

Caprine Arthritis and Encephalitis

*Caprine Arthritis-Encephalitis,
Small Ruminant Lentivirus Infection*

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Importance

Caprine arthritis and encephalitis (CAE) is an economically important viral disease of goats. The caprine arthritis encephalitis virus (CAEV), a lentivirus, infects its hosts for life. Although most infections are subclinical, a minority of animals develops progressive, untreatable disease syndromes including polyarthritis in adults and encephalomyelitis in kids. This virus also causes indurative mastitis, resulting in decreased milk production. CAEV infections decrease lifetime productivity in dairy goats, particularly when the prevalence of infection is high within a herd. In addition, CAEV is a barrier to the exportation of goats from countries where it is endemic, including the United States.

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

Etiology

Caprine arthritis and encephalitis results from infection by caprine arthritis encephalitis virus, a member of the genus *Lentivirus* in the family Retroviridae (subfamily Orthoretrovirinae). Several genetically distinct isolates circulate in goats.

Phylogenetic analyses have demonstrated that CAEV is closely related to the maedi-visna virus, a lentivirus found most often in sheep. 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 SRLV 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

Caprine arthritis encephalitis virus infects goats and, to a lesser extent, sheep. The frequency of cross-species transmission is unknown. It has rarely been demonstrated under natural conditions, but management may play a role.

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

CAEV is common in dairy goats in most industrialized countries. This virus is rarely found in the indigenous breeds of developing nations unless they have had contact with imported goats.

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Transmission

CAEV is mainly transmitted from infected dams to their kids; by the ingestion of virus-containing colostrum or milk, transmission usually occurs early in life. Horizontal transmission can also occur by direct contact, exposure to fomites when feeding, or exposure to contaminated milk in milking parlors. Iatrogenic transmission can occur on contaminated needles and other blood-contaminated fomites. The existence of *in utero* transmission is controversial; most sources suggest it is of minor importance. CAEV has been found in semen, but this route has not been investigated further. Humans can spread CAEV between herds on fomites.

CAEV infects goats for life, but viral burdens vary between animals. Both asymptomatic and symptomatic animals can transmit CAEV.

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 CAEV.

Incubation Period

The incubation period is highly variable. Most goats become infected when they are very young, and develop disease months or years later. Encephalitis usually occurs in kids 2 to 6 months of age, but it has been reported in a one-month-old kid, and in older goats. Polyarthritis is generally seen only in adults.

Clinical Signs

Most infected goats remain asymptomatic, but a minority develops clinical signs. Encephalomyelitis (progressive paresis) occurs primarily in 2-6 month-old kids, but has also been reported in a one-month-old kid and older animals including adults. The initial symptoms in kids may include lameness, ataxia, hindlimb placing deficits, hypertonia and hyperreflexia. Initially, many kids are bright and alert, and continue to eat and drink normally. The neurologic signs gradually worsen to paraparesis, tetraparesis or paralysis. Some affected kids may also appear depressed or exhibit head tilt, circling, blindness, nystagmus, opisthotonos, torticollis, facial nerve deficits, paddling or dysphagia. Variable increases in body temperature have been reported. Affected kids are either euthanized for welfare/ economic reasons or eventually die of secondary causes such as pneumonia or exposure. Although it is rare, some goats have apparently recovered.

Neurological signs are rarely reported in adults. These cases are characterized initially by minor gait aberrations, lameness and knuckling, which progress to paralysis over weeks to months. The reflexes remain intact. Other signs such as coarse tremors, nystagmus, trismus, salivation and blindness are occasionally reported.

Chronic, painful polyarthritis, accompanied by synovitis and bursitis, is the main syndrome in adult goats. Early symptoms include distention of the joint capsule and a variable degree of lameness. The carpal joints are most often affected, but symptoms can also occur in other joints. Although the course of disease is slow, it is always progressive. In late stages, goats may walk with their front legs flexed or become recumbent. Affected animals also lose condition and tend to have coarse, dull coats.

Indurative mastitis can occur in does. These goats have a swollen, firm mammary gland and produce decreased amounts of normal-appearing milk. In severe cases, there is agalactia at parturition. In some goats, the mammary gland may soften and milk production may approach normal; milk yield remains low in others. Overall, milk production is estimated to decrease by 10% in affected herds.

Occasionally, goats with serologic evidence of CAEV infection may develop chronic interstitial pneumonia and progressive dyspnea. Other syndromes that have been described in seropositive goats include lower birth weights in offspring, slower growth and increased reproductive failure.

Post-Mortem Lesions

In goats with polyarthritis, there is thickening of the joint capsule, with proliferation of the synovial villi. The joint capsules, tendon sheaths and bursae may be calcified. In severe cases, there may be severe cartilage destruction, ruptured ligaments and tendons, and periarticular osteophyte formation. In the neurologic form, the gross lesions consist of focal, asymmetric, brownish pink areas 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. Goats with caprine arthritis and encephalitis may also have interstitial pneumonitis. The lungs are firm and gray-pink, contain multiple small white foci, and do not collapse. The bronchial lymph nodes are enlarged in goats with lung lesions. Indurative mastitis may be observed in some does.

Microscopically, caprine arthritis and encephalitis is characterized by inflammation that consists of an interstitial, mononuclear cell reaction. Large aggregates of lymphoid cells and follicle formation may sometimes be seen. The histopathologic lesions found in joints include synovial cell hyperplasia, synovial edema and necrosis, villous hypertrophy and subsynovial mononuclear cell infiltration. In kids with encephalomyelitis, the lesions are characterized by multifocal, mononuclear cell inflammatory infiltrates and varying degrees of demyelination. Chronic interstitial pneumonia may be seen in the lungs, with mononuclear cell infiltrates in the alveolar septae and the perivascular and peribronchial regions. Indurative mastitis is characterized by mononuclear infiltration of the periductular stroma; these cells obliterate the normal mammary tissue. Vasculitis can be seen in the kidney.

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Morbidity and Mortality

In many industrialized nations, CAEV infections are widespread in dairy goats. In the U.S., surveys have demonstrated seroprevalence rates of 38% to 81% in dairy goat herds. Control programs have reduced the incidence in some countries. In Switzerland, an eradication program has reduced the prevalence of seropositive goats from a high of 60-80% to the current level of 1%. CAEV infections are uncommon in meat- or fiber-producing goats. The reason for this disparity is unknown, but possible causes include genetic factors or management practices. Approximately 30% of infected goats develop clinical signs. Encephalomyelitis or polyarthritis is progressive and untreatable once these syndromes appear. Most affected goats are eventually culled for welfare and/or economic reasons, or die from secondary causes. 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.

Diagnosis

Clinical

Caprine arthritis and encephalitis should be suspected in adults with polyarthritis and/or indurative mastitis, and kids with progressive paresis, particularly when more than one syndrome occurs in a herd. A presumptive diagnosis can be based on the clinical signs and history.

Differential diagnosis

The differential diagnosis for arthritis caused by CAEV includes traumatic arthritis and infectious arthritis caused by *Mycoplasma* species. In young kids with progressive paresis, enzootic ataxia, cerebrospinal nematodiasis, spinal cord trauma or abscess, and congenital anomalies of the spinal cord and vertebral column should be considered. In goats with symptoms of brain involvement, the differential diagnosis also includes poliоencephalomalacia, listeriosis and rabies. The pulmonary form in adult goats can resemble the pulmonary form of caseous lymphadenitis.

Laboratory tests

Caprine arthritis and encephalitis 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.

This disease can also be diagnosed using a combination of serology and clinical signs, together with histological examination of tissues when necessary. Agar gel immunodiffusion (AGID) and ELISAs are the most commonly used serological tests. Immunoblotting (Western blotting) is generally performed only in specialized laboratories, but may be valuable when sera give equivocal results in other tests. Radioimmunoprecipitation and radioimmunoassay are generally used only

in research. Serologic diagnosis of this disease has some limitations. Seroconversion typically occurs after months, rather than weeks, and can be unpredictable. Some goats may remain seronegative, and goats with low titers can transiently become seronegative. Maternal antibodies can interfere with detection in kids. In adult goats, a positive result indicates that the goat is persistently infected with CAEV but, because most infected goats do not become symptomatic, it does not confirm that the symptoms in an individual animal are caused by this virus. Due to these limitations, serology is of greater value in screening herds 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, can be low in blood and may fluctuate over time. CAEV is isolated by co-culturing peripheral blood or milk leukocytes from live animals with goat synovial membrane (GSM) cells or other appropriate cell lines. CAEV can also be isolated from affected tissues at necropsy. In GSM 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 broncho-alveolar 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, and possibly joint fluid aspirates. At necropsy, CAEV is isolated from affected tissues such as the lung, synovial membrane, brain and spinal cord, or udder. The specific sample varies with the syndrome. 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.

Treatment

There is no specific treatment for caprine arthritis and encephalitis, but supportive therapy can make affected goats more comfortable. Measures may include regular foot trimming, the provision of additional bedding material, and the administration of NSAIDs to goats with arthritis. High-quality, readily digestible feed should be provided.

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Recommended actions if caprine arthritis and encephalitis is suspected

Notification of authorities

Caprine arthritis and encephalitis 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/vs/area_offices.htm
State Veterinarians:
<http://www.aphis.usda.gov/vs/sregs/official.html>

Control

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.

CAEV is often introduced into a herd in live animals. Additions to uninfected herds should come from CAEV-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. Sheep may also be able to transmit SRLV to goats. In Switzerland, virus transmission of SRLV serotype A4 (MVV) from sheep was shown to be responsible for the re-introduction of seropositivity into a CAEV-free herd. No vaccines are currently available.

CAEV can be eradicated from a herd, or reduced in prevalence, by isolating kids permanently from seropositive dams immediately at birth and raising them on pasteurized milk or milk replacer. Sources of colostrum that have been recommended include heat-treated colostrum [56°C (133°F) for 60 min], colostrum from CAEV-negative goats and bovine colostrum. Small amounts of CAEV were isolated from heat-treated colostrum in one study. The herd should also be tested frequently for CAEV, and seronegative and seropositive goats should be maintained separately. Any equipment shared between the seronegative and seropositive herds should be disinfected. Seropositive goats should eventually be culled. In nationwide eradication programs, quarantines of infected herds aid the final stages of the program.

Lentiviruses are susceptible to 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 herds.

Public Health

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

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/eng/normes/mmanual/a_summry.htm
- OIE International Animal Health Code
http://www.oie.int/eng/normes/mcode/A_summry.htm

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