Practical Strategies for Treating Mastitis

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Introduction

Mastitis is the most frequent and costly disease of dairy cattle. Losses due to mastitis occur for both subclinical and clinical disease. Losses caused by clinical mastitis are often apparent and consist of discarded milk, transient reductions in milk yield and premature culling (Fetrow, 2000). Perceived financial losses for clinical mastitis vary widely. In 2002-2003, farmers participating in milk quality programs in Wisconsin (n = 117) estimated that each clinical case of mastitis cost approximately $97.00 USD, but estimates ranged from zero to $260 per case. Discarded milk accounted for more than half of the cost ($54.00 USD).

The amount of mastitis that a herd experiences is determined by the rate that new infections develop and the length of time that existing infections persist (Ruegg, 2003). Prevention of mastitis is the most cost-effective strategy to control mastitis but effective treatment is necessary for production of high quality milk. Treatment is required when a cow is obviously sick but in many instances, treatment of mastitis is voluntary. Many mild cases of clinical mastitis appear to resolve spontaneously and milk from cows with subclinical mastitis appears normal and may be sold. Treatment of mild cases of clinical mastitis should be considered when the probability of cure is high, the rate of recurrence is expected to decrease with treatment and a financial benefit to the farm is expected. Cure rates are related to the type of bacteria that are causing the mastitis. The decision to use antibiotics to treat mastitis should be made based upon knowledge of the herd history of mastitis and the likelihood of obtaining a successful cure. This paper will discuss practical considerations related to treatment of mastitis infections.

Characteristics of Mastitis Pathogens

The probability of successful elimination of mastitis infections is related to several innate characteristics of the pathogens (Table 1). Many strains of contagious mastitis pathogens are able to survive because they establish subclinical infections that persist for long periods of time without detection. These pathogens may cause periodic episodes of mild to moderate mastitis that seem to resolve without treatment. In most instances, the cow remains subclinically infected and the infections are simply alternating between subclinical and clinical states. Bacteria are often shed intermittently and antibiotics (during lactation or at dry off) are required for treatment.

In contrast, opportunistic bacteria that reside in the environment of the cows tend to be less adapted to survival in the udder and often stimulate an acute immune response when they infect the udder. The immune response is usually successful in eliminating these pathogens resulting in a high rate of spontaneous

cure. Consequently, the natural duration of infection is often relatively short and the only sign of infection may be a brief period of abnormal milk with or without changes in appearance of the udder. For example, we recently collected quarter milk samples (n = 156) from mild to moderate cases of mastitis on 5 commercial dairy farms. These cases of mastitis were from cows that had abnormal milk but did not exhibit any systemic signs of disease (such as fevers, anorexia or pain). Bacteria were isolated from 66% of the cases (n = 103) and Gram-negative bacteria (mostly E. coli and Klebsiella) were responsible for 40% of these mild cases. It is likely that some of the bacteriologically negative samples also originated from infections caused by Gram-negative pathogens.

Table 1. Selected Characteristics of Some Mastitis Pathogens

Pathogen	Usual Mode of Spread	Natural Duration of Infection	Usual method of detection	Site of Infection in Udder	Reported Cure Rates during lactation
Staph aureus	Contagious	Long	Increased SCC, occasional clinical cases	Microabscesses within secretory cells	<35% (chronic infections)[1,2] up to 70% (new infections)[1,2]
Strep agalactiae	Contagious	Long	Increased SCC	Surface of secretory cells	>90%[3]
Strep dysgalactiae	Environmental	Variable	Increased SCC & clinical cases	Surface of secretory cells	>75%[4]
Strep uberis	Environmental & Contagious	Variable	Increased SCC & clinical cases	Surface of secretory cells; some invasive	>70%[4,5]
Coliforms (E. coli, Klebsiella etc.)	Environmental	Short	Mild to severe clinical mastitis	Surface of secretory cells; sometimes bacteria in bloodstream	High rate (>85%) of spontaneous cure[4]
Coagulase-negative Staph spp.	Environmental	Variable	Increased SCC, mild clinical cases	Surface of secretory cells	High rate (>70%) of spontaneous cure[4]
Mycoplasma bovis	Contagious	Long	Increased SCC, agalactiae, clinical mastitis	Surface of secretory cells; bacteria in bloodstream	Very low rate of cure

[1]Sol et al, 1997; [2]Owens et al, 1997; [3]Erskine and Eberhart, 1990;[4]Wilson et al., 1999; [5]Hillerton et al., 2002

The site of infection within the udder is another characteristic that can influence the probability of successful cure (Erskine et al., 2003) Some pathogens (such as *Staph aureus* and some strains of *Strep uberis*) may be highly invasive and penetrate into the secretory alveoli of the udder (Table 1). Successful antibiotic treatment of invasive pathogens is dependent upon selection of an antibiotic that can diffuse into the tissue in a high enough concentration to kill the bacteria. The high rate of treatment failure for cows chronically infected with *Staph aureus* indicates the ability of this pathogen to survive in spite of treatment with common intramammary antibiotics.

The surface of the secretory cells and epithelial cells lining the milk ducts is the site of infection for many mastitis pathogens (Table 1). In these instances, the concentration of antibiotics delivered by intramammary tubes is often sufficient to successfully kill the bacteria and high cure rates for these drugs are often reported.

Treatment of mastitis caused by Specific Pathogens

Strep ag: *Strep ag* lives only in the udder of cows and 80-90% of infected cows are often cured by intramammary treatment using penicillin type drugs. To eradicate *Strep ag*, all 4 quarters of all culture positive cows in the herd should be treated with an appropriate commercially marketed intramammary antibiotic (Erskine, 2001). A small percentage of animals will not be cured, therefore cows that continue to have high SCC values should be resampled and cultured at 30-day intervals. Cows that remain infected can be retreated but should be segregated from the herd to prevent reinfection. Treatment of the herd should be accompanied by an effective teat dipping program and comprehensive dry cow therapy. Treatment of cows subclinically infected with *Strep ag* usually results in increased production and dramatic decreases in bulk tank SCC values. Virtually all mastitis experts concur with treatment recommendations for this organism.

Environmental Streptococci: The spontaneous cure rate for mastitis caused by environmental Streps (usually *Strep uberis* and *Strep dysgalactiae*) may exceed 50%, but cows with clinical infections caused by environmental streptococci have frequent relapses if they do not receive appropriate antibiotic therapy (Morin et al, 1998). Clinical cases of mastitis caused by environmental streps should be treated with approved intramammary antibiotic products for an appropriate number of treatments. The use of extended treatment periods (up to 6 days of intramammary treatment) to treat Strep uberis infections have been shown to result in cure rates that exceed 90% (Hillerton and Kleim, 2002).

Staph aureus: During the lactation period, it is not considered cost-effective to treat most cows that are chronically infected with *Staph aureus* because cure rates are generally less than 20%. However, there may be some instances when treatment should be attempted for clinical mastitis caused by *Staph aureus*. There are a number of factors that influence the cure rate for cows infected with *Staph aureus* (Owens et al., 1997; Sol et al., 1997). One study reported that bacteriologic cure rates for newly acquired (< 2-weeks duration) *Staph aureus*

infections were 70% (Owens, et al., 1997). The study used intramammary treatment with a commercially available penicillin novobiocin product. Cure rates for chronic (> 4-weeks duration) *Staph aureus* infections were only 35%. Cure rates for mastitis caused by *Staph aureus* have been shown to decrease with age (from 81 % for cows ≤48 months of age to 55% for cows ≥96 months), the number of infected quarters (from 73% for 1 infected quarter to 56% for 4 infected quarters) and SCC (Sol et al., 1997). In the study, cows infected in more than 1 quarter were less than half as likely to be cured as compared to cows with only 1-quarter infected. In general, treatment of cows infected with *Staph aureus* may be successful when infections are of short duration (< 2-weeks), in young cows and in early lactation. The use of extended duration of intramammary therapy (8 days) may further improve cure rates (Deluyker et al., 2001).

Coagulase-negative Staphylococci: CNS are frequently isolated from milk samples in herds that have controlled major pathogens (Harmon et al, 1995). The SCC of infected cows can vary, but a typical SCC for a cow infected with this type of pathogen would range between 250,000 – 400,000. While CNS are not a frequent cause of clinical mastitis, surveys in herds that have controlled major pathogens generally attribute 3-10% of clinical cases to CNS. CNS live on teat skin and can colonize the teat canal. Dry cow therapy is usually effective in controlling these organisms. The rate of spontaneous cure is high but intramammary treatment of cows infected with CNS is often highly successful (Wilson et al., 1999).

Gram-negative bacteria: Most mastitis caused by Gram-negative bacteria is mild or moderate. The immune response of the cow is highly successful in destroying these bacteria. As the bacteria are destroyed, they release endotoxin from their cell walls. In 5-15% of these cases, enough endotoxin is released to result in seriously ill cows. These cows require rapid diagnosis and immediate supportive therapy. The hydration status of the cows should be evaluated and cows should be given hypertonic or isotonic fluid therapy and appropriate anti-inflammatories. In more than 40% of severely ill animals, bacteria may escape the udder and circulate throughout the bloodstream (Wenz, et al., 2001). A recent study indicated more favorable clinical outcomes for cows with severe clinical coliform mastitis that received IM ceftiofur once daily as compared to cows that received only supportive therapy (Erskine et al., 2002).

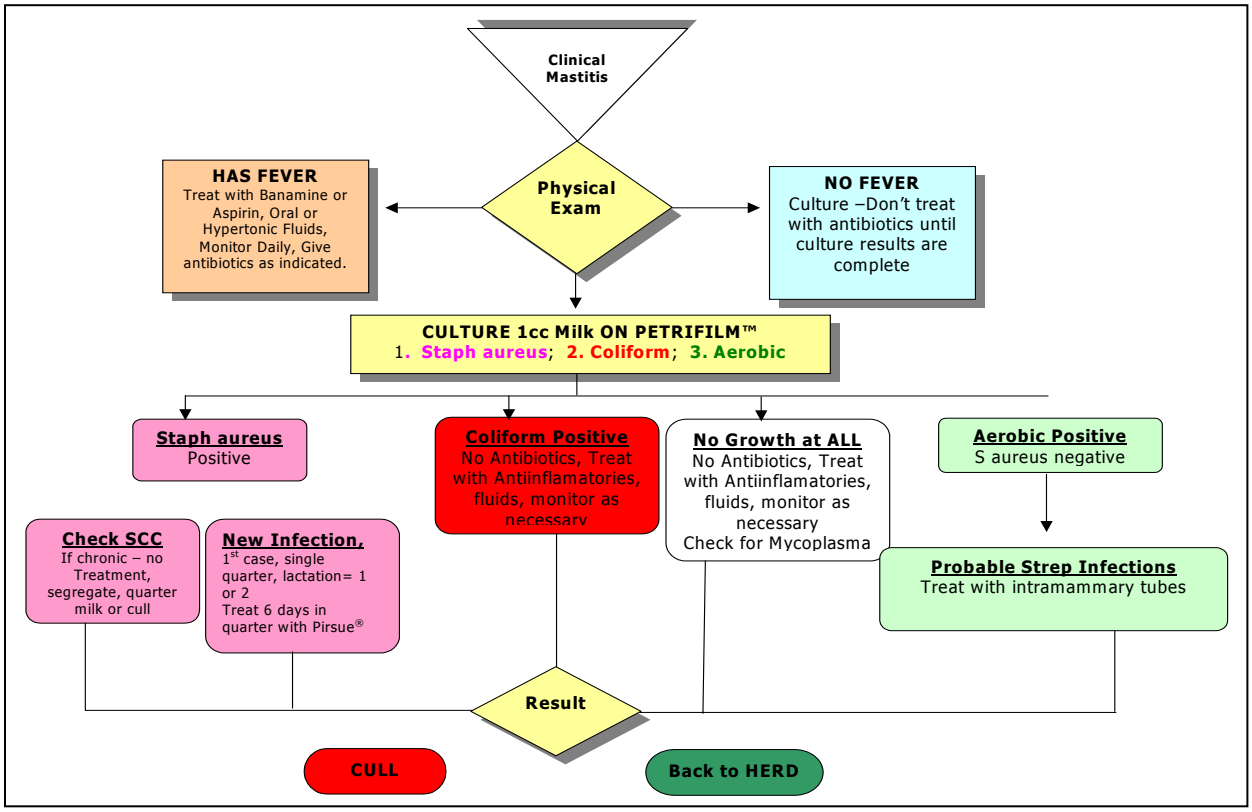
Using On-Farm Treatment Protocols for Clinical Mastitis

It is extremely important to have a treatment plan for clinical mastitis that is based upon the individual herd history and a likely diagnosis of the suspected pathogen. Even when milk samples are routinely collected from cases of clinical mastitis, treatment of clinical mastitis will usually occur before the diagnosis is known. A history of previous diagnosis and a careful physical exam should be used to guide treatment decisions. With the exception of chronic infections caused by *Staph aureus*, intramammary antibiotic therapy should be used to

treat cases that are suspected to caused by Gram-positive bacteria. The use of intramammary and systemic antibiotics to treat mastitis that is probably caused by Gram-negative bacteria should be reserved for seriously ill cows. Antibiotics should be given for appropriate periods of time. Aggressive treatment with intramammary tubes may include extended time periods or tubes given at each milking rather than once per day (Hillerton and Kliem, 2003).

The use of treatment protocols based on culture results has been described (Hess, et al., 2003). We recently modified this procedure to use a commercial culture system to guide mastitis therapy on a large dairy farm (Figure 1). Farm personnel performed the cultures and read them after 24 hours of incubation.

Figure1. Treatment protocol using on-farm culturing to direct therapy.



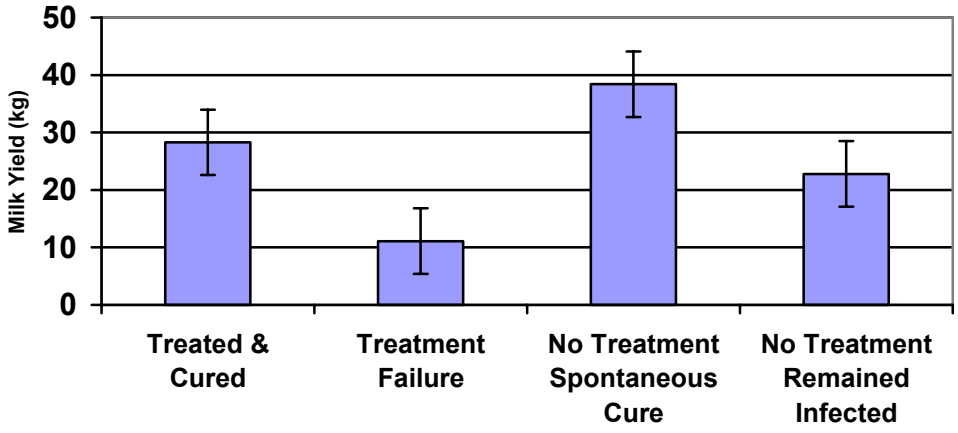
We compared the clinical outcomes of 240 cases of clinical mastitis that were treated according to this protocol to outcomes of 100 cases of clinical mastitis that occurred immediately before the protocol was adopted. In the pretrial period, milk was discarded for an average of 20 days for each mastitis case as compared to milk discarded for 8 days during the trial. Only 13 of 100 (13%) of the pretrial cases did not receive intramammary antibiotics as compared to 161 (67%) cases treated during the protocol period. In this herd, the use of a standardized treatment protocol and directed antibiotic therapy resulted in less antibiotic usage and more favorable clinical outcomes.

Treatment of Subclinical Mastitis

With the exception of Strep ag infections, treatment of cows affected with subclinical mastitis is usually discouraged because discarding saleable milk may result in considerable financial loss. Treatment of subclinical infections has generally occurred at dry off. Maintaining cows with subclinical infections within the dairy herd has some potentially negative consequences. Cows infected with subclinical mastitis have higher SCC values and the farmer may receive a lower price for milk because of decreased quality premiums. Cows with subclinical mastitis may have periodic clinical episodes that require milk withholding or antibiotic treatments. Untreated infections allow invasive pathogens the opportunity to establish chronic infections that are unlikely to respond to antibiotic therapy. Cows with subclinical mastitis infections increase the potential exposure of uninfected cows to contagious pathogens shed in milk from infected cows. Finally, cows with subclinical mastitis infections are known to produce less milk. Each doubling of SCC above 50,000 cells/ml has been shown to result in a loss of 0.4 and 0.6 kg of milk per day in first lactation and older cows, respectively (Hortet and Seegers, 1998).

In many herds, much of the subclinical mastitis is caused by *Staph aureus* and/or environmental Streptococci. Effective treatment of subclinical mastitis caused by these pathogens may require the use of intramammary tubes for up to 8 days (Deluyker et al., 2001). The cost of treatment must be balanced against the loss of saleable milk. In a small, preliminary study, we compared cure rates and daily milk yields of cows treated for subclinical mastitis infections (*Staph aureus* and env. Streps.)(Ruegg and Araujo, 2002). Three weeks after receiving 5 days of intramammary treatment, 10 of 14 treated quarters (71%) were defined as cured as compared to 6 of 13 control quarters (46%). Post-treatment milk yields for the 4-weeks following treatment for cows affected by *Staph aureus* were influenced by treatment (Figure 2). The results of this small study are not conclusive but do indicate the need for more research about potential economic benefit of treating subclinical mastitis infections.

Figure 2. Daily Milk Yields of Cows Treated for Subclinical S aureus Infections



Treatment of Non-lactating Heifers

Many dairy heifers are subclinically infected with mastitis pathogens before calving. In some studies, bacteria have been isolated from more than 50% of quarters of prepartum heifers (Owens, et al., 2001; Oliver et al., 2003). Staphylococci (including *Staph aureus* and CNS) are the most frequent isolates but environmental streptococci have also been isolated. These early mastitis infections are costly because of the potential effect of these infections on future milk yields. The use of dry cow therapy to treat heifers has been shown to be highly effective in treating prelactating heifers and cure rates for Staphylococcal infections frequently exceed 90% (Owens et al., 2001). High cure rates have also been demonstrated for lactating cow therapy administered 14 days before the expected calving date (Oliver et al., 2003). In that study, heifers that received antibiotic treatment before calving had lower SCC and produced 531 kg more milk than control heifers that were not treated. Treatment of heifers before calving is a mastitis control strategy that should be considered by herds that have demonstrated problems with heifer mastitis.

Treatment during the dry period

Dry cow therapy has been shown to eliminate up to 80% of existing infections at dry off and prevent up to 80% of new infections during the dry period. The use of antibiotics to treat all quarters of all cows has been questioned in recent years because of concerns about the development of antibiotic resistant bacteria. There is no evidence that use of dry cow therapy contributes to the development of resistance to antibiotics and decreased resistance has been noted for some antibiotics (Erskine et al., 2001, Makovec and Ruegg, 2003). There is however, strong evidence that cows that do not receive dry cow therapy develop more intramammary infections, even when the cows are uninfected before dry off (Table 2).

Table 2. Infection Rate Based on Dry Cow Therapy[a]

	No Dry Cow Treatment	Cephalosporin Dry Cow Treatment
Clinical Mastitis in Dry Period	12 of 134 cows (8.96%)	0 of 117 cows (0.0%)
New Infection at Calving	42 of 122 cows (34.4%)	12 of 117 cows (10.3%)

[a]adapted from Berry and Hillerton, 2000

While DCT remains an effective practice, the cure rates for chronic mastitis caused by *Staph aureus* remain relatively low and producers often experiment with additional treatments such as the use of multiple intramammary tubes or systemic antibiotics. Several studies have examined the use of adjuncts to DCT. One study compared the use of a single dry cow treatment using benzathine cloxacillin to use of 3 treatments (dry off, 7-days post-dry off and 14-days post-dry off) with the same product (Cummins and McCaskey, 1987).There was no

significant effect of the use of multiple dry cow treatments on the rate of new intramammary infections or the cure rate of existing infections.

At least two-studies have examined the use of systemic antibiotics in cows chronically infected with *Staph aureus*. One study compared the use of intramammary dry cow therapy (300 mg cephapirin benzathine) to the same product plus 11mg/kg intramuscular oxytetracycline given daily on day 7, 8, 9 and 10 after dry off (Erskine et al., 1994). The cure rate at 60-days post-calving was not significantly different (21.2% and 22.5%) between the groups. A more recent study compared the use of intramammary cephapirin benzathine to two subcutaneous injections of tilmicosin (5 mg/kg at dry off and 4-day later). The cure rate for intramammary treatment with cephapirin was considerably higher (78%) as compared to the cure rate for subcutaneous tilmicosin (9%) (Nickerson et al., 1999). The vast majority of studies do not currently support the use of additional therapies at dry off.

Conclusion

Treatment is an important aspect of mastitis control. The most effective treatment strategies include presumed identification of mastitis pathogens and the use of antibiotics for an appropriate duration for the expected pathogen. Researchers are continuing to evaluate the cost to benefit ratio of treatment of subclinical mastitis during the lactation period but it is important to recognize that the decision not to treat subclinical mastitis may have some unintended negative consequences. The use of intramammary antibiotics to treat prepartum heifers should be considered by many herds and the use of dry cow therapy remains integral to the production of high quality milk.

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