Maedi-Visna (Ovine Progressive Pneumonia) Management Strategies

Anthony P. Knight, *BVSc, MS, MRCVS, DACVIM*
College of Veterinary Medicine & Biomedical Sciences, Colorado State University, Fort Collins, CO 80523

Abstract

Maedi-visna (ovine progressive pneumonia) is a lentivirus-induced lymphoid-proliferative disease syndrome of sheep characterized by chronic progressive pneumonia, encephalopathy, swollen joints causing lameness, and indurative lymphocytic mastitis. The primary mode of transmission is via the colostrum from infected ewes and to a lesser extent by management conditions that favor close proximity of sheep to one another. Seroprevalence to range from 19 – 97%, according to North American and European serological surveys of sheep.

Affected sheep typically show progressive weight loss, and dyspnea due to lymphocytic infiltration of the lungs. Neurological signs leading to paralysis, swollen joints causing lameness, and palpably hard, unproductive udders or "hard bag" may occur concurrently or separately in affected sheep. Once infected with the ovine lentivirus, antibodies are produced to the virus that do not confer resistance to the disease, which is ultimately fatal. Definitive diagnosis of maedi-visna can be made from the clinical signs, histopathology, and AGID and/or the ELISA tests that detect the presence of circulating antibody. The ELISA test has greater sensitivity and specificity than the AGID test.

Maedi-visna is best managed by eradicating the virus. Eradication strategies include removing new born lambs at birth from their infected dams before they can suckle colostrum, and then raising them in isolation. Serological testing of all sheep over three years of age and culling infected animals and their progeny will reduce seroprevalence in the flock. Repeated annual testing is required until the herd has at least two negative herd tests.

Introduction

Lentivirus infections of sheep were first recognized in Iceland in 1954, and given the name of maedi (meaning dyspnea) and visna (meaning shrinking of the spinal cord).[25,33] The introduction of maedi-visna into Iceland was traced to the importation of a herd of Karakul sheep from Germany in 1933. In 1970 a disease called Montana sheep disease was first reported in the United States, and has subsequently been called ovine progressive pneumonia (OPP).[4, 10] Since then, maedi-visna has been identified in most sheep raising areas of the world, with the exception of Australia and New Zealand. The disease has been referred to as " old ewe syndrome" because it manifests itself as a weight losing syndrome in older sheep With the advent of new technologies including the polymerase chain reaction (PCR) and the enzyme-linked immunosorbent assay (ELISA), it is now evident that OPP and maedi-visna are caused by the same lentivirus. In most countries with the exception of the United States, maedi-visna or ovine lentivirus disease is the widely accepted and preferred terminology for this complex disease syndrome.[14] The caprine arthritis encephalitis (CAE) lentivirus is also serologically similar to the ovine lentivirus responsible for maedi-visna.[3] Ovine pulmonary carcinoma or adenomatosis (Jaagsiekte) is caused by a distinctly different retrovirus.[10] It was first described in South Africa as Jaagsiekte ("driving sickness"), but has since been found in many other sheep producing countries, including the United States.[16,34]

Both the ovine lentivirus of maedi-visna and the Jaagsiekte retrovirus may be present in sheep concurrently.[17,32] Unlike maedi-visna, sheep with Jaagsiekte develop a broncho-alveolar carcinoma with excessive fluid production in the lungs.[17,34] A unique feature of the disease is the volume of fluid that runs out the nose when the sheep's hind legs are raised and the head lowered.

Sheep breed susceptibility to maedi-visna virus

A variety of sheep breeds appear resistant to maedi-visna while other breeds, especially Corriedales or any breed with Corriedale in its ancestry, appear especially prone to developing the disease.[11,33] Among the common breeds of sheep in North America, the Corriedale and Corriedale crosses (Targhee and Columbia), Finnish Landrace and Finn-crosses, Dorsets, Border Leicester, and Texel breeds are most susceptible to developing clinical signs of maedi-visna. However, all breeds of sheep are susceptible to infection with the ovine lentivirus, and will develop antibodies to the virus without necessarily developing clinical signs.[21]

Etiology

Maedi-visna virus (MVV) is a non-oncogenic lentivirus belonging to the retroviridae family. The CAE virus is genetically and antigenically closely related to the maedi-visna virus,[7] and the two viruses can cross-infect sheep and goats.[3] In fact, the CAE virus ELISA test has high specificity for detecting sheep infected with MVV.[20] The MVV primarily attacks and is transmitted through, the mononuclear cells.[22] Infection is characterized by a long, asymptomatic incubation period in which the virus persists in the presence of a strong humoral and cellular response. Clinical signs of Maedi-visna depend upon the organs involved in the proliferative lymphoid inflammatory response induced by the virus.[25] The incubation period varies from 2 to10 years before clinical signs become evident. Maedi-visna infections generate high titers in sheep that can be detected by the agar gel immunodiffusion test (AGID) and a whole virus enzyme linked immunosorbent assay (ELISA).[23,28] A new test utilizing recombinant viral protein and a synthetic peptide derived from the MVV, has recently been developed that provides greater sensitivity and specificity than the AGID test.[28]

Primary mode of transmission of the ovine lentivirus appears to be through the infected colostrum of infected ewes.[9,12] Lambs ingesting colostrum containing ovine lentivirus become infected and will develop antibodies to the virus, even though some individuals may never develop clinical disease. Lambs that have received adequate colostrum high in antibodies to MVV probably do not become infected during the first month of life due to the protective effects of colostrum.[33] Horizontal transmission of the virus may also occur under management situations that keep sheep in close proximity to each other.[9,33] There is evidence that transplacental transmission of the ovine lentivirus occurs, as the virus has been isolated from fetal and newborn lambs.[18] Similarly, the virus has been detected in lambs obtained via hysterectomy.[19,20] In addition, ovine lentivirus DNA has been detected in peripheral blood mononuclear cells in lambs immediately removed from their dams at birth.[21]

Ovine lentivirus has been detected in the semen of rams with epididymitis due to *Brucella ovis* as the result of the inflammatory process allowing infected white blood cells to enter the semen.[22,23] However, it has not been demonstrated that an infected ram can transfer infection via its semen to a susceptible ewe or her lambs.

Prevalence of Maedi-visna virus

Prevalence of maedi-visna virus in sheep flocks across the world ranges from 19% to 97%.[8,25] In the 2001 National Animal Health Monitoring Survey conducted by the U S Department of Agriculture, the prevalence of MVV in US flocks was found to be 34.4%. This national survey, however, revealed the prevalence of MVV varied considerably from small farm flocks with 17.1% of the sheep positive for MVV, to open range flocks with 45.1% of tested sheep positive for MVV. (www.aphis.usda.gov/vs/ceah/cahn)

Clinical signs

Because of its long incubation period, maedi-visna virus does not typically appear clinically until infected sheep are over two to three years of age. Characteristically infected sheep lose weight, and have little tolerance for exercise or stress due to the presence of a progressive pneumonia. Infected sheep often maintain a good appetite. After a while, the infected sheep cannot keep up with the flock and are often referred to as "lungers".[25,33,34] A dry cough is often present. An increased respiratory rate and labored breathing often lead to a diagnosis of bronchopneumonia that does not respond well to antibiotic therapy. It is, however, not unusual for affected sheep to have secondary bacterial pneumonia and/or caseous lymphadenitis concurrently. Reproductive efficiency of affected ewes declines as body condition deteriorates. Many ewes fail to raise their lambs because of reduced or lack of milk production. Maedi-visna is steadily progressive and eventually kills the animal.

Variance in the clinical manifestations of MVV infections is possibly related to differences in the strains of the virus.[6] A small percentage of infected ewes will develop swollen joints due to synovitis and arthritis leading to lameness. In addition to the respiratory signs, some ewes may develop "hard bag" as a result of the invasion of the mammary glands by lymphoid tissue. The hard, painless udder produces little or no colostrum or milk, and can result in the ewes losing their lambs to starvation.[25]

The visna form of the disease is much less common than the respiratory form (maedi). Visna is characterized by progressive hind leg weakness and ataxia, with eventual posterior paralysis.[25,33] Other neurologic signs may develop. The digestive and respiratory systems are generally unaffected in the neurologic form of the disease.

Diagnosis

Ovine lentivirus infections (maedi-visna) can be definitively diagnosed from typical clinical signs, gross and histopathological lesions, and by detecting serum antibodies to the virus using the AGID and ELISA tests.[23] Seroconversion to MVV occurs from four to six weeks following experimental infection, and antibody

levels tend to remain constant.[26] Colostral antibody to ovine lentivirus has been shown to persist for six months. Therefore, sheep should not be tested for ovine lentivirus until they are over six months of age. A positive AGID or ELISA test in sheep more than six months of age is indicative of infection with the ovine antivirus. Once infected with ovine lentivirus, sheep are infected for life. AGID and ELISA tests can give false-negative results if a sheep has been recently infected and has not had time to produce antibody to the virus. The ELISA test has fewer false-negative results than the AGID test.[28] A small percentage of infected animals never develop antibodies to the virus, and remain a source of infection to other animals in the flock. Some seropositive ewes will become seronegative shortly after lambing as a result of depleting circulating antibody through the colostrums. In general, the older the sheep, the greater the chance it will be seropositive. Infected sheep less than one year of age have been shown to have a 4-11% seroprevalence, while sheep over four years of age were 34% seroprevalent, and those over seven years had 93% seroprevalence.[13,31] The ovine lentivirus can be detected in bone marrow, blood macrophages and pulmonary lymphoid tissue from infected sheep using PCR methods.[35]

Postmortem findings

Sheep that have died from ovine lentivirus (maedi) disease are usually emaciated and have characteristic enlarged, heavier-than-normal lungs. The lungs do not collapse when the thorax is opened, and frequently retain the impression of the ribs on the lung surfaces. (Figure 1), The bronchial and mediastinal lymph nodes are usually markedly enlarged. The dorsal aspects of the lungs are most frequently affected, giving the surface a mottled grayish appearance. On the cut surfaces of the lung there is usually the grayish speckling, and in severe chronic cases, the lung is meaty and homogeneously grayish in color. There is no fluid in the bronchi, unless there is concurrent bronchial pneumonia or ovine pulmonary carcinoma (Jaagsiekte).[19]

Histologically, the most characteristic features of maedi are the extensive lympho-proliferative lesions in the perivascular and peribronchial areas. Bronchial and mediastinal lymph nodes show chronic, hyperplastic lymphadenitis. Examination of the joints will show a chronic, proliferative synovitis and arthritis, especially in animals with swollen joints. Ewes that have "hard bag" exhibit a diffuse lymphoid infiltration of the mammary glands.[18,19]

Sheep with neurologic signs of hind-leg paralysis (visna) commonly show no lung pathology. Lesions in the brain and spinal cord consist of patchy, demyelinating encephalomyelitis, primarily involving the white matter.[31]

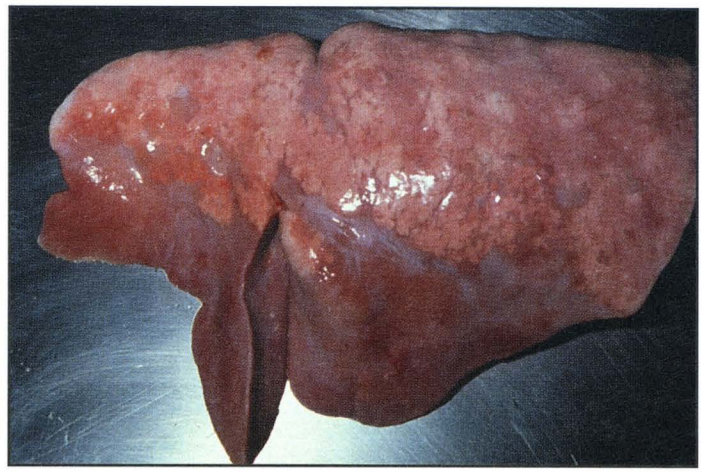

Figure 1. Gross appearance of sheep lungs with maedi. Dorsal aspects of the lungs are enlarged, and non-collapsed due to lymphoid infiltration, while the ventral aspects (dark red) are consolidated due to secondary bronchopneumonia.

Control and eradication

Since there are no effective treatments or vaccines currently available for ovine lentivirus infections (maedi-visna), the disease must be managed to prevent further spread of the virus, and to eradicate infected sheep.[1,2,21,30,33] The means of controlling and/or eradicating the disease must be customized to the individual flock and available resources. What can be implemented in a small farm flock will likely be quite different in a large range commercial sheep ranch. In the large flock with a high MVV seroprevalence, it may be necessary to take several years to reduce the number of infected animals so as to not have major economic impact on the operations of the sheep ranch.

Eradication programs for MVP follow four basic steps:

1. Serological testing (AGID or ELISA) of all sheep over six months of age. This is best accomplished in the fall, and prior to the breeding season.
2. Seropositive sheep should be culled from the flock, or at least separated and moved to a location where they are not in contact with seronegative sheep.
3. All sheep over six months of age should be retested at six to 12 month intervals, and new seropositive animals removed immediately. This testing procedure should be repeated until there are two annual tests in which there are no new cases. At this stage, the flock can be considered free of ovine lentivirus. To remain certifiably free of MVV, the flock should continue to have annual serological testing because of the very

long incubation period, insidious nature of the disease, and lack of sensitivity of currently available serological tests.

4. All replacement animals for the flock should originate from a certified ovine lentivirus-free flock, or the acquired animals should be quarantined until shown to be seronegative to the ELISA test.

This basic protocol can be customized for individual flocks and can work well for small flocks. However, it may be economically crippling to a large sheep operation, especially if there is a high seroprevalence of MVV in the flock. In such cases, it is possible to structure an eradication program that does not become economically unacceptable. Instead of immediately culling all seropositive animals, seronegative animals should be sorted and moved to clean premises so that all will be separated geographically from the infected animals. The "clean" flock must henceforth be managed to ensure no contact with the infected animals. Standard biosecurity measures should be implemented in the farm management system to reduce the chance of ovine lentivirus transmission to the seronegative flock. It is critical that colostrum from infected ewes never be fed to lambs in the seronegative flock. Similarly, colostrum from CAE positive does should not be fed to lambs.

Seropositive sheep or those clinically affected should be culled. The non-clinical seropositive ewes can/should be bred to a different set of rams, so as to maintain next year's lamb crop. The entire lamb crop from the seropositive ewes, however, should be considered infected with MVP and sold as market lambs for slaughter. Eventually the seropositive animals will be reduced by culling clinically affected animals, while the seronegative breeding flock will increase annually to permit eventual elimination of all seropositive animals.

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