EFFECTS OF NUTRITION ON THE HEALTH OF DAIRY CALVES

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INTRODUCTION

It is well documented that dairy calves are extremely susceptible to gastro-intestinal diseases and mortality during the first few weeks of life (Roy, 1990). Recent reports from the USDA's National Animal Health and Monitoring System (NAHMS, 1993; 1996; 2007) report that the national mortality rate of heifer calves from 48 hours of life to weaning is approximately 7.8 to 10.8%. Producer perceived records indicate that scours account for 56.5 to 60.5% of all pre-weaned deaths. Approximately ¼ of all pre-weaned calves are therapeutically treated for scours, and the major causes of death from scours are either dehydration or the pathogen gains access to the body and causes septicemia. The high incidences of disease indicate we have much to learn about improving gastro-intestinal disease resistance among pre-weaned calves. How much and the composition of fluid fed to pre-weaned calves and the use of additives such as different prebiotics, probiotics, and proteins from either hyper-immunized eggs or spray-dried plasma all may improve the health of pre-weaned calves. In addition, there are a few data that indicate that early life nutrition can have long-term impacts on leukocyte responses and disease resistance (Ballou, 2012; Ballou et al., *In Review*). This is an exciting area of research that needs to be addressed further and will be briefly discussed in this article.

PLANE OF NUTRITION

Dairy calves, like all mammalian species, are not exposed to microorganisms prior to birth. Furthermore, while *in utero* the calf is receiving its nutrients from placental transfer; therefore, the gastro-intestinal tract was never exposed to enteric nutrients. Immediately following birth the calf is no longer in a sterile environment and is required to get all its nutrition orally. Many components of the immune system are functional at birth; however, some aspects of the adaptive and soluble components of the immune system further develop as the calf ages. Colostrum has a lot of antibodies, and during the first few days of life the calf is able to absorb those antibodies into their body, which helps protect them from enteric and systemic disease. Colostrum also has a lot of other bioactive molecules that may influence gastrointestinal physiology and ultimately improve health, and the effects of these bioactive molecules effects on gastro-intestinal integrity and health warrant further investigation. Calves that do not receive colostrum are at an increased risk of developing scours and 74 times more likely to die in the first 21 days of life (Wells et al., 1996).

Colostrum is only part of the equation; many calves that receive adequate colostrum still develop gastro-intestinal disease. Data indicate that most scours occur during the first 3 weeks of life (Roy, 1990). Interestingly, by the time the calf is 3 weeks old, more than half of the antibodies it received from the colostrum are gone and not much has really changed regarding the calves cellular or humoral immune system (Kampen et al., 2006). So why are calves not as likely to develop gastro-intestinal disease despite having reduced passively derived immunoglobulins? Remember, when a calf is born the gastro-intestinal tract must quickly adapt to digesting and absorbing enteric nutrients and preventing the colonization and migration of potentially pathogenic microorganisms. Guilloteau et al. (2009) reported that many changes occur in the first few days to week regarding the structure of the cells that line the gastro-intestinal tract. Specifically, they reported fetal-type cells are replaced with more adult-like cells within 5 to 7 days after birth. The cells that make up the gastro-intestinal tract are very important and form the first line or the physical barriers of the immune system. Therefore, my lab hypothesizes that the physical barriers of the gastro-intestinal tract are impaired during the first week(s) of life, which increases the risk of developing scours. More research is needed to understand how we can manage the calf during that first week(s) after calving, while they are adapting to the *ex utero* environment. More research is needed on how nutrition, specifically colostrum quantity, quality, how much and frequency of milk (replacer) feeding influences the gastro-intestinal integrity and resistance to gastro-intestinal diseases during the first few weeks of life.

The interest in the plane of nutrition that calves are fed during the pre-weaned period has increased primarily because data indicate that calves fed a greater plane of nutrition have decreased age at first calving and they may have improved future lactation performance (Soberon et al., 2012; Soberon and Van Amburgh, 2013). More large prospective studies in various commercial settings should confirm that calves fed greater planes of nutrition during the pre-weaned period have improved future lactation performance. Most data on how plane of nutrition influences the health of calves during the first few weeks of life is limited to small, controlled experiments with fecal scores as the primary outcome variable (Nonnecke et al., 2003; Ballou, 2012). Many studies observed that the calves fed the greater plane of nutrition had more loose feces or greater fecal scores (Nonecke et al., 2003; Bartlett et al., 2006; Osorio et al., 2012; Hengst et al., 2012; Ballou et al., unpublished), while others showed no differences in fecal scores (Ballou, 2012; Obeidat et al., 2013). It is important to note, that no study has reported greater fecal scores among calves fed a lower plane of nutrition when compared to calves fed a greater plane of nutrition. It has been suggested that the greater fecal scores were not due to a higher incidence of infection or disease, but may be associated with the additional nutrients consumed. A couple of recent studies from my lab are confirming that calves fed greater quantities of milk solids early in life have greater fecal scores; however, when the dry matter percentage of the calves feces were determined there were no differences between calves fed differing quantities of milk solids.

It was unknown whether the digestibilities of nutrients of calves fed varying planes of nutrition were different during the first week of life. Decreased nutrient digestibilities would likely increase the risk of enteric disease because the increased supply of nutrients to the lower gastro-intestinal tract could provide a more favorable environment for pathogenic microorganisms to thrive. My lab recently tested the hypothesis that feeding a higher plane of nutrition during the first week of life would decrease the percentage of dietary nutrients that were digested and absorbed (Liang and Ballou, unpublished). Our justification for this hypothesis was that the reduced plane of nutrition during the first week of life would allow the gastro-intestinal tract time to adapt to enteric nutrition, without overwhelming the system. However, after conducting a metabolism trial with Jersey calves during the first week of life we had to reject that hypothesis. In fact, there was no difference in the percentage of intake energy that was captured as metabolizable energy, averaging 88% across treatments for the first week of life. We separated the first week of life up into 2 three-day periods and observed a tendency (*P*=0.058) for more of the intake energy to be captured as metabolizable energy during the 2nd period (85.9 versus 91.2 ± 2.0; 1st and 2nd period, respectively). There was a treatment x period interaction (*P*=0.038) on the percentage of dietary nitrogen that was retained. The calves fed the greater plane of nutrition had improved nitrogen retention during the first period (88.0 versus 78.7 ± 1.20; *P*=0.004), but was not different from calves fed the reduced plane of nutrition during the second period (85.3 versus 85.0 ± 1.20; *P*=0.904). Most of the difference in nitrogen retention during the first period could be explained by differences in nitrogen digestibility. These data suggest that feeding a greater plane of nutrition from 1 to 4 days of life improves protein digestion and/or absorption. In the same study we evaluated the urinary recovery of D-xylose, which is a highly absorbable carbohydrate that isn't metabolized. During the first period more D-xylose was recovered (45.2 versus 31.5 ± 4.29%; *P*=0.015) from the calves fed the lower plane of nutrition after an oral dose in between the 2 daily milk replacer feedings. There was no difference in the quantity of D-xylose recovered during the second period (34.6%). The significance of the greater recovery of D-xylose is not completely clear within the context of nutrient and energy digestion and absorption, especially since the calves fed the greater plane of nutrition from 1 to 4 days of life had greater nitrogen digestibility and retention at the same time they had reduced D-xylose recovery. The data from the metabolism study indicate that calves not only tolerate greater quantities of milk during the first week of life, but they incorporate those nutrients into lean tissue growth. The gastrointestinal integrity and implications to enteric health should further be investigated.

Over the past 5 years, my laboratory has conducted research to better understand the how plane of nutrition during the pre-weaned period influences leukocyte responses and resistance to infectious disease during the pre- and immediate post-weaned periods (Ballou, 2012; Obeidat et al., 2012; Ballou et al., unpublished; Liang and Ballou, unpublished). The results indicate that plane of nutrition influences leukocyte responses of calves (Ballou, 2012; Obeidat et al., 2013; Ballou et al., unpublished). In 2 studies, we reported that when calves were fed a lower plane of nutrition their neutrophils were more active during the pre-weaned period, as evident by increased surface concentrations of the adhesion molecule L-selectin (Figure 1) and a greater neutrophil oxidative burst (Obeidat et al., 2013; Ballou et al., unpublished). After weaning the elevated neutrophil responses were no longer apparent in either of those studies. The exact mechanisms for the more active neutrophils among the low plane of nutrition calves are not known, but could be due to increased microbial exposure because of increased non-nutritive suckling or reduced stress among the calves fed the low plane of nutrition. If the neutrophils are more active because of increased microbial exposure, calves fed a lower plane of nutrition could be at an increased risk for disease during the pre-weaned period. Ongoing research in my laboratory is trying to understand the behavior and potential microbial exposure when calves are fed varying planes of nutrition and its influence on immunological development. In fact, a few studies have shown that plane of nutrition during the pre-weaned period influence adaptive leukocyte responses. Pollock et al. (1994) reported that antigen-specific IgA and IgG_2 were reduced when calves were fed more milk. In agreement, Nonnecke et al. (2003) reported that less interferon-γ was secreted when peripheral blood mononuclear cells were stimulated with T-lymphocyte mitogens. However, not all data indicate that adaptive leukocyte responses are reduced when greater quantities of milk are fed; Foote et al. (2007) did not observe any difference in either the percentage of memory CD4+ or CD8+ T lymphocytes or antigen-induced interferon-γ secretion. All the leukocyte response data taken together suggest that calves fed lower planes of nutrition may have more active innate leukocyte responses driven by increased microbial exposure, which may explain the greater adaptive leukocyte responses. In a relatively sanitary environment this increased microbial exposure may improve adaptive immune development in the absence of clinical disease, but in a dirty environment it would likely increase enteric disease.

How plane of nutrition influences resistance to enteric disease is even less clear than how the leukocyte responses are affected. Quigley et al. (2006) reported that feeding a greater plane of nutrition to high-risk Holstein bull calves, purchased from a sale barn and raised on bedding contaminated with coronavirus, increased the number of days calves had scours by 53% and also increased the number of days calves received antibiotics, 3.1 versus 1.9 days. In contrast, a more recent study reported that calves fed a greater plane of nutrition had improved hydration and fecal scores improved faster when they were challenged with *Cryptosporidium parvum* at 3 days of age (Ollivett et al., 2012). In a recent study from my lab, we orally challenged calves fed either a restricted plane of milk replacer or calves fed a greater plane of milk replacer at 10 days of age with an opportunistic pathogen, *Citrobacter freundii* (Liang and Ballou, unpublished). The calves fed the greater plane of nutrition had a greater clinical response to the challenge as evident by increased rectal temperatures (P = 0.021) and numerically greater peak plasma haptoglobin concentrations (511 versus 266 ± 108 µg/mL; P = 0.118). Larger data sets with naturally occurring disease incidence and more experimentally controlled relevant disease challenges are needed before definitive conclusions on the role that plane of nutrition plays on enteric health of calves during the first few weeks of life.

In addition, plane of nutrition during the pre-weaned period may have effects on leukocyte responses that persist beyond the pre-weaned period (Ballou, 2012; Ballou et al., unpublished). Jersey bull calves that were fed a greater plane of fluid nutrition had improved neutrophil and whole blood *E. coli* killing capacities after they were weaned when compared to Jersey calves fed a more conventional, low plane of nutrition (Figure 2; Ballou, 2012). These effects were only observed among the Jersey calves in this study and not the Holstein calves. During this study, all calves were fed the same calf starter. In a follow-up study, Jersey calves that were previously fed a greater plane of milk replacer had a more rapid up-regulation of many leukocyte responses, including neutrophil oxidative burst and the secretion of the pro-inflammatory cytokine tumor necrosis factor-α, after they were challenged with an oral bolus of 1.5 x 10^7 colony-forming units of a *Salmonella typhimurium* (data not shown; Ballou et al., unpublished). The increased activation of innate leukocyte responses among the calves previously fed the greater plane of nutrition calves tended (P=0.098; Figure 3) to prevent the increase in plasma haptoglobin and those calves also had greater concentrations of plasma zinc (data not shown). The calves fed the greater plane of nutrition also had improved intake of calf starter beginning 3 days after the challenge (P = 0.039; Figure 4). These data indicate that the Jersey calves previously fed a greater plane of nutrition had improved disease resistance to an oral *Salmonella typhimurium* challenge approximately a month after weaning. Our 2 studies indicate that at least among Jersey calves, feeding a greater plane of nutrition during the pre-weaned period may influence the health of calves during the immediate post-weaned period. More data are needed to understand how plane of fluid nutrition influences the resistance to diseases that are common during the life cycle of dairy cattle, including: gastro-intestinal, respiratory disease, metritis, and mastitis. Further, more data are needed in Holstein calves to see if the responses observed in Jersey calves would be true in Holsteins.

PREVENTING PATHOGEN & HOST INTERACTIONS

In addition to plane of nutrition, many of the current strategies to improve the health of pre-weaned calves are focused on preventing the interaction of potentially pathogenic microorganisms with the gastro-intestinal tract of the calf, and the use of prebiotics, probiotics, or proteins from hyper-immunized egg or spray-dried plasma have shown some merit. Prebiotics are dietary components that are not digested by the calf, but are used by bacteria in the gasto-intestinal tract to improve their growth. At first glance this may seem bad, why would be want to improve the growth of bacteria in the gastro-intestinal tract? The gastro-intestinal tract is not sterile. Soon after birth, a wide range of bacterial species colonizes the gastro-intestinal tract of calves. Most of these bacterial species do not pose any immediate threat to the survival of the calf and in the past were called "good bacteria" and, of which, many of the common probiotic species are routinely classified as, including: *lactobaccilus* species, *bifidobacteria*, *Enterocooccus faecium*, and *Bacillus* species. There are many plausible mechanisms explaining how both prebiotics and probiotics would reduce the interaction of more pathogenic microorganisms with the gastro-intestinal tract of the calf. Many of the probiotic species had a direct bactericidal activity (Midolo et al., 1995) or compete with the more pathogenic microorganisms for limited resources. In addition, probiotics are themselves bacteria and they may "prime" the immune system of the calf by staying alert, as even the immune system recognizes the "good" bacteria as foreign (Blum et al., 2002; Lomax and Calder, 2009). The common, commercially-available prebiotics available are the fructooligosaccharides (FOS), mannanoligosaccharides (MOS), lactulose, and inulin.

Data on the influence of prebiotics and probiotics alone on the health of dairy calves is equivocal. There are data that show improvements in reducing scouring and improving growth (Abe et al., 1995; Heinrichs et al., 2003), whereas equally as many studies show no benefits to including either prebiotics or probiotics in milk (Morrill et al., 1995; Hill et al., 2008). The lack of a clear effect in calves is likely due to many environmental factors. Research does however support that many prebiotics and probiotics are generally safe and do not have any adverse effects on calf health of performance. In fact, most regulatory agencies around the world classify most prebiotics and probiotics as Generally Regarded As Safe (GRAS). I currently look at adding prebiotics and probiotics as an insurance policy; you do not know when you will need them, but when you do, it is good to have them. Lastly, it is important to note that not all probiotic species and further, not all strains of a specific species, ie: not all *Lactobaccilus acidophilus* strains, behave similarly. Therefore, I would recommend only using probiotic species and strains that have been reported, through 3rd party research, to improve health and performance of calves.

Another strategy to reduce the interaction of pathogenic microorganisms is to feed egg protein from laying hens that were vaccinated against the very microorganisms that cause gastro-intestinal diseases in calves. The laying hens will produce immunoglobulins (IgY) and concentrate those proteins in their eggs, which can recognize the pathogen, bind to it, and prevent its interaction with a calf's gastro-intestinal tract. Inclusion of whole dried egg from these decreased the morbidity due to various bacteria (Hennig-Pauka et al., 2003) and viruses (Kuroki et al., 1993; Ikemori et al., 1997). In addition to the use of hyper-immunized egg protein, spray-dried plasma proteins can improve gastro-intestinal health of calves. Spray-dried plasma is exactly what it sounds like, plasma is spray dried to preserve the functional characteristics of the diverse group of proteins in plasma. The use of spray-dried plasma has been used for many years in the swine industry to improve the performance and health during the post-weaned period. The addition of spray-dried plasma proteins in milk replacer reduced enteric disease in calves (Quigley et al., 2002; Hunt et al., 2002; Quigley and Wolfe, 2003).

In 2010, my lab evaluated the effects of supplementing a blend of prebiotics, probiotics, and hyper-immunized egg proteins to Holstein calves during the first 3 weeks of life (Ballou, 2011). Calves given the prophylactic treatment (n=45) were administered directly into the milk 5 x 10^9 colony forming units per day (from a combination of *Lactobacillus acidophilus*, *Bacillus subtilis*, *Bifidobacterium thermophilum*, *Enterococcus faecium*, and *Bifidobacterium longum*), 2 grams per day of a blend of MOS, FOS and charcoal, and 3.2 grams per day of dried egg protein from laying hens vaccinated against K99+ *Escherichia coli* antigen, *Salmonella typhimurium*, *Salmonella Dublin*, coronavirus, and rotavirus. Control calves (n=44) were not given any prebiotics, probiotics, or dried egg protein. All calves were fed 2 Liters of a 20% protein / 20% fat, non-medicated milk replacer twice daily. Prior to each feeding fecal scores were determined by 2 independent trained observers according to Larson et al. (1977). Briefly 1 = firm, well-formed; 2 = soft, pudding-like; 3 = runny, pancake batter; and 4 = liquid splatters, pulpy orange juice. The prophylactic calves refused less milk (P<0.01) during the first 4 days of life (57 vs 149 grams of milk powder). There were no differences in starter intake or average daily gain due to treatments. However, calves that received the prophylactic treatment had decreased incidence of scours (P<0.01) during the first 21 days of life (25.0 vs 51.1%). Scours were classified as a calf having consecutive fecal scores ≥ 3. The intensity of disease in this study was low and only 1 out of 90 calves died during the experiment. These data support that a combination of prebiotics, probiotics, and hyper-immunized egg protein improve gastro-intestinal health and could be an alternative to metaphylactic antibiotic use. Future research should determine the efficacy of that prophylactic treatment in calves that are at a higher risk of developing severe gastro-intestinal disease and subsequently death.

IMPLICATIONS

Dairy calves are extremely susceptible to disease in the first few weeks of life, which may be related to the naïve gastro-intestinal tract of calves. Increasing the plane of nutrition in the first week or 2 appears to increase fecal scores, although the dry matter percentages of the feces were not different. Additionally, the digestibility of nutrients during the first week of life are great and does not appear to be impaired by feeding a greater quantity of milk replace solids. However, resistance to enteric disease during the first few weeks of life does appear to be influenced by plane of nutrition, but more data are needed before more definitive conclusions can be made. Some early data are suggesting that plane of nutrition during the pre-weaned period may influence leukocyte responses and disease resistance of calves that extend beyond the pre-weaned period, but as with the effects of plane of nutrition on risk for enteric disease, more data are needed before we fully understand how early life plane of nutrition influences disease resistance later in life.

In addition to plane of nutrition, the uses of prebiotics, probiotics, and proteins from hyper-immunized egg or spray-dried plasma were all shown to reduce the incidence of gastro-intestinal disease. If you have a high early mortality I would recommend you look into using a research-backed product with prebiotics, probiotics, or proteins from hyper-immunized egg or spray-dried plasma.

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REFERENCES

Abe, F., N. Ishibashi, and S. Shimamura. 1995. Effect of administration of Bifidobacteria and Lactic Acid Bacteria to newborn calves and piglets. J. Dairy Sci. 78:2838-2848.

Ballou, M.A. 2011. Case Study: Effects of a blend of prebiotics, probiotics, and hyperimmune dried egg protein on the performance, health, and innate immune responses of Holstein calves. Prof. Anim. Sci. 27:262-268.

Ballou, M.A. 2012. Immune responses of Holstein and Jersey calves during the preweaning and immediate postweaned periods when fed varying planes of milk replacer. 95:7319-7330.

Ballou, M.A., D.L. Hanson, C.J. Cobb, B.S. Obeidat, T.J. Earleywine, J.A. Carroll, M.D. Sellers, and A.R. Pepper-Yowell. 2014. Plane of nutrition influences the performance, innate leukocyte responses, and the pathophysiological response to an oral *Salmonella typhimurium* challenge in Jersey calves. *Unpublished - In Review*.

Bartlett, K. S., F. K. McKeith, M.J. VandeHaar, G.E. Dahl, and J.K. Drackley. 2006. Growth and body composition of dairy calves fed milk replacers containing different amounts of protein at two feeding rates. J. Anim. Sci. 84:1454-1467.

Blum, S., J. Haller, A. Pfeifer, and E. J. Schiffrin. 2002. Probiotics and immune response. Clin. Rev. Allergy and Immuno. 22: 287-309.

Foote, M. R., B. J. Nonnecke, D. C. Beitz, and W. R. Waters. 2007. High growth rate fails to enhance adaptive immune responses of neonatal calves and is associated with reduced lymphocyte viability. J. Dairy Sci. 90:404-417.

Frei R, Lauener RP, Crameri R, O'Mahony L. Microbiota and dietary interactions – an update to the hygiene hypothesis? 2012 Allergy; 67: 451–461.

Guilloteau, P., R. Zabielski, J.W. Blum. 2009. Gastrointestinal tract digestion in the young ruminant: ontogenesis, adaptations, consequences and manipulations. J. Physiol. Pharmacol. 60:37-46.

Heinrichs, A. J., C. M. Jones, and B. S. Heinrichs. 2003. Effects of mannan oligosaccharide or antibiotics in neonatal diets on health and growth of dairy calves. J. Dairy Sci. 86: 4064-4069.

Heinnig-Pauka, I., I. Stelljes, and K. H. Waldmann. 2003. Studies on the effect of specific egg antibodies against *Escherichia coli* infections in piglets. Deutsche Tierarztliche Wochenschrift 110: 49-54.

Hengst, B.A., L.M. Nemec, R.R. Rastani, and T.F. Greesley. 2012. Effect of conventional and intensified milk replacer feeding programs on performance, vaccination response, and neutrophil mRNA levels of Holstein calves. J. Dairy Sci. 95:5182-5193.

Hill, T. M., H. G. Bateman II, J. M. Aldrich, and R. L. Schlotterbeck. 2008. Oligosaccharides for dairy calves. Prof. Animal Sci. 24: 460-464.

Hunt, E. Q. Fu, M.U. Armstrong, D.K. Rennix, D.W. Webster, J.A. Glanko, W. Chen, E.M. Weaver, R.A. Argenzio, and J.M. Rhoads. 2002. Oral bovine serum concentration improves cryptosporidial enteritis in calves. Pediatr. Res. 51:370-376.

Ikemori, Y., M. Ohta, K. Umeda, F. C. Icatlo Jr, M. Kuroki, H. Yokoyama, and Y. Kodama. 1997. Passive protection of neonatal calves against bovine coronavirus-induced diarrhea by administration of egg yolk or colostrum antibody powder. Vet. Microbiol. 58: 105-111.

Kampen, A.H., I. Olsen, T. Tollersrud, A.K. Storset, and A. Lund. 2006. Lymphocyte subpopulations and neutrophil function in calves during the first 6 months of life. Vet. Immunol. Immunopathol. 113:53-63.

Kuroki, M., Y. Ikemori, H. Yokoyama, R.C. Peralta, F.C. Icatlo Jr, and Y. Kodama. 1993. Passive protection against bovine rotavirus-induced diarrhea in murine model by specific immunoglobulins from chicken egg yolk. Vet. Microbiol. 31: 135-146.

Larson, L.L., F.G. Owen, J.L. Albright, R.D. Appleman, R.C. Lamb, and L.D. Muller. 1977. Guidelines toward more uniformity in measuring and reporting calf experimental data. J. Dairy Sci. 60:989-991.

Liang, R. and M.A. Ballou. 2014. Influences of plane of nutrition during the first few weeks of life on nutrient digestibility, metabolism, and resistance to an opportunistic, *Citrobacter freundii*, infection. *Unpublished*.

Lomax, A.R., and P. C. Calder. 2009. Prebiotics, immune function, infection and inflammation: a review of the evidence. Br. J. Nutr. 101: 633-658.

Midolo, P. D., J. R. Lambert, R. Hull, F. Luo, and M. L. Grayson. 1995. In vitro inhibition of *Helicobacter pylori* NCTC11637 by organic acids and lactic acid bacteria. J. Applied Bacteriol. 79: 475-479.

Morrill, J. L., J. M. Morrill, and A. M. Feyerherm. 1995. Plasma proteins and a probiotic as ingredients in milk replacer. J. Dairy Sci. 78: 902-907.

National Animal Health Monitoring System. 1993. Dairy heifer morbidity, mortality, and health management focusing on preweaned heifers. Ft. Collins, CO: USDA:APHIS:VS.

National Animal Health Monitoring System. 1996. Part 1: Reference of 1996 Dairy Management Practices. Ft. Collins, CO: USDA:APHIS:VS.

National Animal Health Monitoring System. 2007. Dairy 2007: Heifer calf health and management practices on U.S. dairy operations, 2007. Ft. Collins, CO:USDA:APHIS:VS.

Nonnecke, B. J., M.R. Foote, J.M. Smith, B.A. Pesch, and M.E. Van Amburgh. 2003. Composition and functional capacity of blood mononuclear leukocyte populations from neonatal calves on standard and intensified milk replacer diets. J. Dairy Sci. 86:3592-3604.

Obeidat, B.S., C.J. Cobb, M.D. Sellers, A.R. Pepper-Yowell, T.J. Earleywine, and M.A. Ballou. 2013. Plane of nutrition during the preweaning period but not the grower phase influences the neutrophil activity of Holstein calves. J. Dairy Sci. 96:7155-7166.

Ollivett, T.L., D.V. Nydam, T.C. Linden, D.D. Bowmann, and M.E. Van Amburgh. 2012. Effect of nutritional plane on health and performance in dairy calves after experimental infection with Cryptosporidium parvum. J. Am. Vet. Med. Assoc. 241:1514-1520.

Osorio, J.S., R.L. Wallace, D.J. Tomlinson, T.J. Earleywine, M.T. Socha, and J.K. Drackley. 2012. Effects of source of trace minerals and plane of nutrition on growth and health of transported neonatal dairy calves. J. Dairy Sci. 95:5831-5844.

Pollock, J. M., T. G. Rowan, J. B. Dixon, and S. D. Carter. 1994. Level of nutrition and age at weaning: Effects on humoral immunity in young calves. Br. J. Nutr. 71:239-248.

Quigley, J.D., III, C.J. Kost, and T.A. Wolfe. 2002. Effects of spray-dried animal plasma in milk replacers or additives containing serum and oligosaccharides on growth and health of calves. J. Dairy Sci. 85:413-421.

Quigley, J.D., III, and T.M. Wolfe. 2003. Effects of spray-dried animal plasma in calf milk replacer on health and growth of dairy calves. J. Dairy Sci. 86:586-592.

Quigley, J.D., T. A. Wolfe and T. H. Elsassert. 2006. Effects of additional milk replacer feeding on calf health, growth, and selected blood metabolites. J. Dairy Sci. 89:207-216.

Raeth-Knight, M., H. Chester-Jones, S. Hayes, J. Linn, R. Larson, D. Ziegler, B. Ziegler, and N. Broadwater. 2009. Impact of conventional or intensive milk replacer programs on Holstein heifer performance through six months of age and during first lactation. J. Dairy Sci. 92:799-809.

Roy, J.H.B. The Calf 5th ed. Volume 1 Management of Health. 1990. Boston, Massachusetts. Butterworth Publishers Inc.

Soberon, F., E. Raffrenato, 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.

Soberon, F., and M.E. Van Amburgh. 2013. Lactation Biology Symposium: The effect of nutrient intake from milk or milk replacer of pre-weaned dairy calves on lactation yield as adults: a meta-analysis of current data. J. Anim. Sci. 91:706-712.

Wells, S.J., D.A. Dargatz, and S.L. Ott. 1996. Factors associated with mortatlity to 21 days of life in dairy heifers in the United States. Prev. Vet. Med. 29:9-19.

FIGURES

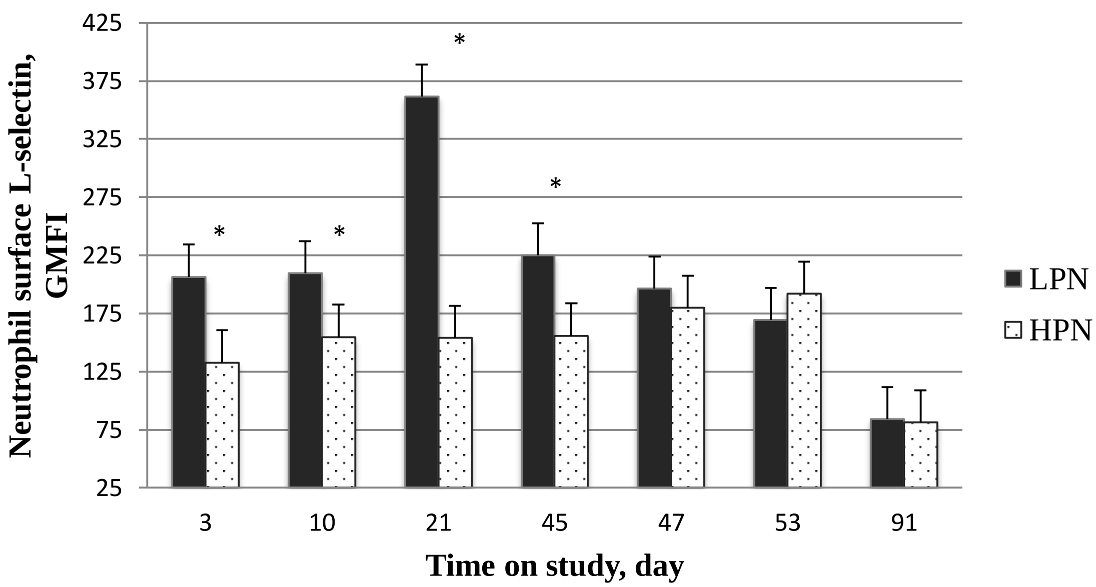

Figure 1: Feeding a lower plane of nutrition (LPN) during the pre-weaned period increased L-selectin concentrations (*P*<0.05) on the surface of neutrophils. An asterix denotes treatment differences (*P*<0.05) sliced by time. Data reported as LS Means ± SEM; from Obeidat et al., 2013.

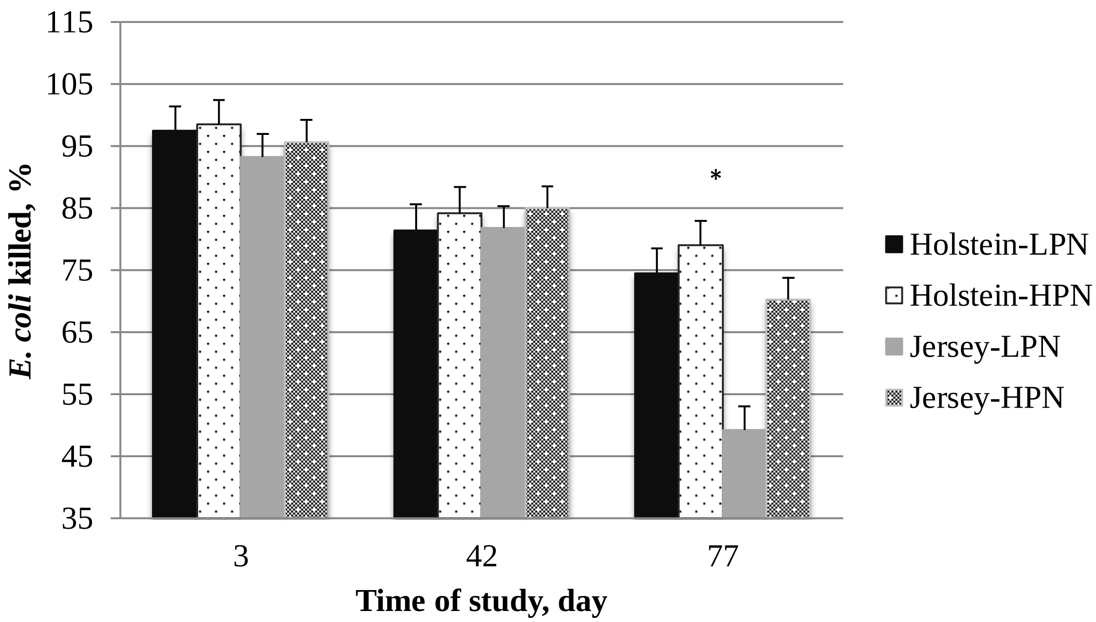

Figure 2: Feeding a higher plane of nutrition (HPN) during the pre-weaned period improved the ability of whole blood from Jersey calves to kill a live *E. coli* at d 77 of the study, during the immediate post-weaned period. An asterix indicates a sliced breed x plane of nutrition contrast at day 77 (P<0.04). Data reported as LS Means ± SEM; from Ballou, 2012.

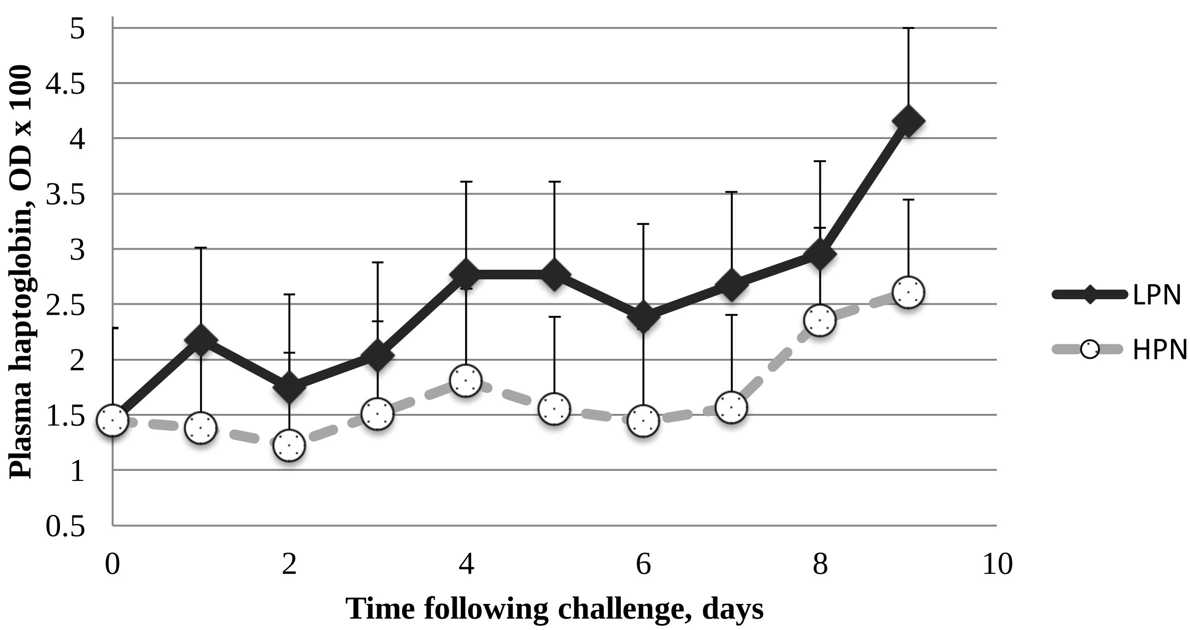

Figure 3: Feeding a higher plane of nutrition (HPN) during the pre-weaned period tended (P=0.098) to reduce plasma haptoglobin concentrations following an oral *Salmonella typhimurium* challenge approximately 1 month after weaning. Data reported as LS Means ± SEM; from Ballou et al., unpublished.

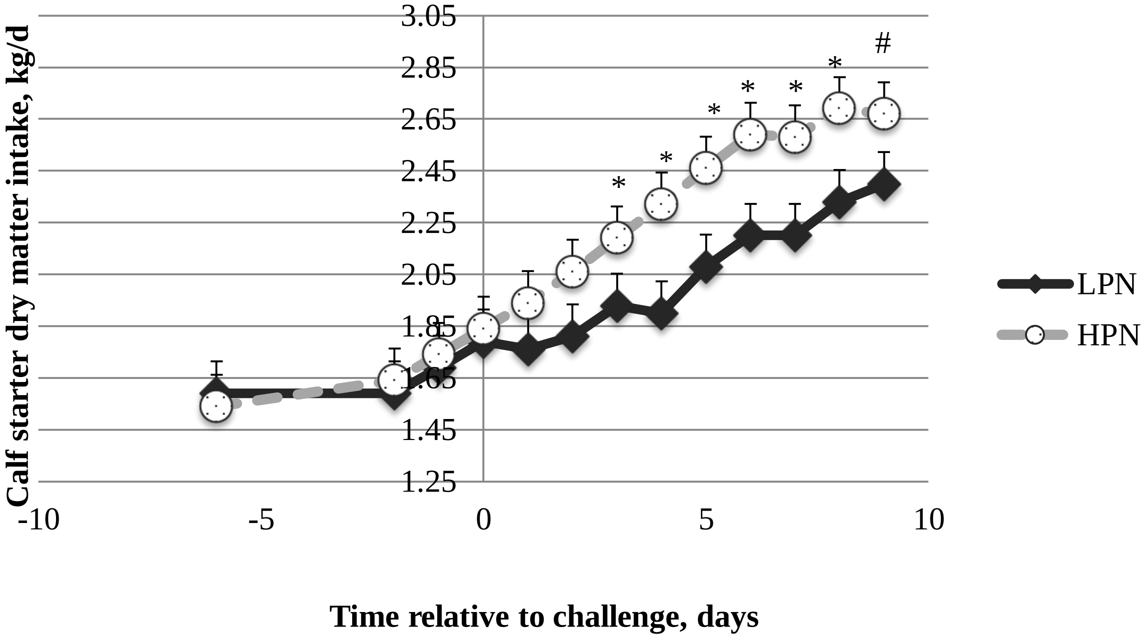

Figure 4: Feeding a higher plane of nutrition (HPN) during the pre-weaned period improved (P=0.039) calf starter intake following an oral *Salmonella typhimurium* challenge approximately 1 month after weaning. An asterix denotes treatment differences (P<0.05) and pound sign indicates a tendency (P<0.10) sliced by time. Data reported as LS Means ± SEM; from Ballou et al., unpublished.