Maedi-Visna

Ovine Progressive Pneumonia,
Marsh's Progressive Pneumonia,
Montana Progressive Pneumonia,
Chronic Progressive Pneumonia,
Zwoegersiekte,
La Bouhite,
Graff-Reinet Disease

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Importance

Maedi-visna is an economically important viral disease of sheep that occasionally affects goats. The maedi-visna virus (MVV), a lentivirus; infects its hosts for life. Although most infections are subclinical, a minority of animals develops progressive, untreatable disease syndromes including dyspnea (maedi) or neurologic signs (visna). Both maedi and visna are eventually fatal. Additional economic costs may include marketing and export restrictions, premature culling, and losses from poor milk production due to indurative mastitis. Economic losses can vary considerably between flocks.

MVV is closely related to the caprine arthritis encephalitis virus (CAEV), a lentivirus found most often in goats. Although documented cases of natural cross-species transmission are currently rare, MVV can infect goats and CAEV can infect sheep. In addition, recombination has recently been demonstrated between MVV and CAEV. These findings suggest that eradication programs for either maedi-visna or caprine arthritis and encephalitis should now address both infections simultaneously.

Etiology

Maedi-visna results from infection by the maedi-visna virus, a member of the genus *Lentivirus* in the family Retroviridae (subfamily Orthoretrovirinae). This virus becomes integrated into leukocyte DNA; infected animals become chronic carriers. Several genetically distinct isolates circulate in sheep.

Phylogenetic analyses have demonstrated that maedi-visna virus is closely related to caprine arthritis encephalitis virus (CAEV), a lentivirus found most often in goats. These two viruses share many features, and are often considered together as the small ruminant lentiviruses (SRLV). Early phylogenetic studies suggested that SRLV can be divided into six sequence clades, I to VI. Clade I contains the prototype Icelandic visna virus and related MVV strains. Clade II consists of North American lentivirus strains isolated from sheep. Clade III consists of Norwegian SRLV, and clade IV of French SRLV. Clade V contains French and Swiss CAEV strains, North American prototype strains, and North American ovine lentivirus strains. Clade VI contains French SRLV. In this analysis, clades III to VI contain related SLRV from both sheep and goats, while clades I and II are more species-specific. These findings suggested that these viruses might be more closely related to each other, in some cases, than to other CAEV or MVV, but they were based on short sequences of nucleic acids.

A new phylogenetic analysis, based on longer genetic sequences, divides these viruses into four principal sequence groups, A to D. Sequence groups A and B are divided further into subtypes. Group A contains at least seven subtypes and group B at least two subtypes. To date, subtypes A5 and A7, and groups C and D have been found only in goats. Subtypes A1 and A2 have been isolated only from sheep. Subtypes A3, A4, A6, B1 and B2 have been found in both species. Recombination between a group A maedi-visna virus and a group B caprine arthritis-encephalitis virus has recently been demonstrated in goats infected with both viruses.

Species Affected

Maedi-visna affects sheep and, to a lesser extent, goats. Breed susceptibility varies. Texel, Border Leicester, and Finnish Landrace sheep appear to be relatively susceptible to disease; Columbia, Rambouillet, and Suffolk sheep seem to be relatively resistant.

Serological evidence of SRLV infections has also been reported in wild ruminants including moufflin, ibex and chamois; however, preliminary evidence suggests that these viruses may be distinct from CAEV and MVV.

Geographic Distribution

Maedi-visna has been found in most sheep-raising countries other than Australia and New Zealand. MVV has been reported from most of continental Europe, the United Kingdom, Canada, the United States, Peru, Kenya, South Africa, Israel, India, Myanmar and the southern regions of the former U.S.S.R.

Transmission

Most animals become infected early in life, from drinking infected colostrum or milk. The virus can also be spread during close contact, probably by the respiratory route. Coinfection with pulmonary adenomatosis (Jaagsiekte) virus increases MVV titers in the respiratory tract, increasing contact transmission between sheep. Transmission has been reported from water contaminated with feces, but indirect spread is generally thought to be rare. Intrauterine spread is thought to be negligible or minor.

MVV infects sheep or goats for life, but viral burdens vary between individual animals. Both asymptomatic and symptomatic animals can transmit this virus.

Sheep can be a source of SRLV transmission to goats, and vice versa. There is little information on the route(s) of transmission between sheep and goats, but the ingestion of contaminated colostrum or milk, or close contact between the two species in crowded barns have been suggested. Under experimental conditions, lambs that have nursed from infected goats can become persistently infected with SRLV.

Incubation Period

The incubation period for maedi is usually more than two years; clinical signs typically develop when animals are three to four years old. The incubation period for visna is somewhat shorter, and symptoms can appear in sheep as young as two years.

Clinical Signs

Most MVV infections are asymptomatic. In animals with clinical signs, the disease can take several forms. Sheep with maedi, the most common form, experience wasting, progressive dyspnea and sometimes a dry cough. Fever, bronchial exudates and depression are not usually seen. Maedi is eventually fatal; death results from anoxia or secondary bacterial pneumonia.

Visna occurs less frequently than maedi in sheep, although it is the more common form reported in goats. Visna usually begins insidiously, with subtle neurologic signs such as hindlimb weakness, trembling of the lips or a head tilt, accompanied by loss of condition. The symptoms gradually progress to ataxia, incoordination, muscle tremors, paresis and paraplegia. Other neurological signs, including rare instance of blindness, may also be seen. The clinical course can be as long as a year. Unattended animals usually die of inanition.

MVV can also cause slowly progressive arthritis with severe lameness, or chronic indurative mastitis with decreased production of normal-appearing milk. Weight gain in lambs may be decreased, possibly due to lower milk yields from dams with indurative mastitis.

Post-Mortem Lesions

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In maedi, the lungs are enlarged, abnormally firm and heavy, and fail to collapse when the thoracic cavity is opened. They are typically emphysematous and mottled or uniformly discolored, with pale gray or pale brown areas of consolidation. Mottling may not be obvious in the earliest stages of the disease. Nodules may be found around the smaller airways and blood vessels, and the mediastinal and tracheobronchial lymph nodes are usually enlarged and edematous. Secondary bacterial pneumonia may mask the primary lesions. On histological examination, lung lesions may include chronic, diffuse interstitial pneumonia, perivascular and peribronchial lymphoid hyperplasia, and hypertrophy of the smooth muscle throughout lungs.

Apart from wasting of the carcass, the only gross lesions seen in visna occur in the brain and spinal cord. Focal, asymmetric, brownish pink areas may be found in the white matter of the brain and spinal cord, as well as on the ventricular surfaces. The meninges may be cloudy and the spinal cord may be swollen. On microscopic examination, the typical CNS lesion is meningoleukoencephalitis with secondary demyelination. In some cases, the inflammatory cell aggregates may be nodular or granulomatous, and necrotic centers may be noted in severe cases.

In ewes with indurative mastitis, the udder is diffusely indurated and the associated lymph nodes may be enlarged. Histologically, the udder is characterized by mononuclear infiltration of the periductular stroma; these cells obliterate the normal mammary tissue.

Arthritis may also be seen in some animals, and the kidneys may have microscopic evidence of vasculitis.

Morbidity and Mortality

MVV is widespread among sheep in many parts of the world. In the United States, the prevalence varies with the region. Infection rates in sheep are highest in the Western and Midwestern States, and can reach nearly 50% in some areas. Control programs have reduced the incidence of MVV in some countries. Maedi visna is uncommon in goats; clinical cases have mainly been reported as visna in adult dairy goats.

Most infections are asymptomatic, but once clinical signs appear, the disease is progressive and usually fatal. When MVV is introduced into a new area, the mortality rate may reach 20-30%. The mortality rate is low in regions where maedi visna is endemic; annual losses rarely exceed 5% in a flock, even when nearly 100% of the flock is infected. Co-infection with Jaagsiekte virus, the retrovirus that that causes ovine pulmonary adenocarcinoma, results in more severe symptoms and increased transmission.

Management practices can influence the prevalence of infection and, thus, the frequency of disease. Clinical signs are not usually seen in herds with a low prevalence of infection. Genetic factors, including the breed of the sheep, influence the outcome of infection.

Diagnosis

Clinical

Maedi-visna should be suspected in animals that are at least 2 years old and have a wasting disease with slowly progressive respiratory distress, neurologic signs, indurative mastitis or arthritis.

Differential diagnosis

The differential diagnosis for maedi includes pulmonary adenomatosis, parasitic lung infections, and caseous lymphadenitis with lung involvement. In cases with neurologic symptoms, scrapie, listeriosis, rabies, louping ill, parasitic central nervous system (CNS) infections and space-occupying lesions of the CNS should also be considered. Caprine arthritis and encephalitis can also resemble maedi visna.

Laboratory tests

Maedi visna may be diagnosed by nucleic acid detection techniques such as polymerase chain reaction (PCR) assays, Southern blotting and *in situ* hybridization. PCR tests are used in some laboratories for rapid diagnosis.

Maedi-visna can also be diagnosed using a combination of serology and clinical signs, together with histological examination of tissues when necessary. Agar gel immunodiffusion and enzyme-linked immunosorbent assays (ELISAs) are the most commonly used tests. Immunoblotting (Western blotting) is generally performed only in specialized laboratories, but may be valuable when sera give equivocal results in other tests. Radio-immunoprecipitation and radio-immunoassay are generally used only in research. Seroconversion generally occurs months after infection. In general, serology is of greater value in screening flocks or other populations than in diagnosing this disease in individual animals. In adult sheep and goats, a positive result indicates that the animal is persistently infected with MVV but, because most infected animals do not become symptomatic, it does not confirm that the symptoms are caused by this virus. Due to these limitations, serology is of greater value in screening flocks than diagnosing this disease in individual animals.

In seropositive, symptomatic animals, histology can confirm the diagnosis in biopsy or necropsy samples. Virus isolation can also be useful; however, viral titers are variable and may fluctuate over time. MVV is isolated by co-culturing peripheral blood or milk leukocytes from live animals with sheep choroid plexus cells, sheep skin fibroblasts or other appropriate cell lines. MVV can also be isolated from tissues at necropsy. In co-cultures that display cytopathic effects, the presence of the virus is confirmed with immunolabelling methods and electron microscopy.

Adherent macrophage cultures established from post-mortem bronchoalveolar lavage can be tested for virus production by electron microscopy or a reverse transcriptase assay. They can also be co-cultured with indicator cells for virus isolation.

Samples to collect

Serum should be collected for serology. Milk can also be tested for antibodies. Virus isolation can be conducted on peripheral blood or milk from live animals. At necropsy, MVV can be isolated from the lung, mediastinal lymph nodes and spleen of animals with maedi. In animals with suspected visna, a sample of the brain should be sent. Alveolar macrophages can also be collected from the lung at necropsy, by post-mortem bronchoalveolar lavage. Samples for virus isolation and alveolar macrophages should be as fresh as possible.

Samples for histology should include all affected tissues such as lung, mediastinal lymph nodes, brain, spinal cord, kidney and/or udder.

Treatment

There is no specific treatment for maedi visna. Supportive therapy may be helpful in individual animals, but it cannot stop the progression of disease.

Recommended actions if maedi-visna is suspected

Notification of authorities

Maedi-visna is a reportable disease in many states. State guidelines should be consulted for more specific information.

Federal: Area Veterinarians in Charge (AVIC):
http://www.aphis.usda.gov/animal_health/area_offices/

State Veterinarians:
http://www.usaha.org/Portals/6/StateAnimalHealthOfficials.pdf

Control

Maedi-visna is a contagious disease. Management practices can influence the prevalence of infection and, thus, the frequency of disease. Clinical signs are not usually seen in herds with a low prevalence of infection.

MVV is often introduced into a herd in live animals. Additions to uninfected herds should come from MVV-negative herds. Other animals should be quarantined and tested before adding them to the herd. Uninfected herds should also be kept from contact with untested or seropositive herds, as horizontal transfer of the virus contributes to transmission. Goats may also be able to transmit SRLV to sheep. No vaccines are currently available.

MVV can be eradicated from a flock, or reduced in prevalence, by isolating lambs permanently from seropositive dams immediately at birth. The lambs are raised on uninfected colostrum and pasteurized milk, milk replacer or milk from seronegative ewes. The flock should also be tested frequently for MVV, and seronegative and

seropositive sheep should be maintained separately. Either of these two techniques may be used alone for controlling maedi visna, but they are most effective in combination. Seropositive sheep should eventually be culled. In nationwide eradication programs, quarantines of infected herds aid the final stages of the program.

Maedi-visna virus cannot survive for more than a few days in the environment, particularly under hot, dry conditions. Lentiviruses can be destroyed with most common disinfectants including lipid solvents, periodate, phenolic disinfectants, formaldehyde and low pH (pH < 4.2). Phenolic or quaternary ammonium compounds have been recommended for the disinfection of equipment shared between seropositive and seronegative sheep.

Public Health

There is no serologic or clinical evidence that humans are susceptible to MVV

Internet Resources

Manual for the Recognition of Exotic Diseases of Livestock
http://www.spc.int/rahs/

The Merck Veterinary Manual
http://www.merckvetmanual.com/mvm/index.jsp

World Organization for Animal Health (OIE)
http://www.oie.int

OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals
http://www.oie.int/international-standard-setting/terrestrial-manual/access-online/

OIE Terrestrial Animal Health Code
http://www.oie.int/international-standard-setting/terrestrial-code/access-online/

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*Link defunct as of 2007