

## **Prepartum management and nutrition effects on calf health, growth and future production**

James D. Quigley

Research & Technical Manager

Cargill

### **Introduction**

The concept of epigenetics, or genetic programming, has taken on considerable interest as an increasing body of research data indicates important effects on animals and their offspring for several generations.

The concept of epigenetics relates to the expression of genes as influenced by the environment (factors other than changes to the underlying DNA sequence). Some of these non-genetic changes are heritable. Thus, these changes in expression of the sequence can pass generations.

### **Physiological basis for epigenetics**

Epigenetic modifications appear to be caused by alterations in gene expression caused by modification in DNA methylation and histone modification. As described by Handy et al. (2011), *“These modifications will alter DNA accessibility and chromatin structure, thereby regulating patterns of gene expression. These processes are crucial to normal development and differentiation of distinct cell lineages in the adult organism. They can be modified by exogenous influences, and, as such, can contribute to or be the result of environmental alterations of phenotype or pathophenotype. Importantly, epigenetic programming has a crucial role in the regulation of pluripotency genes, which become inactivated during differentiation.”*

One of the earliest examples of epigenetic programming were reported during the Second World War. The first of these occurred during the “Dutch Hunger Winter” of 1944-1945 when the population of Western Netherlands was subjected to dramatically reduced caloric intake due to an embargo of supplies into the region.

The Dutch winter was also bitterly cold, which caused further deprivation and stress on the population. During this period, the people of the Western Netherlands were forced to survive on about 30% of the calories of a normal diet. More than 20,000 people died by the end of the German blockade in May, 1945. The effects of the Winter went far beyond the people who suffered deprivation during the war. In fact, children of women born from "Hunger" mothers were affected by the effects of the stress. If the fetus was exposed in mid to late gestation, the

resulting children were smaller with lower rates of obesity and lower glucose tolerance than others in similar demographic profile. Further, the offspring of these children (the grandchildren of the "Hunger" mothers) remained smaller. On the other hand, if the fetus was exposed during early gestation, the resulting children had elevated rates of obesity and altered lipid profiles. They also suffered greater rates of cardiovascular disease as well as reduced cognitive function, especially in later life (Roseboom et al., 2001).

Most researchers have reported on the effects of prepartum nutrition and stress on expression of the fetal genotype, others have suggested that expression of the genotype may also be influenced postnatally, by consumption of colostrum and milk by the neonate. For example, Bagnell et al. (2009) reported that porcine milk contains immunoreactive relaxin that is absorbed into the circulation of the newborn during the colostrum nursing period. The absorbed relaxin may interact with relaxin receptors in the porcine female reproductive tract at birth. It has been hypothesized that the transmission of relaxin via colostrum may influence reproduction in pigs in later life. Others (Van Amburgh et al., 2014) have suggested similar potential in newborn calves, though this concept has not been supported experimentally in at least some studies (Quigley, 2012).

A significant amount of work has been conducted in this interesting area, as the ramifications to on farm management are significant. Here, we will review some more recent studies that suggest the impact of epigenetic programming in animals of agricultural importance.

### **Research with neonates – piglets, beef cattle**

Research with newborn piglets (Tuchscherer et al., 2002) shows the effect of prenatal stress on acquisition of passive immunity very well. In this study, the researchers used 33 Landrace × Duroc sows. Seventeen of these sows were exposed to an acute stress during weeks 12 to 16 of gestation. Sows were stressed by restraining them with a nose sling for five minutes per day between 10:00 and 10:30 a.m. Control sows (n = 16) were not restrained. During the final week of gestation, all sows were moved to farrowing pens and all animals were unrestrained.

Restraining the sows increased concentration of cortisol in their blood. Cortisol concentration in control pigs averaged 34 nmol/ml of serum compared to 112 nmol/ml in restrained sows when measured 10 minutes after the animals were restrained.

Effects of prepartum stress on piglet passive immunity and health were dramatic. Piglets born from stressed sows tended to be more likely stillborn (11.3% of piglets vs. 7.4% in control piglets  $P = 0.18$ ), more likely to have disease and die (by nearly 3×) compared to piglets born to control sows (Table 1).

An interesting observation in this study was that serum IgG concentration was significantly reduced in piglets born to stressed sows. The reduction occurred in spite of the fact that colostrum IgG concentration was unaffected by prepartum stress.

Why would pigs have lower serum IgG concentration at one day of age? The two possible reasons either that piglets consumed less colostrum or they were less efficient in absorbing the colostrum they were fed.

The researchers also reported the lymphocyte proliferation (Table 1 reported as “lymphocyte index”). This index measured the ability of lymphocytes to respond to various antigens (pokeweed mitogen, lipopolysaccharide, and

concanavalin A). At one day of age, lymphocytes from piglets born from stressed sows were less responsive to stressors, indicating that these piglets were more susceptible to disease. Some of these impairments were observed as late as five weeks of age.

These data show clearly that the newborn’s ability to mount an immune response (i.e., the cellular immune response) is very sensitive to events that occur prior to birth. Cellular immunity is an essential part of the overall immune response and, if depressed, will make the newborn animal much more susceptible to disease and death. Thus, if prenatal stress impairs the cellular immune response of newborn animals, poor management during gestation may increase the risk of problems with newborns.

What forms of stress are likely to cause similar responses? Some stressors include heat stress, cold stress, prepartum disease, nutritional imbalance, transport and handling and many others. It’s clear that the latter stages of gestation are critically important to the development of the calf’s immune system and we can impair that development by stressing the cow prior to calving. The research we’ve investigated used sows as the experimental animal. Would we expect a similar response with cattle – beef or dairy? This answer is less clear. There are some data that suggest that stressors can affect calves immunity negatively. For example, Hough et al. (1990) reported that calves fed colostrum from cows that were fed inadequate amounts of nutrition achieved lower serum IgG concentration at 24 hours after birth. Stott (1980) also concluded that stress has been a “ready explanation” for poor IgG absorption in newborn calves. The most likely contribution to this observation is due to prepartum stress in the cow and subsequent effects on the calf.

#### **Effect of pre-partum nutrition on beef cattle**

The first study was conducted at the University of Wyoming (Long et al., 2012). Cross-bred beef cattle were bred artificially and 45 days thereafter, pregnancy was confirmed and the cows were placed into groups – Control (fed at 100% of NRC recommendations), Restricted (fed at 70% of the Control cattle) and R+AA (fed at 70% of NRC but had amino acids to provide the same level of protein/amino acids as

Item	Contro	Stres	P
Stillbirths, %	7.4	11.3	0.18
Disease, %	12.3	28.2	0.000
Died, %	5.6	13.6	0.000
Colostrum IgG, g/L	35.7	38.2	NS
Serum IgG, g/L	46	41	0.01
Lymphocyte Index*	1.9	1.6	0.001

Table 1. Effect of prenatal stress on absorption of IgG by newborn piglets. From: Tuchscherer et al., 2002.

Control cattle). Cows were fed their experimental diets until 185 days of gestation. Thereafter, cows were grouped together and fed the control diet.

Calves born in each group were fed and managed as one group along with their dams until weaning at 214 d and then were backgrounded for 28 d. After birth, calves were raised normally – bull calves were castrated at 2 months of age; weaned at 210 d; and backgrounded for 28 days prior to entering the feedlot for 195 days. Calves were slaughtered and carcass characteristics were determined.

At the end of the experimental period, cows fed the restricted diets without additional amino acids were about 40 kg lighter than control cows and had lower body condition score. Cows fed restricted diet with added amino acids were lighter than control cows, but the difference was not statistically significant.

There was no effect of maternal nutrition on calf BW at birth (average 36, 39, and 41 kg for Control, Restricted + AA and Restricted treatments, respectively) or at slaughter. However, the body composition of calves was affected by the diet of their dams during gestation. Calves fed Restricted (without added AA) had higher yield grades (3.42 vs. 3.01 and 3.03 for Restricted, Control and Restricted + AA, respectively). Beef carcasses are graded numerically on a 1 to 5 scale with 1 being highest quality and 5 lowest quality. More information on how yield grades are determined is available [here](#). Thus, a score of 3.4 would be lower quality compared to a yield grade of 3.0.

In addition, the composition of fat in Restricted calves had increased adipocyte (fat cell) size and composition. Differences in adipocyte composition suggest that the metabolism of calves had changed and calves from nutrient Restricted cows had different metabolism of fat cells. Perhaps this altered metabolism was responsible, in part, for lower carcass quality.

This study suggested that when the dam receives improper nutrition, the metabolism of the newborn can be affected – even much later in life. This interesting study may have important implications to newborn dairy calves, also.

Effects of maternal nutrition on calf growth was evaluated in a second study conducted in Nebraska with grazing beef cattle (Martin et al., 2007). In this 3-year study, cows were fed 0 or 1 lb (0.45 kg/d) of a protein supplement while grazing during late gestation.

Birth statistics (dates, size) of the 170 heifer calves born from supplemented and unsupplemented cows were similar (calves weighed 36 kg at birth). However, BW at 205-days were higher in calves born from dams that received protein supplement (226 vs. 218 kg). Heifers from supplemented cows were also heavier at time of pregnancy diagnosis (400 vs. 386 kg). Also, more of these heifers became pregnant (93%) compared to heifers born from dams that were unsupplemented (80%).

Late gestation nutrient restriction of the mother appeared to have a profound effect on performance of calves – even manifested later in life.

Finally, a study was reported by Laporte-Broux et al. (2011) using dairy goats. Dams were fed control diets (100% of NRC recommendations) or Restricted diets (50-70% of nutrient intake of Control) during the last third of gestation. Restricted goats lost 8% of their BW during the experimental period compared to a loss of 1.3% of BW for Control goats.

Kids born to the Restricted goats were lighter and had smaller abdominal girth than kids born to Control goats. In addition, male kids in the Restricted group used fatty acids differently than other kids,

suggesting an alteration in nutrient metabolism due to maternal diet. However, other tests of behavior and metabolism indicated little long-term effect of maternal nutrient restriction. The researchers evaluated behavioral and metabolic parameters, but few varied between treatments.

The results of this study should be evaluated in context. Newborn kids from Restricted goats were smaller and had higher concentrations of fatty acids in their blood. Clearly, their metabolism differed from kids born from dams on the Control diet. It's possible that kids were not evaluated long enough to see the long-term effects of nutrient deprivation on metabolism. For example, in the Wyoming study, changes in body composition were determined only at slaughter. On the other hand, it's possible that nutrient deprivation during the final trimester of gestation may have less of an effect than earlier nutrient deprivation. However, since most fetal BW is deposited during the final trimester, it's unlikely that nutrient deprivation during this critical time in the development of the fetus wouldn't have an effect.

### Effects of prepartum nutrition on dairy cows

Research by Gao et al. (2012) was conducted with Holstein dairy cows (n = 30) assigned to one of three diets during the last 21 days prior to calving. Cows were assigned to a low energy group (net energy of lactation (NEL) = 5.25 MJ/kg of DM); medium energy group (NEL = 5.88 MJ/kg of DM); and high energy group (NEL = 6.48 MJ/kg of DM). The diets consisted of a combination of straw, hay and grains to attain a CP of 13% of DM and increasing amounts of net energy (Table 2).

Unfortunately, the authors did not report how much each cow was fed, so it's impossible to say exactly the differences among treatments in energy intake.

#### Effects on the cow

Feeding lower energy diets to cows during the last three weeks prepartum had several significant effects on the cow.

Cow BW (Table 3) was not significantly affected by differences in prepartum diet though cows on the high energy diet numerically gained

Ingredient, % of DM	Low	Medium	High
<b>Straw</b>	36.5	17.0	0.0
<b>Corn silage</b>	0.0	19.9	36.5
<b>Chinese wild rye</b>	26.9	24.9	22.9
<b>Alfalfa hay</b>	16.1	7.5	0.0
<b>Corn</b>	8.4	15.7	23.2
<b>Wheat gluten</b>	2.2	2.4	2.8
<b>Proteins<sup>1</sup></b>	8.7	11.3	13.2
<b>Premix</b>	1.2	1.3	1.4
<b>Nutrients, % of DM</b>			
<b>Protein</b>	13.0	13.1	13.1
<b>NDF</b>	56.3	49.9	43.5
<b>NEL, MJ/kg of DM</b>	5.25	5.88	6.48

Table 2. Composition of diets fed to cows on different level of energy (NEL)

<sup>1</sup>Proteins = soybean meal, cottonseed meal, rapeseed meal, DDGS and extruded full fat soy.

Item	Low	Medium	High
<b>BW, kg</b>			
<b>21 d pp</b>	693	695	685
<b>7 d pp</b>	689	689	700
<b>Change</b>	-4	-6	15
<b>Blood glucose, mM/L</b>			
<b>21 d pp</b>	3.58 <sup>a</sup>	3.53 <sup>a</sup>	3.52 <sup>a</sup>
<b>7 d pp</b>	3.50 <sup>a</sup>	3.65 <sup>ab</sup>	3.86 <sup>b</sup>
<b>Change</b>	-0.08	0.12	0.34
<b>Blood NEFA, mM/L</b>			
<b>21 d pp</b>	136.4 <sup>a</sup>	137.6 <sup>a</sup>	133.1 <sup>a</sup>
<b>7 d pp</b>	366.5 <sup>a</sup>	183.7 <sup>b</sup>	146.1 <sup>b</sup>
<b>Change</b>	230.1	46.1	13.0

Table 3. Effects of diet energy content on cow BW and blood metabolites.

<sup>a,b</sup>Means in rows with different superscripts are different ( $P < 0.05$ ).

Adapted from Gao et al., 2012.

BW whereas cows on the lower energy diets did not.

Concentrations of glucose and non-esterified fatty acids varied with differences in diet. Cows fed the low energy diet had lower concentrations of glucose and the content of glucose in the blood declined from 21 to 7 days prepartum. In addition, there was a large increase in the NEFA concentration from 21 to 7 days prepartum. This suggests that these cows were in negative energy balance during the immediate prepartum period. Other assays conducted by the researchers supported these observations.

#### Effects on the calf

The interesting concept of the study was whether prepartum diets affected the calf at birth (and, potentially, throughout life). Results shown in Table 4 suggest that the calf was profoundly affected by the prepartum diet.

Birth weight, body height, body length, abdominal circumference, thoracic girth, umbilical girth, and levels of CD4, CD4:CD8, IL-2, IL-4, and superoxide dismutase were decreased in calves of the L group compared with those of the H group.

Taken together, these results suggest that maternal energy density during the last 21 d prepartum negatively affected growth, development, immunity, and antioxidant capability of neonatal calves.

The implications of the study are significant. What affects the cow during the dry period appears to affect the calf in many ways. These data support an increasing amount of research that tells us that we need to give special consideration to the prepartum period. Although this research focused on the last 21 days of gestation, other studies also suggest that the fetus can be affected early in gestation.

Item	Low	Medium	High
Birth BW, kg	39.2 <sup>a</sup>	42.1 <sup>ab</sup>	43.9 <sup>b</sup>
Birth height, cm	74.7 <sup>a</sup>	76.6 <sup>b</sup>	78.0 <sup>b</sup>
Birth length, cm	72.6 <sup>a</sup>	73.6 <sup>ab</sup>	74.2 <sup>b</sup>
Lymphocyte markers, %			
CD4	5.39 <sup>a</sup>	8.92 <sup>a</sup>	14.21 <sup>b</sup>
CD8	11.45 <sup>a</sup>	10.98 <sup>a</sup>	9.91 <sup>a</sup>
CD21	10.26 <sup>a</sup>	10.63 <sup>a</sup>	9.87 <sup>a</sup>
Plasma IL, ng/ml <sup>1</sup>			
IL-2	4.47 <sup>a</sup>	5.23 <sup>ab</sup>	6.46 <sup>b</sup>
IL-4	0.77 <sup>a</sup>	0.81 <sup>a</sup>	1.20 <sup>b</sup>
IL-6	0.23 <sup>a</sup>	0.20 <sup>a</sup>	0.25 <sup>a</sup>

Table 4. Effects of diet energy content on calf BW and blood metabolites.

<sup>a,b</sup>Means in rows with different superscripts are different ( $P < 0.05$ ).

<sup>1</sup>Plasma interleukin concentration.

Adapted from Gao et al., 2012.

#### Effects of maternal heat stress on offspring

Research continues to show that prenatal stress can affect metabolism of the offspring. This appears to hold true for many different species of animals, including cattle. One stress that consistently affects pregnant dairy cows is heat stress. Previous research has shown that prenatal heat stress on the dam affects calf body weight (calves from heat stressed cows are up to 5 kg lighter than calves from cooled cows), and immune function (Tao et al., 2012).

The Research

Researchers at the University of Florida (Tao et al., 2014) housed 20 dry cows in a cooled (CL) or non-cooled, heat stress (HT) environment at drying off. When calves were born, they were immediately separated from their dams and fed 3.8 L of high quality colostrum by 1 hr after birth and then 1.9 L of colostrum again in about 12 hr. From d 2 to 42, calves were fed pasteurized milk (1.9 to 3.8 L/day) and decreasing amounts to weaning at d 49. Calf starter and water were available for ad lib consumption from 2 d of age. On d 55, calves were exposed to two different metabolic tests, a glucose tolerance test (GTT) and an insulin challenge (IC). Descriptive statistics for these animals are in Table 5.

Table 5. Descriptive statistics for cows exposed to cooled (CL) or heat stress (HT) environments and their calves on d 55 of age.

Item	CL	HT	SE	P
n	10	10	...	...
THI	74.4	75.2		NS
Cow rectal temp, °C	38.7	39.0		0.05
Cow respiration, bpm	49.1	69.7		0.05
Calf BW, kg	45.0	40.2	1.4	0.03
BW gain, kg	28.0	26.3	2.2	NS
Calf glucose, mg/dl	65.2	70.7	2.5	0.14
Calf insulin, ng/ml	0.26	0.26	0.02	NS
Calf NEFA, $\mu$ Eq/dl	442.8	434.6	55.3	NS

Source: Tao et al., 2014.

The goal of the GTT is to find out how calves respond when a dose of glucose is infused into the jugular vein. Typically, blood glucose will increase after administering the glucose into the vein, followed by an increase in blood insulin concentration. The body secretes insulin into the circulation to regulate blood glucose; as glucose rises, insulin is secreted, which promotes uptake of the glucose from the circulation into many different body tissues. In this way, blood glucose can be closely regulated by the animal.

In the study by Tao et al., the concentration of both glucose and insulin in calves in both groups increased up to two hours after glucose infusion. Although there was no effect on insulin concentrations, the concentration of plasma glucose was lower in calves from HT cows. This suggests that when glucose was infused, calves from HT cows were more efficient in moving glucose from the circulation into other body tissues, so the pool of circulating glucose remained lower. So, it appears that other tissues, including fat cells, utilized glucose more efficiently when calves came from HT cows. Although we want calves and heifers to utilize glucose efficiently, we also want to avoid directing that glucose towards adipose tissue, when it may contribute to over-fattening instead of good growth.

Results of the insulin sensitivity test (Table 6) also showed little effect of insulin injection on blood insulin AUC (area under the curve, a measure of concentration over time). However, when insulin was injected, calves born from HT cows had lower glucose AUC compared to calves from CL cows.

Taken together, these data suggest that basal metabolism of calves is affected by the stress imposed on the mother during gestation. This study shows that the way calves use glucose is altered.

Whether this alteration in metabolism of glucose affects the animal's predisposition is not completely clear; however, other data suggest that increased uptake of glucose in response to GTT or IC does predispose animals to increased risk of adipose deposition.

Table 6. Response of calves to glucose tolerance and insulin sensitivity in calves from cows exposed to cooled (CL) or heat stress (HT) environments.

Item	CL	HT	SE	P
Glucose tolerance test				
Insulin AUC <sup>1</sup>				
30 min	10.91	9.74	3.20	NS
60 min	17.41	14.81	3.75	NS
120 min	25.59	20.37	3.98	NS
Glucose AUC <sup>2</sup>				
30 min	1,838	1,633	56	0.02
60 min	3,074	2,642	177	0.11
120 min	3,796	3,146	371	NS
Insulin sensitivity test				
Insulin AUC <sup>1</sup>				
30 min	46.46	42.02	2.53	NS
60 min	54.12	48.24	3.11	NS
Glucose AUC <sup>2</sup>				
30 min	-505	-648	41	0.03
60 min	-1,392	-1,783	98	0.01

Source: Tao et al., 2014.

<sup>1</sup>AUC: ng x min /dl

<sup>2</sup>AUC: mg x min/dl

Managing the environment of cows is important to their health and continued productivity. Results from this study suggests that cooling dry cows is also important for the health and, perhaps, future productivity of the calf.

Research from the University of Florida (Monteiro et al., 2016) summarizes the compilation of five different research trials wherein dry cows were either cooled or not cooled for the last six weeks before calving and the effects of cooling on growth, insemination and first lactation milk production.

Data were compiled from five experiments conducted during five summers (2007-2011) at the research dairy at the University of Florida. Multiparous Holstein cows were dried off about 45 days before their calving date and assigned to either cooling or non-cooling groups. Cooled cows were housed in a freestall barn equipped with sprinklers, fans and shade. The non-cooled cows had access to shade, but no sprinklers or fans. All cows were in the same barn.

Newborn calves were fed 3.8 L of colostrum and then fed pasteurized milk to weaning at d 49, plus ad libitum access to starter and water. Thereafter, calves were managed normally - transitioning from calf starter to TMR; inseminated at a minimum of 1.3 m in height, 340 kg body weight at 13 months of age. Calves in each treatment group were managed similarly, so differences in results could be attributed to the effect of cooling of the dams. A total of 146 records were analyzed (72 heifers in the cooled group and 74 in the non-cooled group).



There was no effect of prepartum treatment on the sex of the calves born, number of DOA's, or calf survival to 4 months of age. However, the number of calves leaving the herd before puberty was higher (8 heifers vs. 1) in the non-cooled group. The number of heifers completing first lactation was also greater in the cooled group (35 vs. 29).

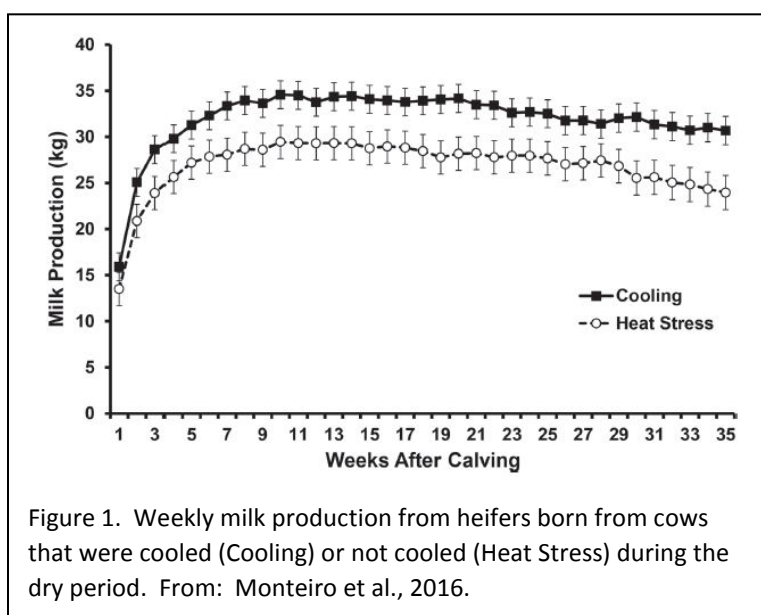
Item	Cooled	Not Cooled	P
Heifers, no	35	29	...
Milk, kg/d	31.9	26.8	0.03
3.5% FCM, kg/d	31.9	26.8	0.01
Milk fat, %	3.55	3.64	0.44
Milk true protein, %	3.00	3.05	0.24

Table 7. Production of heifers through 35 weeks from dams that were cooled or not cooled prior to calving. From: Monteiro et al., 2016.

Results from the study also confirmed previous research that calves born to stress cows were lighter (39.1 vs. 44.8 kg) at birth. The calves gained similar amounts of weight to 12 months of age (299 vs. 306 kg for stressed vs. non-stressed calves, respectively).

Milk production averages for the first lactation are in Table 7. Heifers born to dams that were cooled produced more milk through 35 weeks of lactation compared to heifers from dam not cooled. The difference was 5 kg/d (31.9 vs. 26.8 kg/d). If we calculate the total difference in production – i.e., 5 kg/d x 7 days/week x 35 weeks = 1,225 kg of milk difference between groups.

First lactation milk production is shown in Figure 1. The difference between groups was consistent throughout lactation. Visually, it appears that cooled heifers had greater consistency later in lactation, but this was not tested in the research trial.



This manuscript documents the latest in an important series of research trials that show clearly that prepartum management has profound effects on the fetus. This study shows that these effects are not just academic – they translate into significant production and significant money. The message is clear: take care of your cows to take care of your calves.

### Post-calving effects (The Lactocrine hypothesis)

Feeding colostrum is important for all newborn calves. High quality first-milking colostrum contains large amounts of immunoglobulins required to provide passive immunity to the newborn. Feeding enough colostrum to provide 150-200 grams of IgG in the first 24 hours of life should be standard practice for all calf raisers.

However, recent research suggests that other parts of colostrum – specifically growth factors and hormones – may play an essential role in growth and development of the newborn. This is called the “lactocrine hypothesis”.

The lactocrine hypothesis “*describes the effect of milk-borne factors, including colostrum in this definition, on the epigenetic development of specific tissues or physiological functions...*” (Soberon et al., 2012). Put another way, the lactocrine hypothesis proposes that some factors in colostrum and milk may permanently affect future calf performance such as growth, efficiency or even future milk production.

Researchers using newborn piglets have reported a role for some proteins in colostrum and milk, including a hormone called relaxin (Bartol et al., 2008; Bagell et al., 2009), which may be involved in development of the reproductive organs in piglets. For example, Chen et al. (2011) allowed some newborn piglets to nurse the mother ad libitum while other piglets were fed a colostrum/milk replacer without or with added relaxin for two days. At the end of the two day period, piglets nursing from the sow had greater indices of uterine development than piglets nursing replacer. Adding relaxin to the replacer improved some, but not all, indices of uterine development.

Researchers at the University of Berne in Switzerland and the University of Hannover in Germany have evaluated the role of protein in colostrum on intestinal growth, metabolism and development of digestive processes in calves fed adequate or inadequate amounts of colostrum (for example, see Rauprich et al., 2000; Hammon and Blum, 2002 and many others). Many of these studies report that feeding maternal colostrum increased the rate and extent of gastrointestinal development compared to calves fed formulas without colostrum proteins.

Taken together, these data suggest that hormones and growth factors in colostrum and milk (i.e., lactocrine factors) may have long-lasting effects on growth and development of the newborn.

How might these “lactocrine factors” affect future production in newborn dairy calves? Well, the answer to this question is still not clear, but may be related to expression of genes that are involved in weight gain, utilization of nutrients, reproductive or mammary development. Thus, it may be necessary or important that a calf be exposed to these factors at the right times and in the right amounts to ensure the calf may be able to express its full genetic potential.

### **The role of colostrum**

Colostrum is that logical source for lactocrine factors for the newborn. First-milking colostrum contains large amounts of protein, including immunoglobulins (IgG, IgM, and IgA) and other proteins such as growth factors (IGF-1, IGF-2 and many others), hormones (insulin, growth hormone, etc.), and other peptides. These proteins are often found in amounts far greater than can be found in normal milk. Indeed, some growth factors (e.g., IGF-1) are specifically “activated” (in the case of IGF-1, separated from binding proteins) right around parturition. Thus, it’s logical that these proteins might play a critical role in establishing a baseline for future calf performance.

Is there a dataset that specifically evaluates this lactocrine hypothesis? That is, are there studies that compare milk production in calves fed with or without maternal colostrum, then grown, allowed to calve and produce milk? Well, indeed there is such a dataset. The study is an excellent evaluation of the

hypothesis that colostrum proteins and growth factors can permanently affect an animal's ability to make milk after calving.

The study by Pithua et al. (2010) utilized 497 heifer calves from 12 dairies in Minnesota and Wisconsin. Calves were born on farms involved with Johne's control programs and the study was originally intended to evaluate the use of colostrum replacers in Johne's control. However, for the purposes of this Calf Note, we'll focus on the consumption of colostrum proteins and the effect of lactocrine factors on future production.

Calves were assigned to receive either 4-6 L of maternal colostrum (including all lactocrine factors contained in colostrum) or 1 dose of a commercial colostrum replacer by 1 hour after birth. Farms that fed an additional dose of colostrum at 12 hours also fed a colostrum supplement at about 12 hours of age to calves fed the replacer. All calves were separated from the dam within 60 minutes of birth and were fed their respective treatments to ensure that calves fed the commercial products did not consume maternal colostrum. After the first 24 hours of life, calves were housed, managed and raised according to the normal management of the farm. They all were fed commercial milk replacer, calf starter and water prior to weaning at 56 days of age. Calves were bred and calved according to normal protocols on the farm and milk production was monitored to about 54 months of age.

Calves were monitored throughout life for growth, breeding efficiency, survival in the herd and production of milk in the first two lactations. Reasons for culling heifers were recorded and all measurements were compared between the two treatment groups.

#### The results

A total of 261 calves were fed maternal colostrum and 236 calves were fed the commercial colostrum products. It's important to note that the commercial colostrum replacer and supplement were based on highly fractionated bovine plasma,

so these products contained little or none of the lactocrine factors found in maternal colostrum. The colostrum fed in the study was high quality with an average of 77 g of IgG/L. So, the average IgG concentration was much greater than the recommended 150-200 grams of IgG in the first 24 hours.

Though the concentration of various growth factors, peptides or hormones were not measured, it is assumed that there were sufficient amounts of these lactocrine factors in the colostrum, whereas little or no lactocrine factors would be present in the commercial products.

Item	MC	CR	P
<b>No. of calves</b>	261	236	...
<b>Died, 0-54 mo</b>	55	58	NS
<b>Culled, 0-54 mo</b>	81	68	NS
<b>Total left the herd, 0-54</b>	136	126	NS
<b>Age 1<sup>st</sup> calving, mo</b>	24.4	24.3	NS
<b>Services per conception</b>			
1 <sup>st</sup> Lactation	2.70	2.74	NS
2 <sup>nd</sup> Lactation	2.54	2.36	NS
<b>Days open</b>			
1 <sup>st</sup> Lactation	138	139	NS
2 <sup>nd</sup> Lactation	121	118	NS
<b>Milk production, kg</b>			
1 <sup>st</sup> Lactation	12,232	11,889	NS
2 <sup>nd</sup> Lactation	11,451	11,972	NS
<b>Total Lactations</b>	22,944	22,681	NS

**Table 8. Production of cows fed maternal colostrum (MC) containing lactocrine factors or colostrum replacer (CR) without lactocrine factors. From: Pithua et al., 2010.**

The researchers monitored growth, culling events, milk yield and breeding performance of both groups of calves. Key production parameters are shown in Table 8. The data clearly show that feeding colostrum or colostrum replacer had no effect on milk production, reproduction or survival to 54 months of age. In a previous study, Pithua et al. (2009) reported that calves fed the colostrum replacer were at less risk to become infected with *Mycobacterium paratuberculosis*, the organism responsible for Johne's disease in cattle.

So, what of the lactocrine hypothesis? In this study, calves fed the colostrum replacer, (which was manufactured using fractionated bovine plasma) produced just as much milk and were just as productive as calves fed 4-6 L of high quality maternal colostrum. Here are some of the potential explanations for the lack of an effect:

The colostrum replacer used in the study provided similar amounts of lactocrine factors. Unlikely. Though the non-Ig proteins of products used in the study were not measured, it's likely that colostrum replacers derived from bovine plasma don't contain the large number of different proteins as found in maternal colostrum. The udder concentrates many blood proteins into higher concentrations than found in serum and manufactures others, so that the profile of proteins in colostrum is very different from that of serum.

Effects of lactocrine factors in colostrum are unimportant or transient. Results in calves (Hammon and Blum, 2002; Rauprich et al., 2002) and piglets (Bagnell et al., 2009; Bartol et al., 2008) suggest that lactocrine factors play a role in the development of the gastrointestinal and reproductive systems. Some of these changes appear to be permanent, so, while the results of Pithua don't support a role of lactocrine factors in future milk production, it's unlikely that they're unimportant to the animal.

Lactocrine factors in milk replacer allowed replacer-fed calves to "catch up". Calves in the study by Pithua et al. (2009; 2010) were fed commercial milk replacer after colostrum feeding and until weaning at 56 days. It's possible that lactocrine factors which are also found in milk proteins might influence the calf so that calves fed the colostrum replacer received enough "lactocrine signals" from the milk replacer for proper development. All calves produced a lot of milk in their first lactation (average was >12,000 kg or 26,000 lbs), so it's unlikely that the lack of lactocrine signals in calves fed colostrum replacer had a negative effect on these calves.

Growth factors and hormones in maternal colostrum likely play an important role in the development of the newborn calf. Very interesting research into how these compounds – lactocrine factors – is being conducted in many species of animals and will shed new light on the roles these compounds play. However, some existing research suggests that the effects of these factors, if any, don't permanently affect the ability of calves to survive, grow and become productive on modern dairy farms.

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