Dealing with maedi visna in UK sheep flocks

Background: Maedi visna (MV) is considered to be one of the ‘iceberg diseases’ of sheep; a group of infectious, production-limiting diseases which are endemic to the UK. Characterised by slow, progressive onset, these diseases lie undetected and can have a large impact on flock efficiency. This group of diseases also includes border disease, caseous lymphadenitis, ovine Johne’s disease and ovine pulmonary adenocarcinoma. The prevalence and effects of these diseases within different UK flock types remains unknown.

Aim of the article: To highlight the increasing importance of MV within the national flock. Here, we discuss the production effects, diagnosis and control options for MV.

What is maedi visna?

Maedi visna (MV) is an infectious, insidious production-limiting disease of sheep, caused by a non-oncogenic retrovirus – maedi visna virus (MVV), a small ruminant lentivirus (SLRV) (Box 1) (Radostits and others 2007). It has a long incubation period ranging from several months to years (Asadpour and others 2014) and leads to a progressive loss of condition, reduced flock production and poor economic performance (Ritchie and others 2012).

The prevalence of MV within the UK sheep flock appears to be rising. It is transmitted between sheep and goats; once infected, animals will produce antibodies, but they are unable to eliminate the virus and so become life-long carriers of the disease (Ritchie and others 2012). The immune response may take up to several months, and the incubation period for the disease may take several years.

Clinical cases may only become obvious when a significant proportion of the flock are infected; however, subclinical signs appear well before this. The disease is incurable and progressive, and there appears to be little chance of development of an effective vaccine, although several control options are suggested, which we will discuss in this article.

Why is maedi visna important now?

MV appears to be widely dispersed in the UK flock. A study by (Ritchie and others) (2012), using a random sample of UK flocks, found that the prevalence of infected flocks appeared to have doubled between 1995/6 and 2010 (1.4 per cent to 2.8 per cent, P=0.015). Although the between-flock prevalence appears to be relatively low, the rate of increase is alarming; some UK flocks have found the within-flock prevalence to reach 85 per cent (Ritchie and others 2012, Priestley 2016).

Six years ago it was estimated that 100,000 ewes within the national flock could be infected with MVV (Ritchie and others 2012) and the rate of increase is likely to be exponential. The apparent increasing prevalence of MV within the UK means that understanding the effects of the disease is increasingly relevant.

Impact on flock production

Only partial data on productivity losses associated with MV infection are available for UK flocks at present. The financial costs may be influenced by several factors (Box 2). In flocks with clinical MV, the within-flock prevalence is often identified between 20 and 60 per cent. A lag period of several years appears to be seen from initial flock infection to diagnosis due to clinical signs or production issues; this is a classic characteristic of an iceberg disease.

Some of the production effects and associated financial implications of MV infection within a
flock have been calculated (Table 1). Although these figures may not be representative of all flocks or systems, it goes some way to identify the potential economic losses associated with prolonged MVV infection within a flock. Further studies are needed to quantify additional effects of subclinical disease, such as ongoing transmission within infected flocks and how this relates to different flock types and management systems where transmission dynamics differ (Leginagoikoa and others 2006b).

Clinical disease
Cases of MV may be difficult to identify due to the long incubation period of the disease, non-specific clinical signs, and the susceptibility of infected sheep to concurrent diseases (Leginagoikoa and others 2006a, Ritchie and others 2012).

Clinically infected sheep may present with one of two disease forms – ‘maedi’ or ‘visna’. Both forms have been documented in the UK and both are produced by infection with MVV (Ritchie and others 2012).

Maedi
The more typical presentation within UK flocks is a chronic, progressive pneumonia in older sheep, typically over three years old (Winter and Clarkson 2012). This interstitial pneumonia leads to a loss of condition, difficulty breathing and is eventually fatal (Winter and Clarkson 2012). Postmortem examination of such affected sheep shows markedly enlarged and heavy lungs with a grey discolouration and obvious impression of the ribs (Minguijón and others 2015) (Box 3). Enlarged mediastinal lymph nodes are usually noted and MV cases are commonly associated with secondary bacterial infection, particularly pneumonic Mannheimiosis. Concurrent cases of ovine pulmonary adenocarcinoma have also been reported (Baird 2010).

Visna
The neurological form of the disease is a slowly progressive disorder with weight loss in older sheep. This may progress from a unilateral conscious proprioceptive deficit in one hind limb to toe dragging (Fig 1) and hind limb paralysis (Winter and Clarkson 2012).

Maedi visna-related death and culling
Despite MVV targeting several organs, only the respiratory and neurological forms of the disease appear to lead to cachexia and death, although viral strains targeting the mammary gland and joints may lead to premature culling due to poor performance (Minguijón and others 2015). Mortality associated with SRLV infection (Box 1) is thought to be low in endemic areas, but is strongly influenced by concurrent disease, husbandry, nutrition and environmental factors (Peterhans and others 2004). Such high mortality in newly infected animals, as documented during the Icelandic epidemic

Fig 1: Toe dragging in a ewe infected with maedi visna virus

**Box 1: Key Facts Relating to Small Ruminant Lentiviruses**

- Maedi visna virus (MVV) is closely related to caprine arthritis encephalitis virus (CAEV).
- MVV and CAEV are small ruminant lentiviruses (SRLVs) from the *Retroviridae* family (Leginagoikoa and others 2006a), and both viruses may be transmitted between sheep and goats.
- SRLVs lead to slow, progressive and fatal lymphoproliferative disease (Berriatua and others 2003).
- Cases of MVV and CAEV infection present differently. Sheep infected with MVV primarily show respiratory signs and lose condition. They may also be affected by mastitis and show progressive neurological signs. Goats infected with CAEV commonly present with a polysynovitis arthritis. Goats may also suffer with a loss of condition, poor haircoat, respiratory signs and mastitis.
- The *Lentivirus* genus also contains human immunodeficiency virus (HIV), feline immunodeficiency virus (FIV), bovine immunodeficiency virus (BIV) and equine infectious anaemia virus (EIAV) (Minguijón and others 2015).

**Box 2: Factors Influencing Financial Costs Associated with Maedi Visna Virus Infection within a Sheep Flock**

- Clinical maedi visna virus disease develops slowly*
- 30% of infected animals develop clinical signs*
- The rate of transmission is influenced by flock prevalence and management factors*
- Host and viral genetics influence the extent of the disease*
- Concurrent disease will influence disease signs**

*Peterhans and others 2004, ** Gonzalez and others 1993
High levels of bacterial and indurative mastitis have also been reported in clinically affected flocks in other studies (Pekelder and others 1994, Ritchie and others 2012).

**Lamb performance**

The effects of reduced milk yield due to MVV-associated mastitis and induration on lamb production has not been accurately assessed within a UK setting. It is plausible that lambs nursing ewes with a high degree of induration and subsequent lower yield may lead to reduced survival and poor lamb growth. In other countries, MV seropositivity has been associated with increased preweaning mortality (Arsenault and others 2003). The effects of MVV infection appear to be more marked with increasing ewe age. Dohoo and others (1987) found that the birthweight of lambs from three- to four-year-old seropositive ewes was 3 to 6 per cent lower than birthweight of lambs from non-infected ewes of the same age. The weaning weight of lambs from four-year-old or older seropositive ewes was associated with a reduction of 0.94 kg (Arsenault and others 2003). These effects may be especially felt in medium- or high-prevalence UK flocks that aim to attain the higher sale prices associated with early lamb sales.

Infected ewes were found to have a reduction of 9 per cent in conception rates compared to uninfected ewes and a 6 per cent reduction in milk yield compared to dairy ewes of similar ages within the same flock (P Davies, unpublished data). Indurative mastitis may be found in infected ewes which inhibits the flow of milk throughout the mammary gland, thus reducing milk yield (Snowder and others 1990). Clinical examination of the udder may be unremarkable, and milk remains normal in appearance (Asadpour and others 2014).

**Ewe health and production**

Many studies have identified production-limiting affects in subclinically infected flocks. MVV infection is suggested to decrease the average life span of infected animals: they may be culled at least a year earlier due to reduced productivity (Peterhans and others 2004).

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**Subclinical disease**

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**Table 1: Production effects and financial implications associated with maedi visna infection within a flock**

| Physical performance          | Baseline (disease free) | Impact of maedi visna (at 20% prevalence based on ELISA seropositivity) |
|-------------------------------|-------------------------|--------------------------------------------------------------------------|
| Ewe empty (%)                 | 4                       | 5.8 Estimated 9% reduction in conception rates of the 20% of ewes infected with maedi visna virus |
| Flock scanning (including empty) (%) | 182.9                  | 178.4                                                                     |
| Stocking density              | 10                      | 10 Ewes/ha                                                               |
| Total lamb mortality (scan to sale) (%) | 12                    | 13.2 Estimated 10% increase in lamb mortality                            |
| Rearing (%)                   | 161.0                   | 154.9                                                                    |
| Live weight (kg)              | 40                      | 40                                                                        |
| Cull ewe value per head (£)   | 50                      | 40 Estimated 20% reduction in cull ewe value due to chronic wasting       |
| Replacement rate (%)          | 21                      | 25.2 Estimated 20% increase in forced culling/replacement                 |
| Replacement female purchase cost (£) | 120                    | 120                                                                       |
| Finishing (%)                 | 140.0                   | 129.7                                                                     |
| Average killing out (%)       | 45                      | 45                                                                        |
| Average carcase weight (kg)   | 18                      | 18                                                                        |
| Price (£/kg dw)               | 4                       | 3.952 Estimated 6% lower milk yield = 6% lower daily live weight gain in 20% of lambs suckling MVV-infected ewes. This reduces the mean market price achieved |
| Variable costs (£ /lamb)      | 51.14                   | 55.21                                                                     |
| Variable cost (£ /kg dw)      | 2.84                    | 3.07                                                                      |
Farm animals

Transmission
MV may be transmitted in a number of ways, although the chief route (vertical or horizontal) is unclear. MVV is spread via pulmonary secretions and milk containing infected macrophages, thus the respiratory route and the ingestion of infected milk and colostrum, known as lactogenic transmission, form the basis for natural MV transmission (Berriatua and others 2003, Leginagoikoa and others 2006a, Radostits and others 2007).

Successful eradication programmes focusing on the removal of lambs at birth and rearing on artificial milk and colostrum (Houwers and others 1987) appear to demonstrate that in utero and intrapartum transmission are of little consequence (Cutlip and others 1981). The virus can also be found in semen, saliva and urine (Houwers 1990, Berriatua and others 2003, Ritchie and others 2012).

The role of postnatal maternal transmission to offspring is of importance, although the primary route of transmission (respiratory or lactogenic) remains unclear. The rate of transmission within a flock appears to be related to management procedures and MV flock prevalence. Although intensively farmed flocks appear to have higher prevalence (Leginagoikoa and others 2006b), thus assuming transmission due to repeated close contact with infected sheep, studies have shown high rates of transmission in flocks with clinically healthy ewes with high MV prevalence, managed under extensive conditions (Pekelder and others 1994).

The genetics surrounding the susceptibility of SRLV infection have been explored; some animals appear to be resistant despite repeated exposure to infection (Berriatua and others 2003, Leginagoikoa and others 2006a, Heaton and others 2012). Genetic selection for MVV resistance should be regarded cautiously: viral strains undergo frequent antigenic drift and so virus adaptation may diminish the benefit of previous genetic selection (Minguijón and others 2015).

It has been suggested that eradication programmes, involving the removal of lambs at birth for artificial rearing, may fail due to poor hygiene and disinfection procedures (Houwers and others 1987). Indeed, fomites are an important consideration during MV eradication, even if survival outside the host is limited.

Diagnosis
Although there is no universally accepted ‘gold standard’ to determine sensitivity and specificity of tests used for MV infection, successful control

**BOX 3: PATHOLOGY SAMPLES FROM MAEDI VISNA-INFECTED SHEEP**

Although useful for visualisation of pathological changes, gross postmortem findings cannot be relied on for confirmation of maedi visna (MV) (Radostits and others 2007). Further diagnostic tests are required, such as:

- Histology may be performed on formalin-fixed samples of lung, bronchial lymph node, mammary gland, synovial membrane and brain;
- Heart blood serum may be collected for serology.

Fig a shows two pairs of lungs from three-year-old Texel rams. Unaffected lungs on the left (from a clinically well, MV-negative ram) deflated on removal from the thoracic cavity and placement on the table revealed the heart. In comparison, the affected lungs on the right (taken from an MV-positive ram) failed to collapse when the chest was opened. They had a firm, rubbery texture and were diffusely pale. The interstitial pneumonia in the animal with MV causes the lungs to appear swollen, which obscures the heart in this image.

Fig b shows a lung infected with MV. On the cut surface the parenchyma of the caudal lobe shows multiple coalescing grey and firm foci.

Picture: Ben Strugnell, Farm Post Mortems
Farm animals

In practice, the tests available are useful in reducing prevalence of infection (Peterhans and others 2004). Serological diagnosis used to detect MV antibody in infected animals is considered the most convenient diagnostic method. However, the time from infection to seroconversion can vary from a few weeks to several months (de la Concha-Bermejillo 1997, De Andrés and others 2005). Repeated testing during diagnosis and eradication programmes is necessary (De Andrés and others 2005), as animals with low antibody titres may become transiently seronegative despite latent infection (Houwers and Nauta 1989), and it has been suggested that some carrier ewes may not test positive on the ELISA due to a disrupted immune response in some infected individuals (Gayo and others 2017).

The most commonly used laboratory techniques in the UK for MV diagnosis are the agar gel immunodiffusion test (AGIDT) and ELISA. The AGIDT is highly specific but less sensitive than ELISA (Synge and Ritchie 2010): it was found to be 76 per cent sensitive and 98 per cent specific when compared to ELISA (De Andrés and others 2005). Therefore, due to its high but subjective specificity and low sensitivity, the AGIDT is used mostly for confirmation of more sensitive ELISA results.

ELISAs are suitable for screening large numbers of animals, are more sensitive than the AGIDT, and are quantitative, allowing for computer-based analysis of raw data (Peterhans and others 2004). Commercial ELISAs have been reported with a claimed sensitivity and specificity of 99.4 per cent and 99.3 per cent, respectively. However, apparently high numbers of false positives have occurred when screening certain UK flocks, thus suggesting a lower specificity under some circumstances. To overcome this, the routine confirmatory testing of positives is recommended using alternative assays.

Milk and bulk milk samples have been tested against SRLV for use and ease in dairy breeds (Minguijón and others 2015). There is an agreement of 90 per cent between ELISA used for blood and milk; therefore, milk samples may be preferable to serology in milking flocks and potentially meat flocks during lactation as they are easier and cheaper to obtain. MVV infection may also be identified from postmortem sampling (Box 3).

In summary, it is vitally important to establish which tests are appropriate for the desired level of confidence and to select the appropriate type (Fig 2) and number of animals to make flock screening valid and robust. Typically, this can be summarised as using a high-sensitivity ELISA for screening followed by a high-specificity ELISA or AGIDT for any resulting positive samples. To establish flock status (ie, for flock-screening tests), the highest risk sheep, which are most likely to have antibodies, should be selected – these are typically thin, older ewes who are more likely to have encountered the disease and seroconverted.

**Control options**

Due to the long course of MVV infection, control methods may span several years and so selecting the right plan is crucial to maximise compliance and plan success. MV control for an infected flock can either be via eradication or by conservative management. Many factors may influence the choice of plan including, flock prevalence, farming
**Farm animals**

Production objectives, cost-benefit analysis, animal health and genetics (Minguijón and others 2015). Analysis of flock production data may allow the effects of MV infection to be seen; for example, assessing ewe longevity and lamb performance may address likely cost-benefit analysis of disease control. Flocks seeking full eradication must ensure that both vertical and horizontal routes of transmission are targeted (Minguijón and others 2015).

Minguijón and others (2015) put together an overview of possible control strategies (Fig 3) (Table 2).

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**Table 2: Summary of maedi visna (MV) control options**

| Control option | Advantages | Disadvantages |
|----------------|------------|---------------|
| **Depopulation and repopulation** | Works well for smaller flocks of low genetic value. Can quickly eliminate the disease if sufficient appropriate stock can be sourced. Was found to be a very successful method in Iceland (Pétursson 1994). | Large financial implications associated with whole flock culling. Loss of genetics. Needs readily available disease-free stock for restocking. |
| Level of control: eradication | The entire flock is culled and restocked with accredited or monitored MV-free sheep. | |
| **Selective culling of infected animals ± their progeny** | May be useful in flocks with low to moderate prevalence; allows rapid reduction in seroprevalence (Reina and others 2009). The diagnostic tests are sufficiently accurate to allow fairly rapid eradication. Culling progeny of infected ewes may reduce vertical transmission and inherited susceptibility (Reina and others 2009). | Flocks with high prevalence may see flock size reduced if culling is greater than the normal culling rate (Reina and others 2009). Expensive in terms of diagnostics and high flock replacements costs. |
| Level of control: eradication | Repeated testing and culling of all stock >12 months old. This method uses high sensitivity ELISA and agar gel immunodiffusion test, as outlined in Fig 2. All sheep on farm are routinely tested twice a year. Flocks frequently cull progeny (one year old) of infected animals as well (Houwers and others 1987, Williams-Fulton and Simard 1989, Radostits and others 2007). Replacements are sourced internally from seronegative mothers, ideally these should be older ewes which may be virus free and transmit resistant genes to their offspring (Berniatiu and others 2003, Radostits and others 2007), or from MV-free monitored or accredited flocks. Eradication can be achieved in one to three cycles. | |
| **Artificial rearing of lambs** | May be used on a larger scale. If thorough hygiene procedures are adhered to, this strategy can be very effective. Embryo transfer may be advantageous and economically viable in flocks with high genetic merit. | Very labour-intensive approach. May be especially expensive if infected flock is not retained, although their continued presence poses a significant risk of horizontal transmission (Radostits and others 2007). Lack of passive lamb immunity and artificial feeding may cause additional problems. |
| Level of control: eradication | Lambs are snatched from their dams at birth; reared on bovine/alternative milk and colostrum (Houwers and others 1983, Williams-Fulton and Simard 1989); or Lambs are fostered onto MV-accredited recipient ewes; or Embryo transfer into MV-accredited recipient ewes. Lamb must be kept separate from the rest of the flock to prevent future horizontal disease transmission (Reina and others 2009). On-going testing is necessary to ensure adequate hygiene measures are in place. | |
| **Separation of flock into two separate flocks** | Works well for moderately/highly infected flocks. Eliminates drastic culling procedures – keeps more stable flock numbers and may be more economically stable than culling positive animals/entire flock (Reina and others 2009, Pérez and others 2013). | Requires strict internal hygiene over three to five years, which is very difficult to maintain, especially around grazing and flock handling. Increased labour, large degree of planning. May have to increase farm facilities to maintain separate flocks – increased costs associated with this. |
| Level of control: conservative | The whole flock (>12 months old) is tested and separated according to infection status. The seronegative group must be kept isolated from the seropositive group and strict hygiene must be adhered to. Repeated testing continues on the seronegative group and any returning seropositive animals are immediately moved into the seropositive group. Replacements only kept from the negative flock. The positive flock is run down over time until all are culled when they become unproductive. | |
| **Young flock, early culling** | May reduce some effects of MV. | The cost of keeping a younger flock with increasing culling and replacement rates may well outweigh the cost of disease eradication in the medium/long term. Horizontal and vertical transmission will continue, and subclinical disease will continue to cause production losses. |
| Level of control: conservative | This method includes keeping a younger flock, increasing replacement rate and increase culling based on body condition score and ewe performance. Flock may be kept in age-stratified groups, and replacements kept from older ewes. Replacements are bought in from MV-accredited flocks and kept separate from older sheep. Batch testing of older and thin ewes is recommended. | |
Farm animals

Strict biosecurity procedures are necessary to ensure adequate control of MV infection or prevent reinfection in cases where eradication has been achieved. A single serological test may not be sufficient to determine the infection status of an individual animal due to differences in time to seroconversion (de la Concha-Bermejillo 1997) and the immune response of infected individuals (Gayo and others 2017). Therefore, replacement ewes and rams should be sourced from MV-monitored or accredited flocks who have undergone multiple serological tests (Radostits and others 2007). As MVV has been found in the male genital system and viral shedding in semen has been shown, only certified MVV-free males should be used as semen donors for artificial insemination to avoid both horizontal and vertical transmission (Minguijón and others 2015).

Farmers selling MV-seropositive stock must be strongly encouraged to sell either through the cull ewe market or direct to slaughter. Although there is the temptation to sell stock through other methods, the moral duty to sell only healthy stock on to fellow farmers must be strongly encouraged.

**UK accreditation scheme for maedi visna**

An MV accreditation scheme was introduced into Great Britain in 1982 and may be credited with limiting the spread of MV in the UK. The scheme parameters initially accredited participating flocks to have a MV prevalence of less than 2 per cent, with a confidence of 95 per cent, tested on a biannual or triannual basis, along with strict biosecurity precautions. Over 3000 flocks have participated in the scheme over the past 37 years.

The high uptake of the scheme among pedigree producers may have had an important effect in limiting transmission within the national flock as these flocks have the greatest ‘contact’ with other, commercial flocks, primarily via the sale of breeding rams. Several hybrid breeds are also subject to similarly rigorous testing to prevent transmission to client flocks independently of the scheme. The scheme has recently been reviewed and now sets a standard of less than 5 per cent prevalence and 95 per cent confidence in order to achieve accreditation. It is important for owners to appreciate the fact that accreditation does not guarantee disease freedom.

The uptake of the scheme has been minimal within the commercial lamb-producing sector. Although the costs associated with testing may be high, the lack of clear cost benefits of disease freedom for commercial lamb producers is also a likely contributing factor.

**Conclusion**

Given that prevalence of MV in the UK flock is rising and likely to accelerate, this disease is destined to become a far more important problem for the UK sheep industry. The effects may be increasingly felt within the lamb-producing industry in the future. Perhaps consumer drive to ensure higher animal welfare may be the turning point, or further research will highlight how much MV is holding back the potential of UK sheep production. It is clear there is a need to engage a far larger proportion of the flock.
