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A 100-Year Review: Metabolic modifiers in dairy cattle nutrition[1]

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ABSTRACT

The first issue of the *Journal of Dairy Science* in 1917 opened with the text of the speech by Raymond A. Pearson, president of the Iowa State College of Agriculture, at the dedication of the new dairy building at the University of Nebraska (J. Dairy Sci. 1:4–18, 1917). Fittingly, this was the birth of a new research facility and more importantly, the beginning of a new journal devoted to the sciences of milk production and manufacture of products from milk. Metabolic modifiers of dairy cow metabolism enhance, change, or interfere with normal metabolic processes in the ruminant digestive tract or alter postabsorption partitioning of nutrients among body tissues. Papers on metabolic modifiers became more frequent in the journal around 1950. Dairy farming changed radically between 1955 and 1965. Changes in housing and feeding moved more cows outside, and cows and heifers in all stages of lactation, including the dry period, were fed as a single group. Rations became wetter with the shift to corn silage as the major forage in many rations. Liberal grain feeding met the requirements of high-producing cows and increased production per cow but introduced new challenges; for example, managing and feeding cows as a group. These changes led to the introduction of new strategies that identified and expanded the use of metabolic modifiers. Research was directed at characterizing the new problems for the dairy cow created by group feeding. Metabolic modifiers went beyond feeding the cow and included environmental and housing factors and additives to reduce the incidence and severity of many new conditions and pathologies. New collaborations began among dairy cattle specialties that broadened our understanding of the workings of the cow. The *Journal of Dairy Science* then and now plays an enormously important role in dissemination of the findings of dairy scientists worldwide that address existing and new technologies.

Key words: metabolic modifier, feed additive, ionophore, 100-year review

INTRODUCTION

The first article in the first issue of the *Journal of Dairy Science* in 1917 was the text of the speech by Raymond A. Pearson, president of the Iowa State College of Agriculture, at the dedication of the new dairy building at the University of Nebraska (Pearson, 1917). Fittingly, this was the birth of a new research facility and, more importantly, the beginning of a new journal devoted to the sciences of milk production and manufacture of products from milk. Approximately 15 papers related to metabolic modifiers were published in the *Journal of Dairy Science* from 1917 to 1940 (Appendix Table A1). Salt was the first metabolic modifier described (Joffe, 1918). Climate, season, and stage of lactation, along with feed-related compounds, were reported as factors affecting milk yield and composition. Sources of metabolic modifiers include microorganisms or their products (e.g., ionophores), feed additives, hormones, and nutrients in feed. Some require exhaustive studies to demonstrate safety and efficacy to the target animal and the environment by regulatory agencies. Animal drugs are regulated in the United States by The Center of Veterinary Medicine (**CVM**), a branch of the Food and Drug Administration (**FDA**). Many feed additives are classified as "generally regarded as safe" (GRAS) substances and have little or no regulatory oversight. Makers of these products often make claims not substantiated in peer-reviewed journals.

Chapter 9 of *Nutrient Requirements of Dairy Cattle* (7th rev. ed.; NRC, 2001) identified and described unique aspects of dairy cattle nutrition during the transition period that covered metabolic disorders, reproductive tract problems, and prevention measures to reduce incidence of these conditions. The final section of that publication, "Performance Modifiers," described feed additives, microbial products, and bovine somatotropin.

THE LACTATION CYCLE AND TRANSITION PERIOD

The day following the conclusion of lactation should be recognized as the first day of the next lactation cycle.

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The dry period is a time for preparing for the ensuing lactation. Fetal growth is greatest during the last 2 mo of pregnancy. At the end of lactation, milking ceases and cows are generally treated with long-acting antibiotics that kill most existing bacteria and protect the gland from infection. Cows are fed a high-NDF forage/low-concentrate diet that rebuilds rumen papillae and musculature. The population of rumen bacteria reverts to a high proportion of gram-positive species. Stoppage of milking puts in motion a series of actions that begin the ensuing lactation. Involution of the mammary gland invokes a series of events that replaces old secretory tissue with new alveolar tissue. Iron needed for bacterial growth is bound by lactoferrin. The teat end is sealed by a keratin plug that prevents entrance of bacteria into the gland.

The transition period lasts from 10 to 14 d before calving to 4 to 6 d after calving. As calving approaches, the proportion of concentrate in the ration is increased. The rumen population switches to a more gram-negative flora. Hormonal changes occur that begin the process of lactation. Colostrum is produced and fills the gland. The cow must supply energy, protein, vitamins, and minerals for colostrum production at a time when feed intake is decreasing. The transition of the cow to the lactating state has begun and, with it, the heightened potential of metabolic conditions and infections.

The transition period is an intersection of multiple digestive and metabolic systems with actions that must be operative at the time of calving. Failure of one or more of these systems leads to metabolic and infectious diseases that compromise the cow's well-being and may lead to culling or death. Loss of a cow represents a major loss of income for the producer.

Large shifts in metabolism occur during the transition period that place cows, especially those in later parities, at high risk for metabolic conditions related to energy, mineral, and vitamin deficits. Dry matter intake begins to decrease, especially in final 2 to 4 d before calving (Bertics et al., 1992), and intake may be 0 to 4 kg on the day of calving. Those cows with a major reduction in DMI are at high risk for an assortment of metabolic and bacterial diseases, notably parturient paresis, ketosis, mastitis, retained placenta, and metritis. Birth of the calf creates abdominal space that increases the odds for displaced abomasum. Inclusion of monensin in the feed or as a controlled release capsule administered precalving reduces clinical ketosis and displaced abomasum after calving (Duffield et al., 2002). Goff and Horst (1997) provide an excellent review on metabolic, mechanical, and infectious diseases in cows during the transition period. Without any metabolic or infectious disease, DMI increases 2 to 4 d after calving with high potential for success.

Parturient Paresis (Milk Fever)

Onset of lactation increases mineral demands, especially calcium for smooth muscle contraction. Hibbs (1950) provided a history of published observations of a disease that occurred around time of parturition that became known as milk fever. One reference to milk fever was described in writings by the German scientist Eberhardt in 1793. In the first half of the 19th century, therapies such as hot packs, blankets, and blood-letting were used. Hibbs (1950) described 30 causes of the disease and many remedies followed but all failed. One recommendation was that if a cow survived a second parturition with treatment for milk fever, "prepare the beast for the butcher."

In 1897, J. J. Schmidt examined colostrums with a microscope from affected cows with the disease and attributed milk fever to a viral infection. Treatment of the affected gland with 1% potassium iodide solution cleared the infection but not the condition. Mortality was reduced from greater than 60% to about 15%. In 1901, udder inflation successfully reduced mortality to 1% and became the treatment of choice. Mastitis increased, however, due to use of unsterilized equipment.

New theories were proposed as the cause of milk fever, including hypoglycemia, hyperglycemia, and parathyroid gland insufficiency—all without success. Scientists in the mid-1930s began to shift the research focus to calcium and phosphorus. Fish (1929) reported that the Ca:P ratio in blood from normal cows was 2.3:1, whereas in cows with milk fever, it was 1:9.

Hibbs et al. (1946) suggested that vitamin D was involved in milk fever because the incidence was higher in winter months when cows were maintained indoors and less exposed to solar radiation than in summer, when cows had access to pasture.

Normal blood calcium is 9 to 10 mg/100 mL (Nelson et al., 2016). As blood calcium declines, cows become subclinical (reduced serum calcium but no outward signs); partial or full paralysis with recumbency occurs at a calcium level of $\leq$5 to 6 mg/100 mL. Various ration strategies for feeding close-up dry cows have been developed that reduce the incidence and severity of parturient paresis. These include the amount and ratio of Ca and P, administration of vitamin D per os or by injection, and manipulating alkalinity in diets. The primary goal of these strategies is to maintain or increase blood calcium.

Cows with parturient paresis may also experience reduced milk production, mastitis, retained placenta, and ketosis, and they are at greater risk for culling than herdmates. Multiparous cows, especially those with a long dry period, are at high risk for parturient paresis. Smooth muscle in intestinal and uterine tissues is in-