



## Therapeutics of Postpartum Uterine Infections

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Postpartum metritis is one of the most important disorders in cattle causing high economic losses due to prolonged days open and inter-calving intervals, resulting in involuntary culling. Various microorganisms are responsible for causing metritis, among which Arcanobacterium pyogenes, coliforms and the Gram-negative anaerobes, Fusobacterium and Bacteroides species are frequently involved. Infections generally gain entry during calving and are often associated with difficult birth (dystocia) and Retention of Fetal Membranes (RFM). Under normal conditions, the normal Uterine Defense Mechanism (UDM) eliminates microorganisms from the uterus during uterine involution. However, when the UDM is compromised due to various factors the clinical symptoms of metritis set in and sometimes lead to the death of the animal. Various therapeutic measures are available to counteract metritis worldwide with their own merits and demerits.

### Postpartum metritis

Postpartum metritis is an inflammation of the uterus that affects both the endometrial and muscular layer (Azawi, 2008). The prevalence of metritis is 28.90% in first calvers and 38.93% in all calvers. The prevalence of uterine infection in buffalo cows was substantially greater than in cows, at 24.7% in India (Gupta *et al.*, 1978; Rao and Sreemannarayana, 1983). The majority of cases occur within the first 10-14 days of delivery and are commonly referred to as toxic puerperal metritis (Sheldon *et al.*, 2004). Postpartum metritis typically occurs after an irregular first or second stage of labour, particularly in cases of severe dystocia. Metritis is also linked to uterine inertia, twin births, RFM, long manipulations, and damage to the vulva and/or birth canal (Noakes, 2002). It has been discovered that up to 40% of animals acquire metritis within the first fourteen days of calving, and in 10 to 15% of these animals, infection persists for at least three weeks, resulting in chronic uterine disease (endometritis). However, clinically, metritis must be distinguished from endometritis. Endometritis is an inflammation of the uterine mucus membrane that causes mucoid, mucopurulent, or purulent discharge from the vulva three weeks after parturition or later.

- **Symptoms:** Animals with metritis exhibit both local and systemic symptoms. Common complications include toxæmia, septicæmia, and pyrexia. Affected cows may have higher temperatures (40-41°C), but are often subnormal. The animal has a fast pulse rate (about 100/minute) and may have increased breathing. Animals suffer from anorexia, dehydration, toxæmia-induced diarrhoea, and shock. The infection can spread from the uterine wall to the peritoneum, resulting in localized or widespread peritonitis (Sheldon *et al.*, 2004). The uterus produces poisonous, fetid, reddish, and serous exudates that include degenerating fetal membranes. Animals frequently exude exudate from their vaginas due to straining. Exploration of the vagina and uterus might induce considerable discomfort and expulsion. The cotyledons are enlarged, and the fetal membranes are often securely

linked. The vaginal mucosa is irritated and thickened, while the cervix is partially open. If left untreated, the cow will quickly become recumbent, dehydrated and emaciated, death may occur within a few hours (Jackson, 2004).

- **Therapy of postpartum metritis:** Postpartum metritis is commonly treated with antibiotics or hormones, alone or in combination. Antibiotics may be administered systemically or are infused intrauterine. In more severe cases other symptomatic therapies like anti-inflammatory agents and intravenous fluid therapy are also advocated.
- A) **Intrauterine Therapy (IU therapy):** To treat metritis and other uterine disorders, intrauterine therapies such as antiseptics, antibiotics, and immune modulators are injected into the uterus. Penicillin is a popular antibiotic for postpartum metritis and endometritis due to its ability to enter all layers of the uterus and effectively treat bacteria that cause septicaemia. There are many antibiotics which are commonly associated with metritis such as third-generation cephalosporins, a combination of ampicillin and oxytetracycline, or cloxacillin. These therapies aim to eliminate bacterial infections, stimulate the uterine defence mechanism, or enhance blood flow. Intrauterine therapy commonly involves infusing iodine solution in water or saline. The following criteria are important for choosing antibiotics for the treatment of uterine infections:
1. The antibiotic should be active against the main uterine pathogens and should maintain its activity in the environment of the uterus. Antibiotics that are ineffective under anaerobic conditions, such as aminoglycosides are not recommended for the treatment of postpartum uterus (Olson *et al.*, 1984; Baron, 2004).
  2. The uterine lochia consists of organic fluids and debris and contains a variety of Gram-positive and Gram-negative aerobic and anaerobic bacteria (Sheldon *et al.*, 2004). Consequently, a broad-spectrum antibiotic that is active in the presence of organic debris is indicated (Bretzlaff, 1986). This eliminates the sulfonamides, which are ineffective in the presence of tissue breakdown products.
  3. The antibiotic should be present in a sufficient concentration at the site of infection (i.e. the sub-endothelium). The preparation should not inhibit the normal defence mechanisms and should be well tolerated and not induce irritation.
  4. Antibiotics must reach MIC (minimum inhibitory concentration) to eliminate any bacterial infection (Deori and Arundhati, 2015)
- B) **Systemic antibiotics:** Antibiotic therapy should be initiated immediately. Penicillin is one of the most preferred antibiotics for postpartum metritis because it penetrates all the layers of the uterus, is less expensive, and most of the bacteria penetrating the endometrium leading to septicaemia are responsive to penicillin. Alternatively, ceftiofur sodium at the rate of 2.2 mg/kg IM may be used as systemic antibiotic therapy for 3 to 5 days with no withdrawal requirement. Ceftiofur sodium has been reported to concentrate in the uterus at levels exceeding the mean inhibitory concentrations for *Arcanobacterium pyogenes*, *Fusobacterium necrophorum* and *Escherichia coli*.
- C) **Non-steroidal anti-inflammatory drugs and fluid therapy:** Flunixin meglumine 2.2 mg/kg was given intramuscularly twice a day for three days to treat clinical metritis and endometritis, acting as an anti-inflammatory, antipyretic, and analgesic overall leading to endotoxic effect. Fluids can be given as 2.0-2.5 litres of 7% v/w NS IV followed by 25 litres of isotonic electrolytes by stomach tube (Negasee, 2020)
- D) **Hormonal therapy:** Treatment with prostaglandin or analogues can effectively evacuate the uterus by uterine contraction when Corpus Luteum (CL) is present in one of the ovaries. Prostaglandins are beneficial for cows between 30-45 days of lactation. Expelling uterine fluids helps cows reach their first postpartum estrus. Oxytocin is another hormone available for use. It contributes significantly to uterine contraction during calving.

Although it can trigger uterine contractions for days after calving, it is unclear if it increases postpartum reproductive success.

- E) **Ozone therapy:** Ozone breaks the cell membranes of microorganisms and has been shown to permeate through the protein covering of viruses' nucleic acids to kill them. When ozone foam (Ringer spray G) is sprayed on cows suffering from metritis and endometritis, it has been shown to heal the disorders and can be an effective alternative therapy with an overall improvement in cow fertility.
- F) **Phytotherapy:** There are a variety of plant-based immunomodulators available to treat bovine reproductive problems. The active component found in these plants is responsible for their immunomodulatory activity. Some examples of active compounds having antibacterial and antifungal properties include allicin in garlic, sitoindosides VII-X and withaferin in ashwagandha, hydroalcoholic and hydroacetic in neem, and eugenol in tulsi (Gupta *et al.*, 2023).
- G) **Immunomodulators:** Treatment of animal endometritis using antibiotics resulted in inconsistent recovery rate, emergence of microbial resistance and reduced innate uterine defence mechanism by poor phagocytic activity of PMN cells, withdrawal in milk. Hence, an alternative therapy by using natural substances as a means of activation of uterine defense mechanism gain importance. Substances like LPS, autologous plasma, leukotrienes B4 (LTB4), oyster glycogen, lysozymes etc can be utilized for therapeutics (Sarkar *et al.*, 2016).
- H) **Miscellaneous Drugs:** Calcium is an essential trace element that causes smooth muscle contraction in the uterus. Most high producing cows become calcium deficient immediately after calving, resulting in uterine muscle atonicity and, ultimately, fetal membrane retention and metritis. As a result, prescribing oral calcium during this time may help to prevent metritis. Cows may lose their appetite after calving, and this can lead to ketosis, which causes displaced abomasum or metritis. In such cases, supplementation with propylene glycol or propionate is useful. Supplementation of antioxidants (vitamin E and Se) and immunomodulators like levamisole can be used as supportive therapy in the treatment of metritis.

## Conclusion

Postpartum metritis is a significant global issue, especially in high-yielding dairy cows. The occurrence of uterine disease depends on the cow's immune response and the type and amount of bacterial infection. Currently, antibiotics and hormones are the primary treatments, but both have limitations. Antibiotics can lead to withdrawal periods, residues in milk and meat, drug resistance, and disruption of the normal uterine microbiome. Hormonal therapies are often expensive and not widely available. Effective strategies should focus on preventing metritis in postpartum cows. Immediate veterinary attention is crucial in cases of difficult births. Regular monitoring and timely veterinary care are vital to ensure a successful recovery and reduce complications, ultimately enhancing the health and reproductive performance of the affected animals.

## References

1. Azawi, O. (2008). Postpartum uterine infection in cattle. *Animal Reproduction Science*, 105(3–4), 187–208.
2. Baron, S. (2004). *Medical Microbiology*. Texas Univ., Medical Branch, Galveston, TX, 312–344.
3. Bretzlaff, K. N. (1986). Factors of importance for the disposition of antibiotics in the female genital tract. In D. A. Morrow (Ed.), *Current Therapy of Theriogenology* (pp. 34–47). W.B. Saunders Co., Philadelphia, PA.



4. Deori, S., & Phookan, A. (2015). Bovine postpartum metritis and its therapeutics: A Review. *Indian Journal of Science and Technology*, 8(23), 1.
5. Gupta, P. P., Singh, B., Mandal, P. C., Gill, B. S., & Grewal, G. S. (1978). A postmortem study of mortality pattern in adult buffaloes in Punjab India. *Indian Journal of Animal Sciences*, 48, 669–673.
6. Gupta, V. K., Mohanty, T. K., Bhakat, M., Dewry, R. K., Katiyar, R., Nain, D., Shah, N., Sethi, M., Rautela, R., Singh, M., & Deori, S. (2023). Bovine reproductive immunoinfertility: Pathogenesis and immunotherapy. *Frontiers in Veterinary Science*, 10, 1248604.
7. Jackson, P. C. C. (2004). *Handbook of Veterinary Obstetrics* (2nd ed.). Elsevier Limited.
8. Negasee, K. A. (2020). Clinical metritis and endometritis in diary cattle: A. *Veterinary Medicine Open Journal*, 5, 51-56.
9. Noakes, D. E., Parkinson, P. J., & England, G. C. W. (2002). *Arthur's Veterinary Reproduction and Obstetrics* (8th ed.). W.B. Saunders Company.
10. Olson, J. D., Ball, L., Mortimer, R. G., Farin, P. W., Adney, W. S., & Huffman, E. M. (1984). Aspects of bacteriology and endocrinology of cows with pyometra and retained fetal membranes. *American Journal of Veterinary Research*, 45, 2251–2255.
11. Rao, A. V. N., & Sreemannarayana, O. (1983). Clinical analysis of reproductive failure among female buffaloes (*Bubalus bubalis*) under village management in Andhra Pradesh. *Theriogenology*, 18, 403–411.
12. Sarkar, P., Patra, M. K., & Kumar, H. (2016). Strategic treatment with immunomodulators to resolve endometritis in cow: A review. *Agricultural Reviews*, 37(3), 186-195.
13. Sheldon, I. M., & Dobson, H. (2004). Postpartum uterine health in cattle. *Animal Reproduction Science*, 64, 295–306.