

COLOSTRAL IMMUNOGLOBULINS AND NEONATAL IMMUNITY IN BOVINE

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The calf has essentially no immune protection at birth because maternal immunoglobulins cannot cross the placenta, and the calf's own immune system is functionally immature. The calves are lymphopenic at birth. Leukocytes from calves produced unusually high concentrations of NO when compared with those produced by cows, thus constituting a possible indicator of the immaturity of the immune system of the neonatal calf. The calf's acquisition of colostrum immunoglobulins through absorption in the intestine is called passive transfer or passive immunity. In addition to disease protection, colostrum also provides the neonatal calf with high quality nutrition and many growth factors and hormones that may be beneficial for initiating function and growth of the digestive tract. "Failure of passive transfer" (FPT) occurs when the acceptable levels of IgG or total protein are not achieved by 24-48 hr after birth. Timely, adequate colostrum intake is the single most important management factor affecting morbidity and mortality in preweaned calves. The two most important factors affecting the amount of IgG absorbed from colostrum are the time of first feeding and the amount of IgG consumed. IgG more than 10g/L is optimal for neonatal survival.

Key words: Bovine, Colostrum, Immunoglobulins, Immunity, Neonates

Raising healthy calves with minimal mortality is crucial in successful dairying. There is no placental transfer of immunoglobulin (Ig) to the fetus. So the new born calf is dependent on colostrum for passive immunity (Quigley and Drewry 1998). Physiological immaturity of neonatal immune system renders them more susceptible to infectious diseases (Rajaraman et al. 1997). Colostrum quality is very critical for enhancement of passive immunity for the first 24 h of life (McGuire et al. 1976; Bush and Staley 1980; Matte et al. 1982). Colostrum is a source of immune components and nutrients to the neonates and contains more protein, immunoglobulins, nonprotein nitrogen, fat, vitamins, and minerals than milk. Absorption of Ig occurs non-selectively by pinocytosis, which moves proteins into the gut epithelium. The period during which the intestines of buffalo and cattle neonates are able to absorb colostrum Ig was reported to be 0 to 40 h (Deutsch 1957), 30 min to 5 h (Westrom et al. 1984; Heinrichs, 1985) after birth. Stott et al. (1979) found that calves fed colostrum after birth had a closure time for IgG absorption at 21 hours, IgM at 23 hours and IgA at 23 hours. Stott and Fellah (1983) reported that the IgG in the colostrum might be influencing apparent efficiency of absorption of immunoglobulins. Immune system of calf is more susceptible to oxidative stress during neonatal period due to immature defense system against superoxide radicals (Inemani et al. 1999). Nitric oxide (NO), a component of bactericidal mechanisms of phagocytic leukocytes, plays a pivotal role in cell-mediated immunity. It acts as an intracellular signaling molecule or as a neurotransmitter when produced in low quantities. Research has addressed many NO-related aspects of neonatal adaptation in the time period immediately following birth (Biban et al. 2001; Colnaghi et al. 2003; Levy et al. 2005, and Christen et al. 2007). Christen et al. (2007) reported that neonatal cattle and in part neonates of other species have many fold higher plasma concentrations of nitrite plus nitrate than mature subjects.

Colostrum Immunoglobulins

Immunoglobulins (Ig) present in the body are produced by plasma cells

that are originally derived from bone marrow cells. These plasma cells are present in various locations in the body and secrete immunoglobulins that collect in the blood and then can be utilized by the calf for required immune response. Immunoglobulins are divided into five classes (IgG, IgM, IgA, IgD and IgE). Each of these classes is then further divided into subclasses. Bovine mammary secretions contain four classes of immunoglobulins. The same immunoglobulins are present in colostrum and in milk, but they are found in much higher concentration in colostrum. While milk has less than 1 g/L of immunoglobulins, colostrums typically contains 50 to 100 g/L (Larson et al., 1980; Roy, 1990). Immunoglobulin G comprises 85 to 90% of colostrum immunoglobulin. Colostrum contains 50 to 200 times more IgG, 60 to 100 times more IgM, and 25 to 85 times more IgA than milk (Foley and Otterby, 1978; Norcross, 1982; Roy, 1990). The two subclasses of IgG i.e. IgG1 and IgG2 are found in similar concentrations in the blood of the dam. However, in colostrum, the majority of IgG is in the form of IgG1. (Larson et al., 1980) reported IgG1 to be seven times more concentrated in colostrum than IgG2 but the two subclasses are found in approximately equal amounts in the blood (Butler, 1983; Roitt et al., 1998; Roy, 1990). Immunoglobulin G1 is the major antibody of secondary immune responses, fixes complement, acts as the principle opsonin for macrophages, and is the primary immunoglobulin involved in transferring passive immunity to the neonate (Butler, 1983; Butler, 1969; Roitt et al., 1998). The mammary gland selectively transports IgG (primarily IgG1) in large amounts from the blood to colostrum via an intracellular transport mechanism (Larson et al., 1980). Immunoglobulin G2 fixes complement, mediates the cytotoxicity of polymorphonuclear neutrophils, and precipitates antigen (Butler, 1983). Immunoglobulins A (IgA) and M (IgM) are also found in colostrum, although in much smaller quantities. The secretory form of IgA, which is a dimer connected by a J-chain and attached to the secretory component, comprises about 5% of colostrum immunoglobulins (Butler, 1969; Larson et al., 1980). Immunoglobulin A protects the surface of mucosal membranes, including the intestine, and prevents pathogens from attaching to the surface of cells (Butler, 1983; Muller and Ellinger, 1981; Roitt et al., 1998). Immunoglobulin M is a pentamer that makes up 7% of colostrum immunoglobulins. Immunoglobulin M is the primary protective mechanism against septicemia, fixes complement, and is the major agglutinating antibody (Butler, 1969; Larson et al., 1980). Both IgA and IgM are synthesized locally by the mammary gland and concentrated in colostrum (Butler, 1969; Larson et al., 1980). Immunoglobulin E (IgE) is also present in bovine colostrum and can be transferred to the neonate. The role of IgE is less understood than the other immunoglobulins, but it does have skin-sensitizing activity (Butler, 1983).

Colostrum quality is very critical for enhancement of passive immunity for the first 24 h of life (McGuire et al., 1976; Bush and Staley, 1980; Matte et al., 1982). It is a source of immune components and nutrients to the neonates and contains more protein, immunoglobulins, nonprotein nitrogen, fat, ash, vitamins, and minerals than milk. Because some of the vitamins do not cross the placental barrier, colostrum constitutes the primary source of these nutrients for the calf after birth. Quigley and Drewry, (1998) reported that there was no placental transfer of immunoglobulins to the fetus. Since the cattle calves are born hypo-gammaglobulinemic (Van de Perre, 2003) transfer of maternal immunoglobulin's is important for providing antibody-mediated immune protection. IgG antibodies express multifunctional activities, including complement activation, bacterial opsonisation and

agglutination, and act by binding to specific sites on the surfaces of most of the infectious agents or products, either inactivating them or reducing infections (Lilius and Marnila, 2001).

The chemical composition of colostrum changes very fast within hours and days. Ganovski (1979) reported that following calving, the dry matter was reduced from 27.61% 2 h post calving to 16.85%; organic matter and proteins declined from 26.21% to 15.88%; and 18.19% to 8.50% respectively, on 7th day. Larson et al., (1980) quantified different fractions of immunoglobulins in colostrum of dairy cows. ImmunoglobulinG (IgG) constituted the principal fraction of total Ig. IgG1 isoform accounted for approximately 80% of total IgG (Holloway et al., 2001). While the ratio of IgG, IgM and IgA was 85–90%, 7% and 5% in dairy cows (Larson et al., 1980), it was to the tune of 86%, 8% and 5%, respectively in buffalo colostrum (Dang et al., 2009). Weaver et al., (2000) showed that colostrum IgG content was affected by volume of colostrum produced, parity, dry period length, vaccination, and many other factors.

	IgG ₁ (g/L)	IgG ₂ (g/L)	IgM (g/L)	IgA (g/L)
Colostrum	75.00	1.90	4.90	4.40
Whole Milk	0.35	0.06	0.04	0.05

Larson; Roy, 1980

Besides immunoglobulins, colostrum contains lymphocytes, cytokines, nucleotides and various growth factors which may affect the development of the immune system postnatally (Boutinaud and Jammes, 2002).

Nutritive components of colostrum

The importance of colostrum as a source of Ig is a well-known fact for most dairy producers. Benefits of feeding colostrum are not however, limited to Ig only. Colostrum also contains numerous nutrients such as protein, fat, carbohydrates, vitamins and minerals.

Colostrum is a good source of energy for the neonatal calf. The fat and lactose, which constitutes energy source in the colostrum, are necessary for the calf to begin thermogenesis (heat production) and maintain body temperature. Without this energy source, the calf would only have about 18 hours until its stores of body fat would have depleted (Davis and Drackley, 1998). In addition to energy, the vitamins and minerals in colostrum are at much higher levels than those found in whole milk (Davis and Drackley, 1998). It has been suggested that these increased amounts may be a way to ensure that the calf receives adequate amounts of these vitamins and minerals to initiate its metabolism and possibly to assist in the development of its digestive system.

Colostrum has two times more total solids, two times more fat, and four times than whole milk (Foley and Otterby, 1978). Colostrum composition and quality vary according to breed, parity, season, production at first milking, postpartum milking number, prepartum milking or leakage, and the health of the mammary gland (Devery-Pocius and Larson, 1983; Foley and Otterby, 1978; Kume and Tanabe, 1993; Maunsell et al., 1998; Muller and Ellinger, 1981; Pritchett et al., 1991; Quigley et al., 1998; Shearer et al., 1992). Jerseys have higher concentrations of IgG than Holsteins (Muller and Ellinger, 1981; Parrish et al., 1950; Quigley et al., 1998; Shearer et al., 1992), and in a small survey (Muller and Ellinger, 1981), Holsteins (n = 19) had the lowest IgG concentration of the five breeds compared. Cows in third or greater lactation have higher IgG content and a broader range of antibodies to more pathogens, regardless of breed (Devery-Pocius and Larson, 1983; Oyeniyi and Hunter, 1978; Pritchett et al., 1991; Quigley et al., 1998; Shearer et al., 1992). The increased concentrations of colostrum components are greatest in the first milking postpartum and decline quickly to normal concentrations by the fourth postpartum milking (Parrish et al., 1950; Stott et al., 1981). Cows milked intensively, or that experience

excessive colostrums leakage before calving, produce colostrum with reduced immunoglobulin content (Petrie, 1984). Nardone et al. (1997) observed that heifers exposed to heat stress in the last 90 d of gestation and in the first wk postpartum produced colostrum with lower IgG, IgA, total protein, and fat than non-heat-stressed heifers. As previously mentioned, colostrum quality is determined by IgG content. Generally accepted quality standards are: less than 20 g/L, poor quality; 20 to 50 g/L, moderate quality; and greater than 50 g/L, excellent quality (Shearer et al., 1992; Stott and Fellah, 1983).

Non-nutritive components of colostrum

In recent years, researchers have discovered that colostrum also contains a number of growth factors and non-specific antimicrobial factors in higher concentration than milk (Koldovsky, 1989; Odle et al., 1996; Reiter, 1978). Insulin-like growth factors I and II, epidermal growth factor, cortisol, and thyroxine (Xu, 1996) insulin, and prolactin concentrations are elevated in colostrum compared to milk (Koldovsky, 1989; Odle et al., 1996). Concentrations of insulin-like growth factor-I in colostrum range from 4 to 62 times those in milk, and epidermal growth factor is 2 to 4 times higher (Odle et al., 1996). In addition colostrums contain lysozyme, lactoferrin, and the components of the lactoperoxidase/thiocyanate/hydrogen peroxide system in quantities greater than those in milk (Reiter, 1978). These antimicrobial substances provide non-specific protection against infection and may aid the newborn during the gap between passive immunity and the development of the active immune system (Reiter, 1978). Several research studies have suggested that these components of colostrum may be beneficial for development and maturation of the digestive system (Davis and Drackley, 1998).

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. Absorption of Ig occurs non selectively by pinocytosis, which moves proteins into the epithelium. This absorption process had been thought to occur only in the terminal portion of the small intestine (Comline et al., 1951a; Hardy, 1969; Staley et al., 1972). However, later work found that absorption occurred throughout the small intestine (James et al., 1979; Jochims et al., 1994), although absorptive activity increased from duodenum to ileum and was greatest in the ileum. The period during which the intestines of buffalo and cattle neonates are able to absorb colostrum Ig was reported to be 0 to 40 h after birth (Deutsch, 1957), 30 min to 5 h (Westrom et al., 1984; Heinrichs, 1985). Stott et al., (1979a) found that calves fed colostrum after birth had a closure time for IgG absorption at 21 hours, IgM at 23 hours and IgA at 23 hours. In another experiment, these authors (Stott et al., 1979b) reported that the ability to absorb IgG across the intestinal epithelium diminishes rapidly after birth and ceases by approximately 24 h of age. They further reported that quantity of colostrum fed at the initial age had a significant effect on serum levels of Ig. Greater the quantity of colostrum, higher was the serum Ig concentration in the calf. Stott and Fellah, (1983) reported that the concentration of IgG in the colostrum might influence apparent efficiency of absorption.

Apparent Efficiency of Absorption (% AEA)

Quigley and Drewry, 1998 calculated apparent efficiency of IgG absorption in cattle calves. Efficiency of IgG absorption was determined by multiplying the estimated plasma volume of the calf by its 48-h serum IgG concentration and dividing this product by the mass of colostrum IgG that was fed. Plasma volume at 48 h was estimated to be 0.08 x BW at 48 h. McEwan et al., (1970) reported a mean plasma volume of 8.3% of BW. Mollerberg et al., (1975) reported a value of 6.5%. Others have reported mean values ranging from 8.7 to 9.3% (McEwan et al., 1968; Quigley and Drewry, 1998). Singh et al. (1992) reported blood volume in buffaloes to be 10% of the body weight. Mean AEA of maternal colostrum averaged 20 to 35% (Drewry, 1998) in cattle. The absorption of Ig is also affected by the environment in which the calf is born. Donovan et al., (1986) demonstrated seasonal effect on

immunoglobulin absorption, with highest total serum protein in February and March while lowest in the elevated environmental temperature. Extreme cold (Olson et al., 1980) but not moderate cold (Olson et al., 1981) was associated with reduced absorption of Ig by calves. Davis and Drackley, (1998) found that the heat stress, severe cold stress and severe dystocia reduced Ig absorption from colostrums.

Passive transfer (FPT) failure

Inadequate absorption of colostrum immunoglobulins through the gut is known as failure of passive transfer (FPT). If serum IgG concentration of less than 10 g/L, it is considered as a case of failure of passive immunity (Pare et al., 1993; Rea et al., 1996; NAHMS, 1993) and the calves are at greater risk of acquiring diseases. The National Animal Health Monitoring Service (NAHMS) evaluated calf and heifer rearing practices in 1991 and 1992 using representative national surveying techniques (NAHMS 1993, NAHMS 1994). The project, the National Dairy Heifer Evaluation Project (NDHEP), found that 64% of calves were fed colostrum by hand feeding and 33.7% were allowed to nurse the dam (more than half of these were unassisted). In addition, 25.6% of calves received less than 1.89 L of colostrum in the first 24 h (NAHMS, 1993). Heinrichs et al. (1994) interpreted these results and suggested that the calves fed less than 1.89 L of colostrum probably suffered FPT based on the average IgG concentration of Holstein colostrum. Furthermore, the NDHEP (NAHMS, 1993) reported 31% of calves had serum IgG concentrations less than 10 g/L. Successful transfer of passive immunity has been determined by measuring the concentration of IgG in the serum of the calf at 24 to 48 hours after birth. If serum IgG concentration exceeds the critical level, then the calf is thought to be relatively well protected against pathogens. Greater the concentration of IgG in the circulation of calves at 24 to 48 hours after birth, greater is the protection against the array of pathogens to which the calf might be exposed during extra uterine life.

Preventing failure of passive transfer

Failure of passive transfer is associated with increased risk of morbidity and mortality in preweaned calves. Therefore, management practices must be implemented to minimize FPT and enhance calf health. Several approaches to the problem of FPT exist. First and foremost, timely feeding of high quality colostrum in adequate amounts must occur. One logical and fairly common way to reduce FPT in calves is to save excess colostrum and freeze it for calves born to dams with low colostrum quality. Colostrum can be frozen in plastic containers or bags in amounts suitable for single feedings. Frozen colostrum can be stored at -18°C to -25°C for at least six mo without changing its quality (Roy, 1990; White, 1993). Colostrum is thawed as needed, typically in warm water, although successful thawing can be accomplished in a microwave oven (Jones et al., 1987). Slow thawing at temperatures below 50°C does not affect colostrum quality, but temperatures above 50°C cause colostrum proteins, including immunoglobulins, to denature (Roy, 1990; White, 1993). Once thawed, colostrum should be used immediately, as repeated freeze-thaw cycles decrease the amount of viable immunoglobulin protein (Roy, 1990; White, 1993). Over the past several years, interest in formulating supplemental products or colostrum substitutes to reduce the occurrence of FPT has grown. Supplement products are generally intended for addition to colostrum, to increase the amount of IgG provided to calves. To be labeled as a colostrum supplement, a product must be tested to demonstrate that it improves serum IgG concentrations compared to colostrum deprivation (Garry et al., 1996; Quigley et al., 2000a).

Colostrum supplements fall into four categories: dried colostrum products, whey protein-based products, serum protein-based products, and injectable products. Dried colostrum products were the first type of supplement investigated. Chelack et al. (1993) compared three methods of drying colostrum and concluded that spray drying was the most cost-effective method. Spray-dried colostrum was then reconstituted and fed to calves. Amounts of IgG fed were equal at 126 g (in two feedings) for spray-dried and frozen colostrum. Serum IgG concentration at 48 h was not different for

calves fed the spray-dried colostrum compared to calves fed frozen colostrum (11.6 g/L and 10.57 g/L respectively). Todd et al. (1993) found that calves fed colostrum plus a fortified colostrum powder, providing 128, 78, or 52 g of IgG depending on amount of powder fed and solvent (colostrum, milk, or water), achieved adequate passive immunity and remained healthy throughout the preweaning period. On the other hand, Zaremba et al. (1993) reported that calves fed 85 g of dried colostrum powder (9.6 g IgG) had lower serum IgG at 24 h than calves fed either 3 kg of pooled colostrum (288 g IgG) or 3 kg of pooled colostrums supplemented with 85 g of dried colostrum powder (297.6 g IgG). The addition of dried colostrum powder did not improve IgG concentrations compared to colostrum alone (Zaremba et al., 1993). Supplement products based on whey protein concentrate have also been introduced. Abel Francisco and Quigley (1993) found a change in the timing of absorption when they fed a colostrum supplement containing lyophilized colostrum and dried whey. The IgG1 concentration was highest in calves fed colostrum plus the supplement (198.7 g IgG1) at 12 h, but at 24 h the colostrum calves (fed 198.8 g IgG1) had the higher IgG1 concentrations. Arthington et al. (2000a) also reported higher IgG concentrations in calves fed colostrums compared to calves fed either of two whey protein-based supplements. Intake of IgG for the three groups was 200, 50, and 60 g for colostrum, supplement 1, and supplement 2, respectively. Garry et al. (1996) fed colostrum and three different supplement products. Calves were fed 164.7, 156.8, 107.7, or 126.0 g IgG in colostrum and supplement groups 1 through 3, respectively. The colostrum group had the highest serum IgG concentrations at 24h and was three times more efficient in absorbing IgG. In addition, the colostrum-fed calves experienced significantly fewer episodes of disease prior to weaning than calves fed supplements. Mee et al. (1996) found calves fed whey protein concentrate as a colostrums supplement (69.1 g IgG) or colostrum substitute (17.7 g IgG) had significantly lower serum IgG and total protein concentrations than colostrum-fed calves (123.6 or 117.2 g IgG). In addition, in one of two trials, calves fed only the supplement product had much greater mortality rate than colostrum-fed calves (27.6 and 3.4%, respectively). On the other hand, Seymour et al. (1995) reported similar health parameters and greater feed efficiency during the preweaning period for calves fed a whey protein concentrate substitute instead of colostrum, total IgG intakes were not reported.

Quigley et al. (1998b) fed colostrum or a colostrum replacer derived from bovine serum to calves in two blocks. Due to differences in colostrum quality between blocks, the amount of replacer fed was changed for block 2. This change provided an interesting result. Calves fed the serum product at a high dose (750 g, 150 g IgG) had reduced efficiency of absorption compared to calves fed the replacer at a low dose (266 g, 53.2 g IgG). At the high dose calves fed the replacer had lower 24 h plasma IgG than colostrum-fed calves (who were also fed 150 g IgG), but at the low dose the replacer calves absorbed more IgG than those fed colostrums (IgG intake was 53.2 g). Quigley et al. proposed that the large mass of non-IgG protein in replacement products might impair IgG absorption by competing for intestinal binding sites. Further investigation by this group led to a series of experiments designed to test the theory of competition for binding sites. They found that the addition of casein or whey protein concentrates to colostrum supplements or maternal colostrum had no effect on plasma IgG concentration unless total protein in the product exceeded 500 g (Arthington et al., 2000b).

In addition, the apparent efficiency of absorption was greater for medium and low quality colostrum diets (Arthington et al., 2000b). Arthington et al. (2000) proposed that bovine serum contains a concentrated source of immunoglobulin that is efficiently absorbed by newborns. Furthermore, supplementing colostrum with bovine serum product or feeding bovine serum product alone can improve passive transfer in newborns. Arthington et al. (2000b) also proposed that the more uniform isotype distribution in serum-based products, compared to colostrum, allowed greater absorption efficiency. Other attempts to prevent FPT have used plasma transfusions and injections of purified immunoglobulins (Crawford et al., 1995; Pederson et al., 2000; Quigley and Welborn, 1996; Zaugg, 1994). Transfusion of plasma obtained from mature cows failed to provide IgG concentrations similar to calves fed colostrum (Zaugg, 1994). Infusion of a purified IgG solution into

calves 3 to 8 d of age failed to increase serum IgG when administered subcutaneously, but did increase serum IgG when administered intravenously (Quigley and Welborn, 1996). Injection of purified IgG increased serum IgG compared to no colostrum, but did not increase it to the concentrations obtained by feeding colostrums (Crawford et al., 1995). More recently, Pederson et al. (2000) reported increased plasma IgG concentrations at 24 h when calves were injected at birth with bovine antiserum. In addition, administration of antiserum increased apparent efficiency of absorption by 42% over colostrum alone (Pederson et al., 2000). Effective replacement products would provide a viable alternative for producers facing low quality or contaminated colostrum supplies.

Neonatal Immune Status

The immune status of the newborn calf is widely accepted as hypogammaglobulinemic (Roy, 1980). The syndesmochorial structure of the bovine placenta prevents passage of immunoglobulins from maternal circulation into fetal circulation (Senger, 1997). Endogenous production of IgG began at 4 wk of age in calves with high initial IgG concentrations (Logan et al., 1974). However, in hypogammaglobulinemic calves, endogenous production began within a wk of birth (Logan et al., 1974). Husband et al. (1972) showed that endogenous production of IgG1 and IgG2 began 8 to 16 d after birth. Using 125I-labeled IgG1, Devery et al. (1979) found endogenous IgG1 production of 1 g/d began around 36 h and continued up to 3 wk of age. In summary, the newborn calf has virtually no passively acquired immunoglobulins at birth to fight infections.

In addition, the calf's own immune system is classified as functionally immature; the humoral immune system is incapable of mounting an effective response to invading pathogens (Roy, 1990). Physiological immaturity of neonatal immune system renders them more susceptible to infectious diseases (Rajaraman et al., 1997). Immune system of calf is more susceptible to oxidative stress during neonatal period due to immature defense system against superoxide radicals (Inemani et al., 1999). Passive immune protection is transferred to the calf by ingestion and absorption of intact immunoglobulins, particularly immunoglobulin G (IgG) from colostrum. Once absorbed, immunoglobulins equilibrate to vascular and extra vascular pools in a ratio of approximately 1:1 (Kruse, 1970; Payne et al., 1967). Reportedly, 68% of cleared immunoglobulin was returned to the lumen of the intestine each d over an 8 d period (Besser et al., 1988), where it retained antigen-binding activity and exerted a local protective effect (Besser, 1993; Besser et al., 1988).

Cell mediated immune functions

The calves are lymphopenic at birth (Outteridge and Duffy 1981; Manak 1986). The concentration gradually increases with age (Osburn et al., 1974; Clover and Zarkowen, 1980). Nagahata et al. (1991) found that antibody producing activity of lymphocytes was lower in calves up to 3 weeks after birth. Osburn et al. (1974) depicted a suppressed PHA-induced lymphocyte blastogenesis in the newborn as compared to bovine fetal lymphoid cells at 90 and 121 days of gestation (Osburn et al., 1974; Renshaw et al., 1977). Clover and Zarkower, (1980) reported that both PHA and PWM-induced blastogenic responses of peripheral blood lymphocyte from 6-hr old, colostrum fed calves were suppressed relative to those from 4-day old calves. Rajaraman et al. (1997) reported that peripheral blood mononuclear cells (PBMC) from 1-wk-old calves fed colostrum and milk were functionally hyporesponsive when compared to PBMC from adult cattle. Person et al., (1983) monitored the blastogenic response of calf lymphocyte to PHA and Con A at various levels for first 3 months of life. This suggested that although the lymphocytes of neonate calves had the ability to respond to mitogens, individual variations were noted in the lymphocyte reactivity. These age-related differences in PBMC functions are likely to contribute to the increased susceptibility of the neonate calf to infectious disease.

Other functional differences includes the capacity of PBMC from young calves to produce inducible NOS, a component of bactericidal mechanisms of phagocytic leukocytes, and interferon- γ (IFN), a pivotal cytokine in cell-

mediated immunity, Reduced secretion of other cytokines (Nonnecke et al., 1993), and reduced neutrophil function (Dore et al., 1991; Higuchi et al., 1997) have also been reported after birth.

Nitric oxide (Plasma nitrite + nitrate)

Nitric oxide (NO), a component of bactericidal mechanisms of phagocytic leukocytes, plays a pivotal role in cell-mediated immunity. It acts as an intracellular signaling molecule or as a neurotransmitter when produced in low quantities. When produced in higher quantities for extended periods, Research has addressed many NO-related aspects of neonatal adaptation in the time period immediately following birth (Biban, et al 2001; Colnaghi et al., 2003; Levy et al. 2005, and Christen et al., 2007). NO is involved in the killing of microorganisms and tumor cells (Nathan, 1995) and in hematopoiesis (Ouaaz, 1995). In cardiovascular adjustments and compensation, NO controls local blood flow, which ensures adequate tissue perfusion (Gow et al., 2002; Gow et al. 2004; Huang et al., 2003)

Leukocytes from calves produced unusually high concentrations of NO when compared with those produced by cows, thus constituting a possible indicator of the immaturity of the immune system of the neonatal calf (Rajaraman et al., 1998). These authors reported that leukocytes from 1-wk-old calves produced less nitric oxide (NO) and were less responsive to mitogenic stimuli than were leukocytes from older calves.

Blum et al. (1998) found very high NOx (=NO₂+NO₃, primarily NO₃) concentration in blood plasma, saliva and urine in new-born calves before the first meal, while concentrations in their cerebrospinal fluid and in the blood plasma and milk of their dams were very low. Christen et al., (2007) reported that neonatal cattle and in part neonates of other species have many fold higher plasma concentrations of nitrite plus nitrate than mature cows and subjects of other species, suggesting an enhanced and needed activation of the nitric oxide (NO) axis at birth. Elevated plasma concentrations of total nitrate plus nitrite, the footprint of enhanced nitric oxide synthase (NOS)-mediated nitric oxide (NO) production from arginine (Gow et al., 2002,2004), as well as several other recent lines of evidence, suggest that the NO axis plays a critical role in the neonate's adjustments to life (Huang et al., 2003).

Summary

It is concluded that the new born calves were immunologically immature at birth. Failure to achieve adequate passive immunity has been associated with increased morbidity and mortality, and poor colostrum feeding and management has been suggested as the primary reason for high mortality in calves. Therefore, calves must consume colostrum, which is rich in IgG, to protect against infection. Immunoglobulins are absorbed, primarily by an indiscriminate pinocytotic process, in the small intestine for about 24 h after birth. The importance of colostrum in determining calf health and survival is well established. Timely, adequate colostrum intake is the single most important management factor affecting morbidity and mortality in preweaned calves.

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