Health and stress management in young calves

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The considerable expense of calf rearing, including feed, veterinary interventions, and management, were Historically thought of as costs. As a result, solutions and management targeted minimizing of costs by transitioning calves onto solid feed as quickly as possible, thereby minimizing expense. In the past ten years, considerable evidence on the long-term impacts of young calf feeding has started to reframe the conversation from cost to investment. Yes, the money spent remains the same (if not more); however, the return now goes away from days-to-weaning towards future milk yield potential. Realizing future milk yield potential is principally driven by the growth and health of young dairy calves.

The most accessible indicator of calf health is weight gain; calves that are healthy will grow faster than calves that are sick. For instance, each pound of gain realized by the first 6 weeks of life nets an average return of 1.8 pounds of milk yield in the calf's subsequent first lactation (Rauba et al., 2019). The rate at which calves grow in the first 6 weeks is dependent, above all, on the net energy available for growth (NE_g). Though important, NE_g is the last sink for dietary energy, after net energy for maintenance (NE_m). NE_m is the base amount of energy needed for the calf to survive; this amount includes both basic metabolism as well as fighting off disease, which uses some 2.2 lb of glucose every 12h in a lactating cow (Kvidera et al., 2017). A sick calf not only repartitions NE_g towards NE_m to fight off disease, but also reduces feed intake, further depressing NE_g.

Rather than calculate the energy partitioning on-farm, we can redirect our performance metrics to cost per gain. A recent analysis of ten studies showed that higher daily milk allowance will increase ADG per pound of body weight, especially pre-weaning (Hu et al., 2022). To realize these potential efficiencies, calf health must be optimal to avoid energy being repartitioned to fighting off disease. Consequently, our calf feeding systems must incorporate a focus of calf health. Focusing on calf health requires capitalizing on the calf immune system, which is uniquely positioned to set the calf up for success.

TRANSFER OF PASSIVE IMMUNITY

Like many mammalian species, calves are born with a naïve immune system. Unlike many mammalian species, calves are not born with passive immunity, making them uniquely dependent on effective post-birth health management. This newborn intestinal environment is immature physiologically, immunologically, and microbiologically. The same conditions that create vulnerability also create opportunities for advancing calf health.

The calf intestine is physiologically immature at birth and remains so for approximately 24h. Physiological immaturity is what allows the intestine to absorb antibodies from colostrum, making effective colostrum feeding of utmost importance to calf health. Colostrum must be fed at 10% of body weight (Godden et al., 2019) by 2 hours of life, contain at least 50 g/L immunoglobulin G (IgG; Bartier et al, 2015), and must be absorbed by the calf to elevate serum IgG levels to at least 18 g/L by 24 – 48h of life (Lombard et al., 2020). Historically, antibody absorption was found to be effectively non-existent after 24h of birth.

Recent studies have shown the antibody uptake ability of the intestine is far more flexible than previously thought. For instance, calves whose colostrum was supplemented with butyrate had a much lower rate of antibody absorption and a greater incidence of failure of transfer (Hiltz and Laarman, 2019). Another study (Pyo et al., 2020) found that calves fed transition milk replacer (half milk replacer, half colostrum replacer) for up to 3 days, indicating the passive immunity transfer window can be extended as well. Current work by our team demonstrated that calves fed colostrum were still able to absorb antibodies throughout the small intestine, while calves not fed colostrum lost their antibody absorption abilities by 24h of life (Hiltz et al., 2023; Figure 1).

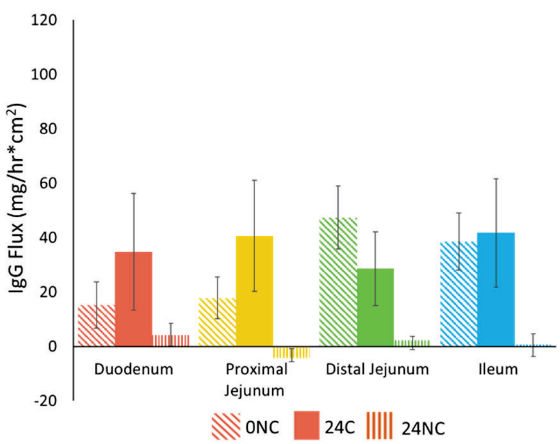

Figure 1. Immunoglobulin G (IgG) antibody absorption rates in different segments of the small intestine at 0h (0NC; diagonal fill) and 24h for calves fed colostrum (24C; solid fill) or not fed colostrum (24NC; vertical fill).

Additionally, work on passive immunity transfer typically only focuses on IgG, which makes up 90% of colostral antibodies (Ahmann et al., 2021). There are actually two other antibody types in colostrum: IgA and IgM. Importantly, IgA is the principal antibody on mucosal surfaces like the gut and the lung, helping identify and fight off infectious bacteria (Woof and Kerr, 2006). In other words, IgA is designed to be secreted, not absorbed, which is borne out in recent studies. For instance, in calves supplemented with an active dry yeast (*Saccharomyces cerevisiae boulardii* CNCM I-1079), IgA secretion increased by 7 days of life (Villot et al., 2020) and reduced the incidence and severity of diarrhea bouts in calves (Villot et al., 2019). The importance of IgA supply in the gut may explain why transition milk feeding has improved antibody action (Pyo et al., 2020). These types of studies highlight some potential benefits of accelerating immune development in young calves.

MICROBIAL DEVELOPMENT

Why are calves born with a poor active immune system? The same immune system that increases vulnerability to disease also increases the ability of healthy bacteria to colonize the gut. At birth, Toll-Like Receptor (TLR) proteins on the intestinal surface can distinguish pathogenic and non-pathogenic microbes; as calves age, these receptors become scarcer (Malmuthuge et al., 2012). During the calf's first week of life, aerobic and facultatively anaerobic bacteria, including *Enterococcus* and *Streptococcus*, colonize the gut (Malmuthuge et al., 2015), depleting the oxygen present. Thereafter, strict anaerobes such as *Bifidobacterium* and *Bacteroides* establish, increasing tolerance to allergies and to symbiotic bacteria (Malmuthuge et al., 2015; Sjögren et al., 2009). In the pre-weaning period, as calves eat more starter, gut microbial diversity increases while most TLR abundance decreases (Malmuthuge et al., 2013). Post-weaning, however, increased calf starter no longer impacts TLR abundance (Sayles et al., *unpublished*). Pre-weaning, restricting the immune response while the immune system is learning to distinguish between pathogenic and non-pathogenic bacteria is crucial.

As a result of reduced immune response to bacteria, the first few weeks of life provide a prime opportunity to modulate the microbiome of calves (Malmuthuge et al., 2015). Recent research showed that *Bifidobacteria* are highly abundant in newborn calves and decrease *E. coli* colonization in the first few hours of life (Malmuthuge et al., 2015). Indeed, the colonization of host-specific microbiota in the gut is key to the efficacy of direct-fed microbials (Chung et al., 2012). In other words, the best probiotics for calves are probiotics from calves. For example, a Canadian team recently developed a cocktail of 4 *Lactobacillus* species derived from a healthy calf and fed this to newborn calves in the first week of life. Calves fed the calf-derived probiotic had lower bacterial shedding until 4 weeks of life (Degenshein et al., 2022), a full 3 weeks after DFM were no longer fed. Currently, our team is exploring the potential of this same probiotic cocktail to mitigate stress during weaning.

EARLY LIFE STRESSORS

While immunological and microbiological underdevelopment are necessary for effective development of a healthy gut microbiome, it coincides with inevitable stressors in our calf management, such as rumen development and weaning. Resilience of calves to these stressors varies widely; it can manifest in growth, health, and localized immune responses.
Rumen development, a key goal of the pre-weaning period, is driven by calf starter intake and fermentation. The short chain fatty acids (SCFAs) produced by fermentation of calf starter create a downward pressure on rumen pH, which may also play an important role in rumen epithelial development. Low rumen pH is regularly observed in pre-weaned calves and

increases with age (Khan et al., 2007; van Niekerk et al., 2020). Performance-wise, depressed rumen pH may cause no difference in body weight gain (Laarman and Oba, 2011) or may have increased body weight gain (McCurdy et al., 2019). In limited cases, low ruminal pH may damage the rumen epithelium, leading to inflammation (Kim et al., 2016). How calf resilience to low rumen pH changes over time is not clear.

In a recent study, our team carried out a study to see how calves' tolerance for rumen pH drops changes as calves age. Unlike the 4-layer rumen barrier, the hindgut barrier consists of only one layer of cells, making it more susceptible to breakdown. In our study, we used cannulated calves to buffer the rumen to a pH of 6.2 or 5.2, with low (10 mM) or very high (285 mM) SCFA. The rumen-buffering was carried out for 4 hours on weeks 3, 5, and 7. Neither rumen pH or SCFA concentration affected intake, growth, blood haptoglobin and cortisol, or histological stress in the liver (Wolfe et al., 2023a). Overall, these preliminary results demonstrate that calves are resilient to changes in the rumen environment throughout the pre-weaning period. The goal of the rumen development stressor, ironically, is to prepare calves for the weaning transition stressor. Weaning-related stress tends to be more visible, especially as a post-weaning growth slump. The key stressor associated with the weaning transition is the drop in milk allowance during the weaning transition; the higher the milk allowance, the greater the stress of weaning. In one study, calves on a high milk allowance weaned over the course of 1 week, where milk allowance is cut by 50% for 1 week before weaning completely. While calf starter intake increased quickly, calves experienced a drop in energy intake for 2 – 3 weeks after weaning began, slowing growth (Eckert et al., 2015). Meanwhile, calves weaned over 2 weeks, from 6 – 8 weeks, showed no slowdown in growth (Laarman et al., 2012; McCurdy et al., 2019). The examples of post-weaning growth slumps are an extreme response, but by no means the only way by which calves exhibit stress.

The above two studies demonstrate the importance of management factors of weaning management: age of the calf and pace of weaning. Compared to abruptly-weaned calves, gradually-weaned calves have greater ADG, ruminal VFA (Khan et al., 2007), more stable rumen pH, and lower heartrates (Wolfe et al., 2023b). As calves age, however, the same weaning pace increases neutrophils and lymphocytes in the blood, indicative of an immune response, and reduces ADG (Wolfe et al., 2023b). In early-weaned calves, abrupt weaning has lower expression of inflammation-related genes (Agustinho et al., 2024). Data from these studies suggest early-weaned calves have lower immunocompetence than older calves. While a lower immune response may be appealing, it is a sign the calf is unable to manage the stress, not that the calf is not experiencing stress. As a result, early weaning is not a desirable option.

OPPORTUNITIES TO IMPROVE HEALTHY CALF REARING

With the underdeveloped immune system of the young calf, how then can producers capitalize on this unique immunological environment to improve calf health? Three key points to be considered (Figure 2):

1) First week of life: During this time, active immunity is underdeveloped to allow for effective colonization by non-pathogenic microbes. Microbial programming to increase beneficial microbes or improve IgA production provides a window to accelerate development of a healthy gut microbiome.
2) Vulnerable period: During this time, microbial colonization slows while active immunity is slowly increasing. Calves are unable to mount an effective response to external stressors like weaning but are resilient to high fermentation rates in the rumen. As calves age, the focus should shift from milk provision to bolster growth, to improving calf starter intake to accelerate rumen development and improve gut microbiome diversity.
3) Immune Maturation: The immune system is starting to mature, and calves are better able to withstand external stressors such as weaning. Weaning should be done in multiple steps over the course of at least two weeks.

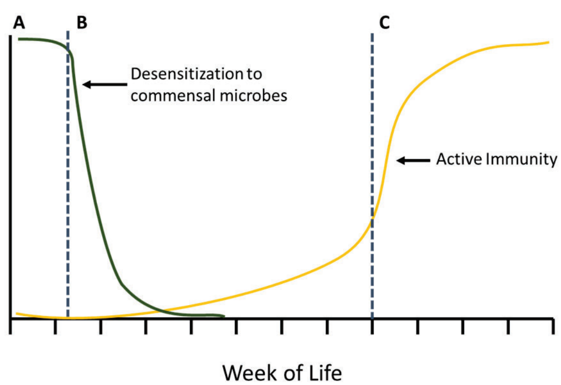

Figure 2. Visualization of immune and microbiome development in early calf life. A – First week of life, where gut microbiome colonization is active; B – Vulnerable period, where gut microbiome colonization is limited and immunocompetence is still low. Calves are vulnerable to disease and unable to respond to external stressors. C – Immune Maturation – Immune system is starting to mature, and calf is better able to withstand external stressors such as weaning.

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