# From newborn to puberty: Promoting calf immunity, development, and health through well-developed nutritional management

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#### Abstract

Proper nutritional management during the first year of the calf's life is essential in maximizing health and productivity. Feeding a sufficient volume of colostrum early in life is crucial to ensure the transfer of passive immunity and research has begun to characterize the additional bioactive compounds in colostrum and transition milk that can benefit calf development. We know that it is important to feed elevated levels of whole milk or milk replacer during the initial weeks of life, when starter intake is negligible, but further research regarding the effects of feeding large volumes of traditional milk replacers compared to whole milk on calf metabolism, health and development is required. When elevated levels of milk are fed preweaning, calves are often susceptible to production challenges during weaning, which can be mitigated by weaning gradually and later in life. It is also becoming clear that postweaning diets, which are often overlooked, can have profound effects on heifer growth and reproductive development. It is clear that a multitude of differing strategies to raise dairy calves exist; yet, it is up to the dairy research and industry communities to educate producers on specific practices that will maximize heifer development, immunity, health and ultimately the profitability of their operations.

Key words: dairy heifer, colostrum, plane of nutrition, weaning

#### Introduction

It is becoming increasingly clear that the calf's growth and health during the pre-weaning stage can have a profound influence on her future productivity as a milking animal.<sup>47</sup> Thus, it is essential that we implement management practices and strategies that promote, rather than hinder, calf health and development. However, there remains a significant need to determine strategies, preferably non-antimicrobial, that reduce the high rates of morbidity (34%) and mortality (5%) in young calves.<sup>51</sup> There are a variety of contributors to calf illness and death, yet, digestive disorders remain the most common culprit.<sup>51</sup> Digestive disorders can often be prevented through the use of well-developed early life nutrition and health management programs. Amongst others, our research group has generated data from the neonatal to post-weaning stages strongly demonstrating that proper nutrition improves calf development and health, and ultimately reduces the high rates of morbidity, mortality, and antimicrobial use during early life.

#### **Colostrum and Transition Milk Feeding**

It is well-known that the calf depends on the feeding of high-quality colostrum during early life to ensure transfer of passive immunity (**TPI**). Yet, failed transfer of passive immunity (**FPTI**), defined as serum IgG < 10 mg/mL at 1 to 7 d of life,<sup>17,50</sup> still occurs in 12.1% of heifer calves in the US.<sup>46</sup> However, re-evaluating the efficacy of this traditional FPTI cut-off point has resulted in new serum IgG cut-point categories: excellent (> 25.0 g/L), good (18.0 to 24.9 g/L), fair (10.0 to 17.9 g/L) and poor (< 10.0 g/L).<sup>34</sup> Current FPTI rates will consequently rise to achieve a minimum of the "good" serum IgG threshold, emphasizing the need to further improve current colostrum and neonatal calf management strategies.

To ensure TPI, it is recommended that calves are fed colostrum containing  $\geq$  50 g of IgG/L at 10 to 12% of birth body weight (~3 to 4 L).<sup>22</sup> In addition, feeding colostrum immediately after birth results in greater serum IgG concentrations compared to calves fed at 6 h and 12 h of life,<sup>13</sup> due to intestinal epithelial cells losing the ability to absorb IgG as time after birth increases.<sup>48</sup> Therefore, it is commonly recommended that colostrum is fed within 4 h after birth to ensure TPI.<sup>22</sup> In terms of feeding method, research has largely shown that feeding  $\geq$  3 L of colostrum and/or colostrum replacer via nipple bottle or esophageal tube feeder does not result in any differences in serum IgG concentrations;<sup>3,8,22</sup> thus, either practice can be used to facilitate adequate TPI. It is important to consider that TPI may be further enhanced by feeding additional meals of colostrum after the initial 3-4 L feeding. Recently, Hare et al<sup>25</sup> fed calves 3-4 L of colostrum within the first 2 h of life, followed by subsequent meals of either colostrum, a 1:1 colostrum:whole milk mixture, or whole milk at 12-h intervals. Calves fed additional meals of colostrum achieved greater serum IgG concentrations (30.4

 $\pm$  0.8 mg/mL) compared to calves fed whole milk (23.9  $\pm$  0.8 mg/mL).<sup>25</sup> Feeding additional meals of colostrum not only improved TPI but also improved gut development, specifically by increasing small intestinal villi height and absorptive surface area (Figure 1).<sup>43</sup> Similar results were observed in calves fed the colostrum:whole milk mixture, demonstrating that colostrum and transition milk (**TM**) play a key role in both providing passive immunity and promoting gut development and maturation.

Nutrients within colostrum may be partially responsible for stimulating intestinal development in neonatal calves. Although protein appears to be the predominant energy source in colostrum, fat actually accounts for  $\sim 60\%$ of digestible energy while protein only supplies ~25%. In addition to fueling the metabolism and thermoregulation of the newborn calf, high levels of fat in colostrum may induce the secretion of glucagon-like peptide (GLP)-2, a gut hormone that is well-known for its role in promoting gut proliferation and development. Feeding colostrum replacer stimulates large increases in plasma concentrations of GLP-28 and feeding colostrum immediately after birth results in greater plasma concentrations of GLP-2 compared to calves fed at 12 h after birth.<sup>27</sup> To corroborate the effect that GLP-2 may have on intestinal development, Fischer-Tlustos et al<sup>15</sup> demonstrated that delaying colostrum feeding did indeed reduce small intestinal villi height compared to feeding immediately after birth.

Colostrum also plays a vital role in the establishment of a healthy intestinal microbial community. The gut microbiome is associated with overall calf health and disease outcomes,<sup>41</sup> emphasizing the importance of a balanced gut microbial community on the development of the immune system and overall physiology of the host. Calves not fed colostrum have a decreased abundance of total bacteria in the small intestine at 12 h of life,<sup>36</sup> and withholding colostrum feeding for 12 h tends to reduce proportions of beneficial bacteria in the colon at 2 d of life.<sup>13</sup> Oligosaccharides, which are present at high concentrations in colostrum compared to whole milk,<sup>16</sup> are associated with the abundance of beneficial bacteria in the small intestine of newborn calves<sup>14,36</sup> and are considered to be one of the major prebiotic compounds influencing the establishment of the intestinal gut microbiome. In addition, colostrum oligosaccharides and their associated constituents may play a key role in inhibiting common intestinal pathogens<sup>38</sup> and enhancing the uptake of IgG into enterocytes.<sup>12,21</sup>

In addition to the aforementioned benefits of colostrum feeding, the first milking contains high levels of growth factors, microRNAs, hormones, cytokines and antimicrobial components that enhance the calf's ability to fight infection and promote development and growth.<sup>2</sup> Many of these compounds, including oligosaccharides,<sup>16</sup> insulin, insulin-like growth factor-1,<sup>2</sup> and nucleotides,<sup>20</sup> are also elevated in transition milk (TM) compared to whole milk. As previously mentioned, calves fed a colostrum:whole milk mixture (to simulate TM) have improved gut development compared to those fed whole milk (Figure 1).43 Specifically, feeding TM promotes intestinal development to the same degree as providing solely colostrum for 3 d, despite containing less nutrients. Therefore, feeding fresh or frozen TM may be a viable and efficient strategy to improve gut development in young calves. A study conducted in Ontario, Canada demonstrated that almost 80% of producers feed TM to calves for an average of 3 d after birth<sup>44</sup> in order to convey enhanced health benefits. Due to the large herd sizes in the US, producers often transition calves directly to whole milk or milk replacer (MR) after the initial colostrum feeding; however, the exact proportion of US heifer calves fed TM is currently unknown.



**Figure 1.** Brightfield microscopy images \*(200 x magnification) of small intestinal tissue from calves consuming either pooled colostrum, a 1:1 colostrum:whole milk mixture (COL:MILK), or whole milk feedings from 12 to 72 h of life after the initial colostrum meal within the first 2 hours of life. Data is published as Pyo et al.<sup>43</sup>

## **Plane of Milk Nutrition**

Dairy calves are typically offered elevated or conventional milk feeding programs. Conventional feeding programs aim to stimulate rumen development<sup>30</sup> via early starter intake and limiting milk consumption to  $\sim 10\%$  of birth body weight (BW; ~4-5 L of milk or 750 g of MR per day). However, calves often have reduced BW gain during the first month of life and suffer from hunger-associated behaviors, leading to both production and welfare concerns.<sup>28</sup> Conversely, offering elevated levels of milk (~20% birth BW, > 8 L or milk or 1.2 kg of MR per day) reduces hunger behavior, and increases BW gain, the potential to produce greater volumes of milk during future lactations, as well as improve mammary development and reproductive efficiency.<sup>28,47,55</sup> Despite the well-known benefits of feeding elevated levels of milk and the ability of calves to consume up to 10 L of milk/d as early as the first week of life,<sup>24</sup> US producers continue to feed an average of 5.7 L of milk/d during the preweaning period.<sup>52</sup> While this rate of milk feeding immediately prior to the weaning may be beneficial, feeding a conventional plane of nutrition during the first month of life will compromise average daily gain (ADG) due to negligible starter intake.<sup>24</sup>

Producers often assume that feeding elevated levels of milk is only feasible with the use of automated feeding technologies. However, 2-week old calves have the ability to consume 5-9 L of milk per meal without ruminal overflow<sup>11</sup> and can consume 4 L of milk/meal without compromising insulin sensitivity.<sup>35</sup> Specifically, calves offered 4 L of milk twice a day were able to slow their abomasal emptying, possibly regulating intestinal glucose delivery and the subsequent insulin response, compared to calves fed 2 L of milk 4 times per day.<sup>35</sup> However, it is important to note that the calves in this study<sup>35</sup> were fed elevated volumes of milk during the first week of life, which may be a critical developmental window in which the calf adapts to consuming high levels of milk.

#### Feeding Whole Milk vs Milk Replacer

Due to the aforementioned benefits of feeding large volumes of milk, the dairy industry is gradually shifting towards feeding elevated planes of whole milk or milk replacer (MR) during the preweaning period. Currently, 60% of US dairy operations feed solely MR or a combination of MR and whole milk.52 Yet, further consideration of traditional MR formulations is required, as MR typically contains greater levels of lactose (40 to 50% vs 33 to 38%)<sup>42</sup> and lower levels of fat (16 to 22% vs 30 to 40%)<sup>1</sup> compared to whole milk. These differences in macronutrient composition have been hypothesized to influence calf growth and development, as well as physiology. For instance, high fat consumption is essential to meeting energy demands and assisting in thermoregulation during early life and is associated with reduced odds of mortality.<sup>51</sup> It is also important to note that the profile of fatty acids (FA) in MR differs from that of whole

milk - specifically MR contains high levels of polyunsaturated FA. Feeding high levels of polyunsaturated FA can reduce nutrient digestibility and growth, as well as increase diarrhea incidence compared to feeding a MR that resembles the FA profile of whole milk.<sup>29</sup> Furthermore, feeding high volumes of MR containing markedly greater lactose concentrations causes concern for gut health and development. High lactose inclusion in MR increases the osmolality of MR (~400-600 mOsm/L) compared to whole milk (~300 mOsm/L), which can potentially disturb gut function in calves.<sup>59</sup> In addition, calves fed a high lactose MR during the first week of life experienced a greater increase in blood glucose and insulin concentrations compared to calves fed a high fat and low lactose MR.57 In this study, calves fed the high fat MR had a reduced rate of abomasal emptying, possibly delaying the delivery of nutrients to the intestine and positively regulating glucose and insulin levels. To date, research investigating the macronutrient and fatty acid composition of MR compared to whole milk is scarce; however, it is important to determine the effects of these feeding practices on heifer physiology and the subsequent influence on development and health.

#### Weaning Strategies

The weaning transition is a period of drastic physical and physiological changes. Ruminal volume increases by 40%<sup>56</sup> and rapid maturation of the rumen transcriptome and microbiome occurs.<sup>6,37,39</sup> Feeding high volumes of milk or milk replacer preweaning can pose a challenge during the weaning transition, especially if weaning occurs prior to 6 weeks of age. Early weaning programs typically aim to encourage early intake of starter and rumen development; however, calves fed elevated levels of milk often consume low amounts of solid feed due to the large amount of energy supplied from milk.<sup>28</sup> This results in decreased digestibility of fiber, dry matter, NDF, CP, and gross energy after weaning, 9,26,49 suggesting that the gastrointestinal tract is unaccustomed to digesting solid feed during and after the weaning transition. Conversely, extending weaning age from 6 to 8 weeks of age in calves fed elevated levels of milk results in greater starter intake, weight gain, and decreased growth depression during weaning.<sup>10,40</sup> Implementing the "step-down" method<sup>31,32</sup> or weaning calves gradually using automation<sup>58</sup> can also improve starter intake and performance measures. Fortunately, the dairy industry has made great strides in improving the onset of weaning, with a reported average weaning age of 9 weeks in the US.52 Yet, only 31% of calves are currently weaned based on their starter intake<sup>52</sup> and may be unequipped to consume and digest large amounts of starter during and after weaning.

In addition to the amount of milk fed preweaning, the impact of the amount and form of starch in calf starter on the development of the gastrointestinal tract and the outcomes of weaning requires further attention. Calves are often fed starter that is high in starch (> 30%), which can result in an accumulation of short chain fatty acids. This can lead to re-

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duced ruminal pH and acidosis, which, if severe, can result in excessive amounts of undigested ruminal starch in the lower gut<sup>33</sup> and eventually in the feces.<sup>10,54</sup> This indicates that the lower gut may experience acidosis, which could potentially lead to the generation of a systemic inflammatory response. In addition, the form of starch, such as whole corn vs steam-flaked corn, can shift the fermentation site to the lower gut<sup>23</sup> and reduce fecal pH.<sup>54</sup> The research community has begun to recognize that significant changes occur in the lower gut during the weaning transition; yet, research investigating the interactions between high planes of milk nutrition and the form and amount of starch in starter and their effects on lower gut functional changes in the lower gut is lacking.

#### Post-weaning and Beyond

Calf research has primarily focused on the pre-weaning and weaning periods and the effects of common nutritional management programs during the initial months following weaning are largely uncharacterized. Although there is data to support the effects of preweaning plane of nutrition on production and health during the adult stage,<sup>31,47</sup> a recent study demonstrated that there was little interaction in growth and development indicators between the pre- and postweaning phases of life.<sup>45</sup> The prepubertal phase is a critical period in heifer development and the industry largely underfeeds heifers during the post-weaning stage. Recent work has demonstrated that improving post-weaning growth by increasing concentrate inclusion in TMR (from 70% to 85%) in post-weaning diets enhances development of the reproductive tract, the number of ovarian follicles during the first estrous cycle, and chances of achieving puberty by 30 weeks of age.<sup>4,5</sup> Furthermore, ADG, serum concentrations of insulin-like growth factor-1 and  $\beta$ -hydroxybutyrate, as well as ruminal concentrations of butyrate, were greater in heifers offered TMR with greater concentrate inclusion.45 This indicates that heifers fed a diet high in concentrate were able to achieve increased growth and ruminal development while simultaneously improving reproductive efficiency. Furthermore, the greater body condition score (BCS) in heifers fed high levels of dietary concentrate suggests an increased conversion of dietary energy to fat at the expense of lean tissue growth for heifers fed greater levels of concentrate in TMR. This is often a concern during the prepubertal period during the allometric mammary growth phase<sup>18,19</sup> and can lead to an accumulation of fat in the mammary fat pad at the expense of parenchymal tissue growth.<sup>7</sup> Although positive associations were observed between greater BCS and reproductive efficiency<sup>4,5,45</sup> further research regarding accelerated growth rates in prepuberal heifers and mammary development and milk production is required.

### Conclusion

During the pre-weaning, weaning and post-weaning phases there are a multitude of common raising strategies that

hinder heifer productivity, development and health. Educating dairy producers and industry representatives on management practices that promote proper calf development is necessary to mitigate the current high rates of morbidity and mortality experienced on farm. However, research pertaining to effects that certain nutritional regimes have on specific physiological mechanisms in the calf, as well as their long-term effects on productivity and health, often requires further investigation. This information is needed to allow the dairy industry to confidently make decisions that promote calf development while ensuring health, welfare and future productivity.

#### References

1. Berends H, van Laar H, Leal LN, Gerrits WJJ, Martín-Tereso J. Effects of exchanging lactose for fat in milk replacer on *ad libitum* feed intake and growth performance in dairy calves. *J Dairy Sci* 2020;103:4275–4287.

2. Blum JW, Hammon H. Colostrum effects on the gastrointestinal tract, and on nutritional, endocrine and metabolic parameters in neonatal calves. *Live Prod Sci* 2000; 66:151–159.

3. Bonk S, Nadalin A, Heuwieser W, Veira D. Lying behavior and IgG-levels of newborn calves after feeding colostrum via tube and nipple bottle feeding. *J Dairy Res* 2016; 83:298-304.

4. Bruinjé TC, Rosadiuk JP, Moslemipur F, Sauerwein H, Steele MA, Ambrose DJ. Differing planes of pre- and postweaning phase nutrition in Holstein heifers: II. Effects on circulating leptin, luteinizing hormone, and age at puberty. *J Dairy Sci* 2021;104:1153-1163.

5. Bruinjé TC, Rosadiuk JP, Moslemipur F, Carrelli JE, Steele MA, Ambrose DJ. Carryover effects of pre- and post-weaning planes of nutrition on reproductive tract development and estrous cycle characteristics in Holstein heifers. *J Dairy Sci* 2019;102:10514-10529.

6. Connor EE, Baldwin RL, Li C, Li RW, Chung H. Gene expression in bovine rumen epithelium during weaning identifies molecular regulators of rumen development and growth. *Funct Integr Genomics* 2013;13:133–142.

7. Davis Rincker LE, Weber Nielsen MS, Chapin LT, Liesman JS, Daniels KM, Akers RM, Vandehaar MJ. Effects of feeding prepubertal heifers a high-energy diet for three, six, or twelve weeks on mammary growth and composition. *J Dairy Sci* 2008; 91:1926-1935.

8. Desjardins-Morrissette M, van Niekerk JK, Haines D, Sugino T, Oba M, Steele MA. The effect of tube versus bottle feeding colostrum on immunoglobulin G absorption, abomasal emptying, and plasma hormone concentrations in newborn calves. *J Dairy Sci* 2018;101:1-12.

9. Dennis TS, Suarez-Mena FX, Hill TM, Quigley JD, Schlotterbeck RL, Klopp RN, Lascano GJ, Hulbert L. 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. *J Dairy Sci* 2018;101:9863-9875.

10. Eckert E, Brown HE, Leslie KE, DeVries TJ, Steele MA. 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* 2015;98:6315-6326.

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

12. Feeney S, Gerlach JQ, Slattery H, Kilcoyne M, Hickey RM, Joshi L. Lectin microarray profiling and monosaccharide analysis of bovine milk immunoglobulin G oligosaccharides during the first 10 days of lactation. *Food Sci Nutr* 2020;7:1564-1572.

13. Fischer AJ, Song Y, He Z, Haines DM, Guan LL, Steele MA. Effect of delaying colostrum feeding on passive transfer and intestinal bacterial colonization in neonatal male Holstein calves. *J Dairy Sci* 2018;101:3099-3109.

14. Fischer AJ, Malmuthuge N, Guan LL, Steele MA. 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* 2018;101:401–407.

15. Fischer-Tlustos AJ, Pyo J, Song Y, Renaud DL, Guan LL, Steele MA. Short communication: Effect of delaying the first colostrum feeding on small intestinal histomorphology and serum IGF-1 concentrations in neonatal male Holstein calves. *J Dairy Sci* 2020;103:12109-12116.

16. Fischer-Tlustos AJ, Hertogs K, Van Niekerk JK, Nagorske M, Haines DM, Steele MA. 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* 2020;103:3683-3695.

17. Gay CC. Failure of passive transfer of colostral immunoglobulins and neonatal disease in calves: A review, in *Proceedings*. 4<sup>th</sup> Int Symp Neonatal Dis Vet Infect Dis Org, Saskatoon, SK, Canada. 1983;4:346-364.

18. Geiger AJ. Review: The pre-pubertal bovine mammary gland: unlocking the potential of the future herd. *Animal* 2019;13:4-10.

19. Geiger AJ, Parsons CLM, Akers RM. Feeding a higher plane of nutrition and providing exogenous estrogen increases mammary gland development in Holstein heifer calves. *J Dairy Sci* 2016;99:7642-7653.

20. Gill BD, Indyk HE, Manley-Harris M. Determination of total potentially available nucleosides in bovine milk. *Int Dairy J* 2011;21:34-41.

21. Gill RK, Mahmood S, Nagpaul JP. Functional role of sialic acid in IgG binding to microvillus membranes in neonatal rate intestine. *Biol Neonate* 1999;76:55-64.

22. Godden SM, Lombard JE, Woolums AR. Colostrum management for dairy calves. *Vet Clin North Am Food Anim Pract* 2019;35:535-556.

23. Gressley TF, Hall MB, Armentano LE. Ruminant nutrition symposium: productivity, digestion, and health responses to hindgut acidosis in ruminants. *J Anim Sci* 2011;89:1120-1130.

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

25. Hare K, Pletts S, Pyo J, Haines D, Guan LL, Steele MA. Feeding colostrum or a 1:1 colostrum:whole milk mixture for 3 d postnatal increases serum immunoglobulin G and apparent IgG persistency in Holstein bulls. *J Dairy Sci* 2020;103:11833-11843.

26. Hill TM, Quigley JD, Bateman II HG, Suarez-Mena FX, Dennis TS, Schlotterbeck RL. Effect of milk replacer program on calf performance and digestion of nutrients in dairy calves to 4 months of age. *J Dairy Sci* 2016;99:8103-8110. 27. Inabu Y, Fischer A, Song Y, Guan LL, Oba M, Steele MA, Sugino T. Short communication: The effect of delayed colostrum feeding on plasma concentrations of glucagon-like peptide 1 and 2 in newborn calves. *J Dairy Sci* 2018;101:6627-6631.

28. Jasper J, Weary DM. Effects of *ad libitum* milk intake on dairy calves. *J Dairy Sci* 2002;85:3054-3058.

29. Jenkins KJ, Kramer JKG, Sauer FD, Emmons DB. Influence of triglycerides and free fatty acids in milk replacers on calf performance, blood plasma, and adipose lipids. *J Dairy Sci* 1985;68:669-680.

30. Khan MA, Weary DM, von Keyserlingk MAG. Hay intake improves performance and rumen development of calves fed higher quantities of milk. *J Dairy Sci* 2011;94:3547-3553.

31. Khan MA, Lee HL, Lee WS, Kim HS, Kim SB, Ki KS, Ha JK, Lee HG, Choi YJ. Pre- and postweaning performance of Holstein female calves fed milk through step-down and conventional methods. *J Dairy Sci* 2007;90:876-885. 32. Khan MA, Lee HJ, Lee WS, Kim HS, Ki KS, Hur TY, Suh GH, Kang SJ, Choi YJ. Structural growth, rumen development, and metabolic and immune responses of Holstein male calves fed milk through step-down and conventional methods. *J Dairy Sci* 2007;90:3376-3387.

33. Li RW, Connor EE, Li C, Baldwin VI RL, Sparks ME. Characterization of the rumen microbiota of pre-ruminant calves using metagenomics tools. *Environ Microbiol* 2012;14:129-139.

34. Lombard J, Urie N, Garry F, Godden S, Quigley J, Earleywine T, McGuirk S, Moore D, Branan M, Chamorro M, Smith G, Shivley C, Catherman D, Haines D, Heinrichs AJ, James R, Maas J, Sterner K. Consensus recommendations on calf- and herd-level passive immunity in dairy calves in the United States. *J Dairy Sci* 2020;103:7611-7624.

35. MacPherson J, Meale SJ, Macmillan K, Haisan J, Bench CJ, Oba M, Steele MA. 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* 2018;13:1385-1393.

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

37. Malmuthuge N, Li M, Goonewardene LA, Oba M, Guan LL. 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* 2013;96:189-200.

38. Martin M-J, Martin-Sosa S, Hueso P. Binding of milk oligosaccharides by several enterotoxigenic *Escherichia coli* strains isolated from calves. *Glycoconj J* 2002;19:5-11.

39. Meale SJ, Li SC, Azevedo P, Derakhshani H, DeVries TJ, Plaizier JC, Steele MA, Khafipour E. Weaning age influences the severity of gastrointestinal microbiome shifts in dairy calves. *Sci Rep* 2017;7:198. doi:10.1038/s41598-017-00223-7.

40. Meale SJ, Leal LN, Martín-Tereso J, Steele MA. 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* 2015;209:268-273.

41. Oikonomou G, Tiexeria AGV, Foditsch C, Bicalho ML, Machadon VS, Bicalho RC. Fecal microbial diversity in pre-weaned dairy calves as described by pyrosequencing of metagenomic 16S rDNA. Associations of *Faecalibacterium* species with health and growth. *PLoS One* 2013;8:e63157.

42. Pantophlet AJ, Gerrits WJJ, Vonk RJ, van den Borne JJGC. Substantial replacement of lactose with fat in a high-lactose milk replacer diet increases liver fat accumulation but does not affect insulin sensitivity in veal calves. *J Dairy Sci* 2016;99:10022-10032.

43. Pyo J, Hare K, Pletts S, Inabu Y, Haines D, Sugino T, Guan LL, Steele M. Feeding colostrum or a 1:1 colostrum:milk mixture for 3 days postnatal increases small intestinal development and minimally influences plasma glucagon-like peptide-2 and serum insulin-like growth factor-1 concentrations in Holstein bull calves. *J Dairy Sci* 2020;103:4236-4251.

44. Renaud DL, Steele MA, Genore R, Roche SM, Winder CB. Passive immunity and colostrum management practices on Ontario dairy farms and auction facilities: A cross-sectional study. *J Dairy Sci* 2020;103:8369-8377.

45. Rosadiuk JP, Bruinje TC, Moslemipur F, Fischer-Tlustos AJ, Renaud DL, Ambrose DJ, Steele MA. Differing planes of pre- and postweaning phase nutrition in Holstein heifers: I. Effects on feed intake, growth efficiency, and metabolic and development indicators. *J Dairy Sci* 2021;104:1136-1152.

46. Shivley CB, Lombard JE, Urie NJ, Haines DM, Sargent R, Kopral CA, Earleywine TJ, Olson JD, Garry FB. 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* 2018;101:9185-9198.

47. Soberon F, Raffrenatio E, Everett RW, van Amburgh ME. Preweaning milk replacer intake and effects on long-term productivity of dairy calves. *J Dairy Sci* 2012;95:783-793.

48. Staley TE, Bush LJ. Receptor mechanisms of the neonatal intestine and their relationship to immunoglobulin absorption and disease. *J Dairy Sci* 1985;68:184-205.

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

50. Tyler JW, Hancock DD, Parish SM, Rea DE, Besser TE, Sanders SG, Wilson LK. 1996. Evaluation of 3 assays for failure of passive transfer in calves. *J Vet Intern Med* 1996;10:304-307.

51. Urie NJ, Lombard JE, Shivley CB, Kopral CA, Adams AE, Earleywine TJ, Olson JD, Garry FB. Preweaned heifer management on US dairy operations: Part V. Factors associated with morbidity and mortality in preweaned dairy heifer calves. *J Dairy Sci* 2018;101:9229-9244.

52. Urie NJ, Lombard JE, Shivley CB, Kopral CA, Adams AE, Earleywine TJ, Olson JD, Garry FB. Preweaned heifer management on US dairy operations: Part I. Descriptive characteristics of preweaned heifer raising practices. *J Dairy Sci* 2018;101:9168-9184.

53. Van Hese I, Goossens K, Vandaele L, Opsomer G. Invite Review: MicroRNAs in bovine colostrum – Focus on their origin and potential health benefits for the calf. *J Dairy Sci* 2020;103:1-15.

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54. Van Niekerk JK, Fischer-Tlustos AJ, Deikun LL, Quigley JD, Dennis TS, Suarez-Mena FX, Hill TM, Schlotterbeck RL, Guan LL, Steele MA. Effect of amount of milk replacer fed and the processing of corn in starter on growth performance, nutrient digestibility and rumen and fecal fibrolytic bacteria of dairy calves. *J Dairy Sci* 2020;103:2186-2199.

55. Vasseur E, Borderas F, Cue RI, Lefebvre D, Pellerin D, Rushen J, Wade KM, de Passille AM. A survey of dairy calf management practices in Canada that affect animal welfare. *J Dairy Sci* 2010;93:1307-1315.

56. Warner RG, Flatt WP, Loosli JK. Dietary factors influencing the development of the ruminant stomach. *Agric Food Chem* 1956;4:788-801.

57. Welboren A, Hatew-Chuko B, Leal L, Martín-Tereso J, Steele M. Effects of a high lactose milk replacer on glucose metabolism in neonatal calves, in *Proceedings.* Western Canadian Dairy Seminar 2019;31:236.

58. Welboren AC, Leal LN, Steele MA, Khan MA, Martín-Tereso J. Performance of *ad libitum* fed dairy calves weaned using fixed and individual methods. *Animal* 2019;13:1891-1898.

59. Wilms J, Berends H, Martin-Tereso J. Hypertonic milk replacers increase gastrointestinal permeability in healthy dairy calves. *J Dairy Sci* 2019;102:1237-1246.