Bluetongue

Sore Muzzle,
Pseudo Foot-and-Mouth Disease,
Muzzle Disease,
Malarial Catarrhal Fever,
Epizootic Catarrh, Beksiekte

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Importance

Bluetongue is a viral disease, transmitted by *Culicoides* midges, that primarily affects sheep and certain wildlife species, including some cervids. Clinical cases range from sporadic to widespread, and mild to rapidly fatal. Additional economic costs result from reproductive losses, damaged wool and decreased milk production. Other mammals are usually infected subclinically, but a few viruses have caused clinical cases, especially when a new serotype enters an area. In particular, systemic illnesses and reproductive losses are seen occasionally in cattle, and rare cases have also occurred in other livestock, some zoo animals, and pregnant dogs.

Bluetongue can be caused by at least 24 serotypes of bluetongue virus, which circulate in different regions. Viruses are introduced periodically to new areas and can become endemic if they become established in competent *Culicoides* vectors. Typically this only occurs in tropical and subtropical regions; however, at least one virus demonstrated the ability to overwinter in colder areas during serotype 8 outbreaks in Europe in 2006. These outbreaks, which sometimes occurred in previously bluetongue-naive populations of animals, were extensive and severe and affected a number of species not previously known to be susceptible. Although this serotype 8 virus apparently disappeared after extensive vaccination programs, it was found again in France in 2015, though its effects have been much milder.

Etiology

Bluetongue is caused by bluetongue virus, a member of the epizootic hemorrhagic disease serogroup in the genus *Orbivirus* and family Sedoreoviridae. Twenty-four 'historical' serotypes are known to cause this disease, each containing multiple strains that can differ in virulence. Several 'atypical' bluetongue serotypes have also been described in the last 20 years. The latter viruses have usually been found in asymptomatic animals and seem to be of limited virulence. Whether they should be considered to cause bluetongue is unclear. Bluetongue viruses can undergo genetic reassortment with each other, as well as with attenuated vaccine strains, to produce new variants.

Species Affected

Among domestic animals, clinical cases mainly occur in sheep, though there are occasional reports of illnesses in other species including cattle, goats, yaks, llamas, alpacas, Bactrian camels and pregnant dogs. Bluetongue has also been seen in some captive or free-living wildlife, including wild relatives of small ruminants (e.g., bighorn sheep, *Ovis canadensis*; mouflon, *Ovis aries musimon*; muskoxen, *Ovibos moschatus*; ibex, *Capra spp.)*; cervids such as white-tailed deer (*Odocoileus virginianus*), marsh-deer (*Blastocerus dichotomus*), brocket-deer (*Mazama* sp.), Reeves' muntjac (*Muntiacus reevesi*) and fallow deer (*Dama dama)*; and various other mammals, such as pronghorn (*Antilocapra americana*), blackbuck (*Antilope cervicapra*), North American (*Bison bison)* and European (*Bison bonasus*) bison, greater kudu (*Tragelaphus cupensis*) and Eurasian lynx (*Lynx lynx*). Virologically confirmed asymptomatic infections have been described in water buffalo, dromedary camels, African buffalo (*Syncerus caffer*), wildebeest (*Connochaetes* spp.), Arabian oryx (*Oryx leucoryx*) and other mammals, with serological evidence for infections in many additional species ranging from elephants, rhinoceros and giraffes to collared peccaries (*Pecari tajacu*), tapirs (*Tapirus* spp.), South American sea lions (*Otaria byronia*) and various felids (including domestic cats), canids, hyaenids and genets. Ruminants are thought to act as the maintenance and amplifying hosts.

Atypical bluetongue virus serotypes have mainly been reported in small ruminants, particularly goats, though one virus was found in an alpaca. Some of these viruses seem to have restricted host specificity, with cattle and sometimes even sheep found to be refractory to experimental inoculation. Most seem to infect animals subclinically, though a few viruses can cause clinical signs in experimentally infected sheep.

Zoonotic potential

There is no evidence that bluetongue virus can cause any illness in humans.

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Iowa State University College of Veterinary Medicine

World Organisation for Animal Health Founded as OIE

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Geographic Distribution

Bluetongue viruses are limited to regions where their *Culicoides* vectors can be found, and occur on all continents, as well as many islands such as Australia and the Caribbean. In general, the endemic areas occur in a worldwide band of tropical and subtropical regions ranging from approximately 35° S to 40° N, though viruses also persist in a few mild climate areas outside this region, such as California. Multiple serotypes can be found in many areas.

Viruses occasionally cause outbreaks outside these regions, but generally do not persist, as the vectors die over the winter. Unusually, a serotype 8 virus overwintered for a time in central and northern Europe after the 2006 outbreaks.

Transmission

Bluetongue virus is transmitted by biting midges in the genus *Culicoides*, which are biological vectors and become persistently infected with the virus. The specific vectors differ between regions, but some important species include *C. sonorensis*, *C. brevitarsis*, *C. imicola* and *C. bolitinos*. Other biting arthropods such as sheep keds (*Melophagus ovinus*), cattle lice (*Haematopinus eurysternus*), ticks and mosquitoes might be capable of mechanical transmission, though their role, if any, is thought to be minor. Bluetongue virus can also be spread mechanically on surgical equipment and needles, and potentially even on re-used needles used for subcutaneous inoculations. How the virus overwintered in northern Europe in 2006 is unclear, though some have suggested that infected midges might have persisted in sheltered locations, such as buildings. Transovarial transmission does not occur in *Culicoides*.

At least some bluetongue viruses can also spread directly between animals in close contact. This is thought to be of little significance for serotype 1-24 viruses, but it may be important for the atypical serotypes, some of which do not seem to replicate readily in *Culicoides*, and also accounts for some infections in carnivores that eat contaminated tissues. The mechanisms of direct transmission between ungulates are still uncertain, but oral transmission has been demonstrated experimentally, and aerosols were implicated in some studies. Serotype 26 viruses have been isolated from ocular swabs in goats, with nucleic acids found at low levels in nasal and ocular secretions. Bluetongue virus can also be found in milk, colostrum and semen, with oral transmission via colostrum shown to occur in young ruminants and venereal transmission demonstrated in cattle. Attenuated vaccine strains, as well as some field strains, can infect the fetus *in utero*. Some dogs became infected from a bluetongue virus-contaminated vaccine.

Serotype 1-24 viruses do not seem to establish persistent infections, even in transplacentally infected animals, but they have been isolated from the blood of some species for several weeks or more. In cattle, live virus was recovered for up to 9 weeks, with viral RNA found much longer. Atypical viruses seem to be more likely to establish long-term or persistent infections. Toggenburg orbivirus (serotype 25) has been recovered from some goats for at least 12-19 months, and its nucleic acids were found for up to 4.5 years.

Disinfection

Sodium hypochlorite and 3% sodium hydroxide are reported to inactivate bluetongue virus, and agents active against other orbiviruses, such as iodine and quaternary ammonium disinfectants, are also likely to be effective.

Incubation Period

The incubation period is estimated to be approximately a week, with a range of 2-10 days.

Clinical Signs

Sheep

Sheep, which are typically the only domestic animal to be affected by bluetongue, may either have asymptomatic infections or become mildly to severely ill. In addition to fever, depression and other nonspecific signs of illness, sick sheep usually have edema on the face and/or muzzle; a serous to mucopurulent nasal discharge, which may crust around the nostrils; and hyperemia of the muzzle, oral and nasal mucous membranes, with petechiae or ecchymoses also present in more severe cases. Oral lesions, which can include erosions, ulcerations and mucosal swelling, can result in drooling and reluctance to eat. In severe cases, the tongue may be cyanotic and protrude from the mouth. Some animals also develop hyperemia on the coronary band, with or without petechiae and ecchymoses, and hot, painful hooves. In addition to lameness, many sheep with foot involvement adopt an arched back posture to keep their weight off the hooves. Some animals also have diarrhea, with or without blood, lesions on the udder and teats, and muscle damage, which can result in torticollis. Pregnant sheep may abort.

Some sheep with bluetongue develop dyspnea from pulmonary involvement and die rapidly. Cardiac complications occasionally lead to sudden death, and secondary bacterial complications may be fatal when the course is more prolonged. Mildly affected sheep usually recover rapidly, but more severely affected animals may have sequelae including loss of condition, hoof deformities, a transient decrease in semen quality, and/or partial to full loss of the wool a few weeks after the illness. Pregnant ewes infected with certain viruses may later give birth to lambs that are stillborn or have congenital lesions, including CNS malformations that can result in neurological signs or "dummy" lambs that cannot nurse or follow the ewe, retinal lesions, skeletal deformities, poor lung development and/or growth retardation. The specific syndromes vary with the stage of gestation, and lambs infected later in the pregnancy are usually normal.

Infections with atypical serotypes are typically asymptomatic; however, some of these viruses can cause mild to moderate illnesses in experimentally infected sheep.

Cattle and goats

Infections in cattle and goats are usually subclinical. Clinical cases can resemble bluetongue in sheep but tend to be milder, and some animals have only nonspecific signs of illness. The muzzle of some cattle was reported to have a "burned" cracked appearance during the 2006-2007 serotype 8 outbreaks in Europe. Some infections were also associated with various skin lesions such as vesicular and ulcerative dermatitis, periocular dermatitis, necrotic lesions and photodermatitis. Reproductive losses can include abortions, stillbirths and congenital abnormalities. Congenital lesions, which occur in calves infected early in gestation, can include blindness and CNS abnormalities (hydranencephaly, microphthalmia), with affected calves usually dying a few days after birth. Some healthy calves infected late in gestation have developed transient corneal opacity from antibody/ antigen complexes after receiving colostrum. Deaths are possible in adult animals, but uncommon.

Atypical serotypes often circulate asymptomatically in goats.

Camelids

Only a few clinical cases have been described in llamas and alpacas. Several fulminant, fatal infections were characterized by brief (< 24 hour) histories of severe respiratory distress, with recumbency or reluctance to rise, followed rapidly by death. Additional signs in some cases included disorientation, paresis and abortion. Some reports described isolated cases; in others, a few additional animals also had dyspnea, or were reported to have had respiratory signs but recovered without a definitive diagnosis of the condition. Small numbers of experimentally infected llamas or alpacas only developed mild signs (anorexia, mild conjunctivitis, unusual recumbency, signs of discomfort, low grade lung sounds) or remained asymptomatic.

Sudden death was reported in one Bactrian camel at a European zoo during serotype 8 outbreaks. Three dromedary camels experimentally infected with a serotype 1 virus remained asymptomatic.

Cervids and other ungulates

Some clinical cases in white-tailed deer, marsh deer and brocket deer are similar to those in sheep, and may include severe respiratory distress. Other individuals had prominent hemorrhagic signs including multifocal hemorrhages in the skin and mucosa, severe bloody diarrhea, or excessive bleeding and hematoma formation at venipuncture sites. Peracute disease characterized by head and neck edema, or acute cases mainly characterized by hemorrhages throughout the body, predominated in some epidemics in white-tailed deer. Many of these cases were fatal. Fallow deer affected by serotype 8 outbreaks at European zoos sometimes developed oral ulcers, excess salivation, difficulty eating and lameness, while others died with few or no clinical signs.

Clinical cases in some other ungulates, such as bighorn sheep or mouflon, resemble bluetongue in sheep, while pronghorn antelope mainly seem to have nonspecific signs of illness, even in fatal cases, or die with few or no preceding signs. Sporadic fatal cases in other hosts have included sudden deaths in captive Alpine ibex (*Capra ibex*) and blackbuck, bluetongue-like signs in captive bison in Europe, and hemorrhagic signs in some hosts. A Siberian ibex (*Capra sibirica*) developed swelling of the head and neck, but survived, while a musk ox had fever, lethargy and conjunctivitis, and aborted.

Carnivores

There are a few reports of bluetongue virus-associated abortions, either with or without systemic illness, in pregnant dogs. Some cases were fatal, typically with dyspnea and/or signs of heart failure. One dog was found dead after apparent recovery from a caesarean section the previous day. Another developed acute dyspnea, together with nonspecific signs of illness, but recovered with supportive treatment and antibiotics. It later aborted, although live fetuses had been detected at discharge. A few experimentally infected, nonpregnant dogs remained well, and the existence of healthy seropositive dogs in some endemic regions suggests that most infections are asymptomatic.

Lethargy was the only sign reported in two bluetongue virus-infected Eurasian lynx. One animal died after 2 days, with hemorrhagic lesions and lung congestion found at necropsy, and virological confirmation of the infection. The other animal died several months later with pneumonia, petechial hemorrhages, anemia and lymphadenopathy. Only serological evidence of bluetongue virus exposure was found at this time.

Post Mortem Lesions

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In addition to the external lesions seen in living animals, bluetongue in sheep is characterized by generalized edema and hemorrhages in the skeletal muscles and various internal organs. Pulmonary edema, which may be accompanied by pleural and pericardial effusion, is common in fatal cases. The heart often contains petechiae, ecchymoses and necrotic foci, including two characteristic bluetongue lesions: focal necrosis in the papillary muscle of the left ventricle and subintimal hemorrhage at the base of the pulmonary artery. The gastrointestinal tract from the mouth to the forestomachs is also affected in many cases, with mucosal hyperemia, hemorrhages, erosions and/or ulcers, particularly at sites of mechanical abrasion such as the buccal surface of the cheek, esophageal groove and omasal fold. Congenital lesions in fetuses and neonates can include hydranencephaly, porencephaly, retinal dysplasia and skeletal abnormalities, as well as reduced lung size and growth retardation.

Similar gross lesions, which sometimes include widespread hemorrhages, may be seen in other species.

Diagnostic Tests

Bluetongue virus, its nucleic acids and antigens may be detected in blood, bone marrow, lymph nodes and internal organs such as the spleen, lung and liver. Virus recovery from blood is most likely to be successful early in the illness. Semen

may also contain the virus. Vaccine strains and (infrequently) a few field strains, including members of serotypes 3, 4 and 8, have been found in fetal and placental tissues.

Clinical cases are often diagnosed by detecting viral RNA with various RT-PCR tests, which can also identify the viral serotype. Antigen capture ELISAs can be used to detect viral antigens in clinical samples, but serotypes cross-react, and false negatives are reported to be common in blood. Serotype 1-24 viruses can be isolated in some mammalian or *Culicoides* cell lines, such as KC cells, or in embryonated chicken eggs. Atypical serotypes are often more difficult to isolate; however, some serotypes previously thought to be uncultivable will grow in certain mammalian or arthropod (e.g., mosquito) cell lines. Isolated viruses are usually identified to the serogroup level by RT-PCR, though immunostaining or group-specific antigen-capture ELISAs can also be used. Viruses can be serotyped by RT-PCR, gene sequencing or virus neutralization tests. Serotyping by virus neutralization may be difficult to interpret due to cross-reactivity between certain serotypes. Animal inoculation in sheep or suckling mice is sensitive but was mostly used in the past.

Serological tests, often used in surveillance, include ELISAs, virus neutralization and agar gel immunodiffusion (AGID). Monoclonal antibody-based competitive ELISAs can distinguish antibodies to bluetongue virus and the closely related epizootic hemorrhagic disease virus, which are indistinguishable by AGID. Rapid immunochromatographic tests have also been developed, and an indirect ELISA can detect antibodies in bulk milk samples.

Treatment

Treatment is supportive and symptomatic.

Control

Disease reporting

Veterinarians who suspect an animal is infected with bluetongue virus should follow their national and/or local guidelines for disease reporting. State authorities should be consulted for any requirements in the U.S.

Prevention

Bluetongue is mainly controlled with vaccines, which must be matched to the viral serotype. Although attenuated vaccines are considered to be more effective than killed vaccines, they have the disadvantage of being transmissible to other animals by *Culicoides* vectors, and can cause fetal malformations in pregnant ewes. In addition, they may occasionally cause illness in highly susceptible animals.

Reduction of exposure to the *Culicoides* vectors might also be helpful, though it is unlikely to be effective as the sole control measure. Some possibilities include avoiding environments where midges are more prevalent (e.g., low-lying, damp pastures), using insect repellents or barriers such as insecticide-impregnated nets, and stabling animals from late afternoon to after dawn to prevent exposure to peak *Culicoides* feeding activity, which occurs around sunset and sunrise in the summer. However, it should be noted that some species of *Culicoides* will enter barns and stables, especially late in the season, and that outdoor feeding activity also begins earlier in the evening as the weather cools. Effective vector control with insecticides or other environmental measures is challenging, due to the extensive breeding sites and large populations of *Culicoides*, as well as the current poor understanding of the degree of control needed to actually reduce disease incidence.

Surveillance of sentinel animals may detect bluetongue viruses before outbreaks occur, allowing vaccination campaigns or other controls to be implemented early. Movement controls for infected animals (including pregnant, seropositive animals) may help limit virus introduction into new areas. Direct contact transmission is thought to have only a minor role in most outbreaks; however, disinfection and other infection control measures might be considered in some situations. In some circumstances, modifications in the breeding schedule might be used to avoid infections during the period when congenital abnormalities are most likely to occur.

Morbidity and Mortality

Bluetongue is a seasonal disease in many areas, due to fluctuations in vector populations caused by cold temperatures or other factors such as changes in rainfall. In regions where multiple serotypes circulate, the dominant serotypes may differ between years. Outbreaks vary in their frequency and severity, and are uncommon in tropical regions where the viruses circulate year round. Extensive epidemics can sometimes be seen when a new virus is introduced into a region. The 2006-2007 epidemic in Europe, which exposed some bluetongue-naive populations for the first time, was particularly severe and affected some mammals that do not usually develop clinical signs. However, this virus was not unusually virulent when inoculated into sheep from North America, and it generally caused much milder illnesses in Europe when it re-appeared in 2015. Immunity to bluetongue viruses appears to be long-lasting, but there is generally little or no protection against other serotypes.

The occurrence and severity of clinical signs in an individual can be influenced by its species, age, general health and previous exposures to bluetongue virus, as well as the viral strain and dose, and stressors such as concurrent illnesses. In endemic regions, sheep are usually the only livestock species that is noticeably affected. Although the morbidity rate among sheep in some endemic regions is < 5%, it can reach or exceed 50-75% if a new virus is introduced or susceptible sheep enter an endemic area. The case fatality rate in sheep is typically < 30%, though there are occasional reports of rates as high as 50-90%. Cattle and goats, which are often affected sporadically, usually have milder illnesses, and deaths are infrequent. Bluetongue virus infections in most other ungulates are subclinical; however, a few wildlife species such as whitetail deer and pronghorn can be severely affected, with morbidity as high as 100% in some local populations, and case fatality rates up to 80-90%. Illnesses appear to be very rare in carnivores, and in dogs, bluetongue only seems to affect pregnant animals.

Internet Resources

European Food Safety Authority. Bluetongue

OIE Bluetongue Reference Laboratory network (OIEBTLABNET)

The Merck Veterinary Manual

United States Department of Agriculture (USDA) Animal and Plant Health Inspection Service (APHIS). Bluetongue

World Organization for Animal Health (WOAH)

WOAH Manual of Diagnostic Tests and Vaccines for Terrestrial Animals

WOAH Terrestrial Animal Health Code

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