

## Treatment of Subclinical Mastitis Infections

Pamela L. Ruegg, Jose Pantoja and Dhananjay Apparao  
University of Wisconsin, Madison

### Take Home Message

- It is possible to achieve satisfactory cure rates using intramammary antibiotics for treatment of subclinical mastitis during the lactation period but the cost effectiveness of the treatments will vary depending on herd & cow specific factors
- Treatment of subclinical mastitis during lactation is not generally cost effective for herds that are able to effectively reduce transmission of contagious pathogens unless there is an alternative use of the milk that would be discarded
- If treatment is undertaken, cow specific risk factors should be considered to identify cows that are most likely to respond to treatment

### Introduction

Mastitis can occur in both a clinical and subclinical form. Clinical mastitis is readily apparent and easily detected by abnormalities in milk or the udder or the occurrence of secondary clinical signs. Treatment decisions for clinical mastitis are generally motivated by a desire to return milk to a saleable state. Detection of subclinical mastitis is more difficult because clinical signs are not apparent and the use of indirect tests (such as enumeration of somatic cells or bacteriological analysis of milk samples) is required for detection. Consequently, subclinical mastitis is often undetected and has the greatest economic consequences because of long term effects on milk yields. Production losses due to subclinical mastitis are estimated to cost the U.S. dairy industry \$1 billion dollars annually (Ott, 1999).

With the exception of infections caused by *Streptococcus agalactiae*, treatment of cows diagnosed with subclinical mastitis is usually discouraged because of discard of saleable milk results in financial loss. However, the maintenance of cows with subclinical mastitis within the dairy herd has some potentially negative unintended consequences. Cows infected with subclinical mastitis have greater somatic cell counts (SCC) and the farmer may be paid less for the milk. Cows with cases of subclinical mastitis may have periodic clinical episodes that require antibiotic treatments and withholding of milk. Herds with bulk tank SCC >400,000 cells/ml have increased risk of antibiotic residue violations (Ruegg and Tabone, 2000). The failure to treat subclinical mastitis may allow invasive pathogens the opportunity to establish chronic infections that are unlikely to respond to antibiotic therapy. Cows with subclinical mastitis maintain a reservoir of infection within the dairy herd and increase the potential exposure of uninfected cows to contagious pathogens. 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 losses of 0.4 kg and 0.6 kg of milk per day in first lactation and older cows, respectively (Hortet and Seegers, 1998). In spite of these potentially negative effects, few mastitis experts advocate treatment of subclinical mastitis during lactation. The objective of this paper is to review recent research examining the efficacy and cost effectiveness of treatment of subclinical mastitis during lactation.

Identification of Cases and Pathogens Causing Subclinical Mastitis

Identification of infected quarters and the arrival at a provisional diagnosis of the most common pathogens is the first step toward making a treatment decision. Both clinical and subclinical mastitis can be caused by a wide variety of pathogens, therefore it is imperative that a sufficient (>25 quarter samples) number of milk samples are submitted for culture. When control procedures have not been successful, contagious pathogens (*Staph aureus* & *Strep ag*) are usually most prevalent but many other pathogens can cause subclinical mastitis (Table 1).

Table 1. Recovery of pathogens from quarters secreting visually normal milk

	Pol & Ruegg, 2007 40 Herds, BTSCC <sup>c</sup> >250,000 cells/ml N = 5672 samples	Pantoja & Ruegg, 2008 1 Herd, milk samples obtained at dry off N = 804	<sup>d</sup> SCC (cells/ml)	Apparao & Ruegg, 2008 5 herds, only milk samples from CMT + quarters N = 426	SCC (cells/ml)
Bacteriological Outcome					
No Growth	53%	88%	90,000	33%	165,500
CNS <sup>a</sup>	15%	8%	220,000	31%	396,000
Strep spp. <sup>b</sup>	7%	3%	994,500	8%	1,024,000
Staph aureus	4%	0%		2%	2,631,300
Gram negative	1%	<1%	2,785,000	8%	1,089,000
Strep ag	1%	0%		0%	
Other	15%	<1%	685,000	10%	384,000
Contaminated	8%	0%	116,000	8%	170,000

<sup>a</sup>Coagulase-negative staphylococci; <sup>b</sup>no Strep ag included; <sup>c</sup>Bulk tank somatic cell count was required to exceed 250,000 cells/ml for enrollment in this study; <sup>d</sup>median SCC of quarter milk samples obtained for those pathogens

When herds have controlled contagious mastitis, most subclinical mastitis is caused by Gram-positive opportunistic pathogens that initiate a moderate to severe inflammatory response. However, the SCC responses of quarters subclinically infected with Gram-negative pathogens can be similar to SCC responses of quarters infected with *Staph aureus* or *Strep spp.*. By definition, milk from subclinically infected quarters appears normal, even when millions of somatic cells are present. Detection of subclinical mastitis is dependent on use of screening tests (such as the CMT) or monthly SCC testing. The ability of these tests to predict the recovery of bacteria from milk samples is fair at best. A quarter SCC threshold of >200,000 cells/ml is generally considered to be evidence of subclinical mastitis. In herds that have not controlled *Staph aureus* or *Strep ag*, about 10-25% of quarters above that threshold will be bacteriologically negative and about the same proportion of quarters below the threshold may be bacteriologically positive (McDermott et al., 1982; Dohoo et al., 1991 and Schepers et al., 1997). When contagious pathogens have been controlled, the rate of “false negatives” (inability to recover bacteria from quarters that exceed the threshold) is even greater. In data obtained from the University of Wisconsin dairy herd, the rate of false negatives increased from 14-70% as the threshold SCC increased from 50,000 to 300,000 cells/ml (Pantoja and Ruegg, unpublished data). Before initiating a treatment program for subclinical mastitis, it is important to perform culturing of milk samples to arrive at a diagnosis of the likely pathogen and also to

select a well defined detection plan for identification of quarters that are candidates for treatment.

Efficacy of Intramammary Treatments for Treatment of Subclinical Mastitis

The use of intramammary antibiotics to treat cows subclinically infected with *Strep agalactiae* is usually successful and results in increased production and dramatic decreases in bulk tank SCC (Erskine and Eberhart, 1990). In contrast, it is not considered cost-effective to treat most cows that are chronically infected with *Staph aureus* because cure rates during lactation are generally quite poor. The difference in these therapeutic outcomes is thought to be related to differences in the site of infection. Some pathogens (*Strep ag*, *CNS* etc.) infect only superficial surfaces (such as the epithelial surface of the ducts). Other pathogens (*Staph aureus*, *Strep uberis* etc.) are invasive and it is more difficult to achieve a therapeutic concentration of antimicrobial at the site of infection. Spontaneous cure rates for some superficial mastitis pathogens are quite acceptable. We recently observed bacteriological cure rates of 61% (control; n = 59 quarters) and 69% (2 treatments with IMM Pirlimycin; n = 58 quarters) for subclinical infections caused by *CNS* (Apparao and Ruegg, unpublished).

Bacteriological cure rates after antimicrobial treatment are often monitored and may appear acceptable but other clinical outcomes may be much more relevant. A randomized, controlled clinical trial was recently conducted to examine short and long term effects of intramammary therapy of subclinical mastitis (Sandgren et al., 2007). Milk samples were obtained from cows with monthly SCC values of >300,000 cells/ml and cows from which *S. aureus* (n = 48), *Str. dysgalactiae* (n = 43) or *Str. Uberis* (n = 35) were isolated were enrolled in the study. Bacteriological cure rates were determined using milk samples collected at 42-52 days after treatment and SCC, milk yield, occurrence of a clinical case and culling were monitored for 10 months after treatment (Table 2). Bacteriological cure rates were 25%, 74% and 60% for infections caused by *Staph aureus*, *Strep dysgalactiae* and *Strep uberis*, respectively. While treatment with antimicrobial compounds initially appeared to improve outcomes, the effect of treatment disappeared as the lactation progressed. As previously reported (Deluyker et al., 2005), the impact of treatment was significantly affected by a number of cow related risk factors. Cure rates were lower for older cows, infections with *Staph aureus* and for cows with greater SCC before treatment. Overall, the authors concluded that beneficial long-term effects of antimicrobial treatment during lactation were not observed for these pathogens.

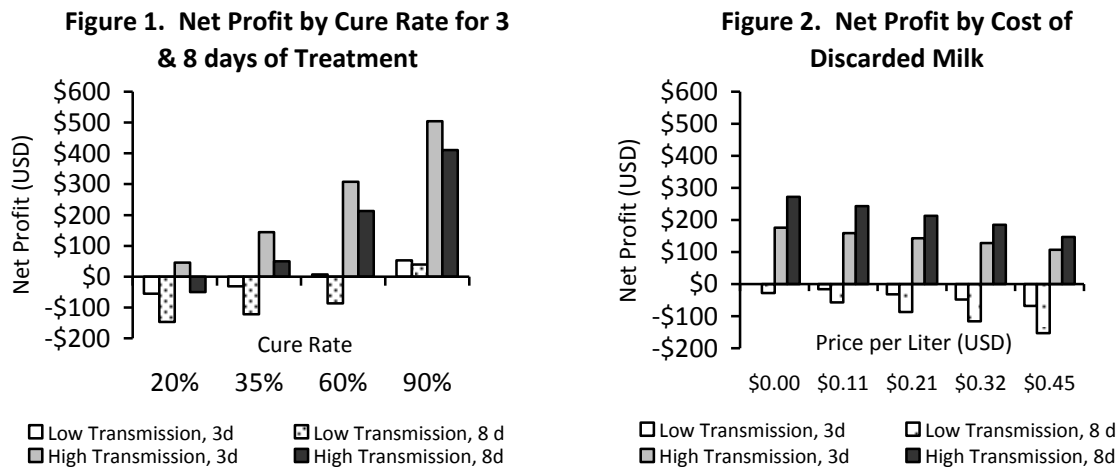
Table 2. Clinical Outcomes after treatment of subclinical mastitis (from Sandgren et al., 2007)

Treatment	N	Bacteriological Cure (%) 42-58 days <sup>a</sup>	SCC (cells/ml x 1000)		Milk (kgs) 2 <sup>nd</sup> test	Recurrence (%)		Culled (%) 10 months
			42-58	2 <sup>nd</sup> test		5 months	10 months	
IM <sup>b</sup>	40	77%	782	243	26.1	10%	25%	24%
IMM <sup>c</sup>	42	65%	439	239	24.5	19%	31%	50%
Control <sup>d</sup>	44	18%*	1353*	419*	26.0	11%	20%	24%

<sup>a</sup>time after treatment; <sup>b</sup>intramuscular benzyl penicillin potassium 15,000iu/kg, 2x for 5 days; <sup>c</sup>intramammary 300,000IU penethamate hydroiodide once daily for 5 days; <sup>d</sup>control group received no treatment; \* $P < 0.05$

### Cost Effectiveness of Treatment

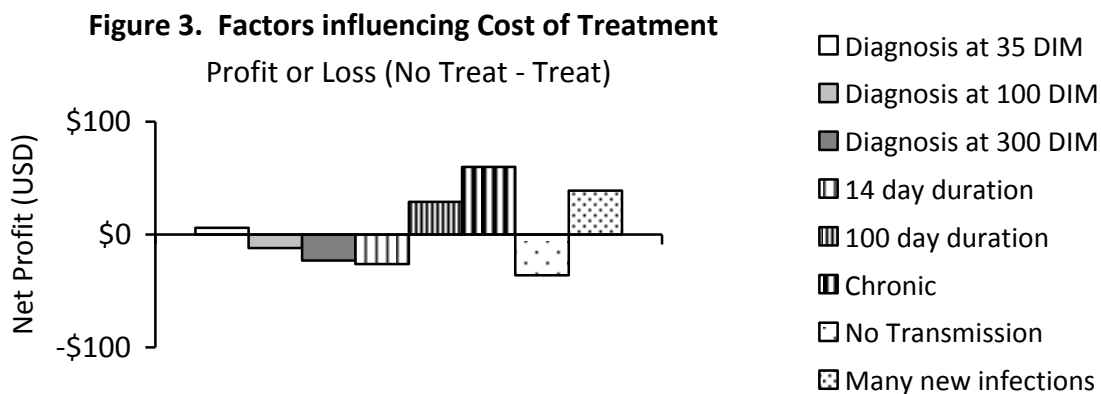
The cost effectiveness of treatment during lactation is driven by the interaction between the value of discarded milk and the potential benefits of treatment. If there is a positive production response to treatment then potential benefits of treatment are more evident. Except for *Strep ag*, very little data that documents significant production responses after lactational therapy of subclinical mastitis is available. A recent study modeled the economic benefits of treatment (3 or 8 days) of subclinical mastitis caused by *Staph aureus* (Swinkels et al., 2005). The researchers created a partial budget that included reduced costs for prevention of clinical mastitis, prevention of new subclinical infections and prevention of culling. Reduced revenues included discarded milk and extra costs associated with treatment and milk cultures. No additional revenue from milk was included. Results were presented for 2 herd scenarios: 1) low probability of contagious transmission (each infected cow infected 0.3 other cows) or 2) high probability of transmission (each infected cow infected 5 other cows). When the probability of transmission was high, the net profit was about \$140 and \$210 USD for 3 day and 8 day treatments, respectively. When the probability of transmission was low, treatment resulted in net losses of \$30-\$85. Importantly, the authors identified that economic benefits of treatment of subclinical mastitis are dependent on the cost of discarded milk and host, pathogen and management factors that influence the probability of cure (Figure 1 & 2).



In low transmission herds, when the probability of cure was high (about 60%), 3 days of treatment was barely profitable. As reported by Sol et al.(1997) cure rates for mastitis caused by *Staph aureus* have been shown to decrease with age (from 81 % for cows  $\leq 48$  months of age to 55% for cows  $\geq 96$  months), the number of infected quarters (from 73% for 1 infected quarter to 56% for 4 infected quarters) and increasing SCC. In herds with low transmission, only treatment of 1<sup>st</sup> or 2<sup>nd</sup> parity cows in early lactation (<100 days in milk) with SCC < 1,000,000cells/ml and single quarter infections were found to be profitable. The authors concluded that treatment of subclinical mastitis may be justified during lactation depending on

factors specific to the herd, the cows and the particular strain of Staph aureus. It is also important to note that this research reinforces the importance of emphasizing management practices that reduce transmission among cows.

A second study by the same group was conducted to evaluate economic effects of treatment of chronic subclinical mastitis caused by Strep uberis (Steenefeld et al., 2007). This study examined the impact of the probability of cure, probability of becoming clinical, transmission to other cows and various physiological effects of mastitis. Overall, the cost of treatment was about \$180 USD as compared to the costs of about \$160 USD if cases were not treated. However, there were important herd and cow level factors that influenced costs (Figure 3) and the authors concluded that treatment decisions should be made on an individual cow basis.



### Recommendations

Subclinical mastitis is caused by a variety of mostly Gram-positive bacteria and many of these cases have a high rate of spontaneous cure. Many subclinical pathogens are responsive to intramammary treatments using commercially available antibiotic products but there are important cow & herd factors that will influence the cost effectiveness of treatment. The decision to treat subclinical mastitis is dependent upon the type of pathogens that are prevalent and diagnostic efforts (milk culturing) must be undertaken before developing a treatment protocol. When Staph aureus is prevalent, treatment of subclinical cases is only advised for animals that have a high probability of cure. If environmental streptococci are common, treatments of chronic infections of cows diagnosed before 100 days in milk may be cost effective. In all instances, the value of the discarded milk must be taken into account and treatment of some subclinical cases of mastitis may be cost effective for herds with alternative uses of discarded milk (for example, pasteurizing and feeding to calves). Overall, treatment is an important aspect of mastitis control but implementation of management practices that reduce transmission of subclinical pathogens are always more cost effective.

### References

1. Deluyker, H. A., S.N. Van Oye, and J. F. Boucher. 2005. Factors affecting cure and somatic cell count after pirlimycin treatment of subclinical mastitis in lactating cows. *J Dairy Sci.*, 88:604-614.
2. Dohoo I.R. and K.E. Leslie. 1991. Evaluation of changes in somatic cell counts as indicators of new intramammary infections. *Prev. Vet. Med.* 10:225–237.
3. Erskine, R. J. and R. J. Eberhart. 1990. Herd benefit to cost ratio and effects of a bovine mastitis control program that includes blitz treatment of *Streptococcus agalactiae*, *J Am Vet Med Assoc* 196:1230-1235.
4. Hortet, P. and H. Seegers. 1998. Calculated milk production losses associated with elevated somatic cell counts in dairy cows: review and critical discussion. *Vet Res.* 29:497-510.
5. McDermott, M. P., H. N. Erb, and R. P. Natzke. 1982. Predictability by somatic cell counts related to prevalence of intramammary infection within herds. *J. Dairy Sci.* 65:1535–1539.
6. Ott, S. Costs of herd-level production losses associated with subclinical mastitis in US Dairy Cows. 1999. Pp 152-156 in Proceedings of the 38<sup>th</sup> annual meeting of National Mastitis Council, Arlington VA. Natl Mast Coun. Madison WI.
7. Pol M, and P. L. Ruegg. 2007. Relationship between antimicrobial usage and antimicrobial susceptibility of Gram-positive mastitis pathogens. *J Dairy Sci* 90:262-273.
8. Ruegg, P.L., and T. J. Tabone. 2000. The relationship between antibiotic residue violations and somatic cell counts in Wisconsin dairy herds. *J Dairy Sci.*, 83:2805-2809.
9. Sandgren, C. H., K. P. Waller, and U. Emanuelson. 2007. Therapeutic effects of systemic or intramammary antimicrobial treatment of bovine subclinical mastitis during lactation. Cited online in early release: *Vet J* (2007), doi:10.1016/j.tvjl.2006.12.005
10. Schepers A.J., T.J. Lam, Y.H. Schukken, J.B. Wilmink and W.J.Hanekamp. 1997. Estimation of variance components for somatic cell counts to determine thresholds for uninfected quarters. *J. Dairy Sci.* 80:1833–1840.
11. Sol, J., O. C. Sampimon and J. J. Snoep and Y. H. Schukken. 1997. Factors associated with bacteriological cure during lactation after therapy for subclinical mastitis caused by *Staphylococcus aureus*. *J Dairy Sci* 80:2803-2808.
12. Steeneveld, W., J. Swinkels, and H. Hogeveen. 2007. Stochastic modeling to assess economic effects of treatment of chronic subclinical mastitis caused by *Streptococcus uberis*. *J Dairy Res* 74:459-467.
13. Swinkels, J.M., H. Hogeveen, and R.N. Zadoks. 2005. A partial budget model to estimate economic benefits of lactational treatment of subclinical *Staphylococcus aureus* mastitis. *J Dairy Sci.* 88:4273-4287.