Slide 1

**Malignant Catarrhal Fever**

Malignant Catarrh, Malignant Head Catarrh, Gangrenous Coryza, Catarrhal Fever, Snotsiekte

Malignant catarrhal fever is an infectious disease of ruminants. It is also referred to as malignant catarrh, malignant head catarrh, gangrenous coryza, catarrhal fever, and snotsiekte, which is a South African word meaning "snotting sickness".

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Overview

- Organism
- Economic Impact
- Epidemiology
- Transmission
- Clinical Signs
- Diagnosis and Treatment
- Prevention and Control
- Actions to Take

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In today's presentation we will cover information regarding the organism that causes Malignant Catarrhal Fever and its epidemiology. We will also talk about the economic impact the disease has had in the past and could have in the future. Additionally, we will talk about how it is transmitted, the species it affects, clinical and necropsy signs seen, and diagnosis and treatment of the disease. Finally, we will address prevention and control measures for the disease as well as actions to take if Malignant Catarrhal Fever is suspected.

(Photo: Hartebeest)

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**The Organism**

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The Organism

- Herpesviridae
  - Genus *Rhadinovirus*
- Multiple serotypes
  - Species and geographically dependent
    - AHV-1 natural host: wildebeest in Africa
    - OHV-2 natural host: domestic sheep and goats worldwide
    - AHV-2 nonpathogenic
    - CpHV-2 natural host: domestic goats

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Malignant catarrhal fever (MCF) is caused by several viruses in the genus *Rhadinovirus* of the family Herpesviridae (subfamily Gammaherpesvirinae). The specific serotype varies depending on species and geographic distribution. Wildebeest in Africa are the natural host species that carry the alcelaphine herpesvirus-1 (AHV-1). All varieties of domestic sheep, as well as goats, in North America and throughout the world are carriers of ovine herpesvirus-2 (OHV-2); this serotype is the major cause of MCF worldwide. Natural hosts of MCF do not experience clinical disease. Alcelaphine herpesvirus-2 (AHV-2) is non-pathogenic but is latently carried by wildebeest, hartebeest, and topi. Most recently it was discovered that worldwide, goats are endemically infected with caprine herpesvirus-2 (CpHV-2), which apparently only causes disease in deer.

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## Importance

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## History

- Cases occur worldwide each year
- MCF in wildebeests in Africa for centuries
- U.S.
  - In cattle since 1920s
  - First bison case in 1973 (South Dakota)
  - Problem in zoo animals
    - New Jersey exotic theme park, 2002
    - AHV-1 diagnosed in Ankoli cattle

Center for Food Security and Public Health, Iowa State University - 2007

MCF cases are reported worldwide in many different species. MCF associated with wildebeests has been recognized in Africa for centuries. Reports of a disease resembling MCF have been present in cattle in the United States since the 1920s. South Dakota reported the first bison case of MCF in 1973. Most recent U.S. infections occurred in October 2002 in an exotic wildlife theme park in New Jersey. AHV-1 was diagnosed using PCR in three Ankoli cattle out of a herd of 31. The virus originated from the fetal fluids of a wildebeest.

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## Economic Impact

- Variable given the carrier status
- Zoologic parks affected through losses of expensive animals
- Not reportable in all 50 states
  - Tracking true losses difficult
- Concern for bison breeders, cattle producers, elk and deer farmers

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Given the carrier status of this virus in the sheep, goat, and wildebeest populations, economic impact could be variable. There are multiple species susceptible to infection as you will see in the coming slides, and many different industries could be affected. Zoologic parks spend hundreds to thousands of dollars on some of their exotic species and could later lose them to infection with MCF. As this is not a reportable disease in all 50 states, tracking the true economic impact is difficult. It is a concern for bison breeders, as well as cattle producers and elk and deer farmers, but hard numbers that quantify the potential losses from this fatal disease were difficult to find.

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## Epidemiology

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## Geographic Distribution

- AHV-1 primarily in Africa
  - Carried by wildebeest, hartebeest, topi
  - Also in zoologic and wild animal parks
- OHV-2 worldwide
  - Carried by domestic and wild sheep and goats
  - Major cause of MCF worldwide

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Malignant catarrhal fever caused by AHV-1 is carried by wildebeest, hartebeests, and topi and is found primarily in the wild in Africa. Wildebeest in zoological and wild animal parks are also asymptomatic carriers. The disease caused by OHV-2 is seen throughout the world, as all domestic and wild sheep appear to have antibodies to this virus. Goats are also carriers of OHV-2. (Top photo: wildebeest, bottom photo: topi antelope)

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## Geographic Distribution

- Positive bison have been found in U.S. and Canada
  - Utah, Wyoming, Colorado, Montana, California, Oregon, Ohio, Kansas, Nebraska, North Dakota, South Dakota
  - Saskatchewan, Ontario, and Alberta
- Often misdiagnosed in bison

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As of February 2000, there were 11 states in the U.S and 3 Canadian provinces that had OHV-2 positive bison or bison herds. These include Utah, Wyoming, Colorado, Montana, California, Oregon, Ohio, Kansas, Nebraska, North Dakota, and South Dakota, and in Canada, Saskatchewan, Ontario, and Alberta. Often the disease gets misdiagnosed, but veterinarians need to be aware of this disease. Data is not as readily available for cattle or elk herds, so it is difficult to know if disease is enzootic in these species.

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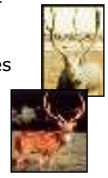
## Morbidity/Mortality

- Carrier species asymptomatic
  - Wildebeest, hartebeest, topi, sheep, goats
- Low morbidity in other species
  - U.S. outbreaks 30 to 40%
  - < 1% in water buffalo, deer
- Mortality 100%
  - Domestic cattle, white-tailed, axis, Pere David's deer



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Carrier species (wildebeest, hartebeest, topi, sheep, and goats) are asymptomatic, and morbidity involving other species is generally low. In the last 30 years, U.S. outbreaks have had morbidity ranging from 30 to 40% and are usually associated with the source animal remaining on the premises. Water buffalo, farmed deer, and fallow deer have low mortality rates, around 1%. Mortality rates can reach 100% in animals with clinical signs, namely domestic cattle, with the highest incidence in those between 6 months and 4 years of age. White-tailed, axis, and Pere David's deer also have extremely high mortality rates.

(Top photo: Pere David's Deer; bottom photo: Axis deer)

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## Transmission

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## Animal Transmission

- AHV-1
  - Wildebeest calves
    - In utero
    - Contact with nasal and ocular secretions
    - Aerosols during close contact
  - Adult wildebeest
    - Cell-associated form
    - Rarely transmitted

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MCF viruses, like other herpesviruses, establish lifelong, latent infections. AHV-1 is transmitted mainly by wildebeest calves, which can become infected *in utero*, by direct contact with other wildebeest, or in aerosols during close contact. Contamination of pastures may also contribute to transmission. Infected calves, particularly animals one to two months of age, shed the virus in nasal and ocular secretions. Wildebeest calves over the age of six months rarely shed virus. In these animals and in adult wildebeest, AHV-1 occurs mainly in a cell-associated, rarely transmitted form; however, cell-free virus can be isolated from the nasal secretions of some animals that are stressed or given corticosteroids. Most cases of wildebeest-associated MCF are seen when susceptible animals are exposed to parturient wildebeest or young calves.

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## Animal Transmission

- OHV-2
  - Respiratory (aerosol)
  - Transplacental rare
  - Contact with nasal secretions
  - Animal-to-animal rare
    - Dead end hosts

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OHV-2 appears to be transmitted mainly by the respiratory route, probably in aerosols. This virus is shed intermittently in nasal secretions, particularly by 6 to 9 month old lambs. OHV-2 DNA has also been reported in the semen of rams. Unlike AHV-1 in wildebeest, OHV-2 is rarely transmitted transplacentally or in colostrum or milk; most lambs do not become infected until they are at least two months of age. Susceptible animals usually become infected when they are in close contact with sheep, but cases have been reported when sheep and cattle were separated by 70 meters, as well as in bison herds up to 5 km from a lamb feedlot. Cattle-to-cattle, bison-to-bison, or deer-to-deer transmission is rare, and these species are considered dead end hosts once infected with OHV-2 or AHV-1.

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## Human Transmission

- MCF has not been documented as causing disease in humans
- Caution at lambing time
  - Equipment used could spread infection to susceptible animals
- Virus quickly inactivated by sunlight
  - Minimizes risk of fomite spread

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MCF has not been documented to cause disease in humans. As the exact transmission of OHV-2 remains unknown, persons assisting in lambing should take precautions not to contaminate cattle areas. This virus is quickly inactivated by sunlight, which helps decrease the chance of fomite spread.

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## Animals and Malignant Catarrhal Fever

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## Species Affected

- Carrier species
  - Sheep, goats, wildebeest, hartebeest, topi
- Susceptible species
  - Cattle, bison, elk, reindeer, moose, domestic pigs, giraffe, antelope, wapiti, red and white-tailed deer, Pere David's deer, white-tailed & white-bearded gnu, gaur, greater kudo, Formosan sika deer, axis deer, nilgai, banteng

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As discussed previously, sheep, goats, wildebeest, hartebeest, and topi are carriers of MCF but are asymptomatic. Other species, including cattle, bison, elk, reindeer, moose, domestic pigs, giraffe, antelope, wapiti, red deer, Pere David's deer, white-tailed deer, white-tailed gnu, white-bearded gnu, gaur, greater kudo, Formosan sika deer, axis deer, nilgai, and banteng are susceptible to MCF and can develop an infection. Water buffalo and farmed deer can also be affected but with much less mortality.

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## Clinical Signs

- Incubation period 9 to 77 days experimentally
  - Unknown in natural infections
  - Subclinical infections develop under stress
- Initial clinical signs
  - Depression, diarrhea, DIC, dyspnea, high fever, inappetence
  - Sudden death

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Experimental infections have an incubation period of 9 to 77 days, but the incubation period is unknown for natural infections. Some animals are subclinically infected and develop disease when they become stressed. Clinical signs initially include depression, diarrhea, disseminated intravascular coagulation (DIC), dyspnea, high fever (105.8-106.7$^{o}$F), inappetence, and often sudden death.

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## Clinical Signs

- Peracute form: sudden death
- Head and eye form
  - Majority of cattle cases
- Intestinal form
  - Initially like head and eye form, but death occurs from severe diarrhea
- Mild form
  - Inoculated animals; recovery expected

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MCF can take four clinical forms in cattle. First is the peracute form in which sudden death can occur. Second is the head and eye form, which is the most common in cattle. It progresses through the early signs of fever, reddened mucosa, and enlarged prescapular lymph nodes. Eventually the lesions become necrotic and death can occur. Third is the intestinal form which has the same early signs as the head and eye form, but the animal dies of severe diarrhea before the lesions become necrotic. The fourth form is mild and only occurred in cattle that were experimentally inoculated with an attenuated virus and recovered. Deer and antelope may have minimal lesions or be less specific than cattle or bison, but many of the same signs occur.

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## Head and Eye Form: Early Stages

- Reddened eyelids
- Bilateral corneal opacity
- Crusty muzzle, nares
- Nasal discharge
- Salivation



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In the early stages of the head and eye form, this disease can cause conjunctivitis, reddened eyelids, and bilateral corneal opacity, as well as serous or thick nasal discharge, crusty muzzles and nares, open-mouthed breathing, and salivation (cattle, bison).

(Photos taken from APHIS USDA FAD training module at www.aphis.usda.gov)

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## Head and Eye Form: Later Stages

Erosions on the tongue

Erosions on the buccal mucosa

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In the later stages of the head and eye form, cattle and bison may have areas of erosions on the buccal mucosa, and necrosis and hyperemia in the oral cavity. The skin can ulcerate, and hardened scabs form on the perineum, udder, and teats.

(Photos taken from USDA APHIS FAD training module at http://www.aphis.usda.gov)

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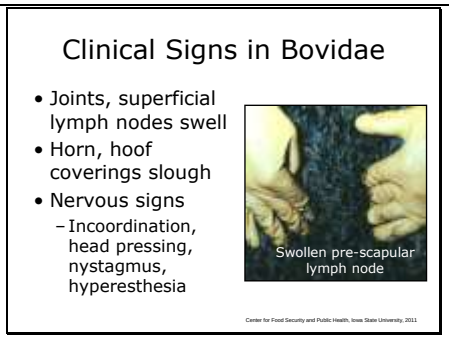


Joints and superficial lymph nodes may swell, and the horn and hoof coverings may slough in some animals. Finally, some animals exhibit nervous signs, such as incoordination, head pressing, nystagmus, and hyperesthesia.

(Photo depicts a swollen prescapular lymph node on a cow. Taken from APHIS USDA FAD training module at www.aphis.usda.gov)

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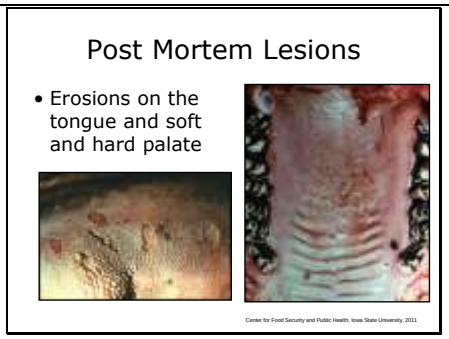


This multisystemic disease can cause post mortem lesions in the gastrointestinal, respiratory, and urinary tracts. The actual severity depends on the course of the illness. The gastrointestinal tract can be affected, starting in the oral cavity (as pictured, erosions on the tongue and the hard and soft palate of a cow).

(Taken from APHIS USDA FAD training module at http://www.aphis.usda.gov)

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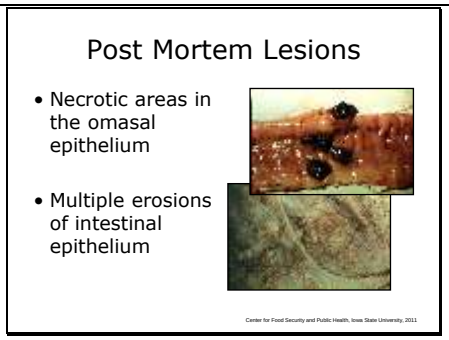


With sudden death, hemorrhagic enterocolitis in the infected animal may be the only sign. Erosions and necrotic areas appear throughout the omasum and intestinal tract.

(Taken from APHIS USDA FAD training module at http://aphis.usda.gov)

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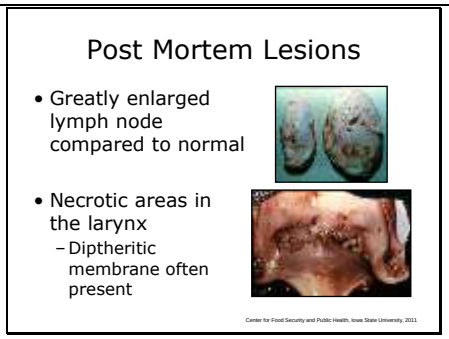


As noted with the clinical signs, the lymph nodes can be greatly enlarged with MCF. The prescapular lymph node is much larger compared to the normal node beside it (above picture). Other cases may exhibit catarrhal accumulations, erosions, and a diptheritic membrane in the respiratory tract. Note the necrotic areas on the larynx in the bottom photo; these are sometimes accompanied by a diptheritic membrane.

(Photos taken from APHIS USDA FAD training module at http://www.aphis.usda.gov)

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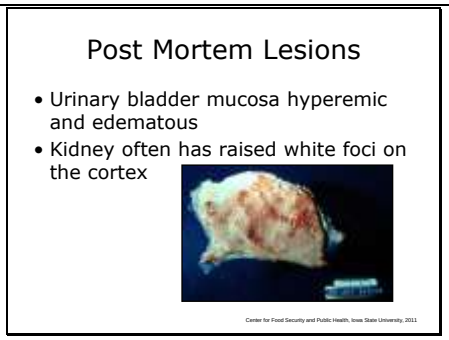


The urinary bladder may have hemorrhagic, edematous areas, and there may be raised white foci on the renal cortex. The mucosa of this bladder (photo) is hyperemic and edematous due to MCF infection.

(Photo taken from APHIS USDA FAD training module at http://www.aphis.usda.gov)

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## Differential Diagnosis

- BVD mucosal disease
- Bluetongue
- Rinderpest
- FMD
- Vesicular stomatitis
- Salmonellosis
- Pneumonia complex
- Oral exposure to caustic materials
- Mycotoxins
- Poisonous plants



Due to the similarity of lesions, differential diagnoses consist of bovine viral diarrhea mucosal disease, bluetongue, rinderpest, foot and mouth disease, vesicular stomatitis, salmonellosis, pneumonia complex, oral exposure to caustic materials, mycotoxins, and some poisonous plants.

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## Sampling

- Before collecting or sending any samples, the proper authorities should be contacted
- Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease



Before collecting or sending any samples from animals with a suspected reportable disease, the proper authorities should be contacted. Samples should only be sent under secure conditions and to authorized laboratories to prevent the spread of the disease.

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## Clinical Diagnosis

- Any susceptible animal with sudden death, fever, erosions of the mucosa, nasal/lacrimal discharge, or bilateral corneal opacity should be tested for MCF
  - Particularly with a history of exposure to sheep, goats, antelope, or wildebeest during parturition



Based on the clinical signs described, MCF should be suspected in susceptible animals if they have been exposed to sheep, goats, antelope or wildebeest, particularly around parturition. Animals that suddenly die or have a fever and erosions of the mucosa, nasal and lacrimal discharge, or bilateral corneal opacity should be tested for MCF.

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## Laboratory Diagnosis

- Histopathology
- PCR
- Virus isolation (AHV-1)
- Serology
  - AHV-1 antibodies in wildebeest
    - Immunofluorescence, immunoblot, VN, ELISA, immunocytochemistry
  - OHV-2 antibodies in sheep
    - Immunofluorescence, immunoblot



Malignant catarrhal fever is often suspected based on histopathologic demonstration of multisystemic lymphoid infiltration, disseminated vasculitis, and degenerative epithelial lesions. Because some MCF viruses cannot be isolated from infected animals, polymerase chain reaction (PCR) tests have become the diagnostic method of choice. PCR can detect both AHV-1 and OHV-2, as well as other MCF viruses. AHV-1 infections, but not OHV-2 infections, can also be confirmed by virus isolation in bovine thyroid cells or other susceptible cell lines. Serology is sometimes helpful, but antibodies may not be found in acute cases, particularly in cervids. Neutralizing antibodies do not usually develop in clinically affected ruminants. In wildebeest, antibodies to AHV-1 can be detected by virus neutralization, immunoblotting, ELISA, immunofluorescence or immunocytochemistry. In sheep, antibodies to OHV-2 can be found by immunofluorescence or immunoblotting.

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## Sample Collection

- Blood in EDTA tube for virus isolation
- Fresh tissue collected and refrigerated immediately after death
  - Spleen, lung, lymph nodes, adrenal glands

- PCR on peripheral blood, fresh tissues
- Paired serum samples

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In order to isolate the virus, 10-20 mls of blood should be collected and put in an EDTA tube. The virus is quickly inactivated in dead animals so spleen, lung, lymph nodes, and adrenal glands should be collected as soon as possible, refrigerated (NOT frozen), and sent for virus isolation, fluorescent antibody, or immunoperoxidase tests. In order to run a PCR test, peripheral blood, fresh tissues, or paraffin-embedded tissue samples must be used. As some animals have antibodies to the virus, paired sera should be used to identify an infection. Serum should be taken 3 to 4 weeks apart, if possible, for serology.

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## Treatment

- Survival is rare if clinically ill
- Mortality reaches 100%
- Supportive therapy, antibiotics for secondary bacterial infection
  - Recovered animals will remain virus carriers

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Mortality in clinically ill animals is nearly 100% and survival in other exposed animals is rare. Supportive therapy (fluids) and antibiotics for secondary bacterial infections can be tried for valuable animals. If recovery occurs, animals will likely remain virus carriers and could spread infection.

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## MCF in Humans

MCF has never been documented to cause infection in humans.

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## Prevention and Control

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## Recommended Actions

- IMMEDIATELY notify authorities
- Federal
  - Area Veterinarian in Charge (AVIC)
    http://www.aphis.usda.gov/animal_health/area_offices/
- State
  - State veterinarian
    http://www.usaha.org/StateAnimalHealthOfficials.pdf
- Quarantine

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If you suspect a case of MCF, state or federal authorities should be notified immediately. Animals suspected with MCF should be isolated, and the farm should be quarantined until definitive diagnosis is determined.

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## Prevention and Control

- Separate infected and carrier animals from susceptible species
  - Carriers: sheep and goats
  - Keep cattle away, especially during parturition

- Zoological parks
  - Introduce seronegative animals only
- No vaccine available

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Should an epidemic occur, clinical and carrier animals should be separated from susceptible species. As domestic sheep and goats are asymptomatic carriers, they should be kept separated from cattle at all costs, especially during parturition. African wildlife, wildebeests, hartebeests, and topi, should also be kept separated from cattle to limit the spread of infection. Zoological parks should only introduce seronegative animals and follow strict quarantine restrictions of newly acquired animals. There is no vaccine currently available, but experimental evidence in cattle has shown some protection from challenge inoculation.

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## Additional Resources

- World Organization for Animal Health (OIE)
  - www.oie.int
- U.S. Department of Agriculture (USDA)
  - www.aphis.usda.gov
- Center for Food Security and Public Health
  - www.cfsph.iastate.edu
- USAHA Foreign Animal Diseases ("The Gray Book")
  - www.usaha.org/pubs/fad.pdf

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## Acknowledgments

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