Chapter 10
Schmallenberg Virus

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Abstract Schmallenberg virus (SBV) infection is an emerging infectious disease of ruminants first discovered in summer 2011 applying metagenomic tools in North-Western Europe and which caused an epidemic proportion and later in the other European countries. It is an enveloped, negative-sense, segmented, single-stranded RNA virus, of the Simbu serogroup, *Orthobunyavirus* genus and the *Bunyaviridae* family, and is arthropod-borne. SBV affects mostly wild and domestic ruminants but has got no zoonotic potential and is horizontally spread by various species of *Culicoides* biting midges. Transplacental transmission can occur during the early part of pregnancy in ruminants after placentomes have been formed and cause teratogenic effects. Schmallenberg virus has also been found to be shed in the semen of cattle and sheep. SBV infection is usually asymptomatic in adult cattle, sheep and goats. The disease is characterised by fever, reduced milk production and diarrhoea in cattle and abortions, stillbirths and foetal abnormalities in sheep and goats when infection of the dam occurs at a critical period of gestation. In response, various molecular and serological tests and inactivated vaccines have been developed rapidly to diagnose and monitor the disease. Schmallenberg virus infections can have an all-round effect on production and considerable economic impact. This chapter details the updated knowledge on the discovery, epidemiology, impact, clinical symptoms, molecular characteristics and diagnostic techniques and the possibilities for preventing infections.

Keywords Schmallenberg virus · Ruminants · Emerging infection · Vector · Risk · Congenital malformations · Abortion · Impact · Diagnosis · Prevention and control

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10.1 Preamble

Schmallenberg virus infection is an emerging threat, first noticed in dairy cattle in the border region of Dutch and Germany where in summer and autumn 2011 a unique syndrome characterised by high body temperature, diarrhoea and fall in milk yield was detected. Investigation for common causes was tested negative, and the aetiology of the syndrome was subsequently identified using metagenomic tools and isolated by cell culture technique. The name Schmallenberg virus is given to this agent as it was first isolated from tissue samples from Schmallenberg in Germany (Hoffmann et al. 2012). Since then, this virus has transmitted to various countries in Europe. SBV is a novel vector-borne orthobunyavirus of Simbu serogroup, member of *Bunyaviridae* family, and transmitted through Culicoides biting midges and also crosses the placenta and causes teratogenic effects with extremely negligible risk for public health. Currently, viruses belonging to the Simbu serogroup reported from Asia, Africa and Australia and the World Organisation for Animal Health (OIE) have not been classified as notifiable. The virus mainly affects domestic ruminants and causes congenital malformations, stillbirth in lambs and goat kids as well as in calves, and abortion (Hoffmann et al. 2012; Bayrou et al. 2014; Peperkamp et al. 2015). The epizootic spread was affirmed in wild ruminants (EFSA 2014). In northern Europe, a significant economic loss was documented due to large-scale SBV outbreak. Consequently, restrictions were imposed on the trade of livestock and its products across the borders (Hoffmann et al. 2012).

Since the first identification of SBV in 2011 considerable information has been acquired about virus origin, emergence, epidemiology, molecular virology, clinical signs, pathogenesis, diagnosis, vaccine development, seroprevalence, potential for further outbreaks and re-emergence and the economic impact of this disease which has been compiled in this chapter and is based on the analysis of the research conducted and the already existing data reported so far on this in scientific journals and Web-based reporting tools.

10.2 History

An unknown disease syndrome in dairy cows was observed in Germany in the year 2011 where herd morbidities were 20–70% and recovery occurred in a few days. At the same time, similar cases with severe scouring were also identified in the Netherlands (Hoffmann et al. 2012; Tarlinton et al. 2012; Bilk et al. 2012; Elbers et al. 2012; EFSA 2012; Beer et al. 2013; Tarlinton and Daly 2013).

In the later part of the year, abortions and stillbirths among newborn lambs but also in goats and cattle along with some dystocia in mature animals were also observed in the Netherlands, Germany and Belgium (van den Brom et al. 2012). In the subsequent year 2012, during February, mid-March, May and August months various outbreaks had been reported from Belgium, Denmark, France, Germany,

Italy, Luxembourg, the Netherlands, Spain, Switzerland and the United Kingdom. Sheep farms were highly infected, followed by cattle and goat farms. The initial cases of congenital abnormalities were investigated in detail, and all suspected aetiological agents were ruled out, and by using metagenomic analysis a new virus was isolated and identified. By metagenomic and full-length sequence analysis, this new virus has shown resemblance to three viruses which were identified in cattle from Japan: Aino virus, Shamonda virus and Akabane virus of the genus Orthobunyavirus viruses and *Bunyaviridae* family (Hoffmann et al. 2012; van den Brom et al. 2012). This agent was subsequently named Schmallenberg virus based on the place of its origin.

In Germany, before this event, there was not a single evidence of SBV protein and RNA based on a retrospective study from 1961 to 2010 in ruminants (Gerhauser et al. 2014). In another study in Turkey, 1 buffalo in 2006 and 12 cows and 1 buffalo sample in 2007 were found positive by antibody ELISA test. However, the viral nucleic acid was only identified in June 2012 (Azkur et al. 2013). Furthermore, in the year 2012, in Mozambique, seropositive sheep, goats and cattle were detected (Blomstrom et al. 2014).

10.3 Disease

Disease in adult cattle causes inapparent or subclinical symptoms (Hoffmann et al. 2012; Schulz et al. 2014). The incubation period ranges from 1 to 4 days, and viraemic stage is very short (1–6 days) which is followed by decreased appetite, high body temperature during high vector activity (more than 40 °C), loss of body condition, reduced milk production (up to 50%) and diarrhoea, followed by recovery within a few days (Hoffmann et al. 2012; Laloy et al. 2015; Lechner et al. 2017). The virus affects equally both the genders (Wernike et al. 2013b).

There may not be any clinical symptoms in adult sheep and goats except for the increased risk of abortions and congenital malformations in offspring. However, some sheep may show very mild clinical signs such as diarrhoea, lethargy, depression, snotty nose and fever (Wernike et al. 2013c; Helmer et al. 2013).

It is a reproductive disorder where dams are capable of transmitting the virus to the foetus, if they get an infection during a certain period of gestation, and develop severe congenital abnormality categorised as arthrogryposis hydranencephaly syndrome (AHS). This includes premature birth, mummified foetuses, stillbirth, disproportionate metatarsus, bent limbs and fixed joints, severe torticollis, ankylosis, flattened skull and brachygnathia inferior (van den Brom et al. 2012; Gelagay et al. 2018). When more than one offspring are infected in utero, only one of them may show clinical symptoms or arthrogryposis may be shown in one and neurological disease in the other. In another situation, one of the twins can be malformed, and the other is viable or only shows delayed growth (van den Brom et al. 2012; Wernike et al. 2014).

The neurological form is manifested by amaurosis, ataxia and/or behavioural abnormalities, recumbency, an inability to suck and occasionally fits ("dummy syndrome"), tetany, paresis, swimming and circling movements. The affected newborn mostly shows multiple malformations of the vertebral column (torticollis, lordosis, kyphosis and scoliosis). Calves are most frequently affected by torticollis and lambs by scoliosis (Bayrou et al. 2014; Peperkamp et al. 2014). Besides the malformations, the body weight of the newborn calves is significantly less (Bayrou et al. 2014).

10.4 Post-mortem Findings

The gross lesions are characterised by arthrogryposis, brachygnathia inferior, and malformations of the vertebral column and central nervous system which include cerebellar hypoplasia hydranencephaly, hydrocephalus, porencephaly, micromyelia and subcutaneous oedema (calves) (van den Brom et al. 2012). The CNS lesions are characterised by cavity formation in white matter, loss of neurons in the cerebrum and cerebellum cortex, nuclei of brainstem and gray columns of the spinal cord. Lambs are more severely affected than calves (Peperkamp et al. 2014; Laloy et al. 2017). Additionally, in case of in utero-infected lambs and calves, the tendons of the affected joints appear smaller, and the related muscles show a change in colour and loss in mass (Bayrou et al. 2014).

10.5 Impacts

Various factors set the impact of the disease, for example, the number of congenitally abnormal lambs, lower milking periods and stage of gestation in which the infection took place (Wuthrich et al. 2016). The direct impact of the disease on adult animals incorporates a rise in body temperature, diarrhoea and decreased milk yield as well as non-pregnancy, repeat breeding, abortion and fatal dystocia. During certain gestational stages, there is a chance of complications featuring deformation and loss of newborn. The vertical transmission during the first half of gestation has the highest visible impact (Hoffmann et al. 2012; Elbers et al. 2012; Bilk et al. 2012; EFSA 2012; Tarlinton et al. 2012; Wernike et al. 2013a; Tarlinton and Daly 2013). During 2012, the observed direct impact was the consequence of the spread of the virus into a host population which was naive. Other consequences of SBV infection are the treatment costs or calving and lambing complications besides the cost of buying the replacement stock to compensate the reproductive losses along with unsold replacement animals, as well as restrictions on the movement (Alarcon et al. 2014).

Although the immediate financial impact of this infection in the ruminants is limited, the appearance of this virus has a major economic impact on international trade and has caused considerable damage to export due to imposed restrictions on

the import of livestock products, such as embryos, semen and live animals from affected countries. Such restrictions on trades have caused considerable financial losses in Europe. During 2011 and 2012, the purebred animals' export value declined by 20%, and in 2012 the bovine semen trade declined by 11–26%, corresponding to 8.9 million doses (EFSA 2014).

At the individual farm level, the impact ranges from minimal to more than 50% losses of young animals (Helmer et al. 2013). In general, the effect of SBV is more on sheep farms experiencing increased numbers of abortions, lamb mortality, dystocia, malformations and lower fertility rate.

In cattle farms, the financial losses owing to the fall in milk yield and return to service are bigger than the congenitally malformed calves (EFSA 2012; Beer et al. 2013). Effect of the virus on domestic goats is lesser than sheep. However, heavy financial loss up to 50% was registered in affected goat farms due to kid's mortality and fall in milk yield (Helmer et al. 2013). Wuthrich et al. (2016) conducted a study in an SBV-infected standardised farm and calculated that the mean loss was 1338 EUR, which at the national scale may be low, but the high fluctuations in losses were observed between farms so that particular farms might have experienced considerable losses (8333 EUR).

10.6 Virus

Within the family *Bunyaviridae*, the largest genus *Orthobunyavirus* is divided into 18 serogroups and the Simbu serogroup holds more than 25 viruses including SBV and is classified into seven species (Simbu virus, Akabane virus, Oropouche virus, Shamonda virus, Sathuperi virus, Shuni virus and Manzanilla virus) on the basis of cross-neutralisation tests and cross-haemagglutination inhibition tests (Goller et al. 2012; Yanase et al. 2012; Hoffmann et al. 2012; Plyusnin et al. 2012).

SBV is an enveloped, spherical (with a diameter ranging 80–120 nm having short surface projections), three-segmented, single-stranded, negative-sense RNA virus. The envelope holds the large (L), medium (M) and small (S) genome segments and forms a panhandle structure using complementary non-coding bases at the end of the segment. These complexes are consociated to a few copies of L polymerase and many copies of the N protein to make ribonucleoproteins (RNPs), the infectious viral particles (Tilston et al. 2017). The L segment codes for an essential protein the viral RNA-dependent RNA polymerase (RdRp) L protein which is accountable for the replication and transcription of the viruses (Kraatz et al. 2018).

The M segment codes for a precursor polyprotein which is co-translationally cleaved by cellular proteases into two surface glycoproteins (Gn and Gc) and a non-structural protein (NSm). Together, Gn and Gc form heterodimeric complexes responsible for virus entry into cells and function as antigenic determinants and are identified by neutralising antibodies whereas NSm protein's role is not fully known, but this protein appears to be involved in the assembly of virus particles. In general, among the S, M and L segments, the M RNA segment is highly variable. Natural

genetic reassortment is responsible for the emergence of new virus strains with a prospective change in their host range, virulence and antigenicity.

The S segment codes for the nucleocapsid protein (N) as well as another small non-structural protein (NSs) in an overlapping ORF. The primary function of this protein is to encapsidate the viral genome and protect its disintegration in the cells and it is also necessary for viral RNA transcription and replication. The N protein is the highly available protein in the virion and infected host cells. Therefore, it is mostly used for molecular and serological identification of SBV (Bilk et al. 2012) and is the major SBV antigen responsible for complement fixation (Goller et al. 2012; Yanase et al. 2012) and also modulates the host innate immune response (Elliott et al. 2013).

10.7 Resistance to Physical and Chemical Action

The virus loses its infectivity at 50–60 °C temperatures in 30 min. Exposure to common disinfectants such as 2% glutaraldehyde, 1% sodium hypochlorite, formaldehyde and 70% ethanol affects the viral virulence and virus does not sustain outside the vector or host for long term (OIE 2017).

10.8 Phylogeny

After the discovery of this virus, the full genome was sequenced by Hoffmann et al. (2012) and the S (830 nucleotides), M (4415 nucleotides) and L (6865 nucleotides) segments were compared with other Orthobunyaviruses and they observed that the small segment was 97% similar to Shamonda virus; the medium segment was 71% similar to Aino virus; and the large segment was 69% similar to Akabane virus, all detected in cattle of Japan. Rooting upon such observations, Schmallenberg virus was placed in the Simbu serogroup as Shamonda-like virus.

Later, Yanase et al. (2012) advocated that SBV emerged as a result of reassortant phenomena between Sathuperi and Shamonda viruses with the small and large segments emerging from Shamonda virus and the medium segment emerging from Douglas and Sathuperi virus. Afterwards, almost complete genome sequences were ascertained for nine viruses of the five species in the Simbu serogroups (i.e. species Shamonda virus (Sango virus, Peaton virus and Shamonda virus), species Sathuperi virus (Douglas virus and Sathuperi virus), species Shuni virus (Shuni virus and Aino virus), species Akabane virus (Sabo virus) and species Simbu virus (Simbu virus)). Upon phylogenetic analysis, it was observed that Schmallenberg virus belongs to the species Sathuperi virus and possibly is not a reassortant virus and as a fact may be an ancestor to Shamonda virus, which itself is a reassortant with small and large segments from Schmallenberg virus and medium segment from an unspecified virus. This conclusion is also assisted by a serological examination

wherein Douglas and Sathuperi viruses are neutralised by anti-SBV serum, but not the Shamonda virus (Goller et al. 2012).

10.9 Epidemiology of Disease

10.9.1 Incidence and Prevalence

Since its first appearance in north-western Europe (Hoffmann et al. 2012), SBV has extended over considerable parts of Europe. SBV infections have been spotted in Germany, the Netherlands and Belgium (seroprevalence up to 99.8%), the United Kingdom, France (seroprevalence up to 90%), Italy, Luxembourg, Spain, Italy, Denmark, Estonia, Ethiopia (seroprevalence up to 56.6%), Northern Ireland, Switzerland, Norway, Austria, Sweden, Finland, Poland and Turkey (Elbers et al. 2012; Azkur et al. 2013; Afonso et al. 2014; Gelagay et al. 2018). After the initial epidemic in 2011–2013, possible recirculation of virus has been reported from several countries, including Germany (Wernike et al. 2015a), Belgium (Delooz et al. 2016) and England and Wales (APHA 2017). Orthobunyaviruses in the Simbu serogroup are identified in Africa, Asia, Australia and the Middle East. Serological studies have shown SBV antibody-positive results from African countries. Since viruses of the Simbu serogroup are spotted in many locations of Africa and due to the paramount issue of cross-reactivity, Mathew et al. (2015) inferred that the seropositivity in ELISA might be due to other viruses of the Simbu serogroup instead of SBV. Likewise, Sathuperi virus (Simbu serogroup) was in the first place to be isolated in India from a pool of *Culex vishnui* mosquitoes and later in Nigeria from dairy cattle and pools of *Culicoides* spp. (Dandawate et al. 1969; Causey et al. 1972). Another member of Simbu serogroup, Kaikalur virus, was isolated from a pool of *Culex tritaeniorhynchus* mosquitoes collected from Krishna district, India (Rodrigues et al. 1977). Because of very close two-way cross-reaction, Kaikalur and Aino viruses are considered identical or varieties of a single virus.

Among cattle, younger animals had lower prevalence than adult (Gelagay et al. 2018). However, Elbers et al. (2012) have not found any age-related difference in seroprevalence in the Netherlands.

10.9.2 Risk Factors

Hitherto, not a single human case has been reported from any country. Thus, the public health risk of SBV should be deemed to be negligible. Simbu serogroup does not have zoonotic implication except Oropouche virus, which causes severe flulike symptoms in humans.

Nevertheless, SBV was expanding and overcame the European boundary. Availability of vectors, reservoirs and susceptible host populations will facilitate it to spread further and/or become endemic as well as determines its persistence. Every fresh batch of animals significantly introduces fresh susceptible hosts. The rate of mixing of a new susceptible host with the existing population will determine the duration and amplitude of inter-annual epidemic cycles. This also depends on herd replacement rates, level of vaccination and durations of immunity. The rate of restocking may vary based on farm management and production systems. In farm enterprises, the regular replacement rate is 20 or 25%, which gives rise to a substantial number of susceptible hosts in a herd annually.

Furthermore, before the introduction of the breeding male(s), if naive females are infected, no unfavourable effects are to be expected. But infection during early pregnancy results in early embryonic death and dams become repeat breeders. Nonetheless, in the next pregnancy, normal results may be expected. When animal health status and meteorological settings become favourable for the vectors and virus, also when a substantial number of the hosts become susceptible, especially at the boundary of the endemic area, the virus can re-emerge.

10.10 Transmission

10.10.1 Susceptible Species

Since the first detection of SBV, the existence of viral RNA and/or antibodies has been investigated in a variety of animals and found that domestic ruminants (cattle, sheep and goats) and multiple wild (alpacas, Anatolian water buffalo, elk, bison, red deer, fallow deer, roe deer, sika deer, muntjac, chamois, moufflons and wild boar) and zoo species (bongo, babirusa, banteng, Congo buffalo, European bison, gaur, gemsbok, greater kudu, Grevy's zebra, moose, Nile lechwe, Nubian goat, onager, reindeer, roan antelope, scimitar-horned oryx, sitatunga and yak) are susceptible to SBV (EFSA 2014). Among domestic ruminants, it is observed that susceptibility of goats is lesser than cattle and sheep.

There is a report indicating that dogs may be infected with SBV and pregnant females show teratogenic effects, but this is possibly a rare phenomenon (Sailleau et al. 2013). Virus infection in pigs has also been reported where it induces seroconversion but does not involve its epizootiology (Poskin et al. 2014). Infection in camelids is also reported (Wernike et al. 2012).

10.10.2 Horizontal Transmission

The virus does not spread through direct contact. The oral route is also not the probable way of spread. Experimental injection by subcutaneous route in cattle (Hoffmann et al. 2012; Wernike et al. 2013b), sheep (Wernike et al. 2013c; Martinelle et al. 2017) and goats (Laloy et al. 2015) and intradermal route in sheep (Martinelle et al. 2017) results in viraemia.

10.10.3 Vector

The SBV is also transmitted by Culicoides biting midges, principally members of the *Culicoides obsoletus* complex, but other *Culicoides* spp. are also capable of spreading, (*Culicoides chiopterus*, *Culicoides dewulfi*, *Culicoides scoticus*, *C. pulicaris*); they are active 1 h before sunrise and sunset (Hoffmann et al. 2012; Bilk et al. 2012; Elbers et al. 2012; Tarlinton et al. 2012; Beer et al. 2013; Wernike et al. 2013a; Tarlinton and Daly 2013).

10.10.4 Vertical Transmission

Vertical transmission is of great significance as SBV gets across the placenta. Transplacental infection occurs when the first placentome appears till the foetus becomes immunocompetent, days 30–150 post-conception in bovine (Bayrou et al. 2014) and days 28–56 post-conception in ovine and caprine (Helmer et al. 2013; Laloy et al. 2017). The clinical manifestation is highly dependent on the age of the foetus (Bayrou et al. 2014). When the dam is infected during the early stage of pregnancy, it can result in foetal death, lower fertility and stillbirth. But if infected later in pregnancy, developed immune system of the foetus is capable of resisting the virus; however mummification, stillbirth and abortion can also occur (Helmer et al. 2013). Infected offspring does not show viraemia, and there is no evidence of virus transmission from the infected progeny to vectors (EFSA 2014).

10.10.5 Semen

The virus can be secreted in the semen of infected animals, and viral nucleic acid has been identified both in the plasma and cell fraction of semen (Kesik and Larska 2016). Semen containing SBV is not likely to infect embryo, but if the dam gets viraemic, vector transmission may occur (Schulz et al. 2014).

10.11 Immunopathobiology

There is not much information on the immune response and duration of immunity following the infection. An innate immune response takes place immediately after the infection in cattle (Wernike et al. 2013b). Nevertheless, SBV alters the innate immune response of the host by suppressing interferon production at the transcription level, particularly mediated by NSs protein. This protein behaves like a virulence factor and antagonises IFN likely by suppressing cellular metabolism. Thus, the innate immune response of the host is vanquished, and effective replication of the virus takes place (Elliott et al. 2013). Seroconversion in cattle occurs after 8–14 days of infection and remains for more than 3 years in naturally infected cows; therefore, a long-standing immunity can be anticipated, but in experimentally infected cattle immunity lasted for at least 8 weeks which was able to prevent reinfection (Wernike et al. 2013b; Elbers et al. 2014; Schulz et al. 2014; Wernike et al. 2015b). Seroconversion in sheep takes place after 6–22 days of infection and lasts for at least 15 months and in goats between 7 and 14 days after infection (Wernike et al. 2013c; Poskin et al. 2015; Laloy et al. 2015). Colostrum feeding is the only way of transferring maternal antibodies to calves, which remains for 5–6 months as the transplacental transfer does not take place in ruminants (Elbers et al. 2014). Furthermore, foetuses are capable of producing neutralising antibodies and are also identified in stillborn or aborted calves and lambs. However, if the foetus is immunocompetent, clinical signs are not visible at birth in case of in utero infection.

10.12 Diagnostics

Clinical diagnosis is usually done through observing clinical evidence of the disease, which may be different in different species. Various laboratory procedures have been described to detect the SBV infections which include (i) real-time reverse transcriptase PCR, (ii) neutralisation and indirect immunofluorescence assays, (iii) ELISA and (iv) isolation and identification of the virus by cell culture technique.

10.12.1 Sample Collection

Schmallenberg virus remains present for a longer time in infected foetuses than adult live animals (4–6 days) and can be detected in malformed newborns (Laloy et al. 2017). From an acutely infected animal, viral nucleic acid could be identified in mesenteric lymph nodes, spleen as well as semen for a long period. Placenta and amniotic fluid are also materials of choice for diagnosis (Bilk et al. 2012).

From acutely infected adults, samples of whole blood in EDTA and serum should be collected and properly packaged and shipped to the designated laboratory under the cold chain. Samples from aborted foetuses or newborn animals may be collected for histopathology (fixed central nervous system, including spinal cord), serology and virological investigations. Brain sample, ideally cerebrum and cerebellum as well as central nervous system, lymphatic organs and blood from dead animals and pre-colostrum blood, serum and meconium samples from live animals should be collected and properly packaged and shipped to the designated laboratory under the cold chain (OIE 2017).

10.12.2 Nucleic Acid Detection

Real-time quantitative reverse transcription PCR is a reliable detection method for viral nucleic acids (L or S segment of the viral genome) in clinical samples. For this purpose, RT-qPCR assay is developed by the FLI (Bilk et al. 2012; Hoffmann et al. 2012).

10.12.3 Virus Isolation in Cell Culture

Virus isolation can be performed from blood collected at the height of temperature from diseased adult animals and from the dead foetus and its brain (Laloy et al. 2017). The virus can be propagated in various cell lines originated from different animal species and humans like Vero cells, sheep choroid plexus cells, bovine foetal aorta endothelial cells, human 293T, Madin-Darby canine kidney cells and baby hamster kidney-21 cells and BSR cells or insect KC (*Culicoides variipennis* larvae) and it induces cytopathic effect (CPE) in most of these cell lines. Among these cell lines, sheep choroid plexus cells were found most sensitive for SBV propagation (Hoffmann et al. 2012; Wernike et al. 2013c; Ilchmann et al. 2017).

10.12.4 Serological Test

The SBV seroprevalence and also the serological status of the individual animal may be determined using virus neutralisation, immunofluorescence assays and ELISA techniques (Loeffen et al. 2012). The gold standard test for SBV diagnosis is virus neutralisation test (VNT) having almost 100% sensitivity and specificity (Loeffen et al. 2012). In spite of the fact that cross-reactions within Simbu serogroup of viruses have been reported, the enzyme-linked immunosorbent assay is a most sensitive, specific, sturdy and approved technique for anti-SBV antibody detection and can be employed for surveillance studies. Bulk milk antibody tests are available and

can be used for surveillance as they indicate herd-level exposure (Hoffmann et al. 2012; Tarlinton et al. 2012; EFSA 2012; Elbers et al. 2012; Bilk et al. 2012; Beer et al. 2013; Tarlinton and Daly 2013). Both ELISA and RT-qPCR kits are commercially available. For multispecies serum or plasma viral antibody detection, competitive ELISA kits are commercially available (ID Screen® Schmallenberg virus Competition Multi-species, IDvet Laboratories, Montpellier, France)

10.12.5 Differential Diagnosis

Differential diagnosis of the disease is important as SBV infection does not show conclusive clinical symptoms in adults; therefore, all potential causes of high body temperature, liquid faecal discharge, lower milk yield stillbirth and abortion must be considered such as bovine viral diarrhoea (BVD), border disease (BD) and other pestiviruses, bovine herpesvirus 1 and other herpesviruses, bovine ephemeral fever, epizootic haemorrhagic disease (EHD), foot and mouth disease (FMD), bluetongue, Rift Valley fever (RVF), and toxic substances, e.g. *Veratrum californicum* and *Lupinus* spp. However, Cache Valley virus, Orthobunyavirus infections (Akabane), genetic factors (e.g. spider lamb syndrome), toxic substances and nutritional deficiencies (e.g. gestational protein deficiency, manganese) must also be taken into consideration while investigating the congenital malformations.

10.13 Prevention and Control

As it is a viral infection, presently, there is no therapy available for this disease; hence, supportive care is an only reliable option for intervention. The direct impact of this disease can be mitigated by the use of a potent vaccine, or by avoiding the risk of pregnancy when vector activity is high. Different inactivated vaccines have been formulated and successfully tested (Wernike et al. 2013c; Hechinger et al. 2014), and two of them, SBVvax (Merial 2013) and Bovilis SBV (MSD Animal Health n.d.), have been given provisional permission to the market in the United Kingdom and France. As per the manufacturer's instruction, the vaccination regime for the large animal is two injections at 28-day interval, and for sheep only one injection is adequate where immunity develops within 3 weeks. Vaccination before the breeding season is the most efficient measure to prevent infection. After vaccination, anti-SBV antibodies develop in a previously uninfected host which protect the foetus from teratogenic effects, once the animal is pregnant, by inhibiting transplacental infection.

Furthermore, the vaccine also protects susceptible animals from sickness and purportedly prevents further transmission of the vector (Tarlinton et al. 2012). DNA immunisation can raise multiple Th response and antibody response. So far, no DNA vaccine is available for this disease. For the development of a prospective DNA vaccine, both the nucleoprotein and the putative GC ectodomain gene have been targeted (Boshra et al. 2017).

One feasible alternative is to control the midge vectors by implementing the procedure like use of insecticides/larvicide and pathogens to natural dwelling where they grow and removal of larva breeding enclosures through environmental interference; adult midges may be controlled by treating either resting sites such as livestock house or its body with insecticides and repellents, e.g. pyrethroids and host kairomones (Carpenter et al. 2008).

Besides, the naive animals or herds with low within-herd seroprevalence can be protected by the improved breeding system. The breeding period may be planned in such a fashion where it falls in late autumn and *Culicoides* spp. are scarce; the animals may be kept mostly inside house, all of the sunsets to sunrise. To protect animals during pregnancy, a susceptible individual may also be shifted to the endemic zone soon enough to raise acquired immunity (Helmer et al. 2013). In calves, maternal antibodies disappear in 5–6 months but in adults specific antibodies persist for a minimum of 2 years (Elbers et al. 2014). Movement restrictions are not imposed as this is not a notifiable disease.

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