



**BLUETONGUE
STANDARD OPERATING PROCEDURES:
1. OVERVIEW OF ETIOLOGY AND ECOLOGY**

FAD PReP

**Foreign Animal Disease
Preparedness & Response Plan**



**United States
Department of
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The Foreign Animal Disease Preparedness and Response Plan (FAD PReP) Standard Operating Procedures (SOPs) provide operational guidance for responding to an animal health emergency in the United States.

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Contents

1.1	Introduction.....	1-2
	1.1.1 Further Information.....	1-2
	1.1.2 Goals	1-2
1.2	Purpose.....	1-2
1.3	Etiology.....	1-3
	1.3.1 Name	1-3
	1.3.2 Virus Characteristics	1-3
	1.3.3 Morphology.....	1-3
1.4	Ecology	1-4
	1.4.1 Susceptible Species	1-4
	1.4.2 Transmission and Vector	1-4
	1.4.3 Morbidity and Mortality	1-7
	1.4.4 General Clinical Signs	1-7
	1.4.5 Bluetongue Virus Serotype 8 Clinical Signs	1-8
	1.4.6 Differential Diagnosis.....	1-9
1.5	Environmental Persistence of Bluetongue Virus	1-10
1.6	Distribution	1-10
	1.6.1 European Distribution and Significance	1-11
	1.6.2 Distribution in North America	1-12
1.7	Vaccines.....	1-13
1.8	Risk of BTV-8 Introduction to the United States	1-14
	Attachment 1.A References and Resources	1-16
	Attachment 1.B Abbreviations.....	1-20

Bluetongue

Etiology & Ecology Quick Summary

Disease

Bluetongue, caused by bluetongue virus (BTV), is also known as sore muzzle, pseudo foot-and-mouth, malarial catarrhal fever, epizootic catarrh, Beksiekte, and muzzle disease.

Mortality & Morbidity

Morbidity in sheep ranges from less than 5 percent to 50–75 percent or higher; mortality can reach up to 100 percent, although generally is less than 30 percent. Cattle and goats have reduced mortality and morbidity is rare.

Clinical Signs

Edema, hemorrhage, and ulceration of mucosae throughout the body.

Susceptible Species

Wild and domestic ruminants: sheep, goats, cattle, buffaloes, deer, bighorn sheep, North American elk, most species of African antelope, and other Artiodactyla, such as camels.

Zoonotic Potential

Not a threat to public health.

Reservoir

Possibly cattle, other ruminant species and/or biting midges of the *Culicoides* species.

Transmission

Primarily vector-borne via *Culicoides* spp. (biting midges). Vertical transmission in hosts occurs; direct transmission plays minor epidemiological role.

Persistence in the Environment

Is not known to persist in fomites or in animal carcasses or products; much is still unknown about environmental persistence.

1.1 Introduction

First described in 1905 among merino wool sheep in South Africa, bluetongue virus (BTV) is an arbovirus which replicates in wild and domestic ruminants causing subclinical to fatal symptoms. Bluetongue has a very wide distribution, historically between 40° North and 35° South, in subtropical and tropical climates, owing to the distribution of its vector, the biting midge (*Culicoides* spp.). Recently, there have been incursions beyond its normal geographic distribution, as observed in the United States and Europe, where strains have moved between geographic regions and adapted to different species of midges.¹ These adaptations, the discovery of new serotypes with unpredictable virulence, and clinical pathology make bluetongue a disease of concern.

Various serotypes of BTV are endemic in the United States. This standard operating procedure (SOP) is concerned primarily with BTV serotype 8 (BTV-8), which does not currently occur in the United States but could have epidemic potential. Incursion of BTV-8 into the United States is concerning due to the significant consequences upon livestock in Europe observed after 2006 when BTV-8 first entered Europe.

1.1.1 Further Information

This document is intended to be an overview of bluetongue, focusing specifically on BTV-8 in domestic livestock. Additional resources as well as the articles referenced in this SOP, are listed in [Attachment 1.A](#). The occurrence of bluetongue infection and laboratory criteria are defined in the World Organization for Animal Health (OIE) Terrestrial Animal Health Code (2016)² and Terrestrial Animal Health Manual (2014),³ respectively. Other Foreign Animal Disease Preparedness and Response Plan documents are available on the Animal and Plant Health Inspection Service (APHIS) public website, <http://www.aphis.usda.gov/fadprep>.

1.1.2 Goals

As a preparedness goal, APHIS will provide etiology and ecology summaries for bluetongue, and update these summaries at regular intervals.

As a response goal, animal health officials and stakeholders will have a common set of etiology and ecology definitions and descriptions, to ensure proper understanding of bluetongue when establishing or revising goals, objectives, strategies, and procedures.

1.2 Purpose

This document provides responders and stakeholders with a common understanding of the disease agent.

¹ World Organization for Animal Health (OIE). (2014). Chapter 2.1.3. Bluetongue. *Terrestrial Manual*. Retrieved from http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.01.03_BLUETONGUE.pdf.

² OIE. (2016). Chapter 8.3. Infection with bluetongue virus. *Terrestrial Animal Health Code*. Retrieved from http://www.oie.int/index.php?id=169&L=0&htmfile=chapitre_bluetongue.htm.

³ OIE. (2014). Chapter 2.1.3. Bluetongue. *Terrestrial Manual*. Retrieved from http://www.oie.int/fileadmin/Home/eng/Health_standards/tahm/2.01.03_BLUETONGUE.pdf.

1.3 Etiology

1.3.1 Name

Bluetongue originally derived its name because the cell injury and necrosis it causes leads to vascular thrombosis, edema, and hemorrhage that may result in a cyanotic or blue tongue. However, the clinical sign of a blue tongue is often not present. Bluetongue is also known as sore muzzle, malarial catarrhal fever, epizootic catarrh, Beksiekte, and muzzle disease.⁴

1.3.2 Virus Characteristics

According to the International Committee on Taxonomy of Viruses,⁵ BTV is categorized as follows:

- Family: *Reoviridae*
- Subfamily: *Sedoreovirinae*
- Genera: *Orbivirus*.

There are currently 27 different serotypes,⁶ of which, all but one can be genetically traced to their original geographic origin;⁷ the exception is BTV-27 due to its recent (2014) discovery. Serotypes differ in virulence, hence the extent of clinical signs may vary. The numerous serotypes are the result of genetic shift (reassortment) and drift (mutation)⁸ from alternating passage of BTV through ruminant and insect hosts.

1.3.3 Morphology

BTV is a non-enveloped, linear, and segmented double-stranded ribonucleic acid (dsRNA) virus. There are 10 segments that code for 10 proteins, 7 structural proteins (VP1–VP7) and 3 non-structural (NS1, NS2, NS3/NS3a) proteins. Two of the structural proteins (VP2 and VP5) make up the icosahedral capsid of the virus. Serotype is primarily determined by VP2, the most variable of the BTV proteins, which interacts with neutralizing antibodies. The geographic origin of the serotypes is reflected in the variable sequence of the segments that make up a specific serotype's genome, allowing further classification of serotypes into topotypes.⁹

⁴ Center for Food Security and Public Health (CFSPH), Iowa State University. (2015). Bluetongue. Retrieved from <http://www.cfsph.iastate.edu/Factsheets/pdfs/bluetongue.pdf>.

⁵ International Committee on Taxonomy of Viruses (ICTV). (2016). Virus taxonomy: 2014 Release. Retrieved from http://www.ictvonline.org/virusTaxonomy.asp?taxnode_id=20143496.

⁶ Jenckel, M., et al. (2015). Complete coding genome sequence of putative novel bluetongue virus serotype 27. *Genome Announcements*, 3(2). <http://dx.doi.org/10.1128/genomeA.00016-15>.

⁷ Maan, N.S., et al. (2015). A quantitative real-time reverse transcription PCR (qRT-PCR) assay to detect genome segment 9 of all 26 bluetongue virus serotypes. *Journal of Virological Methods*, 213, 118–126. <http://dx.doi.org/10.1016/j.jviromet.2014.11.012>.

⁸ MacLachlan, N.J., & Guthrie, A.J. (2010). Re-emergence of bluetongue, African horse sickness and other Orbivirus diseases. *Veterinary Research*, 41(6), 35–46. <http://dx.doi.org/10.1051/vetres/2010007>.

⁹ Dal Pazzo, F., et al. (2009). Bovine infection with bluetongue virus with special emphasis on European serotype 8. *The Veterinary Journal*, 182(2), 142–151. <http://dx.doi.org/10.1016/j.tvjl.2009.05.004>.

1.4 Ecology

1.4.1 Susceptible Species

Most wild and domestic ruminants are susceptible to BTV infection, including, sheep, goats, cattle, water buffalo, African buffalo (*Syncerus caffer*), bison, deer, bighorn sheep, elk, most species of African antelope, and other Artiodactyla such as camels. Recent studies have also suggested that BTV could be infecting carnivorous species such as dogs, cats, cheetahs, lions, etc.^{10,11} However, BTV infection does not always result in disease: cattle, goats, dromedaries, and some wild ruminants often have subclinical infections¹² and may be reservoirs of the disease (especially cattle). Sheep most commonly show clinical signs. The severity of the disease may be influenced by breed, immunological conditions, strain, and environmental factors. In North America, bluetongue (of various serotypes) have been detected in wild species including: white-tailed deer, pronghorn, bighorn sheep, as well as captive Reeve's muntjac and captive greater kudu.

The serotype of concern, BTV-8, infects both domestic and wild ruminants; however, to-date, cattle and sheep are most frequently affected. BTV-8 has also been found in deer, goats, zoo animals, and a Eurasian lynx (carnivore).¹³ In addition, it is believed that South American camelids are susceptible to BTV-8 based on seroprevalence, though other research notes negligible epidemiological significance of camelid infection.^{14,15}

1.4.2 Transmission and Vector

BTV can be transmitted both mechanically and biologically. Surgical equipment and needles can also transfer the virus between ruminants, however this is thought to be insignificant compared to biological means. The biting midge (*Culicoides* spp.), commonly referred to as gnats, are the primary vector transmitting BTV. These insects become infected by feeding on viremic animals and remain infective for the duration of their lives, up to 3 months,¹⁶ replicating the virus in their

¹⁰ Oura, C.A.L. & Harrak, M. EL. (2011). Midge-transmitted bluetongue in domestic dogs. *Epidemiology and Infection*, 139(09), 1396–1400. <http://dx.doi.org/10.1017/S0950268810002396>.

¹¹ Alexander, K.A., et al. (1994). Evidence of natural bluetongue virus infection among African carnivores. *American Journal of Tropical Medicine and Hygiene*, 51(5), 568–576. Retrieved from https://www.researchgate.net/profile/Kathleen_Alexander/publication/15212990_Evidence_of_natural_bluetongue_virus_infection_among_African_carnivores/links/004635228bcec4dc84000000.pdf.

¹² OIE. (2013). Bluetongue. Technical Disease Card. Retrieved from http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/BLUETONGUE.pdf.

¹³ CFSPH. (2015). Bluetongue. Retrieved from <http://www.cfsph.iastate.edu/Factsheets/pdfs/bluetongue.pdf>.

¹⁴ Schulz, C., et al. (2012). Cross-sectional study of bluetongue virus serotype 8 infection in South American camelids in Germany (2008/2009). *Veterinary Microbiology*, 160(1), 35–42. <http://dx.doi.org/10.1016/j.vetmic.2012.05.028>.

¹⁵ Zanolari, P., et al. (2010). Serological Survey of Bluetongue Virus Serotype-8 Infection in South American Camelids in Switzerland (2007–2008). *Journal of Veterinary Internal Medicine*, 24(2), 426–430. <http://onlinelibrary.wiley.com/doi/10.1111/j.1939-1676.2009.0464.x/epdf>.

¹⁶ Purse, B.V., et al. (2015). Bionomics of temperate and tropical *Culicoides* midges: knowledge gaps and consequences for transmission of *Culicoides*-borne viruses. *Annual Review of Entomology*, 60, 373–392. <http://dx.doi.org/10.1146/annurev-ento-010814-020614>.

salivary glands every 6–8 days.¹⁷ Vector activity is directly influenced by temperature—increasing with the rising temperature maximizing at 28 to 30°C and decreasing or ceasing at cooler temperatures.¹⁸

After a bite by a BTV infected *Culicoides* midge, it has been demonstrated that the virus can persist in animal blood for 5–9 weeks, as demonstrated in cattle, and in viral ribonucleic acid (RNA) much longer.^{19,20} Prolonged viremia may have been seen in other species as well, though the existence and characteristics of the carrier state in any species is not yet well understood.

Some serotypes, including BTV-8, appear to have the ability to survive over winter, though it appears to be uncommon. This overwintering may be the result of midge survival in warmer environments during colder months, such as indoors. A recent example of overwintering occurred during the 2015–2016 European outbreak where BTV-8 resurfaced in France: genetic testing resulted in 95 percent homology to European strains that circulated in 2006–2008, but full typing is still being performed.²¹ The exact method(s) in which overwintering can occur remain unknown: research has presented evidence that latent virus found in ruminants may play a role, others have posited that it may be possible for *Culicoides* larvae to extend development through the winter, though lengthy cold temperatures will still kill the pupae.^{22,23,24} There are many theories about overwintering but little confirmed evidence from field conditions.

Additionally, field observations and experimental studies have shown that BTV-8 is capable of transplacental (vertical) transmission and oral transmission in cattle²⁵ and sheep.²⁶ BTV-8 is

¹⁷ OIE. (2013). Bluetongue. Technical Disease Card. Retrieved from

http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/BLUETONGUE.pdf.

¹⁸ Saegerman, C., et al. (2008). Bluetongue epidemiology in the European Union. *Emerging Infectious Diseases*, 14(4), 539. <http://dx.doi.org/10.3201%2F1404.071441>.

¹⁹ Di Galleonardo, L., et al. (2011). The length of BTV-8 viraemia in cattle according to infection doses and diagnostic techniques. *Research in Veterinary Science*, 91(2), 316–320.

[doi:http://dx.doi.org/10.1016/j.rvsc.2010.12.017](http://dx.doi.org/10.1016/j.rvsc.2010.12.017).

²⁰ Singer, R. S., MacLachlan, N. J., & Carpenter, T. E. (2001). Maximal Predicted Duration of Viremia in Bluetongue Virus—Infected Cattle. *Journal of Veterinary Diagnostic Investigation*, 13(1), 43–49. doi: 10.1177/104063870101300109.

²¹ Roberts, H., & Smith, J. (2015). Bluetongue virus (BTV-8) in France. *Department for Environment, Food and Rural Affairs Animal and Plant Health Agency Veterinary & Science Policy Advice Team—International Disease Monitoring*. Retrieved from https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/471263/poa-update2-btv8-france.pdf.

²² Luedke, A.J., et al. (1977). Overwintering mechanism for bluetongue virus: biological recovery of latent virus from a bovine by bites of *Culicoides variipennis*. *The American Journal of Tropical Medicine and Hygiene*, 26(2), 313–325.

²³ Purse, B.V., et al. (2015). Bionomics of temperate and tropical *Culicoides* midges: knowledge gaps and consequences for transmission of *Culicoides*-borne viruses. *Annual Review of Entomology*, 60, 373–392.

<http://dx.doi.org/10.1146/annurev-ento-010814-020614>.

²⁴ Takamatsu, H., et al. (2003). A possible overwintering mechanism for bluetongue virus in the absence of the insect vector. *Journal of General Virology*, 84(1), 227–235. <http://dx.doi.org/10.1099/vir.0.18705-0>.

²⁵ Backx, A., et al. (2009). Transplacental and oral transmission of wild-type bluetongue virus serotype 8 in cattle after experimental infection. *Veterinary Microbiology*, 138(3), 235–243.

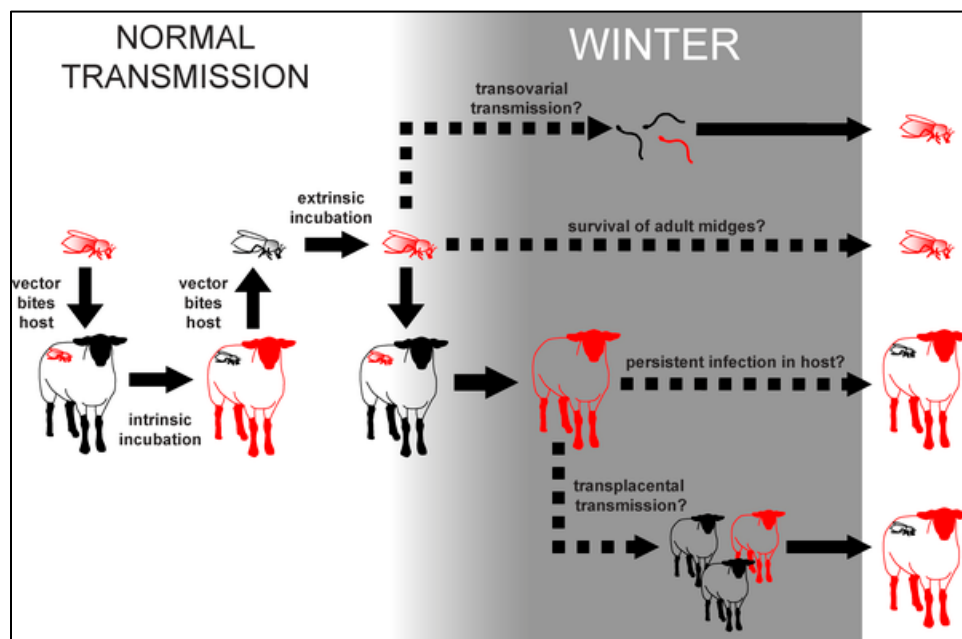
<http://dx.doi.org/10.1016/j.vetmic.2009.04.003>.

²⁶ van der Sluijs, M., et al. (2011). Transplacental transmission of Bluetongue virus serotype 8 in ewes in early and mid gestation. *Veterinary Microbiology*, 149(1), 113–125. <http://dx.doi.org/10.1016/j.vetmic.2010.11.002>.

known to be shed in semen from cattle²⁷ and also has been detected in rams.²⁸ The method of carnivore infection is unknown, but it is speculated carnivores become infected by eating infected carcasses or being bitten by *Culicoides*.²⁹ Like overwintering, additional evidence remains needed on these transmission methods; the complete scope of close-contact transmission for BTV-8 is not well understood, though it is presumed to be of minor epidemiological significance. BTV-25, also known as Toggenburg orbivirus, along with BTV-26, lack the typical replication patterns seen in Culicoid vectors, suggesting that alternative or additional transmission pathways may exist for these new viruses.³⁰

Figure 1 depicts the normal BTV transmission pathway and some of the suspected overwintering mechanisms for the virus. Midges and sheep are colored based on infection—those in black are non-infected and those in red are infected.

Figure 1. Bluetongue Virus Transmission in Summer (Left) and Winter (Right)³¹



Note: This figure expresses an example of BTV transmission in sheep including secondary routes that may be taken by some serotypes suggestive of overwintering pathways. Please note that other species are affected; sheep were chosen as a representative species. This figure does not show mechanical, sexual, or direct transmission.

²⁷ Vanbinst, T., et al. (2010). A duplex real-time RT-PCR for the detection of bluetongue virus in bovine semen. *Journal of Virological Methods*, 169(1), 162–168. <http://dx.doi.org/10.1016/j.jviromet.2010.07.019>.

²⁸ Leemans, J., et al. (2012). Viral RNA load in semen from bluetongue serotype 8-infected rams: Relationship with sperm quality. *The Veterinary Journal*, 192(3), 304–310. <http://dx.doi.org/10.1016/j.tvjl.2011.06.028>.

²⁹ CFSPH. (2015). Bluetongue. Retrieved from <http://www.cfsph.iastate.edu/Factsheets/pdfs/bluetongue.pdf>.

³⁰ Jenckel, M., et al. (2015). Complete coding genome sequence of putative novel bluetongue virus serotype 27. *Genome Announcements*, 3(2). <http://dx.doi.org/10.1128/genomeA.00016-15>.

³¹ Wilson, A., et al. (2008). Where does bluetongue virus sleep in the winter. *PLoS Biology*, 6(8), 1612–1617. <http://dx.doi.org/10.1371/journal.pbio.0060210>.

1.4.2.1 Incubation Period

The incubation period of BTV is approximately 5–10 days and may vary with the atmospheric temperature. Cattle with subclinical infections have been found to be viremic as early as 4 days after initial infection.³² It is suspected that during the BTV-8 European outbreak, cattle and sheep had similar incubation times consistent with normal BTV incubation.³³

1.4.3 Morbidity and Mortality

Morbidity and mortality vary widely by species (even by breed in sheep), serotype of virus, prior exposure, and uncharacterized environmental factors. Most species usually experience subclinical infections; ruminants, primarily sheep, do show clinical signs. Morbidity ranges from less than 5 percent to 50–75 percent or higher and mortality can reach up to 90 percent although generally less than 30 percent. Cattle and goats typically present with reduced morbidity and mortality is rare. In endemic regions, morbidity is as low as 1–2 percent or even absent.³⁴

1.4.3.1 Bluetongue Virus Serotype 8 Morbidity and Mortality

BTV-8, as seen during the 2006–2008 European outbreak, resulted in atypical morbidity and mortality. Cattle, normally asymptomatic, presented clinical signs including reproductive disorders. During 2007 in Germany, case fatality rates were calculated to be as high as 13 percent;³⁵ however this was not indicative of the entire outbreak. Overall, it was reported that there was approximately a mortality rate of less than 1 percent mortality rate in Europe.^{36,37} On the other hand, wild whitetail deer and pronghorn antelope had morbidity rates as high as 100 percent and case fatality rates up to 80–90 percent.³⁸ In Germany, one of the few countries where detailed data was available, the case fatality rate during the BTV-8 outbreak was 37 percent for sheep³⁹ and 26 percent for goats.⁴⁰

1.4.4 General Clinical Signs

For most strains of the 27 serotypes known to cause disease, serious clinical signs are rarely seen outside of sheep and a few cervid species. The predominant mechanism of disease is vascular injury resulting in edema, hemorrhage, and ulceration of mucosa throughout the body. Infected

³² OIE. (2013). Bluetongue. Technical Disease Card. Retrieved from http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/BLUETONGUE.pdf.

³³ Guyot, H., et al. (2008). Clinical aspects of bluetongue in ruminants. In *Bluetongue in Northern Europe*, C. Saegerman, F. Reviriego-Gordejo, & P.-P. Pastoret, (Eds.) Paris: OIE. Retrieved from <http://www.oie.int/doc/ged/D11509.PDF>.

³⁴ CFSPH. (2015). Bluetongue. Retrieved from <http://www.cfsph.iastate.edu/Factsheets/pdfs/bluetongue.pdf>.

³⁵ Conraths, F.J., et al. (2009). Epidemiology of bluetongue virus serotype 8, Germany. *Emerging Infectious Diseases*, 15(3), 433. Retrieved from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2681128/>.

³⁶ OIE. (2013). Bluetongue. Technical Disease Card. Retrieved from http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/BLUETONGUE.pdf.

³⁷ Conraths, F.J., et al. (2009). Epidemiology of bluetongue virus serotype 8, Germany. *Emerging Infectious Diseases*, 15(3), 433. Retrieved from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2681128/>.

³⁸ CFSPH. (2015). Bluetongue. Retrieved from <http://www.cfsph.iastate.edu/Factsheets/pdfs/bluetongue.pdf>.

³⁹ Conraths, F.J., et al. (2009). Epidemiology of bluetongue virus serotype 8, Germany. *Emerging Infectious Diseases*, 15(3), 433. Retrieved from <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2681128/>.

⁴⁰ CFSPH. (2015). Bluetongue. Retrieved from <http://www.cfsph.iastate.edu/Factsheets/pdfs/bluetongue.pdf>.

animals, such as sheep and deer, can experience death within 8–10 days or have an extended recovery period with subsequent alopecia, sterility, and growth delay.⁴¹ In general, the severity of infection and clinical signs expressed are dependent on the serotype, which can result in rapid fatality to mild infection and quick recovery.

1.4.4.1 Sheep Clinical Signs

Sheep are the most susceptible to BTV infection, which may be subclinical or result in mild to severe clinical signs. Signs of illness can include fever, excessive salivation, depression; dyspnea and panting; nasal discharge that becomes mucopurulent and crusts around the nostrils; hyperemia, congestion, and edema of the head and facial tissues; and ulceration and necrosis of the oral mucosa. The coronary bands of the hooves may become hyperemic and can result in lameness due to the pain. Pregnant ewes infected with BTV may abort their fetuses or give birth to malformed lambs. Torticollis, pneumonia, emaciation, and conjunctivitis may be additional clinical signs.⁴²

1.4.4.2 Cattle and Goat Clinical Signs

Typically cattle and goats have subclinical infections, but in clinical cases, the presentation is similar to that in sheep. If present, signs of illness may include facial edema, oral inflammation with vesicles or ulcers in the mouth, excess salivation, nasal discharge, crusting around the muzzle, edema of the distal limbs, hyperemia of the coronary band with lameness, udder and teat lesions, decreased milk production, and abortions or births with Central Nervous System lesions resulting in “dummy” lambs. Specifically, cattle can have skin lesions varying in severity, including photodermatitis that leads to thickening, cracking, and sloughing.⁴³

1.4.4.3 Clinical Signs in Wildlife and Other Species

Species of cervids can present with clinical signs depending on the serotype; however, subclinical infections are most common. White-tailed deer tend to have the following signs in addition to those presented in sheep: severe fever, depression, anorexia, and loss of normal fear responses. Pronghorn may suddenly die or have prolonged sickness. There is little information on other cervid species.⁴⁴

There have been only a few incidents where carnivore species have been infected by BTV. They are suspected to remain predominately asymptomatic. Known infections resulted in clinical signs including, but not limited to, abortions, unspecified illness, and dyspnea.⁴⁵

1.4.5 Bluetongue Virus Serotype 8 Clinical Signs

Until 2006, infection of cattle was largely subclinical; clinical signs were believed to be linked to confounding factors. The 2006–2008 BTV-8 epidemic in Northern and Central Europe was

⁴¹ OIE. (2013). Bluetongue. Technical Disease Card. Retrieved from http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/BLUETONGUE.pdf.

⁴² CFSPH. (2015). Bluetongue. Retrieved from <http://www.cfsph.iastate.edu/Factsheets/pdfs/bluetongue.pdf>.

⁴³ CFSPH. (2015). Bluetongue. Retrieved from <http://www.cfsph.iastate.edu/Factsheets/pdfs/bluetongue.pdf>.

⁴⁴ CFSPH. (2015). Bluetongue. Retrieved from <http://www.cfsph.iastate.edu/Factsheets/pdfs/bluetongue.pdf>.

⁴⁵ CFSPH. (2015). Bluetongue. Retrieved from <http://www.cfsph.iastate.edu/Factsheets/pdfs/bluetongue.pdf>.

notable because cattle were more frequently infected than sheep, although it is unclear if this is attributed to herd populations or virulence.⁴⁶ These cattle were considered a naïve population, which could have added to the multitude of factors that gave way to such a large and significant outbreak.

Signs of illness caused by BTV-8 in cattle are similar to those observed in sheep and cervids infected with various other serotypes. In both cattle and sheep, the type and frequency of signs that can be seen are highly variable, affecting every organ system. Commonly observed signs included anorexia, lethargy, ulcerated and necrotic muzzle tissue, rash on the muzzle, edema localized to the distal limbs, lesions on the udder skin, decreased milk production, and an increased rate of reproductive disorders (abortion, stillbirth, and congenital abnormalities). Cattle predominately experienced a reduced milk yield or reproductive disorders, whereas sheep experienced hyperthermia, in addition to general signs associated with BTV-8.⁴⁷ The high rate of reproductive disorders observed is believed to be correlated with the virus' affinity for trophoblast cells or its ability to cross the placenta.⁴⁸

1.4.6 Differential Diagnosis

Bluetongue presents with clinical signs similar to the following conditions:⁴⁹

- Contagious ecthyma
- Foot-and-mouth disease
- Vesicular stomatitis
- Malignant catarrhal fever
- Bovine virus diarrhea
- Infectious bovine rhinotracheitis
- Parainfluenza-3 infection
- Sheep pox
- Photosensitization
- Pneumonia
- Polyarthritis, footrot, foot abscesses
- Plant poisonings (photosensitization)
- Peste de petits ruminants

⁴⁶ Dal Pazzo, F., et al. (2009). Bovine infection with bluetongue virus with special emphasis on European serotype 8. *The Veterinary Journal*, 182(2), 142–151. <http://dx.doi.org/10.1016/j.tvjl.2009.05.004>.

⁴⁷ Guyot, H., et al. (2008). Clinical aspects of bluetongue in ruminants. In *Bluetongue in Northern Europe*, C. Saegerman, F. Reviriego-Gordejo, & P.-P. Pastoret, (Eds.) Paris: OIE. Retrieved from <http://www.oie.int/doc/ged/D11509.PDF>.

⁴⁸ Dal Pazzo, F., et al. (2009). Bovine infection with bluetongue virus with special emphasis on European serotype 8. *The Veterinary Journal*, 182(2), 142–151. <http://dx.doi.org/10.1016/j.tvjl.2009.05.004>.

⁴⁹ OIE. (2013). Bluetongue. Technical Disease Card. Retrieved from http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/BLUETONGUE.pdf.

- Coenurosis (*Oestrus ovis* infestation)
- Epizootic hemorrhagic disease of deer.

1.5 Environmental Persistence of Bluetongue Virus

To date, there is no evidence that BTV can persist in the environment, as it is unable to persist outside of the vector species or host species. If it is able to persist in the environment where, for example, protein is present, there is no evidence that this persistence has led to transmission or is epidemiologically relevant. Table 1 presents other environmental persistence characteristics of BTV.

Table 1. Resistance of Bluetongue Virus to Physical and Chemical Action⁵⁰

Action	Resistance
Temperature	Inactivated by 50°C/3 hours; 60°C/15 minutes
pH	Sensitive to pH < 6.0 and > 8.0
Chemicals/Disinfectants	Inactivated by sodium hypochlorite, 3% sodium hydroxide, ⁵¹ β-propiolactone, iodophores, and phenolic compounds
Survival	Very stable in the presence of protein (e.g., has survived for years in blood stored at 20°C). No evidence of persistence in the natural environment without a vector or host species.

1.6 Distribution

BTV has been found on every continent except Antarctica. Historically, the distribution has been throughout temperate and tropical climates according to the distribution of competent *Culicoides* species vectors, specifically between 40° North and 35° South. Distribution of different BTV serotypes are typically determined by the appropriate species of *Culicoides* and its habitat. There are approximately 1,400 species of *Culicoides* throughout the world; only about 30 have been shown to be competent biological vectors.⁵²

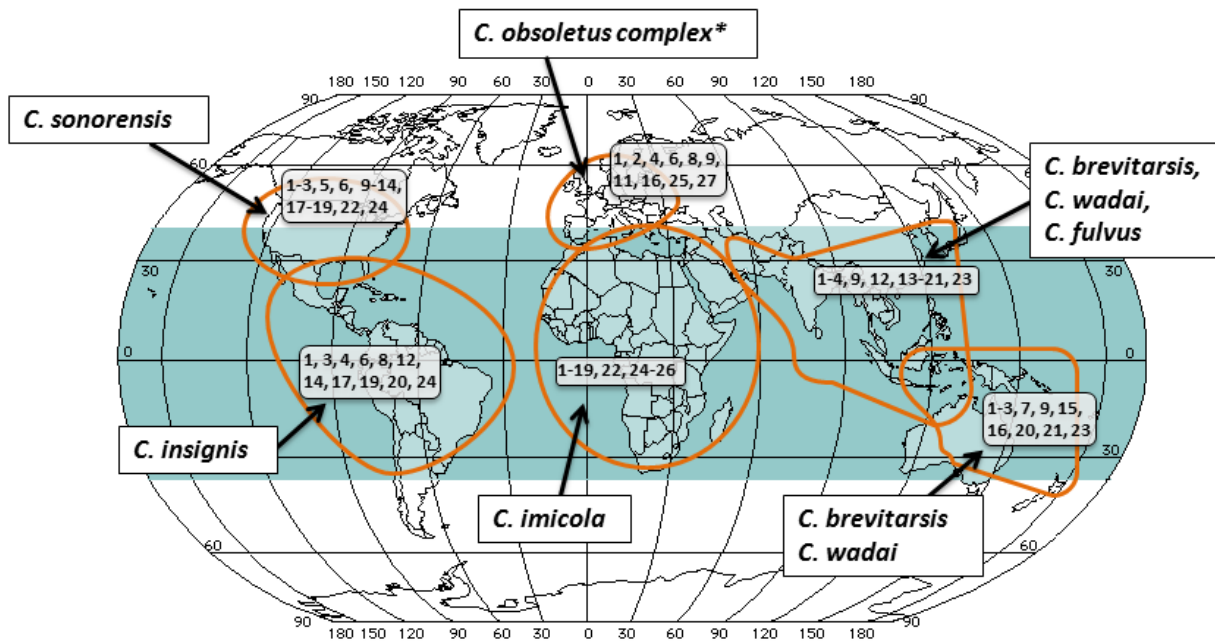
Figure 2 illustrates the relationship between the major *Culicoides* vectors, their predominant geographic location, and the presence of BTV serotypes (indicated within the black boxes).

⁵⁰ OIE. (2013). Bluetongue. Technical Disease Card. Retrieved from http://www.oie.int/fileadmin/Home/eng/Animal_Health_in_the_World/docs/pdf/Disease_cards/BLUETONGUE.pdf.

⁵¹ CFSPH. (2015). Bluetongue. Retrieved from <http://www.cfsph.iastate.edu/Factsheets/pdfs/bluetongue.pdf>.

⁵² The Merck Veterinary Manual. (2014). Overview of Bluetongue. Retrieved from http://www.merckvetmanual.com/mvm/generalized_conditions/bluetongue/overview_of_bluetongue.html.

Figure 2. Approximate Geographic Distribution of Bluetongue Virus Serotypes and Major Vectors⁵³



* The *C. obsoletus* complex comprises of several other closely related species of midges. This particular complex and its various species is not all inclusive to the European region, but is the primary species in addition to *C. imicola* which resides in the Mediterranean area.

1.6.1 European Distribution and Significance

In recent years, bluetongue outbreaks have occurred in North and Central Europe (Figure 2), regions of Asia, and Western North America as far as 50° North. These areas were previously believed to be not at risk for bluetongue. The means of introduction into Northern Europe has not been conclusively determined, although it is believed that climate change factored into BTV expanding beyond its traditional boundaries.⁵⁴

Research has implicated the *C. obsoletus* complex, including *C. dewulfi*, as competent vectors for transmission of BTV-8. However, the recent migration of *C. imicola* into the Mediterranean region, historically only a resident of Africa, tested positive for BTV-8, attributing to serotype 8 transmission.⁵⁵ The introduction of BTV-8 into Europe has resulted in significant economic losses due to animal morbidity/mortality and trade restrictions.

⁵³ Adapted from Tabachnick W.J., University of Florida, Institute of Food and Agricultural Sciences (UF/IFAS). (2008). Bluetongue. Retrieved from <http://edis.ifas.ufl.edu/pdf/IN/IN76800.pdf>.

⁵⁴ MacLachlan, N.J. & Guthrie, A.J. (2010). Re-emergence of bluetongue, African horse sickness and other Orbivirus diseases. *Veterinary Research*, 41(6), 35–46. <http://dx.doi.org/10.1051/vetres/2010007>.

⁵⁵ Goffredo, M., et al. (2015). Vector species of *Culicoides* midges implicated in the 2012–2014 Bluetongue epidemics in Italy. *Veterinaria Italiana*, 51(2), 131–138. Retrieved from http://www.izs.it/vet_italiana/2015/51_2/131.htm.

The distribution of serotypes 1, 2, 4, 8, and 16 are currently found within Europe.⁵⁶ Interestingly, cases of BTV-8 in France, along with other present serotypes, unexpectedly (based on known transmission information) continued through cold winter temperatures.⁵⁷ At this point, the cause of these continued detections is unclear: it is possible that diagnostic testing may be detecting RNA, but not infectious virus,⁵⁸ it could signify new methods of transmission, or overwintering may be occurring. Further research is necessary.

1.6.2 Distribution in North America

In North America, serotypes 10, 11, 13, and 17 are endemic, coincident with *C. sonorensis* distribution. Serotype 2, also endemic, previously was restricted to the southeastern United States, corresponding to the distribution of *C. insignis*; however, recently it was detected in California indicating translocation and reassortment due to unknown viral spread.⁵⁹ Since 1999, isolates of 11 previously unrecognized non-endemic serotypes (1, 3, 5, 6, 9, 12, 14, 18, 19, 22, and 24) have also been found in the southeastern United States—concentrating mostly in Florida. Bluetongue is seasonally absent in the central and northwestern States; the northern and northeastern regions are BTV free.

Figure 3 was created by the National Veterinary Services Laboratory (NVSL) to illustrate detections of BTV serotypes within the United States between 1992 and 2015; therefore, this map does not reflect any type of national surveillance data.

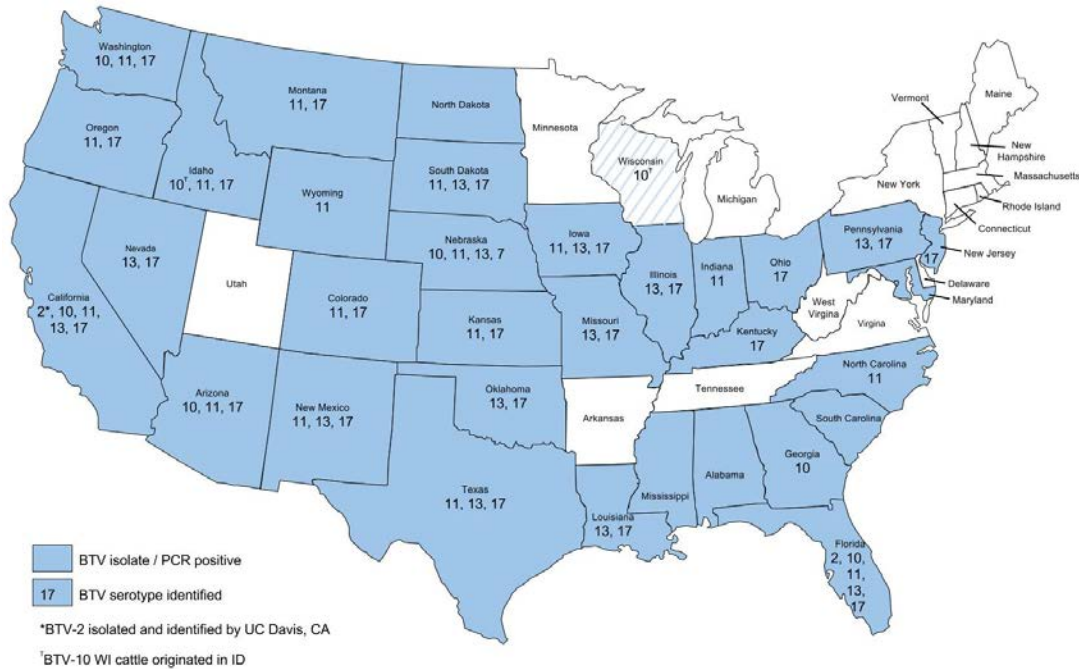
⁵⁶ European Commission—Animals. (2016). Bluetongue restriction zones established by Member States. *Bluetongue*. Retrieved from http://ec.europa.eu/food/animals/animal-diseases/control-measures/bluetongue/index_en.htm.

⁵⁷ European Commission. (2016). Bluetongue seasonally vector free periods. *Bluetongue*. Retrieved from http://ec.europa.eu/food/animals/docs/ad_control-measures_bt_overview_seasonally_vfp_2015-2016.pdf.

⁵⁸ Di Gialleonardo, L., et al. (2011). The length of BTV-8 viremia in cattle according to infection doses and diagnostic techniques. *Research in Veterinary Science*, 91(2), 316–320. Retrieved from <http://www.hachaklait.org.il/files/441204.pdf>.

⁵⁹ Maclachlan, N.J., et al. (2013). Novel serotype of bluetongue virus, western North America. *Emerging Infectious Diseases*, 19(4), 655–666. <http://dx.doi.org/10.3201%2F1904.120347>.

Figure 3. NVSL Bluetongue Virus Isolation and RNA Identification in the United States between 1992 and 2015*



Note: This map represents results that were obtained by the NVSL for reasons other than surveillance and therefore do not necessarily reflect the true bluetongue distribution in the United States.

* This map and data are used with permission from Dr. E. Ostlund and the Equine/Ovine Diagnostic Veterinary Laboratory branch at the NVSL.

1.7 Vaccines

Effective BTV vaccine development is largely a challenge; however, there are a limited number of modified live attenuated vaccines available for use in the United States. The only nationally approved and available vaccine is for BTV-10 produced by the Colorado Serum Company.⁶⁰ In addition, Poultry Health Laboratories produced modified live vaccines for BTV-10, -11, and -17 for approved use in healthy California sheep.⁶¹ The use of attenuated vaccines pose significant health risks to livestock that include reduced milk production, abortion, and teratogenesis. Furthermore, midges feeding on attenuated vaccinate animals can become infected and disseminate the virus where reassortment can occur with wild-type BTV in the environment resulting in novel progeny.⁶²

⁶⁰ Center for Veterinary Biologics. (2016). Veterinary Biological Products Licensees and Permittees. *United States Department of Agriculture*. Retrieved from https://www.aphis.usda.gov/animal_health/vet_biologics/publications/CurrentProdCodeBook.pdf.

⁶¹ Center for Veterinary Biologics. (2016). Veterinary Biological Products Licensees and Permittees. *United States Department of Agriculture*. Retrieved from https://www.aphis.usda.gov/animal_health/vet_biologics/publications/CurrentProdCodeBook.pdf.

⁶² United States Department of Agriculture (USDA) Agricultural Research Service (ARS). (2013). Orbiviruses Gap Analysis: Bluetongue and Epizootic Hemorrhagic Disease. *ARS Workshop Report*. Retrieved from <http://go.usa.gov/BJ5F>.

Inactivated vaccines are not available in the United States, although considered a safer alternative than attenuated vaccines. During the incursion of BTV-8 in Europe, inactivated BTV-1, and -8 vaccines were available in two doses, but not until 2008—2 years after the outbreak began. These inactivated vaccines are no longer available for use.⁶³

Currently, both inactivated and live-attenuated BTV vaccines do not have the capability to differentiate infected and vaccinated animals (also known as the DIVA strategy); however, virus-like particle vaccines could provide an alternative as research progresses.⁶⁴

1.8 Risk of BTV-8 Introduction to the United States

In the United States, there are now a total of 16 BTV serotypes that have been isolated—starting as early as 1950, but mostly detected after 1998. Incursive serotypes are continually pressing the U.S. southern border. It is believed that the majority of these serotypes originated in the Caribbean and Central America, brought in by *Culicoides* spp. that were carried by prevailing winds or by large weather events such as tropical storms and hurricanes. BTV-8 has not been detected in the United States, but it has been identified in Central America.⁶⁵ The initial introduction of BTV-8 into Northern and Central Europe in 2006 was also believed to be through wind-borne insects, with subsequent transmission by local insects. This recent expansion of BTV-8 and the movement of the *C. imicola* vector from Africa into Europe clearly indicates that vector patterns and host-ranges are rapidly changing: BTV incursions into the United States are possible, including BTV-8, particularly given its presence in Central America.

Once a novel BTV serotype or BTV-8 enters the United States, there are also significant challenges: there are both competent vectors that can transmit the virus and significant populations of wild cervids which could be a potential virus reservoir. There are 1,357 species of *Culicoides* midges⁶⁶ and 110 species of *Culicoides* found in North America.⁶⁷ While the exact number of competent vectors for BTV-8 in the United States is unknown, it is clear that there is the potential that at least one or more Culicoid vectors could transmit BTV-8 (or another novel serotype) if it was introduced. In addition, USDA ARS, Arthropod-Borne Animal Diseases Research Unit, and the USDA APHIS National Wildlife Research Center have conducted experiments on U.S. white-tailed deer—excellent sentinel animals for *Orbivirus* activity⁶⁸—with European BTV-8. When experimentally infected, white-tailed deer developed clinical signs and

⁶³ USDA ARS. (2013). Orbiviruses Gap Analysis: Bluetongue and Epizootic Hemorrhagic Disease. *ARS Workshop Report*. Retrieved from <http://go.usa.gov/BJ5F>.

⁶⁴ USDA ARS. (2013). Orbiviruses Gap Analysis: Bluetongue and Epizootic Hemorrhagic Disease. *ARS Workshop Report*. Retrieved from <http://go.usa.gov/BJ5F>.

⁶⁵ Mo, C.L., et al. (1994). Bluetongue virus isolations from vectors and ruminants in Central America and the Caribbean. Interamerican Bluetongue Team. *American Journal of Veterinary Research*, 55(2), 211–215. Retrieved from <http://europepmc.org/abstract/med/8172409>.

⁶⁶ Purse, B.V., et al. (2015). Bionomics of temperate and tropical *Culicoides* midges: knowledge gaps and consequences for transmission of *Culicoides*-borne viruses. *Annual Review of Entomology*, 60, 373–392. <http://dx.doi.org/10.1146/annurev-ento-010814-020614>.

⁶⁷ Stelljes, K.B. (1999). The bluetongue triangle. *USDA Agricultural Research Magazine*, 47(7), 4–6. Retrieved from <http://agresearchmag.ars.usda.gov/1999/jul/blue/>.

⁶⁸ USDA ARS. (2013). Orbiviruses Gap Analysis: Bluetongue and Epizootic Hemorrhagic Disease. *ARS Workshop Report*. Retrieved from <http://go.usa.gov/BJ5F>.

exhibited viremia for as long as 28 days.⁶⁹ These results suggest that white-tailed deer may exhibit disease and could pose as reservoirs for BTV-8 in the United States.

As with any emerging disease or re-emerging disease, it is difficult to predict transmission pathways and epidemiological patterns in advance; more field research is needed on initial introduction pathways, vector competence, transmission, disease incidence, and carriers. However, the recent BTV-8 experience in Europe clearly demonstrates the impact bluetongue disease can have on animal agriculture. Particularly for BTV-8 and any novel serotype that affects cattle as well as other ruminants, the economic impact could be serious: for example, the U.S. beef industry had a retail equivalent value of \$95 billion in 2014.⁷⁰ Trade restrictions, lost production, and costs from controlling and containing the disease may all contribute to negative economic consequences and give reason to maintain vigilance against BTV-8 and novel BTV serotypes in the United States.

⁶⁹ Drolet, B.S., et al. (2011). The Netherlands Strain of BTV 8 in White-Tailed Deer. *114th Annual Meeting of the United States Animal Health Association*. November 11–17, 2010. Kansas City: Richardson Publishing. <http://www.usaha.org/Portals/6/Proceedings/USAHAProceedings-2010-114th.pdf>.

⁷⁰ USDA Economic Research Service (ERS). (2015). U.S. Cattle & Beef Industry. *Statistics and Information*. Retrieved from <http://www.ers.usda.gov/topics/animal-products/cattle-beef/statistics-information.aspx>.

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Attachment 1.B Abbreviations

APHIS	Animal and Plant Health Inspection Service
ARS	Agricultural Research Service
BTV	Bluetongue virus
BTV-8	Bluetongue virus serotype 8
CFSPH	Center for Food Security and Public Health
EHDV	Epizootic Hemorrhagic Disease virus
ERS	Economic Research Service
FAD PReP	Foreign Animal Disease Preparedness and Response Plan
ICTV	International Committee on Taxonomy of Viruses
NVSL	National Veterinary Services Laboratory
OIE	World Organization for Animal Health
PCR	polymerase chain reaction
qRT-PCR	quantitative real-time reverse transcription PCR
RNA	ribonucleic acid
RT-PCR	reverse transcriptase polymerase chain reaction
SOP	standard operating procedure
UF/IFAS	University of Florida, Institute of Food and Agricultural Sciences
USAHA	United States Animal Health Association
USDA	United States Department of Agriculture