

# Evidence for the Use of Ceftiofur for Treatment of Metritis in Dairy Cattle



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## KEYWORDS

• Dairy cattle • Metritis • Uterine disease • Ceftiofur • Cephalosporin

## KEY POINTS

- Uterine disease, such as metritis, is frequently diagnosed in postpartum dairy cattle.
- The treatment of puerperal metritis includes the use of antibiotics.
- Evidence supports the use of ceftiofur for the treatment of metritis.

## INTRODUCTION

Uterine disease, such as metritis, is common in postpartum dairy cows. Metritis is capable of affecting a large number of animals in a herd and is associated with production losses.<sup>1,2</sup> Microbial infections of the reproductive tract can result in infertility by disrupting normal uterine and ovarian function. The incidence of uterine disease within the first week postpartum has been documented to be as high as 40%.<sup>3</sup> Herd incidence of metritis largely depends on the definition of disease. Several large surveys have identified ranges of clinical metritis and puerperal metritis to be between 36% and 50%<sup>4,5</sup> and 18% and 21%,<sup>6,7</sup> respectively. Despite being an important production disease in dairy cattle, clinical metritis and puerperal metritis have only been recently defined. The lack of a uniform clinical definition has made interpretation of current research, treatment, and prognosis challenging. In 2006, Sheldon and colleagues<sup>8</sup> proposed definitions for clinical and puerperal metritis to provide guidelines for treatment and prognosis. Both clinical and puerperal metritis are characterized by an enlarged uterus with fetid red-brown uterine discharge within the first 21 days in milk.<sup>8</sup> The definition distinguishes clinical and puerperal metritis by the presence of a fever and systemic involvement in the latter. Histologically, metritis is characterized by inflammation of all layers of the uterine wall with edema, infiltration of leukocytes, and degeneration of the myometrium.

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The author does not have anything to disclose.

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Inflammation of the uterine mucosa is associated with leukocyte infiltration secondary to uterine infection with *Escherichia coli*, *Trueperella pyogenes*, and *Fusobacterium necrophorum*.<sup>9–11</sup> The severity of disease associated with puerperal metritis warrants treatment with supportive care and antibiotics. Antibiotic treatments for metritis have included penicillin and ceftiofur.<sup>8,12,13</sup> In 2012, the Food and Drug Administration (FDA) issued a final rule prohibiting certain extralabel uses of cephalosporins in food animals.<sup>14</sup> This ruling limits the extralabel use of cephalosporins in food animals to only those cephalosporins with an approved regimen in that species, and use for any purpose in food animals must conform to the label regimen, with the exception of the first-generation cephalosporin, cephapirin. At the time of this publication, only ceftiofur hydrochloride (Excenel RTU-EZ; Zoetis, Madison, NJ) and ceftiofur crystalline-free acid (Excede Sterile Suspension; Zoetis) are labeled for the treatment of bovine metritis in the United States. This article analyzes the available evidence for the use of ceftiofur for the treatment of metritis in postpartum dairy cattle.

## PATIENT EVALUATION

Metritis is found in dairy cattle within the first 21 days in milk and most commonly within the first 7 days postpartum. The severity of the disease and distinction between puerperal and clinical metritis is associated with the presence or absence of systemic illness. In 2006 Sheldon and colleagues<sup>5</sup> proposed the following definitions to aide in diagnosis and classification of puerperal and clinical metritis:

- Puerperal metritis: enlarged uterus with a fetid watery red-brown uterine discharge, associated with systemic signs of illness including decreased milk production, depression, anorexia, and other signs of toxemia and fever greater than 39.5°C (103.1°F), within 21 days postpartum
- Clinical metritis: enlarged uterus and purulent uterine discharge within 21 days after parturition

Abnormalities in rectal temperature and evaluation of vaginal discharge have been the mainstay for clinical diagnosis of puerperal and clinical metritis. However, it is important that rectal temperature and vaginal discharge be interpreted together because there is evidence that a portion of healthy postpartum dairy cows have an elevated rectal temperature within the first 10 days in milk.<sup>15</sup>

Risk factors for the development of metritis include retained fetal membranes, dystocia, twins, stillbirth, and ketosis.<sup>16–18</sup> A large field study performed by Markusfeld<sup>4</sup> provided evidence that primiparous cows may be at greater risk for development of metritis when compared with multiparous cows. Rapid and accurate diagnosis of metritis is necessary to allow for initiation of appropriate treatment, detection of severity of disease, and prognostication for future fertility of the animal.

## PHARMACOLOGIC TREATMENT OPTIONS

### ***Antibiotic Therapy***

Animals affected by puerperal metritis have moderate to severe systemic disease and should be treated. The basis of treatment has been antibiotics and supportive care. The focus of treatment in this article was the administration of systemic antibiotics for the treatment of puerperal metritis, hereafter referred to as metritis. The drug chosen to treat metritis should be effective against those pathogens isolated from the infected uterus. The most common bacteria associated with metritis include *E coli*, *T pyogenes*, and a range of anaerobes including *Prevotella* species and *F necrophorum*.<sup>19–21</sup> The diverse group of organisms isolated from cows with metritis warrants

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