Bloodborne pathogens in beef herds – a Kansas practitioner's perspective

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Abstract

Management options for bloodborne diseases depend on prevalence (herd level and geographic), disease stage and production class. Opportunities to manage disease can be classified according to disease stage. Newer studies show that, in contrast to older studies, there is not currently a known legal way to clear animals of anaplasmosis. The only currently labeled products for treatment of acute clinical anaplasmosis are injectable oxytetracyclines. For a time, an enrofloxacin product (Baytril-CA) was marketed with a label for treatment of anaplasmosis, but the conditional approval application has been withdrawn. Opportunities for leukosis management are limited to exposure control as there are no effective treatments for animals in the clinical stage and no effective methods to clear infected non-clinical animals. Due to the relatively high prevalence in beef herds, a strict test-and-cull strategy is not practical. Instead identifying animals with high pre-viral load who are most infectious provides an option to decrease disease levels with reasonable economics at the farm level. More research is necessary to fully quantify production effects for carrier animals of both bovine leukosis and anaplasmosis.

Key words: anaplasmosis, leukosis, beef cattle

Anaplasmosis

Prevalence and epidemiology

The prevalence of anaplasmosis varies across geographic regions of the United States and is summarized in Table 1. A few highlights from these studies are listed in the paragraphs that follow.

Seroprevalence across herds can vary dramatically even for geographically close herds. Spare et al. found that herd prevalence ranged from 17% to 87% within the state of Kansas.[1] In 2014, Curtis et al. took a close look at seroprevalence (cELISA) in Florida cattle that were under the same ownership but managed as 12 separate herds. Seroprevalence across herds ranged from 2.6% to 85%. The overall individual cow positive rate was 50% across all herds. Unsurprisingly, a comparison between the percent mortality during the 2014 outbreak and percentage of open cows in April 2015 indicated that herds with high mortality had a higher percentage of open cows.[2] Less relationship was found between the ratio of seronegative to seropositive animals and the mortality rate. However, this relationship is more difficult to interpret due to many unknowns in the historic seroprevalence and historic mortality in these groups.

Seroprevalence in Arkansas was evaluated by a randomized sample of 578 mature beef cattle (> 2 years). Samples were evaluated by both PCR and cELISA; prevalence ranged by region from 37% to 94%, with an overall prevalence of 68%.[3] Test results for PCR and cELISA were not identical in all cases.

Strain matters, both for disease progression and severity as well as response to treatment. Multiple strain types can be found within a herd. One study evaluated animals born into a closed herd over a 9 yr period and found 11 different strains. They also detected a few animals infected with more than one strain.[4]

Infection prevention

Obviously, prevention of disease exposure is the ultimate goal in management for anaplasmosis. However, it is extremely difficult to achieve in areas where the disease is endemic. A complex model looking at disease effects and control options concluded that "efforts should be aimed at improving and maintaining good hygiene practices; furthermore, the added benefit of culling infected cows is only minimal and not cost-efficient."[11] Challenges for interpretation of this model include specifics of animal class and marketing strategy (purebred vs. commercial).

A few studies have looked at breed and/or genetic resistance primarily between *Bos indicus* and non-*Bos indicus* or *Bos indicus* crosses. The results are unclear and show a small difference but not enough evidence to change management strategy based on breed at this time.[12,13]

Vaccination

The search for a safe and effective vaccine has been ongoing. Some have indicated that they are skeptical that a sufficiently effective vaccine is possible.[14] There is one vaccine currently marketed in the U.S. on a conditional license.[15] There are no published effectiveness data. However the technology used in a field trial in Mexico has been documented as being similar.[14] The results of this study are challenging to interpret. The authors suggest that the vaccine provided at least some protection compared to controls; however, they are quick to point out that there are strain similarities between the vaccine strains and the local strains to which cattle were exposed.[16] The vaccine strain in the conditionally licensed product is the Mississippi strain.[15] The level of cross protection this strain provides when challenged with common field strains is unknown, but numerous strains have been identified.[17]

In 2020, Curtis et al. published work that compared different adjuvants used with an ear implant vaccine.[18] Results showed some response to some combinations, but there is no published evidence that a product is near a clinical stage. Attempts have been made to identify protective antigens such as the 3 novel protein targets identified by an in silico model in 2020.[19] Numerous other attempts have been made to find good targets for vaccine development.[20]

Tick transmission

Ticks have long been known to be important in transmission of Anaplasmosis and tick control has often been recommended as a control measure. As chemical control of ticks becomes more challenging there are other tick control strategies on the horizon. In 2013, Octavio et al. reviewed the protective antigens that

Table 1: Examples of recent anaplasmosis prevalence studies.

Region	Year	Animal class	Test method	Animals sampled (n)	Percent positive animals(%)	Percent positive herds (%)	Citation
Iowa	2023-2021	Diagnostic Samples	PCR (ct < 35)	1,125	28	–	Villar et al.[5]
North Carolina	2005-2012	Diagnostic Samples	cELISA	10,581	9.8	–	Okafar et al.[6]
North Carolina	2013-2015	Slaughter Beef Cows (> 18 Month)	cELISA	195	3.9	–	Okafar et al.[6]
Georgia	2018-2019	Beef Cattl (> 2 years)	cELISA	1,059	8.1	42	Jones et al.[7]
Georgia	2013-2014	Slaughter Beef Cows (> 18 Month)	cELISA	293	4.4	–	Okafor et al.[8]
Kansas	2016-2017	Beef Cows (> 2 years)	cELISA	9,250 (925 herds)	–	52	Spare et al[1]
Arkansas	~2020	Beef Cattle (> 2 years)	cELISA	578	68	–	Apple et al[3]
Florida	2015	12 Beef Herds (> 2 years)	cELISA	1,085	50 (2-85 within Herd)	–	Curtis et al.[2]
Mississippi	2013-2014	Slaughter Beef Cow (> 18 Month)	cELISA	207	19	–	Okafor et al.[9]
Mississippi	2002-2018	Diagnostic Samples	Card test, CFT, cELISA	5,182	16	–	Okafor et al.[9]
Kentucky	2013	Slaughter Beef Cows (> 18 Month)	cELISA	232	10.8	–	Okafor et al.[10]
Kentucky	2002-2012	Diagnostic Samples	CFT, cELISA	2,573	11.6	–	Okafor et al.[10]

could be used to create vaccines against ticks.[21] This strategy strives to control vector-borne pathogens in 2 ways. First by reducing vector populations, which in turn reduces host exposure to vector borne disease. Second, by reducing the tick's capacity for transmission. There are currently no tick vaccines on the market in U.S., but at least one company is known to be actively pursuing development of vector vaccines.

Diagnosis

There are multiple ways to identify disease, but stage of disease influences which diagnostics are most useful. Table 2 summarizes available diagnostics and stage of disease where they are most useful.

Clinical

Physical exam findings include lethargy and/or aggression, pale or icteric mucous membranes, inappetence, increased respiratory rates, increased heart rate (+/- murmur). Photos of gross and histopathologic lesions of 6 animals are well described in Das et al.[22] Common post mortem lesions include icterus, splenomegaly/friability.

Laboratory

A. margninale organisms can easily be seen on the margins of red blood cells in a blood smear in acutely infected animals.[22] In persistently infected animals there are frequently less than 100 parasitized erythrocytes per mL whole blood.[23] Therefore blood smears are not a good method of detection unless animal is in the acute phase of the disease.

Acutely affected animals showing clinical signs will also have a low packed cell volume (PCV). A hematocrit tube can be placed inside a regular blood tube and spun in a standard centrifuge if a microcentrifuge is not available. For valuable animals, this can provide relatively efficient cow side evidence of whether or not transfusion is warranted.

Options for testing either to confirm clinical signs in acute infection or to identify carriers include cELISA and PCR testing. For an individual in the acute phase of the disease, PCR testing is most logical as they should have a high number of organisms and may have not had sufficient time to mount an antibody response. The cELISA is cheaper and generally used as a screening test, which can be followed by confirmatory PCR testing. While interpretation of testing is generally straightforward,

Table 2: Diagnostics and associated stage of disease where they are appropriate.

Diagnostic indicator	Acute infections	Chronic carriers
Fever, pale membranes, +/-Icterus, increased RR, increased HR (+/-murmur), lethargy and/or aggression, inappetence	X	Not present
Blood smear – visible organisms	X	Not Identifiable
Low packed cell volume (PCV)	X	Normal values
PCR – low ct count	X	X
cELISA – high % inhibition	Not useful	X

a recent study demonstrated that some care should be taken when interpreting cELISA positive results that have a low percent inhibition.[24] A study by Grayson Robbins looked at positive animals from 2 herds that had been previously tested with cELISA.[24] They found that 19/168 animals tested cELISA positive in one herd, and 21/162 cows tested cELISA positive on the other herd. However, 0/19 and 3/21 tested positive on PCR. The takeaway from this should be to confirm positive cELISA results if using for making decisions about culling or sale/purchase.

Treatment

It appears that at least at some doses chlortetracycline, oxytetracycline, and enrofloxacin can affect organism levels in chronically infected individuals.[23,25-27] However, none of the currently legal regimens were effective in clearing the disease.[23,26] And no studies using current diagnostic methods involving adult animals demonstrated clearance regardless of regimen.

Oxytetracycline

Oxytetracycline has long been used for treatment of anaplasmosis. Multiple oxytetracycline products are on the market and labeled to be used for treatment. Historically, this drug was also recommended for clearance of chronic carriers. Newer studies demonstrate that clearance regimens previously recommended are not effective.[26] Oxytetracycline showed a decrease in bacteremia when levels were high (shortly after injection), but by day 3, when drug levels were at their trough, bacteremia levels rose to pretreatment levels.[26]

A recent robust challenge study looking at the effect of oxytetracycline against current field strains is not available. However, it seems reasonable to assume that oxytetracycline is still a good choice for treatment of acute infection as it did demonstrate a significant reduction in infection levels (*A. marginale* organisms/ml blood) for all 7 steers in a study that looked at its effects on chronic carriers of current field strains.[23]

Enrofloxacin

In 2020, a challenge study using a field strain from Oklahoma was used to evaluate the effectiveness of enrofloxacin compared to saline for treatment of acute anaplasmosis. Mortality due to severe anaplasmosis disease in saline treated cattle was 47% (n = 16), and 3% (n = 1) in enrofloxacin treated cattle.[28] PCV continued to drop until day 7 in both groups, but the change in PCV between day zero (treatment) and day 7 was significantly less in the enrofloxacin treated group. If treatment occurred later in the disease course, the drop in PCV may have already occurred and therefore treatment is likely to be less effective. However, this model provided a strong disease challenge and enrofloxacin successfully mitigated many disease effects and lessened severity. A challenge in interpreting this model in the field is ascertaining whether or not the treatment can be administered promptly enough and with as little stress as possible. There are some older studies that also looked at the effect of enrofloxacin but they are not as robust or easy to apply clinically. [29,30]

CTC

There are no current studies that provide any evidence that CTC would be useful as a treatment for acute disease at any dose. It is acknowledged that there are times when a CTC dose for an alternative indication has been used to treat a group of cattle breaking with clinical anaplasmosis. While the ease of administration to the group without handling obviously has its advantages, there is zero published evidence that this is effective for animals with acute disease.

Control

Numerous studies have looked at the effect of different treatments with the goal of eliminating anaplasmosis carriers. While the older studies showed this was possible,[25,31-36] more recent studies indicate that with current legally available treatment options elimination is not possible.[23,26]

CTC

Five years ago the literature available indicated that 0.5 mg/kg might be effective for anaplasmosis elimination but the only evidence was an old challenge study.[32] We now have evidence that a 0.5 mg/lb (1.1 mg/kg) dose is not effective at clearing carrier animals.[26,27] A study by Spare is highly clinically relevant as it looked at bunk feeding CTC at 0.5 mg/lb/day to developing bulls. Of the entire bull population, 38/827 (4.6%) were cELISA-positive for anaplasmosis. All bulls were fed CTC for 80 days with a total study duration of 128 days. The bulls that initially tested positive (day -10), were retested on days 40, 80, and 128+ using cELISA. Some bulls changed status (by day 40) while on the CTC. However, these bulls had a lower inhibition percentage at initial testing.[27] CTC at this dose was not effective in consistently decreasing the mean percent inhibition on the cELISA test. This is in contrast to Reinbold et al. where percent inhibition as measured by cELISA dropped significantly by day 128.[25] It is unknown whether this difference in results is related to strain, dose or other factors.

Oxytetracycline

Several studies report failure of oxytetracycline to eliminate carrier status by using multiple regimens. [23,26,27] Attempts to use oxytetracycline to clear carriers are not recommended.

Enrofloxacin

Although enrofloxacin can legally be used for control of respiratory disease, it cannot be legally used for anaplasmosis control. In addition to that, carrier elimination with enrofloxacin was evaluated and found to be ineffective at clearing the infection. For a short time it caused a decreased parasitemia which then reverted to pretreatment levels within a few weeks.[23]

Summary

Recommendations for anaplasmosis management are dynamic. There is great potential for new technologies in molecular fields to improve our tools to manage anaplasmosis in the future. For now, the legal management options are shown in Table 3.

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Table 3: Tools available for anaplasmosis management.

Action or goal	Current (legal) tools available	Level of evidence
Infection prevention	Nothing	High
Vector reduction	Parasiticide application	Low
Diagnosis	Clinical signs – acute infections cELISA – carrier stage, surveillance PCR – acute or chronic infections	High
Treatment of acute disease	Benign neglect, oxytetracycline,blood transfusion	Moderate
Vaccination	Conditionally licensed vaccine	Low
Antimicrobial control	CTC	Low (strain-dependent?)
Clearance of latent infections	Nothing	High

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