
SCHMALLEMBERG VIRUS

CASE DEFINITION & GUIDANCE

1. Disease background and pathogen information

1.1 History: Since August 2011, a newly-identified infectious disease has been reported in cattle, sheep, goats, and bison in Europe. This disease was first reported in German dairy cows that exhibited signs of fever, anorexia, reduced milk yield, and loss of condition. Herd morbidities were high (20-70 percent) over 2-3 weeks, with affected individuals recovering in a few days. Reports of disease among cattle in Germany, and subsequently in the Netherlands, persisted throughout September and into October.

By November 2011, farmers began reporting abortions and stillbirths associated with congenital malformations, mostly among sheep but also in goats and cattle. Some dystocias, with no other clinical signs, were observed in mature animals. Laboratory testing at the Friedrich Loeffler Institut (FLI) in Germany ruled out a number of infectious diseases of ruminants and tentatively identified a novel virus in the family Bunyaviridae, genus *Orthobunyavirus*. Samples from clinical cases were positive for novel virus material, whereas control cases were not. The virus caused fever, viremia, and diarrhea in a small number of experimentally infected calves (Hoffmann et al. 2012). By mid-March 2012, the virus had been identified on more than 2,100 farms in eight European countries. Most infected premises have been sheep farms (85 percent), followed by cattle (11 percent) and goat farms (4 percent) (FluTrackers.com).

1.2 Causative agent: This new virus is provisionally named Schmallenberg virus (SBV) after the town in Germany where the first positive samples were found. Genomic studies have shown that SBV closely resembles viruses in the Simbu serogroup of the genus *Orthobunyavirus*. Closely-related viruses include Shamonda, Aino, and Akabane viruses (Hoffmann et al. 2012).

1.3 Geographic distribution: As of March 2012, cases of Schmallenberg virus infection have been confirmed in Germany, the Netherlands, Belgium, France, the United Kingdom, Luxembourg, Italy and Spain. Spread of SBV from mainland Europe to Great Britain has been tentatively linked to natural movements of insects from infected areas, similar to the pattern of bluetongue virus in 2008 (European Commission 2012). It is unknown when and where SBV originated (FLI 2012) and its emergence is the first detection of the Simbu virus serogroup in Europe (Hoffmann et al. 2012). SBV is not known to exist in the United States. Orthobunyaviruses in the Simbu serogroup are known in Africa, Asia, Australia, and the Middle East (European Commission 2012).

1.5 Incubation period: In experimental challenge trials, three calves inoculated intravenously or subcutaneously with blood that was PCR positive for SBV became infected and had positive PCR results 2-5 days post-inoculation. The viremic stage in cattle seems to be short, as viral detection was negative in all three infected animals 6 days after inoculation, and clinical signs subsided within a few days (Hoffmann et al. 2012). Similarly, in Akabane virus infection, adult animals are typically asymptomatic, but viremia usually occurs 1 to 6 days post-infection. Fetal infections are inapparent until the animal is aborted or born with severe defects (CFSPH 2009).



1.5 Differential diagnosis: Many of the clinical signs of SBV are similar to other diseases or agents (viral, bacterial, genetic, toxic or nutritional, etc.) that cause abortion, congenital malformations, and transient systemic problems in cattle, sheep, and goats. These diseases include bovine viral diarrhea virus and other pestiviruses, bovine herpesvirus type 1, foot-and-mouth disease virus, bluetongue virus, epizootic hemorrhagic disease virus, Rift Valley fever virus, Cache Valley virus, bovine ephemeral fever virus, toxicities (e.g. *Veratrum californicum*, *Lupinus* spp.), nutritional deficiencies (e.g. gestational protein deficiency, manganese), and genetic abnormalities (e.g. spider lamb syndrome).

1.6 Transmission and reservoirs: All known orthobunyaviruses are spread by arthropod vectors, principally midges (*Culicoides* spp.) and mosquitoes. Transplacental transmission has also been demonstrated in orthobunyaviruses (European Commission 2012). The role of biting midges in the transmission and spread of Schmallenberg virus was confirmed with the detection of SBV in two species of *Culicoides* in Belgium collected during September and October 2011 (European Livestock Association 2012a). The examined insect pools consisted exclusively of heads, suggesting that midges act as amplification vectors and were not simply SBV positive after ingesting a blood meal on viremic animals. The further spread of SBV in Europe will be determined by the natural history of the virus (e.g., whether it overwinters in arthropod hosts), environmental temperatures, and number and distribution of vector species and ruminant hosts. Because Akabane virus can infect domestic and wild ruminants as well as pigs (CFSPH 2009), it is similarly assumed that SBV can infect wildlife and swine, although evidence is lacking (FLI 2012). Potential wildlife hosts for SBV in Europe include roe deer (*Capreolus capreolus*), fallow deer (*Dama dama*), red deer (*Cervus elaphus*), mouflon sheep (*Ovis aries*), bison (*Bison bonasus*), and wild boar (*Sus scrofa*). Should SBV enter North America, potential wildlife hosts would include several species of Cervidae as well as American bison (*B. bison*) and feral swine.

1.7 Epidemiology: Infections with SBV likely occurred during the summer and fall of 2011 (assuming an insect vector) with exposed fetuses and neonates of small ruminants showing signs around parturition. In some sheep flocks, 20-50 percent of lambs were deformed, and many were born dead (Kupferschmidt 2012). Data from the Netherlands suggested that SBV caused a small percentage of cattle abortions and neonatal deformities in 2011 (2 out of 101 sera from cows that had aborted in September-October were PCR positive for the virus). However, scientists are expecting more neonatal cases in cattle during spring of 2012, when bovines conceived in 2011 are due to be born (Kupferschmidt 2012). Genomic studies have shown that SBV is most closely related to Simbu serogroup viruses, in particular Shamonda virus, which does not cause disease in humans. Because of this close relationship and the absence of reports of clinical signs in people, the risk to humans is currently judged as very low to negligible, but cannot be entirely excluded (RIVM 2011, Hoffmann et al. 2012). The European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (ECDC) are closely monitoring the SBV situation with respect to public health (EFSA 2012).

2. Laboratory criteria

2.1 Sampling procedure: Blood (serum or EDTA-preserved whole blood) is the preferred tissue for SBV detection in adult animals. Samples should be collected during the acute stage of clinical infection (e.g., fever, reduced milk yield, diarrhea). Brain is the preferred tissue, along with spleen and blood (serum or EDTA-preserved whole blood), for detection of the virus in aborted, stillborn, and malformed fetuses and neonates (FLI 2012).

2.2 Agent isolation and identification: The FLI has developed a real-time reverse transcriptase PCR (rRT-PCR) for Schmallenberg virus detection. All suspect cases of SBV reported in Germany, the Netherlands,

Belgium, France, and the United Kingdom are currently being confirmed using this rRT-PCR test. The FLI has also shared its PCR protocol for use by laboratories in Italy, Denmark, and the United States. Other supplemental confirmatory tests used on a case-by-case basis include indirect immunofluorescence and virus neutralization assays (FLI 2012). In addition, scientists in the Netherlands and Germany have recently developed an antibody-based test (viral neutralization) that is suitable for mass testing for SBV (i.e., measuring past exposure in animals via antibody production to this virus) (AHVLA 2012, EFSA 2012, European Livestock Association 2012b).

3. Clinical signs

3.1 Fetuses and neonates (primarily sheep and goats)

- Congenital malformations in fetuses and newborns are the major clinical signs and are similar to those seen in Akabane virus infection.
- These congenital anomalies are classified as arthrogryposis hydranencephaly syndrome (AHS).
- Signs of AHS include: stillbirth, premature birth, mummified fetuses, arthrogryposis, hydranencephaly, ataxia, paralysis, muscle atrophy, joint malformations, torticollis, kyphosis, scoliosis, behavioral abnormalities and blindness.
- Specific AHS signs reflect the stage of gestation when the virus infected the dam and fetus.

3.2 Adult animals

- Adult sheep and goats are generally asymptomatic except for increased incidence of abortions and congenital malformations in offspring characteristic of AHS.
- Adult cattle are asymptomatic or display few clinical signs: transient fever, decreased appetite, general malaise, reduced milk production, and diarrhea. Animals generally recover within a week.
- Acute clinical signs are thought to coincide with abundance of insect vectors (biting midges—*Culicoides* spp.).

4. Case definition (modified from EFSA 2012)

4.1 Fetuses and neonates

4.1.1 Suspect case: Susceptible species with clinical signs consistent with SBV.

4.1.2 Confirmed case: Confirmation of viral infection in a suspect case by rRT-PCR, virus isolation, or other method of SBV antigen detection.

4.2 Adult animals – past exposure to virus

4.2.1 Suspect case: Ruminants or other susceptible species with pregnancies terminating in abortions, stillbirths, and congenital malformations in offspring characteristic of AHS.

4.2.2 Confirmed case: Confirmation of SBV antibodies by ELISA or other method of detection in herds with confirmed cases of SBV by antigen detection.

4.3 Adult animals – acute infection

4.3.1 Suspect case: Susceptible species (especially cattle) exhibiting clinical signs consistent with SBV infection.

4.3.2 Confirmed case: Confirmation of viral infection in a suspect case by rRT-PCR, virus isolation, or other method of SBV antigen detection.

4.4 Flock/herd case definition: Any flock/herd with one or more animals confirmed with SBV infection per case definitions above.

5. Reporting criteria

5.1 Currently, viruses belonging to the Simbu serogroup of the genus *Orthobunyaviruses* are not classified as notifiable by the World Organization for Animal Health (OIE). However, affected EU member states have notified the OIE of the presence of Schmallenberg virus under required reporting procedures for emerging diseases. The Dutch Ministry of Agriculture has declared SBV a reportable disease in the Netherlands.

5.2 SBV infection is not known to exist in the United States. Suspected cases should be reported to the respective State animal health official or the APHIS Veterinary Services Area Veterinarian-in-Charge.

6. Disease response

6.1 The EFSA, ECDC, and several laboratories and experts of the EU member states are engaged in studies and investigations of Schmallenberg virus (European Commission 2012). Although SBV has been isolated and propagated in the laboratory, a serologic assay was developed for mass testing of exposure to the virus only recently. Scientists in the Netherlands used a new viral neutralization assay to demonstrate a 70 percent prevalence of antibodies against SBV in the country's dairy cattle population (European Livestock Association 2012b). The FLI in Germany is developing a prototype inactivated vaccine for SBV, although it is unknown when such a vaccine will become available.

6.2 Given the evidence that Schmallenberg virus is largely a vector-borne disease, once SBV is established within one or more competent indigenous vectors and host species, it is unlikely to be contained except in very limited situations. At a local scale, housing animals indoors at night during critical periods of pregnancy could reduce exposure to SBV-infected midges, possibly mitigating the incidence and consequences of SBV infection (Veterinary Record 2012). Enforcing risk mitigations that are currently in place for other ruminant viral diseases, and which are imposed on imported animal-derived material, may also help minimize the immediate risk of importing SBV into the United States.

6.3 The United States is considering surveillance activities for Schmallenberg virus, including testing of ruminant livestock and potential insect vectors that could sustain SBV infection in the event of an outbreak. APHIS – VS has provided a guidance document to U.S. veterinary diagnostic laboratories for passive surveillance of ruminants with clinically compatible signs of SBV infection. Surveillance and mitigation recommendations may change as new epidemiological information becomes available.

6.4 When the first U.S. case of SBV is **confirmed** (currently through virus isolation from an aborted/malformed fetus or RT-PCR of samples from clinically ill animals), APHIS – VS would recommend the following actions:

- 6.4.1** An initial hold order placed on the affected herd/flock where the virus was found. This hold order will remain in place during an investigation that will answer the following:
- a. Is this positive viral case related to an import?

- b. Is the disease likely to be containable? (This includes consideration of location, vector season, potential source, etc.)

The hold order may have provisions to allow some animal movement from the affected premises after assessing the continued potential for viremic animals to be present.

6.4.2 After the initial finding, we recommend surveillance in the immediate surrounding area to answer the following:

- a. Is the virus localized to a confined area or geographically dispersed?
- b. Is the disease situation containable?

The passive surveillance would target sick animals (abortions/malformed fetus, etc.) throughout the State where first isolated. Movements will not be restricted from the surrounding area, except with the general understanding that clinically ill animals should not be moved.

6.4.3 Recommendations for serological evidence of Schmallenberg virus **without** confirmation by antigen detection:

- a. Conduct an epidemiologic investigation to determine the likelihood that the virus was or is present in the herd/flock and if it is likely that the virus can be contained to the premises.
- b. The investigation will include:
 - i. History of relevant clinical signs in the flock/herd.
 - ii. History of imported EU semen (If yes, place a hold order)
 - iii. With clinical signs, collect samples for antigen detection and place hold order pending results.
 - iv. A serology representative sampling from herd/flock:
 - 1. If all negative – presume false positive
 - 2. If additional positives – presume exposure and increase monitoring of herd and surrounding areas.

6.4.4 Recommendations after confirmation of Schmallenberg virus over geographically distinct areas over multiple time periods:

Schmallenberg virus is largely a vector borne disease, once SBV is established within one or more competent indigenous vectors and host species, it is unlikely to be contained except in very limited situations. Therefore, if there are several confirmed geographically distinct cases over multiple time periods, disease from the Schmallenberg virus would be treated the same as other non-program endemic diseases. Movement restrictions or extensive surveillance activities are not likely of value after the virus becomes established with a competent indigenous vector.

References

- AHVLA. Schmallenberg virus: a novel viral disease of cattle, sheep and goats in northern mainland Europe. AHVLA-briefing note. 11 January 2012. Animal Health and Veterinary Laboratories Agency, Department for Environment, Food and Rural Affairs (Defra), United Kingdom. Available online: <http://www.defra.gov.uk/animal-diseases/files/schmallenberg-brief-120112.pdf>
- Davies I, Watkins G. Enhanced surveillance for the risk of incursion of Orthobunyavirus infection into Great Britain. 21 Dec 2011. <http://www.highlandcattlesociety.com/downloads/technical/7.pdf>
- European Centre for Disease Prevention and Control (ECDC). Risk assessment: new Orthobunyavirus isolated from infected cattle and small livestock – potential implications for human health. December 2011. Available online: http://ecdc.europa.eu/en/publications/Publications/231112_TER_Risk_assessment_Schmallenberg_virus.pdf
- European Commission. Information note, Schmallenberg virus. 25 January 2012. Available online: http://ec.europa.eu/food/animal/diseases/schmallenberg_virus/docs/information_1818_note_240112_en.pdf
- European Food Safety Authority (EFSA). "Schmallenberg" virus: likely epidemiological scenarios and data needs. Supporting Publications 2012:EN-241. [31 pp.]. Available online: <http://www.efsa.europa.eu/en/supporting/doc/241e.pdf>
- European Livestock Association. Belgium: Pools of Culicoides spp. found positive for Schmallenberg virus by RT-qPCR. 2012a; accessed 14 March 2012. Available online: <http://ela-europe.org/ELA%20teksten/Schmallenberg%20virus/Pools%20of%20Culicoides%20found%20positive%20for%20Schmallenberg%20virus%20by%20RT-qPCR.pdf>
- European Livestock Association. Antibodies against Schmallenberg virus [SBV] in 70 per cent of the dairy cattle population in the Netherlands. 2012b; accessed 14 March 2012. Available online: <http://ela-europe.org/ELA%20teksten/Schmallenberg%20virus/antibodies%20against%20SBV.pdf>
- FluTrackers.com. Schmallenberg virus in Europe 2012. Updated 9 March 2012. Available online at: <http://www.flutrackers.com/forum/showthread.php?t=183181>
- Friedrich Loeffler Institut (FLI). Responses to questions on "Schmallenberg virus". Updated 30 January 2012. Available online: http://www.fli.bund.de/fileadmin/dam_uploads/tierseuchen/Schmallenberg_Virus/FAQ_Schmallenberg-Virus_120130-en.pdf
- Gibbens N. Schmallenberg virus: a novel viral disease in northern Europe. Vet Rec 14 January 2012; 170 (4): 58. doi: 10.1136/vr.e292.
- Hoffmann B, Scheuch M, Höper D, Jungblut R, Holsteg M, Schirrmeier H, et al. Novel Orthobunyavirus in cattle, Europe, 2011. Emerg Infect Dis [serial on the Internet] 2012 Mar [date cited]. Available online: <http://dx.doi.org/10.3201/eid1803.111905> DOI: 10.3201/eid1803.111905
- Iowa State University: The Center for Food Security & Public Health (CFSPH): *Akabane Disease*. 2009. Available online: <http://www.cfsph.iastate.edu/Factsheets/pdfs/akabane.pdf>

Kupferschmidt K. New animal virus takes northern Europe by surprise. Science NOW. 13 January 2012. Available online: <http://news.sciencemag.org/sciencenow/2012/01/new-animal-virus-takes-northern-.html>

RIVM. Nota: Risk profile human Schmallenberg virus. 21 December 2011. Rijksinstituut voor Volksgezondheid en Milieu, Ministerie van Volksgezondheid, Welzijn en Sport. 8 pp. Available online: <http://www.rivm.nl/dsresource?objectid=rivmp:60483&type=org&disposition=inline>

Veterinary Record. Scenarios for the future spread of Schmallenberg virus. Vet Rec 10 March 2012; 170: 245-246. doi: 10.1136/vr.e1598.

World Organisation for Animal Health. OIE Technical Factsheet – Schmallenberg Virus. 27 February 2012. 4 pp. Available online: http://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/A_Schmallenberg_virus.pdf