General Session I

"Infectious Diseases"

Moderator: **Carlos Risco**

Bovine Anaplasmosis

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Anaplasmosis is an infectious, noncontagious, transmissible disease of cattle caused by the intra-erythrocyte parasite *Anaplasma marginale.* In the United States, anaplasmosis is enzootic in the southern Atlantic states, the Gulf Coast states, the lower plains and western states but is reported as sporadic in the northern states.

Transmission

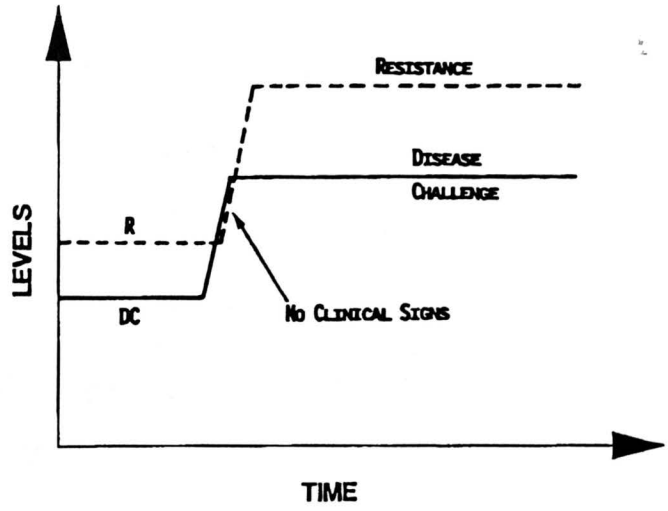
The prinicipal means of *A. marginale* transmission are the mechanical transfer of parasitized erythrocytes and the transfer of the tick stage of *A. marginale* during certain tick feeding, referred respectively as mechanical and biological transmission. Mechanical transmission occurs by direct inoculation of infected erythrocytes into susceptible cattle on blood contaminated hypodermic needles, surgical or dehorning instruments, or on the mouthparts of biting flies. Horse flies, deer flies, stable flies, and less importantly mosquitos, *Dermocenter andersoni* and *Dermocentor occidentalis* ticks can all spread anaplasmosis and have been implicated as the major means of transmission in enzootic areas of the southern U.S. These natural mechanical and biological vectors are usually quite seasonal and most outbreaks of anaplasmosis coincide or immediately follow the vector seasons.

Contaminated surgical instruments, dehorners, and hypodermic needles are known mechanical vectors used by man. This type of mechanical transmission takes place only when the disease organism is exchanged immediately — within minutes. When this type of transmission occurs, a large number of cattle in the herd show signs of anaplasmosis at nearly the same time, without a few earlier cases having appeared.

Clinical Signs

All ages of cattle may become infected with anaplasmosis. However, the severity of illness and the percentage of deaths increases with age. Calves, under 6 months of age become infected and remain carriers when challenged with *A. marginale;* however, they seldom exhibit any clinical signs of anaplasmosis.

Calf Response to *A. marginale* Challenge



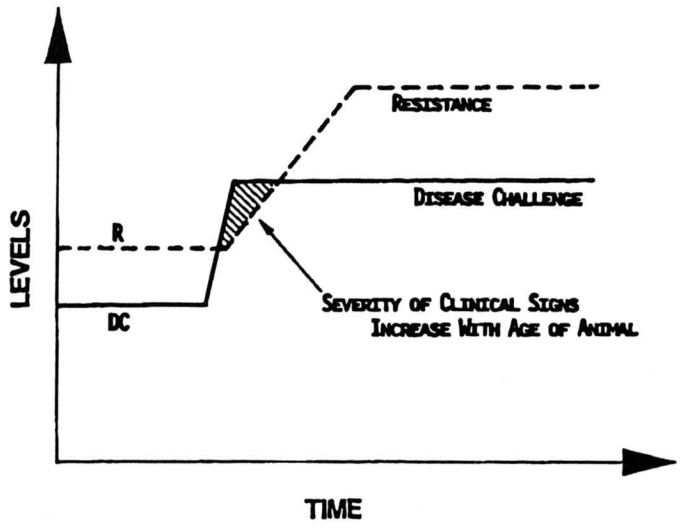
Cattle, aged 6 months to 3 years become increasingly ill and more deaths occur with advancing age.

After 3 years of age, a 30 to 50% mortality rate occurs in cattle exhibiting clinical anaplasmosis.

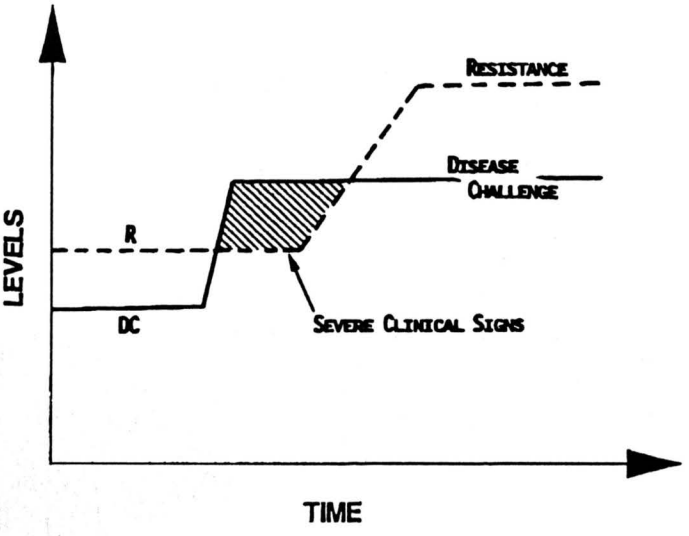
The clinical signs found in bovine anaplasmosis are predominantly signs related to acute anemia. However, a febrile response is noted coinciding with the beginning of a detectable parasitemia in the blood system. The fever usually persists through the period of increasing parasitemia and may reach 27° C (106° F); however, subnormal temperatures are noted prior to death.

The acute anemia results in pallor of the mucosa, muscular weakness, depression, dehydration, anorexia, increased heart rate and, upon exertion, respiratory distress. The animal may be belligerent if inadequate tissue oxygenation has affected the brain. Examination of the blood

Response in Cattle 6 mo-3 yrs of Age
to *A. marginale* Challenge



Response in Cattle Over 3 yrs of Age
to *A. marginale* Challenge



shows it to be grossly thin and watery. Since the disease is characteristically a hemolytic disease in which the parasitized erythrocytes are destroyed in the reticuloendothelial system without release of free hemoglobin, hemoglobinuria is not seen in anaplasmosis.

Pathogenesis

Anaplasmosis can be divided into four stages: incubation, developmental, convalescent, and carrier. The INCUBATION STAGE is that time from introduction of the anaplasma organism into a susceptible animal until the time 1% of the red blood cells are infected. The length of this stage appears to vary directly with the number of organisms introduced into the animal. Under natural conditions, the time may be from three to eight weeks although shorter and longer times have been recorded. No clinical signs can be seen during this stage. The end of the period coincides with the first rise in body temperature.

The DEVELOPMENTAL STAGE refers to that time when the characteristic anemia is developing. It begins at the time of 1 percent infected red blood cells and ends when the reticulocytes appear in the peripheral circulation. The length of this stage varies from four to nine days. During this period, most of the signs characteristic of anaplasmosis appear. The infected animal usually shows the first clinical signs about midway, or about the third or fourth day, of the developmental stage. This is the time when owners who observe their cattle carefully each day will notice the animal is ill.

Laboratory values during this stage reflect a severe hemolytic anemia. The percentage of parasitized erythrocytes can range from 10% to greater than 75% in acute infections and are characterized by numerous 0.5-1.0 micron sized basophilic punctate bodies in the margin of Wright's or Giemsa stained erythrocytes.

Typical Clinical Laboratory Findings
in ACUTE ANAPLASMOSIS

Parasitized RBC (%)	10.0	- 75.0
Packed cell volume (%)	5.0	- 15.0
Total # RBCs (10/mm)	1.5	- 4.0
Bilirubin (mg/100ml)	2.0	- 7.0
Direct	0.25	- 7.0

The CONVALESCENT STAGE extends from the appearance of reticulocytes to the return to normal of the various blood values. The length of this stage varies greatly and may extend from a few weeks to a few months.

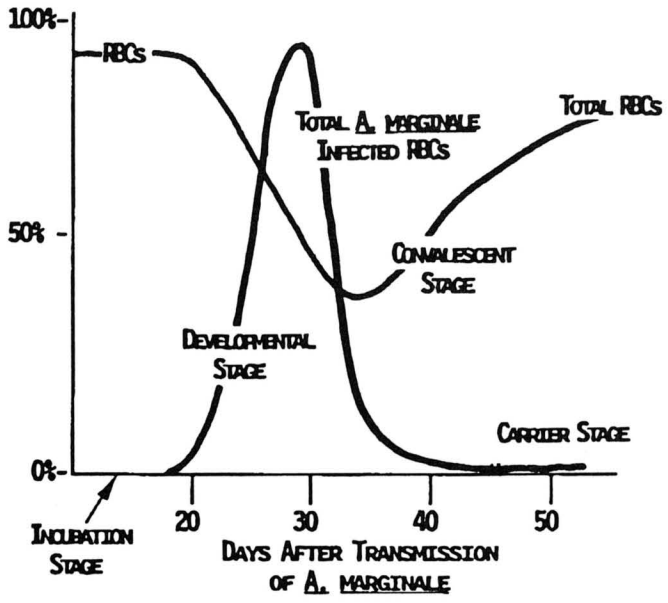
The differentiation between developmental and convalescent stages is evidence of increased erythropoiesis on the stained blood smears. The signs of increased erythropoiesis in the peripheral blood, which identifies the convalescent stage are reticulocytes, polychromatophils, basophilic stippled cells, normoblasts, increased hemoglobin and an increase in the total white cells.

Death losses due to anaplasmosis usually occur during late developmental stage or early convalescent stage.

Post-mortem findings are principally attributable to the severe hemolytic anemia. All tissues are pale and blood is thin and watery; icterus may be present if the animal dies in the later stages of acute infection. The spleen is frequently enlarged and a deep red-brown. An enlarged liver and a gall bladder distended with dark bile are common. On a thin blood smear, stained with Giemsa or Wright's, the *A. marginale* bodies appear as spherical granules 0.2 to 0.5 microns in diameter located near the periphery of the red blood cell. The anaplasma bodies would be most easily detected during the developmental and convalescent stages.

The CARRIER STAGE is usually thought of as that

A. marginale Infestation of RBCs and Change in Total RBCs During the Different Stages of Anaplasmosis



time extending from the disappearance of discernible anaplasma bodies sometime during the convalescent stage to the end of the animal's life. Clinically recovered animals remain carriers with a non-detectable parasitemia and thus act as a resevoir of the disease.

Serology

The rapid card test (agglutination) is the most common serological test used for the detection of anaplasma titers. Infected animals begin to exhibit positive reactions at about the same time that anaplasma bodies can first be seen in the red blood cells. The test reaction is, therefore, negative throughout the incubation period and positive during the developmental, convalescent, and carrier stages. Because the serological test will not differentiate between the latter three stages, the use of serological reactions is of little use when a definitive diagnosis of anaplasmosis is required.

Diagnosis

A tentative diagnosis of anaplasmosis may rely upon suspicion of transmission, characteristic clinical signs, necropsy findings, serologic testing, or clinical laboratory values. However, definitive diagnosis requires the identification of *A. marginale* parasitized erythrocytes during the developmental or convalescent stages.

A brief summary of the presence of parasitemia, serologic reactions and clinical signs in relationship to the stage of disease is tabulated as follows.

FINDINGS DURING DIFFERENT STAGES OF ANAPLASMOSIS

Stage of Disease	*A. marginale* on Blood Smear	Reaction to Serologic Test	Clinical Signs
Unexposed	No	Negative	None
Incubation	No	Negative	None
Developmental	Yes	Positive	Present
Convalescent	Yes*	Positive	Present
Carrier	No	Positive	None

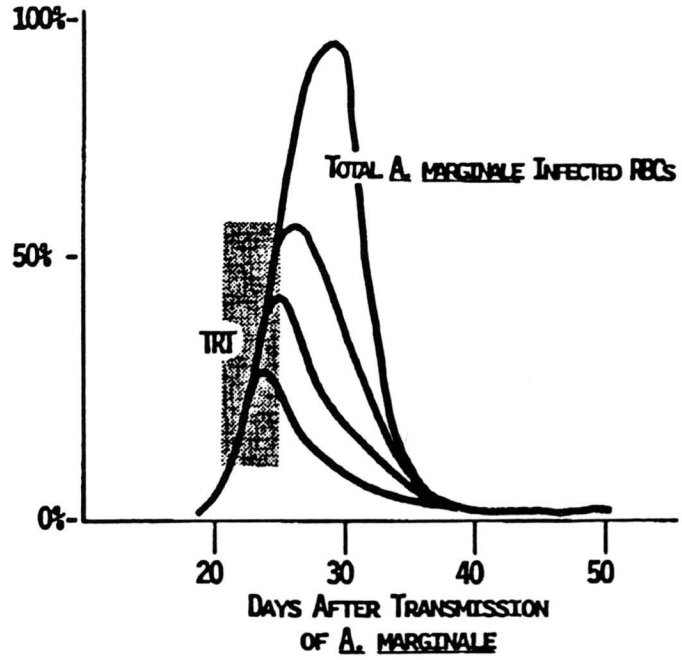
*Immature RBCs also present

Treatment of Acute Anaplasmosis

A **single parenteral injection** of oxytetracycline (OTC) can be very effective in reducing the severity of the disease when administered while the percentage of infected cells is less than 15% (about mid-way of the developmental stage). Animals treated parenterally with OTC at this time have better than average chance for recovery. The OTC will stop the increase in infected red cells and since it is mainly the infected red cells that are destroyed to produce the anemia. the red cell count hopefully will not drop below a critical level.

When percentages of infected cells about 15% are encountered, the effectiveness of the OTC is reduced and recovery of the animal will be due to the natural ability of the bone morrow to produce red cells in sufficient numbers to compensate for the loss of the infected cells.

Effect of Oxytetracycline on *A. marginale* Infestation of RBCs



Toward the end of the developmental stage and the beginning of the convalescent stage, frequently the best treatment is no treatment. There are two reasons for considering not to treat at this time. First, the animal may

suddenly die from anoxia if it is forced to move or becomes excited. Second, OTC treatments do little or nothing to change the outcome of the disease when given at this time. OTC acts only to reduce the number of infected red blood cells; the number of infected red blood cells has already peaked and are being rapidly destroyed by the reticuloendothelial system. Hematinic drugs do not have enough time to stimulate erythropoiesis and a blood transfusion in sufficient amount to be beneficial may overload the anoxia-weakened heart.

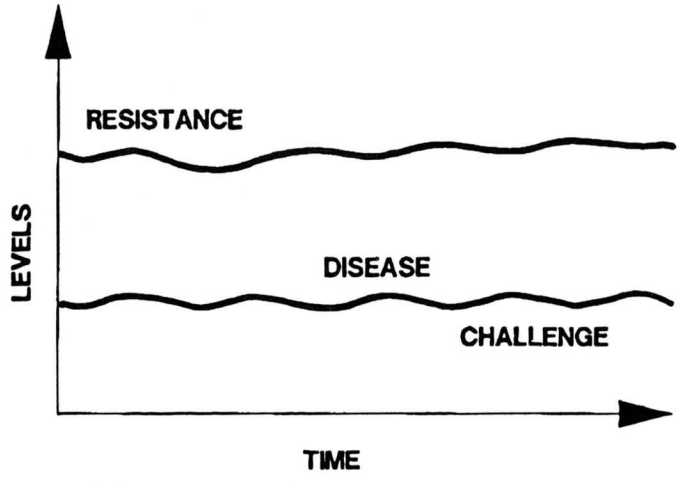
Management of Anaplasmosis

Anaplasmosis outbreaks are related to having NO CONTROL program, having both anaplasmosis CARRIERS and SUSCEPTIBLE ANIMALS present in the herd, and having VECTOR TRANSMISSION.

As with any disease situation, an animal remains healthy or unaffected as long as the animal's "resistance" level remains above the "disease challenge" level.

Relying solely on natural resistance and/or lack of disease exposure to keep the "resistance" level above the "disease challenge" level is not a very comfortable position for a herd to be in. Any rise in the disease challenge level would result in clinical anaplasmosis.

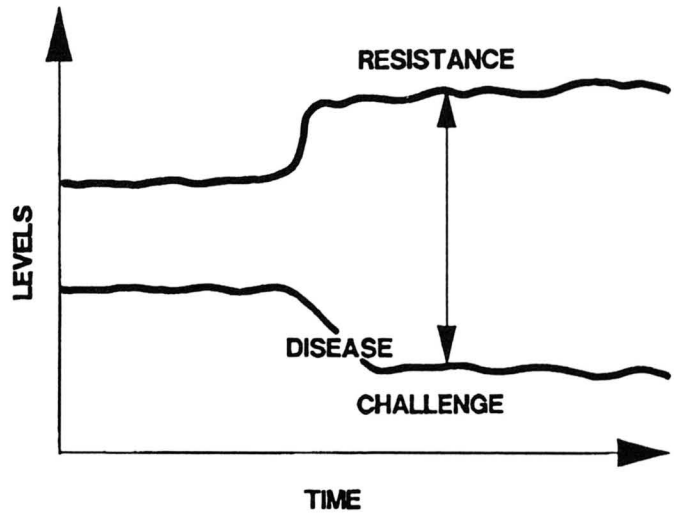
A Healthy Herd Exists When The Resistance Level is Maintained Above the Level of Disease Challenge



Certain TOOLS have been identified that can assist the herd owners control anaplasmosis by preventing outbreaks and halting outbreaks when they occur. Those TOOLS, either RAISE the RESISTANCE or REDUCE the DISEASE CHALLENGE.

It is to the herds owner's advantage to create a greater spread between the "resistance" and "disease challenge" levels. A wider spread provides a more comfortable situation.

A Comfortable Spread Between the Resistance Level and the Level of Disease Challenge



In general, to utilize both tool types (to increase resistance & reduce challenge) simultaneously can be very expensive; therefore, simultaneous use is primarily limited to stopping outbreaks of anaplasmosis, whereas control programs to prevent clinical anaplasmosis in a herd usually utilize only one tool type at a time.

Programs to Prevent Anaplasmosis

1. *Test the herd and REMOVE carriers to prevent anaplasmosis:*

This program necessitates bleeding each animal, identifying the carriers, and removal of the carrier animals.

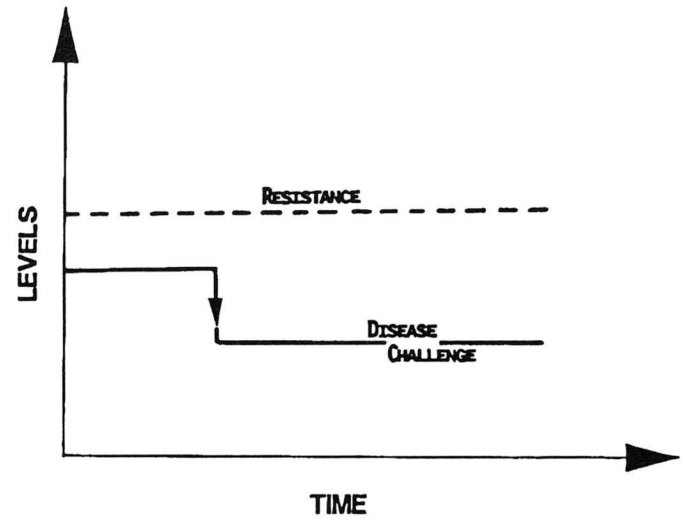
An alternative to disposing of the carriers would be to separate the carrier animals from the "clean" animals and maintain two herds, an anaplasmosis infected herd and an anaplasmosis "clean" herd; there are no susceptible animals in a 100% carrier herd. New additions must be protected, however; and there are regulations governing interstate movement of carrier animals.

2. *Test the herd and CLEAR the CARRIERS of infection to prevent anaplasmosis:*

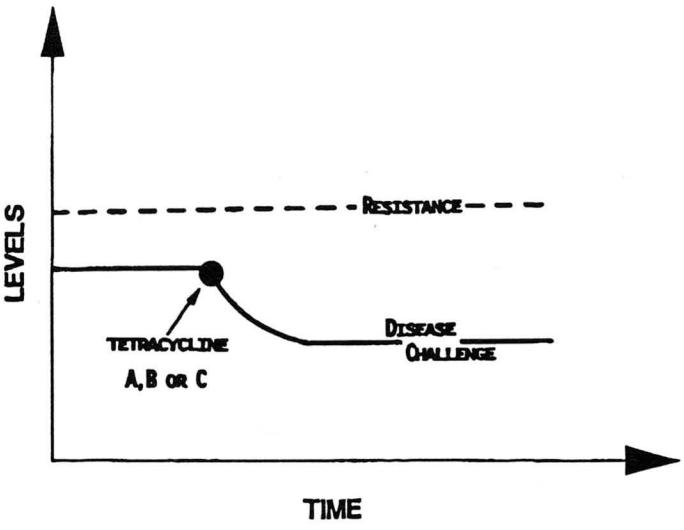
Anaplasmosis carrier cattle may be cured of the infection by treatment with certain tetracycline antibiotics.

Carrier state elimination programs must include post-medication serologic testing. The animal can test positive for months after treatment, but may be free of infection. When testing, six months after treatment ceases, all positive reactors should be considered as "treatment failures". Failures should be retreated or separated from the rest of the herd. Animals cleared of the carrier state are susceptible to reinfection, but are known to exhibit resistance to clinical anaplasmosis for up to 30 months after treatment.

Test & Removal of Carrier Animals as A Control Program for Preventing Anaplasmosis



Test & Eliminate the Carrier State as A Control Program for Anaplasmosis



Elimination of the carrier state should be conducted after the vector season has ended. The effect of a continuous field challenge exposure while attempting a carrier elimination program has not been fully investigated.

A: OTC (50-100 mg/ml)to eliminate carrier stages:

22 mg/kg (10 mg/lb) body weight daily for FIVE DAYS.

11 mg/kg (5 mg/lb) body weight daily for TEN DAYS.

INTRAMUSCULAR: inject not over 10 ml per site.
INTRAVENOUS: dilute with physiological saline or administered by a veterinarian.

B: OTC (LA-200) to eliminate carrier stages:

Treat each animal 4 TIMES WITH LA-200 AT 3 DAY INTERVALS. Inject 20 mg/kg (9 mg/lb) body weight. Each dose should be divided between two sites and given by deep intramuscular injection.

C: CHLORTETRACYCLINE (CTC) to eliminate carrier stages:

60-DAY Treatment with CTC

It is recommended that CTC be fed at a level of 11 mg/kg (5 mg/lb) body weight daily for 60 days. When fed daily at this level, CTC will eliminate the carrier stage. Oral administration permits treatment on a herd basis and the use of economical antibiotic premixes. This oral dose may cause diarrhea, anorexia and weight loss during the first week, but the cattle return to normal rapidly after that time. The medicated feed should nevertheless be kept before them during this time.

120-DAY Treatment with CTC

Fed at the rate of 1.1 mg/kg (0.5 mg/lb) body weight daily for 120 days, CTC eliminates the carrier state. This low dosage fed for 120 days makes the clearing of the carrier state very simple while winter feeding range cattle.

3. *Continuous OTC medication during the vector season to prevent anaplasmosis:*

An injection of OTC administered every 28 days, beginning with the start of the vector season and ending 30 to 60 days after the vector season ends, will prevent clinical anaplasmosis from developing. The recommended dose is 6.6-11 mg/kg (3-5 mg/lb) body weight when using 50-100 mg/ml OTC or 20 mg/kg (9 mg/lb) body weight when using LA-200.

4. *Continuous chlortetracycline medication during the vector season to prevent anaplasmosis:*

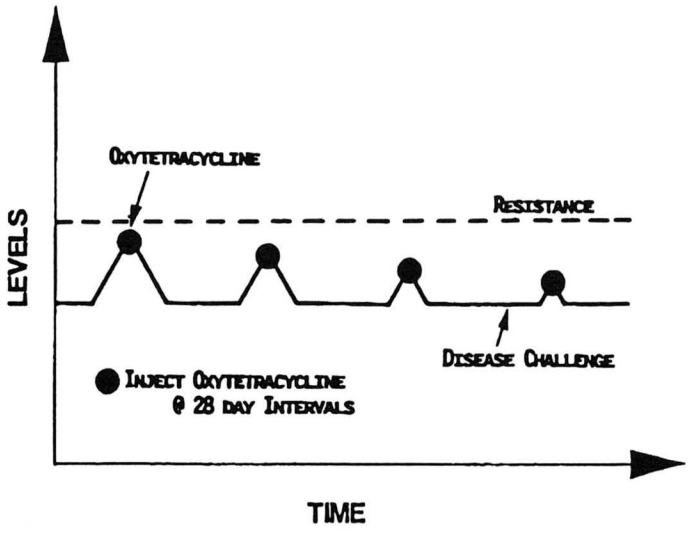
CTC consumed at the rate of 1.1 mg/kg (0.5 mg/lb) body weight daily during the vector season will prevent the transmission of anaplasmosis to susceptible animals.

CTC at this dose may be administered by use of medicated feed fed daily, medicated salt-mineral mixes offered free choice, and medicated feed blocks. Consumption data should be available from feed or salt-mineral manufacturers.

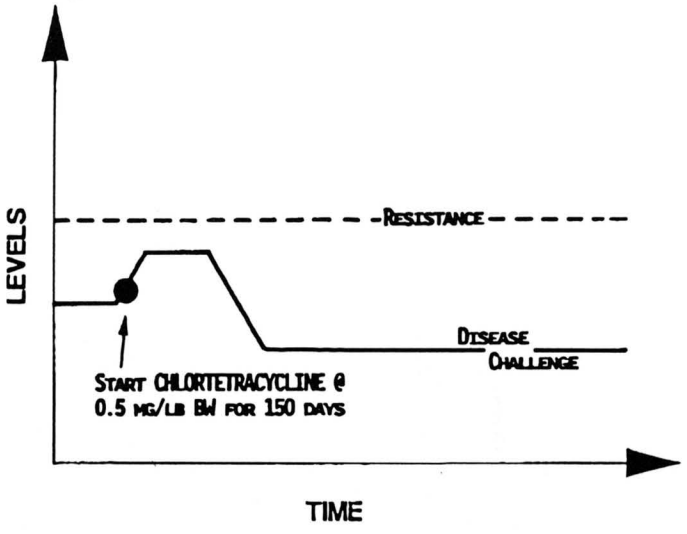
5. *Continuous chlortetracycline medication year round to prevent anaplasmosis:*

CTC administered in daily doses of 0.22 to 0.55 mg/kg

Inject OTC @ 28 Day Intervals Throughout The Vector Season as a Control Program For Anaplasmosis



CTC Administered During the Vector Season as a Control for Anaplasmosis

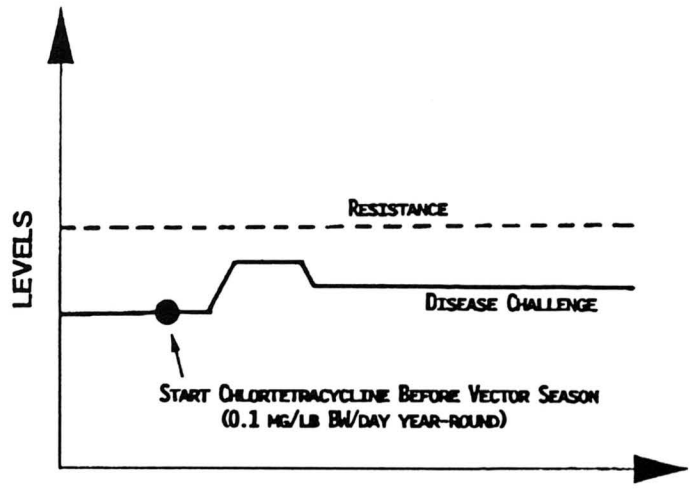


(0.1 - 0.25 mg/lb) body weight will prevent clinical anaplasmosis. However, transmission of the *A. marginale* organism has been reported when using this low dose. If the CTC is withdrawn shortly after transmission occurs you could expect clinical anaplasmosis to appear in the herd after a delayed incubation stage. For this reason, CTC at this dose must be administered year-round. CTC added to salt-mineral mixes is a convenient way to administer this low dose.

When using salt-mineral mixes or feed blocks as the vehicles for administering CTC, it requires placing the mix or blocks near water holes, providing sufficient protection from the sun and rain, and replenishing the mix at frequent intervals. It is advisable to routinely check to insure that the cattle are consuming the medicated mix.

Bulls apparently do not consume adequate chlortetracycline and require additional protection, such as vaccination.

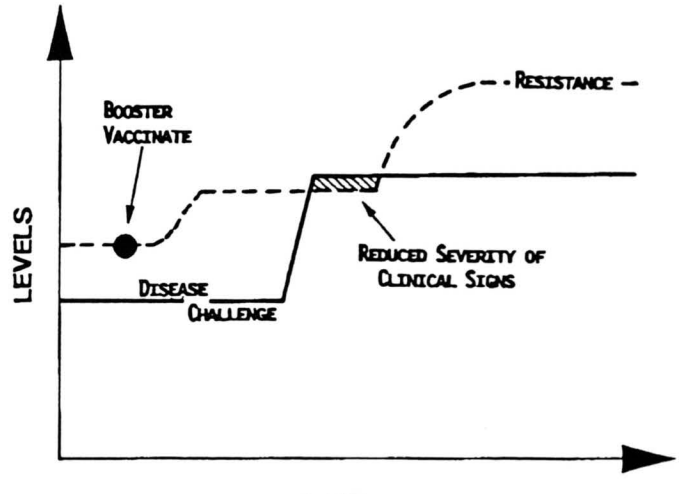
CTC Administered Year-round as a Control Program for Anaplasmosis



6. *Anaplasmosis vaccine to prevent severe cases of clinical anaplasmosis:*

The INITIAL VACCINATION schedule, which consists of 2 doses given 4 weeks apart, is scheduled so that the second dose is given at least 2 weeks before the vector season begins. Each year thereafter a booster should be given 2 weeks or more before the vector season begins. A vaccinated animal is still capable of becoming infected with *A. marginale* and subsequently can become a carrier. The vaccine does not prevent infection, but aids in prevention or reduction in the severity of clinical anaplasmosis.

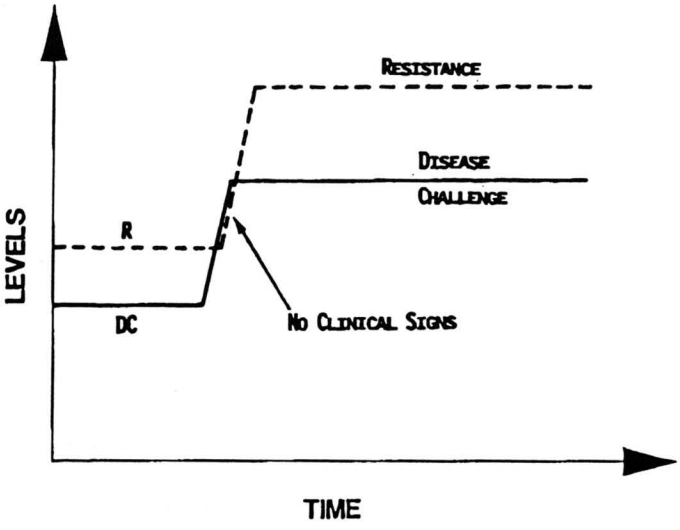
Vaccination to Reduce the Severity of Clinical Disease as a Control Program for Anaplasmosis



7. *Pre-immunization of calves to prevent clinical anaplasmosis:*

Before the development of the TOOLS to prevent anaplasmosis, calves were deliberately inoculated with *A. marginale* to provide life-time protection. 2ml. of citrated whole blood, freshly collected from a known *A. marginale* infected animal, was injected subcutaneously into calves under 6 months of age. The inoculated calves would become infected and remain carriers without exhibiting clinical anaplasmosis. Too high a volume into too old an animal can result in clinical disease. It has been noted that the injection of 5 ml. of *A. marginale* infected blood into yearling heifers has resulted in severe clinical anaplasmosis and death.

Calf Response to a Challenge by
A. marginale



8. *Reduce Vector Transmission:*

Applications of insecticides that reduce the biting insect population will substantially reduce the number of clinical cases occurring in a herd. Periodic spraying and dipping, as well as forced use of dust bags and back rubbers, are the common methods of insecticide application.

Since man often transmits the disease by carrying the organism from a carrier animal to a susceptible animal via blood-contaminated instruments; a quick rinse of the contaminated instruments in clean water or disinfectant between animals will prevent transmission.

Stopping an Outbreak

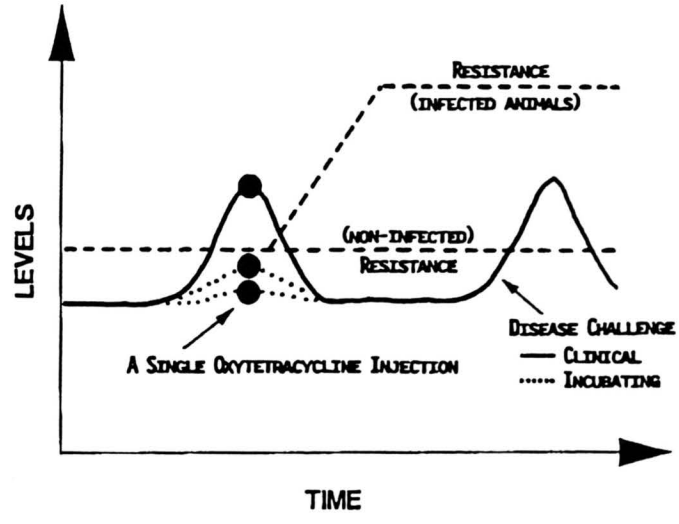
Regardless of the availability of adequate control programs, many cattle producers either choose not to use a program or have no reason to do so. In either event, it is necessary to describe the methods available to a veterinarian and producer for halting an anaplasmosis outbreak in a herd. The proper handling of an outbreak should include the treatment of clinically ill animals AND provide adequate protection for the remainder of the herd. The clinically ill animal may only be the first of many that will become ill or exposed to anaplasmosis.

In addition to treating the clinically ill animals, the remainder of the herd must be adequately protected. Since no clinical symptoms are being exhibited by the animals in the remainder of the herd it is assumed that they could be categorized as being UNEXPOSED, in the INCUBATION STAGE, in the CONVALESCENT STAGE, or in the CARRIER STAGE. The unexposed animals and the animals in the incubation stage must be provided with temporary protection until prolonged protection can be established.

The TOOLS used to prevent an anaplasmosis outbreak in a herd can also be used to STOP an outbreak. They can be used to provide both temporary and prolonged protection to the herd.

Temporary protection is accomplished by administering parenteral injections of OTC. Parenteral injections of OTC prior to exposure has no effect on the course of a later infection, but animals injected with a single parenteral dose of OTC during the incubation stage exhibit a prolongation of the incubation stage for 2 to 3 weeks and a single dose of OTC administered to animals early in the developmental stage will suppress clinical disease for 3 to 4 weeks. In both cases, clinical anaplasmosis is delayed for approximately 28 days.

Response of *A marginale* Infections to One
Oxytetracycline Injection

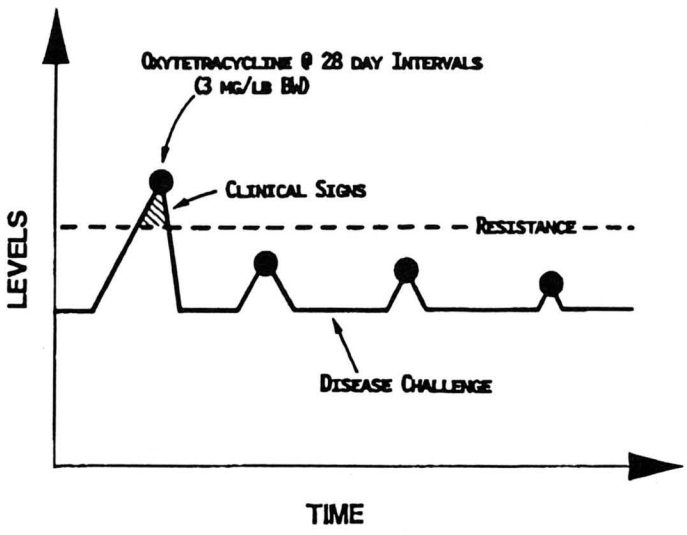


1. Use of INJECTABLE OTC to STOP an OUTBREAK:

At the first indication of anaplasmosis, gather all susceptible animals and administer a single dose of OTC at the rate of 6.6-11 mg/kg (3-5 mg/lb) body weight for tem-

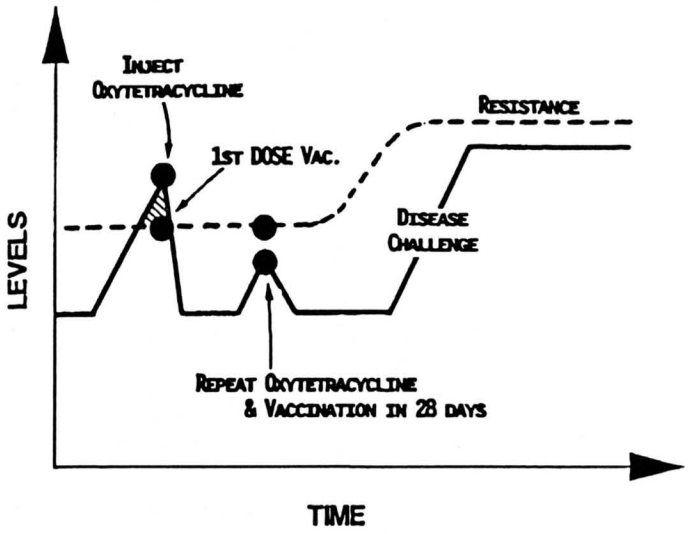
porary protection. For prolonged protection this treatment must be repeated at 28 day intervals throughout the vector season. After withdrawal of the OTC medication, close observation should continue for symptoms of anaplasmosis that may have been only delayed, not aborted, in some cattle.

OTC Injections Used to Stop an Outbreak of Anaplasmosis



2. Use of OTC & VACCINATION to STOP an OUTBREAK:

OTC + Vaccination Used to Stop an Outbreak of Anaplasmosis

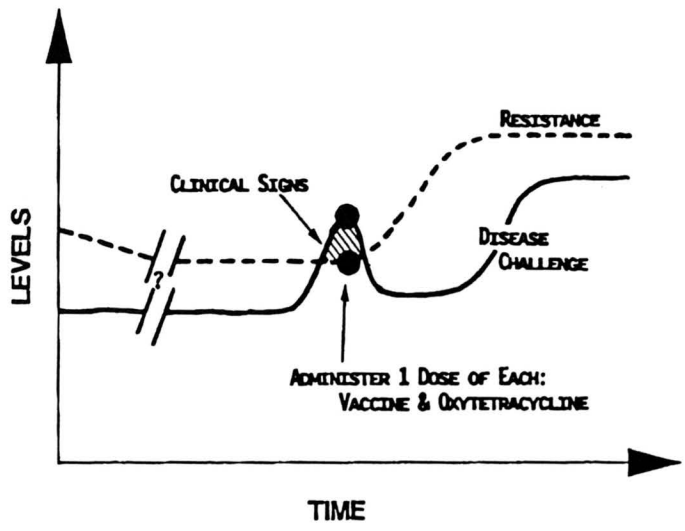


At the first indication of anaplasmosis, gather all susceptible animals and administer a single dose of OTC at the rate of 6.6-11 mg/kg (3-5 mg/lb) body weight for temporary protection. For prolonged protection give each animal the 1st dose of ANAPLAZ vaccine. Twenty eight days later, give the 2nd dose of vaccine and another dose of OTC.

3. Use of OTC & VACCINATION to STOP an OUTBREAK in a PREVIOUSLY VACCINATED HERD:

If anaplasmosis occurs because a VACCINE booster was skipped, administer a single dose of OTC at the rate of 6.6-11 mg/kg (3-5 mg/lb) body weight and 1 dose of vaccine to each susceptible animal. Any previously non-vaccinated animals should receive a second dose of both VACCINE and OTC in 28 days.

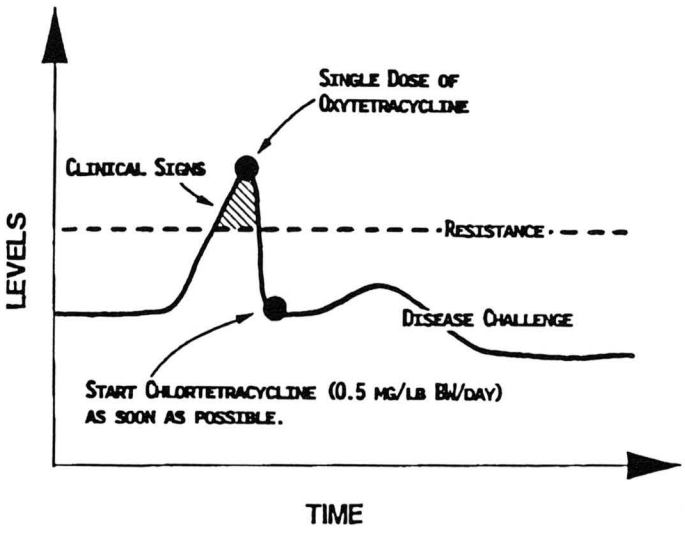
Using Vaccine Boosters and OTC to Stop an Outbreak of Anaplasmosis in a Previously Vaccinated Herd



4. OTC and CHLORTETRACYCLINE to STOP an OUTBREAK:

At the first indication of anaplasmosis, gather all susceptible animals and administer a single dose of OTC at the rate of 6.6-11 mg/kg (3-5 mg/lb) body weight for temporary protection. For prolonged protection, immediately offer chlortetracycline free choice at the rate of 1.1 mg/kg (0.5 mg/lb) body weight in a medicated salt-mineral mix or feed blocks. CTC-medicated mixes or blocks should be offered for at least 60 day.

OTC & CTC Used to Stop an Outbreak of Anaplasmosis



Tetracycline treatment regimens for anaplasmosis control, elimination of the carrier stage, and handling outbreaks are illustrated in the following table:

Tetracycline Treatment Regimens for Anaplasmosis Management

Use & Drug	Route	Dose (mg/kg BW)	Frequency of Treatment
PREVENTION:			
Chlortetracycline	Oral	0.22-0.55	Daily Year-Round
Chlortetracycline	Oral	1.1	Daily During Vector Season
Oxytetracycline (50-100 mg/ml)	IV or IM	6.6-11	Every 28 days During Vector Season
Oxytetracycline (LA-200)	IM	20.0	Every 28 days During Vector Season
CARRIER ELIMINATION:			
Chlortetracycline	Oral	1.1	Daily for 120 days
Chlortetracycline	Oral	11.0	Daily for 60 days
Oxytetracycline (50-100 mg/ml)	IV or IM	11.0	Daily for 10 days
Oxytetracycline (50-100 mg/ml)	IV or IM	22.0	Daily for 5 days
Oxytetracycline (LA-200)	IM	20.0	4 Rx at 3 day intervals
TREATMENT of SICK:			
Oxytetracycline (50-100 mg/ml)	IM	11.0	Usually one treatment
Oxytetracycline (LA-200)	IM	20.0	One treatment
TEMPORARY PROTECTION DURING OUTBREAKS:			
Oxytetracycline (50-100 mg/ml)	IM	11.0	One treatment
Oxytetracycline (LA-200)	IM	20.0	One treatment
PROLONGED PROTECTION DURING OUTBREAKS:			
Oxytetracycline (50-100 mg/ml)	IM	11.0	Every 28 Days During Vector Season.
Oxytetracycline (LA-200)	IM	20.0	Every 28 Days During Vector Season.
Chlortetracycline	Oral	1.1	Daily for 60 days

NOTE: Vaccine is used to stimulate prolonged resistance; however, until the resistance is established, OTC injections should be used simultaneously with each dose of vaccine to temporarily reduce the *A. marginale* challenge.