Oxytocin and Other Alternatives to Antibiotic Therapy of Clinical Mastitis

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Abstract

Mastitis is the most common cause of antibiotic use in adult dairy cows. Antibiotic treatment of clinical mastitis incurs the cost of the drugs used, the discarded milk, and the loss of the option to cull the cow until after the withdrawal time has elapsed if treatment fails. Oxytocin (OT) has been proposed by practitioners as an alternative to antibiotic therapy of mild clinical mastitis. Efficacy of OT has not been established against untreated controls. Safety of OT is reviewed; OT at doses used for milk ejection appears safe, but at higher doses it may affect the estrous cycle and may cause abortion in heat-stressed cattle. Efficacy of intramammary antibiotics in clinical mastitis caused by environmental pathogens is not well established in controlled research. A recent study by the author comparing OT to intramammary cephapirin or amoxicillin used according to the label in mild clinical environmental mastitis showed no overall difference in bacterial or clinical cure rates. Antibiotics did have higher clinical cure rate than OT in infections due to pathogens other than coliforms and streptococci. Protocols for treatment of clinical mastitis on dairy farms should be developed cooperatively by producers and veterinarians based on knowledge of the pathogens involved on each farm. Treating every mastitic quarter with intramammary antibiotics in a herd with mostly environmental mastitis is not economically justifiable. Records of mastitis treatment should be kept so that chronic cows can be identified. On farms with mostly environmental mastitis, antibiotics should be used selectively. Antibiotic therapy of quarters from which no pathogen can be isolated and coliform quarters is difficult to justify. For certain infections combinations of intramammary and systemic antibiotic therapy may be necessary. Use of OT to increase milk ejection, increased frequency of milkout, and anti-inflammatory therapy may be important elements of mastitis treatment protocols. Chronic cows in environmental mastitis herds are unlikely to respond to treatments that have already failed, and should be culled, dried, or segregated.

Introduction

Mastitis is the most common cause of antibiotic use in adult dairy cows. In surveys of well-managed herds with somatic cell counts (SCC) under 150,000 and virtually no mastitis due to coagulase-positive *Staphylococcus aureus* (*Staph.*) or *Streptococcus agalactiae* (*Strep. ag.*), 35-55% of lactations had one or more incidents of clinical mastitis.[2,4,7,8,9] In such herds, 15-40% of the clinical cases had no bacteria isolated from the milk, 21-43% had coliforms, and 9-32% had environmental streptococci.[1,2,4,7] This contrasts with high SCC herds with a significant prevalance of *Staph.* and *Strep. ag.*, where most of the clinical mastitis is caused by those organisms.[4] As more herds respond to quality incentives and stricter SCC standards by controlling the contagious pathogens, we can expect the relative importance of the environmental pathogens to continue to increase.

Antibiotic treatment of clinical mastitis incurs the cost of the drugs used, the discarded milk, and the loss of the option to cull the cow until after the withdrawal time has elapsed if treatment fails. It also incurs the risk of contaminating the bulk tank with antibiotics, and all of the expensive regulatory consequences of violative antibiotic residues under the revised Pasteurized Milk Ordinance, including a significant loss of revenue from milk. Those who design treatment protocols should be sure that the benefit of antibiotic treatment outweighs these very real economic costs.

Some dairymen and veterinarians have already decided that the risks of antibiotic use in most clinical mastitis cases exceed the benefits and have stopped treating clinical mastitis cows with antibiotics in herds with a low prevalence of the contagious organisms. They emphasize protocols of frequent milkout aided by oxytocin (OT) injections and anti-inflammatory drugs, along with heightened attention to management of housing, bedding, and premilking hygiene to prevent infection with environmental pathogens. While the anecdotal reports about such programs are favorable, there is no published data about the rate of chronic or recurring infections in such herds compared to herds using antibiotics, nor on the effects of these infections on bulk tank SCC or subsequent milk yield.

Efficacy and Safety of Oxytocin

I have been unable to find controlled research studies in the literature that document the effectiveness of OT therapy in clinical mastitis. One study[15] showed that OT levels were higher in cows inoculated with 12.5 or 25 mcg of *Escherichia coli* endotoxin in two quarters

than in cows infused with saline. This suggests that lack of OT is not the reason for the often-observed failure of milk letdown in cows with clinical coliform mastitis.

The optimal dosage of OT and the optimal time of administration has not been established by research. Some clinicians have expressed the opinion that a small dose should be given at the end of milking, to aid in the expulsion of residual milk and to reduce strippings. The label dose for aid in milk letdown is 10-20 IU, while that for obstetrical use is 100 IU. One researcher recently confirmed that 20 IU would elicit milk letdown in 1.5-2 minutes and would also aid in ejection of strippings milk.[16]

Oxytocin is rapidly inactivated in the body and the potential for toxicity is low. Occasional anaphylactic reactions are reported in women given OT at parturition. No ill effects on health were found in a study in which cows received twice daily doses of 20 IU OT at milking throughout lactation.[16] Reproductive performance was the same in the treated and control groups in this study.

Oxytocin is part of the normal control mechanism of luteolysis in the estrous cycle in cattle. Oxytocin is secreted by thecorpus luteum and acts on uterine receptors in the estrogen-primed uterus during late diestrus.[17] The binding of OT to the uterine receptors in turn triggers the pulsatile secretion of prostaglandin F2α(PGF) by the uterus. This positive feedback mechanism causes luteolysis and allows estrus to occur. Injection of 230 IU of OT in cows on days 2-6 of the estrous cycle caused a significant increase in PGF concentration in the blood and shortened the cycle of two of six treated cows to 10-12 days.[18] However in another study injection of about 230 IU (.33 IU/kg) at days 5, 10, and 15 of the cycle had no effect on cycle length, estradiol, or progesterone concentrations.[19] On the other hand, continuous infusion of OT in open heifers caused lengthened estrus cycles.[17] ThePGF response to OT injection is suppressed after day 6 of the cycle and restored at d 13-16.[20] Immunization of sheep against OT prolongs the luteal phase of the estrous cycle.[21] OT also has a direct inhibitory effect on gonadotrophin-stimulated steroid hormone (progesterone, in particular) in isolated luteal cells.[21] Exogenous OT does not induce parturition in late-gestation cattle.

Oxytocin also has a role in the effects of heat stress on reproduction. Chronically heat-stressed ewes have smaller lambs than unstressed ewes, partly in response to reduced uterine blood flow.[22] The decrease in uterine blood flow is accompanied by a 60% increase in serum OT. Uterine blood flow was also reduced by exogenous OT and antidiuretic hormone (ADH) injections. OT and ADH are similar in structure and are both secreted by the posterior pituitary. Heat stressed pregnant heifers tended to have a higher PGF response to the injection of 100 IU OT. Five of six heat stressed pregnant heifers, compared to ⅕ nonstressed heifers, were classified as responders to OT (PGF concentration >193 pg/ml).[23] It would appear from this study that heat stress antagonizes the suppressive effect of the embryo on uterine secretion of PGF in response to OT.

In summary, OT used at the low doses used for milk ejection has little toxic potential aside from rare anaphylactic reactions. However at higher doses it has been reported to affect cyclicity of cows in the early and late parts of the cycle and the level of progesterone secreted by the corpus luteum. Heat-stressed animals may be slightly more likely to abort due to OT-induced PGF release from the uterus, and chronic OT administration may reduce uterine blood flow and fetal size and viability. One study reported no health or reproductive effects from twice-daily injections of 20 IU of OT.[16] Since endotoxin can cause prostaglandin release and luteolysis it would be hard to determine whether altered cyclicity or abortion was due to mastitis itself or to OT used as an aid in mastitis therapy.

Antibiotic Therapy of Mild Clinical Mastitis

There is no published evidence that the benefits of antibiotic treatment of mild clinical mastitis outweigh the risks and costs. We have found only one study on intramammary antibiotic treatment of mastitis under field conditions that includes untreated controls. In this abstract[25] results of three treatments were reported. Treatments occurred over an eight year period. Treatment A was 100,000 IU penicillin and 150 mg novobiocin used twice. Treatment B was the same medication used three times. Treatment C was 200 mg of cephapirin used twice. Treatments A and B were used from 1979-1985 and treatment C from 1985-87. Group D were untreated controls, which were split into two groups contemporaneous with the antibiotic-treated groups. No contagious pathogens were reported. The abstract does not state whether the treated quarters were clinically abnormal, and only bacterial cure rates are reported. For environmental staphylococci, cure rates were 62.9%, 70.4%, 67.3%, and 0-7.3% for A, B, C, and D. For environmental streptococci, cure rates were 50.2l%, 58.3%, 48.7%, and 1.9-7.7%. For all coliforms cure rates were 23.2%, 13.0%, and 7.9-13.4% for B, C, and D. For *Klebsiella* sp., cure rates were 20.4%, 6.5%, and 6.3-7.7% for B, C, and D. For *E. coli* alone, cure rates were 40.9%, 25.9%, and 20-47.7% for B, C, and D. Statistical tests of results were not reported but group numbers ranged from 20 to 413. It would appear that these antibiotics were of benefit in the staphylococcal and streptococcal infections, and of marginal or no benefit in the coliform infections.

Chamings[3] reported an 87% clinical cure rate in cows that were not treated with antibiotics for mild

clinical mastitis caused by *Staph.* and *Streptococcus uberis*. The bacteriological cure rate for both organisms was 19-20% This study did not have a positive control group for comparison. This type of mastitis is treated on most dairies with mastitis tubes, possibly in conjunction with extralabel parenteral antibiotics or anti-inflammatory drugs. All of the approved intramammary mastitis preparations on the market in the United States as of June, 1992 were tested against subclinical infections with gram-positive organisms. Only one has a label claim for mastitis caused by Escherichia coli, which is the most frequently isolated udder pathogen in many outbreaks of clinical mastitis in herds with low SCC.

The pharmacology of mastitis therapy has recently been reviewed.[6,13,14] Reasons why antibiotic therapy might fail are summarized in Table 1. The underlying assumption of research on mastitis to date has been that the primary aim of therapy is to kill bacteria, and that the normal state of milk in the udder is sterility. Yet subclinical infections with environmental and contagious pathogens probably exist in every herd.[4] Clinical mastitis may be due to the flareup of subclinical infection in a stressed cow, and often signs of clinical mastitis persist after bacteria can no longer be isolated from the affected quarter. In the short run, the economically important clinical outcome in the treatment of clinical mastitis is not the absence of bacteria, but rather the return of milk and udder to their normal state, so that the cow's milk can once again be sold.

Table 1. Reasons for Failure of Antibiotic Therapy of Clinical Mastitis

A. Drug can not reach all sites of infection
   1. Microabscess formation (*Staph.*)
   2. Blockage of ducts with clots of denatured milk.
   3. Poor distribution of drug in udder, due to swelling, edema, or intrinsic properties of drug.
   4. Abscessation.
   5. Fibrosis.
   6. Intracellular bacteria (*Staph.*)

B. Bacteria already killed by cow's immune system before therapy begins.

C. Inadequate concentration of drug to effect killing.
   1. Poor distribution of drug in udder.
   2. Absorption of drug from milk into systemic circulation.
   3. Failure of drug to be absorbed by affected tissues.
   4. Drug milked out at subsequent milking.
   5. Failure of parenteral drug to cross blood-milk barrier.
   6. Failure of client or veterinarian to repeat treatments in time to maintain MIC in tissue long enough to effect killing.

D. Bacteria refractory to killing by drug.
   1. Bacteria not in rapid growth phase required for drug to act.
   2. Organism is resistant to usable antibiotics (e.g., *Pseudomonas, Mycoplasma*, yeasts, etc.)
   3. Drug with gram-positive spectrum used on gram-negative infection.
   4. Acquired resistance by organism.
   5. Emergence of L-forms, "naked" acapsular forms that resist beta-lactam antibiotics.

E. Reinfection of affected quarter.

Antibiotic Therapy of Specific Mastitis Pathogens.

Only one common pathogen, *Streptococcus agalactiae*, is highly sensitive to and easily cured by approved intramammary antibiotics used according to the label. In most herds with low SCC the prevalence of *Strep. ag.* is low or zero. Many such herds have no *Strep. ag.* isolated from bulk tank samples or clinical cows for years. In herds with *Strep. ag.* infected cows, use of intramammary antibiotics is easily justified on medical, if not economic grounds because it stops the shedding of bacteria by the cow with clinical mastitis and because *Strep. ag.* is very sensitive to all of the antibiotic tubes on the market. Treatment of clinical mastitis in lactating cows is not effective, however, in reducing prevalence in the herd unless it is part of a total control program.[11] Only an integrated program of teat dipping, milking machine maintenance, milking hygiene, and dry cow treatment can bring about a long-term reduction in prevalence.

While all mastitis tubes carry a label claim for *Staph.*, thecure rate is so low that dairymen are best advised to consider it negligible.[10,11,12] The cure rate in *Staph.* cows is low because the organism forms microabscesses in the udder tissue outside the ducts, where intramammary drugs can not reach it. It also can survive inside white blood cells, makes L-forms, and can acquire resistance to commonly used antibiotics.[10] The best hope for successful antibiotic treatment of Staph-infected cows is in young cows with recent infections. Parenteral treatment may increase the chance of a cure.[10] In herds with a high prevalence of *Staph.* infections, the emphasis should be on teat dipping, culling, milking machine maintenance, milking hygiene, and segregation of infected cows to gradually reduce the prevalence of the infection. Antibiotic treatment may reduce shedding of Staph. by clinical mastitis cows and thus help reduce the spread, but it will not reduce overall prevalence in the herd significantly.[11]

In herds with low SCC and low prevalence of contagious pathogens, clinical experience and published surveys[1,2,4,7] show that about 15-40% of pretreatment

milk samples from cows with clinical mastitis are negative for bacterial growth on blood agar. We presume that these samples containing too few organisms for a positive culture result reflect the ability of the cow's immune system to rid the affected quarter of pathogens. Antibiotic treatment of these cows is difficult to justify; the problem is that we can not know which cows they are until after treatment has to be initiated. The aim of treatment should be to return the quarter and the milk to normal, not to prevent the spread of infection. Anti-inflammatory drugs or immune modulators would seem indicated, rather than antibiotics.

A fairly large group of so-called "minor" pathogens --minor in prevalence in the industry, not to the infected cow or her owner--are refractory to all antibiotic treatment. This group includes the genera *Mycoplasma, Pseudomonas, Pasteurella, Serratia, Prototheca, Mycobacterium, Nocardia, Bacillus,* the yeasts and fungi, and *Actinomyces pyogenes.*

In surveys of clinical mastitis in herds with low SCCs, coliform organisms account for about one-third of isolates from clinical cows. Coliform organisms can cause mastitis of severity ranging from subclinical to peracute. Erskine[5,6] has shown that clinical signs appear in experimental coliform mastitis after bacterial numbers in milk have peaked, and that treatment of these cows with intramammary gentamicin did not affect clinical outcome. Toxic mastitis can be reproduced by infusing endotoxin without living organisms into the udder; most of the clinical signs of coliform mastitis are thought to be due to the effects of endotoxin.[5] Treatment should therefore aim primarily at removing endotoxin from the udder with frequent and complete milkout and at counteracting the effects of endotoxin with appropriate antiinflammatory and supportive treatments. The most important part of a treatment protocol for coliform cows is to milk the quarter out completely and often, possibly with the help of OT injections. Unfortunately, treatment must begin before the organisms involved can be identified, and the appearance of the abnormal secretions alone is not a reliable basis for an etiologic diagnosis, except perhaps in the most severe cases.

The environmental streptococci and the coliforms account for the majority of environmental clinical mastitis cases where a diagnosis is obtained. Philpot[11] cited a cure rate for clinical mastitis caused by environmental streptococci of 36%. Erskine[6] states that acceptable cure rates (>75%) are attainable with a combination of intrammary antibiotics and intramuscular procaine penicillin G. Tyler[13] states that response of clinical *Streptococcus uberis* infections to antibiotic therapy during lactation is poor, although a combination of parenteral and intramammary erythromycin appears to be the most efficacious treatment. More research is needed on these organisms, particularly on any long-range benefit from antibiotic treatment in eliminating chronic infections during lactation.

The challenges in treating clinical mastitis in a herd with low SCC are the impossibility of establishing an etiologic diagnosis at the time of first treatment, the fact that about a third of cows being treated have already cleared the infection, and the fact that in the case of the coliforms at least, the primary aim of treatment has to be to counteract the effects of endotoxin rather than reducing bacterial numbers. This must be accomplished without incurring undue risk of antibiotic contamination of milk, in the absence of clear experimental evidence from controlled trials that antibiotic treatment of mastitis is efficacious or cost-effective. Clearly more research is needed.

California Study of Efficacy of Intrammary Antibiotics.

A controlled study of intramammary treatment for mild clinical mastitis caused by environmental bacteria was recently completed at the Veterinary Medicine Teaching and Research Center of the University of California, Davis.[24] We compared the efficacy of cephapirin and amoxicillin mastitis tubes to that of OT alone in the treatment of mild clinical environmental mastitis in 254 quarters. Both tubes were used according to label instructions. Oxytocin cows received 100 units of OT intramuscularly just before milking. No other treatments were used on cows in the study. No contagious pathogens were isolated from any of the clinical cases. Cows treated in the study had mild mastitis, that is, abnormal milk with or without udder swelling, and no signs of systemic illness, and were randomly assigned to one of the three treatments. Cows that did not improve or got worse during the observation period were called treatment failures and withdrawn from the trial. A clinical cure was the return of the affected quarter and milk to normal at the eighth milking after initial diagnosis and treatment. A bacteriologic cure was the failure to isolate the primary pathogen present at the first milking at the eighth milking and at 20 days after initial treatment. Results are shown in in tables 2, 3, and 4. There were no significant differences in overall clinical cure rates by milking 9 after diagnosis or in bacterial cure rate by day 21 between antibiotic- and OT-treated quarters, although there was a significant effect of antibiotics on clinical cure in the category of "other bacteria," which were pathogens other than coliforms and streptococci.

In this study only short-term effects have been analyzed so far. Analysis of the long-term differences between mastitic quarters treated with OT and those treated with antibiotics is still underway. In this study tubes were used strictly according to label (two doses of

Table 2. Pretreatment bacterial isolates of 3 treatment groups in randomized field trials of therapies for milk clinical mastitis, California, 1991-1992 (%)+.

Variable	Treatment			P value
	Oxytocin	Amoxi-mast	Cefa-lak	
Coliform	33.3	41.9	37.3	0.93
Streptococcus sp.	26.7	23.0	26.7	
Other	15.2	10.8	13.3	
Negative	24.8	24.3	22.7	
Number of cows	105	74	75	

+ Of the 94 coliforms, 81 (86%) were *E. coli*. Of the 65 *Streptococcus* sp., 27 (42%) were *S. uberis*, 19 (29%) were *S. dysgalactiae*, and 14 (22%) were *S.viridans*. Of the 34 "Other" bacteria, 14 (41%) were *Staphylococcus* sp. (primarily *S. hyicus*), 9 (26%) were mixed infections, 3 (9%) were *Bacillus* sp., and 3 (9%) were *Corynebacterium* sp.

Table 3. Bacterial and clinical cure (%) by treatment group and herd in randomized field trial of therapies for mild clinical mastitis, California, 1991-1992.

Herd	Treatment			P value
	Oxytocin	Amoxi-mast	Cefa-lak	
Bacterial cure %+				
Herd 1 (n=64)	10/26 (38.5)	9/20 (45.0)	11/18 (61.1)	0.33
Herd 2 (n=31)	6/10 (60.0)	6/10 (60.0)	6/11 (54.5)	0.96
Herd 3 (n=43)	12/21 (57.1)	3/11 (27.3)	5/11 (45.5)	0.27
Total (n=138)	28/57 (49.1)	18/41 (43.9)	22/40 (55.0)	0.61
Clinical cure %				
Herd 1 (n=82)	23/33 (69.7)	20/24 (83.3)	17/25 (68.0)	0.41
Herd 2 (n=86)	19/36 (52.8)	12/25 (48.0)	16/25 (64.0)	0.50
Herd 3 (n=86)	28/36 (77.8)	18/25 (72.0)	17/25 (68.0)	0.69
Total (n=254)	70/105 (66.7)	50/74 (67.6)	50/75 (66.7)	0.99

+ Of 254 cases, 61 were culture negative prior to the 1st treatment, 43 were given additional treatment prior to 9th milking, 2 were treated between 9th milking and 21 days, 2 were dried prior to 21 days, 4 were culled before 9th milking, and 4 were culled before 21-day sample.

cephapirin and three of amoxicillin) and OT was given at three consecutive milkings. The protocol may not correspond with the way in which OT and antibiotic tubes are actually used on most dairy farms.

Protocols for Mastitis Treatment on Dairy Farms

In the past, the standard recommendation was to treat all cows with clinical mastitis with antibiotic tubes used according to the label. In herds with low SCC where all clinical mastitis is caused by environmental bacteria, we can design better treatment protocols that minimize antibiotic use, reduce the risk of residues, and still allow flexibility to beef affected cows if treatment does not work. A responsible treatment protocol requires that permanent records of clinical mastitis be kept so that a cow's past history can be consulted before treatment is initiated.

Table 4. Bacterial and clinical cure (%) by treatment group and bacterium isolated at pretreatment sampling in randomized field trial of therapies for mild clinical mastitis, California, 1991-1992.

Herd	Treatment			P value
	Oxytocin	Amoxi-mast	Cefa-lak	
Bacterial cure %+				
Coliforms (n=63)	15/26 (57.7)	8/21 (38.1)	8/16 (50.0)	0.41
Streptococcus sp. (n=49)	10/21 (47.6)	6/13 (46.2)	11/15 (73.3)	0.23
Other bacteria (n=26)	3/10 (30.0)	4/7 (57.1)	3/9 (33.3)	0.48
Positive cultures (n=138)	28/57 (49.1)	18/41 (43.9)	22/40 (55.0)	0.61
Clinical cure %				
Coliforms (n=94)	22/35 (62.9)	21/31 (67.7)	14/28 (50.0)	0.36
Streptococcus sp. (n=65)	17/28 (60.7)	9/17 (52.9)	14/20 (70.0)	0.56
Other bacteria (n=34)	7/16 (43.7)	7/8 (87:5)	9/10 (90.0)	0.02
No bacteria isolated (n=61)	24/26 (92.3)	13/18 (72.2)	13/17 (76.5)	0.18
Total cultures (n=254)	70/105 (66.7)	50/74 (67.6)	50/75 (67.7)	0.99

+ Of 254 cases, 61 were culture negative prior to the first treatment, 43 were given additional treatment prior to 9th milking, 2 were treated between 9th milking and 21 days, 2 were dried prior to 21 days, 4 were culled before 9th milking, and 4 were culled before 21 day sample. There were no contagious pathogens cultured.

Clinical mastitis should be classified before treatment as mild or severe. Mild mastitis would be characterized by abnormal milk and slight udder swelling, while severe mastitis would include abnormal milk, severe swelling, the risk of losing the quarter, and systemic illness (fever, off feed, diarrhea).

Before a protocol is put in place, the veterinarian should collect and analyze the results of sampling of clinical mastitis cows to determine the pathogens generally involved on the particular farm in different seasons. On a farm with a significant incidence of clinical mastitis caused by *Strep. ag.*, for example, antibiotic tubes should probably be used on most clinical cases, while on a farm where a third of the clinical samples show no growth, another third yield *E. coli*, and no *Strep. ag.* is ever found antibiotic use is hard to justify.

Dairy personnel should be trained to look at the cow's record before beginning a course of lactating cow treatment. The people making the treatment decisions, usually milkers or herdsmen, need to be trained and trusted to make these decisions properly. The veterinarian and the owner should develop a treatment protocol based on the known past history of pathogens in the herd, age of the cow, reproductive status, milk yield, relative value in the herd, past mastitis history, other unsoundnesses (locomotor problems, poor udder conformation, etc.), and the severity of clinical signs. For example, a cow that is below the herd average, open, and late in lactation will most likely be culled eventually anyway and might as well be culled now that she has mastitis. An average first-lactation cow that is late in gestation should be dried off early, since dry cow preparations are stronger, stay in the udder longer, are more likely to clear up the infection than lactating cow tubes, and present less risk of contaminating the bulk tank with antibiotics. Cows with persistent or recurring

infections despite past treatment are unlikely to respond to a repetition of the same treatment protocol. The risky approach on these cows is to turn to extralabel use of parenteral antibiotics, with all of the risk of illegal residues it entails. A safer approach is to evaluate the cow's record and the severity of the infection and decide either to cull the cow, dry her off, treat her, or to let her recover on her own. A young, high-yielding cow in early lactation with mild mastitis might be treated aggressively, with an emphasis on frequent and complete milkout.

Treatment protocols should be modified to fit the culling philosophy and goals of each dairyman. A dairyman who is trying to build up herd numbers, for example, may be more inclined to dry off a clinical mastitis cow than one whose facility is overcrowded and is looking for room for a new heifer. A dairyman may be unwilling to cull his purebred cows under any circumstances.

On large dairies an aid in the management of clinical mastitis is to have a designated mastitis string, which is milked last, just before the hospital or antibiotic string. The mastitis string is milked into the bulk tank. It contains all cows that have had clinical mastitis during the current lacatation, chronic high SCC cows, and cows known to be infected with *Staph.* that the owner does not want to cull. On some dairies it might include slow-milking cows and cows with poor udder shape that require extra attention at milking time. On others the slow cows are in a separate group. Cows in the mastitis string are generally not to be treated with antibiotics when they get clinical mastitis again. They are either culled, or milked out with the aid of OT injections until their milk is normal. Since abnormal milk may not be put into the bulk tank, these cows with clinical mastitis must either be milked into a separate bucket or put in the hospital string until their milk is normal. Cows may leave the mastitis pen only to be dried-off or culled, or if their individual SCC remains below 200,000 for three consecutive test days and they are not known to be infected with a contagious pathogen.

On dairy farms where facilities permit, one small pen may be designated a non-antibiotic hospital. This pen can then be milked at twice the frequency of the other pens by bringing the cows to be milked in the middle of each shift. Since no antibiotics are used in this pen, the pipeline does not have to be washed after it is milked, and the milk can be diverted to calf milk or down the drain.

Treatment of clinical mastitis is the most common use of antibiotics on dairy farms and the most common cause of illegal antibiotic residues. On well-managed dairy farms most mastitis is caused by the environmental pathogens. There is no data from well-controlled studies demonstrating the efficacy of antibiotic treatment of clinical mastitis caused by the environmental pathogens, nor on any benefit of antibiotic treatment on chronic or persistent infections. However even in the absence of data the veterinarian can be very helpful in developing treatment protocols that greatly reduce the use of antibiotics and decrease the risk of violative residues.

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