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Review article

Interactions between negative energy balance, metabolic diseases, uterine health and immune response in transition dairy cows

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ABSTRACT

The biological cycles of milk production and reproduction determine dairying profitability thus making management decisions dynamic and time-dependent. Diseases also negatively impact on net earnings of a dairy enterprise. Transition cows in particular face the challenge of negative energy balance (NEB) and/or disproportional energy metabolism (fatty liver, ketosis, subacute, acute ruminal acidosis); disturbed mineral utilization (milk fever, sub-clinical hypocalcemia); and perturbed immune function (retained placenta, metritis, mastitis). Consequently NEB and reduced dry matter intake are aggravated. The combined effects of all these challenges are reduced fertility and milk production resulting in diminishing profits. Risk factors such as NEB, inflammation and impairment of the immune response are highly cause-and-effect related. Thus, managing cows during the transition period should be geared toward reducing NEB or feeding specially formulated diets to improve immunity. Given that all cows experience a reduced feed intake and body condition, infection and inflammation of the uterus after calving, there is a need for further research on the immunology of transition dairy cows. Integrative approaches at the molecular, cellular and animal level may unravel the complex interactions between disturbed metabolism and immune function that predispose cows to periparturient diseases.

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1. Introduction

Whereas the dry period in cows may be considered to be a resting phase between lactations, in reality considerable fetal growth, mammary tissue remodeling and high nutritional demands occur. The recognition of the importance of the period from late pregnancy until the adaptation phase of early lactation has led to the development of the concept of the transition period, which is commonly defined as the period from 3 weeks before to 3 weeks after calving (Drackley, 1999). Nutrient requirements of the fetus reach maximal levels three weeks prepartum, yet dry matter intake (DMI) decreases by 10–30% (Bell, 1995). Within three weeks of the onset of lactation, milk yield, milk proteins, fat and lactose increase rapidly and exceed feed intake (Bertoni et al., 2009). Moreover, the diet of most dairy cows changes sharply at calving from being mainly forage-based to concentrate-rich diets. Postpartum milk production and the requisite nutritional adaptations induce a physiological state of negative energy balance (NEB). In recent times, genetic selection and improved nutrition have increased milk yield per cow. However, the increased milk output has been accompanied by a decline in fertility in many countries. Pregnancy rates after insemination have declined by 0.45–1% annually in UK and Northern American herds (Royal et al., 2000; Butler et al., 2003; Dobson et al., 2007) while the culling rate is 20–35% (Smith et al., 2000; Rajala-Schultz and Frazer, 2003). Thus, the conclusion reached by many is the existence of an overall antagonism between milk yield and reproduction (VanRaden et al., 2004; Chagas et al., 2007; Lucy, 2007; McCarthy et al., 2007; Mee, 2007). However, recent studies now provide evidence for high milk yield not necessarily being associated with low fertility (López-Gatius, 2003; López-Gatius et al., 2006; Patton et al., 2007). An USDA study has shown that fertility of dairy cattle in Northern America has rebounded since the incorporation of genetic merit for daughter pregnancy rate (DPR) with no apparent slowing down in milk yield and fertility (VanRaden et al., 2011).

There is no arguing that milk yield and reproductive performance are the standard economic barometers of dairy production. It is thought that the reproductive status of a cow is the single most important factor influencing culling decisions on farms and that uterine infection likely contributes indirectly to the high rates of involuntary culling (Gröhn et al., 2003). Understanding the key role of immune responses in numerous transition cow disorders may help to explain links between these diverse conditions. At the molecular level, the activation of local and systemic host defense mechanisms induce inflammation; furthermore, significant gene expression changes occur as an adaptation to the demands of lactation, maintenance and the rapidly involuting uterus. A host of signaling molecules are released by activated immune cells including inflammatory mediators such as prostaglandins and cytokines. The systemic levels of immune molecules such as haptoglobin (HP) and interleukin 8 (IL8) are significantly elevated around calving (Bionaz et al., 2007; Bertoni et al., 2008; Huzzey et al., 2009). Cows even show typical inflammatory changes prior to calving (Trevisi et al., 2002; Trevisi and Bertoni, 2008). Cytokines play a key role in stimulating systemic inflammatory responses, including increased body temperature and heart rate, and decreased feed intake (Dantzer and Kelley, 2007). Furthermore, given the interplay between the immune, endocrine and metabolic systems (Stofkova, 2009; Pittman, 2011), diminished immune competence at calving increases host susceptibility to infections (Trevisi et al., 2011).

Physiological conditions associated with insufficient energy supply predispose dairy cows to metabolic and microbial diseases such as milk fever, endometritis, ketosis, displaced abomasum and retained placenta (Drackley, 1999; Duffield and Herdt, 2000). Clearly the role of inflammatory responses in the decline in fertility is not known, given the range of effects on various physiological processes. An improved understanding of the inflammatory pathways at the molecular level which play an important role in normal immune function, metabolism and reproduction may improve our ability to predict and prevent transition cow disorders. The major interactions between the immune, endocrine and metabolic systems in dairy cows during the transition period are summarized in Fig. 1.

2. Metabolic and physiological changes during the transition period: inflammation, energy balance, endocrine changes and immunosuppression

The primary challenge faced by cows is a sudden increase of nutrient requirements for milk production at a time when dry matter intake (DMI) and nutrient supply lags behind. High nutrient demands for