



Prevention, Treatment, and Clearance of Anaplasmosis Using Drugs

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Prevention

We think of it as prevention, but...

- The actual label indication is...
 - For beef and non-lactating dairy cattle: as an aid in the **control** of active infection of anaplasmosis caused by *Anaplasma marginale* susceptible to chlortetracycline.

Type C Medicated Cattle Free Choice Mineral Feed

For beef and non-lactating dairy cattle: as an aid in the control of active infection of anaplasmosis caused by *Anaplasma marginale* susceptible to chlortetracycline.

Chlortetracycline

6,000 g/ ton

Guaranteed Analysis

Sodium ^a (Min)	_____	%
Sodium ^b (Max)	_____	%
Magnesium ^a (Min)	_____	%
Potassium ^a (Min)	_____	%
Copper ^a (Min)	_____	ppm or % ^c
Selenium ^a (Min)	_____	ppm or % ^c
Zinc ^a (Min)	_____	ppm or % ^c
Vitamin A ^a (Min)	_____	IU/lb

^a Guarantee required only when nutrient added except when the feed is intended, represented or serves as a principal source of the nutrient.

This free-choice medicated feed is required to be manufactured according to the formula and/or specifications published in 21 CFR 558.128(e)(6)(i) as follows: 46.20% Dicalcium Phosphate, 15.00% Sodium Chloride (Salt), 10.67% Magnesium Oxide, 10.00% Cottonseed Meal, 3.80% Trace Mineral/Vitamin Premix (content may be varied, but should be comparable to mixes used for other free choice feeds), 3.50% Calcium Carbonate, 3.00% Dried Cane Molasses, 2.00% Potassium Chloride, 2.00% Mineral Oil, 0.50% Iron Oxide, 3.33% Chlortetracycline Type A medicated article (90 gram/lb). Formulation modifications require FDA approval prior to marketing.

the supplement by the manufacturer within the limits of the formula).

Feeding Directions

Feed a non-medicated mineral supplement for 14 days prior to feeding Blue Bird Aureo FC, then feed Blue Bird Aureo FC continuously on a free choice basis. Pasture and roughage should be adequate to assure consumption of 0.0027 to 0.011 oz/lb body weight/day of this product, which will provide 0.5 to 2.0 mg chlortetracycline per lb body weight per day. If cattle consume more or less than these amounts, move feeder further or closer to the general resting or watering areas. If consumption of the Blue Bird Aureo FC is greater than 0.011 oz/lb body weight per day after moving feeder further from general resting or watering areas, provide salt in a separate feeder to help decrease consumption of Blue Bird Aureo FC.

NET WEIGHT ON BAG OR BULK

This means...

- 1500 lb cow
 - 6000 g/ton is equivalent to 3 grams of chlortetracycline per pound of mineral
 - A 1500 lb cow at 2 mg/lb per day would need 3 grams.
 - Therefore, a 1500 lb cow would need to eat a pound of mineral a day to get 2 mg CTC/lb of bodyweight per day.
 - 4 ounces of mineral would give her $\frac{1}{4}$ of a pound of mineral, which would be 750 mg.
 - 750 mg divided by 1500 lbs equals 0.5 mg CTC/lb of bodyweight per day.
- A bull?

In-feed Control

- Cattle (beef, under 700 pounds)
 - Amount: **350 milligrams per head per day.**
 - Indications: For the control of active infection of anaplasmosis caused by *Anaplasma marginale* susceptible to chlortetracycline.
 - Limitations: A withdrawal period has not been established for this product in preruminating calves. Do not use in calves to be processed for veal.
- Cattle (beef, over 700 pounds)
 - Amount: **0.5 milligrams per pound of body weight per day in feed.**
 - Indications: For the control of active infection of anaplasmosis caused by *Anaplasma marginale* susceptible to chlortetracycline in beef cattle over 700 pounds.
 - Limitations: No limitations are included in the CFR for this species when using this product in this amount.

There is...

- No legal extra-label use in feed. The term “feed” includes.
 - Feed
 - Mineral
 - Milk replacer
- Practices which would be illegal
 - Using a soybean meal/salt carrier in conjunction with 50 g/lb chlortetracycline (a Type A feed) for Anaplasmosis control.
 - Adding the Type A CTC to supplement a mineral which does not result in the labeled concentration of 6000 g/ton or the proper formulation.
 - Feeding a Type B feed (a supplement) as a Type C feed (the final feed ready for feeding).



Treatment

Here in the U.S. our only real option is...

- Oxytetracycline injectable
 - There are multiple labeled products
- Our biggest treatment challenge in adult cattle is to impede the growth of *Anaplasma marginale* while there are enough red blood cells to allow for recovery.
 - This is why older cattle do much worse than calves.
 - The calves can regenerate



Clearing Infected Cattle

Clearing Anaplasmosis Carriers

- There are no drugs labeled for this purpose in the United States
 - This means that any use in the feed for this purpose is illegal.
 - Injectable and water regimens may be used for this purpose within the confines of the Animal Medicinal Drug Use Clarification Act (AMDUCA) regulations.
 - Valid VCPR

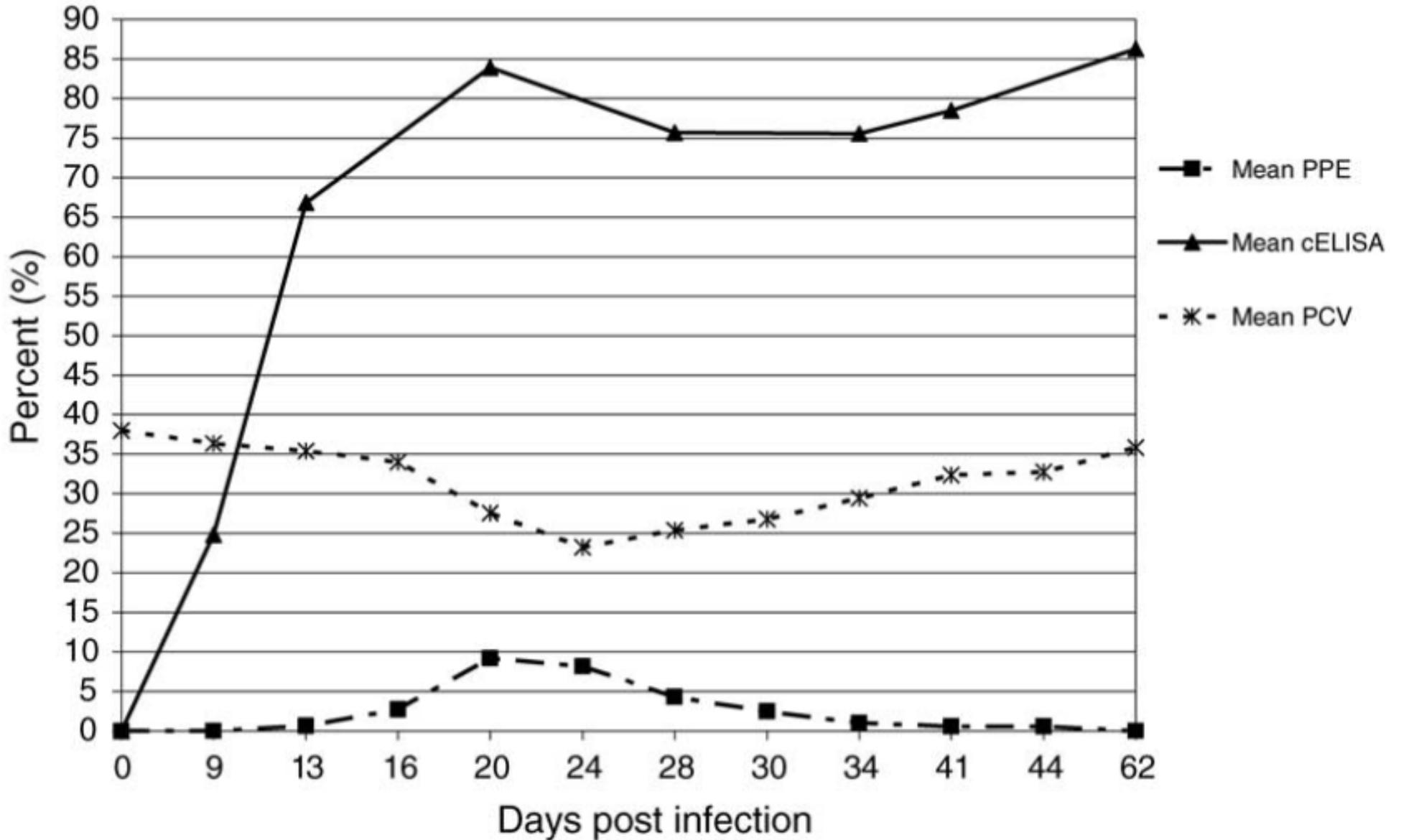
Can we even clear cattle?

- Coetzee, et al. 2005 Comparison of three oxytetracycline regimens for the treatment of persistent *Anaplasma marginale* infections in beef cattle. *Veterinary Parasitology* 127:61-73.
- Crossbred Iowa steers weighing 470 to 760 lbs (160-230 days old) were split into 4 groups. All were inoculated with an oxytetracycline-susceptible isolate of *Anaplasma marginale* from Oklahoma.

Coetzee, et al.

- For 62 days after initial inoculation, the steers were monitored for
 - Percent parasitized erythrocytes (PPE)
 - cELISA
 - Packed cell volume

What happens in calves inoculated with *Anaplasma marginale*



Coetzee, et al.

- After meeting the criteria for being carriers, the treatments were administered.
- Treatments were
 - Untreated controls
 - 300 mg/ml oxytetracycline at 13.6 mg/lb IM, once
 - 300 mg/ml oxytetracycline at 13.6 mg/lb IM, twice, 5 days apart
 - 200 mg/ml oxytetracycline at 10 mg/lb, IV, once daily for 5 days.

Coetzee, et al.

- None of the standard regimens for clearing carrier cattle were effective.
- This was confirmed by
 - DNA testing (for *A. marginale* DNA)
 - cELISA testing
 - Inoculation into splenectomized calves 60 days after treatment

Why do the textbooks say we can?

- Magonigle, et al.,(1975) used the daily IV treatment we used to clear 11, 2-3 year old serologically positive cattle.
 - The clearance was confirmed in splenectomized calves by inoculating them with blood from the treated cattle 4-12 months post-treatment.
- Roby, et al, (1978), gave two injections of 200 mg/ml oxytetracycline, 9 mg/lb, 7 days apart.
 - Clearance confirmed by inoculating splenectomized calves 83 days after treatment.

What Coetzee, et al., means

- None of these short-term injectable regimens in this study, including the OIE standard regimen for clearing carriers (the daily IV OTC), were successful in clearing these documented carriers.
- Other studies did, as confirmed with inoculation of splenectomized calves.
- Differences due to...
 - Age of carriers?
 - Time from carrier establishment to treatment?
 - The *Anaplasma marginale* isolate?

Can we even clear cattle?

- Reinbold, et al. 2010 The efficacy of three chlortetracycline regimens in the treatment of persistent *Anaplasma marginale* infection. Vet Micro 145:69-75.
- *Anaplasma marginale* infected Holstein steers, confirmed by both cELISA and RT-PCR.
 - Virginia isolate
- The steers received either 2, 5, or 10 mg CTC/lb BW per day for 80 days
 - 5 infected steers and 1 splenectomized control steer per treatment group
 - Also 6 infected steers and 1 splenectomized steer in the control group

Results

- All steers were negative by RT-PCR at 46, 46, and 49 days for the 2, 5, and 10 mg/lb groups respectively.
- The cELISA results did not become negative until 18, 54, and 18 days after the 80 day feeding period for the 2, 5, and 10 mg/lb groups respectively.
- Chemosterilization was confirmed by inoculating splenectomized calves with pooled blood samples collected from chemosterilized steers at 50 days past the end of the 80 day feeding period.
 - None of the 3 splenectomized calves developed anaplasmosis over a 6 week monitoring period.

Results

- Five steers were selected for a reinfection study.
 - Antibodies to the Virginia isolate were detected as early as 10 days. All 5 steers were cELISA positive by 24 days post inoculation.
 - RT-PCR detection of infection occurred by 10 days in 4 steers and by day 17 in the fifth steer.

What Reinbold, et al., means

- We can clear cattle infected with the Virginia isolate of *Anaplasma marginale* by feeding CTC at 2, 5, or 10 mg/lb bodyweight for 80 days
 - They were negative by RT-PCR by 50 days.
 - The negative controls in the study were later chemosterilized by a single injection of 300 mg/ml oxytetracycline followed by 2 mg/lb BW CTC per day for 30 days.
- Once cleared, cattle may be reinfected.

Extrapolation warning

- These cattle were all getting the full dose as evidenced by the plasma concentration monitoring.
 - Sporadic and variable (individual animal intake) intake may not work the same (e.g., mineral)
- This was for the Virginia isolate
 - It could be different for other isolates
- Could this work through the water?

Summary

- Control?
 - Yes, but how much is necessary considering variation in intake?
- Treatment?
 - Yes, a balance between RBC regenerative capabilities and shutting down infection
- Clearance?
 - Yes we can, but, no label for this
 - Consistency?