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Calf Note 177 – The interaction of plane of nutrition and immunity in young dairy calves – a review

Introduction

The interaction between nutrition and calf immunity is well established and beyond debate. Proper nutrition has a positive influence on the immune system, and often, calf health. Improper nutrition, but particularly protein / calorie malnutrition – can impair immunity and predispose calves to disease. A question often asked is whether there is benefit to increasing the amount of nutrients (i.e., plane of nutrition) fed to calves' immune response. If some nutrients are good, are more nutrients better? Would a much "higher plane" of nutrition make calves more resistant to disease and make them grow better?

Well, the answer to this question is a qualified "not necessarily". Though claims may be made in popular press articles and advertising campaigns, the research data suggests a much more complex answer to the question. This review will summarize some of the recent, published, research regarding plane of nutrition and immunity to provide a more complete answer.

It's important to understand that there are many "parts" to the immune system and no single laboratory or animal test can evaluate the overall status of immunity in a comprehensive way. Typically, researchers evaluate one component of the immune response (e.g., response to a vaccination, or the ability of immune cells to kill pathogens in culture) based on tests that can be done in the laboratory. Different researchers may utilize different tests; therefore, it's sometime difficult to extrapolate to the overall animal response. Also, many research studies evaluate overall animal health responses – i.e., survival, incidence of disease, health scores, etc. These measures are all economically important and get to a "bottom line" answer to the question of health and nutrition, but there are many non-nutritional factors that can affect animal health, so large numbers of animals are often needed.

Immunity at or below maintenance intake

Maintenance level of intake – particularly maintenance energy intake – appears to be an important threshold for immunity. That is, when calves are fed below maintenance intake, immune response is impaired. We define maintenance energy intake amount of energy (calories) required by the animal to maintain its current body weight (**BW**). Of course, young calves are trying not only to maintain their BW, but also to grow. Thus, we normally feed calves more energy than maintenance energy intake. However, when calves are fed limited amounts of calf milk replacer (**CMR**; e.g., 454 g/d, of 1 lb/d), particularly in cold weather, we may not provide them with enough calories to meet their maintenance energy requirement. In these situations, calves will lose BW and their immune systems are depressed.

There are several studies to suggest that inadequate metabolizable energy (**ME**) intake can impair immune response. For example, Godden et al. (2005) reported that calves fed whole, pasteurized milk had markedly lower rates of treatment and mortality compared to calves fed similar amounts of CMR, particularly in winter (Table 1).

In a well-publicized report from Cornell University, Ollivett et al. (2012) reported that calves fed a high plane of nutrition responded better to an oral challenge of *Cryptosporidium parvum* than calves fed "conventional nutrition". Calves fed on the conventional program were fed 0.49 kg of a 20/20 CMR per day (to provide 0.13 Mcal ME/kg $BW^{0.75}$) until d 21 whereas high plane calves were fed 0.85 to 1.11 kg of a 28/20 CMR per day (to provide 0.23 to 0.30 Mcal ME/kg $BW^{0.75}$ until d 1-7 and 8-21, respectively). No calf starter was fed to the calves. Under these conditions, calves fed the "conventional" program lost an average of 48 g of BW/d and calves fed high plane of nutrition gained 433 g of BW per day.

There was little effect of diet on health scores, which suggested that the cryptosporidial challenge was insufficient to cause severe morbidity or mortality. Calves fed the high plane of nutrition showed improved lymphocyte responses and lower change in packed cell volume (an indication of dehydration) than conventional calves. On the other hand, more calves on the high plane of nutrition refused at least some CMR during the study (64% of calves refused at least one meal) compared to conventional program (11% of calves).

Table 1. Effect of feeding CMR or whole, pasteurized milk on calf morbidity and mortality.

Item	CMR	WPM	*P*
Morbidity, %			
Overall	32.1	12.1	0.01
Winter	52.4	20.4	0.01
Summer	12.7	4.4	0.02
Mortality, %			
Overall	11.6	2.2	0.01
Winter	21.0	2.8	0.01
Summer	2.7	1.7	NS

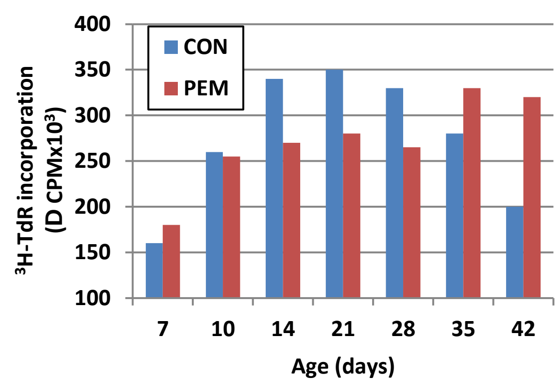
Source: Godden et al., 2005.

The important consideration in both of these studies is that "conventionally" fed calves were fed below their maintenance energy intake. Most morbidity and mortality in the study by Godden et al. (2005) occurred in the winter months. Control calves were fed 454 g of CMR/day (1 lb), which would fulfill maintenance requirements and allow a calf to gain about 250 g (about ½ lb) per day. Although the amount of CMR was increased in cold weather, the increase was likely insufficient to cover the increase maintenance below about 5°C. Since it's often colder than 5°C in the winter in Minnesota (even in a greenhouse barn), calves fed the CMR diet were likely fed below maintenance energy levels for at least part of their lives. Unfortunately, growth rates in summer and winter were not reported. Because whole, pasteurized milk contains more ME and protein than CMR, calves fed the milk diet suffered less malnutrition and less depression of immunity. The observations of Godden et al. (2005) are similar to those of Williams et al. (1981), who reported increased mortality in calves fed 0.3 to 0.4 kg of a CMR daily.

Feeding below maintenance protein and energy intake has been shown to impair numerous aspects of the animal's immune response. For example, Griebel et al. (1987) found that immune cells taken from calves fed diets limited in protein and energy were less able to respond to challenge with an antigen (concanavalin A; Figure 1). However, when calves were switched from the low plane of nutrition to one similar to controls calves, the ability of lymphocytes to respond to challenge increased within seven days to those at or above pretreatment levels. Thus, it appears that reversing nutrient deprivation may not have long lasting effects on the calf's immune response, at least in terms of lymphocyte blastogenesis.

Protein and energy malnutrition is, unfortunately, a common human condition. There are many studies available that document the depressing effect of malnutrition on immunity (for a good review, see Chandra, 1997). The consensus in the scientific literature is that protein and (or) calorie malnutrition impairs immunity, particularly in children and the elderly. That similar results were observed in calves fed below maintenance should be no surprise. Malnutrition impairs immunity. Feeding calves insufficient energy, particularly during cold weather, impairs immunity. Thus, for adequate calf health, it's essential that adequate nutrition be provided.

Figure 1. Response of circulating lymphocytes to an in vitro challenge with concanavalin A at various ages.



Source: Griebel et al., 1987.

Immunity above maintenance

Is there additional benefit to the immune response when feeding calves a much higher "plane" of nutrition? This theory has been tested by several researchers in the past several years. The recommendation that calves be fed larger amounts of ME and protein (often, up to 1 kg of a 28% CP calf milk replacer) to increase growth is often accompanied by claims that such feeding programs also improve health.

From the standpoint of whole animal health, few data support the idea that additional nutrients improve calf health. For example, data from Davis-Rincker (2011) reported that feeding calves additional CMR (CON calves were fed a 20/20 CMR at 1.2% of BW and INT calves were fed a 30/15 CMR at 2.1% of BW) had no effect of days with fever or days treated with antibiotics compared to control calves (Table 2). However, days with diarrhea and fecal scores were *worse* when calves were fed the intensified program.

Table 2. Health measures in calves fed conventional or intensified feeding programs preweaning.

Item	CON	INT	SE	*P*
Serum IgG, g/L	26.6	25.5	0.9	NS
Days with fever	1.18	1.25	0.22	NS
Fecal score[1]	3.01	3.21	0.07	0.03
Days with diarrhea	2.79	4.04	0.29	0.01
Days treated	2.38	2.73	0.62	NS
No. heifers at calving	33	34	…	…

[1]Score of 1 = normal to 5 = watery.

Source: Davis Rincker et al., 2011.

In another study, Hengst et al. (2012) reported that calves fed an intensified CMR feeding program had greater incidence of diarrhea and more respiratory problems compared to calves fed a "standard" feeding program (Table 3). There was no effect of feeding program on the animal's ability to produce specific antibodies when vaccinated with ovalbumin. Some proponents of intensified feeding suggest that feeding additional nutrients well in excess of maintenance levels may improve the animal's ability to make antibodies when vaccinated or exposed to a pathogen. However, in this study, the lack of effect of plane of nutrition on vaccination response suggests that this is unlikely.

The increase in respiratory scores is an interesting observation that has been observed by other authors (e.g., Nonnecke et al, 2003). Hengst et al. (2012) wrote: "*Respiratory scores also tended to be higher for INT calves during wk 5 (P = 0.09). Nonnecke et al. (2003) similarly found that calves fed using an intensified milk replacer feeding program had increased respiratory scores compared with a conventional program. Across their observational period, respiratory scores were 1.55 for calves fed using an intensified program compared with 1.10 in control calves. Both the present study and that of Nonnecke et al. (2003) indicate that increased rates of milk replacer feeding increase measures of respiratory distress.*"

Table 3. Effect of intensified milk feeding program (INT) versus a standard program (CON) on indices of preweaning health.

Item	CON	INT	SE	*P*
Respiratory score[1]	1.01	1.05	0.01	0.05
Fecal score[2]	1.65	1.74	0.15	0.02
Anti-OVA IgG, $\log_{10}$ OD	0.26	0.30	0.03	NS

[1]Score of 1 = normal to 6 = fever.

[2]Score of 1 = normal to 5 = watery.

Source: Hengst et al., 2012.

Increased fecal scores are also commonly seen in calves fed intensified feeding programs. Proponents claim that more liquid feces is neither indicative of poor health nor neonatal infection; rather is simply a response to the additional nutrients presented to the calf. Possibly, calves fed intensified rations have lower proportional digestibility and, consequently, excrete more nutrients that are more liquid in nature.

Other researchers (e.g., Osario et al., 2013) have not reported the same increase in respiratory scores. This may be related to times of sampling, methods used and amount of respiratory stress to which the animals were exposed.

A final example of the response to increased nutrition preweaning is from Cowles et al (2006). Calves in this study were fed a conventional CMR (562 g/d of a 20/20 CMR) or intensified CMR (712 to 1,358 g/d of a 28/20 CMR, fed on a BW basis) without or with additional lactoferrin (an antimicrobial peptide found in milk, fed at 1 g/d). As can be seen in Table 4, calves fed the intensified CMR program were treated more than conventionally fed calves. There was no effect of added lactoferrin on any index of whole animal calf health.

Table 4. Effect of a control (CON) or intensified (INT) milk feeding program without (-) or with (+) added lactoferrin on indices of preweaning health.

Item	CON -	CON +	INT-	INT +	SE	*P*
Days treated						
Preweaning	0.88	1.89	2.56	2.86	0.60	0.02
Wk 7 (weaning)	0.63	0.00	0.44	0.43	0.46	NS
Post-weaning	0.00	0.00	0.00	0.00	0.00	NS
Overall	1.50	1.89	3.11	3.29	0.78	0.05

Source: Cowles et al., 2006.

P = effect of intensified feeding. There was no effect of lactoferrin.

Effects of stress

Stress and failure of passive transfer (**FPT**) can affect the response to an intensified CMR feeding program. Quigley et al. (2006), using transported Holstein bull calves purchased from sale barns (most with FPT), reported that days treated and fecal scores were increased in calves fed an intensified CMR program (Table 5). Also, preweaning mortality tended ($P < 0.10$) to be greater when calves were fed more CMR; 3 CON calves (7.6%) died prior to weaning whereas 14 INT calves (17.5%) died preweaning. High rates of morbidity and mortality preweaning seemed to be greater than other studies and was likely due to the stress of FPT, transport and other stressors imposed on the calves.

Aspects of immune response and nutrition

Many researchers have evaluated specific aspects of the immune response to better understand, from a mechanistic level, if and how nutrition may affect immunity. As mentioned above, many different tests have been conducted to evaluate different aspects of immunity. Table 6 summarizes some of these findings. Generally, few data support the idea that added nutrients improve immunity responses. Indeed, many of these studies reported that at least one measure of immunity were ***impaired*** when high levels of liquid were fed to calves preweaning. For more information on specific tests, or interpretation of results, it is recommended that the specific papers be consulted.

Table 5. Effect of intensified milk feeding program (INT) without (-) or with (+) added serum containing feed additive on indices of preweaning health.

Item	CON	INT-	INT +	*P*
Mortality, %	8.6	22.3	12.6	NS
Fecal scores	1.44	1.60	1.56	0.02
Days with fever	0.04	0.05	0.07	NS
Days with scours	1.7	2.7	2.5	0.03
Days treated	1.9	3.0	3.2	0.05

Source: Quigley et al., 2006.

P = effect of intensified feeding. There was no effect of feed additive.

Summary

Providing additional nutrients to calves prior to weaning by feeding more milk or milk replacer can increase rates of BW gain, height and other measures of size of calf. However, data published to date in the scientific literature suggest that there is little effect of additional nutrients on immunity *as long as animals are fed at or above maintenance levels*. Indeed, much of the published data suggest that whole animal health, days scouring, treatment for scours and respiratory infections may actually be increased when calves are fed high levels of nutrition. Likely, there are important interactions of rates of passive immunity, stress, and level of nutrition that await further investigation.

Table 6. Effects of additional nutrients fed to calves preweaning (INT) on measures of specific immune responses.

Author	Measurement	Effect of INT
Foote et al., 2005a	Proliferation of mitogen-stimulated CD4+, CD8+, and γδT-cell receptor+ cells	Reduced
	CD25 expression by mitogen-stimulated CD4+ and CD8+ cells	Reduced
	CD44 expression by mitogen-stimulated CD8+ cells	Reduced
Foote et al., 2005b	PBMC CD4+, γδTCR+ monocyte %	No effect 1-5; higher wk 6
	Change in γδTCR+, B cell %	No effect
	Percent CD4+ cells with IL-2 receptor	Reduced
	IFN-g and nitric oxide secretion	Reduced
	Antigen hypersensitivity	No effect
Foote et al., 2007	Mono and polymorphonuclear leukocyte % in blood	No effect
	Percentage of CD4+ T cells	No effect
	Percentage memory CD4+ and CD8+ T cells	No effect
	Antigen specific serum IgG	No effect
	IFN-γ and nitric oxide secretion	No effect
	Antigen-elicited cutaneous delayed-type hypersensitivity responses	Reduced
	Viability of CD4+, CD8+, and γδTCR+ T cells	Reduced
	Nitric oxide production from resting cells	Increased
Nonnecke et al., 2003	Total numbers of blood leukocytes and the	No effect
	Composition of the mononuclear leukocyte population	No effect
	Mitogen-induced DNA-synthesis and IgM secretion	No effect
	Blood leukocyte IFN-γ and nitric oxide secretion	Reduced
Ballou, 2012	Blood glucose following LPS challenge	Increased
	Plasma haptoglobin after LPS challenge	Increased
	Neutrophil oxidative burst intensities when co-cultured with *E. coli* for 10 min.	Increased d 77
	Neutrophil oxidative burst capacity and whole blood *E. coli* killing	Increased in Jerseys at d 77
	Secretion of IFN-γ by T lymphocytes	No effect
Pollock et al., 1994	Antibody response to KLH injection	Reduced
	Anti-HRBC titers	Reduced
	Total serum Ig concentration	No effect
Pollock et al., 1993	Skinfold thickness to vaccination	Lower at 9 wk None at 13 wk
	Lymphocyte blastogenesis	Increased 14 wk Decreased 10 wk
	PBMC numbers, activity	None

References

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. J. Dairy Sci. 95 :7319–7330.

Chandra, R. K. 1997. Nutrition and the immune system: An introduction. Amer. J. Clin. Nutr. 66:460S-463S.

Davis Rincker, L. E., M. J. VandeHaar, C. A. Wolf, J. S. Liesman, L. T. Chapin, and M. S. Weber Nielsen. 2011. Effect of intensified feeding of heifer calves on growth, pubertal age, calving age, milk yield, and economics. J. Dairy Sci. 94:3554–3567.

Foote, M. R., B. J. Nonnecke, M. A. Fowler, B. L. Miller, D. C. Beitz, and W. R. Waters. 2005a. Effects of age and nutrition on expression of CD25, CD44, and L-Selectin (CD62L) on T-cells from neonatal calves. J. Dairy Sci. 88:2718–2729.

Foote, M. R., B. J. Nonnecke, W. R. Waters, M. V. Palmer, D. C. Beitz, M. A. Fowler, B. L. Miller, T. E. Johnson, and H. B. Perry. 2005b. Effects of intensified nutrition on antigen-specific, cell mediated immune responses of milk replacer-fed calves. Int. J. Vitam. Nutr. Res. 75:357–368.

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.

Godden, S. M., J. P. Fetrow, J. M. Feirtag, L. R. Green, S. J. Wells, 2005. Economic analysis of feeding pasteurized nonsaleable milk versus conventional milk replacer to dairy calves. J. Amer. Vet. Med. Assoc. 226:1547–1554.

Griebel, P. J., M. Schoonderwoerd and L. A. Babiuk. 1987. Ontogeny of the immune response: Effect of protein energy malnutrition in neonatal calves. Can. J. Vet. Res. 51: 428-435.

Hengst, B. A., L. M. Nemec, R. R. Rastani, and T. F. Gressley. 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.

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.

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

Osorio, J. S., E. Trevisi, M. A. Ballou, G. Bertoni, J. K. Drackley, and J. J. Loor. 2013. Effect of the level of maternal energy intake prepartum on immunometabolic markers, polymorphonuclear leukocyte function, and neutrophil gene network expression in neonatal Holstein heifer calves. J. Dairy Sci. 96:3573–3587.

Pollock, J. M., T. G. Rowan, J. B. Dixon, S. D. Carter, D. Spiller, and H. Warenius. 1993. Alteration of cellular immune responses by nutrition and weaning in calves. Res. Vet. Sci. 55:298-306.

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. British J. Nutr. 71:239-248.

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

Williams, P.E.V., D. Day, A. M. Raven, and J. A. McLean. 1981. The effect of climatic housing and level of nutrition on the performance of calves. Anim Prod 32:133–141.