PEER REVIEWED

Colostrum Replacers – A Review for Veterinary Practitioners

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Abstract

Veterinary practitioners must understand the differences in immunoglobulin G (IgG) content between different types of colostrum replacers, as well as the efficiency of immunoglobulin absorption from various sources. In a disease control program, to protect against *Mycoplasma bovis*, *Mycobacterium avium* subsp *paratuberculosis* exposure, and the potential for exposure to bovine leukemia virus, a colostrum replacer is a viable option to feeding maternal colostrum that might be contaminated with these potential pathogens. Veterinarians should also weigh the convenience, relative simplicity, and accuracy of administering a colostrum replacer versus the expense and intricate protocol necessary to properly manage maternal colostrum. Dried colostrum-derived colostrum replacers supply predominately IgG1, while colostrum replacers derived from bovine plasma or serum supply 50% IgG1 and 50% IgG2 immunoglobulins. It is acceptable to utilize colostrum replacers of proven quality in place of raw, pooled or pasteurized maternal colostrum, providing the necessary amount of total IgG is administered for the birth weight of the calf. If administered properly, colostrum replacers can provide passive transfer of immunity for neonatal calves.

Keywords: colostrum, colostrum replacers, pasteurization, biosecurity, passive transfer of immunity

Résumé

Les vétérinaires praticiens doivent comprendre les différences dans la teneur en immunoglobulines G (IgG) des différents types de colostrum de remplacement de même que l'efficacité de l'absorption des immunoglobulines provenant de différentes sources. Dans un programme de contrôle de la maladie, afin de protéger contre l'exposition à *Mycoplasma bovis* et *Mycobacterium avium* subsp *paratuberculosis* et pour contrer l'exposition potentielle au virus de la leucémie bovine, le colostrum de remplacement est une alternative valable à l'utilisation de colostrum maternel qui pourrait être contaminé par ces pathogènes. Les vétérinaires devraient aussi balancer la commodité, la simplicité relative et la justesse de l'administration d'un colostrum de remplacement versus les dépenses et le protocole sophistiqué nécessaires pour bien régir le colostrum maternel. Le colostrum de remplacement dérivé de colostrum déshydraté fournit principalement de l'IgG1 alors que le colostrum de remplacement dérivé de plasma ou de sérum bovin fournit 50% des immunoglobulines IgG1 et IgG2. Il est acceptable d'utiliser un colostrum de remplacement de qualité éprouvée à la place de colostrum maternel non-traité, mélangé ou pasteurisé en autant que la quantité nécessaire d'immunoglobuline G soit ajustée en fonction du poids du veau à la naissance. Lorsqu'administré adéquatement, le colostrum de remplacement peut accomplir le transfert passif de l'immunité chez les veaux nouveau-nés.

Biosecurity

The need for biosecurity against potential bovine pathogens such as *Mycobacterium avium* subsp *paratuberculosis* (MAP), *Mycoplasma* spp, *Listeria monocytogenes, Campylobacter* spp, *Mycobacterium bovis, Salmonella* spp, *Escherichia coli,* and intracellular pathogens such as bovine leukemia virus (BLV) has generated renewed interest in utilizing complete colostrum replacers.[8,12,28,38,42,48,54,65,72,113,122,126]

Research published in 2005 demonstrated that although colostrum collected directly from the mammary gland is relatively free of bacteria, contamination frequently occurs during harvest of colostrum.[115] These data confirmed colostrum stored for any length of time at warm ambient temperatures (the average ambient temperature during the study was 73°F (22.8°C)) results in a rapid increase in bacteria counts. In addition, colostrum stored at refrigerated temperatures (39°F; 3.9°C) reached total plate counts (mean of $\log_{10}$ 6.03 and 6.17 compared to ambient of 6.62 and 6.63) and total coliform counts (mean of $\log_{10}$ 5.55 and 5.91 compared to ambient

of 4.96 and 4.48) by 48 and 96 hours, respectively, greater than or equal to that of colostrum maintained at ambient temperatures.[115] Stored colostrum bacteria counts quickly increase, allowing unfrozen stored maternal colostrum to become a significant source of potentially pathogenic bacteria. These authors advised that newly collected and refrigerated maternal colostrum, stored at 39°F, should be utilized within 24 hours post-collection.[115] It was discovered that bacterial counts in refrigerated colostrum continued to increase when stored, while natural processes of fermentation for colostrum stored at ambient temperatures, resulting in lowering of the pH of the stored colostrum, began to reduce and stabilize bacterial counts. This study clearly demonstrated that storage of colostrum at refrigerated temperatures does not prevent bacterial multiplication. Others reported that 82% of colostrum samples evaluated exceeded the industry standard of 100,000 cfu/mL total plate count.[91,92] There is a negative association between bacteria counts in colostrum and IgG absorption.[91,92]

Colostrum replacers have become an important management tool to more conveniently supply clean colostrum during night births or other time periods when labor is inadequate, or when only poorly trained labor is available to manage colostrum, which includes procedures or protocols for appropriate pasteurization, volume of colostrum administered to each neonatal calf, and assessment of colostrum quality prior to administration. Producers sometimes choose colostrum replacers after comparing their cash outlay to the true costs of appropriately and consistently managing maternal colostrum administration on-farm. Use of a quality colostrum replacer assures a known, consistent colostral mass is administered to every neonatal calf.

Assessing the IgG Concentration of Colostrum

An electronic, temperature-compensated BRIX refractometer has adequate power and specificity to predict immunoglobulin content on the farm.[26] A refractometer with a BRIX scale measures the concentration of sugars dissolved in a water solution. This type of refractometer can be used to assess colostrum quality, but in comparison to serum total protein evaluation, the line of demarcation will be wider and less distinct for colostrum due to its fat content. This fat does not dissolve in the colostrum liquid, causing the light to be refracted with a blurry line on the refractometer rather than a distinct line of demarcation. For that reason, it is recommended the scale on the BRIX refractometer read at least 22 or 23 before the colostrum is considered to be of adequate quality. Colostrum testing 22 or better on the BRIX scale is expected, with good specificity, to contain adequate antibody content.[26] Fresh colostrum should provide a value of 22 to 23 BRIX to correlate to 50 grams of IgG immunoglobulin per quart of colostrum. If a floating hydrometer or a non-temperature-compensated refractometer is utilized to measure IgG concentration, the temperature of the colostrum collected from the udder must be cooled to the recommended temperature for measurement, usually about 70 to 75°F (21.1 to 23.9°C), or inaccurate measurements will result.[26] This requirement makes use of an electronic temperature-compensated BRIX refractometer an attractive alternative for quick, reliable assessment of IgG content in fresh colostrum collections.

Since a small volume (a few drops for each reading, about 0.3 mL[26]) of colostrum is actually placed on the prism of a BRIX refractometer during testing, it is important that the sample is representative of colostrum actually fed to the calf. A recently published study revealed if cistern colostrum (colostrum accumulated in the teats and cistern of the mammary gland at parturition) is tested, the IgG content may be overestimated. The IgG content of cistern colostrum was shown to be greater than the actual IgG content in the entire colostrum volume milked from the udder after parturition.[45] The authors caution producers about testing the first fraction of colostrum removed in forestripping, and instead recommend a composite sample of the entire colostrum milking be tested after thoroughly mixing the entire colostrum collection.

Fresh colostrum must be collected within two hours post calving, or the udder content will be diluted with milk secretions, reducing immunoglobulin concentration below optimal levels of 50 grams IgG per quart of maternal colostrum.[77] Predicting the IgG content of colostrum by weight of first milking is unreliable, with a R^2 value of 0.03.[26]

Immunoglobulin Sources

Immunoglobulins in colostrum replacers are collected from four basic sources: dried bovine colostrum; dried bovine whey; freeze-dried bovine colostrum or whey; or spray-dried bovine plasma or serum.

Although egg immunoglobulins (IgY) are utilized in numerous commercial products for calves, IgY antibodies are not commonly used in colostrum replacers or colostrum supplements intended for neonatal calves. IgY fed to neonatal calves are absorbed, but IgY half-life is five days,[36] less than half that of bovine IgG.[110] As a result, egg powder should be fed after the first 48 hours of life.[36] Porcine serum was evaluated as a source of IgG in a small colostrum supplement experiment which examined administration of 45 grams of IgG from maternal colostrum, bovine serum or porcine serum.[4] Calves that received bovine serum had higher 24-hour serum IgG concentrations than calves fed porcine serum or maternal colostrum.[4]

Immunoglobulin types in bovine plasma or serum are distinctly different from bovine colostrum or whey. Bovine colostrum contains a 7 to 1 ratio of IgG1 versus IgG2, with some studies reporting that 90% of all immunoglobulins in colostrum are IgG1.[11,14,15,16,17] Immunoglobulins in colostrum are derived from immunoglobulins circulating within the maternal blood system, and little local synthesis of immunoglobulin occurs[11,18,60] unless the mammary gland is responding to a local infection.[20,21]

Whey-based immunoglobulin concentrates mirror the proportions of IgG1 and IgG2 found in bovine colostrum. The mean amount of IgG1 in 349 individual milk samples from normal lactating cows with uninfected quarters was 0.46 mg/mL.[21] The mean amount of IgG2 in 355 samples from lactating cows with uninfected quarters was 16 to 17 ug/mL.[20] The IgG content of dried whey has a preponderance of IgG1, while bovine plasma and serum have approximately equal amounts of IgG1 and IgG2.[11,14,15,16,17]

Based on published studies, IgG1 and IgG2 are differentiated by their electrophoretic movement, their electrophoretic motility or speed of movement, and their electronic charge or reactivity.[34,67] Although the molecular weight of IgG1 and IgG2 are similar, about the same molecular weight as IgA immunoglobulins (150,000),[34,121] it is postulated that IgG1 is more reactive.[34,58] The increased reactivity of IgG1 is also proposed to improve antigen recognition, attachment, and neutralization in vivo.[34,58] These studies demonstrated IgG1 is an important component of the antigen recognition processes in the neonatal calf, which mirrors relevance with similar findings in humans.

In human studies, a two-fold lower concentration of IgG1, compared to IgG2, resulted in a 50% reduction in *Haemophilus influenzae* Type *b* activity.[1] A 1988 study showed that IgG1 was superior to IgG2, IgG3, and IgG4 when chimeric murine-human antibody's anti-tumor activity (human colorectal carcinoma cells) was measured in an antibody-dependent, cell-mediated cytotoxicity assay.[114] Another report showed that human IgG1 and IgG3 are superior to other IgG subclasses in complement activation, attachment to cell membranes through Fc receptors (fragment crystallizable region of an immunoglobulin), which subsequently enhances phagocytosis, and mediation of antibody-dependent cytotoxicity.[85] An Israeli study reported that human IgG2 was the major component in anti-*Shigella flexneri* subclass response, while the anti-*Shigella sonnei* response was dominated by IgG1. This study further determined that levels of IgG1 before exposure to organisms from either of the *Shigella* serogroups correlated with a lower risk of developing symptomatic infection.[103]

IgG1 is the major secreted immunoglobulin in the bovine lung,[63] lacrimal secretions, nasal secretions, vaginal secretions, and saliva.[34] Likewise, the main immunoglobulin class secreted into the bovine intestinal tract is IgG,[8,10,23] and additional research has shown IgG1 to be the predominant immunoglobulin subclass secreted into the bovine intestinal tract.[9]

Allowing functional immunoglobulins to be included in daily milk replacer meals by feeding colostrum to calves during the first 14 days of life reduced diarrheal disease in preweaned calves on calf ranches, and reduced the number of antimicrobial treatments.[6] The immunoglobulin source was 10 grams of supplemental IgG in the form of 70 grams of dried colostrum powder. It appears that some percentage of immunoglobulins fed through a milk replacer meal remain functionally reactive during passage through the abomasum and into the intestinal tract, retaining their antigen recognition properties. Research in humans demonstrated 19 ± 3% of ingested bovine colostrum IgG is recovered in feces and remains immunologically reactive.[105]

This concept has been further studied in non-human primates. Administration of a parenteral dose of rotavirus-specific IgG infused intravenously suppressed or delayed rotavirus infection in rotavirus challenged macaques.[128] This passive transfer of immunity from the bloodstream into the intestinal tract was previously documented in the bovine.[74] Cows were immunized at six and three weeks before calving by intramuscular injection of an autogenous rotavirus particle preparation.[74] Rotavirus neutralizing antibody titers in the immunized and non-immunized cows' colostra were 1:500,000 and 1:12,000, respectively. Another study reported that IgG1 appeared in the gastrointestinal tract of neonatal calves, and the IgG1 was derived predominantly from rotavirus immunoglobulins circulating within the calf's bloodstream.[9] The source of neutralizing immunoglobulins in this study was either bovine colostral whey administered as a subcutaneous injection at 24 hours of age, or natural colostrum derived from Holstein cows immunized with a commercially available rotavirus vaccine administered twice prior to calving. The colostrum was given as either a one quart (.95L) or a 3.5 quart (3.3L) dose at five hours of age. Intestinal immunoglobulin titers of IgG1 correlated well with serum levels of immunoglobulin transferred passively across the intestine at five hours of age or that supplied by the subcutaneous injection of colostral whey. Calves with high serum immunoglobulin concentrations, assessed as those calves with 30 mg/mL of plasma IgG,[74] were relatively resistant to diarrhea caused by rotavirus infection.[9,74] These studies, and several others, demonstrate protection against rotavirus infection is provided by the secretion of serum IgG1 rotavirus immunoglobulin into the intestinal lumen.[8,9,23,74,75,107]

One study was performed in calves to determine how much IgG are excreted in feces.[8] It was estimated that calves fed 100 grams of IgG would secrete one to four

grams of IgG back into the intestinal tract on a daily basis for the first two weeks of life. If the predominate IgG secreted into the intestinal tract is indeed IgG1, it could require 56 grams of IgG1 (14 days times four grams per day secreted) be removed from the bloodstream to meet the rate of secretion identified by the authors in this study. This amount correlates well with the determined plasma half-life of IgG1, which is 11.5 days.[110] Since IgG absorption from the intestine at or near birth is about 25 to 30% efficient, it would require a dose of four quarts of colostrum containing at least 83 grams of IgG per quart to provide enough absorbed IgG1 for this normal rate of intestinal secretion.[3] These data provide evidence immunoglobulins absorbed across the intestinal wall into the bloodstream of the neonatal calf are secreted into the intestinal tract and other organ systems. The demand for secretion is high during the first two weeks post-colostrum administration.[9,51,110]

With high demand for IgG1 secretion into the intestinal tract, the passive transfer of immunoglobulin into the bloodstream of the newborn calf from the intestinal tract during the first 12 hours of age should provide some quantity of IgG1. Since bovine plasma and serum is about 50% IgG1 and 50% IgG2, it would be difficult to supply the needed amount of IgG1 in a 100-gram dose of plasma or serum-derived IgG immunoglobulins. Including the IgG1 that is excreted and secreted into other systems, the amount secreted into the intestinal tract concurrently with other systems would utilize all the IgG1 supplied by a 100-gram dose of plasma or serum-derived IgG.

A comparative investigation measuring the efficiency of immunoglobulin absorption across the intestinal wall in neonatal calves determined that the efficiency of IgG absorption is greater for serum-derived IgG compared to colostral IgG.[3] Compared to two milk-derived colostrum supplements (about one-half the amount of IgG per dose, 50 and 60 grams of IgG versus 90 grams of IgG), the serum-derived immunoglobulins demonstrated a better efficiency of absorption. This study also determined that increasing the mass of IgG fed did not increase the efficiency of absorption. Increasing the mass of IgG offered actually decreased the efficiency of immunoglobulin absorption, indicating there is a point of diminishing efficiency when the amount of IgG offered is increased beyond a certain total gram level.[3,7] Although serum-derived immunoglobulins would have approximately equal amounts of IgG1 and IgG2, thereby providing a lower gram intake of IgG1 and a lower circulating level of IgG1 available for secretion into the digestive tract, no differences were detected in percent mortality across treatments when compared to two different milk-derived colostrum supplements and pooled colostrum.[3]

A second study confirmed IgG absorption was greater for serum-derived colostrum replacer (26% and 19%, depending on treatment) compared to maternal colostrum (14%).[101] In this study, IgG mass fed was much greater for maternal colostrum (429 grams IgG) compared to serum-derived colostrum replacer (100 grams IgG). No differences were noted in 60-day body weight gain or incidence of medical treatments. These researchers also determined addition of animal fat to serum-based colostrum replacer had no impact on IgG absorption, and a second feeding of 100 grams IgG of serum-derived colostrum replacer increased plasma IgG, but efficiency of absorption was reduced.[101]

A third study comparing 250 or 180 grams IgG fed as a serum-derived colostrum replacer or as pooled maternal colostrum to neonatal Holstein or Jersey calves, respectively, found no differences in IgG absorption or in any 29-day performance or health parameter, with the exception of feed conversion. Calves fed maternal colostrum used feed more efficiently compared to calves fed serum-derived colostrum replacer.[57]

Knowing the rate at which IgG1 is excreted in feces, and that calves do not manufacture endogenous IgG1 in appreciable quantity until about three to four weeks of age,[34,51,64] it is necessary that newborn calves consume some source of IgG1 prior to closure of intestinal absorption of whole immunoglobulins at 12-14 hours of age.[33,62] Since deprivation of passive transfer of immunity in a newborn calf results in a 74-fold greater risk of mortality during the first 21 days of life in heifer calves, provision of a source of immunoglobulins at or near birth is essential.[127]

Immunoglobulin Absorption

A well-recognized study conducted in Great Britain indicated that for adequate immunity to be passively transferred to the newborn calf, the IgG concentration in the blood should be at least 10 mg per mL of plasma or serum.[70] This number has remained a basic standard of the measure of adequate transfer of passive immunity in the neonatal calf, and various biochemical methods exist to adequately measure the amount of IgG absorbed into the bloodstream from the intestinal tract of the newborn calf.[71] The practitioner should also be reminded that poor management, such as allowing maternal colostrum or colostrum replacer to become adulterated,[91,92] will overcome apparent adequate passive transfer of immunity.

Calculating the amount of IgG that must be fed to the newborn calf to reach the recognized level of 10 mg/mL or 1,000 mg/dl or 10 grams/liter of serum or plasma is complicated by the efficiency of absorption, the age of the calf, and the source of the IgG.[3,7,68,118,119,120] If the plasma volume of a newborn calf is 6.5% of its birth weight,[69] a calf weighing 90 lb (40.8 kg) would have a plasma volume (approximately same as the serum volume) of 5.85 lb (2.65 kg). One gallon of blood weighs 8.5

lb or 3860 grams. Using those values, 5.85 lb of plasma or serum would equal 2650 grams. One milliliter of plasma or serum weighs approximately one gram. One thousand milliliters equals one liter, so a 90-lb calf has approximately 2.65 liters or quarts of plasma or serum. Knowing this number, to reach an accepted level of 10 mg/mL of plasma or serum, simply multiply by 1000 to reach the amount of 10 grams of IgG per liter or quart of plasma or serum. To simplify, 26 grams (2.6 quarts x 10 grams per quart = 26 grams) of IgG needs to be absorbed into the bloodstream from the intestinal tract to reach the accepted level of 10 mg/mL of plasma or serum.

Unfortunately, not all IgG consumed orally by the newborn calf is actually absorbed into the bloodstream. The efficiency of absorption has been reported to vary,[59,99] but an average of 25% absorption efficiency is practical for determining the amount of IgG needed to be fed at birth or very shortly following birth.[59,68] Accepting the 25% absorption as an average of immunoglobulin absorption efficiency for a colostrum replacer, a newborn 90-lb calf would require 104 grams of IgG to be fed orally in one feeding, preferably within two hours of birth. Accepting these values, it is possible to quickly calculate the total grams of IgG that must be fed to a newborn calf in order to achieve the recommended 10 mg/mL of IgG in the plasma or serum (Table 1).

There is considerable variation in birth weight of Holstein dairy calves. Although the 2007 National Animal Health Monitoring System (NAHMS) survey does not include actual birth weight data on newborn calves, it does provide estimates based on heart girth measures. Their survey of 751 Holstein heifer calves less than seven days of age reports 25th percentile 91 lb (41.3 kg), median 97 lb (43.9 kg), and 75th percentile 105 lb (47.6 kg).[81] Published California data collected from 204 Holstein heifer calves reported an average measured birth weight of 90.6 lb (41.1 kg), while 203 male calves averaged 97.4 lb (44.2 kg).[2] Researchers collected birth weights from 2003 to 2007 on research dairies in Kentucky, Virginia, and North Carolina, and determined the mean birth weight of 243 purebred Holstein calves. Calves from primiparous dams weighed 87.08 lb (39.5 kg) (minimum 60.05 lb (27.2 kg) and maximum 110.09 lb (49.9 kg)), and calves from multiparous dams weighed 94.22 lb (42.7 kg) (minimum 86.11 lb (39.1 kg) and maximum 139.13 lb (63.1 kg)).[83] The same researchers reported mean birth weight of 153 purebred Jersey calves: calves from primiparous Jersey dams weighed 51.63 lb (23.4 kg) (minimum 34.04 lb (15.4 kg) and maximum 64.07 lb (29.1 kg)), and calves from multiparous dams weighed 59.52 lb (26.9 kg) (minimum 38.03 lb (17.3 kg) and maximum 86.67 lb (39.3 kg)).[83] Birth weight of 360 Jersey-Holstein-cross calves was determined to be 69 lb (31.3 kg) from primiparous dams, and 77.12 lb (34.9 kg) from multiparous dams.[83]

Table 1. Corresponding grams of IgG necessary for pounds of body weight of newborn calf for potential passive transfer of immunity.

Body weight at birth (lb)	Grams of IgG needed to reach 10 mg/mL of IgG in the plasma or serum
50	60
60	71
70	87
80	95
90	104
100	118
110	130
120	142
130	154

Colostrum Administration Volume

The IgG levels in natural colostrum vary dramatically, and unless a method is utilized to accurately measure the IgG content, it is generally recommended that four quarts of colostrum, containing at least 50 grams IgG per quart, be administered to a newborn calf as soon as possible after birth.[41] Research has demonstrated that 31% of newborn Holstein heifer calves failed to consume two quarts of colostrum by suckling from a bottle.[124] While some of the calves would consume three quarts (43.75%), and calves that drink aggressively should be offered as much colostrum as they desire, this study confirmed that force-feeding colostrum to Holstein calves in two-quart quantities with an esophageal feeder is required to obtain the recommended two-quart intake.[124] As has been addressed previously, increasing the quantity of total grams of IgG actually decreases the efficiency of IgG absorption. It is necessary to understand that natural colostrum contains many factors besides immunoglobulins of the IgG class.[84] Growth factors, functional proteins, white blood cells, hormones, other classes of immunoglobulins besides the IgG class, and nutrient proteins, carbohydrates, and lipids are just a few of the factors provided to the newborn calf by maternal colostrum.[84]

Colostrum Provision and Future Dairy Heifer Performance

Significant research evaluations have been performed to measure the impact of proper colostrum provision to newborn heifer calves. The impact of plasma or serum immunoglobulin levels has also been defined.[10,32,82,104] Heifers receiving inadequate colostrum, as identified by low immunoglobulin levels in plasma or serum, grew slower, had increased morbidity, and

produced less milk during their first lactation. As expected, heifer calves with inadequate colostrum intake were not as capable of mounting an immune response against pathogens, but those heifers that had adequate colostrum could mount a sufficient immune response, and do so with less energy expenditure. A 1989 study identified a quantifiable relationship between immunoglobulin levels and milk production.[32] Heifer calves with lower immunoglobulin levels produced less milk, which was hypothesized to be a negative response to immune challenges.[32]

More recent research suggests the correlation between colostrum intake and milk production may not be as strong as previously thought, but did determine Brown Swiss heifer calves fed full four quarts of good quality colostrum (at least 50 grams IgG per quart) within one hour of birth produced 2,263 lb (1,029 kg) more milk by the end of their second lactation.[37] Obviously, to obtain the benefit to growth, development, immune status, and milk production, adequate amounts of good quality colostrum must be fed following birth, with the general recommendation to "feed the sooner the better".

Colostrum Handling

Freezing fresh colostrum properly, followed by proper thawing just prior to feeding, has no negative impact on IgG concentration or intestinal absorption.[53] Recent research demonstrated that colostrum pasteurized at 145°F (63°C) for 30 minutes, then poured into two-quart plastic freezer bags, frozen for 24 hours, thawed in water at 122 to 131°F (50 to 55°C) for 15 minutes, and fed three times to each calf during the first 22.1 hours of life could successfully provide passive transfer of immunity measured by the serum total protein level of 5.5 grams/dl of serum.[76] For this farm study, calves receiving slightly less pooled unpasteurized colostrum had fewer calves with total serum protein below 5.2 grams/dl of serum. Although pasteurizing colostrum is an acceptable practice to provide improved biosecurity and disease prevention against such contagious disease organisms as *Mycoplasma bovis*, it has been demonstrated that a significantly higher IgG concentration in the blood is obtained in calves fed unpasteurized colostrum. Calves fed unpasteurized colostrum achieved serum IgG levels of 19.1 mg/mL, while calves fed pasteurized colostrum achieved a serum IgG level of 9.7 mg/mL.[46] The researchers hypothesized this might have been due to prolonged exposure of IgG to heat, particularly when pasteurized in large batches. It is essential that pasteurization maintain the chemical and immunological integrity of immunoglobulins.

Three studies demonstrated that colostrum pasteurization must be accomplished utilizing proper temperatures, proper agitation, and proper length of time. If colostrum is pasteurized with care at 140°F (60°C), and with appropriate gentle agitation for one hour, there is no negative impact on immunoglobulin absorption, nor is there any negative impact on treatment expectations or growth parameters for calves administered the pasteurized colostrum.[35,56,73]

Pasteurization of pooled colostrum is an accepted management practice to control relatively easily inactivated pathogens, like *M. bovis*.[90,91] The ability for various colostrum pasteurization protocols to inactivate MAP, the acid-fast bacteria that causes Johne's disease, is debatable. *M. paratuberculosis* bacteria have a tough and thick cell wall structure that prevents a guaranteed kill of these microorganisms, although there is research that advocates pasteurizing waste milk to inactivate the organism.[112] MAP organisms were not found following heat treatment of raw colostrum at 140°F (60°C) for one hour, and the authors concluded that pasteurization at 140°F should be sufficient to eliminate MAP from colostrum in most situations.[47] To determine presence of MAP, researchers examined bacterial growth at four, eight, and 12 weeks using PCR analysis.

Staphylococcus aureus bacteria contained within the cellular structure of a leukocyte, or bovine leukemia virus (BLV) particles contained within the cellular structure of a lymphocyte, may also be difficult to inactivate in the colostrum pasteurization process if proper protocols are not rigorously followed.[125] These pathogens are protected by their intracellular location. A colostrum pasteurizer must agitate the colostrum as it is being pasteurized in order to prevent bacteria from being protected against the pasteurization process by becoming incorporated into a blood clot, a milk clot, a biofilm, or an unusually thick portion of the colostrum mix. Agitating the colostrum while pasteurizing allows even distribution and exposure to the heat of pasteurization. It is also important to understand that pasteurization is not sterilization. For these reasons, some producers have opted not to feed pooled colostrum to replacement dairy heifers. While it is acceptable to save colostrum from Johne's, *Mycoplasma bovis*, and BLV-free dams, Johne's disease in particular is not always diagnosable before shedding of MAP organisms occurs.[122] It is possible to have a negative blood test to Johne's, after which the cow begins to shed the organisms and then tests positive several months later.[29]

While it is accepted that a single exposure to MAP is insufficient to cause a dairy replacement heifer to develop Johne's disease, it is a prudent goal to prevent initial exposure to MAP bacteria at birth.[52] The only viable option to prevent possible exposure to pathogens that might be found in colostrum is to feed a pathogen-free colostrum replacer. Clinical trials utilizing 497 newborn Holstein heifer calves born on 12 Johne's-endemic midwestern dairy farms, comparing a

plasma-derived colostrum replacement product to raw bovine maternal colostrum, confirmed calves exclusively fed colostrum replacement product were less likely to become infected with MAP compared to those fed raw maternal colostrum.[89]

Commercial Colostrum Replacers

There are numerous manufacturers of colostrum replacers. As previously discussed, dried colostrum and whey-based colostrum replacers contain predominately IgG1. This is the primary fraction of the IgG class of immunoglobulins naturally supplied to a newborn calf by maternal colostrum. It is also the fraction of IgG that has high demand for secretion into the lung, saliva, tears, reproductive tract, and the intestinal tract. Since the natural demand is for IgG1, it should be supplied in any colostrum replacer. Perhaps the ideal colostrum replacer product would have a mixture of dried colostrum or whey and bovine plasma or serum. The colostrum or whey would supply a dense source of IgG1, while the bovine plasma or serum-based IgG would balance out the product with a blend of IgG1, IgG2, and any other functional proteins that survived the manufacturing processes.

As previously stated, plasma and serum-based colostrum replacers provide a near equal proportion of IgG1 and IgG2. Research demonstrates serum-based IgG products have an absorption efficiency advantage over milk-derived IgG, but it should be noted that in the study cited, the serum-based product provided 90 grams of IgG in two doses, while the two milk-derived products provided 50 and 60 grams of IgG in two doses.[3] All three products were identified as colostrum supplements, not colostrum replacers.[3] The efficiency of IgG absorption was not significantly different between the serum-derived immunoglobulins and one of the two milk-derived immunoglobulin sources or pooled maternal colostrum. This study, along with another study,[40] demonstrated two important findings related to the total dose of IgG, and the volume in which it was administered: 1) while more is better when providing a newborn calf with IgG, increasing the mass of IgG per dose does not equate to an increase in the efficiency of absorption,[119] and 2) absorption efficiency of IgG is improved by feeding the proper dose in one feeding as compared to two feedings at seven-hour intervals.[50] This concept had previously been demonstrated comparing the efficiency of IgG absorption from one quart of colostrum containing 100 grams of IgG per quart to two quarts of half-strength (50 grams IgG/quart) provided as two separate feedings.[117]

In regards to importance of IgG1 verses IgG2 to calf health, and the ongoing debate over whether a colostrum-based colostrum replacer is superior to a plasma or serum-based colostrum replacer, it is important to understand that orally supplementing spray-dried plasma or serum prophylactically in milk replacers, at concentrations that provide an estimated 2 to 4 grams of IgG daily (50:50 blend of IgG1 and IgG2), the same quantity of IgG proven to be secreted daily from the calf's bloodstream into the intestinal lumen,[8] is shown to improve gain[78,96] and reduce diarrhea,[55,93,98,100] mortality,[99,100] and morbidity.[98,100] These data, and other disease challenge trials, demonstrated improved calf health when supplementing much higher feeding rates of spray-dried serum to calves challenged with *Cryptosporidium parvum*[55] and corona virus,[5] indicating oral supplementation of a near equal blend of IgG1 and IgG2 is beneficial to calf health and growth.

Serum-based colostrum replacers have high apparent efficiency of IgG absorption (AEA)[50,57,99,101] and comparable[50,57] or superior[101] AEA to pooled maternal colostrum. However, in one published trial, bovine serum resulted in a reduction in AEA compared to pooled maternal colostrum.[94]

Bovine serum has also been extensively researched as a colostrum supplement, supplying approximately 50 grams of IgG per dose, again showing high apparent efficiency of IgG absorption in trials[3,4,31,50,94,97,101,109] and again, comparable[31,50,97,109] or superior[3,4,94,101] AEA to pooled maternal colostrum. Colostrum supplements are useful and cost-effective tools to standardize poor quality colostrum and improve likelihood that all calves receive adequate IgG mass to achieve passive immunity. Colostrum supplements are particularly useful when feeding colostrum of unknown immunoglobulin quality.

These data, and others examining spray-dried colostrum,[39,43,111] prove high apparent efficiency of immunoglobulin absorption of spray-dried functional proteins, and a rate of adequate passive immunity equivalent to maternal colostrum for both spray-dried bovine colostrum and bovine serum.

Because raw material collection and processing procedures can be variable and potentially deleterious to product quality, attention should be paid to assurances that commercial products – whether colostrum, whey, plasma or serum based – have sound data proving high apparent efficiency of IgG absorption. These authors contend the IgG1 content of a colostrum replacer may be immaterial for consideration of which colostrum replacer to choose for clients because research clearly shows both colostrum and serum-based colostrum replacers achieve desired goals of calf production.

Table 2 summarizes published colostrum replacer trials. Practitioners will note a sizable body of published work demonstrating high AEA of spray-dried bovine serum and colostrum used in colostrum replacers. Caution should be taken in comparing AEA results between trials as calculations used to determine AEA can vary between researchers. The authors of this paper believe

there is an adequate quantity of peer-reviewed research to confidently utilize properly handled and processed spray-dried colostrum and bovine serum to manage colostrum status of neonatal calves.

Colostrum Administration

When colostrum or colostrum replacer is administered utilizing an esophageal feeder, the esophageal groove does not close.[25] This means the colostrum or colostrum replacer will enter the reticulo-rumen compartment. A radiographic study demonstrated overflow into the abomasum occurred after about 0.8 pint (400 mL) was administered by esophageal tube feeding. It has been further demonstrated, utilizing radiographic studies, that the remainder of the administered dose volume does make its way into the abomasum, and that the reticulo-rumen contents will empty into the abomasum within three hours after feeding.[61]

Results from a recent study demonstrated if a larger volume (200 total grams of IgG in a three quart feeding) of colostrum replacer was fed, the method of administration, either natural suckling from a nipple bottle or esophageal tube feeding, produced no difference in passive transfer indices.[44] For calves fed a smaller volume of colostrum replacer (100 grams of IgG in 1.5 quarts), acceptable passive transfer rates and AEA were significantly greater for calves fed with a nipple bottle.[44] This study further evaluated the amount of IgG fed as a colostrum replacer compared to feeding four quarts of maternal colostrum. All calves fed 200 grams of IgG in a colostrum replacer powder, mixed into three quarts of approximately 100°F (37.8°C) water, achieved adequate passive transfer of immunity as measured at 24 hours of age, versus 54% of calves fed 100 grams of IgG as a colostrum replacer in 1.5 quarts. Calves fed four quarts of maternal colostrum achieved passive transfer of immunity in 91% of calves evaluated.[43,44] Colostrum was fed within two hours of birth via esophageal tube feeder in all instances.[43,44]

Care must be taken to hygienically administer colostrum replacers and supplements. Research on seven Central California dairies with 800 to 4,000 adult cows determined 40.29% of calves were fed contaminated (>100,000 cfu/mL) colostrum.[129] Three of the dairies utilized a colostrum supplement to standardize colostral immunoglobulin content. Standardization was important because 36.26% of calves suffered from failure of passive transfer (FPT), with a range by dairy from 9.59% to 76.81%.[130] These researchers found the colostrum supplement utilization process was grossly mishandled, particularly on one dairy, resulting in 57.37% of supplemented colostrum becoming contaminated compared to 17.5% of unsupplemented raw colostrum fed to neonatal calves.[129] Using a colostrum replacer not only eliminates maternal colostrum, but also the additional risk of further contamination of colostrum when necessary standardization with a colostrum supplement occurs.

Variables in Passive Transfer of Immunity

Adequate passive transfer of immunity in calves provided a colostrum-derived colostrum replacer is dependent upon total content of antibody provided, volume administered, and method of administration.[43,44] Through studies conducted on maternal colostrum, it has been determined that if milk-clotting proteins are present in a colostrum replacer, or the colostrum replacer is derived from dried or freeze-dried colostrum or a colostrum replacer in which some form of dried milk or milk protein concentrate has been added in the manufacturing process, abomasal clotting of milk-clotting proteins is necessary to maximize immunoglobulin absorption.[30] If the colostrum replacer is manufactured from whey, blood plasma or serum, or the milk-clotting proteins have been removed, clotting does not occur, and is immaterial to immunoglobulin absorption. Abomasal clotting, or milk curd formation, is also immaterial for calf milk replacers manufactured utilizing whey (clotting proteins are retained in the cheese curd formation), compared to calf milk replacers manufactured from ingredients where milk-clotting proteins are present.[22,49,102] If the milk-clotting proteins are present in a calf milk replacer or a bovine colostrum-derived colostrum replacer fed to a neonatal calf, milk protein clotting is essential for proper nutrient digestion and absorption.[102]

Casein is a general term utilized to identify caseinate proteins in milk, the clotting or curd forming proteins contained in milk or colostrum. If too much added casein protein is present, it may be deleterious to immunoglobulin absorption. Research examining the addition of 200 and 400 grams of either casein or whey protein concentrate to bovine serum-based colostrum supplement did not enhance or adversely affect immunoglobulin absorption, compared to pooled maternal colostrum or otherwise equivalent bovine serum-based colostrum supplement fed without additional milk proteins. The exception was when 400 grams of casein was included, which resulted in significant reduction in immunoglobulin absorption.[31]

Trypsin is a pancreatic enzyme which acts on peptide linkages to begin protein digestion in the small intestine. Maternal colostrum derived from species that provide their offspring passive immunity from the ingestion of colostrum has measurable trypsin inhibitor activity provided by its glycoprotein trypsin inhibitor content.[24,88] The amount or capacity of trypsin inhibitor contained in bovine colostrum has been quantified.[108] Trypsin inhibitor activity was measured to be identical in cow and mare colostrum, quantified as 0.5 mL of serum

Table 2. Summary: Colostrum replacer apparent efficiency of IgG absorption (AEA) research. Full reference citations found in Reference section in this paper.

Journal article	IgG source	N	IgG (g)	Admin. post-calving	AEA (1)
Morrill[79]	Dried bovine colostrum (BC)	10	132 + 66	132g 45 min; 66g 6 hrs	26.8% (2)
	BC + 19.5 g sodium bicarb	10	132 + 66	132g 45 min; 66g 6 hrs	29.6% (2)
	Dried bovine colostrum (BC)	10	132 + 66	132g 45 min; 66g 6 hrs	25.5% (2)
	BC + 19.5 g sodium bicarb	10	132 + 66	132g 45 min; 66g 6 hrs	32.9% (2)
Shea[111]	Dried bovine colostrum (BC)	6	105	within 90 min	41.3% (3)
	BC + 0.5 g/d lactoferrin	6	105	within 90 min	37.9% (3)
	BC + 1.0 g/d lactoferrin	6	105	within 90 min	32.1% (3)
	BC + 2 g/d lactoferrin	6	105	within 90 min	36.3% (3)
	Dried bovine colostrum (BC)	6	210	within 90 min	31.0% (3)
	BC + 0.5 g/d lactoferrin	6	210	within 90 min	24.5% (3)
	BC + 1.0 g/d lactoferrin	6	210	within 90 min	26.4% (3)
	BC + 2 g/d lactoferrin	6	210	within 90 min	26.7% (3)
Godden[43]	Maternal colostrum	22	271.2	<2 hours	31.87%[a]
	Dried bovine colostrum	24	100	<2 hours	35.5%[a]
	Dried bovine colostrum	23	200	<2 hours	36.5%[a]
Campbell[19]	Bovine serum replacer (BSR)	11	130	1 hour	34.3% (4)
	BSR 3 - 5 kGy irradiation	11	130	1 hour	31.5% (4)
	BSR 15 - 20 kGy irradiation	11	130	1 hour	25.8% (4)
	BSR 3 - 5 kGy irradiation	11	160	1 hour	29.8% (4)
	BSR 3 - 5 kGy irradiation	12	190	1 hour	26.6% (4)
Hammer[50]	Pooled maternal colostrum	7	282	1 & 8 hrs (50:50)	29% (6)
	Serum replacer + GF (5)	7	150	1 hrs (50:50)	30% (6)
	Bovine serum replacer only	7	150	1 hrs (50:50)	35% (6)
	B. serum supplement + GF	7	150	1 & 8 hrs (50:50)	24% (6)
	Bovine serum supplement only	7	150	1 & 8 hrs (50:50)	30% (6)
Santoro[109]	Pooled maternal colostrum	12	approximately 100	within 90 min.	21%[a]
	Pooled MC + trypson inh.	12	approximately 100	within 90 min.	21.4%[a]
	Bovine serum supplement	12	45.4	within 90 min.	22.7%[a]
	B. serum supp. + tryp. inhibitor	12	45.4	within 90 min.	19.6%[a]
Jones[57]	Pooled Maternal colostrum	39	250 Holstein, 180 Jersey	1.5 h & 13.5 h (50:50)	19.2% (7)
	Bovine serum replacer	39	250 Holstein, 180 Jersey	1.5 h & 13.5 h (50:50)	20.3% (7)
Quigley[99]	Bovine serum replacer	16	187	1 & 8 hrs (50:50)	30%[a]
	Bovine serum supplement	16	95	1 & 8 hrs (50:50)	33%[a]
Quigley[101]	Pooled maternal colostrum	15	429	ASAP & 8 hrs (50:50)	14% (9)
	Bovine serum replacer A	14	100	ASAP (8) after birth	26% (9)
	Bovine serum replacer B	14	100	ASAP after birth	19% (9)
	Bovine serum supplement	14	100	ASAP & 8 hrs (50:50)	25% (9)
Quigley[97]	Pooled maternal colostrum	12	156	ASAP & 12 hrs (50:50)	20%[a]
	Bovine serum supplement	48	90	ASAP & 12 hrs (50:50)	20%[a]
Arthington[4]	Pooled maternal colostrum (MC)	12	95.8	<4 hours	25%[a]
	MC + B. serum (47% of IgG)	12	95.2	<4 hours	37%[b]
	MC + B. serum (70% of IgG)	12	98.8	<4 hours	38%[b]
Arthington[3]	Pooled maternal colostrum	10	200	<2 & 12 hours (50:50)	22%[a,b] (10)
	Milk derived supplement 1	10	50	<2 & 12 hours (50:50)	16%[b] (10)
	Milk derived supplement 2	10	60	<2 & 12 hours (50:50)	24%[a,c] (10)
	Bovine serum supplement	10	90	<2 & 12 hours (50:50)	28%[c] (10)

(Table 2 continued)

Journal article	IgG source	N	IgG (g)	Admin. post-calving	AEA (1)
Davenport[31]	Pooled maternal colostrum	8	90	1.5 hour	31% (11)
	Bovine serum supplement	8	69	1.5 hour	30% (11)
	B. serum suppl. + 200g casein	8	69	1.5 hour	29% (11)
	B. serum suppl. + 400g casein	8	69	1.5 hour	19% (11)
	B. serum suppl. + 200g WPC	8	74.5	1.5 hour	34% (11)
	B serum suppl. + 400g WPC	8	80.5	1.5 hour	32% (11)
Quigley[94]	Pooled maternal colostrum	7	149.6	1.5 & 13.5 hrs (50:50)	25%[a]
	Bovine serum replacer	7	150	1.5 & 13.5 hrs (50:50)	15%[b]
Quigley[94]	Pooled maternal colostrum	3	53.2		24%[a]
	Bovine serum supplement	3	53.2		38%[b]

[a,b,c] Values within row are significantly different ($P<0.05$). Lack of subscripts does not necessarily mean absence of statistical significance, rather infeasibility to demonstrate differences within table confines.

1.) AEA = apparent efficiency of absorption of IgG

2.) Groups 1 and 2 dams fed diet w/o anionic salts (dietary cation-anion difference of +77mEq/kg). Groups 3 and 4 dams fed diet with anionic salts (dietary cation-anion difference -100 mEq/kg) three weeks prior parturition. Sodium bicarbonate increased absorption of IgG $P<0.04$. Anionic salt + bicarb $P<0.08$

3.) AEA reduced with 210 g vs 105 g $P<0.0001$. Linear effect of lactoferrin $P<0.12$. Quadratic effect of lactoferrin $P<0.03$

4.) Linear effect of irradiation dose w/130 g of IgG $P<0.0015$; linear effect of IgG mass with a low dose of irradiation $P<0.0562$

5.) GF = spray-dried IGF-I and TGF beta growth factors added

6.) Contrasts: MC vs CR NS; supplements vs replacers $P<0.02$; 5% GF vs 0% GF $P<0.03$; supplement GF vs replacer GF $P<0.07$

7.) Average between measures of two groups. 2 X 2 study also examining plasma in milk replacer

8.) ASAP = reported in paper as "as soon as possible after birth"

9.) Contrasts: MC vs all supplements or replacers $P<0.01$; supplement vs ((CR A + CR B)/2) NS; CR A vs CR B $P<0.01$

10.) AEA percent estimated from bar graph (Figure 1, *J Dairy Sci* 83:1465, 2000.)

11.) Contrasts: MC vs all supplements NS; supplement vs supplement + 200 or 400 casein NS; supplement vs WPC 200 or 400 NS; Supplement + 200 casein vs supplement + 400 casein $P<0.03$; supplement + 200 WPC vs supplement + 400 WPC NS

required to inactivate 1 mg trypsin. Known amounts of trypsin were incubated with known volumes of colostrum for a recognized time. The remaining trypsin was then analyzed within the incubated sample by adding known volumes of bovine serum with trypsin inactivating properties. Trypsin inhibitor levels in bovine mammary gland secretions were reduced 100 times by one week into lactation.[108] Although this is an older study utilizing rather crude analytical methods in comparison to current biochemical analytical methodology, species that provide passive transfer of immunity to their offspring by colostrum consumption were proven to have measurable and quantifiable levels of trypsin inhibitor in their colostrum, collected immediately following parturition. The action of trypsin inhibitor activity in bovine colostrum is to prevent the digestion of immunoglobulins prior to their absorption into epithelial cells of the small intestine by the process of pinocytosis.[13]

There is conflicting data in the literature concerning the impact of adding a measured amount of trypsin inhibitor to maternal colostrum or a serum-derived colostrum replacer. In a 1994 study, the addition of one gram of trypsin inhibitor per quart of maternal colostrum administered to Jersey calves increased serum immunoglobulin and serum total protein, regardless of the age of first feeding, 0, 12, 24, and 48 hours. Concentrations of serum IgG and IgM were increased 16 and 30%, respectively, when trypsin inhibitor was fed.[95] Conversely, a study performed in 2004 found no advantage to adding trypsin inhibitor. One gram of trypsin inhibitor was added at the initial two feedings of either maternal colostrum or a serum-derived colostrum replacer. Trypsin inhibitor did not affect serum IgG concentration or absorption of IgG. Particularly, it was determined that adding trypsin inhibitor to a serum-derived colostrum replacer did not enhance serum IgG concentrations in neonatal calves.[109]

In another study evaluating additives for a colostrum replacer and a colostrum supplement, the addition of plasma fractions containing elevated concentrations of IGF-1 (insulin-like growth factor – 1) and TGF-β (transforming growth factor – β), both functional proteins, actually decreased IgG absorption of blood-derived immunoglobulins in the neonatal calf.[50]

Researchers have also examined the effect of pH of bovine serum-derived colostral supplements between

5.0 and 7.5, and determined no marked influence of pH on the efficiency of immunoglobulin absorption.[97] These same researchers examined the utilization of polyethylene glycol to manufacture a bovine serum that is much denser in immunoglobulin content.[101] This chemical manufacturing process was considered as a method for purifying immunoglobulins in various functional protein-containing products, but unfortunately it was proven to reduce AEA of immunoglobulins in calves.[101]

Researchers also examined supplementing lactoferrin to spray-dried bovine colostrum-based colostrum replacer.[111] Lactoferrin is an iron binding glycoprotein present at much higher concentrations in colostrum (2 to 100X) than in milk.[111] These researchers postulated lactoferrin might inhibit bacterial growth, increase intestinal cell growth, and stimulate glucose absorption. One or two doses of colostrum replacer (105 or 210 grams IgG) was supplemented with either 0, 0.5, 1.0, or 2.0 grams/day of lactoferrin, resulting in a negative quadratic effect on AEA of IgG from spray-dried colostrum.[111]

Timing of Colostrum Administration

With the first consumption of colostrum, absorption efficiency begins to diminish from that point, until at 12 hours when efficiency is poor. By 24 hours, the efficiency of immunoglobulin absorption is reduced even further.[118,120] Prepartum stressors on the dam, particularly high environmental temperatures, can negatively impact absorption efficiency of immunoglobulins from colostrum. Early researchers determined that calves born from Holstein cows housed under cooled shades (78.8 - 96.8°F or 26 - 36°C) had significantly greater IgG absorption compared to calves born from cows housed under shades not cooled (95 - 113°F or 35 - 45°C).[116] Couple this knowledge with the impact of IgG mass and volume administered, and it becomes important to provide the newborn calf with the proper grams of IgG based on birth body weight. This proper dose, particularly if utilizing a colostrum replacer, should be fed as soon after birth as possible in a single two-quart feeding.[118,119,120] Review suggests producers should offer another feeding of IgG about five to seven hours after the first feeding,[117] although there is published data to support the use of one dose of 150 grams bovine serum-derived IgG fed in one dose, which provided better absorption efficiency of IgG when compared to administering 150 grams of bovine serum-derived IgG in two doses seven hours apart.[50]

These data should compel the bovine veterinary practitioner to advise clients to provide the proper grams of IgG for the body weight of the neonatal calf in one feeding by natural suckling, if possible. Additional feedings can be provided, but sufficient time should elapse. Research supports waiting at least seven hours before the second feeding is administered.[50,118]

Serum Total Protein

Serum total protein analysis is an accepted method to measure adequate colostrum provision and absorption. Measurement of blood levels of protein, and specifically IgG, is a good tool to assess the amount of colostrum fed and the efficiency of its absorption.[57] The correlation of serum total protein to the amount of immunoglobulin absorbed is high.[57] When utilizing colostrum replacers alone that contain concentrated IgG fractions, serum total protein measurement may not correlate accurately to the amount of immunoglobulin absorbed. Colostrum contains many proteins besides IgG, which are all included in total serum protein. An IgG quantitative analysis should be performed to assess the amount of immunoglobulin absorbed from the intestinal tract when a colostrum replacer is utilized independent of maternal colostrum.[94]

To measure absorption of IgG from a colostrum replacer, it is necessary to measure the serum level of IgG. One study has evaluated survival and health of calves fed only a colostrum replacer derived from bovine plasma.[57] This study demonstrated that the rate of FPT of immunity did not differ between groups fed natural colostrum or colostrum replacer. No difference was found in mortality or treatment intervention between the two groups. Serum IgG levels in the colostrum replacer treated group were determined by specific IgG testing, not by serum total protein levels.

Colostrum Replacer Manufacturing

It is generally accepted that the process used to manufacture colostrum replacers, whether derived from colostrum, whey, bovine plasma or serum sources, reduces the potential pathogen load to near zero. Pasteurization prior to spray drying and irradiation procedures are generally considered sufficient to inactivate pathogenic agents. Polymerase chain reaction (PCR) diagnostic tests identify the DNA or RNA of a virus particle, or the DNA of a bacterial contaminate in dried colostrum. Research data demonstrate that pasteurization temperatures, and times utilized to pasteurize fresh or frozen colostrum prior to spray drying, inactivates BLV.[106] Unfortunately, for these same manufacturing processes, there is no available research suggesting bovine virus diarrhea virus is inactivated when colostrum is pasteurized at 140°F (60°C) for one hour. However, pasteurization and spray drying does inactivate lymphocytes, other white blood cells, and may have some detrimental effect on heat sensitive proteins, chemical messengers, and growth factors found in fresh or frozen maternal colostrum. Serum proteins processed using spray drying procedures, and orally supplemented to calves exposed to and exhibiting signs of cryptosporidial enteritis, re-

sulted in less intestinal damage and improved intestinal morphology. These researchers hypothesize that because serum contains specific growth factors and stimulates cultured intestinal cell proliferation and migration, supplementing serum results in improved intestinal repair function when calves are exposed to *Cryptosporidium parvum*.[55] Spray drying and processing did not appear to negatively impact the functional response of these bovine serum-derived growth factors.[55]

Some manufacturers of colostrum replacer use irradiation to further assure product suitability for the neonatal calf. However, care should be taken to assure colostrum replacer is not subjected to excessive levels of irradiation. A recent study examined the effects on absorption of IgG and incidence of FPT of 3 - 5 kGy (3,000 - 5,000 Gray units of energy) or 15 - 20 kGy irradiation energy exposure to bovine serum-based colostrum replacer.[19] Although the study showed a linear negative effect of increasing irradiation dose on absorption of 130 grams of IgG in colostrum replacer, the lower level of irradiation provided an identical 80.8% rate of successful passive transfer in calves receiving an otherwise identical non-irradiated colostrum replacer dose. It is important to note that 130 grams of IgG irradiated with higher 15 - 20 kGy, rates that are more likely to result in sterilization, resulted in a FPT rate of 54.6%. This higher rate of irradiation significantly reduced IgG absorption from 31.5% in the group administered colostrum replacer exposed to 3 - 5 kGy irradiation, to 25% in the group administered colostrum replacer exposed to 15 - 20 kGy irradiation.[19]

Colostrum replacer manufacturers should utilize protocols or Hazard Analysis and Critical Control Points plans to guarantee the end-user a colostrum replacer product is not exposing calves to viable pathogens.[125] Inactivation of MAP organisms through pasteurization is complex,[27,66,86,87] with published data indicating a high temperature is required to inactivate the tough MAP bacteria. Colostrum replacer manufacturers should perform real time PCR testing on products offered for use in neonatal calves to ensure replacer is not contaminated with MAP. Since DNA is chemically and thermally stable at temperatures above the recommended temperature of pasteurization of colostrum, 140°F or 60°C, colostrum replacer suppliers must insure a positive PCR test for MAP does not equate to the presence of viable MAP bacteria. Suppliers of liquid colostrum for dried colostrum manufacturers must implement protocols for routine vaccinations, disease control, and proper colostrum handling post-calving.[125]

Use of a quality colostrum replacer should be encouraged for dairy or beef herds if raw colostrum is suspected of being a biosecurity threat. For those interested in utilizing a colostrum replacer to manage a disease and biosecurity control program for dairy replacement heifers, a number of commercial products are derived from dried colostrum or whey providing 100 grams of IgG or more, with the proper proportions of IgG1 found in natural maternal colostrum. These products are generally produced from pasteurized and spray-dried dairy cow colostrum. Considering an immunoglobulin absorption efficiency of 25%, 100 grams of immunoglobulin is sufficient colostrum replacement for calves weighing up to 85 to 90 lb (39 to 41 kg). More IgG is necessary to provide adequate colostrum replacement for calves with a birth weight exceeding 90 lb. Research has demonstrated the efficiency of absorption of IgG is different among commercially available colostrum replacers.[39]

Several reports support use of spray-dried colostrum[43] and bovine serum-derived[50,57,99,101] colostrum replacers. Veterinary practitioners should request absorption data from the commercial supplier of any colostrum replacer, regardless of IgG source, to ensure the product has proven AEA. Post-administration performance data would enhance the decision-making processes for the bovine practitioner recommending a specific colostrum replacer to his or her clients.

Colostrum or Colostrum Replacer

In a 2007 study, 12 commercial Holstein dairy farms were enrolled in a colostrum feeding study using either maternal colostrum or 125 grams immunoglobulin provided from a plasma-derived colostrum replacer. Products were administered either by esophageal tube feeder or nipple suckling. Of 457 newborn heifer calves in the study, 28% of calves administered maternal colostrum failed to achieve adequate passive transfer of immunity, and 93.1% of the calves administered the plasma-derived colostrum replacer failed to achieve adequate passive transfer of immunity. The expectation to have 100% of calves properly managed for colostrum provision, either by providing maternal colostrum or a colostrum replacer to achieve adequate passive transfer of immunity, is unrealistic.[123] However, providing some source of colostrum or colostrum replacer is realistic, and calves not provided colostrum are at a significant disadvantage for survival, cost of production, and future milk production expectation.

In the above study, the proportion of calves treated for illness was not statistically different for calves fed either maternal colostrum or the plasma-derived colostrum replacer. Total number of days treated and death loss between the groups was also similar.[123] The death loss for heifers administered maternal colostrum in this study was 10.0%, while that for the heifers administered the plasma-derived colostrum replacer was 12.4%, very close to the National Dairy Heifer Evaluation Project national average.[80] This project also reported over 40% of dairy heifer calves failed to achieve adequate transfer of passive immunity, as measured by serum IgG levels

of 10 mg/mL or above between one and two days of age. There is room for much improvement in colostrum provision management on dairy production facilities in the United States. The authors of this review are hopeful this information will provide bovine veterinarians with in-depth information necessary to assist dairy clients in making that improvement.

Conclusions

This review illustrates that immunoglobulin absorption for the neonatal calf has many variables. In a disease control program designed to protect against *Mycoplasma bovis*, MAP exposure, and BLV, utilization of a good quality colostrum replacer is a viable option to feeding maternal colostrum that might be contaminated with potential pathogens. Bovine serum-derived colostrum replacers can serve as an alternative to feeding maternal colostrum, and serum-based colostrum replacer can provide passive transfer of immunity to neonatal calves. Likewise, a colostrum replacer manufactured from dried bovine colostrum has been confirmed to provide passive transfer of immunity to neonatal calves. Considering the intricate protocols necessary to properly and consistently manage colostrum in a commercial setting, colostrum replacers hold much promise for not only reducing disease transmission associated with feeding raw or improperly pasteurized colostrum, but also for feeding a more consistent mass of colostral proteins to newborn calves on a timely basis.

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