

# Bovine Anaplasmosis: An Overview

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## Introduction

Bovine Anaplasmosis is an infectious disease of adult cattle caused by the hemotrophic rickettsial parasite *Anaplasma marginale*. Cattle of all ages may become infected with *Anaplasma marginale*, but clinical disease increases in severity with age. Anaplasmosis is rarely observed in calves less than six months of age. Cattle over three years of age are most susceptible and have the highest mortality rate (30-50%).<sup>1,2</sup>

Anaplasmosis is a cyclical disease with outbreaks occurring every five to seven years.<sup>1</sup> The American National Cattlemen's Association has considered anaplasmosis as a major disease problem with annual losses and disease control estimated to be \$300 million.<sup>3</sup>

## Incidence and Prevalence

In the United States, anaplasmosis is most prevalent in the southeast, western mountain region and California.<sup>4</sup> It is becoming more prevalent in the midwestern states. A serological survey conducted in Missouri indicates that the prevalence in cattle is 7.08%.<sup>1</sup> In Iowa, a serological survey is currently being conducted by the National Animal Health Monitoring Service (NAHMS).<sup>6</sup> The survey was initiated in 1984. Results are recorded for each animal and each herd tested. Individual animals are either positive or negative for *Anaplasma marginale*. If only one individual in a herd is positive, then the herd is considered suspect. However, if more than one individual animal is positive, the entire herd is identified as a positive herd for *Anaplasma marginale*. The results for the 1984 to 1988 period are listed in Table 1.

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Table 1. Incidence of Anaplasmosis in tested herds throughout Iowa.

	<u>84 -85</u>	<u>86-87</u>	<u>1988-current</u>
#HerdsTested	15	17	19
# Positive	0	0	1
# Suspect	4 <sup>a</sup>	0	3
% Positive	0.0	0.0	5.3
# Cows Tested	145	170	175
# Positive	4	0	4
% Positive	2.8	0.0	2.3

a The suspects were from four separate herds.

## Transmission

The spread of anaplasmosis is very complicated due to transmission by vectors, iatrogenically, wildlife reservoirs and subclinical carriers.

Ticks are the only proven biological vector that can transmit anaplasmosis. *Boophilus spp.* and *Dermacentor spp.* are thought to be the most important vectors.<sup>4</sup> However, *Boophilus spp.* have been eradicated from the United States and *Dermacentor andersoni* has been identified as the major vector of *Anaplasma marginale*.<sup>1</sup>

Several studies have been done to gain a better understanding of the transmission of *Anaplasma marginale* from ticks to cattle. A study conducted by Kocan et al. was done to determine when the rickettsia were transmitted from ticks to cattle.<sup>7</sup> Adult ticks were allowed to feed on calves from one to nine days. Calves that had infected ticks on for one to six days did not become infected with *Anaplasma marginale*. However, ticks that fed on calves for more than six days transmitted anaplasmosis to all the calves. The long feeding time required for ticks to transmit *Anaplasma marginale* suggests a progressive development of the organism within the tick. Regurgitation or salivary

secretions are the most likely method of transmission. However, if regurgitation played a role then transmission would likely occur prior to day six of the feeding period. *Anaplasma marginale* has not been isolated from saliva or the salivary glands.

Horse flies and eye gnats are mechanical vectors. Studies conducted at Mississippi State University have shown that anaplasmosis can be transmitted from infected calves to susceptible calves with as few as ten bites and that horse flies can transmit for at least 60 minutes after a partial blood meal.<sup>1</sup> Outbreaks due to horse flies are most common in the late summer or early fall because the incubation period of anaplasmosis may be 4-6 weeks.

Blood contaminated instruments can also transmit the organism from one animal to another.<sup>1,2,8</sup> Instruments commonly incriminated are vaccinating needles, dehorning equipment, tattoo pliers and surgical instruments. When this type of transmission occurs, a large number of cattle that had the instruments used on them will show signs of anaplasmosis at the same time.

In utero transmission of *Anaplasma marginale* has been reported.<sup>9</sup> Fetal death and subsequent abortion has been observed in pregnant cows exposed during the third trimester of gestation.

Chronic carrier cattle are thought to have a major part in maintaining anaplasmosis as an enzootic infection. Zaugg, et al. indicated that male ticks may act as intrastadial vectors and have the potential to initiate field epizootics of acute anaplasmosis by transferring from chronic carriers without a detectable parasitemia to susceptible cattle.<sup>10</sup>

### Clinical Signs

Anaplasmosis is conventionally divided into the following four stages: incubation, developmental, convalescent and carrier.<sup>2</sup> No clinical signs are observable during the incubation period which can last from three to eight weeks. This period is defined as that time from the introduction of *Anaplasma marginale* in an animal until the time when 1% of the red blood cells are infected.

The developmental stage begins when the animal becomes febrile and the animal develops anemia. The majority of the clinical signs associated with anaplasmosis are due to the

anemia. Anaplasmosis stimulates both a cell mediated and humoral immune response. The humoral response occurs with the production of autoantibodies. Experimental evidence suggests that these autoantibodies coat infected and normal red blood cells and activate complement. Macrophages in the liver and spleen readily remove the opsonized red blood cells resulting in clinical disease.<sup>1</sup> Clinical signs become apparent when the pack cell volume (PCV) drops below 20%.<sup>10</sup> These signs include pale mucous membranes, rapid respirations, fever (104-106 F), muscular weakness, anorexia, and dehydration.<sup>2,4</sup> More severe cases will be icteric and may be belligerent due to hypoxia associated with the anemia. This acute stage can last from four to seven days. These signs will carry over into the convalescent stage.

When reticulocytes are apparent in peripheral blood smears again, the animal is considered to be in the convalescent stage. This stage lasts from weeks to months and concludes with the animal regaining normal blood values. Sometime during this stage, the anaplasmic bodies become undetectable in peripheral blood smears and the animals are considered carriers. The clinically recovered animals remain carriers for the rest of their life.<sup>2,4</sup>

Occasionally, the only clinical sign noted is acute death. Differential diagnosis would include anthrax, clostridial infections, bloat, lightning, bacillary hemoglobinuria, and acute toxicoes.<sup>4</sup>

Necropsy findings are usually associated with anemia and red blood cell destruction. The blood is thin and watery, tissues are pale and may be icteric. The spleen is enlarged due to the massive erythrocyte destruction. The liver is also enlarged and has rounded edges and the gallbladder is distended with thick, dark bile.

### Diagnosis

There are several methods of diagnosing anaplasmosis. Diagnosis during outbreaks can be based on clinical signs, necropsy results and the presence of *Anaplasma marginale* on Wright's or Giemsa-stained peripheral blood smears.<sup>2</sup> The majority of the organisms are located on the margin of the red blood cells and are detected during the developmental and early convalescent stages. Blood smears are not helpful during the carrier stage of anaplasmosis because there is no detectable parasitemia during

this stage.

A rapid blood staining procedure for anaplasmosis has been developed using Diff-Quik stain.<sup>11</sup> The study showed that the Diff-Quik method will detect a higher number of *Anaplasma marginale* organisms in the red blood cells than the same sample stained with Giemsa or Wright's stain. The Diff-Quik method is also faster and more accurate due to fewer staining artifacts which can be mistaken for infected erythrocytes.

Serological testing is useful in the developmental, convalescent or carrier stages of the disease. Both the rapid card agglutination test and the complement-fixation test are effective.<sup>1</sup> Serologic tests will not detect anaplasmosis during the incubation period because antibodies are not present in the animal until about the same time that the *Anaplasma marginale* is detectable in peripheral blood smears.<sup>2</sup>

Recently, a DNA probe has been developed to diagnose anaplasmosis in both cattle and ticks.<sup>3</sup> The probe is marked with a special compound that produces a purple color when the probe comes in contact with *Anaplasma* DNA. In the past, ticks suspected of carrying *Anaplasma marginale* had to be ground up and inoculated into calves. After the incubation period of three to eight weeks, it could be determined if the ticks transmitted anaplasmosis to the calves. Now, the DNA probe allows researchers to detect *Anaplasma marginale* in ticks and cattle, even during the incubation period, within a matter of hours.

**Treatment and Control**

As stated earlier, vectors and carrier animals are very important in outbreaks of anaplasmosis. Therefore, it is important to concentrate primarily on these areas when trying to control anaplasmosis. Control of ticks and biting insects can be very difficult. However, the use of dust bags, fly tags, insecticide sprays and dips can help reduce the insect population and the potential for the transmission of anaplasmosis by insect vectors.<sup>2,4</sup>

To prevent transmission of anaplasmosis by needles, surgical instruments, dehorner and other veterinary equipment, a quick rinse in water or dilute disinfectant is very effective.<sup>1,2</sup>

The method of treatment and control chosen for anaplasmosis should be dependent on the situation at hand. Several programs have been

developed to control and prevent outbreaks of anaplasmosis. These programs must include post-treatment serologic testing to determine if they were successful. Animals that have been cleared from the carrier stage remain resistant to anaplasmosis for about 30 months.

Many of these programs include the use of tetracyclines. Tetracyclines have been shown to be very effective especially if given early when the *Anaplasma marginale* is in the multiplication phase of the incubation period. The various programs using tetracyclines for the control and treatment of anaplasmosis are listed in Tables 2 and 3.<sup>2,12</sup> The best results usually occur if therapy is initiated before the PCV falls below 15%.<sup>10</sup>

Table 2. Programs to Control Anaplasmosis

**Elimination of the carrier stage:<sup>a</sup>**

<u>Drug</u>	<u>Dose</u>	<u>Route</u>	<u>Treatment</u>
Oxytet	22mg/kg	IM or IV	SID for 5 days
Oxytet	11mg/kg	IM or IV	SID for 10 days
LA-200 <sup>b</sup>	20mg/kg	IM	4 treatments at 3 d. intervals
Chlortet	11mg/kg	PO	daily for 60 days
Chlortet	1.1mg/kg	PO	daily for 120 days

**Medication during the vectors season:<sup>c</sup>**

<u>Drug</u>	<u>Dose</u>	<u>Route</u>	<u>Treatment</u>
Oxytet	6.6-11 mg/kg	IM or IV	every 21 to 28 days
LA-200	20mg/kg	IM	every 21 to 28 days
Chlortet	1.1mg/kg	PO	medicated feed, medicated salt, mineral mixes

**Medication during the entire year:**

<u>Drug</u>	<u>Dose</u>	<u>Route</u>	<u>Treatment</u>
Chlortet	1.1mg/kg	PO	daily

Note: Table 2 and 3 information taken from Richey, EJ. in: *Current Veterinary Therapy-Food Animal Practice*, 2nd ed. JL Howard, ed. W.B. Saunders, 1986.

Table 3. Treatment of acute anaplasmosis outbreaks

Treatment of clinically ill animals:

<u>Drugs</u>	<u>Dose</u>	<u>Route</u>	<u>Treatment</u>
Oxytet	11mg/kg	IM	one or more as needed
LA-200 <sup>a</sup>	20mg/kg	IM	one dose

Temporary protection for the remainder of the herd:

<u>Drug</u>	<u>Dose</u>	<u>Route</u>	<u>Treatment</u>
Oxytet	6.6-11 mg/kg	IM	one dose
LA-200	20mg/kg	IM	one dose

Prolonged protection for the remainder of the herd:

<u>Drug</u>	<u>Dose</u>	<u>Route</u>	<u>Treatment</u>
Oxytet	6.6-11mg/kg	IM	every 21 to 28 days
Anaplaz <sup>bc</sup> +Oxytet	6.6-11mg/kg	IM	revaccinate in 28 days, +6.6-11mg/kg Oxytet
Oxytet	6.6-11mg/kg	IM	one dose
+Chlortet	1.1mg/kg	PO	daily for 60 days

Table 2 (con.)

<sup>a</sup> should be conducted after the vector season ends.

<sup>b</sup> Liguamycin LA-200, Pfizer Inc.

<sup>c</sup> begin with the start of the vector season and continue until 1-2 months after the vector season ends.

<sup>d</sup> prevents clinical anaplasmosis but not the carrier stage.

<sup>e</sup> bulls require additional protection, i.e. vaccination.

One program that does not require the use of tetracyclines is the test and isolate program.<sup>2</sup> This program requires that all animals in the herd be identified and blood tested. The herd is then separated into a carrier herd and a non-carrier herd. The two herds must be isolated from each other during the vector season or one of the herds must be eliminated. New additions into either herd must be tested to determine their status prior to entry.

If a very valuable animal or a very small group of animals are acutely affected, symptomatic treatment may be very useful and practical.<sup>4</sup> Blood transfusions of 4-12 liters may help an anemic animal. Dextrose and fluids may also be helpful. It is important to remember to treat the animals as quietly as possible and to minimize the amount of stress. Any additional stress could lead to hypoxia and death. If the PCV falls to 10% or lower, often the best treatment is no treatment.<sup>10</sup> With these conditions, the hazards of restraint and handling are greater than the benefits of the therapy.

Immunization

Immunization against anaplasmosis is available to help reduce the severity of clinical disease.<sup>1,13</sup> As listed in Table 3, the vaccine can also be combined with a treatment program to provide prolonged protection in the event of an acute outbreak. However, vaccinated animals can still become infected and become chronic carriers of anaplasmosis.

The vaccination program must be completed at least two weeks before the beginning of the vector season to be effective.<sup>1</sup> The vaccine is

Table 3 (con.)

<sup>a</sup> Liguamycin LA-200, Pfizer Inc.

<sup>b</sup> Product of Fort Dodge Laboratories.

<sup>c</sup> dose according to label instructions.

administered in two doses four weeks apart. The duration of immunity is estimated to be greater than one year; however, bi-annual boosters are recommended to insure adequate protection. Only open cows should be vaccinated. If pregnant cows are vaccinated, there is a potential for neonatal isoerythrolysis in the calves. High levels of isoantibodies may develop because the vaccine is derived from anaplasma infected bovine erythrocytes.<sup>1,13</sup>

Recently, researchers identified the protective antigen of *Anaplasma marginale* and cloned the gene which codes for this antigen.<sup>1</sup> This new information will make it possible for the future development of new subunit and vaccinia vector vaccines.

### Conclusions

Anaplasmosis can be a devastating disease in the cattle industry. To help prevent future outbreaks and to control the spread of anaplasmosis to naive herds should be a high priority goal for the veterinary profession in the years to come. Veterinarians will be instrumental in the recognition of anaplasmosis in the field and should have a good working knowledge of the control programs that are available, and be able to initiate them readily to curb the losses associated with an anaplasmosis outbreak. Intra-state and interstate movement of cattle should be monitored closely to help prevent the spread of anaplasmosis into uninfected herds.

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