

## MALIGNANT CATARRHAL FEVER

(Malignant head catarrh, malignant catarrh, snotsiekte)

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### Definition [top](#)

Malignant catarrhal fever (MCF) is a generalized viral disease of domestic cattle and buffaloes and many species of wild ruminants characterized by high fever, profuse nasal discharge, corneal opacity, ophthalmia, generalized lymphadenopathy, leukopenia, and severe inflammation of the conjunctival, oral, and nasal mucosae with necrosis in the oral and nasal cavities sometimes extending into the esophagus and trachea. Occasionally central nervous system (CNS) signs, diarrhea, skin lesions, and nonsuppurative arthritis are observed.

### Etiology [top](#)

The etiologic agent of MCF in Africa is a highly cell-associated lymphotropic herpesvirus of the subfamily *Gamma herpesvirinae*. Two viral strains have recently been designated: alcelaphine herpesvirus-1 (AHV-1) and alcelaphine herpesvirus-2 (AHV-2), although some continue to designate this agent as bovid herpesvirus-

3. This agent is carried as a latent infection by African antelope of the family Bovidae, subfamily Alcelaphinae which includes wildebeest (*Connochaetes* sp.), hartebeest (*Alcelaphus* sp.), and topi (*Damaliscus* sp.). The wildebeest herpesvirus of MCF (AHV-1) was first isolated by Plowright from a blue wildebeest (*Connochaetes taurinus taurinus*) in 1960.

Epidemiologic evidence suggests that domestic and wild sheep and goats may be additional major reservoirs of a virus causing MCF. Serologic evidence also suggests this virus may be related but not identical to the alcelaphine herpesvirus-1.

Sheep-associated MCF herpesviruses were isolated from domestic cattle in Minnesota in 1977 and from domestic cattle in Austria in 1990. On the basis of morphology and molecular DNA mapping, both isolates appear similar to AHV-1.

Viruses identical or closely related to AHV-1 and AHV-2 have been isolated from several captive wild ruminant species in two U.S. zoos located in Oklahoma City and San Diego. Animals infected with AHV-1 were white-tailed gnu, white-bearded gnu, gaur, greater kudu, Formosan sika deer, axis deer, and nilgai. The AHV-2 was isolated from a topi and a hartebeest at the San Diego Wild Animal Park.

The agent of MCF on deer farms in Scotland and New Zealand has not yet been demonstrated by electron microscopy or isolation of cell-free virus in a cell culture system. However, it has been passaged in lymphocyte cultures, rabbits, and deer.

### Host Range [top](#)

All species of wildebeest, hartebeest, and topi are considered carriers of alcelaphine MCF virus. There is serologic evidence that several other African wild ruminants, such as various species of oryx and addax, may also be reservoir hosts, although MCF virus has not been isolated from these species.

Domestic and wild sheep and goats are also considered reservoir hosts for MCF virus.

Many exotic ruminant species in zoos have been reported affected with MCF, including several wild bovines such as bison, water buffalo, gaur and banteng, and several deer (including white-tailed deer) and antelope species. Interestingly, no cases of MCF have been reported from antelope species that normally cohabitate wildebeest grazing areas in Africa.

In cattle and susceptible wild ruminants, MCF affects all ages, breeds, and sexes.

## **Geographic Distribution** [top](#)

Sheep-associated MCF occurs worldwide. The alcelaphine antelope-associated form in cattle occurs chiefly in Africa in the natural habitat of wildebeest, hartebeest, and topi. This form of MCF has, however, occurred in zoos and wild animal parks that also kept wildebeest. The increasing popularity in North America and other areas of the world of wild game animal ranches, often in association with domestic cattle raising, increases the possibility that MCF will become a more prevalent disease in cattle and ranched exotic ruminants. There is increasing serologic evidence that cattle may develop low levels of neutralizing antibodies following exposure to MCF, especially of sheep or goat origin, without manifesting clinical disease. There is evidence that stress or some other immunosuppressive effector may be necessary as a precursor of clinical sheep-associated MCF.

## **Transmission** [top](#)

The MCF virus in wildebeest, hartebeest, and topi is largely cell-associated in adult animals and hence rarely transmissible. However, neonatal wildebeests have been found to shed cell-free MCF virus in nasal and ocular secretions and in feces. Cell-free MCFV has also been demonstrated in nasal secretions of captive adult wildebeests after stress or administration of corticosteroids. Transmission to cattle or other susceptible species may occur by inhalation of cell-free virus in infectious aerosol droplets, ingestion of feed or water contaminated with infectious secretions or feces, or possibly mechanically by arthropods. Masai herdsmen believed cattle acquire MCF by contact with wildebeest placentas or birth hair of neonates. Recent studies have failed to demonstrate infective MCFV in fetal fluids or placentas of wildebeest probably owing to the rapid inactivation of virus by sunlight. The mode of transmission of sheep-associated MCF remains unknown, although relatively close contact between cattle and sheep, especially lambing ewes, is believed necessary. MCF-affected cattle appear to shed only cell-associated virus, and thus cattle-to-cattle transmission is thought to be rare or nonexistent, although there are documented instances where this has occurred.

## **Incubation Period** [top](#)

The incubation period in natural cases is not known, but epidemiologic evidence indicates it may be as long as 200 days. Experimentally, the incubation period has varied from 9 to 77 days.

## **Clinical Signs** [top](#)

Clinical MCF in cattle has arbitrarily been divided into four forms as follows:

1. Peracute form: Fever, severe inflammation of the oral and nasal mucosae and hemorrhagic gastroenteritis with a course of 1 to 3 days.
2. Intestinal form: Fever, diarrhea, hyperemia of oral and nasal mucosae with accompanying discharges, and lymphadenopathy with a course of 4 to 9 days (Fig. 75).
3. Head and eye form: This is the typical syndrome of MCF with fever, nasal, and ocular discharges progressing from serous (Fig. 76) to mucopurulent and purulent. Encrustation of the muzzle and nares occurs in later stages, causing obstruction to the nostrils and dyspnea, open-mouthed breathing, and drooling (Fig. 77). There is intense hyperemia and multifocal or diffuse necrosis of the oral mucosa (usually on the lips, gums, and hard and soft palate) and buccal mucosa. Erosion of the tips of buccal papillae, leaving them reddened and blunted, is often encountered (Fig. 78).

Ocular signs referable to ophthalmia include lacrimation progressing to purulent exudation, photophobia, hyperemia, and edema of the palpebral conjunctiva and injection of scleral vessels. Corneal opacity, starting peripherally and progressing centripetally, results in partial to complete blindness (Fig. 79). Hypopyon may also be seen. Corneal opacity is usually bilateral but occasionally is unilateral. Fever is common and usually high (104-107° F [40-41.6° C ]) until the animal becomes moribund, at which time it is hypothermic. Clinical features at early onset have included reddening of the skin of the udder, the coronary bands and interdigital spaces, and marked hyperemia of the oral cavity. Increased thirst accompanies the fever, and anorexia is seen in late stages. Constipation is common in this form of MCF, but terminal diarrhea is sometimes observed.

Nervous signs are not frequently seen but may be manifested by trembling or shivering, uncoordinated gait, and terminal nystagmus.

Necrotic skin lesions occasionally are seen, and horn and hoof coverings may be loosened or sloughed in some cases. The course of the head and eye form, which is invariably fatal, is usually 7 to 18 days.

4. Mild forms: These are syndromes caused by experimental infection of cattle with attenuated viruses and are usually nonfatal.

There is considerable variation and overlap among these artificial categories, and their use has little value.

Although the manifestations of the "head and eye" form of MCF are considered the typical syndrome in cattle, clinical signs in exotic ruminants are often less dramatic and not usually specifically diagnostic, except in members of the subfamily *Bovinae* (i.e., wild cattle). In deer and antelope species MCF tends to be more subtle clinically and usually is manifested by conjunctivitis, photophobia, moderate corneal clouding (often unilateral), fever, depression, variable lymphadenopathy, occasionally diarrhea, and usually a mild serous nasal discharge. Death may be sudden following a brief course of hemorrhagic diarrhea. Inflammation of the oral and nasal cavity is usually less severe than in cattle and only occasionally progresses to mucosal erosions.

There is some suggestion from studying cases of MCF among exotic ruminants of a host-dependent modification with respect to the clinical and pathologic manifestations of MCF virus infection.

### Gross Lesions [top](#)

Gross lesions vary considerably, depending on the form or severity and course of the disease. Animals that die of the peracute disease may have few lesions other than a hemorrhagic enterocolitis.

In the more protracted acute to subacute disease (intestinal and head and eye forms), the carcass may be normal, dehydrated, or emaciated. The muzzle is often encrusted and raw. Cutaneous lesions sometimes occur as a generalized exanthema with exudation of lymph causing crusting and matting of the hair. Where skin is unpigmented, hyperemia is apparent. These lesions are frequently seen in the ventral thorax and abdomen, inguinal region, perineum and loins, and sometimes on the head.

Enlarged lymph nodes are characteristic findings in MCF. All nodes may be involved, but those in the head and neck and periphery are the most consistently prominent (Fig. 75). Affected nodes are grossly enlarged and edematous and sometimes have patchy reddened or beige-brown areas on cut surfaces. Hemolymph nodes are also enlarged and prominent. The spleen is slightly enlarged, and Malpighian corpuscles are prominent. Pale areas may be seen in the heart muscle.

Lesions in the respiratory system range from mild to severe. When the clinical course is short, there is slight serous nasal discharge and hyperemia of the nasal mucosa. Later the discharge becomes more copious and mucopurulent to purulent and is accompanied by intense nasal mucosal hyperemia, edema, and small focal

erosions.

Occasionally a croupous pseudomembrane formation is seen. Lesions in the nasal passages and turbinates may extend to the frontal sinuses. The pharyngeal and laryngeal mucosae are hyperemic and edematous and later develop multiple erosions, often covered with gray-yellow pseudomembranes (Fig. 80). Inflammation and sometimes petechiation and ulceration are seen in the tracheobronchial mucosa. The lungs are often edematous and sometimes emphysematous but in some cases may appear normal. A bronchopneumonia may complicate chronic cases.

The alimentary tract mucosa may have no gross lesion in peracute cases. When the course is longer, alimentary lesions are commensurately more severe and include mild to severe mucosal inflammation (hyperemia and edema), erosions, and ulcerations— especially on the dental pad and gingival surfaces, the palate (Fig. 81), tongue, and buccal papillae. Mucosal inflammation, hemorrhage, and erosions may also be found in the rest of the digestive tract including the esophagus, rumen, omasum, abomasum, small intestines, colon, and rectum. Petechiation may be seen. Feces are usually scant, dry, pasty, or blood stained.

Urinary tract lesions include hyperemia and sometimes marked distention and prominence of bladder mucosal vessels and mucosal edema, perhaps with petechial to severe hemorrhage and occasionally epithelial erosion and ulceration. Kidneys may appear normal or mottled with patches of beige, discolored raised areas. Petechiae or ecchymoses may occur in the renal pelvis and ureters.

The liver is usually slightly enlarged, and, upon close examination, has a prominent reticular pattern. There may be hemorrhages and erosions in the gallbladder mucosa.

In most cases, small arterioles are very prominent and tortuous and have thickened walls. This is usually seen in subcutaneous vessels and those in the thorax, abdomen, and CNS.

Fibrinous polyarthritis is seen in many cases of MCF.

### **Morbidity and Mortality [top](#)**

Clinical MCF in cattle in the United States is usually sporadic. However, in an outbreak in a Colorado feedlot, morbidity was 37 percent. Morbidity in nonalcelaphine MCF outbreaks in Malaysia ranged from 28 percent to 45 percent. The prognosis in MCF is poor. Once clinical signs are observed, mortality is usually

greater than 95 percent (90-100 percent). In some parts of New Zealand, MCF is, along with tuberculosis, the most important cause of mortality in the deer-farming industry.

## Diagnosis [top](#)

### Field Diagnosis [top](#)

A history indicating contact with sheep, goats, or alcelaphine antelope, especially around the period of parturition, associated with typical clinical features of MCF, provides grounds for a tentative diagnosis of MCF.

Gross necropsy lesions consisting of corneal opacity; enlarged lymph nodes; inflammation and erosions in nasal passages, alimentary tract mucosa, and urinary bladder; and prominent tortuous small arteries in the subcutaneous tissue, thorax, and abdomen, provide further evidence for a presumptive diagnosis of MCF.

### Specimens for the Laboratory [top](#)

1. For animal transmission and inoculation at least 300 to 500 ml blood in EDTA (1 mg/ml blood), heparin, or ACD solution should be collected and carried or shipped iced, not frozen. For virus isolation in cell culture, 10 to 20 ml of blood in EDTA is preferred. This should also be shipped cold but not frozen.
2. Tissues for virus isolation, FA, or immunoperoxidase examination should also be refrigerated (iced) but NOT FROZEN and should include pieces of spleen, lung, lymph nodes, adrenals, and thyroids as well as unclotted blood. These should be collected as soon after death as possible, for the virus becomes inactivated rapidly in an animal dead more than 1 hour. The most useful specimens for animal inoculation or virus isolation attempts are those collected from a moribund animal immediately after euthanasia.
3. Tissues for histopathology, fixed as thin pieces in 10 percent neutral buffered formalin, should include lung, kidney, liver, adrenals, lymph nodes, eyes, oral epithelium, esophagus, Peyer's patches, urinary bladder, carotid rete, thyroid, heart muscle, skin (if lesions are present), and whole brain.
4. Serum for serology should consist of paired samples taken 3 to 4 weeks apart (i. e., the first during the acute phase of disease and the second during convalescence or at death). Serologic methods currently preferred include virus neutralization and competitive inhibition enzyme-linked immuosorbent assay for

MCF antibody.

## Laboratory Diagnosis [top](#)

Microscopic lesions of an extensive fibrinoid necrotizing vasculitis, perivasculitis, and lymphoreticular proliferation in lymphoid organs with mononuclear infiltrations in kidney, liver, adrenals, CNS, etc., are pathognomonic for MCF and are a sound, practical basis for a confirmed diagnosis.

Virologic and serologic examinations provide additional information that may also ultimately lead to a better understanding of the epizootiology and differences between viral strains and the clinical manifestations. Methods used consist of virus isolation, identification of viral isolates, demonstration of the appearance, or rising titers of MCF antibodies and molecular techniques using viral DNA probes, or target DNA amplifying methods such as the polymerase chain reaction (PCR). Because of the presence of MCF antibodies in asymptomatic U.S. cattle, a single antibody positive serologic sample is of limited value in establishing an etiologic diagnosis. The PCR method for demonstrating MCF DNA segments is proving to be useful for identifying MCF carriers as well as diagnosing overtly diseased animals.

## Differential Diagnosis [top](#)

Clinical MCF must be distinguished from other diseases and factors that produce inflammation and erosions and ulcerations of the nasal and alimentary tract mucosas such as BVD mucosal disease, bluetongue, rinderpest, vesicular diseases (FMD, VS), ingested caustics, and some poisonous plants and mycotoxins. The inability to differentiate the alcelaphine clearly from the sheep-associated MCF by clinical observations, lesions, or laboratory means presents an enigma in evaluating the possibility of a foreign animal disease. With our current knowledge, history of association with sheep, goats, or with alcelaphine antelope remains the only practical means of differentiating one form from the other.

## Vaccination [top](#)

Cattle and experimentally infected rabbits recovered from MCF have a solid immunity against all strains of MCF virus.

An effective vaccine is not available for MCF. Some viral strains have undergone limited attenuation after serial passage in cell cultures and offer hope for a future modified live virus vaccine. Experimental killed virus vaccines have been inconsistent in inducing protection against virulent virus challenge, although some have induced significant titers of serum virus neutralizing antibodies

## Control and Eradication [top](#)

Cattle should be kept separated from potential reservoir hosts such as sheep, goats, and wildebeest — especially during lambing, kidding, or calving seasons, respectively.

The stocking of cattle ranches with alcelaphine antelope, wild sheep, or goats should be discouraged or should require a negative MCF serologic test, preferably by the serum-virus neutralization method, or a negative PCR test for any wild ruminants destined for such a facility. Similar testing of such wild ruminants before being placed in, or transferred between, zoos is also recommended as a means to prevent the introduction of potential carriers of MCF virus.

Containment of an outbreak usually means the immediate separation of cattle or the susceptible host from sheep and goats in the case of the domestic disease and the susceptible host from alcelaphine or wild ruminants in the case of alcelaphine MCF.

## Public Health [top](#)

There is no evidence that MCF is infectious for humans.

## GUIDE TO THE LITERATURE [top](#)

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