Influence of Pre-partum Nutrition on Measures of Health and Productivity of Offspring

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Introduction

In recent years increasing interest has been placed on the influence of maternal nutritional status during gestation and subsequent consequences on the offspring. These efforts have been viewed in both man and animals. Certainly, the importance of some of these nutritional impacts have been realized for many years, like the emphasis of prepartum folic acid nutrition and the resulting decrease in birth defects in children. However, how might prepartum nutrition impact the productivity of animals, specifically livestock?

In human and rodent models this area of study has created the term "fetal programming". In essence, fetal programming is described as a specific prepartum insult that may result in altered or compromised health and productivity of the offspring. The coining of this term has caught the attention of many research groups. As I examined current literature on this topic, I was surprised to find that a www.pubmed.com search of "fetal programming" resulted in 580 different documents. Within this list, nearly 90% have been published in the past 10 years. The term "programming" is also present in the mainstream press. During a recent flight I picked up the carrier's company magazine (Continental.Com Magazine, Gene Genie, January 2006). In that issue I read an article describing the impact of nutritional "programming" on longevity in rodents and humans. This is certainly a young area of research, rich for investigation; however, much of the current data relates to the consequences of fetal programming on subsequent incidences of cardiovascular disease and blood pressure (Langley and Jackson, 1994; Godfrey and Barker, 2000) or diabetes (Desai et al., 1995). Identifying economically influential impacts of fetal programming in livestock species is less compelling, but nonetheless interesting as a potential research topic.

In this specific area of investigation, our program has focused its efforts on research directed toward the significance of maternal nutrition on post-partum anestrus and pregnancy. In essence, we have not considered subsequent impacts on offspring health and productivity. Specifically, our research efforts have focused on management systems that would provide adequate supplementation to hasten post-partum interval and improve pregnancy of cows, but could these periods of nutritional restriction be impacting the productivity of offspring? As I considered the significance of this topic in cattle, I initially felt the impact to be of limited economic significance. My reasoning relates to an important difference shared among production systems involving beef and dairy cattle, which differs from all other food animal livestock enterprises. Unlike swine, poultry, and even beef feedlot systems, cow-calf and dairy production systems rely on an annual fluctuation in quality and quantity of nutritional assets available to the cow (beef cows) and the level of nutrient loss through the production of milk (beef and dairy cows). These fluctuations result in an expected annual change in cow nutritional status and production level. These conditions, therefore, result in annual fluctuations in cow body condition. Some or all nutrients may be deficient in a cow's diet at certain times of the year, but I question whether these conditions impact the health and productivity of the developing offspring. Nevertheless, in certain events, which may be unique or extreme in nature, prepartum nutritional insults may indeed create situations where the health and performance of the offspring could be compromised. I will attempt to address some examples in this paper.

Energy, Protein, and General Dietary Restriction

In livestock, one of the most studied outcomes of this research area is related to birth weight. One commonly reported study addressing this topic found that nutritionally restricted beef heifers gave birth to lighter calves, although calving difficulty was not impacted (Corah et al., 1975). Interestingly, up to the time of weaning, these lighter calves never caught up to their contemporaries born to dams provided adequate prepartum nutrition. This response may be the result of a lighter initial body weight or a lesser milk production observed in nutritionally restricted dams. Further, calves born to nutritionally restricted dams were more likely to die prior to weaning, suggesting a decrease in calf vigor or viability. In another study (Prior and Laster, 1979), variations in prepartum dietary energy did not impact fetal calf development. The differing results of these two studies are likely related to the degree of nutrient restriction imposed.

This decrease in calf vigor may be explained in part by a reduced ability to generate heat in calves born to undernourished dams. In one study (Carstens et al. 1987), calves born to dams that were protein restricted during gestation were found to have a lesser ability to generate body heat. This response was also related to calf body weight, whereas lighter calves produced less body heat than larger calves. This altered ability to produce adequate body heat may make these calves more susceptible to common environmental stressors. Interestingly, the altered ability to produce body heat might not be associated with brown adipose fat, an important thermoregulatory tissue for newborn calves (Smith et al., 2004); because further studies have shown that protein-restricted diets did not alter the amount or composition of this unique fat reserve (Martin et al., 1997).

Both the availability and quality of nutrients vary seasonally for grazing animals. Generally, grazing animals require nutrient supplementation during at lease some months of the year or they will experience body weight loss and potential reductions in fertility. These instances of nutrient restriction may have an important influence on subsequent developmental outcomes of the offspring. Vonnahme et al. (2003) reported that ewes provided a nutrient-restricted diet during early gestation (day 28 to 78) had smaller fetuses compared to ewes maintained on a nutrient-adequate diet. In contrast, Wallace et al. (1999) found that ewes maintained on a high vs. moderate plane of nutrition during the second and third trimester had shorter gestational length and reduced fetal placental weight. These authors concluded that rapid growth rates of pregnant adolescent ewes, as a result of a high plane of nutrition, results in restricted placental growth and reduced birth weight.

Protein restriction does appear to impact the cow and fetus differently (Du et al., 2005). In a gestating cow study, both dam and fetus experienced reduced protein synthesis of skeletal muscle when the dam was provided a protein-restricted diet. Indices of protein degradation of skeletal muscle were only evident in the dam, not the fetus, suggesting differential impacts of the dietary insult. In another study by the same researchers (Du et al., 2004), nutrient-restricted cows were found to have lesser calpastatin activity compared to control cows provided a nutrient adequate diet. In contrast, muscle calpastatin activity of calves was found to be greatest in those gestated by nutrient-restricted versus nutrient-adequate dams, suggesting the existence of a protective mechanism to preserve fetal muscle development in a nutrient restricted dam. Indeed, although cow carcass weight and longisssmus muscle area were less in nutrient restricted versus nutrient adequate dams, there were no differences in measures of body and carcass weight of the fetus (Table 1).

Table 1. Carcass characteristics for cows and fetuses[a]

	Nutritional treatment			
Item[b]	Control	Restricted	SEM	P-value
Cows				
Carcass weight, kg	858	697	28	< 0.001
LM[c] area, cm^2	72	60	2	0.016
Fetuses				
Body weight, g	948	884	27	0.158
Carcass weight, g	730	692	21	0.188

[a]Obtained from Du et al. (2004).
[b]Carcass weights of cows obtained following removal of head, skin, and organs; fetal carcass weight determined after removal of organs.
[c]LM = longissmus muscle.

Pre-partum nutritional programming may also impact reproductive development of offspring. An excellent review of this topic is provided by Rhind et al. (2001). In their manuscript, the authors describe several examples of how the nutritional status of the dam during varying stages of gestation may impact the development of the offspring’s reproductive system.

Micronutrients

There are numerous research examples that link prepartum micronutrient nutrition to viability of rodent offspring. One of the most studied micronutrients is zinc and a comprehensive review of the literature is available (Keen and Hurley, 1987). Inadequate maternal zinc nutrition results in embryonic (Mieden et al., 1986) and fetal (Hurley, 1981) abnormalities. Additionally, rats born to dams provided a mineral-restricted diet have been shown to have increased body fat compared to rats born to dams consuming a mineral-adequate diet (Venu et al., 2004). Prior to parturition, dams fed the mineral-restricted diet had lesser plasma iron, zinc, magnesium, and hemoglobin concentrations, a greater abortion rate, and a lesser pup birth weight compared to rats provided a mineral-adequate diet.

In my opinion, one of the most intriguing research results related to this topic is a mouse study linking prepartum zinc deficiency to immunodeficiency in offspring over several generations (Beach et al., 1982). In that study, offspring of parent mice fed a diet deficient in zinc experienced a marked reduction in lymphocyte responsiveness and immunoglobulin formation to antigen challenge. Although to a lesser extent, the second and third generation of offspring also experienced similar immunodepression. The authors designed the study well, whereas the mice pups were fostered onto parents receiving the control diet to eliminate the influence of consuming a zinc-deficient milk diet (Dorea, 1993). I am unaware of similar research findings in livestock species.

Pre-partum micronutrient nutrition may also impact the immune competence of offspring through alterations in the trace mineral and immunoglobulin composition of colostrum (de Toledo and Perry, 1985; Mahan, 2000). This would not be considered an impact of fetal programming, *per se*, but may likely be an important component of prenatal nutrition on postnatal health and performance. In one study, prepartum injectable selenium was found to increase immunoglobulin-M concentrations in the colostrum of sows (Table 2; Hayek et al., 1989), while dietary selenium increased immunoglobulin-G in the colostrum of cows (Awadeh et al., 1998).

Table 2. Effect of prepartum selenium injection on sow immunoglobulin (Ig) content in colostrum[a]

	Treatment[b]		
Ig Class	Control	Selenium	SEM
IgA	13.8	14.5	1.9
IgM	8.4	10.0	0.8
IgG	54.0	64.3	7.0

[a]Data derived from Hayek et al., 1989.
[b]Treatments provided to sows at 100 days of gestation. The study also contained a Vitamin E injection treatment, which did not significantly impact Ig concentration of colostrum.
Units of measures were not provided, but we assume they are mg/mL.

In terms of copper nutrition, our group has attempted on two occasions to create a model whereas copper-deficient dams would give birth to copper-deficient offspring. Both attempts were unsuccessful. Although moderate to severe copper deficiency was achieved in the dams, the calves were born in adequate copper status. These findings suggest that the cow has an ability to pull minerals from nutrient reserves to support the mineral status of the developing fetus at the expense of her own mineral nutritional needs. Similar results have been shown in horses (Gee et al., 2000), whereas maternal copper status had no impact on subsequent copper status of the newborn foal.

Unlike copper, prepartum selenium nutrition has often been shown to significantly impact the selenium status of offspring in cattle. Research in this area has provided important management considerations for the control of "white muscle disease" in calves, which is a condition linked to selenium deficiency. In one study, selenium supplementation to deficient cows resulted in significant increases in the selenium status of the offspring (Enjalbert et al., 1999; Table 3).

Table 3. Effect of late gestation selenium (Se) supplementation to Se-deficient beef cows on cow and calf red blood cell Se status[a]

Se, mg/d[b]	Cow, initial	Cow, day 15	Calf, day 15
	------------------- U / g of hemoblobin -------------------		
13.0	2.33	122.4	186.2
32.5	1.67	161.7	236.1
45.5	5.30	197.8	378.8
SE	1.14	14.4	15.2

[a]Derived from Enjalbert et al., 1999.
[b]Selenium supplemented to cows for 15 days during late gestation

Although these results are intriguing, rats and mice are not livestock species. In nearly all of the rodent studies reviewed, the authors utilize a purified or semi-purified diet to achieve the physiological responses reported. These types of diets are impractical and certainly not applicable to normal livestock production systems. This unique dietary model is important when considering the significance of research outcomes derived from rodent versus livestock species.

Environment

Pre-partum environmental impacts on birth weight have been examined in livestock, rodents, and humans. A commonly cited research effort in beef cattle was conducted by Ferrell (1991). In that study, embryos derived from Brahman and Charolais donor cows were transferred into both Brahman and Charolais recipient cows in a 2 x 2 factorial arrangement of treatments. By day 274 of gestation, Charolais fetuses carried in Charolais recipient cows were heavier in than both Charolais and Brahman fetuses carried in Brahman cows (Table 4). These results suggest that the maternal environment is able to program fetal growth, thus impacting birth weight in cattle.

Temperature is another environmental factor that has been shown to impact birth weight in livestock. For example, it is a widely observed phenomenon that calf birth weight in the seasonally warm climate of Florida is lesser than birth weights from cattle of similar genetics in a temperate climate. It appears however that this environmental impact may be altered by management. Collier et al. (1982) showed that birth weight of Holstein calves could be lessened in Florida by the provision of shade during the later stages of gestation. This response is likely due to a reduction in uterine and umbilical blood flow during gestational exposure to increased environmental heat (Reynolds et al., 1985), which may contribute to a reduction in nutrient transfer to the developing fetus.

Table 4. Fetal weight of Charolais and Brahman calves gestated in both Charolais and Brahman recipient cows.

Fetus Breed	Recipient breed	Fetus wt (232 d)	Fetus wt (274 d)
		---------------------- kg	----------------------
Charolais	Charolais	22.4	46.9
Charolais	Brahman	23.7	33.9
Brahman	Brahman	13.2	25.5
Brahman	Charolais	12.9	27.6

Table adapted from Ferrell (1991).

In contrast to high heat environments, birth weights are typically increased when the dam experiences cold temperatures during gestation. In one study (Thompson et al., 1982), ewes exposed to chronic cold stress during the final six weeks of gestation gave birth to heavier lambs compared to ewes gestating in a thermoneutral environment. In an accompanying study the authors found that fetal blood glucose concentrations increased when ewes were exposed to acute cold stress. The authors conclude that gestating ewes are able to repartition nutrients from dam to fetus in response to cold stress. This effect may be responsible for the observed increase in birth weight.

In the field of embryo transfer it is evident that additional environmental factors can also contribute to viability of the offspring. An example of this is the condition known as the 'Large Offspring Syndrome" in embryo transferred cattle. This condition appears to be related to environmental factors associated with the process of embryo transfer (i.e. culture media) and not the recipient dam (Young et al., 1998).

Concluding Remarks

In nearly all livestock management systems occurring in the developed world, the influence of minor prepartum nutritional deficiency will unlikely result in a noticeable impact on offspring health and performance. However, there continues to be a growing body of evidence supporting the potential link for unique nutritional circumstances to impacts on offspring viability. We believe this impact may be most pronounced in the deficiency or toxicity of microminerals. These events are not easily recognizable in the dam as they seldom impact cow body condition as is usually evident during a deficiency of energy or protein.

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