Passive Immunity in Newborn Calves

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Summary (Take Home Message)

The neonatal immune system at birth is naïve to the wide variety and types of pathogens present in the environment. Consumption of colostrum to provide circulating IgG prior to the cessation of macromolecular transport ("closure") is essential to ensure healthy calves. There are a tremendous number of factors that may influence the absorption of IgG by calves; therefore, blanket recommendations for feeding one amount of colostrum to all calves is inappropriate. A model to evaluate factors affecting IgG absorption has been developed and those factors are discussed. Colostrum supplement products have been developed and are available in the marketplace. Unfortunately, many of these products provide little additional circulating IgG. Therefore, it is essential that producers carefully evaluate claims for improve circulating IgG and animal survival.

Introduction

The replacement enterprise is a pivotal component of most modern dairy farms. By providing a consistent and economical supply of high quality replacements to the lactating herd (or for sale to other herds), the replacement enterprise can be viewed as a profit (or loss) center for the dairy. This enterprise approach to calf rearing, which requires sound business and management decisions, can allow producers to evaluate the replacement enterprise and identify areas where the enterprise may be improved.

Calves are born with a predetermined genetic potential, which may be permanently affected by management decisions implemented throughout the rearing period and by environmental factors. A calf's genetic potential may be viewed as an upper limit that is expressed only if proper decisions are implemented at the appropriate time. Studies have shown that the level of management has a profound effect on calf morbidity and mortality (Curtis et al., 1985; Waltner-Toews et al., 1986a, 1986b). Proper management of young stock, particularly during the neonatal period, can markedly reduce morbidity and mortality, whereas improper management will lead to economic losses from increased cost of veterinary intervention, death losses, reduced growth, and suboptimal reproductive performance. In addition, poor management of young stock can reduce the lifetime productivity of the individual cow and the herd as a whole.

The most critical time in the life of the dairy replacement is during the first few days, when morbidity and mortality are greatest. A USDA study of farms throughout the U.S. with more than 30 cows (NAHMS, 1992) indicated that preweaning mortality of calves born alive was 8.4%, whereas mortality after weaning was only 2.2%. Clearly, the loss of calves prior to weaning is a major concern for all dairy producers. More recent estimates (NAHMS, 1996) indicated that preweaning mortality was 11%, with little change in postweaning mortality.

▪ Absorption of Immunoglobulins

Absorption of intact macromolecules across the intestinal epithelium into the neonatal circulation is possible for approximately 24 hours after the calf is born. The absorption of Ig occurs by an active process called *pinocytosis,* which moves Ig (and other molecules) across the intestinal epithelium. After leaving the epithelium, Ig molecules move into the lymph and then to the circulation. Maturation of the small intestine begins shortly after birth and the ability of the intestine to absorb macromolecules without digestion is lost by about 24 hours after birth. This loss of absorptive ability appears related to the development of the digestive apparatus in intestinal epithelial cells and turnover of cell populations. After about 24 hours of age, the chance to provide the calf with antibodies is gone. However, it is important to continue to feed colostrum for 2 to 3 days after birth. The Ig in colostrum will bathe the calf's digestive tract and make it difficult for bacteria to attach to the intestinal wall. This "local effect" can reduce the incidence of scours during the first several weeks of life.

Traditionally, determination of successful transfer of passive immunity has been by measuring the concentration of IgG in the serum of the calf at 24 to 48 hours after birth. If the serum IgG concentration exceeds some critical level, then the calf is thought to be relatively well protected against pathogens. The critical level for determining failure of passive transfer of immunity (**FPT**) is usually considered at 10 g/L (1,000 mg/dl), although some researchers have used other threshold serum IgG concentrations. Calves with less than 10 g/L of serum IgG are at increased risk of disease than calves with greater serum IgG concentrations. Of course, the concentration of serum IgG is a continuum of risk – that is, calves with < 10.1 of IgG/L of serum are not at markedly greater risk than calves with 9.9 g of IgG/L. Generally, it is well accepted that the greater the concentration of IgG in the circulation of calves at 24 to 48 hours after birth, the greater the protection against the array of pathogens to which the calf might be exposed.

There are many factors that influence the concentration of IgG in the blood of the calf at 24 to 48 hours. These include:

- Mass of IgG consumed
- Apparent efficiency of IgG absorption (**AEA**)
- Plasma or serum volume of the calf

These factors can be summarized as:

Serum IgG (g/L) = IgG consumed (g) × AEA (%) / serum volume (L) [1]

We can use equation [1] to calculate the AEA with which IgG are absorbed

AEA (%) = serum IgG (g/L) × serum volume (L) / IgG consumed (g) [2]

The concept of AEA is not well understood by many veterinarians or nutritionists, but encompasses many of the concepts universally accepted as important to successful passive transfer.

Blood volume

The amount of IgG in the bloodstream is, necessarily, affected by the size of the plasma or serum pool. Intuitively, it is logical that calves with a larger blood volume will attain a lower IgG concentration than calves with smaller blood volume if they are fed the same mass of IgG. This, then requires prediction of plasma volume in some manner. Prediction of blood/serum volume is often carried out using dye dilution methods (McEwan et al., 1968, 1970). McEwan et al., (1970) reported a mean plasma volume of 8.3% of BW. Others have reported mean values of 8.7 to 9.3% (McEwan et al., 1968; Quigley et al., 1998) and 6.5% (Möllerberg et al., 1975). The value of 7% of BW has been used widely in other research trials in which AEA was estimated.

A practical method of estimating plasma volume is to assume that 9% of the animal's body weight at 24 hours is plasma volume.

Colostrum and Ig intake

The amount of IgG absorbed depends on the AEA and the mass of IgG consumed. The mass of IgG consumed is a function of the quantity of IgG ×

the IgG concentration of the colostrum. The concentration of Ig in colostrum varies according to the cow's disease history, volume of colostrum produced, season of the year, breed, and other factors. Research from Washington (Pritchett et al., 1991) indicated the average concentration of IgG_1 (a sub-fraction of IgG) in colostrum from 919 Holstein cows was 48.2 g/L with a range of 20 to >100 g/L. A Tennessee study (Quigley et al. 1994b) measured colostrum from 96 Jersey cows and found that samples averaged 66 g/L of IgG, with a range of 28 to 115 g/L. The difference between 20 and 100 g/L of IgG in colostrum can mean the difference between FPT and successful passive transfer.

The amount of Ig in colostrum depends on a large number of factors, including the disease history of the cow. That is, cows tend to produce Ig in response to pathogens to which they have been exposed. Therefore, cows exposed to a greater number of pathogens tend to produce colostrum with greater Ig than cows exposed to fewer pathogens. This is often why older cows will produce colostrum containing more Ig than younger cows. However, if older cows are not exposed to many pathogens, the colostrum produced may not have high levels of Ig. This is also why a good dry cow vaccination program can improve the quality of colostrum. Moreover, cattle raised on a farm will produce colostrum with antibodies *specific for the organisms on that farm* which is an added benefit. Finally, prepartum milking or leaking of milk from the udder prior to calving can reduce the concentration of Ig in colostrum.

Research has also indicated that the volume of colostrum produced will influence colostral Ig concentration. In general, colostrum produced in large volumes will have lower Ig concentration than colostrum produced in smaller volumes. This is only a general rule, however, and the relationship between Ig concentration and volume is not constant.

The large variation in Ig content makes accurate colostrum management and feeding difficult. Colostral IgG can be measured in the laboratory with great accuracy; unfortunately, the assays involved are time-consuming and expensive. A measurement of colostrum specific gravity using a device called a colostrometer is one method to estimate Ig content of colostrum (Fleenor and Stott, 1980). This device is based on the relationship between Ig in colostrum and specific gravity. Unfortunately, components of colostrum other than Ig affect specific gravity, so the relationship is variable. Also, the relationship between specific gravity and IgG is dependent on temperature and other factors (Mechor et al., 1991, 1992; Morin et al., 2001; Pritchett et al., 1994). However, the colostrometer may give a gross (qualitative) estimate of colostrum quality - particularly if the colostrum is of poor quality.

The amount of colostrum consumed by the calf is the only factor in the equation of serum IgG that is easily manipulated on the farm. Therefore, many veterinarians and dairy professionals have increased the recommended amount of colostrum in an attempt to reduce the incidence of FPT. While this approach serves a useful purpose, it does not address all factors that need to be considered in attempting to maximize successful passive transfer of immunity.

■ Factors affecting AEA

There are many components to AEA – the ability of the calf to absorb ingested IgG into the circulation. It should be noted that the efficiency of IgG absorption is apparent – it is not an estimate of the total IgG absorbed into the animal.

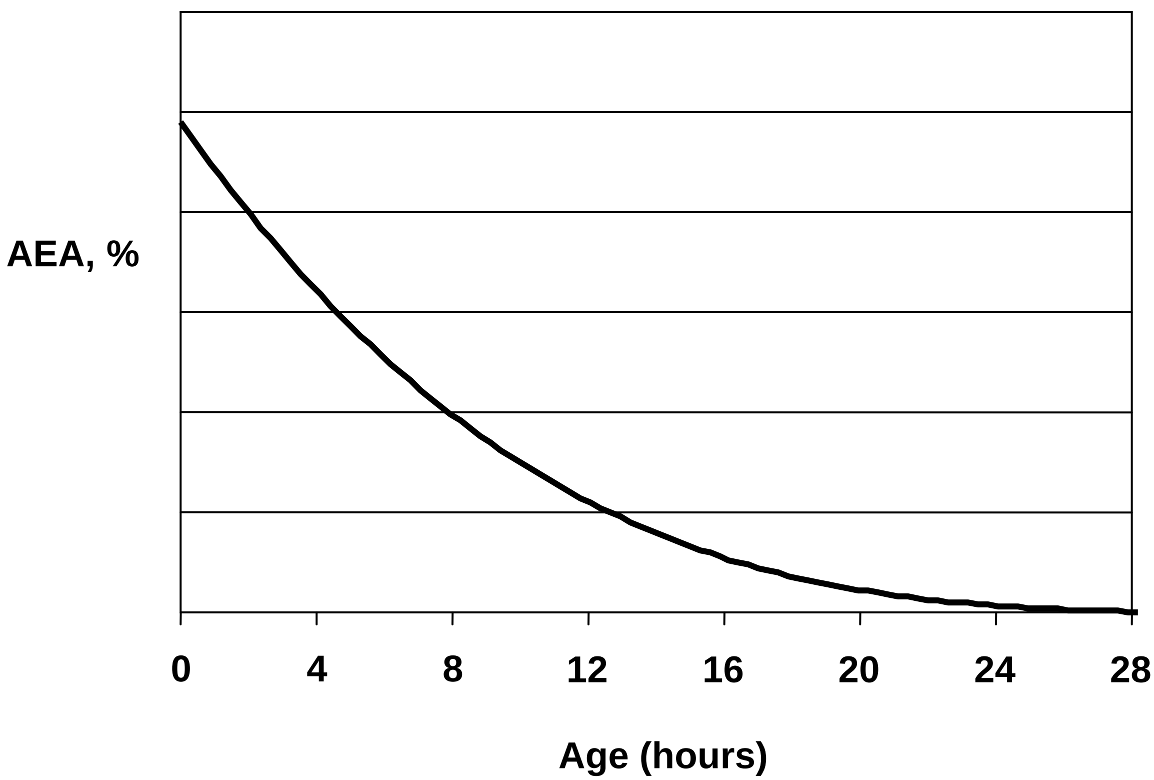

Figure 1. Changes in apparent efficiency of IgG absorption (AEA) with increasing age in newborn calves.

Many IgG will be initially be absorbed into the circulation and then later move out of the blood and into other body pools. The extent to which IgG leave the circulation is not well defined, but estimates are that approximately 50% of absorbed IgG will move out of the circulation. Theoretically, then, the maximum possible AEA is about 50%. However, much more research is required to completely understand the factors affecting the equilibration of IgG into intravascular and extravascular pools and variability among animals in this regard.

1. Age at First Feeding

The most important factor affecting AEA is the time after birth at which colostrum is fed. This concept is long established in the literature. However, age at first feeding is more properly classified as a loss of efficiency of absorption rather than a loss of IgG concentration *per se*. Maturation of intestinal epithelial cells, establishment of intestinal bacteria, and increasing production of intestinal enzymes will all reduce AEA.

The decline in AEA with increasing age is often assumed to be curvilinear (Figure 1). While this has been reported in some studies (Stott and Fellah, 1983), others indicate a linear decline in AEA with advancing age (Kruse, 1970). Still others indicate little change in AEA to 12 hours of life (Quigley et al., 1995). Therefore, although the curvilinear decline in AEA is generally accepted in the literature, it is not well supported in the literature. Generally, however, it is well accepted that calves fed the same mass of IgG will be less efficient in absorbing those IgG if they are fed at a later age.

Current theories (Bush and Staley, 1980; Jochims et al., 1994; Staley and Bush, 1985) suggest that intestinal epithelial cells lose their ability to absorb intact macromolecules after about 24 h because of maturation of the cells and development of the intracellular digestive apparatus. This maturation begins shortly after birth. Rajala and Castrén (1995) reported a decline in serum IgG concentration of 2 g/L at 30 min after birth; regression of serum IgG concentration on age at first feeding in calves fed maternal colostrum (Abel and Quigley, 1993) also indicated a reduction of AEA within 1 h of birth. Clearly, there is a compelling reason to feed calves as soon as possible after birth to maximize the acquisition of passive immunity.

In addition to the maturation of intestinal cells, the secretion of digestive enzymes may also contribute to lower AEA by degrading IgG prior to absorption. At birth and for a limited period thereafter, the secretion of digestive enzymes remains limited to allow macromolecules such as IgG to escape digestion and allow absorption (Guilloteau et al., 1983; Thivend et al., 1980). By about 12 h, enzyme secretion becomes more marked, thereby reducing the ability of IgG to reach the peripheral circulation without being degraded. Supplementation of colostrum with soybean trypsin inhibitor increased the absorption of IgG (Quigley et al., 1995), indicating the deleterious effects of proteolytic enzymes on AEA.

Establishment of microbial populations in the intestine may also be involved in reduced AEA with time after birth. The intestinal tract of the neonate is sterile at birth; however, within a few hours, environmental bacteria begin to colonize the intestine. This colonization can be hastened by an environment that promotes the growth of pathogens (i.e., a dirty environment). James et al. (1981) reported that the presence of bacteria in the intestine may actually increase the rate of intestinal closure, thereby reducing AEA and acquisition of passive immunity.

Logan et al. (1977) studied the effects of early colonization of pathogens on neonatal calves. Calves were fed colostrum and challenged with *E. coli*. The first group was fed colostrum, then challenged; group 2 were challenged, then fed colostrum. Nearly all calves in the second group became morbid and about 75% of the group died. Conversely, calves fed colostrum prior to *E. coli* challenge did not become sick and none died.

Quigley et al., (1994a) reported that calves removed from their dams at birth showed different temporal acquisition of enteric pathogens from birth to 35 days compared to those left with the dam for 24 hours. Clearly, the dam and the calving environment can contribute significantly to the amount and type of bacteria to which the calf is exposed shortly after birth.

2. Colostrum IgG Concentration And Amount Of Colostrum Fed

The relationship between serum IgG and colostral IgG intake (colostrum IgG concentration × amount of colostrum fed) is linear in most experiments (McEwan et al., 1970, Stott and Fellah, 1983), which suggests that AEA is constant throughout the range of IgG intake. This also suggests that the limit to absorption of IgG from the intestine is outside the range of typical IgG intake. However, others (Besser et al., 1985, 1991) have reported a curvilinear relationship between IgG intake and serum IgG concentration, suggesting that there is a maximal amount of Ig that can be absorbed from the intestine. Consequently, it is possible that a maximal amount of colostrum fed exists above which absorption of Ig becomes inefficient.

The concentration of IgG in colostrum may influence AEA. Stott and Fellah (1983) reported that calves fed 1 L of colostrum containing various amounts of IgG were more efficient in absorbing IgG than were calves fed the same mass of IgG in 2 L. Stott and Fellah (1983) also suggested that large amounts of colostrum containing a low concentration of IgG would not be absorbed adequately; instead, limited amounts of high IgG colostrum may be more important. The ability of the intestine to extract Ig from colostrum may be improved when more concentrated (higher Ig) colostrum is fed. However, other research is needed to confirm this finding.

Concentration of Ig in colostrum from the first milking may be inadequate to ensure the transfer of an adequate mass of Ig when ≤2 L are fed. Besser et al. (1991) suggested that the prevalence of failure of passive transfer in dairy herds could be minimized by artificially feeding calves large volumes (3 to 4 L) of fresh or refrigerated colostrum within the first 24 h. It is not clear whether the absorption of Ig in calves is affected by feeding a similar volume of colostrum in one or two feedings. Halliday and Williams (1976) reported that one feeding of colostrum fed to lambs reduced AEA compared with results for two feedings 6 h apart. Increased serum IgG concentration was attributed to improved absorption of the first feeding as a result of the second. Research (Hopkins and Quigley, 1997) suggests that absorption of IgG is similar whether calves are fed 4 L in one or two feedings.

3. Colostrum Protease Inhibitor Concentration

Colostrum from cows normally contains unique proteins, protease inhibitors, that protect IgG from digestion in the intestine. The most common of these proteins, trypsin inhibitor is normally found in very high concentrations in first-milking colostrum, then declines with the onset of lactation. The addition of soybean trypsin inhibitor can increase serum IgG concentrations in calves (Quigley et al., 1995), most likely by protecting IgG from intestinal digestion

4. Colostrum processing

Manipulation of the physical or chemical characteristics of colostrum (freezing, pasteurization, etc.) can affect the AEA (Lakritz et al., 2000). Most of these effects will be specific for the processing. Generally, however, processes that alter protein structure, expose colostrum to extremes of heat or cold will reduce AEA to varying degrees.

5. Protein intake

The mass of protein and IgG may play a role in AEA. Addition of bovine serum albumin to colostrum (Besser and Osbourn, 1993) or addition of casein or whey to a colostrum supplement (Davenport et al., 2000) reduced, to varying degrees, the absorption of IgG. It is possible that large amounts of non-Ig protein compete with Ig at binding sites in the intestine, thereby reducing IgG absorption. However, additional research is needed to adequately determine the nature of this response.

6. Sex of the Calf

The sex of the calf may influence AEA; heifer calves generally have higher serum IgG concentrations than do bull calves (Roy, 1990). It is not clear whether gender of the calf may be related more to blood volume than to AEA.

A second possibility is that the larger size of bull calves may influence the metabolic state of the calves, thereby affecting Ig absorption. Further research in this area is warranted. However, Vann et al. (1995) reported no effect of calf gender on AEA in *Bos indicus* or *Bos taurus* calves.

7. Breed

Roy (1990) summarized several studies and concluded that breed differences exist in the efficiency of Ig absorption. Holstein calves had a greater AEA than Ayrshire calves and Friesian × Ayrshire calves. Differences in BW, gender, blood volume, metabolic state of the calf, and method of feeding have not been adequately accounted for in these studies, so the effect of breed is unclear. Mowrey (2001) reported that calculated AEA of Jersey calves fed colostrum or a colostrum replacement product were 24% higher than AEA for Holstein calves fed similar products.

8. Method of Colostrum Feeding

Calves that were allowed to nurse the dam generally achieve lower serum IgG concentrations and are far more susceptible to morbidity and mortality than are calves fed colostrum by nipple bottle (Brignole and Stott, 1980; Logan et al., 1981). Calves allowed to nurse the dam often consume less colostrum than do calves fed by nipple bottles (Brignole and Stott, 1980), thereby lowering IgG intake. In addition, calves allowed to nurse the dam often begin consuming colostrum later than calves fed by nipple bottle, thereby lowering AEA by allowing maturation of the intestinal epithelium.

Research that has controlled (or measured) the intake of IgG by calves allowed to nurse the dam early have reported AEA better than for calves fed by nipple bottle (Selman et al., 1970; Stott et al., 1979). Those researchers (Selman et al., 1970; Stott et al., 1979) have hypothesized that a neural effect of the presence of the dam or some labile component in colostrum may be responsible for improved AEA in the calf.

The use of the esophageal feeder to feed large quantities of colostrum has been associated with reduced AEA and slightly lower serum IgG concentration compared with colostrum administered by nipple bottle (Lee et al., 1983). Colostrum administered by esophageal feeder enters the rumen before moving into the abomasum and intestine (Lateur-Rowet and Breuink, 1983). Thereafter, it takes 2 to 4 h for the colostrum to leave the rumen. This interval may actually be the reason for lower AEA, because the intestine may mature during this time, thereby reducing the number of actively absorbing cells in the intestine. However, many veterinarians recommend feeding 4 L of colostrum as soon as possible after birth to ensure that all colostrum is consumed. Others (Adams et al., 1985; Molla, 1978) support the use of esophageal feeders to provide large amounts of colostrum without significant effect on serum IgG concentrations.

9. Metabolic state of the calf

A strong correlation exists between calf perinatal mortality metabolic or respiratory acidosis (Szenci, 1985), which is common at birth (Besser et al., 1990; Garry, 1993; Szenci, 1985). Some researchers (Garry, 1993; Kasari, 1994; Szenci, 1985) view this relationship as physiological, but others (Besser et al., 1990; Boyd, 1989) consider it abnormal and a threat to the health and survival of the neonate. The prevalence of respiratory acidosis immediately postpartum could inhibit the ability of the neonate to adapt to the extrauterine environment. Normal birth is generally accompanied by a brief period of hypoxia or ischemia. Often the increase in partial pressure of CO_2 (P_{CO2}) lowers pH, resulting in mild acidosis (Garry, 1993). Metabolic, respiratory, and mixed acidosis occur frequently, but significant alkalosis is rarely observed (Garry, 1993). Risk factors associated with postnatal acidosis include the duration of observed second stage labor >2 h; dystocia requiring traction; and weakness of a calf at birth (Besser et al., 1990). Mean arterial P_{CO2} concentrations range from 43 to 59 mm Hg (Adams et al., 1993; Eigenmann et al., 1984). By comparison, normal arterial P_{CO2} in adult awake mammals ranges from 35 to 45 mm Hg (Kirk, 1983). Mean venous P_{CO2} concentrations in healthy calves not exhibiting respiratory distress syndrome were 58 ± 2 mm Hg (Szenci, 1985).

Respiratory acidosis may affect AEA and the acquisition of passive immunity. Although metabolic acidosis usually resolves within 2 h of birth, respiratory acidosis may persist for > 24 h (Besser et al., 1990; Boyd, 1989). Serum IgG_1 (a sub-fraction of IgG) concentrations may be reduced in calves that have lower blood pH and elevated P_{CO2} (Besser et al., 1990). Boyd (1989) reported that birth P_{CO2}, but not pH, was inversely correlated to serum IgG_1 concentrations. Conversely, several others (Ayers and Besser, 1992; Drewry et al., 1999; López et al., 1994) did not find a significant relationship between P_{CO2} (arterial or venous) and plasma IgG concentration or AEA in calves. Tyler and Ramsey (1991) suggested that hypoxia in calves immediately after birth may delay the absorption of IgG but not affect peak plasma IgG concentration.

Calves born from cows fed anionic diets may be affected by respiratory or metabolic acidosis, which may, in turn, affect AEA (Guy et al., 1996; Joyce and Sanchez, 1994). Conversely, Tucker et al. (1992) reported that the cation-anion balance of the diet (either -30 or +90 mEq/kg of DM) consumed by 120 dry cows and heifers did not affect the acid-base status or the plasma mineral content of their calves. Guy et al. (1996) reported increased serum IgG_1 concentrations when calves were fed an oral paste of sodium bicarbonate 0.5 h after the first colostrum feeding. Calves were born from cows fed diets with a dietary cation-anion difference of +445 or +75 mEq/kg of DM for 3 wk prepartum. Calves born from cows fed the cationic diet had higher serum IgG_1 concentration at 24 h than did calves from cows fed more acidotic diets, although venous blood P_{CO2} was not affected (Guy et al., 1996). Conversely, Ayers and Besser (1992) reported no improvement in serum IgG_1 concentration of calves injected with either doxapram HCl (2 mg/kg of BW) or sodium bicarbonate (3 mEq/kg of BW), although pH was increased and P_{CO2} was decreased by treatment with doxapram HCl alone or in combination with sodium bicarbonate. Further research is required to determine the total effect of neonatal acid-base status on the ability of the calf to absorb colostral Ig and to determine whether treatments are effective or necessary.

9. Effects of Environment

The absorption of Ig may be affected by the environment in which the calf is born. Extreme cold (Olson et al., 1980a), but not moderate cold (Olson et al., 1981a,b), reduces the absorption of Ig by calves. The effects of ambient temperature outside the thermoneutral range for calves may involve direct effects on intestinal absorption and transport (Olson et al., 1981a) as well as the ability of the calf to stand and nurse (Olson et al., 1980b; Stauber, 1976).

10. Stress Hormones

The degree of dystocia may affect survival of calves. The relationship between dystocia and lower plasma Ig concentrations has been determined conclusively. However, research by Stott and Rienhardt (1978) suggested that dystocia did not influence concentrations of circulating cortisol or affect AEA. Concentrations of glucocortocoids affect absorption of Ig in calves. Administration of ACTH has been reported to increase IgG absorption in calves (Johnston and Oxender, 1979; Stott, 1980), but may be dependent upon the degree of maturation of the calf at birth (Stott, 1980).

■ Colostral Supplements

Maternal colostrum is almost always the preferred source of IgG. The IgG in maternal colostrum are derived from the dam's bloodstream and are based on the disease history to which the cow has been exposed. The industry has long recognized that management of colostrum on the farm is time consuming, tedious and prone to error. Statistics, including neonatal morbidity, mortality and the proportion of calves with FPT are clear evidence that colostral management is often inadequate and there is a need for improved management of colostrum feeding.

Poor colostrum quality (low IgG concentration or contamination) or a lack of colostrum prompted the search for alternative sources of IgG for neonatal calves. Currently, the only sources of IgG are from animals. However, colostral supplements have been introduced to the industry and have been used to supplement (increase colostral IgG concentration) or replace maternal colostrum. Maternal colostrum may be replaced by a supplement when it is unavailable, of poor quality (low IgG concentration) or may contain pathogenic organisms, such as *Mycobacterium paratuberculosis.* The three readily available sources of IgG are lacteal secretions (colostrum and milk), blood and eggs.

1. Supplements Derived From Lacteal Secretions

Colostral supplements derived from whey and cow colostrum have been evaluated at several locations. Absorption of IgG from supplements derived from lacteal secretions have been reported to be poor (Abel Francisco and Quigley, 1993; Garry et al., 1996; Morin et al., 1997; Zaremba et al., 1993; Mee et al., 1996; Ikemori et al., 1997) although the reasons for poor IgG absorption have not been defined clearly.

Abel Francisco and Quigley (1993) added a colostral supplement to maternal colostrum from 32 cows. Colostrum ranged from very high to low concentration of IgG, and averaged 59 g of IgG/liter. Calves were fed colostrum by 2 hours of birth, and again 12 hours later. No effect of colostral supplement was observed on serum IgG concentrations taken 24 or 48 hours after birth. These data suggested that when maternal colostrum was fed, there was no benefit to adding a colostrum supplement. When only the poor quality colostrum samples (<20 g of IgG/L) were evaluated, the results were similar. Even when poor quality colostrum was fed, there was little benefit to adding a colostral supplement.

In a second study, use of colostral supplements based on whey and colostrum were reevaluated by feeding newborn calves 2 quarts of dam's colostrum as soon as possible after birth and again 12 hours later. This study reconfirmed our previous finding that colostrum supplements do not affect serum IgG concentrations when added to good quality colostrum. Generally, the use of the current generation of colostrum supplements based on whey or colostrum has shown poor absorption and only limited increases in serum IgG concentrations when fed at or above manufacturer's recommendations (Garry et al., 1996).

2. Supplements Derived From Chicken Eggs

Preparations derived from chicken eggs have been evaluated in some studies (Erhard et al., 1995, 1997). Typically, these preparations contain IgY obtained from hyperimmunization of chickens. The resulting product contains specific activity against the antigen administered. However, absorption of the IgY into the circulation appear to be relatively low and, therefore, these preparations may be most useful in post-closure applications (Erhard et al., 1997).

3. Supplements Derived From Bovine Serum

A colostrum supplement based on serum proteins (Lifeline, APC, Inc., Ames, IA) is significantly more effective in providing circulating IgG and improved survival of neonatal calves when fed alone or added to maternal colostrum (Arthington et al., 2000a,b; Quigley et al., 1998, 2000, 2001). Studies have indicated that the apparent efficiency of IgG absorption from serum derived colostral supplements is equal to maternal colostrum – usually averaging approximately 25 to 35%. In addition, serum derived colostral generally contain more IgG than supplements based on whey or cow colostrum.

Colostrum supplements derived from serum contain primarily IgG_1 and IgG_2 in approximately equal proportions. This is somewhat different from supplements derived from colostrum, which contain mostly IgG_1. Therefore, the absorption kinetics and half-life of these products may be expected to vary significantly. Furthermore, IgG derived from serum are usually significantly less expensive – therefore, it is more economical to collect, process and manufacture supplements derived from serum. Serum is a high quality product and a recent summary of risks assessment conducted by Harvard University School of Public Health for the USDA indicates the safety of blood products with respect to BSE transmission. The survey found that current regulations prohibiting the feeding of ruminant proteins – with the exception of blood products, milk, gelatin and plate waste – dramatically reduce the risk of establishing BSE in North America. If BSE were introduced by importation of infected cattle or infected meat and bone meal, the existing regulations would also stop the spread of the disease.

Recommendations

The terms “colostrum supplements” and “colostrum replacers” are poorly defined in the literature and in the industry. Many products are currently marketed as colostrum replacers, but have neither a sufficient mass of IgG nor the nutritional supplementation required by the calf. Recent developments (Quigley et al., 2001) indicate that true colostrum replacement products will be available in the near future.

The term “colostrum supplement” should refer to those preparations intended to provide < 100 g of IgG/dose and are not formulated to completely replace colostrum. Supplements should be formulated to be fed in conjunction with colostrum and to increase IgG concentration and provide nutrients that are inherently variable in maternal colostrum (e.g., vitamin E). Additional research is needed to identify components critical to successful CS formulation.

In addition to an adequate mass of IgG (>100 g of IgG/dose), colostral replacers must provide nutrients required by the calf. Energy as carbohydrate and lipid is needed to allow the calf to thermoregulate and to establish homeostasis. Digestible protein sources are required as a source of amino acids for gluconeogenesis and protein synthesis, and vitamins and minerals are essential to successful colostral replacer formulation. Colostrum is a highly concentrated source of fat soluble vitamins, as placental transfer of these vitamins is limited. Additional research is also required to define requirements for hormones and growth factors that are found in high concentrations in maternal colostrum. Inclusion of viable leukocytes normally found in maternal colostrum is not possible presently.

Colostrum supplement products that contain IgG are regulated in the U.S. by the USDA Center for Veterinary Biologics. Regulatory approval of products for prevention or treatment of failure of passive transfer requires that products produce an increase in circulating IgG concentration in at least 20 neonatal animals fed a dose of the product above a minimum standard for the specific species (9 CFR 113.499). To date, no approved CS has been shown to increase IgG concentration above the species standard (10 g/L). Recently, we reported that plasma IgG exceeded the bovine species standard in calves fed 122 or 244 g of IgG (Quigley et al., 2001). Our data suggest that mass of IgG and method of processing are critical to ensure adequate transfer of passive immunity. It is important to recognize that products providing less than 100 g of IgG/dose should not be used to replace colostrum; rather two discrete classes of products (supplement vs. replacer) with unique functions and formulation should be recognized.

■ Summary

A more complete understanding of the factors that affect the incidence and severity of FPT are needed if meaningful improvements are to be made regarding neonatal morbidity and mortality. Although the mass of IgG that is consumed by the calf is important, other factors affecting the ability of the animal to absorb Ig are also meaningful. New technologies to increase the mass of IgG (e.g., colostral supplements and replacers) will provide an increased ability to manage the colostrum feeding program. However, other technologies, including measurement of colostral quality, determining the potential AEA of a calf, and others, need to be determined to provide optimal immune protection to the calf.

■ References

Abel Francisco, S.F. and J. D. Quigley, III. 1993. Serum immunoglobulin concentration in response to maternal colostrum and colostral supplementation in dairy calves. Am. J. Vet. Res. 54:1051-1054.

Adams, G. D., L. J. Bush, J. L. Horner, and T. E. Staley. 1985. Two methods for administering colostrum to newborn calves. J. Dairy Sci. 68:773.
Adams, R., R. B. Garry, B. M. Aldridge, M. D. Holland, and K. G. Odde. 1993. Physiologic differences between twin and single born beef calves in the first two days of life. Cornell Vet. 83:13.
Arthington, J. D. M. B. Cattell, J. D. Quigley, III, G. C. McCoy, and W. L. Hurley. 2000a. Passive immunoglobulin transfer in newborn calves fed colostrum or spray-dried serum protein alone or as a supplement to colostrum of varying quality. J. Dairy Sci. 83:2834–2838.
Arthington, J. D., M. B. Cattell and J. D. Quigley, III. 2000b. Effect of dietary IgG source (colostrum, serum, or milk-derived supplement) on the efficiency of IgG absorption in newborn Holstein calves. J. Dairy Sci. 83:1463-1467.
Ayers, M. W., and T. E. Besser. 1992. Evaluation of colostral IgG_1 absorption in newborn calves after treatment with alkalinizing agents. Am. J. Vet. Res. 53:83.
Besser, T. E., A. E. Garmedia, T. C. McGuire, and C. C. Gay. 1985. Effect of colostral immunoglobulin G1 and immunoglobulin M concentrations on immunoglobulin absorption in calves. J. Dairy Sci. 68:2033.
Besser, T. E., C. C. Gay, and L. Pritchett. 1991. Comparison of three methods of feeding colostrum to dairy calves. J. Amer. Vet. Med. Assoc. 198:419.
Besser, T. E., and D. Osbourn. 1993. Effect of bovine serum albumin on passive transfer of immunoglobulin G1 to newborn calves. Vet. Immunol. Immunopathol. 37:321–327.
Besser, T. E., O. Szenci, and C. C. Gay. 1990. Decreased colostral immunoglobulin absorption in calves with postnatal respiratory acidosis. JAVMA 196:1239.
Boyd, J. W. 1989. Relationships between acid-base balance, serum composition and colostrum absorption in newborn calves. Br. Vet. J. 145:249.
Brignole, T. J. and G. H. Stott. 1980. Effect of suckling followed by bottle feeding colostrum on immunoglobulin absorption and calf survival. J. Dairy Sci. 63:451.
Bush, L. J., and T. E. Staley. 1980. Absorption of colostral immunoglobulins in newborn calves. J. Dairy Sci. 63:672.
Curtis, C. R., H. N. Erb, and M. E. White. 1985. Risk factors for calfhood morbidity and mortality on New York dairy farms. Proceedings of Cornell Nutrition Conference, pp. 90-99.
Davenport, D. F., J. D. Quigley, III, J. E. Martin, J. A. Holt, and J. D. Arthington. 2000. Addition of casein or whey protein to colostrum or a colostrum supplement product on absorption of IgG in neonatal calves. J. Dairy Sci. 83:2813-2819.
Drewry, J. J., J. D. Quigley, III, D. R. Geiser, and M. G. Welborn. 1999. The effect of elevated arterial carbon dioxide tension on efficiency of immunoglobulin G absorption in calves. Am. J. Vet. Res. 60:609-614.

Eigenmann, U.J.E., H. A. Schoon, D. Jahn, and E. Grunert. 1984. Neonatal respiratory distress syndrome in the calf. Vet. Rec. 114:141.

Erhard, M. H., E. Gobel, B. Lewan, U. Losch, and M. Stangassinger. 1997. Systemic availability of bovine immunoglobulin G and chicken immunoglobulin Y after feeding colostrum and whole egg powder to newborn calves. Arch. Tierernahr. 50:369-380.

Erhard, M. H., U. Losch, and M. Stangassinger M. 1995. Intestinal absorption of homologous and heterologous immunoglobulin G in newborn calves. Z. Ernahrungswiss. 34:160-163.

Fleenor, W. A., and G. H. Stott. 1980. Hydrometer test for estimation of immunoglobulin concentration in bovine colostrum. J. Dairy Sci. 63:973-977.

Garry, F. B. 1993. Clinical aspects of acidosis in newborn calves. Proc. of the 3rd Inter. Conf. on Vet. Perinatol. Davis, CA.

Garry, F., R. Adams, M. B. Cattell, and R. P. Dinsmore. 1996. Comparison of passive immunoglobulin transfer to dairy calves fed colostrum or commercially available colostral-supplement products. J. Amer. Vet. Med. Assoc. 208:107.

Guilloteau, P., T. Corring, P. Garnot, P. Martin, R. Toullec, and D. Durand. 1983. Effects of age and weaning on enzyme activities of abomasum and pancreas of the lamb. J. Dairy Sci. 66:2373.

Guy, M. A., W. K. Sanchez, J. J. Higgins, R. L. Crill, and J. G. Giesy. 1996. Effect of an oral paste of sodium bicarbonate given at parturition on immunoglobulin status of neonatal calves. J. Dairy Sci. 79(Suppl. 1):198. (Abstr.).

Halliday, R., and M. R. Williams. 1976. Passive immunity in the lamb. Effects of a second feed of colostrum on antibody absorption from the first feed. Res. Vet. Sci. 21:173.

Hopkins, B. A., and J. D. Quigley, III. 1997. Effects of method of colostrum feeding and colostral supplementation on serum IgG concentrations in neonatal calves. J. Dairy Sci. 80:979.

Ikemori Y, M. Ohta, K. Umeda, F. C. Icatlo, M. Kuroki, H. Yokoyama, and Y. Kodama. 1997. Passive protection of neonatal calves against bovine coronavirus-induced diarrhea by administration of egg yolk or colostrum antibody powder. Vet Microbiol. 58:105-111.

James, R. E., C. E. Polan, and K. A. Cummins. 1981. Influence of administered indigenous microorganisms on uptake of I^{125}-g-globulin in vivo by intestinal segments of neonatal calves. J. Dairy Sci. 64:52.

Jochims, K., F. J. Kaup, W. Drommer, and M. Pickel. 1994. An immunoelectron microscopic investigation of colostral IgG absorption across the intestine of newborn calves. Res. Vet. Sci. 57:75.

Johnston, N. E. and W. D. Oxender. 1979. Effect of altered serum glucocorticoid concentrations on the ability of the newborn calf to absorb colostral immunoglobulin. Am. J. Vet. Res. 40:32.

Joyce, P. W. and W. K. Sanchez. 1994. Dietary cation-anion difference and forage type during the dry period: effect on lactational performance and metabolic disorders of cows and health of calves. J. Dairy Sci. 77(Suppl. 1):97. (Abstr.).

Kasari, T. R. 1994. Physiologic mechanisms of adaptation in the fetal calf at birth. Vet. Clin. North Am. Food Anim. Pract. 10:127.

Kirk, R. W. 1983. Current Veterinary Therapy VIII: Small Animal Practice. W. B. Saunders Co., Philadelphia, PA.

Kruse, V. 1970. Absorption of immunoglobulin from colostrum in newborn calves. Anim. Prod. 12:627.

Lakritz J., J. W. Tyler, D. E. Hostetler, A. E. Marsh, D. M. Weaver, J. M. Holle, B. J. Steevens, and J. L. Denbigh. 2000. Effects of pasteurization of colostrum on subsequent serum lactoferrin concentration and neutrophil superoxide production in calves. Am. J. Vet. Res. 61:1021-1025.

Lateur-Rowet, H.J.M. and H. J. Breuink. 1983. The failure of the oesophageal groove reflex, when fluids are given with an oesophageal feeder to newborn and young calves. Vet. Quart. 5:68.

Lee, R.B., T.E. Besser, C.C. Gay, and T.C. McGuire. 1983. The influence of method of feeding on IgG concentrations acquired by calves. Proceedings, 4th International Symposium on Neonatal Diarrhea. VIDO, Saskatoon, Saskatchewan, Canada. pp. 373-377.

Logan, E. F., B. D. Muskett, and R. J. Herron. 1981. Colostrum feeding of dairy calves. Vet. Rec. 108:283.

Logan, E. F., G. R. Pearson, and M. S. McNulty. 1977. Studies on the immunity of the calf to colibacillosis - VII: The experimental reproduction of enteric colibacillosis in colostrum-fed calves. Veterinary Record. 101:443-446.

López, A., J. Löfstedt, R. Bildfell, B. Horney, and S. Burton. 1994. Pulmonary histopathological findings, acid-base status, and absorption of colostral immunoglobulins in newborn calves. Am. J. Vet. Res. 55:1303.

McEwan, A. D., E. W. Fisher, and I. E. Selman. 1968. The effect of colostrum on the volume and composition of the plasma of calves. Res. Vet. Sci. 9:284.

McEwan, A. D., E. W. Fisher, and I. E. Selman. 1970. An estimation of the efficiency of the absorption of immune globulins from colostrum by newborn calves. Res. Vet. Sci. 11:239.

Mechor, G. D., Y. T. Gröhn, and R. J. Van Saun. 1991. Effect of temperature on colostrometer readings for estimation of immunoglobulin concentration in bovine colostrum. J. Dairy Sci. 74:3940-3943.

Mechor, G. D., Y. T. Gröhn, L. R. McDowell, and R. J. Van Saun. 1992. Specific gravity of bovine colostrum immunoglobulins as affected by temperature and colostrum components. J. Dairy Sci. 75:3131-3135.

Mee, J. F., K. J. O'Farrell, P. Reitsma, and R. Mehra. 1996. Effect of a whey protein concentrate used as a colostrum substitute or supplement on calf immunity, weight gain, and health. J. Dairy Sci. 79:886-894.

Molla, A. 1978. Immunoglobulin levels in calves fed colostrum by stomach tube. Vet. Rec. 103:377.

Möllerberg, L., L. Ekman, and S. O. Jacobsson. 1975. Plasma and blood volume in the calf from birth till 90 days of age. Acta Vet. Scand. 16:178.
Morin, D. E., G. C. McCoy and W. L. Hurley. 1997. Effects of quality, quantity, and timing of colostrum feeding and addition of a dried colostrum supplement on immunoglobulin G1 absorption in Holstein bull calves. J. Dairy Sci. 80:747-753.
Morin D. E., P. D. Constable, F. P. Maunsell, and G. C. McCoy. 2001. Factors associated with colostral specific gravity in dairy cows. J. Dairy Sci. 84:937-943.
Mowrey, C. M. 2001. Influence of feeding pooled colostrum or colostrum replacement on IgG levels and evaluation of animal plasma as a milk replacer protein source. MS Thesis, Virginia Tech, Blacksburg, VA.
National Animal Health Monitoring System. 1992. Dairy herd management practices focusing on preweaned heifers. USDA, Animal and Plant Health Inspection Service, Veterinary Services, Fort Collins, CO.
National Animal Health Monitoring System. 1996. Dairy herd management practices focusing on preweaned heifers. USDA, Animal and Plant Health Inspection Service, Veterinary Services, Fort Collins, CO.
Olson, D. P., R. C. Bull, L. F. Woodward, and K .W. Kelley. 1981a. Effects of maternal nutritional restriction and cold stress on young calves: absorption of colostral immunoglobulins. Am. J. Vet. Res. 42:876.
Olson, D. P., C. J. Papasian, and R. C. Ritter. 1980a. The effects of cold stress on neonatal calves. 2. Absorption of colostrum immunoglobulins. Can. J. Comp. Med. 44:19.
Olson, D. P., L. F. Woodward, R. C. Bull, and D. O. Everson. 1981b. Immunoglobulin levels in serum and colostral whey of protein-metabolizable energy restricted beef cows. Res. Vet. Sci. 30:49.
Olson, D. P., C. J. Papasian, and R. C. Ritter. 1980b. The effects of cold stress on neonatal calves. 1. Clinical condition and pathological lesions. Can. J. Comp. Med. 44:11.
Pritchett, L. C., C. C. Gay, T. E. Besser, and D. D. Hancock. 1991. Management and production factors influencing immunoglobulin G_1 concentration in colostrum from Holstein cows. J. Dairy Sci. 74:2336-2341.
Pritchett L. C., C. C. Gay, D. D. Hancock, and T. E. Besser. 1994. Evaluation of the hydrometer for testing immunoglobulin G1 concentrations in Holstein colostrum. J. Dairy Sci. 77:1761-1767.
Quigley, J. D., III, J. J. Drewry, and K. R. Martin. 1998. Estimation of plasma volume in Holstein and Jersey calves. J. Dairy Sci. 81:1308-1312.
Quigley, J. D., III, D. L. Fike, M. N. Egerton, J. J. Drewry, and J. D. Arthington. 1998. Effects of a colostrum replacement product derived from serum on immunoglobulin G absorption by calves. J. Dairy Sci. 81:1936-1939.
Quigley, J. D., III, P. French, and R. E. James. 2000. Effect of pH on absorption of immunoglobulin G in neonatal calves. J. Dairy Sci. 83:1853-1855.

Quigley, J. D., III, K. R. Martin, D. A. Bemis, L.N.D. Potgieter, C. R. Reinemeyer, B. W. Rohrbach, H. H. Dowlen, and K. C. Lamar. 1994a. Effects of housing and colostrum feeding on the prevalence of selected organisms in feces of Jersey calves. J. Dairy Sci. 77:3124.

Quigley, J. D., III, K. R. Martin, H. H. Dowlen, and K. C. Lamar. 1995. Addition of soybean trypsin inhibitor to bovine colostrum: Effects on serum immunoglobulin concentrations in Jersey calves. J. Dairy Sci. 78:886.

Quigley, J. D., K .R. Martin, H. H. Dowlen, L. B. Wallis, and K. Lamar. 1994b. Immunoglobulin concentration, specific gravity, and nitrogen fractions of colostrum from Jersey cattle. J. Dairy Sci. 77:264-269.

Quigley, J. D., III, R. E. Strohbehn, C. J. Kost, and M. M. O'Brien. 2001. Formulation of colostrum supplements, colostrum replacers and acquisition of passive immunity in neonatal calves. J. Dairy Sci. 84:2059–2065.

Rajala, P., and H. Castrén. 1995. Serum immunoglobulin concentrations and health of dairy calves in two management systems from birth to 12 weeks of age. J. Dairy Sci. 78:2737.

Roy, J.H.B. 1990. The Calf. Volume 1. Management of Health. Butterworths, Boston, MA.

Selman, I. E., A. D. McEwan, and E. W. Fisher. 1970. Serum immune globulin concentration of calves left with their dams for the first two days of life. J. Comp. Pathol. 80:419.

Staley, T. E., and L. J. Bush. 1985. Receptor mechanisms of the neonatal intestine and their relationship to immunoglobulin absorption and disease. J. Dairy Sci. 68:184.

Stauber, E. H. 1976. Weak calf syndrome: a continuing enigma. JAVMA 168:223.

Stott, G. H. 1980. Immunoglobulin absorption in calf neonates with special consideration of stress. J. Dairy Sci. 63:681.

Stott, G. H., and A. Fellah. 1983. Colostral immunoglobulin absorption linearly related to concentration for calves. J. Dairy Sci. 66:1319.

Stott, G. H., D. B. Marx, B. E. Menefee, and G. T. Nightengale. 1979. Colostral immunoglobulin transfer in calves. IV. Effect of suckling. J. Dairy Sci. 62:1908.

Stott, G. H. and E. J. Rienhard. 1978. Adrenal function and passive immunity in the dysotical calf. J. Dairy Sci. 61:1457.

Szenci, O. 1985. Role of acid-base disturbances in perinatal mortality of calves. Acta Vet. Hung. 33:205.

Thivend, P., R. Toulec, and P. Guilloteau. 1980. Digestive adaptation in the preruminant. Page 561 *in* Digestive Physiology and Metabolism in Ruminants. Y. Ruckebusch and P. Thivend, ed. AVI Publ. Co., Westport, CT.

Tucker, W. B., J. F. Hogue, G. D. Adams, M. Aslam, I. S. Shin, and G. Morgan. 1992. Influence of the dietary cation-anion balance during the dry period on the occurrence of parturient paresis in cows fed excess calcium. J. Anim. Sci. 70:1238.

Tyler, H., and H. Ramsey. 1991. Hypoxia in neonatal calves: effect on intestinal transport of immunoglobulins. J. Dairy Sci. 74:1953.

Vann, R. C., J. W. Holloway, G. E. Carstens, M. E. Boyd, and R. D. Randel. 1995. Influence of calf genotype on colostral immunoglobulins in Bos taurus and Bos indicus cows and serum immunoglobulins in their calves. J. Anim. Sci. 73:3044.

Waltner-Toews, D., S. W. Martin, A.H. Meek, and I. McMillan.1986a. Dairy calf management, morbidity and mortality in Ontario Holstein herds. Prev. Vet. Med. 4:103-117.

Waltner-Toews, D., S. W. Martin, and A.H. Meek. 1986b. Dairy calf management, morbidity and mortality in Ontario Holstein herds. IV. Association of management with mortality. Prev. Vet. Med. 4:159-171.

Zaremba, W., W. M. Guterbock and C. A. Holmberg. 1993. Efficacy of a dried colostrum powder in the prevention of disease in neonatal Holstein calves. J. Dairy Sci. 76:831-836.