Bluetongue: a review

A. Sperlova, D. Zendulkova

University of Veterinary and Pharmaceutical Sciences, Brno, Czech Republic

ABSTRACT: Bluetongue is a non-contagious disease of domestic and wild ruminants caused by a virus within the *Orbivirus* genus of the family *Reoviridae* and transmitted by *Culicoides* biting midges. It is a reportable disease of considerable socioeconomic concern and of major importance for the international trade of animals and animal products. In the past, bluetongue endemic areas were found between latitudes 40°N and 35°S; however, bluetongue has recently spread far beyond this traditional range. This is in accordance with the extension of areas in which the biting midge *Culicoides imicola*, the major vector of the virus in the "Old World", is active. After 1998 new serotypes of bluetongue virus (BTV) were discovered in Southern European and Mediterranean countries. Since 2006 BTV-serotype 8 has also been reported from the countries in Northern and Western Europe where *Culicoides imicola* has not been found. In such cases, BTV is transmitted by Palearctic biting midges, such as *C. obsoletus* or *C. dewulfi,* and the disease has thus spread much further north than BTV has ever previously been detected. New BTV serotypes have recently been identified also in Israel, Australia and the USA. This review presents comprehensive information on this dangerous disease including its history, spread, routes of transmission and host range, as well as the causative agent and pathogenesis and diagnosis of the disease. It also deals with relevant preventive and control measures to be implemented in areas with bluetongue outbreaks.

Keywords: *Orbivirus*; ruminants, *Culicoides* spp.; pathogenesis; control; prevention

Contents

Supported by the Ministry of Education, Youth and Sports of the Czech Republic (Grant No. MSM 6215712403).

1. Introduction

Bluetongue is an infectious, non-contagious disease of ruminants and camelids transmitted by *Culicoides* biting midges. It is caused by the bluetongue virus (BTV) and is placed in the Office International des Epizooties list of diseases. The manifestations of bluetongue range from an inapparent to a fatal outcome depending on the serotype and strain of the virus and the species, breed and age of the infected animal; older animals are generally more susceptible (Elbers et al., 2008b). Clinical signs are usually detected in fine-wool breeds of sheep and the white-tailed deer (*Odocoileus virginianus*) and include fever, facial oedema, haemorrhages into, and ulceration on, the oral mucosa and coronitis. Bluetongue typically occurs when susceptible animal species are introduced into areas with circulating virulent BTV strains, or when virulent BTV strains extend their range to previously unexposed populations of ruminants (Zientara et al., 2010). The worldwide economic losses due to bluetongue have not been expressed in exact numbers, but the estimate is 3 billion US$ a year (Tabachnick, 1996). The losses are both direct (death, abortions, weight loss or reduced milk yield and meat efficiency) and, what is more important, indirect as a result of export restrictions for live animals, their semen and some products such as foetal bovine serum. The costs of preventive and control measures should also be taken into account. In cases of a wider spread of bluetongue, these measures could have a serious impact on the quantity of meat and animal products available for the consumer market; therefore, bluetongue is considered a potential biological weapon (Blancou and Pearson, 2003; Zendulkova and Pospisil, 2007).

2. History and distribution

Bluetongue was first recorded at the end of the 18th century in South Africa after an import of fine-wool sheep from Europe (Spreull, 1905). It was first referred to as fever, malarial catarrhal fever of sheep or epizootic malignant catarrhal fever of sheep (Hutcheon, 1902; Spreull, 1905). In 1933 it was first diagnosed in cattle (Bekker et al., 1934) and, because its clinical signs were similar to those of foot-and-mouth disease, it was called pseudo-foot-and-mouth disease, seerbeck or sore-mouth (Vellema, 2008). "Bluetongue", the name used today, has been derived from the African "bloutong", which was coined by South-African farmers who noticed tongue cyanosis in seriously diseased animas (MacLachlan et al., 2009). In 1906 Theiler was the first to report that the infecting agent was a filtrable virus (Mehlhorn, 2008; Vellema, 2008).

Bluetongue can develop and spread when susceptible hosts, BTV and competent insect vectors are all present at the same time. Traditionally, the virus was present in a geographic band between the latitudes 40°N and 35°S where its vectors, certain species of biting midges, were living (Rodriguez-Sanchez et al., 2008; Vellema, 2008; Wilson and Mellor, 2009). In North America and China the virus spread even further, up to 50°N (Mellor et al., 2000). Before the 1940s the occurrence of bluetongue was limited to South Africa (MacLachlan et al., 2009). The first well recorded epidemic beyond the African continent dates back to 1943 in sheep in Cyprus (Gambles, 1949; MacLachlan, 2004), but there are indications that bluetongue had been there since 1924 (Polydorou, 1978; Rodriguez-Sanchez et al., 2008). In 1943–1944 bluetongue was found in Israel (Shimshony, 2004), in 1948 it was reported in Texas, USA (Hardy and Price, 1952), between 1956 and 1957 a large epidemic broke out on the Iberian peninsula, and subsequently bluetongue was also found in the Middle East, Asia and Southern European countries (Gibbs and Greiner, 1994; Mellor and Wittmann, 2002; MacLachlan, 2004). In Australia it first appeared in 1977 (Gibbs and Greiner, 1994), and in South America it was found in the 1980s (Rosadio et al., 1984; Lopez et al., 1985; Tamayo et al., 1985; Clavijo et al., 2002). Bluetongue is also present in Central America and Mexico, Papua New Guinea, Thailand, China, Japan, the Indian subcontinent, Mediterranean countries (Greece, Spain, Italy, Corsica), Portugal, Bulgaria and other countries (Baylis and Mellor, 2001; Mellor and Wittmann, 2002; Tweedle and Mellor, 2002; Anonymous, 2007; Mehlhorn et al., 2007; Mellor et al., 2008).

2.1. Bluetongue epidemiology after 1998

2.1.1. Southern Europe

During the 20th century, only short outbreaks of bluetongue were occasionally recorded in Southern European countries (Spain, Portugal, Greece and

Cyprus) (Mellor and Boorman, 1995; Hendrickx, 2009). However, since 1998 BTV has been present in Southern European and Mediterranean countries from which it has gradually spread to areas previously free of the virus. This finding of BTV in the countries north of the Alps is considered to be associated with recent global climatic changes and the related spread of the main BTV vector *Culicoides imicola* (Purse et al., 2005; Randolph and Rogers, 2010). In 1998 the disease was recorded in Greece, in 1999 in Turkey and Bulgaria, then also in Serbia, Montenegro, Kosovo and Macedonia. In 2000 bluetongue was found in Sardinia, Sicily, mainland Italy, and in Corsica, Menorca and Mallorca. In 2001 it was first found in Croatia and the following year in Bosnia and Albania. Up to now serotypes 1, 2, 4, 9 and 16 have been isolated in the region of Southern Europe (Mellor and Wittmann, 2002; Anonymous, 2007; Mellor et al., 2008; Saegerman et al., 2008).

2.1.2. Northern Europe

In August 2006 bluetongue epidemics broke out suddenly and unexpectedly in Northern Europe – first in The Netherlands and shortly afterwards in Belgium, Germany and the north of France (Thiry et al., 2006; Carpenter et al., 2009; Wilson and Mellor, 2009). They were caused by the BTV serotype 8 (Elbers et al., 2008a; Mintiens et al., 2008) that is common in Kenya (Davies, 1978), Nigeria (Sellers, 1984), Sudan (Mohammed and Taylor, 1987), Malawi (Haresnape et al., 1988), South African Republic (Nevill et al., 1992), India (Prasad et al., 1992b) and Central America and the Caribbean (Gibbs and Greiner, 1994; Mo et al., 1994). This serotype had never been reported in Europe before 2006 (Mehlhorn et al., 2007; Mintiens et al., 2008) and up to now its origin has not been traced (Mintiens et al., 2008; Wilson and Mellor, 2009). There are several theories explaining its introduction, for instance, import of animals at a viraemic stage of the disease, infected semen or embryos, inadvertent shipment of infected biting midges together with animals or plants, or the introduction of biting midges either through their own flight over long distances or with the aid of wind (Saegerman et al., 2008).

By the end of 2006, BTV-8 had further been discovered in Luxembourg (Carpenter et al., 2009; Wilson and Mellor, 2009). Owing to survival over the winter, the BTV-8 appeared in these countries again the next year, and even spread to Great Britain, Switzerland, Denmark and the Czech Republic (Saegerman et al., 2008; Schwartz-Cornil et al., 2008; Hendrickx, 2009). New outbreaks of bluetongue were reported in Hungary, Austria and Sweden in 2008 (Carpenter et al., 2009; Agren et al., 2010; Kampen and Werner, 2010; Lewerin et al., 2010) and in Norway at the beginning of 2009 (Anonymous, 2009b). The BTV-8 strain that has invaded Northern Europe is highly virulent not for only sheep, but also cattle or South American camelids and, in addition, it can cross the placenta, which was not typical of the field strains of BTV in the past (MacLachlan, 2010). The BTV-8 epidemic in Northern Europe has probably caused greater economic damage than any previous single-serotype bluetongue outbreak (Wilson and Mellor, 2008).

In 2008 BTV-6 was identified in the Netherlands and Germany and BTV-11 in Belgium. Both viruses were derived from the vaccine strains (De Clercq et al., 2009; Eschbaumer et al., 2010) most likely introduced to Europe through the illegal use of attenuated vaccines (MacLachlan, 2010).

A new virus, similar to BTV, and infecting goats was discovered in Switzerland in early 2008. It was named *Toggenburg orbivirus* (Hofmann et al., 2008), and is a so far unknown orbivirus with low pathogenicity and a potential BTV serotype 25 (Hofmann et al., 2008; Chaignat et al., 2009). And similarly in the Arab countries, in 2010, a potential serotype 26 of BTV was identified in sheep and goats in Kuwait (Maan et al., 2011).

2.1.3. USA, Australia, Israel

As in Southern Europe, new BTV serotypes were identified in the USA, Australia and Israel during the last decade. In the USA, in addition to the serotypes 2, 10, 11, 13 and 17 found in enzootic outbreaks before 1999, BTV serotypes 1, 3, 5, 6, 9, 12, 14, 19, 22 and 24 were newly isolated. In Australia serotypes 2 and 7 were newly identified in 2007 and 2008. The situation was similar in Israel where, in addition to the previously recorded BTV serotypes 2, 4, 6, 10 and 16, serotypes 8, 15 and 24 were discovered after 2006 (MacLachlan, 2010).

3. Aetiology

Bluetongue virus is a member of the genus *Orbivirus* in the family *Reoviridae*. It is similar in mor-

phology to other orbiviruses, such as epizootic hemorrhagic disease virus, African horse sickness virus or equine encephalosis virus. So far 24 BTV serotypes have been identified world-wide (Roy and Noad, 2006; Schwartz-Cornil et al., 2008) with the already mentioned potential serotypes 25 and 26 recently isolated in Switzerland and Kuwait, respectively (Hofmann et al., 2008; Chaignat et al., 2009; Maan et al., 2011). Bluetongue virus is a non-enveloped virus, 90 nm in diameter, with a triple-layered icosahedral protein capsid (Huismans and Erasmus, 1981; Prasad et al., 1992a; Grimes et al., 1998; Mertens and Diprose, 2004; Nason et al., 2004; Roy and Noad, 2006). Its genome consists of ten double-stranded (ds) RNA segments coding for seven structural proteins (VP1–VP7) and four non-structural proteins (NS1–NS3 and NS3A) (Kar et al., 2007; Roy, 2008). The outer layer consists of two major proteins, VP2 and VP5 (Verwoerd et al., 1970, 1972; Nason et al., 2004; Roy and Noad, 2006). The VP2 protein determines the serotype, is responsible for receptor binding, haemagglutination and eliciting host-specific immunity (Huismans and Erasmus, 1981; Cowley and Gorman, 1987; Mertens et al., 1989; Hassan and Roy, 1999; Roy, 1992, 2008). The VP5 protein interacts with the host cell endosomal membrane and plays a minor role in eliciting an antibody response (Hassan et al., 2001; Roy, 2008).

The middle layer or inner capsid (core) is formed by the VP7 protein (Prasad et al., 1992a; Roy, 1992; Nason et al., 2004) which is the main determinant of serotype specificity (Inumaru et al., 1987; Oldfield et al., 1990; Anthony et al., 2007) and provides an epitope in ELISA tests for detection of antibodies against BTV. The innermost layer (subcore) consists of the VP3 protein (Grimes et al., 1998) and three smaller structural proteins, VP1, VP4 and VP6, involved in transcription and replication of viral RNA (Prasad et al., 1992a; Nason et al., 2004; Schwartz-Cornil et al., 2008).

The role of the NS1 non-structural protein is not yet clear; the present data indicate an involvement in viral morphogenesis (Brookes et al., 1993; Owens et al., 2004). The NS2 protein is the major component of viral inclusion bodies (Brookes et al., 1993; Owens et al., 2004; Lymperopoulos et al., 2006; Schwartz-Cornil et al., 2008) and is also involved in recruitment of BTV mRNA for replication (Fukusho et al., 1989; Kar, 2007; Roy, 2008). The NS3 protein acts as a viroporin, which enhances permeability of the cytoplasmic membrane and thus facilitates virus release from mammalian or insect cells (Hyat et al., 1991; Roy, 1992, 2008; Han and Harty, 2004). In addition, NS3 also allows BTV particles to leave host cells by a budding mechanism (Wirblich et al., 2006). This probably operates in insect cells where no cytopathic effect is induced by BTV (Schwartz-Cornil et al., 2008).

The segmented nature of the BTV genome allows for reassortment of ds-RNA segments if the host cell is concurrently infected by several different serotypes or strains (Oberst et al., 1987; Samal et al., 1987; Stott et al., 1987; Belyaev and Roy, 1993; Batten et al., 2008). The reassortment event plays an important role in the development of viral diversity (Carpi et al., 2010) and gives rise to changes in virulence and serological characteristics of the virus (Cowley and Gorman, 1989; Mertens et al., 1989; Nuttall et al., 1992; O'Hara et al., 1998; Batten et al., 2008).

BTV remains stable in the presence of proteins and can survive for years, for instance, in blood stored at 20 °C (Anonymous, 2009a). It is sensitive to 3% NaOH, organic iodine complex, phenol and b-propiolactone (Radostits, 1994; Anonymous, 2009a).

4. Transmission

4.1. *Culicoides* biting midges

Bluetongue is almost always transmitted by biting midges of the genus *Culicoides* (Diptera: *Ceratopogonidae*) and therefore outbreaks depend on the concomitant presence of competent insect vectors and susceptible ruminants. The genus *Culicoides* at present includes 1300 to 1400 species (Mellor et al., 2000; Borkent, 2005), but only about 30 of them are BTV vectors (Meiswinkel, 2004). Although biting midges are ubiquitous (Mellor et al., 2000), they are most frequently present in warm, damp and muddy areas which are rich in organic matter, and plentiful in animal hosts they can feed on. They are most active from about one hour before sunset until one hour after sunrise (Mellor et al., 2000).

The midge life cycle lasts for two to six weeks (Veronesi et al., 2009), is direct and involves an egg, four larval instars, a pupa and an adult (Mellor et al., 2000). Adults usually live for only ten to 20 days, but can survive for up to 90 days in colder conditions (Mellor, 2000; Lysyk and Danyk, 2007). Females of

some midge species need to take a blood meal three to four days prior to egg laying and feed at roughly four-day intervals; males feed on plant juices (Birley and Boorman, 1982; Mellor et al., 2000). By sucking the blood of infected ruminants, midges acquire BTV which then replicates in their digestive tract. Progeny virus is then released into the haemocoel from where the secondary target organs, including the salivary glands, are infected. Subsequent to virus replication in the salivary glands, transmission can take place. The whole cycle from infection to transmission takes between ten to 15 days at 25 °C and individual vectors once infected usually remain so for life (Chandler et al., 1985; Eaton et al., 1990; Mellor, 1990, 2000, 2004).

The ability of biting midges to transmit BTV is markedly influenced by ambient temperature, air humidity and total seasonal rainfall (Mullens et al., 1995; Wellby et al., 1996; Mellor, 2000). The virus in vectors can replicate at a temperature above 15 °C (Mellor et al., 2000), with the intensity of replication growing with increasing temperature (Van Dijk and Huismans, 1982). The recent "global warming" has allowed for longer activity of biting midges and thus longer periods during which they are capable of BTV transmission (Tweedle and Mellor, 2002). In addition, the higher temperatures recently experienced in northern Europe have increased the competence of indigenous *Culicoides* species to transmit BTV (Gale et al., 2009; MacLachlan, 2010). In the temperate zone the adults of biting midges usually do not survive the first frost and bluetongue thus has a seasonal nature (Radostits et al., 1994), with peaks of activity in spring and autumn (Purse et al., 2005).

Biting midges are regarded as exophagic and exophilic insects (i.e., feeding on animals outdoors and remaining outside, respectively), but some species, such as *C. dewulfi* and *C. obsoletus*, have shown endophagic behaviour (i.e., feeding inside) which increases in intensity with decreasing ambient temperatures (Baldet et al., 2008).

Biting midges can fly over a maximum distance of two km, but because of their small size (one mm to three mm) they can easily be carried on the wind; their passive transport up to a distance of 700 km has been reported (Ducheyne et al., 2007).

In the "Old World" the species *Culicoides imicola,* the most widely spread midge on the globe, is regarded as the major BTV vector. It is a thermophilic species requiring an average ambient temperature of above 12 °C to survive and over 15 °C for virus replication in the organism. It shows the highest activity in the temperature range from 13 °C to 35 °C (Tweedle and Mellor, 2002). It reproduces in damp or wet soils fertilised with manure (Meiswinkel et al., 1994) and feeds on cattle, sheep and horses (Mellor and Wittmann, 2002). *Culicoides imicola* has been found in Africa, the south of Asia, Portugal, Spain, Greece, Cyprus, Corsica, Italy, Israel, Turkey, Yemen, Oman and other countries (Mellor, 1990). It does not live in Northern and Central Europe. Here, psychrophilic species of biting midges are found, such as *C. obsoletus, C. pulicaris* and other species, which are potential BTV vectors (Mehlhorn et al., 2007).

In the epidemic caused by BTV-8 in Germany in 2006–2007, bluetongue was transmitted by *C. obsoletus* (Mehlhorn et al., 2007), the species from which BTV was isolated as early as 1977 during the Cyprus epidemic (Mellor and Pitzolis, 1979) and later in outbreaks in Italy (Savini et al., 2005), The Netherlands (Meiswinkel et al., 2008), and again in Germany (Hoffmann et al., 2009). In Sicily and Germany BTV was isolated from the species *C. pulicaris* (Caracappa et al., 2003; Hoffmann et al., 2009) and in the Netherlands from *C. dewulfi* (Meiswinkel et al., 2007) and *C. chiopterus* (Dijkstra et al., 2008).

The species *C. obsoletus* is one of the commonest species in Central and Northern Europe (Tweedle and Mellor, 2002) and together with *C. scoticus* is included in the *Obsoletus* complex (Savini et al., 2003; Meiswinkel et al., 2004). The females of these two species are very similar in morphology, which makes their differentiation hard (Campbel and Pelham-Clinton, 1960; Meiswinkel et al., 2004; Savini et al., 2005), but species identification is possible with the use of molecular methods (Nolan et al., 2007; Balczun et al., 2009, Stephan et al., 2009). *C. obsoletus* midges proliferate among wet decaying leaves, in water-filled tree cavities or manure heaps (Anonymous, 2007). *C. pulicaris* and *C. punctatus* midges are members of the *Pulicaris* complex (Carpenter et al., 2006; Dijkstra et al., 2008; Hoffmann et al., 2009). *C. pulicaris* midges go to rain-pools on peat moorland for reproduction (Anonymous, 2007). Similarly to *C. obsoletus,* they are widespread in Northern and Central Europe, but probably play only a minor role in BTV transmission (Mehlhorn et al., 2009). The females of species included in the *Pulicaris* and *Obsoletus* complexes preferably attack cattle (Bartsch et al., 2009; Ninio et al., 2011). The occurrence of *C. dewulfi* biting midges is closely related to the rearing of cattle

and horses whose manure heaps are ideal breeding sites for the insects (Kettle and Lawson, 1952; Campbell and Pelham-Clinton, 1960; Meiswinkel et al., 2007). *C. chiopterus* midges are also coprophilic and preferably feed on cattle and horses (Kettle and Lawson, 1952; Campbell and Pelham-Clinton, 1960; Dijkstra et al., 2008; Zimmer et al., 2008). Both species exhibit strong endophagic behaviour (Baldet et al., 2008).

In North America the species *C. sonorensis* is known as the major BTV vector (Mellor, 1990); *C. insignis* is considered to be less important (Tanya et al., 1992). The species *C. insignis* and C. *pusillus* act as BTV vectors in South and Central America (Kramer et al., 1985; Mo et al., 1994) and *C. brevitarsis, C. fulvus, C. wadai* and *C. actoni* in Australia (Mellor et al., 2000).

4.2. Other ways of transmission

Biting midges are responsible for BTV transmission in the majority of cases, but occasionally some other vectors can be involved. In addition to biting midges, BTV has been isolated from some arthropods, e.g., sheep ked (*Melophagus ovinus*) (Luedke et al., 1965) or some species of ticks (Stott et al., 1985; Bouwknegt et al., 2010) and mosquitoes (Brown et al., 1992). However, these are mechanical vectors with only a negligible role in disease epidemiology (Radostits et al., 1994).

Bull semen can also transfer the virus, but it can be infected only when the bull is viraemic (Bowen and Howard, 1984; Howard et al., 1985; Osburn, 1994; Kirkland et al., 2004) and when semen contains red or white blood cells with which the virus is associated (Osburn, 1994; Wilson et al., 2008).

The passage of BTV across the placenta is another mode of transmission. It has been recorded in cattle (Gibbs et al., 1979; Thomas et al., 1986; De Clercq et al., 2008; Desmecht et al., 2008; Menzies et al., 2008; Backx et al., 2009; Darpel et al., 2009; Lewerin et al., 2010; Santman-Berends et al., 2010), sheep (Richardson et al., 1985; Flanagan and Johnson, 1995; Saegerman et al., 2011) and in dogs (Wilbur et al., 1994).

Recently, an until now unique route of transmission was described in ruminants. This involved ingestion of the placenta of a BTV-infected bovine foetus (Menzies et al., 2008). In an experimental study it was possible to infect a newborn calf with BTV-contaminated colostrum (Backx et al., 2009). Transmission with colostrum has also been reported by Mayo et al. (2010). This is the first report of BTV or its nucleic acids naturally occurring in colostrum. Oral transmission has been described in carnivores (Alexander et al., 1994; Jauniaux et al., 2008) and has recently been experimentally confirmed in type1 interferon receptor-deficient mice (Calvo-Pinilla et al., 2010).

Bluetongue can also be spread by live attenuated vaccines against BTV, or even by vaccines against other antigens contaminated with BTV (Wilbur et al., 1994; Evermann, 2008).

5. Host range

All ruminants are susceptible to infection with bluetongue, but clinical disease is most often manifested in sheep; a serious disease also develops in white-tailed deer (*Odocoileus virginianus*) (Howerth and Tyler, 1988; Parsonson, 1990; Johnson et al., 2006). In cattle, which play an important role in the epidemiology of BTV mainly because of prolonged viraemia, the disease has in the past mostly been reported to have a subclinical course (Tweedle and Mellor, 2002). However, in the epidemics caused by BTV-8 in Western and Central Europe, even cattle showed clinical disease (Thiry et al., 2006; Darpel et al., 2007; Elbers et al., 2008a). Under natural conditions the disease may also be present in wapiti (*Cervus elaphus canadensis*), proghorn *(Antilocapra americana)*, African antelopes and other wild ruminants (Howerth et al., 2001), but it can also affect camelids (Rivera et al., 1987; Henrich et al., 2007; Meyer et al., 2009) and elephants (Erasmus, 1990; Mushi et al., 1990). Bluetongue has also been recorded in axis deer (*Axis axis*), fallow deer (*Dama dama*), sika deer (*Cervus nippon*), red deer (*Cervus elaphus*), roe deer (*Capreolus capreolus*), mouflon (*Ovis orientalis musimon*), Spanish ibex (*Capra pyrenaica*) and captive yak (*Bos grunniens grunniens*) (Murray and Trainer, 1970; Corn et al., 1990; Fernandez-Pacheco et al., 2008; Linden et al, 2008; Mauroy et al., 2008; Ruiz-Fons et al., 2008; Garcia et al., 2009; Rodriguez-Sanchez et al., 2010a,b).

Although bluetongue is a disease found in ruminants and camelids, under certain circumstances it can also be transmitted to carnivores. In dogs, for instance, bluetongue has been reported following the use of a BTV-contaminated vaccine (Wilbur et al., 1994; Evermann, 2008). Bluetongue has also

been recorded in Eurasian lynxes (*Lynx lynx*) kept in a Belgian zoo; the cats were fed on aborted or stillborn foetuses of ruminants raised on neighbouring farms (Jauniaux et al., 2008). Specific antibodies to BTV were also identified in African carnivores including lions, cheetahs, wild dogs, jackals, hyenas and large-spotted genets (Alexander et al., 1994). These findings can also be explained by ingestion of flesh and organs of BTV-infected animals. In the USA antibodies against BTV have been found in Florida black bears (*Ursus americanus floridanus*), Florida panthers (*Puma concolor coryi*) (Dunbar et al., 1998) and domestic dogs (*Canis familiaris*) (Howerth et al., 1995).

6. Overwintering

The survival of virus from one "vector season" to the next is called "overwintering", but the mechanism involved is still poorly understood. However, BTV can survive in the absence of adult vectors for nine to 12 months of cold weather in an infected host with no detectable viraemia, disease or seroconversion (Taylor and Mellor, 1994; Takamatsu et al., 2003; Osmani et al., 2006; Wilson et al., 2007). One way in which overwintering may be achieved is by the infection of adult vectors (Wilson et al., 2008). Although the average life span of these is usually ten to 20 days (Mellor, 2000), they can occasionally live for up to three months (Lysyk and Danyk, 2007). During the winter of 2006–2007, which was exceptionally mild in Europe (Wilson et al., 2008), some small numbers of adult *Culicoides* midges were recorded in Belgium (Losson et al., 2007). This suggests that under favourable conditions some biting midges can live long enough to survive the period between two vector seasons (Wilson et al., 2008). Possibilities for BTV to survive at different stages of the *Culicoides* life cycle have also been investigated. It has previously been shown that, in biting midges, small RNA fragments, but not the whole virus, can pass through pores of vitelline membrane (Nunamaker et al., 1990). Further evidence was provided by White et al. (2005) who detected BTV RNA in midge larval stages; however, transfer of virus in larvae has not been demonstrated. Takamatsu et al. (2003) have shown in an *in vitro* study that BTV can persistently infect ovine T-cells, a process that may also occur during infection and viraemia in mammalian hosts, thus providing a mechanism for virus persistence. This hypothesis, however, has not been confirmed (Lunt et al., 2006; Wilson et al., 2008). In some instances, the virus could overwinter in cattle owing to prolonged BTV viraemia, which can occasionally last up to 100 days (Sellers and Taylor, 1980), or due to latent BTV infection (Luedke et al., 1977). Another mechanism suggested for BTV overwintering is transplacental infection (De Clercq et al., 2008; Menzies et al., 2008; Backx et al., 2009; Darpel et al., 2009; Lewerin et al., 2010; Santman-Berends et al., 2010). Pregnancy in cattle is long enough for BTV to survive during a period free of competent insect vectors (Wilson et al., 2008). Mechanical vectors may also be involved in virus overwintering; BTV has been isolated from the sheep ked (Luedke et al., 1965) and some tick species (Stott et al., 1985; Bouwknegt et al., 2010), which are arthropod species living much longer than *Culicoides* midges. In addition, the trans-stadial passage found in hard ticks and trans-ovarial passage in soft ticks suggests their role in virus transmission (Bouwknegt et al., 2010). Mechanical vectors should therefore be regarded as potential reservoirs for BTV (Wilson et al., 2008; Bouwknegt et al., 2010).

7. Pathogenesis

After introduction through the bite of an infected midge, the virus is transported by the host dendritic cells from the skin to the local lymph nodes (Hemati et al., 2009), the sites of initial virus replication (MacLachlan, 2004). Subsequently, it spreads to the blood circulation inducing a primary viraemia which seeds secondary organs, i.e., lymph nodes, spleen and lungs (Barratt-Boyes and MacLachlan, 1994; Sanchez-Cordon et al., 2010). The virus replicates in vascular endothelial cells, macrophages and lymphocytes (MacLachlan et al., 1990, 2009; Barratt-Boyes and MacLachlan, 1994; MacLachlan, 2004; Drew et al., 2010a). In early viraemia virus is associated with all blood elements, while at later stages of viraemia it exclusively associates with erythrocytes (MacLachlan et al., 1990, 2009; MacLachlan, 2004). Virus particles appear to be sequestered in invaginations of the erythrocyte membrane (Brewer and MacLachlan, 1994; MacLachlan, 2004), allowing prolonged viraemia in the presence of neutralizing antibodies (Richards et al., 1988; Brewer and MacLachlan, 1994). Free virus in low titres is found in blood plasma only at the initial stages of infection (MacLachlan et

al., 1990; MacLachlan, 1994; Barratt-Boyes and MacLachlan, 1994).

Infection with BTV results in cell necrosis and apoptosis (Barratt-Boyes et al., 1992; DeMaula et al., 2001; Mortola et al., 2004) and, by activating the p38MAP kinase, the virus increases vascular permeability (Chiang et al., 2006; Drew et al., 2010b). In addition, it induces the production of TNFα, IL-1, IL-8, IL-6, IFN-I and cyclooxygenase-2, and enhances plasma concentration of prostacyclin and thromboxane, which frequently leads to an excessive inflammatory response and subsequent damage to the cells and tissues of the infected animal (MacLachlan and Thompson, 1985; DeMaula et al., 2001, 2002; Schwartz-Cornil et al., 2008; Drew et al., 2010a). The pathogenesis of bluetongue is characterised by injury to small blood vessels in target tissue, resulting in vascular occlusion and tissue infarction. Virus-induced vasoactive mediators produced by thrombocytes, dendritic cells, macrophages and BTV-infected endothelial cells increase damage to the endothelium, interfere with its function and increase vascular permeability; this leads to the development of oedema and effusions (MacLachlan et al., 2009; Drew et al., 2010a).

7.1. Viraemia and immune response

Viraemia in infected animals has a prolonged course, but is not persistent (Barratt-Boyes and MacLachlan, 1995; Bonneau et al., 2002; Melville et al., 2004). Its duration depends on the longevity of erythrocytes to which virus is bound, in contrast to the other blood cells, even at the late stage of infection (MacLachlan et al., 2009). It is also related to the species and breed of the infected animal. Viraemia lasts 14 to 54 days in sheep and 19 to 54 days in goats (Barzilai and Tadmor, 1971; Luedke and Anakwenze, 1972; Koumbati et al., 1999). In cattle, viraemia may last as long as 60 or, even 100 days (Sellers and Taylor, 1980), which makes this animal an important host from the epidemiological point of view.

The infected animals react to BTV with interferon production and humoral and cell-mediated immune responses (MacLachlan and Thomson, 1985; MacLachlan, 1994). Serotype-specific neutralising antibodies against the VP2 protein confer protection against homologous strain reinfection (Cowley and Gorman, 1987; Hassan and Roy, 1999; Roy, 1992; Schwartz-Cornil et al., 2008). Neutralising antibodies are also induced, to a lesser degree, by the VP5 protein (Roy, 1992; Lobato et al., 1997). The sera of infected ruminants also contain serogroup-specific antibodies induced by the VP7 protein, as well as antibodies against other structural and non-structural proteins (MacLachlan et al., 1987; Richards et al., 1988; MacLachlan, 2004). The cell-mediated immune response to BTV can probably reduce the spread of virus in the organism early after infection, but cannot eliminate the virus completely (MacLachlan, 1994; Barratt-Boyes et al., 1995). By producing a cytotoxic effect in infected cells, CD8+ T-lymphocytes play the most important role (MacLachlan, 1994; Barratt-Boyes et al., 1995; Schwartz-Cornil et al., 2008).

8. Clinical signs

Bluetongue in sheep is manifested as an acute, chronic or subclinical condition; fine wool breeds are most susceptible. An incubation period of four to eight days (Tweedle and Mellor, 2002) is followed by fever, apathy, tachypnea, and hyperaemia of the lips and nostrils with excessive salivation and serous nasal discharge that is initially clear, then becomes mucopurulent and upon drying may form a crust around the nostrils. Oedema of the tongue, lips, submandibulum and sometimes ears appears, petechiae develop on the conjunctiva and ulcers on the oral mucosa. Cyanotic tongues are found in rare cases. In some cases, dyspnoe, profuse haemorrhagic diarrhoea or vomiting that can cause aspiration pneumonia is recorded. At the end of the pyrexia stage, affected sheep may have coronitis, laminitis or paresis and necrosis of striated muscles and, as a result, stand with an arched back and are reluctant to move. Torticollis, dermatitis and breaks in the wool may also develop (Brewer and MacLachlan, 1994; Tweedle and Mellor, 2002; Anonymous, 2004; Darpel et al., 2007; Elbers et al., 2008a, 2009; Kirschvink et al., 2009). Infection in pregnant ewes may lead to abortion, foetal mummification and the birth of weak calves with potential congenital defects (hydrocephalus, cerebral cysts, retinal dysplasia, etc.) (Osburn et al., 1971; Osburn, 1994; MacLachlan et al., 2000; Tweedle and Mellor, 2002; Saegerman et al., 2011). Chronically affected sheep may succumb to other diseases such as bacterial pneumonia (MacLachlan and Gard, 2009).

Goats are less frequently infected with BTV, and rarely show any signs of clinical disease. If they do, the signs are similar to but less severe than in sheep.

In the 2006 epidemic in the Netherlands, the diseased goats showed a sudden drop in milk production, high temperature, oedema of the lips and head, nasal discharge and scabs on the nose and lips, erythema of the skin of the udder and small subcutaneous haemorrhagic lesions (Dercksen et al., 2007).

In cattle clinical disease is rare (Tweedle and Mellor, 2002) with the exception of BTV-8 infection in which clinical signs are manifested in large numbers of animals (Elbers et al., 2008b). Clinical infection is considered a hypersensitivity reaction mediated by the IgE antibody (Anderson et al., 1987). The early stages are characterised by fever, apathy and depression followed by erosion and necrosis of the oral and nasal musocae, nasal discharge, excessive salivation, conjunctivitis, lameness and stiffness, ulcerative dermatitis, coronitis, occasional bloody diarrhoea, oedema and hyperaemia. The skin of teats is often inflamed and may crack and peel (Tweedle and Mellor, 2002; Thiry et al., 2006; Williamson et al., 2008; Elbers et al., 2008a, 2009). Milking cows show reduced milk production (Thiry et al., 2006; Mehlhorn et al., 2008; Elbers et al., 2009). Infection of dams in early stages of pregnancy can result in early death and resorption of the embryo; other consequences involve abortion or the birth of malformed and weak calves (MacLachlan et al., 2000; Tweedle and Mellor, 2002; Elbers et al., 2008a; Desmecht et al., 2008). If dams survive, the foetuses infected between 70 and 130 days of gestation develop serious CNS malformations (hydrocephalus, cerebral defects) while those infected a few weeks before delivery usually have only mild encephalitis (Waldvogel et al., 1992; MacLachlan et al., 2000).

In white-tailed deer bluetongue has, similarly to epizootic haemorrhagic disease of deer, an acute course manifested as haemorrhagic diathesis as a sequela to disseminated intravascular coagulation (Waldvogel et al., 1992; MacLachlan et al., 2000). It is characterised by widespread haemorrhages throughout the body, swelling of the head and neck, hypersalivation, blood-stained nasal discharge and bloody diarrhoea (Radostits et al., 1994; Howerth et al., 2001).

9. Pathology

Necropsy findings in affected animals reveal subcutaneous tissues infiltrated with gelatinous fluid in the head, haemorrhages in the tunica media of the pulmonary artery or even aorta, hyperaemia, or occasionally cyanosis, of the oral mucosa with petechiae and ecchymoses. Erosions with coats of necrotic tissue may be present in the lips, tongue and cheeks. There may be hyperaemia of the ruminal pillars and reticular folds. The spleen, lymphatic nodes and tonsils are enlarged and haemorrhagic, occasionally with petechiae. The tongue root, pericardial sac, kidney, gut (particularly at the iliocaecal junction) and subcutaneous tissues may have petechiae. The skeletal and heart musculature shows light necrotic areas. In addition, inflammation of the upper respiratory tract, pulmonary oedema, pleuritis, pericarditis or enteritis may be present (Tweedle and Mellor, 2002; Darpel et al., 2007; Mauroy et al., 2008; MacLachlan et al., 2009).

Histological findings include hypertrophy of endothelial capillaries, perivascular oedema and infiltration of skeletal and cardiac muscle with macrophages and lymphocytes, vascular congestion with subsequent tissue infarction leading to epithelial tissue hypoxia and cell desquamation. In acute cases heart and skeletal muscles have haemorrhage and necrosis which, in chronic cases, results in fibrosis and infiltration with mononuclear cells (Brodie et al., 1998; Tweedle and Mellor, 2002; MacLachlan et al., 2009).

10. Diagnosis

A preliminary diagnosis based on clinical signs, post-mortem findings and epidemiological assessment should be confirmed by laboratory examination (Afshar, 1994).

Samples to be examined in the laboratory should include non-coagulated blood (use of ethylenediaminetetraacetic acid or heparin is preferred), blood serum, post-mortem tissue samples of spleen, lymph nodes, lungs, liver, bone marrow and, when indicated, heart and skeletal muscles; in addition, brain tissue is collected in foetuses (Stott et al., 1983; Parsonson, 1990; Afshar, 1994; Tweedle and Mellor, 2002).

For transport, blood serum samples should be frozen at –20 °C and the other samples should be kept on ice (Tweedle and Mellor, 2002). Full blood samples can be stored at +4 °C for a long time; isolated blood cells in 10% dimethyl sulphoxide require storage at a temperature of –70 °C (Thomas, 1984).

10.1. Bluetongue virus isolation

Bluetongue virus can be propagated in embryonated chicken eggs, cell cultures or in sheep.

Embryonated eggs, nine to 12 days old, are used for BTV isolation (Anonymous, 2004) and intravenously inoculated with the material examined. This method is 100- to 1000-fold more sensitive than yolk sac inoculation (Goldsmit and Barzilai, 1985), but is demanding in terms of technical skills and experience (Clavijo et al., 2000). The material obtained from embryonated eggs can either be further propagated in cell culture or directly examined using molecular methods (PCR or *in situ* hybridisation) (Schoepp et al., 1991; Katz et al., 1994; Wang et al., 1988; Clavijo et al., 2000).

Bluetongue virus can also be isolated in cell lines of insect origin, such as the KC line derived from *Culicoides sonorensis* cells or the C6/36 line from *Aedes albopictus* (AA) cells; the mammalian BHK-21, CPAE or Vero cell lines can also be used (Wechsler and McHolland, 1988; Anonymous, 2004; Mecham, 2006). The cytopathic effect produced by BTV is observed only on cell lines of mammalian origin at three to five days after inoculation and appears as foci of rounded and refractile cells (Clavijo et al., 2000). The isolation of virus in cell culture is usually preceded by its passage in embryonated chicken eggs which are more susceptible to BTV than cell lines (Afshar, 1994; Clavijo et al., 2000).

Sheep can provide a sensitive and reliable system for BTV isolation; however, today they are used only occasionally, e.g., in cases when a sample contains a very low virus titre (Afshar, 1994; Anonymous, 2004).

10.2. Antigen identification

A direct identification of BTV in blood or tissue samples is possible with use of the reverse transcription-polymerase chain reaction (RT-PCR) method that allows for serotyping and can detect BTV RNA in samples as late as six months after infection (Katz et al., 1994; MacLachlan et al., 1994). A quantitative assessment of RNA in an examined sample is possible by real time-RT-PCR (Shaw et al., 2007; Toussaint et al., 2007). The identification of a BTV serotype is carried out in the virus neutralisation test. Other available diagnostic methods include antigen-capture ELISA, immunospot and immunofluorescence tests (Anonymous, 2004), but they are rarely used.

10.3. Antibody identification

Serogroup-specific antibodies against BTV can be detected by a competitive ELISA test targeted to the VP7 protein. This is a rapid method permitting determination of serum or plasma antibody as early as the 6th post-infection day (Koumbati et al., 1999). There are other commercial ELISA kits developed recently by which early antibodies or antibodies against BTV in individual or bulk milk samples can be detected (Mars et al., 2010). In addition, serogroup-specific antibodies can be identified by an agar-gel immunodiffusion test, which, however, may produce cross-reactions with other orbiviruses (Afshar et al., 1989), a complement-fixation test and a haemagglutination-inhibition test (Anonymous, 2004). The serum neutralisation test has the highest specificity and sensitivity of all the tests, but is also most expensive and time-consuming (Reddington et al., 1991; Hamblin, 2004).

11. Differential diagnosis

The clinical signs of bluetongue can easily be mistaken for those of other ruminant diseases such as orf (contagious pustular dermatitis), foot-and mouth disease, acute photosensitisation, acute haemonchosis (with depression and submandibular oedema), facial eczema, *Oestrus ovis* infestation, pneumonia, plant poisoning, salmonellosis, sheep pox, peste des petits ruminants (Tweedle and Mellor, 2002; Williamson et al., 2008), malignant catarrhal fever, pododermatitis, rinderpest, infectious bovine rhinotracheitis, bovine viral diarrhoea, bovine popular stomatitis, bovine herpes mamillitis and epizootic haemorrhagic disease (Frank and Willis 1975; Mehlhorn et al., 2008; Williamson et al., 2008; Savini et al., 2011).

12. Prevention and control

There is no specific therapy for animals with bluetongue. Symptomatic therapy includes gentle handling of affected animals, their stabling and, if indicated, administration of non-steroidal antiphlogistic drugs (Radostits et al., 1994; Tweedle and Mellor, 2002).

An immediate ban on animal import from countries with bluetongue is the priority measure, followed by the monitoring of farms raising domestic ruminants which include clinical examination and

serological and virological testing, and a monitoring of insect vectors. Prophylactic immunisation and the removal of vectors or prevention of vector attacks can also be used.

12.1. Prophylactic immunisation

Vaccination can prevent clinical bluetongue or at least mitigate its course by interrupting the BTV cycle in the environment; it thus reduces the economic losses due to animal infection and makes transfer and trading of animals from BTV enzootic regions possible (Savini et al., 2008; Bhanuprakash et al., 2009; Caporale and Giovannini, 2010). Bluetongue vaccines are serotype-specific (Bhanuprakash et al., 2009) and therefore, before use in a given area, the serotypes present in the environment should be taken into account. Two types of vaccines, inactivated and live attenuated, are currently available.

12.1.1. Live attenuated vaccines

Live attenuated vaccines were until recently the only bluetongue vaccines commercially available (Caporale and Giovannini, 2010), and were originally used in endemic situations where multiple serotypes of virus are common (e.g., South Africa). In these regions multivalent live attenuated vaccines against the serotypes present there are still used (Veronesi et al., 2005). One dose of attenuated vaccine is enough to provide good protection for at least one year. Their production is inexpensive, which is another advantage (Savini et al., 2008; Bhanuprakash et al., 2009), but they may lose efficiency at temperatures over 35 °C (Hammoumi et al., 2003) and may provide poor protection against infection with a heterologous BTV serotype (Tweedle and Mellor, 2002). However, there are growing concerns about the use of BTV attenuated commercial vaccines (Veronesi et al., 2005) which can result in clinical signs of bluetongue, abortion, reduced milk production, temporary poor semen quality in rams (Breard et al., 2007; Savini et al., 2008) and foetal malformation if pregnant ewes are vaccinated (Flanagan and Johnson, 1995; Tweedle and Mellor, 2002; Bhanuprakash et al., 2009). For these reasons it is recommended to vaccinate ewes nine to 15 weeks before mating, and rams after the mating period (Bhanuprakash et al., 2009) but at least six weeks before the beginning of the following period (Savini et al., 2008). Attenuated vaccine virus can also produce viraemia lasting over two weeks in vaccinated sheep (Veronesi et al., 2005). There is a possibility that vaccine virus will infect vectors and revert to virulence, or will produce a recombinant progeny virus with novel properties after the reassortment of genes from wild and vaccine virus in the vaccinated animal or the vector (de Mattos et al., 1994; Tweedle and Mellor, 2002; Veronesi et al., 2005; Savini et al., 2008). However, Caporale and Giovannini (2010) consider these possibilities as only hypothetical and they remain unsupported by factual scientific data.

12.1.2. Inactivated vaccine

If properly produced, inactivated vaccines can induce reliable and protective immunity that, for a good and lasting effect, requires re-vaccination (Savini et al., 2008, 2009). Although their production is rather expensive, at present they are the best compromise in terms of safety and efficiency (Schwartz-Cornil et al., 2008; Bhanuprakash et al., 2009). Well inactivated vaccines can prevent the development of clinical disease in susceptible hosts, reduce direct economic losses due to infection, facilitate safe trading in animals and prevent the development of vireaemia, or make it less severe, following infection with a homologous BTV serotype (Tweedle and Mellor, 2002; Bhanuprakash et al., 2009). After the 1998 outbreaks of bluetongue in Southern Europe, monovalent inactivated vaccines were first prepared against BTV-2, then against BTV-4; bivalent vaccines were made against BTV-2 and BTV-4 (Savini et al., 2008). Today monovalent vaccines against BTV-1, BTV-8 and BTV-9 are available (Zientara et al., 2010). Strategies for differentiating infected from vaccinated animals (DIVA) are theoretically possible with inactivated vaccines, but have not yet been developed (Bhanuprakash et al., 2009).

12.1.3. New-generation vaccines

At the present moment new types of vaccines are being developed; they include, for instance, recombinant vector vaccines, sub-unit vaccines and others which would offer advantages such as no risk of

virus transmission, rapid onset of immune response or options to make them polyvalent or as DIVA vaccines (Savini et al., 2008; Bhanuprakash et al., 2009; Roy et al., 2009). However, they are expected to have a considerably higher price, which would be a disadvantage (Bhanuprakash et al., 2009).

12.2. Vector control

Understandably, it is impossible to completely eliminate *Culicoides* midges in the natural environment. It is possible, however, to reduce midge populations to ineffective levels, or to prevent vector attacks by stabling susceptible animals overnight since midges have nocturnal feeding habits. In addition, the protection of animals in stables can be improved by door and window screens made of a fine mesh or a coarse fabric impregnated with insecticide (Radostits et al., 1994; Calvete et al., 2010). Alternative approaches involve moving the animas from insect resting and breeding sites or complete elimination of such sites. The species *C. imicola*, *C. obsoletus* and *C. pulicaris* breed in wet soils rich in organic matter and such grounds should be drained and dried.

The control of adult midges can be carried out by use of approved insecticides (Schmahl et al., 2009a,b) applied outside or inside (in areas with *C. dewulfi* occurrence) the stable or directly to the susceptible animals. The latter approach is allowed only with agents of low toxicity to mammals such as synthetic pyrethroids (deltamethrin, cyfluthrin, permethrin and fenvalerate); these agents provide protection for three to five weeks (Mehlhorn et al., 2009; Schmahl et al., 2009a,b) and can be used in the form of insecticide-impregnated ear tags. Animals can also be protected by systemic invermectins administered intradermally or subcutaneously. The larvicide Abate (5% temephos granulated with gypsum) can be applied to midge breeding grounds. Insect repellents can also be used for direct protection of animals; diethyl toluamide (DEET), for instance, is effective for up to four hours (Tweedle and Mellor, 2002).

12.3. Measures for bluetongue control

In accordance with European Union Council Directive No 2000/75/EC, in the case of bluetongue, three zones of restriction are defined, namely, a zone of 20-km radius around the infected premises, and a protection zone and a surveillance zone together of at least 150-km radius around the infected premises (Caporale and Giovannini, 2010). In the European Union, Commission Regulation (EC) No 1266/2007, as amended, lays down rules for the control, monitoring, surveillance and restrictions on movements of animals, in relation to bluetongue, in and from the restricted zones. Veterinary investigations are carried out, suspect animals are examined and samples are taken for laboratory tests. The reference laboratory for bluetongue in the European Union is the Pirbright Laboratory of the AFRC Institute for Animal Health in the United Kingdom.

13. Situation in the Czech Republic

A total of 14 bluetongue outbreaks have so far been reported in the Czech Republic and all occurred in cattle herds. In contrast to Western Europe, the disease had a mild course and only one out of 25 affected animals showed clinical signs. Similarly to other European countries (Caporale and Giovannini, 2010), the compulsory vaccination of all domestic ruminants all over the country, with an inactivated vaccine against BTV-8, was started in 2008. Currently, due to favourable bluetongue status, the vaccination is only voluntary for all domestic ruminants, since April 2011. Monitoring of insect vectors and other measures are implemented in accordance with Commission Regulation (EC) No. 1266/2007. The State Veterinary Institute in Jihlava serves as the Czech national reference laboratory for bluetongue. The Department of Parasitology, Faculty of Science, Charles University in Prague, is responsible for insect vector monitoring and examination.

14. REFERENCES

Afshar A (1994): Bluetongue: laboratory diagnosis. Comparative Immunology, Microbiology and Infectious Diseases 17, 221–242.

Afshar A, Thomas FC, Wright, PF, Shapiro JL, Anderson J (1989): Comparison of competitive ELISA, indirect ELISA and standard AGID tests for detecting bluetongue virus antibodies in cattle and sheep. Veterinary Record 124, 136–141.

Agren ECC, Burgin L, Sternberg Leverin S, Gloster J, Elvander M (2010): Possible means of introduction of

bluetongue virus serotype 8 (BTV-8) to Sweden in August 2008: comparison to results from two models for atmospheric transport of Culicoides vector. Veterinary Record 167, 484–488.

Alexander KA, MacLachlan NJ, Kat WP, House C, O'Brien SJ, Lerche NW, Sawyer M, Frank GL, Holekamp K, Smale L, McNutt WJ, Laurensen MK, Mills MGL, Ossburn BI (1994): Evidence of natural bluetongue virus infection among african carnivores. The American Journal of Tropical Medicine and Hygiene 51, 568–576.

Anderson GA, Scott JL, Gershwin LJ, Osburn BI (1987): Identification of bluetongue virus specific immunoglobulin E in cattle. Journal of General Virology 68, 2509–2514.

Anonymous (2004): Manual of diagnostic test and vaccines for terrestrial animals. 5th ed. Chapter 2.1.9. Bluetongue, Office International Des Epizooties, Paris. http://web.oie.int/fr/normes/mmanual/A_00032.htm (accessed June 29, 2011)

Anonymous (2007): Scientific Report of the Scientific Panel on Animal Health and Welfare on request from the Commission (EFSA-Q-2006-311) and EFSA Self-mandate (EFSA-Q-2007-063) on bluetongue. EFSA Journal 479, 1–29; 480, 1–20.

Anonymous (2009a): Bluetongue. Animal disease data. Office International des Epizooties, Paris. http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/BLUETONGUE_FINAL.pdf (accessed July 29, 2010).

Anonymous (2009b): Bluetongue, Norway (Immediate notification: 20/02 2009), Ref OIE: 7815. Anonymous http://web.oie.int/wahis/public.php?page=single_report&pop=1&reportid=7815 (accessed March 20, 2011).

Anthony S, Jones H, Darpel KE, Elliott H, Maan S, Samuel A, Mellor PS, Mertens PP (2007): A duplex RT-PCR assay for detection of genome segment 7 (VP7gene) from 24 BTV serotypes. Journal of Virological Methods 141, 188–197.

Backx A, Heutink R, van Rooij E, van Rijn P (2009): Transplacentar and oral transmission of wild-type bluetongue virus serotype 8 in cattle after experimental infection. Veterinary Microbiology 138, 235–243.

Balczun C, Vorsprach B, Meiser CM, Schaub GA (2009): Changes of the abundance of Culicoides obsoletus s.s. and Culicoides scoticus in southwest Germany identified by PCR-based differentiation. Parasitology Research 105, 345–349.

Baldet T, Delecolle JC, Cetre-Sossah C, Mathieu B, Meiswinkel R, Gerbier G (2008): Indoor activity of Culicoides associated with livestock in the bluetongue virus (BTV) affected region of northern France during autumn 2006. Preventive Veterinary Medicine 87, 84–97.

Barratt-Boyes S, MacLachlan NJ (1994): Dynamics of viral spread in bluetongue virus infected calves. Veterinary Microbiology 40, 361–371.

Barratt-Boyes S, MacLachlan NJ (1995): Pathogenesis of bluetongue virus infection of cattle. Journal of the American Veterinary Medical Association 206, 1322–1329.

Barratt-Boyes SM, Rossitto PV, Stott JL, MacLachlan NJ (1992): Flow cytometric analysis of in vitro bluetongue virus infection of bovine blood mononuclear cells. Journal of General Virology 73, 1953–1960.

Barratt-Boyes SM, Rossitto PV, Taylor BC, Ellis JA, MacLachlan NJ (1995): Response of the regional lymph node to bluetongue virus infection in calves. Veterinary Immunology and Immunopathology 45, 73–84.

Bartsch S, Bauer B, Wiemann A, Clausen P-H, Steuber S (2009): Feeding patterns of biting midges of the Culicoides obsoletus and Culidoides pulicaris groups on selected farms in Brandenburg, Germany. Parasitology Research 105, 373–380.

Barzilai E, Tadmor A (1971): Multiplication of bluetongue virus in goats following experimental infection. Refuah Veterinarith 23, 11–20.

Batten CA, Maan S, Shaw AE, Maan NS, Mertens PPC (2008): A European field strain of bluetongue virus derived from two parenteral vaccine strains by genome segment reassortment. Virus Research 137, 56–63.

Baylis M, Mellor PS (2001): Bluetongue around the Mediteranean in 2001. Veterinary Record 149, 659.

Bekker JG, de Kock G, Quinlan JB (1934): The occurrence and identification of bluetongue in cattle – the so-called pseudo foot-and-mouth disease in South Africa. Onderstepoort Journal of Veterinary Science and Animal Industry 2, 393–507.

Belyaev AS, Roy P (1993): Development of baculovirus triple and quadruple expression vectors: co-expression of three or four bluetongue virus proteins and the synthesis of bluetongue virus-likeparticles in insect cells. Nucleic Acids Research 21, 1219–1223.

Bhanuprakash V, Indrani BK, Hosamani M, Balamurugan V, Singh RK (2009): Bluetongue vaccines: the past, present and future. Expert Reviews Vaccines 8, 191–204.

Birley MH, Boorman JPT (1982): Estimating the survival and biting rates of haematophagous insect with particular reference to Culicoides obsoletus group in Southern England. Journal of Animal Ecology 51, 135–148.

Blancou J, Pearson JE (2003): Bioterrorism and infectious animal diseases. Comparative Immunology, Microbiology and Infectious Diseases 26, 431–443.

Bonneau KR, DeMaula CD, Mullens BA, MacLachlan NJ (2002): Duration of viremia infectious to Culicoides sonorensis in bluetongue virus-infected cattle and sheep. Veterinary Microbiology 88, 115–125.

Borkent A (2005): The biting midges, the Ceratopogonidae (Diptera). In: Marquardt WH (ed.): Biology of Disease Vectors. Elsevier Academic Press, Burlington, Massachusetts. 113–126.

Bouwknegt C, van Rijn PA, Schipper JM, Holzel D, Boonstra J, Nijhof AM, van Rooij MA, Jongejan F (2010): Potential role of ticks as vectors of bluetongue virus. Experimental and Applied Acarology, 52, 183–92.

Bowen RA, Howard TH (1984): Transmision of bluetongue virus by intrauterine inoculation or insemination of virus-containing bovine semen. American Journal of Veterinary Research 45, 1386–1388.

Breard E, Pozzi N, Sailleau C, Durand B, Catinot V, Sellem E, Dumont P, Guerin B, Zientara S (2007): Transient adverse effects of an attenuated bluetongue virus vaccine on the quality of ram semen. Veterinary Record 160, 431–435.

Brewer AW, MacLachlan NJ (1994): The pathogenesis of bluetongue virus infection of bovine blood cells in vitro: ultrastructural characterization. Archives of Virology 136, 287–298.

Brodie SJ, Wilson WC, O'Hearn PM, Muthui D, Diem K, Pearson LD (1998): The effects of pharmacological and lentivirus-induced immune suppression on orbivirus pathogenesis: assessment of virus burden in blood monocytes and tissues by reverse transcription – In situ PCR. Journal of Virology 72, 5599–5609.

Brookes SM, Hyat AD, Eaton BT (1993): Characterization of virus inclusion bodies in bluetongue virus-infected cells. Journal of General Virology 74, 525–530.

Brown ES, Gorman BM, Tesh RB, Knudson DL (1992): Isolation of bluetongue and epizootic hemorrhagic disease viruses from mosquitoes collected in Indonesia. Veterinary Microbiology 32, 241–251.

Calvete C, Estrada R, Miranda MA, Del Rio R, Borras D, Beldron FJ, Martinez A, Calvo AJ, Lucientes J (2010): Protection of livestock against bluetongue virus vector Culicoides imicola using insecticide-treated netting in open areas. Medical and Veterinary Entomology 24, 169–175.

Calvo-Pinilla E, Nieto JM, Ortego J (2010): Experimental oral infection of bluetongue virus serotype 8 in type I interferon receptor-deficient mice. Journal of General Virology 91, 2821–2825.

Campbell JA, Pelham-Clinton EC (1960): A taxonomic review of the British species of Culicoides Latreille. Proceedings of the Royal Society of Edinburgh (B) 67, 181–302.

Caporale V, Giovannini A (2010): Bluetongue control strategy, including recourse to vaccine: a critical review. Revue Scientifique et Technique-Office International des Epizooties 29, 573–591.

Caracappa S, Torina A, Guercio A, Vitale F, Calabró A, Purpari G, Ferrantelli V, Vitale M, Mellor PS (2003): Identification of a novel bluetongue virus vector species of Culicoides in Sicily. Veterinary Record 153, 71–74.

Carpenter S, Lunt HL, Arav D, Venter GJ, Mellor PS (2006): Oral susceptibility to bluetongue virus of Culicoides (Diptera: Ceratopogonidae) from the United Kingdom. Journal of Medical Entomology 43, 73–78.

Carpenter S, Wilson A, Mellor PS (2009): Culicoides and the emergence of bluetongue virus in northern Europe. Trends in Microbiology 17, 172–178.

Carpi G, Holmes EC, Kitchen A (2010): The evolutionary dynamics of bluetongue virus. Journal of Molecular Evolution 70, 583–592.

Chaignat V, Worwa G, Scherrer N, Hilbe M, Ehrensperger F, Batten C, Cortyen M, Hofmann M, Thuer B (2009): Toggenburg orbivirus, a new bluetongue virus: Initial detection, first observations in field and experimental infection of goats and sheep. Veterinary Microbiology 138, 11–19.

Chandler LJ, Ballinger ME, Jones RH, Beaty BJ (1985): The virogenesis of bluetongue virus in Culicoides variipennis. Progress in Clinical and Biological Research 6, 245–253.

Chiang ET, Persaud-Sawin DA, Kulkarni S, Garcia JG, Imani F (2006): Bluetongue virus and double-stranded RNA increase human vascular permeability: role of p38 MAPK. Journal of Clinical Immunology 26, 406–416.

Clavijo A, Heckert RA, Dulac GC, Afshar A (2000): Isolation and identification of bluetongue virus. Journal of Virological Methods 87, 13–23.

Clavijo A, Sepulveda L, Riva J, Pessoa-Silva M, Tailor-Ruthes A, Lopez JW (2002): Isolation of bluetongue virus serotype 12 from an outbreak of the disease in South America. Veterinary Record 151, 301–302.

Corn JL, Kavanaugh DM, Osborn DA, Denariais S, Milke CM, Nettles VF (1990): Survey for diseases and parasites in exotic ruminants in Texas. Proceedings of the United States Animal Health Association 94, 530–540.

Cowley JA, Gorman BM (1987): Genetic reassortments for identification of the genome segment coding for the bluetongue virus hemagglutinin. Journal of Virology 61, 2304–2306.

Cowley JA, Gorman BM (1989): Cross-neutralization of genetic reassortants of bluetongue virus serotypes 20 and 21. Veterinary Microbiology 19, 37–51.

Darpel KE, Batten CA, Veronesi E, Shaw AE, Anthony S, Bachanek-Bankowska K, Kgosana L, Bin-Tarif A, Carpenter S, Muller-Doblies UU, Takamatsu H-H, Mellor PS, Mertens PPC, Oura CAL (2007): Clinical signs and pathology shown by British sheep and cattle infected with bluetongue virus serotype 8 derived from the 2006 outbreak in northern Europe. Veterinary Record 161, 253–261.

Darpel KE, Batten CA, Veronesi E, Williamson S, Anderson P, Dennison M, Clifford S, Smith C, Philips L, Bidewell C, Bachanek-Bankowska K, Sanders A, Bin-Tarif A, Wilson AJ, Gubbins S, Mertens PPC, Oura CA, Mellor PS (2009): Transplacental transmission of bluetongue virus 8 in cattle, UK. Emerging Infectious Diseases 15, 2025–2028.

Davies FG (1978): Bluetongue studies with sentinel cattle in Kenya. Journal of Hygiene (London) 80, 197–204.

De Clercq K, De Leeuw I, Verheyden B, Vandemeulebroucke E, Vanbinst T, Herr C, Meroc E, Bertels G, Steurbaut N, Miry C, De Bleecker K, Maquet G, Bughin J, Saulmont M, Lebrun M, Sustronck B, De Deken R, Hooyberghs J, Houdart P, Raemaekers M, Mintiens K, Kerhofs P, Goris N, Vandenbussche F (2008): Transplacental infection and apparently immunotolerance induced by a wild-type bluetongue virus serotype 8 natural infection. Transboundary and Emerging Diseases 55, 352–359.

De Clercq K, Mertens P, De Leeuw I, Oura C, Houdart P, Potgieter AC, Maan S, Hooyberghs J, Batten C, Vandemeulebroucke E, Wright IM, Maan N, Riocreux F, Sanders A, Vanderstede Y, Nomikou K, Raemaekers M, Bin-Tarif A, Shaw A, Henstock M, Breard E, Dubois E, Gastaldi-Thiery C, Zientara S, Verheyden B, Vandenbussche F. (2009): Emergence of bluetongue serotypes in Europe, Part 2: The occurrence of a BTV-11 strain in Belgium. Transboundary and Emerging Diseases 56, 355–361.

De Mattos CC, de Mattos CA, Osburn BI, MacLachlan NJ (1994): Heterogeneity of the L2 gene of field isolates of bluetongue virus serotype 17 from the San Joaquin Valley of California. Virus Research 31, 67–87.

DeMaula CD, Jutila MA, Wilson DW, MacLachlan NJ (2001): Infection kinetics, prostacyclin release and cytokine-mediated modulation of the mechanism of cell death during bluetongue virus infection of cultured ovine and bovine pulmonary artery and lung microvascular endothelial cells. Journal of General Virology 82, 787–794.

DeMaula CD, Leutenegger CM, Bonneau KR, MacLachlan NJ (2002): The role of endothelial cell-derived inflammatory and vasoactive mediators in the pathogenesis of bluetongue. Virology 296, 330–337.

Dercksen D, Groot Nibbelink N, Paauwe R, Backx A, van Rijn P, Vellema P (2007): First outbreak of bluetongue in goats in The Netherlands (in Dutch). Tijdschrift Diergeneeskunde 132, 786–790.

Desmecht D, Vanden Bergh R, Sartelet A, Leclerc M, Mignot C, Misse F, Sudraud C, Berthemin S, Jolly S, Mousset B, Linden A, Coignoul F, Cassart D (2008): Evidence for transplacental transmission of the current wild-type strain of bluetongue virus serotype 8 in cattle. Veterinary Record 163, 50–52.

Dijkstra E, Ven van der IJK, Meiswinkel R, Hözel DR, Van Rijn PA, Meiswinkel R (2008): Culicoides chiopterus as a potential vector of bluetongue virus in Europe. Veterinary Record 162, 422.

Drew CP, Heller MC, Mayo C, Watson JL, MacLachlan NJ (2010a): Bluetongue virus infection activates bovine monocyte-derived macrophages and pulmonary artery endothelial cells. Veterinary Immunology and Immunopathology 136, 292–296.

Drew CP, Gardner IA, Mayo CE, Matsuo E, Roy P, MacLachlan NJ (2010b): Bluetongue virus infection alters the impedance of monolayers of bovine endothelial cells as a result of cell death. Veterinary Immunology and Immunopathology 136, 108–115.

Ducheyne E, De Denken R, Becu S, Codina B, Nomikou K, Mangana O, Georgiev G, Purse BV, Hendrickx G (2007): Quitifying the wind dispersal of Culicoides species in Greece and Bulgaria. Geospatial Health 2, 177–189.

Dunbar MR, Cunningham MW, Roof JC (1998): Seroprevalence of selected disease agents from free-ranging black bears in Florida. Journal of Wildlife Disease 34, 612–619.

Eaton BT, Hyatt AD, Brookes SM (1990): The replication of bluetongue virus. Current Topics of Microbiology and Immunology 162, 89–118.

Elbers ARW, Backx A, Meroc E, Gerbier G, Staubach C, Hendrickx G, van der Spek A, Mintiens K (2008a): Field observations during the bluetongue serotype 8 epidemic in 2006 I. Detection of first outbreaks and clinical signs in sheep and cattle in Belgium, France and the Netherlands. Preventive Veterinary Medicine 87, 21–30.

Elbers ARW, Backx A, Mintiens K, Gerbier G, Staubach C, Hendrickx G, van der Spek A (2008b): Field observations during the bluetongue serotype 8 epidemic in 2006 II. Morbidity and mortality rate, case fatality and clinical recovery in sheep and cattle in Netherlands. Preventive Veterinary Medicine 87, 31–40.

Elbers ARW, van der Spek AN, van Rijn PA (2009): Epidemiologic characteristics of bluetongue virus serotype 8 laboratory-confirmed outbreaks in The Netherlands

in 2007 and a comparison with the situation in 2006. Preventive Veterinary Medicine 92, 1–8.

Erasmus BJ (1990): Bluetongue virus. In: Dinter Z., Morein B. (eds.): Virus Infections of Ruminants. Elsevier, New York, USA. 227–237.

Eschbaumer M, Hoffmann B, Moss A, Savini G, Leone A, Konig P, Zemke J, Conraths F, Beer M (2010): Emergence of bluetongue virus serotype 6 in Europe-German field data and experimental infection in cattle. Veterinary Microbiology 143, 189–195.

Evermann JF (2008): Accidental introduction of viruses into companion animals by commercial vaccines. Veterinary Clinics of North America-Small Animal Practise, 38, 919–929.

Fernandez-Pacheco P, Fernandez-Pinero J, Aguero M, Jimenez-Clavero MA (2008): Bluetongue virus serotype 1 in wild mouflons in Spain. Veterinary Record 162, 659–660.

Flanagan MM, Johnson SJ (1995): The effects of vaccination of Merino ewes with an attenuated Australian bluetongue virus serotype 23 at different stages of gestation. Australian Veterinary Journal 72, 455–457.

Frank JF, Willis NG (1975): Bluetongue and epizootic hemorrhagic disease. Journal of Wildlife Diseases 10, 228.

Fukusho A, Yu Y, Yamaguchi S, Roy P (1989): Completion of the sequence of bluetongue virus serotype 10 by the characterization of a structural protein, VP6, and a non-structural protein, NS2. Journal of General Virology 70, 1677–1689.

Gale P, Drew T, Phipps LP, David G, Wooldridge M (2009): The effect of climate change on occurrence and prevalence of livestock diseases in Great Britain: a review. Journal of Applied Microbiology 106, 1409–1423.

Gambles RM (1949): Bluetongue of sheep in Cyprus. Journal of Comparative Pathology, 59, 176–190.

Garcia I, Napp S, Casal J, Perea A, Allepuz A, Alba A, Carbonero A, Arenas A (2009): Bluetongue epidemiology in wild ruminants from Southern Spain. European Journal of Wildlife Research 55, 173–178.

Gibbs EPJ, Greiner EC (1994): The epidemiology of bluetongue. Comparative Immunology and Microbiology and Infectious Diseases 17, 207–220.

Gibbs EPJ, Lawman MJP, Herniman KAJ (1979): Preliminary observations on transplacentar infection of bluetongue virus in sheep – A possible overwintering mechanism. Research of Veterinary Sciences 27, 118–120.

Goldsmit L, Barzilai E (1985): Isolation and propagation of bluetongue virus in embryonating chicken eggs. In: Barber TL, Jochim MM, Osburn BI (eds.): Bluetongue and Related Orbiviruses. American Journal of Tropical Medicine and Hygiene 34, 307–318.

Grimes JM, Burroughs JN, Gouet P, Diprose JM, Malby R, Zientara S, Mertens PP, Stuart DI (1998): The atomic structure of the bluetongue virus core. Nature 395, 470–478.

Hamblin C (2004): Bluetongue virus antigen and antibody detection, and the application of laboratory diagnostic techniques. Veterinaria Italiana 40, 538–545.

Hammoumi S, Breard E, Sailleau C, Russo P, Grillet C, Cetre-Sossah C, Albina E, Sanchis R, Pepin M, Guibert J-M, Zientara S (2003): Studies on the safety and immunogenicity of the South African bluetongue virus serotype 2 monovalent vaccines: specific detection of the vaccine strain genome by RT-PCR. Journal of Veterinary Medicine B 50, 316–321.

Han Z, Harty RN (2004): The NS3 protein of bluetongue virus exhibits viroporin-like properties. Journal of Biological Chemistry 279, 43092–43097.

Hardy WT, Price DA (1952): Soremuzzle of sheep. Journal of American Veterinary Medical Association 120, 23–25.

Haresnape JM, Taylor WP, Lungu SAM (19898): The epidemiology of bluetongue in Malawi. Epidemiology and Infection 100, 493–499.

Hassan SS, Roy P (1999): Expression and functional characterization of bluetongue virus VP2 protein: role in cell entry. Journal of Virology 73, 9832–9842.

Hassan SH, Wirblich C, Forzan M, Roy P (2001): Expression and functional characterization of bluetongue virus VP5 protein: role in cellular permeabilization. Journal of Virology 75, 8356–8367.

Hemati B, Contreras V, Urien C, Bonneau M, Takamatsu H-H, Mertens PPC, Breard E, Sailleau C, Zientara S, Schwartz-Cornil I (2009): Bluetongue virus targets conventional dendritic cells in skin lymph. Journal of Virology 83, 8789–8799.

Hendrickx G (2009): The spread of blue tongue in Europe. Small Ruminant Research 86, 34–39.

Henrich M, Reinacher M, Hamann HP (2007): Lethal bluetongue virus infection in an alpaca. Veterinary Record 161, 764.

Hofmann MA, Renzullo S, Mader M, Chaignat V, Worwa G, Thuer B (2008): Genetic characterization of Toggenburg orbivirus, a new bluetongue virus from goats, Switzerland. Emerging Infectious Diseases 14, 1855–1861.

Hoffmann B, Bauer B Bauer C, Batza HJ, Beer M, Clausen PH, Geier M, Gethmann JM, Kiel E, Liebisch G, Liebisch A, Mehlhorn H, Schaub GA, Werner D, Conraths FJ (2009): Monitoring of putative vectors of bluetongue virus serotype 8, Germany. Emerging Infectious Diseases 15, 1481–1484.

Howard TH, Bowen RA, Pickett BW (1985): Isolation of bluetongue virus from bull semen. Progress in Clinical and Biological Research 178, 127–134.

Howerth EW, Tyler DE (1988): Experimentally induced bluetongue virus infection in white-tailed deer: ultrastructural findings. American Journal of Veterinary Research 49, 1914–1922.

Howerth EW, Dorminy M, Dreesen DW, Spires EA, Stallknecht DA (1995): Low prevalence of antibodies to bluetongue and epizootic hemorrhagic disease viruses in dogs from southern Georgia. Journal of Veterinary Diagnostic Investigation 7, 393–394.

Howerth EW, Stallknecht DE, Kirkland PD (2001): Bluetongue, epizootic hemorrhagic disease, and other orbivirus related diseases. In: Williams ES, Barker IK (eds.): Infectious diseases of wild mammals. 3rd ed. Iowa State University Press, Iowa. 77–97.

Huismans H, Erasmus BJ (1981): Identification of the serotype-specific and group-specific antigens of bluetongue virus. Onderstepoort Journal of Veterinary Research 48, 51–58.

Hutcheon D (1902): Malarial catarrhal fever of sheep. Veterinary Record 14, 629–633.

Hyatt AD, Gould AR Coupar B, Eaton BT (1991): Localization of the non-structural protein NS3 in bluetongue virus infected cells. Journal of General Virology 72, 2263–2267.

Inumaru S, Ghiasi H, Roy P (1987): Expression of bluetongue virus group-specific antigen VP3 in insect cells by a baculovirus vector: its use for detection of bluetongue virus antibodies. Journal of General Virology 68, 1627–1635.

Jauniaux TP, De Clerq KE, Cassart DE, Kennedy S, Vandenbussche FE, Vandemeulebroucke EL, Vanbinst TM, Verheyden BI, Goris NE, Coignoul FL (2008): Bluetongue in Eurasian Lynx. Emerging Infectious Diseases 14, 1496–1498.

Johnson DJ, Ostlund EN, Stallknecht DE, Goekjian VH, Jenkins-Moore M, Harris SC (2006): First report of bluetongue virus serotype 1 isolated from a white-tailed deer in the United States. Journal of Veterinary Diagnostic Investigation 18, 398–401.

Kampen H, Werner D (2010): Three years of bluetongue disease in central Europe with special reference to Germany: what lessons can be learned? Wiener Klinische Wochenschrift 122, 31–39.

Kar AK, Bhattacharya B, Roy P (2007): Bluetongue virus RNA binding protein NS2 is a modulator of viral replication and assembly. BMC Molecular Biology 8, 4.

Katz J, Alstad D, Gustafson G, Everman J (1994): Diagnostic analysis of the prolonged bluetongue virus RNA presence found in the blood of naturally infected cattle and experimentally infected sheep. Journal of Veterinary Diagnostic Investigation 6, 139–142.

Kettle DS, Lawson JWH (1952): The early stages of British biting midges Culicoides Latreille (Diptera: Ceratopogonidae) and allied genera. Bulletin of Entomological Research 43, 421–467.

Kirkland PD, Melville LF, Hunt NT, Williams CF, Davis RJ (2004): Excretion of bluetongue virus in cattle semen: a feature of laboratory-adapted virus. Veterinaria Italiana 40, 497–501.

Kirschvink N, Raes M, Saegerman C (2009): Impact of a natural bluetongue serotype 8 infection on semen quality of Belgian rams in 2007. Veterinary Journal 182, 244–251.

Koumbati M, Mangana O, Nomikou K, Mellor PS, Papadopoulos O (1999): Duration of bluetongue viremia and serological responses in experimentally infected European breeds of sheep and goats. Veterinary Microbiology 64, 277–285.

Kramer WL, Greiner EC, Gibbs EPJ (1985): Seasonal variations in population size, fecundity and parity rates of Culicoides insignis (Diptera: Ceratopogonidae) in Florida, USA. Journal of Medical Entomology 22, 163–169.

Lewerin SS, Hallgren G, Mieziewska K, Treiberg Berndtsson L, Chirico J, Elvander M (2010): Infection with bluetongue virus serotype 8 in Sweden in 2008. Veterinary Record 167, 165–170.

Linden A, Mousset B, Grégoire F, Hanrez D, Vandenbussche F, Vandemeulebroucke E, Vanbinst T, Verheyden B, De Clerck K (2008): Bluetongue virus antibodies in wild red deer in southern Belgium. Veterinary Record 162, 459.

Lobato ZI, Coupar BE, Gray CP, Lunt R, Andrew ME (1997): Antibody responses and protective immunity to recombinant vaccinia virus-expressed bluetongue virus antigens. Veterinary Immunology and Immunopathology 59, 293–309.

Lopez WA, Nicoletti P, Gibbs EPJ (1985): Antibody to bluetongue virus in cattle in Ecuador. Tropical Animal Health and Production 17, 82.

Losson B, Mignon B, Paternostre J, Madder M, De Deken R, De Deken G, Deblauwe I, Fassotte C, Cors R, Defrance T, Delecolle J-C, Baldet T, Hubruge E, Frederic F, Bortels J, Simonon G (2007): Biting midges overwintering in Belgium. Veterinary Record 160, 451–452.

Luedke AJ, Anakwenze EI (1972): Bluetongue virus in goats. American Journal of Veterinary Research 33, 1739–1745.

Luedke AJ, Jochim MM, Bowne JG (1965): Preliminary bluetongue transmission with the sheep ked Melophagus ovinus (L.). Canadian Journal of Comparative Medicine of Veterinary Science 29, 229–231.

Luedke AJ, Jones RH, Walton TE (1977): Overwintering mechanism for bluetongue virus: Biological recovery of latent virus from a bovine by bites of Culidoides variipennis. American Journal of Tropical Medicine and Hygiene 26, 313–325.

Lunt RA, Melville L, Hunt N, Davis S, Rootes CL, Newberry KM, Pritchard LI, Middleton D, Bingham J, Daniels PW, Eaton BT (2006): Cultured skin fibroblast cells derived from bluetongue virus-inoculated sheep and field-infected cattle are not source of late and protracted recoverable virus. Journal of General Virology 87, 3661–3666.

Lymperopoulos K, Noad R, Tosi S, Nethisinghe S, Brierley I, Roy (2006): Specific binding of bluetongue virus NS2 to different viral plus-strand RNAs. Virology 353, 17–26.

Lysyk TJ, Danyk T (2007): Effect of temperature on life history parametres of adult Culicoides sonorensis (Diptera: Ceratopogonidae) in relation to geographic origin and vectorial capacity for bluetongue virus. Journal of Medical Entomology 44, 741–751.

Maan S, Maan NS, Nomikou K, Batten C, Antony F, Belaganahalli MN, Samy AM, Reda AA, Al-Rashid SA, El Batel M, Oura CAL, Mertens PPC (2011): Novel bluetongue virus serotype from Kuwait. Emerging Infectious Diseases 17, 886–889.

MacLachlan NJ (1994): The pathogenesis and immunology of bluetongue virus infection of ruminants. Comparative Immunology, Microbiology and Infectious Diseases 17, 197–206.

MacLachlan NJ (2004): Bluetongue: pathogenesis and duration of viraemia. Veterinaria Italiana 40, 462–467.

MacLachlan NJ (2010): Global implications of the recent emergence of bluetongue virus in Europe. Veterinary Clinics of North America: Food Animal Practise 26, 163–171.

MacLachlan NJ, Gard G (2009): Clinical signs and pathology. In: Mellor P, Baylis M, Mertens PPC (eds.): Bluetongue. Academic Press, London. 285–293.

MacLachlan NJ, Thompson J (1985): Bluetongue virus-induced interferon in cattle. American Journal of Veterinary Research 46, 1238–1241.

MacLachlan NJ, Heidner HW, Fuller FJ (1987): Humoral immune response of calves to bluetongue virus infection. American Journal of Veterinary Research 48, 1031–1035.

MacLachlan NJ, Jagels G, Rossitto PV, Moore PF, Heidner HW (1990): The pathogenesis of experimental bluetongue virus infection of calves. Veterinary Pathology 27, 223–229.

MacLachlan NJ, Nunamaker RA, Katz JB, Sawyer MM, Akita GY, Osburn BI, Tabachnick WJ (1994): Detection of bluetongue virus in the blood of inoculated calves: comparison of virus isolation, PCR assay, and in vitro feeding of Culicoides variipennis. Archives of Virology 136, 1–8.

MacLachlan NJ, Conley AJ, Kennedy PC (2000): Bluetongue and equine viral arteritis viruses as models of virus-induced fetal injury and abortion. Animal Reproduction Science 60–61, 643–651.

MacLachlan NJ, Drew CP, Darpel KE, Worwa G (2009): The Pathology and Pathogenesis of Bluetongue. Journal of Comparative Pathology 141, 1–16.

Mars MH, van Maanen C, Vellema P, Kramps JA, van Rijn PA (2010): Evaluation of an indirect ELISA for detection of antibodies in bulk milk against bluetongue virus infections in The Netherlands. Veterinary Microbiology 146, 209–214.

Mauroy A, Guyot H, De Clercq K, Cassart D, Thiry E, Saegerman C (2008): Bluetongue in captive yaks. Emerging Infectious Diseases 14, 675–676.

Mayo CE, Crossley BM, Hietala SK, Gardener IA, Breitmeyer RE, MacLachlan NJ (2010): Colostral transmission of bluetongue virus nucleic acid among newborn dairy calves in California. Transboundary and Emerging Diseases 57, 277–281.

Mecham JO (2006): Detection and titration of bluetongue virus in Culicoides insect cell culture by an antigen-capture enzyme-linked immunosorbent assay. Journal of Virological Methods 135, 269–271.

Mehlhorn H, Walldorf V, Klimpel S, Jahn B, Jaeger F, Eschweiler J, Hoffmann B, Beer M (2007): First occurrence of Culicoides obsoletus-transmitted Bluetongue virus epidemic in Central Europe. Parasitology Research 101, 219–228.

Mehlhorn H, Walldorf V, Klimpel S, Schmahl G (2008): Outbreak of bluetongue disease (BTD) in Germany and the danger for Europe. Parasitology Research 103, 79–86.

Mehlhorn H, Walldorf V, Klimpel S, Schaub G, Kiel E, Focke R, Liebisch G, Liebisch A, Werner D, Bauer C, Clausen H, Bauer B, Geier M, Horbrand T, Batza H-J, Conraths FJ, Hoffmann B, Beer M (2009): Bluetongue disease in Germany (2007–2008): monitoring of entomological aspects. Parasitology Research 105, 313–319.

Meiswinkel R, Nevill EM, Venter GJ (1994): Vectors: Culicoides spp. In: Coetzer JAW, Thomson GR, Tustin RC (eds.): Infectious Diseases of Livestock with Special Reference to Southern Africa. Vol. 1. Oxford University Press, Cape Town. 68–89.

Meiswinkel R, Gomulski LM, Delecolle J-C, Goffredo M, Gasperi G (2004): The taxonomy of Culicoides vector complexes – unfinished business. Veterinaria Italiana 40, 151–159.

Meiswinkel R, van Rijn P, Leijs P, Goffredo M (2007): Potential new Culicoides vector of bluetongue virus in northern Europe. Veterinary Record 161, 564–565.

Meiswinkel R, Baldet T, de Deken R, Takken W, Delecolle J-C, Mellor PS (2008): The 2006 outbreak of bluetongue in northern Europe – The entomological perspective. Preventive Veterinary Medicine 87, 55–63.

Mellor PS (1990): The replication of bluetongue virus in Culicoides vectors. Current Topics of Microbiology and Immunology 162, 143–161.

Mellor PS (2000): Replication of arboviruses in insect vectors. Journal of Comparative Pathlogy 123, 140–146.

Mellor PS (2004): Infection of the vectors and bluetongue epidemiology in Europe. Veterinaria Italiana 40, 167–174.

Mellor PS, Boorman J (1995): The transmission and geographical spread of African horse sickness and bluetongue viruses. Annals of Tropical Medicine and Parasitology 89, 1–15.

Mellor PS, Pitzolis G (1979): Observations on breeding sites and light-trap collections of Culicoides during an outbreak of bluetongue in Cyprus. Bulletin of Entomological Research 69, 229–234.

Mellor PS, Wittmann EJ (2002): Bluetongue virus in the Mediterranean basin 1998–2001. Veterinary Journal 164, 20–37.

Mellor PS, Boorman J, Baylis M (2000): Culicoides biting midges: Their role as arbovirus vectors. Annual Review of Entomology 45, 307–340.

Mellor PS, Carpenter S, Harrup L, Baylis M, Mertens PP (2008): Bluetongue in Europe and the Mediterranean Basin: History of occurrence prior to 2006. Preventive Veterinary Medicine 87, 4–20.

Melville LF, Hunt NT, Davis SS, Weir RP (2004): Bluetongue virus does not persist in naturally infected cattle. Veterinaria Italiana 40, 502–507.

Menzies FD, McCullough SJ, McKeown IM, Forster JL, Jess S, Batten C, Murchie AK, Gloster J, Fallows JG, Pelgrim W, Mellor PS, Oura CAL (2008): Evidence for transplacental and contact transmission of bluetongue virus in cattle. Veterinary Record 163, 203–209.

Mertens PPC, Diprose J (2004): The bluetongue virus core: a nano-scale transcription machine. Virus Research 101, 29–43.

Mertens PPC, Pedley S, Cowley J, Burroughs JN, Corteyn AH, Jeggo MH, Jennings DM, Gorman BM (1989): Analysis of the roles of bluetongue virus outer capsid proteins VP2 and VP5 in determination of virus serotype. Virology 170, 561–565.

Meyer G, Lacroux C, Leger S, Top S, Goyeau K, Deplanche M, Lemaire M (2009): Lethal bluetongue virus serotype 1 infection in llamas. Emerging Infectious Diseases 15, 608–609.

Mintiens K, Meroc E, Mellor PS, Staubach C, Gerbier G, Elbers ARW, Hendrickx G, De Clercq K (2008): Possible routes of introduction of bluetongue virus serotype 8 into the epicentre of the 2006 epidemic in north-western Europe. Preventive Veterinary Medicine 87, 131–144.

Mo CL, Thompson LH, Homan EJ, Oviedo MT, Greiner EC, Gonzales J, Saenz MR (1994): Bluetongue virus isolations from vectors and ruminants in Central America and the Caribbean. Interamerican Bluetongue Team. Americal Journal of Veterinary Research 55, 211–215.

Mohammed ME, Taylor WP (1987): Infection with bluetongue and related orbiviruses in the Sudan detected by the study of sentinel calf herds. Epidemiology and Infection 99, 533–545.

Mortola E, Noad R, Roy P (2004): Bluetongue virus outer capsid proteins are sufficient to trigger apoptosis in mammalian cells. Journal of Virology 78, 2875–2883.

Mullens BA, Tabachnick WJ, Holbrook FR, Thompson LH (1995): Effects of temperature on virogenesis of bluetongue virus serotype 11 in Culicoides variipennis sonorensis. Medical Veterinary Entomology 9, 71–76.

Murray JO, Trainer DO (1970): Bluetongue virus in North American elk. Journal of Wildlife Diseases 6, 144–148.

Mushi EZ, Hill FWG, Daweb P, Riess R (1990): Antibodies to bluetongue and African horse sickness viruses in the sera of elephants in Zimbabwe. Bulletin of Animal Health and Production in Africa 38, 475.

Nason EL, Rothagel R, Murkherjee SK, Kar AK, Forzan M, Prasad BV, Roy P (2004): Interactions between the inner and outer capsids of bluetongue virus. Journal of Virology 78, 8059–8067.

Nevill EM, Venter GJ, Edwards M (1992): Potential Culicoides vectors of livestock orbiviruses in South Africa. In: Walton T, Osburn B (eds.): Bluetongue, African Horse Sickness and Related Orbiviruses. CRC Press, Boca Raton. 455–459.

Ninio C, Augot D, Delecolle J-C, Dufour B, Depaquit J (2011): Contribution to the knowledge of Culicoides (Diptera: Ceratopogonidae) host preferences in France. Parasitology Research 108, 657–663.

Nolan DV, Carpenter S, Barber J, Mellor PS, Dallas JF, Mordue Luntz AJ, Piertney SB (2007): Rapid diagnostic PCR assay for members of the Culicoides obsoletus and Culicoides pulicaris species complexes, implicated

vectors of bluetongue virus in Europe. Veterinary Microbiology 124, 82–94.

Nunamaker RA, Sieburth PJ, Dean VC, Washington JG, Nunamaker CE, Mecham JO (1990): Absence of transovarial transmission of bluetongue virus in Culicoides variipennis: Immunogold labelling of bluetongue virus antigen in developing oocytes from Culicoides variipennis (Coquillett). Compendium of Biochemistry and Physiology A 96, 19–31.

Nuttall PA, Jacobs SC, Jones LD, Carey D, Moss SR (1992): Enhanced neurovirulence of tick-borne orbiviruses resulting from genetic modulation. Virology 187, 407–412.

Oberst RD, Stott JL, Blanchard-Channell M, Osburn BI (1987): Genetic reassortment of bluetongue virus serotype 11 strains in the bovine. Veterinary Microbiology 15, 11–18.

O'Hara RS, Meyer AJ, Burroughs JN, Pullen L, Martin LA, Mertens PPS (1998): Development of a mouse model system and identification of individual genome segments of African horse sickness virus, serotypes 3 and 8 involved in determination of virulence. Archives of Virology 14, 259–279.

Oldfield S, Adachi A, Urakawa T, Hirasawa T, Roy P (1990): Purification and characterization of the major group-specific core antigen VP7 of bluetongue virus synthesized by a recombinant baculovirus. Journal of General Virology 72, 449–451.

Osburn BI (1994): The impact of bluetongue virus on reproduction. Comparative Immunology, Microbiology and Infectious Diseases 17, 189–196.

Osburn BI, Silverstein AM, Prendergast RA, Johnson RT, Parshall CJ (1971): Experimental viral-induced congenital encephalopathies. I. Pathology of hydranencephaly and porencephaly caused by bluetongue vaccine virus. Laboratory Investigation 25, 197–205.

Osmani A, Murati B, Kabashi Q, Goga I, Berisha B, Wilsmore AJ (2006): Evidence for presence of bluetongue virus in Kosovo between 2001 and 2004. Veterinary Record 158, 393–396.

Owens RJ, Limn C, Roy P (2004): Role of an arbovirus nonstructural protein in cellular pathogenesis and virus release. Journal of Virology 78, 6649–6656.

Parsonson IM (1990): Pathology and pathogenesis of bluetongue infections. Current Topics of Microbiology and Immunology 162, 119–141.

Polydorou K (1978): The 1977 outbreak of bluetongue in Cyprus. Tropical Animal Health and Production 10, 229–232.

Prasad BVV, Yamaguchi S, Roy P (1992a): Three-dimensional structure of single-shelled bluetongue virus. Journal of Virology 66, 2135–2142.

Prasad G, Jain NC, Gupta Y (1992b): Bluetongue virus infection in India: a review. Revue Scientifique et Technique 11, 699–711.

Purse BV, Mellor PS, Rogers DJ, Samuel AR, Mertens PPC, Baylis M (2005): Climate change and the recent emergence of bluetongue in Europe. Nature Reviews Microbiology 3, 171–181.

Radostits OM, Blood DC, Gay CC (1994): A Textbook of the Diseases of Cattle, Sheep, Pigs, Goats and Horses. 8th ed. VB Saunders Company Ltd. 1028–1033.

Randolph SE, Rogers DJ (2010): The arrival, establishment and spread of exotic diseases: patterns and predictions. Nature Reviews Microbiology 8, 361–371.

Reddington JJ, Reddington GM, MacLachlan NJ (1991): A competitive ELISA for detection of antibodies to the group antigen of bluetongue virus. Journal of Veterinary Diagnostic Investigation 3, 144–147.

Richards RG, MacLachlan NJ, Heidner HW, Fuller FJ (1988): Comparison of virologic and serologic responses of lambs and calves infected with bluetongue virus serotype 10. Veterinary Microbiology 18, 233–242.

Richardson CC, Taylor WWP, Terlecki SS, Gibbs EEP (1985): Observations on transplacental infection with bluetongue virus in sheep. American Journal of Veterinary Research 46, 1912–1922.

Rivera H, Madewell B, Ameghino E (1987): Serologic survey of viral antibodies in the Peruvian alpaca (Lama pacos). American Journal of Veterinary Research 48, 189–191.

Rodriguez-Sanchez B, Iglesias-Martin I, Martinez-Aviles M, Sanchez-Vizcaino JM (2008): Orbiviruses in the Mediterranean Basin: updated epidemiological situation of bluetongue and new methods for the detection of BTV serotype 4. Transboundary and Emerging Diseases 55, 205–214.

Rodriguez-Sanchez B, Gortazar C, Ruiz-Fons F, Sanchez-Vizcaino JM (2010a): Bluetongue virus serotypes 1 and 4 in red deer, Spain. Emerging Infectious Diseases 16, 518–520.

Rodriguez-Sanchez B, Sanchez-Cordon PJ, Molina V, Risalde MA, Perez de Diego AC, Gomez-Villamandos JC, Sanchez-Vizcaino JM (2010b): Detection of bluetongue serotype 4 in mouflons (Ovis aries musimon) from Spain. Veterinary Microbiology 141, 164–167.

Rosadio RH, Evermann JF, Demartini JC (1984): A preliminary serological survey of viral antibodies in llamas (Lama glama) in Argentina. Zentralblatt fur Veterinarmedizin B 46, 157–161.

Roy P (1992): Bluetongue virus proteins. Journal of General Virology 73, 3051–3064.

Roy P (2008): Functional mapping of bluetongue virus proteins and their interactions with host proteins dur-

ing virus replication. Cell Biochemistry and Biophysics 50, 143–157.

Roy P, Noad R (2006): Bluetongue virus assembly and morphogenesis. In: Roy P (ed.): Reoviruses: Entry, Assembly and Morphogenesis. Current Topics in Microbiology and Immunology. Springer, Berlin, Heidelberg. 87–116.

Roy P, Boyce M, Noad R (2009): Prospects for improved bluetongue vaccines. Natural Reviews Microbiology 7, 120–128.

Ruiz-Fons F, Reyes-Garcia AR, Alcaide V, Gortazar C (2008): Spatial and temporal evolution of bluetongue virus in wild ruminants, Spain. Emerging Infectious Diseases 14, 951–953.

Saegerman C, Berkvens D, Mellor PS (2008): Bluetongue epidemiology in the European union. Emerging Infectious Diseases 14, 539–544.

Saegerman C, Bolkaerts B, Baricalla C, Raes M, Wiggers L, de Leeuw I, Vandenbussche F, Zimmer JY, Haubruge E, Cassart D (2011): The impact of naturally-occuring, trans-placental bluetongue virus serotype 8 infection on reproductive performance in sheep. Veterinary Journal 187, 72–80.

Samal SK, El-Hussein A, Holbrook FR, Beaty BJ, Famig RF (1987): Mixed infection of Culicoides variipennis with bluetongue virus serotypes 10 and 17: Evidence for high frequency reassortment in the vector. Journal of General Virology 68, 2319–2329.

Sanchez-Cordon PJ, Rodriguez-Sanchez B, Risalde MA, Molina V, Pedrera M, Sanchez-Vizcaino JM, Gomez-Villamandos JC (2010): Immunohistochemical detection of bluetongue virus in fixed tissue. Journal of Comparative Pathology 143, 20–28.

Santman-Berends IMGA, van Wuijckhuise L, Vellema P, van Rijn PA (2010): Vertical transmission of bluetongue virus serotype 8 in Dutch dairy herds in 2007. Veterinary Microbiology 141, 31–35.

Savini G, Goffredo M, Monaco F, De Santis P, Meinswinkel R (2003): Transmission of bluetongue virus in Italy. Veterinary Record 152, 119.

Savini G, Goffredo M, Monaco F, Di Gennaro A, Cafiero MA, Baldi L, de Santis P, Meiwinkel R, Caporale V (2005): Bluetongue virus isolations from midges belonging to the Obsoletus complex (Culicoides, Diptera: Ceratopogonidae) in Italy. Veterinary Record 157, 133–139.

Savini G, MacLachlan NJ, Sanchez-Vizcaino JM, Zientara S (2008): Vaccines against bluetongue in Europe. Comparative Immunology, Microbiology and Infectious Diseases 31, 101–120.

Savini G, Hamers C, Conte A, Migliaccio P, Bonfini B, Teodori L, Di Ventura M, Hudelet P, Schumacher C, Caporale V (2009): Assessment of efficacy of a bivalent BTV-2 and BTV-4 inactivated vaccine by vaccination and challenge in cattle. Veterinary Microbiology 133, 1–8.

Savini G, Afonso A, Mellor P, Aradaib I, Yadin H, Sanaa M, Wilson W, Monaco F, Domingo M (2011): Epizootic haemorragic disease. Research in Veterinary Science 91, 1–17.

Schmahl G, Klimpel S, Walldorf V, Al-Quraishy S, Schumacher B, Jatzlau A, Mehlhorn H (2009a): Pilot study on deltamethrin treatment (Butox, Versatrine) of cattle and sheep against midges. Parasitology Research 104, 809–813.

Schmahl G, Mehlhorn H, Abdel-Ghaffar F, Al-Rasheid K, Schumacher B, Jatzlau A, Pohle H (2009b): Does rain reduce the efficacy of Butox 7.5 pour on (deltamethrin) against biting midges (Culicoides specimens)? Parasitology Research 105, 1763–1765.

Schoepp RJ, Blair CD, Roy P, Beaty BJ (1991): Detection of bluetongue virus RNA by in situ hybridization: comparison with virus isolation and antigen detection. Journal of Veterinary Investigation 3, 22–28.

Schwartz-Cornil I, Mertens PPC, Contreras V, Hemati B, Pascale F, Brerad E, Mellor PS, MacLachlan NJ, Zientara S (2008): Bluetongue virus: virology, pathogenesis and immunity. Veterinary Research 39, 46.

Sellers RF (1984): Bluetongue in Africa, the Mediterranean region and the Near East – disease, virus and vectors. Preventive Veterinary Medicine 2, 371–378.

Sellers RF, Taylor WP (1980): Epidemiology of bluetongue and the import and export of livestock, semen and embryos. Bulletin of Office international des Epizooties 92, 587–592.

Shaw AE, Monaghan P, Alpar HO, Anthony S, Darpel KE, Batten CA, Guerico A, Alimena G, Vitale M, Bankowska K, Carpenter S, Jones H, Oura CAL, King DP, Elliott H, Mellor PS, Mertens PPC (2007): Development and initial evaluation of a real-time RT-PCR assay to detect bluetongue virus genome segment 1. Journal of Virological Methods 145, 115–126.

Shimshony A (2004): Bluetongue in Israel – a brief historical overview. Veterinaria Italiana 40, 116–118.

Spreull J (1905): Malarial catarrhal fever (bluetongue) of sheep in South Africa. Journal of Comparative Pathology and Therapeutics 18, 321–337.

Stephan A, Clausen P-H, Bauer B, Steuber S (2009): PCR identification of Culicoides dewulfi midges (Diptera: Ceratopogonidae), potential vector of bluetongue in Germany. Parasitology Research 105, 367–371.

Stott JL, Osburn BI, MacLachlan NJ (1983): Diagnosis of bluetongue virus infection in cattle: virus isolation or serology? Proceedings of the American Accociation of Veterinary Laboratory Diagnosticians 26, 301–318.

Stott JL, Osburn BI, Alexander L (1985): Ornithodoros coriaceus (pajaroello tick) as a vector of bluetongue virus. American Journal of Veterinary Research 46, 1197–1199.

Stott JL, Oberst RD, Channell MB, Osburn BI (1987): Genome segment reassortment between two serotypes of bluetongue virus in a natural host. Journal of Virology 61, 2670–2674.

Tabachnick WJ (1996): The genetics of Culicoides variipennis and the epidemiology of bluetongue disease in North America. Annual Review of Entomology 45, 20–40.

Takamatsu H, Mellor PS, Mertens PPC, Kirkham PA, Burroughs JH, Parkhouse RME (2003): A possible overwintering mechanism for bluetongue virus in the absence of the insect vector. Journal of General Virology 84, 227–235.

Tamayo R, Schoebitz R, Alonso O, Wenzel J (1985): First report of bluetongue antibody in Chile. Progress in Clinical and Biological Research 178, 555–558.

Tanya VN, Greiner EC, Gibbs EP (1992): Evaluation of Culicoides insignis (Diptera: Ceratopogonidae) as a vector of bluetongue virus. Veterinary Microbiology 32, 1–14.

Taylor WP, Mellor PS (1994): Distribution of bluetongue virus in Turkey, 1978–1981. Epidemiology and Infection 112, 623–633.

Thiry E, Saegerman C, Guyot H, Kirten P, Losson B, Rollin F, Bodmer M, Czaplicki G, Toussaint J-F, De Clercq K, Dochy J-M, Dufey J, Gilleman J-L, Messeman K (2006): Bluetongue in northern Europe. Veterinary Record 159, 327.

Thomas FC (1984): Comparison of some storage and isolation methods to recover bluetongue virus from bovine blood. Canadian Journal of Comparative Medicine 48, 108–110.

Thomas FC, Randall GC, Myers DJ (1986): Attempts to establish congenital bluetongue virus infections in calves. Canadian Journal of Veterinary Research 50, 280–281.

Toussaint JF, Sailleau C, Breard E, Zientara S, De Clercq K (2007): Bluetongue virus detection by two real-time RT-qPCRs targeting two different genomic segments. Journal of Virological Methods 140, 115–123.

Tweedle N, Mellor PS (2002): Technical review – bluetongue: The virus, hosts and vectors. Version 1.5. Report to the Department of Health, Social Services and Public Safety U.K. (DEFRA), 25 p. http://archive.defra.gov.uk/foodfarm/farmanimal/diseases/atoz/documents/bluetongue_technical.PDF (accessed July 28, 2011).

Van Dijk AA, Huismans H (1982): The effect of temperature on the in vitro transcriptase reaction of bluetongue virus, epizootic haemorrhagic disease virus and African horse sickness virus. Onderstepoort Journal of Veterinary Research 49, 227–232.

Vellema P (2008): Bluetongue in sheep: Question marks on bluetongue virus serotype 8 in Europe. Small Ruminant Research 76, 141–148.

Veronesi E, Hamblin C, Mellor PS (2005): Live attenuated bluetongue vaccine viruses in Dorset Poll sheep before and after passage in vector midges (Diptera: Ceratopoginidae). Vaccine 23, 5509–5516.

Veronesi E, Venter GJ, Labuschagne K, Mellor PS, Carpenter S (2009): Life-history parameters of Culicoides (Avaritia) imicola Kieffer in the laboratory at different rearing temperatures. Veterinary Parasitology 163, 370–373.

Verwoerd DW, Louw H, Oellermann, RA (1970): Characterization of bluetongue virus ribonucleic acid. Journal of Virology 5, 1–27.

Verwoerd DW, Els HJ, De Villiers EM, Huismans H (1972): Structure of bluetongue virus capsid. Journal of Virology 10, 783–794.

Waldvogel AS, Anderson GA, Phillips DL, Osburn BI (1992): Association of virulent and avirulent strains of bluetongue virus serotype 11 with premature births of late-term bovine fetuses. Journal of Comparative Pathology 106, 333–340.

Wang L, Kemp MC, Roy P, Colloson EW (1988): Tissue tropism and target cells of bluetongue virus in the chicken embryo. Journal of Virology 62, 887–893.

Wechsler SJ, McHolland LE (1988): Susceptibility of 14 cell lines to bluetongue virus infection. Journal of Clinical Microbiology 26, 2324–2327.

Wellby M, Baylis M, Rawlings P, Mellor PS (1996): Effect of temperature on survival and rate of virogenesis of African horse sickness virus in Culicoides variipennis sonorensis (Diptera: Ceratopogonidae) and its significance in relation to the epidemiology of the disease. Bulletin of Entomological Research 86, 715–720.

White DM, Wilson WC, Blair CD, Beaty BJ (2005): Studies on overwintering of bluetongue viruses in insect. Journal of General Virology 86, 453–462.

Wilbur LA, Evermann JF, Levings RL, Stott IR, Starling DE, Spillers CA, Gustafson GA, McKeirman AJ (1994): Abortion and death in pregnant bitches associated with a canine vaccine contaminated with bluetongue virus. Journal of American Veterinary Medicine Association 204, 1762–1765.

Williamson S, Woodger N, Darpel K (2008): Differential diagnosis of bluetongue in cattle and sheep. Practise 30, 242–251.

Wilson AJ, Mellor PS (2008): Bluetongue in Europe: vectors, epidemiology and climate change. Parasitology Research 103 (Suppl. 1), S69–S77.

Wilson AJ, Mellor PS (2009): Bluetongue in Europe: past, present and future. Philosophical Transactions of the Royal Society B-Biological Sciences 364, 2669–2681.

Wilson A, Carpenter S, Gloster J, Mellor PS (2007): Re-emregence of bluetongue in northern Europe in 2007. Veterinary Record 161, 487–489.

Wilson A, Darpel K, Mellor PS (2008): Where does bluetongue virus sleep in winter? PLOS Biology 6, 1612–1617.

Wirblich C, Bhattacharya B, Roy P (2006): Nonstructural protein 3 of bluetongue virus assists virus release by recruiting ESCRT-I protein Tsg101. Journal of Virology 80, 460–473.

Zendulkova D, Pospisil Z (2007): Bluetongue and its possible impact on production and quality of food of animal origin (in Czech). Scientific Report for the Veterinary Committee for Food Safety, Brno, 18 pp.

Zientara S, MacLachlan NJ, Calistri P, Sanchez-Vizcaino J-M, Savini G (2010): Bluetongue vaccination in Europe. Expert Reviews Vaccines 9, 989–991.

Zimmer J-Y, Haubruge E, Francis F, Bortels J, Simonon G, Losson B, Mignon B, Paternostre J, De Dekken R, De Deken G, Deblauwe I, Fassote C, Cors R, Defrance T (2008): Breeding sites of bluetongue vectors in northern Europe. Veterinary Record 162, 131.

Received: 2011–04–15
Accepted after corrections: 2011–08–26

Corresponding Author:

MVDr. Adela Sperlova, University of Veterinary and Pharmaceutical Sciences Brno, Department of Infectious Diseases and Microbiology, Palackeho 1–3, 612 42 Brno, Czech Republic
Tel. +420 541 562 249, +420 732 820 504, E-mail: adelasperlova@centrum.cz