

Louping Ill

*Ovine Encephalomyelitis,
Infectious Encephalomyelitis of
Sheep, Trembling-Ill*

Last Updated: August 24, 2009



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Importance

Louping ill is a tick-borne, zoonotic, viral disease that is most important in sheep and red grouse. Severe clinical signs can be seen in naive sheep flocks moved into endemic areas. Many animals may develop neurological disease, and up to 60% of the flock can die. In endemic areas, most losses occur among unvaccinated younger sheep that are no longer protected by maternal antibodies. Louping ill is a serious problem in red grouse populations; few chicks may survive in some endemic areas. The mortality rate can be as high as 80% in experimentally infected birds. Cases of louping ill are also reported occasionally in other species including goats, llamas, alpacas, swine, horses and deer. Humans can develop flu-like symptoms or neurological signs after exposure, but the illness is rarely fatal.

Etiology

Louping ill results from infection by louping ill virus, a member of the genus *Flavivirus* in the family *Flaviviridae*. This virus is closely related to tickborne encephalitis virus (TBEV) and is a member of the same viral complex.

Four subtypes of louping ill virus – the British, Irish, Spanish and Turkish subtypes – have been identified; however, a recent genetic analysis suggests that the Turkish subtype (Turkish sheep encephalitis virus) is more closely related to TBEV than louping ill virus, and should be reclassified.

Species Affected

Sheep are the most important hosts for louping ill virus. Clinical cases have also been documented in other mammals including cattle, goats, horses, llamas, alpacas, pigs, dogs, deer and European elk. Fatal cases have been reported among grouse and their relatives, including experimentally infected ptarmigan (*Lagopus mutus*) and willow grouse (*Lagopus lagopus*), and naturally or experimentally infected red grouse (*Lagopus lagopus scoticus*). Louping ill virus can also infect a number of small mammals including shrews, wood mice, voles, rats, hares and rabbits. Humans seem to be accidental hosts.

Sheep appear to be the most important reservoir hosts, but grouse can also amplify louping ill virus, and mountain hares (*Lepus timidus*) have been implicated as maintenance hosts via non-viremic transmission between co-feeding ticks. One study suggests that horses might sometimes develop viremia that is sufficient to amplify this virus.

Geographic Distribution

Louping ill occurs mainly in the British Isles. This disease been reported throughout upland areas of Scotland, Ireland, northern England, and Wales wherever the tick vector *Ixodes ricinus* is found. Louping ill virus or a close relative causes a very similar disease in Norway, and a Spanish subtype of the virus has been documented in the Basque region of Spain. Similar viruses might also occur in other parts of continental Europe; however, it is difficult to determine louping ill virus's geographic distribution because it is so closely related to TBEV, a common virus in Europe.

Transmission

Louping ill is transmitted mainly by ticks. The principal vector is the three-host tick *Ixodes ricinus*. Transstadial transmission and overwintering of the virus have been documented in this species, but transovarial transmission does not seem to occur. Several other species of ticks including *Rhipicephalus appendiculatus*, *I. persulcatus* and *Haemaphysalis anatolicum* are also capable of transmitting louping ill virus, but they do not seem to be important in the epidemiology of this disease. Only sheep and red grouse consistently develop viremia sufficient to infect ticks and amplify the virus. Sheep appear to be the most important reservoir hosts. Grouse can act as amplifying hosts for a short period, but die very quickly. Viremia sufficient for virus amplification has also been reported in experimentally infected horses, but the viral titer was much lower than in sheep, and importance of this finding is uncertain.

Mountain hares have been implicated as maintenance hosts via non-viremic transmission between co-feeding ticks.

Louping ill virus can also be transmitted by other routes. This virus is shed in the milk of goats, and to a lesser extent, sheep; lambs and kids may become infected when they nurse. Red grouse can be infected by eating ticks, and one group of pigs became ill after they ingested raw meat from infected lambs. Iatrogenic spread can occur on needles or surgical instruments. Louping ill virus can also be transmitted to humans via infected tissues or cultures. Little is known about how long flaviviruses can survive in the environment, but the yellow fever virus is reported to remain viable in liquid for a few days at 37°C (98.6°F).

Incubation Period

The incubation period for louping ill is six to 18 days in sheep. Parenterally inoculated red grouse develop clinical signs in 2 to 8 days.

Clinical Signs

In sheep, louping ill is characterized by an initial febrile viremic stage, which may be accompanied by depression and anorexia, followed in some cases by neurological signs. In endemic areas, many animals develop mild or subclinical infections. In animals with encephalitis, the clinical signs may include muscle tremors and/or rigidity, incoordination, ataxia, hypersensitivity, salivation and nervous nibbling, progressing in some cases to head pressing, posterior paralysis, recumbency, convulsions and/or coma. Affected sheep may develop an unusual hopping gait, called a “louping gait,” during which they move both hindlegs, then both forelegs, forward in unison. Death is common among animals with neurological signs, often within a few days. Peracute deaths can also be seen. Surviving animals may have residual CNS deficits. Concurrent infection with *Anaplasma phagocytophilum* can increase the severity of the clinical signs, probably by suppressing the immune system.

Similar clinical signs can occur in other mammalian species. The louping gait does not seem to have been reported in species other than sheep. However, incoordination and ataxia are common, and exaggerated ‘goose-stepping’ of the hindlimbs was documented in a llama.

The clinical signs in experimentally infected red grouse include depression, anorexia, regurgitation of the crop contents during handling, and muscle weakness, followed by death. Although central nervous system (CNS) lesions can be found, obvious neurological signs have not been reported in these birds. Decreased body weight and poor survival of chicks, as well as deaths in birds of all ages, have been reported among wild

populations. Some other species of grouse and ptarmigan also develop fatal disease after experimental inoculation.

Post Mortem Lesions

Louping ill affects the CNS but does not cause any gross lesions. Congestion of the meningeal vessels or secondary pneumonia may be seen in some animals.

In mammals, the histopathological lesions are characterized by nonsuppurative meningitis and encephalomyelitis. In sheep, these changes are seen primarily in the brainstem and cerebellum, as well as in the ventral horn of the spinal cord. Nonsuppurative meningoencephalitis has also been reported in experimentally infected grouse, but the lesions occurred mainly in the cerebrum and the optic lobes of the midbrain.

Morbidity and Mortality

Most cases of louping ill occur in spring, early summer and fall, when ticks are most common. Morbidity and mortality vary with the animal’s immune status, concurrent infections and other factors. In endemic areas, the mortality rate is usually 5–10%, and most cases occur in animals that are less than two years old. Lambs born in these areas are usually protected by maternal antibodies for the first few months of life, and older animals have developed immunity. All ages are affected in newly introduced flocks, and the mortality rate can reach 60%. Once a sheep has developed encephalitis, the case fatality rate is approximately 50%. Both fatal cases and recovery have been reported in other species of mammals.

Red grouse appear to be very susceptible to louping ill. Up to 84% of the adult birds may be seropositive in areas where *Ixodes ricinus* is common. The mortality rate can be as high as 80% in parenterally inoculated red grouse. Deaths have also been reported in wild birds, and the survival of chicks may be very low in endemic areas.

Diagnosis

Clinical

Louping ill should be suspected in sheep with fever and neurological signs, particularly when the flock has recently been introduced to tick-infested pastures. It should also be a consideration in grouse with a fatal illness.

Differential diagnosis

The differential diagnosis in mammals includes other causes of acute neurological disease. Scrapie, pregnancy toxemia, maedi-visna, rabies, coenurosis, listeriosis, hypocalcemia, hypocuprosis and various toxicities are among the considerations in sheep. The clinical signs appear to be nonspecific in grouse, and a wide variety of diseases must be considered.

Laboratory tests

Louping ill can be diagnosed by virus isolation, the detection of viral nucleic acids or antigens, and serology. Louping ill virus may be recovered from the blood during the acute phase of the disease, or from the brain and spinal cord of animals with neurological signs. This virus can be isolated in porcine or ovine kidney cell lines, as well as in embryonated eggs. It may also be recovered by intracerebral inoculation of suckling mice.

Viral antigens or nucleic acids can be detected in the CNS by immunohistochemical staining or with a reverse transcriptase polymerase chain reaction (RT-PCR) assay, respectively. Histopathology can be helpful.

Serological tests include hemagglutination inhibition, serum neutralization, enzyme-linked immunosorbent assay (ELISA) and complement fixation. The detection of virus-specific IgM in the hemagglutination inhibition test indicates that the infection is recent. Cross-reactions can occur with other flaviviruses in serological tests.

Samples to collect

Before collecting or sending any samples from animals with a suspected foreign animal disease, the proper authorities should be contacted. Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease. Louping ill is zoonotic; samples should be collected and handled with all appropriate precautions.

Louping ill virus can be isolated from blood samples for a few days during the initial fever; samples of uncoagulated blood should be collected. The viremia has usually ended by the time the animal develops neurological signs. At necropsy, the brain and upper portion of the spinal cord are collected. Samples for virus isolation should be kept cool and transported to the laboratory as soon as possible. The brain and spinal cord are also submitted for RT-PCR, immunohistochemistry and histopathology.

The hemagglutination inhibition test can detect virus-specific IgM, allowing a recent infection to be diagnosed with a single serum sample. Paired serum samples may also be collected.

Recommended actions if louping ill is suspected

Notification of authorities

State and federal veterinarians should be notified immediately of any suspected cases of louping ill.

Federal: Area Veterinarians in Charge (AVIC):

http://www.aphis.usda.gov/animal_health/area_offices/

State Veterinarians:

<http://www.aphis.usda.gov/vs/sregs/official.html>

Control

If louping ill is introduced into a new region, it might be eradicated by euthanasia of infected animals, quarantines, movement controls and other measures, combined with effective tick control. It is critical to prevent the virus from becoming established in tick populations.

In endemic regions, sheep can be protected by vaccination, or by preventing exposure to habitats where ticks are found. Lambs born to vaccinated or naturally infected ewes are usually protected by maternal antibodies for the first few months of life. Vaccines have also been used in cattle and goats. Acaricides can reduce tick populations, but it is difficult to protect animals by this method alone. There is no specific treatment for louping ill, but supportive therapy including good nursing may be helpful. Enveloped viruses such as louping ill virus are generally susceptible to most common disinfectants.

Public Health

Humans can be infected via tick bites or by contact with the virus in tissues or laboratory cultures. Louping ill virus may be transmitted through skin wounds, and aerosol exposure has been reported in laboratories. It might be possible to acquire this virus by drinking unpasteurized milk; particularly high viral titers occur in goat milk. There are relatively few documented cases of louping ill. Many of these cases were seen in laboratory workers, but other occupations are also at risk. One study reported that approximately 8% of abattoir workers are seropositive. Louping ill has also been reported in shepherders, veterinarians and others. In people, this disease begins 2-8 days after exposure, as a nonspecific, influenza-like illness with symptoms such as fever, headache, joint pain and malaise. In the second stage of the illness, some patients develop meningoencephalitis or paralytic neurological signs that resemble polio. Hemorrhagic fever has also been reported. Deaths are very rare, but convalescence can be prolonged.

Internet Resources

United Kingdom. Department for Environment, Food and Rural Affairs
<http://www.defra.gov.uk/animalh/diseases/default.htm>

United States Animal Health Association.
Foreign Animal Diseases
<http://www.usaha.org/pubs/fad.pdf>

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

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