AKABANE
STANDARD OPERATING PROCEDURES:
1. OVERVIEW OF ETIOLOGY AND ECOLOGY

FAD PReP
Foreign Animal Disease Preparedness & Response Plan

United States Department of Agriculture

United States Department of Agriculture • Animal and Plant Health Inspection Service • Veterinary Services

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The Foreign Animal Disease Preparedness and Response Plan (FAD PReP) Standard Operating Procedures (SOPs) provide operational guidance for responding to an animal health emergency in the United States.

These draft SOPs are under ongoing review. This document was last updated in **January 2015.** Please send questions or comments to:

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Akabane

Etiology & Ecology Quick Summary

Disease

Akabane disease, congenital arthrogryposis-hydranencephaly syndrome, congenital bovine epizootic A-H syndrome, acorn calves, curly lamb disease, curly calf disease.

Mortality and Morbidity

Morbidity ranges from 5 to 80 percent in cattle and 15 to 80 percent in sheep; mortality is very high in newborns.

Susceptible Species

Cattle, sheep, and goats experience clinical disease; wild ruminants also are infected, but the effects on their offspring are unknown.

Zoonotic Potential

Not a threat to public health.

Transmission

The virus is both vectorborne, by *Culicoides* biting midges and mosquitoes, and tranmitted vertically across the placenta where it infects the fetus.

Persistence in the Environment

Akabane virus can be destroyed by common disinfectants, including bleach, detergents, chlorhexidine, alcohol, and phenols, and heat above 50°C; it does not persist when exposed in the environment.

Animal Products and By-Products

Akabane virus is not maintained in animal tissues.

1.1 Introduction

Akabane disease, caused by an arbovirus, is mainly characterized by congenital defects in ruminants. First isolated in 1959 from mosquitoes in Japan, it is named for the village where it was discovered. Akabane disease has also been detected in Australia, Israel, and Korea, and reported throughout much of the African continent[1] as well as in Israel and Turkey.[2,3]

Akabane virus (AKAV), which causes Akabane disease, is spread by biting midges and/or mosquitoes. It can also be transmitted vertically from mother to fetus. Adult ruminants typically experience inapparent infections, though certain strains cause encephalomyelitis in cattle.[4] The disease is considered endemic over two ranges: one extending from Japan to Australia and the other from the Middle East to South Africa.[5]

1.1.1 Goals

As a preparedness goal, the Animal and Plant Health Inspection Service (APHIS) will provide etiology and ecology summaries for Akabane disease and update these summaries at regular intervals.

As a response goal, the Unified Command and stakeholders will have a common set of etiology and ecology definitions and descriptions, to ensure proper understanding of AKAV when establishing or revising goals, objectives, strategies, and procedures.

1.1.2 Further Information

This document is intended to be an overview, focusing on Akabane disease in domestic ruminants. Resources are listed in Attachment A.

Publicly available documents are available at http://www.aphis.usda.gov/fadprep or on the APHIS Intranet at http://inside.aphis.usda.gov/vs/em/fadprep.shtml for APHIS employees.

1.2 Purpose

This document provides responders and stakeholders with a common understanding of the disease agent.

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[1] Al-Busaidy S, Hamblin C, Taylor WP. 1987. "Neutralising antibodies to Akabane virus in free-living wild animals in Africa". *Tropical Animal Health and Production*. 19(4): 197–202.
[2] Merck Veterinary Manual. 2012. "Akabane Virus Infection." Accessed from http://www.merckmanuals.com/vet/generalized_conditions/congenital_and_inherited_anomalies/akabane_virus_infection.html (January 21, 2015).
[3] Geoghegan JL, Walker PJ, Duchemin JB, Jeanne I, Holmes EC. 2014. "Season Drivers of the Epidemiology of Arthropod-Borne Viruses in Australia." *PLoS Neglected Tropical Diseases.* Online before print.
[4] Oem JK, Kim YH, Kim SH, Lee MH, Lee KK. 2014. "Serological characteristics of affected cattle during an outbreak of bovine enzootic encephalomyelitis caused by Akabane virus. *Trop Anim Health Prod.* 46: 261–263.
[5] Center for Food Security and Public Health, Iowa State University (CFSPH). 2009. "Akabane Disease". *Technical Factsheet.* www.cfsph.iastate.edu.

1.3 Etiology

1.3.1 Name

This disease is most commonly known as Akabane disease, but it may also be referred to as congenital arthrogryposis-hydraencephaly syndrome, congenital bovine epizootic A-H syndrome, acorn calves, curly lamb disease, and curly calf disease. [6]

1.3.2 Virus Characteristics

According to the International Committee on Taxonomy of Viruses, this disease has the following characteristics:[7]

- Family: Bunyaviridae
- Genera: *Orthobunyavirus*
- Baltimore Classification: Group V (-) ssRNA.

1.3.3 Morphology

AKAV is enveloped with a genome made up of three distinct single strands of RNA. These are designated the large (L), medium (M), and small (S) RNA, and code for the large virion protein, two envelope glycoproteins, and a nucleoprotein and nonstructural protein, respectively. [8,9]

1.3.4 AKAV Strains and Isolates

AKAV belongs to the Simbu serogroup of the Bunyaviridae family. There are many different strains and isolates of AKAV[10], including Tinaroo virus, Sabo virus, Yaba-7 virus, and the Iriki strain; groupings of AKAV are geographically distinct and highly variable in their levels of virulence.[11]

The Aino virus, a member of the same serogroup as AKAV, has a nearly identical etiology and ecology, and observations of infection with both viruses have been made in cattle.[12] Aino virus appears to occur more rarely.[13] Though sometimes referred to interchangeably, AKAV and Aino viruses can be differentiated by real-time reverse-transcriptase polymerase chain reaction.[14] In

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[6] CFSPH, 2009.
[7] International Committee on Taxonomy of Viruses. 2012. ICTV Taxonomy History for Akabane virus. http://ictvonline.org.
[8] Akashi H, Inaba Y. 1997. "Antigenic diversity of Akabane virus detected by monoclonal antibodies". *Virus Research*. 47: 187–196.
[9] Stram Y, Kuznetzova L, Guini M, Rogel A, Meirom R, Chai D, Yadin H, Brenner J. 2004. "Detection and quantitation of Akabane and Aino viruses by multiplex real-time reverse transcriptase PCR". *Journal of Virological Methods*. 116(2): 147–154.
[10] Oem JK, Lee KH, Kim HR, Bae YC, Chung JY et al. 2012. "Bovine Epizootic Encephalomyelitis caused by Akabane Virus infection in Korea." *Journal of Comparative Pathology.* 147(2-3):101–105.
[11] Kono R, Hirata M, Kaji M, Goto Y, Ikeda S et al. 2008. "Bovine epizootic encephalomyelitis caused by Akabane virus in southern Japan." *BMC Veterinary Research.* 4:20.
[12] Stram et al., 2004.
[13] Akashi H, Onuma S, Nagano H, Ohta M, Fukutomi T. 1999. "Detection and differentiation of Aino and Akabane Simbu serogroup bunyaviruses by nested polymerase chain reaction". *Archives of Virology*. 144: 2101–2109.
[14] Stram et al., 2004.

addition to AKAV and Aino virus, the Schmallenberg virus is also a member of the Simbu serogroup.

1.4 Ecology

1.4.1 General Overview

AKAV is endemic over two distinct geographic ranges. One stretches over east and southeast Asia south to Australia, affecting Australia as well as Japan, Korea, and Taiwan. In the other range, AKAV is endemic from the Middle East to South Africa, where reporting countries also include Turkey, Cyprus, and Israel. Outbreaks of clinical disease tend to occur at the edges of the virus' endemic ranges, often where climatic variability stretches the area where conditions for the disease are favorable. Epizootics tend to occur seasonally.[15]

1.4.2 Susceptible Species

Clinical signs have been reported exclusively in cattle, sheep, and goats. Akabane disease primarily presents a danger to ruminant neonates. It is possible that wild ruminants may be affected by congenital defects associated with AKAV, but this has not been confirmed. Viral antibodies have also been isolated from horses, donkeys, buffalo, deer, and camels.[16,17]

1.4.3 Introduction and Transmission of AKAV

AKAV is transmitted by *Culicoides* biting midges and mosquitoes, and vertically across the placenta during pregnancy. In areas where the disease is endemic, ruminants typically are immune by the time they reach sexual maturity, so congenital defects are not observed.

However, when environmental conditions are favorable, the vector and virus can spread outside of its normal range and affect ruminants with no immunity.[18] AKAV is not known to be spread through contact with infected animals or their tissues, sera, or excretions; accordingly, fomites and mechanical vectors are not considered important in transmission.

1.4.3.1 Vertical Transmission

Akabane is most damaging as a disease of fetal ruminants; transmission across the placenta is an important route of infection. Vertical transmission of the virus occurs when a pregnant animal is bitten by an infected insect and develops a viremia; the virus is transmitted across the placenta to the fetus. Past studies indicate that bulls infected with AKAV were not likely to pass the virus to their offspring.[19]

[15] Kono R. et al. 2008.
[16] Cybinski DH, St George TD, Paull NI. 1978. "Antibodies to Akabane virus in Australia." *Aust Vet J.* 54(1): 1–3.
[17] Yang DK, Kim BH, Kweon CH, Nah JJ, Kim HJ et al. 2008. "Serosurveillance for Japanese encephalitis, Akabane, and Aino viruses for Thoroughbread horses in Korea." *J Vet Sci.* 9(4):381–385.
[18] Merck Veterinary Manual. 2012.
[19] Parsonson IM, Della-Porta AJ, Snowdon WA, O'Halloran ML. 1981. Experimental infection of bulls with Akabane virus". *Research in Veterinary Science.* 31(2): 157–160.

1.4.3.2 Vector Transmission

Multiple species within the *Culicoides* genus of midges are known vectors, and several mosquito species have been identified to carry AKAV. In Japan, horizontal transmission is mainly by *Culicoides oxystoma,* but the mosquitoes *Aedes vexans* and *Culex tritaeniorhyncus* have been implicated as well. In Australia, the vector of note is *Culicoides brevitarsis*, but *C. wadei*, *C. fulvus,* and *C. actoni* may also contribute.[20] AKAV is reported to be transmitted more efficiently in Australia than bluetongue viruses and can be spread by relatively small vector populations.[21] African AKAV is transmitted by the midges *C. milnei* and *C. imicola* as well as the mosquito *Anopheles funestus*. *Culicoides nubeculosus* and *C. variipennis* have also been found competent to transmit AKAV in experimental settings.[22]

1.4.3.3 Wildlife

Wild species of ruminants can become infected with AKAV. No fetal defects in wildlife have been observed, but the occurrence remains possible due to the difficulty of witnessing wild births. Antibodies to the virus have been recovered from buffalo, deer, and various African wildlife species.[23]

1.4.4 Incubation Period

Infection is typically inapparent in adult animals, but viremia, which can lead to vertical transmission, occurs 1 to 6 days after infection.[24]

1.4.5 Morbidity and Mortality

Where AKAV is endemic, susceptible animals attain immunity by the time they reach sexual maturity. The morbidity and mortality rates differ by species, viral strain, and the timing of an infection with AKAV. A morbidity rate of 5 to 50 percent can be observed in cattle, whereas in sheep the rate is between 15 and 80 percent. Infected newborns experience very high mortality, as almost none are viable and either die soon after birth or must be euthanized.

1.4.5.1 Clinical Signs

AKAV is most commonly associated with fetal and postnatal complications, which are frequently severe enough to cause abortions, stillbirths, premature births, and congenital defects. Cases involving affected fetuses typically involve malformations of the joints, muscles, and brain, and pregnant animals do not show signs of illness. Infected fetuses are only known at birth or in the event of disease-induced abortion.

The effects of AKAV infection of a fetus depend on when during gestation the infection occurs; this is more evident in cattle, due to their longer gestation periods:

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[20] Geoghegan JL et al. 2014.
[21] Kirkland PD. 2012. "Akabane Virus– Epidemiology, Pathogenesis and Impact". Scientific Seminar on Management of Schmallenberg Virus, Brussels, Belgium. http://ec.europa.eu/food/animal/diseases/schmallenberg_virus/docs/akabane_other_sbv_en.pdf.
[22] CFSPH, 2009.
[23] Al-Busaidy S, et al. 1987.
[24] CFSPH, 2009.

- Congenital lesions in the brain may be present in calves born to cows infected early in pregnancy. These calves exhibit behavioral abnormalities even though their motor faculties seem normal. Neurological signs may occur, and calves may be blind, deaf, depressed, or unaware of surroundings; they may have difficulty suckling and generally die soon after birth or must be euthanized.
- Infection in the second trimester of pregnancy is likely to result in a calf born with arthrogryposis, or rigid joints with atrophied muscles.
- Fetuses infected at a later stage tend to be aborted, stillborn, or premature; often signs of disease are not noticeable until examination of the cranial cavity reveals hydranencephaly.
- Newborn calves may be alert but typically cannot stand, and they are likely to be uncoordinated, partially or fully paralyzed, have bulging or tearing eyes, and make unusual vocalizations.[25] The Iriki strain, in particular, is known to cause intense nervous signs in calves.[26]

In cases where AKAV infection causes clinical disease in adult or postnatal ruminants, encephalomyelitis in cattle may result in tremors, ataxia, lameness, paralysis, involuntary eye movement, muscle spasms, and hypersensitivity. However, it is common for adult cattle to be infected without demonstrating clinical signs.[27]

In sheep and goats, similar signs are seen in fetuses and newborn animals, but they often occur together. Lambs and kids are particularly likely to experience defects and contortions of the neck and spine as well as having incompletely developed lungs.[28] Lambs and kids are typically stillborn or die soon after birth.[29]

Other diseases presenting with similar signs to Akabane include:

- Schmallenberg virus;
- disease caused by Aino or Cache Valley (Chuzan) viruses;
- bovine viral diarrhea virus;
- border disease;
- Wesselsbron disease;
- bluetongue (in sheep); and
- other nutritional, genetic, and toxic diseases.

[25] CFSPH, 2009.
[26] Miyazato S, Miura Y, Hase M, Kubo M, Goto Y, Kono Y. 1989. "Encephalitis of cattle cause by Iriki isolate, a new strain belonging to Akabane virus". *Japanese Journal of Veterinary Science*.51(1): 128–136.
[27] Oem JK, Lee KH, et al. 2012.
[28] CFSPH, 2009.
[29] Merck Veterinary Manual. 2012.

1.5 Environmental Persistence

Members of the Bunyaviridae family are destroyed by common disinfectants, such as hypochlorite (bleach), detergents, chlorhexidine, alcohol, and phenols, and are sensitive to temperatures above 50°C for 30 minutes. AKAV does not persist in infected animal tissues or fluids and will not endure in the environment for any significant period of time (Table 1). [30]

Table 1. California Serogroup (Orthobunyaviruses) Resistance to Physical and Chemical Action

Action	Resistance
Temperature	Infectivity lost (or significantly reduced) at 50–60° C (122–140° F) for at least 30 minutes.
Chemicals/Disinfectants:	Susceptible to common disinfectants: 1% sodium hypochlorite, 2% glutaraldehyde, 70% ethanol, formaldehyde.
Survival	Does not survive outside the host or vector for long periods.

Source: OIE. 2013. "Schmallenberg Virus" *Technical Factsheet*. www.oie.int.

1.6 Risk of Introduction into the United States

Livestock in the United States are considered to be susceptible to Akabane, and indigenous arthropod species may be competent to transmit the virus. A similar arbovirus of the same family, Cache Valley virus, has been found in North America. Naïve populations are more likely to see high rates of mortality, as each year the United States is home to over 35 million calves and 3 million lambs.

Preventing contact with insect vectors is an important method of controlling the spread of Akabane, particularly in environments and seasons where midges and mosquitoes thrive. Vaccine is available for AKAV, though it is not licensed in the United States.[31]

[30] World Organization for Animal Health (OIE). 2013. "Schmallenberg Virus" *Technical Factsheet*. www.oie.int.
[31] CFSPH. 2014. Vaccine Database: Akabane. Accessed from http://www.cfsph.iastate.edu/Vaccines/disease_list.php?disease=akabane (January 21, 2015).

Attachment A. References and Selected Resources

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Attachment B. Abbreviations

APHIS	Animal and Plant Health Inspection Service
FAD PReP	Foreign Animal Disease Preparedness and Response Plan
AKAV	Akabane virus
RNA	ribonucleic acid
SOP	standard operating procedure
TDD	telecommunications device for the deaf
USDA	United States Department of Agriculture