

MASTITIS OF SHEEP - OVERVIEW OF RECENT LITERATURE

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Introduction

Mastitis is by definition, inflammation of the mammary gland. Inflammation is most commonly due to infection with a pathogen (intramammary infection or IMI) but may also be due to injury and less commonly due to allergy and neoplasm. If inflammation is present without a detectable IMI, it may be that the udder was injured, it is recovering from an infection that has self-cured, the infection is not due to a bacteria, or that the sampling and culturing technique was faulty. The literature varies considerable in what is considered to be pathogenic level of inflammation or significant infection with a pathogen. However, if IMI and / or presence of inflammation adversely affects the level of production or the quality of milk products, then it is significant to the sheep industry.

Clinical Picture

Quinlivan in 1968 developed a classification system of ovine clinical mastitis that can still be applied today: The four categories of small ruminant mastitis:

1. A small fibrotic lesion within the mammary tissue. Secretions were within normal range. Thought to be chronic in nature.
2. A more extensive fibrosis of the udder. Milk ranged from normal to purulent to cheesy or no milk due to teat occlusion with fibrous tissue. Again thought to be chronic.
3. Extensive swelling of the udder. Milk was found to be white, watery, serum-like or purulent. Udders could also be abscessed or ruptured due to previous gangrenous mastitis. Likely acute mastitis.
4. Peracute mastitis. Complete udder involvement with severe inflammation. Secretions were serum-like with varying amounts of fibrin and purulent material. Mammary lymph nodes were enlarged and body temperature generally elevated.

Cases of clinical mastitis can occur at any time of lactation or of the dry period. The highest incidence of severe clinical or peracute mastitis seems to be approximately 2 to 4 weeks post-lambing and again just post-weaning. There is little well documented evidence to support this impression, however. Mastitis that develops during the dry period or late lactation is often not noticed until the subsequent lambing as well as, in the case of non-dairy sheep, at shearing time.

Peracute Mastitis

In peracute mastitis, the clinical picture is generally dominated by depression, initial fever which may be followed by hypothermia, dehydration, anorexia and a swollen, discoloured gland.

Occasionally, lameness may be an important presenting sign. The skin of the affected gland may become reddish to purple and cold to the touch. The discolouration often extends beyond the gland to the belly wall and groin area. Secretions are serum-like and reddish and may contain gas. The animal is weak and may become recumbent. Case fatality rates due to the effects of toxæmia are high (30 to 40%) if left untreated. If it survives the initial disease, the gangrenous gland and surrounding tissue are sloughed over a period of weeks and the wound heals by secondary intention. Commonly, *Staphylococcus aureus* is cultured from these cases, as well as occasionally *Pasteurella* spp and coliforms. Clostridial organisms are sometimes demonstrated on gram stain, and may be present perhaps as secondary invaders of anoxic tissues.

Acute and Chronic Clinical Mastitis

Clinical mastitis is characterized by palpable changes in the consistency of the glandular tissue, i.e. hard, fibrotic, abscesses, gland size (either swollen or shrunken) and / or appearance of the milk, which may contain flakes, purulent material and be discoloured. In cases of sheep raised for meat production it may not be possible to tell the duration of the mastitis as the udder may only be examined at lambing or at weaning or if the animal is clinically ill.

Subclinical Mastitis

The definition of subclinical mastitis is an inflammation that is not readily detected clinically but adversely affects production. What constitutes subclinical mastitis in sheep in terms of level of somatic cell counts (SCC), California Mastitis Test (CMT) results and bacteriological culture results are not as clearly defined as for dairy cattle.

PREVALENCE OF MASTITIS

How common mastitis is in sheep is extremely variable. Studies of cull ewes at slaughter in Britain show a very high prevalence ranging from 13 to 50% , indicating that clinical mastitis is likely an important cause of culling of ewes in the UK. In American range flocks, prevalence of clinical mastitis ranges from 1 to 3%, but the prevalence is much higher if the udders are cultured as well (5 to 30%) or a positive SCC reaction is obtained (14 to 20%). Dairy sheep have been reported to have a prevalence of mastitis, as determined by a positive milk culture, of up to 35% of ewes and by positive SCC and milk culture of 4 to 17%.

ETIOLOGIC AGENTS

***Staphylococcus aureus*:** is a very common isolate from cases of clinical sheep mastitis, up to 35% of clinical cases may be due to this bacteria.

***Pasteurella* spp:** *Pasteurella haemolytica* is a very important cause of peracute and clinical mastitis of sheep. Experimental infection of ewes' udders with as few as 10 colony forming units (cfu) of *P haemolytica* isolated from ovine and bovine pneumonic lesions or the nasal cavities of healthy lambs, produces clinical cases that resemble naturally occurring disease. These findings strongly support the theory that the source of udder infection with *P haemolytica* is from the nose and throats of nursing lambs.

Coliforms: Commonly isolated coliforms from sheep include *E. coli*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* as the most common, with *Salmonella* spp being more rarely isolated. *Pseudomonas aeruginosa* has been implicated in outbreaks of acute mastitis with high levels of mortality in lactating dairy sheep.

Environmental *Streptococcus* spp: In most sheep surveys, environmental streps are also rarely isolated with the exception of one UK survey which found it to be more common than coagulase negative staphylococcus.

Coagulase Negative *Staphylococcus*. (CN-S): There are many different species of CN-S which have variable capacity to cause mastitis in sheep, for example *S. chromogenes*, *S. hyicus*, *S. epidermidis*, *S. simulans*, and *S. warneri*. As a group they are the most common isolates from subclinical mastitis in ewes across all stages of lactation including at dry-off or weaning. Many of species of CN-S have been isolated from sheep and many are likely of very low pathogenicity, however some species have been shown to cause as severe a clinical mastitis as *S aureus*. However, not all C-NS isolates are associated with inflammation. One report found that 87% of 400 clinically normal milking ewes, had C-NS cultured as the primary isolate and also exhibited a low SCC of 200,000 cells/ ml of milk or less.

Contagious Agalactia: If the clinical picture of mastitis in a sheep flock includes arthritis and conjunctivitis with or without pneumonia, contagious agalactia should be considered as a diagnosis. The causative agent of this disease syndrome is *Mycoplasma agalactiae*. This agent is a common pathogen of sheep in the Mediterranean and Alpine areas of Europe, but (fortunately) is classified as an foreign disease agent to North America but it has been isolated from a case of mastitis in a California goat.

Maedi Visna: Maedi-visna virus (MV-v), also known as Ovine Progressive Pneumonia virus (OPP-v) has been implicated in chronic progressive pneumonia and weight loss as well as changes to the ovine mammary gland. Clinically at lambing, the udder is hard and appears to be full of milk but little milk can be expressed from the glands. “Hard bag” and decreased milk is far more prevalent in MV-v serologically positive flocks when compared to MV-v negative (63.1% vs 8.0% in one study). MV-v can be isolated from the mammary tissues and from the milk. Much higher levels of virus are found in colostrum at parturition than in milk suggesting that colostrum is an important method of infection of lambs.

Unfortunately this viral form of mastitis has a detrimental effect on ewe productivity. Some western US sheep producers reported culling as many as 10% of ewes each year due to “hard bag”. Another study found that ELISA positive ewes were less productive in terms of lamb growth (8.5 lb per ewe lambing) although it isn’t known if this difference is due to mastitis or other effects of the disease. However it has been found that there is a significant negative correlation between lamb weaning weight and the damage in ewes’ udders due to MV-v. Lambs nursing the most affected ewes, weighed 5 kg less at weaning than lambs nursing unaffected ewes.

Miscellaneous Infections. *Serratia marcescens* has been associated with contaminated teat cups. Aspergillosis has also occurred involving the mammary gland subsequent to treatment with antibiotics prior to lambing.

DIAGNOSIS

Clinical Examination

As mentioned previously, there have been good attempts to try to categorize mastitis based on clinical examination of the gland and milk. The difficulty in meat or fibre sheep is in early recognition as the udder may only be routinely inspected at lambing, shearing or sometimes at weaning whereas infection in this type of animal may occur at any time but most often 2 to 3 weeks post parturient and after weaning. Some producers also have difficulty identifying mild changes to the udder during lactation and sometimes clinical changes only become evident during the dry period. In meat animals, it is important to identify chronic clinical mastitis prior to breeding so that ewes or does with compromised udders can be culled at that time.

Milk Culture

The protocol for obtaining milk samples is as follows:

- The sample vial should be labelled with date, farm ID, sheep ID and left or right or “C” for composite.
- The udder should be free of mud and manure.
- If the udder is dirty, it should be washed and dried with a clean towel.
- Hands should be washed with an antibacterial soap and dried with a clean towel.
- The fore-milk (milk that is sitting in the teat and cistern) should be stripped, ideally into a strip cup.
- Teat ends should be disinfected with alcohol-soaked cotton swabs until the swabs are clean.
- The far teat should be disinfected first and sampled last to avoid contamination.
- A sterile milk vial should be used.
- Take care not to touch the inside of the lid or vial nor have dirt fall into the vial when sampling.
- The container should be half-filled (minimum) and the cap replaced.
- The sample should be refrigerated and transported to the lab as soon as possible, or frozen if no somatic cell counts are to be done and the sample won't be transported for at least 24 hrs.

A positive culture is a pure culture with a minimum of 5 colony-forming-units (CFU's)

Somatic Cell Counts

Measuring somatic cell levels in the milk is a surrogate measure of mastitis, i.e. inflammation as a response to infection. Many factors other than infection will elevate SCC. What is most important is what levels of SCC are associated with decreased milk production.

Levels Indicating Significant Intramammary Infection (IMI):

In normal ewes' milk, 50 to 70% of the cells are macrophages with PMN's making up another 15-40%, lymphocytes 6-14% and other cells types (epithelial, eosinophils, etc.) making up less than 5%. Unlike goat SCC determination, it doesn't matter which type of counter is used (Coulter, Fossomatic, Direct Microscope), all are highly accurate for determining ovine SCC levels. There are various opinions as to an appropriate SCC cut-point to use for selecting which sheep should be sampled for culture. Suggested threshold values vary from a low of 100,000 SCC to a high of 1,000,000, with the most common level suggested being 1,000,000. However, using the same threshold value as for cattle (250,000) will ensure that almost all truly infected sheep are sampled and thus detected.

Factors other than IMI that affect SCC level:

Stage of Lactation. Sheep SCC levels will rise towards the end of lactation without IMI, but not to the same degree as in goats.

Lactation Number. First lactation Italian dairy sheep have a much lower mean SCC of 57,000 cells/ ml milk suggesting that this group of sheep may have a lower normal value than multiparous dairy ewes. However, lactation number accounts for only 6.6% of the variability in SCC, indicating that lactation number is not very important when interpreting SCC flock levels.

Time of Day. Milk samples taken in the morning milking had 7 to 22% higher SCC level than those taken in the evening.

Freezing and Storage. Freezing does not adversely affect SCC levels to the degree where they can't be interpreted, however it is still recommended to perform SCC determination on fresh milk samples for the most accurate determination. Storage greater than 7 days will cause significant decreases in SCC values (14%).

Indirect Measure of Inflammation

California Mastitis Test (CMT)

The CMT reagent reacts with DNA present in epithelial and inflammatory cells. More DNA = more gelling of the milk. In each well of the paddle, equal amounts of milk and CMT reagent are mixed (5 ml each) and immediately evaluated. Results are generally reports as:

- negative no gelling seen at all
- trace small amounts of gel noticed when the paddle is tipped
- 1+ significant amounts of gel seen when tipped
- 2+ when paddle is swirled, gel tends to clump in the middle
- 3+ mixture completely gelled and clumps in middle when swirled

There is fair to good correlation between CMT and SCC, remembering that CMT is a subjective test. With regards to predicting presence of IMI, CMT is better able to classify udders as not infected as opposed to correctly identifying infected glands. If CMT values of 1 + or higher are used to select animals for culture, then most infected sheep will be sampled.

RISK FACTORS FOR MASTITIS (IMI & ELEVATED SCC)

Teat & Udder Damage. The occurrence of IMI in non-dairy sheep has been hypothesized to be predisposed by the size of the lambs nursing the ewe. Two early investigators of mastitis speculated that because heavy lambs can be rough when nursing, this may lead to bruising and eventually invasion of *Pasteurella* spp organisms. There is little written about the relationship between visible udder or teat lesions and the risk of mastitis but one study did not find any association.

Udder Conformation. Poor udder conformation (supernumery teats, unconventional teats or poorly shaped udders) has a significant but minor effect on the frequency of IMI in sheep. An inconvenient approach for lambs to suckle the udders might explain the inefficient evacuation of milk from the glands and predisposition to IMI.

Number nursing. The number of lambs born has been found to have a positive correlation with incidence of IMI but only accounts for a small proportion of its total variability. This suggests that the damage from frequent and vigorous suckling of lambs may cause udder damage that predisposes ewes to IMI.

Age. Overall there was a significant positive association between the prevalence of IMI and ewe age.

Stage of Lactation. The prevalence of subclinical mastitis increased with later stages of lactation.

Milking Systems and Management. Sheep that are hand-milked tend to have a higher level of subclinical IMI, particularly with *S. epidermidis*. High stocking density has an adverse effect on milk production and udder health of sheep. Sheep housed at 2 m²/animal were healthier than those housed at higher densities.

Level of milk production. A study of dairy sheep at the farm level found that farms with higher milk production had significantly higher prevalence (48%) of subclinical mastitis compared to the lower production farms (22%). It was hypothesized that high producing ewes associated with high milk yield farms were more susceptible to IMI than low producing ewes associated with low milk yield farms.

Genetic resistance. The heritability of resistance to mastitis in sheep, i.e. how many years the ewes produced without coming down with mastitis, was estimated to be only 0.13. This suggests that selection for longevity to not developing mastitis might be valuable to include in some breeding programs, perhaps particularly in high incidence flocks but that genetic progress will likely be slow.

IMPACT OF MASTITIS ON PRODUCTIVITY

Mortality and Culling. Abattoir studies have shown that mastitis or abnormal udders are a common finding in culled ewes, leading to speculation that it is an important reason for culling. In one British study, 46% of all ewes culled from two large lowland flocks, were removed due to udder problems. In a Scottish study, in a three year survey on sheep losses mastitis accounted for 8.4% of all ewe deaths.

Milk Yield & Composition. IMI in ewes has a well-documented effect on milk production with reduced milk production of 20 to 37%. Lactose concentration is also decreased by IMI and elevated SCC, thus adversely affecting cheese production.

Offspring Performance and Mortality. An important cause of perinatal lamb mortality is starvation due to mismothering estimated at 34% in one study, of which an important component is due to mastitis or lack of milk. Infection also reduces average daily gain of up to 20 gm/day and up to 4 kg by weaning. Another study found that for an increase of 10 gm in the average daily gain of lambs, there was a decrease in IMI prevalence by 0.09%.

Treatment and Prevention

Use of Antimicrobial Drugs in Dairy Sheep. Very few drugs are approved for use in lactating dairy sheep in Canada and the USA as indicated by the Bureau of Veterinary Drugs (Canada) (http://hwcweb.hwc.ca/food-aliment/english/veterinary_drugs/index.html) and the Centre for Veterinary Medicine (USA) (<http://dil.vetmed.vt.edu/FDA/NADA/NADA.cfm>) although there is movement with respect to streamlining the approval process in the USA (<http://www.fda.gov/cvm/fda/TOCs/minortoc.html>). Veterinarians in North America are allowed to prescribe drugs in an off-label manner but they are then obligated to assure that residues do not enter the food chain. Sparse literature exists on appropriate withdrawal periods for the milk of dairy sheep. One study showed that a commercial lactating cow intramammary infusion product (Synulox LC which contains amoxicillin, clavulanate and prednisolone) required a withdrawal period of 112 hrs after its use in healthy goats, over twice recommended on the label for bovine. Studies using commercial dry cow products have found the occasional goat with antimicrobial residues at the subsequent kidding, even when the dry period was as long as 100 days. This contradicts earlier findings that suggest that the bovine withdrawal period is suitable for most intramammary infusion products. It is strongly recommended to consult FARAD (<http://www.farad.org/>) and to use antimicrobial detection tests for milk whenever antimicrobial drugs are used to treat dairy sheep, although false positives and negatives are possible when bovine kits are used in these species particularly if the milk is heated or a preservative is added.

Clinical Mastitis. There is very little scientifically supported information on the appropriate treatment of clinical mastitis in lactating sheep. If the sheep is systemically ill (e.g. fever, poor appetite), treatment should be systemic and supportive therapy (fluids, anti-inflammatory agents) as well systemic antibiotics should be used. A veterinarian should be contacted to provide the best care. Sheep with gangrenous mastitis are at grave risk of dying. No recently published information exists on treatment of dairy sheep with intramammary infusion products during lactation. In dairy cows, response to treatment with intramammary infusions during lactation is poor (*S. aureus*) to fair (CN-S and environmental infection).

Dry period therapy. The use of dry cow intramammary therapy in sheep has been well studied. There is evidence of improved cure rates and decreased level of new infections, although these levels vary considerably between studies. One study showed an improvement in milk production in the group that received procaine penicillin at weaning, although a 72 hr fast post-weaning produced a similar improvement. In a study conducted recently in Ontario, the prophylactic injection of tilmicosin one month prior to lambing (at the same time as the routine pre-lambing clostridial vaccination was done) has been shown to be of benefit in terms of a 43% reduction in udder abnormalities at weaning, and increased weaning weights of lambs (0.52 kg heavier than the control group). The decision to use a form of dry period antimicrobial therapy needs to be based on the prevalence of mastitis in the flock as well as ease of treatment (e.g. injection vs intramammary infusion) and withdrawal considerations.

Milking Management. The following recommendations are a summary of the current recommendations for the milking of sheep in Europe, USA and Argentina. More official recommendations for small ruminant milking machines will be forthcoming soon from the International Dairy Federation and will be published in Bulletin 354 (<http://www.fil-idf.org/Welcome.html>).

Vacuum Pump Capacity. Israel recommends 75 l / min per unit whereas Holland recommends values based on ISO Standard 5707 that takes into account effective reserve, air consumption of different components of the milking machine and air demand for cleaning, for example 650 l / min for 6 units; 1500 l/min for 24 units; and 1950 l/min for 30 units.

Pulsation Characteristics. Sheep are milked with a much faster pulsation rate than goats. The recommendations are 120-180 cycles/min and a pulsator ratio of 50%. 180 cycles/min was found to have the lowest SCC level in sheep.

Vacuum Levels. Sheep are milked at lower vacuum level at the claw than is recommended for cattle (32-40 kPa) but there are many differences depending on the milking system used. Recommendations vary from 33-36 kPa for lowline and bucket systems to 44-48 kPa for high line systems. 36 kPa has been recommended for dairy ewes in a system with the line 0.9 m above the platform.

Clusters. Dairy sheep producers tend to use cylindrical or hemispherical claws with a volume of between 60 and 200 cm³. The claw should also have a shut-off valve.

Other. Automatic cluster removal systems are rarely used for sheep although automatic cleaning systems are popular in large dairies. Some producers use udder holders to straighten teat placement.

Maintenance. Routine maintenance of small ruminant milking machines is at best sporadic. Problems such as liner cracks, vacuum fluctuations due to equipment malfunction, accumulation of dirt and milk stone in the system, can all lead to poor milk quality and increased incidence of IMI.

Units per Person. This varies greatly depending on the design of the parlour. For platform type parlours, 2 to 4 units/person are recommended for single platform and 2 to 7 for double platform. Milk-out time for sheep is very short (1.5 to 3 min) and over-milking is likely a common feature in many automated dairies.

Teat Dips. Very little work has been published on the evaluation of teat dips in small ruminants. More work needs to be published to be able to determine the level of efficacy in preventing new cases of IMI in sheep.

Udder Preparation. Because milk out time is very short in small ruminants, udder preparation needs to be done quickly as well, to prevent the loss of the effect of the udder stimulation on let-down. If udders are washed in preparation for milking, it is very important that they are dried sufficiently to prevent environmental mastitis, in particular *P. aeruginosa* mastitis, due to wet udders. One study compared goat herds that washed and dried udders with individual towels to herds that used a common wash towel and air dried the udder, and found that the latter practice was associated with higher rates of IMI. It may be better to only selectively wash dirty udders or reduce the number of units per milker to allow more time to properly dry udders, to help avoid this problem.

Other Treatments

The administration of vitamin E and selenium to dairy ewes during the dry period resulted in a reduction of SCC levels, particularly PMN's but not in the incidence of clinical mastitis or prevalence of IMI.

Zoonotic Considerations of Sheep Milk

The sale of raw milk is illegal in Ontario despite some people's view that it is a health food. It can contain many disease agents that can cause illness in humans. *S. aureus* is a commonly found bacteria in bulk tank milk with an average of 2 to 3 cfu / ml milk and has been isolated from up to 13% of cheese . Verocytotoxin-producing *E coli* H7:0157 has been isolated from raw sheep milk in Italy and is known to survive the processing system for soft Italian cheeses. *Listeria monocytogenes* has been isolated from store-bought semi-soft and soft sheep cheeses and from the milk, mammary lymph node and feces of sheep with subclinical mastitis. *Coxiella burnetii* is a common infection in sheep and outbreaks of human disease, in which people were hospitalized with severe illness, have been linked to the handling and consumption of raw goats' milk . Other pathogenic contaminants of milk include *Yersinia enterocolitica*, *Salmonella* sp, *Klebsiella* sp, *Streptococcus faecalis* and *E coli*.

Conclusions

In the last two decades, there has been a tremendous increase in knowledge of mastitis in sheep, particularly with respect to the infectious agents responsible for IMI and the interpretation of SCC levels. But if veterinarians are to effectively understand and control mastitis in sheep, the large gaps in our knowledge of the disease must continue to be addressed. With the increasing popularity in North America of dairy sheep milk products, better guidelines are required for the use of not just intramammary antimicrobial agents in the treatment of mastitis, but for all classes of drugs that might be beneficial for maintaining the health of this minor species that produce milk for human consumption.