Malignant catarrhal fever (MCF)

Author: Prof Moritz van Vuuren


Licensed under a Creative Commons Attribution license.

EPIDEMOLOGY

Only AlHV-1 has been isolated and characterized; OvHV-2 has consistently proved impossible to isolate using conventional methodologies and has only been identified by applying molecular techniques to detect the viral DNA.

It was not until 1960 that the causal virus of the wildebeest-associated disease was identified by Plowright and co-workers as a herpesvirus that could be isolated in cell culture provided that infected intact cells were included in the inoculum.

The genome of AlHV-1 is characteristic of the gammaherpesviruses, and consists of a 130 kb unique region together with 25 to 30 kb multiple direct repeats of approximately 1 kb each located terminally. The cloning and structural analysis of the complete genome of the virulent isolate C500 was completed in 1997.

The aetiological agent of the sheep-associated form of MCF has remained elusive. Despite several reports to the contrary, no aetiological virus has ever been isolated either from cases of this form of MCF or from sheep. Evidence for the existence of a virus antigenically related to AlHV-1 that infects sheep was based on the detection of antibody that reacted with AlHV-1 in an indirect immunofluorescence antibody (IIFA) test in virtually every sheep serum examined, as well as on the detection of antibody in sheep sera which reacted with the major structural proteins of AlHV-1 in immunoblots. In addition, hamsters experimentally infected with tissues from cattle and deer that had contracted this form of MCF were found to develop antibody to AlHV-1.

Despite consistent failure to isolate an aetiological virus from cases of the sheep-associated form of MCF, it has been possible to generate lymphoblastoid cell lines originating from cattle and deer suffering from this form of the disease. The DNA from such cell lines was found to hybridize with a number of DNA clones of the unique region of the AlHV-1 molecule and subsequent screening of a genomic library from these cells enabled the identification of several viral clones which were established to be OvHV-2. Sequence data from one of these clones has formed the basis of a polymerase chain reaction (PCR) specific for OvHV-2 which allows the detection of the virus both in sheep and MCF-affected cattle, domestic pigs, several species of farmed deer, bison, water buffalo, African buffalo as well as a number of exotic hoofstock in zoological collections.

The disease occurs worldwide but its importance varies as it is markedly dependent on both the source of virus and the species affected. The two blue wildebeest subspecies and the black wildebeest may be a source of AlHV-1. This form of MCF occurs throughout the natural distribution of
these antelope in Africa, as well as in zoological collections when mixed populations of members of the Artiodactyla (hoofstock), including wildebeest, are kept. In the latter instance a variety of susceptible species may be affected.

Transmission of AlHV-1 in free-living populations of wildebeest is extraordinarily efficient with all calves becoming infected within the first few months of life. Following the isolation of the virus from wildebeest calves in East Africa in 1960, Plowright et al embarked on an exhaustive study of transmission in free-living C. t. albojubatus. These studies established that all adults had neutralizing antibody to the virus and that virus could be recovered from a proportion of their foetuses. Furthermore, sera from wildebeest calves examined for antibody to the virus were usually positive. These data suggest that most calves receive colostral antibody and are infected either in utero or during the first few months of life when maternal antibody is still present. Virus has been recovered from nasal or ocular secretions of wildebeest calves aged six to eight weeks suggesting that the respiratory tract is the likely route of contagious spread. Thus, in free-living wildebeest, a proportion of foetuses are infected in utero which is followed by intense transmission within the population during which all calves become infected in the first few months of life.

Following infection, AlHV-1 establishes a latent infection with virus only on occasion being detectable. The work of Plowright suggested that wildebeest cows may become viraemic in the late stages of pregnancy, while a study by Rweyemamu et al. in 1974 found that reactivation with excretion of virus occurred in captured adult wildebeest at the time of confinement following abrupt changes in diet and following betamethasone (corticosteroid) treatment at the dosage rate of 40 mg daily for seven days.

In all the numerous studies of AlHV-1 infection in wildebeest, no evidence of clinical disease or pathological lesions has been reported.

Direct transmission of AlHV-1 to MCF-susceptible indicator hosts only occurs from wildebeest; all reports consistently confirm the observation that horizontal spread does not take place from MCF-affected animals or from the few that survive the disease, although vertical (transplacental) transmission in cattle has been described.

Although the actual method of transmission has not been fully established, it is noteworthy that an outbreak of MCF in cattle has been described in the USA where wildebeest situated a substantial distance away were almost certainly the source of AlHV-1. In South Africa, too, there are reports of MCF occurring in cattle separated from wildebeest by up to 800 metres. This has led to speculation that spread by arthropod vectors may occur. However, the known physical characteristics of the herpesviruses, the extraordinarily efficient spread amongst wildebeest calves, and observations on the transmission of the closely related OvHV-2 support the view that natural spread is generally, if not exclusively, by aerosol with many of the apparent anomalies being explained by prolonged incubation periods occurring in some animals.

In the Maasai areas of East Africa, the seasonal occurrence of MCF in cattle which is predominantly in March and April in northern Tanzania and from April to July in southern Kenya, has been associated with blue wildebeest (C. t. albojubatus) calving seasons. Therefore, the disease is more common in cattle in these areas when the wildebeest calves are two to three-months-old. In South
Africa, blue wildebeest (*C. t. taurinus*)-associated MCF occurs regularly in provinces where free-living or semi-captive wildebeest are present. However, the majority of cases occur in the Limpopo and North-West Provinces where ecotourism has expanded and the number of game farms increased significantly during the 1990s. Two peaks in the prevalence of the disease are encountered; one in January to May (with the highest number of cases occurring in early April) following the wildebeest calving season in December, January and February, and a second, in which the prevalence is higher, from September to November (the highest number of cases being in mid-September) when the wildebeest calves are nine to 11 months old. The disease is rare in the summer months of December, January and February, as well as in mid-winter. The ages of cattle (excluding congenital cases) that develop clinical signs vary from 4.5 months to a few years with the majority being between eight and 18 months old.

South Africa is the only natural habitat of the black wildebeest. Although the blue wildebeest has thus far been regarded as the most important carrier of AlHV-1, indications are that black wildebeest are equally important transmitters of MCF virus. This increase can be ascribed to the increase in the number of farms on which black wildebeest are kept. Whereas the black wildebeest was a few decades ago regarded as a threatened species, its area of distribution is now even bigger than that of the blue wildebeest. All black wildebeest herds tested thus far in South Africa were serologically positive for antibodies against AlHV-1.

As with AlHV-1 infection amongst wildebeest, OvHV-2 is transmitted to a proportion of lambs *in utero* and this is followed by an intense transmission in the periparturient flock with all becoming infected within three months of birth. However, more recent research has shown that lambs do not shed virus occurs until after 5 months of age.

The sheep form of the disease occurs wherever domestic sheep are kept, including African countries, although the susceptibility of recipient animal species varies considerably. Cattle (*Bos taurus* and *B. indicus*) are relatively resistant to infection with OvHV-2 and cases of MCF usually occurs only sporadically although outbreaks affecting many animals have been recorded. Other species, such as Bali cattle of Indonesia (*Bos javanicus*) and Père David’s deer (*Elaphurus davidianus*), are extremely susceptible to infection and must be kept well separated from sheep if heavy mortality is to be avoided. Other species of deer and the water buffalo have an intermediate susceptibility between cattle and the extremely susceptible hosts. The disease has also been described in zoological collections affecting a variety of species belonging to the subfamilies Bovinae and Tragelaphinae as well as in giraffe, although the identity of the causal virus has not always been established. With the increasing interest in the farming of bison in North America, the sheep-associated form of MCF is proving to be a common cause of mortality in them.

Another anomaly for which no satisfactory explanation has been forthcoming is the relatively common occurrence of SA-MCF in domestic pigs in Norway, although it has also been reported in Finland, Sweden, Germany and Switzerland. The occurrence of the disease in pigs does not appear to be determined by the breed of pigs or sheep involved, and the amplicon derived by PCR from pigs had a nucleotide sequence identical to that obtained from other sources. Incidents tend to occur in small holdings where sheep and pigs are housed in the same air space and generally several pigs become affected over a few days. However, no feature of the management could be identified to explain why
Malignant catarrhal fever

disease in pigs should be so restricted to these countries. Malignant catarrhal fever has not been reported in pigs in Africa.

As with animals suffering from MCF following infection with AlHV-1, horizontal spread from animals with SA-MCF does not occur. Transmission is thus only from sheep to the susceptible host, but the factors playing a role in this phenomenon are poorly understood and there are many irreconcilable features that cannot yet be explained.

The sheep-associated disease in domestic cattle occurs sporadically usually affecting only one or a few animals. This may occur following intimate contact with sheep and personnel or fomites that have had contact with sheep, as well as where no obvious contact with sheep can be established. Infection, however, can result in outbreaks in which substantial losses may occur over weeks or months while on occasion the disease recurs annually when several animals are affected during the course of several years. This is associated with certain groups of sheep becoming more efficient in transmitting the infection to cattle.