



## Bluetongue and Epizootic Haemorrhagic Disease

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### Etiology

Bluetongue (BT) and Epizootic Haemorrhagic Disease (EHD) are caused by Orbiviruses within the family Reoviridae. Both viruses are multi-typic and currently 26 serotypes of BT virus (BTV) and 7 of EHD virus (EHDV) are recognized. Both viruses are also arboviruses and are transmitted biologically between their hosts by the bites of Culicoides (Diptera, Ceratopogonidae) biting midges.

### Affected species (wildlife, domestic animals, humans)

BTV can infect all ruminant species but in domestic ruminants severe disease is usually restricted to improved breeds of sheep. Cattle rarely suffer severe disease and so act as covert and transient virus reservoirs. Goats and camels (*Camelus* spp.) rarely exhibit obvious clinical signs.

In African wild ruminants infection is inapparent. In N. American wild ruminants acute disease and death occurs in: white-tailed deer (*Odocoileus virginianus*), bighorn sheep (*Ovis canadensis*) and pronghorn antelope (*Antilocapra americana*). Disease has also been reported in spotted deer (*Axis axis*) in India, Rusa deer (*Cervus timorensis*) on Reunion island, and in captive American bison (*Bison bison*), European bison (*B. bonasus*), Siberian ibex (*Capra siberica*) and Musk ox (*Ovibos moschatus*) but not in European deer species. The occurrence of disease in N. American and Asiatic wild ruminant species suggests the historical link between them and BTV is more recent than with native African ruminants.

Among carnivores, domestic dogs are susceptible when inoculated with BTV and may die or abort. BTV antibodies have also been detected in the larger African carnivores and captive Eurasian lynx (*Lynx lynx*) have died from BT. However, carnivore species are not considered epidemiologically important.

Like BTV, EHDV is probably able to infect all or most ruminant species but infection is usually subclinical or mild. However, a variant of EHDV-2 (Ibaraki) has caused morbidity and mortality in Japanese cattle and EHD has also been reported in cattle in N. America, northern Africa, Israel and Turkey. In wildlife, EHDV has not been reported as causing disease in most species though it may occasionally do so in elk (*Cervus canadensis*), bighorn sheep, mule deer (*O. hemionus*) and pronghorn antelope. An exception to this rule is a severe and fulminating haemorrhagic disease that often occurs in white-tailed deer in N. America.

### Epidemiological characteristics and disease course

The vast majority of BTV and EHDV infections occur via the bites of vector insects - Culicoides biting midges. Consequently, the distribution of these viruses is limited to areas where vectors occur, to seasons when they are active and to regions where ambient temperature is sufficient to allow virus multiplication in them. In tropical areas such conditions occur all year and so does virus transmission. In temperate areas the peak transmission period is usually limited to summer and autumn. Should the winter be long in such areas, BTV and EHDV are usually unable to overwinter and annual re-introduction is necessary to perpetuate an outbreak. However, recently, oral and transplacental transmission of BTV-8 has been demonstrated which potentially facilitates persistence of this virus between years in regions as far north as N. Europe. It is not known whether other BTV or EHDV types can be transmitted in this way. Recent work in S. Europe indicates that in some areas red deer may play an important role in maintaining BTV outbreaks. After inoculation by vector bite both viruses are

disseminated throughout the body. Replication occurs in monocytes, macrophages, dendritic cells and vascular endothelial cells. Virus may be isolated from the circulation from 3-6 days p.i. and viraemia peaks at 7-8 days p.i. However, as most circulating virus is cell-associated and protected from antibody there may be an extended viraemia (up to 60 days).

### **Clinical signs**

Animals with acute BT may have any combination of: fever, anorexia, dyspnoea, excessive salivation, nasal and ocular discharges, petechial and ecchymotic haemorrhages in oro-nasal mucosa, oral erosions, lameness, coronitis, oedema of the head and neck, and cyanosis of the tongue. Pregnant animals may abort. White-tailed deer and improved sheep breeds are very susceptible and may develop a bleeding tendency which is usually associated with consumptive coagulopathy in white-tailed deer. Most animals succumbing to acute BT die within 14 days. Survivors may have a long convalescence. In them muscle injury and necrosis may prevent normal gait and can lead to torticollis. Wool of sheep and, hooves of sheep and white-tailed deer may be shed and many chronically affected animals may succumb to secondary infections. EHD is clinically indistinguishable from BT.

### **Gross lesions**

Characteristic lesions of BT and EHD: congestion, haemorrhage and oedema. The mucosa of the digestive tract may be oedematous with petechial haemorrhages and sometimes bloody diarrhoea. There may also be subcutaneous haemorrhages. Haemorrhage at the base of the pulmonary artery has been considered pathognomonic but is not always seen. Interlobular and interstitial oedema in the lungs leads to froth in the bronchial tract and dyspnoea. A gelatinous, reddish fluid infiltrates subcutaneous and inter-muscular connective tissues. The skeletal musculature may be grayish and marbled due to degeneration.

### **Histological lesions**

Depending on the stage of infection there can be widespread damage to the endothelium of small blood vessels resulting in vascular permeability, thrombosis and tissue infarction. In epithelial tissues this can lead to sloughing. Haemorrhage, mononuclear cell infiltration and necrosis of the myocardium may occur.

### **Differential diagnosis**

Pox, foot and mouth disease, Akabane disease, peste des petits ruminants, contagious ecthyma, vesicular stomatitis, Rift Valley fever, pneumonia, photosensitization, and copper deficiency.

### **Criteria for diagnosis**

Because clinical disease is rare and the clinical signs are largely unspecific, diagnosis usually requires isolation and/or identification of BTV or EHDV, or their nucleic acids.

### **Recommended diagnostic method(s) and preferred samples (incl. recommended amount and appropriate storage)**

Virus and/or nucleic acid detection: first using group-specific then type-specific RT-PCRs. Real time assays are preferred (increased sensitivity and specificity) but conventional PCRs based upon seg. 7 may be used.

Isolation of BTV via embryonating hens eggs (preferred) or cell culture, and of EHDV via cell culture: followed by virus identification, first using group-specific conventional or real time RT-PCRs, then type-specific RT-PCRs or VNTs. PCRs are preferred as they do not require virus adaptation to cell culture.

Despite high sensitivity, specificity and speed, a major disadvantage of PCRs is that they detect RNA, not infective virus. Isolation must be used in addition to PCRs to confirm infective virus.

Samples: Blood (10 ml) collected into EDTA tubes during the febrile phase or any solid tissue from the haematopoietic system (10 g), e.g. spleen, lung, lymph nodes. Spleen and whole blood are preferred. Tissue samples should be stored at +4°C, as freeze-thawing will lyse the erythrocytes and release virus which may then be inactivated by antibody. The erythrocytes should be washed to remove any antibody before isolation procedures commence. Long term storage of virus samples should be at -80°C

Serology: Identification of BTV or EHDV antibodies using a group-specific antibody detection VP7 competition ELISA followed by the type-specific SNT. Serum samples may be stored at -20°C.

### **APHAEA protocol (for harmonization at large scale)**

A monoclonal antibody-based competitive ELISA that detects serogroup specific BTV antibodies is recommended and is an OIE prescribed test (OIE 2014). Should BTV nucleic acid detection/identification also be required, prescribed methods are similarly described in OIE (2014).

**Laboratories that can be contacted for diagnostic support**

BT and EHD are notifiable. The EU reference laboratory is the Pirbright Institute UK and OIE reference laboratories are: Onderstepoort Veterinary Institute RSA, National Veterinary Services Laboratories USA, Pirbright Institute UK, IZS dell'Abruzzo e del Molise, Italy and Australian Animal Health Laboratory Australia (see: [www.oie.int](http://www.oie.int)).

**Recommended literature**

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