

Bovine Anaplasmosis

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Class of 2005

What is it?

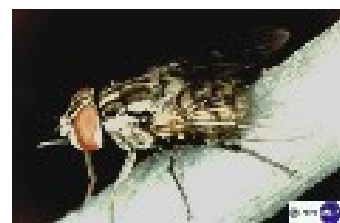
Bovine anaplasmosis is a disease caused by the rickettsial organism *Anaplasma marginale*. The disease is characterized by progressive anemia and icterus without hemoglobinemia or hemoglobinuria. *Anaplasma centrale* is a species thought to cause only mild disease in cattle, but is used in some countries to vaccinate animals against disease caused by *A. marginale*. A different species, *Anaplasma ovis*, causes anaplasmosis in sheep and goats, but does not establish persistent infection in cattle. In the United States, annual losses in beef cattle due to the effects of anaplasmosis are estimated at greater than \$300 million.

How do cattle become infected?

The organism can be transmitted to animals by multiple routes, depending on geographic location and management factors. The principal source for infection is a persistent carrier, which acts as a reservoir for tick transmission or mechanical transmission. The carrier state is reached when an animal either survives the acute phase of the disease or is vaccinated with a live vaccine.

Tick transmission is one primary route of infection, with *Dermacentor variabilis* and *D. andersoni* being the vectors of interest in the United States, *Rhipicephalus simus* in South Africa, and *Boophilus annulatus* transmitting the bacteria in Israel, Central America, South America, and Mexico. In areas where tick vectors are uncommon or do not occur, mechanical transmission via bloodsucking flies (*Tabanus*, *Stomoxys*, misquitoses) can be the major route of infection.

Another very important means of infecting cattle with *A. marginale* is by performing routine procedures in which blood contaminated equipment is used for many cattle. Examples of such equipment include castration devices, tattooing instruments, ear-tagging tools, multiple use of needles, and dehorning equipment. It has also been shown that calves can become infected in utero during gestation, although this is probably not as common as other means of infection.



What are the signs of disease?

After an animal is inoculated with *A. marginale* infected blood, the organisms invade mature red blood cells (RBCs). The RBCs are then consumed (phagocytized), which results in the development of anemia. The incubation period is variable (7-60 days), but

averages one month. Clinical signs develop when one percent of the animal's RBCs have been infected with *Anaplasma* organisms. However, up to 70% of an animal's red blood cells can become infected during the acute phase of anaplasmosis. The individual clinical signs that are seen are dependant on many factors, including age, possibly breed, and geographic region. In general, the severity of disease increases with the age of the animal. Young calves are typically asymptomatic. Calves up to two years of age generally have mild to moderate disease while adult cattle are often severely affected.

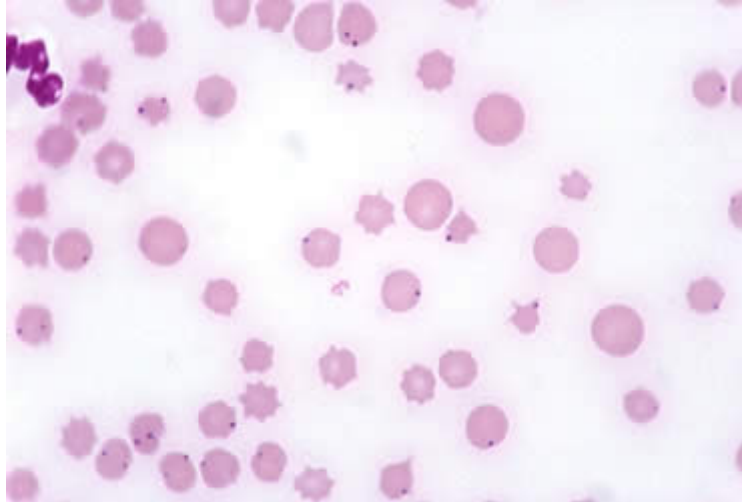
The first sign of disease is often fever of 103°-106° F. Anorexia, lethargy, and decreased milk production are also early signs of disease. Early in the disease process, mucous membranes are pale. Good areas to assess the mucous membrane color are the vulva, sclera, and oral cavity. If the animal survives past two or three days, the mucous membranes become icteric. Affected animals are usually constipated, with dark brown feces containing mucus. Cattle may demonstrate aggressive behavior, thought to be due to cerebral hypoxia from anemia. **It is important to not stress the animal during this time of severe anemia for danger of causing collapse and death.**

As mentioned earlier, hemoglobinemia and hemoglobinuria are **NOT** signs of anaplasmosis. If infection occurs late in gestation, abortion is possible. Animals that survive this acute phase of disease will go through a convalescent period that can last three to four weeks. Icterus and weight loss are very commonly seen during this time. Recovered animals are persistently infected and possess lifelong immunity.

There may also exist breed differences in susceptibility to disease caused by *A. marginale*, with *Bos taurus* cattle possibly more vulnerable to tick-borne diseases than *Bos indicus*. This could make genetic improvement a very difficult task in tropical areas, since survival of imported cattle might be reduced compared to native cattle. The region in which animals are located can affect disease severity due to the strain of the organism within that region, the possible routes of transmission, the existing prevalence of disease, and other environmental factors.

How is it Diagnosed?

An accurate history along with the previously mentioned clinical signs should arouse suspicion of anaplasmosis. However, differential diagnoses would include leptospirosis, babesiosis, bacillary hemoglobinuria, hepatotoxic plant poisonings, and other causes of anemia or icterus. Anemia can be established by assessing the packed cell volume. In the acute phase of disease, *A. marginale* organisms can be detected within red blood cells by microscopic examination of stained (Wright's, new methylene blue, Giemsa) blood smears. The organisms are basophilic staining and are found at the margin, within the erythrocytes, in small clumps of two to eight organisms referred to as a morula.



After cattle recover from acute anaplasmosis, up to 0.1% of the erythrocytes remain infected, which makes identification of inclusion bodies very difficult. Therefore, the best way to diagnose persistently infected cattle is by serology, which is not as useful for acutely affected animals.

Serological methods have historically included complement fixation and card agglutination tests. However, in recent years a competitive inhibition ELISA kit has been developed and studied. The new ELISA kit has a reported sensitivity of 96% and specificity of 95%, making it a very useful tool in screening to identify carrier cattle. Lesions that might be noted at necropsy include paleness or icterus, thin and watery blood, splenomegaly, hepatomegaly with yellow-orange discoloration, and pericardial petechiae.

How is it Treated?

Oxytetracycline (11 mg/kg IV for 3-5 days, or 1-2 doses of 20 mg/kg IM long-acting oxytetracycline every 72 hours) is currently the treatment of choice for treating acute anaplasmosis. If the packed cell volume drops below 15%, a blood transfusion allows for a better prognosis. The treatment mentioned above is not adequate to clear the organism from a persistently infected animal. Long-acting oxytetracycline at 20mg/kg must be administered every 72 hours for four successive treatments to obtain complete clearance. Even then, not all carrier animals will be cleared of the infection.

How is it Prevented?

Prevention and control measures may vary depending on the infection rate, route of transmission, and purpose of livestock production. Practicing tick or fly control in areas where one or both of these are primary means of transmission can be beneficial. The added benefits such as pinkeye control and weight gain make this a very realistic control measure. Practicing adequate hygienic procedures can be used to control and eliminate anaplasmosis when transmission is found to be iatrogenic. Good hygiene will also limit the spread of other pathogens that are propagated by way of blood contamination. In endemic areas, cattle are often allowed to become infected at a young age so that disease is mild or subclinical, developing lifelong immunity thereafter. In some countries with

lower transmission rates, the use of live vaccines containing less pathogenic isolates of either *A. marginale* or *A. centrale* is used to accomplish the same goal. The live *A. centrale* vaccine is the most widely used anaplasmosis vaccine worldwide, and has been shown to protect against clinical disease caused by *A. marginale*. An important drawback to live vaccines is the risk of transmitting other diseases through the vaccine, such as bovine leucosis. Another alternative prevention is the use of a killed vaccine. In the United States, killed vaccines have been the only approved vaccination option for anaplasmosis. Unlike live vaccines, which should produce persistent lifelong infection after one dose, killed vaccines require a yearly booster and result in a lower level of protective immunity than their live counterparts. Recently, a cell culture method of propagating *A. marginale* organisms has been developed. Although more research is needed, this system may allow for the production of a killed vaccine without the need to use cattle in order to harvest their infected red blood cells. Both live and killed vaccines afford some protection against developing clinical anaplasmosis; however, no vaccine currently available is capable of preventing infection.

For protection against infection and disease caused by anaplasmosis, much research and development is being performed on DNA vaccines. These novel vaccines rely on specific *Anaplasma* antigens that can be used to elicit the desired immune response and may also be used to decrease transmission of organisms. There is much more to be learned, but these vaccines show promise in helping to prevent both disease and infection in cattle.

References

1. Aiello, Susan E. 1998. Anaplasmosis. *The Merck Veterinary Manual*. 8:21-23
2. Bock, R.E.; Kingston, T.G.; Vos, A.J. de. 1999. Effect of Breed of Cattle on Innate Resistance to Infection with *Anaplasma marginale* transmitted by *Boophilus microplus*. *Australian Veterinary Journal*. 77(11):748-751.
3. Kocan, Katherine M.; Fuente, Jose de la; Guglielmone, Alberto A.; Melendez, Roy D. 2003. Antigens and Alternatives for Control of *Anaplasma marginale* Infection in Cattle. *Clinical Microbiology Reviews*. 16(4):698-712.
4. Shkap, V.; Molad, T.; Fish, L.; Palmer, G.H. 2002. Detection of the *Anaplasma centrale* Vaccine Strain and Specific Differentiation from *Anaplasma marginale* in Vaccinated and Infected Cattle. *Parasitology Research*. 88(6):546-552.
5. Smith, Bradford P. 2002. Anaplasmosis. *Large Animal Internal Medicine*. 3:1049-1051.