

Treatment of Postpartum Metritis in Dairy Cows

K. W. Pulfer, DVM
R. L. Riese, DVM, DACT

Introduction

Bovine postparturient metritis is an economically significant problem in most dairy herds. Although mortality is low, morbidity is often high, and systemic illness may result in lowered feed consumption and decreased milk production, as well as losses incurred because of milk dumping due to antibiotic residues in milk from treated cows. Metritis significantly increases days to conception and services per conception, leading to losses from reduced milk production associated with longer calving intervals and higher insemination costs. Fertility may be permanently impaired in some cows, causing higher culling rates and the associated increase in replacement costs. Culling because of decreased fertility often results in a loss of freedom to cull for other factors such as low production, and may result in the culling of genetically superior animals.^{1,2,3}

Pathogenesis

Many factors are associated with the development of postparturient metritis. Retained fetal membranes and dystocias, along with the uterine manipulation that often accompany these conditions are most often incriminated.^{1,3,4} Other factors include the development of concurrent metabolic and infectious diseases, nutritional deficiencies, hormonal imbalances, or unsanitary calving conditions.^{1,5,6} It must be realized that metritis is at times iatrogenic, as increased incidence has been associated with some intrauterine treatment choices.

* Dr. Pulfer is a 1990 graduate of the College of Veterinary Medicine.

**Dr. Riese, formerly an assistant professor of Veterinary Clinical Sciences at Iowa State University, is in private practice in Melbourne, Iowa.

Etiology

Much work has been done to identify the species of bacteria associated with metritis. It has been found that most, if not all, bovine uteri are bacterially contaminated in the immediate postpartum period. Culture at this time will usually yield a wide range of bacteria, including *Actinomyces pyogenes*, *Streptococcus*, *Staphylococcus*, and *Clostridium* spp., coliforms, and gram negative anaerobes.^{1,2,4,7,8,9} The presence of these organisms at this time should not be considered abnormal. In the normal postpartum uterus, bacterial numbers should drop rapidly after parturition, and bacteria will be absent or present only in very low numbers within three to four weeks of calving. Metritis results because of an alteration in the normal clearing of these organisms from the uterus. In the early postpartum period, retained fetal membranes and/or uterine inertia often result in an explosion of coliform and *Clostridium* spp. bacteria. The retained membranes provide an ideal substrate for bacterial growth. The lack of mechanical expulsion is a major factor in this increase.⁴ Bacterial exotoxin and endotoxin absorption may result in toxic metritis at this time.

Later in the postpartum period, the bacterial species commonly associated with metritis include *Actinomyces pyogenes* and anaerobic gram negative bacteria, usually *Fusobacterium necrophorum* or *Bacteroides* spp.⁸ Coliform bacteria are an uncommon finding at this time.^{1,7,8} These later infections are rarely associated with systemic illness and because there is often little or no external drainage of purulent material from the vagina, these infections often go unnoticed.

Diagnosis

Metritis is often suspected because of the presence of a purulent, malodorous vaginal discharge. This is often seen as a puddle under the vulva when the cow is lying down or as exudate on

the perineum, tail and vulva. The exudate is usually reddish-brown or white, depending on the type and stage of infection present. The viscosity and the odor of the exudate should be noted as the normal postpartum uterine exudate will be quite high in mucus and without an offensive odor. However, absence of noticeable drainage by no means rules out the presence of infection. Examination of the vulva manually or with a speculum may reveal purulent exudate in the anterior vagina or clinging to the external cervical os.

Many cows with metritis will have a clean vagina upon examination and no apparent discharge. Thus, uterine palpation per rectum should always be performed when metritis is suspected. An infected uterus and cervix will have delayed involution, one horn is usually larger than the other, fluid may be present in one or both horns, or the uterine wall feels thickened and "doughy". Care should be taken when palpating an enlarged or pus-filled uterus as the uterine wall may be friable which could result in rupture or perforation leading to peritonitis. Infection of the uterus extending to the serosal surface is known as perimetritis and often leads to adhesion which may impair fertility. Exudate from the uterus may also infect the oviducts, ovaries, bursas and other surrounding structures.

Toxic metritis

Signs of toxemia may be noted in some cows with metritis. These include anorexia, pyrexia (not always), depression, and dehydration. Mortality, while not common, is possible. Usually, toxic metritis occurs in cows shortly (2-14 days) after calving.⁷ There is good blood supply to the uterus at this time enhancing the absorption of bacterial toxins produced by gram negative bacteria in the uterus at this stage of the postpartum period. High numbers of gram negative bacteria elaborate large amounts of endotoxin, making endotoxemia the most likely etiology of this condition.¹

Toxic metritis is a condition that requires prompt and aggressive medical intervention. Therapy should be aimed at removing as much of the toxic uterine material and treating the animal for systemic signs of toxemia. Uterine lavage with a dilute chlorhexidine solution is very useful in these situations. Dilute iodine solutions may also be used, but have the disadvantage of being more caustic and irritating than chlorhexidine. A stomach tube is passed through the cervix into the previously pregnant horn and the solution pumped

into the uterus or allowed to infuse via gravity. The tube is then disconnected and held below the level of the uterus to set up a siphon effect. Approximately one liter of solution is infused or until some of the solution flows back through the cervix. Care must be taken that the uterus is not overly distended with fluid. Over distention may lead to the forcing of purulent material up through the oviducts or to uterine rupture.

An effort should be made to keep the fluid as close to body temperature as possible, since a cold or hot solution will cause irritation that may lead to straining. A hot solution poses the additional threat of causing uterine hyperemia which may increase the absorption of intraluminal toxins, thereby precipitating a toxemic crisis. The infusion and drainage should be repeated until the draining fluid is about the same color as the infused fluid.⁷ The flushing may be followed by infusion of an antibiotic into the uterine cavity.

Systemic signs should be treated as one would treat most toxemias. A combination of systemic antibiotics, antiinflammatory drugs, and supportive therapy will usually be very helpful.⁷ Systemic penicillins or tetracyclines are often used because of their combination of efficacy, economy, safety, and reasonable milk withdrawal times. As with all antibiotic administration to lactating dairy cows, the milk should be tested and found free of antibiotic residues before it is saved.¹⁰ Many anti-inflammatory agents have been used in the treatment of toxic metritis with varying claims of efficacy. Flunixin meglumine may be especially useful in this situation, considering the role of absorbed endotoxin. This is however, an extra-label drug use. Intravenous electrolytes and glucose are often indicated and should be administered in large amounts (10-20 liters).

Treatment

Treatment of metritis which is not causing systemic problems, while not a medical emergency, is extremely important for the future reproductive performance of the animal. The goals of metritis treatment should be to clear the uterus of the infection with minimal trauma to the tissues. This allows for conception soon after treatment. Many of the treatments commonly employed do not allow for early conception due to the ineffectiveness of the drug or to uterine damage caused by the drug. Persistent infection of a uterus undergoing repair may not prevent estrus and breeding, but likely will affect conception or the life

of the early embryo. Increased days open is often seen as a problem with intrauterine therapy.^{1,12} Treatments commonly fall into three areas: antibiotic therapy, chemical disinfectants, and hormonal therapy.

Antibiotic therapy in the treatment of metritis should be directed at presenting a sufficient concentration of an appropriate antibiotic to the site of the infection. Since, in metritis, the infection is present into the deeper structures of the uterus and possibly even to the serosal surface, inappropriate antibiotics or antibiotics in too low a concentration may not be absorbed and presented to the site of the infection. Other structures such as the oviducts and ovaries may also be infected and these would not necessarily be treated by antibiotics placed into the uterine cavity. Antibiotics infused into the uterus are absorbed into the systemic circulation and may appear in the milk or meat.¹⁰ uterine infusion of antibiotics does not mean that milk and meat withdrawal times do not apply. The amount of antibiotic absorbed depends on the drug, its form, its carrier, the amount used, and the disease status of the uterus it is infused into.¹¹ Appropriate caution should be taken when marketing meat and milk products from treated cows.

Although only neomycin is labeled for bovine intrauterine therapy,¹³ many other antimicrobials including penicillin, tetracyclines, aminoglycosides, nitrofurazone, and sulfonamides, with and without potentiation, have been used for extra-label applications.^{11,14}

Sulfonamides inhibit bacterial folic acid formation and their activity against causative organisms appears good in vitro. Pus and necrotic debris present in the infected uterus provide the metabolites needed by the bacteria to produce folic acid. This antagonizes the action of sulfonamides and renders them ineffective.¹⁴ Sulfonamides can also be quite irritating to the endometrium.

Aminoglycosides also demonstrate a good spectrum of activity in vitro, however their uptake by bacteria depends on the presence of oxygen for oxidative phosphorylation to provide the energy needed for active transport of the drug across the bacterial membrane. Therefore, their effectiveness is extremely diminished in the oxygen-deficient atmosphere of the infected uterus.¹⁴

Nitrofurazone, in its commonly available concentrations, has difficulty meeting the minimum inhibitory concentration necessary for bacterial inhibition. It also has reduced effectiveness in the

presence of pus, blood and necrotic debris and is also quite irritating to the endometrium.^{1,14}

The action of tetracyclines is not affected by the presence of pus, blood or necrotic debris in the uterus, making them a good choice for treating the mixed-bacterial infection in the early postpartum uterus. One resistant bacteria also does not provide protection for the others. Dosages range from 0.5-5.0 grams and the infusion should be repeated every 1-2 days until the infection is under control. Tetracyclines can be quite irritating to the endometrium and may be detrimental to uterine defense mechanisms. However, if used in a sufficient volume of carrier, usually distilled water or saline, they remain a good choice for use with the mixed infections of the early postpartum period.

Penicillin is less irritating to the endometrium but resistance patterns of the mixed bacterial flora of the early postpartum uterus make it a poor choice. One resistant bacteria provides protection for the rest. Penicillin is very effective against the bacteria seen in the later postpartum period, namely *Actinomyces pyogenes*, *Fusobacterium necrophorum*, and *Bacteriodes* spp. Dosages range from 1-10 million units and should be repeated daily for optimum effect.^{11,14} Dilution of the antimicrobial in 10-100 ml of a sterile solution such as saline or distilled water has been advocated to allow better distribution of the compound within the uterine lumen.¹¹ It is felt by some that the lack of irritation seen with penicillin versus tetracycline will lead to improved endometrial health and more rapid conception.¹⁰

Parenteral antimicrobial therapy for metritis which is not causing systemic signs may be a viable alternative to intrauterine therapy, especially if the producer realizes that all milk from treated cows needs to be discarded, regardless of the route of therapy. Parenteral therapy will generally produce adequate antibiotic levels in all genital tissues, not just the uterine lumen. This route may also eliminate drug induced damage to the endometrium and allows repeated treatment without the risk of introducing new infection. The choice of antibiotic used should rely on the therapeutic considerations previously discussed regarding intrauterine therapy, with penicillin and tetracyclines most commonly used.¹¹

Intrauterine infusion of disinfectants such as iodine, chlorhexidine, or cresol derivatives has been advocated for metritis treatment. Studies have shown that strong iodine solutions will cause endometrial necrosis and return to estrus within 4-

7 days. The irritation caused by the disinfectant has been demonstrated to invoke a prostaglandin release with subsequent luteolysis and return to estrus.¹⁵ This is most likely true for other disinfectants as well. They are also quite detrimental to uterine defense mechanisms. Since their primary role appears to be luteolysis, the advent of more efficacious luteolytic agents has made their use of questionable value.

Hormone Therapy

Hormone therapy for metritis has become increasingly popular with the introduction of more effective compounds and the tighter control of antibiotic milk residues. Hormones have the added advantage of quick and easy administration, as most are effective when given intramuscularly. In addition, there is usually enhancement rather than interruption of uterine defense mechanisms.

Hormones are used to stimulate uterine evacuation and improve the effectiveness of uterine defenses. In general, agents can be divided into those that directly affect the uterus and those that induce estrus or an estrus-like state. Oxytocin and ergonovine fall into the first category and estrogens and prostaglandins fall into the latter. Oxytocin is often used immediately postpartum to facilitate placenta removal. While the efficacy of its use here is often in contention, it is agreed that oxytocin will induce uterine contractions in animals with high levels of circulating estrogen. Therefore, it is relatively useless in animals that are more than 2-3 days postpartum and not in the follicular stage of their cycle. Oxytocin's short half-life also makes repeat treatments necessary. Ergonovine is a fungal derivative and not actually a hormone. Empirical evidence has been the main basis for its use. Controlled trials have shown little or no effect on myometrial contraction.¹¹

Estrogen stimulation of the uterus causes increased myometrial tone and activity, as well as stimulating the uterine immune mechanisms.⁷ Estrogen may be used alone for metritis treatment. Recommended doses of estradiol range from 3-10 mg and doses may be repeated twice at 3 day intervals.¹¹ A major problem with the administration of exogenous estrogens is the fact that the uterus will contract regardless of the patency of the cervix. This has the potential to force purulent material up the oviducts, a process which can cause salpingitis, oophoritis, and adhe-

sions, all of which will have a detrimental effect on future reproductive performance.⁷ However, estrogen is the only therapeutic agent which will consistently produce uterine contractions in animals at all stages of cyclicity, and it has been found to be at least as effective as prostaglandins when given before day 40 postpartum.⁷

Induction of estrus is the ideal treatment for metritis. During estrus there is very effective expulsion of uterine contents and stimulation of uterine defense mechanisms to a very high level. In addition, the corpus luteum (CL) formed may be destroyed with estrogen or prostaglandin after 6-8 days, leading to another estrus; in effect a repeat treatment for the metritis. As prostaglandin's direct effect on the uterus is fairly minimal, it is essential that the cow have an active CL in order to derive maximal benefit from its administration. Successful induction of estrus occurs 80-90% of the time following prostaglandin administration to a cow in the luteal stage of her cycle compared to 55-60% success following estrogen administration.¹¹

Conclusion

Treatment of bovine metritis should focus on several goals. First, any systemic involvement should be treated to protect the immediate health of the cow. Treatment of the metritis itself and preservation of future fertility are also of primary importance and need to be considered together. Many commonly used treatments for metritis have been shown, in controlled studies, to decrease the future fertility of the cow, thus increasing the days to conception and raising the chances that the treated cow will be culled for reproductive reasons. Treatments, therefore, need to be chosen and applied cautiously with the above considerations in mind.

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Dr. Ila Davis