Practical Methods for Mastitis Control

Christina S. Petersson-Wolfe¹, Andrea R. Tholen¹, John Currin² and Ken E. Leslie³

¹Virginia Tech, Department of Dairy Science, Blacksburg VA 24061
²Virginia Maryland Regional College of Veterinary Medicine, Blacksburg VA 24061
³Ontario Veterinary College, Guelph ON N1G 2W1
Email: milk@vt.edu

■ Take Home Messages

• Mastitis is a common and economically important problem caused by a wide variety of pathogens.
• One of the major costs may be related to dairy cattle welfare, which remains largely unexplored.
• Recommended prevention and control measures remain relatively constant. However, advancements in detection and therapy options have occurred in recent years.
• Novel tools for the detection of disease include in-line milk analyzers and behavior monitoring systems.
• Pain is an unpleasant sensory and emotional experience associated with tissue damage. It is highly variable and difficult to quantify in dairy cattle.
• Observations of both physiological and behavioral changes should be considered when monitoring for disease.
• There is clear benefit to the use of non-steroidal anti-inflammatory drugs (NSAIDs) for management of inflammation and alleviation of pain.

■ Introduction

Despite the widespread implementation of mastitis control programs, clinical mastitis is a commonly occurring and economically important disease for the worldwide dairy industry (Olde Riekerink et al., 2008). In recent years, there has been a general decline of the incidence of clinical mastitis (Bradley, 2002). However, with an incidence rate of 23 cases per 100 cow years in Canadian herds (Olde Riekerink et al., 2008), a focus on research and extension on this issue is still greatly needed. Mastitis can be attributed to an annual economic loss of approximately $400 million for dairy producers.
Economic costs associated with mastitis include milk production losses, treatment costs, and potential long-term damage to the mammary gland as a result of inflammation (Fetrow et al., 2000). Indirect costs from mastitis can include somatic cell count (SCC) penalties and increased culling rates (Blowey and Edmondson, 2010). In summary, clinical and subclinical intramammary infection (IMI) is a major issue for the dairy industry with broad ranging impacts and consequences. Aspects of proper mastitis control include disease prevention, timely detection and appropriate treatment. Although the underlying principles of mastitis control are universal, individual operations must develop control programs that are both practical and farm-specific. This paper will provide information on mastitis-causing pathogens and practical ways to prevent, detect and treat mastitis.

## Mastitis-causing pathogens

In order to develop farm-specific mastitis control programs, we must first have an understanding of common mastitis-causing pathogens. These are often categorized into two main groups; contagious and environmental. Contagious pathogens are spread from cow to cow predominantly at milking time while environmental mastitis pathogens, as the name suggests, are found in the cow’s environment. A summary of the control, prevention and treatment of common mastitis causing pathogens is shown in Table 1 (adapted from: http://pubs.ext.vt.edu/404/404-230/404-230_pdf.pdf). Gaining an understanding of the types of pathogens that cause intramammary infections on an individual farm will help in the development of farm-specific mastitis control programs. This knowledge can be gleaned from routine milk culturing of quarters prior to dry-off, at freshening and at the event of clinical mastitis. Some farms may have predominantly contagious pathogens, while others will experience primarily environmental pathogens and as such, the respective mastitis control programs will differ.

## Prevention and Control

The Recommended Mastitis Control Program published by the National Mastitis Council (NMC) continues to be the cornerstone of all on-farm mastitis control programs and can be found at: http://www.nmconline.org/docs/NMCchecklistNA.pdf. These practices should be applied to all operations as standard operating procedures for the prevention and control of both environmental and contagious pathogens. The 10-point program laid out in this document includes:

- Establishment of udder health goals
- Maintenance of a clean, dry and comfortable environment for the cows
- Proper milking procedures
Practical Methods for Mastitis Control

- Maintenance of milking equipment
- Good record keeping
- Appropriate management of clinical mastitis
- Effective dry cow management
- Maintenance of biosecurity for contagious pathogens and chronic infections
- Monitoring udder health status
- Review of mastitis control programs

As mastitis is one of the most costly diseases to dairy producers, prevention is key and the adherence to this 10-point program will aid not only in prevention, but also control. Although these guidelines are relatively static, the information regarding the detection and treatment of mastitis continues to evolve and as such, will be covered in greater detail.

Detection

Detection of mastitis can be achieved in many different ways. The most common detection methods include observation of clinical signs, somatic cell count (SCC) testing, which is commonly measured through the Dairy Herd Improvement Association (DHIA), bacteriological culturing, the California Mastitis Test (CMT), and using more recent advancements, through the use of in-line milk analyzers.

The detection of clinical mastitis through observation of clinical signs (i.e. off color, flakes, clots, swelling or redness of the gland) is performed prior to milking. However, this method is subjective and furthermore, subclinical mastitis is not detected by forestripping. Another method to detect mastitis is through SCC measuring, commonly performed by DHIA (Laevens et al., 1997). Knowledge of SCC can be useful for identifying subclinical mastitis, as it is an indirect measure of infection status. Consequently, monitoring of SCC is a useful tool in mastitis detection. Historically, this testing has been performed monthly and therefore should not be the only method of mastitis detection on-farm. More recent advancements in in-line milk analyzers and biosensors may allow for measurement at each milking.
<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Contagious or Environmental</th>
<th>Source</th>
<th>Spread</th>
<th>Control</th>
<th>Treatment*</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Staph. aureus</em></td>
<td>Contagious</td>
<td>Infected udders, hands of milkers</td>
<td>Milking time</td>
<td>Post dip, DCT‘, segregation and cull if necessary</td>
<td>Early lactation – 5-7d pirlimycin, do not treat chronic infections</td>
</tr>
<tr>
<td>Coagulase (-) staph. &amp; <em>S. hyicus</em></td>
<td>Neither</td>
<td>Skin flora &amp; occasionally environment</td>
<td>Infect teat canal from skin sources</td>
<td>Post dip, DCT</td>
<td>Treat clinical cases (broad spectrum), DCT</td>
</tr>
<tr>
<td><em>Strep. agalactiae</em></td>
<td>Contagious</td>
<td>Infected udders</td>
<td>Milking time</td>
<td>Milking time hygiene, post dip, DCT</td>
<td>Label recommendations for broad spectrum antibiotics</td>
</tr>
<tr>
<td><em>Strep. dysgalactiae</em></td>
<td>Contagious &amp; Environmental</td>
<td>Infected udders and environment</td>
<td>Milking time &amp; environmental contact</td>
<td>Milking time hygiene, pre &amp; post dip, DCT, teat seal</td>
<td>Label recommendations for broad spectrum antibiotics</td>
</tr>
<tr>
<td><em>Strep. uberis</em></td>
<td>Environmental</td>
<td>Environment – early dry period</td>
<td>New IMI^2 during early dry period</td>
<td>Milking time hygiene, pre &amp; post dip, DCT, teat seal</td>
<td>IMM^3 Therapy 4-5d penicillin systemically (3.5cc/100lbs body weight)**</td>
</tr>
<tr>
<td>Environmental strep &amp; <em>Enterococcus spp.</em></td>
<td>Environmental</td>
<td>Environment</td>
<td>Environmental contact</td>
<td>Milking time hygiene, pre &amp; post dip, DCT, teat seal</td>
<td>Do not treat local cases. Systemic cases – 2-3L hypertonic saline IV, followed by oral fluid therapy, NSAID**** and injectable antibiotics</td>
</tr>
<tr>
<td><em>Escherichia coli</em></td>
<td>Environmental</td>
<td>Bedding, manure, soil</td>
<td>Environmental contact</td>
<td>Cows clean &amp; dry, use of sand bedding, pre dip, a J5 vaccine</td>
<td>Do not treat local cases. Systemic cases – 2-3L hypertonic saline IV, followed by oral fluid therapy, NSAID**** and injectable antibiotics</td>
</tr>
<tr>
<td><em>Klebsiella spp.</em></td>
<td>Environmental</td>
<td>Organic bedding</td>
<td>Environmental contact</td>
<td>Avoid sawdust &amp; recycled manure, pre dip, J5 vaccine</td>
<td>Do not treat local cases. Systemic cases – 2-3L hypertonic saline IV, followed by oral fluid therapy, NSAID**** and injectable antibiotics</td>
</tr>
</tbody>
</table>

\(^1\)DCT = Digital Cooling Test
\(^2\)IMI = Intramammary Inoculation
\(^3\)IMM = Intramammary Medication

**Petersson-Wolfe et al.**
<table>
<thead>
<tr>
<th><strong>Enterobacter spp.</strong></th>
<th>Environmental</th>
<th>Bedding, manure, soil</th>
<th>Environmental contact</th>
<th>Cows clean &amp; dry, use of sand bedding, pre dip, a J5 vaccine</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serratia spp.</strong></td>
<td>Environmental</td>
<td>Soil and plants</td>
<td>Environmental contact</td>
<td>Cows clean &amp; dry, pre dip (no chlorhexidine products)</td>
</tr>
<tr>
<td><strong>Pseudomonas spp.</strong></td>
<td>Environmental</td>
<td>Water &amp; wet bedding</td>
<td>Environmental contact</td>
<td>No water use in parlor, no cooling ponds, sand bedding, a J5 vaccine</td>
</tr>
<tr>
<td><strong>Proteus spp.</strong></td>
<td>Environmental</td>
<td>Bedding, feed &amp; water</td>
<td>Environmental contact</td>
<td>Not much known, use of sand bedding, a J5 vaccine</td>
</tr>
<tr>
<td><strong>Pasteurella spp.</strong></td>
<td>Probably contagious</td>
<td>Upper respiratory tract of mammals and birds</td>
<td>Unknown – likely cow to cow</td>
<td>Prevent teat injuries, remove affected cows from herd</td>
</tr>
<tr>
<td><strong>Mycoplasma spp.</strong></td>
<td>Contagious</td>
<td>Infected udders</td>
<td>Cow to cow</td>
<td>Identify and remove infected cows from herd</td>
</tr>
<tr>
<td><strong>Yeast &amp; mold</strong></td>
<td>Environmental</td>
<td>Soil, plants, water</td>
<td>Dirty infusions</td>
<td>Aseptic infusions</td>
</tr>
<tr>
<td><strong>Corynebacterium bovis &amp; other coryneforms</strong></td>
<td>Contagious</td>
<td>Infected udders</td>
<td>Cow to cow</td>
<td>Post dip</td>
</tr>
<tr>
<td><strong>Prototheca</strong></td>
<td>Environmental</td>
<td>Soil, plants, water</td>
<td>Dirty infusions, infected udders</td>
<td>Aseptic infusions, eliminate infected cow</td>
</tr>
<tr>
<td><strong>Bacillus spp.</strong></td>
<td>Environmental</td>
<td>Soil, water, air</td>
<td>Dirty infusions</td>
<td>Aseptic infusions</td>
</tr>
<tr>
<td><strong>Arcanobacterium pyogenes</strong></td>
<td>Environmental</td>
<td>Teat injuries</td>
<td>Flies</td>
<td>Fly control</td>
</tr>
</tbody>
</table>

**These are general treatment recommendations – actual recommendations may vary from herd to herd. Please consult your veterinarian.**

**Extra label usage; Please consult your veterinarian before starting this protocol.**

**Nonsteroidal anti-inflammatory drugs, ¹ – DCT, dry cow therapy; ² – IMI, intramammary infection; ³ – IMM, intramammary**
Another useful tool in the detection of mastitis is bacteriologic culturing of milk. Milk culturing can be done on-farm or samples can be sent to a laboratory for analysis. Results from laboratory analyses may take several days to obtain and therefore, treatment decisions are often made prior to knowing the causative pathogen. However, the development of several on-farm culture systems has afforded dairy producers the opportunity to perform milk culturing on-site. The implementation of on-farm culturing allows dairy producers to make culture-based treatment decisions without detrimental effects on the cow (Lago et al., 2011a, b).

The CMT test can give rapid results and be a useful cow-side test for farmers and veterinarians. A small amount of milk is added to a small amount of bromocresol-purple-containing detergent that breaks down the cell membrane of somatic cells to create a viscosity proportional to leukocyte number. Advantages of this test include cost, as this test averages $12 for 350 tests, results are produced rapidly, and the test can be used cow-side. Although this test has many advantages, the results can often be difficult to interpret and with a relatively high number of false negatives.

Recent advancements in in-line milk analysis systems and animal behavior monitoring systems provide daily cow measurements, are less laborious than the previously discussed methods of detection and may allow for the detection of disease prior to the onset of clinical signs that may reduce the cost per case. Electrical conductivity (EC) is arguably the most widely used milk characteristic and was first introduced as an indicator of mastitis in the 1940’s. Since then, numerous studies have examined its ability to detect mastitis. This measurement determines the ability of a solution to conduct an electric current between two electrodes, or the resistance of a material to an electric current. The elements most important in determining the electrical conductivity of milk include Na\(^+\), K\(^+\), and Cl\(^-\). During a mastitis infection tight junctions become leaky and allow Na\(^+\) and Cl\(^-\) to pass through the junctions and into the lumen of the alveolus, while K\(^+\) moves out of milk. Therefore, Na\(^+\) and Cl\(^-\) concentrations are increased while K\(^+\) concentrations are decreased during mastitis. If EC readings deviate outside the normal range of 4.0 to 5.0 mS, there is a greater probability for a mastitis infection. The use of EC for the identification of sick animals has been previously validated as a reliable method of detection (Milner et al., 1996; Norberg et al., 2004). One study reported that changes in electrical conductivity were able to predict 92% of mastitis cases prior to or on the day clinical signs were present (Milner et al., 1996).

Although milk components remain relatively constant in a healthy gland, substantial changes occur during cases of clinical mastitis (Forsback et al., 2010). Many studies have examined changes in milk components after the onset of clinical signs during naturally-occurring mastitis or around the onset of clinical signs following intramammary challenge, but only recently have
studies begun to examine changes prior to onset during naturally-occurring clinical mastitis using in-line milk analyzers. One study found not only overall changes in milk components, but also pathogen-specific changes in milk components prior to onset of naturally occurring clinical mastitis (Tholen et al.). The utilization of these data will become more apparent as research continues to examine the specific changes associated with clinical and subclinical mastitis.

It has also been suggested that milk protein percent might also be useful in the early detection of clinical mastitis. Milk contains numerous proteins, the primary group being caseins and the secondary group being whey. During a mastitis infection there is an increase in the amount of plasmin, a proteolytic enzyme that can causes damage to casein, thus reducing its concentration in milk according to one study (Uallah et al., 2005). However, it has also been reported that milk protein concentrations increase during a mastitis infection, primarily due to an increase in whey proteins. A number of serum proteins, a part of the whey protein group, include serum albumin, immunoglobulins, and transferrin. These proteins pass into milk because of leaky tight junctions and as a result may increase protein concentrations in milk. With these contradictory results, it is obvious that further work is needed to understand the change in milk protein concentration around the onset of naturally-occurring clinical mastitis.

Changes in milk fat concentration during clinical mastitis have been previously reported. Fat concentration in unhealthy quarters (4.40% ± 0.33%) was reportedly less (P<0.01) than healthy quarters (4.72% ± 0.31%) (Nielsen et al., 2005). These reported differences may be due to impaired milk fat synthesis due to epithelial cell damage or due to an increase in lipase concentration in the gland as this enzyme causes the breakdown of triglycerides releasing free fatty acids, which in turn can cause off flavors in milk and decrease fat concentrations in milk.

Some studies have examined changes in milk lactose concentration during clinical mastitis. Nielsen et al., (2005) analyzed lactose concentrations throughout milking in cows with healthy and unhealthy quarters. Results suggest that cows with unhealthy quarters had significantly (P<0.001) lower lactose concentrations (4.37% ± 0.06%) compared to healthy quarters (4.70% ± 0.05%) throughout the milking process (Nielsen et al., 2005). These changes in milk lactose concentration may be due to tissue damage and/or bacterial utilization of the sugar.

The body temperature of a dairy cow averages 38.6°C, whereas the temperature of milk is 0.09°C lower than the normal body temperature. In quarters defined as healthy, a consistent milk temperature indicates regular milk flow from the udder to the cistern. Deviations in milk temperature may illustrate problems associated with milk flow from alveoli and fine ducts to the
cistern which could be caused by epithelial damage as a result of mastitis. A total of 19 of 25 cows with clinical mastitis had a significant increase in milk temperature and a decrease in milk yield, or a rise in milk temperature alone before clinical signs appeared (Maatje et al., 1992). Infrared thermography (IRT), which utilizes the generation of heat captured in images, has also been studied as a potential mastitis detection tool. An infrared camera measures the amount of radiation emitted from an object and that radiation is a function of surface temperature making it possible for the camera to calculate and display the temperature. Infections can cause a localized increase in temperature due to the inflammatory response. One study showed udder skin surface temperature for 94 healthy quarters (SCC ≤400,000 cells/mL) averaged 33.45°C ± 0.09°C, which was less than subclinical quarters (35.80°C ± 0.08°C; SCC >400,000 cells/mL; n = 135) (Polat et al., 2010). Although milk temperature has been evaluated since the 1970’s, progress towards implementing it as a tool for early detection of mastitis on farms is still in the research stage. New technology, such as IRT, could prove to be a more beneficial and rapid method for detecting clinical mastitis, but more research needs to be done to examine these new technologies.

Mastitis has a significant effect on milk yield. During an IMI, an influx of neutrophils will pass between the milk producing cells of the mammary gland and into the lumen of the alveoli to help destroy bacteria. As a result, secretory cells are damaged. Once leukocytes reach the lumen they will aggregate and form clots which can block milk ducts and result in incomplete milk removal. If milk ducts remain clogged, secretory cells revert to a non-producing state, and alveoli begin to shrink being replaced by scar tissue, thus causing a reduction in milk yield. Studies have showed that cows in first lactation that eventually developed clinical mastitis produced significantly more milk before diagnosis compared to cows that never developed clinical mastitis. A similar trend was found with multiparous cows that developed clinical mastitis (Schukken et al., 2009). Additionally, pathogen-specific effects have been shown for milk yield, with the greatest impacts attributed to Gram-negative infections (Grohn et al., 2004). Milk production loss as a result of clinical mastitis occurs predominantly after signs of clinical mastitis. Milk yield loss based on current findings suggests that this variable alone may not be sufficient enough to detect cases of clinical mastitis. However, when milk yield is combined with other milk component data it may serve as a valuable method for early detection of clinical mastitis in dairy cows.

In addition to changes in milk components, altered animal behavior during disease has been widely reported and may be a useful tool for the detection of disease. In fact, the daily monitoring of animal activity has proven to be a successful method to identify animals at risk for periparturient disease. Cows that experienced a metabolic or digestive disease showed an increase in step activity 8 or 9 d prior to clinical diagnosis. This activity then decreased until clinical diagnosis. Overall, cows diagnosed as unhealthy walked 8-14 steps/h
less than healthy cows (Edwards and Tozer, 2004). In another study, cows later diagnosed with mastitis showed a decreased resting time on d -2 and d -1 (349 ± 43 min and 391 ± 43 min, respectively) relative to diagnosis as compared to non-mastitic cows (481 ± 17 min and 488 ± 16 min, respectively) (Yeiser, 2011), which could be attributed to pain or discomfort. Furthermore, cows later diagnosed with subclinical ketosis displayed more rest bouts on d -1 (16 ± 2 bouts) relative to diagnosis as compared to animals without detectable disease (12 ± 1 bouts) (Yeiser, 2011).

The lying behavior of the cow may also indicate a mastitis infection. The laterality of cows that had mastitis was found to be significantly different than those without the infection (Kikkers et al., 2006). Animals that tended to lie more so on their left side had an increased risk of having mastitis in the right quarter even though the relationship was not significant. Significance of this relationship may have been observed if lying position had been visually recorded more often than just four times throughout the day (Kikkers et al., 2006). The use an automatic data logger could provide measurements every minute to determine the true relationship of infected quarters and lying side.

Similar behavioral changes were also observed with cows that were experimentally challenged with lipopolysaccharide (LPS) where the animals’ resting behavior changed (Hänninnen et al., 2007). Cows rested for a longer period of time immediately after being challenged compared to d -1, relative to infusion. Following that period of rest, the hourly rest time decreased. In another study, a similar change in behavior was observed in the first 12 h after LPS infusion, where cows infected spent less time lying in their stalls (40.7 ± 4.0%) as compared to the control animals (47.9 ± 3.4%). These infected animals also reduced the time spent eating (16.9 ± 0.8% versus 21.0 ± 1.2%) and cud chewing (35.8 ± 2.3% versus 39.8 ± 1.5%) (Zimov et al., 2011). An E. coli infection induced similar responses as cows stood idly longer on the day of the infection with associated decreases in DMI and feeding time (Fogsgaard et al., 2012). The experimental challenge model is an effective way to help understand the behavioral changes prior to and after the onset of clinical mastitis. However, naturally occurring cases of mastitis should also be considered as severity and infective pathogen may cause differences in behavioral responses. These studies suggest activity parameters could be used as a valid method for proactively monitoring herd health on dairy operations.

### Treatment

Traditional antimicrobial treatment of mastitis has been and still is the generally recommended practice for clinical mastitis. Treatment regimes have been heavily researched and as such, some treatment protocols are discussed in Table 1. Increasing consumer awareness of antimicrobial usage on-farm and animal welfare issues related to sick cows has dairy producers...
interested in not only reduced antimicrobial usage but also therapies to address the mitigation of pain. Having said that, the effects of mastitis on cow behavior and welfare remain largely unexplored. A wide variety of tools and techniques are now available and validated for the assessment of animal behavior and welfare. However, the assessment of pain due to mastitis has not been adequately studied. Many researchers contend that animals suffering from mastitis have compromised welfare, and are in need of supportive pain management therapy. Furthermore, some authors have asserted that appropriate analgesic treatment of clinical mastitis, to provide relief from suffering caused by pain, discomfort and distress, should be mandatory (Hillerton, 1998). Several non-steroidal anti-inflammatory drugs (NSAIDs) are available as supportive therapies for clinical mastitis, even though documented evidence of efficacy and regulatory approvals for treatment of clinical mastitis are very limited. As the treatment of mastitis with antimicrobials has been widely discussed in other publications, the remainder of this paper will discuss our general therapy and effects of mastitis on cow behavior and welfare.

Treatment of inflammation relies on relieving the pain and other systemic effects that commonly accompany inflammation, and slowing any further tissue damage. NSAIDs are commonly used in animals to reduce inflammation (anti-inflammatory), reduce pain (analgesic), reduce pain sensitivity (anti-hyperalgesic), and decrease overall body temperature (anti-pyretic). These drugs act by inhibiting cyclooxygenase, which in turn prevents prostaglandin synthesis.

Around the world, commercially available NSAIDs are approved for anti-inflammatory and anti-pyretic indications. The actual intended pharmacological effect of NSAID administration has not been documented, meaning that the frequency of use of NSAIDs in cattle with an intention to mitigate pain is not well understood. However, as research continues to evolve in this area, it is becoming apparent that the incorporating NSAID therapy into treatment protocols for a variety of clinical problems, including clinical mastitis, should improve the welfare of diseased animals and correspondingly, decrease the economic losses to food animal producers (Barrett, 2004).

Treatment decisions for animals with severe clinical mastitis most often involve veterinary intervention. Survey research has shown that both dairy producers and veterinarians generally agree that severe cases of mastitis can cause the animal significant pain and distress (Todd et al., 2010). As such, it is common practice to provide the severely mastitic cow with NSAID therapy, in addition to antibiotics. Finally, there is mounting evidence for this use in both induced and naturally-occurring cases of clinical mastitis, even though formal regulatory approval is rare.
The use of NSAIDs has been shown to decrease rectal temperatures, decrease signs of inflammation, maintain rumen motility, and reduce heart rates in cows challenged with an intramammary infusion of LPS endotoxin to mimic early coliform mastitis, as compared with their non-treated counterparts (Anderson et al., 1986; Wagner and Apley, 2004; Zimov et al., 2011). Decreased heart rate could be interpreted as a result of a decrease in animal distress or alleviation of pain by the NSAID. There was also an observed reduction in fever of treated animals. As previously stated, fever is a strategy used by animals to combat infection. As such, it is unknown whether the reduction of fever is actually advantageous for animals with an early case of clinical mastitis. There is generally a lack of published literature supporting the beneficial or detrimental effects of reducing fever in these cases.

Milk measurements and behavioral activity was monitored to examine the effects of flunixin meglumine given 4 hours post-infection during endotoxin-induced clinical mastitis (Zimov et al., 2011). The frequency of rumen sounds was numerically increased in challenge animals, but dry matter intake was not affected by the infection or treatment. The lack of difference in intake was likely due to the feeding management, or the actual length of the infection time during the study. However, treated-cows did show an increased eating time 9-12 h after administration, as well as an increase in cud chewing compared to the non-treated control group. While infected cows spent less time lying in the first 12 hours after infection, flunixin treatment had no effect on the lying behavior (Zimov et al., 2011).

Ketoprofen is another NSAID utilized by the dairy industry. The effectiveness of ketoprofen in experimental LPS-induced clinical mastitis cases has been evaluated. Three treatment groups were studied where two groups of experimental animals were inoculated with LPS and compared to an untreated control group. The two groups of experimental animals were given ketoprofen either orally or intramuscularly 2 hours after LPS mastitis was induced (Banting et al., 2008). Untreated control animals showed an increase in rectal temperature to an average of 40.5°C with differences between the groups seen at 6, 8 and 10 hours post-challenge. By 2 hours post-challenge, respiratory rates were increased in all groups. The respiratory rates in the two treated groups started to decline by 6 hours, and were normal after 24 hours. Rumen contractions were reduced by 50% in the 2 hours post-challenge for all animals. Within 6 hours, ketoprofen-treated animals began to recover with full recovery by 24 hours whereas the control group did not recover until day 7. As the udder of the animals was palpated, a visual analogue scale assessed the pain experienced. Ketoprofen allowed for a more rapid decline in pain scores as compared to the untreated control. Further, milk thromboxane β₂ levels, an indicator of the general inflammatory status of an animal, were reduced at 6 hours post-challenge, as compared to 12 hours post-challenge in the control animals.
Anderson and Muir (2005) reviewed numerous articles concerning the use of NSAIDs in dairy cattle, which clearly demonstrated an improved response to treatment in affected animals after a variety of veterinary procedures. These animals also returned to a normal physiological state more quickly when an NSAID was administered prior to specific procedures. When cows were infused with *E. coli* and given a NSAID prior to the development of clinical signs of infection, it was found that two NSAIDs almost entirely blocked the febrile response and delayed the decrease in rumen activity of affected animals (Lohuis et al., 1989). Other studies with experimentally-induced coliform mastitis have also shown improved recovery in these treated animals (Vangroenweghe et al., 2005). Oral and intravenous NSAIDs provided equal systemic responses (Odensvik and Magnusson, 1996). In a similar experiment, it was found that NSAIDs decreased mammary inflammation and rectal temperature, but did not prevent milk production losses or appetite reduction (Morkoc et al., 1993). In very recent research, the use of flunixin meglumine was evaluated during experimentally induced *E. coli* mastitis (Yeiser et al., 2012). It was concluded that *E. coli* mastitis altered physiological parameters, animal resting activity, dry matter intake, and milk production thus having a negative impact on animal well-being. There was improvement in dry matter intake and milk production with flunixin therapy providing evidence for using an NSAID as supportive therapy in alleviating the adverse effects associated with *E. coli* mastitis (Yeiser et al., 2012).

The effect of NSAIDs on naturally-occurring clinical mastitis is not well documented in the literature. As it is difficult to perform research on naturally-occurring infections, most of the published literature reports on results obtained from experimentally-induced infections. Both induced and naturally-occurring infections result in increases in milk SCC, body temperature, concentrations of TNF-α, mammary gland swelling, and a decrease in milk production (Van Oostveldt et al., 2002). Thus, there are many similarities between clinical symptoms for natural infections and experimentally-induced infections. However, it may be inappropriate to directly compare cases of clinical mastitis resulting from LPS endotoxin infusion or even experimental-challenge using live organism with cases of naturally-occurring mastitis. Early research in this area documented the administration of antibiotics and one intravenous treatment of NSAID at the time of first physical examination after the detection of severe endotoxic naturally-occurring clinical mastitis (Dascanio et al., 1995). These researchers found no difference in body temperature, milk production or need for additional therapy between treatment groups, when monitoring animal responses every 24 hours.

Another early study evaluated the therapeutic usage of flunixin meglumine administered intravenously to animals with naturally occurring clinical mastitis in order to determine whether or not cows with clinical mastitis suffered pain over time, and if treatment with a NSAID would help with pain alleviation (Fitzpatrick et al., 1998). Cows with mild or moderate mastitis were given an
NSAID, either by intramammary or intravenous route of administration. Pain thresholds were determined using a mechanical device that exerted pressure to the hind limb of each cow. Cows with mild and moderate cases of clinical mastitis showed a heightened responsiveness to pain that persisted for days or weeks after onset. The cows with mild clinical mastitis exhibited reduced sensitivity to pain when treated with a NSAID intravenously. A beneficial effect of the relief of pain was documented. However, similar results were not found with the moderate cases of clinical mastitis, which may have been attributed to the dosage of NSAID being too low. In addition, the observed pain relief by the NSAID in that study was short-lived, and it was recommended that repeated doses of intravenous NSAID might allow for more long-term pain relief (Fitzpatrick et al., 1998).

In a study in Israel, it was found that giving ketoprofen intramuscularly for five days allowed affected cows to return to 75% of their daily milk production recorded prior to their mastitis infection (Shpigel et al., 1994). Upon initial diagnosis of clinical mastitis, the animals were given antimicrobials in combination with ketoprofen. A secondary part of the study included ketoprofen treated versus a placebo treated control group. The animals treated with ketoprofen had an average 93.5% recovery rate based upon production parameters as compared to the average recovery rate from the control groups of 78.4%. Furthermore, only 1 of 39 (3%) of ketoprofen-treated cows were culled that lactation versus 9 of 41 (22%) of control animals.

In another study, 100 dairy cows with both mild and moderate naturally-occurring cases of mastitis were assessed for pain (Milne et al., 2004). It was found that the respiratory rate, rectal temperature and heart rate were all significantly higher in cases of moderate mastitis, when compared to mild clinical mastitis cases. Animals were administered the NSAID, meloxicam, in either a single or a three-dose regimen. Pain threshold levels were then measured. Animals treated with NSAID returned to their normal threshold levels for these outcome variables significantly faster than untreated animals. The effect was similar whether an animal received one or three doses of meloxicam. It was concluded that by promoting recovery of moderate or mild mastitis by alleviating pain associated with a case of mastitis, cattle welfare would be improved. Other studies that have treated cows with meloxicam have recorded the alleviation of pain and discomfort associated with mastitis by reducing heart and respiratory rates and pain responses (Banting et al., 2003).

The use of NSAIDs for the treatment of mastitis has been most commonly prescribed for cases of severe endotoxic mastitis, and has not been widely adopted as a standard treatment for cases of mild and moderate clinical mastitis. It is well recognized that for such cases, treatment decisions do not often directly involve veterinarians. Usually, the therapy of these cases at the time of their detection is up to the discretion of the dairy producer or farm
manager. Farm personnel often follow a treatment protocol that is designed by both farm staff and the herd health advisory team. It is desirable to create a set of standard operating procedures as a treatment protocol for all cases of clinical mastitis, such as found with the Canadian Quality Milk Program, and to consult with a veterinarian about how to carry these plans out efficiently. As such, there may be an opportunity for greater use of NSAID therapy in mild and moderate clinical mastitis cases.

In a field study conducted in New Zealand, treatment of mild and moderate clinical mastitis with a combination of meloxicam and a parenteral antibiotic (penethamate hydriodide) was evaluated for its effect on SCC, milk yield losses, clinical outcomes, and culling rates as compared with antibiotic therapy alone (McDougall et al., 2009). Cows were treated with 5 g of penethamate hydriodide daily for three days after the clinical detection of mastitis. Half of these cows were also treated with 250 mg of meloxicam and the other half were treated with a placebo (control group). It was found that there was no difference between treatment groups in the number of cows that were defined as treatment failures (i.e., re-treated within 24 days of initial treatment, died, or the treated gland stopped producing milk). There was also no difference in milk yield for the cows treated with meloxicam compared with the control cows. However, SCC was lower in the meloxicam-treated group compared with the control group after treatment (550 ± 48 vs. 711 ± 62 (×1,000/mL), respectively) and fewer meloxicam-treated cows were removed from the herds (39/237 (16.4%) vs. 67/237 (28.2%), respectively). It was concluded that treating cows with a combination of meloxicam and penethamate resulted in a lower SCC and a reduced risk of removal from the herd (culling) as compared with the penethamate treatment alone (McDougall et al., 2009).

Conclusions

As mastitis is currently one of the most costly diseases for the dairy industry, prevention, control and treatment practices should receive utmost attention. Although prevention and control protocols have remained relatively constant over the years, new detection and therapy options have been researched and show promise. Furthermore, it is clear that clinical mastitis has severe detrimental effects on the animal and negative economic impacts for dairy producers. Therefore, attention to behavioural and physiological indicators should be given to monitor animal health. New technologies may allow dairy producers to identify clinical mastitis in its very early stages, or even before clinical changes occur. Furthermore, automated measures of activity, such as step counts and lying time show promise as predictors of clinical problems. These new technologies, in addition to other automated measures, have the potential for improving the screening methods for pre-clinical mastitis and accurately predicting the onset of a clinical mastitis event. With this opportunity for very early detection of infection, there is a potential for early
intervention with NSAID therapy, which may allow for maximum efficacy from its use. As the health and well-being of dairy cattle continue to be scrutinized by consumer groups, it is essential that attention be placed on prevention, detection and the alleviation of any perceived pain or discomfort associated with clinical mastitis.

References


Milne, M. H., A. M. Nolan, and P. J. Cripps. 2004. Preliminary results on the effects of meloxicam (Metacam) on hypersensitivity in dairy cows with clinical mastitis. in World Buiatrics Congress, Quebec City, QC.


