Anaplasmosis:

Treatment and Management Options Available to the Veterinarian and Herd Owner During an Acute Outbreak

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With the addition of the Anaplasmosis Card Test (1) and Anaplasmosis Vaccine* to the arsenal for control of anaplasmosis, it can be confusing to veterinarians and herd owners to choose an approach for curbing or modifying an anaplasmosis outbreak in a herd.

In order to properly evaluate an anaplasmosis outbreak and to determine an approach to modify the disease pattern, one must have a simple knowledge of the pathogenesis of anaplasmosis. We will not discuss the specific symptoms of the disease but rather present a description of the stages of the disease encountered, methods of differentiating the stages, options available for treatment during an acute outbreak, and preventative measures prior to the vector season. Quite often the veterinarian encounters one animal showing clinical symptoms of anaplasmosis. His concern, quite naturally, is directed toward this animal, but in fact his primary concern should be directed toward the remainder of the herd. The clinically ill animal may be the first of many that will become ill or exposed to anaplasmosis.

With this in mind, we will briefly describe the stages of anaplasmosis, their respective serological and hematological characteristics, and the value of treatment during certain stages. Brock (3) has shown that anaplasmosis can be conveniently divided into four stages: incubation, developmental, convalescent, and carrier. The incubation stage is that time from the 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 loosely with the first rise in temperature.

The developmental stage refers to that time when the characteristic anemia is developing. It begins at the time of 1% infected red blood cells and ends when 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.

Convalescence 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 carrier stage is usually thought of as that time extending from the disappearance of discernible bodies sometime during the convalescent stage to the end of the animal's life.

Treatment and management options that are available to the veterinarian and herd owner during an acute outbreak of anaplasmosis are as follows: (a) treat clinical disease as it is detected, (b) parenteral antibiotic treatment of herd members at 28-day intervals through the vector season, (c) simultaneous vaccination and antibiotic treatment of herd animals, and (d) serological test with subsequent vaccination and antibiotic treatment or serological test with subsequent antibiotic treatment.

When considering option A, treating clinical anaplasmosis as it is detected, it must be realized that the important stages for veterinarians who must treat acute cases of anaplasmosis are the developmental and convalescent. It is during one of these two stages that the veterinarian first sees the sick animal. The best management of the case depends upon an accurate estimate of the stage of the disease.

The infected animal usually shows the first clinical signs of the disease about mid-way, or about the third or fourth day, of the developmental stage. This is the time owners who observe their cattle carefully each day will notice the animal's being ill. Animals treated with the tetracyclines at this time have better than average chance for recovery. Any delay in treatment during the developmental stage decreases the animal's chance for recovery.

Midway in the developmental period, with 10-15% infected red blood cells, a single parenteral injection of a tetracycline drug at the rate of 3-5 mg/lb. body

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weight can be very effective in reducing the severity of the disease. The tetracycline antibiotics will stop the increase in infected red cells and since it is probably the infected red cells that are destroyed to produce the anemia, the red cell count will not drop below a critical level.

When percentages of infected cells above 15% are encountered, the effectiveness of the tetracycline antibiotics is reduced. Recovery then becomes due to the natural ability of the bone marrow to produce red cells in sufficient numbers to compensate for the loss of the infected cells.

Toward the end of the developmental stage and the beginning of the convalescent stage, frequently the best treatment is no treatment. At all times anaplasma infected cattle should be handled gently and without excitement, but it is especially true at this time when the anemia is most severe. There are two reasons for no treatment at this time. First, the animal may suddenly die from anoxia if it is forced to move or becomes excited. Second, treatments do little or nothing to change the outcome of the disease when given at this time. The tetracyclines are of little value since they act only to reduce the number of infected red blood cells and the number is already decreasing rapidly. Hematinic drugs do not have enough time to stimulate erythropoiesis and blood transfusions in sufficient amounts to be beneficial may overload the already anoxia-weakened heart.

The need, therefore, is a reasonably simple and accurate way to differentiate between the developmental and convalescent periods. The crucial point between these two periods is the stimulation of the bone marrow to increased erythropoiesis. The signs of increased erythropoiesis in the peripheral blood are reticulocytes, polychromatophils, basophilic stippled cells, normoblasts, increased hemoglobin, and an increase in the total white cells.

The most easily determined sign of convalescence is the presence of reticulocytes. Normally, no reticulocytes are present in the peripheral blood of cattle. Any of these cells found on a slide are a sign that the animal is beginning to increase its rate of red cell production, although the actual red cell count may decrease for one to four additional days. While most cattle will recover after showing any reticulocytes, the greater the percentage of red cells that are reticulocytes, the more positive one can be of recovery.

Also, on a smear stained with Wright's or Giemsa stain, but usually following the appearance of reticulocytes by one to five days, are the other forms of immature red cells. These include large grayish staining red cells, the polychromatophils; with purple-black dense nuclei, the normoblasts. Normoblasts are the last to appear and indicate that the animal is well on the way to recovery.

With the above in mind, it is possible to determine the stage of anemia quickly from a slide. The developmental stage is characterized by no reticulocytes, normal appearing red cells, except that many are infected, and a normal number of white cells. In contrast, the convalescent stage shows reticulocytes, large polychromatophilic and basophilic stippled red cells, normoblasts and increased numbers of white cells (Table I). This entire section simply means that by smearing and staining a small drop of blood, one can tell the owner that this animal is over the hump, and if left quietly alone, it will recover, or that the animal has a way to go and should be treated.

When considering the entire herd, we can see no advantage, other than treating sick animals, in using *option A.* **Major disadvantages of this approach include the lack of protection for the remaining susceptible animals, and the undetection of carrier animals (from which the disease originated) which remain in the herd to provide a reservoir for the disease.**

Option B: During an acute outbreak, a producer may wish to stop the appearance of additional acute cases and provide some degree of protection to the remaining herd members without using the anaplasmosis vaccination program. He may do so by first removing all clinically ill animals and treating following the technique discussed in Option A; second, treating the remaining herd members with parenteral injections of tetracycline at rate of 2 gms per animal, repeated at 28 day intervals throughout the vector season. After stopping the acute outbreak with the first treatment of parenteral tetracycline it is also possible to provide protection of the herd by oral

Table 1

Blood Changes in Anaplasmosis

These Values Can be Used to Determine the Stage of Anaplasmosis in Acute Cases

PERIOD	SLIDE			COUNTS			SEROL. TEST
	Retic.	Inf. RBC	Polych. Normbl.	RBC	Hb.	Ht.	C.F. or Card
Non-exposed	None	None	None	Normal	Normal	Normal	–
Incubation	None	None	None	Normal	Normal	Normal	–
Developmental	None	Present	None	Low	Low	Low	+
Convalescent	Present	Present	Present	Low	Low	Low	+
Carrier	None	None	None	Normal	Normal	Normal	+

administration of 0.25 mg of tetracycline per pound of body weight per day for the vector season.

Brock (4) found that a single treatment prior to infection has no effect on the course of a later infection but the same treatment during the incubation period, while not preventing infection, substantially reduces the number of clinical cases encountered.

A parenteral tetracycline treatment during the developmental and convalescent stages was previously discussed under Option A. Allowing for a minimal incubation stage of 21 days and an average developmental stage of seven days, repeated parenteral injections at 28 day intervals will fall within either the incubation or developmental stage of newly infected animals. Treatment of an animal during either stage would be beneficial to the animal.

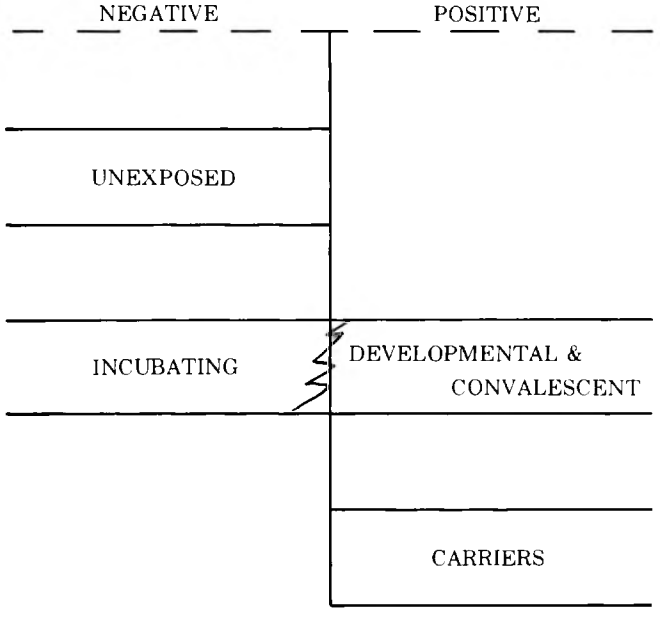
The major disadvantage in this option is that carriers are not identified and remain in the herd as reservoirs of the disease.

Option C: Option C, a method developed by Bedell and Slater (2), consists of simultaneous treatment of all herd animals with parenteral injections of 3-5 mg/lb body weight of tetracyclines and inactivated anaplasmosis vaccine.

This method is supported by the fact that anaplasmosis vaccine, as an aid in reducing the clinical symptoms of bovine anaplasmosis, necessitates that the two (2) doses of vaccine be given at least four (4) weeks apart and two (2) weeks prior to exposure to the disease. This requires a minimum of six (6) weeks from the initial dose of vaccine before any degree of protective immunity is present in the vaccinated animal. Therefore, the animal requires some type of protection during the six (6) week waiting period and can be provided by parenteral injections of tetracyclines as noted in Option B.

Table 2

Antibody Titers
of Animals Within a Herd
During an Outbreak of Anaplasmosis



When anaplasmosis is diagnosed in a herd, immediately separate the clinically ill animals and treat each following the method described in Option A above. To each remaining herd member, administer the first dose of anaplasmosis vaccine and 2 gms per animal of tetracycline intramuscularly. Four weeks later, administer the second dose of anaplasmosis vaccine and repeat the tetracycline treatment. This results in the simultaneous temporary protection and immunization against anaplasmosis in the susceptible herd at the time of an acute outbreak.

The advantage of this approach is that protection from clinical anaplasmosis is afforded all susceptible animals. Disadvantages include the vaccination of animals which are in the incubation, developmental, and carrier stages; and undetected carriers remain in the herd as reservoirs of the disease. Keep in mind that a vaccinated animal is still capable of becoming infected with anaplasmosis and subsequently can become a carrier. The vaccine does not provide complete immunity, but only aids in prevention of clinical symptoms of bovine anaplasmosis.

Option D: This option includes serological testing with subsequent vaccination and antibiotic treatment or serological testing with antibiotic treatment only, for control and management of an anaplasmosis outbreak.

With the development of the Anaplasmosis Card Test and the continued use of the Complement Fixation Test, serological testing of bovine serums for the detection of antibodies to *Anaplasma marginale* is readily available. The serological distribution of herd members into positive and negative titered animals during an outbreak of acute anaplasmosis is very helpful to the veterinarian. Referring to Table 2, we can see that unexposed and incubating animals have a negative titer while the animals in the developmental, convalescent and carrier stages have a positive titer.

First, segregate those animals showing symptoms of anaplasmosis. The disease stage of each clinically ill animal needs to be determined and each treated accordingly (refer to Option A).

Second, each herd member not included with the clinically ill animals is to receive parenterally 3-5 mg of tetracycline per pound of body weight, and in addition, blood samples must be obtained for serological testing and slide examination (EDTA sample for slide, serum for serological test).

Third, after receiving the serological test results, separate the herd into positive or negative titered groups. The positive group will include those animals in the carrier, convalescent, and developmental stages of the disease. The negative titered animals will include the unexposed animals and the animals in the incubating stage.

Fourth, examine the blood film slides of the positive titered group to determine the stage of dis-

ease and treat accordingly.

Fifth, negative titered animals can be handled in one of two ways. (1) Immediately administer the first dose of anaplasmosis vaccine and an additional injection of tetracycline. Both the vaccine and tetracycline need to be repeated in 28 days. (2) Four to six weeks after the first tetracycline treatment and serological test, repeat the treatment and test to identify those animals which were in the incubation stage at the time of the first test. The positive titered animals detected with the second test must be considered infected and thus segregated. The negative titered animals are to be considered unexposed and can be protected with additional tetracycline treatments or herd segregation.

The advantages of this method are that animals in the developmental, convalescent, and carrier stages, all of which have been infected with *A. marginale,* can be identified as reservoirs of the disease and segregated from the rest of the herd. All negative titered animals (unexposed and incubating) will be afforded the tetracycline or vaccine plus tetracycline protection as discussed in Options B and C.

Preseason Protection: The measures taken, prior to the vector season, that will reduce losses due to anaplasmosis include vaccination, serological testing with segregation or treatment, and low level feeding of tetracyclines continuously through the vector season.

An anaplasmosis vaccination program must be completed at least two (2) weeks prior to the beginning of the vector season to allow the vaccinates to obtain an antibody level which will afford sufficient protection to reduce the clinical symptoms of anaplasmosis.

Serological testing with subsequent segregation or treatment consists of using the anaplasmosis card test or complement fixation test to identify the carrier animals in a herd. The carrier animals then could be segregated from the "clean" animals or treated to cure the carrier state.

Anaplasmosis carrier cattle may be cured of the infection by sufficiently large doses of the tetracycline antibiotics. The parenteral injection of 5 mg of tetracycline per pound of body weight daily for ten days or the same daily dosage orally for 60 days will destroy carrier infection. The high oral dosage will cause diarrhea, anorexia and weight loss for the first week, but the cattle return to normal rapidly after that time. The antibiotic feed should nevertheless be kept before them during this time.

The use of oral tetracycline medication combined with feed or salt mineral mixes needs to begin several weeks prior to exposure to the disease. The oral

Table 3

Summary of Treatment and Control for Anaplasmosis

Stage	Identification	Treatment	CONTROL
Unexposed	Serology during off season.	Not necessary	Parenteral tetracyclines in doses of 3-5 mg per lb of body weight repeated at 28 day intervals, vaccination, or low level feeding of tetracyclines.
Incubation	None, can be a problem	Parenteral tetracyclines, 3-5 mg/lb body weight, may reduce incidence of clinical anemia.	Treatment at 28 day intervals, serological testing with vaccination and treatment, or serological testing with treatment at 28 day intervals.
Developmental	Anaplasma bodies and serology	Parenteral tetracycline: 3-5 mg/lb body weight.	Treatment and segregation
Convalescent	Anaplasma bodies, immature red cells, and serology.	No treatment may be more beneficial. Evaluate each case and use whole blood accordingly.	Segregation
Carrier	Serology	Tetracyclines for clearing of carrier state only. Parenteral: 5 mg/lb body wt. daily for 10 days. Oral: 5 mg/lb body weight daily for 60 days.	Segregation or treatment

dosage of 0.5 mg of tetracycline per pound of body weight per day during the vector season will prevent transmission of anaplasmosis and will also effectively halt the infection if given within the first week of the incubation period. Smaller oral dosages of 0.1 to 0.25 mg per pound of body weight per day fed continuously thru the vector season may prevent clinical anaplasmosis, but will allow carrier infections to develop or prolong the incubation period allowing clinical anaplasmosis to appear sometime after medication has ceased.

Medicated salt mineral mixes can be provided free choice from June 1 through September 30 each year to provide oral medication beginning prior to the vector season and continuing until the vectors disappear.

The treatment and control is summarized on Table 3.

References

1. Amerault, T. E. and Roby, T. O.: A Rapid Card Agglutination Test for Bovine Anaplasmosis. J.A.V.M.A., 153 (1968) 1828-1834. - 2. Bedell, D. M. and Slater, M.: The Use of a Combination of the Therapeutic and Immunological Regiment in an Anaplasmosis Epizootic. Biochemic Review, Vol. 33/2. - 3. Brock, W. E.: Anaplasmosis Control and Treatment: The Oklahoma Veterinarian, Sept. 1959. - 4. Brock, W. E.: Unpublished Data.

Abstracts of the Literature

Early Pregnancy Diagnosis in Cattle

Progesterone concentrations in peripheral plasma and in milk were determined by competitive protein - binding assay each day throughout the oestrus cycle of heifers and a dairy cow, also in animals after insemination. The accuracy of detecting and forecasting pregnancy and non-pregnancy was assessed in studies involving blood sampling of heifers on the 20th and 23rd day after mating. The high degree of accuracy obtained with this procedure for an early pregnancy diagnosis would be particularly useful in herds involved in a controlled breeding program.

D. F. Wishart, B.V.M.S., M.R.C.V.S., V.A. Head, B.Sc. and C. E. Horth, B.Sc: Veterinary Record (1975) 96. 34-38.

Prenatal Diagnosis of Sex in Cattle by Amniocentesis

A method for the aspiration of amniotic fluid from pregnant cows at 70 to 100 day gestation and the subsequent cultivation of amniotic cells *in vitrio* is described. The unit for aspirating amniotic fluid includes a sterile Plexitron tubing fitted with a 60 ml syringe on one end and a 12 in. needle (No. 18 gauge) partially encased in a 6 in. AI pipette on the other. Aspiration of fluid is accomplished through the vaginal route by piercing the dorsal formix. Chromosome analysis is performed on amniotic cells after cultivation *in vitrio* for four to seven days. This method, which is simple and accurate, provides a safe diagnostic procedure for the prenatal detection of sex and cytogenetic defects in cattle.

T. A. Bongso, V.V.Sc., M.Sc. and P. K. Basnur, B.Sc., M.Sc., Ph.D., Veterinary Record (1975) 96. 124-127.

Results from 35 animals were accurate in all cases where the sex of the foetus was confirmed as male - 17 out of 35 - from the gonadal sex.

Treatment of Clinical Mastitis: Two Intramammary Formulations Compared

Two hundred cases of mild clinical mastitis were treated on two farms using two intramammary preparations in quick release bases. One preparation contained penicillin and streptomycin; the other contained lincomycin, neomycin and prednisolone. Fifty-eight percent of cases were clinically and bacteriologically cured using the first preparation; 61% of cases with a similar range of organisms, using the second. The main infections were *Strept. uberis* and coliform; all but three of the infections were sensitive *in vitro* to one or both of the antibiotic preparations.

On the farm with 100 cows, 69% of cases were cured while only 52% were cured on the farm with 300 cows. It is suggested that it is more difficult to detect and treat cases in the larger herd. A number of reservations about the interpretation of the results are discussed, but the results support the view that success in mastitis therapy is strictly limited by the reaction of the mammary gland to infection and that other new intramammary preparations of antibiotics are likely to produce similar results.

W. B. Faull, B.Sc., F.R.C.V.S., and W. R. Ward, Ph.D., B.V.Sc., M.R.C.V.S.: Veterinary Record (1975) 96. 127-129.