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From pre- to postweaning: Transformation of the young calf's gastrointestinal tract[1]

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ABSTRACT

The ruminant gastrointestinal tract (GIT) faces the challenge of protecting the host from luminal contents and pathogens, while supporting the absorption and metabolism of nutrients for growth and maintenance. The GIT of the calf in early life undergoes some of the most rapid microbial and structural changes documented in nature, and these adaptations in GIT function make the young calf susceptible to GIT diseases and disorders. Despite these challenges, the calf's GIT has a certain degree of plasticity and can sense nutrient supply and respond to bioactive ingredients. Calf GIT research has historically focused on the transition during weaning and characterizing ruminal papillae development using microscopy and digesta metabolite responses. Through the use of new molecular-based approaches, we have recently shown that delaying the age of weaning and providing a step-down weaning protocol is associated with a more gradual shift in ruminal microbiota to a postweaned state. In addition to ruminal adaptations during weaning, nutrient flow to the lower gut changes dramatically during weaning, coinciding with a wide array of structural and microbiological changes. Structural and gene expression changes suggest that the lower gut of the dairy calf undergoes alterations that may reduce barrier function when solid feeds are consumed. More recently, in vivo data revealed that the weaning transition increases total gut permeability of the calf. Interestingly, the lower gut may be able to communicate with the forestomach, meaning that a nutrient can be sensed in the lower gut and cause subsequent adaptations in the forestomach. An improved understanding of how diet, microbiota, and functional ingredients interact to affect growth and barrier function of the intestinal tract would greatly benefit the dairy calf industry. A mechanistic understanding of such adaptations would also aid in the formulation of specific management regimens and provision of functional ingredients required to characterize and enhance gut function in young calves.
Key words: forestomach, rumen, lower gut, calf

INTRODUCTION

The primary function of the gastrointestinal tract (**GIT**) is the digestion and absorption of nutrients. Of equal importance is the role of the GIT in protecting the host from a continually fluctuating mixture of microorganisms, toxins, and chemicals in the lumen, and to prevent unregulated translocation into portal circulation (Gäbel et al., 2002). To achieve this, the GIT continuously senses the luminal composition and adapts to support the maintenance of its integrity and enhance nutrient absorption (Furness et al., 2013). Maintaining a healthy and functional GIT is also important to animal energetics as it uses 20% of oxygen in the ruminant and accounts for 30% of metabolic and protein synthesis activities (Cant et al., 1996). Thus, the metamorphosis undergone by the GIT can affect many biological systems within the animal, making the maintenance of its function and health of great importance in dairy production systems.

With respect to GIT health in dairy production systems, digestive disorders in lactating dairy cows, such as ruminal acidosis, dominate the scientific literature. Yet, the calf is the most susceptible animal on the farm with the highest incidence of mortality and morbidity, compared with the rest of the herd. According to the most comprehensive survey available in the North American dairy industry (USDA, 2007), morbidity rates in preweaned dairy calves were estimated to be as high as 46% and mortality rates at 10%, with GIT ailments being the number 1 cause. A recent survey

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conducted on commercial dairy farms in Ontario (Canada) and Minnesota (United States; 2,874 calves from 0 to 3 mo) reported that GIT infections were the first ailment experienced in the calf's life, with 23% of these calves receiving antibiotic treatment for diarrhea (Windeyer et al., 2014). Along with a high degree of infection, antibiotic treatments, and stress during the preweaning phase, weaning represents one of the most dramatic GIT transformations in nature and is associated with distress, depressed growth, and impaired GIT health (Khan et al., 2011, 2016). Consequently, the period from birth to weaning is a time of extreme GIT challenges, yet the short- and long-term biological outcomes of altered GIT development are still poorly understood.

Physiological development of the GIT has been characterized using dissection techniques and the analysis of digesta and blood metabolite responses in calves for some time. Yet, the advancement of different fields of science, such as high-throughput sequencing, have effectively opened the door to new capabilities of characterizing GIT compartments under specific nutritional programs or challenges. In addition to the evolution of scientific techniques, the dairy industry has also undergone a change in feeding regimen, from feeding restricted levels of milk that limit growth rates preweaning to feeding elevated levels of milk that are close to ad libitum or natural intakes and yield greater growth rates preweaning. This change undoubtedly affects GIT physiology, molecular biology, and microbiology; however, there remains a paucity of information in this area that limits further enhancements in calf biology and management.

Therefore, this review aims to summarize our current knowledge of the transformation the calf GIT undergoes during the pre- and postweaning periods. We begin with the forestomach, which has received most of the attention in dairy calf research, followed by the lower gut. The biological relevance of new molecular-based research on calf performance, GIT health and function, and overall animal welfare are discussed, and the largest knowledge gaps around GIT biology are pinpointed. Furthermore, we attempt to elucidate potential control mechanisms of gut function by reviewing microbial-host and host-host signaling (Figure 1).

FORESTOMACH ADAPTATIONS

In the newborn calf, dietary requirements are fulfilled by the uptake of colostrum, which is digested in the abomasum and subsequent GIT to provide energy, essential nutrients, as well as immunity molecules. Continuing through the preweaning phase the majority of energy intake originates from milk or milk replacer (**MR**), which due to reflexive closure of the reticular groove, bypasses the rumen and directly enters the abomasum (Baldwin et al., 2004). The role of the abomasum is often overshadowed by the rumen, yet many digestive disorders and ailments during the preweaning phase are related to impaired abomasal function. For example, there is concern regarding the development of depressed abomasal pH (Ahmed et al., 2002), ulceration (Ahmed et al., 2002; Marshall, 2009) and overflow of milk into the rumen (termed ruminal drinking; Berends, 2014) and reduced insulin sensitivity (Bach et al., 2013) in calves fed an elevated level of milk with a low meal frequency (<2 meals per day). Several recent studies, however, have challenged our understanding of abomasal capacity in young calves (Ellingsen et al., 2016) and by showing a limited effect of larger meals (4 L, 2 times per day) on hyperglycemia (MacPherson et al., 2016). In the second experiment, calves adapted to larger meal sizes by reducing their abomasal emptying rate (MacPherson et al., 2016), a process that has been linked to the control of pancreatic insulin secretion (Stahel et al., 2016), suggesting that nutrient sensing likely occurs in lower gut neuroendocrine cells which transmit feedback that affects functionality of the forestomach, namely the abomasum.

Most research on the transformation of the calf GIT focuses on rumen maturation, which is believed to be initiated by the consumption of solid feed, but arguably starts much earlier, with solid food intake fueling a rapid increase in ruminal fermentation. The production and absorption of resulting fermentation end products (i.e., VFA) stimulate ruminal papillae development (Sander et al., 1959; Baldwin et al., 2004; Suárez et al., 2006), whereas the physical structure of substrates such as roughages contribute to muscular development and expansion of ruminal volume (Tamate et al., 1962; Stobo et al., 1966), and stimulate rumination and saliva flow to the rumen (Hodgson, 1971). The main enzymatic activities (fibrolysis, amylolysis, proteolysis, and ureolysis) of ruminal microbiota have been observed in the rumen from 4 (Sahoo et al., 2005) or 10 (Kmet et al., 1986) d of age. In excess of 60 glycoside hydrolase microbial genes are present in the rumen at early stages of life, suggesting great potential for plant carbohydrate metabolism even in the absence of regular plant cell wall intake (Li et al., 2012), which is confirmed by the measurement of fibrolytic activities in the young calf rumen (Rey et al., 2012; Jiao et al., 2015). Rey et al. (2012) measured both ruminal enzyme activities and fermentative capacity in dairy calves from birth through weaning. In the first month after birth, high levels of enzymatic activities were measured in addition to changes in ruminal pH, which decreased in a time pattern contrary to that of total VFA concentration. At