Drug therapy for mastitis treatment and control has been a hotly debated issue in the US. The initial issue was the effect of drugs, chiefly antibiotics, on cheese manufacturing processes. Reports in the press highlighting contamination of milk and other dairy products with antibiotics and other animal drugs quickly raised the issue of food safety and resulted in the intervention of governmental agencies regulating the use of animal medications in dairy cattle. Guidelines for drug use in dairy cattle established by FDA and on-farm quality assurance programs developed by the National Milk Producers Federation and the American Veterinary Medical Association have successfully prevented accidentally contaminated milk from reaching the processing and consumer level of the dairy industry. Most recently global concerns for developing antimicrobial drug resistance and the need to develop more prudent and judicious use of animal drugs have caused the veterinary profession to reconsider the intervention methods of treating and controlling mastitis in dairy cattle.

**Antibiotic Susceptibility Testing**

Antibiotic susceptibility testing is of limited value when addressing the treatment needs of specific cases of mastitis. The inherent delay in obtaining the necessary information may allow the infection to become more firmly entrenched and resistant to treatment. Treatment decisions need to be made early and should be based on clinical diagnosis not on culture results or pending antibiotic susceptibility tests. However, antibiotic susceptibility testing may prove more useful when determining the susceptibility patterns of persistent pathogens in the herd such as environmental streptococci and, to some degree, coliform infections. More importantly it may indicate which antimicrobial products would not likely be effective. Antibiotic resistance in vitro is likely to predict antibiotic resistance in vivo. However antibiotic susceptibility in vitro will not necessarily translate to antibiotic susceptibility in vivo. Specific pathogen defense mechanism may not be apparent in vitro but can effectively resist treatment in vivo. Some drugs such as erythromycin, penicillin, penicillin-novobiocin and cephalirin, which can alter neutrophil function, may affect treatment outcome in a negative way.

**Subclinical Mastitis**

Subclinical mastitis is responsible for the greatest financial losses associated with mastitis. It is estimated to cause 70% of the total losses. These losses however are difficult to demonstrate to producers since they are associated with decreased milk production caused by the effects of chronic inflammation of the mammary gland. Subclinical mastitis can be controlled with:

1.) Effective dry cow therapy.
2.) Effective and consistent application of sanitary procedures during milking.
3.) Identification of farm specific risk factors for mastitis and development of management protocols to eliminate or minimize those factors.
4.) Selective culling of chronically infected cows.
5.) Adequate treatment of clinical cases.

Infections caused by *Streptococcus agalactiae* historically have been a major cause of subclinical mastitis in the US. It is the only specific pathogen to cause subclinical mastitis that warrants the immediate treatment of lactating cattle as infections are identified. The fact that it is an obligate parasite of the udder and is very sensitive to many of the commonly available approved medications make treatment of *Strep ag* infections during lactation a positive economic investment. Other agents such as
*Staphylococcus aureus* and environmental streptococci that may cause a significant number of subclinical infections are less likely to be successfully treated during lactation and are more likely to respond to appropriate treatment at dry off or should be considered for culling. Subclinical infections due to environmental *Strep* sp. may be more amenable to treatment in early lactation if they are identified and treated in early lactation. Environmental Staphylococci and Streptococci infections generally last about 70 days but may endure through the current lactation. This treatment approach to environmental *Streptococcus* infections will require careful scrutiny and monitoring of new infections, culture results and treatment protocol design.

In herds where contagious mastitis has been eliminated or new infections are controlled, environmental infections are the predominant cause of subclinical infection. Eradication of these organisms as a source of infection is unreasonable. They are best controlled by means of sanitary milking procedures; a high level of environmental hygiene that result in minimal exposure of the teat end to pathogens; immunization (Coliforms) and optimization of overall nutrition and health.

**Clinical Mastitis**

The signs and severity of clinical mastitis vary considerably. Clinical signs are dependant upon both host and pathogen factors. Pathogen factors include such things as species of bacteria, virulence of the strain, and size of the inoculum. Host factors include parity, stage of lactation somatic cell count, level of immunity and the presence of concurrent disease.

Mild and moderate cases of mastitis are most often treated by and at the discretion of the milkers or herd management. Selection of the treatment regimen is often based upon clinical impression of effectiveness.

Today many herd managers are adopting written standard operating procedures (SOP) for the assessment, treatment and outcome evaluation of clinical mastitis. The SOP approach to disease management on the farm is largely due to concern for drug residue violations. Other reasons for adopting SOP’s include a desire to minimize drug use, provide drug therapy to those situations and animals that will most benefit, prevent over-treatment or inappropriate treatment, and to provide consistency and accountability to treatments. Veterinary involvement in creating standard operation procedures is essential. It can provide the practitioner with the opportunity to influence drug use and purchases, to ensure proper and adequate treatment, and the ability to assess treatment outcomes and, thereby, alter treatment protocols when necessary.

Establishing case assessment criteria, treatment protocols and outcome assessment algorithms should be kept relatively simple and easy to follow. Examples of these algorithms are available within the mastitis module.

**Acute Clinical Mastitis**

Veterinarians are most frequently called to treat acute or peracute mastitis. These are typically severe cases characterized by systemic signs including high fever, anorexia, swollen and painful quarter(s), weakness, diarrhea and recumbence. These signs are typically associated with endotoxemia associated with coliform mastitis or with septicemia from coliform, streptococcus, *Staphylococcus aureus* or other environmental pathogen. A separate document concerning the pathobiology of acute mastitis is available at this site. It contains an extensive explanation of the pathogenesis of mammary gland infection and the relationships among infection, endotoxemia, lesions and systemic disease.

The use and effectiveness of antimicrobials for acute mastitis is still being debated. In many instances of acute mastitis the infection has been cleared by the host by the time the infection has been detected. In these cases, it is argued that intervention with antibiotics is unnecessary, that the signs observed are due to endotoxemia not infection. In these cases treatment should concentrate on supportive therapy such as fluid replacement and countering the inflammation associated with endotoxemia.

Septicemia is another potential complication of acute mastitis, although some researchers consider this to be an uncommon occurrence. Others have estimated the occurrence of septicemia to be as high as 30% of all coliform infections. Another complication of infection is the development of chronic infection in those
situations where the acute infection was not cleared during the early pathogenesis of the disease. Clearly preventing septicemia or the development of chronic infection would justify the use of antibiotics as part of the treatment scheme for acute mastitis. Research has identified some of the risk factors associated with the severity of signs of acute mastitis as well as the development of septicemia and chronic infection. More severe clinical signs often characterize acute mastitis during the peripartum or early postpartum period. This is in all likelihood associated with the level of immunosuppression present at this time. Cows with very low somatic cell levels (<50,000 cells/ml) in milk frequently suffer from more severe signs of infection and are more likely to develop bacteremia or chronic infection of the gland.

Acute mastitis in animals with moderate to high somatic cell counts is less common and less severe as is acute mastitis in animals in late lactation (>150 DIM), or those receiving core antigen vaccination for coliform mastitis. Under these circumstances the use of antibiotics either systemically or locally (IMM) is probably not necessary. Routine analysis of treatment records and outcomes of a specific herd should be helpful in determining treatment guidelines for acute mastitis including the need for antimicrobial therapy.

Treatment Modalities

Attempt to limit opportunities for accidental contamination of bulk milk with drugs has led to the recommendation of frequent stripping of the affected quarter with the aid of oxytocin to enhance milk let-down. This recommendation is based on the fact that many mild cases of clinical mastitis are self-limiting and that the animals own defense mechanisms can successfully clear the infection. This approach has been used successfully in many herds, however there is a need to continually monitor infection rates, particularly chronic infection rate and somatic cell counts. Over time chronic infection rates can increase causing slow but progressive increases in bulk tank somatic cells. Treatment trials in California comparing treatment of mild cases of clinical mastitis with cephalixin, amoxicillin or oxytocin with frequent stripping of the affected quarter demonstrated no differences in clinical cure rate by the ninth day or bacteriological cure rate by day 21 among treatment groups for cows with environmental streptococcus and coliform infections. However the oxytocin treated cows had more relapses and additional infections due to environmental streptococci. The net result was no difference in days of discarded milk, milk yield, or culling when antibiotics were used as opposed to use of oxytocin alone.

The availability of antibiotics for parenteral use against coliform mastitis in the US is very limited. Macrolides such as erythromycin and tilmicosin are not effective against coliform bacteria. Gentocin and other aminoglycosides have been shown to also be ineffective in vitro against mastitis and there is a voluntary ban on their use in cattle in the US because of concern for tissue residues. Penicillin, oxytetracycline, ceftiofur and florfenicol offer some choices, although penicillin and ceftiofur do not penetrate udder tissue well. Their use, all be it extra-label, does provide some options for treatment.

In a published study done at the University of Illinois cows with clinical mastitis were treated with antibiotics and supportive treatment or with supportive treatment alone. The antibiotic treatment group received intramammary cephalixin twice daily until clinical signs had resolved and oxytetracycline IV once daily if systemic signs were present. Supportive measures included oxytocin and frequent stripping, flunixin meglumine every eight hours if systemic signs were present and fluid therapy if the animal was dehydrated. Cows with coliform and environmental streptococcus mastitis that were treated had significantly higher clinical cure rates by the tenth milking than did cows not receiving antibiotics. When all cases of mastitis were considered, treatment with antibiotics resulted in a higher cure rate by 14 days, fewer recurrent coliform mastitis infections, and fewer new infections in other quarters and reduced severity of disease. Although these treatment choices are extra-label this work does show that there are effective options available for treatment of acute clinical mastitis.

Supportive Treatment

Treatment with a variety of anti-inflammatory drugs is indicated and can be beneficial when fever and a swollen, painful quarter characterize clinical mastitis. Choice of anti-inflammatory agents will depend on the severity of the disease. Currently only the corticosteroid drugs
dexamethasone (Azium®) and isoflupredone (Prefef 2X®) are approved for use in lactating dairy cattle. Their use systemically or directly in the mammary gland may be indicated in initial treatment of acute coliform mastitis. Systemic effects of the drugs and potential consequences in pregnant animals (dexamethasone) must be considered before administration.

Non-steroidal anti-inflammatory drugs (NSAIDS) such as flunixin meglumine, aspirin, phenylbutazone, and ketoprofen have also been used extensively to treat the signs of inflammation and endotoxemia. None of these drugs are however approved for use in dairy cattle. Their use in acute clinical mastitis is warranted to relieve the pain and swelling of infection. They have been shown to return near normal appetites to affected cows. Recent published findings indicate that tissue residues of phenylbutazone in culled cattle at slaughter are a concern. The prolonged half-life of the drug in cattle and the nature of phenylbutazone sensitivity of humans suggest that this drug not be used in cattle. Flunixin meglumine (Banamine) is probably the logical drug of choice in most cases. It is approved for use in cattle as an adjunct treatment for pneumonia but not for use in lactating cattle. Slaughter withdrawal times are established and milk withhold recommendations are available from Food Animal Residue Avoidance Databank (FARAD).

Fluid replacement is necessary for those animals showing signs of dehydration. Treatment with hypertonic saline solution (4ml/kg) will provide immediate expansion of extracellular fluid volume and temporarily counter some of the effects associated with endotoxemia. Follow up fluid therapy is also indicated in the form of oral supplementation or long term administration of parenteral fluids which often requires the administration of 10 to 20 liters. The state of hydration of affected animals should be assessed several times daily.

Hypocalcemia and hypokalemia are not uncommon occurrences associated with acute coliform mastitis. Administration of calcium by injection or orally is indicated and oral administration of potassium chloride may be indicated in anorexic cattle. After initial administration blood levels can easily be monitored.

**Conclusions**

Public and regulatory concerns for food safety and quality will have a continuing and greater influence on animal disease treatment and drug availability in the future. Treatment choices must be based on sound scientifically based strategies. It is imperative that veterinarians become involved in the development and administration of farm specific treatment protocols (SOP’s) and encourage early detection of infections. Infection rates, treatment outcomes and milk quality parameters should be monitored and reviewed routinely. Farms should have well established milk quality and mastitis goals that are communicated to all involved parties. Effective use of SOP’s will require educating farm labor on the early detection, administration and recording of treatments. Records should be kept in accordance with PMO and AMDUCA requirements.