Nutritional Regulation of Gut Function and Development During the Pre-Weaning and Weaning Period of the Dairy Calf

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Introduction

Raising healthy and productive calves is the key to the long-term success of the dairy industry. Unfortunately, amongst all animals on the dairy farm, calves suffer from the highest rates or morbidity and mortality, reaching up to 34% and 5%, respectively (Urie et al., 2018a). In 2010, the Dairy Calf and Heifer Association (**DCHA**) reported that the target morbidity rate for calves 24 to 60 d of age is less than 25% (DCHA, 2010; Urie et al., 2018a), demonstrating that there is still a significant need to reduce the high prevalence of morbidity. Digestive disorders are the most common cause of morbidity and mortality and can often be mitigated through sound early life nutrition and health management programs. As such, knowledge centered on nutritional strategies that promote optimal gut health in young calves is fundamental to ensuring the sustainability and profitability of the dairy industry. Therefore, this paper will focus on how gut function and development are regulated by differing nutritional strategies during the colostrum, transition milk, and whole milk or milk replacer feeding periods, as well as during the weaning transition.

Colostrum Feeding

Ensuring Passive Transfer

The bovine placenta prevents the passive transfer of immunoglobulins (**Ig**) to the calf in utero, and as a result, the neonatal calf is born immune-deficient. Thus, the calf relies on the timely feeding of adequate volumes of high-quality colostrum during early life to ensure that passive transfer of IgG is achieved. Specifically, it is recommended that calves are fed 3 to 4 L of colostrum containing > 50 g of IgG/L and a total bacterial count < 100,000 cfu/mL (McGuirk and Collins, 2004) before 6 hours of life (Stott et al., 1979; Fischer et al., 2018a). Unfortunately, failure of passive transfer (**FPT**, serum IgG < 10 mg/mL) still occurs in 12.1% of heifer calves (Shivley et al., 2018), which appears to be an improvement from recent FPT rates of 19.1% (Beam et al., 2009) and 40% (USDA, 1993). However, there has recently been a push to increase the FPT threshold from the dated recommendation of 10 mg/mL (Tyler et al., 1996; BAMN, 2001) to 15 mg/mL (Furman-Fratczak et al., 2011) or even 20 mg/mL (Chigerwe et al., 2015), as these concentrations better favour the absence of morbidity and mortality. Although this would result in on-farm FPT rates concurrently rising, this can be considered a positive push for dairy producers to improve colostrum and newborn calf management.

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As previously mentioned, one of the most critical factors in achieving successful passive transfer of immunity is the timely feeding of colostrum. It is widely accepted that the gut is no longer permeable to IgG after approximately 24 h of life; however, 41% and 23% of dairy producers reported only occasionally or never feeding colostrum overnight, respectively, which is when the majority of calvings occur (Winder et al., 2018). These practices are concerning, as research from the 1970s and 1980s has shown that serum IgG decreases in a linear trend as calves age (Stott et al., 1979; Bush and Staley, 1980). To our knowledge, Fischer et al. (2018a) was the first study to determine the effect of delaying colostrum feeding after birth using current colostrum recommendations, feeding an average of 3.2 L and 198 g of IgG, and standardizing colostrum intake by feeding pooled colostrum at 7.5% of birth body weight (**BW**). Calves fed within 1 h after birth had higher serum IgG concentrations (22.3 mg/mL) at 24 h compared to calves fed at 6 and 12 h after birth, which did not differ (17.0 mg/mL). This suggests that serum IgG concentrations may decrease in a non-linear trend with colostrum feeding time, and that the closure of the intestine may progress to a finite degree between 1 and 6 h of life (Fischer et al., 2018a). Previous work has shown that the ability to non-selectively absorb macromolecules during early life is unique to fetal intestinal cells (El-Nageh, 1967), which are completely absent by the third day of life (Smeaton and Simpson-Morgan, 1985). However, little is known about the factors that control the turnover of permeable fetal intestinal cells and future research is needed to determine the mechanisms by which gut closure occurs in the absence of colostrum feeding.

In addition to the quickness, quality, quantity, and cleanliness of colostrum feeding, additional factors can influence serum IgG concentrations of the neonatal calf. For instance, Hare et al. (unpublished data) demonstrated that feeding multiple meals of colostrum resulted in a greater maximum serum concentration of IgG (30.4 mg/mL) compared to calves only fed one meal of colostrum followed by whole milk (23.9 mg/mL). In addition, serum IgG concentrations were more persistent – i.e., remained at a greater proportion of the maximum IgG concentration reached – in calves fed multiple colostrum meals compared to those only fed one meal. Feeding multiple meals of colostrum, and thus improving IgG persistency, is likely to assist in preventing early life morbidity by reducing the high prevalence of digestive disorders. In addition, although previous work has found that tube feeding can reduce passive transfer (Godden et al., 2009), recent work by Desjardins-Morrissette et al. (2018) found no differences in IgG concentrations between calves fed 3 L of colostrum via tube or bottle. These conflicting findings likely arise from tube feeding small volumes of colostrum (e.g. 1.5 L) resulting in a large proportion of the meal remaining in the rumen compared to when 3 L is fed. Therefore, tube-feeding can be used as an efficient method to deliver colostrum and achieve passive transfer in neonatal calves, permitting that $\geq$ 3 L is fed.

Establishing a Healthy Gut

Although colostrum is well known for promoting the acquisition of passive immunity, it also plays a fundamental role in establishing the calf gut bacterial community, known as the microbiome. The gut microbiome plays a key role in shaping early life gut development and maturation. As such, dysbiosis of the microbiome can lead to increased risk of digestive disorders and bacterial infections, which are the main cause of morbidity, mortality and economic loss in the dairy industry. Feeding colostrum during the first hour of life accelerates the bacterial colonization of the calf small intestine, with calves fed fresh colostrum reaching a total bacteria density of 10^{10} 16S rRNA gene/g at 12 h of life compared to calves not fed colostrum, who only achieve 10^{8} 16S rRNA gene/g (Malmuthuge et al., 2015) at 12 h of life – total bacterial levels similar to newborn calves. Similarly, calves fed colostrum immediately after birth tended to have an increased prevalence of *Bifidobacteria* and *Lactobacillus* - which are well-known for their beneficial roles in the newborn gut - associated with the colon at 48 h compared with calves fed colostrum at 12 h of life (Fischer et al., 2018a). Furthermore, Malmuthuge et al. (2015) found that not feeding colostrum increased the prevalence of *Escherchia coli* in the small intestine compared with calves fed colostrum, and recent research has demonstrated an association between late colostrum feeding and the abundance of opportunistic pathogens, namely *Enterococcus* and *Streptococcus* (Ma et al., 2019). Together, these results suggest that bacterial colonization occurs at a slower rate in the absence of colostrum feeding and delaying the first colostrum meal may increase the risk of pathogen colonization and subsequent infection and disease.

In addition to fresh colostrum promoting an optimal gut bacterial community, feeding heat-treated colostrum may have even greater benefits. Specifically, feeding heat-treated colostrum to calves results in a greater prevalence of *Bifidobacteria* in the small intestine compared to calves fed fresh colostrum (Malmuthuge et al., 2015), which may explain the reported reduction in enteric infections with heat-treated colostrum feeding (Godden et al., 2012). Further work in the study by Malmuthuge et al. (2015) revealed that heat-treated colostrum contained 3 times more 3’sialyllactose (**3’SL**), the primary sialylated oligosaccharide (**OS**) in bovine colostrum, compared to fresh colostrum (Fischer et al., 2018b). Bovine colostrum OS can act as the primary energy substrate for beneficial gut bacteria (Yu et al., 2013), suggesting high concentrations of OS may mediate the early establishment *Bifidobacteria* in the calf intestine. To date, over 50 bovine OS have been detected (Aldredge et al., 2013; Albrecht et al., 2014), with concentrations of the primary sialylated bovine OS, 3’SL, 6’sialyllactosamine (**6’SLN**), disialyllactose (**DSL**) and 6’sialyllactose (**6’SL**), present at 15, 72, 22, and 5 times greater concentrations in colostrum compared to whole milk, respectively (Fischer-Tlustos et al., 2020). In addition to promoting beneficial bacterial colonization in the gut, bovine colostrum OS can inhibit adhesion of pathogens to the intestinal surface (Martin et al., 2002), indirectly support intestinal barrier and immune function (Chiclowski et al., 2012), and may enhance the binding of IgG to the intestinal epithelium and its subsequent uptake (Gill et al., 1999). Large quantities of bovine OS can be extracted during cheese whey processing (Barile et al., 2009; Aldredge et al., 2013), which may provide the opportunity for dairy producers to supplement these compounds in colostrum or colostrum replacer to promote optimal calf gut health.

In addition to OS, colostrum contains high levels of growth factors, namely insulin-like growth factor (**IGF**)-I, which is the most abundant growth factor and is thought to have a positive indirect effect on the growth of the intestine (Baumrucker et al., 1994; Blum and Hammon, 2000). Colostrum also has elevated levels of antimicrobial compounds, such as lactoferrin, lysozyme and lactoperoxidase, which help to maintain a healthy gut (Pakkanen and Aalto, 1997). Furthermore, high levels of nutrients in colostrum stimulate the production of the beneficial gut hormones glucagon like peptide (**GLP**)-1 and -2 (Desjardins-Morrissette et al., 2018; Inabu et al., 2018), which is not observed with milk feeding. Delaying colostrum feeding up to 12 h after birth can suppress the amount of GLP-1 and -2 produced compared to calves fed immediately after birth (Inabu et al., 2018). This may compromise early life growth and gut maturation, as GLP-2 is known to directly stimulate gut development, while GLP-1 promotes insulin release resulting in increased uptake of glucose for energy use by peripheral tissues. Therefore, although the majority of these compounds have been largely overlooked, it is clear that colostrum has a greater role in calf health and development than simply providing IgG.

Transition Milk

After 1 to 2 colostrum feedings during the first day of life, calves are often transitioned directly to whole milk or milk replacer (**MR**). This is a stark contrast to nature, in which calves would consume transition milk (**TM,** milkings 2 to 6) from suckling the dam (Blum and Hammon, 2000). Not feeding TM to calves may be a missed opportunity to improve gut health, as TM contains elevated levels of growth hormones, IGF-1, insulin (Blum and Hammon, 2000), nucleotides (Gill et al., 2011), and OS (Fischer-Tlustos et al., 2020) compared to whole milk. Furthermore, TM contains elevated proportions of omega-3 fatty acids (**FA**) (Hare et al., 2019), which have been shown to benefit antioxidant status and long-term immune response when supplemented to neonatal calves (Opgenorth et al., 2019). Although a previous study showed no benefit of TM feeding on serum IgG concentrations (Conneely et al., 2014), recent work by Hare et al. (unpublished data) demonstrated that serum IgG was more persistent (91% of maximum concentration, Cmax) in calves fed a colostrum:whole milk mixture (**MIX**, 1:1 ratio to simulate TM) compared to calves fed whole milk (75% of Cmax). Furthermore, calves fed MIX tended to have increased production of GLP-1 (Inabu et al., 2019) and displayed increased small intestinal surface area and cell proliferation in certain intestinal segments at 3 days of life compared to calves fed whole milk (Pyo et al., 2020). Although this work is promising, further research to determine the specific role each bioactive molecule may play in promoting optimal gut development is needed.

Milk Nutrition

Plane of Nutrition

Pre-weaning milk or MR feeding programs typically consist of feeding a conventional or elevated plane of nutrition. A conventional milk feeding program aims to encourage starter intake by limiting milk consumption to 10% of birth BW (4-5 L of milk/d or 750 g of MR powder/d). By decreasing milk intake, these programs can result in increased rumen development due to increased starter intake during early life

(Tamate et al., 1962), which may result in less susceptibility to health and production challenges during weaning. Furthermore, conventional feeding programs are often associated with a reduced feeding cost compared to feeding greater volumes of milk. However, lower BW gains (300-500 g/d) are often observed during the first month of life and calves often suffer from hunger, leading to animal welfare concerns (Jasper and Weary, 2002). In contrast, elevated programs feed milk or MR *ad libitum* or at approximately 20% of birth BW (> 8 L of milk/d or 1.2 kg of MR powder/d), which improves animal welfare as it reduces hunger-associated behaviours. A recent study by Haisan et al. (2019) showed that all calves (n = 26) offered large volumes of milk were able to consume over 8 L of milk/d and up to 10 L/d using an automated calf rail during the first week of life, demonstrating that this type of feeding program is synergistic with the calf's natural ability to consume large volumes of milk during this time. Furthermore, calves fed > 8 L/d achieved an average daily gain (**ADG**) of 750 g/d during the first three weeks of life, while calves restricted to 5 L/d only gained 350 g/d. This result is likely due to starter intake being negligible during early life and thus the majority of metabolizable energy is consumed directly from milk, regardless of the feeding program. In addition to increased BW gain and animal welfare, elevated feeding programs have the potential to result in more milk during lactation, improved mammary development, and reduction in age at first calving (Khan et al., 2007a; Soberon et al., 2012).

Despite the well-known benefits of feeding elevated levels of milk, Canadian (Vasseur et al., 2010) and United States (Urie et al., 2018b) dairy producers continue to feed an average of 5.5 and 5.7 L of milk/d, respectively. It is typically thought that feeding elevated planes of nutrition is only feasible through automated feeding, given concerns around feeding large volumes of milk in only 2 meals/d. However, a recent study (Ellingsen et al., 2016) demonstrated that 2-week old calves were able to consume 5 to 9 L of milk/meal without any overflow into the rumen, suggesting that we have largely underestimated how much calves are able to consume in a single feeding. Furthermore, work by MacPherson et al. (2018), demonstrated that there are no differences in insulin sensitivity in calves fed 8 L of milk over 2 meals from the first week of life compared to calves fed 8 L over 4 meals. Calves fed only 2 meals/d had a slower abomasal emptying rate, indicating that glucose delivery was slowed, which may have regulated the insulin response. Therefore, it may be important to begin feeding elevated planes of milk during the first week of life, as this may be a critical metabolic developmental window in which the calf adapts to consuming high volumes of milk.

Whole Milk vs. Milk Replacer Composition

In the United States, solely MR or a combination of MR and whole milk is fed on 60% of dairy operations (Urie et al., 2018b). Furthermore, the majority of dairy producers feed MR containing an average of 20.2% fat (Urie et al., 2018b). This is a stark contrast to whole milk, which contains approximately 30% fat. High fat consumption is essential for calves during early life because it is crucial in meeting energy demands and assisting with thermoregulation. Moreover, the odds of mortality are 3 times higher for calves fed < 0.15 kg of fat/d compared with calves fed > 0.22 kg of fat/d (Urie et al., 2018a). In addition to containing low amounts of fat, MR contains significantly more lactose than whole milk (45% vs. 35%). With the recent shift in calves being progressively fed larger volumes of MR, there is concern around how feeding large volumes of MR containing a high amount of lactose and a low amount of fat may impact gut development and health. Specifically, high lactose inclusion in MR increases the osmolality of MR (~400-600 mOsm/L) compared to whole milk (~300 mOsm/L), which has been shown to increase intestinal permeability and potentially disturb gut function in calves (Wilms et al., 2019). Moreover, feeding high amounts of lactose could negatively affect glucose homeostasis, resulting in high concentrations of blood glucose and insulin that may eventually lead to insulin resistance. Recent work by Welboren et al. (2019a) showed that calves fed 6 L of MR with high lactose and low fat (**HL**) content twice daily during the first week of life experienced a greater rise in blood glucose and insulin concentrations compared to calves fed a high fat and low lactose (**HF**) MR. Calves fed HF-MR tended to have slower abomasal emptying compared to HL-fed calves, which may have delayed the digestion of nutrients, namely fat and glucose, resulting in the positive effects observed on glucose regulation. To date, research investigating how current MR macronutrient compositions affect calves fed elevated planes of nutrition, especially long-term, is lacking. Moreover, future research is needed to evaluate the specific mechanisms by which MR compositions directly affect calf gut barrier function, development and overall metabolism and health.

Weaning Transition

Current Weaning Strategies

In nature, calves can consume over 10 L of milk/d in 8 to 12 small meals and will be fully weaned between 7 and 14 months of age (Reinhardt and Reinhardt, 1982). This is in contrast to current weaning practices, in which the average weaning age is approximately 9 weeks (Urie et al., 2018b). Furthermore, many operations often practice early weaning programs, with weaning occurring from 4-6 weeks of life, in order to limit milk feeding costs, encourage early intake of starter and thus stimulate rumen development. However, calves fed elevated levels of milk experience a challenge at weaning, especially if weaning occurs before 6 weeks of life, because of low pre-weaning solid feed intake (Jasper and Weary, 2002). This has been shown to result in decreased digestibility of dry and organic matter, neutral detergent fiber, crude protein, and gross energy after weaning (Terre et al., 2007; Hill et al., 2016; Dennis et al., 2018), suggesting that the digestive tract of calves fed elevated planes of nutrition are not equipped to digest solid feed following weaning. Previous research has demonstrated that calves fed an elevated plane of nutrition had greater starter feed intake and weight gain when the weaning transition was extended from 6 to 8 weeks (Eckert et al., 2015) and extending weaning can decrease the reduction of weight gain at weaning (Meale et al., 2015).

In addition to delaying the age of weaning, the “step-down” weaning method can be used to mitigate potential negative outcomes when weaning from elevated levels of milk. Khan et al. (2007a,b) was the first to report on the step-down protocol, in which calves either received elevated levels of milk at 20% of BW until d 23, followed by a step-down to 10% of BW from d 23 to d 44, or were fed at 10% of BW until d 44. The results showed that intake of solid feed and weight gain increased in calves fed according to the step-down protocol, suggesting that this is a feasible and efficient strategy to maximize weight gain while simultaneously achieving early weaning. When using automation, linear declines in milk intake can be implemented without increasing labor costs. For instance, reducing MR allowance by 2.5% daily from 6 L/d at d 36 to 2 L/d until d 63, results in increased performance compared to reducing milk intake by abrupt 2 L intervals (Welboren et al., 2019b). In contrast to these current protocols, it has long been recommended that calves should be weaned based on starter intake - specifically, calves should consume at least 700 to 900 g of starter for 2 to 3 consecutive days prior to weaning (BAMN, 2003). Despite this, only 31% of calves are currently weaned based off starter intake (Urie et al., 2018b), which is a practice that needs to be further investigated on dairy farms.

Weaning and Gut Function

Prior to weaning, calf gut function is similar to that of a monogastric, with glucose from milk providing the primary energy source. As starter intake increases, the rumen will gradually become the main site of fermentation and short chain fatty acids (**SCFA**) will account for 80% of the calf's energy source after weaning. As such, the weaning transition is a period in which the calf gut undergoes drastic physical changes, with total volume of the rumen increasing from 30% to 70% of the entire forestomach (Warner et al., 1956). The rumen transcriptome and microbiome also undergo rapid maturation, with enhanced expression of metabolic (Connor et al., 2013) and gut barrier (Malmuthuge et al., 2013) genes and altered microbial populations (Meale et al., 2017), resulting from exposure to substrates in the form of calf starter. Interestingly, the lower gut also undergoes significant changes, with microbial diversity increasing (Li et al., 2012); however, there is currently a lack of research characterizing the functional changes that occur to initiate these changes in the lower gut during weaning.

Calves are often fed high starch (>30%) in the form of calf starter in an effort to initiate rapid rumen development. However, this can result in an accumulation of SCFA and reduced ruminal pH, which may lead to ruminal acidosis. Recent work by Van Niekerk et al. (2017) demonstrated that it can take up to 5 weeks after weaning for the rumen environment of calves fed elevated levels of milk to be in a state that is not considered ruminal acidosis. If acidosis is severe, excessive amounts of starch can reach the hindgut (Li et al., 2012), resulting in high levels of fecal starch during weaning for calves fed elevated levels of milk (Eckert et al., 2015; Van Niekerk et al., 2018). This is likely a result of the calf gut lacking the necessary gut adaptations required to digest high amounts of starch at this time. These outcomes are unfavourable, as acidosis of both the rumen and hindgut can lead to systemic inflammatory responses. In addition, the site of fermentation – i.e. the rumen or hindgut – may be shifted depending on the processing of the source of starch in starter. For instance, feeding processed grain, such as steam-flaked corn, increased the risk of ruminal acidosis (Krause and Oetzel, 2006), while whole corn shifted fermentation to the lower gut (Gressley et al., 2011).

Van Niekerk et al. (2018) found that feeding an elevated level of milk combined with whole corn in calf starter resulted in decreased fecal pH 2 weeks after weaning compared to calves fed starter containing flaked corn, indicating that whole corn may shift the site of fermentation to the lower gut, possibly resulting in hindgut acidosis. However, there is currently a paucity of information regarding the influence of preweaning feeding regimes and weaning on the intestinal function of calves.

Conclusions

From the multitude of aforementioned research, it is clear that nutritional management can have a large impact on growth performance, health, and gut function and development. While ensuring passive transfer of newborn calves is of great importance, colostrum and transition milk also contain additional bioactive molecules beyond IgG that can have beneficial effects on gut function and development. In addition, maximizing whole milk or MR intake during the pre-weaning period is essential to animal welfare and growth when starter intake is negligible. Calves are often susceptible to health and production challenges during weaning when fed elevated levels of milk during the pre-weaning period, but this can be mitigated through the use of a step-down weaning program or weaning based on starter intake. Overall, further research is needed to determine the long-term effects that differing nutritional strategies during the first days, weeks and months of life may have on calf gut development and function. This will allow industry representatives and producers to make confident decisions that promote calf health, welfare, and productivity in order ensure the long-term success of the dairy industry.

References

Albrecht, S., J.A. Lane, K. Marino, K.A. Al Busadah, S.D. Carrington, R.M. Hickey, and P.M. Rudd. 2014. A comparative study of free oligosaccharides in the milk of domestic animals. Br. J. Nutr. 111:1313-1328.

Aldredge, D.L., M.R. Geronimo, S. Hua, C.C. Nwosu, C.B. Lebrilla, and D. Barile. 2013. Annotation and structural elucidation of bovine milk oligosaccharides and determination of novel fucosylated structures. Glycobiology. 23:664-676.

BAMN (Bovine Alliance on Management and Nutrition). 2001. A guide to colostrum and colostrum management for dairy calves. Accessed Jan. 6, 2020. https://www.aphis.usda.gov/animal_health/nahms/dairy/downloads/bamn/BAMN01_Colostrum.pdf

BAMN. 2003. A guide to dairy calf feeding and management. Bovine Alliance on Management and Nutrition (BAMN). Accessed Jan 6, 2020. https://www.aphis.usda.gov/animalhealth/nahms/dairy/downloads/bamn/BAMN03GuideFeeding.pdf.

Barile, D., M. Arlorio, J.B. German, J.D. Coisson, N. Tao, and C.B. Lebrilla. 2009. Permeate from cheese whey ultrafiltration is a source of milk oligosaccharides. Int. Dairy J. 19:524-530.

Baumrucker, C. R., D. L. Hadsell, and J. W. Blum. 1994. Effects of dietary insulin-like growth factor 1 on growth and insulin-like growth factor receptors in neonatal calf intestine. J. Anim. Sci. 72:428-433.

Beam, A.L., J.E. Lombard, C.A. Kopral, L.P. Garber, A.L. Winter, J.A. Hicks, and J.L. Schlater. 2009. Prevalence of failure of passive transfer of immunity in newborn heifer calves and associated management practices on US dairy operations. J. Dairy Sci. 92:3973-3980.

Blum, J.W. and H. Hammon. 2000. Colostrum effects on the gastrointestinal tract, and on nutritional, endocrine and metabolic parameters in neonatal calves. Live. Prod. Sci. 66:151-159.

Bush, L.J. and T.E. Staley. 1980. Absorption of colostral immunoglobulins in newborn calves. J. Dairy Sci. 63:672-680

Chiclowski, M., G. De Lartigue, J.B. German, H.E. Raybould, and D.A. Mills. 2012. *Bifidobacteria* isolated from infants and cultured on human milk oligosaccharides affect intestinal epithelial function. J. Pediatr. Gastroenterol. Nutr. 55:321-327.

Chigerwe, M., J. V. Hagey, and S. S. Aly. 2015. Determination of neonatal serum Immunoglobulin G concentrations associated with mortality during the first 4 months of life in dairy heifer calves. J. Dairy Res. 82: 400-406.

Conneely, M., D.P. Berry, J.P. Murphy, I. Lorenz, M.L. Doherty, and E. Kennedey. 2014. Effect of feeding colostrum at different volumes and subsequent number of transition milk feeds on the serum immunoglobulin G concentration and health status of dairy calves. J. Dairy Sci. 97:6991–7000.

Connor, E. E., R. L. Baldwin, C. Li, R. W. Li, and H. Chung. 2013. Gene expression in bovine rumen epithelium during weaning identifies molecular regulators of rumen development and growth. Funct. Integr. Genomics.13:133–142.

Dairy Calf and Heifer Association. 2010. Gold standards. Accessed Jan. 10, 2020. http: / / calfandheifer .org/ gold standards/ index .php.

Dennis, T.S., F.X. Suarez-Mena, T.M. Hill, J.D. Quigley, R.L. Schlotterbeck, R.N. Klopp, G.J. Lascano, and L. Hulbert. 2018. Effects of gradual and later weaning ages when feeding high milk replacer rates on growth, textured starter digestibility, and behavior in Holstein calves from 0 to 4 months of age. Journal of dairy science. 101(11):9863-75.

Desjardins-Morrissette, M., J.K. van Niekerk, D. Haines, T. Sugino, M. Oba, and M.A. Steele. 2018. The effect of tube vs. bottle feeding colostrum on IgG absorption, abomasal emptying and plasma hormone concentrations in newborn calves. J. Dairy Sci. 101:4168–4179.

Eckert, E., H. E. Brown, K. E. Leslie, T. J. DeVries, and M. A. Steele. 2015. Weaning age affects growth, feed intake, gastrointestinal development, and behaviour in Holstein calves fed an elevated plane of nutrition during the preening stage. J. Dairy Sci. 98:6315-6326.

Ellingsen, K., C.M. Mejdell, N. Ottesen, S. Larsen, and A.M. Grondahl. 2016. The effect of large milk meals on digestive physiology and behaviour in dairy calves. Physiol. Behav. 154:169–174.

El-Nageh, M.M. 1967. Relation entre l'arret de la resporption intestinale des anticorps et le renouvellement de l'epithelium intestinal. Ann. Med. Vet. 111:400-405.

Fischer, A.J., Y. Song, Z. He, D.M. Haines, L.L Guan, and M.A. Steele. 2018a. Effect of delaying colostrum feeding on passive transfer and intestinal bacterial colonization in neonatal male Holstein calves. J. Dairy Sci. 101:3099-3109. https://doi.org/ 10.3168/jds.2017-13397

Fischer, A. J., N. Malmuthuge, L. L. Guan, and M. A. Steele. 2018b. Short communication: The effect of heat treatment of bovine colostrum on the concentration of oligosaccharides in colostrum and in the intestine of neonatal male Holstein calves. J. Dairy Sci. 101:401-407.

Fischer-Tlustos, A.J., K. Hertogs, J.K. Van Niekerk, M. Nagorske, D.M. Haines, and M.A. Steele. 2020. Oligosaccharide concentrations in colostrum, transition milk, and mature milk of primi- and multi-parous Holstein cows during the first week of lactation. J. Dairy Sci. In Press: Accepted Dec 6, 2019.

Furman-Fratczak, K., A. Rzasa, and T. Stefaniak. 2011. The influence of colostral immunoglobulin concentration in heifer calves' serum on their health and growth. J. Dairy Sci. 94:1536-1539.

Gill, R.K., S. Mahmood, and J.P. Nagpaul. 1999. Functional role of sialic acid in IgG binding to microvillus membranes in neonatal rate intestine. Biol. Neonate. 76:55-64.

Gill, B.D., H.E. Indyk, and M. Manley-Harris. 2011. Determination of total potentially available nucleosides in bovine milk. Int. Dairy J. 21:34–41.

Godden, S.M., D.M. Haines, K. Konkol,and J. Peterson. 2009. Improving passive transfer of immunoglobulins in calves. II: Interaction between feeding method and volume of colostrum fed. J. Dairy Sci. 92:1758–1764.

Godden, S.M., D.J. Smolenski, M. Donahue, J.M. Oakes, R. Bey, S. Wells, S. Sreevatsan, J. Stabel, and J. Fetrow. 2012. Heat-treated colostrum and reduced morbidity in preweaned dairy calves: results of a randomized trial and examination of mechanisms of effectiveness. J. Dairy Sci. 95:4029-4040.

Gressley, T.F., M.B. Hall, and L.E. Armentano. 2011. Ruminant nutrition symposium: productivity, digestion, and health responses to hindgut acidosis in ruminants. J. Anim. Sci. 89(4):1120-30.

Haisan, J., M.A. Steele, D.J. Ambrose, and M. Oba. 2019. Effects of amount of milk fed, and starter intake, on performance of group-housed dairy heifers during the weaning transition. Appl. Anim. Sci. 35:88–93.

Hare, K.S., K. Hertogs, A. Fischer, P. Vahmani, M.E.R. Dugan, and M. Steele. 2019. Omega-3 and -6 fatty acids are more abundant in colostrum than transition and whole milk. J. Dairy Sci. 102(Suppl. 1):154.

Hill, T.M., J.D. Quigley, H.G. Bateman II, F.X. Suarez-Mena, T.S. Dennis, and R.L. Schlotterbeck. 2016. Effect of milk replacer program on calf performance and digestion of nutrients in dairy calves to 4 months of age. J. Dairy Sci. 99(10):8103-10

Inabu, Y., A. Fischer, Y. Song, L.L. Guan, M. Oba, M.A. Steele, and T. Sugino. 2018. Short communication: The effect of delayed colostrum feeding on plasma concentrations of glucagon-like peptide 1 and 2 in newborn calves. J. Dairy Sci. 101:6627-6631.

Inabu, Y., J. Pyo, S. Pletts, L.L. Guan, M.A. Steele, and T. Sugino. 2019. Effect of extended colostrum feeding on plasma glucagon-like peptide-1 concentration in newborn calves. J. Dairy Sci. 102:4619–4627.

Jasper, J., and D. M. Weary. 2002. Effects of ad libitum milk intake on dairy calves. J. Dairy Sci. 85:3054–3058.

Khan, M. A., H. J. Lee, W. S. Lee, H. S. Kim, S. B. Kim, K. S. Ki, J. K. Ha, H. G. Lee, and Y. J. Choi. 2007a. Pre- and postweaning performance of Holstein female calves fed milk through step-down and conventional methods. J. Dairy Sci. 90:876–885.

Khan, M. A., H. J. Lee, W. S. Lee, H. S. Kim, K. S. Ki, T. Y. Hur, G. H. Suh, S. J. Kang, and Y. J. Choi. 2007b. Structural growth, rumen development, and metabolic and immune responses of Holstein male calves fed milk through step-down and conventional methods. J. Dairy Sci. 90:3376–3387.

Krause, K. M., and G. R. Oetzel. 2006. Understanding and preventing subacute ruminal acidosis in dairy herds: A review. Anim. FeedSci. Technol. 126:215–236

Li, R.W., E.E. Connor, C. Li, R.L. Baldwin VI, and M.E. Sparks. 2012. Characterization of the rumen microbiota of pre-ruminant calves using metagenomics tools. Environ. Microbiol. 14:129-139.

Ma, T., E. O'Hara, Y. Song, A. Fischer, Z. He, M.A. Steele, and L.L. Guan. 2019. Altered mucosa-associated microbiota in the ileum and colon of neonatal calves in response to delayed first colostrum feeding. J. Dairy Sci. 102:7073-7086.

MacPherson, J., S.J. Meale, K. Macmillan, J. Haisan, C.J. Bench, M. Oba, and M.A. Steele. 2018. Effects of feeding frequency of an elevated plane of milk replacer and calf age on behavior, and glucose and insulin kinetics in male Holstein calves. Animal. 13:1385–1393.

Malmuthuge, N., M. Li, L. A. Goonewardene, M. Oba, and L. L. Guan. 2013. Effect of calf starter feeding on gut microbial diversity and expression of genes involved in host immune responses and tight junctions in dairy calves during weaning transition. J. Dairy Sci. 96:189-200.

Malmuthuge, N., Y. Chen, G. Liang, L.A. Goonewardene, and L.L. Guan. 2015. Heat-treated colostrum feeding promotes beneficial bacteria colonization in the small intestine of neonatal calves. J. Dairy Sci. 98:8044-8053.

Martin, M.J., A. Martin-Sosa, and P. Hueso. 2002. The sialylated fraction of milk oligosaccharides is partially responsible for binding to enterotoxigenic and uropathogenic *Escherichia coli* in human strains. J. Nutr. 132:3067-3072.

McGuirk, S.M. and M. Collins. 2004. Managing the production, storage and delivery of colostrum. Vet. Clin. North Am. Food Anim. Pract. 20:593-603.

Meale, S. J., L. N. Leal, J. Martín-Tereso, and M. A. Steele. 2015. Delayed weaning of Holstein bull calves fed an elevated plane of nutrition impacts feed intake, growth and potential markers of gastrointestinal development. Anim. Feed Sci. Tech. 209:268–273.

Meale, S. J., S. C. Li, P. Azevedo, H. Derakhshani, T. J. DeVries, J. C. Plaizier, M. A. Steele, and E. Khafipour. 2017. Weaning age influences the severity of gastrointestinal microbiome shifts in dairy calves. Sci. Rep. 7: doi:10.1038/s41598-017-00223-7.

Opgenorth, J., L.M. Sordillo, and M.J. VandeHaar. 2019. Colostrum supplementation with omega-3 fatty acids and α-tocopherol decreases indicators of oxidative stress and alters plasma fatty acid profile in newborn calves during the first week of life. J. Dairy Sci. 102(Suppl. 1):86.

Pakkanen, R. and J. Aalto. 1997. Growth factors and antimicrobial factors of bovine colostrum. Int. Dairy J. 7(5):285-297.

Pyo, J., K. Hare, S. Pletts, Y. Inabu, D. Haines, T. Sugino, L. L. Guan, and M. Steele. 2020. Feeding colostrum or a 1:1 colostrum:milk mixture for 3 d postnatal increase small intestinal development and minimally influences plasma GLP-2 and serum IGF-1 concentrations in Holstein bull calves. J. Dairy Sci. In Review.

Reinhardt, V. and A. Reinhardt. 1981. Natural sucking performance and age at weaning in zebu cattle (Bos indicus). J. Agric. Sci. 96:309–312.

Shivley, C.B., J.E. Lombard, N.J. Urie, D.M. Haines, R. Sargent, C.A. Kopral, T.J. Earleywine, J.D. Olson, and F.B. Garry. 2018. Preweaned heifer management on US dairy operations: Part II. Factors associated with colostrum quality and passive transfer status of dairy heifer calves. J. Dairy Sci. 101:9185-9198.

Smeaton, T.C. and M.W. Simpson-Morgan. 1985. Epithelial cell renewal and antibody transfer in the intestine of the foetal and neonatal lamb. Aust. J. Exp. Biol. Med. Sci. 36:181-198.

Soberon, F., E. Raffrenatio, R.W. Everett, and M.E. van Amburgh. 2012. Preweaning milk replacer intake and effects on long-term productivity of dairy calves. J. Dairy Sci. 95:783-793.

Stott, G.H., D.B. Marx, B.E. Menefee, and G.T. Nightengale. 1979. Colostral immunoglobulin transfer in calves II. The rate of absorption. J. Dairy Sci. 62:1766-1773.

Tamate, H., R. Getty, A. D. McGilliard, and N. L. Jacobson. 1962. Effect of various dietaries on anatomical development of stomach in calf. J. Dairy Sci. 45:408-420.

Terré, M., M. Devant, and A. Bach. 2007. Effect of level of milk replacer fed to Holstein calves on performance during the preweaning period and starter digestibility at weaning. Livest. Sci. 110:82–88.

Tyler, J.W., D.D. Hancock, S.M. Parish, D.E. Rea, T.E. Besser, S.G. Sanders, and L.K. Wilson. 1996. Evaluation of 3 assays for failure of passive transfer in calves. J. Vet. Intern. Med. 10:304-307.

Urie, N.J., J.E. Lombard, C.B. Shivley, C.A. Kopral, A.E. Adams, T.J. Earleywine, J.D. Olson, and F.B. Garry. 2018a. Preweaned heifer management on US dairy operations: Part V. Factors associated with morbidity and mortality in preweaned dairy heifer calves. J. Dairy Sci. 101:9229–9244.

Urie, N.J., J.E. Lombard, C.B. Shivley, C.A. Kopral, A.E. Adams, T.J. Earleywine, J.D. Olson, and F.B. Garry. 2018b. Preweaned heifer management on US dairy operations: Part I. Descriptive characteristics of preweaned heifer raising practices. J. Dairy Sci. 101:9168-9184.

USDA, 1993. Transfer of maternal immunity to calves. USDA_APHISVS_CEAH, Fort Collins, CO. Accessed Jan 6, 2020. https://www.aphis.usda.gov/aphis/ourfocus/animalhealth/monitoring-and-surveillance/nahms/nahms_dairy_studies

Van Niekerk, J. K., M. Middeldorp, and M.A. Steele. 2017. Ruminal pH in Holstein dairy bull calves from pre-weaning to post-weaning. J. Dairy Sci. Vol. 100 (Suppl. 2):178.

Van Niekerk, J. K., A.J. Fischer, L.L. Deikun, T.M. Hill, J.D. Quigley, R.L. Schlotterbeck, and M.A. Steele. 2018. Can processing corn influence growth performance, nutrient digestibility and ruminal and hindgut fermentation in calves fed low or high plane of milk replacer? J. Dairy Sci. Vol. 101 (Suppl. 2): 235-236.

Vasseur, E., F. Borderas, R.I. Cue, D. Lefebvre, D. Pellerin, J. Rushen, K.M. Wade, and A.M. de Passille. 2010. A survey of dairy calf management practices in Canada that affect animal welfare. J. Dairy Sci. 93:1307–1315.

Warner, R. G., W. P. Flatt, and J. K. Loosli. 1956. Dietary factors influencing the development of the ruminant stomach. Agric. Food Chem. 4:788–801.

Welboren, A., B. Hatew-Chuko, L. Leal, J. Martín-Tereso, and M. Steele. 2019a. Effects of a high lactose milk replacer on glucose metabolism in neonatal calves. WCDS Proc. 31:236.

Welboren, A.C., L.N. Leal, M.A. Steele, M.A. Khan, and J. Martín-Tereso. 2019b. Performance of ad libitum fed dairy calves weaned using fixed and individual methods. Animal. 1-8.

Winder, C.B., C.A. Bauman, T.F. Duffield, H.W. Barkema, G.P. Keefe, J. Dubuc, F. Uehlinger, D.F. Kelton. 2018. Canadian National Dairy Study: Heifer calf management. J. Dairy Sci. 101:10565-10579.

Yu, Z-T., C. Chen, and D.S. Newburg. 2013. Utilization of major fucosylated and sialylated human milk oligosaccharides by isolated human gut microbes. Glycobiology. 23(11):1281-1292.

SESSION NOTES