# “Cherries on Top”

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## Introduction

Mastitis is a common disease of the udder found in lactating dairy ruminants that causes major economic loss through decreased milk quality and production.[4] Mastitis refers to the inflammation of the mammary gland, most likely secondary to infection or trauma.[1,4] Other less common causes include neoplasia or allergic reactions.[4] Mastitis causes physical and chemical changes in the milk and can cause pathological changes in the udder.

Mastitis can be categorized into environmental or contagious, depending on which bacteria are present and cultured. Contagious mastitis is caused by pathogens found within the mammary gland and passed from animal to animal, mainly through fomites during milking.[5,7] Pre dipping teats prior to milking can help aid in prevention. Pathogens found in the environment lead to environmental mastitis and can be managed through maintaining clean, dry living areas and post teat dipping.[7] Ensuring udders are clipped, cleaned, and dried with one use towels can also decrease spread of disease.[2,4] Mastitis can be difficult to treat, which is why prevention and control are key factors in maintaining a mastitis free herd.

Mastitis can range from subclinical to peracute to acute and chronically clinical.[4] The subclinical form can often only be determined through Somatic Cell Count (SCC) levels due to the absence of clinical signs. [1] Somatic cells are made up of epithelial cells and white blood cells, so in animals with infections, these levels increase.[1,2,3] Detecting subclinical cases can help prevent spread to other animals. Clinical cases are based on causative agent, severity of clinical signs, and duration of illness. Peracute mastitis causes more systemic infections (depression, fever, anorexia) leading to mortality rates in the 30-40%.[4] Acute and chronic mastitis are mainly localized to the udder.[4] Chronically infected animals should be culled or isolated from the herd. [1]

An infection caused by *Staphylococcus aureus* is the most common and important cause of clinical mastitis in a majority of dairy goats.[1,2,5,6] It is also a main cause of subclinical mastitis, which can develop into clinical.[4,5,9] *S. aureus* mainly resides in teat lesions caused during milking but can be found on the skin (teat, muzzle nostrils) of healthy animals and is quick to invade injured tissue.[2] It is transmitted during milking, making this a contagious pathogen. *S. aureus* infections can be found in many mammals, and though most strains are species specific, it carries a potential zoonotic health risk if contaminated milk is consumed.[6,7] One study showed that 67% of S. aureus isolates produced at least one enterotoxin gene in caprine and ovine milk.[6] *Staphylococcus aureus* can be difficult to treat because it is an intracellular organism that has the potential to form a biofilm and creates micro abscesses that antibiotics are unable to penetrate leading to antibiotic resistance.[2]

Other common pathogens of mastitis infecting the caprine species that will not be discussed include *Streptococci* spp. (*S. agalactia* most common), *Pasteurella haemolytica* (suckling kids), *Corynebacterium pseudotuberculosis* (herd abscess problem), and less commonly, *Mycoplasma* spp.[1]

**History and Presentation**

Under Destiny Triple Cherries, nick named Cherries, is a 1.5 year old Lamancha doe that was found Monday June 24, 2019 with a swollen udder and ventral edema. Owners suspected a snake bite and began treating her at home with flunixin meglumine, penicillin, florfenicol, and diphenhydramine. After no success, on June 25$^{th}$, she was taken to her rDVM where she was treated with furosemide and dexamethasone to help reduce udder edema. The swelling decreased throughout the evening but was still apparent, so on June 26$^{th}$, the owners elected to bring her to MSU-CVM Food Animal Services for further examination and workup.

Upon presentation, Cherries was bright, alert, and responsive. She weighed 53.2 kg (117 lbs) and had an ideal body condition score of 5/9. She exhibited a head tilt that the owner associated with a previous ear infection treated in May 2018. On physical examination, she was tachycardic with a heart rate of 168 beats per minute and tachypneic with a respiration rate of 60 breaths per minute, though both heart and lungs auscultated normally. She was normothermic with a temperature of 100.9, and her mucous membranes were a pale pink. Her sclera was moderately injected. She had mild discharge from both ears with crusting around the edges. Her ventral abdomen showed moderate fluid accumulation extending from her sternum to her udder. No snake bites or other puncture wounds were appreciated. The left teat was swollen, cold to the touch and complete sensation was absent. The exterior surface of the teat was a dark purple in color. The right teat had the same coloring on the caudal aspect but normal pink flesh cranially.

**Diagnostic Approach**

Blood was pulled for a complete blood count and large animal chemistry profile. The complete blood count showed a severe leukocytosis (39.9; NRI (5-17)) with a mature neutrophilia (33117; NRI (700-7600)) and monocytosis (3990; NRI (70-570)) indicating there was an ongoing infection. An increased PCV and Hgb indicates that she was dehydrated. The chemistry profile revealed moderate hypokalemia (2.13; NRI (3.4-5.7)) along with other mild electrolyte imbalances, moderate hyperglycemia (182; NRI (45-70)), and azotemia with an increased BUN (40; NRI (19-31)) and creatinine (1.46 (0.7-1)). She also had an increase in total bilirubin (1 (0-0.1)) and CK (3590 (104-219)).

Bloody milk was extracted from the left side of the udder while normal appearing milk came from the right. A milk sample was taken from both teats for culture and sensitivity. Though a California Mastitis Test (CMT) can be used for the diagnosis of mastitis in the goat, goat milk

naturally has a higher somatic cell count (SCC) than the bovine.[4] A CMT score yielding a negative (0), trace, or 1 can be seen in noninfected goats, so a score of 2 or 3 indicates a diagnosis of mastitis.[5] Furthermore, a North American dairy goat farm survey showed no bacterial growth in the milk of ~50% goats with SSC levels greater than the recommended $10^6$ cells/ml of milk.[4] An intramammary infection can be presumed if SSC is greater than 1,500,000 cells/ml.[5] Infections caused by S. aureus cause a dramatic increase of SSC (4-8 x $10^6$ cells/ml), making a CMT a good diagnostic tool in the field for this particular bacteria.[4,9] Since Cherries clinical presentation was diagnostic for mastitis, a CMT was not performed. Instead, samples from the teat were collected to identify the pathogen to pursue proper treatment. Culture and sensitivity allows for the most appropriate antibiotic selection to ensure treatment efficacy.

Culture and sensitivity results revealed growth of *Staphylococcus aureus* (>10,000 cfu/ml milk) and a gram-negative organism (100 cfu/mL milk) in the left teat with no growth in the right teat. Antibiotic susceptibility showed only resistance to Ampicillin while this *S. aureus* strain was susceptible to Ceftiofur, Cephalothin, Erythromycin, Novobiocin, Oxacillin, Penicillin, Penicillin/Novo, Pirlimycin, and Tetracycline. Based on clinical presentation and culture results, Cherries was diagnosed with gangrenous mastitis caused by *Staphylococcus aureus*.

**Pathophysiology**

*Staphylococcus aureus* is a gram-positive, aerobic cocci bacterium that is catalase positive and coagulase positive.[11] S. aureus has a variety of virulence factors, making its pathogenesis multifactorial.[12]

*S. aureus* first enters the teat canal through a lesion in the skin at or just after milking.[7] It invades the epithelium through surface protein adherence with the help of toxins (hemolysins, leukotoxin, leucocidin) that lyse cell membranes, initiating an inflammatory response.[2,7,12] *S. aureus's* capsule, along with Protein A, helps with phagocytosis resistance by the white blood cells recruited.[2,3,7,12] If phagocytized, *S. aureus* keeps dormant until the leukocytes die off, which enables the spread of infection.[2] *S. aureus* then migrates up the gland cistern, causing damage that leads to the formation of scar tissue.[2] The bacteria ascend through the ducts into the alveoli, which are the milk secreting cells.[1,2] Once in the alveoli, the immune system forms an abscess in attempt to isolate the infection.[2] This allows *S. aureus* to be undetected by the body and can even prevent antibiotics from penetrating the bacteria.[2] This intermittent shedding makes it difficult to treat the infection and allows the pathogen to spread easily through the mammary gland.[7]

The affected area becomes ischemic due to vasoconstriction from the production of alpha toxins by *S. aureus*.[3,10] Strains that produce these toxins are the most common cause of mastitis leading to gangrene and ultimately sloughing of the necrotic tissue.[3,7]

**Treatment and Management**

Medical management of gangrenous mastitis alone is not always successful, and a mastectomy is often the most effective treatment.[8] With *S. aureus*, it is important to perform an antibiotic sensitivity test to ensure there's not antibiotic resistance.[2,4]

On June 26th 2019, Cherries underwent a teat amputation. This was done in hopes to preserve the right teat for future kidding and lactation, as studies have shown to be successful.[8] Stay sutures were placed in the remaining tissue to assist in proper drainage. A tube of

cephapirin sodium was administered into the right teat canal as a preventative measure. There are few drugs approved for the use in dairy goats, and none for mastitis; therefore, medical treatment must be administered extra-labelly through a veterinarian with a valid VCPR.[4] Cherries was given oxytetracycline intravenously as a broad spectrum antibiotic while awaiting culture and sensitivity results. Cherries was also started on Procaine Penicillin G and ceftiofur sodium subcutaneously. The administration of ceftiofur sodium subcutaneously was done so extra-labelly, and is prohibited in cattle, swine, chickens and turkeys. Doing this may result in illegal residue, and therefore should not be used in animals intended for slaughter. She was started on intravenous lactated ringer solution at double maintenance rate, and once hypokalemia was revealed on biochemistry, potassium (20 mEg/L) was added to the fluids. Flunixin meglumine intravenously was added to combat endotoxins and inflammation. Covexin 8 (clostridial vaccine) was also administered at that time due to tissue necrosis and concern of developing tetanus. She received Butorphanol for pain control throughout the first night.

On June 27th 2019, Cherries was dull and uncomfortable. Quadrifusion (Ketamine, Butorphanol, Xylazine, Acepromazine) was added to her fluids to better aid in pain control. Vitamin B was also supplemented into the bag at this time for appetite stimulation. Due to anorexia and likely bacteremia, dextrose 2.5% was added to her fluids to keep her glucose in normal ranges. The gangrene further spread cranially up her ventral abdomen to include her caudal epigastric vasculature. Furthermore, the medial aspect of her right teat surface was beginning to necrose as well. Icing her ventral abdomen and udder three times a day was included in her treatment regimen due to the progression of swelling and darkening pigment changes. Throughout the evening, her hyporexia improved as she began to graze.

The morning of June 28th 2019 a blood glucose performed revealed she was hypoglycemic (59 g/dl), despite her increased appetite. She was administered a bolus of dextrose 50%. Further spread of the infection was not appreciated. There was considerably less drainage and discharge from the amputated teat. Cherries fluids were increased to 5% Dextrose solution due to her continued inability to maintain normal glucose levels; however, that evening her glucose was 92 g/dl, so fluids were decreased to 1.5 maintenance.

Cherries began to improve on June 29th 2019, as she seemed more comfortable and her mentation improved. She maintained her glucose through the night, so fluids were decreased to maintenance and the 2.5% dextrose solution was discontinued and replaced with lactated ringers solution.

On June 30th, her fluid rate was decreased to half maintenance to encourage her to drink on her own. Her blood glucose remained within normal limits. The infected skin from the gangrenous mastitis on her udder and ventral abdomen continued to declare itself with a tan ring dividing the infected tissue from the healthy.

On July 1st 2019, she was discontinued from fluids. Debridement of her left teat was performed to remove the necrotic tissue. An incision was made in the subcutaneous layer on her ventrum and up the right teat where necrotic tissue was present to allow drainage.

**Case Outcome**

On July 2nd 2019, Cherries was discharged to her owner and scheduled for a 2 week recheck. She was sent home on ceftiofur sodium and Penicillin Pen G. Owners were instructed to keep her in a dry place with adequate fly control to ensure the wound cleanliness and prevent myiasis. Though the wound would take weeks to months to completely heal, Cherries had

recovered systemically. The owners were made aware that the tissue will begin to slough, and further debridement may be necessary for proper granulation tissue formation. They were instructed to monitor her right teat for heat, swelling, discoloration or further spread. If she became depressed, lethargic, or hyperthermic, she was to return for reevaluation.

Cherries returned on July 17th 2019 for a recheck. She had greatly improved and there was a large scab over most of her wound and partially on her right teat, which was debrided and scrubbed with chlorhexidine. Her final recheck was on August 21st 2019. The wound was healing properly, and a healthy bed of granulation tissue had formed. The key to successful healing and future prevention is through the practice of good hygiene and biosecurity.[7]

Prognosis in animals with gangrenous mastitis is normally guarded to grave due to the risk of septicemia.[13] Individuals infected with mastitis are often culled to aid in prevention of further spread throughout their herds, or due to production losses.[1,13] Early treatment with the appropriate antibiotics and surgical intervention can result in successful outcomes, however, sometimes it's not economically feasible. In Cherries case, she was economically valuable enough to perform a teat amputation and future use of her as a breeding doe with the understanding future kids may need milk supplementation. Ultimately, Cherries treatment was successful and is normal as of 11 months post-infection and teat amputation.

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