw for up to 55 days. Lower temperatures and mixing the bacteria with wood shavings, hay, straw and faeces appeared to lengthen the bacterial survival time.

## Maedi Visna (MV)

Maedi Visna (MV) is a highly infectious disease of sheep caused by a virus in the same family as jaagsiekte sheep retrovirus (JSRV), the cause of ovine pulmonary adenocarcinoma (OPA). MV is characterised by a long incubation period of several months to years and leads to a progressive loss of condition, reduced flock production and poor economic performance. Once infected, the sheep will produce antibodies to the virus, typically within weeks or months of infection. The disease is incurable; infected sheep become life-long carriers because they are unable to eliminate the virus. Currently, no vaccine is available.

## Disease levels

The prevalence within the national flock (including England, Scotland and Wales) appears to be increasing. The prevalence of infected flocks appears to have doubled from 1.4% to 2.8%. However, this national figure obscures the significant regional variation in counties, such as Leicestershire and Gloucestershire, where flock level prevalence is 15%.

Prevalence within flocks varies, with evidence of up to 85% of sheep affected within some flocks.

## Transmission

The MV virus is spread via lung discharges and milk containing infected white blood cells. If the animals are affected by other diseases, such as OPA, which increases the number of white blood cells in lung secretions, this will increase the level of transmission. The virus can also be found in semen, saliva and urine and in utero infections can occur.

The virus is unstable in the environment. Straw, hay or shavings may harbour the virus, but more research is required to determine this.

Some research has been conducted on genetic susceptibility. Indeed, some sheep with a variation in the gene do seem more susceptible to infection than others.

Data suggest that UK hill breeds such as Herdwick, Rough Fell and Dalesbred are less likely to carry the highly susceptible gene. Genetic information could be used to select less susceptible animals within flocks to control MV infection, but needs further investigation.

## Ovine paratuberculosis, or ovine Johne's disease (OJD)

Ovine paratuberculosis, or ovine Johne's disease (OJD), is a bacterial disease of the small intestine. It is caused by *Mycobacterium avium* spp. *paratuberculosis*, which causes chronic inflammation, poor absorption of nutrients and reduced metabolic efficiency leading to reduced fertility and progressive weight loss. In Europe, Johne's was first reported in cattle in 1895 and has spread throughout the world. The disease is well recognised as a major production-limiting disease that affects multiple species.



Some ewes in this group were subsequently diagnosed with Johne's

Photo source: Dr F. Lovatt, Flock Health Ltd

The impact of Johne's on the UK sheep industry has received almost no attention, while the equivalent disease in cattle has had control schemes in place for decades. This is likely to be because of the differences in clinical disease symptoms. In cattle, clinical Johne's presents as profuse, chronic diarrhoea accompanied by progressive weight loss and eventual emaciation, which is obvious to the farmer and their vet.



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In sheep, diarrhoea is rarely a symptom and the progressive weight loss and reduction in productivity are often attributed to aging, resulting in culling without further diagnosis or consultation with a vet. Greater awareness of Johne's is needed among farmers and vets.

Johne's is caused by one of the two strains of the bacteria: sheep (S) or cattle (C). Sheep are susceptible to both C and S strains. The C strain is believed to be more common, however, the distribution and abundance of the S strain may be underestimated because it is more challenging to culture under laboratory conditions. Cattle appear to be relatively resistant to infection and disease from the S strain. In lambs, the strain of bacteria has a strong influence over the immune and pathological responses developed by the host. To control the disease in both species, it is vital to consider contact between sheep and cattle, for example, cattle could be an indirect source of contamination of sheep pasture via co-grazing or slurry application. The bacteria are highly prevalent in UK dairy cattle systems and seasonal grazing of sheep on slurry-treated pastures is widely practiced. In addition, sheep may represent a reservoir of both C and S strains that may re-infect cattle herds where attempts to eradicate the disease are made.

Three different disease states have been described for Johne's, each of which produces a different antibody and immune response. Asymptomatic animals are those that appear to have contained or overcome infection and have neither histological lesions nor shed the bacteria.

### Disease levels

In several European countries, ELISA tests or faecal culture has revealed a prevalence of Johne's in ewes of between 0% and 60% and between 0% and 29% in flocks. However, the very poor sensitivity of the ELISA tests used means that the true prevalence is likely to be higher than these estimates.

In the UK, a recent survey of larger commercial sheep enterprises, which employed polymerase chain reaction (PCR) tests on faeces, found 64% of samples to be positive for Johne's bacteria. Initial data from this study not only suggest that the bacteria are present in the UK, but that life expectancy of breeding ewes within flocks with the highest prevalence of Johne's positive samples is significantly shorter than those in flocks where no bacteria were detected.

### Transmission

Johne's infection mostly results from faecal–oral exposure routes, with entry via the intestinal tract then the lymphatic system. The disease can also be contracted from drinking contaminated colostrum or milk. In a study of 142 late-pregnant ewes from two heavily infected flocks, all five ewes with clinical disease had infected fetuses, compared with only one of 54 ewes with subclinical disease.

Almost all clinical disease is seen in ewes older than 2–3 years old. However, the key risk period for infection is exposure to the bacteria in early life, while the intestinal immune system is developing. The first 3–4 months are critical. After six months, the risk of infection and disease following exposure to the bacteria declines significantly. This has major implications for control measures.

Some sheep may be capable of temporarily or even permanently clearing the infection, especially during the early stages of infection. The fate of an animal exposed to the infection appears to depend on its own genetic susceptibility.

### Ovine pulmonary adenocarcinoma (OPA)

OPA, also commonly known as jaagsiekte, is a disease seen in sheep with a contagious lung tumour caused by infection with JSRV. This group of viruses is related to MV, but is genetically distinct. The disease has a worldwide distribution, with the exception of Australia and New Zealand, where it has never been reported. Iceland is the only country to have eradicated the disease.

Tumour growth impairs lung function, which affects the efficiency of the cardiovascular system. Symptoms include respiratory distress with excessive fluid production in some but not all cases. Body condition loss, reduced reproductive performance, impaired immunity and reduced milk yield are often seen. The production impacts have not been robustly investigated, especially in the subclinical disease phase.

### Disease levels

Abattoir cull ewe and fallen stock surveys have reported a prevalence of between 0.9% and 5.6%. It is difficult to truly know the UK prevalence or regional or breed variation in flock-level prevalence.

There is a correlation between OPA prevalence and the spread of MV virus infection.

### Transmission

Transmission via oral discharges, as well as milk and colostrum, has been frequently demonstrated, while transplacental or lambing transmission has not been proven. Some studies have suggested that the virus may survive outside of the host, on equipment or in housing, since detectable virus was present for several weeks. However, it is not clear how long the virus remains viable and infectious in the farm environment. Buildings or pasture should be rested between batches of infected or potentially infected and uninfected sheep. In the Icelandic eradication programme, a rest period of two months was used, which appears to have been sufficient.

Susceptibility to OPA is age-dependent, with long incubation periods (between six months and three years). The disease is rarely seen in lambs, with most clinically affected sheep aged between three and four years old. However, young lamb infection plays an important role in the transmission of the disease. Increased culling of unproductive ewes with undiagnosed subclinical OPA may occur in younger ewes.

# Impact of disease

## Animal welfare

No published research has yet addressed the welfare implications of these five diseases. However, from the clinical signs and subclinical affects, welfare will certainly be affected.

MV, OPA and Johne's all cause suffering to affected individuals through chronic respiratory insufficiency and emaciation.

Border disease impairs the normal behaviour of hairy shaker lambs, causing suffering through mucosal disease and premature death.

The clinical impact of CLA is poorly understood compared with the other diseases, but the development of external and internal abscesses may be uncomfortable or painful, as well as having chronic physiological effects.

The indirect welfare impact of these diseases on the lambs of affected ewes is more difficult to assess. However, it can be assumed that affected ewes have reduced quantity and quality of colostrum and lower milk yields, which would reduce lamb growth rates and overall survival.

Limited information is available on the subclinical impact of iceberg diseases on ewe performance, longevity, fertility and lamb survival or growth rate. This is particularly true for OPA, which is difficult to diagnose in live animals because of its long incubation period.

## Reproductive efficiency

### Border disease

There is no detailed data on production losses caused by reduced conception rate or abortion.

One study of a flock with a severe, acute outbreak of disease over one lambing period estimated a reduction in lamb output of 50%. This figure should be considered as the upper level of losses that could occur in a naive flock experiencing an epidemic.

By generalising the reduction in conception rate observed in cattle exposed to BVD and applying it to the replacement female component of an endemically infected sheep flock, it is reasonable to expect an additional 2–8% empty ewes per year attributed to BD virus exposure during pregnancy.

### Maedi Visna

Ewes infected with MV had a 9% reduction in conception rates compared with uninfected ewes of a similar age within the same flock.

### Ovine Johne's disease

Negative effects on fertility have been reported in dairy sheep, but only in older ewes (parity of five and above), with an average of 19% fewer lambs born alive.

## Ewe and ram longevity

### Caseous lymphadenitis

In North America, a clear association has been found between 'thin ewe' syndrome (ewes being thin despite having a good appetite and no parasitic infection) and the form of CLA disease that affects the nervous system, leading to large production losses and increased culling rates.

CLA can cause mastitis in sheep and this is most likely associated with infection of a lymph node. It may present as acute mastitis, or as a chronic abscess within the mammary gland leading to increased culling rates and lower milk yields.

### Maedi Visna

In the UK, the major clinical sign of MV infection is chronic progressive pneumonia in older sheep (typically those over three years old), leading to weight loss, reduced fertility and milk yield. The significance of MV may only be recognised when the prevalence within a flock reaches 50%. In addition, infected sheep that show symptoms such as loss of condition or pneumonia may be culled for other reasons without further investigation.

The long incubation period and nature of the disease means that many studies have identified production-limiting effects associated with subclinical MV. The average lifespan of infected animals appears to decrease because of reduced productivity and they are culled at least a year earlier than uninfected cohorts.







### **Ovine Johne's disease**

Recent data from a UK study of 63 flocks indicated that, on average, only 17% of lowland breeding ewes in flocks infected with Johne's were retained for more than three years, compared to 40% in uninfected flocks.

### **Ovine pulmonary adenocarcinoma**

While there have been individual reports of flocks experiencing 20% mortality in adult sheep in a single year, a mortality or culling rate of 1–5% each year is a more common presentation in flocks known to be affected by OPA.

### **Lamb survival**

#### **Border disease**

No research data is available to quantify the impact on postnatal lamb survival. The immunosuppressive effect of the virus could increase susceptibility to a variety of other pathogens. One small study revealed that lambs infected with BD have a 2.1-fold higher risk of showing diarrhoea and respiratory signs in the first six weeks of life compared with uninfected lambs.

### **Lamb growth rate and carcase quality**

#### **Border disease**

There is evidence that infected lambs grow 20% slower during the first six weeks of life than uninfected lambs, equating to a 2.5 kg difference in liveweight by six weeks of age.

### **Caseous lymphadenitis**

There is no direct evidence that CLA has an effect on growth rate. However, the potential impact on milk yield and lamb growth rate during lactation may be inferred from studies that have examined other production outcomes linked to physiological efficiency of the ewe.

In Western Australia, 4–7% of clean fleece weight is lost when an animal is infected with CLA, although this would have limited importance within the UK. The reduction in wool growth is likely to be associated with stress, reduced milk yield and colostrum yield and quality.

In South Africa and Canada, CLA has been identified as the leading cause of sheep carcase condemnation attributed to extra trimming to remove lesions.

### **Maedi Visna**

The milk yield of infected ewes is reported to reduce by 6–7%. The weaning weight of lambs born to MV-positive ewes over four years old reduced by 0.94 kg. These are subclinical effects from ewes without clinical signs of disease.

At present, there is no robust data on productivity losses under UK flock management systems. Individual case studies suggest that losses can be significant when within-flock prevalence reaches high levels. For example, in one UK flock of 1,500 Masham mule ewes with clinical signs of MV, flock productivity was estimated to reduce by 20–40%. This was characterised by smaller, weak lambs, lower weaning weights and high replacement rates, equating to a cost of £30,000–£50,000.

# Investigation and diagnosis

## Diagnostic techniques

There are a variety of diagnostic techniques that can be applied to these five diseases.

### Immunology or serology

In the UK, test kits are commercially available to detect antibodies against the causative agents of BD, CLA, MV and Johne's. At present, this is not the case for OPA.

These tests rely on the immune reaction of the individual being high enough to reach the detection threshold of each test. This is often the case in animals experiencing clinical disease, but is less consistently true of animals that are incubating or suffering from subclinical disease. For MV and CLA, sheep undergo periods of high and low immune response and antibody production after infection. With Johne's, antibody levels often remain low until the clinical phase of the disease. This makes disease screening using blood tests less straightforward. However, it can be overcome by appropriate sample size selection and by communicating with the owner as to the likelihood of some individuals having inconsistent results over a period of time as their immune response to the infection varies.

In contrast to MV, CLA and Johne's viruses, the serological response to BD virus is more typical of viral pathogens, which means blood tests for this disease are more reliable. A rapid increase in antibodies after infection is followed by a slow reduction in antibody levels over time to the point where, years after infection, previously infected animals may have undetected levels of BD antibodies. This does not apply if a foetus was infected mid-gestation, in which case it becomes persistently infected because it has no immune response to the virus.

It is also important to note that maternally derived antibodies to BD, CLA, MV and Johne's are indistinguishable from the lambs' own antibodies, so testing lambs under the age of 2–3 months is problematic.

### Antigen detection

Direct detection of the pathogen by PCR tests or culture is useful for disease states in which serological responses are low or absent.

Commercial antigen detection PCR tests are available for BD virus (blood) and Johne's (faeces).

Bacteriological culture is available for CLA pus or Johne's faeces.

Experimental tests using PCR have been developed for MV and OPA, but are not currently available as commercial tests.

PCR tests are highly specific as long as the gene primers selected are highly conserved. PCR sensitivity can be limited by the biology of the disease, for example, levels of MV virus can be very low during the incubation phase of the disease and are at low concentrations in blood or nasal secretions.

In PCR or culture tests, interpretation of low levels of the bacteria causing Johne's is subject to debate in both cattle and sheep because the minimum pathogen concentration threshold correlating with clinical or subclinical disease remains unclear. Further validation work is needed in sheep to understand the diagnostic relationship.

### Samples from culled animals or fallen stock

Routine post-mortem examination (PME) of a sample of cull animals or fallen stock allows a variety of diseases and abnormalities to be simultaneously examined and detected. At a PME, gross pathology plus histopathology has been shown to be highly informative and a cost-effective surveillance method for MV, Johne's, OPA and CLA, plus other common and rare endemic diseases.

### Post-mortem examination for diagnosing iceberg diseases

Although many diagnostic options are available for live animals, in some situations, PME and additional testing may be most appropriate for diagnosing iceberg diseases.

**It must be made clear that absence of disease on a PME does not rule out the presence of disease on farm.**

Farmers and their vets must consider the best place for a PME to be performed based on available resources and expertise.



Thin ewes that were subsequently diagnosed with ovine pulmonary adenocarcinoma

Photo source: Dr F. Lovatt, Flock Health Ltd

For most of the iceberg diseases, a typical presentation may be a thin ewe or an increase in the number of thin sheep. The differential list for thin sheep may be quite extensive, including CLA, MV, Johne's and OPA, as well as other common endemic diseases, such as chronic liver fluke, or malnutrition either from poor teeth or insufficient feed supply.



Before carrying out a PME, vets should:

- Take a thorough history – most of the iceberg diseases have long differential diagnoses lists and so accurate history-taking is important to ensure the right samples or carcasses are selected
- Appreciate whether the carcass is appropriate for examination – carcasses should be fewer than 24 hours old, especially in hot weather, because poor carcass quality may provide false or inconclusive results, leading to a waste of time and money
- Consider their own expertise, the resources available to them (including appropriate PME tools) and their time availability – it may be more cost-effective to send the carcass to a post-mortem provider, e.g. APHA, SRUC Veterinary Services or independent operators at fallen stock collection centres

### Fresh tissue sampling for histology

Sample the lesion and the border between healthy and diseased tissue. Sections fixed for histology should be no more than 1 cm<sup>3</sup>

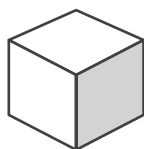


Figure 4. Sections fixed for histology should be no more than 1 cm<sup>3</sup> (exact size of box)

- Place section to be fixed in 10% neutral buffered formalin as soon as possible
- Ensure samples sent to labs are appropriately packaged, following the guidelines of the receiving lab

### Samples for Border disease

Although vets typically associate ‘hairy shaker’ lambs with BD, flocks may have had BD for several years before a classic ‘hairy shaker’ lamb is seen.

Consider testing for BD in cases of reduced or poor ewe fertility, high levels of abortions or weak lambs with or without neurological symptoms.

Tissues from PI lambs contain high levels of virus, which may be more easily identified than those associated with aborted or stillborn lambs. Therefore, if sampling abortive material does not lead to diagnosis, sampling weak lambs may be more likely to lead to a diagnosis of BD.

Table 1. The samples needed to test for Border disease

Disease	Scenario	Samples
Border disease	Abortion	Foetal tissue – fresh spleen and thymus Placenta – ideally including cotyledon
	Weak or hairy shaker lambs	Fresh spleen, thyroid, thymus, kidney, brain, lymph nodes or gut lesions for virus isolation

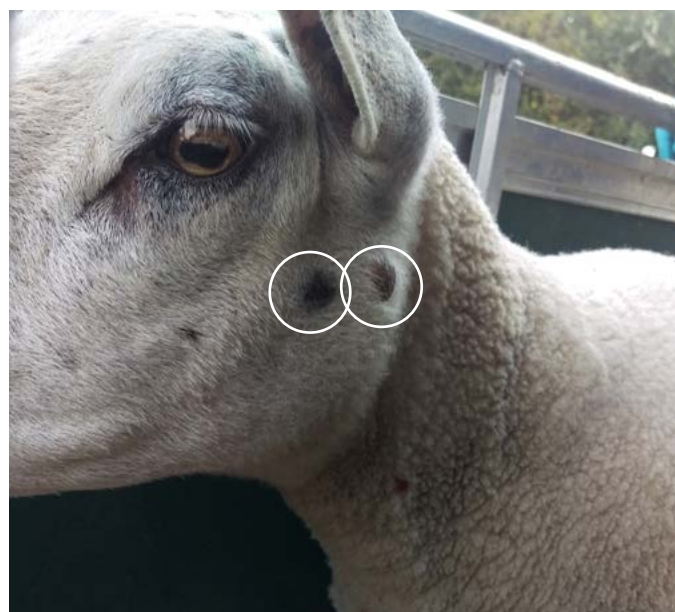
Lambs affected by BD may present in different ways, including clinically normal, weak and small with failure to thrive, or as classic ‘hairy shaker’ lambs with nervous signs and fleece changes (increased crimp or increased pigmentation of the fleece).



Photo source: Farm Post Mortems Ltd

### Samples for caseous lymphadenitis

Although CLA lesions are typically thought of as external, evidence from UK studies suggests that CLA lesions may be found internally.



A ewe with external CLA lesions associated with the parotid lymph node

Photo source: Dr F. Lovatt, Flock Health Ltd.

Consider testing for CLA in cases of:

- External pus-filled lesions
- Thin ewes with or without respiratory signs
- Poor fleece quality
- Poor fertility in rams
- Poor body condition score (BCS) or poor weight gain
- Pus-filled lesions found internally on PME

Table 2. The samples needed to test for caseous lymphadenitis

Disease	Scenario	Samples
Caseous lymphadenitis	Pus-filled lesion found on clinical examination or PME	Swabs collected for bacteriological culture



Two pairs of lungs from three-year-old Texel rams

Photo source: Dr P. Davies, Pro Ovine Ltd



A large CLA lesion in the mediastinal lymph node within the chest cavity. Note the concentric rings of an onion-like lesion, however, this should not be used to definitively diagnose CLA. For confirmation, bacterial culture is required to isolate *C. pseudotuberculosis*

Photo source: Farm Post Mortems Ltd

### Samples for Maedi Visna

Consider MV in cases of:

- Ewes with respiratory disease that may or may not be thin
- Increased ewe deaths
- Poor young lamb performance
- Poor or reduced ewe fertility

The lungs (top of column 2) on sheep affected by MV are heavier than those of their uninfected counterparts and can weigh up to 4.5 kg. The lungs on the left are normal and the lungs on the right are from a ram infected with MV. Note the increased size and swollen nature of the affected lungs. When placed on the table the heart is obscured, unlike the lungs on the left.

Table 3. The samples needed to test for Maedi Visna

Disease	Scenario	Samples
Maedi Visna	Thin ewe for clinical investigation or cull ewe screen	Histology may be performed on formalin-fixed samples of lung, bronchial lymph node, mammary gland, synovial membrane and brain  Blood serum from the heart may be collected for serology



An area of MV within an infected lung. Note the swollen tissue where the lung has been cut and the pinkish-grey discoloration

Photo source: Farm Post Mortems Ltd

### Samples needed for ovine Johne's disease

The most definitive diagnostic test for clinical Johne's is gross pathology at PME with histological confirmation. Some cases present with thickening (and pigmentation) of the small intestine, but this should not be used as a definitive diagnosis and samples should be collected for histology. As Johne's can present differently, if there are no obvious areas of thickening or pigmentation then consider sampling from multiple sites along the intestines.



Unlike cattle, sheep with Johne's do not scour as a direct result of the infection. However, concurrent high worm burden associated with debilitation may lead to scouring.

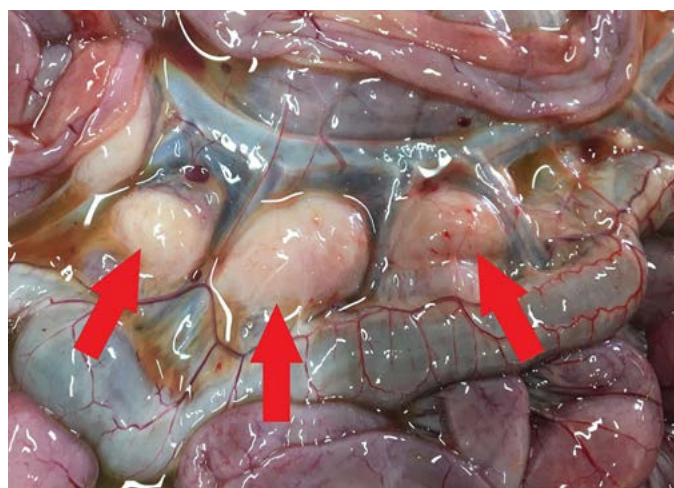
Consider Johne's in cases of:

- Thin/poor BCS sheep
- Flocks that have a low proportion of older sheep or high culling rates
- Poor young lamb performance potentially caused by reduced milk yield



Cases of Johne's with areas of thickened, sometimes pigmented intestines

Photo source: Farm Post Mortems Ltd



Enlarged lymph nodes (arrows) and oedema may also occur in cases of Johne's and may accompany intestinal thickening and pigmentation

Photo source: Farm Post Mortems Ltd

Table 4. The samples needed to test for ovine Johne's disease

Disease	Scenario	Samples
Ovine Johne's disease	Thin ewe for clinical investigation or cull ewe screen	Collect area (1–2 cm) of thickened small intestine from a few sample sites for histology

#### Samples for ovine pulmonary adenocarcinoma

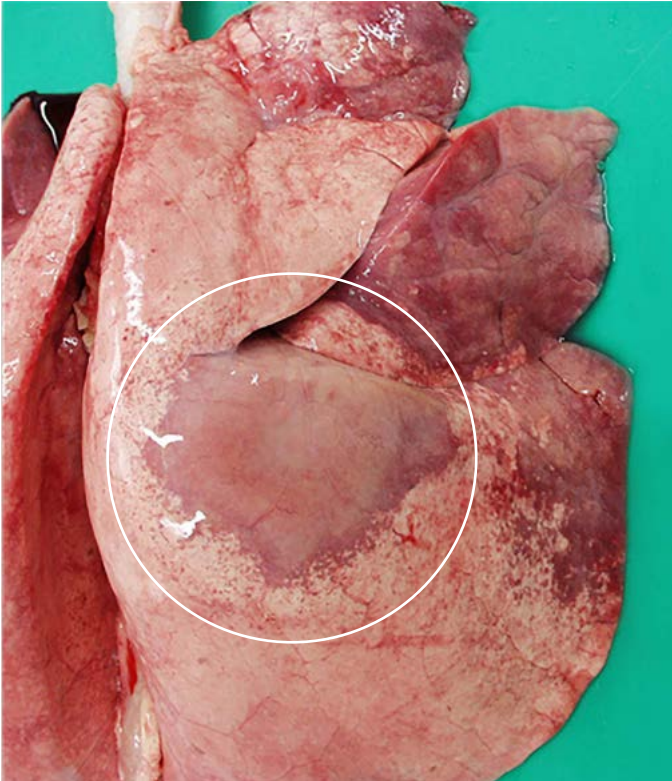
In OPA, tumours are found throughout the lungs. They will be hard, grey areas within the lung and may be large and consolidated, or smaller and more spread out. OPA lesions are firm when palpated. The tumours are associated with a large amount of frothy fluid, which may ooze from the lung surface when cut or be found throughout the trachea when it is split open. It is worth checking for lungworm.

Consider OPA in cases of:

- Sheep with respiratory disease, which may or may not be thin
- Increased ewe mortality rate

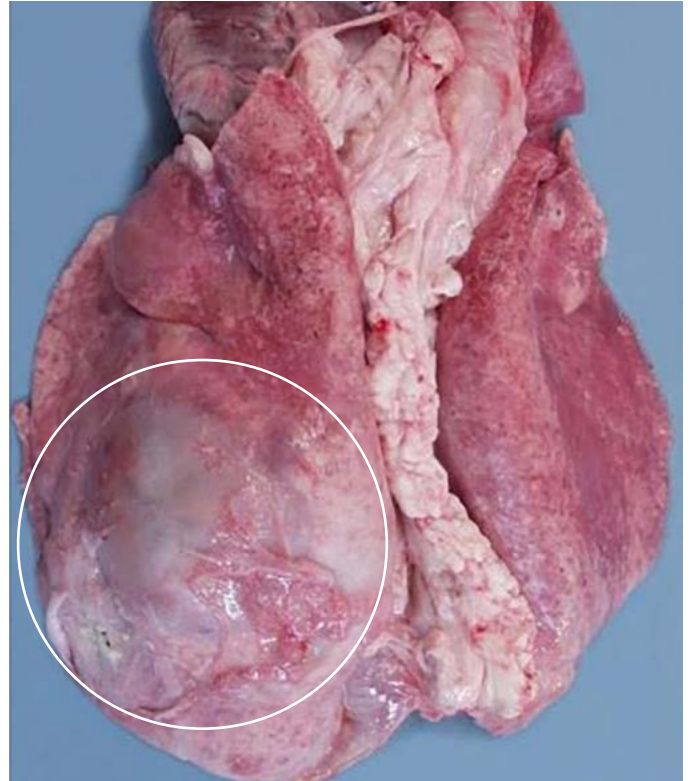
Table 5. The samples needed to test for ovine pulmonary adenocarcinoma

Disease	Scenario	Samples
Ovine pulmonary adenocarcinoma	Thin ewe for clinical investigation or cull ewe screen	Collect multiple samples (1 cm <sup>3</sup> ) of affected lung, as well as samples from the border of diseased and healthy lung for histology



A classic lesion of OPA, although the tumour may be found throughout the lungs

Photo source: Hal Thompson, Richard Irvine and Noelia Yusta, School of Veterinary Medicine, University of Glasgow



This is an abscess, although the colour and shape of the lesion looks very similar to OPA. OPA would be differentiated by palpation (abscesses are capsulated and feel smooth, whereas OPA lesions do not have a capsule and are solid)

Photo source: Hal Thompson, Richard Irvine and Noelia Yust, School of Veterinary Medicine, University of Glasgow



OPA lesions may contain areas of abscess. Histology will help to differentiate if lesions are just abscesses, or abscesses in combination with OPA

Photo source: Farm Post Mortems Ltd



# Test selection

## Test characteristics

The effectiveness of a diagnostic test is described in terms of the test characteristics of sensitivity and specificity, which relate to the proportion of animals correctly or incorrectly classified by the test as being positive or negative.

Sensitivity, or the 'true positive rate', is a measure of the proportion of infected individuals that are correctly identified as such.

Specificity, or the 'true negative rate', is a measure of the proportion of uninfected individuals that are correctly identified.

These test characteristics are generated experimentally by testing samples from known populations of diseased or infected animals and from known disease-free animals. However, there is considerable variation between individuals, particularly between individuals at different stages of disease, which means that the characteristics of a given diagnostic test can vary dramatically depending on the population of interest. For example, the test characteristics for antibody ELISA assays for MV or Johne's are more sensitive and specific for animals showing symptoms than in the earlier incubating or subclinical phases. This presents some major problems for disease screening of asymptomatic animals when attempting to calculate appropriate sample sizes and confidence of result interpretation.

For example, a test that has only moderate sensitivity or specificity would be unhelpful in a flock where the target disease is of low prevalence. It may, however, be of some clinical use when the disease prevalence is very high.

## Sample size calculation

Appropriate sample size selection is essential to be confident in the result. Sampling too few individuals can easily lead to the assumption that a flock is free from disease, when in fact the testing protocol was inadequate to find the disease.

Determining the necessary sample size is dependent on several factors:

- The test characteristics
- Sensitivity
- Specificity
- The level or confidence required by the vet and farmer
- The prevalence that is judged to be clinically important

If the sample size is too small, then a high confidence in the accuracy of a flock health screening result can only be achieved for a disease with a high prevalence.

If the aim is to eradicate disease, such as in the MV accreditation scheme, a confidence level of 98% at a prevalence of 2% is set and this is combined with the test characteristics of the ELISA assay and the flock size to give the required sample size. However, this approach

is not always appropriate. For several reasons, lower confidence or higher threshold prevalence may be accepted as clinically relevant to reduce the number of samples and the cost of testing.

Sampling a high-risk group within a flock can increase the confidence of the correct flock-level result.

- For BD, the most appropriate strategy depends on the question to be answered:
  - Current disease circulation patterns – sample homebred lambs over the age of three months for BD virus antibodies
  - Reproductive investigations – samples should be collected from ewes who scan empty, abort or give birth to dead or abnormal lambs
- For CLA, test all stock rams, plus older and thin ewes and any animal with superficial lymph node enlargement or scars at those sites
- For MV and Johne's, preferentially test ewes older than four years that are in poor body condition
- For OPA, select old, thin ewes for PME or those showing some breathing difficulties

Transthoracic (chest) ultrasound scanning may be valuable to further refine candidates for PME, however, variability between operators in interpreting images, along with as yet unquantified sensitivity and specificity of the technique as a screening test, means that caution must be taken. It is anticipated that more data on these two critical aspects of the transthoracic ultrasound technique will be published in the near future, which should increase the confidence when interpreting the results.

## Examples

The following examples illustrate how a diagnostic test with a given level of sensitivity and specificity for a disease can be used and how the outcome of the testing can be interpreted with the farmer.

A farmer with 400 ewes wants to investigate a disease with a prevalence of 10% using a test with 95% sensitivity and 95% specificity. They want to attempt disease eradication by test and cull.

- In this scenario, there should be 40 ewes (10% of 400) that would be classed as true infected animals
- However, the test has a sensitivity (or true positive rate) of 95%, so it will correctly identify 95% of the true infected animals (38 of the 40 ewes) and these are called true positive animals
- This leaves two true infected ewes that will be classed as false negatives, i.e. they are infected but the test has failed to identify them
- The test has a specificity (or true negative rate) of 95%, so it will correctly identify 95% of the true uninfected ewes as negative, i.e. 342 ewes would be identified as true negative, which is 95% of the 360 uninfected ewes
- This means that this test would misclassify 18 ewes (5% of the 360 uninfected ewes) as false positives

The number of animals that appear to be infected based on the test results is a sum of the true positive (38) and false positive (18) (see Table 6). In this example, this equates to 56 ewes, so there is an apparent disease prevalence of 14%.

At this stage, the positive predictive value (PPV) is used as an indicator of the accuracy of a test in a flock with a given expected prevalence. It combines the test characteristics of sensitivity and specificity with the prevalence of the disease in a given flock or subgroup of a flock. The PPV is defined as follows:

From page 15 for this example the sensitivity = 95% and prevalence = 10%

$$PPV = \frac{\text{Sensitivity} \times \text{Prevalence}}{(\text{Sensitivity} \times \text{Prevalence}) + ((1 - \text{Specificity}) \times (1 - \text{Prevalence}))}$$

To increase the PPV for the 400 ewe flock x by ewe number.

$$\frac{((0.95 \times 0.1) \times 400)}{+ ((0.05 \times 0.9) \times 400)} = \text{True positive (38) + false positive (18)} = 56$$

$$PPV = \frac{38}{56} = 0.68 \text{ or } 68\%$$

In this example, if the farmer culled all the positive ewes as part of the eradication scheme, then 56 ewes would be removed but only 68% of these are true positives. Two false negative ewes would be left on the farm. It is likely that the farm would re-test the ewes as part of an eradication programme.

Table 6 shows how, in a low-prevalence (3%) flock, a test with sensitivity and specificity of 95% generates more false positives than it identifies true positives.

Table 6. Summary of the disease prevalence examples (number of sheep rounded to nearest whole sheep from 400 ewe flock)

Group	Number of sheep in a flock with 10% disease prevalence	Number of sheep in a flock with 3% disease prevalence
True infected	40	12
True uninfected	360	388
True positive	38	11
True negative	342	369
False positive	18	19
False negative	2	1

This is very significant if culling decisions are based on these results. Additional testing in the live animal to confirm positive test results is frequently required and advised to avoid unnecessary and incorrect culling of uninfected animals.

### Careful interpretation is required

A large number of diagnostic tests are currently commercially available for BD, CLA, MV and Johne's. Many of these are ELISA-based, with reference sensitivity and specificity values generated by the test kit manufacturer against a reference set of example samples from UK or other sources. These samples may not accurately represent the immunological response in a UK flock because of, for example, pathogen strain diversity, breed and age variability in susceptibility or stage of disease (advanced clinical case versus incubating stage). Given these limitations, the vet must keep in mind that the sensitivity and specificity of a given test in the particular situation in which they wish to use it may differ from that stated by the test kit manufacturer.

The use of a highly sensitive (true positive) ELISA test generally results in lower specificity (true negative) and an increased number of false positives. These need testing to confirm the result, either by agar gel immunodiffusion test (AGIDT) or by an alternative ELISA with higher specificity.

For example, the diagnosis of MV must be recognised as a process requiring interpretation rather than an easy one-step test. This can be difficult for clients to accept unless they are fully aware of and prepared for the testing programme from the outset.

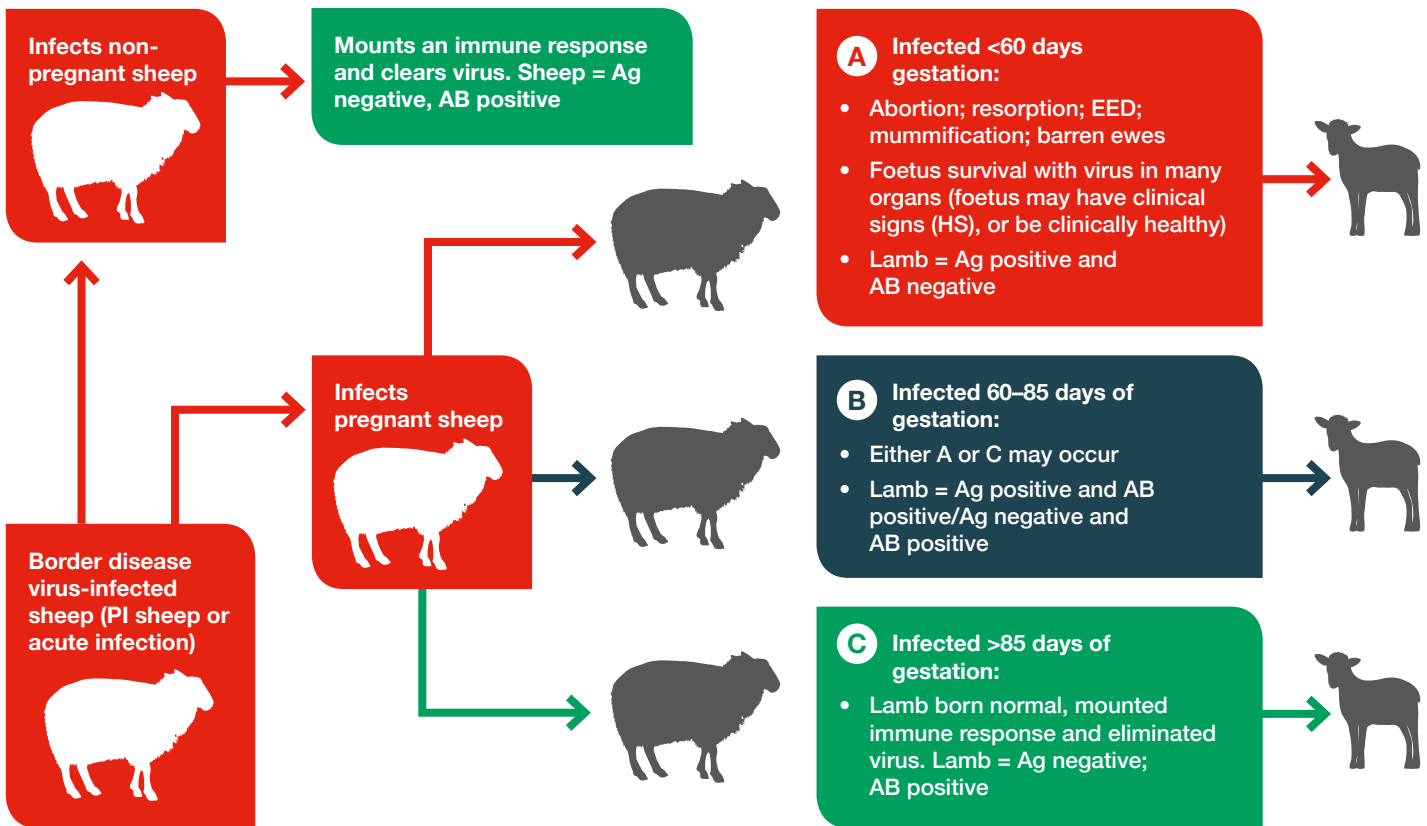
Estimates of the false positive rates in a given flock can be made from the declared specificity of the test kits. However, these have been shown to differ between populations and infection stages. For example, one ELISA kit tested in the EU had specificity greater than 99%, but in Canadian flocks, specificity of the same test was less than 88%. The vet must be cautious and manage the client's expectations, especially when large numbers of false positive results compromise the client's confidence in the screening process.

Different commercial laboratories operate different levels of test validation for each disease and can provide guidance on test selection and interpretation.



# How to test for Border disease

BD is complex because what happens to the lamb depends on when a pregnant ewe encounters the virus. Figure 4 shows that if a pregnant ewe is infected within the first 60 days of gestation (A), it may lead to abortion or the production of a PI lamb. If the infection occurs after 85 days of gestation, (C), the lamb is born normal. If the pregnant ewe is infected between 60 and 85 days of gestation, then either A or C could happen.



Key: Ag = antigen, AB = antibody, EED = early embryonic death, HS = hairy shaker, PI = persistently infected

Figure 4. The Border disease transmission cycle

## Clinical Border disease

In cases where abortions are occurring, foetal tissue (fresh spleen and thymus) and placenta samples should be collected for virus isolation. This can be difficult because the thymus is very small and easy for an inexperienced vet to miss and the ewe often consumes the placenta before discovery. Additionally, blood from aborting or barren ewes can be tested for the virus or immune response.

Currently in the UK, PCR tests are used to detect antigens in tissues or blood and an ELISA test is used to detect antibodies in serum. Since 2004, APHA has screened BVD virus antigen ELISA samples with TaqMan reverse transcription PCR (RT-PCR) to distinguish between BVD virus 1, BVD virus 2 or Border disease virus. This may be of use if cross-infection from cattle is suspected and there is a desire to investigate further in individual cases.

In suspected PI cases (hairy shakers), which may be weak or scouring lambs, blood should be taken from live lambs and then clotted and heparinised in tubes for testing. Care should be taken when sampling during the first two months of life because colostral antibodies produced by the dam of a PI animal may mask the virus.

A real-time RT-PCR assay may give more accurate results because it has high sensitivity. To confirm virus persistence in the blood, re-test the affected animals using PCR 3–6 weeks after the initial test.

BD virus can be detected in ram semen, making semen a potential transmission vector from PI or transiently infected rams. Some PI animals over the age of four years appear to develop antibodies to BD virus. However, these may be in response to encountering slightly different strains or mutations of BD virus in adulthood, causing an immune response that cross-reacts with the BD virus ELISA test.

Suspect cases of acute infections of adult or healthy newborn lambs may be diagnosed by blood-testing a representative number of sheep. To diagnose acute outbreaks, paired sera from the same animal should be tested on the same plate to provide a reliable comparison. An interval of 2–4 weeks should be sufficient to identify rising antibodies from the two samples.

### Border disease health status screening

For those sampling on suspicion of underlying disease or for surveillance purposes, blood serum tests can be used to determine the prevalence within a flock, region or country. Antibodies to BD virus may be detected in sheep blood using virus neutralisation or an ELISA test.

Screening tests are most likely to be representative of the virus circulation within a flock if conducted on homebred replacement ewes because high levels of neutralising antibody produced by in-contact sheep may persist for at least a year. Therefore, high antibody levels from bought-in or older ewes may indicate historic exposure.

For flocks that lamb indoors at high stocking density, it is suggested to take surveillance samples during the early summer, given that BD virus can spread through foetal fluids at lambing time. This may allow time for antibodies to develop from contact with affected ewes and simultaneous sampling of the current lamb crop.

Detecting antibodies in bulk milk is widely used for BVD surveillance in cattle and has been suggested as a potentially important tool for the surveillance and control of BD within milking sheep. Although the number of milking flocks within the UK is relatively low (approximately 200), this might be a useful tool for flock-wide surveillance purposes, especially as milking flocks stand a higher chance of disease transmission associated with intensive husbandry procedures. Collecting a representative number of individual milk samples would also be possible from indoor-lambing, non-dairy flocks at the point of lambing or in individual lambing pens.

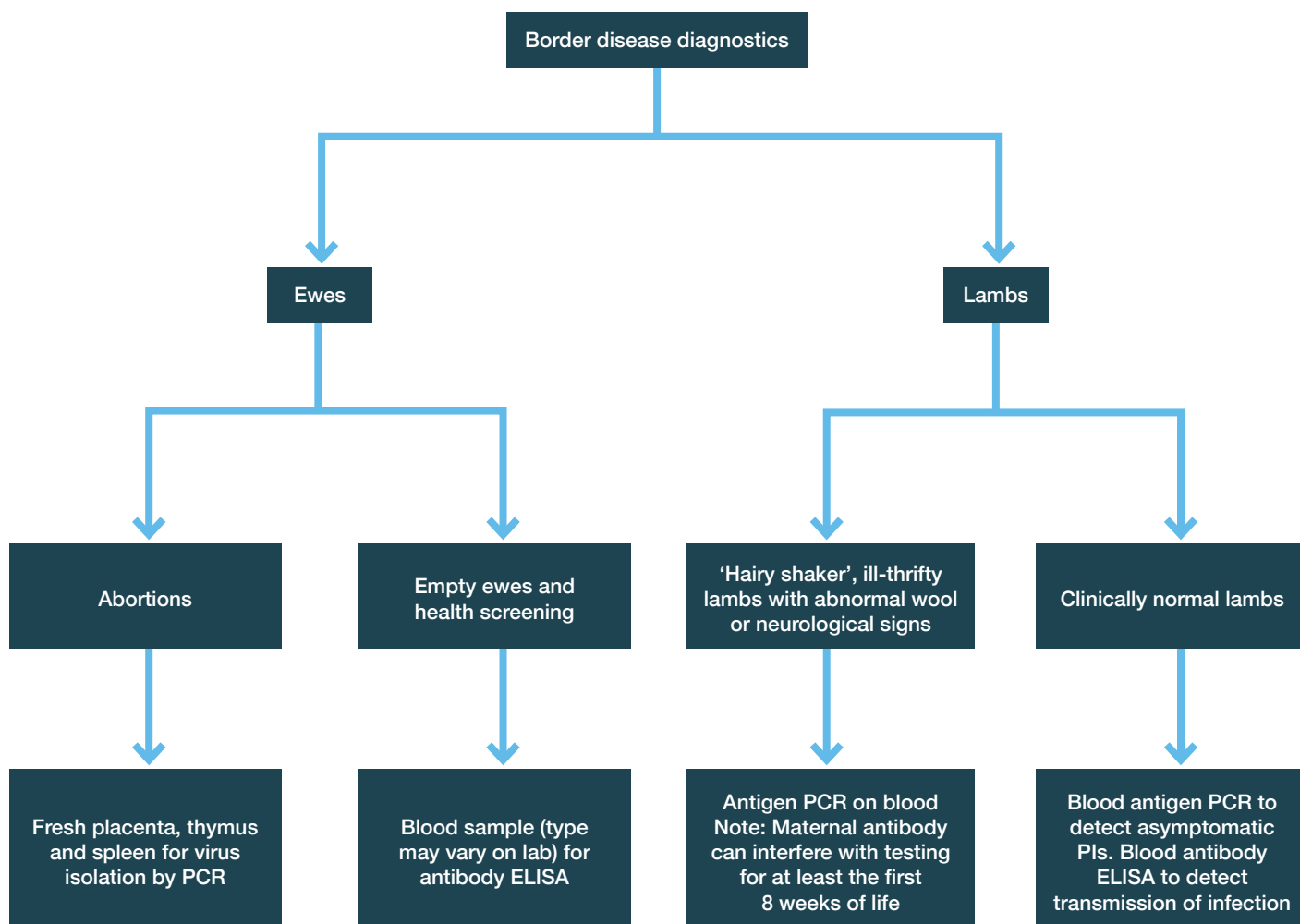


Figure 5. Summary of diagnostic decision tree for Border disease



# How to test for caseous lymphadenitis

Diagnosis of CLA can be a clinical diagnosis based upon the presence of lesions (internal or external) or upon an antibody response to bacteria in the blood.

Diagnosis of flock health status can be done by examining animals for clinical signs or by blood-testing for exposure to the pathogen. This response indicates exposure but not necessarily disease or lesions, as exposed animals may not develop symptoms or experience production losses. The proportion of positive animals that develop clinical CLA has not been established.

The blood tests available have only moderate sensitivity, indicating that a diagnostically useful immune response to the infection is not a typical feature of the disease. The ELISA tests currently available are highly specific for exposure but, as described above, this does not necessarily equate to eventual disease.

When using clinical signs as a diagnostic tool in the live animal, the slow progression of CLA makes it extremely difficult to identify a high proportion of infected animals because the period between infection and the development of CLA abscesses can vary from three weeks to six months. This is typically longer than routine quarantine protocols, so the introduction of an infected animal cannot be fully ruled out under normal procedures.

Western blot testing is normally used to increase the specificity of screening programmes. A novel, whole-blood interferon-gamma assay has been used experimentally for the diagnosis and trial eradication of CLA with some promising results, showing test sensitivity and specificity of 91% and 98%, respectively. However, further work is required to validate these findings in a representative sample from infected flocks.

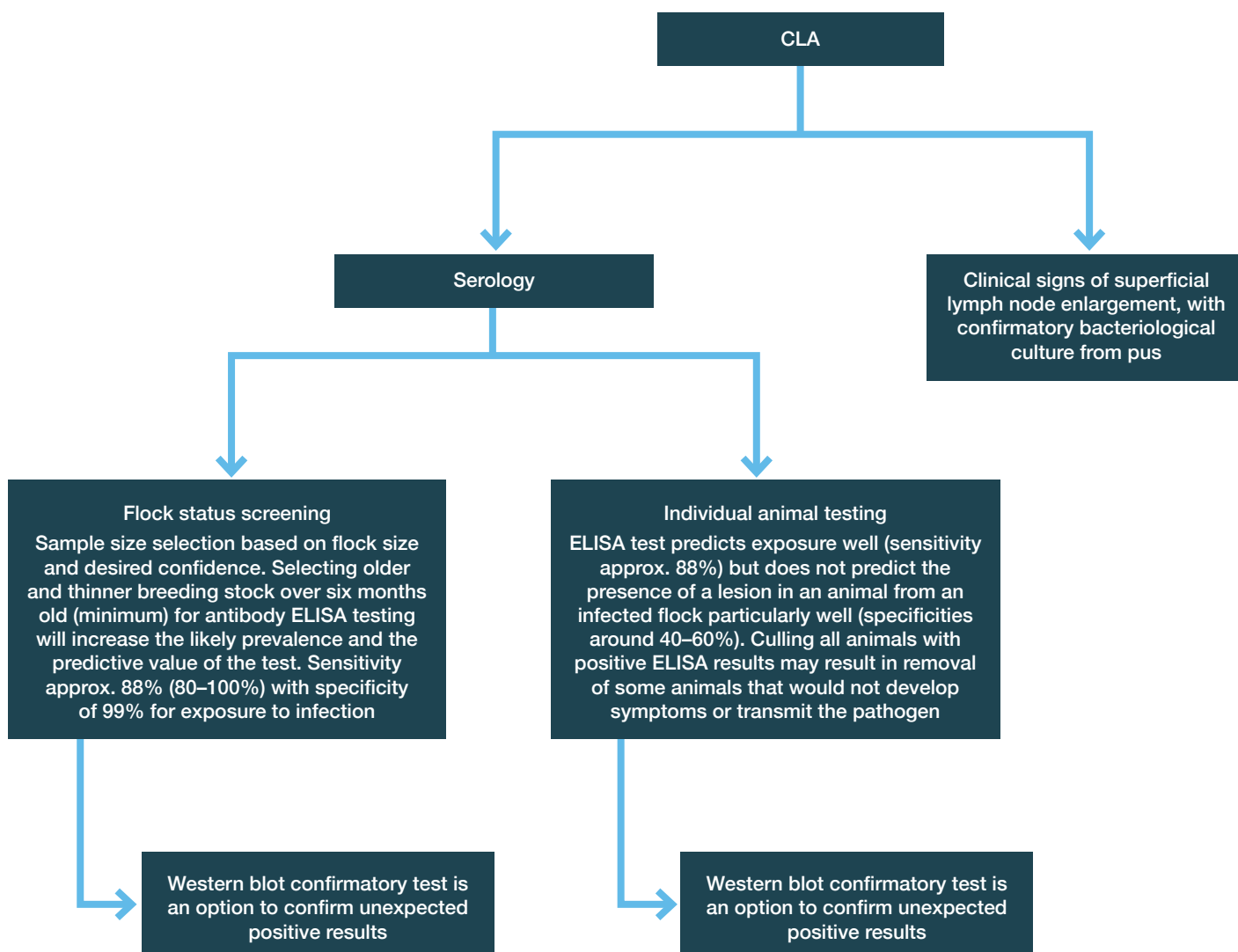


Figure 6. Summary of diagnostic decision tree for caseous lymphadenitis

# How to test for Maedi Visna

Wide variation in virus genetics and host interactions may reduce the validity of diagnostic tests. However, in general, antibody or viral detection using various blood testing methods is appropriate for early diagnosis. Although there is no universally accepted 'gold standard' to determine the sensitivity and specificity of the tests used for MV infection, successful control programmes indicate that the tests available are useful for reducing infection prevalence.

Serological diagnosis used to detect antibodies in infected animals is considered the most convenient way to diagnose MV infections. However, the time between infection and the production of antibodies (seroconversion) can vary widely, with reports suggesting a few weeks to several months. The time between infection and the development of antibodies appears to be shorter in heavily infected flocks compared with those with lower levels of infection. Additionally, animals with low antibody levels may have a negative test result for a brief period. This may be an issue in MV diagnosis and eradication, but it should improve with repeated testing.

There are a variety of laboratory techniques that can be used for this purpose, with AGIDT and ELISA being most common in the UK.

The AGIDT was found to be 76% sensitive and 98% specific compared with ELISA because of this high but subjective specificity, AGIDT is mostly used to confirm ELISA results.

More than 30 different ELISA tests have been produced. Given that there are wide variations in viral strains, the antigen used should reflect that which is currently circulating in the local area to achieve acceptable accuracy. ELISA tests are suitable for screening large numbers of animals; they are more sensitive than AGIDT and are quantitative, allowing for computer-based analysis of raw data. Commercial ELISA tests have reportedly achieved a sensitivity of 99.4% and a specificity of 99.3%, although the accuracy and specificity of several UK flocks screened using this ELISA have been questioned. Sampling has shown that ELISA tests can detect antibody development at an earlier stage compared with the AGIDT. Overall, ELISA tests appear far more sensitive than PCR (because of a very low viral load in blood or secretions), except in young animals. However, PCR appears able to detect some infected animals before the development of antibodies.

There is an agreement of 90% between ELISA tests of blood and milk, therefore it may be preferable to take milk samples rather than blood samples in milking flocks (and potentially meat flocks during lactation) because they are easier and cheaper to obtain.

In summary, it is important to establish the tests that are appropriate for the desired level of confidence and to select the appropriate type and number of animals to make flock screening valid and robust. Typically, a high-sensitivity ELISA test for screening, followed by a high-specificity ELISA or AGIDT test for any resulting positive samples, will be most appropriate. To establish flock status, sheep at highest risk that are most likely to have antibodies should be selected i.e. thin, old ewes that may be suffering from clinical disease.

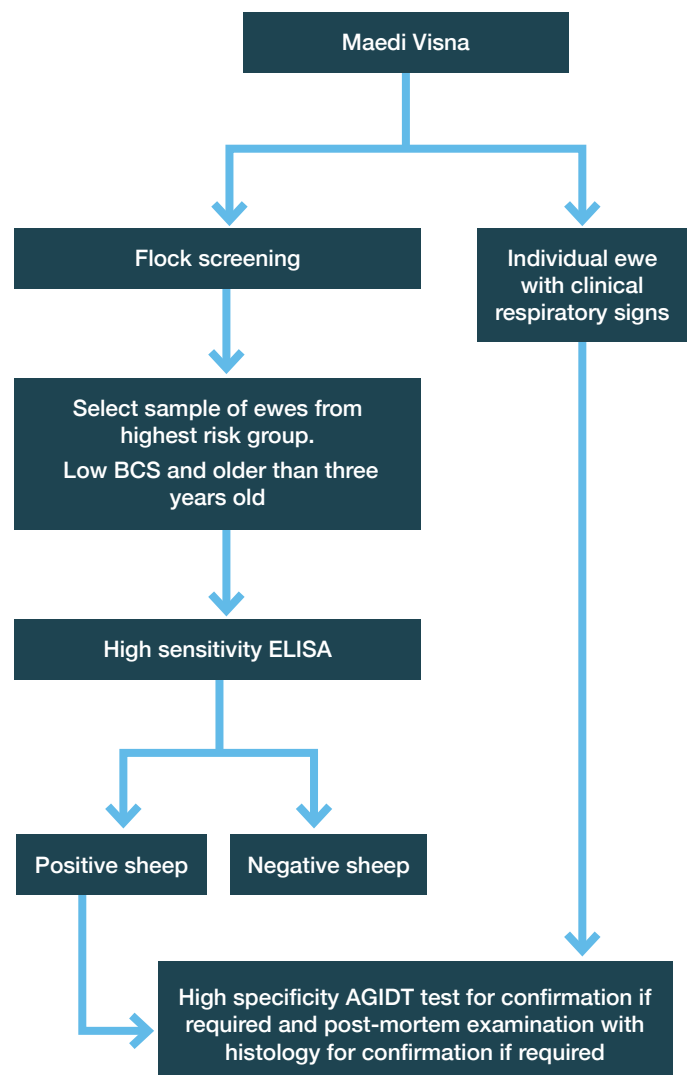


Figure 7. Summary of diagnostic decision tree for Maedi Visna



# How to test for ovine Johne's disease

Johne's can be complex because some animals clear the infection and do not develop disease, while others do (see Figure 8).

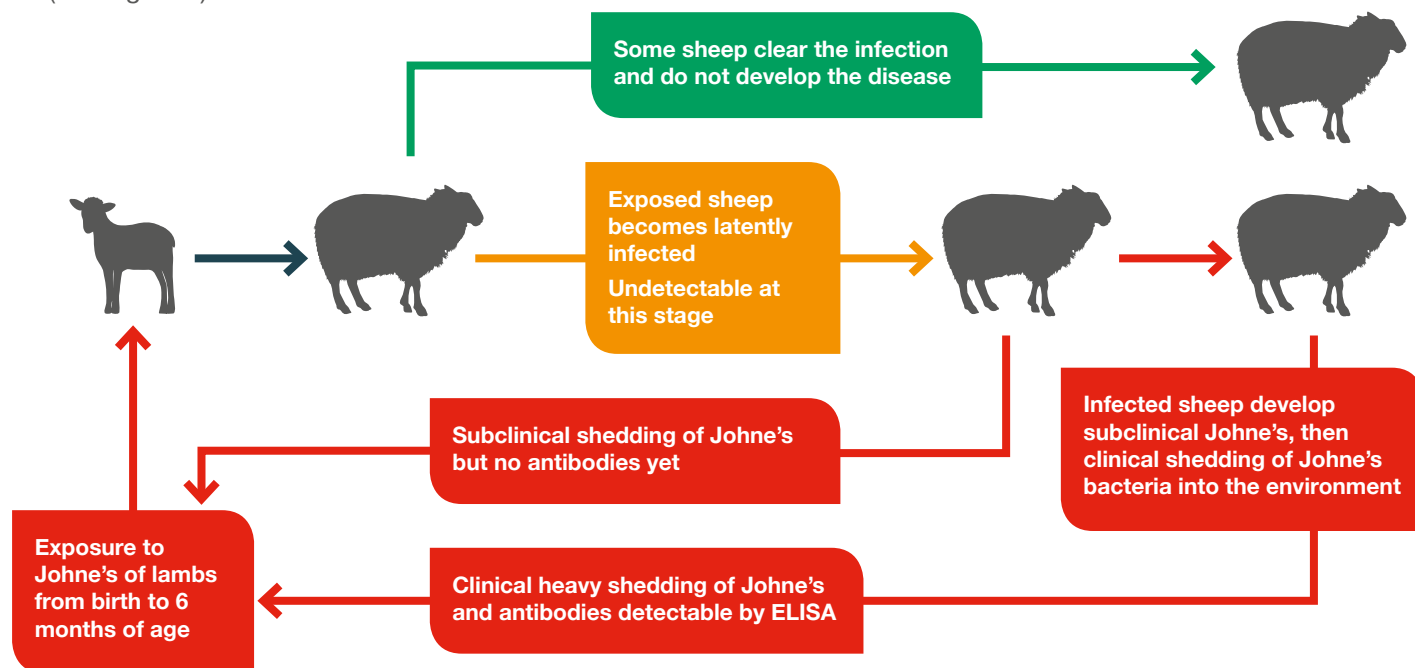


Figure 8. The ovine Johne's disease transmission cycle

The most definitive diagnostic test for clinical Johne's is gross pathology at PME with histopathological confirmation. This is very useful as part of the routine screening of cull and fallen stock, but may not be sufficiently sensitive to establish flock status quickly or cheaply enough to be useful for small or medium-sized flocks where prevalence may be low.

The greatest challenge for Johne's is the low sensitivity of available diagnostic tests. This is worsened by the inability to identify dormant and subclinical Johne's infections, particularly as faecal shedding of the organism can be intermittent in these animals and tends to precede antibody responses. For these reasons, large sample sizes are necessary to achieve sufficient confidence to identify low or moderate prevalence.

Identifying the bacteria by PCR is generally accepted as the most sensitive means of detecting infection within a flock. In contrast, antibody tests with a strong response to the bacteria are taken as being more specific, while they generally represent a later point in the infection and are less sensitive.

For both PCR antigen and ELISA antibody tests, there is significant uncertainty when low results are regarded as inconclusive and require repeat or confirmatory testing.

In Australia, a testing programme called SheepMAP has been established for over 20 years. In the UK, no such testing programme is currently available, with laboratories recommending small pools of five or 10 animals, which significantly increases the cost to achieve the same sensitivity. The UK Johne's scheme relies upon blood ELISA samples from every animal, which is uneconomical to be of use in most flocks.

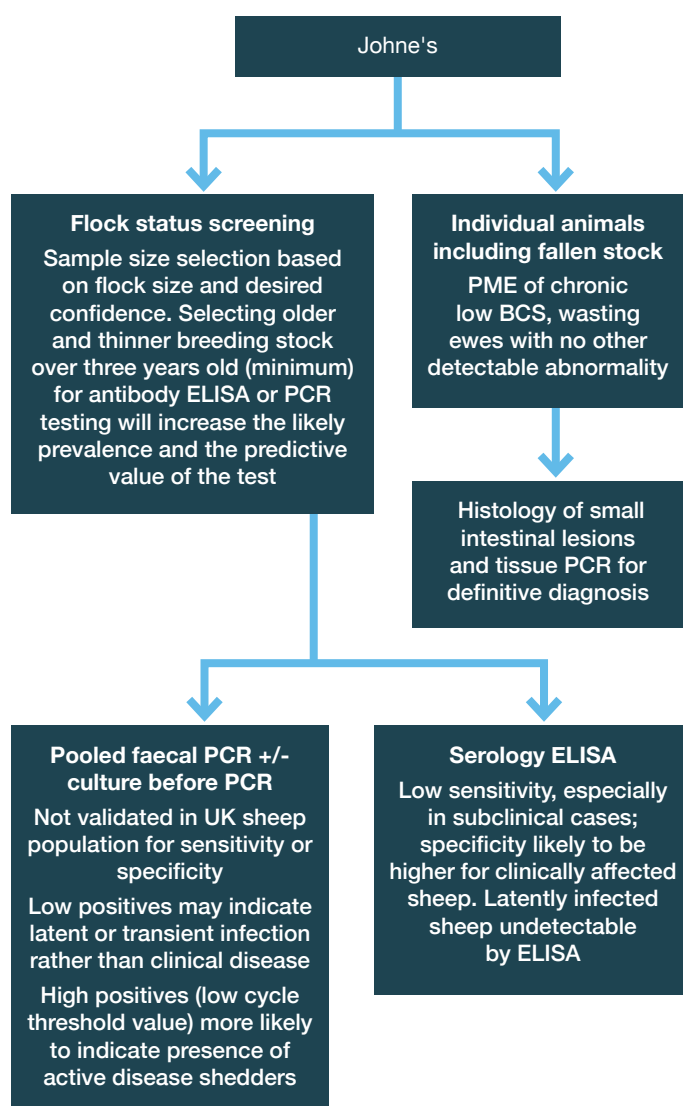


Figure 9. Summary of diagnostic decision tree for ovine Johne's disease

# How to test for ovine pulmonary adenocarcinoma

Currently, there are no commercially available serological or antigen assays for OPA. Diagnosis in the live animal is by clinical signs and/or transthoracic ultrasound examination.

The most definitive and reliable diagnosis is achieved by PME, with gross pathology supported by histopathology. However, even this approach is surprisingly insensitive. A study has shown that 25% of those sheep found to be histologically positive for OPA had no visible gross lesions. Of the 75% with some visible lesions, most of the OPA-positive animals had multiple, easily recognisable typical histological lesions, but some had only a single, small lesion. Furthermore, on gross visual PME, 13% of suspect OPA cases were false positives following histological examination.

These test characteristics and the lack of any confirmatory test or alternative lab-based test in the live animal, present significant challenges to the surveillance of the disease for individual flocks.

Transthoracic ultrasound examination can be useful as a diagnostic tool in the symptomatic, thin ewe to gain

additional diagnostic information. It has a place in the hands of experienced practitioners dealing with high-prevalence flocks in which the positive predictive value is high. Early culling before the appearance of symptoms would enhance animal welfare, with a lower risk of accidentally culling false positive animals.

In the hands of an inexperienced operator, there is a risk of low specificity, as lungworm lesions, abscesses or the liver can be confused with an OPA tumour. Even in the hands of an experienced operator, sensitivity is low for early cases when lesions are too small to detect.

The low sensitivity and specificity, combined with operator subjectivity, makes transthoracic ultrasound examination an unproven tool for screening disease in asymptomatic animals or flocks with low or unknown prevalence. The substantial risk of false negative results means that it should not be used to claim disease freedom.

Also, repeated application of this technique cannot guarantee eradication of the disease.

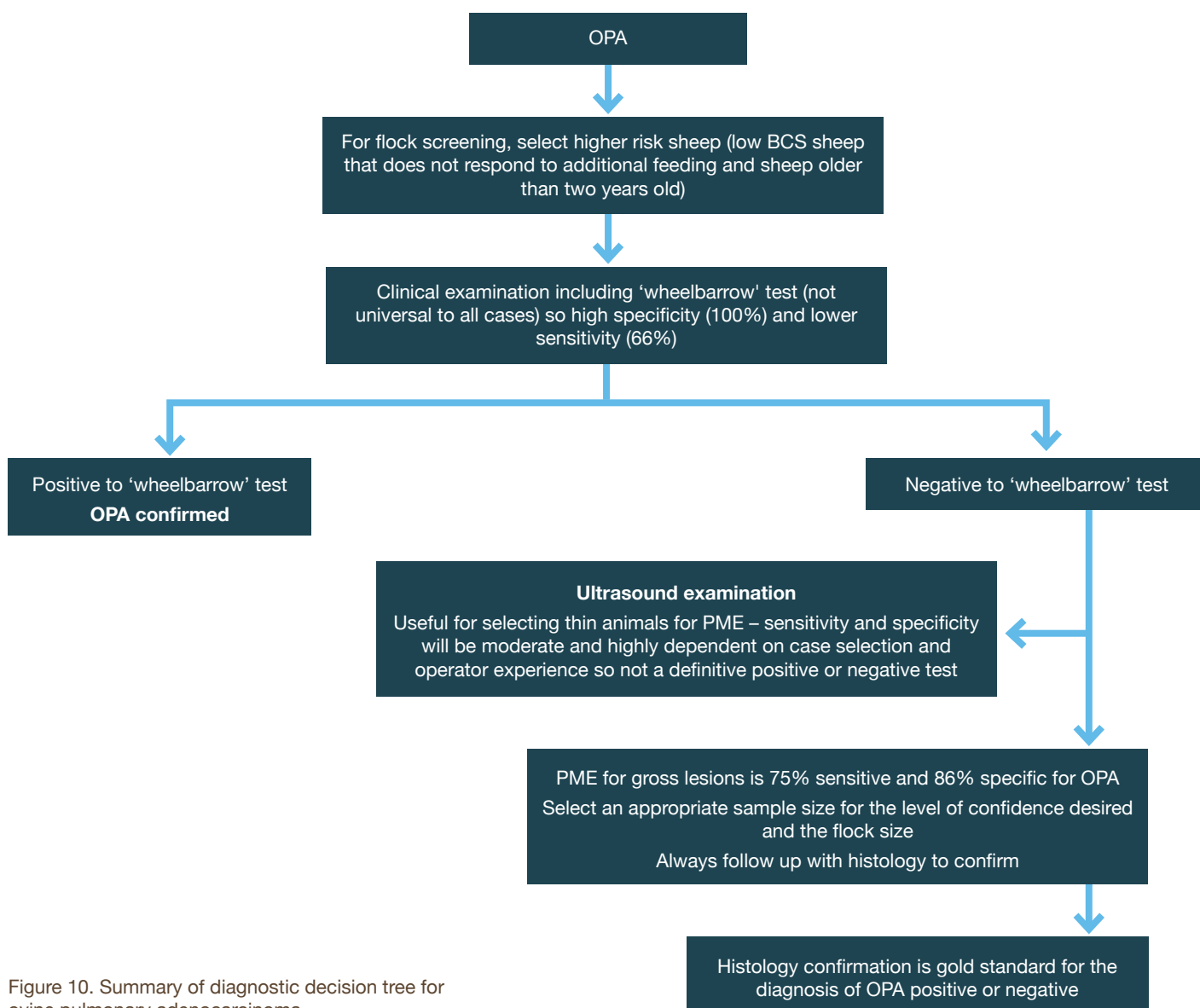


Figure 10. Summary of diagnostic decision tree for ovine pulmonary adenocarcinoma



## Impact on trade and exports

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The diagnosis of any of these diseases in a flock may prevent owners from exporting stock to specific countries or territories, depending on the disease status and the receiving country's policy at that time.

In some cases, individual animals will require testing prior to export, e.g. for MV, while in other cases, a declaration of no known disease in the flock made by the owner or vet may be all that is required.

However, if farmers wish to export stock, specific export requirements should be clarified with Defra before any disease screening or the introduction of a vaccination control programme. This is important because the vaccination status of stock may prevent or hinder export of stock to certain destinations and requirements may change at any time.



These were part of the 128 Shropshire sheep going to Belgium, Holland and France in 2018. They came from 14 Shropshire breeders and went out to 6 different buyers.

Photo source: Sue Farquhar

# Control options

## Border disease

The characteristics of the disease suggest that, in a newly infected flock, the most noticeable production losses will occur during rapid disease spread. Once endemic disease has been established within that flock, disease symptoms will become less apparent. Farmers should be made aware of this, as well as the potential for ongoing hidden losses, as part of the consultation with their vet. Farmers of flocks who purchase replacements on an annual basis from several sources could find there is a very unpredictable disease risk. A naive group of sheep has the potential to be exposed to BD virus from an endemically infected flock, giving rise to rapid disease spread.

There is also the potential for ongoing transmission of the virus in the absence of PI animals. Some sheep can only infect other susceptible sheep for a limited time because they can recover quickly and develop immunity. This needs to be considered before very expensive 'PI hunts' are undertaken. Transmission within large flocks is not sufficiently understood to provide confidence that flock-level infection can be controlled in the same way as in cattle.

'Natural vaccination' by exposure to a PI or mixing replacements with an endemically infected flock has been widely discussed as a means of control. However, multiple case reports suggest that transmission is slow and this approach does not result in a high proportion of immune ewes in most cases and instead, the disease will persist in a flock. Discuss control methods with your vet for your specific farm situation.

## BVD and Border disease transmission and control between cattle and sheep

There is limited evidence that BD virus and BVD virus can be transmitted between cattle and sheep. Cattle have been found to develop an immune response to BD virus infection under natural conditions and cattle persistently infected with BD virus have been reported. Pregnant heifers housed with a PI bull tested positive for BD virus and PI was diagnosed in three of the six unborn foetuses at PME.

Housing cattle and sheep in the same building was identified as the most important risk factor for BD virus infection in cattle.

Differences in the transmission of BD within the sheep population and BVD within the cattle population have been highlighted. The risk period for BD PI production is shorter than that of cattle and during this time sheep are not routinely housed and so risk of transmission is thought to be lower.

As the UK moves towards eradicating BVD, the transmission of BVD and BD between cattle and sheep may be increasingly relevant as an increasingly susceptible cattle population develops. This risk should not be ignored.

Herds in which BVD eradication is taking place should screen in-contact sheep for BD and carry out a risk assessment to identify the appropriate biosecurity changes to make. For example, pregnant sheep should never be mixed with cattle or vice versa and sheep and cattle should never be housed in a shared air space.

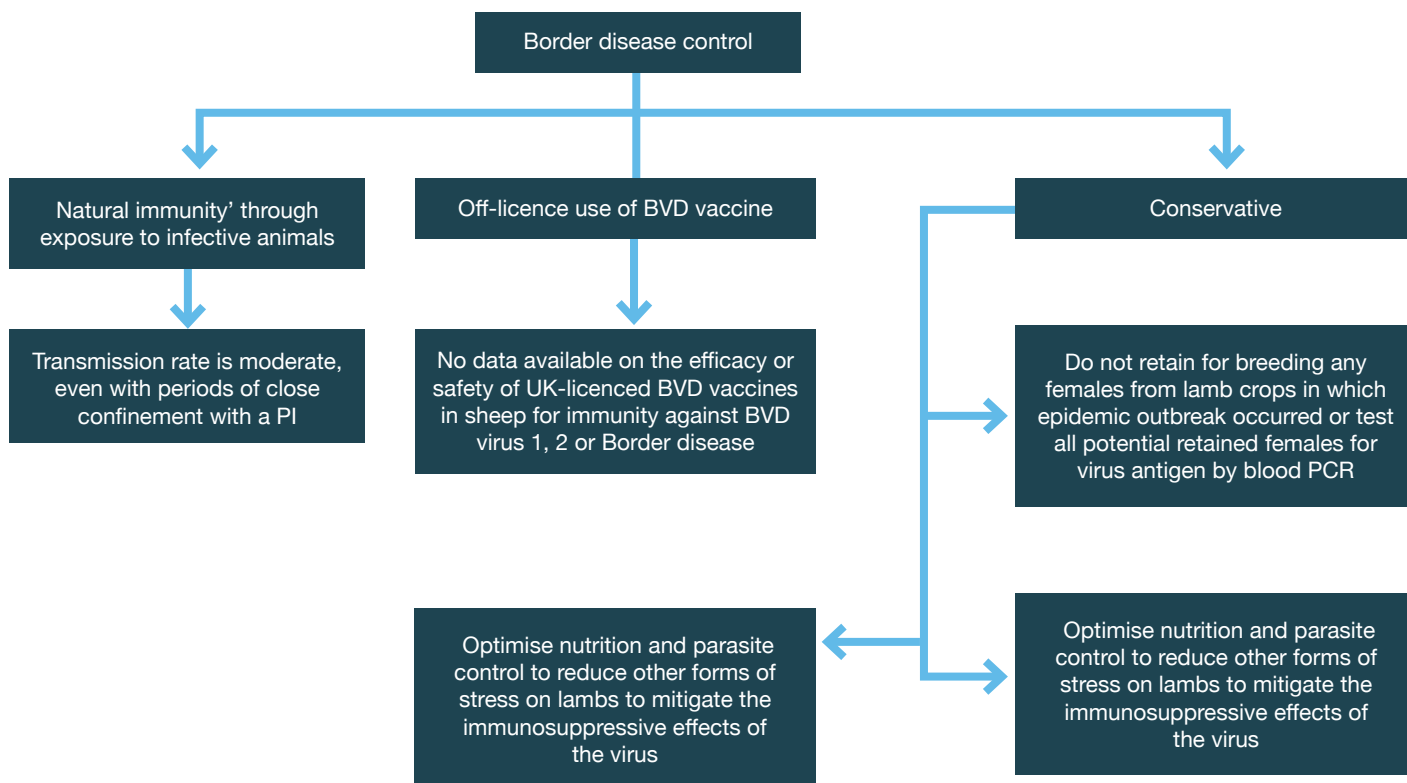


Figure 11. Summary of control measures for Border disease



Routine procedures such as tag and testing, which have formed an important element of BVD control, are not validated for BD in the UK. Reliance on blood testing in sheep flocks may hinder BD control because of the cost and time associated with traditional blood sampling procedures. Tissue and milk-based testing protocols would provide more flexible and possibly cheaper diagnostic options for producers.

### Case study flock: Border disease

#### Background

The farmer reports that very strange lambs were the initial issue, with an increasing barren rate. At the initial investigation in 2012, the vet was worried about trace element levels; however, all mineral levels were adequate. The issue continued and, in 2014, the farmer reports poor, woolly, stiff lambs that would sometimes shake. These lambs would often die within 24 hours of birth and be from apparently fit and healthy ewes. The affected lambs sampled positive for BD virus. The farmer was not able to identify when BD was introduced onto the farm.

Table 7. Flock outline

Farm size	142 hectares rented
Farm type	Open flock – ewe lambs last purchased in August/September 2017
Sheep details	Medium-sized flock, with a mixture of homebred ewe lambs and bought-in shearlings and ewe lambs used as replacements
Cattle numbers	Small suckler herd All calves are sold as stores Cattle are vaccinated for BVD Unknown status for Johnne's Cows and sheep may graze the same fields, but very rarely at the same time
Production aims	Produce prime lamb sold liveweight at the local market A few ewe lambs will be sold as breeding stock and remaining lambs sold as store lambs towards the end of the season
Scanning rate	Average 187% (2008–2018)
Source of replacements	Replacement shearlings sourced from local market Crossbred ewes by a terminal sire are homebred Ewe culling rate: 17% Ewe replacement rate: 21%
Vaccination protocol	Ewes, tups and lambs vaccinated with Heptavac™ P plus Ewes vaccinated with Scabivax™ Forte two months pre-lambing Ewes and tups are vaccinated with Footvax™
Start of lambing	Mid-February and 1 April 2018

#### Farm management

Excellent flock records have allowed detailed monitoring of flock performance. This flock is lambed indoors, with ewes and lambs turned out 2–3 days post-lambing. Early and late lambing groups are kept separately until weaning. Once weaned, ewes are grouped according to BCS. Half of the replacement ewe lambs spend time away from the farm on winter keep, but have no contact with other livestock.

On average, 4% of ewes die on farm and 17% will be sold as cull ewes each year. Ewes are culled for age, vaginal prolapses, mastitis and recurring lameness. Replacement crossbred shearlings are purchased from the local market and, in the past, in-lamb shearlings have also been bought. Replacement tups are bought from one farm.

All new stock introduced onto the farm are dosed with monepantel (Zolvix™, Elanco), foot-bathed and then housed for three days before being turned out with the main breeding flock. New tups are kept separately until tupping time.

#### Performance figures

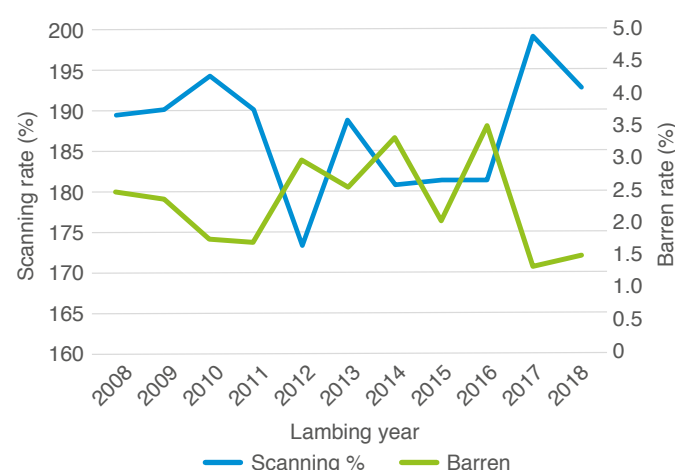


Figure 12. Ewe fertility, 2008–2018

Overall, the scanning figures are very good, with over 180% achieved in most years. There is a noticeable drop in fertility in 2012, associated with both a reduction in scanning rate and an increase in barren rate (Figure 12). Unlike the scanning rate, the barren rate does not recover to below the target of 2% until the last two years. This reduction may indicate that this was the year in which BD was introduced to the flock and certainly ties in with the farmer's history. The farmer reports no age distinction in the barren ewes.

The number of lamb losses appears to increase (Figure 13). Interestingly, there is a sharp rise in 2011; the season before fertility issues were seen in the ewes. The losses appear to be spread between scanning and sale (target scanning to turnout <11%, target turnout to sale <4%). The increase in lamb losses may be attributed to the presence of BD virus on farm, leading to increased secondary diseases. Targeted PME's may help to reduce the number of losses.

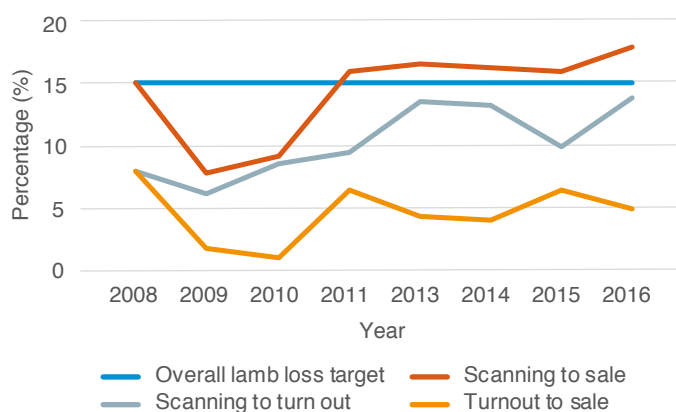


Figure 13. Total lamb losses, 2008–2016 (excluding 2012 as data was missing)

### Intervention since diagnosis

The farmer sought advice from Moredun Research Institute and a sheep consultant working in conjunction with the vet. Ewes with affected lambs were tagged and culled the following year if they had affected lambs again. Gradually, the number of hairy shaker lambs has reduced, with just one being identified in the 2017 lambing season.

Replacement shearing ewes are mixed with the main flock (ewes with lambs) from the first week of May until tupping. This is to allow them time to become exposed to BD virus prior to first tupping.

### Farmer's view

The farmer indicates that the initial veterinary advice received was conflicting: they were told their older sheep would be most at risk, when in fact the opposite is true. They acknowledge that relatively little was known about the disease at the time of diagnosis, but felt the vets could have done more to investigate other flocks' control methods.

The most useful advice was to mix their replacement ewes with the main flock for a long period pre-tupping to maximise the chance of developing BD virus antibodies. The farmer has targeted good husbandry and aims to keep ewes in good condition to try to reduce the effects of BD within the flock.

The farmer acknowledges that clinical signs may come and go over the years, but is prepared to tag ewes with affected lambs and remove any affected lambs.

### Considerations for the case study

Data collected by the farmer is incredibly useful to allow the analysis of flock performance. Further data on the age of the barren ewes would help to assess which ewes are most affected.

The gradual increase in lamb losses should not be overlooked, although it is just above the target of overall lamb losses of 15%. Lamb sale data would have been useful to analyse the effect of BD on lamb growth rate.

It is difficult to assess the level of circulating BD virus antibody without sampling a proportion of the flock. Two ages of sheep could be assessed, including young lambs at approximately eight weeks old when

maternally derived antibodies have waned and a group of maiden ewes prior to tupping. If antibody levels in the maiden ewes are adequate, they will be protected by 'auto-vaccination', i.e. exposure to the virus during the period with the rest of the flock.

All replacement stock should be quarantined for a period of 21 days to reduce the risk of introducing several disease issues into the flock.

## Caseous lymphadenitis

The chronic and often subclinical nature of this disease makes it difficult to control. Experience from other countries shows that, if left uncontrolled, up to 60% of adults within a flock may become infected.

Control strategies include vaccination, eradication by test and cull or conservative management by culling animals with symptoms at the earliest opportunity.

In the UK, the vaccine *Glanvac*<sup>TM</sup> may be imported under licence from the Veterinary Medicines Directorate or, alternatively, an autogenous vaccine can be prepared within the UK. However, the cost benefit of vaccination in the control of infection in commercial UK flocks is unknown. *Glanvac*<sup>TM</sup> has been shown to provide between 25% and 90% protection in the Australian sheep population; reports from users in the UK indicate a reduced prevalence of clinical lesions.

Vaccinated animals produce a response that is indistinguishable from natural infection, so blood tests cannot be used with a vaccination strategy. However, clinical examination and culling individuals with lesions can be used in addition to vaccination.

Test and cull strategies whereby all breeding stock are blood-tested at six-month intervals and all positive animals are culled (inconclusive can be confirmed by western blot) have effectively reduced exposure to the pathogen to zero in 4–5 years. The moderate sensitivity of the ELISA test means that culling rates may be high and more rounds of testing are required compared with equivalent eradication strategies for MV or BD. The lack of robust data on the productivity implications of endemic CLA means it is currently challenging to make cost-benefit decisions at an individual flock level.

Regardless of the strategy adopted, basic hygiene practices should be adopted, such as handling older animals last if possible and shearing older sheep after younger ones to avoid cross-contamination. Similarly, disinfection with most agents will kill the pathogen.



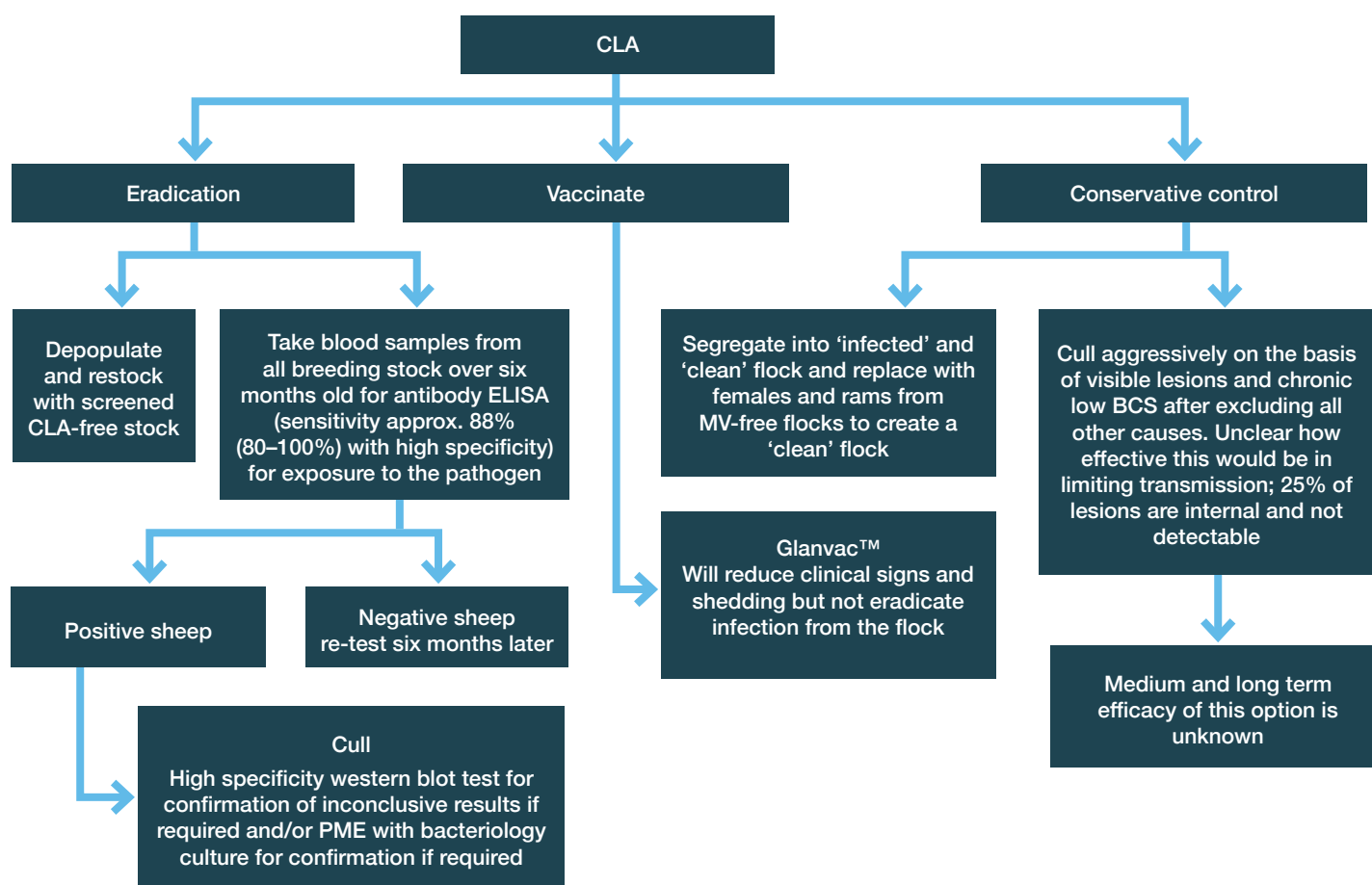


Figure 14. Summary of control measures for caseous lymphadenitis

### Case study flock: CLA and Border disease

#### Background

Formed in 2009, the flock comprised a mixture of pedigree ewes. The farmer subsequently bought 80 crossbred ewes from their father's flock.

The father's crossbred flock had a history of CLA during the early 2000s. There were more clinical signs in some breeds than others, despite no difference in management. Sheep in the old flock had large pus-filled lesions around the face and neck and less commonly around the udder.

Control measures were not put in place on the father's farm. Lesions started to develop in the breeding tups for sale in the new flock, so the farmer sought advice on containing the disease. CLA was diagnosed on the basis of clinical signs and response to vaccination. The farmer reports no obvious effects in lamb production or the culling rate of the ewes in either affected flock.

In 2013, four hairy shaker lambs were born within the early lambing group. In the first year, they encountered hairy shaker lambs; both lambing groups encountered serious issues with coccidia in the growing lambs. Since then, lambs in both lambing groups have been born with similar signs. BD virus was diagnosed based on the typical clinical signs seen in the affected lambs.

Table 8. Flock outline

Farm size	194 hectares rented
Farm type	Lowland pedigree and commercial flock Open flock – 50 ewes and 4–5 rams bought in per year
Sheep details	850 ewes and 14 stock tups (pedigree terminal sire breeds) 200 replacement lambs (50 tupped in 2017)
Cattle numbers	50 youngstock and 10 cows to sell to local farm shop (at 32 months old) Cows and sheep will co-graze. Unknown BVD and Johne's status in cattle
Production aims	Produce prime lamb, sold deadweight, aiming for 3L grade and to sell pedigree shearling tups as breeding stock; 200 lambs are sold direct to the local farm shop Future aims: increase the number of pedigree sheep, which may slightly reduce overall flock numbers; aiming to be MV accredited for all breeding stock that will be sold
Scanning rate	January lambing 2018: 175% March/April lambing 2018: 185%

Table 8. Flock outline continued

Source of replacements	Homebred replacements are kept where appropriate New genetics are sought from a variety of sources 0–50 ewes bought in per year; approximately four tups bought in per year
Vaccination protocol	Ewes' replacements are vaccinated with Toxovax™ and Enxovax™, Bravoxin™ 10 and Ovipast™ Plus Lambs are vaccinated with Ovivac™ P Plus All breeding stock and replacements are vaccinated with Glanvac™ 6
Start of lambing	Lamb in two groups: mid December 2017 and beginning of March 2018

### Farm management

Most ewes lamb early to meet the Easter market for new season lamb. Pedigree ewes are tupped later to breed tups for the shearling ram sales the following year.

Both lambing groups are housed five days before the start of lambing. Ewes and lambs are turned out 24 hours after lambing. Lambs are creep-fed from two weeks old with feed that contains a coccidiostat, given that the flock has previously had significant coccidia issues. They are weaned at 12 weeks.

After weaning, the later-lambing ewes are split according to BCS at weaning. In the last few years, the farmer has paid more attention to BCS and this has become noticeably more consistent.

The farmer may buy in whole pedigree flocks that are going out of business and pedigree tups may be sourced from individual farms or ram sales. On arrival, new sheep receive monepantel and a long-acting wormer, two doses of closantel and Glanvac™ 6. New tups will be turned out with the rest of the tups straight away, but ewes may be kept separate until tupping time.

Ewes and tups are culled on BCS, teeth, lameness, mastitis and poor mothering ability. The farmer is more lenient with sheep that initially cost more.

### Intervention since diagnosis

In 2014, all breeding ewes, tups and replacement lambs were vaccinated with Glanvac™ 6 for CLA control. All replacement stock animals receive two doses at six months old and new animals introduced onto farm are vaccinated as soon as possible. All breeding stock animals receive an annual booster. Since vaccination was initiated, there has been a dramatic decrease in the clinical signs associated with CLA. Roughly, 80% of breeding tups are sold at the farm gate and these are advertised as vaccinated for CLA.

Since the first hairy shaker lamb was identified on farm in 2013, the farmer has culled any clinically affected lambs. Ewes that give birth to hairy shaker, strange or poor lambs have been culled and ewes bought in the year previously to the outbreak were culled. The farmer

was advised to cull all ewe lambs born in 2013, but was unable to do so as it was not financially viable. The farmer reports no affected lambs in 2018 to date.

### Farmer's view

The issue with CLA had been allowed to rumble on in the previous flock but, as the farmer did not want their reputation to be affected by selling poor tups, the disease issues were investigated. The farmer also mentions that vaccine unavailability prevented them from starting vaccination sooner. It is difficult to get new stock onto the vaccine regimen because of the vaccine bottle size (250 doses per bottle) and buying in stock throughout the year. The farmer is incredibly pleased with the response seen since vaccination was introduced. They have noticed one lesion in the last 12 months; however, they feel that this animal may have missed its initial start-up course.

BD virus control on farm was more difficult. The farmer should have culled all affected sheep as soon as possible. They are unsure whether the heavy burden of coccidia among the lambs in 2013 was from the introduction of BD virus into the flock or attributed to the weather conditions that year.

The farmer aims to breed rams for commercial breeders and to sell all breeding stock as MV accredited.

### Considerations for the case study

It is difficult to analyse the effects of either disease without production data. The high expansion rate could be a disease concern if rigorous biosecurity measures are not put in place. The farmer's desire to maintain flock numbers at around 800–850 should reduce the need to purchase stock and this will be further limited if MV accreditation is sought.

If the vaccination regimen is not followed closely, levels of CLA circulating within the flock may build again and animals may display more clinical signs. Although tups sold at the farm gate are declared as vaccinated, the sale of vaccinated tups through market without declaring the Glanvac™ vaccination makes future testing of these animals difficult to interpret.

Currently, no diagnostic test for CLA is able to differentiate between an infected and a vaccinated animal.

### Maedi Visna

In an infected flock, control can be achieved either through eradication or conservative management. The eradication protocol involves either culling followed by restocking with accredited or monitored MV-free sheep, or repeated test and cull to eliminate infection from the existing flock using high sensitivity ELISA assays (and potentially AGIDT for additional confirmation if required). The tests are sufficiently accurate to allow rapid eradication using this process.



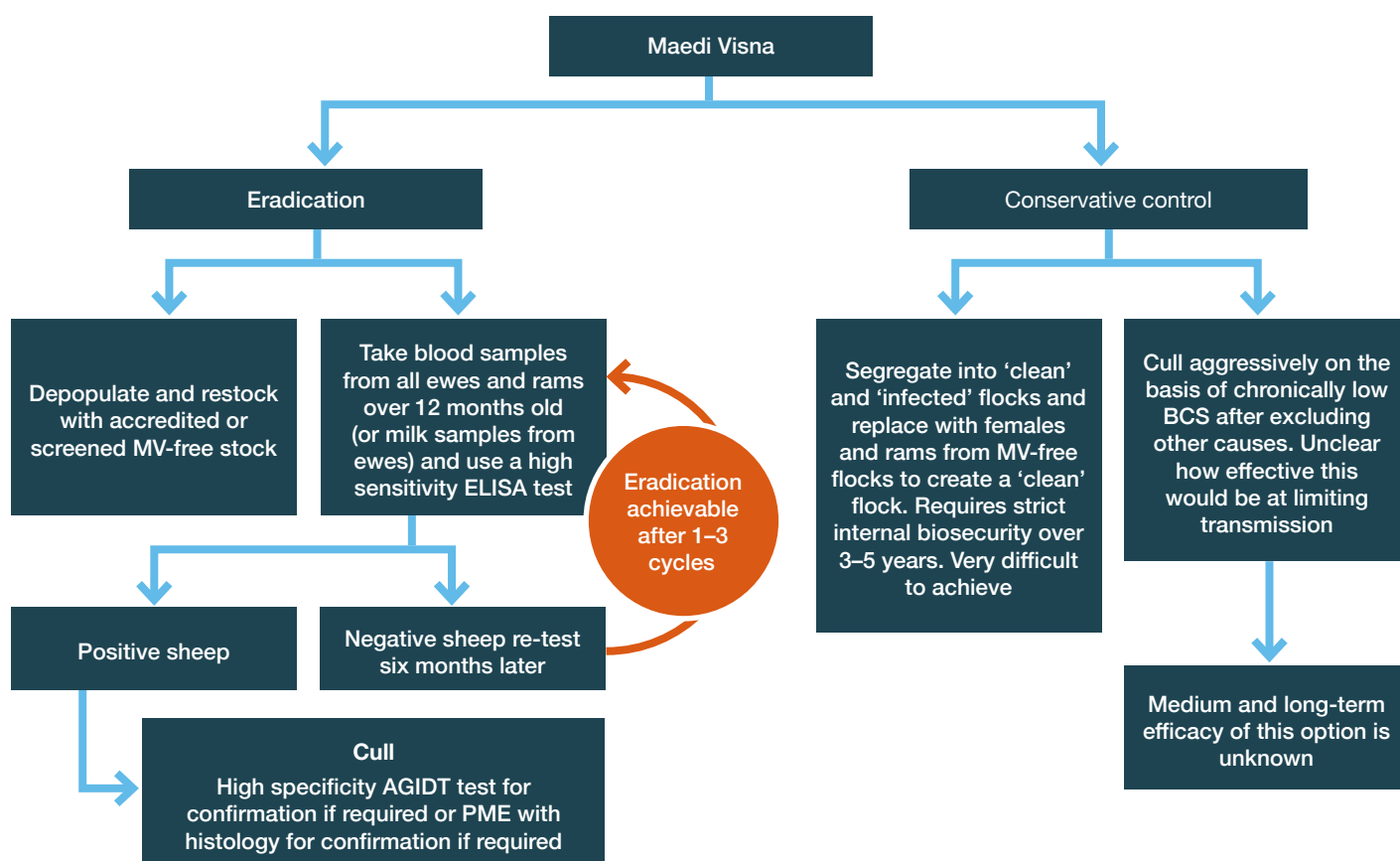


Figure 15. Summary of control measures for Maedi Visna

For farmers of flocks who are unable to embark upon an eradication programme, ‘conservative control’ strategies are another option. These include keeping a younger flock, increasing the replacement rate and increasing culling based on BCS and output, or only buying sheep from MV accredited flocks and keeping them separate from older sheep. However, transmission and subclinical disease will continue to cause production losses. The cost of keeping a younger flock and increasing culling and replacement rates may outweigh the cost of disease eradication in the medium and long term.

The Maedi Visna Accreditation Scheme was introduced in Great Britain in 1982. In 2018, participating flocks needed to have an MV prevalence of less than 5%, with a confidence of more than 98% tested on a biannual or triannual basis, along with strict biosecurity precautions. Independently of this scheme, rigorous testing of several hybrid breeds also helps to prevent transmission to client flocks.

The Scottish Agricultural College (SAC) uses a more targeted MV monitoring scheme, which has a focus on older, thinner ewes as a starting point to help establish flock status. It is highly cost-effective and allows confidence and prevalence to be calculated retrospectively. The use of milk samples collected by the farmer for MV testing could also reduce the costs of sampling for health status screening that does not require veterinary time.

### Case study flock: MV

#### Background

The farmer sells a small number of pedigree rams each year. In 2016, a purchaser who did an MV screen of 12 sheep on farm reported that a ram they had purchased from the case study flock was positive for MV.

The case study farmer then sampled 12 cull ewes for a thin ewe screen, with 11 out of 12 ewes returning a positive result. A further 100 sheep were tested and 66% of these were found to be positive for MV. All young positive sheep from the screen were kept because neither the individual sheep nor the main flock had any symptoms.

In hindsight, the farmer reports they may have had a higher replacement rate than necessary. There were no obvious clinical signs, sheep maintained good rearing rates, ewes were in good condition and lambs performed well. It was unknown how long MV had been present on the farm prior to the diagnosis in 2016.

At shearing in the winter of 2016, 30 ewes were culled because of poor BCS. The rest of the flock was in good condition and scanned at 200%.

However, by early 2017, the farmer noticed that many ewes had lost condition after being shorn. At lambing, a large proportion of the ewes were noticeably thin. Many were turned out with single lambs because of poor condition or a lack of milk. The farmer reports no respiratory signs among the ewes. Of the 490 ewes that lambed, the farmer reared 130 pet lambs.

Table 9. Flock outline

Farm size	57 hectares of permanent pasture
Farm type	Lowland/upland flock Open flock, stock last purchased in August 2017
Sheep details	420 ewes, six tups and 120 replacements Planning to increase flock size following whole flock cull in 2016/2017
Cattle numbers	No other stock on farm
Production aims	Prime lamb sold deadweight – aim for 20 kg Sell pedigree Texel rams – approximately 15 sold each year Sheep enterprise is not the primary source of income on farm
Scanning rate	200% (lambing 2016)
Source of replacements	Most replacement ewes sourced from within the flock and replacement tups are bought in All purchased replacement stock is MV accredited; replacement rate is 25%, they are bred for the first time as shearlings
Vaccination protocol	All breeding stock is vaccinated with Footvax™ and Heptavac™ P Shearlings are also vaccinated with Toxovax™
Lambing started	Beginning of March 2018

### Farm management

This flock of ewes has targeted high genetic merit to maintain excellent rearing rates and carcase quality. Ewes lamb inside throughout March, with all lambs sold as deadweight from May onwards.

The farmer purchased the current farm in 2001. All rams bought were MV accredited, with most straight from farm. Since 2008, all stock bought onto the farm was MV accredited. A high proportion of good quality ewe replacements drove a replacement rate of 25%.

Ewes are foot-bathed, winter-sheared, vaccinated for footrot and treated for liver fluke on housing in December. Once lambled, ewes are penned with their lambs for 24 hours before being placed in a group pen for a few days before being turned out. Lambs are weaned at approximately 12–14 weeks old.

New stock is housed overnight, wormed with a monepantel and then kept in a separate field for 14 days before mixing with the rest of the flock. New stock is also vaccinated with Heptavac™ P plus and Footvax™.

### Intervention since diagnosis

Following a difficult lambing season in 2017, the whole flock was culled. The farmer reports that 20–40 ewes were culled each week from December 2016 to July 2017.

The farm was restocked with approximately 500 breeding ewes from a variety of sources. All sheep were from accredited stock, except for a small group of mixed-breed sheep that had been kept separately on farm and were considered MV-negative following two clear tests.

### Lambing figures

Table 10. Lambing performance figures 2016

Number of ewes to tup	634 (including ewe lambs)	Key parameters (%)
Number of lambs scanned	1,268	Scanning rate = 200
Number of lambs born (including any mummified etc.)	1,219	Lambing rate = 192
		Lamb losses = 12.5
Number of lambs retained on farm	140	Rearing rate = 175
Number of lambs sold	969	Rearing rate = 175

Table 11. Cost of culling and replacing the whole flock

	Number of sheep	Average price per head (£)	Total (£)
Culls sold (December 2016–July 2017)	548 ewes	66	36,000
Replacement sheep**	Ewes Tups Ewe lambs	150 800 85	73,100 5,600 10,300 = 89,000
Net cost associated with whole flock cull			53,000

\*\*Note: all stock animals were MV accredited. Most were pedigree, therefore were more expensive than commercial ewes. Farmer estimates that this cost £18,200 more than re-stocking with commercial ewes alone.

### Farmer's view

The farmer is unsure as to how the disease entered the flock. Since the flock started in 2001 they had only bought MV accredited stock. The farm has no borders with other flocks. The farmer doesn't think any clinical signs of the disease were present until winter 2016. The effect of MV was then devastating for lambing the following spring.

The farmer acknowledges that it was difficult to buy enough MV accredited stock, but they are worried that other issues may have been brought onto the farm, such as Johne's or liver fluke.



Other farmers had worrying reactions to the news that this farmer has MV on the farm. Some were indifferent, others asked, “you are selling lots of lambs, so what is the problem?” The farmer was also asked why they were not selling the ewes for breeding.

**More work needs to be done to improve farmer awareness of the disease and to understand its clear limitations to flock health, welfare and production.**

### Considerations for the case study

This flock demonstrates that good lambing figures can be achieved despite the presence of MV, possibly masked by a high genetic turnover. However, this case study also shows that good lambing figures are not sustainable with MV infection. The flock prevalence of 66% is similar to other flocks in which clinical signs associated with MV infection started to become apparent. Once prevalence has reached this level, control options for MV are very limited.

One question that is likely to remain unanswered is the source of disease. Introduction of infected non-accredited animal(s) in 2001, or a breakdown in an MV accredited source flock appear to be the only explanations. The relatively long housing period over the winter may be a key time for disease transmission because of close and prolonged contact with other sheep.

Ewe death rates within the last three years appear to be within the national ewe mortality rate (4–6%), however, they are slightly above a target rate of 4%. The figures of 2017 should be carefully considered. The farmer culled 30 ewes at scanning because of poor condition. The mortality rates would have likely been much higher had the farmer not acted quickly to cull ewes that were losing condition and then ultimately culled the whole flock. Ewe mortality for 2018 is higher than the farmer would have liked, however, they note that more ewes than normal were lost to mastitis. Stress and poorer nutrition associated with a poor spring may have increased mastitis rates.

### Ovine Johne's disease

The three main approaches to dealing with Johne's in ruminants have been attempted and their pros and cons in sheep are outlined in this section.

#### Management changes to decrease transmission of ovine Johne's disease

In the largely extensive production systems practised in the UK, ‘snatch-lambing’ with artificial rearing will not be economically viable, except for dairy flocks or extremely high-value pedigrees. However, other management protocols, such as lambing high-risk shedding ewes (older and thinner) away from the younger breeding ewes in separate pens or separate lambing fields, would be feasible for most enterprises.

The possibility of selecting replacement females exposed to infection would also be limited by only selecting younger ewes. To be most effective, segregation throughout the rearing period to at least six months of age would be desirable. However, the longer the segregation, the more challenging the management of the growing lamb crop becomes with competing priorities such as grass supply.

It is logistically difficult to kill bacteria on equipment and in housed lambing systems through disinfection. Prudent measures to adopt to control Johne's and other pathogens, particularly at lambing time, are practising good hygiene, physical separation with clean bedding and, potentially, adding lime or sand to absorb moisture. Bacteria can also be spread via manure, however, in the context of Johne's in sheep, any risk attributed to manure spreading (whether cattle or sheep manure) has not been sufficiently investigated. Similarly, the role of wildlife vectors remains unclear in the epidemiology of Johne's transmission.

#### Test and cull to eliminate the sources of infection

Test and cull has been tried but has repeatedly failed in sheep. This failure is associated with a combination of persistent environmental reservoirs of infection, inaccurate individual animal tests, expensive testing protocols using existing tests relative to individual ewe value and resistance of farmers to engage with the policies when implemented at a regional or national level. Compared with cattle, in which blood-testing of dairy herds, in particular, is very common in the UK, there is no realistic prospect that this approach will be more cost-effective in sheep than the alternative of vaccination and transmission management.

#### Vaccinate replacements to increase their resistance to infection

As a way to control Johne's in small ruminants, vaccination has been highly effective. Importantly, vaccination does not prevent infection, but it significantly reduces the occurrence of clinical cases and the rate of bacterial excretion from infected animals.

The *Gudair*<sup>TM</sup> (316F strain) vaccine is believed to be effective against both C and S strains of the bacteria causing Johne's. In Australia, effective vaccination underpins the national Johne's control programme, along with a risk-based trading system, SheepMAP.

The Australian vaccination programme starts with the vaccination of all lambs between 4 and 16 weeks of age. This practice should be continued annually. Non-vaccinated animals are gradually removed for reasons of age, production or if they are clinically suspect. The value of vaccinating adult animals is limited.

Vaccination reduces deaths caused by the disease by 90% and delays and reduces faecal shedding of the causative organism. Bacterial excretion was reduced by more than 90% in vaccinated animals; however, given that occasional cases of disease and shedding have been reported in vaccinated animals, the vaccine is not 100% effective in high-challenge situations.

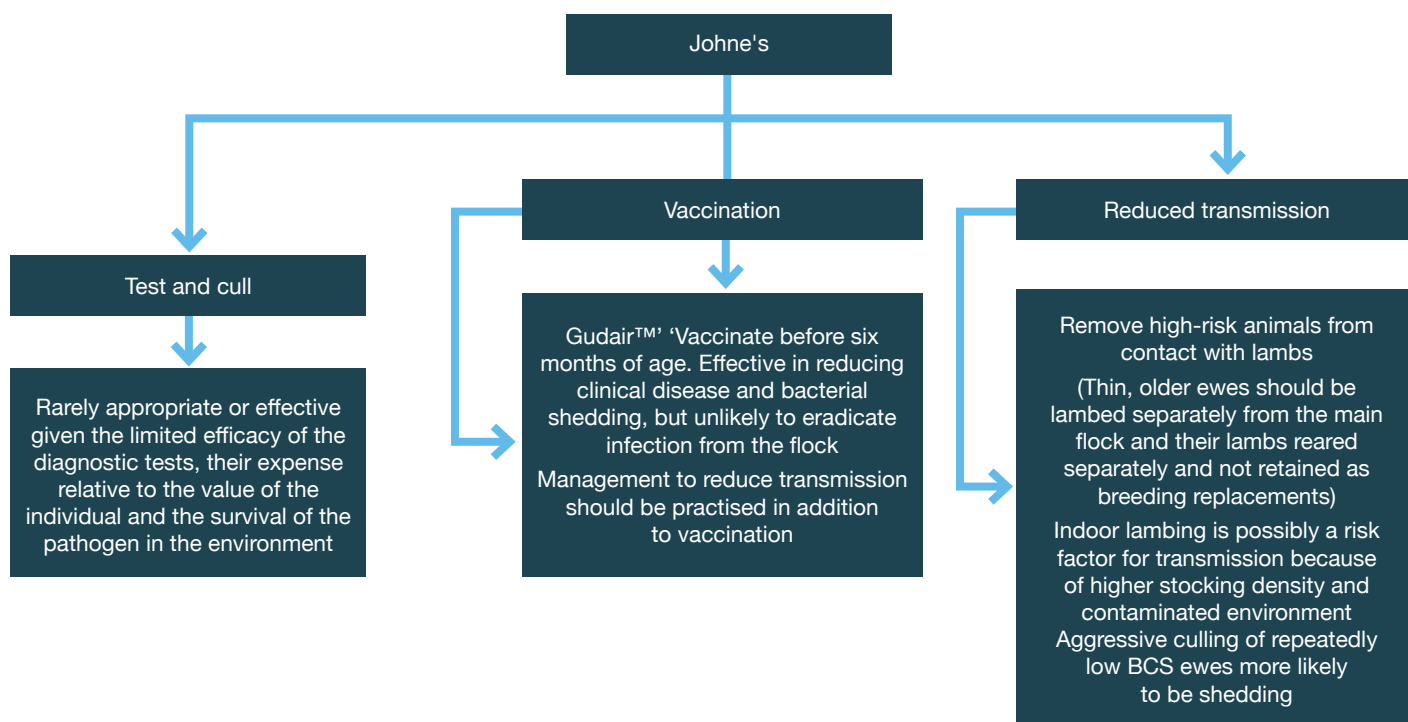


Figure 16. Summary of control measures for ovine Johne's disease

In sheep, vaccine injection site lesions were detected in almost 50% of sheep after two months and persisted for at least four years in 20–25% of vaccinated animals. This is an important consideration, especially for flocks in which visual appearance is important for marketing stock. A study has shown that vaccination injection site lesions at slaughter occurred in 18% of adult sheep and 65% of lamb carcasses. This may present additional trimming costs for processors in the UK.

### Case study flock: ovine Johne's disease

#### Background

Initially, two separate flocks were run: a hill flock and a lowland flock comprising draft ewes and mule ewes crossed to a terminal sire. Limited hill land caused the flocks to breed insufficient numbers of female sheep to be self-contained. The farmer was wary of purchasing sheep because of the risk of introducing infectious diseases.

During this period, the flock was diagnosed with Johne's. The farmer said the mule ewes appeared to be more susceptible to the disease than the Scotch Blackface ewes. Changes in management strategy, including lambing outside and feeding from a snacker on the floor rather than in troughs, as well as heavy culling, were put in place. The farmer notes that symptoms reduced and they felt able to get on top of the disease. Despite this, pressure remained to change breed on the farm to better suit the land. Traditional breeds were considered but, at the time, the farmer felt their genetic merit was poorly documented and sought genetics from abroad. Hence, 15 years ago, a new breed was introduced onto the farm.

The farmer recalls that the flock never reached its full potential. Initially this was blamed on trace elements in the soil, particularly cobalt, selenium and copper. Repeated blood tests returned different results. The soil was found to contain high levels of molybdenum. Consequently, several treatments were suggested, including top-dressing the pasture with cobalt sulphate. However, the same issues with performance remained.

Mortality increased from 2–5%, reaching 10% among the breeding ewes. Lean ewes with lambs at foot started to be seen. Repeated blood tests and PME were performed, but no diagnosis was reached. Further thin ewes were found at weaning (BCS 1.5–2), which failed to improve despite worming, drenching for liver fluke and good nutrition. This led the farmer to consider that the problem must be related to digestion. Finding Johne's in their college notes, they discussed the likelihood of this disease with their vet. Consequently, blood samples revealed Johne's.

Before diagnosis, the farmer noticed that they were culling too many young sheep. Despite there being enough land to keep 1,900 sheep, increased culling rates maintained numbers around 1,700.



Table 12. Flock outline

Farm size	405 hectare farm
Farm type	Lowland flock Open flock, 5–6 tups purchased annually
Sheep details	1,200 breeding ewes, 30 tups, 500 replacement ewes Some ewes are tupped by a terminal sire ram to produce fast-growing prime lamb
Cattle numbers	No other stock on farm
Production aims	Prime lambs sold as deadweight Aim to sell 70–80 ewe lambs Arable is primary source of income, with sheep a close second
Scanning rate	170–175%
Source of replacements	All ewe replacements are sourced from within the flock (500–550/year) Tup replacements are sourced annually, direct from two pedigree breeders
Vaccination protocol	Lambs are vaccinated with Ovivac™ P plus Shearling ewes are vaccinated with Toxovax™ and Campyvac™ 4 and move onto Heptavac™ P plus All breeding stock is vaccinated with Gudair™
Start of lambing	Mid-April 2018

### Farm management

This lowland flock lambs outside in late April, producing prime lamb that is sold throughout the winter. The flock has sought high genetic merit tups to overcome significant problems spanning many years.

Both ewes and tups are grouped according to age, remaining in their age groups for life. The ewes are housed in January, where they are scanned and winter-shorn. Ewes remain in their age groups, but are grouped within these according to the number of lambs scanned.

All ewes lamb outside. Twin-bearing ewes are turned out onto good grass 4–5 weeks pre-lambing, with singles following two weeks pre-lambing. Lambs are weaned from 12 weeks and approximately 200 may be finished inside.

Ewes are culled for a variety of reasons. Each year, 5–6 tups are selected from two breeders and are sourced for their well-recorded genetics. On arrival, new stock is wormed with monepantel and moxidectin, treated for liver fluke and dosed with long-acting oxytetracycline. They are also vaccinated with Heptavac™ P plus, housed overnight and then turned out into an isolation paddock.

### Intervention since diagnosis

Since diagnosis, all sheep in the breeding flock have been vaccinated with Gudair™. As soon as replacement ewe lambs are identified, they are vaccinated around weaning. All females sold as breeding stock are vaccinated before sale. Additionally, the farmer culls very heavily; subsequently the mortality rate has reduced to 3–4%. They are able to put weight on thin ewes that they intend to sell for slaughter.

### Farmer's view

The farmer was incredibly pleased to reach a diagnosis. They acknowledged that vets did not know very much about the disease, or appear to understand the large economic losses suffered by the clinical signs observed.

The farmer cannot identify when Johne's was introduced to the flock, but thinks it may have originated from two adjacent fields. Sheep grazed in these fields over two wet summers seemed most susceptible to the disease. The undulating terrain meant that sheep were kept close together as the water pooled in certain areas. The farmer cannot discount the possibility of rabbit involvement. Clinical signs in sheep from these fields were not identified until months later, but they were able to link them by their location across the summers.

The farmer recounts that all of the possible vaccination information was collated at the time because there was very little information on its use within the UK. When contacting Moredun Research Institute, the farmer found out about a successful sheep vaccination programme in Spain, using the South African produced Gudair™.

### Considerations for the case study

This case is interesting, given that the farmer struggled to get the vets to diagnose the disease. The flock was identified as positive more than five years ago and more is now known about Johne's in the UK.

The clinical signs associated with Johne's remain present despite vaccination. Susceptibility to Johne's appears to be strongly dependent on age.

**Minimising the risk of contaminating replacement ewes at a young age is important for disease control.**

Sheep can be vaccinated from as young as four weeks of age, so this may help to reduce clinical signs and transmission. Additionally, keeping replacements from only the youngest ewes may help to reduce shedding.

It would be very interesting to analyse flock production data, especially the ages of ewes within the flock.

It is important to note that the practice of routinely dosing all new stock animals with antibiotics on arrival is strongly discouraged because it increases the risk of developing antibiotic resistance on farm. Veterinary advice should be sought based on individual farm circumstances and reviewed regularly to ensure targeted and responsible antibiotic use.

# Ovine pulmonary adenocarcinoma

In Iceland, the national eradication of OPA was achieved in a programme involving a rigid policy of culling all flocks in endemically infected areas and enforcing a two-month quarantine period prior to introducing stock from other ‘low risk’ areas. This is practically, economically and politically impossible in most countries, including the UK.

Individual flock depopulation and repopulation with disease-free stock is also an option. However, defining or guaranteeing disease freedom is not possible without a suitable testing protocol that allows results to be confirmed results in the live animal.

This problem is not limited to OPA but is common to all of the five production-limiting diseases. However, it is most acute for OPA, given the lack of suitable diagnostic tests to establish flock-level OPA status.

Ongoing research at the Moredun Research Institute into the use of transthoracic ultrasound scanning at regular intervals may allow assessment of the costs and benefits of that approach. In high-prevalence flocks, identifying sufficient numbers of preclinical cases might justify the expense of scanning every we at regular intervals.

However, this approach is unlikely to be cost-effective for low-prevalence flocks. Indeed, the additional risk of culling a larger number of false positives than true positives would make the intervention counter-productive.

It is therefore essential that the vet has accurate validated estimates of the sensitivity and specificity of the technique in asymptomatic sheep. Then, they can discuss fully with the client the potential benefits and risks of applying this control measure to a given flock. Vets must also consider their own experience with the technique, as well as the subjectivity and interoperator variability that arises with such a technique.

Farmers of many flocks will opt for aggressive culling based upon repeated low BCS as a means of identifying those animals that cannot cope physiologically with the farming system used. This is a crude tool, but one with potential merit that is worthy of further assessment as a means of limiting the production impact of all the wasting diseases – OPA, Johne’s, MV and potentially, CLA – on the flock.

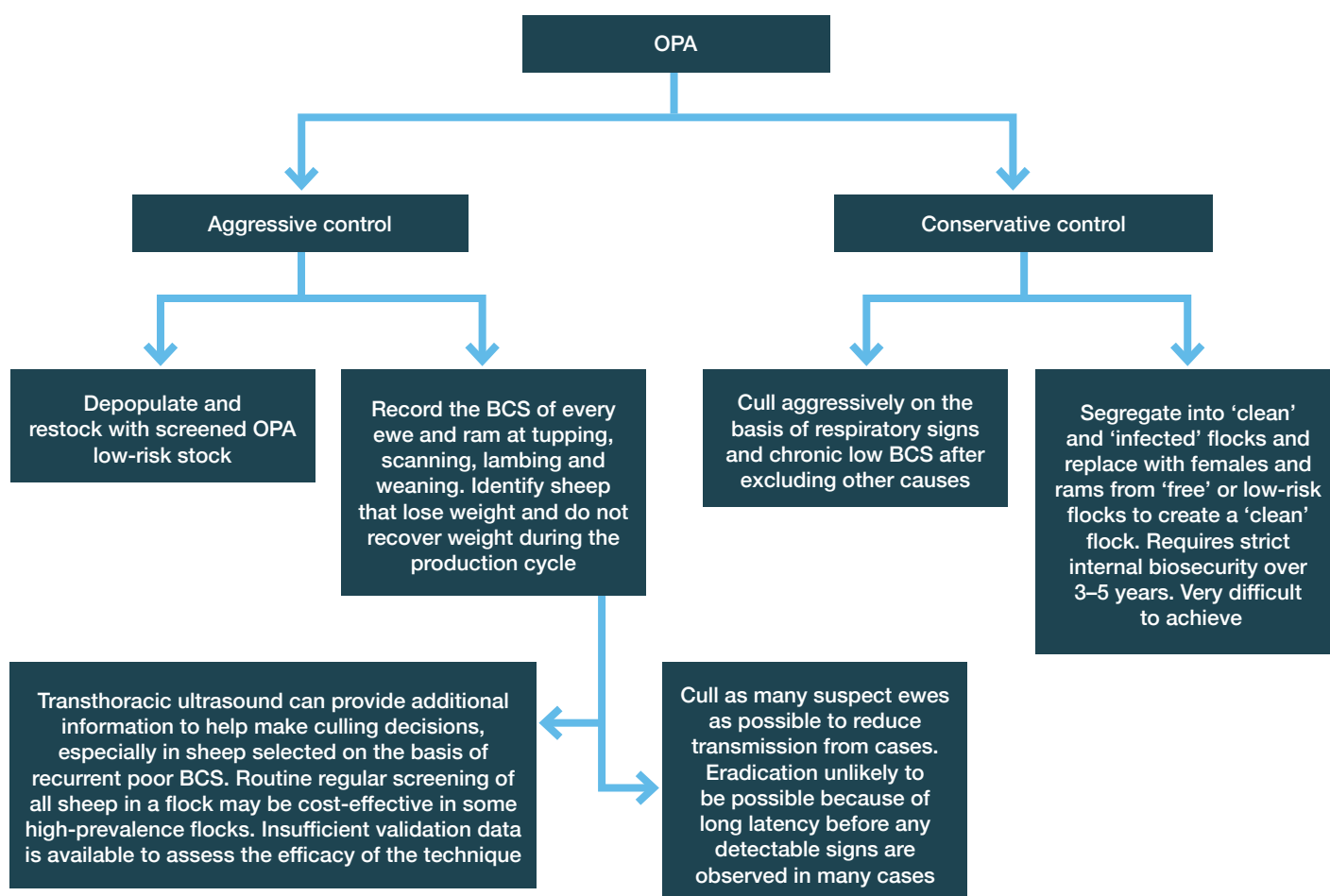


Figure 17. Summary of control measures for ovine pulmonary adenocarcinoma

## Case study flock: OPA

### Background

In 2015, the farmer noticed that they were losing more ewes than in previous years and could not explain the reasons for death. Ewe losses continued to increase, in 2017 the farmer recounts that 1–2 ewes died every two weeks as they started drawing lambs to be sold. Initially, they thought it was associated with stress and the hot weather at the time, assuming that it was caused by pneumonia.

In 2017, a total of 20 ewes died, all from the older group of ewes. Some ewes would gradually decrease in condition, but other – seemingly fit – ewes would be found dead. The repeated gathering of the group to collect the lambs appeared to increase the issue. The farmer also recalls an increase in coughing among the group of affected ewes. However, there was no difference in lamb performance between the affected group and the non-affected group of ewes.

The increase in death rate led the farmer to seek advice from his local vet. OPA was diagnosed at PME with secondary pasteurellosis.

Table 13. Flock outline

Farm size	450 hectares over three flocks
Farm type	Lowland and hill flock Open flock, tups purchased in autumn 2017
Sheep details	The farm comprises three separate flocks totalling 1,700 sheep The lowland flock is made up of 500 breeding ewes, 11 tups and 150 replacement ewe lambs
Cattle numbers	125 suckler cows Cattle and sheep have nose-to-nose contact Cattle are positive for BVD virus and results indicate a PI animal is likely to be present All youngstock are being tag and tested The herd have unknown status for Johne's
Production aims	Both sheep and cattle enterprises form the farmer's main source of income Primary aim is to produce prime lambs, selling deadweight (averaging 18.5 kg)
Scanning rate	189% average over 2017 and 2018 lambing seasons
Source of replacements	Ewe replacements sourced as ewe lambs from the hill flocks on same farm and are then mated as ewe lambs Replacement tups source from large commercial breeding company
Vaccination protocol	Ewes, tups and replacements receive Heptavac™ P plus Ewe lambs receive Toxovax™ prior to first tupping
Start of lambing	Late February 2018

### Farm management

This flock lambs indoors throughout March, with lambs creep-fed from three weeks of age through to finishing.

Triplet and twin-bearing ewes are housed for 3–4 weeks pre-lambing. Single-bearing ewes are brought inside once there is enough space. Ewes are turned out with one or two lambs; one triplet lamb will be removed and reared on a milk machine. Once turned out, ewes are grouped according to age: shearlings and four-tooths are grazed together.

The lambs are weaned at 16 weeks old, aiming to get all gone by the end of August. Once weaned, ewes are kept in their age groups.

Replacement tups are bought from a breeding centre that screens all flocks for MV and Johne's. All tups sold are individually screened for BD antigen. Before leaving the farm of origin, the tups are bolused, drenched with a dual wormer containing derquantel and abamectin and boosted with a multivalent vaccine Ovivac™ P plus. Any new stock animals are housed for 24–48 hours and will receive a mineral drench.

Ewes are culled for a variety of the usual reasons, with no one cause being reported as a particular issue.

### Intervention since diagnosis

After shearing in 2017, the affected group of ewes was systematically examined using transthoracic ultrasound. Thirty ewes from this group were found to have ultrasound changes consistent with OPA and were subsequently culled. No further ewes have died since ultrasound scanning. A repeated ultrasound scanning session is planned for the following summer.

As the groups of ewes are not mixed, they remain separate from the younger sheep. New tups were introduced to the clean group during tupping in 2017; all other tups were assumed to be OPA-positive and will be kept separately from the clean tups and ewes. All thin sheep will be removed and culled. No screening for the hill flock is planned.





## Lambing figures

Table 14. Flock performance figures 2017

Number of ewes to the tup	490	Key parameters (%)
Barren	12	Barren rate = 2.4
Singles	114	Scanning rate = 184
Twins	290	Scanning rate = 184
Triplets	70	Scanning rate = 184
Total number of lambs scanned	904	Losses between scanning and marking = 8.2
Number of lambs marked at 7 weeks old	830	Losses between marking and sale = 0.8
Number of lambs weaned and sold	823	Total lamb losses 9.0
Number lambs lost scanning to sale	101	Rearing rate = 164
Number of ewes died	20	Ewe death rate = 4.1
Number of ewes culled	128	Ewe cull rate = 26.1

The scanning rate achieved in 2017 was high and was repeated the following year with a scanning rate of 193% for the 2018 lambing season. Total lamb losses were below the 13% target, which is reflected in a rearing rate of 164 lambs per 100 ewes put to the tup.

### Farmer's view

The farmer is determined to get on top of the issue. It only affects management of the sheep at the moment and keeping the two groups separate is difficult. At present, the level of infection does not seem to affect lamb growth or production.

### The referring vet's view

Two vets carried out thoracic ultrasound. Culling all positive ewes was recommended, as well as a PME to confirm diagnosis and investigate any other underlying disease.

Costs of scanning:

- Visit fee: £28.60
- Scanning hourly rate: £77.74
- Scanning 250 ewes (at a rate of 50 ewes/hour): £417.28 (ex. VAT)

The referring vet recommends six-monthly scanning initially, reducing this to annual scanning once the flock prevalence reduces. The vet feels that disease is unlikely to be eliminated within this flock because of difficulties in identifying very early cases. Since the farm is surrounded by single fences, disease re-introduction is also possible.

### Considerations for the case study

The results achieved during the 2017 lambing season are fantastic, especially in the face of clinical cases of OPA. If affected ewes are effectively culled before clinical signs occur, this control strategy may be enough to sustain good lambing results.

It is interesting that 92% of all lamb losses occurred before the first seven weeks of life. It would be useful to define exactly when these losses occurred, e.g. pre-birth or within the first 48 hours of life. The farmer reported that some ewes were thin before showing respiratory signs. Ewes in poorer condition are known to have lambs with lower birth weights and reduced colostrum quality, ultimately leading to reduced survival. Lambs that do survive are likely to have reduced daily liveweight gains, so are sold later in the season. However, in 2018, most lambs were away by the age of 16 weeks.

Ultrasound scanning the flock in summer 2017 appeared to halt the rate of ewe deaths, however, this may be coupled with a reduction in stress, heat and mixing of ewes (e.g. for repeated gathering of the flock for lamb selection). Farmers of several flocks that have had OPA for some years have started ultrasound scanning every six months or so, because lesions were developing quicker than previously expected. Maintaining age groups may also help to lower transmission levels and coupled with regular thoracic scanning, this may be sufficient to maintain control of OPA within this flock.

Ultrasound scanning the hill flocks would have a huge cost in terms of time and money, but performing PMEs on a selection of cull ewes from these flocks might ensure that the disease is not present here too.

Overall, the effects of OPA have been seen as an increase in ewe deaths on farm over the last summer. It will be interesting to assess ongoing flock surveillance in the coming years.

## Flock biosecurity

For the iceberg diseases, as well as almost all other livestock diseases, most of the risk of transmission comes from the movement of live animals between farms. In comparison, shearers and ultrasound scanners pose only a small risk. Farmers, vets and the wider industry must realise that good biosecurity is not just putting a foot dip at the farm gate, but also involves considering the risk when purchasing rams or replacements of unknown health status from a sale.

Closed flocks (for which rams are only purchased) are inherently at lower risk than open or 'flying' flocks because of far fewer purchased animals potentially harbour disease. However, many closed flocks have long-standing endemic disease, so they cannot be considered as higher health status without the confirmatory testing that would be appropriate for any other flock. In these situations, options exist for the owner, such as splitting the flock into clean and dirty groups with strict internal biosecurity, or gradually culling out the infected flock. This is a good option where the scale and layout of the enterprise allows.

Alternatively, depopulation and repopulation of the breeding flock is an option, along the lines of the pig or poultry industries. However, in the sheep sector, this is more challenging because of the lower availability of replacement stock of guaranteed health status and equal genetic merit. Until these barriers are overcome, many closed flocks with endemic disease will pursue conservative control measures, such as aggressive culling, if no more commercially viable options exist.

## Accreditation and flock health status

In the UK, there is currently one sheep higher health status accreditation programme: the Premium Sheep and Goat Health Scheme (PSGHS). It offers an MV accreditation scheme, a commercial flock 'one-off' MV package for thin ewes and a Johne's risk level scheme. Enzootic abortion of ewes and scrapie schemes are also administered by PSGHS. Other general monitoring or diagnostic testing for these and other diseases is available from several laboratories in the UK. Details of the schemes change over time; up-to-date information on testing and biosecurity requirements can be found on the PSGHS website, [www.psghs.co.uk](http://www.psghs.co.uk)

## Integrated flock screening of cull ewes and fallen stock

Screening cull ewes and fallen stock is highly cost-effective and is the simplest way of testing the 'high risk' group of any flock in which the prevalence of CLA, MV, Johne's and OPA is highest. This approach is not as useful for BD, in which case screening the lamb crop is most appropriate. The expected prevalence of these four diseases in the thinner, older cull ewes would be substantially higher than in most of the flock. Ewes with poor teeth may be excluded from testing on the assumption that this is the cause of low BCS. Other common causes of weight loss should also be ruled out first, such as gut parasites, liver fluke and undersupply of energy and protein.

Table 15 shows the results from a recent survey of more than 50 large commercial flocks by PME of 12–25 cull ewes per flock. The work demonstrates the flock level prevalence of iceberg diseases.

Table 15. Prevalence of iceberg diseases from flock health status survey by post-mortem examination and serology of cull ewes

Disease	Farm level prevalence (%)
Border disease	15
Caseous lymphadenitis	4
Maedi Visna	2
Ovine Johne's disease	64
Ovine pulmonary adenocarcinoma	7

## Pre-purchase screening

Pre-purchase screening is possible for private sales, using the same sample size and prevalence calculations as would be used for flock health status monitoring. Difficulty often arises over when and who conducts the tests and how to interpret results from small sample sizes of purchased stock. This is especially true for individual rams when many of these diseases are latent for months or years before becoming detectable, which limits the efficacy of individual tests. BD (ELISA antibody for group exposure or PCR antigen for individual PI status), MV and CLA are the most useful pre-sale tests and can be repeated after quarantine for several weeks to provide additional assurance of accurate results. Bearing in mind that OPA and Johne's have long incubation periods, an idea of the status of the source flock is more helpful than attempting to determine the status of the purchased individuals. The risk of false positive results is high given their young age and the tests currently available.

## Quarantine

Quarantine facilities and periods can be difficult to practically enforce for hidden diseases, especially for MV in which antibodies may be produced up to seven months after exposure.

An initial minimum quarantine period of three weeks in a shed or dedicated paddock is necessary to allow time to return test results and complete vaccination courses. Segregating purchased females until and including the next lambing season is advisable for BD control, as well as infectious abortion control.

The exact length of the quarantine period should depend upon the specific health planning priorities of the farm and should be considered in detail between the farmer and vet. No one duration or set of interventions is appropriate for all flocks, so this is a key element of the active flock health planning process. If disease issues are identified, it is important to discuss and establish how this information will be used, e.g. can the problem be controlled or mitigated? Or, if an animal is identified as infected, is the owner willing to cull, sell or return it?

## Summary

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In researching and writing this manual and in the course of speaking to vets and farmers throughout the UK, it has become increasingly evident that there is enthusiasm to identify and tackle these five production-limiting diseases among a motivated minority of well-informed stakeholders. However, in general, awareness of these diseases is relatively low compared with the obvious clinical conditions that preoccupy sheep vets and farmers on a daily basis. Beyond basic awareness of the existence and manifestation of the iceberg diseases, the availability of simple and effective control measures, such as vaccines, was seen by most vets as the key driver to encourage more farmers to address these diseases.

Vets and farmers must both deal with significant uncertainty when choosing suitable tests for these diseases and in interpreting the diagnostic results. It is very difficult for individuals to weigh up the potential impact of these diseases on a flock, especially when relatively little peer-reviewed research on the production impact of iceberg diseases has been conducted under UK management conditions. It is hoped that this manual will clarify what is currently known and identify the questions that vets and farmers should discuss.

The starting point for many conversations about iceberg diseases will probably be to identify a particular production or health issue in a flock, or the diagnosis of an iceberg disease by PME. However, it would be beneficial for awareness within the sheep sector to reach a point at which these diseases were routinely discussed as a part of a broader flock health planning process, with screening for flock health status and for pre-purchase of replacements.

Dealing proactively with infectious disease at a herd or flock level has allowed the pig and poultry livestock sectors to cut the impact of disease on their costs and productivity. The cattle sector is making a concerted effort to deal with BVD and Johne's – both diseases that likely involve sheep as reservoirs of infection. As the impact of the iceberg diseases on UK sheep systems becomes clearer through more focused research on the current knowledge gaps, it is hoped the sheep sector will move in the same direction. Reducing the unnecessary waste and welfare implications of the five iceberg diseases should make individual farmers, and the sector as a whole, more efficient and more resilient in the future.



# Glossary

**Asymptomatic** Producing or showing no symptoms

**Clinical disease** A disease that has recognisable symptoms

**Endemic** A disease that is regularly present in a certain population, region or environment

**Histology** The study of the microscopic structure of tissues

**Lymph nodes** Small bean-shaped organs located throughout the body that are part of the body's immune system

**Mediastinal lymph nodes** Glands located in the part of the chest between the sternum and spinal column

**Pathogenic** The ability of an organism to cause disease

**Prevalence** The number of cases of a disease present in a particular population at a given time

**Serology** Testing blood serum

**Seropositive** A positive result in a test of blood serum

**Subclinical disease** A phase of disease that shows no symptoms

**Viraemic** When the virus are replicating in the blood

**Virology** Testing for viruses

**Within-flock prevalence** Prevalence of contaminated sheep within a contaminated flock

## Abbreviations

**AGIDT** Agar gel immunodiffusion test

**APHA** Animal and Plant Health Agency

**BCS** Body Condition Score

**BD** Border disease

**BVD** Bovine Viral Diarrhoea

**CLA** Caseous lymphadenitis

**ELISA** Enzyme-linked immunosorbent assay

**JSRV** Jaagsiekte sheep retrovirus

**MV** Maedi Visna

**OJD** Ovine Johne's disease

**OPA** Ovine pulmonary adenocarcinoma

**PCR** Polymerase chain reaction

**PI** Persistently infected

**PME** Post-mortem examination

**PPV** Positive predictive value

**PSGHS** Premium Sheep and Goat Health Scheme

**RT-PCR** Reverse transcription polymerase chain reaction

**SAC** Scottish Agricultural College

**SRUC** Scotland's Rural College



# References

There is the full literature review on the **AHDB Beef & Lamb website**, the references can be found in this document.

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