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Bovine Respiratory Disease Influences on Nutrition and Nutrient Metabolism

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Key points

- Inflammation caused by bovine respiratory disease (BRD) continues to be one of the greatest challenges facing beef cattle producers and feedlot managers.
- BRD results in decreased intake, daily gain, and feed efficiency in feedlot calves, decreasing growth rate and increasing required days on feed.
- Morbidity caused by BRD has been associated with decreased hot carcass weight and poor carcass characteristics.
- Acute phase protein production in the liver, initiated by proinflammatory cytokines, may shift the priority for amino acid and energy use by the host animal during periods of sickness.
- Nutrient requirements for stressed calves seem to be the same as for nonstressed calves; however, nutrients should be concentrated early in the receiving period to account for low dry matter intake.

Keywords: Acute phase response, Feedlot cattle, Inflammation, Nutrient requirements, Stress

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Introduction

The bovine respiratory disease (BRD) complex is the major cause of morbidity and mortality in growing and finishing cattle. BRD is a multifaceted disease generally caused by a combination of stress and viral and bacterial infections. The primary stressors encountered by calves during the marketing process include removal from dam, feed and water deprivation, exposure to new animals and pathogens, and castration/dehorning.[1] These stressors can weaken the immune system and allow infection to occur. The major viruses normally involved in BRD are infectious bovine rhinotracheitis virus, bovine viral diarrhea viruses (BVDVs), parainfluenza type-3 virus, and/or bovine respiratory syncytial virus (BRSV). Viruses can weaken the immune defenses and allow secondary infection by bacteria to occur in the lungs of the compromised calf. Bacteria most commonly isolated from lungs of calves infected with BRD are *Mannheimia haemolytica*, *Pasteurella multocida*, *Histophilus somni*, and *Mycoplasma bovis*. Bovine viral diarrhea virus has been isolated alone or in combination with other viral and bacterial pathogens in animals diagnosed with BRD. Cattle persistently infected with BVDV have been reported as the main source of disease transmission in feedlot settings,[2] and the presence of an animal persistently infected with BVDV in a feedlot pen has been reported to increase the risk of antimicrobial treatment of BRD by 43% compared with nonexposed cattle.[3]

The impact of BRD on nutrient requirements has been studied and debated for many years. Because nutrition and stress are interrelated, it is important to consider how both can be managed to minimize the potential impact of BRD on animal health and performance. Stress can produce or aggravate nutritional deficiencies, and nutritional deficiencies can produce a stress response. Because stress can alter the steady state of the body and challenge physiologic adaptive processes,[4,5] management of stress in cattle should involve removal of the cause of stress, and management of the physiologic changes observed in animals caused by stress. Theoretically, meeting nutrient requirements of calves should help them overcome the physiologic changes associated with stress. In contrast, it has become clear through several experiments that, after calves get sick, the economics of all subsequent segments of the beef industry are negatively affected.[6–12] These experiments have compared the economics and performance of cattle that become sick and require treatment with those that remain healthy throughout the growing and finishing phase. Results consistently show that, if an animal gets sick, the combination of mortality, medical costs, decreased performance, and poorer carcass quality results in decreased net returns for morbid calves compared with calves that remain healthy throughout the growing/finishing phase of production.

Calves of known origin and background or preconditioned calves, where health management practices (*e.g.*, dehorning, castration, vaccination, and weaning at least 30 days before transport) are known, have decreased risk for BRD compared with market-sourced calves with unknown history. Step and colleagues[13] reported that newly weaned calves shipped directly from a ranch to a receiving facility and maintained separately showed less morbidity, lower health cost, and greater daily gains than calves purchased from multiple sources and commingled before shipment. Health costs and daily gains from commingled groups made up of freshly weaned calves shipped immediately from the ranch and market-sourced calves were not different from market-sourced calves that were not commingled. However, compared with ranch calves weaned and then immediately shipped or market-sourced calves, this experiment indicated that weaning calves for 45 days on the ranch of origin before shipping resulted in less morbidity and lower medicine costs when they arrived at the receiving facility whether they were maintained separately or commingled with market-sourced calves.[13]

Preweaning interventions can also provide potential benefits. Creep feeding or limit feeding calves for 6 to 8 weeks before weaning seems to have economic benefits compared with a program in which calves are weaned and fed ad libitum for 4 weeks before marketing.[14] Whether ranch sourced, preconditioned, or market-sourced calves are purchased, the objectives of the receiving health and nutrition program are to assist the calf in recovering from stress, optimize the immune response, and shorten the time to begin productive weight gain during the next phase of production.

Stress effects on nutrient metabolism

Inflammation resulting from BRD or other diseases or injury serves to protect tissues, which maintains homeostasis and supports animal survival. However, sustained stimulation of the inflammatory response impairs normal growth and development, and may prevent an animal from attaining its full genetic potential for growth and carcass merit. Direct interactions between proinflammatory molecules and muscle, fat, mammary, and intestinal epithelial cells result in modifications of their metabolic and anabolic functions. When viral and bacterial pathogens, trauma, or stress overcome host defenses, the innate immune system initiates a rapid and systemic acute phase response (APR). Molecules from pathogens are detected by toll-like receptors, which stimulate the production of proinflammatory cytokines (*e.g.*, tumor-necrosis factor-alpha, interleukin [IL]-1a, IL-1b, IL-6) and leads to an APR, fever, anorexia, muscle catabolism, coagulation, increased glucocorticoid hormone levels, changes in liver protein synthesis, and leukocytosis.[15–17] Although such a response is invaluable to the health of the animal, it can have consequences for growth and other physiologic outcomes. A sustained systemic immune response can increase risk of sepsis, organ failure, and mortality.[18,19]

The APR provides an early nonspecific defense against pathogen challenge through a process that involves metabolic changes.[20] As part of the early defense mechanism, acute phase proteins (APP) are produced in the liver.[21,22] APP production is initiated by proinflammatory cytokines.[23] In addition, Cooke and Bohnert[24] showed that increased circulating levels of cortisol resulted in increased levels of IL-6 and haptoglobin (Hp), indicating that the APR can be activated by systemic increases in the stress marker cortisol. As a component of the APR, the liver alters metabolism to increase or decrease the production of APP. The increased demand for amino acid (AA) for production of APP by the liver is likely supplied by muscle protein catabolism and subsequent AA uptake by the liver.[25] In addition, the liver provides energy substrates to the peripheral tissues in exchange for the AA substrates needed for protein synthesis. Whether the negative impact of BRD on growth could be prevented by supplying the proper array of AA and energy substrate to meet demands of the liver during inflammation needs further study.

It is unclear how or whether an APR can negatively affect long-term growth and carcass characteristics. Berry and colleagues[26] observed sustained increased Hp levels in calves requiring multiple treatments for BRD. Hp levels remained high for 28 days, indicating that calves receiving multiple treatments experience a sustained APR. In contrast, Burciaga-Robles and colleagues[27] showed a short APR in a BRD challenge model. There is limited information regarding APP levels or the APR throughout for multiple treatments for naturally acquired BRD and subsequent harvest. Because the APR can be stimulated by cortisol,[24] it might be difficult to distinguish between increased levels of APP in response to animal handling or other stressors versus increased levels caused by illness. It is clear that increased APP levels are associated with decreased daily gain,[28,29] and the APR and inflammatory responses, regardless of initiator, alter metabolic function in a variety of tissues.

Cattle are different from other species in that Hp and serum amyloid A (SAA) are the major APPs with levels that are observed to increase during infections.[16,17] Changes in Hp levels have been observed caused by several bacterial and viral infections, including *M haemolytica* and *P multocida*, BVDV, and BRSV, all of which are common BRD pathogens.[17,20] In addition, SAA is a second definitive positive APP in cattle and levels have been shown to be increased during acute inflammation and BRD.[30,31] The significant changes in protein synthesis that occur in the liver likely modify AA requirements for the host animal. Waggoner and colleagues[32] challenged beef steers with endotoxin, and plasma concentrations of isoleucine and leucine decreased 4 hours after infusion with lipopolysaccharide compared with unchallenged controls. Reeds and colleagues[33] α-glycerophosphate, α_1-antitrypsin, SAA, and Hp) and muscle protein and calculated that the demand for the aromatic AAs (*i.e.*, phenylalanine, tyrosine, and tryptophan) would lead to more than twice the amount of AA in skeletal muscle needed to be mobilized to accommodate APP synthesis. This need for specific AAs indicates the detriment that an APR may have on muscle in beef cattle with BRD. Future research is needed to describe changes in liver and peripheral tissue metabolism in calves affected by BRD and the immunologic signals that are responsible for long-term growth impairment and potential changes in carcass composition.

Influence of nutrition on bovine respiratory disease

A consistent response in stressed calves that show clinical signs of BRD is a decrease in dry matter intake (DMI). In addition, technologies that allow the determination of feeding behavior have shown that changes in patterns of feeding behavior and DMI are good predictors of calves that will be treated for BRD.[34,35] Feed intake by lightweight stressed calves averages only 1.5% of body weight (BW) during the first 2 weeks after arrival to a feeding facility[36,37] (**Table 1**). In a summary of 18 experiments involving transit-stressed calves, 83.4% of morbid calves and 94.6% of healthy calves had consumed any feed by day 7 following arrival to the feedlot.[36] In addition, measured DMI of morbid calves was 58%, 68%, and 88% of healthy calves across days 1 to 7, 1 to 14, and 1 to 56, respectively. Similarly, Sowell and colleagues[38] observed that 94% of calves identified as healthy and 87% of morbid calves visited the feed bunk on the day of arrival, and 100% of healthy calves and only 91% of morbid calves had visited the bunk by day 3. In a second experiment,[38] only 13% and 10% of healthy and morbid calves, respectively, visited the feed bunk on day 1. All healthy calves had visited the bunk by day 4, but only 76% of morbid calves were observed at the feed bunk. In both experiments, healthy calves had more overall feeding events per day and spent more time at the bunk daily than morbid animals, both during the first 4 days and throughout the 32-day experiment. Total calves identified as sick were 52% in experiment 1 and 82% in experiment 2,[38] which likely explains the greater variation in feeding behavior. In both experiments, 80% of morbid calves were identified within 10 days of arrival.

It is apparent that newly received, highly stressed calves consume less feed than healthy calves exposed to fewer stress factors. As such,

Table 1. Dry matter intake (percentage of body weight) of newly arrived calves transported from Tennessee to Texas

Days After Arrival	*Healthy Calves*	*Sick Calves*
0–7	1.6	0.9
8–14	1.9	1.4
15–28	2.7	1.8
28–56	3.0	2.7

current recommendations are for nutritionists to increase the density of nutrients in diets of stressed calves so that animal requirements for nutrients are met even when intake is low.[39] In commercial settings, it is unclear whether disease causes decreased intake or decreased intake is responsible for disease incidence. After recovery, DMI may remain low or be similar compared with nontreated animals. However, there is evidence that, on recovery, morbid animals experience compensatory gain compared with nontreated animals. This compensation may be caused by recovering gastrointestinal fill or reduced competition for nutrients when cattle are moved from preconditioning pens to pasture[40] or are adapted to a finishing diet.[41] McBeth and colleagues[41] segregated heifers by the number of BRD treatments (0 or 1) administered during a 42-day preconditioning period and observed subsequent finishing performance. At the beginning of the finishing phase, no difference in BW between healthy and morbid steers existed. However, daily gain was increased 14.4% and 5.8% for treated heifers during day 0 to 28 and day 0 to 112, respectively. Although DMI was not different at any time during the 140-day finishing period, the increase in daily gain resulted in treated heifers being more efficient during the first 28 days on feed. An experiment by Holland and colleagues[42] showed that receiving-phase and overall (arrival to end) daily gain were 59% and 8.7% lower, respectively, for heifers treated 3 times for BRD compared with heifers that remained healthy throughout the feeding period. After the low growing phase gain by morbid animals, a compensatory response occurred in those animals, such that overall finishing-phase daily gain was similar across BRD treatment categories, and feed efficiency was improved. Therefore, segregation according to previous number of BRD treatments during finishing may result in a compensatory response in daily gain and improved feed efficiency for treated animals. Similar results were observed by Wilson and colleagues.[43] Although increased days on feed may be required to reach similar final BW and carcass characteristics, a restart program may be a viable alternative to realizing or railing animals treated multiple times for BRD.

Energy concentration and source

Energy deficiency in cattle can severely depress the immune system[44]; however, excess dietary energy can also have detrimental effects. Feedlot studies suggest that the incidence of BRD in market-transport stressed calves is increased when the diet contains more than 60% concentrate. Although it is unlikely that the energy concentration of the diet is excessive in most receiving diets, it is possible that an energy deficit could occur because of poor forage quality and/or an inadequate supply of forage. Lofgreen[45,46] reported that calves fed low-quality hay diets on arrival were not able to compensate for their lost early weight gain later in the feeding period.

A series of experiments with market-stressed calves was conducted to determine optimal dietary energy concentrations of receiving diets.[47] In experiment 1, diets with concentrations of 0.84, 1.01, and 1.10 Mcal/kg of net energy for gain (NE_g) (dry matter [DM] basis) were fed for 29 days followed by all treatment groups being fed the 1.01 Mcal/kg of NE_g diet for an additional 34 days. Calves received on the intermediate-energy and high-energy dietary treatments consumed more feed and gained more weight during the 29-day receiving period, with the calves consuming 1.10 Mcal/kg of NE_g gaining more than the intermediate-energy treatment group at similar DMI. Calves on the high-energy and low-energy diets had lower morbidity rates than calves on the intermediate-energy treatment. Given the outcome of this study, Lofgreen and colleagues[47] replaced the 0.84 Mcal/kg of NE_g diet with a 1.19 Mcal/ kg NE_g diet to determine whether gain would increase further with increased dietary energy concentration. Intake decreased when the higher-energy diet was added and daily gain was not increased. In contrast with the previous study, calves on the 1.10 Mcal/kg of NE_g diet consumed more feed than calves on the 1.01 Mcal/kg of NE_g diet. Morbidity tended to increase with increasing energy concentration.

Fluharty and Loerch[48] fed corn silage–based diets with 1.15, 1.21, 1.25, or 1.30 Mcal/kg of NE_g to individually housed steers in a 28-day receiving study. There was a linear increase in DMI with increasing dietary energy concentration but there was no difference in daily gain, feed efficiency, or health status for the 28-day period. Similarly, DMI was improved and daily gain was not different between high-energy (1.17 Mcal/kg NE_g) and low-energy (1.01 Mcal/kg NE_g) diets in a 28-day preconditioning study conducted by Pritchard and Mendez.[49] Berry and colleagues[50] attempted to sort out the confounding effects of roughage and energy concentrations by feeding high-starch and low-starch concentrations within each of 2 dietary roughage concentrations. Energy concentration did not influence performance or overall morbidity, but morbid calves fed diets with the greater concentration had less shedding of *P multocida* and *H somni* than those fed the lower-energy diets. Dietary roughage concentration varied over a narrow range of 35% to 45% in the Berry and colleagues[50] study, and therefore comparison with results from experiments with greater variation in roughage/energy concentration is difficult. Rivera and colleagues[51] analyzed data to evaluate relationships between BRD and dietary roughage concentration in lightweight, stressed cattle. Diets ranged from all-hay to 75% concentrate. Morbidity (*i.e.*, percentage of calves treated for BRD using visual observation and rectal temperature) decreased as dietary roughage concentration increased [morbidity, % = 49.59 (0.0675 roughage, %); *P* 5 .003]. Average daily gain and DMI were decreased by increasing the dietary roughage concentration. In addition, economic analysis indicated that the slightly lesser morbidity noted with greater roughage concentrations would not offset the loss in profit resulting from decreased average daily gain. Rivera and colleagues[51] concluded that milled diets with greater levels of concentrate would provide the optimal receiving diet for lightweight, highly stressed, newly received cattle, with limited effects on BRD. Grain type used in receiving diets does not seem to affect calf health or performance.[39] Spore and colleagues[52] reported that limit feeding high-energy rations based on low-starch corn by-products such as Sweet Bran (Cargill Corn Milling, Blair, NE) resulted in greater feed efficiency without affecting health of newly received, stressed cattle. Limit feeding a high-energy diet (1.32 Mcal of net energy [NE]/kg of DM) containing 40% Sweet Bran during the receiving and growing phase improved feed efficiency by 22% compared with a low-energy diet (0.99 Mcal of NE/kg of DM) fed *ad libitum*.

Protein concentration and source

Dietary protein requirements for beef cattle can be calculated using the National Academies of Sciences, Engineering, and Medicine (NASEM)[39] metabolizable protein model, which integrates BW and energy intake. Energy intake is the first-limiting nutrient involved with weight gain; therefore, protein deposited in gain largely depends on energy intake.[53] Because newly received stressed calves often have very low intakes during the first few days, protein requirements might be low. Requirements would then increase as energy intake increases.

Effects of various protein levels and sources for newly received calves have been characterized. Galyean and colleagues[54] fed 3 levels (12%, 14%, or 16%) of supplemental crude protein (CP) from soybean meal to 120 calves (185 kg) in a 42-day receiving experiment. Daily gain increased and DMI tended to increase linearly with increasing CP concentration. Morbidity was higher for calves fed the high-protein diet compared with the 14% CP diet. Fluharty and Loerch[55] conducted a series of experiments to access protein requirements of newly arrived cattle. In experiment 1, newly weaned Simmental x re fed increasing CP concentrations (12%, 14%, 16%, or 18%) from spray-dried blood meal or soybean meal. Feed efficiency improved linearly with increasing CP concentration for the first 7 days and for the entire 42-day feeding period. Daily gain increased linearly with increasing CP concentration during the first week after arrival. For the entire receiving period, calves fed the blood meal diets had a 7.4% increase in gain compared with calves fed the soybean meal diets. Similar to data reported by Galyean and colleagues,[54] morbidity also increased linearly with increasing CP concentration, with cattle on the 12%, 14%, 16%, and 18% CP diets experiencing 38%, 50%, 45%, and 68% morbidity, respectively. A second experiment was conducted in which 246-kg Simmental Angus steers were fed 11%, 14%, 17%, 20%, 23%, or 26% CP diets with protein supplied by spray-dried blood meal or soybean meal.[55] DMI was not affected by CP concentration. Daily gain and feed efficiency both responded quadratically, with the 20% CP diet yielding the greatest performance. There were no differences in health status between treatment groups. In a summary of several experiments, Galyean and colleagues[56] noted that, as the protein concentration in receiving diets increased up to approximately

20% of DM, animal performance improved, but the incidence of BRD increased slightly. Cole[14,57] suggested that a CP concentration of approximately 14.5% is optimal for newly received calves and would meet their protein requirements.

Pritchard and Boggs[58] indicated that dried distiller's grains could effectively replace soybean meal as a protein supplement for incoming feedlot cattle. Morbidity rates in their study were very low (<3%). Van Koevering and colleagues[59] reported that replacing soybean meal with dried distiller's grains in a receiving supplement decreased performance but did not affect the incidence or severity of BRD.

In general, young calves have a limited capacity to use dietary urea. The NASEM[39] suggests that intakes of 30 g/d can be tolerated by stressed calves during the first 2 weeks of feeding. The use of ingredients high in ruminally undegraded protein (RUP) has been beneficial in some studies with calves on forage-based diets. It seems that RUP concentrations of 5.4% of dietary DM are generally adequate for stressed calves.[39]

Minerals

Because of low feed intakes, the concentrations of most minerals need to be increased in receiving diets. However, with the possible exception of K, the mineral requirements (*i.e.*, grams per day) of stressed calves do not seem to be increased.[56]

Cu, Zn, and Se have been shown to be essential for optimal immune function. Although several studies have reported a beneficial effect of supplemental Cu, Se, and Zn on some indicators of immune function, data have been inconsistent, and few studies have shown a positive effect on animal health or performance when the control diet was not deficient in these minerals. In general, beneficial effects of supplementing these trace minerals on immunity or the incidence of BRD in beef calves would most likely occur in animals with marginal or deficient mineral status. Because the mineral status of calves is rarely known, it is advantageous to supplement with these minerals, especially because most forages are marginal or deficient in at least 1 of these minerals or contain increased concentrations of antagonists, such as Mo and S. However, feeding excessive quantities of the trace minerals may not be helpful and is potentially harmful. A good rule of thumb is to provide 50% or more of mineral requirements in the daily supplement.

Although some studies have reported improved immune responses when calves were supplemented with organic forms of Cu, Zn, Se, or Mn (proteinates, AA complexes, and so forth), other studies have reported no effect.[1,56] Garcia and colleagues[60] reported that varying level and source of trace minerals did not affect growth performance or morbidity in newly received cattle, and Ryan and colleagues[61] reported that source of Cu, Zn, and Mn had no effect on growth performance, morbidity, average antibiotic cost, plasma Cu and Zn concentrations, or antibody titer response to bovine viral diarrhea virus vaccination in shipping-stressed cattle over a 42-day to 45-day backgrounding phase. Supplying minerals in an AA-chelated form reduced the number of treatments required for morbid calves to recover from BRD compared with a complex mineral form, although morbidity and mortality did not differ.[62] In addition, an injectable trace mineral did not improve performance or morbidity when the incidence was low.[63]

The NASEM[39] noted that results of recent experiments indicate a need for supplemental Cr in some situations. Reports by Chang and Mowat[64] and Moonsie-Shageer and Mowat[65] indicated that BW gain by feeder calves was increased by supplements of 0.2 to 1.0 mg of Cr per kilogram of diet. The effect on morbidity was inconsistent. Bernhard and colleagues[66] fed 221-kg steers 0, 0.1, 0.2, or 0.3 mg/kg of Cr (DM basis) from Cr-propionate. Cr-supplemented steers had improvements in DMI, feed efficiency, and daily gain within the first 28 days of the experiment, when cattle would have been under nutritional and physiologic stress. Through the remainder of the experiment, Cr-supplemented steers maintained these advantages.

Vitamins

Experiments with B-vitamin supplementation to newly weaned/received cattle have resulted in variable responses, with decreased morbidity and increased performance in some studies and little or no response in others.[14] In a review of several experiments, Cole[14] noted a 3% decrease in BRD morbidity, a 4.2% increase in BW gain, and a 5.1% improvement in feed efficiency with supplemental B vitamins.

Supplemental vitamin E in receiving diets seems to be beneficial for decreasing morbidity and improving performance. Several studies with feedlot diets suggest that feeding vitamin E in excess of requirements may be beneficial to animal health. In general, results have been better when vitamin E was fed than when it was injected.[14,57] In a summary of results of cattle feedlot receiving studies, Elam[67] noted that, as vitamin E supplementation increased from 0 to 2000 IU/d, BRD decreased 0.35% for every 100-IU increase in vitamin E intake. Results with supplementation of other fat-soluble vitamins have been inconsistent.[14]

Duff and Galyean[1] concluded that, with the possible exception of K, the stressors of weaning, marketing, transport, and disease do not seem to increase total nutrient requirements of calves. However, because of low feed intakes, the concentrations of nutrients in the diet need to be increased to meet the nutrient requirements of the animals (**Table 2**).[14,39,57]

Table 2. Recommended nutrient concentrations in diets for stressed calves (dry matter basis)

Nutrient	*Concentration*	*Comments*
Dry Matter (%)	80–85	Limit extreme high-moisture feeds
NE_m (Mcal/kg)	1.3–1.6	Higher first 7–14 d
NE_g (Mcal/kg)	0.8–0.9	Higher first 7–14 d
CP (%)	12.5–14.5	Limit urea to <30 g/d
Ca (%)	0.6–0.8	—
P (%)	0.4–0.5	—
K (%)	1.2–1.4	Avoid high Cl levels
Na (%)	0.2–0.3	Check water
Mg (%)	0.2–0.3	—
S (%)	0.15–0.25	Check water
Mn (ppm)	40–70	—
Co (ppm)	0.1–0.2	—
Cu (ppm)	10–15	Higher if high S or Mo
Fe (ppm)	100–200	—
Zinc (ppm)	75–100	—
Se (ppm)	0.1–0.2	—
Vitamin E (IU/d)	400–500	Concentrate if pelleted

Summary

Nutritional management of newly received calves is key to recovery from stressors associated with weaning and marketing. Because of low initial intakes, nutrient deficiencies are difficult to meet and may limit the recovery process. More nutrient-dense diets should be formulated to aid calves in recovery, although it may take several days to return stressed calves to positive energy and protein balances. If deficiencies can be compensated for, energy and protein source seem to have minimal impact on health and performance of newly received, stressed calves. However, continued research in the area of nutrient requirements of calves facing immune challenges could prove beneficial in formulating nutritional management plans for stressed calves. This outcome would be especially beneficial for meeting nutrient/metabolic requirements during an APR, with potential consequences for long-term outcomes.

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