

## AKABANE

*(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)*

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### Definition [top](#)

Congenital arthrogryposis-hydranencephaly (A-H) syndrome is an infectious disease of the bovine, caprine, and ovine fetus caused by intrauterine infection and interference with fetal development after transmission to the dam by biting gnat- or mosquito-transmitted Akabane virus and some other antigenically related members of the Simbu group of arboviruses (1,7). Fetal infection may cause abortions, stillbirths, premature births, mummified fetuses, and various dysfunctions or deformities of fetuses or liveborn neonates. Adult animals are not clinically affected while actively infected with virus (17).

### Etiology [top](#)

The etiologic agents of congenital A-H syndrome are arboviruses of the Simbu group of the family Bunyaviridae. Akabane virus was the first member of the Simbu group to be incriminated in congenital A-H syndrome, but other members (namely Aino, Peaton, and Tinaroo viruses) have the capacity to produce fetal defects (3,10,13,18). In recent years, Cache Valley virus, a mosquito-borne member of the Bunyaviridae outside the Simbu group, has been found to reproduce a similar syndrome in ruminants within the United States (2). The Simbu group of viruses are spread only by insect vectors. Spread by contact, infected tissues, exudates, or fomites does not occur.

### Host Range [top](#)

Congenital A-H syndrome associated with Akabane virus and other Simbu group viruses has been reported only in cattle, sheep, and goats. Although antibody against these viruses has been detected in horses, no clinical evidence of fetal infection has been reported. Infections of wild ruminants do occur, and fetal damage must be considered but has not been reported.

### Geographic Distribution [top](#)

In Japan, the periodic outbreaks of AH syndrome have been reported since 1949. Enzootic Akabane virus (and presumably other Simbu group virus) activity has occurred in the northern half of Australia since at least 1931 with occasional temporary epizootic incursions southward dependent on favorable seasons (18). Reports of A-H syndrome in Israel (8) and other countries in the Middle East, Cyprus (8,18,19), Korea, Zimbabwe, and South Africa have been published in the last decade. Serological surveys indicate that the virus occurs throughout Africa, Asia, and Australia but not Papua New Guinea, the Pacific Islands, or the Americas.

### Transmission [top](#)

The occurrence of A-H syndrome is seasonally and geographically restricted. The location and timing of the infection of the fetus during early pregnancy is consistent with the seasonality of transmission by hematophagous insects. Akabane virus has been isolated from *Aedes vexans* and *Culex triteeniorhynchus* mosquitoes in Japan; *Anopheles funestus* mosquitoes in Kenya; *Culicoides milnei* and *C. imicola* in Africa; *C. oxystoma* in Japan; and *C. brevitarsis* and *C. wadei* gnats in Australia (3,13,17,18). Confirmation of the biologic transmission by these species is lacking; however, epidemiologic evidence incriminates them. In Australia, *C. brevitarsis* is believed to be the principal vector of Akabane virus. Cache Valley virus has been isolated from at least nine different mosquito species,

and antibodies to this virus have been detected in man, as well as wild and domestic animals in the Americas.

There is no indication that Akabane virus, other Simbu group viruses or Cache Valley virus is transmitted in any other way than by a vector. Transmission happens months before disease in the fetus is evident.

### **Incubation Period** [top](#)

Infection of adult animals produces no overt clinical sign, but viremia generally occurs 1-6 days after infection. A natural viremia may last 4 to 6 days before antibodies to Akabane virus are detectable (17). However, infection of pregnant animals during the first months of gestation may result in fetal infection that is not apparent until much later in pregnancy or at term (6).

Timing of the infection relative to the stage of gestation is critical to the development of defects in the fetus. In pregnant sheep, the gestational period for the occurrence of fetal abnormalities has been shown to vary from 30-36 days to 30-50 days (6,14,15). This variation in the reported results has been ascribed to (a) differences in the virulence of virus strains used, (b) differences in the passage level of the virus strain used, or (c) differences caused after growth of the virus in the arthropod vectors. Inoculation of pregnant cattle with virus between 62 and 96 days of gestation resulted in fetal lesions; in pregnant goats, the critical period in the gestational cycle was about 40 days (10,12).

### **Clinical Signs** [top](#)

Congenital A-H syndrome is manifested as a seasonally sporadic epizootic of abortions, stillbirths, premature births, and deformed or anomalous bovine, caprine, and ovine fetuses or neonates. The pregnant dam has no clinical manifestation at the time of infection with virus. Sentinel cattle under close observation have no clinical sign during viremia induced by natural infection. If infection develops during the first third of pregnancy, gross fetal damage may occur. At the other end of the disease spectrum, damage to the central nervous system (CNS) may be minor and produce changes in behavior of the new born or young animal. Dystocia at parturition may occur owing to the deformities in the fetus. Badly deformed fetuses are usually dead at birth, and the limbs are locked in the flexed or extended position. Most live neonates have central nervous system degeneration and muscle lesions that prevent the animal from standing or suckling. Torticollis, scoliosis, brachygnathism, and kyphosis may coexist with arthrogryposis. Lesions in the central nervous system are manifested clinically as blindness, nystagmus, deafness, dullness, slow suckling, paralysis, and

incoordination.

Mildly affected calves or lambs may improve their mobility with time. However, most eventually die by 6 months as a result of blindness and other neurological defects (5,7,10,12,14,15,17).

### **Gross Lesions** [top](#)

An individual fetus or newborn may have arthrogryposis and hydranecephaly or both syndromes. Lesions are associated with damage to the enervation of the musculature and to the central nervous system. Arthrogryposis is the most frequently observed lesion. Affected joints cannot be straightened even by application of force because of ankylosis of the joint in the extended or flexed position (Fig. 23). Torticollis, scoliosis, and brachygnathism are observed. There may be shallow erosions about the external nares and muzzle and between the distal digits. Hypoplasia of the lungs and skeletal muscles, fibrinous polyarticular synovitis, fibrinous navel infection, ophthalmia, cataracts, and presternal steatosis occur. Within the CNS, hydranencephaly (Fig. 24), hydrocephalus, agenesis of the brain, microencephaly, porencephaly and cerebellar cavitation, fibrinous leptomeningitis, fibrinous ependymitis, and agenesis or hypoplasia of the spinal cord are variously reported (5, 16, 20). The cerebellum appears intact. Lesions due to Akabane tend to be symmetrical. However, some asymmetry occurs when Aino virus is involved. Akabane virus was isolated from fetuses of naturally infected pregnant cows or ewes by the use of predictive serology. When the mothers seroconverted from negative to positive in Akabane virus neutralization tests, Akabane virus was isolated from the fetus (4,11).

### **Morbidity and Mortality** [top](#)

In endemic areas, animals are exposed and become immune before becoming pregnant; thus, congenital abnormalities are seldom seen in native animals, for antibodies prevent virus from spreading from the site of the bite to the fetus. However, when the infected vector spreads (e.g., during an extended humid summer) to an area where the animals are not immune, A-H syndrome can occur months later in many animals. The disease can also appear when pregnant animals from a disease-free area are moved into an endemic area.

There is no reported damage to the dam in congenital A-H syndrome. Most live-born affected calves, lambs, or kids die shortly after birth or must be slaughtered for humane reasons. Some mildly affected calves do improve gait and learn to follow the herd.

## Diagnosis [top](#)

### Field Diagnosis

A field diagnosis of congenital A-H syndrome can be made on the basis of the clinical condition, gross pathologic lesions, and the epidemiology. The sudden onset of aborted, mummified, premature, or stillborn fetuses with arthrogryposis and hydranencephaly should be suggestive. The dam will have had no clinical history of disease. A retrospective study would indicate that the first third of pregnancy occurred during a time of biting insect activity.

### Specimens for the Laboratory [top](#)

The following specimens should be collected for virus isolation: placenta, fetal muscle, cerebrospinal fluid, and fetal nervous tissue; for serology: fetal or precolostral serum, and serum from the dam. For histopathology send pieces of spleen, liver, lung, kidney, heart, lymph nodes, affected muscle, spinal cord and brain in 10 percent buffered formalin.

If the specimens can be delivered to a laboratory within 24 hours, they should be placed on ice. If delivery will take longer, quickfreeze the specimens and do not allow them to thaw during transit.

### Laboratory Diagnosis [top](#)

Virus isolation should be attempted from placenta, fetal muscle, or fetal nervous tissue. The chances of success are very low except with a fetus and placenta aborted before antibodies are generated within an immunocompetent fetus. In the absence of viral isolations, a serologic diagnosis is usually made by demonstrating antibodies in precolostral or fetal serum samples. In adult animals, seroconversion or a demonstrable rise in antibody titer indicates that there was infection. A microtiter neutralization test and an immunofluorescence test are available for detecting and assaying antibodies (18). Tissues of the dam are free of virus by the time the damage is observed in the fetus or newborn. Low titers (<10) in unpaired serum samples should not be taken as diagnostic because of cross-reaction problems.

### Differential Diagnosis [top](#)

The demonstration that Cache Valley virus, a Bunyavirus that is ubiquitous within the United States, can cause the A-H syndrome means that serological tests are

essential to distinguish exotic from enzootic etiologies (2). It is a reasonable assumption that other Bunyaviridae will be proven to be teratogenic in livestock in the Americas. A variety of nutritional, genetic, toxic, and infectious diseases will produce fetal wastage and deformities. Fetal brain lesions resulting from bluetongue vaccine virus infections of pregnant ewes are similar to those produced within the congenital A-H syndrome. Bluetongue presents the greatest difficulty in the initial differential diagnosis of hydranencephaly. Bovine virus diarrhea infection can cause cerebellar dysplasia in calves. Border disease virus infection can cause undersized, excessively hairy lambs with muscular tremors and skeletal defects. Wesselsbron virus infection can cause congenital porencephaly and cerebral hypoplasia in calves. Serology of the dam and fetus will resolve any confusion.

### **Vaccination** [top](#)

A formalin-inactivated, aluminum phosphate, gel-absorbed vaccine and an attenuated vaccine have been developed in Japan for Akabane virus. An effective killed vaccine for Akabane virus has been developed but not marketed in Australia (7,9). These vaccines induce immunity in the cow or ewe, and the circulating antibodies prevent the virus from reaching the fetus. The vaccines are used prior to exposure to infected vectors. Vaccine is no longer available for economic reasons. Immunizing agents for other Simbu group viruses are not currently available and are not expected to be developed.

### **Control and Eradication** [top](#)

Techniques for the control of the viral agents that cause congenital A-H syndrome are those typically recommended for other vector-transmitted agents. Control of the vector depends upon disruption of breeding sites, reduction of vector populations with pesticides, and protection of host animals from feeding by the vectors. In addition to these procedures, animals should be vaccinated before breeding.

### **Public Health** [top](#)

There is no evidence that humans can be infected by Akabane virus.

### **GUIDE TO THE LITERATURE** [top](#)

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