Treatment of gram-negative Mastitis

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Gram-negative mastitis is caused by bacteria which persist and propagate in the farm environment. Feces, bedding, and water sources often are implicated. Examples of environmental pathogens include *Escherichia coli, Klebsiella sp.,* and *Enterobacter sp.* There probably exist real differences in the clinical behavior of mastitis caused by different environmental pathogens, but this hypothesis is not supported by scientific observations. Although contagious spread of these bacteria is possible, transmission from the environment is more likely.

Two approaches are available to the control of mastitis. These approaches are cow-centered and environment-centered intervention. Cow-centered approaches are appropriate for contagious mastitis syndromes. Infected cattle are identified and treated, isolated, or culled. Transmission between cows is targeted because the infected cow is the primary reservoir of infection.

These strategies will have minimal impact in herds with environmental mastitis problems, because the environment, rather than the infected cow is the reservoir of infection. There is no treatment regimen with proven efficacy for gram-negative mastitis. Furthermore, the microbiologic cure of infected cattle will not eliminate reservoirs of infection. Consequently, control strategies which emphasize the identification and treatment of cattle with environmental pathogens are doomed to failure. General recommendations for the control of environmental mastitis center on improving the general level of environmental hygiene and maximizing immune responses with good nutrition and vaccination programs. Use of water is limited in the milking parlor. Only clean and dry cows are milked. Cows are provided with fresh palatable feedstuffs immediately after milking, encouraging them to remain standing while the teat sphincter closes. Cows are provided with a clean comfortable area to lie down and only bacteriologically inert bedding is used.

Environmental infections generally cause transient infections. The majority of these infections will cause transient inflammation with mild clinical signs. A small number of cows will have severe systemic manifestations of disease. Typically, milk bacterial numbers peak prior to the onset of clinical signs. Most gram-negative infections will undergo spontaneous cures within four weeks following infection; however, some gram-negative infections, particularly *Klebsiella sp.* and *Serratia sp.* may persist for extended periods of time. Therapeutic intervention with either intramammary or systemic antibiotics has never been proven to either cure or beneficially alter the course of clinical or subclinical gram-negative mastitis.

The self-limiting nature of environmental infections and the absence of effective therapy suggests that aggressive treatment of subclinical and mild clinical gram-negative mastitis is contraindicated. We must recognize the limited efficacy and negative economic consequences of treatment. In addition to labor, veterinary, and drug costs, these programs will necessitate extensive milk and slaughter withdrawals. Furthermore, the present regulatory climate creates substantial disincentives for antibiotic use. Mild cases of mastitis should be treated using local therapy only. Local therapy entails milking of the affected quarter at 2 to 3 hour intervals. Some practitioners also will use an intramammary infusion of a commerically available antibiotic tube.

Administration of oxytocin will aid in the removal of milk and inflammatory mediators from the inflamed gland. Proven efficacy of antimicrobial therapy of lactating cow mastitis is limited to Streptococcal pathogens. Consequently, herds which have eradicated or controlled *S. agalactiae* may gain little from antibiotic therapy of cows with mild clinical mastitis. Cows which have abnormal milk persisting after 3 days of therapy will probably not respond to antimicrobial therapy.

More aggressive therapy may be indicated in individual cows with acute disease. The goal of treatment is to salvage the productivity and health of the individual

cow. Treatment of individual cows will have no bearing on the herd incidence of mastitis. Selective screening and treatment protocols based on either milk somatic cell counts or cultures to identify subclinical gram-negative mastitis are specifically contraindicated. Systemic therapy of mastitis in lactating cows should be limited to cows with systemic clinical signs; fever (rectal temperature > 103.5 F), poor appetite, lack of rumen motility, dehydration, and scleral injection. Systemic therapy may include parenteral antibiotics, anti-inflammatory agents, and fluid and electrolyte therapy. The costs associated with drugs, veterinary services, and milk and meat withdrawals associated with aggressive systemic therapy dictate that local and systemic disease be clearly differentiated.

The lack of mastitis treatment regimens with demonstrated efficacy has led to the use of empirical and often irrational treatments. Such treatments place livestock health, well-being, and productivity at risk. Development of rational treatment regimens is dependent on a conscientious physical examination, identification of the etiologic agent, an unbiased assessment of treatment efficacy, and development of treatment plans which consider individual cow health, economic constraints, and avoidance of milk and meat residues.

The ideal antibiotic for treatment of acute coliform mastitis would be readily concentrated in the mammary gland, be effective against gram-negative bacteria, and have short milk and meat withdrawal times. No such antibiotic is currently approved for use in lactating dairy cattle. Penicillins, cephalosporins, and aminoglycosides are poorly distributed to the mammary gland following systemic therapy. Aminoglycoside antibiotics have prohibitively long slaughter withdrawals following intravenous or intramuscular therapy. Sulfonamides generally have poor activity against gram-negative bacteria. Tetracyclines and macrolide antibiotics like erythromycin are readily transferred to the mammary gland following systemic therapy; however, macrolide antibiotics have greatly reduced activity in inflammatory secretions. Although oxytetracycline and erythromycin penetrate the mammary gland, gram-negative mastitis pathogens are frequently resistant to these antibiotics. Antibiotics with favorable patterns of *in vitro* sensitivity and distribution properties will likely become available in the next decade (fluoroquinolones, fluphenicol, and thiamphenicol). It should be noted that *in vitro* sensitivity is not equivalent to *in vivo* efficacy. Few of the antibiotics we have mentioned here are approved for use in lactating dairy cattle.

The decision whether or not to administer antibiotics continues to be a source of debate among dairy practitioners. Most veterinarians agree that antibiotics have minimal impact on the course of intramammary infections. Some practitioners will withhold antibiotics. They contend that the systemic manifestations of disease noted in cows with gram-negative mastitis are systemic manifestations of mediator-induced shock which have been activated by a local gram-negative infection. This point-of-view is supported by the results of one study in which the percentage of cows with acute mastitis with positive blood cultures was negligible. Other practitioners will administer antibiotics because some cows with gram-negative mastitis may be bacteremic or have decreased resistance to secondary infections. Many cows with acute gram-negative mastitis are severely neutropenic, consequently, there exists a reasonable rationale for the administration of prophylactic antibiotics. This approach is supported by one recent study which observed that a significant number of cows with gram-negative mastitis did have positive blood cultures. If our sole goal is to treat circulating bacteremia, the antibiotic distribution to the mammary gland becomes a minor concern. This is the train of thought which supports many practitioners' decision to administer antibiotics to cows with severe, acute gram-negative mastitis. **However, we should emphasize that no antimicrobial regimen has demonstrated efficacy, either medical or economic, in the treatment of clinical gram-negative mastitis. Consequently, the role of antimicrobial therapy remains limited.**

Most cows with systemic signs of acute mastitis will probably benefit from anti-inflammatory therapy. Several experimental studies have demonstrated the beneficial effects of these compounds in ameliorating clinical and biochemical manifestations of gram-negative mastitis. The most commonly used anti-inflammatory agents are flunixin meglumine, phenylbutazone, and glucocorticoids. Anti-inflammatory agents are not innocuous compounds. Glucocorticoids (dexamethasone, betamethasone, prednisolone, and prednisone) are potentially immunosuppressive and will induce abortions in some animals. Non-steroidal anti-inflammatory agents can cause kidney damage and abomasal ulcers. Adverse reactions occur most frequently in severely dehydrated cattle that are given repeated doses. Phenylbutazone has an exceptionally long half-life in cattle and dosage intervals shorter than 48 hours are contraindicated. Dimethylsulfoxide (DMSO) is probably contraindicated in septic shock states due to its diuretic properties. Generally, anti-inflammatory agents are administered early in the course of acute systemic disease and discontinued after one or two treatments.

Although many clinicians recognize the importances and value of fluid therapy in the treatment of acute mastitis there is little documented evidence substantiating the efficacy of this procedure. Cost, safety, and speed of administration all favor oral fluids. A gen-

eral rule is that oral fluids are most effectively used in subjects with a primary dehydration, normal gastrointestinal absorption, and less than < 10% dehydration. Many cows with acute mastitis are effectively excluded using these criteria. Intravenous fluid therapy is a therapeutic option which deserves strong consideration. Effective fluid therapy is probably one of the most beneficial treatment option in cases of endotoxin-induced shock. Intravenous fluids may be administered rapidly in the first hour of treatment (15 to 20 ml/lb or a total volume of 20 L) and at a reduced rate (5 to 10 ml/lb) thereafter. Total doses will vary from 20-60 L depending on cow size, hydration status, and presence of ongoing fluid losses. Most cows with acute gram-negative mastitis will have a mild azotemia and hypokalemia, hyperglycemia, moderate to severe hypocalcemia and normal acid-base status. In the absence of serum chemistry results, near-isotonic sodium chloride based solutions, judiciously supplemented with calcium and potassium, are likely the most suitable choices for intravenous fluids in cattle with acute mastitis. Excessive glucose administration in already hyperglycemic cows should be avoided because this type of therapy may cause an osmotic diuresis and further contraction of circulating blood volume.

The bulk of informed opinion currently recognizes that antibiotic therapy of mastitis should ideally be restricted to instances where the practitioner is reasonably certain of therapeutic efficacy and economic benefit (either production or reductions in the reservoir of infectious bacteria offsetting direct and indirect treatment costs). Clinical trials and experimental studies have demonstrated no benefits to antibiotic therapy in cattle with gram-negative mastitis. Systemic antibiotic therapy should be restricted to cows with systemic clinical signs. Given that a large percentage of cattle with clinical coliform mastitis will not remaining productive following clinical disease, extended milk or meat withdrawal times should be avoided. Rational therapeutic plans for severe cases of mastitis will require extra-label drug use. Such plans will necessitate the existence of a valid veterinarian-client-patient relationship. Consultation with a veterinary practitioner will aid in the selection of efficacious and safe compounds and doses. **Practitioners, in consultation with the Food Animal Residue Avoidance Database, can set appropriate times and testing procedures to prevent the sale of residue contaminated milk.**

References

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Abstract

Effects of treatment with topical ivermectin three and eight weeks after turnout on nematode control and the performance of second-season beef suckler cattle

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Two groups of yearling suckled beef calves born between January and May of the preceding year and another two groups of lighter and slightly younger calves born between the previous March and July were grazed during their second year on four separate paddocks known to be contaminated with infective larvae of gastrointestinal nematodes. One of the heavier and one of the lighter groups were treated with a topical formulation of ivermectin three weeks and eight weeks after turnout. The treatment of the heavier group had only relatively minor parasitological effects and no effect on weight gains, whereas the treatment of the lighter cattle resulted in increased weight gains due to effective nematode control. The paper highlights that small differences in previous performances, age and exposure to parasites can have a substantial impact on the benefits accrued from anthelmintic treatment.