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Biological Characteristics of Schmallenberg Virus - an Overview

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Abstract

Schmallenberg virus disease was originally reported in Germany in 2011. The new disease was diagnosed in the UK in January 2012. Currently, little information has been collected about the pathogen of the Schmallenberg virus. The virus genetically belongs to the Bunyaviridae family (Orthobunyavirus genus and Simbu serogroup). The clinical symptoms of acute SBV infection are unspecific in sheep and goats. This study characterized the origin, emergence, transmission, spread in Europe and Azerbaijan, clinical signs, and the diagnosis of this virus. Currently, the Shmallenberg disease is known to be a serious threat to Veterinary Public Health.

Keywords: Schmallenberg virus, trans missive infections, spread, Azerbaijan

Introduction

Structure of the virus

Schmallenberg Virus (SBV) is an infectious disease of ruminants. The virus belongs to *the Orthobunyavirus* genus of the *Bunyaviridae* family, the Simbu serogroup. Besides the *Orthobunyavirus* genus, the *Bunyaviridae* family has more than 350 viruses divided into five genera based on serological, morphological, and biochemical characteristics: Nairovirus, Phlebovirus, Hantavirus, and Tospovirus with additional unclassified viruses (Charles, 1994; ICTVI, 2006). Although viruses in the Bunyaviridae family share a tripartite RNA genome in common, they significantly differ in their geographic distribution, disease characteristics, and transmission mode (Bishop & Beaty, 1988; Charles, 1994; Horne & Dana, 2014). Viruses within the Orthobunyavirus, Nairovirus, and Phlebovirus genera are transmitted by hematophagous arthropods, whereas hantaviruses are transmitted among rodents, and tospoviruses are transmitted between plants by non-hematophagous thrips (Horne & Dana, 2014; ICTVI, 2006).

A little information has been collected on the pathogen of the Schmallenberg virus, at the moment. These are a single-stranded, negative-sense, tripartite RNA genomes with viral genes on one of three segments: the negative sense large (L) segment, coding for the RNA-dependent RNA polymerase for transcription and replication; the negative sense or ambisense (tospovirus) medium (M) segment, which encodes the Gn and Gc viral glycoproteins and a non-structural protein (NSm). Surface proteins are involved in attachment, cell fusion, and hemagglutination; therefore, they contain important determinants of virulence. Neutralizing antibodies are directed against the epitopes of the surface glycoproteins G1 and G2, while antibodies to the glycoprotein G2 have protective properties (Fischer *et al.,* 2013; Coupeau *et al.,* 2013). The composition of virionic lipids corresponds to the composition of the cell membranes, which is used for culturing the virus (Hofmann et al., 2012; Martinelle *et al.,* 2017).

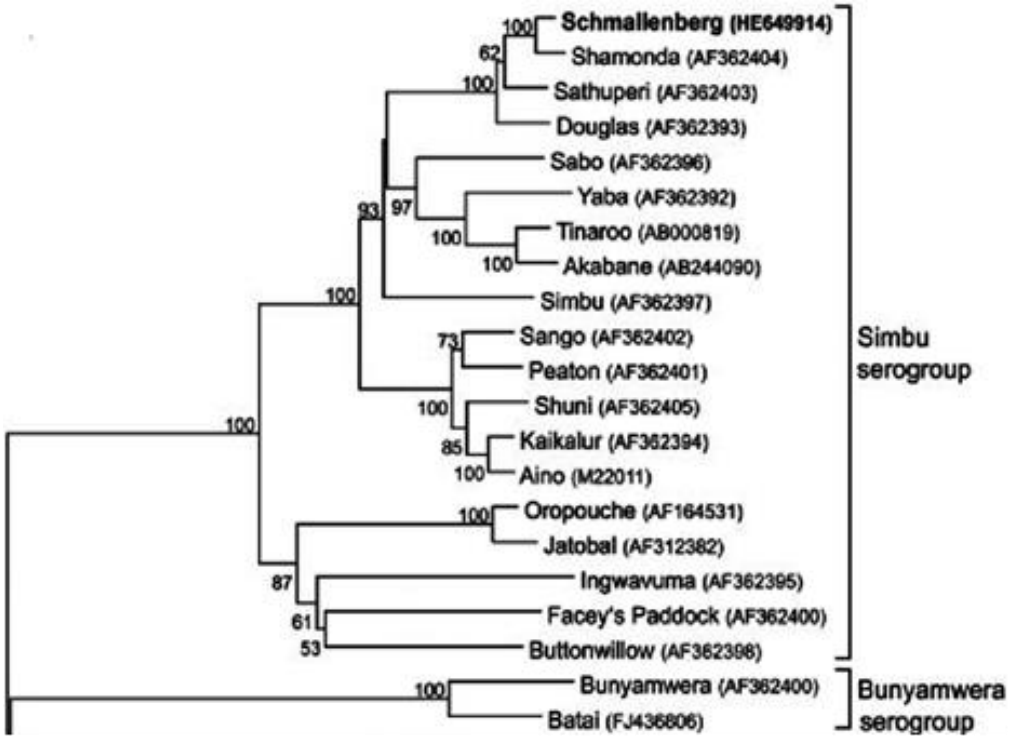


Figure1. Phylogenetic relationship between the Schmallenberg virus and orthobunyaviruses of the Simbu, Bunyamwera, and California serogroups, adapted from Hoffmann et al. (2012).

The most famous representatives of this group are the Crimean-Congolese hemorrhagic fever virus, the Nairobi disease virus, the Akabane disease virus, Rift Valley fever virus (Saeed *et al.,* 2001; Goller *et al.,* 2012; Kirkland, 2015**)**. A part of the viruses of this family is susceptible to humans, and a fatal outcome is possible. Bunyaviruses are thermosensitive, i.e. they are quickly inactivated at a temperature of 56 ° C, die when irradiated with ultraviolet rays, sensitive to fat solvents and detergents, acids (Yanase *et al.,* 2012; Elliott, 2009; Sanders *et al.,* 2011).

Spread of Shmallenberg virus

This group of bunyaviruses is more often allocated to the African continent where they were found, and also in the countries of Asia and Australia. However, some of them have been circulating in Europe for several decades (Elliott, 2009; Elbers *et al.,* 2011; Stokes *et al.,* 2015). The first reports of unidentified disease of dairy cattle were obtained from farms located in the Netherlands and Germany (in the city of Schmallenberg were discovered three dairy cows with unexplored symptoms) in August 2011 (Tarlinton *et al.,* 2012; De Regge *et al.,* 2013; Wernike *et al.,* 2014; Berhanu *et al.,* 2018). This new virus named after a German city where infects ruminant artiodactyls (cattle, sheep, goats) has been detected in 7 EU countries: Germany, the Netherlands, Great Britain, France, Luxembourg, Italy, and Belgium (Hofmann *et al.,* 2012; SVE, 2014; Gubbins *et al.,* 2014; Brülisauer *et al.,* 2017). There is a tendency towards the territorial and quantitative spread of infection, both in the number of dysfunctional sites and in the number of infected animals in these countries (ProMED, 2012; Tarlinton *et al.,* 2012; Briese *et al.,* 2013; Bilk *et al.,* 2012).

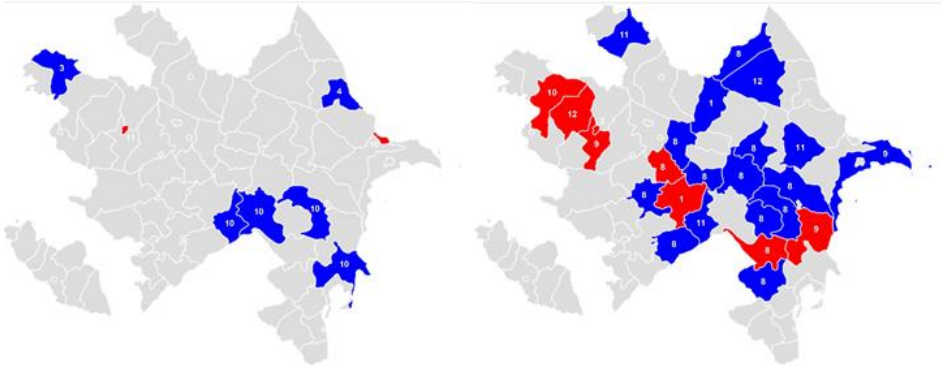
According to the source, TSN FEDERAL state reporting system, as of March 14, 2012, 944 confirmed cases of Schmallenberg virus were detected in livestock enterprises in Germany in federal lands, of which 124 cases were detected in livestock enterprises where cattle are kept, 780 cases in sheep farms and 40 - goat-breeding enterprises (according to publications of the Friedrich Lefler German Institute) (Lievaart-Peterson *et al.,* 2012; Conraths *et al.,* 2013).

The high SBV within-flock seroprevalence (up to 98.03%) in geographic areas having reported SBV outbreaks in late 2011 and 2012 was expected to limit the reemergence of the virus in 2012 (Wernike *et al.,* 2014; EFSA, 2014)

Figure 2. Geographical spread of SBV in Europe

The occurrence of Shmallenberg diseases in Azerbaijan

In 2012, there was an unexpected increase of abortions in cattle and sheep in Azerbaijan, which was unrelated to infections with Brucella or Chlamydia. Due to the similarities of the overall symptomology observed, the then just recently described Schmallenberg virus was suspected as a potential cause. This surveillance study was hence launched to determine if the Schmallenberg virus had made it to Azerbaijan and to monitor the situation (Gubbins *et al.*, 2014; Zeynalova & Vatani, 2019).



2012/13 October – June 2013/14 July – June

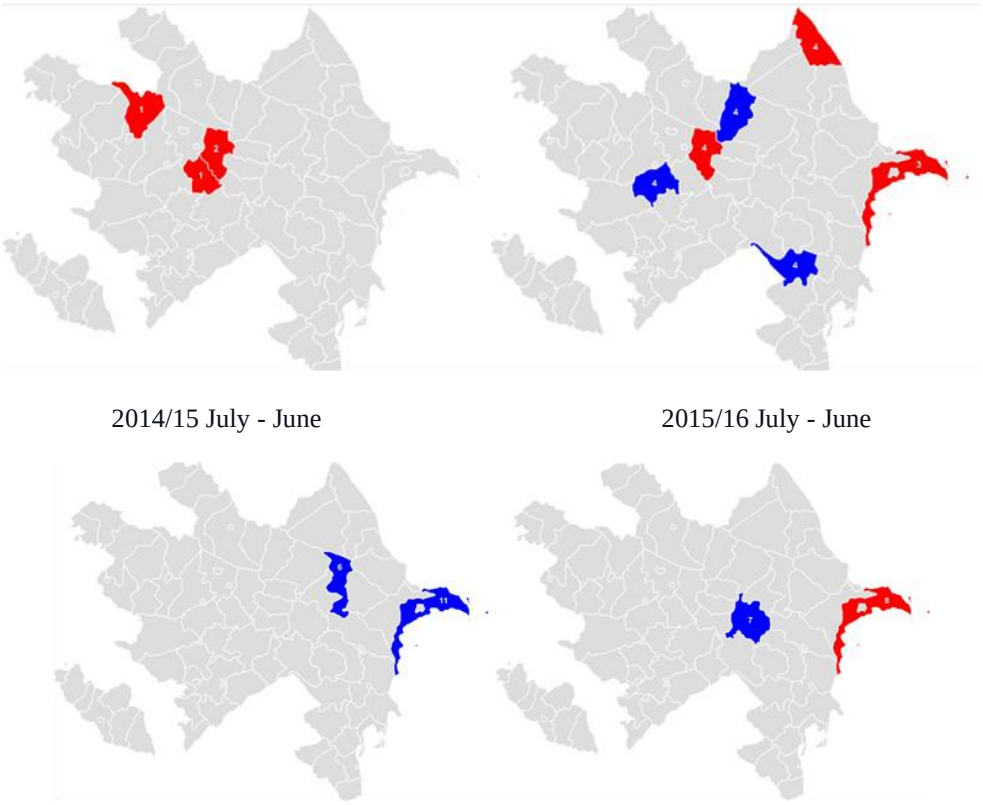


Figure 3. Spread of Shmallenberg disease in Azerbaijan (Zeynalova *et al.*, 2019).

The first wave of Schmallenberg virus infections was detected in 2012/2013 and limited mainly to the southern part of the country. In the second and bigger wave in 2013/2014, cases were found throughout most of the country (Zeynalova *et al.*, 2019).

Susceptible animals, transmission routes

It is proved that the transmission of *Bunyavirus* viruses is carried out by vectors. Most of these vectors live in Asia or Africa, which include biting midges or mosquitoes. After the appearance of the SBV virus in 2011, biting midges of the species *Culicoides Obsoletus* coming from the genus Ceratopogonid Culicoides were identified as SBV vectors. Studies have shown that the viral genome was present in different species of Culicoides (Culicoides dewulfi, Culicoides chiopterus, Culicoides punctatus, etc.) (Labuda, 1991; Rasmussen *et al.*, 2012).

The virus was isolated in the salivary glands of woodlice in Belgium. In laboratory conditions, virus RNAs were detected in biting midges *Culicoides Obseletus* collected in Denmark in 2011 (Davies & Daly, 2013; De Regge *et al.*, 2014; SVE, 2014). The absence of β-actin mRNA in ruminants and high titers of the virus in these samples indicate the replication of the virus in the insect organism, that is, Culicoides punctatus biting midges are biological carriers of the Schmallenberg disease virus (Figure 4) (Burgin *et al.*, 2013; EMS, 2014; Collins *et al.*, 2017).

Biting midges of the genus Culicoides are involved in the transmission of several viruses of the Simbu serogroup. They were recognized as the main carriers of Bluetongue virus in northern and central Europe during the outbreak in 2006 (White *et al.*, 2017; Nick, 2017; Rossel, 2018). Some members of the Simbu serogroup are zoonoses (Oropouche virus). Since the Schmallenberg virus has appeared recently, the transmission of the disease to humans has not yet been studied. There is no evidence of human morbidity, although studies conducted at the Dutch National Institute for Health and the Environment do not exclude the possibility of human infection with the Schmallenberg virus. At present, there are two ways of infection of animals: First is horizontal - with bites of blood-sucking insects of midges and mosquitoes. Second is vertically - from the mother to the fetus during fetal development (transplacental), accordingly in pregnant animals, infection leads to the birth of fetuses with congenital deformities (De Regge *et al.*, 2013; Luttikholt *et al.*, 2014; Afonso *et al.*, 2014; ProMED, 2014). The third route of infection should not be ruled out - iatrogenic, by veterinary specialists during veterinary prophylactic (vaccinations, chemotherapeutic treatments, subcutaneous, intramuscular injections, etc.) and diagnostic measures (taking blood, scrapings). However, no signs of horizontal transmission (from animal to animal) were found. Many questions remain regarding the pathogenesis of SBV infection in pregnant animals, their transmission by the embryo and / or gametes, and the dynamics of the virus to and within the fetus (Lehmann *et al.*, 2012; Hoffmann *et al.*, 2012; Briese *et al.*, 2013; Poskin *et al.*, 2014).

Figure 4. *Culicoides punctatus*

Clinical signs

Symptoms of the disease in cattle: in adult animals, fatigue, loss of appetite, fever, diarrhea, premature birth are first observed, part of the livestock die, milk yield decreases sharply, abortions occur in the last half of pregnancy and cases of stillbirths (Lievaart-Peterson *et al.,* 2012; Davies & Daly, 2013; Kauffold *et al.,* 2017). In sheep and goats, SBV infection remains subclinical. The nonspecific febrile syndrome was recorded in the summer and fall of 2011 in adult dairy cows in the Netherlands and Germany (Garigliany *et al.,* 2012; EFSA, 2014; White *et al.,* 2017). The disease is more severe in sheep and goats: there is a higher percentage of death, depletion of animals, damage to the reproductive organs in the maternal population. Sacral cleft of the spine was observed in two SBV-positive stillborn lambs in 2013 (De Regge *et al.,* 2013; Brülisauer *et al.,* 2017). In newborn animals, blindness, dropsy of the chest and abdominal cavities, paralysis, swelling in the subcutaneous tissue, and pathology of the lower jaw are noted. Such offspring, as a rule, die immediately after birth, the percentage of deaths varies from 20 to 50% in herds infected with the virus. An autopsy revealed common malformations of the central nervous system (CNS), including hydranencephaly, porencephaly, lissencephaly, hydrocephalus, cerebellar and cerebral hypoplasia, and micromyelia (Tsuda *et al.,* 2004; Hofmann *et al.,* 2012; Van den Brom *et al.,* 2012; Bilk *et al.,* 2012).

Figure 5. Clinical signs of Shmallenberg disease in the aborted fetuses

Laboratory diagnosis and prophylaxis of disease

Laboratory diagnostics

Diagnostics is carried out employing the PCR test (test - a system for determining the nucleic acid fragments of pathogens by polymerase chain reaction (PCR) in biological material). The test is extremely effective in identifying difficulties to cultivate cultures, pathogens that are not cultivated, latent forms of microorganisms in chronic and latent forms of infection. The use of PCR diagnostics is a highly effective method for determining intracellular parasites and viruses with high antigenic variability. The method can identify a pathogen fragment in the material from the animal, environmental objects (soil, water, etc.) (Lehmann *et al.,* 2012; Veronesi *et al.,* 2013). A significant drawback of this reaction is its high cost; the test takes a lot of time; it is carried out only in laboratory conditions with the appropriate equipment. DEFRA (UK Department of the Environment, Food, and Agriculture), as well as several institutes in Europe, are looking for a simple, easy-to-use, inexpensive test to determine the virus or its fragments. The virus itself was found in the intestinal contents of animals, the brain of sick and dead animals, blood samples, samples of intraperitoneal fluid, and blood-sucking insects (Rasmussen *et al.,* 2012; McGrath & More, 2018).

The first indirect enzyme-linked immunosorbent assay (ELISA) to detect Shmallenberg-specific antibodies in serum or milk samples became commercially available shortly after the emergence of SBV (Elbers *et al.,* 2012; Burgin *et al.,* 2013; Berhanu *et al.,* 2018). The most known kits are: the indirect ELISA kit for the detection of anti-Schmallenberg virus (SBV) antibodies in ruminant serum and plasma from multiple species, including cattle, sheep, and goats; competitive ELISA for the detection of antibodies directed against the Schmallenberg virus nucleoprotein in serum or plasma from multiple species (Humphries & Burr, 2012; Van der Poel *et al.,* 2014; Bréard *et al.,* 2013; Poskin *et al.,* 2015; Collins *et al.,* 2017).

Based on the available official data, the European Union does not consider vaccination mandatory during the spread of the disease. Currently, there is no information on the transmission of the virus with meat and milk and the vaccination against the virus is not required, however the ruminants that give birth to non-viable calves are considered as immunized. In the case of disease, the troupe of stillborn animals and afterbirth should be disposed of in accordance with local (national) regulations (EFSA, 2014; Zeynalova *et al.,* 2019).

So, despite some information, the Schmallenberg disease virus has not been sufficiently studied. It is still not clear how the virus occurs in Europe. The

evidence presented indicates that a lot of laboratory research and genetic tests are needed.

Abbreviations

SBV – Shmallenberg Virus
TSN- Animal Disease Reporting System
RNA- Ribonucleic acid
ELISA- Enzyme-linked Immunosorbent Assay
PCR- Polymerase chain reaction
DEFRA- Department for Environment, Food and Rural Affairs

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