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Hot topic: new research highlights the need for holistic thinking about transition cows

Abstract
In the past, efforts to improve the transition to lactation have focused largely on preventing infections and maximizing energy intake in transition cows, and these issues have generally been treated independently. New models, however, are emerging to explain the development of numerous transition disorders. A combination of insults, including social stress, negative energy balance, heat stress, endotoxin exposure, and oxidative stress may promote inflammation, suppress feed intake, and impair both metabolic and immune function during the transition period. These models suggest that transition cow management must be viewed holistically, because the cow’s environment, nutrition, and immune function interact in many complex ways. Fortunately, a number of practical approaches can be used to improve the overall health of transition cows, which can decrease the cull rate in early lactation and improve both productivity and reproductive success.; Dairy Day, 2012, Kansas State University, Manhattan, KS, 2012; Dairy Research, 2012 is known as Dairy Day, 2012

Keywords
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Hot Topic: New Research Highlights the Need for Holistic Thinking about Transition Cows

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Summary
In the past, efforts to improve the transition to lactation have focused largely on preventing infections and maximizing energy intake in transition cows, and these issues have generally been treated independently. New models, however, are emerging to explain the development of numerous transition disorders. A combination of insults, including social stress, negative energy balance, heat stress, endotoxin exposure, and oxidative stress may promote inflammation, suppress feed intake, and impair both metabolic and immune function during the transition period. These models suggest that transition cow management must be viewed holistically, because the cow’s environment, nutrition, and immune function interact in many complex ways. Fortunately, a number of practical approaches can be used to improve the overall health of transition cows, which can decrease the cull rate in early lactation and improve both productivity and reproductive success.

Key words: transition cow

Physiological Interactions in the Transition Dairy Cow
Traditionally, experts on dairy cattle have focused on isolated components of dairy management: nutritionists work on diets, veterinarians respond to disease outbreaks, and others design facilities to maximize cow comfort. Today, we are learning how much nutrition, pathogens, and environmental challenges interact to influence the physiology of the cow.

One such interaction is the effect of energy balance on immune function. Nearly all transition cows experience at least 3 weeks of negative energy balance, a situation in which they require more energy for maintenance and milk production than is consumed from their diet. Recent work has demonstrated that blood metabolites that are elevated during this time, including nonesterified fatty acids (NEFA) and beta-hydroxybutric acid (BHBA), may directly impair the function of multiple types of immune cells. These effects may help to explain at least some of the decrease in immune function during negative energy balance.

Another common nutrition-related issue is the subclinical hypocalcemia that occurs in most transition cows. This issue is most commonly discussed in terms of the risk for milk fever; hypocalcemia can cause paresis because of the critical role of calcium in initiating muscle contractions and transmitting nerve signals. Calcium, however, is an important signal transducer in many other cell types, including immune cells. Monocytes from cows experiencing hypocalcemia were recently demonstrated to have low intracellular calcium stores. An inability of monocytes to utilize intracellular calcium for cell signaling is expected to dampen functional responses and the ability of these immune cells to fight pathogens. Such findings may provide a physiological basis for the long-observed links between hypocalcemia and mastitis in transition cows.

These findings are shedding light on why nutritional deficiencies and metabolic disorders can depress immune function and promote infectious disorders in the transition period. In fact, de-
creased feed intake was observed before calving in cows that ended up with subclinical ketosis or metritis after calving in several studies, suggesting that behavioral changes and nutrient imbalances can precede key transition problems by days, if not weeks. Another line of work focuses on the other side of this relationship: why biological stressors promote metabolic problems.

**Stress, Sources of Stress, and the Consequences**

Stress is defined as “the non-specific response of the body to any demand for change,” which does not necessarily imply that stress is negative; in fact, some necessary components of the transition to lactation are certainly stressful by this definition. Although stress is difficult to define clearly and impossible to measure directly, it is worth considering because it is one way through which the intricate links between behavior, nutrition, and physiology can be understood. Common stress responses include decreased feed intake and inflammation, both of which have been implicated in most transition disorders. Social stress, infection, metabolic stress, and heat stress will be discussed as key sources of stress in the transition cow.

**Social Stress**

The best-studied source of social stress in transition cows is overcrowding. Competition at the feed bunk has been shown to decrease DMI of multiparous cows in the critical final week of gestation in spite of the fact that cows in this stage of production eat less than half as much dry matter as cows at peak lactation. Cows competing for access to feed also spent more time standing; standing time during the transition period has recently been documented as a key risk factor for claw horn lesions later in lactation. Feed bunk competition also results in cows consuming fewer and larger meals, which could increase the risk for ruminal acidosis, at least after the transition to a lactation ration. Although few controlled studies have been conducted to evaluate the effects of regrouping cows, anecdotal evidence suggests that repeated regrouping can induce similar stress and may likewise suppress feed intake and promote lameness.

**Infection**

Infectious disorders cause both specific and nonspecific responses. Among the most important stress responses to infection is inflammation. Mammary and uterine infections clearly result in both local and systemic inflammation, which can affect nearly all organs. The nonspecific inflammatory stress responses to infection promote the development of metabolic disorders by suppressing feeding behavior and directly impairing metabolic function of the liver.

**Metabolic Stress**

Inflammation may be a key contributor to metabolic disorders in transition cows. A retrospective study of cows on 3 commercial Italian dairies suggested that liver inflammation is associated with a problematic transition to lactation: cows with the strongest inflammatory profiles were at 8-fold greater risk for experiencing one or more transition disorders, had lower plasma calcium concentrations, took longer to re-breed, and produced less milk in the first month of lactation.

Metabolic stress can be initiated by a variety of factors, including inflammation from infection (discussed above), oxidative stress, and translocation of endotoxin from the gut. One effect of increased delivery of NEFA to the liver in early lactation is an increase in the production of reactive oxygen species, a condition commonly referred to as oxidative stress. This is especially true for cows with high body condition, likely because plasma NEFA concentrations are more elevated in these cows. Reactive oxygen species are a concern because they can damage cellular
proteins and DNA and are potent activators of inflammatory pathways. Endotoxin is a component of the cell wall of gram-negative bacteria, and detection of endotoxin by immune cells initiates a strong inflammatory response. Recent studies have demonstrated that sub-acute ruminal acidosis increases both ruminal and plasma endotoxin concentrations, which causes liver inflammation.

Metabolic inflammation can be derived from at least 3 sources: infection, oxidative stress, and endotoxin translocated from the gut. Several recent studies have shown that causing sterile inflammation in dairy cattle promotes conditions leading to fatty liver and ketosis, two of the most prevalent metabolic disorders in transition cows. In addition to promoting metabolic disorders by stimulating inflammation, oxidative stress can directly suppress immune function by damaging lipids, proteins, and DNA of immune cells. Oxidative stress may play a key role in the poor immune function observed in transition cows, a hypothesis that is supported by numerous studies demonstrating beneficial effects of supplementing antioxidants in the transition period.

Heat Stress
Another common stressor for transition cows is excessive heat load. Many operations cool lactating animals, either because these cows have the highest heat burden or because the benefits of cooling lactating cows are so easy to observe in daily milk weights during heat waves. The stress of such environments on dry cows has not received as much attention. Recent work showed that heat stress during the dry period decreased dry matter intake (DMI) during the week of calving by nearly 50%, decreased the function of immune cells after calving, and decreased peak milk production by more than 10 lb/day. Although the exact mechanisms linking heat stress to these long-term effects remain unclear, substantial costs are clearly associated with allowing dry cows to experience sustained heat stress.

Practical Implications
These findings suggest a number of focus areas for dairy managers aiming for a holistic management scheme to accommodate the complex nutritional, environmental, and behavioral needs of the transition dairy cow.

Housing
The clear implication of recent findings from the group at the University of British Columbia is that overcrowding dry cows is a mistake. During the financial difficulties of the past several years, numerous stories have circulated about farms decreasing stocking rates of lactating cows from 120% to 100% without losing milk in the bulk tank. Perhaps these instances are a reminder about the importance of adequate space (both in free stalls and bunk line); if anything, literature suggests that space is even more critical in the dry period. Behavioral responses to overstocking are expected to cause greater lameness and more negative energy balance and to increase the transition disorders associated with these issues. With the recent findings from the University of Florida, similar negative effects can be expected in cows that are exposed to heat stress through the dry period. Providing adequate space and keeping cows cool should be high priorities in any dry cow management plan.

Another factor worth considering is the grouping of cows. For many years, separating dry cows in far-off and close-up pens was recommended to allow different diets to be fed during these periods; however, with the information available on one-group dry cow strategies (see below), this procedure is no longer necessary. According to some, the reduced stress of not moving cows an
extra time is reason enough to make the change to a one-group dry cow system. When considering grouping strategies for dry cows, realize that subordinate cows, those who are bullied away from the feed bunk, eat less feed, and spend more time standing when overcrowded, are the most susceptible to social stress. As a result, these cows are also the most susceptible to transition disorders if not properly managed. If possible, it is wise to pen close-up heifers separately from dry cows; subordinate cows (small or simply submissive cows) can be housed with heifers if necessary. Finally, remember that pen movements affect not only the cow that is moving, but also the entire group. Even if a single pen is used to house all dry cows on a farm, the weekly influx of new cows constantly disrupts the social structure in the pen and serves as a potential source of stress. Although certainly not practical on all farms, some larger operations are experimenting with “all-in, all-out” management schemes, where a group of dry cows all enter the pen together and end up in a fresh cow pen together after all have calved. This type of system has the potential to minimize the amount of social stress for transition cows.

Nutrition
The primary goal in transition cow nutrition has been crystallized in the past decade: control body condition. No other factor that we can measure is a better predictor of a disastrous transition period than a body condition score (BCS) of 4 or greater. In fact, most academics who focus on transition disorders for this period advocate a target BCS of 3 or even less at calving because the consequences of high BCS have proven far more serious than those of low BCS. Cows suffering from “fat cow syndrome” experience greater decreases in feed intake than healthy cows, have greater increases in plasma NEFA, and are far more likely to have clinical cases of ketosis and even infectious disorders. The goal of controlling body condition is often best met by feeding relatively low-energy diets throughout the dry period, although a wide variety of formulations can potentially be used to accomplish this goal. The devil, of course, is in the details: preventing excessive sorting, promoting sufficient feed intake to meet energy requirements, and balancing for dietary cation-anion difference are all problems to address.

As with social stress, nutritional needs of close-up heifers can be best met by housing them separately. Because these heifers are still growing and are less susceptible to "fat cow syndrome," it is probably logical to offer them a slightly higher energy diet than multiparous cows. Likewise, anionic diets that benefit multiparous transition cows can dramatically decrease feed intake of heifers. Heifers rarely experience severe hypocalcemia, so it is best to feed them diets without added sources of anions.

Disease Prevention
The immune dysfunction that cows experience during the transition period suggests several management strategies that may help limit disease pressure and associated stress during this time. Clearly, dairies are interested in reducing pathogen loads for all cows, but if an opportunity to improve the cleanliness of certain pens arises, it would be wise to invest in fresh pens where the majority of mastitis and metritis cases occur. In addition, vaccination protocols should be designed to avoid vaccinating cows during the final 3 weeks of gestation, because the decreased function of the adaptive immune system during this period limits the effectiveness of vaccines and produces potentially harmful inflammation during a critical time.

Conclusions
Even on farms with relatively low incidence of transition cow disorders, suboptimal social settings, environmental conditions, feed intake, metabolic status, or immune function may impair
the ability of transition cows to reach their genetic potential for peak milk yield, resulting in significant economic losses throughout lactation. Although the mechanisms underlying some of these interactions remain elusive, some clear messages stand out from recent research:

- Transition cows need adequate bunk and stall space; heat stress during this period has long-term negative effects.
- Separating heifers from dry cows and minimizing group changes during the transition period encourages improved nutritional management and decreased social stress.
- Because of the numerous interactions between different physiological systems, improving feed intake after calving, improving metabolic function, or decreasing infections should positively affect the other factors, ultimately increasing health and productivity.