Heartwater

Cowdriosis, Malkopsiekte, Péricardite exsudative Infectieuse, Hidrocarditis Infecciosa, Idropericardite dei Ruminanti

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Importance

Heartwater, a rickettsial disease of ruminants, is one of the most important diseases of livestock in Africa. This tick-borne illness can significantly decrease productivity in regions where it is endemic. It is particularly serious in non-indigenous livestock that are moved into heartwater areas; many of these animals may die. Wild ruminants can also be infected. Most wildlife species appear to carry the organism asymptomatically, but serious illness has been reported in lechwe moved into endemic areas, as well as in experimentally infected white-tailed deer.

Heartwater is readily introduced into new regions in infected animals or ticks. Known and potential host ticks are widely distributed, and can be found on a variety of animals including reptiles. On at least one occasion, leopard tortoises and African spurred tortoises imported into Florida were found to be carrying infected ticks. Once the tick vector becomes established, eradication of heartwater is difficult. One host tick, *Amblyomma variegatum*, was introduced into the Caribbean early in the 19th century. During the 1970s and early 1980s, this tick spread rapidly from island to island; in some cases, it may have been carried by cattle egrets. The presence of heartwater in the Caribbean increases the risk of introducing this disease into the Americas. Ongoing programs are attempting to eradicate *Amblyomma variegatum* from the Caribbean. To date, these programs have succeeded in reducing the numbers of ticks on some islands and eradicating them from others, but complete eradication throughout the Caribbean remains elusive.

Etiology

Heartwater results from infection by *Ehrlichia* (formerly *Cowdria*) *ruminantium*, a small, Gram negative, pleomorphic coccus in the family Anaplasmataceae and order Rickettsiales. This organism is an obligate intracellular parasite. Strains of *E. ruminantium* are very diverse; while some strains are highly virulent, others appear to be non-pathogenic. *E. ruminantium* has a high level of genomic plasticity. Gene segments are often deleted or inserted, and genes may be disrupted. Several different genotypes can co-exist in a geographic area, and may recombine to form new strains.

Species Affected

*E. ruminantium* mainly infects domesticated and wild ruminants. Cattle, sheep, goats and water buffalo can be affected. Among wild ruminants, *E. ruminantium* has been proven to infect blesbok (*Damaliscus pygargus*), black wildebeest (*Connochaetes gnou*), blue wildebeest (*Connochaetes taurinus*), African buffalo (*Syncerus caffer*), eland (*Taurotragus oryx*), giraffes (*Giraffa camelopardalis*), greater kudu (*Tragelaphus strepsiceros*), sable antelope (*Hippotragus niger*), lechwe (*Kobus leche kafuensis*), steenbok (*Raphicerus campestris*), springbok (*Antidorcas marsupialis*), sitatunga (*Tragelaphus spekii*), Timor deer (*Cervus timorensis*) and chital (*Axis axis*). White-tailed deer (*Odocoileus virginianus*) have been infected experimentally. Other wild ruminant species are also thought to be susceptible, but confirmation is lacking.

Experimental infections have been established in some non-ruminant species including ferrets, laboratory mice, four-striped grass mice (*Rhabdomys pumilio*) and southern multimammate mice (*Mastomys coucha*). Leopard tortoises (*Geochelone pardalis*) and helmeted guinea fowl (*Numida meleagris*) were reported to be susceptible in earlier studies, but this was not confirmed in a recent report. The scrub hare (*Lepus saxatilis*) may also be a host, but this has not been proven.

Recently, an organism closely resembling *E. ruminantium* was found in African vipers and other snakes with a fatal disease that resembled heartwater. It has not yet been determined whether this organism is *E ruminantium* or a closely related species.

Geographic Distribution

Heartwater is endemic in most of Africa south of the Sahara desert, as well as in surrounding islands such as Madagascar, and in the Caribbean.
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Transmission

Heartwater is transmitted by ticks in the genus *Amblyomma*. Ticks become infected as larvae or nymphs, and can transmit the disease as nymphs or adults. Transovarial passage is not significant in the epidemiology of heartwater, and may not occur. Cattle egrets have been implicated in the dispersal of *Amblyomma* ticks in the Caribbean. At least twelve species of *Amblyomma* can transmit *E. ruminantium*. *A. variegatum* (the tropical bont tick) is the major vector in Africa and the Caribbean. Other known vectors include the bont tick *A. hebraeum* (in southern Africa), *A. lepidum* (in East Africa and the Sudan), *A. astrion*, and *A. pomposum*. *A. sparsum*, *A. gemma*, *A. cohaerans*, *A. marmoreum* and *A. tholloni* (the elephant tick) are capable of transmitting experimental infections. Two North American species, *A. maculatum* (the Gulf Coast tick) and *A. cajennense*, can transmit *E. ruminantium* in the laboratory, but neither has been implicated in natural infections. *E. ruminantium* gene segments have been found, by PCR, in the ticks *Rhipicephalus evertsi*, *Hyalomma truncatum* and *Hyalomma marginatum*; however, the organism was not isolated.

Ticks become infected by feeding on acutely ill or subclinically infected animals. Experimentally infected carrier sheep can infect ticks for at least seven months. Cattle can infect ticks for a minimum of eight months. Blesbok, black wildebeest, blue wildebeest, African buffalo, eland, giraffe, greater kudu and sable antelope can also become carriers. Infections have been detected for up to six months in some wild ruminants. *E. ruminantium* is very fragile and does not survive outside a host for more than a few hours at room temperature. However, cows may transmit the infection to their calves in colostrum.

Incubation Period

The incubation period in natural infections is usually two weeks, but it can be as long as a month. The incubation period after intravenous inoculation is seven to 10 days in sheep and goats, and 10 to 16 days in cattle.

Clinical Signs

Peracute disease is usually seen in Africa in non-native breeds of sheep, cattle and goats. Heavily pregnant cows are particularly susceptible to this form. Peracute disease is characterized by sudden death preceded by a brief interval of fever, severe respiratory distress, hyperesthesia, lacrimation and, in some breeds of cattle, severe diarrhea. Terminal convulsions may be seen. This form of heartwater is relatively rare.

Acute disease is the most common form of heartwater in domesticated ruminants. This syndrome is seen in non-native or indigenous cattle, sheep and goats. The symptoms begin with a sudden fever, anorexia, listlessness and dyspnea. Some animals, particularly cattle, may also develop diarrhea. These symptoms are followed by neurological signs that may include chewing movements, protrusion of the tongue, twitching of the eyelids, and circling, often with a high-stepping gait. Affected animals sometimes stand rigidly with muscle tremors. Some animals may become aggressive or anxious. As the disease progresses, the neurologic signs become more severe, and the animal goes into convulsions. In the terminal stages, lateral recumbency with paddling or galloping movements, opisthotonos, hyperesthesia, nystagmus and frothing at the mouth are common. Animals with the acute form of heartwater usually die within a week. On rare occasions, heartwater occurs as a subacute disease with a prolonged fever, coughing and mild incoordination. CNS signs are inconsistent in this form. In subacute disease, the animal either recovers or dies within 1 to 2 weeks.

Mild or subclinical infections may be seen in young calves, lambs or kids; partially immune livestock; some indigenous breeds; and some wild ruminants. The only symptom may be a transient fever. This form of the disease is known as “heartwater fever.”

Post Mortem Lesions

Hydropericardium, with straw–colored to reddish pericardial fluid, gives heartwater its name; this lesion is more consistently found in sheep and goats than in cattle. Other common lesions include pulmonary and mediastinal edema, intestinal congestion, hydrothorax, ascites, and edema of the mediastinal and bronchial lymph nodes. Petechial hemorrhages are often found on the epicardium and endocardium. Submucosal and subserosal hemorrhages may also be seen in other organs. Splenomegaly may be noted, particularly in sheep and goats. Congestion and meningaeal edema are sometimes found in the brain.

Morbidity and Mortality

The mortality rate in susceptible livestock ranges from 6% to 90%. Breeds of domesticated ruminants vary in their susceptibility, with higher morbidity and mortality rates in non-native than indigenous breeds. Up to 80% of merino sheep may die, but the mortality rate can be only 6% in Persian or Afrikander sheep. Angora and Saanen goats are also very susceptible to heartwater, while Creole goats in Guadeloupe are resistant. Similarly, *Bos indicus* breeds of cattle tend to be more resistant than *Bos taurus*. Genetic resistance has been demonstrated in some breeds.

Most infections in wild ruminants appear to be subclinical or mild, but high mortality rates have been reported in lechwe introduced into endemic areas, and in experimentally infected white-tailed deer. Occasional cases of heartwater have also been reported in other wild ruminants in Africa. Heartwater was suspected to be cause of death of a dromedary, but this was not proven.
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Diagnosis

Clinical
Heartwater should be suspected in animals with the typical symptoms including neurological signs, and post-mortem lesions consistent with this disease. The presence of *Amblyomma* ticks supports the diagnosis.

Differential diagnosis
The peracute form of heartwater can be confused with anthrax. The acute form may resemble rabies, tetanus, bacterial meningitis or encephalitis, babesiosis, anaplasmosis, cerebral trypanosomiasis, or theileriosis. It must also be differentiated from poisoning with strychnine, lead, ionophores and other myocardial toxins, organophosphates, arsenic, chlorinated hydrocarbons, or some poisonous plants (*Cestrum laevigatum*, *Pavetta* species, and *Pachystigma* species). Accumulations of fluid similar to heartwater are also sometimes seen in heavy helminth infestations.

Laboratory tests
Heartwater is often diagnosed by observing *E. ruminantium* colonies in the brain or intima of blood vessels. Brain smears are air dried, fixed with methanol and stained with Giemsa. *E. ruminantium* occurs as clumps of reddish-purple to blue, coccoid to pleomorphic organisms inside capillary endothelial cells. These organisms are often found close to the nucleus, and may be in a ring or horseshoe. *E. ruminantium* can also be detected in formalin-fixed brain sections using immunoperoxidase techniques. Colonies can be difficult or impossible to find in some animals that have been treated with antibiotics. Only a few colonies may be found in animals with peracute disease.

In tissues, *E. ruminantium* can be detected with DNA techniques including polymerase chain reaction (PCR) tests. PCR can find this organism in the blood from just before the onset of the fever to a few days after recovery, but detection in carrier animals is inconsistent. Positive PCR reactions are sometimes seen in areas where neither heartwater nor its tick vectors are known to exist, possibly due to cross-reactions with other *Ehrlichia* species.

Heartwater can also be diagnosed by isolating *E. ruminantium* from the blood. However, culture is time-consuming, and other diagnostic technique may be preferred. *E. ruminantium* can be grown in many primary ruminant endothelial cells or endothelial cell lines. In cultures, the organism is identified by microscopic examination, or by immunofluorescence/ immunoperoxidase staining. In some cases, heartwater may be diagnosed by inoculating fresh blood into a susceptible sheep or goat.

Serology can be used to screen animals for heartwater before importation, or to check the immune status of vaccinated animals. Serological tests include indirect immunofluorescence, enzyme-linked immunosorbent assays (ELISA), and immunoblotting (Western blotting). Cross-reactions with other *Ehrlichia* species occur in all serological tests. ELISAs that use recombinant antigens are more specific and reliable than other assays, but must still be interpreted with care.

Heartwater carriers are difficult to detect. Rickettsial colonies are difficult to find in these animals, and animal inoculation may be unsuccessful except during the first few weeks after recovery. Carriers may sometimes be found by PCR, or by feeding ticks on the animal and testing the ticks by PCR. Some carriers can be seronegative.

Samples to collect
Before collecting or sending any samples from animals with a suspected foreign animal 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.

Heartwater is often diagnosed in brain samples at necropsy. The best samples to collect are well-vascularized portions of the brain such as the cerebrum, cerebellum or hippocampus. Brain tissue can be collected at necropsy by driving a large nail through the unopened skull, and aspirating a sample with a syringe. Another technique is to cut off the head and collect tissue through the foramen magnum with a curette. *E. ruminantium* colonies can be found for up to two days in brains stored at room temperature, and for up to 34 days in refrigerated brains. *E. ruminantium* can also be found in smears made from the intima of large blood vessels.

In clinically ill animals, blood samples should be collected for PCR. PCR can sometimes detect organisms in the blood or bone marrow of carriers. For culture, blood is collected into an anticoagulant and diluted in culture medium; details are available in the OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals. Samples should be kept refrigerated and shipped with ice packs.

Serum may be collected for serology.

Recommended actions if heartwater is suspected

Notification of authorities
Heartwater must be reported to state or federal authorities immediately upon diagnosis or suspicion of the disease.

Federal Area Veterinarians in Charge (AVIC):
http://www.aphis.usda.gov/vs/area_offices.htm

State Veterinarians:
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Control

*E. ruminantium* cannot survive outside a living host for more than a few hours at room temperature. For this reason, heartwater is usually introduced in infected animals, including asymptomatic carriers, or in ticks. In heartwater-free countries, susceptible ruminants from endemic regions are tested before importation. All animals that may carry *Amblyomma*, including non-ruminant species, must be inspected for ticks before entry. In addition, ticks may be carried into a country on illegally imported animals or migrating birds. Outbreaks are usually controlled with quarantines, euthanasia of infected animals and tick control. During an outbreak, ticks should not be allowed to feed on infected animals. Iatrogenic transfer of blood between animals must also be avoided.

In endemic areas, animals with heartwater can be treated with antibiotics. Tetracycline is effective during the early, febrile stages of this disease, but animals often die before treatment can be administered. Antibiotic treatment alone is not always successful in later stages.

In endemic regions, heartwater can be prevented by tick control and vaccination. Alternatively, animals moved into endemic areas may be protected by prophylactic treatment with tetracycline. Vaccination currently consists of infection with a live *E. ruminantium* strain, then treatment with antibiotics when a fever develops. Alternatively, the vaccine may be given to young kids or lambs during their first week of life, or to calves less than 5-8 weeks of age; young animals possess non-specific resistance to infection, and do not always require treatment. Vaccination does not protect animals from all field strains, and revaccination is risky due to the possibility of anaphylactic reactions. Improved vaccines are in development. Intensive tick control may increase the susceptibility of animals to heartwater, because it eliminates the immune boosting effect of persistent exposure to small doses of organisms.

Heartwater can be eradicated from a region by eliminating its vectors. *Amblyomma* ticks can be difficult to eradicate due to their high rate of reproduction, the wide variety of hosts they infest, and acaricide resistance. A regional program (The Caribbean *Amblyomma* Program) has been established to eradicate *Amblyomma variegatum* ticks from English and Dutch-speaking islands in the Caribbean. A complementary eradication program (POSEIDOM Vétérinaire Programme) has been conducted on French-speaking islands. To date, these programs have succeeded in reducing the numbers of ticks on some islands and eradicating them from others, but complete eradication throughout the Caribbean remains elusive.

Public Health

*E. ruminantium* is not thought to be zoonotic. Recently, positive PCR results for this organism were obtained in three fatal cases of human ehrlichiosis. Two cases occurred in children with encephalitis, vasculitis of the brain, and pulmonary edema. Clinical details were not available for the other case. *E. ruminantium* was not proven to be the cause of death in any of the three people, and it remains to be determined whether this organism can cause human disease.

Internet Resources

Manual for the Recognition of Exotic Diseases of Livestock
http://www.spc.int/rah/
The Caribbean Amblyomma Programme (CAP)

The Merc Veterinary Manual.
http://www.merckvetmanual.com/mvm/index.jsp

United States Animal Health Association. Foreign Animal Diseases

World Organization for Animal Health (OIE)
http://www.oie.int

OIE Manual of Diagnostic Tests and Vaccines for Terrestrial Animals
http://www.oie.int/eng/normes/mmanual/a_summry.htm

OIE Terrestrial Animal Health Code
http://www.oie.int/eng/normes/mcode/A_summry.htm

References


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*Link defunct as of 2007.*