

# MALIGNANT CATARRHAL FEVER

Aetiology Epidemiology Diagnosis Prevention and Control References

## **AETIOLOGY**

### ***Classification of the causative agent***

Virus family Herpesviridae, subfamily Gammaherpesvirinae, genus *Macavirus*. The MCF subgroup of viruses, called MCFV, contains at least 10 members, five of which are currently known to cause disease.

Wildebeest-associated MCF: alcelaphine herpes virus 1 (AIHV-1). Endemic in wildebeest populations worldwide.

Sheep-associated MCF: ovine herpesvirus 2 (OvHV-2). 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

### ***Resistance to physical and chemical action***

Temperature: No data available, but virus is very labile.

pH: Mostly stable between pH 5.5–8.5

Disinfectants/chemicals: Inactivated by common disinfectants including sodium hypochlorite (3% solution if heavy organic debris present)

Survival: Inactivated rapidly by sunlight. Cell-associated virus survives 72 hours outside the host; cell-free virus is inactivated quickly in dry environments but may survive over 13 days in humid environments

## **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 AIHV-1 and OvHV-2 can give rise to epizootics. The disease has been most often described as affecting species of the subfamily Bovinae 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.

#### AIHV-1:

- Transmission in wildebeest occurs perinatally; 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

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

## Transmission

### AIHV-1

- Transmission of AIHV-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 six months of age is rare
- 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
- Congenital transmission of AIHV-1 within infected domestic cows can occur with varying disease latency periods in newborn calves

### OvHV-2

- Transmitted mainly by the respiratory route, probably in aerosols
- Shed intermittently in nasal 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.
- 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 DNA detected in semen of domestic rams)

## Occurrence

MCF viruses are found worldwide. AIHV-1- associated disease has been reported mainly in sub-Saharan Africa where cattle and wildebeest congregate, but can cause disease in zoological parks wherever carriers and susceptible species cohabitate. OvHV-2 - associated disease occurs throughout the world.

**For more recent, detailed information on the occurrence of this disease worldwide, see the OIE World Animal Health Information Database (WAHID) Interface**

[<http://www.oie.int/wahis/public.php?page=home>] or refer to the latest issues of the *World Animal Health* and the *OIE Bulletin*.

## **DIAGNOSIS**

Incubation period is variable, ranging from 11–34 days or up to 9 months

### ***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 protracted 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***

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, hyperplasia and 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***

- Rinderpest
- Bovine viral diarrhoea mucosal disease
- Infectious bovine rhinotracheitis
- Bluetongue
- Epizootic haemorrhagic disease
- Foot and mouth disease
- Vesicular stomatitis
- 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 identified formally, although lymphoblastoid cell lines propagated from affected animals contain OvHV-2-specific DNA and virus particles have been observed in these cells.

Both AIHV-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 is becoming the method of choice for diagnosing both forms of the disease.

### **Samples**

#### *Virus isolation and viral detection*

- Refrigerate but do not freeze tissues.
- AIHV-1 is inactivated quickly in dead animals – the most useful samples are collected immediately after euthanasia or death.
- Tissues for virus isolation: anticoagulated blood- 10–20 ml 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 tissues

### **Procedures**

#### *Identification of the agent*

- Virus isolation from peripheral blood leukocytes (AIHV-1) or lymphoid cells.
  - Most monolayer cultures of ruminant origin are probably susceptible and develop cytopathic effect (CPE). Bovine thyroid or turbinata cell cultures have been used extensively.
  - Primary isolates typically produce multinucleated CPE in which viral antigen can be identified by immunofluorescence or immunocytochemistry.
- PCR (AIHV-1 and OvHV-2)

#### *Serological tests*

##### AIHV-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, ELISA or immunoblotting.

- Virus neutralisation
- Immunoblotting

- Enzyme-linked immunosorbent assay (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 2.4.15 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 AIHV-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 be culled. 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 are not available for any MCF virus.

**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*.**

## **REFERENCES AND OTHER INFORMATION**

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The OIE will periodically update the OIE Technical Disease Cards. Please send relevant new references and proposed modifications to the OIE Scientific and Technical Department ([scientific.dept@oie.int](mailto:scientific.dept@oie.int)). Last updated June 2013.