

Wesselsbron Disease

Wesselsbron Fever

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Importance

Wesselsbron disease is caused by a mosquito-borne virus that can infect a number of species, including humans. This virus seems to be widespread in Africa, where it can cause reproductive losses and neonatal mortality in small ruminants. The effects of Wesselsbron virus on other animal species are still unclear; however, occasional reproductive losses have been described in experimentally infected cattle. This virus was also implicated in neurological disease in two horses, and isolated from the brain of a dead dog. A limited number of clinical cases have been described in humans, often associated with exposure in the laboratory or during necropsies. All of these cases were characterized by a mild, self-limited, influenza-like illness, with the exception of one laboratory-acquired infection where the person also developed encephalitic signs. The overall burden of disease in animals and humans is hard to evaluate: Wesselsbron disease resembles other illnesses such as Rift Valley fever, and laboratory testing may be done infrequently in resource-poor areas. Wesselsbron virus might have the potential to become established outside Africa, similarly to other flaviviruses such as West Nile virus and Zika virus. Relatively little research has been published on Wesselsbron disease in the last 30 years.

Etiology

Wesselsbron disease is caused by Wesselsbron virus, a member of the yellow fever group of the genus *Flavivirus*, family *Flaviviridae*.

Species Affected

Wesselsbron disease has been described mainly in sheep and goats, but experimental infections suggest that this virus can also affect cattle. Experimentally infected horses and pigs had few or no clinical signs, but two unpublished cases of neurological disease in horses were attributed to Wesselsbron virus in 2008. This virus was isolated from the brain of a dead dog, and it has also been recovered from camels and farmed ostriches. Antibodies to Wesselsbron virus have been found in a number of domesticated animals, including horses, donkeys, pigs, camels and dogs, and in wild zebras, wild ruminants and lemurs. Experimental infections have been established in a few species not known to be infected in nature, such as rabbits, guinea pigs, mice and nonhuman primates. At least some of these infections were by unnatural routes such as intracerebral or intraperitoneal inoculation.

Domesticated ruminants have been proposed as reservoir hosts, based on the high seroprevalence in these species. Viremia in sheep and cattle is sufficient to infect mosquitoes. Other proposed reservoir hosts have included wild birds and wild rodents, such as gerbils (e.g., the Cape short-eared gerbil, *Desmodillus auricularis*).

Zoonotic potential

Wesselsbron virus affects humans.

Geographic Distribution

Virological and/ or serological evidence suggests that Wesselsbron virus circulates in a number of countries in sub-Saharan Africa, including the island of Madagascar. This virus was apparently isolated from mosquitoes in Thailand in 1966, but there is no recent evidence for its presence outside Africa.

Transmission

Wesselsbron virus is transmitted by mosquitoes. Members of the genus *Aedes* are thought to be the major vectors, but it has also been detected in other genera including *Culex*, *Anopheles* and *Mansonia*. There is at least one report of virus isolation from an ixodid tick, but the significance of this finding, if any, is uncertain.

Experimental infections have been established in animals by intranasal, subcutaneous and intravenous inoculation. However, there is no evidence that Wesselsbron virus is transmitted between ruminants or other animals, except via mosquitoes.

Wesselsbron Disease

People have been infected by handling contaminated material and virus cultures in the laboratory, and tissues during necropsies. Transmission in mosquito bites is also thought to account for some cases. There is no evidence for person-to-person transmission.

The Wesselsbron virus is relatively fragile, and it is unlikely to remain infectious for more than a few days in carcasses or animal products in the field.

Disinfection

Although there are no studies describing the disinfectant sensitivity of Wesselsbron virus, other flaviviruses are sensitive to temperatures above 40°C (104°F), detergents and lipid solvents.

Infections in Animals

Incubation Period

One source estimates the incubation period in small ruminants to be 3-6 days. Most experimentally infected sheep and goats developed clinical signs after 1-4 days.

Clinical Signs

Sheep and goats

Wesselsbron disease has been described most often in sheep, where it mainly affects pregnant ewes and newborn lambs. The typical presentation can include abortions, stillbirths, mummified fetuses and weak lambs that die soon after birth. Some aborted fetuses may have congenital CNS defects and arthrogryposis. At least one congenitally infected but healthy lamb was described after experimental inoculation of the dam. The clinical signs in neonatal lambs can be nonspecific, with fever, anorexia, weakness, a rough hair coat and an elevated respiratory rate. Some descriptions also mention mucoid diarrhea, melena, pale mucous membranes, blood-stained nasal discharges, icterus, edema of the head or encephalitic signs. Some affected lambs can die within a few days. Pregnant sheep may also have systemic signs, with one study describing a moderate fever, mild lethargy, decreased appetite and an elevated respiratory rate after experimental inoculation. Reproductive complications, such as metritis and pregnancy toxemia, can be fatal. There is a field report of hydrops amnii (excessive accumulation of amniotic fluid in the amniotic cavity) associated with a live vaccine strain and also with field strains of the virus. Nonpregnant sheep generally seem to develop a brief, mild, nonspecific febrile illness or have no clinical signs. More severe signs (i.e., nasal discharge, diarrhea, jaundice and subcutaneous edema of the head, with a high mortality rate) were reported during one epidemic in the 1950s, but other illnesses might have also contributed to this syndrome.

Most sources report that Wesselsbron disease in goats resembles the illness in sheep. However, one group reported that experimentally infected, nonpregnant 4-5 month old

goats became severely ill after an unusually prolonged incubation period (up to 24 days), with signs of fever, edema of the head, and mucoid diarrhea, and 2 of the 4 infected goats died, 21-25 days after inoculation. The same authors reported severe, acute illnesses and fatalities in another experiment in nonpregnant pygmy goats. The incubation period in this case was short, and more typical of Wesselsbron disease. As of 2017, these findings have not been confirmed by other investigators.

Other species

Laboratory studies suggest that Wesselsbron virus can cause occasional reproductive losses in pregnant cattle. Abortions, congenital defects (e.g., porencephaly, cerebellar hypoplasia), and weak, congenitally infected calves, which died soon after birth, have been described. However, most calves born to experimentally infected, pregnant cattle seem to be healthy and uninfected. Some pregnant or nonpregnant cattle, including neonatal calves, developed a nonspecific, mild febrile illness after being inoculated with Wesselsbron virus. Other nonpregnant cattle only had a fever, with no overt clinical signs. One of 6 neonatal calves died in an experiment where calves were inoculated with this virus to study viremia, but no additional details were provided.

Two cases of neurological disease in horses, one fatal, were attributed to Wesselsbron disease in South Africa in 2008. To date, there is no further information about these cases. Fever alone was reported in experimentally infected horses and pigs.

In early studies, nonpregnant guinea pigs and rabbits inoculated intraperitoneally did not develop clinical signs, but pregnant animals aborted or had young that died shortly after birth.

Post Mortem Lesions

Congenital malformations of the CNS (e.g., porencephaly, cerebellar hypoplasia, hydranencephaly) and arthrogryposis have been reported in ovine and bovine fetuses.

Young lambs frequently have hepatomegaly with a yellowish to orange-brown liver, and moderate to severe icterus. There may also be white, pinpoint necrotic foci in the liver. The gastrointestinal tract may contain hemorrhagic lesions, including petechiae and ecchymoses in the abomasal mucosa, and hemorrhagic lesions of varying severity in the intestines. Petechiae and ecchymoses can sometimes be detected on the fascia and serosal surfaces of other organs, and there may be blood-stained fluid in the abdominal and thoracic cavities. Pulmonary congestion, splenomegaly and subcutaneous edema have also been described. On histopathology, there is usually mild to extensive necrosis of the liver parenchyma, with foci of necrotic hepatocytes. Lesions in adult animals are similar but usually much milder.

Wesselsbron Disease

A newborn calf infected *in utero*, which died soon after birth, had hepatic lesions resembling those seen in lambs, together with congestion, edema and hemorrhages of the brain, respiratory tract, myocardium, spleen and small intestinal mucosa.

Diagnostic Tests

Wesselsbron virus can be isolated from many organs and tissues of neonatal ruminants and fetuses, particularly the blood, serum, liver and brain of aborted fetuses, and the spleen and liver of dead lambs. Only a limited number of facilities can handle the live virus, as it is a biosafety level 3 pathogen. Systems that have been employed for virus isolation include BHK or lamb kidney cells, as well as suckling mice and chick embryos. The identity of the virus can be confirmed by virus neutralization, but a polymerase chain reaction (PCR) assay and nucleic acid sequencing were used in one recent (human) investigation. Whether PCR assays are routinely used for diagnosis in Africa is unclear. One report suggested that immunohistochemistry, using formalin-fixed liver tissues, may be helpful for confirming the disease in newborn lambs.

Serological tests that have been described include hemagglutination inhibition, complement fixation and virus neutralization. Although there is a high degree of cross-reactivity with other flaviviruses in hemagglutination inhibition tests, homologous Wesselsbron titers are usually much higher than heterologous titers. An ELISA has been described in the literature.

Treatment

There is no treatment for Wesselsbron disease, except supportive and symptomatic care.

Control

Disease reporting

Veterinarians who encounter or suspect Wesselsbron disease should follow their national and/or local guidelines for disease reporting. In the U.S., state or federal veterinary authorities should be informed immediately of any disease outbreaks caused by agents not present in the U.S.

Prevention

It would be prudent to avoid moving pregnant and neonatal small ruminants into endemic areas, especially if they have not been exposed previously to Wesselsbron virus. In the past, an attenuated vaccine for sheep was available in some areas. If given to pregnant ewes, this vaccine could cause reproductive losses similar to field strains of Wesselsbron virus. It is reported to have been discontinued.

Although vector control is theoretically possible, it is not usually practical for protecting small ruminant flocks.

Morbidity and Mortality

Serosurveys suggest that ruminants in some parts of Africa are commonly infected with Wesselsbron virus, with some surveys reporting exposure rates as high as 50% in cattle, sheep and goats. However, some of these studies might have also measured cross-reactive antibodies to other flaviviruses. Infections seem to occur year-round in some regions. In others, outbreaks are seen mainly when heavy rains favor the replication of mosquitoes that breed in floodwaters.

The overall prevalence of Wesselsbron disease in small ruminants is uncertain, as it resembles other illnesses such as Rift Valley fever, and samples may not be sent to a diagnostic laboratory. Some sources suggest that clinical cases are probably infrequent in Africa, although some large outbreaks were reported in the past. Wesselsbron disease is thought to be milder than Rift Valley fever; however, mortality rates as high as 20-30% have been reported in newborn lambs and kids. Some sources estimate a mortality rate of 20% in pregnant sheep, but it is possible that concurrent diseases or inadequate veterinary care (i.e., for pregnancy complications) contribute to these deaths. Most infections in nonpregnant adult ruminants are thought to be subclinical or mild. A limited number of field studies and experiments in cattle suggest that, while reproductive losses are possible in this species, they are probably uncommon.

Infections in Humans

Incubation Period

The incubation period in humans is estimated to be 2-4 days.

Clinical Signs

Most infections seem to be subclinical or mild. Most of the reported clinical cases have been characterized by an acute, influenza-like illness. Commonly reported symptoms included fever, headache, arthralgia and myalgia. Although the fever usually disappeared after 2-3 days, the muscle pains sometimes persisted for much longer. Some people also had mild skin rashes. Neurological signs were reported in one laboratory-confirmed case in 1957. This person, who had been splashed in the eye with virus, presented with an encephalitic syndrome, including dementia, and temporary hearing loss. Impaired vision was reported in another case.

Diagnostic Tests

Wesselsbron virus has been isolated from the blood of febrile patients, and from a pharyngeal wash. Serology was used to diagnose some cases.

Treatment

Treatment is symptomatic.

Prevention

People who work with Wesselsbron virus or contaminated tissues should wear protective clothing, including gloves, to prevent contact with the virus. Techniques that could aerosolize the virus should be avoided. Personal mosquito bite prevention measures, such as repellants and mosquito netting, are likely to be helpful.

Morbidity and Mortality

Subclinical infections are thought to be common among people in sub-Saharan Africa. Seroprevalence rates of 1% to 35% have been reported in various surveys; however, cross-reactions between flaviviruses could have caused false positive reactions in some people. Only a few laboratory-confirmed clinical cases have been reported. Most occurred in laboratory workers or field personnel who handled Wesselsbron virus or contaminated material, or who were collecting mosquitoes. In 2010-2011, two cases of Wesselsbron disease were confirmed in livestock farmers during an outbreak of Rift Valley fever.

Almost all of the cases described, to date, have been mild, but one person presented with signs of encephalitis. He had been splashed in the eye with virus, and the route of exposure might have influenced the symptoms. Fatal infections have not been reported in humans, as of 2017.

Internet Resources

The Merck Veterinary Manual

<http://www.merckvetmanual.com/mvm/index.html>

United States Animal Health Association. Foreign Animal Diseases

http://www.aphis.usda.gov/emergency_response/downloads/naheims/fad.pdf

University of Pretoria. Center for Viral Zoonoses - Emerging Arbo and Respiratory Virus Program

<http://www.up.ac.za/zoonoses-research-unit>

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*Link defunct as of 2017