Review

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Passive Transfer of Colostral Immunoglobulins in Calves

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Passive transfer of colostral immunoglobulins has long been accepted as imperative to optimal calf health. Many factors, including timing of colostrum ingestion, the method and volume of colostrum administration, the immunoglobulin concentration of the colostrum ingested, and the age of the dam have been implicated in affecting the optimization of absorption. The practice of colostrum pooling, the breed and presence of the dam, and the presence of respiratory acidosis in the calf also may affect passive transfer. Various tests have been reported to accurately measure passive transfer status in neonatal calves. The radial immunodiffusion and the enzyme-linked immunosorbent assay (ELISA) are the only tests that directly measure serum IgG concentration. All other available tests including serum total solids by refractometry, sodium sulfite turbidity test, zinc sulfate turbidity test, serum γ-glutamyl transferase activity, and whole blood glutaraldehyde gelation estimate serum IgG concentration based on concentration of total globulins or other proteins whose passive transfer is statistically associated with that of IgG. This paper presents a comprehensive review of the literature of passive transfer in calves including factors that affect passive transfer status, testing modalities, effects of failure of passive transfer on baseline mortality, consequences of failure of passive transfer, and some treatment options. Many previously accepted truisms regarding passive transfer in calves should be rejected based on the results of recent research.

Key words: Cattle; Management; Mortality; Neonate; Testing.

The transfer of immunoglobulins from the dam to the neonate, termed passive transfer, is important in the protection of neonates from infectious disease. Failure of passive transfer (FPT) is not a disease, but a condition that predisposes the neonate to the development of disease. Currently, as many as 35% of dairy calves are estimated to suffer from FPT.[1,2] Although less frequent in other animal industries, FPT is observed in beef calves, lambs, and neonatal swine.[3–5] This makes FPT a major economic consideration for livestock producers.

In domestic large animals, the placenta prevents transmission of immunoglobulins from the dam to the fetus in utero. The syndesmochorial placenta of the cow forms a syncytium between the maternal endometrium and the fetal trophectoderm, separating the maternal and fetal blood supplies and preventing the transmission of immunoglobulins in utero.[6] Consequently, calves are born agammaglobulinemic, rendering ingestion and absorption of adequate amounts of colostral immunoglobulins essential for establishing passive immunity.

The primary immunoglobulin in bovine colostrum is IgG1, which is derived from maternal serum IgG1.[7–11] Transport of immunoglobulins from the serum to the mammary gland begins several weeks before parturition and reaches a peak 1–3 days before parturition in the cow.[7,12] Concentration of IgG1 in colostrum is facilitated by receptors on the mammary alveolar epithelial cells.[8] Glandular epithelial cells cease expressing this receptor at the beginning of lactation.[13] Altered expression most likely occurs in response to rising prolactin concentration.[13]

In addition to immunoglobulins, immunologically active cells and soluble mediators such as lactoferrin are transferred from the dam to the neonate through the colostrum.[14] Lakritz et al[15] demonstrated that some measurements of neutrophil function are decreased in calves that failed to absorb colostral lactoferrin, suggesting that soluble mediators absorbed from colostrum enhance the immunologic capabilities of the neonate.

Leukocytes in mammary secretions are immunologically active and may gain access to the fetal circulation.[16–18] This finding is supported by results of a study in which bovine colostral lymphocytes were fed to colostrum-deprived rabbits.[19] Sheldrake and Husband[20] demonstrated the presence of radiolabeled maternal lymphocytes in the lymph and mesenteric lymph nodes of lambs after these cells were infused into the neonatal duodenum. The overall contribution of soluble factors and cellular transfer in the neonatal immune response remains to be completely elucidated.

Factors Influencing Immunoglobulin Transfer

Factors that often are cited as having an effect on passive transfer in the calf are the timing of colostrum ingestion, the method and volume of colostrum administration, the immunoglobulin concentration of the colostrum ingested, and the age of the dam. The practice of colostrum pooling, the breed and presence of the dam, and the presence of respiratory acidosis in the calf also may affect passive transfer.

Timing of Ingestion

The neonatal enterocyte has the unique ability to absorb protein macromolecules. During the first 24–36 hours of life the enterocytes of the small intestine will nonselectively absorb a variety of macromolecules, including immunoglobulins, by pinocytosis.[21] Immunoglobulins are transported across the cell and into the lymphatics by exocytosis.[22] The immunoglobulins then gain access to the circulatory

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system through the thoracic duct. The nonselectivity of this process is substantiated by the fact that other protein macromolecule concentrations and enzyme activities such as γ-glutamyltransferase (GGT) are increased in neonates after the ingestion of colostrum.[22,23]

The cessation of macromolecule absorption is termed closure, and occurs at different times depending on the species. The exact mechanism behind closure has yet to be elucidated, but it probably reflects a combination of exhaustion of pinocytotic capability and enterocyte replacement by a more mature population of gut epithelial cells.[24,25] In calves, closure occurs at approximately 24 hours postpartum.[1] If feeding is delayed, closure may be extended to 36 hours.[1] In piglets and lambs, various feeding or dietary regimens can influence time to closure.[26] The same does not seem to be true in calves.[27,28] Peak serum immunoglobulin concentration is not seen until 32 hours postpartum because of ongoing transport of immunoglobulins across the enterocytes.[1] Despite the length of time to gut closure, immunoglobulin transfer across the gut epithelium is optimal in the first 4 hours postpartum and begins to decline rapidly after 12 hours postpartum.[29–31] Calves fed earlier will have significantly higher serum IgG concentrations than those fed later when similar concentrations and volumes of colostrum are fed.[32]

Method and Volume of Colostrum Feeding

The act of suckling will close the esophageal groove.[33] Based on this observation, the hypothesis that suckled colostrum would have enhanced absorption has been put forth.[34] Comparison of nipple bottle and esophageal tube administration of equal volume and IgG mass of colostrum demonstrated that calves allowed to suck a nipple bottle had slightly higher average serum IgG concentrations.[34] However, this difference was neither statistically nor clinically significant.

Far more important than the method of colostrum administration are colostral immunoglobulin concentration and the volume of colostrum ingested by the calf. High rates of FPT have been associated with dairy calves that are left with the dam and allowed to suckle naturally.[2,34,35] This issue was illustrated by Besser et al[35] when they observed FPT rates of 61, 19, and 10% in dairy calves that received colostrum via suckling the dam, suckling a nipple bottle, and esophageal tube administration, respectively. Clearly, esophageal tube feeding dairy calves can insure a lower rate of FPT. Dairy calves allowed to nurse to satiety will not ingest an adequate volume of the relatively dilute dairy cow colostrum to meet their immunoglobulin requirements.[36,37] The rate of FPT was dramatically decreased in calves that received greater than 100 g of colostral IgG.[35] In the same study, the investigators noted that only 36% of colostrum samples would have provided an adequate IgG mass (>100 g IgG) to the calf if 2 L of colostrum was fed. However, greater than 85% of the colostrum samples would have provided an adequate mass if 4 L was fed. Clearly, dairy calves are unable to achieve adequate passive transfer without dramatic intervention.

Colostrum Quality

Differentiating high-immunoglobulin-concentration colostrum from low-immunoglobulin-concentration colostrum is problematic. Fleenor and Stott[38] advocated the use of the hydrometer for this purpose. They demonstrated that colostral specific gravity was associated with colostral total solids (r^2 = .763), colostral total protein (r^2 = .900), and colostral immunoglobulin concentration (r^2 = .699). The strength of the association between colostral specific gravity and colostral immunoglobulin concentrations found by subsequent researchers (r^2 = .469) has been poorer than original reports, suggesting that the hydrometer probably is inadequate for routine screening of colostrum.[39] Using recognized test endpoints, specific gravity >1.050 and colostrum IgG concentrations >50 g/L, the sensitivity of the hydrometer in the detection of low-immunoglobulin colostrum is only 0.32.[39] This procedure would classify 2 of every 3 low-quality colostrum samples as acceptable. Test sensitivity can be improved by raising the endpoint specific gravity above 1.050. However, test specificity is severely compromised causing an excessive proportion of colostrum samples to be classified as immunoglobulin deficient and inordinately limiting the volume of colostrum available to feed calves. As shown by Fleenor and Stott,[38] components other than colostral immunoglobulin concentration contribute to colostral specific gravity. The core problem with the use of the hydrometer is that low- and high-immunoglobulin-concentration colostrum samples have specific gravity distributions that overlap. Additionally, hydrometers are plagued by temperature-based variation, which may contribute to colostrum misclassification.[40,41]

An alternative tool for the selection of high-quality colostrum is the weight of the 1st-milking colostrum. In a study of 919 Holstein dairy cows, Pritchett et al[42] observed that colostrum derived from cows producing less than 8.5 kg of milking colostrum had a significantly higher colostral IgG1 concentration (P = .0001). This difference was present in cows of all ages, but was most pronounced in 2nd-lactation cows. That study demonstrated that discarding 1st-milking colostrum samples that weighed >8.5 kg would substantially increase the percentage of high-immunoglobulin colostrum samples. This practice would insure an adequate IgG1 concentration to provide adequate passive transfer in most calves fed 3 L of colostrum in a timely manner.[42]

Parity

A common recommendation is to discard the colostrum from 1st-lactation cows.[43] Although these recommendations initially were formed to insure that high-quality colostrum was provided to the calves, recent work has demonstrated that this practice may be counterproductive. Muller and Ellinger[44] demonstrated the lack of a statistical difference in colostral immunoglobulin concentrations based on parity. In that study, no difference was found in colostral immunoglobulin concentrations in cows in their 1st, 2nd, and 4th lactation or greater (59.1 g/L, 62.6 g/L, and 74.9 g/L, respectively). However, cows in their 3rd lactation did have significantly higher immunoglobulin concentrations (81.5 g/L). Another study examined the immunoglobulin concen-

tration of 1st-milking colostrum samples in 919 Holstein cows.[42] Cows in their 1st lactation produced colostrum with a mean IgG1 concentration equal to that of 2nd-lactation cows.[42] Cows in their 3rd or greater lactation produced colostrum with the highest IgG1 concentration. The IgG concentration of colostrum from cows in the 3rd lactation was significantly higher than that of cows in their 2nd lactation, but not from those in the 1st lactation. Tyler et al[45] confirmed that no significant difference existed between colostral IgG concentrations and lactation number in the 1st and 2nd lactations. However, cows in their 3rd or greater lactation did have significantly higher immunoglobulin concentrations.

Based on these reports, we strongly discourage discarding colostrum from 1st-lactation cows. If discriminations are to be made using lactation number, only the colostrum from cows of 3rd lactation or greater should be used. This recommendation is unlikely to prove workable or useful. Discarding colostrum from 1st- and 2nd-lactation cows would mean that roughly 30% of the cows in their 3rd or greater lactation must produce colostrum for 100% of the calves. Furthermore, the magnitude of the anticipated colostral IgG concentration change from the 1st to the 3rd lactation is relatively small and other factors probably are more important.

Pooling

The logic behind pooling colostrum was that this process would minimize the influence of low-immunoglobulin colostrum samples. Unfortunately, this is not the case because cows that produce larger colostrum volumes tend to have lower immunoglobulin concentrations. For example, cow A produces 15 kg of colostrum containing 20 g/L of IgG and cow B produces 5 kg of colostrum containing 40 g/L of IgG. If we mix the colostrum from these 2 cows, the pooled colostrum will not have 30 g/L of IgG. This pooled colostrum will contain 25 g/L of IgG ([(20)(15) + (40)(5)]/20). Low-immunoglobulin, high-volume colostrum will be overrepresented in any pooled colostrum. Consequently, the practice of pooling colostrum should be strongly discouraged.

Breed of the Dam

Several studies have compared the colostral immunoglobulin concentrations of various breeds of cattle.[44–46] One study found the immunoglobulin concentrations of 1st-milking colostrum of Ayrshire, Brown Swiss, Guernsey, Jersey, and Holstein cows to be 80.8, 65.7, 63.1, 90.4, and 55.9 g/L, respectively.[44] Cows of the Ayrshire and Jersey breeds had significantly higher immunoglobulin concentrations than did Holsteins. Colostrum IgG concentraitons in Brown Swiss and Guernsey cows were not significantly different than those in Ayrshires, Jerseys, and Holsteins. Tyler et al[45] found a significant difference in the colostral IgG concentrations of Guernsey and Holstein cattle. Guernsey colostrum samples had IgG concentrations that exceeded those of the Holsteins by 36 g/L.

Lactogenic capability of the dam also may play a role in colostral IgG concentration. Guy et al[47] observed multiple parameters in dairy and beef breeds to determine differences in colostrogenesis. That study demonstrated similar concentrations of IgG1 in prepartum mammary secretions in both beef and dairy cattle. Two weeks prepartum, dairy cattle demonstrated a dramatic decline in serum IgG concentration and a concomitant rise in serum α-lactalbumin concentration relative to that of the beef cows. This finding may support the idea that dairy cattle transport a higher mass of IgG from the serum to the mammary gland, but the concentration of IgG in the colostrum is diluted because of high production. However, several alternative explanations that may account for this difference remain to be evaluated.

Presence of the Dam

In a study of colostral immunoglobulin absorption in 20 calves, Selman et al[48] noted that immunoglobulin absorption was increased in calves that were housed in close proximity to their dam, when compared to calves housed separately from their dam. All calves were allowed to suckle their dam to satiety at 6 and 12 hours postpartum. Calves that were left with their dams were muzzled to prevent intake at other times. No difference was found in the intake volume between the 2 groups of calves. However, calves that remained in the presence of their dam had higher average serum immunoglobulin concentrations at 48 hours postpartum. In an attempt to account for colostral IgG concentration, a follow-up study was performed.[49] Ten calves were allotted to the mothered group and 10 to the nonmothered group. All calves were fed colostrum from a pool with an immunoglobulin concentration of 6.8 g/dL colostral whey. The only management variable that differed between the 2 groups was the presence of the dam. Similar to the previous study, calves that were left with their dam had significantly higher serum immunoglobulin concentrations at 9, 24, and 48 hours postpartum. In a comparison of calves that were left with the dam to a group removed from the dam immediately postpartum and fed by nipple bottle, Stott et al[36] found that calves left with the dam had consistently higher rates of immunoglobulin absorption and serum IgG concentrations. However, all of the calves that received 2 L of colostrum had adequate passive transfer and neither the difference in the rate of IgG absorption nor the final serum IgG concentration in bottle-fed calves was significantly different from that of the naturally suckled calves.

From these studies, it is apparent that calves left with the dam have higher rates of IgG absorption and serum IgG concentrations. However, calves removed from the dam can attain adequate passive transfer if sufficient quantities of colostrum are fed. The risk of FPT is greater in naturally suckled calves because of intake of inadequate colostrum volume and IgG mass,[35–37] and the mothering effect does not provide suitable gain to advocate leaving calves with the dam.

Metabolic Disturbances

Respiratory or metabolic acidosis can develop during prolonged parturition. In fact, calves with prolonged calving times are more likely to be acidotic than calves resulting from a normal parturition.[50] Besser et al[51] demonstrated that serum immunoglobulin concentration is decreased in calves

with respiratory acidosis. However, it should be noted that venous blood samples were used to determine the presence of respiratory acidosis and the calves were not sampled for serum IgG concentration beyond 12 hours postpartum.

In another study, Tyler and Ramsey[52] observed that hypoxic calves had delayed IgG absorption in the first 18 hours postpartum. However, unlike the normoxic calves, the hypoxic calves had appreciable IgG absorption after a 2nd colostrum feeding. Time to closure was increased from a mean of 20.5 hours in the normoxic calves to 40.5 hours in hypoxic calves. Despite the difference in absorptive time, the absorptive capacity of the 2 groups was not statistically different.[52] Similarly, Drewry et al[53] observed that respiratory acidosis had no effect on serum IgG concentrations in calves at 13, 25, and 37 hours of age.

One possible conclusion drawn from this body of work is that calves with metabolic or respiratory acidosis have the potential to absorb an adequate amount of immunoglobulin. The increased rate of FPT seen in these animals may occur because they are less likely to get up and nurse in a timely fashion, rather than as a result of abnormalities in absorptive capacity. In summary, the effect of dystocia, hypoxia, and respiratory acidosis on the rate of FPT remains an area of open debate.

Testing for Passive Transfer Status

Many tests have been developed to assess passive transfer status in domestic animals. The radial immunodiffusion and the enzyme-linked immunosorbent assay (ELISA) are the only tests that directly measure serum IgG concentration. All other available tests including serum total solids by refractometry, sodium sulfite turbidity test, zinc sulfate turbidity test, serum GGT activity, and whole-blood glutaraldehyde gelation estimate serum IgG concentration based on concentration of total globulins or other proteins whose passive transfer is statistically associated with that of IgG.

Serum Total Solid Concentration by Refractometer

The measurement of serum total protein by refractometer as an estimate of serum immunoglobulin concentration was 1st proposed by McBeath et al.[54] In a study of 185 calves, serum protein measurement by refractometer was demonstrated to have good correlation with serum immunoglobulin concentration measured by radial immunodiffusion ($r = .72$).[54]

In another study comparing the performance of commonly used tests for passive transfer, serum total protein by refractometry faired well.[55] That study demonstrated that a serum protein concentration of 5.2 g/dL was equivalent to an IgG concentration of 1,000 mg/dL. Depending on the endpoint chosen, this test correctly classified >80% of the calves.[55] The 5.0-g/dL endpoint maximized specificity at 0.96, but had a sensitivity of only 0.59. However, the 5.5-g/dL cutoff maximized sensitivity at 0.94 with a specificity of 0.74. By maximizing specificity, the 5.0-g/dL cutoff will limit the number of false-positive test results (ie, calves that are classified as FPT that actually have adequate passive transfer). By maximizing sensitivity, the 5.5-g/dL cutoff will minimize the number of animals with inadequate serum IgG concentrations that are classified as adequate passive transfer (false negatives). The selection of test endpoints should be guided by the costs of false-positive versus false-negative test results, the prevalence of FPT, and the planned application of test results.

This test is excellent for herd monitoring and is easily performed by practitioners. Despite widespread skepticism and concerns regarding the effects of age and hydration status, refractometry seems to provide a reasonably accurate assessment of passive transfer status in moribund calves, but a test endpoint of 5.5 g/dL may be preferable in clinically ill calves.[56] On a healthy, adequately hydrated calf a serum total protein of 5.2 g/dL or greater is associated with adequate passive transfer.[55]

Sodium Sulfite Turbidity Test

The sodium sulfite turbidity test historically has been described as a 3-step semiquantitative test using 14, 16, and 18% sodium sulfite test solutions.[57] The test solutions cause selective precipitation of high molecular weight proteins, including immunoglobulins. This precipitation results in turbidity, which is the measured endpoint. Increasing concentrations of reagent or salt solution will induce turbidity at lower concentrations of high molecular weight proteins. Consequently, turbidity using a 14% test solution is indicative of higher serum immunoglobulin concentrations than turbidity using a 16% test solution. Similarly, turbidity using a 16% test solution is indicative of higher serum immunoglobulin concentrations than turbidity using a 18% test solution. Unfortunately, the test endpoint using the lower 2 dilutions, 14 and 16%, corresponds with inordinately high serum IgG concentrations.[55] Use of either the 14 or 16% test solution concentrations will tend to misclassify large numbers of calves with adequate serum immunoglobulin concentrations as having FPT. In a recent study, the mean serum IgG concentrations of calves at the 1+, 2+, and 3+ endpoints were 1,250, 2,116, and 2,948 mg/dL, respectively.[55]

When 242 calves were examined using the sodium sulfite turbidity test, the 1+ endpoint, corresponding to turbidity at the 18% test solution, correctly classified a higher percentage of calves than the 2+ or 3+ test endpoints, 86% versus 71 and 37%, respectively. The 1+ endpoint had a lower sensitivity, 0.85, than the 2+ and 3+ endpoints, which both had a sensitivity of 1.0. However, the 1+ endpoint had a dramatically better specificity of 0.87 versus 0.56 and 0.03 for the 2+ and 3+ endpoints. Consequently, optimal diagnostic utility is attained using an 18% test solution. Furthermore, the higher immunoglobulin concentrations necessary to cause turbidity using the 14 and 16% test solutions are difficult, if not impossible, to attain on a consistent basis in dairy calves. In this same study, less than 2% of dairy calves had positive turbidity using a 14% test solution and only 37% of calves had positive turbidity using a 16% test solution. Consequently, the sodium sulfite turbidity test is best used as a single dilution procedure using an 18% test solution.

Zinc Sulfate Turbidity Test

The zinc sulfate turbidity test operates on the same basic principle as the sodium sulfite turbidity test. The test was

originally described by McEwan et al[58] to be read spectrophotometrically. Modification of the original test methodology has created a less cumbersome, farm-friendly test. It typically is performed as single dilution assay in which 0.1 mL of serum is added to 6 mL of 208 mg/L zinc sulfate solution. The assay is allowed to incubate at room temperature for 30 minutes and turbidity is checked. At this dilution, the test has an inappropriately high endpoint, which was demonstrated by Tyler et al.[55] At this concentration, the test demonstrated a very poor specificity of 0.52 and only correctly classified 69% of the calves tested.

Test performance can be readily improved by increasing the concentration of the test solution, but this refinement has not been widely adopted. In a study of zinc sulfate performance in 235 Holstein calves, the test correctly classified an increasing percentage of calves at higher solution concentrations.[59] Increasing test solution zinc sulfate concentration from 200 mg/L to 350 mg/L would cause a minimal decrease in sensitivity (1.0 to 0.94) while dramatically improving specificity (0.255 to 0.765) and positive predictive value (0.53 to 0.83). Other major limitations of this test are the effect of hemolysis and the fact that the solutions are not stable when exposed to atmospheric carbon dioxide.[55,59,60] One, 3, and 5% hemolysis has been shown to increase the estimated immunoglobulin concentration by 2.2, 7.6, and 12.6 mg/mL, respectively.[60] Aged solutions that are not stored in a low-CO_2 atmosphere will yield a high proportion of calves with low serum IgG concentrations being misclassified as having adequate passive transfer.[55,59,60] The significant influence of hemolysis and CO_2 make this test cumbersome for routine use.

ELISA

An ELISA recently has become available for use in calves. This test gives a semiquantitative immunoglobulin concentration and is similar to radial immunodiffusion in accuracy. The test currently marketed for calves[a] is low in cost. In preliminary testing, this test seemed to perform similarly to the 18% sodium sulfite turbidity test or refractometry procedures (Doug Hostetler, personal communication).

GGT Activity

The enzyme GGT is produced by the ductile cells of the mammary gland and as a result is found in colostrum.[61] In calves that have ingested colostrum, serum GGT concentrations will be high compared to those of adult cows.[23,62,63] In a study that evaluated serum GGT activity in calves, increased serum activity was noted in all calves that had evidence of colostral ingestion as determined by serum protein concentration and serum protein electrophoresis.[23] GGT was noted to rise quickly after the ingestion of colostrum. A precipitous decrease in activity was seen over the next 24 hours followed by a more gradual decline over the next 2 months. Based on these findings, the conclusion that serum GGT activity increased in neonatal calves as a result of the ingestion of colostrum was made.

This hypothesis was confirmed by Braun et al[62] in a study that evaluated GGT activity in the serum of 16 calves and the in colostrum of their dams. Increased serum GGT activity was seen in all calves that received colostrum. The 2 calves that received alternative products, milk replacer and boiled cow milk, did not demonstrate an increase in serum GGT activity over precolostral values. The colostral GGT activity varied widely from cow to cow. Serum GGT activity in the colostrum-fed calves also varied widely from calf to calf. No significant association was present between the GGT activity of the colostrum and the subsequent serum GGT activity in the calves ($P > .05$). However, a correlation was present between the log serum GGT activity and serum globulins ($r = .41$; $P < .01$). That study hypothesized that GGT could be used as an indicator of passive transfer status in calves, although no attempt was made to establish cutoff values.

Perino et al[63] demonstrated increased serum GGT activity in a study of 48 calves after the ingestion of colostrum. An association between serum GGT and serum IgG was observed, but the strength of the association was low. Serum GGT could be used to confirm ingestion of colostrum, but did not permit accurate assessment of serum IgG concentration. Parish et al[64] confirmed the findings of previous researchers in a study of serum GGT activity in 71 dairy calves. In that study, a model to predict passive transfer status as a function of age and serum GGT activity was created ($r^2 = .40$) for calves under 11 days old. From that model, recommendations were made for the interpretation of serum GGT activity in calves and the passive transfer status of the calf. In 1-day-old calves, serum GGT activity should be >200 IU/L. In 4-day-old calves, serum GGT activity should be >100 IU/L. In 1-week-old calves, serum GGT activity should be >75 IU/L. Calves that have serum GGT activity <50 IU/L within the first 2 weeks of life should be considered to have FPT. In sharp contrast to the results of Parish et al,[64] Wilson et al[3] were unable to substantiate the utility of serum GGT activity in the prediction of passive transfer status in 69 beef calves. In summary, serum GGT activity has no advantage relative to other methods for assessing passive transfer status in calves and its use should be discouraged.

Whole-Blood Glutaraldehyde Coagulation Test

The whole-blood glutaraldehyde coagulation test initially was introduced as a method to detect hypergammaglobulinemia in adult cattle.[65] This test takes advantage of the fact that uncharged amino groups on proteins will form cross-linkages with aldehyde groups forming a visable clot.[65,66] A low concentration of glutaraldehyde will not react with albumin. However, glutaraldehyde will form cross-linkages with fibrinogen, but this effect was considered negligible. Thus, the clot formation was attributed to the gelation of gamma globulins. Liberg[67] later demonstrated that hyperfibrinogenemia can significantly influence the results of the glutaraldehyde coagulation test. In a study of 82 cows with traumatic reticuloperitonitis, he demonstrated that hyperfibrinogenemia in the absence of hypergammaglobulinemia would cause clot formation on the addition of glutaraldehyde to a whole-blood sample.

Tennant et al[68] described a modification of the glutaraldehyde coagulation test to estimate gamma-globulin concentrations in neonatal calves. This method used serum as

opposed to whole blood, eliminating the potential interaction of fibrinogen. In that study, 50 μL of 10% glutaraldehyde was added to 0.5 mL of serum. The samples then were observed for clot formation for 1 hour. Samples with no clot formation within the hour were deemed hypogammaglobulinemic.

Recently, a whole-blood glutaraldehyde clot test was marketed for use in cattle.[b] To perform this test, 1.5 mL of whole blood is added to a preprepared glutaraldehyde solution and the time to clot formation is recorded. Clot formation in <5 minutes is indicative of adequate passive transfer. In a study that examined test performance in 242 calves, test performance was determined to be inadequate for routine use.[69] Sensitivity and specificity of the test were endpoint-dependent, with sensitivity ranging from 0.41 to 0.00 and specificity ranging from 0.85 to 1.00.

The Effects of Passive Transfer on Baseline Mortality

With regard to passive transfer, more is not better. Previous authors suggested that 5.5 g/dL total serum solid concentration or alternatively a serum IgG concentration of 1,500 mg/dL should be used as goals.[70,71] The wisdom of this goal should be questioned. In 1 recent study, mortality was followed in 3,479 calves in which serum protein was measured in the 1st week of life. The relative risk of mortality in each stratum then was calculated.[72] Based on the results of that study, a serum protein concentration of 5.5 g/dL probably is not a consistently achievable goal in dairy calves.

Tyler et al[72] observed that <40% of dairy calves exceeded this goal concentration. The relative risk of mortality for calves with serum protein concentration between 5.0 and 5.5 g/dL was only modestly increased, with a relative risk of 1.3. Furthermore, no decrease in mortality was observed as serum protein concentrations increased above 5.5 g/dL. Consequently, no justification exists for setting a goal of serum protein concentration >5.5 g/dL, and little justification exists for setting a goal >5.0 g/dL. If the goal concentration was reduced to 5.0 g/dL, >65% of the calves studied exceeded this threshold value. More importantly, calves classified as having FPT had substantial increases in mortality, with a relative risk of 2.0. Because the increased risk of mortality is concentrated in the lowest passive transfer stratum, monitoring failure (% of calves <5.0 g/dL) or pass rates rather than mean serum IgG or protein concentrations is better.

Another common misconception is that calves reared under conditions of high baseline mortality can be reared successfully if passive transfer is sufficiently improved. Recent studies have demonstrated that the risk associated with varying levels of passive transfer is independent of baseline mortality rate.[72] On any farm, a baseline mortality rate exists, which reflects the inputs of pathogens, nutrition, and hygiene. As serum immunoglobulin concentrations decrease from a threshold concentration (5.5 g/dL total protein) the risk of mortality increases relative to this farm's specific baseline mortality. Improved passive transfer will decrease calf mortality until this threshold serum IgG concentration is achieved. Serum protein concentrations >5.5 g/dL will not further decrease mortality. Improved passive transfer results in dramatic decreases in mortality in hypogammaglobulinemic calves, but improvement from adequate to superlative passive transfer will not result in decreased baseline mortality. Furthermore, analysis of the data presented by Tyler et al[72] substantiated that the majority of calves (77%) with complete FPT (<4 g/dL serum protein) would survive. Likewise, adequate or excellent passive transfer status does not guarantee survival, demonstrated by the 5% baseline mortality that persisted in the highest passive transfer strata.

Consequences of FPT

Increased neonatal mortality due to FPT is a well-accepted consequence of FPT. However, the potential long-term effects have been largely overlooked. Robison et al[73] demonstrated a significant increase in average daily gain in dairy heifers that had adequate passive transfer when compared to those with FPT ($P < .01$). In that study, heifers with FPT also had higher mortality rates than those with adequate passive transfer, particularly during the postweaning period.

In a study of the effects of passive transfer status on production in dairy heifers, DeNise et al[74] demonstrated that heifers with FPT had significantly lower mature equivalent milk production during the 1st lactation ($P < .05$). In that study, heifers with FPT also had a greater tendency to be culled in the 1st lactation when compared with those that had adequate passive transfer.

In studies on the health and performance of beef calves related to postcolostral IgG concentration, Wittum and Perina[75] found that calves with FPT had increased risk of neonatal and preweaning mortality as well as preweaning morbidity when compared to calves with adequate passive transfer. The calves with FPT also had poorer production in the feed lot, with an increased risk of mortality and respiratory tract morbidity when compared to calves with adequate passive transfer. In that study, an indirect effect of passive transfer status on weaning weight and average daily gain was present because of the effect of passive transfer status on calf morbidity.

Treatment of FPT

Newborn calves are hypogammaglobulinemic at birth. However, they are immunocompetent and produce approximately 1 g IgG1 per day.[76] Despite the production of endogenous antibody, they remain unable to respond to some antigens, such as lipopolysaccaride, until 30 days of age.[77] Therefore, although calves suffering FPT are at a greater risk for developing disease, they can survive if they are placed in a clean environment with low exposure to infectious pathogens.

The decision to treat a calf with FPT should be based on several factors including its age, value, surrounding environment, and the ability to collect and administer plasma or whole blood. Treatment of FPT in an otherwise normal neonate is addressed via the administration of plasma at a dosage of 20 mL/kg IV. Whole blood also can be used, but the dosage should be increased to account for the presence of red blood cells. Cross-matching rarely is necessary be-

cause of the large number of blood types in cattle. In addition, we have been unable to locate a documented case of transfusion reaction in calves for a 1st-time transfusion. Despite this, calves should be monitored for adverse reactions (eg, lethargy, dyspnea) during the procedure. To avoid the cost of intravenous catheter placement, plasma or whole blood also can be administered via the intraperitoneal (IP) route. To administer plasma or whole blood IP, an area in the left paralumbar fossa is clipped and surgically prepared. A 14- to 16-gauge, 1.5-inch needle is used to penetrate the skin, abdominal musculature, and peritoneum in the center of the left paralumbar fossa.

In addition to plasma or whole-blood transfusions, oral colostrum supplementation beyond the period of closure is logical to provide protection at the level of the gut lumen. Some clinicians advise oral supplementation with plasma beyond the period of closure. This practice should be questioned because serum contains significantly lower immunoglobulin concentrations than does colostrum. In addition, if one goes to the trouble and expense of collecting serum, it is logical to administer it in a manner that maximizes systemic absorption.

Finally, the prophylactic use of broad-spectrum, parenteral antimicrobials in calves with FPT is a rational consideration. However, use of prophylactic antimicrobials must be combined with management practices that minimize pathogen exposure because antimicrobials will not negate the effects of a high pathogen load.

Summary

Many factors influence the absorption of immunoglobulins and serum IgG concentration in the neonate. Most important are the volume and IgG mass that the calf receives. All calves should receive 4 L of high-quality colostrum by esophageal tube. Colostrum quality should be assessed by the weight of the 1st-milking colostrum as opposed to parity of the dam or colostrometer measurements. Calves that receive less volume or those that are allowed to nurse to satiety are at greater risk for FPT because of inadequate mass of IgG ingested.

An understanding of the appropriate testing procedures is imperative to provide high-quality neonatal care. Many assays are available to directly measure or infer serum IgG concentration in calves. The whole-blood glutaraldehyde gelation test is inadequate for clinical use. Modifications to the turbidimetric assays, especially the sodium sulfite turbidity test, make them useful in clinical practice. Despite concerns about refractometry, this method of assessment can provide adequate results in both healthy and moribund calves.

Immunoglobulin concentrations measured in the neonate are simply guidelines based on statistical analysis of large populations. Several factors interact in conjunction with the amount of passively acquired immunoglobulin to determine the occurrence of disease. These factors include (but are not limited to) management, environment, hygiene, infection pressure, virulence of infectious organisms, and antibody specificity. Although neonates that suffer FPT are at increased risk for disease, low serum immunoglobulin concentrations do not guarantee disease if the neonate resides in a clean environment and is not exposed to highly virulent organisms. Similarly, neonates with adequate passive transfer can easily suffer disease if placed in a filthy environment or exposed to highly virulent organisms.

Footnotes

[a] Quick Test Calf IgG Kit, Midland Bioproducts Inc, Boone, IA
[b] Gamma-check B, Veterinary Dynamics, Inc, San Luis Obispo, CA

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