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Epizootic Haemorrhagic Disease an emerging disease!

Introduction

Epizootic haemorrhagic disease (EHD) is a vector-borne infectious viral disease of domestic and wild ruminants, primarily affecting white-tailed deer and cattle. The first identification of the virus was in white-tailed deer (WTD) populations in the USA in 1955. It has been reported in various regions worldwide since and has significant welfare, social and economic implications. The disease is closely related to Bluetongue Virus (BTV) and the global range of this virus with its associated diseases has changed remarkably in recent years. This article provides an overview of current knowledge about EHD.

Etiology

The etiological agent of EHD is the epizootic haemorrhagic disease virus (EHDV). This RNA virus belongs to the family Reoviridae, genus Orbivirus and shares many morphological and structural characteristics with the other members of the genus such as bluetongue virus (BTV) and the African horse sickness virus [1]. Like BTV, the primary determinant of serotype specificity is the outer capsid VP2 protein. VP2 is also mainly responsible for the induction of virus neutralizing antibodies. Rapid, sensitive and specific molecular typing assays have been developed by identification of segment 2 nucleotide regions unique to each EHDV serotype. There are 7 different serotypes described up to today [2,3].

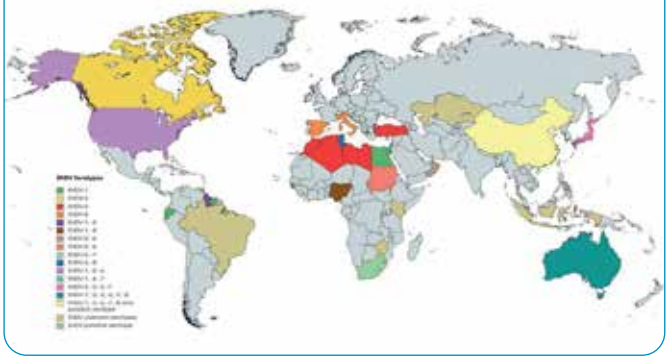
Epidemiology

EHD is a vector-borne viral disease; its distribution is consequently limited to the distribution of competent vectors. EHDV as well as BTV is transmitted between its ruminant hosts by species of Culicoides biting midges. Horizontal transmission through direct contact or fomites has not been observed, emphasizing the role of vectors in EHD epidemiology. Available data suggest that the species of Culicoides that transmit EHDV are likely to be similar, though not necessarily the same, as for BTV. Transmission occurs when infected midges feed on susceptible hosts. Culicoides can fly 5 km in a few days, but they can also be transported over longer distance by the wind, especially over the sea [6]. Environmental factors, such as temperature, precipitation and humidity, influence vector abundance and activity. The vector is more active during the warm season. Consequently, the number of new infections decreases at the beginning of winter and increases again at the beginning of summer when the insect population is most active. The WTD infected with EHDV in the USA in 1955 were severely affected showing high mortality [4]. Since then, the EHDV has spread worldwide and has been isolated in North and South America, Africa, Asia, the Middle East, Oceania and Europe *(Figure a)*. To date, it is endemic in parts of North America, Australia and certain countries of Asia and Africa [5].
EHD appeared for the first time in Europe in October 2022 in the south of Italy. The serotype 8 strain in Italy was with very high probability the same as the Tunesia strain of 2021 and has spread rapidly in Spain and Portugal. In September 2023, a first case of EDHV serotype 8 was diagnosed in France and in 2024 France counted over 4500 outbreaks *(Figure b)*.

Pathogenesis

EHDV is capable of infecting wild and domestic ruminants. Historically, it has been associated with disease in wild cervids, particularly white-tailed deer (Odocoileus virginianus). Following infection, EHDV initially replicates in endothelial cells of the lymphatic vessels and in the lymph nodes draining the site of infection. In the blood the virus is associated with lymphocytes and in particular red blood cells where it is present in high titres

Figure a:



Epidemiology of EHDV across the world

Figure b:

Localisation of EHD outbreaks in Europe
in period July 2022- January 2025
(Source: https://animal-diseases.efsa.europa.eu/EHDV/#Geographicaldistribution)

for longer periods of time. The replication of EHDV in endothelial cells leads to cell lysis and the release of pro-inflammatory cytokines. This causes increased vascular permeability, haemorrhage and oedema. The disruption of blood vessel integrity is central to the clinical signs observed in infected animals.

As for other vector borne viruses, duration of viraemia represents a key element for the spread of the infection. In an infection trial with EHDV-1 in white tailed deer, neutralising antibodies were first detected between days 10 and 14 post infection. Neutralising antibodies, however, were not able to completely remove the virus from circulation.

Gard and Melville [7] carried out a study on the duration of viraemia in cattle naturally infected with EHDV *(Table 1)*.

Table 1:

Duration of viraemia in 130 sentinel cattle (Adapted from Gard and Melville, 1992).

	Duration of viraemia in weeks (viral isolation)				
	<1	1-2	2-3	3-4	4-5
EHDV-2	46*	24	6	4	1
EHDV-5	31	3	0	1	1
EHDV-7	0	1			
EHDV-8	12				

* Number of viraemic animals per week

An EHDV-6 pathogenesis study in cattle found that viremia and seroconversion were more variable in cattle challenged with the same virus as WTD, and none of the cattle demonstrated clinical, hematologic or pathologic abnormalities [8].

Cattle vaccinated with the recombinant VP2 proteins of EHDV-2 and EHDV-6 produced virus-neutralizing antibodies against their homologous virus serotypes; the ability to neutralize heterologous viruses was limited [9].

A recent cattle challenge study, designed to generate a panel of bovine reference sera, provided data regarding the presence and absence of cross-neutralization between serotypes. In seven calves, each challenged with one virus representing one of the seven EHDV serotypes (EHDV-1-2, and -4-8), viral RNA was detectable in all animals and all seven seroconverted [10]. No, or only weak cross-neutralizing reactivity was observed with most of the sera, with stronger cross-reactivity observed between some isolates of EHDV-2 and -7, and EHDV-6 and -8.

Clinical Signs

EHDV clinical signs were observed in white-tailed deer, cattle and other wild and domestic ungulates. In white-tailed deer the infection might be characterised by high mortality and morbidity while in cattle mortality is usually low and morbidity might vary from 1% to 18%.

The clinical presentation of EHD in cattle can range from subclinical infection to severe disease. Factors influencing disease severity include the virulence of the EHDV strain, environmental stressors and the immune status of the host [11,12,13].

In many cases, cattle infected with EHDV show no overt clinical signs of disease. Subclinical infections are particularly common in regions where EHDV is endemic, and animals have developed partial immunity.

In mild to moderate disease cases clinical signs are present. They often include pyrexia, lethargy and reduced appetite, mild lameness and hyperaemia of the mucous membranes in particularly in the oral cavity and nose.

In more severe cases, cattle may exhibit swelling of the head, neck and tongue (oedema), ulceration of the oral mucosa, excessive salivation and nasal discharge, petechiae or ecchymoses on mucous membranes and the skin, respiratory distress due to pulmonary oedema. Sudden death occurs in acute cases, often associated with vascular collapse.

Sheep infected with EHDV rarely show clinical signs and the infection is usually subclinical. The same applies to goats, which often show no viremia or symptoms, only seroconversion [14,15].

Diagnosis

Clinical signs of EHD in wild ruminants and cattle are indistinguishable from those of BT and are similar to signs found in other cattle diseases like BVD-MD, IBR, food and mouth disease, vesicular stomatitis and malignant catarrhal fever. For a definitive diagnose of EHDV infection, specific laboratory testing is required. For virus detection a multiplex real time RT-PCRs is available which is capable to distinguish EHDV from BTV [16]. For serological detection of antibodies several different Elisa tests, beside the classical serum neutralisation (SN) and compliment fixation test (CFR), are also available.

Control and prevention

Effective control strategies focus on vector management and vaccination.

Increased biosecurity measurements for managing Culicoides populations is essential in reducing EHD transmission. The proper biosecurity approach includes environmental management with eliminating or treating breeding sites, such as moist soil, and decaying vegetation to disrupt midge life cycles. Additionally, chemical control measures can be taken by applying insecticides in areas with high midge activity. However, this method's effectiveness can be limited due to the extensive habitats of midges and potential environmental concerns. Using insect repellent sprays, pour-on products with deltamethrin or macrocyclic lactones like ivermectin can help to control vector populations but deltamethrin and ivermectin will not prevent the Culicoides vectors from blood feeding.

Specific EHDV serotype vaccines can protect animals in certain regions. In some EU countries like Belgium and France vaccination campaigns with a specific serotype 8 vaccine are in place. However, the ability of the vaccines under development to generate durable universal immunity that can cross-protect between different EHDV serotypes remains uncertain.

Animals affected by the EDHV that develop moderate to severe symptoms, should be treated with a supportive therapy with anti-inflammatory drugs to reduce pyrexia, pain, swelling, and oedema. Antimicrobials are only required in case of secondary bacterial infections.

Conclusion

EHD poses a varying threat to cattle, depending on environmental and epidemiological factors. While often subclinical, the disease can cause significant morbidity and mortality under favourable conditions for viral transmission. The expanding geographic distribution of various EHDV serotypes and their vectors, and the increasing severity and frequency of outbreaks in both deer and cattle, makes EHDV control a top priority for governments, scientists and farm managers.

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