

TEN MYTHS OF MASTITIS THERAPY

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1. Once a *Staph aureus* cow, always a *Staph aureus* cow.

Although a difficult therapeutic challenge, intramammary infections (IMI) caused by *Staph aureus* are not necessarily incurable. Depending on the herd, 30 to 70% of individual quarters may be cured during the dry period. Thus, if a little judgement is exercised in selection of cows as therapeutic targets, treatment can be reasonably effective and economical. The dry period offers the best time to administer therapy because milk withholding expenses are negligible, residue risks are reduced, and it is the optimum time in the lactation cycle of the cow to enhance the synergy between antimicrobial activity and the immune system. It is potentially beneficially to administer systemic antimicrobials to dry cows in addition to intramammary therapy to enhance the elimination of IMI. This combination may be beneficial to lactating cows as well, however the costs of therapy and potential decreased efficacy should be considered carefully before treating lactating cows. Prolonged use of intramammary therapy (multiple regimens of labeled doses) may also increase efficacy, and vaccination prior to therapy may augment efficacy as well. However, cows with multiple infected quarters, or that are chronically infected (several months with elevated SCC) are poor therapeutic candidates. Additionally, it is highly recommended to use culture and susceptibility information to assist drug selection and dosing regimens.

References:

- Erskine, RJ, et al, JDS, 77:3347, 1994
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2. It doesn't pay to treat clinical mastitis / All clinical mastitis cases should be treated.

This is dependent on the severity and history of the affected cow. Although many herds have reduced the use of antimicrobials for the therapy of clinical mastitis, it can not be assumed that treatment is not necessary for all cases in all herds. Severe clinical mastitis (cow displaying systemic signs) should almost always be treated initially until a clinical evaluation can be made, in addition to bacteriology, on the second or third day after the onset of the mastitis.

The usefulness of intramammary antimicrobials in affecting the outcome of clinical mastitis caused by coliform bacteria is questionable, although systemic therapy may be beneficial. Additionally, severe mastitis caused by other organisms such as staphylococci and streptococci are likely to benefit from therapy, even if only to control the infection to a less severe state. Therapy should be discontinued within one to two days after severe clinical cases have responded to the point where the cow has started to recover dry matter intake and milk production, despite continued swelling or abnormal milk. It is difficult to correctly determine the causative bacteria for a severe clinical mastitis case from clinical signs of the cow. This forces a therapeutic decision before we have culture results available. Additionally, it is typical for 30 to 35% of all clinical mastitis cases that are sampled to yield no bacteria on culture.

Interest in a non-therapy approach to mastitis was initiated by a California study in which bacteriologic cures for mild clinical mastitis caused by streptococci or coliforms did not differ between cows treated with cephalosporin, amoxicillin, or no antibiotic (oxytocin and stripping). However, an economic analysis of this study determined that although milk production and survival in herd did not differ between antimicrobial and non-treated cows, the rate of recurring cases was higher in the non-treated cows, especially for streptococcal IMI. A case report from Colorado supported this concern for non-therapy of streptococcal cases. A marked increase in the incidence of clinical mastitis caused by streptococci and an increase in herd somatic cell count was reported following the initiation of a non-antimicrobial program for clinical mastitis. Additionally, an Illinois study determined that bacteriologic cure and return to normal udder appearance occurred more frequently when clinical mastitis caused by streptococcal mastitis was treated with IV oxytetracycline, intramammary cephalosporin, and supportive care, as compared to supportive care only. Thus, initial cases may benefit from therapy, particularly if the causative agents are streptococci. Nonetheless, therapy of mild clinical mastitis is not likely to be effective or economical when treating chronic, recurring cases. It is important to monitor success of therapy by SCC and rate of recurring cases, in some herds, minimal therapy may be beneficial.

References:

- Erskine, RJ, et al., *AJVR*, 53:375, 1992
- Pyorala, S, et al., *JDS*, 77:453, 1994
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- Morin, DE, et al., *JAVMA*, 213:676, 1998
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3. Oxytocin and stripping is the way to treat.

Although popular, frequent stripping of the quarter may not be beneficial for all cases. For severe mastitis cases where the secretion of the gland is watery and discolored, frequent stripping may actually be more harmful than beneficial. Certainly, if cows are having difficulty releasing or ejecting milk because of clots and flakes that plug the teat canal, these

should be stripped out. However, more frequent stripping has not been demonstrated in a clinical study to be any more beneficial than regular milking intervals.

In study from the U.K., 20 IU of oxytocin before each milking for 6 milkings only cleared 25% of experimental *Strep uberis* infections. However, after the oxytocin dosing, sustained use of intramammary antibiotics was found to effectively eliminate all infections. Thus, oxytocin use alone was not beneficial as compared to antibiotic use.

Reference:

Hillerton, JE, et al., JDS, 82:93, 1999.

4. Keep on treating a clinical mastitis case until the milk returns to normal.

The immune system of the cow eliminates infectious organisms, antimicrobials act in a supporting role towards this goal. While initial recognition of a clinical mastitis case should initiate immediate therapeutic decisions, non-responsive cases need to be recognized as failures of the immune system. This is especially the case for chronic recurring infections. Following coliform mastitis cases, it is typical for the cow's immune system to continue to react, even after a successful elimination of the infection. The quarter may go agalactic (give up milking). This is a normal response to inflammation and cannot be "turned off" with antibiotics. Many cows milk well with three quarters, and in the case of coliform mastitis, affected quarters are likely to come back to full production in the following lactation. Additionally, non-responsive quarters are often the sign of a resistant organism, including yeasts and *Pseudomonas*. Thus, it should be a very rare situation where a clinical mastitis case is treated for more than 4 to 5 days. If the average number of days that milk is discarded per case of clinical mastitis in a herd is greater than 5, the therapy protocol should be reviewed.

5. Commercial infusion tubes today aren't as good as the old days.

It may appear in the literature that we are not achieving cure rates that are comparable to previous reports from twenty-five years ago, however current assessment of efficacy is more critical in determining a true cure than was previously reported. Previous results had less rigorous definitions of cures and had greater levels of *Streptococcus agalactiae* as part of the data. Antimicrobial susceptibilities for many of the mastitis organisms isolated from laboratories have not changed over the years. The problem is our therapeutic regimens, not the drugs we select.

References:

MacDonald, TJ, et al., AJVR, 37:1185, 1976

Mackie, DP, Vet Record, 123:515, 1988

Erskine, RJ in *Antimicrobial Therapy in Veterinary Medicine*, 3rd ed Iowa State Univ Press, p.712, 2000.

6. A double dose of tubes is better.

Excepting aminoglycosides and fluorquinolones, the most critical factor in successful antimicrobial therapy is the length of time that the drug concentration in milk and mammary tissue is above the MIC (minimum inhibitory concentration) for the causative bacteria, not how much higher the maximum drug concentration achieves over the MIC. Increasing the dose only gains one half-life of effective concentration. It is much more beneficial to extend the therapeutic time period, beyond the typical two to three days for most commercial preparations.

7. Extra label products are more effective.

The pharmacokinetics and antimicrobial activity for most antimicrobials has not been tested in relation to the presence of milk and mammary inflammation. Some of the typical extra-label drugs used for mammary infusions have been demonstrated to be detrimental to leukocyte function at the concentrations achieved in milk after administration. Most drugs that are available for systemic use in cattle penetrate into the gland very poorly, with the exception of macrolides, fluorquinolones, or oxytetracycline. Drug clearance and withholding for extra-label drugs is unknown, especially in mastitic cows. The majority of studies that have investigated extra-label drug use for the treatment of mastitis have determined that there is little positive effect as compared to cure rates achieved by labeled drug regimens. This is especially true for intramammary infusions.

References:

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Shpigel, NY, et al., JDS, 80:327, 1997
Morin, DE, et al., JAVMA, 213:676, 1998
Erskine, RJ, et al., AJVR, 53:375, 1992

8. If after two treatments there are still clots and flakes, I need to switch to a new antibiotic.

This is the opposite of sound pharmacodynamics. The key to successful therapy is staying with the same drug as long as possible. Thus it is better to stay with the same drug for a longer period of time, rather than switching. Switching drugs starts the therapeutic clock all over again, and can lead to bacterial resistance. Thus, if the best potential of therapy is to be realized, then consideration should be given to staying with the same therapy rather than switching. This concept is in contrast to the approach to mastitis therapy that tends to minimize milk withholding periods. If not achieving desirable results with extended therapy, consider if it is an IMI that should not be treated, i.e, bacteria not susceptible, or a recurring chronic infection. Use of susceptibility results can be useful for predicting therapeutic efficacy for streptococcal and non-chronic IMI.

Reference:

Owens, WE, et al., JDS, 80:313-317, 1997.

9. First generation cephalosporins and synthetic penicillins are more effective treatments for clinical mastitis because they are active against Gram-positive pathogens and coliforms.

Antimicrobial susceptibility data suggests that 50 to 80% of *E. coli* isolates from mastitis cases are susceptible to ampicillin. However, susceptibility data based on disk assay methods can be misleading. The “breakpoints” or zones of inhibition that determine susceptibility of the bacteria to the drug are generally based on human drug metabolism and clinical experience. It is difficult to maintain inhibitory concentrations of ampicillin for greater than 50% (MIC₅₀) of *E. coli* isolates if the drug is administered IM, virtually impossible to maintain inhibitory concentrations for 90% (MIC₉₀) of the isolates. Less than 5% of *Klebsiella* isolates are susceptible to this drug. Coliform organisms have been demonstrated to be susceptible to first generation cephalosporins 70 to 90% of the time. However, systemic formulations for use in cattle are not available or pharmacologically practical. Thus, in order to achieve potentially high enough concentrations of these drugs for the treatment of coliform mastitis, intramammary therapy would be the preferred route of administration. However, the reality is that intramammary infusions of these products, or any current antimicrobial is not likely to affect the outcome of clinical coliform mastitis.

The practical problem when facing a therapeutic decision regarding clinical mastitis is whether it is a mild or severe case. In either situation, intramammary infusions are indicated for severe cases and perhaps non-chronic mild cases to cover the potential for Gram-positive bacteria. All the labeled products on the market for use as an intramammary infusion in dairy cattle demonstrate good efficacy against Gram-positive bacteria. If there is concern regarding a severe clinical mastitis case that may be a potential coliform mastitis, intramammary drug infusions should be given to address the possibility of streptococci and staphylococci infections, and an antibiotic that may have activity against coliform organisms should be administered systemically.

References:

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10. My mastitis therapy program is doing OK even if I don't keep records. I'll just do what the (choose one or all) a) other farms are doing, b) what I read about in the trade magazine, c) my vet or local feed mill has in stock, d) what I used for the last cow that I treated.

This is the most critical problem in most herds. Without knowing the causative agents, the risk factors associated with clinical mastitis cases in a herd (lactation, days in milk, season, etc), and clinical outcomes (SCC, milk production, rate of recurring cases, days out of tank, and culling) after therapy, it is impossible to know if a therapy plan is a good one. A good method to measure success of a clinical mastitis prevention and therapy program is to ask “have we discarded less milk from clinical mastitis cases this year than last year?” How much milk did you discard in your herd last year?

Editor’s Note: This paper is included in the proceedings as an addendum to Dr. Gary Neubauer’s presentation “Mastitis Treatment Strategies: Old Myths and New Facts”.