ADSA Foundation Scholar Lecture and
Ruminant Nutrition Symposium: Dietary Methyl Donor Supplementation and Hepatic Health in Transition Dairy Cows

529  ADSA Foundation Scholar Presentation (Production):
Influencing hepatic metabolism: Can fatty acids and methyl donors modulate nutrient partitioning to support metabolic health in the transition dairy cow? H. White*, University of Wisconsin Madison, Madison, WI.

Hepatic de novo production of glucose and oxidation of fatty acids (FA) are critical in supporting milk production during the transition to lactation period. During this period of metabolic challenge, there is an increase in FA taken up by the liver. Although the optimal fate for these FA is complete oxidation through the TCA cycle, alternative fates include incomplete oxidation via ketogenesis or storage within the liver as triglycerides (TG). Influencing the relative capacity of these pathways may prevent ketosis and fatty liver and improve hepatic efficiency. Hepatic nutrient partitioning reflects complex regulation of key enzymatic steps modulated by FA, substrates, and methyl donors. Fatty acids mobilized from adipose tissue have regulatory effects on genes such as pyruvate carboxylase; however, both in vivo and vitro work suggests there may be other influences present which can result in differential regulation between cows that subsequently develop sub-clinical ketosis and that some FA may be preferentially stored or oxidized. Supporting TG export or subsequent lipolysis is also important for minimizing liver TG accumulation. Although there is biochemical overlap between choline and methionine within both methyl donor metabolism and cellular lipid packaging, there is evidence that each of these nutrients have their own metabolic priorities. Increased FA oxidation and TG export with choline treatment may support both decreased cellular TG and ketone body secretion. Together, these shifts in pathway flux may also support the increased cellular glycogen observed in vitro and give reason to further examine gluconeogenic capacity in cows supplemented with choline. While further research is needed to continue refining our understanding of the intricate balance that regulates hepatic metabolism, shifting nutrient partitioning via oxidative pathways may be key in supporting both efficiency and metabolic health.

Key Words: gluconeogenesis, oxidation, choline

530  Methyl donor metabolism and nutrition in the transition dairy cow: Should we consider fatty acid nutrition simultaneously? J. W. McFadden*, Cornell University, Ithaca, NY.

One-carbon metabolism involves the folate and methionine (Met) cycles that work in unison to support lipid, nucleotide, and protein synthesis, as well as methylation reactions and the maintenance of redox status. Methyltetrahydrololate is utilized by Met synthase to couple the folate and Met cycles. Methionine may also be formed by the transformation of choline-derived betaine by betaine hydroxymethyltransferase. Within the Met cycle, S-adenosylmethionine is formed and used to synthesize phosphatidylcholine. Such actions are considered important for hepatic very-low density lipoprotein assembly and triglyceride secretion. Following methylation, homocysteine is formed and utilized to synthesize glutathione within the transsulfuration pathway, which scavenges reactive oxygen species. These biochemical complexities play a major role in the transition dairy cow that experiences a demand for compounds with a labile methyl group. Indeed, dietary methyl donor supplementation has merit when we consider research demonstrating improved lactation performance, and prevention of hepatic triglyceride deposition, inflammation, and oxidative stress with this feeding strategy. However, our understanding of methyl donor utilization and efficacy to maintain peripartal health deserves consideration within the context of fatty acid supply and metabolism. In non-ruminants, transmethylation-dependent phosphatidylcholine synthesis favors phosphatidylethanolamine enriched in very-long chain polyunsaturated fatty acids (PUFA). Because hepatic PUFA depletion is a feature of fatty liver in transition cows, inadequate hepatic PUFA concentrations may limit the ability of methyl donors to stimulate phosphatidylcholine synthesis and prevent steatosis. Moreover, fatty acid oversupply or composition may counteract the potential benefits of dietary methyl donor supplementation on redox homeostasis and immune status. Although work has focused on methyl donor co-supplementation (e.g., choline and Met), future studies should determine whether specific dietary fatty acid feeding regimens optimize methyl donor efficacy in the transition cow.

Key Words: liver, methyl donor, transition cow

531  Potential impacts of betaine supplementation on dairy cattle during the transition period and under heat stress. S. Tao*, J. K. Bernard, R. M. Orellana Rivas, T. N. Marins, and Y. Chen, University of Georgia, Tifton, GA.

Betaine (tri-methylglycine) is a natural compound present in bacteria, plant and animal cells. It is an important nutrient in human and animal diets and exerts functions in osmolality regulation, maintenance of cell function as a chaperone and one-carbon metabolism as a methyl donor. Betaine in the animal body can be synthesized endogenously by choline oxidation or absorbed from the diet. As a methyl donor, betaine is catalyzed by betaine-homocysteine methyltransferase and donates a methyl group to homocysteine for re-synthesizing methionine, primarily in liver. This potentially spares choline or methionine as methyl donors, and promotes the production of S-adenosylmethionine, a universal methyl donor. As an organic osmolyte, betaine regulates cell volume and organizes water structure in a cell, stabilizing cellular proteins, especially under stress conditions. Therefore, betaine has numerous functions in an animal’s body. In laboratory animals, betaine supplementation is reported to alleviate hepatic fat accumulation and other symptoms associated with alcohol or non-alcohol related liver injury. In coccidia-infected poultry, betaine stabilizes intestinal structure and maintains gut health and function. In swine and poultry, betaine is used as a “carcass modifier” to increase lean tissue synthesis. In ruminants, limited research suggest that supplementation of betaine influences rumen fermentation, improves nutrient digestibility, and increases milk yield during lactation. Because it functions as a methyl donor and an organic osmolyte, betaine has the potential to be utilized in dairy cattle diet during the transition period and summer to improve hepatic health and improve stress responses. However, convincing evidence is still limited and extensive research is warranted.

Key Words: betaine, transition period, heat stress

532  Folic acid and vitamin B12 requirements of mature cows: Importance of endogenous production of methyl donors from the...
Methionine (Met) is the precursor of S-adenosylmethionine (SAM), donor of methyl groups in more than 50 metabolic reactions, among them synthesis of creatine and phosphatidylcholine and DNA methylation. In the transmethylation pathway (TM), after giving its methyl group, SAM is converted into S-adenosylhomocysteine (SAH) and then into homocysteine (Hcy). The latter can be catabolized into cysteine or remethylated into Met. The role of the remethylation cycle is to ensure a constant supply of SAM, even when Met supply is low. Remethylation of Met can be achieved using preformed labile methyl groups provided by choline and betaine or by methylneogenesis. For endogenous production of methyl groups, tetrahydrofolate (THF) accepts a 1-carbon unit, mostly provided by catabolism of serine, glycine or formate, to form 5,10-methylene-THF which can be irreversibly converted into 5-methyl-THF. The latter transfers its methyl group to the vitamin B12 coenzyme which acts as an intermediary for the transfer of the methyl group to Hcy to regenerate Met and THF. In multiparous dairy cows, when Met supply is above 2.2% MP, a supplement of folic acid and vitamin B12 has no effect on TM but when Met supply is lower than 1.9% MP, the vitamin supplement increases TM. In the latter, the supplement of vitamins also increases \( AHCY \) (SAH hydrolase) supporting the previous observation that, when Met supply is low, methylneogenesis allows maintaining TM. The fate of Hcy flowing TM, however, varies according to plasma Met concentration. When plasma Met is low, plasma Hcy and Cys are decreased by the vitamin supplement; methylneogenesis reduces the need for Met by increasing the number of times that a molecule of Hcy is remethylated within hepatic cells before being catabolized. However, when plasma Met is high, this effect is reduced and plasma Hcy and Cys increased. Providing an adequate supply in folic acid and vitamin B12 allows for sufficient endogenous production of methyl groups to support TM, which is likely to be especially of critical importance when methionine supply is low.

Key Words: dairy cow, B vitamin, S-adenosylmethionine

533 Methionine supplementation during the transition period: Fine-tuning immunometabolism. Z. Zhou*, Michigan State University, East Lansing, MI.

Around parturition in dairy cows, the increased demand for nutrients to sustain fetal growth and lactation, coupled with depressed feed intake, impose tremendous metabolic stress. Consequently, the metabolic challenge and inflammation incurred during this period have been shown to lead to health problems and compromised lactation performance. Various nutrients are known to promote a smooth transition from gestation to lactation by fine-tuning immunometabolism. Methionine, an essential amino acid (AA) engaged in various key physiologic events, has been underscored as a limiting AA for milk protein synthesis. Apart from its apparent key role in mammary gland and liver protein synthesis, methionine also serves as a substrate for sulfur-containing antioxidants, namely glutathione and taurine. Additionally, as a key component of one-carbon metabolism, hundreds of methylation reactions acquire methyl groups from methionine via S-adenosyl methionine. Recent research has highlighted the milk production and health benefits from methionine supplementation during the transition period. This presentation will provide a brief review of the impact of methionine on transition dairy cow health and productivity as well as the underlying alterations in immunometabolism. Specifically, this presentation will discuss results from studies showing the role of methionine supplementation in inducing metabolic changes in (1) plasma AA profile and utilization; (2) liver and skeletal muscle metabolome; (3) hepatic sulfur-containing antioxidant pool and metabolism; and (4) hepatic one-carbon metabolism in vivo and in vitro. In the future, the opportunity and challenge will be to continue to improve our understanding of how functional nutrients affect immunometabolism in dairy cows and effectively apply this knowledge to feeding and management in the dairy industry.

Key Words: methionine, transition period, immunometabolism