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Failure of passive transfer of immunity - A Comprehensive review

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Abstract

Newborn calves are essentially agammaglobulinemic. The syndesmochorial placenta of domestic large animals does not allow the fetus to acquire maternal immunoglobulins during pregnancy. Therefore, neonates rely entirely on Passive Immunity Transfer (PIT) of immunoglobulins, mainly Immunoglobulin G (IgG), obtained from maternal colostrum during the first hours after birth. Failure of Passive Transfer (FPT) occurs when a neonate does not absorb sufficient colostral antibodies and is associated with increased preweaning morbidity, septicemia, respiratory tract disease, and neonatal mortality. This extensive review presents the physiological mechanism of immunoglobulin transfer, the significant risk factors of FPT, the common diagnostic techniques, and the efficient herd management strategies to prevent the illness.

Keywords: Passive transfer, immunity, calves, calves, colostrum, immunoglobulin g, herd management

Introduction

Passive Immunity Transfer (PIT) is the mechanism by which immunoglobulins are passed from mother to newborn. Calves rely on the PIT of IgG from maternal colostrum consumed within the first few hours of life (McGrath *et al.* 2016) [59]. The placenta in domestic large animals prevents immunoglobulin transmission from the mother to the fetus in pregnancy. The cow's syndesmochorial placenta divides the fetal and maternal blood supply and prevents immunoglobulin transfer in utero by generating a syncytium between the fetal trophoctoderm and the maternal endometrium (Arthur *et al.* 1996) [3]. Failure of passive transfer (FPT) transpires when a newborn lacks the capacity to absorb antibodies from colostrum (Beam *et al.* 2009) [9]. As a result of this failure, a newborn is more susceptible to diseases since it lacks the necessary immunity to protect against microorganisms. FPT is not a medical problem, but rather a condition that enhances the probability of disease development in neonates. FPT is seen in newborn pigs, lambs, and cattle calves, despite its lower prevalence in other animal industries. According to Wilson *et al.* (1999) and Tessman *et al.* (1997) [86, 100], this makes FPT an important economic concern for animal producers. The most important factor influencing calf health and survival is effective colostrum administration and regulation. Colostrum is essential for creating antibodies and strengthening immunity to infections and diseases. Immunoglobulins (Ig) in high-quality colostrum cause a passive transfer of immunity when absorbed by the calf's digestive tract. Immunoglobulins are classified into five categories: IgA, IgG, IgM, IgD, and IgE, each having a distinct concentration in colostrum. IgG, the main immunoglobulin in cows, is connected with disease resistance. IgA in saliva protects against intestinal infections and inhibits the growth of rumen bacteria, thus it is abundant. Although IgM is produced in smaller quantities than IgG, it is more effective at eradicating viruses and plays an important role in the initial exposure to antigens. The concentration of immunoglobulin and colostrum is important in passive transmission in neonatal calves. To guarantee beneficial absorption rates, administer four quarts of colostrum to the calf between delivery and four hours after birth. To achieve passive transfer, blood Ig levels should be at

Least 10 g/L (Kirk 2011) ^[47]. According to Bush and Staley (1980) ^[16, 84], IgG absorption from epithelial cells to the bloodstream begins after 12 hours of age and ends after 24 hours. According to Leece and Morgan (1962) ^[50], gut closure occurs when the gut is unable to absorb and transport macromolecules into the bloodstream. Although Stott *et al.* (1979a) ^[81] investigated how colostrum accelerated cessation and how colostrum-deprived calves had delayed gut closure, an earlier study stated that nutrition had no effect on gut closure (Patt, 1977) ^[69]. Additionally, Stott *et al.* (1979b) ^[83] established that colostrum feeding stimulates pinocytosis, the process by which immunoglobulins are delivered. After that, macromolecule absorption begins to decelerate, yet circulatory transport continues. Furthermore, Stott *et al.* (1979c) ^[83] report that gut closure in calves can reduce macromolecule absorption after colostrum ingestion. Although the exact mechanism dictating this permeability is unknown (Weaver *et al.*, 2000) ^[98], it is believed that either mature epithelial cells replace enterocytes or pinocytotic activity is diminished, resulting in gut closure (Smeaton and Simpson Morgan, 1985) ^[78]. The timing of colostrum administration to a newborn calf is also important because studies have shown that absorption efficiency decreases with increasing time between birth and first colostrum feeding (Bush and Staley, 1980) ^[6]. A more recent study by Fischer *et al.* (2018) discovered that delaying colostrum feeding for more than six hours after delivery lowered IgG transfer when compared to calves fed promptly after birth, confirming the idea that calves should be fed right away. Immunoglobulins move from the serum to the mammary gland several weeks before parturition, peaking one to three days before (Sasaki *et al.* 1976) ^[75]. The receptors on dam's alveolar epithelial cells contribute to the levels of IgG1 in colostrum (Barrington *et al.* 1997a) ^[4]. At the start of lactation, glandular epithelial cells quit expressing this receptor. Altered expression is most likely caused by increased prolactin concentrations (Barrington *et al.* 1997b) ^[4]. Immunoglobulins, immunologically active cells, and soluble mediators such as lactoferrin are all transmitted from dam to calf via colostrum (Reiter *et al.* 1975) ^[74].

(Lakritz *et al.* 2000) ^[49] Shown that soluble mediators ingested from colostrum boost newborn immunological capacities and that specific neutrophil function assessments are lowered in calves that are unable to absorb colostral lactoferrin. Leukocytes in mammary secretions are immunologically active and may enter the fetal blood (Concha *et al.* 1980) ^[19]. Until its immune system develops, the neonatal calf relies on Ig from colostrum to provide passive immunity. The concentrations of serum immunoglobulin G (IgG) can indicate how protective colostrum is. IgG levels of less than 10 g/L indicate that passive immunity has not been conferred (Besser *et al.*, 1985) ^[10]. As an alternative, if healthy calves younger than one week are tested more than six hours after consuming colostrum, serum total protein (STP) concentrations provide a reasonable estimate of IgG and are helpful for analyzing FPT at the herd level (McGuirk and Collins, 2004) ^[58]. FPT has been linked to higher morbidity, mortality, and slower calves' growth rates, according to Cuttance *et al.* (2017) ^[21]. Lower levels of serum IgG raise the likelihood of developing respiratory disease (Virtala *et al.*, 1999; Pardon *et al.*, 2015) ^[68, 95]. Donovan *et al.* (1998) ^[25] discovered that when STP concentration (at 2-8 days of age) rose linearly from 40 to 80 g/L, the prevalence of septicemia in infants under 45 days of age decreased. Additionally, they discovered that the risk of death decreased

from 0 to 6 months of age when STP levels increased from 40 to 60 g/L, but not after that. Calves with STP concentrations below 40 g/L had a 4.6-fold higher risk of dying than those with concentrations above 60 g/L, according to Tyler *et al.* (1998) ^[91]. It is less clear how FPT and growth rates are related; it has been demonstrated that calves with lower IgG concentrations grow more slowly at different developmental stages (Furman-Fratczak *et al.*, 2011; Pardon *et al.*, 2015) ^[31, 68]. Overall, it is hypothesized that calves that consume colostrum, which provides stronger immune protection, are more likely to live longer and grow more quickly.

Risk factors of FPT

Problems with calf antibody absorption, inadequate colostrum consumption, and poor colostrum quality are risk factors. Additional characteristics associated with FPT include male gender, colostrum feeding assistance, and calving support. When the absorption of macromolecules stops, closure happens. Bovine neonates can absorb colostral Ig from the colon at different times, according to several studies: 3-5 hours (Westrom *et al.*, 1984 ^[99]; Heinrichs, 1985) ^[38]; 12-23 hours (McCoy *et al.*, 1970) ^[55]; and 0-40 hours (Deutsch and Smith, 1957) ^[27]. Additionally, different antibody types have variable closure periods, according to Stott *et al.* (1979) ^[81]. The closure times for IgG, IgM, and IgA absorption were 21 hours, 23 hours, and 23 hours, respectively, for the calves that received colostrum after delivery. The IgG content of colostrum may change the perceived effectiveness of immunoglobulin absorption, according to Stott and Fellah's (1983) ^[79] hypothesis. Due to the direct costs of calf losses and treatment, as well as long-term effects on production performance, calfhood illnesses have a substantial impact on the financial sustainability of dairy operations (Donovan *et al.*, 1998) ^[25]. The primary risk factors associated with poor calf rearing include: failure to disinfect the newborn's navel; delayed identification and calf monitoring; inappropriate housing systems adopted for calves; lack of surveillance during calving, especially at night; and a lack of colostrum quality checks and poor colostrum management (Vasseur *et al.* 2010) ^[93]. Serum IgG concentration was found to be significantly impacted by being a twin, born to a heifer, and needing calving help (Waldner and Rosengren, 2009) ^[96]. According to Filteau *et al.* (2003) ^[29], the only factors that significantly affected FPT were the type of indoor calving facility and the degree of assistance the calf required for feeding; dam parity and dam body condition had no influence. Serum IgG levels were higher in calves that got more feeding assistance. The importance of calf vigor at birth was emphasized by Herpin *et al.* (1998) ^[39] since it may influence a calf's inclination to consume colostrum. According to Vasseur *et al.* (2009) ^[94], combining the calf's birth weight and vigor is the most accurate method of predicting colostrum intake. Calves that were smaller and less active consumed less colostrum. Ig absorption is significantly influenced by the amount and timing of colostrum consumption. Jaster (2005) ^[44] discovered that decreased blood Ig concentrations resulted from the delayed delivery of colostrum of poor quality and quantity. Additionally, after feeding different amounts of high-quality and low-quality colostrum at different times after birth, the author compared the absorption of Ig. After prolonged calving or dystocia, calves usually have poorer vitality and colostrum consumption skills, as well as poorer suckling responses and longer time to sternal recumbency. Dystocia has a significant role in reduced calf vitality and colostral Ig absorption, which inhibits the transmission of

passive immunity (Barrier *et al.*, 2013) ^[6]. Longer calving periods increase the risk of respiratory or metabolic acidosis in calves. Calves with respiratory acidosis had decreased serum Ig concentrations, according to Besser *et al.* (1990) ^[11]. According to Tyler and Ramsey (1991) ^[89], hypoxic calves exhibited delayed IgG absorption within the first 18 hours following calving. However, the hypoxic calves showed significant IgG absorption during the second colostrum feeding. Beam *et al.* (2009) ^[9] found that calves given pooled milk had a higher chance of FPT than calves allowed to nurse or given colostrum by hand after four hours of birth. Author also mentioned neglecting to seek veterinary care during a difficult birth and neglecting to provide dystocia calves with a source of heat during cold weather are two other management practices that increase the risk of FPT. Calves' capacity to absorb immunoglobulins from colostrum is hampered when housed in an unheated environment during cold weather, increasing the risk of calf death from cold stress (Olson *et al.*, 1980; Norheim and Simensen, 1985) ^[64, 65]. Higher rates of FPT were observed in dairy calves who were allowed to nurse normally from the dam; this could be due to the calf's inability to eat adequate colostrum and IgG mass (Weaver *et al.* 2000) ^[98]. According to James *et al.* (1981) ^[43], management situations that result in bacterial contamination of colostrum are concerning because pathogenic bacteria can either directly cause disorders like scours or septicemia or interfere with the passive absorption of colostrum antibodies into the calf's circulation, reducing calf immunity. According to Gelsinger *et al.* (2015) ^[32], a higher bacterial count in colostrum decreased the calves' plasma total protein and IgG concentrations as well as the effectiveness of their IgG absorption.

Factors influencing immunoglobulin transfer

Several parameters are commonly mentioned as influencing passive transfer in the calf, including the dam's age, the time of colostrum intake, the method and volume of colostrum delivery, and the immunoglobulin concentration of the ingested colostrum. The calf's respiratory acidity, the breed and presence of the dam, and the colostrum pooling method can all affect passive transfer.

Timing of ingestion

The neonatal enterocyte has a unique ability to absorb protein macromolecules. During the first 24 to 36 hours of life, the enterocytes in the small intestine will pinocytose a variety of macromolecules, including immunoglobulins, and non-selectively absorb them as observed by Broughton *et al.* (1970) ^[15]. According to Staley *et al.* (1972) ^[84], immunoglobulins are transported via exocytosis from cells into lymphatics, from there they pass through the thoracic duct and into the circulatory system. Neonatals who consume colostrum have higher levels of various protein macromolecules and enzyme activity, including gamma-glutamyltransferase (GGT). Thompson *et al.* (1981) ^[87] suggested that closure, which occurs at different times depending on the species, is the end of macromolecule absorption. Immunoglobulin transport across the gut epithelium is greatest in the first 4 hours after delivery and starts to sharply decrease after 12 hours, regardless of how long the gut closure lasts (Stott *et al.* 1979a) ^[81]. When given comparable amounts and concentrations of colostrum, calves fed earlier have blood IgG concentrations that are significantly higher than those fed later. (Stott *et al.* 1979b) ^[83].

Method and volume of colostrum feeding

Suckling will cause the esophageal groove to close (Leek 1993) ^[52]. The idea that suckled colostrum would have improved absorption has been proposed in light of this data. Calves given a nipple bottle were shown to have somewhat higher average serum IgG concentrations when compared to calves given colostrum by esophageal tube administration of same volume and IgG mass (Adam's *et al.*, 1985) ^[1]. The amount of colostrum the calf consumes and the colostrum immunoglobulin concentration are far more significant than the colostrum administration technique. Dairy calves that are left with the dam and permitted to nurse naturally have been linked to high rates of FPT. Besser *et al.* (1991) ^[12] provided an illustration of this problem, allowing dairy calves to nurse until they are satisfied will prevent them from consuming enough of the somewhat diluted colostrum from dairy cows to meet their immunoglobulin needs. FPT rates of 61, 19, and 10% were noted by Lee *et al.* (1983) ^[51] in dairy calves that were given colostrum by esophageal tube administration, suckling the mother, and suckling a nipple bottle, respectively. He said that feeding dairy calves via esophageal tubes can guarantee a decreased FPT rate.

Colostrum quality

To overcome the challenge of distinguishing between colostrum with high and low immunoglobulin concentrations, Fleenor and Stott (1980) ^[80] recommended the use of a hydrometer. They showed that the concentration of colostral immunoglobulin, colostral total solids, and colostral total protein were all related to colostral specific gravity. However, the author discovered that test specificity is seriously weakened, leading to an excessive percentage of colostrum samples being labeled as immunoglobulin deficient and significantly reducing the amount of colostrum that can be fed to calves. The measured weight of the first-milking colostrum is an additional method for choosing high-quality colostrum. Colostrum from cows who produced less than 8.5 kg of milking colostrum had a considerably higher colostral IgG1 concentration, according to Pritchett *et al.* (1991) ^[70], who studied 919 Holstein dairy cows. Although this difference existed in cows of all ages, it was particularly noticeable in cows that were in their second lactation. According to that study, the percentage of high-immunoglobulin colostrum samples would significantly rise if first milking colostrum samples weighing more than 8.5 kg were discarded. In most calves given 3 L of colostrum in a timely way, this procedure would guarantee a enough IgG1 concentration to ensure effective passive transfer. According to Shearer *et al.* (1992) ^[77], colostrum with an Ig concentration of less than 20 g/L is considered poor quality, 20 to 50 g/L is considered intermediate quality, and more than 50 g/L is considered outstanding quality. High-quality colostrum has been defined as having a colostrum IgG concentration of greater than 50 g/L (Kehoe *et al.*, 2011) ^[46]. Colostrum IgG concentrations ranged from 8.3 to 128.6 g/L, with 29.1% of the samples having less than 50 g/L of IgG, according to Bartier *et al.* (2015) ^[7]. The cattle's parity affects the colostral IgG concentrations. Colostral IgG concentrations were higher in cows with third or greater parity than in cows with second parity or first parity. IgG levels in colostrum ranged from 7.1 to 159.0 g/L, with 16.0% of samples having fewer than 50 g/L, according to Quigley *et al.* (2013) ^[71]. Morrill *et al.* (2012) ^[63] reported that Ig concentrations ranged from 1.8 to 200.2 g/L, with 29.4% of samples having less than 50 g/L. Furthermore, the calving season may have an impact on the

colostrum quality in terms of the concentration of colostral IgG. Wintertime colostral IgG levels were lower than those of other seasons, according to Gulliksen *et al.* (2008) [36].

Presence of the dam

In the study of colostral immunoglobulin absorption in 20 calves, Selman *et al.* (1971) [76] observed that, in contrast to calves kept apart from their dam, immunoglobulin absorption was higher in calves housed near to their dam. At 6 and 12 hours after giving birth, all calves were permitted to nurse their mother until they were satisfied. In order to prevent intake at other times, calves that were left with their dams were muzzled. The intake volume of the two calves' groups did not differ from one another. At 48 hours postpartum, however, calves that stayed with their mother had greater average serum immunoglobulin concentrations.

Metabolic disturbance

Prolonged parturition may result in metabolic or respiratory acidosis. Compared to calves born after a normal parturition, calves with longer calving times are more likely to be acidotic (Szenci 1983) [85]. Calves with respiratory acidosis had lower serum immunoglobulin concentrations, as shown by Besser *et al.* (1990) [11]. It should be mentioned, nonetheless, that the calves were not collected for serum IgG concentration beyond 12 hours postpartum, and venous blood samples were used to assess the existence of respiratory acidosis. In a different investigation, Tyler and Ramsey (1991) [89] found that during the first eighteen hours after giving birth, hypoxic calves exhibited delayed IgG absorption. However, following a second colostrum feeding, the hypoxic calves showed significant IgG absorption in contrast to the normoxic calves. The normoxic calves' average time to closure was 20.5 hours, but the hypoxic calves was 40.5 hours. This set of research may lead to the conclusion that calves with respiratory or metabolic acidosis are capable of absorbing enough immunoglobulin. These animals may have a higher rate of FPT because they are less likely to wake up and nurse on time, rather than because of anomalies in their absorptive capacity. In conclusion, there is ongoing discussion on the impact of respiratory acidosis, hypoxia, and dystocia on the rate of FPT.

Diagnosis - Direct and indirect method and cut off values

To evaluate the state of passive transmission in domestic animals, numerous assays have been created. The only methods that quantify blood IgG levels directly are the enzyme-linked immunosorbent assay (ELISA) and radial immunodiffusion. Every other test that is currently available, such as whole-blood glutaraldehyde gelation, sodium sulfite turbidity, zinc sulfate turbidity (ZST), serum GGT activity, and serum total solids by refractometry, calculates serum IgG concentration by measuring the concentration of total globulins or other proteins whose passive transfer has a correlation to that of IgG. Radial immunodiffusion (RID) remains the gold standard (Donovan *et al.* 1998) [25]. Standard RID is costly, involves a large amount of laboratory time (18-24 hours), and requires skilled workers. Etzel *et al.* (1997) [28] created a less expensive automated turbidimetric immunoassay that used anti-bovine IgG and produced precise IgG concentration readings in 15 minutes, but the samples still required laboratory processing. In more recent times, a portable analyzer has been developed to employ the turbidimetric immunoassay (Alley *et al.* 2012) [2]. This offers quick cow-side FPT diagnosis, but because a portable

analyzer is less cost efficient. ELISA is an alternate technique for directly measuring serum IgG level. This makes it possible to automate the process, which lowers the time needed to a fifth of RID and the cost per test to roughly a tenth of RID (Gelsing *et al.* 2015) [32]. According to Cuttance *et al.* (2019) [22], the ELISA may be used as a screening and confirming test for FPT when blood IgG concentrations were less than 5 g/L, but only as a screening test when serum IgG concentrations were greater than 5 g/L. Total protein (TP) or total solids in serum or plasma, γ -glutamyl transferase (GGT) activity, total solids measured using a Brix refractometer, and turbidimetric tests employing sodium or zinc sulfate are examples of indirect methods for measuring IgG quantities. Tests based on estimating concentrations of TP in serum or plasma have been widely used to diagnose FPT because immunoglobulins make up a significant portion of the circulating proteins found in the serum of neonatal calves and the non-immune proteins are comparatively constant between calves (Godden 2008) [34]. Two techniques have been employed to estimate TP concentrations in cattle: the colorimetric Biuret method (Busher 1990) [17] and refractometers, which measure the serum or plasma's refraction index and use a conversion factor to convert it to TP concentrations (Vandeputte *et al.* 2011) [92]. It has been demonstrated that measuring TP concentrations in serum gives a reasonable estimate of IgG concentrations in serum and can be used to investigate FPT at the herd level if healthy calves younger than one week are tested, as long as it has been more than six hours since they were fed colostrum (McGuirk and Collins 2004) [58]. A range of cut-points, from 50 to 55 g/L, have been proposed for the diagnosis of FPT using TP concentrations (Cuttance *et al.* 2017) [21]. The discrepancy in cut-points indicates variations in the connection between TP and IgG concentrations between studies, as well as variations in whether sensitivity or specificity is maximized. A refractometer can also be used to estimate TP concentrations (Quigley *et al.* 2013) [71]. The serum's refractive index can be determined using Brix or a direct measurement of total solids, which corresponds to TP (g/L). Although serum is used in the majority of TP concentration estimation methods, plasma can also be used. In samples from 61 calves, MacFarlane *et al.* (2014) [57] evaluated the agreement and correlation between TP concentrations in serum and plasma. Although the two tests had extremely excellent agreement, the authors noted that different cutpoints would be needed for serum or plasma in order to define FPT. For instance, 52 g/L TP was ideal when utilizing serum, but 56 g/L TP is recommended when using plasma.

The majority of mammalian tissues contain the enzyme GGT, which is involved in the transport of amino acids. It is present in large concentrations in bovine colostrum and is produced by the ductile cells of the mammary gland (Baumrucker 1979) [8]. Proteins other than IgG, like GGT, are also absorbed since macromolecules are not selectively absorbed by the calves' small intestine during the first 24 hours of life (Parish *et al.* 1997) [67]. GGT and IgG may, however, have distinct uptake patterns; the rise in GGT activity is more temporary, and its absorption is less effective than that of IgG (Hadorn and Blum 1997) [37]. However, it has been found that calves who had colostrum ingested had >60 times higher serum GGT activity than those that had not (Thompson and Pauli 1981) [87]. According to reports, measuring GGT activity can yield a helpful indication of colostrum ingestion and, consequently, IgG concentrations (Perino *et al.* 1993) [66]. However, GGT

activity declines over time after birth, in contrast to IgG and TP concentrations, which remain rather stable until one week of age (Braun *et al.* 1982) ^[14]. Using amounts of IgG <10 mg/mL as the threshold for identifying FPT, Parish *et al.* (1997) ^[67] developed a set of age-based GGT activity levels that may be used to diagnose FPT. Calves that were one day old had a GGT activity threshold of less than 200 IU/L, four-day-old calves less than 100 IU/L, and one-week-old calves less than 75 IU/L. Furthermore, GGT activity <50 IU/L was suggestive of FPT for any calf younger than 14 days. Due to its applicability as a non-laboratory-based test, the ZST test has been widely utilized worldwide but not in New Zealand (McEwan *et al.* 1970) ^[56]. When zinc sulfate is added to serum, globulins precipitate, producing turbidity that is proportionate to the globulin content (Kunkel 1947) ^[48]. This technique has been modified to estimate serum IgG concentrations and, thus, diagnose FPT. A colorimeter can be used to determine the turbidity objectively, or samples can be evaluated subjectively. If the turbidity is high enough to make newspaper unreadable through the sample tube, the samples are said to contain enough IgG (Tyler *et al.* 1996) ^[41]. Shortly after RID was initially created, this method was presented as a way to identify FPT (Ritzmann 1978) ^[72]. It was not contrasted with this gold standard or with other direct IgG assays. Standardizing the ZST test is challenging since the turbidity generated can change depending on the concentration of the test solution, the wavelength of light used to read the reaction, and the amount of time the reaction is allowed to continue before measurement (Hudgens *et al.* 1996) ^[41]. Hogan *et al.* (2016) ^[40] examined the specificity and sensitivity over a range of wavelengths, concentrations, and times in an effort to standardize the test. Additionally, there are no obvious benefits to the ZST over simpler tests, like measuring TP concentrations, because the high sensitivity reported was dependent on cut-points that changed with zinc sulfate concentration, reaction time, and turbidity measurement wavelength.

Effects of passive transfer and consequences of failure of passive transfer

Weaver *et al.* (2000) ^[98] stated that excessive passive transfer can be detrimental. This demonstrates the potential negative repercussions of excessive passive transfer, which can be ineffective or even destructive in some contexts. Boyd *et al.* (1974) ^[13] suggested that the optimal cutoff values be either a serum IgG concentration of 1,500 mg/dL or a total serum solid content of 5.5 g/dL. Irwin (1974) ^[42] analyzed mortality in 3,479 calves whose serum protein was measured during their first week of birth and concluded that it is improbable that dairy calves will consistently reach a blood protein concentration of 5.5 g/dL. The average daily growth of dairy heifers with suitable passive transfer was much higher than that of dairy heifers with FPT. As explained by Robison *et al.* (1988) ^[73]. According to De Nise *et al.* (1989), heifers with FPT were more likely to be culled than those with adequate passive transfer and produced noticeably less mature equivalent milk during the first lactation. Calves with FPT were found to have a higher risk of preweaning morbidity and neonatal and preweaning mortality than calves with adequate passive transfer (Wittum and Perino, 1995) ^[66, 101]. FPT calves were more likely to die and experience respiratory tract morbidity, and they generated less in the feed lot than calves with adequate passive transfer. Additionally, he pointed out that while passive transfer status impacted calf morbidity, it indirectly impacted weaning weight and average daily gain.

Prevention and management of fpt

The main strategy to avoid gastro-intestinal (GI) infection-related morbidity is to control FPT. According to Lopez & Heinrichs (2022) ^[53], in order to accomplish this, newborn calves should be given approximately 8% of their body weight in hygienic, premium colostrum (>50 IgG/L) during the first two hours of life. Maternal vaccination against GI pathogens during colostrogenesis, the month prior to calving, may improve the efficacy of this regimen (Chambers *et al.*, 2022) ^[18]. Although studies show mixed results, giving prebiotics or probiotics to newborn calves can prevent diarrhea (Wang *et al.*, 2023; Medrano-Galarza *et al.*, 2018) ^[61, 97]. Regular prophylactic or metaphylactic antimicrobial usage (AMU) is no longer advised to lower the risks of antimicrobial resistance (AMR), according to Mee *et al.* (2022) ^[62]. As with the majority of infectious disorders in neonates, FPT is a risk factor for GI, according to Deepak *et al.* (2021) ^[24], as are co-infection with numerous respiratory pathogens and co-morbidity with GI infections. Lorenz *et al.* (1921) ^[54] mentioned that in order to prevent respiratory illnesses, modifiable risk factors must be addressed. According to Gorden and Plummer (2010) ^[33], the most important actions are to reduce FPT and stocking rate, avoid head space with older cattle, improve ventilation in the housing, and, if diagnostic testing indicates it, implement a vaccine program.

The most important preventive strategies are better cleanliness and dietary control. Important nutritional considerations include limiting the volume of liquid feed (<3 L), limiting the osmolality (<500 mOsm/L), and preparing milk replacer according to the manufacturer's instructions (e.g., thorough mixing, correct mixing rate, and temperature). Cleaning feeding supplies and changing out broken teats are two aspects of improved hygiene (Cooke, 2019) ^[20]. Colostrum pooling raises the risk of FPT, hence it is not advised. Without routine on-farm screening, FPT is more likely to happen (Beam *et al.* 2009) ^[9]. Therefore, the most practical approach in the field is to quantify serum total protein using a refractometer. The IgG level of 48-hour-old calves should be assessed on a regular basis to assess colostrum management compliance. Colostrum can be pasteurized at 60 °C for 60 minutes to reduce the bacterial burden while maintaining safe feeding levels for viscosity and colostral IgG content (Donahue *et al.* 2012) ^[26]. When compared to batches of colostrum of lower or intermediate grade, higher-quality batches suffer a significantly greater percentage of IgG loss (Mc Martin *et al.* 2006) ^[60]. Compared to calves fed unpasteurized colostrum, calves fed pasteurized colostrum showed significantly greater blood IgG concentrations, serum protein levels, and/or an apparent efficiency of absorption (Godden *et al.* 2012) ^[35]. In the gastrointestinal lumen, bacteria attach themselves to free IgG, blocking the absorption and passage of IgG molecules via intestinal epithelial cells. Additionally, the incidence of treating diarrhea was significantly reduced for calves fed pasteurized colostrum (Godden *et al.* 2012) ^[35]. To find out if weak-born calves experience the rapid transfer of Ig from the reticulorumen to the abomasum, more investigation is required. Additionally, tube feeding may result in severe depression or make the switch to nipple bucket drinking more challenging (Kaske *et al.* 2005) ^[45]. According to Trotz-Williams *et al.* (2008) ^[88], calves raised by female employees have a lower likelihood of receiving FPT. Probably because when a newborn calves refuse to nurse, females are more understanding. FPT is more likely to develop in calves with

dystocia (Furman-Fratczak *et al.* 2011) [31]. This can be explained by either having a lower apparent absorption efficiency or consuming insufficient amounts of colostrum. Dusty *et al.* (2000) state that giving plasma intravenously at a dosage of 20 mL/kg is the recommended treatment for FPT in a newborn who is otherwise healthy. Although whole blood can also be used, the dosage needs to be increased to account for the red blood cells.

Conclusions

Newborns must be fed maternal colostrum, a very nutritious feed, as soon as they are born. Immunoglobulins, which are proteins that create a calf's immune system through passive transfer, are abundant in it. Diverse immunoglobulins are found in colostrum, but the IgG class is the most crucial for immunity transfer. Serum IgG concentration should be determined directly at 24 hours of life to see whether a calf received an acceptable level of IgG. Indirect measures of IgG, such STP or Brix%, can be useful when calves are fed maternal colostrum. Serum IgG measurement will be more accurate when calves are given Colostrum replacer, but other cutoff values might be needed. After 24 hours, the amount of IgG in a calf's bloodstream will depend on the quality of the colostrum, which includes its IgG concentration and bacterial levels. Colostrum should be administered within two hours of delivery and include at least 50 mg/mL of IgG. The small intestine can absorb immunoglobulin proteins during this rapid feeding before progressively decreasing its permeability; complete closure occurs 24 hours after birth. Colostrum replacer may be used in situations where premium colostrum is not available for rapid feeding. The amount of immunoglobulin that is acquired passively is one of the factors that affect how the disease develops. Management, environment, cleanliness, infection pressure, virulence of infectious organisms, and anti-body specificity are some of the factors to consider. Even though neonates with FPT are more likely to get sick, if they live in a clean environment and are not exposed to highly virulent pathogens, low blood immunoglobulin concentrations may not always indicate illness. Similarly, if exposed to highly pathogenic bacteria or kept in an unclean environment, newborns with good passive transfer may quickly get illness.

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