Reducing Failure of Passive Immunoglobulin Transfer in Dairy Calves

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SUMMARY

The dairy calf is unique in that its only source of early immunity is obtained passively from colostrum after birth. There are many factors that impact the early immune status of the dairy calf. Primary factors include the quality of colostrum fed, time of feeding and amount fed. Managing an effective colostrum program should consider these factors, which will result in high level of circulating maternal immunoglobulins present in the blood of the one day old dairy calf. The resulting condition when blood IgG levels are not met is termed failure of passive transfer or FPT. Failure of passive transfer of immunoglobulins results in increased morbidity and mortality for the young calf thus is of great economic importance to the dairy industry. Increased exposure from pathogens makes calves prone to FPT and more susceptible to morbidity and mortality. Recent research has shown methods to pasteurize colostrum to reduce bacterial loads in colostrum. Pasteurization has shown the additional effects of improving immunoglobulin absorption by the calf. The objective of this review is to summarize the literature of achieving proper levels of passive immunity in calves, including the importance of colostrum for the neonate, IgG absorption, and effects of pasteurization on bacterial load, and IgG levels.

Keywords: Dairy calf, colostrum, failure of passive antibody transfer, health, neonatal nutrition, pasteurizing colostrum.

RÉSUMÉ

Réduire le défaut de transfert passif d'immunoglobulines chez le veau laitier

Le veau nouveau-né est totalement privé d'immunité propre à la naissance et acquiert cette immunité passivement via l'absorption de colostrum après sa naissance. De nombreux facteurs peuvent influencer le statut immunitaire du veau dans les premiers jours de vie. Les facteurs principaux comportent la qualité du colostrum fourni, le moment de l'alimentation colostrale ainsi que la quantité apportée. Un programme d'alimentation colostrale efficace doit considérer ces facteurs afin d'atteindre un niveau élevé d'immunoglobulines maternelles circulantes dans la circulation générale du veau au lendemain de sa naissance. Dans le cas où le niveau sanguin d'IgG atteint est inferieur à la valeur seuil recherchée, on parle alors d'un défaut de la transmission passive d'immunité ou FPT. Ce défaut de transmission passive d'immunité provoque une morbidité et une mortalité accrue chez les jeunes veaux, qui engendrent des pertes économiques conséquentes pour les élevages bovins laitiers. Une pression sanitaire forte augmente l'exposition du jeune veau à divers pathogènes et le rend également plus susceptible au FPT et donc morbidité et mortalité sont accrues. Des travaux de recherche récents ont évalué l'impact de diverses méthodes de pasteurisation du colostrum sur sa contamination bactérienne. La pasteurisation a également démontré des effets bénéfiques sur le niveau d'absorption des immunoglobulines par le veau nouveau-né. L'objectif de cet article est de synthétiser la littérature disponible quand aux façons d'atteindre un niveau d'immunité passive adéquat pour le veau nouveau-né, en incluant l'importance du colostrum pour le nouveau-né, l'absorption des IgG et les effets de la pasteurisation du colostrum sur sa contamination bactérienne et les niveaux d'IgG absorbés par le veau.

Mots clés : veau, colostrum, défaut de transfert d'immunité passive, santé, nutrition néonatale, pasteurisation.

Introduction

Colostrum feeding is a critical step in raising healthy calves as a result of the unique physiology and metabolism of the bovine. This physiological aspect relates to the inability of the placenta of the bovine to transmit maternal immunoglobulins *in utero* [1]. Although newborn calves prior to colostrum feeding are capable of mounting a small immune response, they are best characterized as being immunonaive [7]. The ingestion and absorption of colostral immunoglobulins are essential for establishing immunity, until the calf's own immune system becomes functional, beginning at 3-6 weeks of age [6, 45].

The transfer of immunoglobulins from the dam to the neonate, termed passive transfer, is important in the protection of the newborn from infectious disease. A condition that predisposes the neonate to the development of disease syndromes that has been termed failure of passive transfer, (FPT). It has been estimated that as many as 35% of dairy calves in the United States suffered from FPT [12, 55], making FPT a major economic consideration for dairy producers [39]. Recent National Animal Health Monitoring System dairy studies reported that mortality rate among pre-weaned dairy heifers on United States farms averaged 7.9% [40], and a great proportion of these deaths could be attributed to failure of passive transfer based on associated research with calf health events.

The small intestine of the newborn calf possesses the capacity to absorb intact large protein molecules, such as immunoglobulins [39, 59]. This is an important step in the process of developing a strong passive immune level in the calf. The conclusion of macromolecule absorption is termed gut closure and occurs at different times depending on the species [13].

While the exact mechanism behind closure has yet to be determined, it has been proposed that it reflects a combination of exhaustion of pinocytotic capability and enterocyte replacement by a more mature population of gut epithelial cells [13]. In calves, closure occurs at approximately 24 h postpartum [55]. For this reason, the absorption of sufficient immunoglobulins that provide passive immunity to the calf must happen before one day of age. The efficiency of absorption however decreases rapidly after birth until 24 h and has been shown to be in a linear manner [13].

Preventing bacterial contamination during the harvest, storage, and feeding processes is an important aspect of a colostrum program [53]. Some management strategies to prevent bacterial proliferation in stored colostrum include freezing, refrigeration, and the use of preservative agents such as potassium sorbate in refrigerated fresh colostrum [53]. One additional method for reducing or eliminating bacterial pathogens is to heat-treat fresh bovine colostrum [38]. Pasteurization studies on colostrum have been done using the same times and temperatures recommended for milk [22]. However, there has been limited laboratory and field studies investigating the practice of heat-treating colostrum and they have reported varying results with respect to effect of heating on both colostral Ig levels and rates of failure of passive transfer. Few studies look at the short- and long-term calf health and performance [29].

The objective of this review is to present a summary of the literature of factors affecting bovine colostrum absorption and factors that may minimize failure of passive transfer of antibodies in the neonate dairy calf. Further review will be related to pasteurizing colostrum to reduce pathogen exposure and improve passive antibody transfer.

Colostrum for the bovine neonate

The immune system of the calf at birth is inefficient in its ability to produce antibodies to help fight infections [39]. Colostrum, the first secretion produced by the mammary gland after parturition, is especially rich in immunoglobulins [6, 21], which provide the calf immune protection during the first weeks of life [42].

Colostrum provides passive immunity for the newborn calf and also has effects on the development of the neonatal intestine, since it contains a number of bioactive and growth-promoting substances such as peptide hormones, growth factors, cytokines, steroid hormones, thyroxine, nucleotides, polyamines, enzymes, lactoferrin, lysozymes, insulin, cytokines, IGF-1, and IGF-2 [20, 33, 43]. Villous circumference, area, height, and height/crypt depth ratio in the duodenum have been shown to be greater for calves fed colostrum compared with colostrum-deprived calves [10, 14]. Calves fed colostrum also have greater plasma xylose concentrations after oral administration of xylose compared with calves fed milk replacer, suggesting enhanced absorptive capabilities in colostrum-fed animals [25, 34].

Colostrum is also important as the first source of nutrients for the calf after birth. It contains nutrients including proteins, essential and nonessential amino acids, fatty acids, lactose, fat and water soluble vitamins, and minerals [21, 32]. Except for casein and lactose, colostrum contains nutrients in greater amounts than does mature milk [11, 21, 33]. Contents of energy, protein, fat and some minerals are markedly higher in colostrum than in mature milk [21]. It is important to emphasize that the concentration of proteins and peptides diminishes quickly after the onset of the lactation [23, 36]. Likewise, the concentration of immunoglobulins is significantly reduced in subsequent milkings [18, 54]. Initial immunoglobulin levels and specificity can be modified through maternal vaccination programs as is often recommended [18].

The importance of immunoglobulins for the bovine neonate

Colostrum contains large quantities of immunoglobulins [32] that are transferred from the cow's bloodstream [4, 16, 35, 48]. Transport of immunoglobulins from the serum to the mammary gland begins several weeks before parturition and reaches a peak 1 to 3 d before parturition in the cow [5, 47]. Immunoglobulin G, M and A are the primary types found in bovine colostrum [17, 43]. The IgG, IgA and IgM typically account for 85, 5, and 7% of the total of Ig in colostrum, respectively [35, 47]. Bovine IgG can be divided into 2 subclasses: IgG_1 and IgG_2 [17], but IgG_1 comprises more than 90% of the total IgG [6, 43]. Although IgG_1 and IgG_2 are present at approximately equal concentration in ruminant blood, only the IgG_1 subclass is transported in large amounts from the maternal plasma across the alveolar epithelial cells into the mammary secretions [2, 35]. This uptake is facilitated by receptors present on these cells [5, 16]. The bovine neonatal Fc receptor for IgG (**FcRn**) was recently cloned and its expression was demonstrated in multiple tissues, including the mammary gland and the small intestine [31]; however, how FcRn is involved in mammary IgG transport has not been directly assessed [37]. Total IgG or IgG_1 in the blood serum accounts for an adequate indicator of the transfer of passive immunity [27].

Increased neonatal mortality and morbidity is a well-accepted consequence of failure of passive transfer. VIRTALA *et al.*, [60] showed that low post-colostral serum IgG level is a significant risk factor for the development of pneumonia in heifer calves. A study by WELLS *et al.*, [62] concluded that lack of colostral feeding was highly associated with neonatal death loss in the United States. Also DONOVAN *et al.*, [19], in a prospective study to determine calf-level factors that affected calf health status between birth and 6 mo of age, showed that there was a clear association between serum total protein (a measure of colostral immunoglobulin absorption) and mortality. Calves with low serum total protein values (< 50 g/L) were 3 to 6 times more likely to die within the first 6 mo of life than those with serum total protein concentrations of > 60 g/L. In a previous study by NOCEK *et al.*, [41], calves deprived of colostrum gained BW poorly and suffered severe and long episodes of scours and high mortality. Calves fed colostrum with high immunoglobulin gained BW from birth to d 4 while those fed colostrum with low immunoglobulin levels lost BW. Overall severity and duration of scours were less for calves fed colostrum with high compared to low immunoglobulin levels. In another study [8] it was demonstrated that calves with high serum IgG concentrations had lower mortality rates from both enteritis and respiratory disease than calves with serum concentrations of less than 10 g/L.

Insufficient serum Ig concentrations at 24 to 48 h could necessitate an immune response by the calf before it is immunologically capable of handling an invasion of pathogenic organisms. Illnesses often associated with such invasions can detract from the normal growth and development of the calf. Calves with adequate serum immunoglobulins often are able to inactivate pathogenic invasions earlier than calves with lower serum immunoglobulins that must mount an immune response for defense. Therefore, calves having adequate serum immunoglobulins will continue to grow normally and not be deterred as would calves with insufficient immunoglobulins [45].

Absorption of Immunoglobulins in the Neonatal Dairy Calf

The fundamental aspects of a successful colostrum management program are age of calf at first feeding, volume of colostrum administered, and immunoglobulin concentration of the colostrum ingested [56, 57, 58]. Colostrum should be fed within 4 to 6 hours after birth at the very most and 4 to 5 L should be fed duing the first two meals or 8 hours after birth [18]. Maternal IgG and other constituents of colostrum are transported across the neonatal intestinal epithelium primarily within the first 24 h of life [30], travel through the lymphatics, and enter blood circulation via the thoracic duct [3, 9, 44]. Non-selective pinocytosis has been suggested as the transport mechanisms for IgG to be transported across the intestinal epithelium [8]. However, recent evidence has pointed toward a role for the neonatal FcRn in these processes. The FcRn is composed of 2 subunits, β2-microglobulin and an integral membrane polypeptide homologous to the major hystocompatability complex class I proteins [49]. It binds IgG in a pH-dependent manner and was first described as an IgG transporter in the neonatal gut of rodents [46].

Pathogens and control of pathogens in Colostrum

Several bacterial pathogens can be transmitted in colostrum and milk, whether by direct shedding from the mammary gland, postharvest contamination, or bacterial proliferation in improperly stored colostrum [53]. Numerous studies have demonstrated that pasteurization of milk and colostrum effectively kills pathogens such as *Mycobacterium bovis, Mycobacterium avium* subsp. *paratuberculosis, Mycobacterium californicum, Escherichia coli, Salmonella sp., Listeria monocytogenes*, and others [15, 50, 51].

A recommendation for controlling the spread of infectious disease within a herd is to feed colostrum from non infected dams. However, these recommendations may be impractical if a large portion of the herd is affected or if the costs of other feeding methods are prohibitive. Analternative may be the use of on-farm batch pasteurizer units (65.5°C for 30 min) that have been shown to destroy *M. avium* subsp. *paratuberculosis* in waste milk [50]. On-farm pasteurization of waste milk held at 65°C for 10 min also destroyed common mastitic mycoplasma such as *Mycoplasma bovis, M. californicum*, and *M. canadense* [15]. STABEL *et al*., [51] concluded that pasteurization is effective for the destruction of *M. paratuberculosis, Salmonella* spp., and *Mycoplasma* spp. in raw milk and effectively destroys *M. paratuberculosis* in colostrum, providing dairy producers with an alternative to purchasing commercial replacement products, resulting in reduced costs and reduced calf morbidity [50].

A field study, using a HTST pasteurization method (72°C for 15 s), reported that total colostral IgG mass received by 150 calves fed pasteurized colostrum (mean = 151.4 g) was significantly lower than for 150 calves fed unpasteurized colostrum (mean = 203.1 g) [26]. The high temperature most likely decreased the functional IgG content as recent studies have shown that high temperatures are a major cause of this denaturation of IgG [22, 29]. Yet, there was no difference in the number of calves experiencing FPT (based on < 10 g/L of total serum IgG measured at 48 to 96 h after colostrum intake) between treatment (16.2%) and control (19.5%) groups. Similarly there was no difference in mean serum IgG concentrations between treatment (14.76 g/L) and control (14.35 g/L) groups. The lack of difference is likely due to the large quantity of IgG fed to both groups of calves.

In a study designed to describe the effect of feeding heat-treated (vs. raw) colostrum on passive transfer of colostral immune and nutritional parameters in neonatal calves [29] found that calves fed heat-treated colostrum had significantly greater serum total protein and IgG concentrations at 24 h and therefore greater apparent efficiency of IgG absorption (total protein = 63 g/L; IgG = 22.3 g/L; apparent efficiency of absorption = 35.6%) compared with calves fed raw colostrum (total protein = 59 g/L; IgG = 18.1 g/L; apparent efficiency of absorption = 26.1%). The authors found no effect of treatment on serum concentrations of IgA, IgM, vitamin A, vitamin E, cholesterol, ß-carotene, or vitamin E to cholesterol ratio, or on serum bovine viral diarrhea virus type I serum neutralization titers. There was no difference between treatment groups when examining calf plasma total leukocyte counts, neutrophil counts, lymphocyte counts, or neutrophil opsonization activity. However, the authors considered the latter results inconclusive since it has to be determined if neonatal calves can absorb non-dam colostral leukocytes and if passive absorption of colostral cellular immune fractions or functions of these cell fractions are affected by heat-treating colostrum.

A further study looked at pasteurizing colostrum at 60°C for 30 min and fed to newborn calves. Calves fed the heat treated colostrum had significantly greater IgG absorption than control calves with no effect on serum protein levels or T-cell numbers [18].

Therefore pasteurization of colostrum may present a way to reduce bacterial populations in the colostrum and increase IgG absorption, thereby reducing the percentage of dairy calves that experience FPT. It has not been demonstrated why feeding heat-treated colostrum may increase IgG absorption. The recommended levels are heating colostrum to 60°C for 30 to 60 mi. This critical temperature will not denature the IgG molecules; however it will significantly reduce bacteria levels without altering the viscosity of the colostrum. The current hypothesis suggests that the presence of bacteria in the small intestine at the time of colostrum administration could interfere with systemic absorption of Ig molecules [27, 28, 52]. Possible mechanisms for this effect could include competition between microbes and IgG molecules for common receptors on the intestinal epithelial cells, or physical binding of colostral IgG by microbes within the intestinal lumen, thus decreasing the availability of transportable IgG [27, 28, 52]. There may be more than one possible explanation to this phenomenon however.

Implications

Failure of passive antibody transfer is a costly problem for dairy farmers around the world. Well defined colostrum management practices have been defined to minimize the risk of FTP, however it remains a farm management problem. It has been established that heat treatment of colostrum utilizing similar times and temperatures recommended for milk, can reduce bacteria loads in colostrum, however there is differing results in the higher temperatures and their result in denaturation of colostral IgG. It appears that some pasteurization procedures can result in increased Ig absorption by calves by using smaller batches and perhaps more controlled pasteurizing temperatures. These systems can lead to similar blood protein levels however higher blood IgG amounts indicating a preferential means of IgG absorption with pasteurized colostrum.

References

1. - BAINTNER K.: Transmission of antibodies from mother to young: Evolutionary strategies in a proteolytic environment. *Vet. Immunol. Immunopathol.*, 2007, **117**, 153-161.
2. - BALFOUR W.E., COMLINE R.S.: Acceleration of the absorption of unchanged globulin in the new-born calf by factors in colostrum. *J. Physiol.*, 1962, **160**, 234-257.
3. - BARRINGTON G.M., BESSER T.E., DAVIS W.C., GAY C.C., REEVES J.J., MCFADDEN T.B.: Expression of immunoglobulin G1 receptors by bovine mammary epithelial cells and mammary leukocytes. *J. Dairy Sci.*, 1997, **80**, 86-93.
4. - BARRINGTON G.M., BESSER T.E., GAY C.C., DAVIS W.C., REEVES J.J., MCFADDEN T.B.: Effect of prolactin on in vitro expression of the bovine mammary immunoglobulin G1 receptor. *J. Dairy Sci.*, 1997, **80**, 94-100.
5. - BARRINGTON G.M., MCFADDEN T.B., HUYLER M.T., BESSER T.E.: Regulation of colostrogenesis in cattle. *Livest. Prod. Sci.*, 2001, **70**, 95-104.
6. - BESSER T.E., GAY C.C.: Septicemic colibacillosis and failure of passive transfer of colostral immunoglobulin in calves. *Vet. Clin. N. Am. Food Anim. Pract.*, 1985, **1**, 445-459.
7. - BESSER T.E., GAY C.C.: The importance of colostrum to the health of the neonatal calf. *Vet. Clin. N. Am. Food Anim. Pract.*, 1994, **10**, 107-117.
8. - BLATTLER U., HAMMON H.M., MOREL C., PHILIPONA C., RAUPRICH A., ROME V., LE HUEROU-LURON I., GUILLOTEAU P., BLUM, J.W.: Feeding colostrum, its composition and feeding duration variably modify proliferation and morphology of the intestine and digestive enzyme activities of neonatal calves. *J. Nutr.*, 2001, **131**, 1256-1263.
9. - BLUM J.W., HAMMON H.: Colostrum effects on the gastrointestinal tract, and on nutritional, endocrine and metabolic parameters in neonatal calves. *Livest. Prod. Sci.*, 2000, **66**, 151-159.
10. - BROUGHTON C.W., LECCE J.G.: Electron-microscopic studies of the jejunal epithelium from neonatal pigs fed different diets. *J. Nutr.*, 1970, **100**, 445-449.
11. - BUHLER C., HAMMON H., ROSSI G.L., BLUM J.W.: Small intestinal morphology in eight-day-old calves fed colostrum for different durations or only milk replacer and treated with long-R3-insulin-like growth factor I and growth hormone. *J. Anim. Sci.*, 1998, **76**, 758-765.
12. - BUTLER J.A., SICKLES S.A., JOHANNS C.J., ROSENBUSCH R.F.: Pasteurization of discard mycoplasma mastitic milk used to feed calves: Thermal effects on various mycoplasma. *J. Dairy Sci.*, 2000, **83**, 2285-2288.
13. - BUTLER J.E.: Bovine immunoglobulins: An augmented review. *Vet. Immunol. Immunopathol.*, 1983, **4**, 43-156.
14. - BUTLER J.E.: Bovine immunoglobulins: A review. *J. Dairy Sci.*, 1969, **52**, 1895-1909.
15. - DAVIS C.L., DRACKLEY J.K.: The Development, Nutrition, and Management of the Young Calf, Iowa State Univ. Press, Ames, Iowa, 1998.
16. - DONOVAN G.A.,DOHOO I.R., MONTGOMERY D.M., BENNETT F.L.: Associations between passive immunity and morbidity and mortality in dairy heifers in Florida, USA. Prevent. *Vet. Med.*, 1998, **34**, 31-46.
17. - FOLEY J.A., OTTERBY D.E.: Availability, storage, treatment, composition, and feeding value of surplus colostrum: A review. *J. Dairy Sci.*, 1978, **61**, 1033-1060.
18. - GODDEN S.M., SMITH S., FEIRTAG J.M., GREEN L.R., WELLS S.J., FETROW J.P.: Effect of on-farm commercial batch pasteurization of colostrum on colostrum and serum immunoglobulin concentrations in dairy calves. *J. Dairy Sci.*, 2003, **86**, 1503-1512.
19. - HADORN U., BLUM J.W.: Effects of feeding colostrum, glucose or water on the first day of life on plasma immunoglobulin G concentrations and γ-glutamyltransferase activities in calves. *J. Vet. Med. A.*, 1997, **44**, 531-537.
20. - HAGIWARA K., KATAOKA S., YAMANAKA H., KIRISAWA R., IWAI H.: Detection of cytokines in bovine colostrum. *Vet. Immunol. Immunopathol.*, 2000, **76**, 183-190.
21. - HAMMON H.M., BLUM J.W.: Prolonged colostrum feeding enhances xylose absorption in neonatal calves. *J. Anim. Sci.*, 1997, **75**, 2915-2919.
22. - HOPKINS B.A., QUIGLEY J.D. III: Effects of method of colostrum feeding and colostrum supplementation on concentrations of immunoglobulin G in the serum of neonatal calves. *J. Dairy Sci.*, 1997, **80**, 979-983.
23. - JAMALUDDIN A.A., HIRD D.W., THURMOND M.C., CARPENTER T.E.: Effect of preweaning feeding of pasteurized and nonpasteurized milk on postweaning weight gain of heifer calves on a Californian dairy. *Prevent. Vet. Med.*, 1996, **28**, 91-99.
24. - JAMES R.E., POLAN C.E.: Effect of orally administered duodenal fluid on serum proteins in neonatal calves. *J. Dairy Sci.*, 1978, **61**, 1444-1449.
25. - JAMES R.E., POLAN C.E., CUMMINS K.A.: Influence of administered indigenous microorganisms on uptake of [Iodine-125] {gamma}-globulin in vivo by intestinal segments of neonatal calves. *J. Dairy Sci.*, 1981, **64**, 52-61.
26. - JOHNSON J.L., GODDEN S.M., MOLITOR T., AMES T., HAGMAN D.: Effects of feeding heat-treated colostrum on passive transfer of immune and nutritional parameters in neonatal dairy calves. *J. Dairy Sci.*, 2007, **90**, 5189-5198.
27. - KACSKOVICS I.: Fc receptors in livestock species. *Vet. Immunol. Immunopathol.*, 2004, **102**, 351-362.
28. - KACSKOVICS I., WU Z., SIMISTER N.E., FRENYO L.V., HAMMARSTROM L.: Cloning and characterization of the bovine MHC class I-like Fc receptor. *J. Immunol.*, 2000, **164**, 1889-1897.

29. - KEHOE S.I., JAYARAO B.M., HEINRICHS A.J.: A survey of bovine colostrum composition and colostrum management practices on Pennsylvania dairy farms. *J. Dairy Sci.*, 2007, **90**, 4108-4116.

30. - KOLDOVSKY O.: Search for role of milk-borne biologically active peptides for the suckling. *J. Nutr.*, 1989, **119**, 1543-1551.

31. - KUHNE S., HAMMON H.M., BRUCKMAIER R.M., MOREL C., ZBINDEN Y., BLUM J.W.: Growth performance, metabolic and endocrine traits, and absorptive capacity in neonatal calves fed either colostrum or milk replacer at two levels. *J. Anim. Sci.*, 2000, **78**, 609-620.

32. - LARSON B.L.: Transfer of specific blood serum proteins to lacteal secretions near parturition. *J. Dairy Sci.*, 1958, **41,** 1033-1044.

33. - LARSON B.L., HEARY H.L., DEVERY J.E.: Immunoglobulin production and transport by the mammary gland. *J. Dairy Sci.*, 1980, **63**, 665-671.

34. - MADSEN B.D., RASMUSSEN M.D., NIELSEN M.O.W.L., LARSEN L.B.: Physical properties of mammary secretions in relation to chemical changes during transition from colostrum to milk. *J. Dairy Res.*, 2004, **71**, 263-272.

35. - MAYER B., DOLESCHALL M., BENDER B., BARTYIK J., BOSZE Z., FRENYO L., KACSKOVICS I.: Expression of the neonatal Fc receptor (FcRn) in the bovine mammary gland. *J. Dairy Res.,* 2005, **72**, 107-112.

36. - MCMARTIN S., GODDEN S.M., METZGER L., FEIRTAG J., BEY R., STABEL J., GOYAL S., FETROW J., WELLS S., CHESTER-JONES H.: Heat treatment of bovine colostrum I: Effects of temperature on viscosity and immunoglobulin G level. *J. Dairy Sci.*, 2006, **89**, 2110-2118.

37. - MOREIN B., BLOMQVIST G., HU K.: Immune responsiveness in the neonatal period. *J. Comp. Pathol.*, 2007, **137**, S27-S31.

38. - MORIN D.E., MCCOY G.C., HURLEY W.L.: 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.*, 1997, **80**, 747-753.

39. - NOCEK J.E., BRAUND D.G., WARNER R.G.: Influence of neonatal colostrum administration, immunoglobulin, and continued feeding of colostrum on calf gain, health, and serum protein. *J. Dairy Sci.*, 1984, **67**, 319-333.

40. - NOUSIAINEN J., KORHONEN H., SYVAOJA E.L., SAVOLAINEN S., SALONIEMI H., HALONEN H.: The effect of colostral immunoglobulin supplement on the passive immunity, growth and health of neonatal calves. *Agric. Sci. Finland*, 1994, **3**, 421-428.

41. - OYENIYI O.O., HUNTER A.G.: Colostral constituents including immunoglobulins in the first three milkings postpartum. *J. Dairy Sci.*, 1978, **61**, 44-48.

42. - PAKKANEN R., AALTO J.: Growth factors and antimicrobial factors of bovine colostrum. *Int. Dairy J.*, 1997, **7**, 285-297.

43. - RADOSTIS O.M., GAY C.C., HINCHCLIFF K.W., CONSTABLE P.D.: Diseases of the newborn. *In*: RADOSTIS and others (éd.): Veterinary Medicine: A Textbook of the Diseases of Cattle, Horses, Sheep, Pigs, and Goats. Saunders Elsevier, Philadelphia, 2007, 127-171.

44. - ROBINSON J.D., STOTT G.H., DENISE S.K.: Effects of passive immunity on growth and survival in the dairy heifer. *J. Dairy Sci.*, 1988, **71**, 1283-1287.

45. - RODEWALD R.: pH-dependent binding of immunoglobulins to intestinal cells of the neonatal rat. *J. Cell Biol.*, 1976, **71**, 666-669.

46. - SASAKI M., DAVIS C.L., LARSON B.L.: Production and turnover of IgG1 and IgG2 immunoglobulins in the bovine around parturition. *J. Dairy Sci.*, 1976, **59**, 2046-2055.

47. - SASAKI M., DAVIS C.L., LARSON B.L.: Immunoglobulin IgG1 metabolism in new born calves. *J. Dairy Sci.*, 1977, **60**, 623-626.

48. - SIMISTER N.E., MOSTOV K.E.: An Fc receptor structurally related to MHC class I antigens. *Nature*, 1989, **337**, 184-187.

49. - STABEL J.R.: On-farm batch pasteurization destroys *Mycobacterium paratuberculosis* in waste milk. *J. Dairy Sci.*, 2001, **84**, 524-527.

50. - STABEL J.R., HURD S., CALVENTE L., ROSENBUSCH R.F.: Destruction of *Mycobacterium paratuberculosis, Salmonella* spp., and *Mycoplasma* spp. in raw milk by a commercial on-farm high-temperature, short-time pasteurizer. *J. Dairy Sci.*, 2004, **87**, 2177-2183.

51. - STALEY T.E., BUSH L.J.: Receptor mechanisms of the neonatal intestine and their relationship to immunoglobulin absorption and disease. *J. Dairy Sci.*, 1985, **68**, 184-205.

52. - STEWART S., GODDEN S.M., BEY R., RAPNICKI P., FETROW J., FARNSWORTH R., SCANLON M., ARNOLD Y., CLOW L., MUELLER K., FERROUILLET C.: Preventing bacterial contamination and proliferation during the harvest, storage, and feeding of fresh bovine colostrum. *J. Dairy Sci.*, 2005, **88**, 2571-2578.

53. - STOTT G.H., FLEENOR W.A., KLEESE W.C.: Colostral immunoglobulin concentration in two fractions of first milking postpartum and five additional milkings. *J. Dairy Sci.*, 1981, **64**, 459-465.

54. - STOTT G.H., MARX D.B., MENEFEE B.E., NIGHTENGALE G.T.: Colostral immunoglobulin transfer in calves I. Period of absorption. *J. Dairy Sci.*, 1979, **62**, 1632-1638.

55. - STOTT G.H., MARX D.B., MENEFEE B.E., NIGHTENGALE G.T.: Colostral immunoglobulin transfer in calves II. The rate of absorption. *J. Dairy Sci.*, 1979, **62**, 1766-1773.

56. - STOTT G.H., MARX D.B., MENEFEE B.E., NIGHTENGALE G.T.: Colostral immunoglobulin transfer in calves III. Amount of absorption. *J. Dairy Sci.*, 1979, **62**, 1902-1907.

57. - STOTT G.H., MENEFEE B.E.: Selective absorption of immunoglobulin IgM in the newborn calf. *J. Dairy Sci.*, 1978, **61**, 461-466.

58. - VIRTALA A.M., GROHN Y.T., MECHOR G.D., ERB H.N.: The effect of maternally derived immunoglobulin G on the risk of respiratory diseases in heifers during the first 3 months of life. *Prevent. Vet. Med.*, 1999, **39**, 25-37.

59. - WELLS S.J., DARGATZ D.A., OTT S.L.: Factors associated with mortality to 21 days of life in dairy heifers in the United States. *Prevent. Vet. Med.*, 1996, **29**, 9-19.