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VM183

Risk Factors for Uterine Disease in Dairy Cows[1]

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Uterine diseases are highly prevalent in high-producing dairy cows. Metritis affects about 20% of lactating dairy cows, with the incidence ranging from 8% to >40% at some farms (Curtis et al. 1985; Galvão et al. 2009a; Goshen and Shpigel 2006; Hammon et al. 2006; Huzzey et al. 2007; Markusfeld 1984). Clinical endometritis also affects about 20% of lactating dairy cows, with the prevalence ranging from 5% to >30% in some herds (Galvão et al. 2009a; LeBlanc et al. 2002; McDougall et al. 2007). Subclinical endometritis is the most prevalent of all uterine diseases; it affects ~40%–50% of lactating dairy cows, with the prevalence ranging from 30% to >70% in some herds (Galvão et al. 2009a; Galvão et al. 2009b; Gilbert et al. 2005; Hammon et al. 2006; Kasimanickam et al. 2004; Kasimanickam et al. 2005).

Traditionally, risk factors associated with metritis include primiparity, dystocia, twins, retained placenta (RP), stillbirth, abortion, prolapsed uterus, and ketosis (Erb et al. 1981a; Erb et al. 1981b; Dohoo and Martin 1984; Markusfeld 1984; Curtis et al. 1985; Markusfeld 1985; Markusfeld 1987; Gröhn et al. 1990; Correa, Erb, and Scarlett 1993; Kaneene and Miller 1995; Goshen and Shpigel 2006; Dubuc et al. 2010). Risk factors for endometritis include dystocia, twins, RP, stillbirth, abortion, metritis, problems with vulval conformation, male offspring, and ketosis (Gröhn et al. 1990; Galvão et al. 2009a; Dubuc et al. 2010; Potter et al. 2010; Cheong et al. 2011). While metritis is more prevalent in primiparous cows (Markusfeld 1985; Markusfeld 1987; Goshen and Shpigel 2006), incidence of endometritis has been found to increase, to decrease, or to be conditional with the level of milk yield in primiparous compared to multiparous cows (Galvão et al. 2009a; Potter et al. 2010; Cheong et al. 2011). Interestingly, multiparous cows have increased bacterial contamination ~50 days after calving compared to primiparous cows (Galvão et al. 2009a). Milk production has a detrimental effect on leukocyte function (Kimura, Goff, and Kehrli 1999; Nonnecke et al. 2003); therefore, leukocytes from multiparous cows are expected to be more severely affected because of greater milk yields. In fact, phagocytic activity of neutrophils in older cows is more markedly reduced after calving compared to younger cows (Kehrli, Nonnecke, and Roth 1989; Gilbert et al. 1993). Therefore, increased levels of pro-inflammatory cytokine production in the uterine endometrium might help to prevent metritis; however, because multiparous cows have greater demands for milk yield, they might be less able to clear an infection completely and, therefore, might be more likely to have endometritis. Another important factor that might be involved in the susceptibility to metritis is the circulating levels of immunoglobulins. Immunoglobulins work as opsonins, which greatly enhance phagocytic capacity. Primiparous cows have lower immunoglobulin content in colostrums, which indicates lower circulating immunoglobulin levels (Muller and Ellinger 1981); therefore, phagocytosis might not be optimal in early lactation in primiparous cows.

Recent studies have focused on the effect of dry matter intake, indicators of energy balance such as nonesterified fatty acids (NEFA) and betahydroxybutyrate (BHBA), haptoglobin, glycogen stores in neutrophils, and calcium

1. This document is VM183, one of a series of the College of Veterinary Medicine, Department of Large Animal Clinical Sciences, Florida Cooperative Extension Service, Institute of Food and Agricultural Sciences, University of Florida. Original publication date May 2012. Visit the EDIS website at http://edis.ifas.ufl.edu.

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on uterine disease (Hammon et al. 2006; Huzzey et al. 2007; Duffield et al. 2009; Dubuc et al. 2010; Galvão et al. 2010; Ospina et al. 2010; Martinez-Patino et al. 2011). Dry matter intake has been recognized as an important risk factor for the development of uterine disease. Recent observations show that cows that developed metritis and endometritis had a decrease in dry matter intake up to two weeks before calving (Hammon et al. 2006; Huzzey et al. 2007). This decrease in dry matter intake was accompanied by an increase in NEFA and BHBA in blood, indicating a greater degree of negative energy balance and immunosuppression in those cows (Hammon et al. 2006; Galvão et al. 2010).

Others have tried to find cutoff levels for NEFA and BHBA pre- and postpartum that can determine the risk of cows developing uterine disease postpartum. Duffield et al. (2009) observed that the best cutoff for BHBA at the first week postpartum to predict metritis was >1200 µml/l. Cows with BHBA >1200 µml/l had 2.1x greater likelihood of developing metritis postpartum. Ospina et al. (2010) found a lower cutoff for BHBA in the first two weeks postpartum as a predictor of metritis (>700 µml/l). Dubuc et al. (2010) observed that NEFA concentrations ≥600 mml/l one week before calving were predictive of metritis postpartum. Ospina et al. (2010) found that NEFA concentrations >360 mml/l either two weeks before or two weeks after calving were predictive of metritis. It is not clear why differences exist in the cutoffs between these two reports because both used Holstein cows and had a similar sample size (about 1,400 cows). The timing of sampling may be the most striking difference. Dubuc et al. (2010) sampled cows one week before calving, which may have resulted in higher concentrations and less variation. In that study (Dubuc et al. 2010), the cutoff for endometritis was found to be ≥1,100 µml/l of BHBA in the first week postpartum.

Neutrophils mainly depend on glucose uptake and glycolysis for the energy required for chemotaxis, but they almost exclusively depend on glycogen stores for phagocytosis and microbial killing even in the presence of extracellular glucose (Weisdorf, Craddock, and Jacob 1982a; Weisdorf, Craddock, and Jacob 1982b). One recent study found that cows that develop metritis or endometritis had decreased neutrophil glycogen stores around the time of calving, which could be a predisposing factor for uterine disease later in lactation (Galvão et al. 2010).

Hypocalcemia has been consistently associated with RP (Curtis et al. 1983; Curtis et al. 1985; Correa, Erb, and Scarlett 1993), and, in some studies, with metritis (Gröhn et al. 1990). Calcium is a key mediator in several cell processes, including activation of immune cells. In a recent study, cows that developed metritis had decreased calcium concentrations in the first two weeks postpartum, and lower calcium was associated with decreased neutrophil function (Martinez-Patino et al. 2011). Interestingly, the ability to maintain calcium concentration in blood in the first three days after calving was more important than the absolute calcium concentration. It has been found that the greater the drop in calcium concentration in the first three days postpartum, the greater the probability of developing metritis later in lactation (Figure 1).

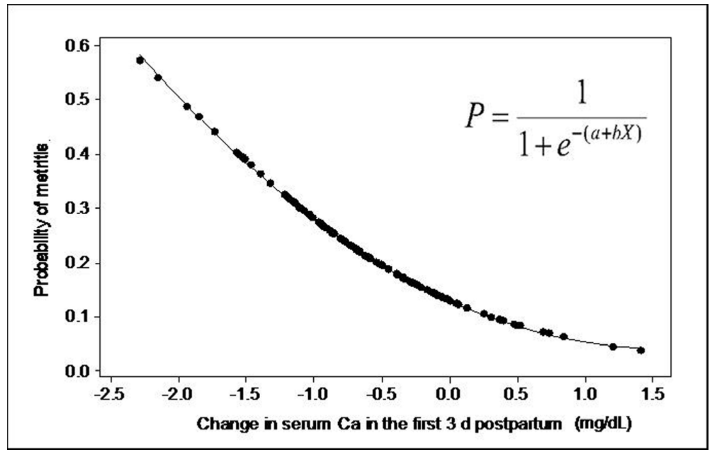

Figure 1. Effect of calcium change in the first three days postpartum on the probability of development of metritis in the first two weeks postpartum.

Credits: Martinez-Patino et al. (2011).

Summary

Uterine diseases are highly prevalent in high-producing dairy cows. Risk factors associated with metritis include primiparity, dystocia, twins, RP, stillbirth, abortion, prolapsed uterus, and ketosis. Risk factors for endometritis include dystocia, twins, RP, stillbirth, abortion, metritis, problems with vulval conformation, male offspring, and ketosis. BHBA blood concentration ≥1,200 µml/l in the first week postpartum is predictive of metritis, while BHBA blood concentration ≥1,100 µml/l in the first week postpartum is predictive of endometritis. NEFA blood concentration ≥600 mml/l in the first week postpartum is predictive of metritis. If samples are collected in the first two weeks postpartum, the cutoff for predicting metritis is ≥700 µml/l for BHBA and ≥360 mml/l for NEFA. Neutrophil glycogen stores and calcium are associated with the development of uterine disease. Particularly, a drop in calcium in the first three days postpartum is a strong predictor of metritis.

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