



HAL
open science

Micronutrients and their impact on high performing dairy cows- A focus on niacin and choline

José Pires, Ric Grummer

► **To cite this version:**

José Pires, Ric Grummer. Micronutrients and their impact on high performing dairy cows- A focus on niacin and choline. Southwest Nutrition and Management Conference, University of Arizona. USA., 2008. hal-02755681

HAL Id: hal-02755681

<https://hal.inrae.fr/hal-02755681v1>

Submitted on 3 Jun 2020

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Micronutrients and Their Impact on High Performing Dairy Cows- A Focus on Niacin and Choline

J.A.A. Pires and R.R. Grummer
Department of Dairy Science
University of Wisconsin - Madison
Corresponding author: rgrummer@wisc.edu

Summary

- Controlled experiments suggest that supplemental choline may prevent and alleviate fatty liver in dairy cows.
- Field studies show increased intake and fat corrected milk production, and decreased incidence of ketosis when cows were fed rumen-protected choline during both close-up period and early lactation.
- Production responses to dietary supplementation of free niacin are difficult to interpret because there is extensive degradation of niacin in the rumen.
- Nicotinic acid, a form of niacin, can decrease plasma NEFA concentrations in the bovine under negative energy balance.
- In the future, nicotinic acid may prove useful in nutritional management of the periparturient dairy cow once a rumen-protected form of nicotinic acid is tested.
- A rate of nicotinic acid delivery that promotes moderate reduction in NEFA concentrations must first be identified. We also need to define strategies to prevent the occurrence of an exaggerated NEFA rebound once treatment is discontinued.
- Research is also warranted on potential synergistic effects between nicotinic acid and choline on modulation of lipid metabolism of periparturient cows.

Introduction

Microbial degradation and synthesis of nutrients makes it difficult to estimate nutrient requirements for ruminant animals. For example, despite decades of research on amino acid nutrition, the most recent NRC subcommittee on Nutrient Requirements of Dairy Cattle (NRC, 2001) declined to establish amino acid requirements due to insufficient data and inadequate models for predicting amino acid flow to the small intestine. Similarly, requirements for choline and B vitamins were not established. In the case of B vitamins, the dogma is that microbial synthesis and dietary sources escaping ruminal degradation provide adequate quantities and supplementation is not required. However, as milk production has increased, that notion has received additional scrutiny.

In an excellent review, Erdman (1992) proposed that folic acid, pantothenic acid, and choline may be limiting for lactating dairy cows. The supply of these nutrients to the small intestine was estimated to be between 3 and 30 percent of potential requirements. Potential requirements were determined by assuming the dairy cow is a larger version of a lactating sow. While on the surface it appears that microbial degradation of nutrients renders the ruminant animal deficient in these nutrients, one must leave open the possibility that ruminants have been able to adapt to limitations in the availability of nutrients. How else can one explain the ability of a modern

dairy cow to maintain itself and produce in excess of 15 times the amount of milk that would be needed to sustain its calf without supplementation of these nutrients? However, this does not mean that increasing the supply of these nutrients to the small intestine could not increase milk production. Additionally, when determining the amount of a nutrient that should be fed to dairy cows, the critical measurement is not always milk or milk solids production. The effects of supplementation on health and reproductive performance of the animal should also be considered. Pharmacological effects of nutrients may warrant inclusion in a diet.

The objectives of this presentation are to examine the potential role of niacin and choline in the diet of high producing dairy cows. Choline was cited by Erdman (1992) as potentially limiting for dairy cows. In contrast, he predicted that intestinal supply of niacin was far in excess of that needed for milk production. Supplementation of free niacin to dairy rations, commonly at a rate of 6 to 12 g/d, has inconsistent and small effects on lactation performance, and questionable economic return (Schwab et al., 2005). Consequently, for niacin, the focus of this paper will be on its pharmacological effects and the role it may have on modifying lipid metabolism. Effects on reproduction will not be discussed as that is the topic of another paper in these proceedings.

Choline

Background

Choline is often referred to as a vitamin or micronutrient, but it does not fit the classical definition. It can be synthesized endogenously, it is not an enzyme cofactor in metabolic pathways, and it is typically supplemented in much larger quantities than vitamins. Choline is an essential nutrient for many animal species including rats, pregnant sows, pre-ruminating sheep, and calves. Choline serves as a methyl donor in biochemical reactions and as a constituent of phosphatidylcholine (PC). Methionine serves as a methyl donor for choline synthesis; therefore, choline and methionine can spare the requirement of each other. Involvement of biotin, folic acid, and vitamin B12 in one-carbon methyl metabolism yields potential interactions between these vitamins and choline. Phosphatidylcholine can be synthesized from tri-methylation of phosphatidylethanolamine or directly from choline. As a component of phospholipids, choline is essential for maintaining cell membrane structure and permeability, and for transport of lipid from the liver as a constituent of very low density lipoproteins (VLDL). Choline deficiency leads to fatty liver in laboratory animals.

Estimates of ruminal choline degradation are 80-98% (Atkins et al., 1988, Sharma and Erdman, 1989b). Differential milk yield response between ruminal and abomasal infusion of choline support in vitro data and suggest ruminal degradation of choline (Sharma and Erdman, 1989a). The main fate of dietary choline is ruminal conversion to trimethylamine followed by conversion to methane. Ruminal production of choline is negligible (Erdman, 1992).

Protected choline supplements have been developed to decrease microbial degradation in the rumen and increase delivery of choline to the small intestine. Low degradation rate in the rumen does not guarantee post ruminal bioavailability. Documentation of extent of ruminal protection and degree of release in the small intestine is scarce due to the difficulty and expense of

obtaining the data. Most published research on protected choline products does not contain that information. Therefore, absence of responses to protected choline supplementation is difficult to interpret. If ruminal protection or duodenal release is inadequate, the absence of a response does not necessarily imply that a response is not possible. Presence of a response indicates some degree of protection and release, however, the extent is unknown. Consequently, it is difficult to generate dose response information.

Milk Production

A summary of milk and milk component responses to choline are shown in Figures 1-3. In each, the control treatment mean has been plotted against the choline treatment mean. Amounts of choline chloride supplied for most of the studies was 15 g/day, although amounts may have been as high as 50 g/day in some of the post-ruminal infusion trials. We plotted the data in this fashion to try and examine if the response was related to level of production or milk components.

In the 16 treatment comparisons summarized in Figure 1, there was a significant increase ($P < 0.05$) in milk yield in 6 comparisons and a trend ($P < 0.15$) toward an increase in one comparison. Response to choline was not dependent on high milk yield because some of the biggest responses were obtained from moderate (30-35 kg/d) producing cows.

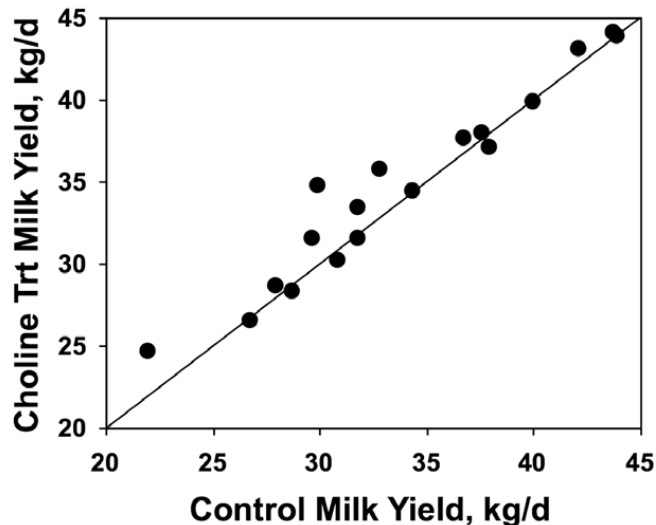


Figure 1. Milk yield response, plotted as control treatment vs. choline treatment, for cows fed rumen-protected choline or post-ruminally infused with choline. References: Abeni et al., 2007; Davidson et al., 2006; Emanuele et al., 2007; Erdman and Sharma, 1991; Hartwell et al., 2000; Janovick Guretzky et al., 2006; Lima et al., 2007; Ondarza et al., 2007; Piepenbrink and Overton, 2003; Sharma and Erdman, 1988; Sharma and Erdman, 1989; Thering et al. 2007; Toghdory et al., 2007; Zahra et al., 2006.

Reasons for the increases in milk yield or variability in milk yield response are not known, however, it may be related to status of other methyl donors (i.e. methionine) or cofactors associated with one-methyl carbon metabolism (folic acid, vitamin B12). In lactating goats it was estimated that 6% of the choline pool in the body is derived from methionine and 28% of the

methionine pool in the body is used for choline synthesis (Emmanuel and Kennelly, 1984). Administration of 2-amino-2-methyl-1-propanol, an inhibitor of choline synthesis from methionine, to lactating dairy cows decreased milk and fat-corrected milk yield during postruminal infusion of methionine but not during postruminal infusion of choline (Sharma and Erdman, 1988). This provided evidence that methionine serves as a methyl donor for choline synthesis in dairy cattle. Feeding rumen-protected choline increased milk yield in late lactation cows (Emanuele et al., 2007) or multiparous cows (Davidson et al., 2006) when compared to feeding rumen-protected methionine, suggesting a role for choline other than sparing methionine. Experiments employing a factorial design have not demonstrated an interaction between supplemental rumen-protected choline and dietary protein (13.0 vs. 16.5% CP; Erdman and Sharma, 1991) or rumen-protected methionine supplementation (0 vs. 14 g/d; Thering et al., 2007). Further studies are needed to establish the relationship between supplemental choline and other nutrients involved in one-carbon methyl metabolism.

Some of the early studies by Erdman and co-workers (Erdman et al., 1984) hypothesized that choline supplementation may increase milk fat percentage. They suggested “choline aided the transport of mobilized free fatty acids from adipose tissue through the liver to the mammary gland”. Figure 2 shows a summary of the responses of milk fat percentage to rumen-protected or postruminally infused choline. Of the 12 studies summarized, fat percentage was increased statistically in 3 of the studies ($P < 0.05$) and tended to increase in 1 of the studies ($P < 0.15$). Interestingly, in three studies employing fresh cows in which milk fat test was high ($> 4.0\%$) and fat mobilization would be high, there was no treatment effect. This does not support Erdman’s hypothesis of enhanced hepatic lipid transport as a mechanism of action for increased milk fat.

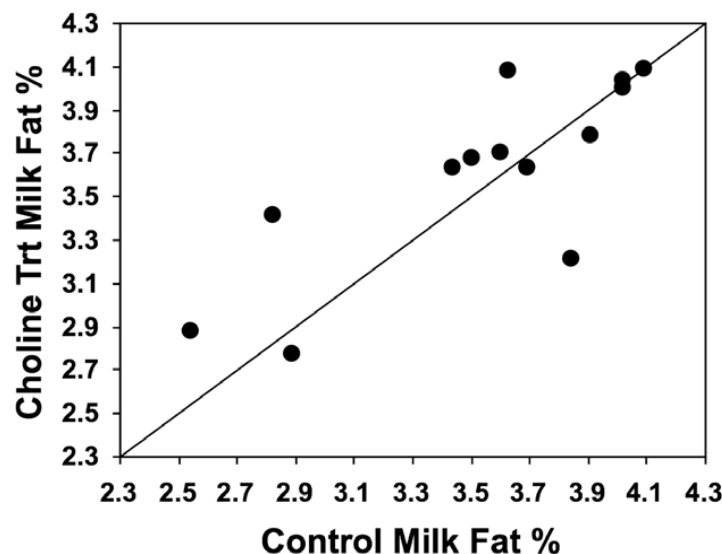


Figure 2. Milk fat response, plotted as control treatment vs. choline treatment, for cows fed rumen-protected choline or postruminally infused with choline. References: Abeni et al., 2007; Davidson et al., 2006; Emanuele et al., 2007; Erdman and Sharma, 1991; Hartwell et al., 2000; Janovick Guretzky et al., 2006; Ondarza et al., 2007; Piepenbrink and Overton, 2003; Sharma and Erdman, 1988; Sharma and Erdman, 1989; Toghdory et al., 2007; Zahra et al., 2006.

Milk protein response to supplemental choline is summarized in Figure 3. The response is neutral with only one study indicating a trend for a change; a decrease ($P < 0.15$). Given the potential ability of choline to spare methionine, it is surprising that positive treatment effects were never observed. In the great majority of studies, diet methionine status was not described.

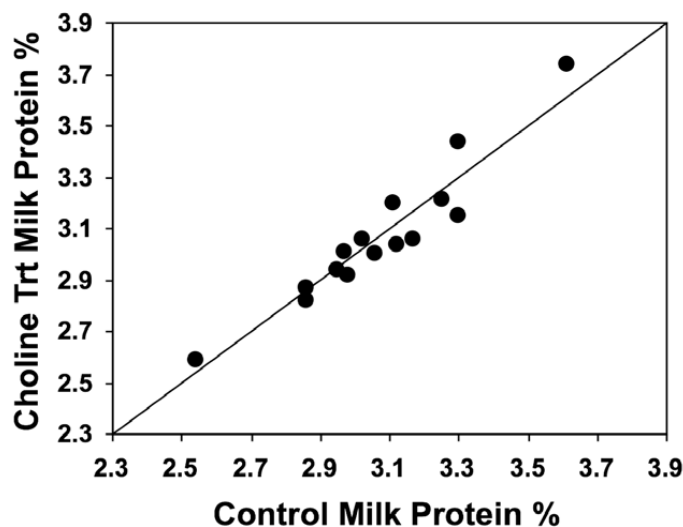


Figure 3. Milk protein response, plotted as control treatment vs. choline treatment, for cows fed rumen-protected choline or postruminally infused with choline. References: Abeni et al., 2007; Davidson et al., 2006; Emanuele et al., 2007; Erdman and Sharma, 1991; Hartwell et al., 2000; Janovick Guretzky et al., 2006; Ondarza et al., 2007; Piepenbrink and Overton, 2003; Sharma and Erdman, 1988; Sharma and Erdman, 1989; Thering et al. 2007; Toghdory et al., 2007; Zahra et al., 2006.

Animal Health

Choline deficiency in rats has been shown to cause an increase in accumulation of triglyceride (TAG) in liver. Triglyceride is transported out of the liver as a constituent of VLDL. As previously mentioned, choline may spare methionine (also a methyl donor) which is an amino acid that is required for synthesis of protein (a constituent of VLDL). Choline also serves as a substrate for synthesis of PC, another constituent of VLDL.

Fatty liver is a metabolic disorder that can affect up to 50% of high producing cows during the transition period, potentially compromising health, production and reproduction. Fatty liver develops when plasma nonesterified fatty acid (NEFA) concentrations are high due to depressed feed intake and altered endocrine status associated with initiation of parturition and lactation. The NEFA concentration at which TAG begins to accumulate in liver is not well established, but is known that the hepatic uptake of NEFA is directly associated with its concentration in blood. Research involving frequent blood and liver sampling in periparturient Holstein cows has shown liver TAG accumulation within 1 d after calving, which was preceded by an acute increase in plasma NEFA concentration and depressed feed intake immediately prior to and at calving (Vazquez-Añon et al., 1994). Therefore, if the flow of choline to the intestine of dairy cattle is

insufficient during the periparturient period when feed intake is low and fat mobilization is high, synthesis of VLDL could be limited and fatty liver could result.

Only recently have the effects of choline on liver TAG been measured directly. Hartwell et al. (2000) fed ruminally protected choline to transition dairy cows but did not see any beneficial effect on liver TAG concentration. However, the degree of ruminal protection of the choline fed in that trial has been questioned by the manufacturer of the product (D. Putnam, personal communication). More recently, an improved protected choline product (D. Putnam, personal communication) was fed to transition dairy cows and a statistically non-significant reduction in liver TAG was observed as level of supplementation was increased (Piepenbrink and Overton, 2004). Liver TAG is a highly variable measurement in dairy cattle immediately after parturition and this study may not have had adequate animal numbers to detect statistically significant treatment differences. Therefore, we attempted to assess whether choline had a role in preventing or alleviating fatty liver using an experimental model that might be more sensitive for detecting a treatment effect.

To conduct these experiments, we used far-off dry cows. In the first study, cows were energy-restricted to approximately 30% of requirements for maintenance and pregnancy for 10 d. This was done to mimic feed intake depression prior to calving and allow for lipid mobilization and development of fatty liver. During the energy restriction, cows were fed an unsupplemented diet or one diet supplemented with rumen-protected choline. This protocol allowed to assess whether choline has a role in the *prevention* of fatty liver. For the second experiment, cows were energy-restricted for 10 days, similar to that in the first experiment. During this time, all cows were fed the same diet. Following the 10-day energy restriction, cows were fed ad libitum for 6 days. During that time cows were fed an unsupplemented diet or one supplemented with rumen-protected choline. Depletion of TAG from the liver was monitored during the ad libitum feeding. This protocol allowed to determine whether choline has a role in the *alleviation* of fatty liver (Cooke et al., 2007).

Feeding 15 g choline/day in a ruminally protected form prevented fatty liver and possibly alleviated fatty liver (Cooke et al., 2007). Supplementation during energy restriction reduced liver TAG after 10 days (Figure 4). Plasma NEFA were also reduced by choline supplementation (Figure 5), therefore, it cannot be distinguished whether the beneficial effects of choline on liver TAG were due to direct effects on the liver or indirect effects on lower plasma NEFA. It is not known how choline affects plasma NEFA. The results of the second experiment are a bit more difficult to interpret. At the end of the 10-day energy restriction, prior to application of treatments, liver TAG content was 6.8 vs. 12.7 ug TAG/ug DNA in cows destined to receive control (without choline supplementation) and choline supplemented diet, respectively. Since treatments had not been applied yet, one would have expected the values to be similar. In an attempt to adjust for this discrepancy, the values for liver TAG after the 10-day energy restriction but prior to treatment were used as covariates in statistical analysis. Covariately adjusted liver TAG on days 3 and 6 of treatment and ad libitum feeding are shown in Figure 6. Additionally, results were expressed as a percentage of liver TAG after the induction phase. On day 3 of ad libitum feeding and treatment, liver TAG content was 60.4 and 52.2 % of that after induction for the control and choline supplemented groups, respectively. On day 6, liver TAG was 48.5 and 29.9% of initial content, for control and choline supplemented groups.

The liver TAG results supported the findings from the first trial and suggest that choline deficiency may contribute to fatty liver.

Demonstrating that choline can prevent fatty liver using a model such as we employed is an important finding, but it does not establish if there is a beneficial effect on animal health. To evaluate effects on animal health, trials employing large animal numbers are required and such studies are necessarily conducted on large commercial farms. Lima et al. (2007) conducted two experiments on separate farms. On one farm, using 363 cows, 0 or 15 g/d of choline in a protected form was fed between 25 d prior to expected calving until 80 d post calving. Postpartum, DMI tended to be greater (22.6 vs. 23.9 kg/d; $P = 0.10$) and fat-corrected milk yield was greater (44.6 vs. 42.8; $P < 0.05$) for cows fed choline. Feeding choline reduced ($P < 0.05$) the incidence of ketonuria (10.7 vs. 28.8%), clinical ketosis (4.0 vs. 11.3%), and the relapse of clinical ketosis (2.3 vs. 6.85). On the second farm, the same treatments were fed, but the duration was only from 25 d prior to expected calving until calving. DMI and fat-corrected milk was not affected by treatment and choline supplementation tended to increase milk yield (27.9 vs. 28.7 kg/d; $P = 0.07$). Parameters related to ketosis were not affected by treatment. The researchers speculated that the absence of a response on the second farm may have been due to the absence of choline supplementation after calving.

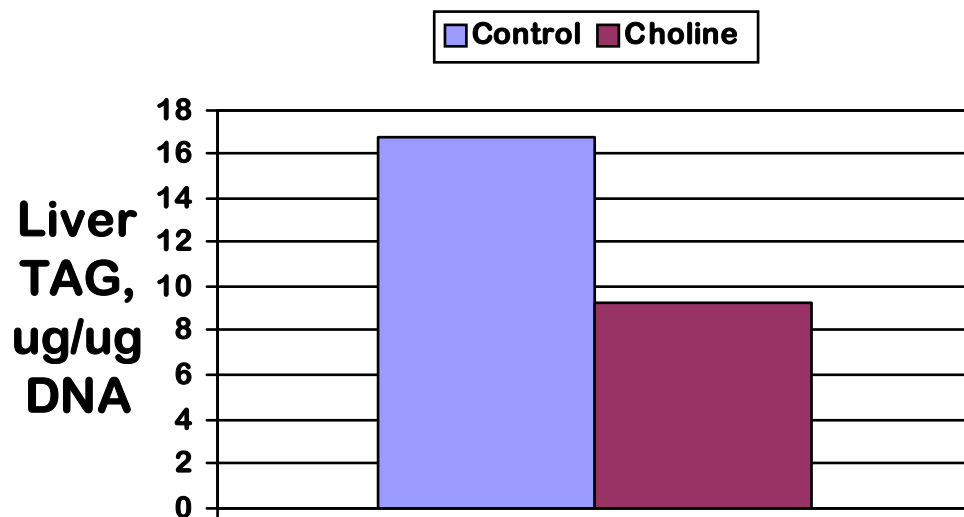


Figure 4. Effect of choline supplementation on liver TAG after 10 days of feed restriction of far-off dry cows (Experiment 1; Cooke et al., 2007).

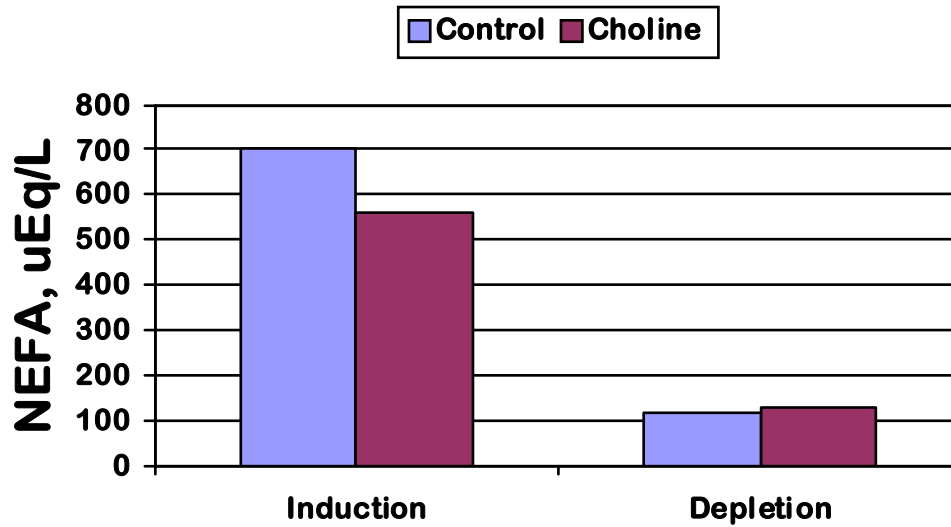


Figure 5. Plasma NEFA during choline supplementation. Induction corresponds to measurements made after 10 days of feed restriction of far-off dry cows (Experiment 1). Depletion corresponds to measurements made during ad libitum feeding that followed 10 days of feed restriction (Experiment 2; Choline was not supplemented during feed restriction; Cooke et al., 2007).

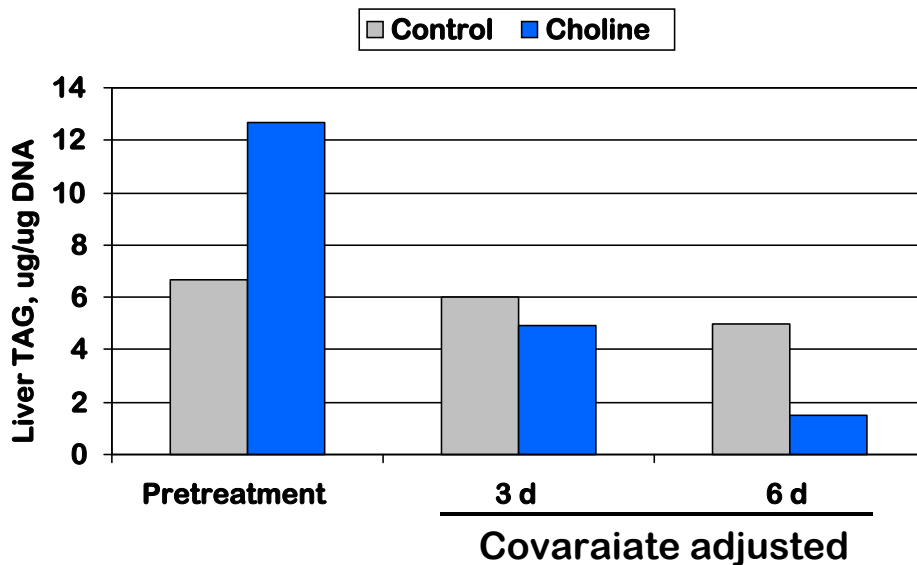


Figure 6. Liver TAG after a 10 day feed restriction (pretreatment with choline) and after three or 6 days of ad libitum feeding during which time cows were or were not supplemented with choline (Experiment 2). Due to the discrepancy in liver TAG pretreatment, the pretreatment values were used for covariate adjustment of data (Cooke et al., 2007).

Niacin

Background

The vitamin niacin is a precursor of the coenzyme nicotinamide adenine dinucleotide (**NAD**) which participates in a large number of oxidation-reduction reactions, both in anabolic (NADPH/NADP) and catabolic (NADH/NAD) pathways. Niacin can be found in two common forms: nicotinic acid (**NA**) and nicotinamide (**NAM**). Both compounds have similar nutritional properties, and both can be used in the synthesis of NAD but have distinct biological properties (Dipalma and Thayer, 1991; Carlson, 2005).

Early studies from the 1960's showed that NA has anti-lipolytic effects in humans. Both oral or intravenous administrations of NA boluses lead to dramatic and acute reductions of plasma NEFA concentrations, followed by a rebound above baseline levels and a subsequent return to baseline (Carlson, 2005). In dairy cows, large oral boluses of NA cause transient decreases in NEFA concentration followed by a rebound (160 g, Waterman and Schultz, 1972; Waterman et al., 1972; 12 or 120 g, Jaster et al., 1983). Pharmacological doses of NA inhibit lipolysis in adipose tissue (Dipalma and Thayer, 1991; Carlson, 2005), but have minimal direct effects on subsequent fatty acid metabolism in the bovine (Waterman and Schultz, 1973). The rebound is thought to occur when NA action in adipose tissue ceases, possibly due to clearance of NA from blood (Waterman and Schultz, 1972).

However, in contrast to NA, NAM does not have anti-lipolytic properties in humans (Dipalma and Thayer, 1991; Carlson, 2005). Accordingly, oral administration of 12 g/d of NAM to feed-restricted cows failed to reduce plasma NEFA or BHBA concentrations (Jaster and Ward, 1990), even though rumen microbes are able to convert NAM to NA (Harmeyer and Kollenkirchen, 1989; Campbell et al., 1994).

Productive performance

The bulk of research on niacin in dairy nutrition has been focused more on its role as a vitamin, and rarely on the anti-lipolytic effects of pharmacological doses of NA. Additionally, dairy researchers have not always specified which form of niacin they used and seldom considered the different metabolic effects of NA and NAM.

A meta-analysis of 27 feeding studies involving NA supplementation to dairy rations showed no improvement in lactation performance when NA was given at a rate of 6 g/d (Schwab et al., 2005). Supplementation of 12g NA/d did not change in milk production (0.4 kg; $P = 0.12$) and resulted in modest increases in fat (25.8 g/d; $P = 0.01$) and protein (17.4 g/d; $P = 0.08$) yields compared to controls (Schwab et al., 2005). The authors questioned the economic return from supplementing free NA in dairy rations due to high variability of results and small production responses.

Plasma NEFA concentrations were reduced in only one out of 11 studies in which periparturient cows were supplemented with niacin (6 to 12 g/d of free NA or NAM; NRC, 2001). Accordingly, meta-analysis of multiple studies involving NA feeding showed no statistical effects of NA in plasma NEFA and BHBA concentrations (Schwab et al., 2005). The

absence of positive results of niacin supplementation in most feeding trials contrasts with the positive effects of NA in reducing NEFA levels in humans, and with the acute reduction in plasma NEFA when supraphysiological doses of NA were given to cows. There are several factors that may explain the lack of success with using niacin to reduce NEFA:

a) The active form of niacin modulating adipose tissue metabolism in humans is NA, not NAM. Therefore, effects would not be expected in the bovine if NAM is fed.

b) Supplemental niacin is extensively degraded or transformed in the rumen. Only 6.7% to 17% of supplemental NA was estimated to reach the duodenum in the bovine (Zinn et al., 1987; Campbell et al., 1994). Absorption of NA through the rumen is probably insignificant (Harmeyer and Kollenkirchen, 1989; Erickson et al., 1991; Campbell et al., 1994).

c) The dosage of niacin fed to periparturient dairy cows (either as NA or NAM) usually ranges from 6 to 12 g/d (NRC, 2001; Schwab et al., 2005). This supplementation level is probably insufficient to elicit a significant and sustained decrease in NEFA, especially when taking into consideration the limited flow of supplemental NA to the lower gut (Zinn et al., 1987; Campbell et al., 1994).

Recent experiments involving the supplementation of periparturient dairy cows with high doses of rumen available NA have produced inconsistent results. Jersey cows supplemented with 48 g/d of free NA from 30 d prepartum until calving had lower levels of plasma NEFA at calving and less DMI decline during the last week of gestation (French, 2004). However, these results were not replicated when both Holstein and Jersey cows were supplemented with up to 98 mg NA/d per kg BW, from 30 d prepartum to 21 d postpartum (Chamberlain and French, 2006). We suspect that only a small fraction of the NA was absorbed because a free form of NA was used. Furthermore, the antilipolytic effects could have been transient, and the inconsistent results on plasma NEFA may have reflected the time of blood sampling relative to NA feeding.

Current research

We hypothesized that, if delivered in sufficient quantities to the intestine, NA would limit lipolysis in adipose tissue and induce sustained reductions in plasma NEFA concentration during periods of negative energy balance. This hypothesis was tested with a series of experiments measuring plasma NEFA responses to post-ruminal infusions of NA in non-lactating, feed-restricted Holstein cows (Pires and Grummer, 2007; Pires et al., 2007).

In experiment 1, we studied the effect of single NA abomasal bolus on plasma NEFA of feed-restricted cows using a 4 x 4 Latin square design (Pires and Grummer, 2007). Treatments were a bolus of 0, 6, 30 or 60 mg NA/kg BW, corresponding to 0, 5, 24 and 49 g of NA, given as a single abomasal infusion each period. Cows were feed-restricted for 48 h prior to abomasal infusion to stimulate mobilization of fatty acids and elevate plasma NEFA concentration. All NA doses caused dramatic reductions of plasma NEFA, followed by a rebound during which NEFA increased transiently above baseline levels (Figure 7). The pattern of plasma NEFA decrease was similar during the first h for the 3 NA treatments. Additionally, the 2 highest doses of NA (30 and 60 mg/kg) caused a similar pattern of NEFA concentrations up to 3 h after the

single infusions. Three h after the abomasal infusion of the 2 highest doses of NA, NEFA concentrations fell to less than 100 uEq/L. The initial pattern of plasma NEFA decrease suggests that blood NA concentrations initially reached a threshold that induced maximum inhibition of adipose lipolysis. The rebound of plasma NEFA followed a pattern observed in other animal models. The magnitude of rebound depended on either the dose of NA or duration of time with decreased NEFA, because the two highest NA doses caused the longest decrease in NEFA, but also the greatest rebound. It is conceivable that smaller boluses of NA may potentially limit the duration and magnitude of NEFA rebound.

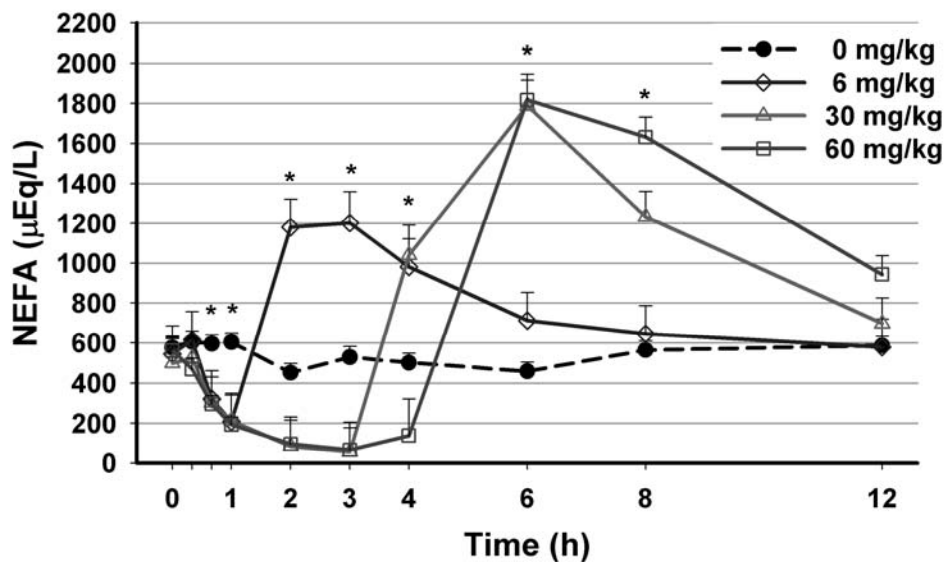


Figure 7. Effects of abomasal infusion of single doses of nicotinic acid on plasma NEFA. Fixed effects in the statistical model: treatment ($P = 0.001$), time and treatment x time interaction ($P < 0.001$). Treatment differences within a time point are indicated by * ($P < 0.001$; Pires and Grummer, 2007).

A second experiment was conducted to assess whether successive abomasal infusions of NA could induce sustained reductions of plasma NEFA concentration (Pires and Grummer, 2007). Six non-pregnant, non-lactating Holstein cows were feed-restricted for 48 h to increase plasma NEFA. At 48 h of feed restriction, cows received 9 hourly abomasal infusions of 0, 6 or 10 mg NA/kg BW per h, which corresponded to 0, 4.9 and 8.3 g NA/h. Both NA treatments reduced plasma NEFA in a similar pattern, from 550 to approximately 100 uEq/L. Again, a dramatic rebound was observed after NA infusions were discontinued at 8 h (Figure 8).

The repeatability of this method to decrease plasma NEFA concentrations was demonstrated in a third experiment, which was designed to establish a cause-effect relationship between elevated plasma NEFA and insulin resistance in Holstein cows (Pires et al., 2007). Six non-lactating, non-gestating, ruminally cannulated Holstein cows were randomly assigned to a sequence of two treatments in a cross-over design. Mobilization of body reserves was stimulated by withdrawing forage for 48 h before initiation of treatments. Treatments consisted of 11 hourly abomasal infusions of water (control) or NA (6 mg/h per kg BW) as an antilipolytic agent

to decrease plasma NEFA concentration. Intravenous glucose tolerance test (IVGTT; 0.25g/kg BW of glucose i.v.) was performed 8 h after initiation of treatments and was followed by 3 h of blood sampling. The reduction of plasma NEFA concentration ($P < 0.001$) enhanced ($P < 0.01$) clearance of glucose during IVGTT (1.9 vs. 1.2 %/min). This occurred despite lower ($P = 0.05$) insulin concentration (70.0 vs. 97.9 uIU/mL), which reflects an increased response to endogenous insulin. Clearance of glucose during IVGTT is a function of glucose uptake and insulin-mediated inhibition of endogenous glucose production. The reduction of plasma NEFA may have enhanced glucose utilization, inhibited endogenous glucose production, or both, by increasing insulin sensitivity.

Data from these experiments suggest that maximal antilipolytic response was achieved with 6 mg NA/kg BW per h. Plasma NEFA decreased from approximately 550 uEq/L to less than 100 uEq/L within 2 h after initiation of treatments, which was below the NEFA concentration observed prior to feed restriction (Pires and Grummer, 2007; Pires et al., 2007). Lower rates of NA infusion may promote more moderate reductions of plasma NEFA concentration.

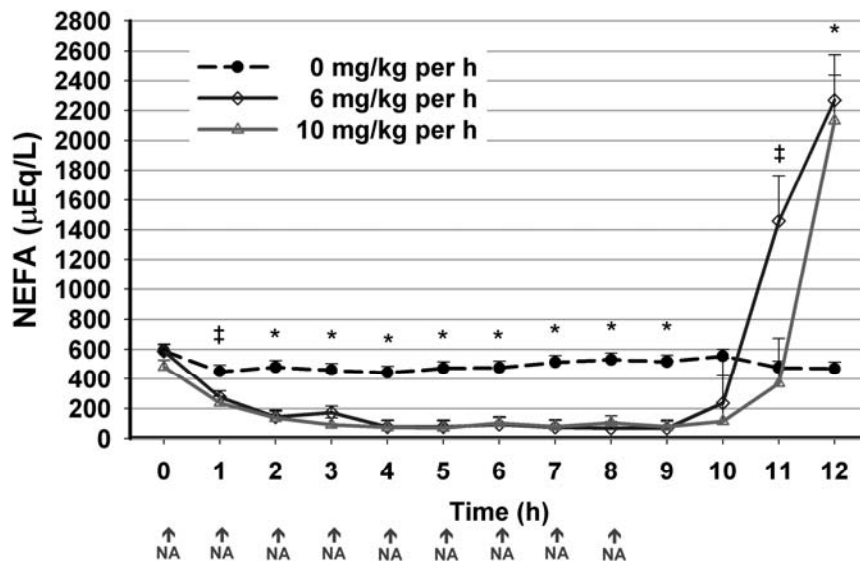


Figure 8. Effects of abomasal infusions of nicotinic acid at a rate of 0, 6, or 10 mg/h per kg of BW on plasma NEFA. Infusion of treatments started at 48 h of feed restriction (time 0) and was repeated at 1, 2, 3, 4, 5, 6, 7, and 8 h thereafter. Fixed effects in the statistical model: treatment ($P = 0.06$), time ($P < 0.001$) and treatment x time ($P < 0.001$). Treatment differences within a time point are indicated by * ($P < 0.001$) and ‡ ($P = 0.05$; Pires and Grummer, 2007).

Conclusions

Supplementation of dairy diets with protected choline has improved milk yield in moderate producing cows (30 - 35 kg/d). There is little evidence supporting beneficial effects in milk fat percent, while protein percent was unchanged in all trials reviewed herein. In addition to productive performance, potential benefits of supplemental choline on modulation of lipid metabolism must be considered. Controlled experiments suggest that supplemental choline prevents liver TAG accumulation and enhances depletion TAG following a protocol for induction of hepatic TAG infiltration. Field studies involving large animal numbers showed increased DMI and FCM production, and decreased incidence of ketosis when cows were fed rumen-protected choline during both close-up period and early lactation.

Previous studies on NA supplementation involved either oral boluses of high doses of NA, which is not feasible in a feeding situation, or incorporated NA in dairy rations (commonly 6 to 12 g/d) and failed to acknowledge the extensive degradation or transformation of NA by ruminal microbes. Therefore, it is not possible to accurately estimate the amount of NA reaching the intestine for absorption, and production responses to dietary supplementation of free NA are difficult to interpret.

Recent research shows that NA is a powerful antilipolytic agent in the bovine under negative energy balance due to feed restriction. Furthermore, data suggest that sustained reductions of plasma NEFA can be achieved if the supply of NA for absorption by the lower gut is maintained. The antilipolytic properties of NA may prove useful in nutritional management of the periparturient dairy cow once a ruminally-protected form of NA is tested. The reduction of plasma NEFA concentration would improve the metabolic profile of the transition cow and prevent energy-related metabolic disorders associated with excessive mobilization of fat reserves, e.g., fatty liver and ketosis. However, we must first identify a rate of NA delivery that promotes moderate rates of lipolysis and NEFA concentrations, because NEFA originating from adipose tissue are an important energy source and precursor for milk fat synthesis in early lactation. Furthermore, a fairly steady supply of NA would have to be maintained in order to avoid the occurrence of a NA-induced NEFA rebound. The rate of rumen-protected NA incorporation in transition diets will have to take into consideration the typical drop in DMI observed immediately prior to and at calving.

Research is also warranted on potential synergistic effects between NA and choline on modulation of lipid metabolism of periparturient cows. The antilipolytic properties of nicotinic acid could be used to prevent excessive lipolysis in adipose tissue and attenuate the increase in plasma NEFA at calving, while choline supplementation would improve hepatic fatty acid metabolism, therefore decreasing TAG accumulation and occurrence of ketosis.

References

- Abeni, F., M. Speroni, M. G. Terzano, L. Migliorati, P. Cavassini, and G. Pirlo. 2007. Effects of rumen protected choline on production responses in Italian Friesian dairy cows. *J. Dairy Sci.* 90(Suppl. 1):354.
- Atkins, K.B., R. A. Erdman, and J. H. Vandersall. 1988. Dietary Choline effects on milk yield and duodenal choline flow in dairy cattle. *J. Dairy Sci.* 71:109-116.
- Brusemeister, F., and K. Sudekum. 2006. Rumen-protected choline for dairy cows: the in situ evaluation of a commercial source and literature evaluation of effects on performance and interactions between methionine and choline metabolism. *Anim. Res.* 55:93-104.
- Campbell, J. M., M. R. Murphy, R. A. Christensen, and T. R. Overton. 1994. Kinetics of niacin supplements in lactating dairy cows. *J. Dairy Sci.* 77:566-575.
- Carlson, L. A. 2005. Nicotinic acid: The broad-spectrum lipid drug. A 50th anniversary review. *J. Intern. Med.* 258:94-114.
- Chamberlain, J. L. and P. D. French. 2006. The effects of nicotinic acid supplementation during late gestation on lipolysis and feed intake during the transition period. *J. Dairy Sci.* 89 (Suppl. 1):232.
- Cooke, R. F., N. S. Del Rio, D. Z. Caraviello, S. J. Bertics, M. H. Ramos, and R. R. Grummer. 2007. Supplemental choline for prevention and alleviation of fatty liver in dairy cattle. *J. Dairy Sci.* 90:2413-2418.
- Davidson, S., B. Hopkins, J. Odle, V. Fellner, and L. Whitlow. 2006. Supplementation of diets with limited methionine content with rumen-protected forms of methionine, choline, betaine in early lactation cows. S. Davidson, B. Hopkins, J. Odle, C. Brownie, V. Fellner, and L. Whitlow. *J. Dairy Sci.* 89(Suppl. 1):142.
- Dipalma, J. R. and W. S. Thayer. 1991. Use of niacin as a drug. *Annu. Rev. Nutr.* 11:169-187.
- Emanuele, S., T. Hickley, and R. Carvalho. 2007. Effect of rumen protected choline (Reashure) and rumen protected methionine on milk yield, and composition in lactating cows. *J. Dairy Sci.* 90(Suppl. 1):352.
- Emmanuel, B. and J. J. Kennelly. 1984. Kinetics of methionine and choline and their incorporation into plasma lipids and milk components in lactating goats. *J. Dairy Sci.* 67:1912-1918.
- Erdman, R. A. 1992. Vitamins. Pages 297-308 in *Large Dairy Herd Management*. H. H. Van Horn and C. J. Wilcox, eds. American Dairy Science Association, Champaign, IL.
- Erdman, R. A., and B. K. Sharma. 1991. Effect of dietary rumen-protected choline in lactating dairy cows. *J. Dairy Sci.* 74:1641-1647.
- Erickson, P. S., M. R. Murphy, C. S. McSweeney, and A. M. Trusk. 1991. Niacin absorption from the rumen. *J. Dairy Sci.* 74:3492-3495.
- French, P. D. 2004. Nicotinic acid supplemented at a therapeutic level minimizes prepartum feed intake depression in dairy cows. *J. Dairy Sci.* Vol. 87 (Suppl. 1):345 (Abstr.).
- Harmeyer, J. and U. Kollenkirchen. 1989. Thiamin and niacin in ruminant nutrition. *Nutrition research reviews* 2:201-225.
- Hartwell, J. R., M. J. Cecava, and S. S. Donkin. 2000. Impact of dietary rumen undegradable protein and choline on intake, peripartum liver triglyceride, plasma metabolites and milk production in dairy cows. *J. Dairy Sci.* 83:2907-2917.

- Janovick Guretzky, N. A., D. B. Carlson, J. E. Garret, and J. K Drackley. 2006. Lipid metabolite profiles and milk production for Holstein and Jersey cows fed rumen-protected choline during the periparturient period. *J. Dairy Sci.* 89:188-200.
- Jaster, E. H. and N. E. Ward. 1990. Supplemental nicotinic acid or nicotinamide for lactating dairy cows. *J. Dairy Sci.* 73:2880-2887.
- Jaster, E. H., D. F. Bell, and T. A. McPherron. 1983. Nicotinic acid and serum metabolite concentrations of lactating dairy cows fed supplemental niacin. *J. Dairy Sci.* 66:1039-1045.
- Lima, F. S., M. F. Sa Filho, L. F. Greco, F. Susca, V. J. A. Magalhaes, J. Garrett, and J. E. P. Santos. 2007. Effects of feeding rumen-protected choline (RPC) on lactation and metabolism. *J. Dairy Sci.* 90(Suppl. 1):174.
- NRC. 2001. Nutrient requirements of dairy cattle. 7th Revised ed. Natl. Acad. Press, Washington, DC.
- Ondarza, M. B., S. Emanuele, and D. Putnam. 2007. Effect of rumen protected choline (reashure) supplemented to high producing cows on milk production, milk components, and intake. *J. Dairy Sci.* 90(Suppl. 1):353.
- Piepenbrink, M. S., and T. R. Overton. 2003. Liver metabolism and production of cows fed increasing amounts of rumen-protected choline during the periparturient period. *J. Dairy Sci.* 86:1722-1733.
- Pires, J. A. A. and R. R. Grummer. 2007. The use of nicotinic acid to induce sustained low plasma nonesterified fatty acids in feed-restricted Holstein cows. *J. Dairy Sci.* 90:3725-3732.
- Pires, J. A. A., J. B. Pescara, and R. R. Grummer. 2007. Reduction of plasma NEFA concentration by nicotinic acid enhances the response to insulin in feed-restricted Holstein cows. *J. Dairy Sci.* 90:4635-4642.
- Schwab, E. C., D. Z. Caraviello, and R. D. Shaver. 2005. A meta-analysis of lactation responses to supplemental dietary niacin in dairy cows. *Professional Animal Scientist*:239-247.
- Sharma, B. K., and R. A. Erdman. 1988. Abomasal infusion of choline and methionine with or without 2-amino-2-methyl-1-propanol for lactating dairy cows. *J. Dairy Sci.* 71:2406-2411.
- Sharma, B. K., and R. A. Erdman. 1989. Effects of dietary and abomasally infused choline on milk production responses of lactating dairy cows. *J. Nutr.* 119:248-254.
- Thering, B. J., J. M. Ramos-Nieves, J. L. Lukas, D. E. Putnam, and T. R. Overton. 2007. Interrelationships of dietary supplies of choline and methionine on productive performance of Holstein dry cows. *J. Dairy Sci.* 90(Suppl. 1):355.
- Toghdory, A., S. Emanuele, T. Choorchi, and A Naerian. 2007. Effect of choline and rumen protected choline on milk production, milk composition and blood metabolites of lactating dairy cows. *J. Dairy Sci.* 90(Suppl. 1):353.
- Vazquez-Añon, M., S. Bertics, M. Luck, R. R. Grummer, and J. Pinheiro. 1994. Peripartum liver triglyceride and plasma metabolites in dairy cows. *J. Dairy Sci.* 77:1521-1528.
- Waterman, R. and L. H. Schultz. 1972. Nicotinic acid loading of normal cows: Effects on blood metabolites and excretory forms. *J. Dairy Sci.* 55:1511-1513.
- Waterman, R. and L. H. Schultz. 1973. 1 carbon 14-labeled palmitic acid metabolism in fasted, lactating goats following nicotinic acid administration. *J. Dairy Sci.* 56:1569-1574.

- Waterman, R., J. W. Schwalm, and L. H. Schultz. 1972. Nicotinic acid treatment of bovine ketosis. I. Effects on circulatory metabolites and interrelationships. *J. Dairy Sci.* 55:1447-1453.
- Zahra, L. C., T. F. Duffield, K. E. Leslie, T. R. Overton, D. Putnam, and S. J. LeBlanc. 2006. Effects of rumen-protected choline and monensin on milk production and metabolism of periparturient cows. *J. Dairy Sci.* 89:4808-4818.
- Zinn, R. A., F. N. Owens, R. L. Stuart, J. R. Dunbar, and B. B. Norman. 1987. B-vitamin supplementation of diets for feedlot calves. *J. Anim Sci.* 65:267-277.