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REVIEW
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Colostrum Management: Keys to Optimizing Output and Uptake of Immunoglobulin G

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Colostrum is essential for the health and wellbeing of dairy cattle. This review provides insight into different means of augmenting or enhancing colostrum quality including colostrum feeding, dry cow management, prepartum cow diets, freezing, pasteurization, colostrum additives, and colostrum replacers. Other components in colostrum such as maternal cells and their importance are discussed. New research is needed regarding the components in colostrum (bioactive peptides and growth factors) and their effects on the neonate. Colostrum replacers and a prediction equation to estimate colostrum quality are reviewed.

Keywords: colostrum, calf, prepartum cow management, immunoglobulin G, colostrum additives, prepartum cow diets

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INTRODUCTION

Colostrum is the initial lacteal secretion produced by the mammary gland after involution and parturition. It contains large amounts of immunoglobulins, growth factors, fat, and water. In preruminant animals, colostrum provides for the initial immunity because the immune system is naïve at birth. This is due to the minimal transfer of immunoglobulins (**Ig**) *in utero* ascribed to the six-layer placenta (three maternal and three fetal layers; Peter, 2013). The Ig of importance for calves are IgG_1 and IgG_2. Colostrum quality decreases as the time after calving to harvest increases while colostrum quality also decreases as the volume produced increases (Morin et al., 2010). Therefore, colostrum must be fed as soon as possible after parturition due to the non-specific absorption occurring during the first 12 h of life. After the first 12 h of life, absorption of Ig is reduced. Colostrum also provides the calf with hydration and also body fat. Neonatal preruminant animals are born with approximately 3% body fat. Good quality colostrum is defined as a concentration of IgG greater than 50 g/L (NAHMS, 2007) or approximately 22% Brix reading on a refractometer. The purpose of this review is to provide information on ways to enhance the quality of colostrum and ultimately the uptake of IgG and other beneficial factors found in colostrum.

COLOSTROGENESIS AND PARITY

The production of colostrum in the mammary gland begins several weeks (3 weeks, Sasaki et al., 1976; 5 weeks, Brandon et al., 1971) before parturition. It has been recently determined that how cows are managed and fed during this time has a direct impact on the production and uptake of Ig by the calf. Research has shown that feeding a diet according to the nutrient requirements of cows in this phase of the lactation cycle results in the production of good quality colostrum.

For several years, producers routinely did not feed colostrum from cows entering their first lactation. This was likely due to these animals not being fed to produce adequate colostrum. Kehoe et al. (2011) have shown that first lactation cows produced adequate quality colostrum (IgG of greater than 50 g/L), but not as high quality as cows with more parities. This is due to the older cow experiencing more disease challenges resulting in producing colostrum of better quality than younger cows.

TRANSFER OF PASSIVE IMMUNITY

Until recently, transfer of passive immunity was defined as calf blood serum IgG concentration of greater than 10g/L at 24 h of age. Calves with serum IgG greater than or equal to 10 g/L at 24 h of age were said to have attained passive transfer and calves that were less than 10 g/L had failure of passive transfer of immunity. As serum IgG increases, calves experience reduced morbidity. Recently, the industry has developed new standards for evaluating the transfer of passive immunity in calves. The new standards for 24 h serum IgG concentrations are as follows: excellent, greater than or equal to 25 g/L; good 18–24.9 g/L; fair, 10–17.9 g/L; and poor, less than 10 g/L (Lombard et al., 2020). To accomplish this, at least 3.8 L of colostrum is fed with most farms feeding in the first few hours after birth. Faber et al. (2005) fed two groups of Brown Swiss calves either 2 or 4 L of good quality colostrum at birth. Results indicated that greater ($P < 0.001$) Average daily gain (ADG) was observed for calves fed 4 L as compared to 2 L of colostrum (1.03 kg/day for calves fed 4 L vs. 0.8 kg/day for calves fed 2 L). Ultimately, calves that were fed 4 L of colostrum produced 1,349 kg more milk ($P< 0.05$) in their second lactation than calves fed 2 L. These data support the earlier work of Denise et al. (1989) where calves having greater serum IgG at birth produced more mature equivalent milk. Possibly, there are components within colostrum that result in positive mammary cell proliferation (Faber et al., 2005).

MANAGEMENT OF THE PREPARTUM DAM AND SUPPLEMENTATION

Until recently, there has been scant research in the area of prepartum cow management in regard to colostrum. However, researchers at the University of Florida have conducted several studies that indicated that providing cooling (fans and misters) to dry cows improved calf health likely through fetal programming (Tao et al., 2012). Calves born of cooled cows were more efficient in absorbing IgG than calves born of heat-stressed cows ($P < 0.01$) and had greater serum IgG over the first 28 days of life ($P = 0.03$). These calves produced more milk when they became cows than their heat-stressed herd mates (Dahl et al., 2016). This research group indicated that 89% of the dry cows in the United States would benefit from cooling (Ferreira et al., 2016) and hence improve the health of their calves. Recently, there have been several studies conducted investigating how feeding the dam affects the health of the calf. One of the earliest experiments was conducted by Hough et al. (1990) who fed 26 Angus cows either 100% or 57% of overall beef nutrient requirements beginning 90 days prepartum (NRC, 1984). The concentration of colostral IgG was similar between treatments (43 g/L vs. 39.5 g/L) for restricted and control fed dams respectively. Calves born from restricted fed dams had higher cortisol 33.8 ng/ml vs. 26.1 ng/ml for the control calves ($P < 0.05$). Calves fed colostrum from dams fed the restricted diet had 24 h serum IgG of 17.2 g/L compared to calves fed colostrum from dams fed the 100% NRC diets (22.2 g/L) tended to have higher 24 h serum IgG ($P = 0.07$) compared to calves fed colostrum from cows fed the nutrient-deficient diet. These data support the concept of how the dam is managed before parturition affects the calf's ability to absorb IgG and calves from dams that are poorly managed tend to be stressed (as evidenced by the increased cortisol), resulting in reduced IgG uptake. Cows fed a low-energy diet (5.25 MJ/kg DM) Dry Matter (DM) compared to cows fed a high energy diet (6.48 MJ/kg DM) had reduced content of CD4 cells in lymphocytes of their subsequent calves (Gao et al., 2012). Colostrum feeding was not discussed in this study, but these results confirm the importance of the diet for the prepartum cow as it can affect the fetus and ultimately the immunity of the calf. Feeding higher energy diets through fatty acid supplementation to prepartum cows had positive effects on IgG uptake and enhanced apparent efficiency of absorption (**AEA**; Garcia et al., 2014). The concentration of IgG in colostrum did not differ among treatments of saturated fats or essential fatty acids compared to control ranging from 83 to 122 g/L. However, colostrum yield was not recorded. Serum IgG at day 1 of life tended to be greater ($P = 0.09$) for calves born from cows fed either 1.7% saturated fat or 2% Ca-salts containing essential fatty acids compared to control. Whereas calves born of cows fed the saturated fats had 24 h serum IgG and tended to be greater ($P = 0.07$) averaging 26.9 and 29.7 g/L for nulliparous and primiparous cows, respectively, compared to calves born of cows fed the essential fatty acid diet that was 25.1 and 23.6 g/L for nulliparous and primiparous cows, respectively. AEA was greater in calves born from cows fed saturated fat compared to calves born from dams in the control treatment. This is usually not the case; AEA is enhanced when calves are fed colostrum with a lower IgG concentration compared to calves fed colostrum with higher IgG concentration. Conneely et al. (2014) fed different amounts of colostrum in relation to birth BW (7.5%, 8.5%, and 10%) and found that 8.5% of BW had the greatest IgG absorption and AEA, but IgG was not similar among treatments.

Feeding high amounts of energy (150% NRC) resulted in lower concentration of IgG in colostrum (96.1 g of IgG/L, 100% NRC; 72.4 g of IgG/L, 150% NRC; P = 0.02; Mann et al., 2016), but cows on the high energy diet produced 1.3 kg more colostrum. These data and the data from the previous experiments (Hough et al., 1990; Gao et al., 2012) indicate that improving the energy status of gravid dry cows enhances their calves' performance. However, over feeding energy is not beneficial in regard to colostrum IgG concentration (Mann et al., 2016). It is not clear whether the effect is *in utero* or through colostrum.

COW DIETS TO REDUCE HYPOCALCEMIA

It is common to feed prepartum cows, a diet containing anionic salts (**DCAD**) to reduce the incidence of hypocalcemia. However, there are limited data on its effect on colostrum yield and quality. Joyce and Sanchez (1994) indicated that feeding cows an anionic salt caused a reduction in blood pH of their calves and suggested that more work be done to evaluate the impact of these diets on the newborn calf. Morrill et al. (2010) observed no effect of supplementation of multiparous cows with either 77 or −100 mEq/kg diets on the serum IgG concentration or AEA at 24 h. However, calves in this experiment were fed a colostrum replacer (**CR**) not their dam's colostrum. More research studies need to be conducted to further refine the effect of DCAD on colostrum production, quality, and calf performance. Zeolites (**Z**) have recently been utilized in the feeding of prepartum cows by reducing the bioavailability of dietary Ca, reducing the potential for hypocalcemia-related disorders (Papaioannou et al., 2005). Marin et al. (2020) fed 90 prepartum Holstein cows either 0, 150, or 300 g of Z per day for one month before parturition. Results indicated that colostrum IgG concentration was greater ($P < 0.05$) for the Z-fed cows (37.28 and 37.45 g/L for the 150 and 300 g/day treatments, respectively) compared to the control cows (35.15 g/L). However, colostrum quality would be considered poor (IgG of less than 50 g/L). Calf serum IgG uptake was not determined in this experiment and performance data were not provided. Further research needs to be conducted to evaluate feeding Z.

ADDITIVES TO PREPARTUM COW DIETS AND THEIR EFFECTS ON COLOSTRUM

Hall et al. (2014) fed Jersey cows Se yeast (105 mg/cow) once weekly in addition to 0.3 mg Se/kg per day for 8 weeks prepartum, or cows with no Se-yeast. At birth calves were fed either colostrum from Se-yeast supplemented cows or control. Results indicated that serum IgG ($P = 0.03$) and AEA ($P < 0.01$) were greater in calves born of cows fed the Se-yeast on day 2 of life regardless of colostrum source, indicating that there was an *in utero* effect of the Se-yeast supplementation. Pavlata et al. (2004) provided Se-deficient cows with either 0, an injection providing 44 mg of Na selenite and 500 mg of α-tocopherol acetate at 4 weeks before parturition, or the same injection, but provided at 8 and 4 weeks prepartum. Colostrum quality was greater ($P < 0.05$) for the cows injected twice compared to the control cows (34.08 and 22.87 turbidity units). Control cows were similar to cows injected once (21.38 turbidity units). Lacetera et al. (1996) observed that cows injected with a combination of Na-selenite and dl-α-tocopheryl acetate during the dry period produced colostrum with similar IgG concentrations as compared to non-injected cows, but 22% more colostrum indicating a greater production of total IgG. Beef cows on Se-deficient pastures were injected with vitamin E and Se (Se of 0.1 mg/kg and vitamin E of 1 mg/kg), or provided Se in the diet (salt mix of 120 mg/kg), or provided Se in the diet with the injection or no supplemental Se or vitamin E. Cows with the dietary Se produced greater IgG/L colostrum and calves had greater serum IgG after suckling (Swecker et al., 1995).

PROBIOTICS

There are limited data on the addition of probiotics to prepartum cows on colostrum quality and absorption of IgG by their calves. Dann et al. (2000) fed 39 Jersey cows either 0 or 60 g/day of a yeast culture. Results indicated that DMI tended ($P = 0.10$) to be increased in cows fed the yeast culture compared to those not receiving it. Colostrum yield and calf performance data were not reported. However, ewes supplemented with 14 g/day yeast culture beginning 14 days prepartum showed no effect on colostrum nutrient content. Immunoglobulin G was not measured in this study (Macedo et al., 2012). Supplementing yeast culture to dairy cows and its effects on colostrum need to be studied.

Utilizing a direct-fed microbial (**DFM**) and enzymes on colostrum quality, yield, and IgG status in calves is limited. Ort et al. (2018) fed 36 multiparous Holstein cows either no DFM or 45.4 g/day of a DFM containing *Saccharomyces cerevisiae* and *Enterococcus faecium* (1.323 billion cfu/g) colony forming units (cfu) or the DFM plus 18.2 of an enzyme combination of cellulase and amylase (**DFME**) beginning 21 days before parturition. There were no effects of the DFM or DFME on DMI or any other growth or performance parameter prepartum. Colostrum yield was variable and not significantly different ($P = 0.12$) ranging from 6.6 kg (DFM) to 10.7 kg for the control treatment. Colostrum quality ranged from 79.1 g/L (control cows) to 91.1 g/L (DFME) IgG, but these results were not different. There were no differences in calf BW, serum IgG, and AEA at 24 h. These data suggest little benefit to supplementing prepartum cows with a probiotic as it pertains to colostrum quality, yield, and day 1 calf immunity.

VITAMINS AND VITAMIN PRECURSORS

β-carotene (**BC**) is the main precursor of vitamin A but has been studied little regarding its effect on the prepartum cow, calves, and colostrum. The BC status of calves is an important indicator

of poor transfer of passive immunity. Calves with failure of passive transfer had lower serum BC than calves that attained passive immunity (Torsein et al., 2011). β-carotene was supplemented to nine multiparous Holstein dairy cows at a rate of 700 mg/day (Aragona et al., 2021) or nine similar cows received no supplementation of BC (control) for 4 weeks prepartum. Results indicated that there was no effect of the supplemental BC on prepartum cow DMI, BW, or body condition score. Cow blood IgG, BC, and ketones were not different between treatments. However, cow non-esterified fatty acid concentrations were reduced at calving for cows fed supplemental BC ($P < 0.01$; 465.4 vs. 656.0 mEq/L for BC and control cows, respectively). Colostrum, yield, quality, and components did not vary between treatments except that total solids content were greater for cows supplemented with BC ($P = 0.03$; 27.75% vs. 22.89% for BC and control cows, respectively). Prom (2016) observed no difference in colostrum yield, but an increase in colostral fat content when comparing cows fed either 0 or 800 mg BC/day. Aragona et al. (2021) fed calves 4 L of their dam's colostrum and then fed a commercial all milk-milk replacer, calf starter grain, and free-choice water for 6 weeks. Characteristics of IgG status did not vary except that AEA was less in the calves fed colostrum from their dams fed BC ($P = 0.03$; 39.5% vs. 52.16% for BC and control treatments, respectively). This response was likely due to the nonsignificant numerically greater IgG concentration in the colostrum from cows fed BC ($P= 0.12$; 79.88 and 57.92 g/L for BC and control cows, respectively). Feed efficiency (ADG/DMI) was greater for calves born of cows fed BC compared to those of control cows ($P = 0.03$; 0.44 vs. 0.33 for BC and control, respectively). Most of this response was due to responses seen in the first two weeks of life where feed efficiency was greater ($P < 0.01$). These data suggest that there may be a component present in the colostrum from BC supplemented cows or that a change occurred in the calves during fetal development. This change likely occurred in the small intestine as the response was most profound when most of the nutrients that were taken in were derived from milk replacer (weeks 1 and 2 of life).

Martinez et al. (2018) fed 79 prepartum Holstein cows supplemental vitamin D as either calcidiol (1,25 dihydroxyvitamin D_3) or cholecalciferol (25-dihydroxyvitamin D_3) at a rate of 3 mg/11 kg DM intake. Cows were fed these products beginning at 255 days of gestation. These cows were also subjected to either 130 or −130 mEq/kg DCAD diet. Results indicated that DCAD did not affect colostrum yield similar to the data of Morrill et al. (2010). However, colostrum yield tended ($P = 0.10$) to be greater when calcidiol (7.82 kg) was fed compared to cholecalciferol (6.04 kg). Colostrum protein, solids-not-fat, and total fat yields were greater for cows fed calcidiol ($P < 0.05$). Immunoglobulin G concentration was greater in cows fed calcidiol compared to cows fed cholecalciferol ($P <0.01$; 58.9 and 47.9 g/L, respectively). The authors speculated that 1,25 dihydroxyvitamin D_3 can modulate immune responses. On the basis of data from Reinhardt et al. (1999) who observed an increase in IgG titers when 1,25 dihydroxyvitamin D_3 was provided when cows were vaccinated with *Escherichia coli J5*. Martinez et al. (2018) speculated that vaccinating the cows prepartum could have resulted in higher serum IgG and possible uptake of these proteins by the mammary cells. Further research needs to be conducted to evaluate the effect of feeding calcidiol on prepartum cows and the subsequent effects on their calves.

There are limited studies on the supplementation of vitamin K on colostrum quality and production. However, Kuroiwa et al. (2022) supplemented 21 Holstein cows with vitamin K3 (50 mg/day; menadione) and compared to 19 cows not supplemented with vitamin K. Transition milk was sampled on day 3 postpartum. Immunoglobulin G concentration was greater on day 3 ($P < 0.05$) compared to cows not provided with supplemental vitamin K. The authors hypothesized that the vitamin K would be absorbed and converted to the active form menaquinone 4 and cause an increase in IgG concentration in the colostrum.

Nicotinic acid (**NA**) supplementation to lactating dairy cows with mixed results. Recently, studies have been conducted with prepartum dairy cows to evaluate NA's impact on colostrum composition, quality, and yield and its effects on their calves. The concept behind supplementation of NA is that it will increase blood flow. During colostrogenesis blood flow will likely go to the mammary gland resulting in more nutrient uptake in the gland. NA remains intact in the rumen longer than nicotinamide (Erickson et al., 1991), and it was shown to increase the production of *Entodiniiae* (Dennis et al., 1982: Erickson et al., 1990; Dorreau and Ottou, 1996). *Entodiniiae* have a symbiotic relationship with bacteria resulting in greater microflora numbers and the potential to aid in the maintenance of rumen health even when higher concentrate diets are fed. Holstein cows fed either 0 or 48 g/day for 4 weeks prepartum resulted in greater colostrum quality when cows were fed 48 g/day ($P = 0.01$; 73.8 and 86.8 g/L for 0 and 48 g NA/day respectively). Calves were fed a **CR** to determine whether there were any effects of NA supplementation *in utero*. There were no effects of cow prepartum NA supplementation on AEA or blood IgG, suggesting that NA does not cause any response *in utero* (Aragona et al., 2016). The addition of NA (0, 16, 32, or 48 g NA/day) to prepartum cow diets was shown to linearly increase urinary purine derivatives—an indicator of rumen microbial protein synthesis (Aragona et al., 2020). The increase in postruminal microbial flow would result in greater amino acid uptake in the cows fed the NA and a likely increase in colostrum quality (greater IgG). Colostrum yield was not different in this study, but colostrum quality linearly increased ranging from 57.6 to 83.5 g/L IgG. Total IgG yield reacted quadratically ($P = 0.03$) with the greatest value for cows fed 32 g/day NA. There were no differences in calf 24 h serum IgG among treatments. There was a trend for a quadratic response (P = 0.07) with calves born of cows fed the 32 g/day NA treatment having the greatest ADG. However, there was a quadratic response ($P = 0.03$) for improved feed efficiency during the 6-week calf growth period with calves born of cows fed the 32 g/day NA treatment resulting in the greatest feed efficiency (0.5; ADG/DMI) compared to the other treatments ranging from 0.34 to 0.36 ADG/DMI. These

results are likely due to improved intestinal development in calves born of cows fed NA because most of the nutrients in the first 6 weeks are in the form of milk, which will pass to the abomasum *via* the esophageal groove. Further, most of the ADG responses occurred in the first 3 weeks after birth.

SOMATIC CELLS COUNT AND COLOSTRUM

Besides IgG concentration, other factors can affect calf immunity one potential challenge is colostrum somatic cell count (**SCC;** Ferdowsi nia et al., 2010) In a comprehensive study, Puppel et al. (2020) compared the colostrum production and SCC of a 250 cow commercial herd. Cows were divided into two groups based on their SCC. In this study, 40 Holstein cows were divided into two groups (less than 400,000 SCC/ml; n = 22) and (greater than or equal to 400,000 SCC/ml; n = 18) based on initial first colostrum samples (collected within 2 h of calving). Cows with the lower SCC had a colostrum IgG concentration of 82.45 g/L, whereas cows with the higher SCC had a colostrum IgG concentration of 41.11 g/L ($P < 0.01$). These data support the data of Kehoe et al. (2007) who showed that herds with a milk SCC less than 200,000 produced higher quality colostrum than herds with a greater milk SCC (greater than 200,000) suggesting that overall better management results in better colostrum quality. Colostral protein concentration was also greater ($P < 0.01$) in the cows with the lower SCC (14.86%) as would be expected with the greater IgG concentration in those cows than in the cows with higher SCC (12.11%). This was not observed in a similar study (Ferdowsi nia et al., 2010). Puppel et al. (2020) observed greater colostral fat content of 7.67% in the colostrum from the lower SCC and 5.11% from the colostrum with the greater SCC ($P \leq 0.01$). They also observed greater lactoferrin concentration in the colostrum from cows with the lesser SCC compared to the cows with the greater SCC ($P < 0.01$). Ferdowsi nia (2010) observed that blood IgG concentration varied at 3 h after being fed colostrum in calves fed colostrum from cows producing a high SCC colostrum (greater than 5,000,000 cells/ml; IgG of 11.4 g/L) when compared to cows fed either lower (960,000 cells/ml; IgG of 16.6 g/L) or moderate (2,000,000 cells/ml; 16.2 g/L) SCC (linear $P = 0.10$). Blood IgG concentration was not determined at 24 h of age. In this study, calves were provided with 2 kg of their dam's colostrum at birth and another 2 kg 12 h later. Serum IgG concentration was determined in blood sampled at parturition and found to be greater for cows producing high SCC (30.1 g/L) colostrum compared to moderate (22.9 g/L) or lower SCC colostrum (17.8 g/L; $P < 0.01$).

Colostrum fat content was linearly reduced in cows with the greater SCC (4.5%) compared to the colostrum from cows with a lesser SCC (6.0%; $P < 0.04$; Ferdowsi nia et al., 2010). They suggested that colostral SCC may have interfered with *de novo* fatty acid synthesis and the production of acyl glycerides and the potential for impaired fatty acid uptake by infected mammary cells. This is especially important as calves are born with only 3% body fat and colostrum provides for the development of the insulator properties required by the neonate. Eicosapentaenoic acid and docosahexaenoic acid concentrations were increased ($P < 0.01$) in the lower SCC colostrum. Both fatty acids can suppress the production of proinflammatory cytokines (Puppel et al., 2020).

Ferdowsi nia et al. (2010) observed that calves fed lesser SCC colostrum had twice as much BW gain compared to calves receiving the high SCC colostrum in the first 30 days of life (5.7 kg vs. 2.5 kg, respectively, $P < 0.01$). These data indicate that calving cows in a clean environment along with dry cow therapy should result in lesser SCC colostrum and better quality colostrum. These data suggest that calves born from these cows and fed the colostrum with a lesser SCC should perform better than their herdmates fed the higher SCC colostrum.

COLOSTRUM FREEZING AND PASTEURIZATION

Freezing and heating colostrum kill a majority of colostral leukocytes (Godden et al., 2019). Langel et al. (2015) evaluated calves fed either whole colostrum or flash-frozen colostrum—known as cell-free colostrum. Flash-frozen colostrum was produced by placing 1 L of colostrum in perflouroalkoxy bags and covering the bags with liquid nitrogen. Bags were turned every 3 min until completely frozen. These researchers used 37 newborn calves (29 Holstein and eight Jersey). Calves received a total of 3.8 L split into two feedings and had blood samples taken at 6 h postcolostrum feeding and on days 1, 3, 7, 14, 21, and 28 to evaluate maternal cells transferred to the colostrum and then transferred to the calf *via* feeding. Results suggest that intact maternal colostral cells can move into circulation. They found that calves fed the fresh colostrum had increased $CD4^+$ T cells compared to the calves fed the flash-frozen colostrum. Donovan et al. (2007) injected all cows with an inactivated bovine viral diarrhea vaccine. They observed that calves that received whole colostrum responded to bovine viral diarrhea antigen, whereas calves fed frozen colostrum did not respond to the antigen one to two days after colostrum ingestion. These data indicated that cell-mediated immunity can transfer by vaccination of the dam. In this study, Holstein calves either were fed 4 L of whole colostrum or whole frozen colostrum (−80°C). Results indicated that freezing colostrum effectively destroyed colostral leukocytes and there was no difference in serum IgG by day 1 (calves received 4 L of colostrum). More research studies need to be conducted to evaluate whether this response would occur in frozen colostrum stored under common conditions (−20°C).

COLOSTRUM PASTEURIZATION

Heating colostrum can decrease or eliminate many pathogens present in colostrum including *Mycobacterium paratuberculosis* ssp. *Avium*, *Salmonella* spp., and *Mycoplasma* ssp. (Godden et al., 2006). Stabel (2008) demonstrated that pasteurization (65°C, for 30 min) of colostrum can decrease the initial

exposure to *M. paratuberculosis*. Feeding colostrum containing M. *paratuberculosis* is a route in which this organism is transferred resulting in Johne's Disease when the calf matures. Godden et al. (2006) inoculated colostrum with various pathogens and then pasteurized colostrum for various times at 60°C from 0 to 120 min, not including a 30-min heat-up stage. Results indicated that pasteurizing colostrum for 120 min resulted in no detectable *M. bovis*, *E. coli*, *S. enteritidis*, *L. monocytogenes*, and *M. paratuberculosis.* They observed very little difference in concentration of IgG (60.5 and 59.1 g/L for raw and pasteurized colostrum, respectively). However, in higher quality colostrum, there was a numerical decrease in IgG in raw versus pasteurized colostrum (76.5 and 70.8 g/L for raw and pasteurized colostrum, respectively). McMartin et al. (2006) in a companion study to Godden et al. (2006) evaluated various temperatures for 120 min as they specifically affected the viscosity of the colostrum. Results indicated that as the temperature increased from 60°C to 63°C gel formation occurred. A reduction in IgG concentration was observed as pasteurization temperature increased from 59°C to 63°C. For example, IgG decreased ($P < 0.05$) from 76.1 g/L for a preheated sample (good quality colostrum) to 43.7 g/L (Poor quality colostrum) after pasteurizing at 63°C for 120 min. There were no differences for IgG when colostrum was pasteurized at 60°C for 120 min (71.6 and 70.4 g/L for preheated and postheated colostrum, respectively). This same research group then evaluated heating colostrum (60°C for 60 min) and feeding it to calves on a commercial dairy (Johnson et al., 2007). Colostrum was heated at 60°C for 60 min and quality characteristics were determined. Immunoglobulin G was similar between the raw and heated samples (72.6 and 67.3 g/L, respectively). The bacterial total plate count was reduced in the heated colostrum ($P < 0.0001$) compared to the raw colostrum. Calves (n = 50) received either pasteurized or raw colostrum. Results indicated that calves fed the pasteurized colostrum had greater ($P = 0.001$) serum IgG at 24 h (22.3 g/L) than calves fed the raw colostrum (18.1 g/L). In addition, AEA was greater ($P < 0.001$) for the calves fed the pasteurized colostrum (35.6%) compared to the calves fed the raw colostrum (26.1%). There were no differences in leukocyte, vitamin A, vitamin E, β-carotene, or cholesterol concentrations between the treatments. Similar results were observed for minerals and vitamins comparing heat-treated and unheated colostrum (Elizondo-Salazar and Heinrichs, 2009). These researchers observed similar values for colostrum whether unheated or heated for IgG concentrations with lesser bacterial counts as determined by standard plate count, and counts of environmental streptococci, coliforms, and non-coliforms ($P < 0.05$). Elizondo-Salazar and Heinrichs (2009) evaluated serum IgG at 0, 4, 8, 12, 16, 20, 24, and 48 h after birth and then weekly until 8 weeks of age. Results indicated that serum IgG was greater for every hour measured and then up to week 5 ($P < 0.05$) indicating that heating colostrum imparts a lasting effect on calf health. The AEA was enhanced for every hour except for 4 h for the heated colostrum compared to calves fed the unheated colostrum ($P < 0.05$). A large study (Godden et al., 2012) involving six dairy farms and 1,071 calves fed either fresh or heat-treated colostrum (60°C for 60 min) reported higher serum IgG ($P < 0.0001$) for calves fed the heated colostrum (18. 0 g/L) compared to the calves fed the fresh colostrum (15.4 g/L) congruous with Elizondo-Salazar and Heinrichs (2009). Results indicated that calves fed the fresh colostrum (36.5%) had an increased risk of treatment compared to calves fed heated colostrum (30.9%). Moreover, calves fed the fresh colostrum also had an increased risk of scours (20.7%) compared to calves fed the pasteurized colostrum (16.5%). Gelsinger et al. (2014) pasteurized (60°C for 30 min) three batches of colostrum with varying IgG concentrations (greater than 75 g/L = high quality, 60–75 g/L = medium quality, and less than 60 g/L = low quality). The final results after pooling colostrum were high-quality colostrum was IgG of greater than 90 g/L, medium quality was IgG of approximately 71 g/L, and low quality was IgG of between 52 and 56 g/L. Similar to the results of Godden et al. (2006), colostrum quality decreased the most when the high-quality colostrum was heated (92.3 g/L) compared to the unheated colostrum (98.8 g/L). There were very few differences between heating the medium quality and low-quality colostrum and the unheated colostrum. Earlier research indicated that pasteurizing colostrum reduced ($P < 0.05$) standard plate count and non-coliform counts regardless of colostrum quality. Over all colostrum qualities, heating improved plasma IgG ($P = 0.03$) and AEA ($P = 0.01$) at 48 h compared to the unheated colostrum (Gelsinger et al., 2014), but not in Gelsinger and Heinrichs (2017) where there were no differences between plasma IgG regardless of heating or not. Interestingly, feeding calves medium quality pasteurized colostrum resulted in similar plasma IgG concentration (22.5 g/L) as calves fed unheated high-quality colostrum fed calves (23.3 g/L). Kryzer et al. (2015) evaluated Jersey colostrum heated (60°C, 60 min) in either feeding bags or heated then stored in the feeding bag, frozen or fresh refrigerated colostrum. Results indicated that the pasteurized colostrum had reduced total plate counts and total coliform counts ($P < 0.01$) compared to the unheated colostrum. Calves fed the pasteurized colostrum had higher IgG and greater AEA at 24 h ($P < 0.01$). The results of these studies are likely due to the pasteurization process increasing IgG absorption by decreasing absorption of other colostral proteins. An important attribute of heat treatment is feeding the colostrum soon after heating. Gelsinger et al. (2015) pasteurized a batch of colostrum, froze half, and then treated the other half with 20 ml of untreated low bacteria colostrum and then incubated at 20°C for 72 h and then frozen. Values for IgG at 48 h after birth indicated that calves fed the bacteria-laden colostrum were less than 10 g/L, indicating the failure of transfer of passive immunity. Allowing the pasteurized colostrum to incubate can result in poor uptake of IgG and AEA with results similar to colostrum that was not pasteurized and allowed to incubate (Gelsinger et al., 2015). Colostrum should be fed immediately after pasteurization or frozen for later use.

Cytokines are present in colostrum and are higher than in whole milk, suggesting that they may be immunomodulatory (Hagiwara et al., 2000). Yamanaka et al. (2003) indicated that there were high concentrations of cytokines in colostrum and

that they may compensate for the immature immune system and contribute to its maturation. There are limited data evaluating cytokines and the effect of heating or freezing on these important components of colostrum. Gelsinger and Heinrichs (2017) pasteurized good quality colostrum at 60°C for 60 min and compared it to unheated colostrum fed to bull calves. At 24–48 h of age, there were no differences between calves regarding IFNγ, but calves fed heated colostrum had a lower concentration of IL1β ($P < 0.01$). On days 14 and 35, calves were injected with 5.0 mg/ml of ovalbumin, and plasma concentrations of ovalbumin-specific IgG, IFNγ, and IL1β were used as markers of B-cell, T-cell, and innate cell activity. Plasma IFNγ was not different for calves injected with ovalbumin on day 14. Plasma IL1β concentrations were lower in the heated colostrum fed calves ($P = 0.03$) on day 14. Results of this study suggest that heating colostrum can impact some cytokine production. Data also suggest that heating colostrum for 60 min at 60°C can decrease colostral concentrations of lactoferrin (**LF**) and IGF-1. Both of these can be linked to intestinal epithelial development and improvement in overall calf health (LF).

In a large study using 587 calves fed either pasteurized colostrum and milk or nonpasteurized colostrum and milk, Armengol and Fraile (2016) observed that pasteurization decreased morbidity and mortality for calves fed pasteurized colostrum and milk to 5.2% and 2.8%, respectively, and calves fed the nonpasteurized colostrum and milk had morbidity and mortality rates of 15% and 6.5%, respectively ($P < 0.01$). These data confirm the on-farm use of pasteurization as a means of improving the health of growing dairy calves.

Another method of processing colostrum was the use of high-pressure processing. Foster et al. (2016) inoculated colostrum with *E. coli*, *S. enterica enterica serovar Dublin*, and *M. paratuberculosis* along with viruses. Results indicated that processing the inoculated colostrum at 300 MPa (30, 45, and 60 min) and 400 MPa (10,15, and 20 min) reduced the amounts of all the viable bacteria except for *M. paratuberculosis*. Calf serum IgG concentration (samples were taken 24 and 36 h after birth) was similar for calves fed the high pressure processed colostrum (17.1 g/L) or the heat-treated colostrum (22 g/L). However, AEA was reduced in calves fed the high pressure treated colostrum compared to heat treated colostrum (22.6% and 38%, respectively; $P < 0.001$).

ADDITIVES TO COLOSTRUM

In an attempt to increase the absorption of IgG, additives have been supplemented in colostrum. One of the earliest studies evaluating an addition to colostrum was the work of Baumwart et al. (1977) where potassium isobutyrate (KIB) was added to colostrum. This was based on data by Hardy (1969) where KIB was added to colostral whey in anesthetized calves and γ globulin absorption was increased. In the study of Baumwart et al. (1977), calves received 2.83 meq KIB/g of colostral γ globulin or a similar amount of distilled water added to colostrum. Results indicated that adding the KIB tended ($P < 0.08$) to reduce IgG uptake.

Laskowski and Laskowski (1951) showed that colostrum contains a trypsin inhibitor (**TI**), and Sandholm and Hokanen-Buzalski (1979) confirmed that it changes in cow colostrum with the greatest amount in colostrum harvested close to calving. Trypsin inhibitor would reduce protein digestion allowing for more intact IgG absorption across the small intestine. One of the first studies to investigate the addition of TI was conducted by Jensen and Pedersen (1982) with colostrum-deprived piglets where they received sow colostrum TI. Results indicated that IgG and IgA were greater ($P < 0.01$) 6 h after feeding compared to piglets receiving saline. In calves, gastric protease is active on day 1 of life (Huber et al., 1961) suggesting that inhibiting trypsin can be beneficial in improving IgG uptake.

Quigley et al. (1995) added 1 g of soybean TI to 1 L of colostrum and fed up to 12 h after birth and then 12 h later to Jersey calves compared to calves not receiving TI. Results indicated that adding TI increased IgG uptake by 16% and IgM by 30% compared to calves not receiving the TI. Calves not receiving TI had excellent 24 h IgG greater than 27 g/L, whereas calves receiving the TI at birth had 34.4 g/L IgG ($P < 0.05$). In a similar study but using colostrum supplement or colostrum, Santoro et al. (2004) fed 1 g soybean TI added at the first two feedings (0.5 g) and observed no beneficial effects regardless of feeding colostrum on IgG uptake or AEA in the first 24 h after birth compared to calves receiving no supplemental TI (IgG of 13.5 and 15.7 g/L; 21.4% and 21.0% AEA, respectively).

Fratric et al. (2005) added Z to colostrum ranging in quality of IgG from 83.11 to 96.75 g/L. Calves were fed either 0.75 or 1.5 L at 12 h intervals on day 1 of life with or without Z (5 g/L). Zeolite increased ($P < 0.01$) serum IgG in calves at 24 h in the calves fed 1.5 L twice per day compared with calves not fed Z (35.2 and 25.4 g/L, respectively). It is not clear how Z supplementation resulted in increased serum IgG. Gvozdic et al. (2007) fed 3.0 L of colostrum with or without a 20-ml suspension of clinoptilolite (a mineral similar to Z) with greater ($P < 0.05$) 24 h serum IgG for calves fed the clinoptilolite (35.2 g/L) compared to calves not fed the suspension (25.3 g/L).

Kamada et al. (2007) and Hall et al. (2014) indicated that adding Se (Na-selenite) to colostrum improved IgG uptake. Kamada et al. (2007) conducted two experiments regarding the effect of adding Se to colostrum. In experiment 1, they added Se to calves fed concentrations of Se from 0.2, 1.0, and 5.0 ppm added to colostrum fed over four feedings (colostrum and transition milk from the subsequent milkings). All colostrum and subsequent milkings came from one cow with IgG concentration ranging from 129 to 24.3 g/L. One liter was fed within 2 h of birth and 2 L of second, third, and fourth milkings were provided at 12, 24, and 36 h of life. Serum IgG concentration at 24 h was 20% greater in selenium supplemented colostrum fed calves compared to control calves ($P < 0.04$). Five parts per million were too much and reduced IgG uptake. In their second experiment, Kamada et al. (2007) found

that adding 1 ppm in the first feeding was as effective as adding it to colostrum and transition milk (calves were fed as in experiment 1). Hall et al. (2014) observed similar results with 3 mg/L Se of colostrum with serum IgG concentrations 56% higher than controls (17.2 and 11.4 g/L for treated and control calves, respectively). Kamada et al. (2007) speculate that a complex forms between the Se and IgG enhancing the uptake of IgG *via* pinocytosis.

The addition of sodium bicarbonate (**SB**;7.3 g/kg) to fermented colostrum to raise the pH to 6.15 resulted in increased absorption of IgG by calves, but not as great as calves fed unfermented colostrum (Foley et al., 1978). Adding SB to colostrum has a bacteriostatic effect on *E. coli* O 111 (Griffiths and Humphreys, 1977) and likely could benefit and enhance IgG uptake. Chapman et al. (2012) added SB to pooled maternal colostrum (9 batches pooled and frozen). Calves were fed 2.68 L of colostrum (82.1 ± 8.5 g/L) with or without 20 g of SB within 75 min of birth and another 1.32 L of colostrum with or without SB 6 h later. Serum IgG was greater than 30 g/L at 24 h of age and AEA was greater than 32% regardless of treatment. Results of this study indicated no benefit of adding SB to colostrum.

Lactoferrin (**LF**) is an iron-binding whey protein found in colostrum at 1–2 g/L (Molenaar et al., 1996). It is involved in the development of the intestine and the immune system in mice and humans (Shah, 2000; Zhang et al., 2001). Connelly and Erickson (2016) added 1 g of supplemental LF or 0 LF between two feedings of 2 L of colostrum fed to 24 bull calves at birth and 8 h later. Immunoglobulin G concentrations were 55.5 and 53.25 g/L for the control and LF treatments, respectively. On day 2 of life calves, were subjected to a xylose challenge (Merritt and Duelly, 1983) to determine any effect of supplementing colostrum with LF on intestinal development. At this time, calves were fed an all-milk, milk replacer. There was no benefit of adding LF to colostrum on day 1 of life as serum IgG at 24 h, and AEA was similar across treatments. Nor were there any changes in serum xylose concentration on day 2 of life indicating no effect of adding LF to colostrum on intestinal epithelium development.

COLOSTRUM PRODUCTION CHALLENGES

Jersey cows produce high-quality colostrum (greater than 50 g/L IgG) but, sometimes, at the expense of production. For example, a study was conducted in the author's laboratory where out of forty multiparous Jersey cows, 10 produced < 2 L with one cow producing no colostrum at the first milking. There were no outward differences among treatments. Recently, Gavin et al. (2018) evaluated a 2,500 cow dairy in Texas to evaluate photoperiod, parity, weather, and various production parameters on colostrum production. Colostrum was collected over a year. In May of 2016, cows average 6.6 kg colostrum, whereas in December, cows averaged 2.5 kg/day. Multiparous cows produced 1.3 kg in December. Cows decreased production of colostrum on average by 0.17 kg/week with multiparous cows declining by 0.22 kg/week from May until December. In December, over 35% of the multiparous cows calving produced no colostrum while 1% of first parity cows produced no colostrum. Apparently, cow age affects colostrum production in Jersey cows. Gavin et al. (2018) used logistic regression to determine what would cause a decrease in the production of at least 2.7 kg of colostrum. Older cows had a 1.38 (37–48 mo), 2.06 (49–60 mo), and 2.27 (older than 60 mo) greater odds of producing less than 2.7 kg of colostrum compared to cows younger than 37 mo. Cows with a shorter dry period (45 days) had 1.88 times greater odds of low colostrum production compared to cows with a 75-day dry period. Cows with a 45-day dry period had a 1.69 greater odds ratio of low colostrum production compared to cows with a 65-day dry period. This response may be due to changes in photoperiod which can affect the production of hormones needed for lactogenesis and colostrogenesis. However, there are no studies evaluating photoperiod specifically on colostrum production and quality.

The environment can affect colostrum quality. Gulliksen et al. (2008) in Norway observed that the best colostrum (highest IgG concentration) was produced in late summer and early autumn. However, data from Ireland (Conneely et al., 2014) observed that the best quality colostrum was produced during the winter and early spring.

COLOSTRUM QUALITY PREDICTION EQUATION

Cabral et al. (2016) developed a model to predict colostrum quality using previous lactation and environmental data from nine Holstein herds (108 samples) and validated it with 27 samples from nine other Holstein herds. The model required some data transformation to a natural logarithm (Ln). The equation to predict colostrum quality (IgG, g/L) is as follows:

Ln IgG = 4.03684 + 2.28887 (Ln FY) − 2.1529 (Ln FP) − 2.25429 (Ln PY) + 2.10609 (Ln PP) + 0.14457 (Ln Par) − 0.00025683 (PTAM) + 0.01553 (D>) − 0.05018 (PASWK); $R^2 = 0.56$, where FY is the previous lactation milkfat yield, FP is the previous lactation milkfat percent, PY is the previous lactation milk protein yield, PP is the previous lactation milk protein percent, Par is the previous lactation parity, PTAM is the predicted transmitting ability – milk, D> is the days when the maximum environmental temperature was over 23°C, and PASWK is the number of weeks during the dry period when a cow was on pasture. These data indicate that previous fat yield, previous protein percent, parity, and days above the thermal neutral zone were all positively related to colostrum quality. Whereas previous fat percent, protein yield, PTAM, and weeks on pasture during the dry period were all negatively related to colostrum quality. There are no models to predict colostrum yield which would benefit the industry as it pertains to low colostrum production.

COLOSTRUM REPLACERS

CRs are an important tool for the dairy producer because cows can sometimes not produce adequate amounts of colostrum, and

it can pass organisms onto the calf such as *E. coli* and *M. bovis*. In addition, colostrum quality can sometimes be a challenge. Gulliksen et al. (2008) observed that in colostrum collected from 1,250 Norwegian dairy cows, 57.8% produced colostrum that failed to meet the 50 g of IgG/L threshold. Whereas Morrill et al. (2012) found that only 39.4% of colostrum samples met the minimum of less than 100,000 cfu/ml for total plate count and the minimum IgG concentration. Therefore, it is necessary for dairy producers to have an alternative source of IgG for neonatal calves. CRs can be a suitable alternative. CRs need to provide more than 100 g of IgG per dose to achieve a fair value for serum IgG at 24 h (at least 10g/L; Quigley et al., 2001). Sources for IgG vary and range from blood-based or colostral-based CR. In one of the earliest studies evaluating CRs, Quigley et al. (2001) evaluated blood serum-based colostrum supplement (CS; 90 g of IgG) to blood-based CR (244 g of IgG) fed to 160 calves. Results indicated that calves fed CR had serum IgG of 14.1 g/L at 24 h, whereas calves fed the CS failed to attain transfer of passive immunity. Shea et al. (2009) compared passive transfer status in calves fed either 1 dose (105 g of IgG) or two doses one at birth and one at 12 h. Lactoferrin was added at a rate of 1g. Results indicated that calves fed only one dose had barely attained passive transfer of IgG by 24 h (10.7 g/L), whereas calves fed two doses had a greater ($P < 0.001$) concentration of serum IgG (14.4 g/L). Supplementing LF in this case reduced AEA. Possibly, LF was competing with IgG for absorption across the small intestine. Adding SB to CR was effective to increase serum IgG ($P < 0.05$) in one study where 20 g of SB was added to 66 g of IgG and 10 g of SB to the next feeding of 66 g of IgG in a CR compared to no addition of SB (IgG of 16.3 and 13.2 g/L, respectively; Morrill et al., 2010). However, in another study (Cabral et al., 2011) conducted in the same laboratory adding graded levels of SB (0, 15, 30, or 45 g SB) with one feeding of CR, a negative linear response was observed. The authors suggested that the 45 g of SB treatment may have caused the calves to enter a metabolic alkalosis. In a follow-up study conducted on a commercial dairy, Cabral et al. (2014) added 30 g of SB to a CR and observed a highly significant reduction in serum IgG ($P < 0.01$). Upon further investigation, dams of calves used in this study were not fed an anionic salt-based diet and the addition of the SB could have caused a metabolic alkalosis in these calves.

From these studies, CR is advantageous as long as more than 100 g of IgG is provided and SB can be beneficial to aid in IgG uptake but only likely in calves born of cows on a diet that causes metabolic acidosis (anionic diet).

CONCLUSION

Colostrum is a critical necessity in a neonatal calf's life through the provision of antibodies, maternal cells, and nutrients. Research is currently being conducted to investigate the effects of other components of colostrum on intestinal epithelial growth and the propensity for calves fed more colostrum to produce more milk as cows. More research studies need to be conducted to fully evaluate the contribution of this important lacteal secretion to the calf and eventually cow performance.

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The author confirms being the sole contributor of this work and has approved it for publication.

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REFERENCES

Aragona, K. M., Chapman, C. E., Pereira, A. B. D., Isenberg, B. J., Standish, R. B., Maugeri, C. J., et al. (2016). Prepartum Supplementation of Nicotinic Acid: Effects on Health of the Dam, Colostrum Quality, and Acquisition of Immunity in the Calf. *J. Dairy Sci.* 99, 3529–3538. doi: 10.3168/jds.2015-10598

Aragona, K. M., Rice, E. M., Engstrom, M., and Erickson, P. S. (2020). Supplementation of Nicotinic Acid to Prepartum Holstein Cows Increases Colostral Immunoglobulin G, Excretion of Urinary Purine Derivatives, and Feed Efficiency. *J. Dairy Sci.* 103, 2287–2302. doi: 10.3168/jds.2019-17058

Aragona, K. M., Rice, E. M., Engstrom, M., and Erickson, P. S. (2021). Effect of β-Carotene Supplementation to Prepartum Holstein Cows on Colostrum Quality and Calf Performance. *J. Dairy Sci.* 104, 8814–8825. doi: 10.3168/jds.2020-19553

Armengol, R., and Fraile, L. (2016). Colostrum and Milk Pasteurization Improve Health Status and Decrease Mortality in Neonatal Calves Receiving Appropriate Colostrum Ingestion. *J. Dairy Sci.* 99, 4718–4725. doi: 10.3168/jds.2015-10728

Baumwart, A. L., l.J. Mungle, M., and Corley, L. D. (1977). Effect of Potassium Isobutyrate on Absorption of Immunoglobulins From Colostrum by Calves. *J. Dairy Sci.* 69, 759–762. doi: 10.3168/jds.S0022-0302(77)83931-3

Brandon, M. R., Watson, D. L., and Lascelles, A. K. (1971). The Mechanism of Transfer of Immunoglobulins Into Mammary Secretions of Cows. *Aust. J. Exp. Biol. Med. Sci.* 49, 613–623. doi: 10.1038/icb.1971.67

Cabral, R. G., Cabral, M. A., Chapman, C. E., Kent, E. J., Haines, D. M., and Erickson, P. S. (2014). Colostrum Replacer Feeding Regimen, Addition of Sodium Bicarbonate, and Milk Replacer: The Combined Effects on Absorptive Efficiency of Immunoglobulin G in Neonatal Calves. *J. Dairy Sci.* 97, 2291–2296. doi: 10.3168/jds.2013-7007

Cabral, R. G., Chapman, C. E., Aragona, K. M., Clark, E., Lunak, M., and Erickson, P. S. (2016). Predicting Colostrum Quality From Performance in the Previous Lactation and Environmental Changes. *J. Dairy Sci.* 99, 4048–4055. doi: 10.3168/jds.2015-9868

Cabral, R. G., Chapman, C. E., Haines, D. M., Brito, A. F., and Erickson, P. S. (2011). Short Communication: Addition of Varying Amounts of Sodium Butyrate to Colostrum Replacer: Effects on IgG Absorption and Serum Bicarbonate in Neonatal Calves. *J. Dairy Sci.* 94, 5656–5660. doi: 10.3168/jds.2011-4235

Chapman, C. E., Cabral, R. G., Marston, S. P., Brito, A. F., and Erickson, P. S. (2012). Short Communication: Addition of Sodium Bicarbonate to Maternal Colostrum: Effects on Immunoglobulin G Absorption and Hematocrit in Neonatal Calves. *J. Dairy Sci.* 95, 5331–5335. doi: 10.3168/jds.2011-5184

Conneely, M., Berry, D. P., Murphy, J. P., Lorenz, I., Doherty, M. L., and Kennedy, E. (2014). Effect of Feeding Colostrum at Different Volumes and Subsequent

Number of Transition Milk Feed on the Serum Immunoglobulin G Concentration and Health Status on Dairy Calves. *J. Dairy Sci.* 97, 6991–7000. doi: 10.3168/jds.2013-7494

Conneely, M., Berry, D. P., Sayers, R., Murphy, J. P., Lorenz, I., Doherty, M. L., et al. (2013). Factors Associated With the Concentration of Immunoglobulin G in the Colostrum of Dairy Cows. *Animal* 7, 1824–1832. doi: 10.1017/S1751731113001444

Connelly, R. A., and Erickson, P. S. (2016). Lactoferrin Supplementation of the Neonatal Calf has No Impact on Immunoglobulin G Absorption and Intestinal Development in the First Days of Life. *J. Anim. Sci.* 94, 196–200. doi: 10.2527/jas.2015-8918

Dahl, G. E., Tao, S., and Monteiro, A. P. A. (2016). Effects of Late Gestation Heat Stress on Immunity and Performance of Calves. *J. Dairy Sci.* 99, 3193–3198. doi: 10.3168/jds.2015-9990

Dann, H. M., Drackley, J. K., McCoy, G. C., Hutjens, M. F., and Garrett, J. E. (2000). Effects of Yeast Culture (*Saccharomyces Cerevisiae*) on Prepartum Intake and Postpartum Intake on Milk Production in Jersey Cows. *J. Dairy Sci.* 83, 123–127. doi: 10.3168/jds.S0022-0302(00)74863-6

Denise, S. K., Robison, J. D., Stott, G. H., and Armstrong, D. V. (1989). Effects of Passive Immunity on Subsequent Production in Dairy Heifers. *J. Dairy Sci.* 72, 552–554. doi: 10.3168/jds.S0022-0302(89)79140-2

Dennis, S. M., Arambel, M. J., Bartley, E. E., Riddell, D. O., and Dayton, A. D. (1982). Effect of Heated or Unheated Soybean Meal With or Without Niacin on Rumen Protozoa. *J. Dairy Sci.* 80, 1200–1206. doi: 10.3168/jds.S0022-0302(82)82391-6

Donovan, D. C., Reber, A. J., Gabbard, J. D., Aceves-Avila, M., Galland, K. L., Hobert, K. A., et al. (2007). Effect of Maternal Cells Transferred With Colostrum on Cellular Responses to Pathogen Antigens in Neonatal Calves. *Am. J. Vet. Res.* 68, 778–782. doi: 10.2460/ajvr.68.7.778

Dorreau, M., and Ottou, J. F. (1996). Influence of Niacin Supplementation on *In Vivo* Digestibility and Ruminal Digestion in Dairy Cows. *J. Dairy Sci.* 79, 2247–2254. doi: 10.3168/jds.S0022-0302(96)76601-8

Elizondo-Salazar, J. A., and Heinrichs, A. J. (2009). Feeding Heat-Treated Colostrum to Neonatal Dairy Heifers: Effects on Growth Characteristics and Blood Parameters. *J. Dairy Sci.* 93, 3265–3273. doi: 10.3168/jds.2008-1667

Erickson, P. S., Murphy, M. R., McSweeney, C. S., and Trusk, A. M. (1991). Niacin Absorption From the Rumen. *J. Dairy Sci.* 74, 3492–3495. doi: 10.3168/jds.S0022-0302(91)78540-8

Erickson, P. S., Trusk, A. M., and Murphy, M. R. (1990). Effects of Niacin Source on Epinephrine Stimulation of Plasma Nonesterified Fatty Acid and Glucose Concentrations, on Diet Digestibility and Rumen Protozoal Numbers in Lactating Dairy Cows. *J. Nutr.* 120, 1648–1653. doi: 10.1093/jn/120.12.1648

Faber, S. N., Faber, N. E., McCauley, T. C., and Ax, R. L. (2005). Case Study: Effects of Colostrum Ingestion on Lactational Performance. *Prof. Anim. Sci.* 21, 420–425. doi: 10.15232/S1080-7446(15)31240-7

Ferdowsi nia, E., Nikkhah, A., Rahmani, H. R., Alikhani, M., Alipour, M. M., and Ghorbani, G. R. (2010). Increased Colostral Somatic Cell Counts Reduce Pre-Weaning Calf Immunity, Health, and Growth. *J. Anim. Phys. Anim. Nutr.* 94, 628–634. doi: 10.1111/j.1439-0396.2009.00948.x

Ferreira, F. C., Gennari, R. S., Dahl, G. E., and de Vries, A. (2016). Economic Feasibility of Cooling Dry Cows Across the United States. *J. Dairy Sci.* 99, 9931–9941. doi: 10.3168/jds.2016-11566

Foley, J. A., Hunter, A. G., and Otterby, D. E. (1978). Absorption of Colostral Proteins by Newborn Calves Fed Unfermented, Fermented, or Buffered Colostrum. *J. Dairy Sci.* 61, 1450–1456. doi: 10.3168/jds.S0022-0302(78)83748-5

Foster, D. M., Poulsen, K. P., Sylvester, H. J., Jacob, M. E., Casulli, K. E., and Farkas, B. E. (2016). Effect of High-Pressure Processing of Bovine Colostrum on Immunoglobulin G Concentration, Pathogens, Viscosity, and Transfer of Passive Immunity to Calves. *J. Dairy Sci.* 99, 8575–8588. doi: 10.3168/jds.2016-11204

Fratric, N., Stojic, V., Jankovic, D., Samanc, H., and Gvozdic, D. (2005). The Effect of Clinoptilolite Based Mineral Adsorber on Concentrations of Immunoglobulin G in the Serum of Newborn Calves Fed Different Amounts of Colostrum. *Acta Vet. (Beograd)* 55, 11–21. doi: 10.2298/AVB0501011F

Gao, F., Liu, Y.-C., Zhang, Z.-H., Zhang, C.-Z., Su, H.-W., and Li, S.-L. (2012). Effect of Prepartum Maternal Energy Density on the Growth Performance, Immunity and Antioxidant Capability of Neonatal Calves. *J. Dairy Sci.* 95, 4510–4516. doi: 10.3168/jds.2011-5087

Garcia, M., Greco, L. F., Favoreto, M. G., Marsola, R. S., Martins, L. T., Bisonotto, R. S., et al. (2014). Effect of Supplementing Fat to Pregnant Nonlactating Cows on Colostral Fatty Acid Profile and Passive Immunity of the Newborn Calf. *J. Dairy Sci.* 97, 392–405. doi: 10.3168/jds.2013-7086

Gavin, K., Neibergs, H., Hoffman, A., Kiser, J. N., Cornmesser, M. A., Amirpour Haredasht, S., et al. (2018). Low Colostrum Yield in Jersey Cattle and Potential Risk Factors. *J. Dairy Sci.* 101, 6388–6398. doi: 10.3168/jds.2017-14308

Gelsinger, S. L., Gray, S. M., Jones, C. M., and Heinrichs, A. J. (2014). Heat Treatment of Colostrum Increases Immunoglobulin G Absorption Efficiency in High-, Medium-, and Low-Quality Colostrum. . *J. Dairy Sci* 97, 2355–2360. doi: 10.3168/jds.2013-7374

Gelsinger, S. L., and Heinrichs, A. J. (2017). Comparison of Immune Responses in Calves Fed Heat-Treated or Unheated Colostrum. *J. Dairy Sci.* 100, 4090–4101. doi: 10.3168/jds.2016-12010

Gelsinger, S. L., Jones, C. M., and Heinrichs, A. J. (2015). Effect of Colostrum Heat Treatment and Bacterial Population on Immunoglobulin G Absorption and Health of Neonatal Calves. *J. Dairy Sci.* 98, 4640–4645. doi: 10.3168/jds.2014-8790

Godden, S., McMartin, S., Feirtag, J., Stabel, J., Bey, R., Goyal, S., et al. (2006). Heat-Treatment of Bovine Colostrum. II: Effects of Heating Duration on Pathogen Viability and Immunoglobulin G. *J. Dairy Sci.* 89, 3476–3483. doi: 10.3168/jds.S0022-0302(06)72386-4

Godden, S.M., Lombard, J.E., and Woolums, A.R. (2019). Colostrum Management for Dairy Calves. *Vet. Clin. Food Anim.* 35, 535—556. doi: 10.1016/j.cvfa.2019.07.005

Godden, S. M., Smolenski, D. J., Donahue, M., Oakes, J. M., Bey, R., Wells, S., et al. (2012). Heat-Treated Colostrum and Reduced Morbidity in Preweaned Dairy Calves: Results of a Randomized Trial and Examination of Mechanisms of Effectiveness. *J. Dairy Sci.* 95, 4029–4040. doi: 10.3168/jds.2011-5275

Griffiths, E., and Humphreys, J. (1977). Bacteriostatic Effect on Human Milk and Bovine Colostrum on Escherichia Coli: Importance of Bicarbonate. *Infect. Immun.* 15, 396–401. doi: 10.1128/iai.15.2.396-401.1977

Gulliksen, S. M., Lie, K. I., Soverod, L., and Osteras, O. (2008). Risk Factors Associated With Colostrum Quality in Norwegian Dairy Cows. *J. Dairy Sci.* 91, 704–712. doi: 10.3168/jds.2007-0450

Gvozdic, D., Stojic, V., Fratric, N., Pesut, O., Jovanovic, I., Kirovski, D., et al. (2007). Efficiency of Immunoglobulin Absorption in Newborn Calves Receiving Oral Clinoptilolite Treatment. *Lucrari Ştiinifice Med. Vet.* 40, 234–242.

Hagiwara, K., Katakoka, S., Yamanaka, H., Kirisawa, R., and Iwai, H. (2000). Detection of Cytokines in Colostrum. *Vet. Immunol. Immunopathol.* 76, 183–190. doi: 10.1016/S0165-2427(00)00213-0

Hall, J. A., Bobe, G., Vorachek, W. R., Estill, C. T., Mosher, W. D., Pirelli, G. J., et al. (2014). Effect of Supranutritional Maternal and Colostral Selenium Supplementation on Passive Absorption of Immunoglobulin G in Selenium-Replete Dairy Calves. *J. Dairy Sci.* 97, 4379–4391. doi: 10.3168/jds.2013-7481

Hardy, R. D. (1969). The Influence of Specific Chemical Factors in the Solvent on the Absorption of Macromolecular Substances From the Small Intestine of the Newborn Calf. *J. Physiol.* 204, 607–632. doi: 10.1113/jphysiol.1969.sp008935

Hough, R. L., McCarthy, F. D., Kent, H. D., Eversole, D. E., and Wahlberg, M. L (1990). Influence of Nutritional Restriction During Late Gestation on Production Measures and Passive Immunity in Beef Cattle. . *J. Anim. Sci* 68, 2622–2627. doi: 10.2527/1990.6892622x

Huber, J. T., Jacobsen, N. L., Allen, R. S., and Hartman, P. A. (1961). Digestive Enzyme Activities in the Young Calf. *J. Dairy Sci.* 44, 1494–1501. doi: 10.3168/jds.S0022-0302(61)89911-6

Jensen, P. T., and Pedersen, K. B. (1982). The Influence of Sow Colostrum Trypsin Inhibitor on the Immunoglobulin Absorption in Newborn Piglets. *Acta Vet. Scand.* 23, 161–168. doi: 10.1186/BF03546802

Johnson, J. L., Godden, S. M., Molitor, T., Ames, T., and Hagman, D. (2007). Effects of Feeding Heat-Treated Colostrum on Passive Transfer of Immune and Nutritional Parameters in Neonatal Dairy Calves. *J. Dairy Sci.* 90, 5189–5198. doi: 10.3168/jds.2007-0219

Joyce, P. W., and Sanchez, W. K. (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.

Kamada, H., Nonaka, I., Ueda, Y., and Murai, M. (2007). Selenium Addition to Colostrum Increases Immunoglobulin G Absorption by Newborn Calves. *J. Dairy Sci.* 90, 5665–5670. doi: 10.3168/jds.2007-0348

Kehoe, S. I., Jayarao, B. M., and Heinrichs, A. J. (2007). A Survey of Bovine Colostrum Composition and Colostrum Management Practices on Pennsylvania Dairy Farms. *J. Dairy Sci.* 90, 4108–4116. doi: 10.3168/jds.2007-0040

Kehoe, S.I., Heinrichs, A.J., Moody, M.L., Jones, C.M., and Long, M.R. (2011). Comparison of Immunoglobulin G Concentrations in Primiparous and Multiparous Bovine Colostrum. *Prof. Anim. Sci.* 27, 176—180. doi: 10.15232/51080-7446(15)30471-X

Kryzer, A. A., Godden, S. M., and Schell, R. (2015). Heat-Treated (in Single Aliquot or Batch) Colostrum Outperforms non-Heated Colostrum in Terms of Quality and Transfer of Immunoglobulin G in Neonatal Calves. *J. Dairy Sci.* 98, 1870–1877. doi: 10.3168/jds.2014-8387

Kuroiwa, T., Ohtani, Y., Obara, Y., Terada, F., Watanabe, K., Shirakawa, H., et al. (2022). Effect of Vitamin K3 Supplementation on Immunoglobulin G Concentration in Colostrum or Periparturient Holstein Dairy Cows. *Anim. Sci. J.* 93(1):e13706. (in press). doi: 10.1111/asj.13706

Lacetera, A., Bernabucci, U., Ronchi, B., and Nardone, A. (1996). Effects of Selenium and Vitamin E Administration During a Late Stage of Pregnancy on Colostrum and Milk Production in Dairy Cows and on Passive Immunity and Growth of Their Offspring. *Am. J. Vet. Res.* 57, 1776–1780.

Langel, S. N., Wark, W. A., Garst, S. N., James, R. E., McGilliard, M. L., Peterson-Wolfe, C. S., et al. (2015). Effect of Feeding Whole Compared With Cell-Free Colostrum on Calf Immune Status: The Neonatal Period. *J. Dairy Sci.* 98, 3729–3740. doi: 10.3168/jds.2014-8422

Laskowski, M., and Laskowski, M. (1951). Crystalline Trypsin Inhibitor From Colostrum. *J. Biol. Chem.* 190, 563–573. doi: 10.1016/S0021-9258(18)56005-1

Lombard, J., Urie, F., Godden, S., Quigley, J., Earleywine, T., McGuirk, S., et al. (2020). Consensus Recommendations on Calf- and Herd-Level Passive Immunity in Dairy Calves in the United States. *J. Dairy Sci.* 103, 7611–7624. doi: 10.3168/jds.2019-17955

Macedo, R. J., Arrendondo, V., Garcia, F., Aguilar, M., Prado, O., and Rodriguez, R. (2012). Effect of Supplemental Yeast Culture and Physiological Factors on Colostrum and Milk Composition in Pelibuey Ewes. *Trop. Anim. Health Prod.* 44, 349–354. doi: 10.1007/s11250-011-0028-6

Mann, S., Leal Yepes, F. A., Overton, T. R., Lock, A. L., Wakshlag, J. J., and Nydam, D. V. (2016). Effect of Dry Period Dietary Energy Level in Dairy Cattle on Volume, Concentration of Immunoglobulin G, Insulin, and Fatty Acid Composition of Colostrum. *J. Dairy Sci.* 99, 1515–1526. doi: 10.3168/jds.2015-9926

Marin, M. P., Porgurschi, E. N., Marin, I., and Nicolae, C. G. (2020). Influence of Natural Zeolites Supplemented With Inorganic Selenium on the Productive Performance of Dairy Cows. *Pak. J. Zool.* 52, 775–783. doi: 10.17582/journal.pjz/20190829190816

Martinez, N., Rodney, R. M., Block, E., Hernandez, L. L., Nelson, C. D., Lean, I. J., et al. (2018). Effects of Prepartum Dietary Cation-Anion Difference and Source of Vitamin D in Dairy Cows: Lactation Performance and Energy Metabolism. *J. Dairy Sci.* 101, 2544–2562. doi: 10.3168/jds.2017-13739

McMartin, S., Godden, S., Metzger, L., Feirtag, J., Bey, R., Stabel, J., et al. (2006). Heat Treatment of Bovine Colostrum. I. Effects of Temperature on Viscosity and Immunoglobulin G Level. *J. Dairy Sci.* 89, 2110–2118. doi: 10.3168/jds.S0022-0302(06)72281-0

Merritt, A.M., and Duelly, P. (1983). Phloroglucinol Microassay for Plasma Xylose in Dogs and Horses. *Am. J. Vet. Res.* 44, 2184—2185.

Molenaar, A. J., Kuys, Y. M., Davis, S. R., Wilkins, R. J., Mead, P. E., and Tweedie, J. W. (1996). Elevation of Lactoferrin Gene Expression in Developing, Ductal, Resting, and Regressing Parenchymal Epithelium of the Ruminant Mammary Gland. *J. Dairy Sci.* 79, 1198–1208. doi: 10.3168/jds.S0022-0302(96)76473-1

Morin, D. E., Nelson, S. V., Reid, E. D., Nagy, D. W., Dahl, G. E., and Constable, P. D. (2010). Effect of Colostrum Volume, Interval Between Calving and First Milking, and Photoperiod on Colostral IgG Concentrations in Dairy Cows. *JAVMA* 237, 420–428. doi: 10.2460/javma.237.4.420

Morrill, K.M., Conrad, E., Lago, A., Campbell, J., and Tyler, H. (2012). Nationwide Evaluation of Quality and Composition of Colostrum on Dairy Farms in the United States. *J. Dairy Sci.* 95:3997—4005. doi: 10.3168/jds.2011-5174

Morrill, K. M., Marston, S. P., Whitehouse, N. L., Van Amburgh, M. E., Schwab, C. G., Haines, D. M., et al. (2010). Anionic Salts in the Prepartum Diet and Addition of Sodium Bicarbonate to Colostrum Replacer and Their Effects on Immunoglobulin G Absorption in the Neonate. *J. Dairy Sci.* 93, 2067–2075. doi: 10.3168/jds.2009-2622

NAHMS (2007) *Dairy 2007. Heifer Calf Health and Management Practices on U.S. Dairy Operations*. Available at: https://www.aphis.usda.gov/animal_health/nahms/dairy/downloads/dairy07/Dairy07_ir_CalfHealth_1.pdf (Accessed April 1, 2022).

NRC (1984). *Nutrient Requirements of Beef Cattle* (Washington, DC: National Academy of Science. National Academies Press).

Ort, S. B., Aragona, K. M., Chapman, C. E., Shangraw, E., Brito, A. F., Schauff, D. J., et al. (2018). The Impact of Direct-Fed Microbials and Enzymes on the Health and Performance of Dairy Cows With Emphasis on Colostrum Quality and Serum Immunoglobulin Concentration in Calves. *J. Anim. Physiol. Anim. Nutr.* 102, e641–e652. doi: 10.1111/jpn.12806

Papaioannou, D., Katsoulos, P. D., Panousis, N., and Karatzias, H. (2005). The Role of Natural and Synthetic Zeolites as Feed Additives on the Prevention and/or Treatment of Certain Farm Animal Diseases: A Review. *Microporous Mesoporous Mater* 84, 161–170. doi: 10.1016/j.micromeso.2005.05.030

Pavlata, L., Prasek, J., Filipek, J., and Pechova, A. (2004). Influence of Parenteral Administration of Selenium and Vitamin E During Pregnancy on Selected Metabolic Parameters and Colostrum Quality in Dairy Cows. *Vet. Med. Czech* 49 (5), 149–155.

Peter, A. T. (2013). Bovine Placenta: A Review on Morphology, Components, and Defects From Terminology and Clinical Perspectives. *Theriogenology* 80, 693–705. doi: 10.1016/j.theriogenology.2013.06.004

Prom, C. M. (2016). Supplementation of β-Carotene During the Close-Up Period on Cows, Colostrum and Calves. MS Thesis. Department of Animal Sciences, University of Illinois at Urbana-Champaign.

Puppel, K., Golebiewski, M., Grodkowski, G., Solarczyk, P., Kostusiak, P., Klopcic, M., et al. (2020). Use of Somatic Cell Count as an Indicator of Colostrum Quality. *PLoS One* 15 (8), e0237615. doi: 10.1371/journal.pone.0237615

Quigley, J. D., Martin, K. R., Dowlen, H. H., and Lamar, K. C. (1995). Addition of Soybean Trypsin Inhibitor to Bovine Colostrum: Effects of Serum Immunoglobulin Concentration in Jersey Calves. *J. Dairy Sci.* 78, 886–892. doi: 10.3168/jds.S0022-0302(95)76702-9

Quigley, J. D., Strohbehn, R. E., Kost, C. J., and O'Brien, M. M. (2001). Formulation of Colostrum Supplements, Colostrum Replacers and Acquisition of Passive Immunity in Neonatal Calves. *J. Dairy Sci.* 84, 2059–2065. doi: 10.3168/jds.S0022-0302(01)74650-4

Reinhardt, T. A., Stabel, J. R., and Goff, J. P. (1999). 1,25 Dihydroxyvitamin D3 Enhances Milk Antibody Titers to *Escherichia Coli* J5 Vaccine. *J. Dairy Sci.* 82, 1904–1909. doi: 10.3168/jds.S0022-0302(99)75425-1

Sandholm, M., and Hokanen-Buzalski, T. (1979). Colostral Trypsin-Inhibitor Capacity in Different Animal Species. *Acta Vet. Scand.* 20, 469–476. doi: 10.1186/BF03546574

Santoro, H. M., Erickson, P. S., Whitehouse, N. L., McLaughlin, A. M., Schwab, C. G., and Quigley, J. D. (2004). Evaluation of a Colostrum Supplement, With or Without Trypsin Inhibitor, and an Egg Protein Milk Replacer for Dairy Calves. *J. Dairy Sci.* 87, 1739–1746. doi: 10.3168/jds.S0022-0302(04)73328-7

Sasaki, M., Davis, C. L., and Larson, B. L. (1976). Production and Turnover of IgG1 and IgG2 Immunoglobulins in the Bovine Around Parturition. *J. Dairy Sci.* 59, 2046–2055. doi: 10.3168/jds.S0022-0302(76)84486-4

Shea, E.C., Whitehouse, N.L., and Erickson, P.S. (2009). Effects of Colostrum Replacer Supplemented with Lactoferrin on the Blood Plasma Immunoglobulin G Concentration and Intestinal Absorption of Xylose in the Neonatal Calf. *J. Anim. Sci.* 87, 2047—2054. doi: 10.2527/jas.2008-1225

Shah, N. P. (2000). Effects of Milk Derived Bioactives: An Overview. *Br. J. Nutr.* 84 (Suppl. 1), S3–S10. doi: 10.1017/S000711450000218X

Stabel, J. R. (2008). Pasteurization of Colostrum Reduces the Incidence of Paratuberculosis in Neonatal Dairy Calves. *J. Dairy Sci.* 91, 3600–3606. doi: 10.3168/jds.2008-1107

Swecker, W. S., Thatcher, C. D., Eversole, D. E., Blodgett, D. J., and Schurig, G. G. (1995). Effect of Selenium Supplementation on Colostral IgG Concentration on

Cows Grazing Selenium-Dependent Pastures and on Postsuckle Serum IgG Concentration in Their Calves. *Am. J. Vet. Res.* 56, 450–453.

Tao, S., Monteiro, A.P.A., Thompson, I.M., Hayen, M.J., and Dahl, G.E. (2012). Effect of Late-gestation Maternal Stress on Growth and Immune Function of Dairy Calves. *J. Dairy Sci.* 95, 7128—7136. doi: 10.3168/jds.2012-5697

Torsein, M., Lindberg, A., Sandgren, C.H., Waller, K.P., Tornquist, M., Svensson, C., et al (2011). Risk Factors for Calf Mortality in Large Swedish Dairy Herds. *Prev. Vet. Med.* 99, 136—147. doi: 10.1016/j.prevetmed.2010.12.001

Yamanaka, H., Hagiwara, K., Kirisawa, R., and Iwai, H. (2003). Proinflammatory Cytokines in Bovine Colostrum Potentiate the Mitogenic Response of Peripheral Blood Mononuclear Cells From Newborn Calves Through IL-2 and CD25 Expression. *Microbiol. Immunol.* 47, 461–468. doi: 10.1111/j.1348-0421.2003.tb03371.x

Zhang, P., Sawicki, B., Hanson, L., Nuijens, J. H., and Neville, M. C. (2001). Human Lactoferrin in the Milk of Transgenic Mice Increases Intestinal Growth in Ten-Day-Old Suckling Neonates. *Adv. Exp. Med. Biol.* 501, 107–113. doi: 10.1007/978-1-4615-1371-1_13

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