HEARTWATER
(Cowdriosis)

Definition top

Heartwater (HW) is an acute noncontagious infectious disease of ruminants affecting cattle, sheep, goats, and antelope and is caused by the rickettsial organism *Cowdria ruminantium*, which is transmitted by ticks of the genus *Amblyomma*. The disease is characterized by fever, nervous signs, hydropericardium, hydrothorax, ascites, edema of the lungs, and high mortality. In some wild ruminants the agent causes subclinical infection. The name "heartwater" is derived from the hydropericardium, which is commonly seen with this disease (Fig. 59).

Etiology top

The disease is caused by *Cowdria ruminantium*, a rickettsial agent. It is the only species of the genus *Cowdria*, in the tribe Ehrlichia, family Rickettsiaceae, order Rickettsiales. The organism multiplies in vascular endothelial cells throughout the body and in the reticulum cells of the lymph nodes. The agent is pleomorphic, usually coccoid, occasionally ring-formed, and measures from 400 to over 1,000 nm in diameter. It usually occurs in clumps of from less than five to several thousand organisms within the cytoplasm of infected capillary endothelial cells, especially in the brain. The HW organism is extremely fragile and cannot persist outside of a host for more than a few hours. Because of its fragility, the organism must be stored in dry ice or liquid nitrogen to preserve its infectivity.

Heartwater strains vary in virulence, and although all are apparently pathogenic for sheep and goats, at least one strain is nonpathogenic for cattle.

Host Range top

Heartwater causes severe disease in cattle, sheep, goats, and water buffalo; mild disease in some indigenous African breeds of sheep and goats; and inapparent disease in several species of antelope indigenous to Africa. The blesbok (*Damaliscus albifrons*), the black wildebeest (*Connochaetes gnu*), the eland (*Taurotragus oryx oryx*) and the springbok (*Antidorcas marsupialis*) have experimentally been shown to be susceptible to HW, and although the natural disease in these animals is usually mild, deaths in springbok have been attributed to HW. The blesbok and wildebeest are known carriers of *C. ruminantium* and are believed to play a role in the maintenance of the disease in nature.

Nonruminant hosts of *C. ruminantium*, such as guinea-fowl, leopard tortoises, and scrub hare, may also be important in the maintenance of the organism in nature because they are all known carriers of the agent. Although the striped mouse and the multimammate mouse have been shown to be susceptible to *C. ruminantium*, they are not hosts of the vector ticks and are not believed to play a role in the epizootiology of HW.

In the United States the most common deer species, *Odocoileus virginianus* (the white-tailed deer), has been shown by experimental inoculation to be susceptible to *C. ruminantium*. Severe clinical signs were noted along with typical postmortem lesions (Fig. 62). The mortality rate was high. *Amblyomma maculatum*, an experimentally proven vector of HW, is a common parasite of white-tailed deer in the southern United States.

The ferret and the albino mouse are susceptible to *C. ruminantium* under experimental conditions, and a mouse agent resembling C. ruminantium has been

isolated in South Africa.

Geographic Distribution top

Heartwater occurs only where vector ticks of the genus *Amblyomma* are active. For decades, the disease has been known to occur in most countries of Africa south of the Sahara Desert and on the island of Madagascar. The disease has also been reported from Tunisia and the former Yugoslavia; however, the Yugoslavian report is probably erroneous. For the last half century or more, the disease has been considered one of the most important livestock diseases in Africa and has been surpassed only by trypanosomiasis and East Coast fever.

Heartwater is now known to occur in the Caribbean, where the vector tick *A. variegatum* (tropical bont tick) has been recognized for many years. This tick, now known to occur on numerous Caribbean islands (e.g., Puerto Rico, Antigua, Guadeloupe, Martinique, St. Lucia, Nevis, St. Kitts) was probably introduced to the French Antilles with a shipment of cattle from Senegal in the 1830's. A fatal disease of cattle with neurologic and hemorrhagic signs, which in retrospect could have been HW, was described from Guadeloupe in 1932. Rapid spread of the tropical bont tick in the West Indies is believed to have occurred only after the introduction of the cattle egret from Africa in the early 1960's. Egrets are now known to be efficient porters of the tick. Heartwater has been diagnosed on the islands of Antigua, Guadeloupe, and Marie Galante. A disease closely resembling HW has also been reported from other Caribbean islands (e.g., Cuba and Antigua), but the diagnoses have not been confirmed. *Cowdria ruminantium* is far more widespread in the Caribbean than was formerly believed. Recent serological surveys (13) have demonstrated HW antibodies in cattle from 10 Caribbean islands (Antigua, Dominica, Granada, Guadeloupe, Martinique, Montserrat, St. Kitts, St. Lucia, St. Martin, and St. Vincent).

Transmission top

Heartwater is transmitted only by ticks of the genus *Amblyomma*. Of the 12 species known to transmit the disease, *A. variegatum* (tropical bont tick) is by far the most important, for it is widely distributed in Africa and has extended its range to include Yemen, Reunion, the Cape Verde islands, and several islands of the West Indies (26). Other major vector species are the bont tick *A. hebraeum* (in southern Africa), and *A. lepidum* (in East Africa and the Sudan). *Amblyomma astrion* (mainly on buffalo) and *A. pomposum* are also natural vectors of the disease, and five other African ticks — *A. sparsum*, *A. gemma*, *A. cohaerans*, *A. marmoreum* and *A. tholloni* (the elephant tick) — have experimentally been shown to be capable of transmitting HW.

Two North American species of *Amblyomma* ticks have been shown by Uilenberg (1982) to be capable of transmitting the disease. They are *A. maculatum* (the Gulf Coast tick) and *A. cajennense*, but neither of these ticks has been incriminated as natural vectors of HW. The former tick is widely distributed in the eastern, southern, and western United States, and was shown by Uilenberg to be as good a vector as one of the principal African vectors, *A. hebraeum*.

Amblyomma ticks are three-host ticks whose life cycles may take from 5 months to 4 years to complete. Because the ticks may pick up the infection as larvae or nymphs and transmit it as nymphs or as adults, the infection can persist in the tick for a very long time. The infection does not pass transovarially. *Amblyomma* ticks are multihost and will feed on a wide variety of livestock, wild ungulates, ground birds, small mammals, reptiles, and amphibians.

Incubation Period top

The incubation period is generally shorter in sheep and goats than in cattle. Experimental intravenous inoculation usually results in a febrile response between the 7th and 10th day after inoculation in sheep and goats, and between the 10th and 16th day after inoculation in cattle. Under field conditions, susceptible animals can be expected to show signs of the disease 14 to 28 days after introduction into an HW-infected area.

Clinical Signs top

Heartwater occurs in four different clinical forms determined by variations in susceptibility of the hosts and the virulence of various strains of the HW agent.

The relatively rare peracute form of the disease is usually seen in Africa in nonnative breeds of cattle, sheep, and goats introduced to an HW enzootic area. Heavily pregnant cows are especially prone to develop the peracute disease. Sudden death occurs, usually preceded only by a fever, severe respiratory distress, and terminal convulsions. Severe diarrhea may be seen in some breeds of cattle (e.g., Jersey, Guernsey).

The acute form of the disease, by far the most commonly observed syndrome, is seen in nonnative and indigenous domestic ruminants. A sudden fever of up to 107° F (42° C) is followed by inappetance, depression, listlessness, and rapid breathing. Nervous signs then develop, the most prominent being chewing movements, twitching of the eyelids, protrusion of the tongue (Fig. 58) and circling, often with highstepping gait. The animal may stand with its legs apart and

head lowered. The nervous signs increase in severity, and the animal goes down in convulsions. Galloping movements and opisthotonos are commonly seen before death. Hyperesthesia is often observed in the terminal stages of the disease, as is nystagmus and frothing at the mouth. Diarrhea is occasionally seen, especially in younger animals. The acute disease is usually fatal within a week of the onset of signs.

Rarely, the disease may run a subacute course characterized by prolonged fever, coughing (a result of lung edema), and mild incoordination; recovery or death occurs in 1 to 2 weeks. A mild or subclinical form of the disease, known as "heartwater fever," is seen in partially immune cattle or sheep, in calves less than 3 weeks old, in antelope, and in some indigenous breeds of sheep and cattle with high natural resistance to the disease. The only clinical sign in this form of the disease is a transient febrile response.

Gross Lesions top

The gross lesions in cattle, sheep, and goats are very similar. Heartwater derives its name from one of the prominent lesions observed in the disease, namely pronounced hydropericardium (Fig. 59). The accumulation of straw-colored to reddish fluid in the pericardium is more consistently observed in sheep and goats than in cattle. Ascites, hydrothorax, mediastinal edema, and edema of the lungs (Fig. 60), all resulting from increased vascular permeability with consequent transudation, are frequently encountered. Subendocardial petechial hemorrhages are usually seen, and submucosal and subserosal hemorrhages may occur elsewhere in the body. Degeneration of the myocardium and liver parenchyma, splenomegaly, edema of lymph nodes, nephrosis, and catarrhal and hemorrhagic abomasitis and enteritis are all commonly encountered. Meningeal congestion and edema are often present. Brain congestion may occur, but brain lesions can be remarkably few when one considers the severity of the nervous signs observed in this disease.

Morbidity and Mortality top

Once signs of the disease have developed, the prognosis is poor for nonnative sheep, goats, and cattle infected with the more virulent strains of the HW organism. The mortality rate in merino sheep may be 80 percent in contrast to 6 percent mortality observed in Persian or Afrikander sheep. Angora goats are extremely susceptible to HW. In cattle, mortality of about 60 percent is not uncommon.

Diagnosis top

Field Diagnosis top

The presence of *Amblyomma* ticks plus the rather characteristic signs and lesions of heartwater allows tentative field diagnosis of the disease, which must then be confirmed by demonstration of the causative organism, its antigens, or its DNA.

Specimens for the Laboratory top

From live animals, collect 10 ml of blood using heparin as an anticoagulant and add sufficent DSMO to make a 10 percent concentration; freeze on dry ice. Collect an additional 50 ml of heparinized blood and 10 ml of serum. From a dead animal, submit smears of cerebral cortex or half of the brain unpreserved and a set of tissues in 10 percent buffered formalin.

Laboratory Diagnosis top

1. Demonstration of the Organism: The HW organism stains purplish-blue with Giemsa stain and can be seen by microscopic examination of brain smears prepared as follows: A small piece of cerebrum, cerebellum, hippocampus, or other well-vascularized portion of the brain is macerated between two microscope slides. The resultant pulp is then drawn across a slide with varying pressure, which results in "ridges and valleys" on the slide. The slide is then air-dried, fixed with methanol, and stained with Giemsa. Under low magnification, the capillaries will be found extending from the "thick" areas of the slide. Examination of the capillary endothelial cells under oil immersion will reveal the blue to reddish-purple clumps of organisms (Fig. 61). A rapid method for obtaining brain tissue for examination is to drive a large nail through the unopened skull and make a smear from the tissue adhering to the nail. The HW organisms can also be observed in smears prepared from the intima of large blood vessels or in stained sections of kidney glomeruli and lymph nodes.

Although microscopic examination of Giemsa-stained brain smears is still widely employed in HW diagnosis, newer and more sensitive techniques such as the use of DNA probes (25) have been applied to detect *Cowdria* nucleic acids in tissues of infected livestock and ticks. These newer techniques should supplant the older methods of diagnosis as facilities and equipment become more available in HW-enzootic areas.

2. Antibody Detection: The indirect fluorescent antibody (IFA) test has extensively been used for HW antibody detection, and the newer competitive enzyme-linked immunosorbent assay (CELISA) (10, 14) promises to be a useful addition to the

meager array of tests available for the detection of HW antibodies. The cross-reactions described with several *Ehrlichia* spp. can now be eliminated with the use of more specific antigens and monoclonal antibodies.

Differential Diagnosis top

The peracute form of HW can be confused with anthrax. The acute nervous form of HW can be confused with rabies, tetanus, chlamydiosis, bacterial meningitis or encephalitis, cerebral trypanosomiasis, piroplasmosis or theileriosis, and various intoxications such as with strychnine, lead, organophosphates, or chlorinated hydrocarbons. Heavy helminth infestations may produce accumulations of fluid similar to those seen in HW. Arsenical poisoning may resemble the enteric form of the disease, and certain poisonous plants (e.g., Cestrum laevigatum, Pachystigma spp., Pavetta spp.) may produce signs and lesions similar to those seen in HW.

Treatment top

Tetracycline antibiotics (especially oxytetracycline) are very effective in the treatment of HW, especially when animals are treated early in the course of the disease. Tetracycline antibiotics administered before signs appear will suppress the disease entirely, but will allow immunity to develop. Doxycycline and rifamycin are both very effective, and a wide variety of sulfonamides have successfully been used in HW treatment. Treatment for ruminal atony, a commonly observed sequel to this disease, may be indicated, and diuretics may be useful to control fluid accumulations in body cavities.

Vaccination top

Animals recovering from the natural disease or from artificial exposure to the organism are solidly immune for a variable period ranging from 6 months to 18 months. Animals exposed to reinfection during this period of resistance will have their immunity reinforced and will remain immune as long as they are periodically reinfected. There is now conclusive evidence that immunity to HW is T-cell mediated (6) and that circulating antibodies play a minor role in immunity.

Calves and lambs are very resistant to *C. ruminantium* in the first 4 weeks of life. This resistance seems to be a true age resistance and has successfully been used in the immunization of cattle and sheep. Calves of less than 4 weeks of age, and lambs in the first week of life can be immunized by intravenous inoculation of HW-infected blood. The infection that follows is usually mild, and upon recovery animals are immune to reinfection because immunity is continuously stimulated by natural exposure to the organism. Older animals or very valuable calves should be

examined daily after immunization and should be treated with antibiotics as soon as the febrile response commences. A subcutaneous implant of doxycycline at the time of immunization will eliminate the labor-intensive tetracycline treatment method. The immunity will not be affected by the antibiotic treatment. Flock immunization of sheep and goats can be accomplished by inoculation followed by mass treatment at the end of the incubation period.

Immunologically different strains of the organism do exist, but present evidence indicates that there is considerable cross-protection between different strains (9), thus allowing successful immunization. However, there are some stains between which there is little cross-protection.

A strain of *C. ruminantium*, attenuated by serial passage in bovine umbilical endothelium cells has been shown to confer solid HW immunity to sheep and goats (9). This finding suggests that a live-attenuated vaccine to HW may soon be available, but because other strains of the organism have not become attenuated by cell-culture passage, the degree of cross-protection between strains still needs clarification. A universally effective vaccine is probably not imminent.

Control and Eradication top

Tick Control top

The HW organism is extremely fragile and cannot persist outside of a host for more than a few hours. The principal mode of bringing the disease into an area is thus through introduction of infected ticks or carrier animals. It is not known for how long wild or domestic ruminants can be a source of infection for ticks in nature, but Andrew and Norval (1989) have shown that experimentally infected sheep, cattle, and African buffalo can be a source of infection for nymphs of the bont tick (*A. hebraeum*) for 223, 246, and 161 days, respectively. After molting to adults, the ticks transmit the disease to susceptible sheep. This prolonged carrier state needs to be considered when animals are moved from HW-enzootic to HW-free areas. It is also not known for how long a tick can remain a carrier of the organism. Careful dipping and hand-dressing followed by inspection to ensure the absence of ticks is recommended for animals in transit to HW free areas.

Vector control measures aimed at eradication of *Amblyomma* ticks by dipping of cattle have failed principally because the vector is a multihost tick with a high rate of reproduction. The development of acaricide resistance has further complicated attempts at tick control. In enzootic areas, tick levels are now allowed to remain at levels high enough to permit reinfection of immune animals to booster the immunity.

Chemoprophylaxis top

Cattle, sheep, and goats moving into an HW-enzootic area can be protected from HW by prophylactic treatment with tetracycline (short or long-acting) either by feeding (15) or by inoculation (22). However, they should be kept under surveillance and individually treated if clinical signs are seen.

Public Health top

Humans are not known to be susceptible to Cowdria ruminantium.

GUIDE TO THE LITERATURE top

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