

Akabane Disease

Congenital Arthrogryposis–Hydranencephaly Syndrome, A–H Syndrome, Akabane Disease, Congenital Bovine Epizootic A–H Syndrome, Acorn Calves, Silly Calves, Curly Lamb Disease, Curly Calf Disease, Dummy Calf Disease

Last Modified: September 2009



the Center for
Food Security
& Public Health

IOWA STATE UNIVERSITY®

College of Veterinary Medicine
Iowa State University
Ames, Iowa 50011
Phone: 515.294.7189
Fax: 515.294.8259
cfsph@iastate.edu
www.cfsph.iastate.edu



INSTITUTE FOR
INTERNATIONAL
COOPERATION IN
ANIMAL BIOLOGICS

an OIE Collaborating Center

Iowa State University
College of Veterinary Medicine
www.cfsph.iastate.edu/IICAB/



Importance

Akabane disease is a viral disease of ruminants that is mainly characterized by fetal damage. Inapparent infections in adults can lead months later to abortions, stillbirths and congenital defects in newborns. Most affected neonates die or must be euthanized. Before vaccines were developed, Akabane disease caused significant economic losses in some countries. Between 1972 and 1975, this virus resulted in the birth of more than 42,000 abnormal calves in Japan. A few strains of Akabane virus can also cause outbreaks of encephalomyelitis in calves and adult cattle. The latter syndrome has been considered rare, but in 2006, an outbreak affected nearly 200 cattle in Japan. There is no treatment for Akabane disease.

Etiology

Akabane virus is an arbovirus in the genus *Orthobunyavirus* and the Simbu serogroup of the family *Bunyaviridae*. Some closely related, named viruses including Tinaroo virus, Sabo virus and Yaba-7 virus are now considered to be strains or isolates of Akabane virus. Strains of Akabane virus may differ considerably in their virulence. Although most isolates only affect unborn ruminants, a few variants like the Iriki strain can cause neurological disease in postnatal cattle. Distinct groups of Akabane viruses circulate in Asia, Oceania and Africa.

Species Affected

Symptomatic infections have been seen only in cattle, sheep and goats. Wild ruminants can be infected with Akabane virus; congenital defects might occur in these species, but there are no reported cases in the literature. Antibodies to Akabane virus have also been found in horses, donkeys, buffalo, deer and camels. One isolate (NT-14) was reported to be widespread among pigs in Taiwan. Mice and hamsters can be infected experimentally.

Geographic Distribution

Akabane virus is thought to be endemic in two large north-south geographical bands. One band extends from Japan through Southeast Asia to Australia. The second occurs from the Middle East to South Africa. Where Akabane virus is constantly present, animals usually become infected before their first pregnancy, and clinical signs do not occur in their offspring. For this reason, clinical cases are usually reported only from the far northern and far southern regions of the virus's distribution. In other endemic regions, outbreaks can occur in recently introduced, naive animals. Some countries that have reported Akabane disease include Japan, Korea, Taiwan, Australia, Israel and Turkey. In Australia, the virus is endemic in the northern half of the country, but occasional outbreaks occur in southern Australia when conditions are favorable for it to spread. Outbreaks of an unusual form of Akabane disease characterized by postnatal encephalomyelitis have been reported in Japan, Taiwan and Korea.

Transmission

Akabane virus is transmitted by biting midges (gnats) in the genus *Culicoides*, as well as by mosquitoes. *Culicoides oxystoma* is the principal vector in Japan. *Culicoides brevitarsis* seems to be the primary vector in Australia, but the virus has also been found in *C. wadei*. *C. milnei* and *C. imicola* can transmit Akabane virus in Africa. Experimentally, virus replication has been demonstrated in *C. nubeculosus* and *C. variipennis*. Akabane virus has also been found in mosquitoes including *Aedes vexans* and *Culex tritaeniorhynchus* in Japan, and *Anopheles funestus* in Africa.

Vertical transmission is important in the epidemiology of this disease. Akabane virus is transmitted across the placenta to the fetus, and the primary effect is on the offspring of infected animals. Akabane does not appear to be contagious by casual contact; horizontal transmission has only been reported via insect vectors. Ruminants do not become long-term carriers of this virus.

Incubation Period

In adult animals, the infection is asymptomatic, but viremia usually occurs 1 to 6 days after infection, and Akabane virus is transmitted across the placenta to the fetus. Fetal infections do not become evident until the animal is either born or aborted due to severe defects.

Clinical Signs

Most strains of Akabane virus infect non-pregnant animals subclinically. A few isolates can cause encephalomyelitis in calves and adult cattle. Neurological signs that have been reported in these animals include tremors, ataxia, lameness, paralysis, nystagmus, opisthotonos and hypersensitivity. Although some individual animals have been febrile, fever was absent in most cases with CNS signs.

More often, Akabane disease is characterized by asymptomatic infections in postnatal animals, and abortions, stillbirths, premature births and congenital defects in fetuses and newborns. Two syndromes can be seen in the fetus: arthrogryposis and congenital malformations of the brain. Some animals (especially calves) have only one of the two syndromes, but others may have both. Encephalitis can also be seen in fetuses infected near term. Birth complications, particularly when the fetus is malformed from arthrogryposis, may cause injuries to the dam that result in infertility or death.

Because Akabane virus has different effects at each stage of gestation, an ordered sequence of events tends to be seen. This is particularly evident in cattle, which have a longer gestation period than small ruminants. In cattle, abortions, stillbirths and premature births may be the first sign of an Akabane outbreak. Aborted fetuses can appear normal on first examination, but severe hydranencephaly may be found if the skull is opened. In some outbreaks, nonsuppurative encephalomyelitis can be seen in calves that were infected late in gestation. These calves may have a variety of neurological signs including flaccid paralysis, exaggerated movements and hyperexcitability. Many cannot stand, and those that can rise with assistance are ataxic. The next calves to be born, which were infected during an earlier stage of their gestation, usually have arthrogryposis at birth. One or more joints are rigid and fixed in flexion (or, less often, in extension), and the associated muscles are often atrophied. The first calves tend to have less severe defects than calves born later. Torticollis, scoliosis, kyphosis and spina bifida may also be seen occasionally.

Affected calves born late in the outbreak, which were affected during an early stage of gestation, have congenital lesions in the brain ranging from small cavitations to severe hydranencephaly. Although these animals can usually stand and walk, they have behavioral abnormalities. Many are blind, depressed or dull, deaf and unaware of their environment; they may wander aimlessly. The suckle reflex can be slow or absent. Other neurological signs may also be

seen, and the gestation is often extended. A few calves may have both arthrogryposis and CNS defects. Most affected neonates die or must be euthanized soon after being born.

The range of fetal and neonatal defects seen in sheep and goats is similar, but there is more overlap. Arthrogryposis and CNS lesions are seen at the same time during the outbreak, and often occur in the same animals. Additional defects including pulmonary hypoplasia have been reported in small ruminants.

Post Mortem Lesions [Click to view images](#)

Fetuses or newborns may have arthrogryposis, hydranencephaly or both syndromes. In animals with arthrogryposis, one or more joints are affected in one or multiple legs. These joints are fixed by abnormalities in the soft tissues, and cannot be straightened. However, if the tendons are cut, the joints may move freely. The muscles may appear fibrotic and gray. CNS lesions can include hydranencephaly (thinning or disintegration of the cerebral cortex), hydrocephalus, agenesis of the brain, microencephaly, porencephaly (small cystic defects) or cerebellar cavitation. The brainstem does not usually have gross lesions even when the cerebral hemispheres are absent. Torticollis, scoliosis, kyphosis, spina bifida and brachygnathism can also be seen, especially in lambs and kids. Hypoplasia of the lungs, thymus and spinal cord can occur in small ruminants. Cataracts and ophthalmia have been reported. Aborted or stillborn fetuses may appear to be normal until they are examined carefully.

Calves infected late in gestation, as well as calves and adult cattle infected postnatally, can have lymphohistiocytic encephalomyelitis. Marked gross lesions are absent in the brains of these animals. Nonsuppurative lymphohistiocytic encephalomyelitis is found on histological examination; these lesions are most common in the pons and medulla oblongata, and the ventral horn gray matter of the spinal cord.

Morbidity and Mortality

Most animals in endemic areas are immune to Akabane virus by sexual maturity. Outbreaks usually occur at the limits of the virus's geographic range, when it is transmitted to susceptible animals during favorable environmental conditions such as a mild, moist autumn. Epizootics are seasonal, and tend to be seen at 4-6-year intervals, probably when immunity to previous viruses has waned. Some outbreaks might occur when infected midges are blown long distances by the wind. Pregnant animals that are moved into endemic areas are also at risk. Subsequent pregnancies are not affected.

The morbidity rate varies with the stage of the pregnancy. In cattle, the most severe defects occur when cows are infected at approximately 80-150 days of gestation, although the fetus can be affected any time after the first two months. Sheep and goats are most susceptible between 28 and 56 days of gestation, particularly at 28-36 days. In cattle, the morbidity rate varies from 5% to

approximately 50%, with the highest rates seen at the beginning of the susceptible period. Morbidity also varies with the strain of the virus. In sheep infected at the most susceptible stage, different isolates have morbidity rates of 15% to 80%. The mortality rate is very high in affected newborns: most animals die soon after birth or must be euthanized.

Encephalomyelitis appears to be uncommon in postnatal animals. Small-scale outbreaks have been reported occasionally among cattle in Japan, Taiwan or Korea. In 2000, an outbreak on five farms in Korea had a morbidity rate of approximately 30%. A larger epizootic occurred in Japan in 2006; approximately 180 cattle were affected between the end of August and mid-December.

Diagnosis

Clinical

Akabane disease should be suspected during an outbreak of aborted, mummified, premature or stillborn fetuses with arthrogryposis and hydranencephaly. No history of disease is expected in the dam. Encephalomyelitis may also be reported in postnatal animals; these outbreaks can occur on farms with no evidence of congenital disease from Akabane virus.

Differential diagnosis

Akabane disease must be differentiated from Aino virus, Chuzan virus or Cache Valley virus infections, bovine virus diarrhea, Border disease, Wesselsbron disease, and a variety of nutritional, genetic, and toxic diseases. Bluetongue is also a consideration in sheep.

Laboratory tests

Akabane disease is often diagnosed by serology in the fetus or presuckle neonate. Virus neutralization and enzyme-linked immunosorbent assays (ELISAs) are frequently used. Other serological tests include agar gel immunodiffusion, hemagglutination inhibition and hemolysis inhibition assays. Most fetuses and full term calves have mounted an antibody response to Akabane virus, but fetuses that were infected before they became immunocompetent may be seronegative. Samples from the dam are most useful in areas where the virus is not endemic. In endemic areas, the lack of a maternal immune response rules out Akabane infection in the fetus, but a positive sample may be due to a pre-existing titer. Serology is occasionally helpful in cases of postnatal encephalitis. Low titers in unpaired serum samples may be due to cross-reactions with related viruses, particularly those in the Simbu serogroup.

Virus isolation and the detection of antigens and nucleic acids are occasionally useful. Akabane virus can be isolated in cell lines including hamster lung (HmLu-1) and baby hamster kidney (BHK-21) cells. Suckling mice may also be used. Antigens may be found in the CNS and skeletal muscles using immunofluorescent or

immunohistochemical staining, and nucleic acids may be detected with reverse transcription polymerase chain reaction assays (RT-PCR). In congenital disease, Akabane virus is difficult to detect because the fetus is often infected long before its effects are seen. Viral antigens are not found in most fetuses or live-born young. Virus isolation from the fetus or placenta is rarely successful unless the animal was aborted before it developed an immune response, and the dam has usually cleared the virus by the time the affected fetus is born. However, viral antigens or nucleic acids have been found in the CNS of cattle with postnatal encephalomyelitis. Virus isolation can also be successful in this situation.

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.

Serum samples should be taken from the dam and the fetus, or the neonate before it is allowed to suckle. Body fluids may also be used; pericardial fluid is the preferred sample, but pleural fluid or peritoneal fluid can also be taken. Samples of the brain, spinal cord, affected muscles, spleen, kidney, heart, lung and lymph nodes should be collected into 10% formalin for histopathology. For virus isolation, immunohistochemistry and RT-PCR, samples should be taken from the placenta and fetal muscle, brain and spinal cord. These samples should be collected from a fresh fetus that was aborted early; in cattle, it should have been aborted before 5 months of gestation and soon after it was infected. Samples for virus isolation should be kept cool and delivered (on ice) to a laboratory within 24–48 hours.

In outbreaks of postnatal encephalomyelitis, CNS tissues have been used to isolate Akabane virus and detect viral antigens and nucleic acids. Serology was also helpful in some cases.

Recommended actions if Akabane disease is suspected

Notification of authorities

Akabane disease should be reported immediately to state or federal authorities upon diagnosis or suspicion of the disease.

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

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

Control

Akabane virus does not appear to be transmitted between animals except by arthropods. If this virus is introduced into an area where it is not endemic, care should be taken to prevent infection by potential vectors such as

mosquitoes or gnats. If disinfection is necessary, enveloped viruses such as the Bunyaviridae are susceptible to most common viral disinfectants including hypochlorite (bleach), detergents, chlorhexidine, alcohol and phenols.

Vaccines are available in some countries including Australia and Japan. Akabane disease can also be controlled by moving susceptible animals into endemic regions in time to develop immunity before they are first bred. Changing herd management to avoid infections during the most susceptible period of pregnancy may be helpful. Insect control techniques, including the use of repellents, can be effective for a few days, but cannot control the disease in the long term.

Public Health

Human infections with Akabane virus have not been reported.

Internet Resources

Animal Health Australia. Akabane
<http://www.animalhealthaustralia.com.au/aahc/index.cfm?7343A4AE-B23E-246B-3D4F-0FCD031B3D97>

Food and Agriculture Organization of the United Nations (FAO). 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>

United States Animal Health Association. Foreign Animal Diseases
http://www.aphis.usda.gov/emergency_response/downloads/nahems/fad.pdf

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

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

References

- Bryant JE, Crabtree MB, Nam VS, Yen NT, Duc HM, Miller BR. Isolation of arboviruses from mosquitoes collected in northern Vietnam. *Am J Trop Med Hyg.* 2005;73(2):470-3.
- Charles JA. Akabane virus. *Vet Clin North Am Food Anim Pract.* 1994;10(3):525-46.
- Garner G, Saville P, Fediaevsky A. Manual for the recognition of exotic diseases of livestock: A reference guide for animal health staff [online]. Food and Agriculture Organization of the United Nations [FAO]; 2003. Akabane. Available at: <http://www.spc.int/rahs/>. Accessed 5 Sept 2009.
- Huang CC, Huang TS, Deng MC, Jong MH, Lin SY. Natural infections of pigs with akabane virus. *Vet Microbiol.* 2003;94(1):1-11.

International Committee on Taxonomy of Viruses Universal Virus Database [ICTVdB] Management. 00.011.0.01.003. Akabane virus. In: Büchen-Osmond C, editor. ICTVdB - The universal virus database, version 4 [online]. New York: Columbia University; 2006. Available at: <http://www.ncbi.nlm.nih.gov/ICTVdb/ICTVdB>. Accessed 1 Oct 2009.

Jennings M, Mellor PS. *Culicoides*: biological vectors of Akabane virus. *Vet Microbiol.* 1989;21(2):125-31.

Kahn CM, Line S, editors. The Merck veterinary manual [online]. Whitehouse Station, NJ: Merck and Co; 2006. Akabane virus infection. Available at: <http://www.merckvetmanual.com/mvm/index.jsp?cfile=htm/bc/50804.htm>. Accessed 5 Sept 2009.

Kahrs RF. Viral diseases of cattle. 2nd ed. Ames, IA: Iowa State University Press; 2001. Akabane and bunyaviruses causing bovine fetal wastage; p. 257-261.

Kirkland PD. Akabane and bovine ephemeral fever virus infections. *Vet Clin North Am Food Anim Pract.* 2002;18(3):501-14, viii-ix.

Kirkland P, Macarthur E. Akabane disease. In: Foreign animal diseases. 7th edition. Boca Raton, FL: United States Animal Health Association; 2008. p. 117-23.

Kono R, Hirata M, Kaji M, Goto Y, Ikeda S, Yanase T, Kato T, Tanaka S, Tsutsui T, Imada T, Yamakawa M. Bovine epizootic encephalomyelitis caused by Akabane virus in southern Japan. *BMC Vet Res.* 2008;4:20.

Lee JK, Park JS, Choi JH, Park BK, Lee BC, Hwang WS, Kim JH, Jean YH, Haritani M, Yoo HS, Kim DY. Encephalomyelitis associated with akabane virus infection in adult cows. *Vet Pathol.* 2002;39(2):269-73.

Nebraska Cooperative Extension. University of Nebraska – Lincoln. Selection and use of disinfectants. Nebraska Cooperative Extension; 2001 May. Available at: <http://ianresearch.unl.edu/pubs/animaldisease/g1410.htm>. * Accessed 3 Oct 2001.

Smith MC, Sherman DM. Goat medicine. Philadelphia; Lea & Febiger; 1994. Akabane disease; p. 82-4.

Stram Y, Brenner J, Braverman Y, Banet-Noach C, Kuznetzova L, Ginni M. Akabane virus in Israel: a new virus lineage. *Virus Res.* 2004;104(1):93-7.

Uchida K, Murakami T, Sueyoshi M, Tsuda T, Inai K, Acorda JA, Yamaguchi R, Tateyama S. Detection of Akabane viral antigens in spontaneous lymphohistiocytic encephalomyelitis in cattle. *J Vet Diagn Invest.* 2000;12(6):518-24.

Yamakawa M, Yanase T, Kato T, Tsuda T. Chronological and geographical variations in the small RNA segment of the teratogenic Akabane virus. *Virus Res.* 2006;121(1):84-92.

*Link defunct as of 2009