Technologies for Delivering Passive Immunity to Newborn Calves

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Maternal-Fetal Environment

Unlike human infants calves are born almost entirely devoid of a competent humoral (antibody) immune system. This is due to the unique form of maternal-fetal placentation during gestation, which allows for little to no transfer of large proteins from maternal to fetal blood. In ruminants, this form of placental attachment probably has important evolutionary significance in that grazing animals may consume toxin-containing plants, which could be harmful to the developing fetus. Although avoiding contact with maternal blood may prove beneficial in some instances it does present an obstacle for delivering immune protection to the newborn.

Attainment of Passive Immunity

Pre-partum Mammary Environment

Attainment of immunity in newborn ruminants is achieved via the oral consumption of immunoglobulin (Ig) rich lacteal secretions shortly after birth. These lacteal secretions are collectively referred to as colostrum. At birth, ruminants possess a highly permeable intestinal epithelium, which both passively and selectively allows for the passage of large molecules. Those, which are viewed most important for influencing passive immunity, are the immunoglobulin proteins. Other factors, which have been shown to have some immunological significance, are also present in colostrum. These will be described later in further detail. During the final weeks of parturition, hormonal changes in the cow cause a rapid and selective accumulation of immunoglobulin in the lacteal secretions. This process is short-lived, as subsequent milkings after parturition reveal a rapid decline in Ig concentration (Foley and Otterby, 1978). These immunoglobulins are antibodies that are derived from the cow's own humoral immune system. They represent a complex cascade of specificities to antigens from which she has been exposed throughout her lifetime. This maternal exposure can be both natural and a product of vaccination. Because older cows have had more opportunity to be exposed to a variety of antigens, coupled with their ability to produce a larger volume of colostrum, cow age tends to affect both the concentration and specificity range of colostral immunoglobulin (Devery-Pocius and Larson, 1983).

Colostrum Consumption and Passive Immunity

The immunity attained through the consumption of colostrum is referred to as passive immunity. Passive immunity is that which is received *passively* from an exogenous source. In almost all instances, passive immunity in calves is quantified by the concentration of immunoglobulin-G found in the bloodstream at 24 to 48 h after birth. Numerous reports have shown a positive correlation between blood IgG concentrations and the incidence of morbidity in calves (Perino and Rupp, 1996; Besser and Gay, 1994; Nousiainen et al., 1994; Gay, 1984; Nocek et al., 1984). As well, the attainment of passive immunity has been shown to affect subsequent calf growth even at later stages of life (Wittum and Perino, 1995). High blood Ig concentrations are not always associated with improved performance. Health within a herd is a balance between the magnitude of pathogen exposure and the level of immunity achieved in the animal. Optimization of passive immunity and/or disease control equally impact subsequent young animal performance.

Attainment of passive immunity, via colostrum, must occur before the calf's intestinal epithelium ceases to be permeable to the large Ig proteins. This is refereed to as gut closure and is a function of both time and stimulation from orally consumed material. Typically, a healthy calf, which has access to liquid feed or has consumed colostrum, will undergo complete gut closure by about 24 hours after birth. Even though some Ig absorption may occur up to 24 hours, the ability to absorb large proteins decreases rapidly within the first couple hours of life (Figure 1). Attainment of adequate passive immunity is often associated with 24 to 48 h blood IgG concentrations $\geq$ 10 g/L. The incidence of illness in calves with blood IgG concentrations below 10 g/L is increased when compared to calves with concentrations above this generic threshold.

Immunoglobulin is not the only colostral factor, which may be important in passive immune support in newborn calves. Cell-mediated immunity may also play a significant role in passive immunity. This type of immunity originates from the viable leukocytes (white blood cells) found in colostrum. The significance of cell-mediated immunity is probably most closely associated with maternal lymphocytes (specifically T-lymphocytes), which may be absorbed following colostrum consumption. Because of their short life span and their tendency to engulf lipid, it is doubtful that non-specific immune cells (neutrophils and macrophages) hold much relevance in the colostral transfer of cellular immunity. One commonly cited study on this subject (Riedel-Caspari, 1991) reported that newborn calves offered colostrum or milk replacer containing colostral leukocytes experienced improved antibody responses to sheep erythrocyte challenge. This response is T-lymphocyte dependent and illustrates the potential importance of their presence in colostral secretions.

Sources of Exogenous Immunoglobulin – Colostrum Supplementation

Many attempts have been taken to control the means by which newborn calves may obtain passive immunity. The beef industry seldom interferes with the cow after calving, allowing the calf to obtain colostrum through voluntary nursing shortly after birth. In contrast, the dairy industry usually does not place significance on maternal characteristics (i.e. mothering abilities) in breeding programs. Nevertheless, the 1994 National Dairy Heifer Evaluation Project showed that nearly 1/3 of all dairy producers relied on the calf to suckle the dam to achieve colostrum consumption. When dairy calves are left to suckle the dam, it is difficult to know when or how much colostrum the calf is actually ingesting. A high proportion of calves forced to obtain their passive immunity in this manner will not achieve adequate transfer of Ig. Therefore, it is always important to have a management plan that optimizes a newborn calf's ability to achieve adequate passive immunity. These plans call for the physical feeding of an immunoglobulin source to the newborn dairy calf.

Feeding Immunoglobulin to Newborn Calves

Several sources of immunoglobulin will be discussed in this review. Each are similar in that they share in the fundamental factors affecting Ig absorption in newborn calves, including, but not limited to, 1) sex of calf, 2) incidence of acidosis at birth, 3) breed of calf, 4) environmental stress, and most importantly 5) Ig concentration of the first feeding, and 6) time of Ig consumption. The concentration of Ig in colostrum is the common determinant of colostral quality. Typically, colostrum containing > 50 g IgG/L is considered to be of high quality. Colostral IgG concentration in a typical 2-L feeding has been shown to be linearly and positively correlated ($r^2 = .77$) to subsequent serum IgG concentrations 24 h later (Stott and Fellah, 1983). As well, the time of colostrum feeding (age of first feeding) has an inverse effect on rate of absorption (Stott et al., 1979), whereas calves offered the same amount of Ig at 24 h of age achieved less than 20% of the total Ig absorption experienced by calves fed Ig immediately after birth.

Immunoglobulin feeding may be achieved by using a nipple bottle feeder or an esophageal tube. Bottle-feeding is the most widely used method for delivering an Ig source to newborn calves. Healthy calves may voluntarily consume two to three liters of colostrum within a few hours of birth. Two ensure adequate Ig intake, two feedings of colostrum within 12 hours of birth is commonly recommended. Subsequent attainment of passive immunity is similar in calves fed high quality colostrum in one or two feedings, providing these feedings are offered with 12 hours of birth (Hopkins and Quigley, 1997). If a producer wishes to offer a larger volume, or if the calf is unable or unwilling to suckle, an esophageal feeder may be used. The esophageal feeder is a long, narrow, rigid tube, which is placed down the esophagus of the newborn calf. A bottle or bag on the other end of the tube contains the fluid, which is then released to flow into the calf's stomach. The use of an esophageal tube has been associated with a slight decrease in the efficiency of Ig absorption. In bottle-fed calves, the suckling action closes the esophageal groove, allowing fluid to bypass the undeveloped rumen. Colostrum from tube fed calves is deposited into the rumen where it may remain for several hours. This time lag probably explains the decrease in Ig absorption efficiency. Nevertheless, the use of an esophageal tube provides a quick and simple method for ensuring delivery of Ig to newborn calves. It is also essential when a producer wishes to deliver volumes larger than a calf may consume voluntarily.

Frozen Colostrum

Producers may wish to have a stored supply of quality colostrum available. This can be achieved by freezing high-quality colostrum collected from the first milking after parturition. Colostrum may be stored frozen for up to a year with no significant loss in Ig concentration. High-quality colostrum is usually defined as a colostrum pool which possessing at least 50 g IgG/L. Measuring colostral quality on the farm can be achieved by the use of a colostrometer. The colostrometer is a hydrometer device calibrated to associate specific gravity of colostrum with Ig concentration. When using this instrument it is important to consider temperature of the colostrum being tested. Variations in colostrum temperature can impact specific gravity. Although researchers have found this instrument to adequately reflect Ig content, they often warn of the precision of this estimate. In practical situations the colostrometer should be used only to identify classes of quality (i.e. high quality versus poor quality). These colostrum pools may be frozen in individual plastic bags in 1-L volumes. It is important to not overheat frozen colostrum during thawing. A good practice to follow is to submerge the sealed frozen bag into a bath of warm water allowing it to thaw slowly over approximately 30 minutes.

Milk-Derived Ig Supplements

Alternative Ig sources have been developed commercially and may be used to fortify or replace natural colostrum. Historically, these commercial products have been derived from lacteal secretions; either dried colostrum or concentrated whey sources. Several researches have investigated the effectiveness of these supplements for both the supplementation as well as the full replacement of natural maternal colostrum (Morin et al., 1997; Mee et al., 1996; Francisco and Quigley III, 1993; Zaremba et al., 1993). Results have not been promising. Their limited effectiveness has been broadly attributed to the low concentration of Ig in most commercial powders (Haines et al., 1990). The efficiency of absorption of commercial sources of supplemental Ig has been investigated. A frequently cited report from Colorado State University compared the efficiency of IgG absorption of three commercial colostrum supplements with natural colostrum (Garry et al., 1996). The colostrum products tested in this study all absorbed at a much lower efficiency than natural colostrum (Figure 2). In this study, the commercial products were fed at a much higher mass of dried powder than is recommended by the manufacturers. This was done in an attempt to increase the mass of Ig offered to the calves to a level that was similar to the amount of Ig offered through the natural colostrum treatment. It is possible that the increase in percent solids of the treatment fluid decreased the efficiency of Ig absorption.

Serum-Derived Ig Supplements

In recent years a new source of supplemental Ig, from processed bovine and porcine serum, has become commercially available. Blood, harvested as a byproduct of the packing industry, contains an abundant supply of Ig concentrated serum. Serum is harvested from plasma, which has been separated from red-blood cells in whole blood (Figure 3). The liquid serum is then spray-dried into a fine, tan powder containing approximately 20 % IgG on a powder basis, as well as other biological proteins (Figure 4). Combined with selected carriers to improve solubility and handling, dried bovine serum products can offer as much as 10 % IgG on a powder basis.

The importance of Ig concentration in commercial powder supplements (discussed earlier) is also relevant to serum-derived supplements. Research has shown that the total percent solids of the fluid offering also affects the absorption efficiency of serum-derived Ig (Quigley et al., 1998). In this study, colostrum deprived calves fed 266 grams of powder had an efficiency of IgG absorption greater than calves fed an equal mass of Ig from pooled colostrum. However, when calves were offered 750 grams of IgG from dried serum powder, the absorption efficiency was greatly reduced. These findings support the importance of utilizing a supplement material, which is concentrated in Ig.

The absorption efficiency of serum-derived Ig from both bovine and porcine sources has been investigated in newborn colostrum deprived calves. In one study (Arthington et al., In Press. J Dairy Sci), calves fed bovine serum-derived Ig had higher 24- and 72-h serum IgG concentrations compared to calves fed maternal colostrum and porcine-derived serum Ig (Table 1). This report is the first illustrating the ability of a dried supplemental Ig source to provide passive immune support at a level equal to or greater than natural colostrum-derived Ig. It also supports the importance of ensuring the use of bovine- versus porcine-derived Ig when selecting a commercial, dried-serum supplement. Porcine-serum derived Ig failed to be absorbed at the efficiency of bovine-serum derived IgG. This may suggest a preferential selection for the absorption of species-specific Ig in the newborn calf. Research with foals suggests that heterologous Ig is not absorbed as efficiently as Ig from mares (Holmes and Lunn, 1991).

Serum-derived Ig appears to be much more effective in delivering passive immune support to newborn calves compared to commercial milk-derived supplements. This theory was tested in a second study where a comparison was made between serum-derived and milk-derived Ig supplements on their ability to deliver passive immunity to colostrum-deprived newborn calves (Arthington et al., 2000). In this study, the efficiency of IgG absorption from a commercial, dried bovine-serum product was compared with natural colostrum and two milk-derived Ig supplements. Colostrum supplement treatments were fed according to manufacturer's recommendations at birth and again at 12 h. This strategy resulted in varying masses of total IgG being offered to the calves (200, 90, 50, and 60 g of IgG for Colostrum, Bovine Serum, Supplement 1, and Supplement 2, respectively). Plasma IgG concentrations at 12 and 24 h differed ($P < .05$) for each treatment (Figure 5). Apparent efficiency of IgG absorption was greatest for Bovine Serum compared with Colostrum and Supplement 1 (Figure 6).

Producers often have an adequate supply of colostrum but realize that there may be a great deal of variation in quality (i.e. Ig concentration). Therefore, in a third experiment, we examined the effectiveness of using bovine serum-derived Ig to fortify poor and medium quality colostral pools. This research, conducted in collaboration with the University of Illinois (Arthington et al., In Press. J Dairy Sci). The results revealed that low and medium quality colostrum, supplemented with bovine serum Ig, can provide calves with as good or better passive immune support compared to calves consuming unsupplemented high-quality colostrum (Table 2). These findings have direct implications on the ability for calf managers to fortify existing colostrum sources with dried, bovine-serum powder, therefore providing calves with a maximal amount of available Ig.

Important Considerations in a Colostrum Management Program

The following points summarize important considerations when developing a quality colostrum management program. Particular points will certainly vary between locations and management styles. In general, however, calf producers who are able to focus and optimize these criteria will realize improved calf health and subsequent improved performance.

1. The calf must consume colostrum as soon after birth as possible. The ability of the calf to absorb IgG falls dramatically as the calf reaches 24 hours of age. Colostrum or colostrum supplement should be fed to the calf within 24 hours of age. If a calf is too weak to suckle colostrum or colostrum supplement from a bottle, an esophageal feeder should be used.

2. Always attempt to utilize high quality colostrum (minimum of 50 g of IgG / L). A colostrometer may be used to identify poor quality colostral pools.

3. When using a commercial supplement to fortify or replace colostrum attempt to obtain a product, which contains dried bovine serum. Dried bovine-serum based supplements will provide calves with an Ig source that is more readily absorbed compared to milk-based colostrum products.

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Tables and Figures

Table 1. Serum IgG concentrations at 24 and 72 h after 1st feeding in colostrum-deprived calves receiving Ig from pooled colostrum (PC), bovine serum (BS), or porcine serum (PS) sources.

	Serum IgG concentration, g/L			
Treatment	24 h	SE	72 h	SE
PC	5.7[a]	0.85	5.7[ab]	0.91
BS	8.3[b]	0.85	7.4[b]	0.85
PS	4.2[a]	0.85	3.5[a]	0.85

[ab]Means within column with different superscripts differ ($P<0.01$).

Table 2. Serum IgG concentrations at 12 and 24 h after 1st feeding, calf birth weight, and apparent efficiency of IgG absorption (AEA) in colostrum-deprived calves receiving IgG from colostrum sources of varying quality.

	Serum IgG concentration, g / L			
Colostrum Treatment[1]	12 h[2]	24 h	BW, kg	AEA, %
High Quality	6.7[a]	6.2[a]	42.5	25[a]
Medium Quality + BS	10.3[b]	9.6[b]	40.0	37[b]
Low Quality + BS	10.7[b]	9.6[b]	42.8	38[b]

[1]IgG concentrations of treatments were 95.8 (0% from bovine serum, BS), 95.2 (47% from BS), and 98.8 (70% from BS) g of IgG / 2 L feeding for high, medium, and low quality colostrum, respectively).
[2]Pooled SEM were 0.49 and 0.50 g of IgG/L for 12 and 24 h means and 1.4 % for AEA, respectively.
[ab]Means within a column with different superscripts differ ($P<0.05$).

Figure 1. Effect of Age on the Percent Absorption Capacity of the Calf Gut Epithelium

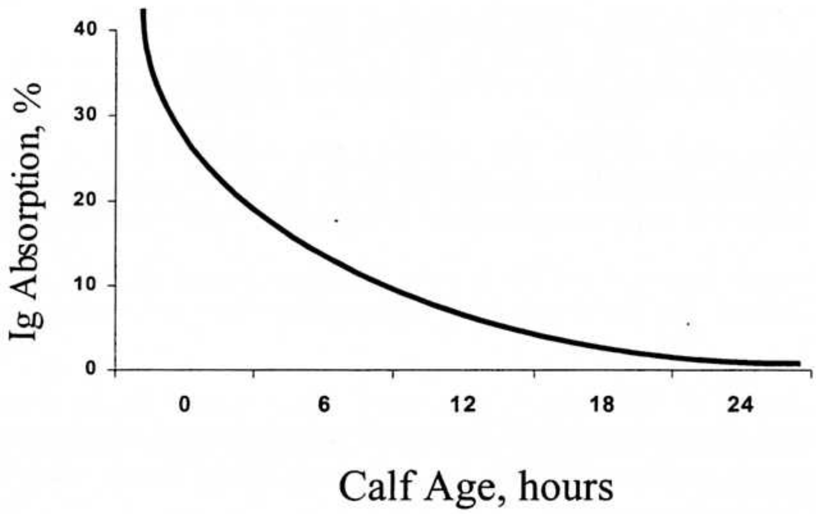
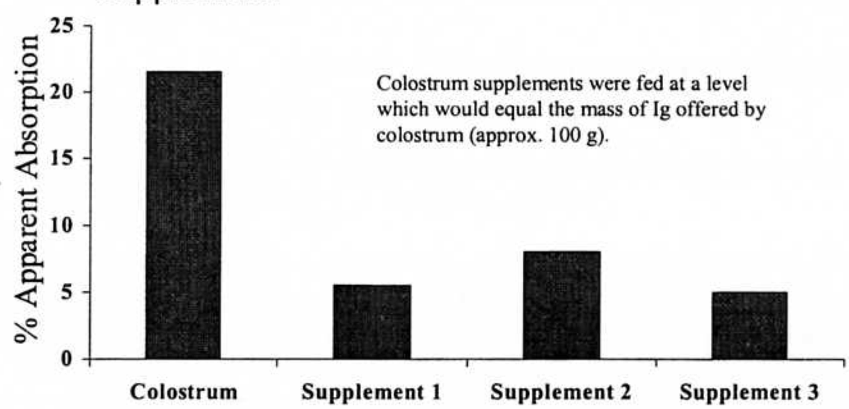


Figure 2. Apparent efficiency of IgG absorption in colostrum-deprived calves fed colostrum or colostrum-supplement.



Data adapted from Garry et al., 1996

Figure 3. Production of Ig Supplements from Whole Blood

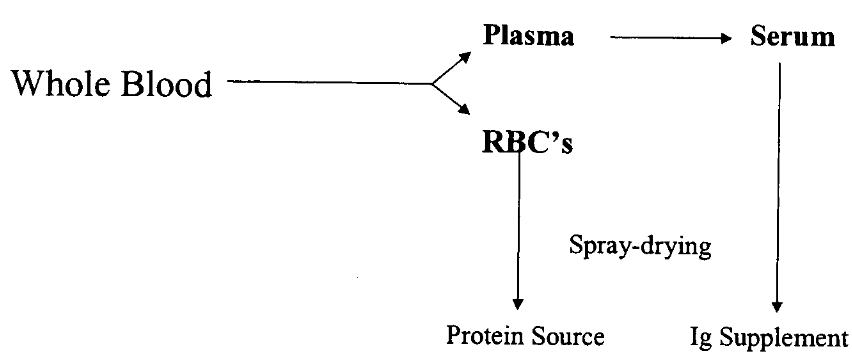


Figure 4. Constituents of Spray-Dried Serum

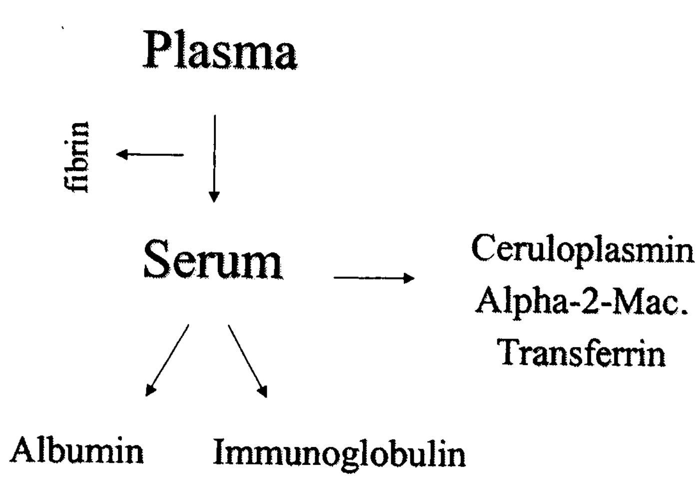
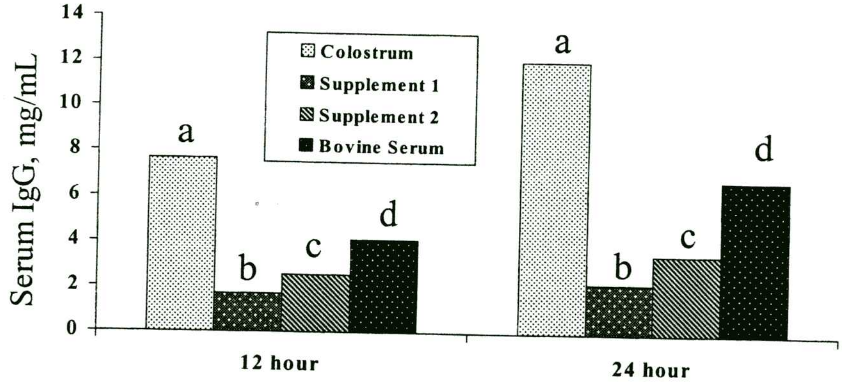


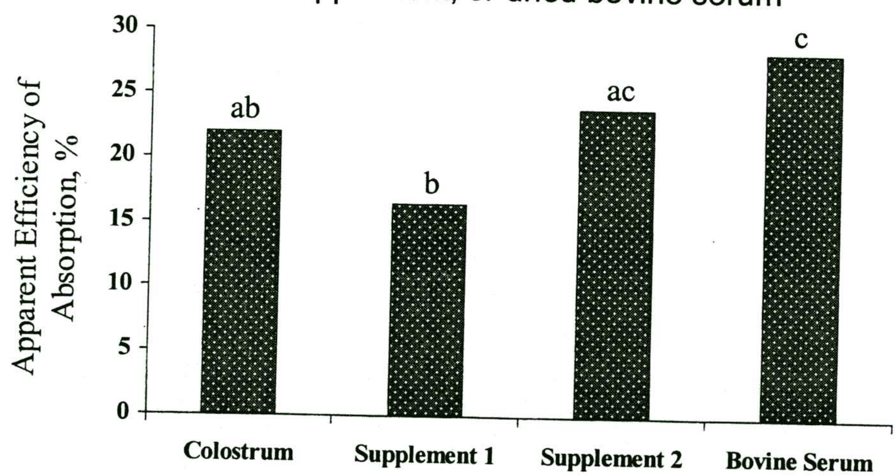
Figure 5. Effect of IgG source on subsequent 12- and 24-h serum IgG concentrations in colostrum-deprived calves.



Means with different superscripts differ, P < .05

Arthington et al., 2000

Figure 6. Apparent efficiency of IgG absorption in colostrum-deprived calves fed colostrum, milk-derived colostrum-supplement, or dried bovine serum



Means with different superscripts differ, P < .05

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