SCHMALLENBERG VIRUS

Schmallenberg virus was first identified in November 2011. The information presented in this technical factsheet reflects the epidemiological observations and research done to date (April 2017), together with data extrapolated from genetically similar viruses of the same genus and serogroup.

AETIOLOGY

Classification of the causative agent

The "Schmallenberg virus" (SBV) is an enveloped, negative-sense, segmented, single-stranded RNA virus. It belongs to the *Bunyaviridae* family, within the *Orthobunyavirus* genus. The Schmallenberg virus is a member of the Simbu serogroup viruses, which includes Shamonda, Akabane, and Aino viruses. Within the Simbu serogroup, the viruses that are most closely related to SBV are Sathuperi and Douglas virus.

Field and laboratory studies indicate a causal relationship between SBV infection and reported clinical signs.

Resistance to physical and chemical action

Data for SBV or extrapolation from the California serogroup of Orthobunyaviruses:

Temperature:	Infectivity lost (or significantly reduced) at 50–60°C 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.

EPIDEMIOLOGY

According to the epidemiological investigations, reinforced by what is already known about the genetically related Simbu serogroup viruses, SBV infects ruminants and is not zoonotic. Transmission among animals is by insect vectors. The virus can also be transmitted vertically by *in utero infection.*

Hosts

- Confirmed by PCR or virus isolation:
  - Cattle, sheep, goats
  - Bison
  - Roe deer
  - Mouflon
  - Dog (a single case of a PCR-positive dog)
- Confirmed by serology only:
  - Red deer
  - Sika deer
  - Fallow deer
  - Alpacas
  - Wild boar
  - Various further wild ruminants and some zoo animals

Transmission

- Epidemiological investigations indicate insect vector transmission.
- Insect vectors include several *Culicoides* species where SBV RNA has been detected.
- Vertical transmission across the placenta has been proven.
- SBV has been found in bovine semen. However, transmission by natural breeding or artificial insemination has not yet been demonstrated.
- Direct transmission from animal to animal has not been reported, and is very unlikely.

Viraemia and incubation period

Experimental infection in cattle and sheep showed no or only mild clinical signs with an incubation period of between 1 and 5 days and a viraemia also lasting for 1 to 5 days.

Sources of virus in the animal host

Material found to be positive by virus isolation

- Blood from affected adults and brain from infected foetuses. Placental tissues collected at birth.

Material found PCR positive

- Blood and serum of acutely infected animals
- SBV RNA can be detected up to several weeks after infection in different tissues such as lymphatic organs, especially in mesenteric lymph nodes and spleen Organs and blood of infected foetuses, and further samples such as placenta, amniotic fluid, and meconium.

Occurrence

Some Orthobunyaviruses had previously been reported in Europe, but viruses from the Simbu serogroup had never been isolated in Europe prior to 2011.

Schmallenberg virus was first detected in November 2011, in Germany from samples collected in summer/autumn 2011 from diseased dairy cattle exhibiting fever and reduced milk yield. Similar clinical signs (including diarrhoea) were detected in dairy cows in the Netherlands where the presence of SBV was also confirmed in December 2011.

Congenital malformations were reported in 2012 in newborn lambs in the Netherlands, and SBV was detected in, and isolated from, the brain tissue. Further spread of SBV to many other countries in continental Europe, the British Isles, the Mediterranean Basin, and Turkey was reported, indicating that Schmallenberg virus was circulating widely across this region in 2012. In the following years, it was detected in new and previously affected countries.

For information on the initial occurrence of this infection, see the *OIE World Animal Health Information Database* (WAHID) interface [http://www.oie.int/wahis/public.php?page=home].

DIAGNOSIS

Clinical Diagnosis

Manifestation of clinical signs varies by species and age. Adult cattle typically exhibit only a mild form of acute disease. Congenital malformations are observed in cattle and other ruminant species e.g sheep, goats and bison. Diarrhoea has been observed in some cattle and sheep.

- Adults
    - Usually inapparent, but non-specific signs including the following:
    - Fever (>40°C)
    - Transitory reduced milk yield
    - Diarrhoea
    - Individuals recover within a few days
    - Abortion

- Malformed newborn animals and stillbirths
    - Arthrogryposis/ Hydranencephaly
    - Brachygnathia inferior
    - Ankylosis
    - Torticollis
    - Scoliosis

The incidence of malformation varies depending on the stage of gestation at the time of infection and the species. In some pregnancy-synchronised sheep flocks, high incidence has been reported. For cattle, the incidence is very low.

Pathological Lesions

In malformed newborn:

- Hydranencephaly
- Hypoplasia of the central nervous system
- Porencephaly
- Subcutaneous oedema (calves)
- Arthrogryposis

The pathology can be summarised as arthrogryposis-hydranencephaly syndrome.

Differential diagnosis

For the acute infection of adults:

The clinical signs are not specific. All possible causes of high fever, diarrhoea, milk reduction and abortion should be taken into account.

For the malformation of calves, lambs and kids:

- Other Orthobunyaviruses
- Bluetongue or Epizootic Haemorrhagic Disease Virus
- Pestiviruses
- Genetic factors
- Toxic substances

Laboratory diagnosis

Samples

Samples should be transported cooled

From live animals for the detection of acute infection:

- EDTA blood
- Serum
  - At least 2 ml, transported cooled

From stillborn or malformed newborn calves, lambs and kids:

- Virus detection:
  - Tissue samples of brain (cerebrum and brainstem)
  - Amniotic fluid
  - From live newborn:
    - Amniotic fluid and placenta
    - Meconium
- Antibody detection:
  - Pericardial fluid
  - Blood (pre-colostral)
- Histopathology:
  - Fixed central nervous system, including spinal cord

Procedures

Identification of the agent

- Real-time RT-PCR (Bilk et al., 2012, Fischer et al. 2013); commercial PCR kits are available
- Cell culture isolation of the virus: insect cells (KC), hamster cells (BHK), monkey kidney cells (VERO)

Serological tests on serum samples

- ELISA: commercial kits available
- Indirect Immunofluorescence
- Neutralisation test

For further information, reference material and advice, refer to Dr. Martin Beer (Martin.Beer@fli.bund.de), Institute of Diagnostic Virology, Friedrich-Loeffler-Institut, Federal Research Institute for Animal Health, Greifswald-Insel Riems, Germany.

Interpretation of the tests:

Serological results (ELISA) for index cases should be confirmed by neutralisation tests.

PCR-positive results for index cases should be confirmed by sequencing.

PREVENTION AND CONTROL

There is currently no specific treatment for Schmallenberg virus.

Inactivated vaccines are commercially available in some countries.

Sanitary prophylaxis

Control of potential *Culicoides* vectors during the vector-active season may decrease the transmission of virus. Reschedule of sheep breeding outside the vector season may decrease the number of foetal malformations.

REFERENCES AND OTHER INFORMATION

- Bouwstra RJ, Kooi EA, de Kluijver EP, Verstraten ER, Bongers JH, van Maanen C, Wellenberg GJ. van der Spek AN, van der Poel WH, 2013. Schmallenberg virus outbreak in the Netherlands: routine diagnostics and test results. *Vet Microbiol.*, Jul 26;**16**5(1-2):102-8. doi: 10.1016/j.vetmic.2013.03.004.
- Beer M, Conraths FJ and Van der Poel WHM, 2013. 'Schmallenberg virus' - a novel orthobunyavirus emerging in Europe. *Epidemiology and Infection*, **141**, 1-8. Available from <Go to ISI>://WOS:000312037600001.
- Bilk S, Schulze C, Fischer M, Beer M, Hlinak A, Hoffmann B. 2012. Organ distribution of Schmallenberg virus RNA in malformed newborns. Vet Microbiol. 2012 Mar 30. [Epub ahead of print]
- Breard E, Lara E, Comtet L, Viarouge C, Doceul V, Desprat A, Vitour D, Pozzi N, Cay AB, De Regge N, Pourquier P, Schirrmeier H, Hoffmann B, Beer M, Sailleau C, Zientara S, 2013. Validation of a Commercially Available Indirect Elisa Using a Nucleocapside Recombinant Protein for Detection of Schmallenberg Virus Antibodies. Plos One, 8, e53446, doi: 10.1371/journal.pone.0053446
- Conraths FJ, Kämer D, Teske K, Hoffmann B, Mettenleiter TC, Beer M, 2013. Reemerging Schmallenbergs Virus Infections, Germany, 2012. *Emerg Infect Dis* **19**, 513-514.
- Delooz, L., C. Saegerman, C. Quinet, T. Petitjean, N. De Regge and B. Cay (2016). "Resurgence of Schmallenberg Virus in Belgium after 3 Years of Epidemiological Silence." *Transbound Emerg Dis*., doi: 10.1111/tbed.12552
- De Regge N, Deblauwe I, De Deken R, Vantieghem P, Madder M, Geysen D, Smeets F, Losson B, van den Berg T, Cay AB Detection of Schmallenberg virus in different Culicoides spp. by real-time RT-PCR. *Transbound. Emerg. Dis.*, 2012 Dec; **59**(6):471-5. doi: 10.1111/tbed.12000. Epub 2012 Oct 1
- De Regge N, van den Berg T, Georges L, Cay B. Diagnosis of Schmallenberg virus infection in malformed lambs and calves and first indications for virus clearance in the fetus. *Vet. Microbiol*., 2013 Mar 23; **162**(2-4):595-600. doi: 10.1016/j.vetmic.2012.11.029. Epub 2012 Nov 29
- Fischer M, Schirrmeier H, Wernike K, Wegelt A, Beer M, Hoffmann B. 2013. Development of a pan-Simbu real-time reverse transcriptase PCR for the detection of Simbu serogroup viruses and comparison with SBV diagnostic PCR systems. *Virol J.*, doi : 10.1186/1743-422X-10-327
- Friedrich-Loeffler-Institut – Update of Information on 'Schmallenberg virus': http://www.fli.bund.de/de/startseite/aktuelles/tierseuchengeschehen/schmallenberg-virus.html
- Friedrich-Loeffler-Institut – New Orthobunyavirus detected in cattle in Germany: http://www.fli.bund.de/fileadmin/dam_uploads/press/Schmallenberg-Virus_20111129-en.pdf
- Friedrich-Loeffler-Institut – Schmallenberg virus factsheet: http://www.fli.bund.de/fileadmin/dam_uploads/tierseuchen/Schmallenberg_Virus/Schmallenberg-Virus-Factsheet-20120119-en.pdf
- Gache K, Touratier A, Bournez L, Zientara S, Bronner A, Dion F, Garin E, Calavas D. Detection of Schmallenberg virus in France since 2012. *Vet. Rec*., 2017 Jan 7; 180(1):24. doi: 10.1136/vr.j38.
- Goller KV, Hoeper D, Schirrmeier H, Mettenleiter TC and Beer M, 2012. Schmallenberg virus as possible ancestor of Shamonda virus. *Emerging Infectious Diseases*, **18**, 1644-1646. Available from <Go to ISI>://MEDLINE:23017842.
- Hahn K, Habierski A, Herder V, Wohlsein P, Peters M, Hansmann F, Baumgartner W, 2012, Schmallenberg virus in central nervous system of ruminants, *Emerging infectious diseases*, **19**, 154-155, doi: 10.3201/eid1901.120764
- Hoffmann B, Schulz C and Beer M, First detection of Schmallenberg virus RNA in bovine semen, Germany, 2012. *Veterinary Microbiology*. Available from http://www.sciencedirect.com/science/article/pii/S0378113513004392.

- Laloy E, Braud C, Bréard E, Kaandorp J, Bourgeois A, Kohl M, Meyer G, Sailleau C, Viarouge C, Zientara S, Chai N. Schmallenberg Virus in Zoo Ruminants, France and the Netherlands. *Emerg. Infect. Dis*., 2016 Dec; **22**(12): 2201-2203. doi: 10.3201/eid2212.150983.
- Martinelle L, Poskin A, Dal Pozzo F, De Regge N, Cay B, Saegerman C. Experimental Infection of Sheep at 45 and 60 Days of Gestation with Schmallenberg Virus Readily Led to Placental Colonization without Causing Congenital Malformations. PLoS One. 2015 Sep 29; 10(9):e0139375. doi: 10.1371/journal.pone.0139375. eCollection 2015
- National institute of public health and the environment – Risk Profile Humaan Schmallenbergvirus: http://www.rivm.nl/dsresource?objectid=rivmp:60483&type=org&disposition=inline
- European Centre for Disease Prevention and Control, Risk assessment: New Orthobunyavirus isolated from infected cattle and small livestock – potential implications for human health: http://ecdc.europa.eu/en/publications/Publications/Forms/ECDC_DispForm.aspx?ID=795
- The Center for Food Security and Public Health, Iowa State University - Akabane Disease. September 2009 – Akabane disease card. Available at: http://www.cfsph.iastate.edu/Factsheets/pdfs/akabane.pdf
- Public Health Agency of Canada - California serogroup - Material Safety Data Sheets http://www.phac-aspc.gc.ca/lab-bio/res/psds-ftss/msds27e-eng.php
- Peaton virus: a new Simbu group arbovirus isolated from cattle and *Culicoides brevitarsis* in Australia - St George T.D., Standfast H.A., Cybinski D.H., Filippich C., Carley J.G., *Aust. J. Biol. Sci.,* 1980, **33** (2), 235–43. http://www.publish.csiro.au/?act=view_file&file_id=BI9800235.pdf
- Poskin A, Van Campe W, Mostin L, Cay B, De Regge N. Experimental Schmallenberg virus infection of pigs. *Vet. Microbiol*., 2014 Jun 4; 170(3-4):398-402. doi: 10.1016/j.vetmic.2014.02.026. Epub 2014 Mar 3
- Hoffmann B, Scheuch M, Höper D, Jungblut R, Holsteg M, Schirrmeier H, et al. Novel orthobunyavirus in cattle, Europe, 2011. *Emerg. Infect. Dis.*, 2012 Mar [08/02/2012]. http://dx.doi.org/10.3201/eid1803.111905
- ProMed Mail from Published Date: 2013-01-23 19:25:46: Subject: PRO/AH/EDR> Schmallenberg virus - Europe (07): (Germany) virus RNA bov semen ; Archive Number: 20130123.1511878
- Sailleau C, Boogaerts C, Meyrueix A, Laloy E, Bréard E, Viarouge C, et al. Schmallenberg virus infection in dogs, France, 2012 [letter]. Emerg Infect Dis [Internet]. 2013 Nov [*11/10/2013*]. http://dx.doi.org/10.3201/eid1911.130464
- Veronesi E, Henstock M, Gubbins S, Batten C, Manley R, Barber J, Hoffmann B, Beer M, Attoui H, Mertens PP, Carpenter S, 2013. Implicating culicoides biting midges as vectors of schmallenberg virus using semi-quantitative rt-PCR, PLoS One, 8(3):e57747. doi: 10.1371/journal.pone.0057747
- Wernike K, Beer M, 2016. Stability of Schmallenberg virus during long-term storage. doi: 10.2376/0005-9366-129-144
- Wernike K, Eschbaumer M, Schirrmeier H, Blohm U., Breithaupt A, Hoffmann B, Beer M, 2013. Oral exposure, reinfection and cellular immunity to Schmallenberg virus in cattle, *Veterinary Microbiology*, accepted 30 January 2013
- Wernike, K., B. Hoffmann, F. J. Conraths and M. Beer (2015). "Schmallenberg Virus Recurrence, Germany, 2014." *Emerg. Infect. Dis.*, **21**(7): 1202-1204.
- Wernike K, Kohn M, Conraths FJ, Werner D, Kameke D, Hechinger S, Kampen H, Beer M, 2013. Transmission of Schmallenberg Virus during Winter, Germany, *Emerg. Infect. Dis*., Oct; 19(10):1701-3. doi: 10.3201/eid1910.130622.
- Wernike K, Nikolin VM, Hechinger S, Hoffmann B, Beer M, 2013. Inactivated Schmallenberg virus prototype vaccines, Vaccine, Aug 2; 31(35):3558-63. doi: 10.1016/j.vaccine.2013.05.062
- Wernike K, Hoffmann B, Bréard E, Bøtner A, Ponsart C, Zientara S, Lohse L, Pozzi N, Viarouge C, Sarradin P, Leroux-Barc C, Riou M, Laloy E, Breithaupt A and Beer M, 2013. Schmallenberg virus experimental infection of sheep. *Veterinary Microbiology*, 166, 461-466. Available from http://www.sciencedirect.com/science/article/pii/S0378113513003453.

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The OIE will update this Technical Factsheet when relevant