MALIGNANT CATARRHAL FEVER

AETIOLOGY

Classification of the causative agent Malignant catarrhal fever (MCF) is caused by a group of viruses that belong to the family Herpesviridae, subfamily Gammaherpesvirinae, genus Macavirus. The MCF subgroup of Macaviruses, called MCFV, contains at least 10 members, five of which are currently known to cause disease. There are two major groups of MCF viruses – the Alcelaphinae/Hippotraginae group and the Caprinae group.

The two most important viruses are Alcelaphine herpesvirus 1 (AlHV-1), which is endemic in wildebeest populations worldwide causing wildebeest-associated MCF; and ovine herpesvirus 2 (OvHV-2), which causes sheep-associated MCF, and is endemic in most sheep populations worldwide. Caprine-associated MCF: caprine herpesvirus 2 (CpHV-2): endemic in most domesticated goat populations worldwide and causes MCF in cervids. Unknown origin: causes MCF in white-tailed deer (MCFV-WTD). Roan antelope origin: Hippotragine herpesvirus-1 was used to experimentally induce MCF in rabbits.

EPIDEMIOLOGY

MCF is a generally fatal disease of cattle and many other species of Artiodactyla, which occurs following infection with certain herpesviruses of the genus Macavirus. Five herpesviruses have been recognised as causing MCF, the best characterised being AIHV-1 and OvHV-2. MCF usually appears sporadically and

affects few animals, though both AlHV-1 and OvHV-2 can give rise to epizootics.

AlHV-1:

• Transmission in wildebeest occurs mainly perinatally, but some calves may become infected in utero; all calves become infected within the first few months of life and remain carriers for life

• Transmission to susceptible hosts occurs only from wildebeest; there is no definitive evidence that MCF-affected animals transmit the disease horizontally to others

• Most cases of wildebeest-associated MCF occur when susceptible animals are exposed to parturient wildebeest or young calves, or pasture contaminated by them

OvHV-2:

• A proportion of lambs are infected in utero with most lambs becoming infected perinatally

• Transmission is only from sheep to susceptible hosts, not horizontally between infected hosts 2 Hosts

• The disease has been most often described as affecting species of the subfamily Bovidae and family Cervidae, but is also recognised in domestic pigs, giraffe and species of antelope belonging to the subfamily Tragelaphinae. Animals that develop MCF are usually dead-end hosts

• Carrier species with inapparent infections include wildebeest, sheep, and goats • Clinical infections occur in members of the families Bovidae; Cervidae, and Giraffidae, such as cattle, water buffalo, bison, deer, and other wild ruminants

• Deer species affected: red deer, axis deer, fallow deer, Formosan sika deer, mule deer, Père David's deer, Reeve's muntjac, swamp deer, white-tailed deer

• Other species affected: antelope, banteng, elk, reindeer, gaur, giraffe, greater kudu, nilgai and wapiti

• Domestic pigs in several countries have recently been confirmed as susceptible, and signs are very similar to those seen in acutely affected cattle

• Laboratory rabbits, Syrian hamsters, guinea-pigs and rats have been experimentally infected

• MCFV DNA has been isolated from other exotic ruminants with unknown disease potential: ibex, musk ox, gemsbok, aoudads, hartebeest and topi

• A species can be susceptible to one MCF virus, but relatively resistant to others Transmission

• MCF viruses, like other herpesviruses, establish lifelong, latent infections in natural hosts

• Inhalation is thought to be the primary means of transmission for all MCF viruses, although ingestion might also be possible AlHV-1

• Transmission of AlHV-1 within free-living wildebeest populations is very efficient: all wildebeest calves are infected within the first few months of life by in utero, direct contact or aerosol routes. Contamination of pastures may also contribute to transmission, as may fomites

• Most transmission by wildebeest calves occurs at 1–2 months of age – transmission after 6 months of age is rare, due to the development of neutralising antibodies

• Virus is shed by wildebeest calves in nasal and ocular secretions, mainly in the cell-free form

• Close contact is usually needed but transmission over one hundred metres has been reported OvHV-2

• Transmitted mainly by the respiratory route, probably in aerosols

• Shed intermittently in nasal and ocular secretions, particularly by 6- to 9-month old lambs

• A proportion of lambs are infected in utero with most lambs becoming infected perinatally, though infection may not occur in some situations till after 3 months of age, potentially due to the effects of maternal antibody

• Close contact with sheep by susceptible species is usually required, but cases have been reported when sheep and cattle were separated by 70 metres, and in bison herds up to 5 km from a lamb feedlot

• There is a wide spectrum of susceptibility: Bos taurus and Bos indicus cattle are relatively resistant to OvHV-2 and cases are usually sporadic; most species of deer, bison (Bison bison) and water buffalo (Bubalus bubalis) are much more susceptible; and Bali cattle (Bos javanicus) and Père David's deer (Elaphurus davidianus) are extremely susceptible Sources of virus

• Nasal and ocular secretions mainly, but also reported in faeces and semen (OvHV-2

Occurrence MCF viruses are found worldwide, but illness occurs only when a carrier species can pass a virus to susceptible hosts. AlHV-1- associated disease has been reported mainly in sub-Saharan Africa where cattle and wildebeest

comingle. This virus is reported to be the most important MCF virus in some parts of Africa, although OvHV-2 associated disease also occurs. AIHV-1 can cause disease also in zoological parks wherever carriers and susceptible species cohabitate. OvHV-2 is the major cause of MCF in domesticated animals throughout the world. Sheep-associated MCF is common among Bali cattle in Indonesia; however, cases in cattle are infrequent in countries where Bos taurus and Bos indicus are the predominant species. OvHV-2 is a serious concern in countries with bison and cervid farms, as these species are very susceptible. OvHV-2 is reported to be the major cause of MCF among ruminants in zoos and wildlife parks. For more recent, detailed information on the occurrence of this disease worldwide, see the OIE World Animal Health Information Database (WAHID) Interface DIAGNOSIS Incubation period is variable according to the virus and host and not yet accurately described, ranging from 11 to 34 days or up to 9 months in experimentally infected MCF-susceptible hosts, while natural exposure of cattle to wildebeest led to recorded cases of MCF between day 70 and 120 after first exposure. Clinical diagnosis The clinical signs of MCF are highly variable and range from peracute to chronic. In general, the most obvious signs develop in the more lengthened cases.

• Peracute: either no clinical signs are detected, or depression followed by diarrhoea and dysentery may develop 12–24 hours prior to death

• In general: high fever, increased serous lachrymation and nasal exudate progressing to profuse mucopurulent discharge, inappetance, and decreased milk yields

• Progressive bilateral corneal opacity, starting at the periphery, is characteristic.

• Skin ulceration and necrosis may be extensive or restricted to the udder and teats

• Salivation and oral hyperaemia may be an early sign, progressing to erosions of the tongue, hard palate, gums and, characteristically, the tips of the buccal papillae

• Superficial lymph nodes may be enlarged and limb joints may be swollen

• Nervous signs such as hyperaesthesia, incoordination, nystagmus and head pressing may occur alone or with signs described above

• A few infected animals may recover following mild or even quite severe clinical reactions Lesions MCF is characterised by inflammation and epithelial necrosis, with lympho-proliferation, infiltration of nonlymphoid tissues by lymphoid cells, and vasculitis. Gross pathological changes reflect the severity of clinical signs, but are generally widespread and may involve most organ systems.

• Erosions and haemorrhages in gastrointestinal tract: contents may be haemorrhagic
• Enlarged lymph nodes, but degree varies within an animal

• Catarrhal exudate, erosions and diphtheritic membranes often observed in the respiratory tract

• Urinary bladder often has characteristic ecchymotic haemorrhages of the epithelial lining, especially in bison

• Interstitial accumulation of lymphoid cells in nonlymphoid organs, in particular the renal cortex and periportal areas of the liver, is typical, and in the case of the kidney may be very extensive with development of multiple raised white foci, each 1–5 mm in diameter

• In the absence of molecular diagnosis, histologic changes are often relied on for diagnosis of MCF and are characteristic: epithelial degeneration, vasculitis, hyperplasiaand necrosis of lymphoid organs, and widespread interstitial accumulations of lymphoid cells in nonlymphoid organs

• The brain may also show a nonsuppurative meningoencephalitis with lymphocytic perivascular cuffing and a marked increase in the cellularity of the cerebrospinal fluid Differential diagnosis

• Bovine viral diarrhoea mucosal disease

• Infectious bovine rhinotracheitis

• Bluetongue

• Epizootic haemorrhagic disease

• Foot and mouth disease

• Vesicular stomatitis

• Rinderpest

• Ingestion of caustic materials or some toxic plants Laboratory diagnosis AIHV-1 may be recovered from clinically affected animals using peripheral blood leukocytes or lymphoid cell suspensions.

Virus can also be recovered from wildebeest, either from peripheral blood leukocytes or from cell suspensions of other organs. OvHV-2 has never been cultured in vitro, although lymphoblastoid cell lines propagated from affected animals contain OvHV-2-specific DNA and virus particles have been observed in these cells. OvHV-2 virus has been recovered from sheep nasal secretions and has been used in a range of studies, including induction of experimental MCF in a range of species. Both AlHV-1 and OvHV-2 have been transmitted experimentally to cattle, rabbits and hamsters, which develop lesions characteristic of MCF. Viral DNA has been detected in clinical material from cases of MCF caused by both AIHV-1 and OvHV-2 using the polymerase chain reaction. PCR has become the

method of choice for diagnosing both forms of the disease. Samples Virus isolation and viral detection

• Refrigerate but do not freeze tissues

• AlHV-1 is inactivated quickly in dead animals – the most useful samples are collected immediately after euthanasia or death

• Tissues for virus isolation: 10–20 ml anticoagulated blood in EDTA, spleen, lung, lymph nodes, and adrenal glands

• Tissues for PCR: anticoagulated blood, kidney, lymph nodes, intestinal wall, brain and other tissues from above. PCR is also possible from fixed tissues with appropriate DNA extraction protocols Serological tests

• Paired serum samples (5 ml) taken 3–4 weeks apart

• **Histopathology • • Cattle:** lung, liver, lymph nodes, skin (if lesions are present), kidney, adrenal gland, eye, oral epithelium, oesophagus, Peyer's patches, urinary bladder, thyroid, heart muscle, carotid rete and brain

• Bison: urogenital and intestinal tract tissue are particularly important

• Other species: wide range of tissuesProcedures Identification of the agent

• Virus isolation from peripheral blood leukocytes (AlHV-1) or lymphoid cells. o Most monolayer cultures of ruminant origin are probably susceptible and develop cytopathic effect (CPE). Bovine thyroid or turbinate cell cultures have been used extensively o Primary isolates typically produce multinucleated CPE in which viral antigen can be identified by immunofluorescence or immunocytochemistry

• PCR (AlHV-1 and OvHV-2) Serological tests AlHV-1 Infected wildebeest develop antibody to AIHV-1, which can be detected in the four assays below. However, the

antibody response of clinically affected animals is limited, with no neutralising antibody developing, so that detection relies on the use of immunofluorescence, enzyme-linked immunosorbent assay (ELISA) or immunoblotting.

• Virus neutralisation

• Immunoblotting

• ELISA

• Immunofluorescence OvHV-2 Antibody to OvHV-2 can be detected by using AIHV-1 as the source of antigen. Domestic sheep consistently have antibody that can be detected by immunofluorescence, ELISA or immunoblotting, although antibody is not always present in more acutely affected animals such as deer.

• Immunofluorescence

• ELISA

• Immunoblotting For more detailed information regarding laboratory diagnostic methodologies, please refer to Chapter 3.4.13 Malignant catarrhal fever in the latest edition of the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals under the heading “Diagnostic Techniques”.

PREVENTION AND CONTROL

Sanitary prophylaxis Prevent contact between carriers and clinically susceptible species

• Separate susceptible animals from sheep, goats, wildebeest or other suspected reservoir hosts. Wildebeest appear to transmit AlHV-1 readily, and should always be separated from cattle

• Cattle should not graze pastures where wildebeest have grazed and given birth

• Wildebeest should also be segregated in zoos

• Cattle rarely develop the sheep-associated form of MCF, but separation from sheep would be advisable, particularly from lambs actively shedding virus. Co-housing of sheep and cattle should be avoided

• Bison, some deer and other highly susceptible species should not be allowed near sheep. Separation by longer distances is particularly important when the host is highly susceptible and the concentration of virus is high (e.g. bison and lambs in feedlots)

• Access to contaminated fomites must be avoided, especially when the species is highly susceptible

• OvHV-2 free sheep can be produced by early weaning and isolation

• During outbreaks, susceptible animals should be separated immediately from the suspected source. Cattle and other incidental hosts are thought to be dead end hosts, and do not need to beculled. Because the incubation period can be very long, cases can continue to occur for months. Stress reduction can help prevent disease in subclinically or mildly affected animals Medical prophylaxis

• Commercial vaccines for MCF virus are under development. For more detailed information regarding safe international trade in terrestrial animals and their products, please refer to the latest edition of the OIE Terrestrial Animal Health Code.