SERUM IMMUNOGLOBULIN LEVELS IN NEONATAL DAIRY CALVES FED A UNIFORM SOURCE OF COLOSTRUM

by

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ABSTRACT

Wide variations in blood serum immunoglobulins (Ig) and hypogammaglobulinemia in newborn calves have been attributed to differences in amount and time of colostral Ig ingestion and/or factors affecting intestinal Ig absorption including stress from difficult birth (dystocia), heat stress and inherent factors in colostrum. This study was designed to determine differences in absorbed colostral IgG serum titers in 29 male and 15 female neonatal Holstein calves. The calves were fed a uniform source (frozen) of colostrum immediately after birth at 2% of birth weight followed by water, 0.2% birth weight, to rinse the nipple bottle. No additional feed was given in the next 24 hours except water at 1% of birth weight was fed at 12 hours.

A blood sample was taken before feeding colostrum and 24 hours later. Calves were penned in open shaded shelters. Absorbed IgG serum titers were not ($P > .05$) related to sex, body weight, dystocia (9 cases) or ambient temperatures of 47 to 114^{o}F. Absorbed IgG in the serum of the 44 calves ranged from 0.24 to 9.18 mg/ml and had a mean of 5.51 ± 1.83 mg/ml. Variations in serum IgG titers, among calves fed a uniform source of colostrum, were apparently

related to differences in intestinal absorption and not to environmental stress or intrinsic factors in the colostrum.

INTRODUCTION

Neonatal dairy calves are born virtually agammaglobulinemic. Early postnatal immunity is passively acquired through intestinal absorption of immunoglobulin (Ig) from the maternal colostrum milk. The colostral Ig blood titer acquired by the calf plays a major role in protecting the animal from disease until its own immune system becomes active at about 4 weeks of age.

The mechanism whereby the calf absorbs whole immunoglobulins from colostrum normally functions only during the first 24 hours of life after which Ig absorption ceases. During this period the degree of intestinal permeability decreases as evidenced by a gradual decline in the rate of Ig absorption. Thus to maximize immunological benefit, calves should ingest a maximum amount of colostrum as early in life as possible.

However, in spite of consuming sufficient amounts of colostral Ig, immediately after birth, marked variations occur in calf serum Ig titers and some calves remain hypogammaglobulinemic. Accordingly increased calf mordidity and mortality have been related to low Ig serum levels.

Several researchers have attributed wide differences in calf serum Ig titers to the amount of colostral Ig

consumed. Others have suggested premature cessation of intestinal absorption and/or other failures of the absorpative mechanism as possible contributing factors. In previous experiments to define the cause of this phenomenon, calves were generally fed varied amounts and/or sources of colostrum with different Ig concentrations. Colostrum from individual cows has been shown to contain varying quantities of chemical factors that influence the rate of intestinal Ig absorption. This study was designed to determine the variability in colostral Ig blood serum titers among newborn Holstein calves fed a uniform source of colostrum in accordance with body weight.

REVIEW OF LITERATURE

Introduction

This review will be primarily concerned with the transmission of maternal immunoglobulin (Ig) to the neonatal bovine calf. References to other species will be included for comparative purposes. Additional information is in more comprehensive reviews on neonatal immunology in the bovine (8, 11, 27) and in other species (8, 38, 40).

Immunoglobulins

Immunoglobulins or antibodies are general terms that refer to a family of high molecular weight proteins having similar physio-chemical characteristics. Their primary purpose is to enhance animal resistance to disease by neutralizing possible toxic effects of foreign molecules (antigens), including bacteria, viruses etc., that gain entrance to the body. That portion of their structure which enables them to combine specifically with an antigen is called the antigenic determinant and represents the basis on which they are separated into classes (11).

The number of Ig classes varies among species however, three classes commonly identified among mammals, including the bovine, have been designated IgG (subclasses

IgG_1, IgG_2) IgM and IgA. Accordingly IgG represents about 80-90% of the total serum Ig whereas IgM and IgA each comprise between 5 and 10% of the total amount (11, 27, 38).

Active and Passive Immunity

When an immunologically competant animal is first exposed to an antigen, antibodies designed to react specifically with the invading agent are actively produced. Following such an antigenic response the animal normally acquires a long lasting resistance or "active immunity" wherein any subsequent exposure to the same antigen results in a copious production of the specific protective Ig. Throughout life an animal becomes actively immune to a great number of antigens to which it has been exposed and experienced an antigenic response (8).

In contrast, the newborn animal which has just emerged from an environment sheltered from most antigenic stimuli, has only a limited capacity to produce Ig. Accordingly, Ig produced by the mother is transferred to the offspring to provide immediate protection "passive immunity" against those antigens with which she has had immunological experience.

Passive immunity, while immediate, lasts only as long as the transferred Ig remain in the circulation. A half-life of 15-20 days has generally been reported for maternal Ig in the calf (6, 15, 17) however, low levels of

detectable antibody titer may persist for several months (29). Although, passive immunity is short lived it plays an important role in the health and survival of the neonate until its own active immune system is readily able to synthesize Ig. The latter reportedly occurs in the calf at about four weeks of age (1, 60).

Transference of Passive Immunity to the Neonate

Provision of the newborn with maternal or passive immunity against environmental diseases is a common feature of mammals, but the mode of transfer and degree of mammalian innate immunity varies among species.

Each species is identified with one of three general categories: (I) The ruminant, horse, and pig are born agammaglobulinemic, having little or no placentally transferred immunity. Passive immunity is acquired almost entirely after birth via the ingestion of Ig in the "colostrum" milk. (II) In the rat, mouse, dog, and cat some transference of Ig occurs before birth via the fetal blood supply. Additional passive immunity is acquired post partum through the ingestion of colostrum (61). (III) The rabbit, guinea pig, human and other primates acquire passive immunity almost entirely prenatally through the placental transport of IgG (61, 77).

These differences have been explained as one of two opposing theories: (I) The yolk sac development theory, and (II) the placental cell layer theory (8). In the former theory it is suggested that the blood level of antibodies at the time of birth is directly related with the development, persistence, and time of withdrawal of the yolk sac into the umbilical cord. The yolk sac is withdrawn into the umbilical cord very early in gestation in animals in category I. This is considered to severely limit prenatal Ig absorption. Animals in categories II and III have a high blood level of antibodies at birth and the yolk sac is exposed to the uterine lumen during most of gestation.

In contrast to the above hypothesis, the more generally accepted "placental barrier theory" attributes the lack of early postnatal antibodies in agammaglobulinemic species to the more complex placental filtering system between the maternal and fetal blood circulation. This complexity of the placenta has been explained in terms of cell layers. Animals with five and six cell layers separating the maternal and placental circulation do not transfer Ig to the fetus in utero. Whereas, Ig is transferred via the placenta in species with four or less placental cell layers.

Colostrum Immunoglobulins

Colostrum is the first milk or lacteal secretion following parturition. The albumin-globulin content is 7-12%, compared to about 0.7% in normal milk (25, 26, 33, 44, 72). The Ig content may represent as much as 90% of the albumin-globulin fraction (25, 72).

Prior to parturition the cow selectively secretes serum IgG, IgM and IgA unchanged into the mammary gland. During this transfer, serum Ig levels decline while colostrum Ig may increase up to five times the serum Ig concentration (9, 29, 43, 65, 72). The subclass IgG1 comprises about 80-90% of the total colostral Ig whereas the closely related IgG2 fraction, for some unknown reason, is transported only in minor amounts (65, 69). In contrast, both IgG subclasses are apparently transported into the mammary gland of the sow. Only IgA generally appears in lacteal secretions of man, the rabbit and mouse (11).

Following parturition, the amount of Ig in the milk declines preciptiously and at 24 hours post-partum is less than one-third of the original colostral concentration (7, 26, 33, 39). The importance of this change is recognized in calf husbandry wherein it is generally recommended that calves be fed only the initial colostrum milk during the first 24-36 hours of life in order to maximize Ig consumption.

Transference of Colostrial Passive Immunity

Since 1922 it has been known that passive immunity in neonatal dairy calves is acquired through the ingestion of colostrum (57). As previously noted the blood serum of the neonatal calf is essentially free of Ig. However, after the calf consumes colostrum, there is a rapid increase in serum Ig (41, 57, 72, 82). The latter has been observed within three hours after colostrum ingestion (3, 10). The Ig in colostrum and that appearing in the serum after its ingestion are apparently identical and have been identified as the agents responsible for passive immunity in the calf (16, 29, 35, 41, 72). Calves deprived of colostrum have a markedly higher morbidity and mortality rate than colostrum fed calves (1, 36, 75). For example when 225 calves were given colostrum, 75% survived, whereas only 9% of 103 colostrum deprived calves lived past three weeks of age (35).

Several investigators have shown that the calf absorbs unchanged colostral Ig via the tall epithelial cells lining the small intestine and that none is absorbed from the abomasum or large intestine (3, 4, 16). It is believed that the absorption mechanism is a micropinocytotic process (cell drinking), which is a means whereby large molecules gain entrance to certain cells (47). Subsequently

the Ig moves out of the cells into the mesenteric lymphatics, and passes through the thoracic duct into the peripheral circulation (3, 15, 32).

Evidence that little or no Ig directly enters the portal circulation in the calf and kid goat was demonstrated by introducing 131-I labelled globulin into the duodenum. Between 12-25% of the labelled globulin was recovered from the thoracic duct lymph in a 5 hour period. No labelled globulin was found in the blood prior to its detection in the lymph (3). This is in contrast to smaller molecules of serum albumin, of which, in addition to the lymph, a considerable proportion is transported by the blood (2). In the neonatal pig, colostral Ig are also apparently transported by the lymph to the circulation (61).

Although concentration of Ig in the colostrum is a selective process absorption by the calf is apparently nonselective since IgG, IGA and IGM are taken up by the intestine equally well (4, 43, 65). In addition, other macromolecular substances including bovine serum globulins, serum albumin, β lactoglobulins and polysaccharides etc., can be absorbed intact by the intestinal mucosa in the newborn calf (2, 4, 18, 29) and pig (47, 60).

Cessation of Intestinal Ig Absorption

The unique ability of the calf to absorb large amounts of whole proteins through the intestinal wall is

transitory. The capacity to directly absorb colostral Ig ceases within about 24 hours after birth (15, 31, 49, 76). No measurable increase appeared in the serum Ig of calves fed colostrum or isolated colostral Ig after calves were more than 24 hours of age (31, 49, 76).

It was suggested that the transitory nature of this absorption might coincide with the development of gastric protein digestion or with a maturation and change in permeability of intestinal epithelial cells (76). To test these theories large amounts of colostrum were introduced directly into the intestinal tracts of calves at 6 to 18 or 48 to 60 hours of age. Subsequent appearance of colostral Ig in the serum of the younger but not older calves indicated that cessation of intestinal absorption was not related to gastric Ig degradation but to a change in the intestinal permeability.

Cessation of intestinal permeability is apparently not delayed and occurs even if the calf does not ingest colostrum or milk, etc. during the first 24 hours of life (15). However, the ingestion of soluble protein before feeding colostrum may influence intestinal Ig absorption. When newborn calves were fed skim milk or bovine serum three hours prior to feeding colostrum, there was no absorption from the colostrum of a neutralizing antibody to

foot and mouth disease but, the latter was readily absorbed when only colostrum was fed (29).

Absorption of colostrol Ig will occur up to 106 hours of age in previously unfed pigs. However, piglets fed colostrum or other soluble protein at birth experience cessation of Ig absorption or intestinal closure 12-24 hours postnatally or accordingly thereafter in relation to time of first feeding (60, 61). In the rat intestinal closure to intact proteins does not occur until approximately three weeks after birth (13).

Closure of intestinal absorption to whole proteins is gradual and not abrupt. In calves, intestinal absorption of Ig, as determined by a somatic antigen of E. coli, was reduced almost 50% at 16 hours after birth (27). When 131-I labeled globulin was introduced directly into the small intestine of neonatal calves, maximum concentration occurred in the lymph between 180 and 200 minutes. Thereafter, a gradual decline generally occurred (3).

A similar decline in the rate of intestinal Ig absorption in the pig suggests a progressive exposure of the epithelial cells to colostral Ig followed accordingly by cell closure (61). Intestinal Ig absorption begins in the anterior section and proceeds along the gut to the posterior portion where absorption continues as anterior cell closure occurs (14, 73).

This cellular maturation or change in permeability agrees with the previously suggested pinocytotic method of absorption which is associated mostly with primitive or immature type cells (14, 47, 61). In the pig these cells may follow the all-or-none phenomenon in which Ig is taken up to the cell's capacity after which absorption ceases and the Ig is subsequently released into the lymphatics (60, 61). However, it has also been proposed that the epithelial cells first lose their ability to release the absorbed Ig and thereafter experience a loss of ability to take up macromolecules from the intestinal lumen (14).

A seven fold increase in alkaline phosphatase activity has been noted in the small intestine of piglets at the time of cell closure (61). A gradual increase in alkalin phosphatase activity was also found to be concomitant with cell closure in the mouse and rat (30, 55). Whether this phenomenon is actually related to the cessation of intestinal absorption or is a result of cellular metabolism is not known.

Injections of cortisone acetate into the mouse and rat (30, 55) or piglet (61) advances the time at which absorption ceases. Starved piglets failed to show Ig absorption when fed colostrum 48 and 72 hours after injection of cortisone whereas absorption continued up to 106 hours in uninjected pigs (61). On the other hand, the

injection of calves with cortisone, adrenocorticotrophic hormone or somatotrophin (growth hormone) did not appear to alter intestinal permeability to Ig absorption (18, 77).

It is apparent that time and rate of cell closure to Ig absorption and factors affecting this phenomenon vary among species. The exact nature of the changes or factors involved in cessation of Ig absorption by the intestinal epithelial cells remain to be determined.

Immunological Significance of Calf Serum Ig Titers

In recognition of the transitory nature of intestinal Ig absorption it is generally recommended that calves be fed colostrum as early in life as possible in order to maximize serum Ig titers and immunological benefit. However, in spite of consuming adequate amounts of colostral Ig immediately after birth, some calves remain virtually agammaglobulinemic (9, 27, 35, 43, 74). It has been reported that 10-30% of calves fed sufficient colostral Ig remain hypogammaglobulinemic (9, 34, 43, 82).

In correlating serum Ig titers to morbidity and mortality, numerous researchers have noted that calves with low serum Ig levels are more apt to succumb to infection than calves with higher serum titers (7, 23, 37, 52, 53, 62, 80, 84). A distribution of deaths and culls in relation

to percentage of Ig in the blood serum of new born calves is shown in Table 1 (84).

Table 1. Distribution of deaths and culls according to percentage of Ig in the blood of calves.

Serum % Ig	No. of Calves	Deaths	Culls	Total Loss	% Loss
1.1 - 6.2	73	8	4	12	16.4
6.3 - 12.0	73	2	1	3	4.1
12.1 - 19.3	73	1	1	2	2.73
19.4 - 46.7	74	0	1	1	1.35

A 1970 farm survey in England, involving 227 calves, showed a significant relationship between low serum Ig levels and a high incidence of disease. The occurrence of calf scours was 21.9% and of other diseases 11.4% in calves having below median serum Ig titers in comparison to 5.3% and 3.5% respectively, in calves with above median Ig levels (7).

In the same year workers in Scotland reported a negative correlation between serum Ig levels and mortality rates in 415 market bull calves, about one week of age.

Figures extrapolated from a bar graph show that a mortality rate of 60% occurred in about 180 calves having the lowest serum Ig levels, 20% died in the median serum Ig group of about 80 calves, while only a 5% death loss occurred among 255 calves having the highest Ig serum titers (53).

In a more recent five month field study in the United States, blood samples were taken from 456 newborn calves in 30 Michigan herds. Serum Ig levels, measured in zinc sulfate units, were significantly lower in calves that died, 5.7 units, as compared to 7.8 units in calves that lived (23).

Various diseases of calves including Streptococcus, Pasteurella and Salmonella etc., are associated with acute diarrhea and rapid death. However, infection due to Escherichia coli is the most common cause of these symptoms (22, 27). Although morbidity in neonatal calves has been related to a lack of Ig against specific strains of E. coli in the colostrum of some cows (27, 35, 36, 73), the primary pathogenic factor concerned with susceptibility of the calf to E. coli is hypogammaglobulinemia (27, 38).

In calves experiencing diarrhea, fecal output and excretion of IgG, and mortality were observed to be highest in calves that initially had the lowest serum Ig titers (24). The amount of IgG excreted was greater among

diarrhetic calves that died versus those that survived but, this difference could not be correlated with changes in serum Ig levels.

These and other studies show that hypogammaglobulinemia is a primary factor in the pathogenesis of disease in newborn calves. This relationship has prompted researchers to identify those factors that may influence serum Ig levels in the neonatal calf.

Factors Influencing Calf Serum Ig Titers

The initial Ig titer acquired by the neonatal calf has been shown to be influenced by several factors.

Amount of Colostrum Ingested

It has been suggested that the wide range in serum Ig titers among calves is primarily due to differences in amounts of colostrum consumed (10, 23). However, it is recognized that the total amount of Ig a calf receives depends not only on the amount of colostrum ingested but also on the concentration of Ig in the colostrum (9, 44, 52).

Several studies show a positive correlation between serum Ig titers and amounts of colostral Ig fed (9, 10, 23, 43, 52). In two studies (9, 10) calves were given specified amounts of colostrum in relation to body size.

Accordingly, 50 and 68% of the variation in blood serum Ig levels could be attributed to differences in amount of Ig consumed per unit body weight.

Results of attempts to relate colostral Ig concentration with calf serum Ig titers have been variable. In some (9, 45) a positive correlation was found whereas others have reported no relationship between colostrum and serum Ig concentrations (10, 43). Three batches of colostrum containing 10.5, 18.8 and 29.8 mg/ml of IgG were fed at two levels, to calves, according to body weight. Absolute amount of IgG consumed, but not its concentration in colostrum, had a significant effect on blood concentration of IgG (10).

Marked variations among individual cows in colostrum yield, 1.0 - 40 lb, and colostrum Ig concentration 1.5 - 11.9%, have been reported (9, 43, 44, 52). In addition, colostral yield and Ig concentration have been observed to differ according to breed and age of cow (44). Mean first lactation colostrum yields of Danish Red, Black and White, and Jersey heifers were found to be significantly lower, 11.4, 7.3 and 4.6 lb, respectively, than cows of the same breeds which at second and third calving produced 20.0, 14.7 and 14.1 lb, respectively. Other investigators have also found higher variability and lower yield of colostral Ig among first-calf heifers (46, 79). These observations have led to the conclusion that at least some

cases of hypogammaglobulinemia are not due to failure of the nursing calf to absorb Ig but instead to a lack of colostral Ig intake.

Time of Colostrum Ingestion

Hypogammaglobulinemia has been found to occur more frequently among calves not given colostrum until 6-12 hours of age (27, 70, 74). Of nine calves not fed colostrum until 10-12 hours after birth, two absorbed no Ig and three had very low serum levels. In contrast only 33% of calves fed earlier were hypogammaglobulinemic (74). These observations are consonant with studies showing that rate of intestinal Ig absorption decreases with time after birth (3, 27, 45).

Environmental Stress

It is well known that the environment, especially weather, plays a major role in the health and well being of newborn calves. Seasonal patterns of morbidity and mortality rates are generally highest in the winter months (48). Surveys in England (7) and Scotland (53) revealed significantly lower serum Ig levels in winter versus summer born calves. However, in addition to climate, these differences may also reflect seasonal changes in management. For example, during the summer grazing season the nursing calf obtains colostrum free choice. Whereas, in the winter

early separation of the dam and calf with limited feeding of colostrum by bucket has been associated with lower serum Ig levels (53).

In a recent Arizona study heat stress was shown to depress calf serum Ig titers (81). Three Holstein calves born the same day and fed a uniform source of colostrum according to body weight were assigned to three housing treatments: (I) in pens under an open shade with evaporative cooling, (II) in pens under an open shade with no cooling, and (III) in individual open sided hutch pens with metal roofs. Average daily peak housing temperatures in order of treatment were 72.4, 79.6 and 81.6^{o}F. Mean serum IgG1 levels 48 hours after birth, for 36 calves on each treatment, were 25.4, 22.0 and 18.6 mg/ml, respectively.

Specific Factors in Colostrum

Colostrum from individual cows has been shown to contain specific factors which influence the rate of intestinal absorption (3, 32, 59). Absorption of Ig, via the epithelial cells of the small intestine, is enhanced by the presence of certain substances in the colostrum whereas in their absence the rate of absorption is extremely low. These accelerating factors are apparently effective only during the period following birth in which intestinal permeability normally occurs. They accelerate but, are not entirely responsible for Ig absorption (3, 32).

In attempts to identify these enhancing factors several substances contained in colostrum have been tested. These include a small unidentified protein, inorganic phosphate, glucose -6- phosphate, lactate, pyruvate and butyrate. All have been shown to independently accelerate Ig absorption to some degree but not to the extent of whole colostrum (3, 32). Although histamine concentration in colostrum is about three times the amount in normal milk, it apparently does not act as an enhancement factor (59).

Intestinal Absorption

Some researchers have attributed variation in calf serum Ig titers to inherent differences in intestinal absorption (9, 43). However, results of these studies may have been confounded when calves were fed varied sources and/or amounts of colostrum irrespective of body size.

Gestation periods of variable length are often suggested to be an influencing factor on intestinal Ig absorption and a possible cause of hypogammaglobulinemia but no relationship has been found in this regard (61, 74, 77). In one study, three calves were taken by Cesarean section 14-19 days prior to their estimated birth date and fed the same source of colostrum. Two of the calves fed colostrum immediately after delivery had normal Ig blood patterns. The third calf showed no Ig absorption when

colostrum was not fed until 38 hours after delivery (77). Also, Ig absorption was not altered in pigs delivered prematurely at 100 days gestation or farrowed late at 118 days (61).

Whether exceptionally low serum Ig titers in calves fed adequate amounts of colostral Ig are due to an absolute defect in the absorption mechanism, premature intestinal closure and/or variations in the source of colostrum fed has not been resolved. A defect in such a universal basic cellular function is said to be difficult to envisage (43). Nevertheless it is probable that calf serum Ig titers are influenced to a considerable degree by differences among calves in their inherent absorption ability.

PROCEDURE

This study consisted of two trials with a total of 44 Holstein calves. Trial I was conducted June 18 to August 14, 1975 with 15 female and 14 male calves at the Harold Kuiper Dairy, Chandler, Arizona. Trial II was conducted February 6 to 10, 1976, with 15 male calves at the Shamrock Dairy, Tucson, Arizona. Experimental procedures were the same in both trials.

Colostrum milk from only the first milking post-parturition was collected from six Holstein cows 2-6 years of age. The colostrum was blended (pooled) and immediately frozen in one-third quart containers. The amount needed was thawed just prior to feeding.

The pooled colostrum was quantitatively analyzed for IgG content (21). A qualatative estimation of specific immunoglobulins in the pooled colostrum was determined by immunoelectrophoretic separation of the colostrum serum proteins. Identification was produced by reaction of the pooled colostrum serum proteins against rabbit anti-bovine whole serum (54).

Calves were taken from their mothers prior to nursing. Subsequently each calf was fed a pooled source of colostrum milk at 2% of its birth weight followed by

water at 0.2% of body weight to rinse the nipple bottle. The calves were penned under an open shade and no additional feed was given during the next 24 hours except water at 1% of birth weight at 12 hours.

A blood sample was taken by jugular venapuncture, using 10 ml vacutainers (5), before (zero hour) and at 24 hours after feeding colostrum. The blood serum was prepared (8) and frozen until analyzed.

Blood serum IgG was quantitated by radial immuno diffusion (21). Using this technique, calf serum was placed in small wells within agarose containing commercial rabbit anti-bovine serum IgG (54). Diffusion of calf serum into the agarose produced antigen-antibody precipitate rings around the wells. Diameter of the rings reflected the serum concentration of the antigen bovine IgG.

Specific calf serum immunoglobulins were analyzed and determined by immunoelectrophocesis (12). Calf serum was electrophocetically separated on ion agar (19) and reacted against rabbit anti-bovine whole serum (54).

Dystocia or difficult birth was defined as mild or severe according to the degree of physical assistance required and the apparent stress exerted on the calf during parturition. Mild dystocia was noted when delivery was relatively easy and a minimum of assistance was needed.

On the other hand, dystocia was recorded as severe when delivery was difficult, prolonged and considerable assistance was required.

Ambient temperatures occurring during the first 24 hours of life for each calf were obtained from local weather summary reports for the Phoenix-Chandler and Tucson areas (83).

Data for both trials were analyzed statistically by analysis of variance independently and combined.

RESULTS AND DISCUSSION

The blended colostrum contained an IgG concentration of 77.28 mg/ml and weighed 1.035 g/ml. This Ig value compares favorably with other reported colostral Ig mean values of 72.56 mg/ml (52) and 74.52 mg/ml (44).

The characteristic low level or lack of IgG in the blood serum of most calves at birth and its subsequent appearance in the post-colostral serum at 24 hours can be readily seen in Tables 2 and 3 and in the radial immunodiffusion (Figure 1) and immunoelectrophocetic (Figure 3) patterns of calves 69 and 444. In contrast, IgG was identified in 27% of the zero hour serum samples of calves at birth including calves 379 and 555 each of which had the highest initial serum IgG titers, 6.04 mg/ml (Figures 1, 2 and 3).

In order to relate the 24 hour serum IgG titer to intestinal absorption it was necessary to differentiate absorbed IgG from the total serum IgG concentration. Therefore, 24 hour IgG absorption is defined in this study as the 24 hour IgG titer minus the serum IgG concentration at birth.

The zero hour serum IgG titers detected in the 12 calves had a range of 1.74-6.04 mg/ml and a mean value of

Table 2. Serum IgG titers in calves at birth and 24 hours after colostrum ingestion, Trial I.

Data are in order of absorbed IgG concentration (total - birth) in the serum.

Calf No.	Sex	Serum IgG Titers 24 hours (mg/ml)		
		Birth	Total	Absorbed
555	M	6.04	6.28	0.24
34	F	0.00	2.29	2.29
318B[a]	F	0.00	2.32	2.32
61	M	0.00	3.86	3.86
58	M	0.00	3.86	3.86
47A	F	0.00	4.35	4.35
47B	F	0.00	4.35	4.35
306	F	0.00	4.35	4.35
59	M	3.02	7.73	4.71
403	F	3.67	8.60	4.93
75	F	1.74	6.76	5.02
379	M	6.04	12.08	6.04
70	M	0.00	6.04	6.04
45	F	0.00	6.04	6.04
409	M	0.00	6.04	6.04
42	M	0.00	6.04	6.04
318A	M	0.00	6.04	6.04
346	F	3.02	9.18	6.16
205	M	0.00	6.28	6.28
79	F	0.00	6.28	6.28
39	F	0.00	6.28	6.28
395	F	0.00	6.52	6.52
444	F	0.00	6.76	6.76
69	M	0.00	6.76	6.76
419	M	0.00	6.76	6.76
426	M	0.00	7.10	7.10
62	M	0.00	7.49	7.49
334	F	0.00	8.69	8.69
343	F	0.00	9.18	9.18

a. A, B indicates twin calves.

Table 3. Serum IgG titers in calves at birth and 24 hours after colostrum ingestion, Trial II.

Data are in order of absorbed IgG (total - birth) in the serum.

Calf No.	Sex	Serum IgG Titers 24 hours (mg/ml)		
		Birth	Total	Absorbed
406	M	0.00	3.02	3.02
401	M	1.67	5.56	3.89
402	M	4.25	8.69	4.44
409	M	2.32	6.76	4.44
414	M	2.32	6.76	4.44
412	M	0.00	4.54	4.54
415	M	0.00	4.54	4.54
410	M	0.00	5.07	5.07
403	M	0.00	5.70	5.70
405	M	0.00	5.80	5.80
411	M	0.00	5.80	5.80
407	M	0.00	6.76	6.76
413	M	0.00	6.76	6.76
408	M	2.42	9.90	7.48
404	M	3.02	12.08	9.06

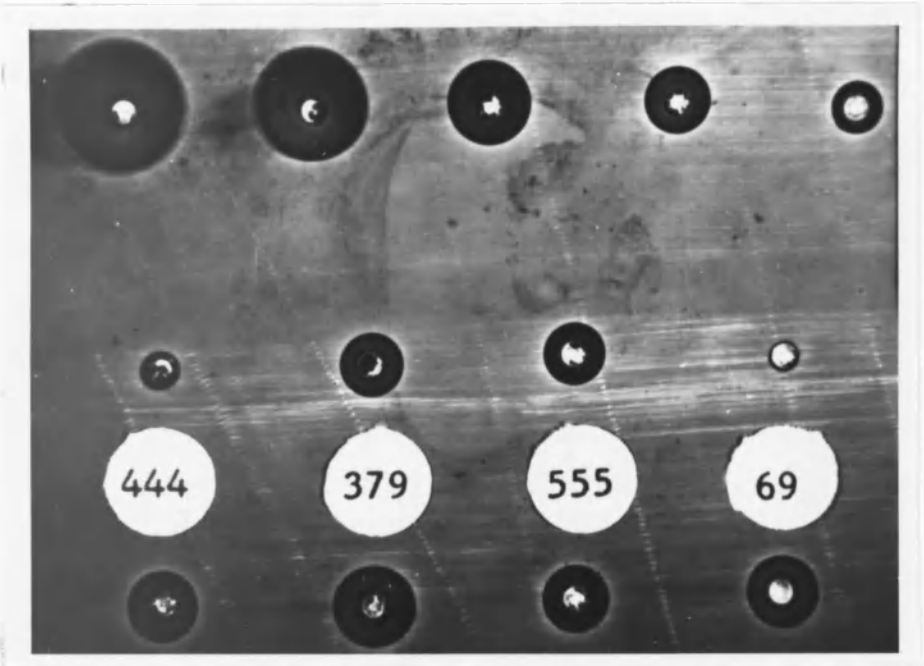

Figure 1. Calf serum IgG radial immunodiffusion patterns.

Top row: Normal bovine serum IgG standard (48.3 mg/ml) dilution precipitate rings (left to right) 0, 1/2, 1/4, 1/8 and 1/16 dilutions. Center row: Zero hour serum IgG titers. Calves 69 and 444. No definite precipitate rings indicate little or no serum IgG at birth. Calves 379 and 555. Precipitate rings = 6.04 mg/ml IgG in serum at birth. Bottom row: IgG serum titers 24 hour post-colostrum ingestion. Precipitate IgG rings for calves 444, 379, 555 and 69 equal 6.76, 12.08, 6.28 and 6.76 mg/ml, respectively. Absorbed IgG (24 hour - 0 hour serum titer) = 6.76, 6.04, 0.24 and 6.76 mg/ml, respectively.

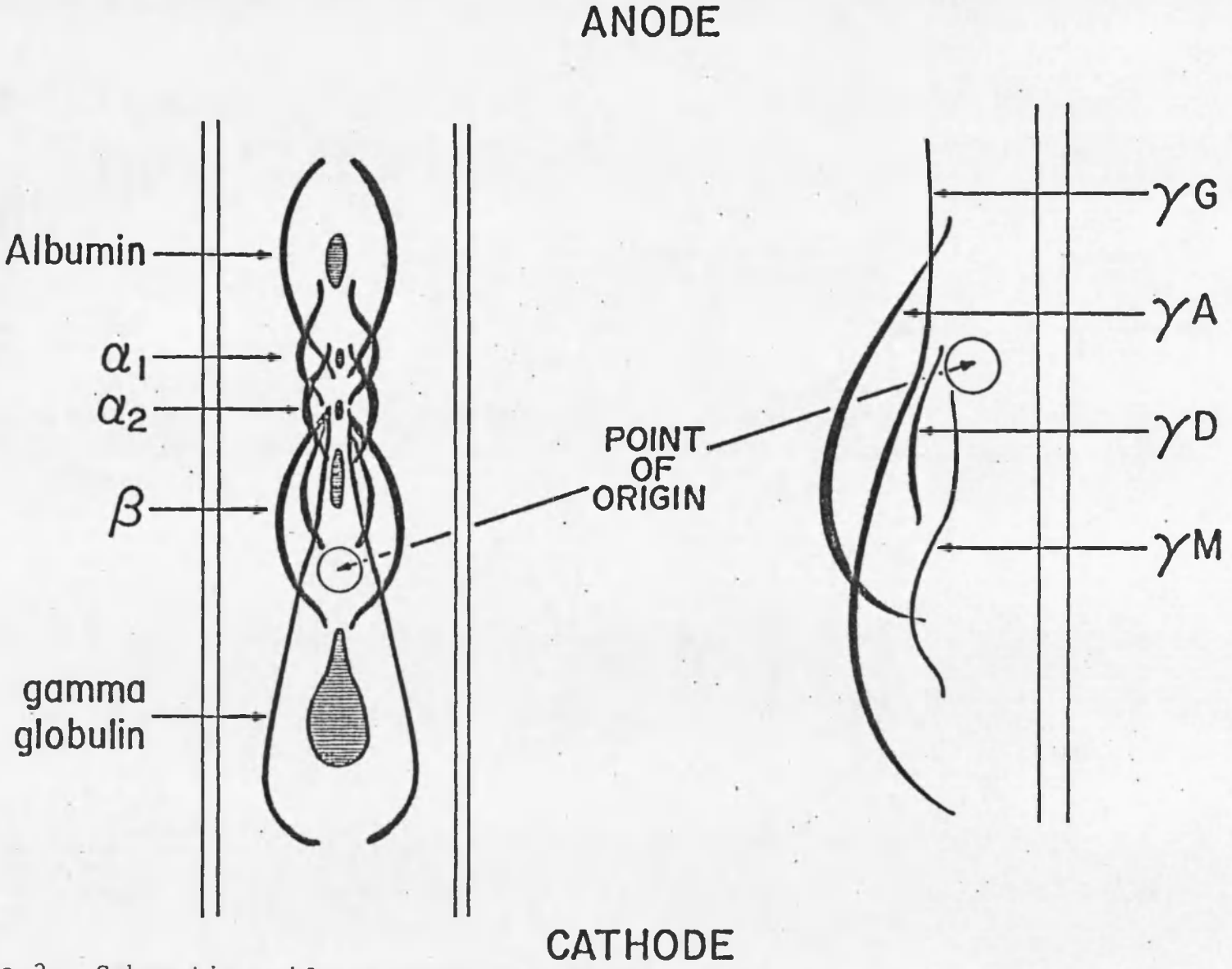

Figure 2. Schematic guide of precipitin bands for immunoelectrophoretograms in Figure 3.

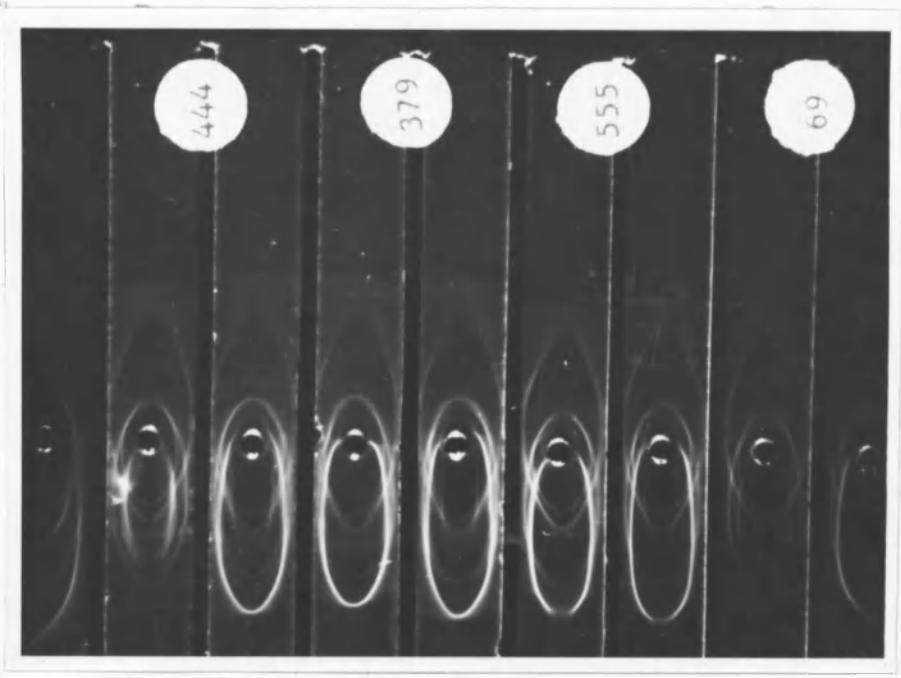

Figure 3. Calf serum immunoelectrophoretograms.

Zero hour immunoelectrophoretograms, on the left side of each calf number, show little or no IgG in the serum of calves 69 and 444 whereas IgG is present in calves 379 and 555. Immunoelectrophoretograms on the right side show IgG in the serum of each calf 24 hours post-colostrum ingestion.

3.29 mg/ml. Similar mean concentrations of Ig, 1.40 to 2.90 mg/ml, have been reported in pre-colostral calf serum in other studies (9, 43, 63, 81). Very low levels of IgG have also been observed in some unsuckled pigs (56, 67).

While the appearance of small amounts of Ig in the serum of some calves at birth is not uncommon the exact nature of its occurrence is not known. Although the newborn calf is immunologically immature, limited Ig production has been demonstrated in utero (20, 22, 78) and during the first few days of life (8, 41, 63). Small amounts of Ig have also been observed to be synthesized in the fetal human (28), lamb (58, 71), rat and chicken (68).

Transplacental transfer of Ig in the pig has been reported (42). The condition has been attributed to damage of the placental barrier by infection and to mechanical or functional defects that may allow maternal blood or body fluids to enter the fetal circulation during gestation or parturition. These studies indicate that the bovine fetus may acquire low levels of serum Ig through antigenic stimulus or an unusual transfer of passive immunity during gestation.

However, irrespective of its occurrence, the initial serum IgG concentration in the 12 calves apparently had little or no subsequent effect on intestinal absorption (Table 2). Their 24 hour absorbed IgG serum concentrations

ranged from .24-9.06 mg/ml and had a mean value of 5.07 mg/ml. These data were not significantly different ($P > .05$) from the range, 2.29-9.18 mg/ml, and mean, 5.68 mg/ml IgG absorption values of the other 32 calves. It is also of interest to note that in the two calves having the highest initial serum IgG titers, calf 379 had 6.04 mg/ml of absorbed IgG in the serum at 24 hours whereas calf 555 had only 0.24 mg/ml (Table 2) (Figures 1, 3).

These observations agree with results of other calf studies (9, 43), wherein initial serum Ig could not be related to post-colostral serum Ig levels. They are also consonant with findings that intestinal Ig absorption in piglets was not altered by high Ig blood levels produced by the injection of fractionated colostral Ig into the peritoneal cavity (61). It appears that intestinal absorption of Ig is markedly altered only when the epithelial cells are exposed to Ig or other soluble protein from the direction of the intestinal villi and not the capillary bed.

In Trial I, the absorbed IgG mean serum titers for male and female calves were 5.52 and 5.57 mg/ml, respectively (Table 2). Since these values were not statistically different ($P > .05$), the data were compared to Trial II, without regard for sex, to determine the effect of climate on the absorbed IgG serum concentrations.

As previously reviewed, heat stress in Arizona has recently been shown to depress Ig serum concentration in calves 48 hours of age (81). In the present study maximum ambient temperatures ranging from 92 to 114°F occurred during the first 24 hours of life for calves in Trial I. Minimum and maximum mean values accordingly were 78.6 and 105.6°F. In contrast peak temperatures during Trial II ranged from 60 to 74°F with minimum and maximum mean values of 51.6 and 69.0°F, respectively. Despite these differences in seasonal temperatures, the absorbed IgG serum values were similar for calves in both trials. The means and standard deviations for absorbed IgG in Trial I, 5.54 ± 1.88 mg/ml and Trial II, 5.45 ± 1.56 mg/ml were not different ($P > .05$). However, in Trial I calves were not exposed to the more severe heat stress conditions experienced by calves in the metal roofed hutch type pens (81).

Since climate apparently had little overall effect on the serum IgG titers of calves in this study the data for Trials I and II were combined (Table 4). The absorbed IgG mean serum value and standard deviation for the combined data of the 44 calves was 5.51 ± 1.83 mg/ml. Seventy percent of the calves had absorbed IgG serum values between 4.0 and 7.0 mg/ml, with approximately 16% being greater than 7.0 and 14% less than 4.0 mg/ml (Table 4).

Table 4. Absorbed IgG and percent of ingested IgG in the serum of calves 24 hours after colostrum ingestion relative to sex, birth weight and dystocia, Trials I and II.

Data are in order of absorbed IgG in the serum.

Trial	Calf No.	Sex	Birth Wt. (lb)	Dystocia	Absorbed IgG Titer mg/ml	Absorbed IgG Titer % of IgG[a] Ingested
I	555	M	66		.24	1.5
I	34	F	82		2.29	14.3
I	318B[b]	F	63		2.32	14.4
II	406	M	117	severe	3.02	18.8
I	61	M	90		3.86	24.0
I	58	M	80		3.86	24.0
II	401	M	78		3.89	24.2
I	47A	F	65	mild	4.35	27.1
I	47B	F	70	mild	4.35	27.1
I	306	F	114		4.35	27.1
II	402	M	101		4.44	27.7
II	409	M	94	mild	4.44	27.7
II	414	M	88		4.44	27.7
II	412	M	110		4.54	28.3
II	415	M	71		4.54	28.3
I	59	M	89		4.71	29.3
I	403	F	75		4.93	30.7
I	75	F	79		5.02	31.3
II	410	M	113		5.07	31.6
II	403	M	99	mild	5.70	35.5
II	405	M	98		5.80	36.1
II	411	M	100		5.80	36.1
I	379	M	84		6.04	37.6
I	70	M	61		6.04	37.6
I	45	F	81		6.04	37.6
I	409	M	86		6.04	37.6
I	42	M	90		6.04	37.6
I	318A	M	73		6.04	37.6
I	346	F	97		6.16	38.4
I	205	M	92		6.28	39.1
I	79	F	79		6.28	39.1
I	39	F	58	mild	6.28	39.1
I	395	F	94		6.52	40.6
I	444	F	58		6.76	42.1
I	69	M	103	mild	6.76	42.1

Table 4. (Continued).

Trial	Calf No.	Sex	Birth Wt. (lb)	Dystocia	Absorbed IgG Titer mg/ml	Absorbed IgG Titer % of IgG[a] Ingested
I	419	M	65		6.76	42.1
II	407	M	98		6.76	42.1
II	413	M	105	mild	6.76	42.1
I	426	M	71		7.10	44.2
I	62	M	83		7.49	42.6
II	408	M	105		7.49	42.6
I	334	F	75	mild	8.69	54.1
II	404	M	98		9.06	56.4
I	343	F	75		9.18	57.2

a. Percent of total IgG ingested present in the serum.

b. A, B indicates twin calves.

There were not significant (P >.05) differences in serum pattern of absorbed IgG with respect to the following independent variables: sex, body weight, and dystocia (Tables 4 and 5). Since calves in this experiment were fed a specified amount of pooled colostrum per unit body weight there was no relationship between amounts of colostrum consumed and subsequent serum levels of IgG. In contrast, when calves were fed different amounts of colostrum, other workers found that 50 and 68% of the variation in blood serum Ig levels could be attributed to differences in amount of Ig consumed per unit body weight (9, 10).

Although nine calves encountered some difficulty during birth only one calf experienced severe dystocia (Table 4). The calf (number 406), was apparently injured and had great difficulty standing on its rear legs. It also had the lowest IgG serum titer, 3.02 mg/ml, of the nine calves in this category.

The amount of ingested IgG present in the serum at 24 hours was determined for comparison with other studies (9, 52). A plasma volume of 93 ml/kg of body weight at 72 hours of age (51) and the 24 hour concentration of absorbed IgG per milliliter of serum were used to calculate the total absorbed IgG contained in the serum 24 hours after colostrum consumption. The figure is expressed as a percent of the total colostral IgG ingested (Table 4).

Table 5. Absorbed IgG range and mean serum titers in calves 24 hours after colostrum ingestion relative to sex, birth weight and dystocia, Trials I and II.

	No. of Calves	Absorbed IgG Titer	
		Range	Mean[a]
Sex			
Males	29	0.24 - 9.06	5.51
Females	15	2.29 - 9.18	5.52
Birth Wt. (3 subgroups)			
58 - 79 (lb)	17	0.24 - 9.18	5.46
80 - 99 (lb)	18	2.29 - 9.06	5.64
100 - 117 (lb)	9	3.02 - 7.49	5.36
Dystocia			
Dystotic	9	3.02 - 8.69	5.60
Non-dystotic	35	0.24 - 9.18	5.49

a. Means within groups did not differ (P >.05).

Between 1.5% and 57.2% of the IgG consumed could be accounted for in the serum of individual calves at 24 hours. The mean value for all calves was 34.3%. This figure is comparable to those obtained in a similar manner by other workers who reported mean absorption efficiencies of 45% (9) and 25% (52) in the serum of calves at 24 and 72 hours of age, respectively. During the first 72 hours of life the intravascular or plasma volume of the calf has been observed to expand approximately 40% and produce a dilution effect of plasma constituents in association with liquid consumption (51). This may account for the higher absorbed IgG serum concentrations obtained at 24 hours in this study and by other workers (9) in comparison to the lower value reported at 72 hours (52). It is also recognized that time of blood sampling does not always coincide with peak concentration of serum Ig which may range between 12 and 48 hours of age (9).

Another factor that gives rise to an apparently low intestinal Ig absorption efficiency based on serum values is that no measure is made of Ig in the extravascular pool. When the latter factor was estimated by the above workers (52), using an extravascular to intravascular ratio of 1.2/1.0, the Ig absorption efficiency was 55% compared to the serum value of 25%. In the present study, using the same ratio, total IgG absorption efficiency was 75.5%.

Proteinuria has been reported to occur in newborn humans, puppies, foals and ruminants following the ingestion of colostrum or milk, etc. (8, 40, 50). The presence of protein in the urine of calves coincides with the appearance of Ig in the serum during the period of intestinal permeability and declines to minimum levels following the cessation of intestinal Ig absorption (8, 18, 64). Accordingly, this phenomenon has been suggested to influence serum Ig levels via the circulatory clearance of Ig by the kidney (9, 66). However, the principle constituent of proteinuria in the calf has been shown to arise mainly from the low molecular weight colostral proteins absorbed with Ig (64). Apparently little if any whole or degraded materials resembling colostral Ig normally appear in the urine of the newborn calf.

Results of this study indicate that variations in IgG concentrations in the serum of calves fed a uniform source of colostrum must be attributed largely or entirely to differences in intestinal absorption and not to intrinsic factors in the colostrum. Therefore, in spite of the generally recommended practice of insuring that calves consume colostrum immediately after birth, some calves will remain hypogammglobulinemic irregardless how other variables related to serum IgG are controlled. Further studies to identify the cause for the wide variations in efficiency of intestinal IgG absorption in dairy calves are needed.

LITERATURE CITED

1. Aschaffenburg, R., S. Bartlett, S. K. Kon, J. H. B. Roy and D. M. Walker. 1951. The Nutritive Value of Colostrum for the Calf. Br. J. Nutr. 5:171.

2. Balfour, W. D. and R. S. Comline. 1959. The Specificity of the Intestinal Absorption of Large Molecules by the Newborn Calf. J. Physiol. Lond. 148:77.

3. Balfour, W. E. and R. S. Comline. 1962. Acceleration of the Absorption of Unchanged Globulin in the Newborn Calf by Factors in Colostrum. J. Physiol. Lond. 160:234.

4. Bangham, D. R., P. L. Ingram, J. H. B. Roy, K. W. G. Shillam and R. J. Terry. 1958. The Absorption of ^{131}I-labelled Serum and Colostral Proteins from the Gut of the Young Calf. Proc. Royal Soc. 149:184.

5. Becton-Dickinson Vacutainer. Division of Becton, Dickinson and Company, Rutherford, New Jersey.

6. Bonewitz, R. 1973. First Five Hours Important for New Calves. Modern Dairyman. March 17:35.

7. Boyd, J. W. 1972. The Relationship between Serum Immune Globulin Deficiency and Disease in Calves; A Farm Survey. Vet. Rec. 90:645.

8. Brambell, F. W. R. 1970. The Transmission of Passive Immunity from Mother to Young. American Elsevier Publishing Company, Inc., New York.

9. Bush, L. J., M. A. Aguilera and G. D. Adams. 1971. Absorption of Colostral Immunoglobulins by Newborn Dairy Calves. J. Dairy Sci., 54:1547.

10. Bush, L. J., M. B. Mungle, L. D. Corley and G. D. Adams. 1973. Factors Affecting Absorption of Immunoglobulins by Newborn Dairy Calves. J. Dairy Sci. 56:312.

11. Butler, J. E. 1969. Bovine Immunoglobulins: A Review. J. Dairy Sci. 52:1895.

12. Campbell, D. H., J. S. Garvey, N. E. Cremer and D. H. Sussdorf. 1970. Methods in Immunology. W. A. Benjamin, Inc., New York.

13. Clark, S. L. 1959. The Ingestion of Proteins and Colloidal Materials by Columnar Absorptive Cells of the Small Intestine in Suckling Rats and Mice. J. Biophysic. and Biochem. Cytol. 5:41.

14. Clarke, R. M. and R. N. Hardy. 1971. Histological Changes in the Small Intestine of the Young Pig and their Relation to Macromolecular Uptake. J. Anat. 108:63.

15. Comline, R. S., H. E. Roberts and D. A. Titchen. 1951. Route of Absorption of Colostrum Globulin in the Newborn Animal. Nature 167:561.

16. Comline, R. S., H. E. Roberts and D. A. Titchen. 1951. Histological Changes in the Epithelium of the Small Intestine during Protein Absorption in the Newborn Animal. Nature 168:84.

17. Crowley, J. W. 1973. The Feeding Value of Colostrum Varies. Hoard's Dairyman. 188:685.

18. Deutsch, H. F. and V. R. Smith. 1957. Intestinal Permeability to Proteins in the Newborn Herbivore. Am. J. Physiol. 191:271.

19. Difco Laboratories, Detroit, Michigan.

20. Divelbiss, R. I. 1975. Immunization Before Birth a Revisited Hope Now Near Reality. Hoard's Dairyman 120:889.

21. Fahey, J. L. and E. M. McKelvey. 1965. Quantitative Determination of Serum Immunoglobulins in Antibody-Agar Plates. J. Immunology 94:84.

22. Fennestad, K. L. and C. Borg-Petersen. 1962. Antibody and Plasma Cells in Bovine Fetuses Infected with Leptospire Saxkoebing. J. Infect. Dis. 110:63.

23. Ferris, T. and J. W. Thomas. 1975. Be Sure Calves Get Enough Colostrum. Hoard's Dairyman 120:947.

24. Fisher, E. W., A. A. Martinez, Z. Trainin and R. Merirom. 1975. Studies of Neonatal Calf Diarrhea. II. Serum and Faecal Immune Globulins in Enteric Colibocillosis. Br. Vet. J. 175:402.

25. Foley, R. C., D. L. Bath, F. N. Dickinson and H. A. Tucker. 1972. Dairy Cattle: Principles, Practices, Problems, Profits. Lea and Febiger Publishing Company, Philadelphia, Pennsylvania.

26. Frandsen, J. H. 1958. Dairy Handbook and Dictionary. Nittany Printing and Publishing Company, State College, Pennsylvania.

27. Gay, C. C. 1965. Escherichia coli and Neonatal Disease of Calves. Bacteriological Rev. 29:75.

28. Gay, C. C., N. Anderson, E. W. Fisher and A. D. McEwan. 1965. Gamma Globulin Levels and Neonatal Mortality in Market Calves. Vet. Rec. 77:148.

29. Graves, J. H. 1963. Transfer of Neutralizing Antibody by Colostrum to Calves Born of Foot-and-Mouth Disease Vaccinated Dams. J. Immunol. 91:251.

30. Halliday, R. 1959. The Effect of Steroid Hormones on the Absorption of Antibody by the Young Rat. J. Endocrinology 18:56.

31. Hansen, R. G. and P. H. Phillips. 1947. Studies on Proteins from Bovine Colostrum. J. Biol. Chem. 171:223.

32. Hardy, R. N. 1969. The Influence of Specific Chemical Factors in the Solvent on the Absorption of Macromolecular Substances from the Small Intestine of the Newborn Calf. J. Physiol. Lond. 204:607.

33. Henderson, J. L. 1971. The Fluid-Milk Industry. 3rd ed. Avi Publishing Company, Inc., Westport, Connecticut, 28.

34. Ingram, D. G., L. B. Corbeil and M. E. Malcomson. 1970. Antibodies to Escherichia coli in Young Calves: K Antigens. Amer. J. Vet. Res. 31:71.

35. Ingram, D. G. and M. E. Malcomson. 1970. Antibodies to Escherichia coli in Young Calves: O. Antigens. Amer. J. Vet. Res. 31:61.

36. Ingram, P. L., R. Lovell and P. C. Wood. 1956. Bacterium Coli Antibodies in Colostrum and their Relation to Calf Survival. J. Path. Bact. 72:561.

37. Irwin, V. C. R. 1974. Incidence of Disease in Colostrum Deprived Calves. Vet. Rec. 94:105.

38. Janeway, C. A., F. S. Rosen, E. Merler and C. A. Alper. 1967. The Gamma Globulins. J. and A. Churchill Ltd., London.

39. Jarret, J. A. 1974. Colostrum from your Older Cows is Best for New Calves. Hoard's Dairyman 119:1300.

40. Jeffcott, L. B. 1972. Passive Immunity and its Transfer with Special Reference to the Horse. Biol. Rev. 47:439.

41. Johnson, P. and A. E. Pierce. 1959. Ultracentrifugal and Electrophoretic Studies on Neonatal Calf Sera and Maternal Colostrum. J. Hyg. 57:309.

42. Kim, Y. B., S. G. Bradley and D. W. Watson. 1966. Otogeny of the Immune Response. I. Development of Immunoglobulins in Germ-Free and Conventional Colostrum-Deprived Piglets. J. Immunol. 97:52.

43. Klaus, G. G. B., A. Bennett and E. W. Jones. 1969. A Quantitative Study of the Transfer of Colostral Immunoglobulins to the Newborn Calf. Immunology 16:293.

44. Kruse, V. 1970. Yield of Colostrum and Immunoglobulin in Cattle at the First Milking After Parturition. Anim. Prod. 12:619.

45. Kruse, V. 1970. Absorption of Immunoglobulin from Colostrum in Newborn Calves. Anim. Prod., 12:627.

46. Larson, B. L. and K. A. Kendall. 1957. Protein Production in the Bovine. Daily Production of the Specific Milk Proteins During the Lactation Period. J. Dairy Sci. 40:377.

47. Lecce, J. G. 1966. In Vitro Absorption of Gamma-Globulin by Neonatal Intestinal Epithelium of the Pig. J. Physiol. 184:594.

48. Martin, S. W., C. W. Schwabe and C. E. Franti. 1975. Dairy Calf Mortality Rate: Influence of Meteorologic Factors on Calf Mortality Rate in Tulare County, California. Amer. J. Vet. Res. 36:1105.

49. McCoy, G. C., A. G. Hunter and J. B. Williams. 1968. Effects of Diet and Time on the Circulating Gamma Globulin Concentration in the Newborn Calf. J. Dairy Sci. 51:964.

50. McDougall, E. I. 1965. Proteinuria of Newborn Suckling Ruminants. Biochem. J. 94:101.

51. McEwan, A. D., E. W. Fisher and I. E. Selman. 1968. The Effect of Colostrum on the Volume and Composition of the Plasma of Calves. Res. Vet. Sci. 9:284.

52. McEwan, A. D., E. W. Fisher and I. E. Selman. 1970. An Estimation of the Efficiency of the Absorption of Immune Globulins from Colostrum by Newborn Calves. Res. Vet. Sci. 11:239.

53. McEwan, A. D., E. W. Fisher and I. E. Selman. 1970. Observations on the Immune Globulin Levels of Neonatal Calves and their Relationship to Disease. J. Comp. Path. 80:259.

54. Miles Laboratories, Inc., Research Products Div., Kankakee, Illinois.

55. Moog, F. 1962. Developmental Adaptations of Alkaline Phosphatases in the Small Intestine. Fed. Proc. 21:51.

56. Myers, W. L. and D. Segre. 1963. The Immunologic Behaviour of Baby Pigs. III. Transplacental Transfer of Antibody Globulin in Swine. J. Immunol. 91:697.

57. Orcutt, M. L. and P. E. Howe. 1922. The Relation Between the Accumulation of Globulins and the Appearance of Agglutinins in the Blood of Newborn Calves. J. Exp. Med. 36:291.

58. Osburn, B. I. and R. K. Hoskins. 1969. Antibody Responses to Brucella ovis in Maternal and Fetal Sheep. J. Infect. Dis. 119:267.

59. Patt, J. A., A. Zarkower and R. J. Eberhart. 1972. Effect of Histamine on Intestinal Absorption of Gamma Globulin in Newborn Calves. J. Dairy Sci. 55:645.

60. Payne, L. C. and C. L. Marsh. 1962. Gamma Globulin Absorption in the Baby Pig: The Nonselective Absorption of Heterologous Globulins and Factors Influencing Absorption Time. J. Nutr. 76:151.

61. Payne, L. C. and C. L. Marsh. 1962. Absorption of Gamma Globulin by the Small Intestine. Fed. Proc. 21:909.

62. Penhale, W. F., G. Christie, A. D. McEwan, E. W. Fisher and I. E. Selman. 1970. Quantitative Studies on Bovine Immunoglobulins. Br. Vet. J. 126:30.

63. Pierce, A. E. 1955. Electrophoretic and Immunological Studies on Sera from Calves from Birth to Weaning. I. Electrophoretic Studies. J. Hyg., Camb. 53:247.

64. Pierce, A. E. 1961. Further Studies on Proteinuria in the Newborn Calf. J. Physiol. Lond. 156:136.

65. Pierce, A. E. and A. Feinstein. 1965. Biophysical and Immunological Studies on Bovine Immune Globulins with Evidence for Selective Transport within the Mammary Gland from Maternal Plasma to Colostrum. Immunology 8:106.

66. Pierce, A. E. and P. Johnson. 1960. Ultracentrifuge and Electrophoretic Studies on the Proteinuria of the Newborn Calf. J. Hyg., Camb. 58:247.

67. Pierce, A. E. and M. W. Smith. 1967. The Intestinal Absorption of Pig and Bovine Immune Lactoglobulin and Human Serum Albumin by the Newborn Pig. J. Physiol. Lond. 190:1.

68. Reade, P. C., C. R. Jenkin and K. J. Turner. 1965. The synthesis by Foetal Chicks and Rats of Serum Proteins Having Some Properties of Immunoglobulins. Aust. J. Exp. Biol. Med. Sci. 43:699.

69. Rice, C. E. and J. Carriere. 1969. Studies of Changes in Serum Proteins in Cows and Calves in a Herd Affected with Johne's Disease. Res. Vet. Sci. 10:188.

70. Selman, I. E., A. D. McEwan and E. W. Fisher. 1970. Serum Immune Globulin Concentrations of Calves Left with their Dams for the First Two Days of Life. J. Comp. Pat. 80:419.

71. Silverstein, A. M., J. Uhr, K. L. Kraner and R. J. Lukes. 1963. Fetal Response to Antigenic Stimulus. II. Antibody Production by the Fetal Lamb. J. Exp. Med. 117:799.

72. Smith, E. L. 1948. The Isolation and Properties of Immune Proteins of Bovine Milk and Colostrum and their Role in Immunity; A Review. J. Dairy Sci. 31:127.

73. Smith, H. C. 1965. The Perennial Problem of Calf Scours. Mod. Vet. Practice 46:51.

74. Smith, H. W., J. A. O'Neil and E. J. Simmons. 1967. The Immune Globulin Content of the Serum of Calves in England. Vet. Rec. 80:664.

75. Smith, T. and R. B. Little. 1922. The Significance of Colostrum to the Newborn Calf. J. Exp. Med. 36:181.

76. Smith, V. R. and E. S. Erwin. 1959. Absorption of Colostrum Globulins Introduced Directly Into the Duodenum. J. Dairy Sci. 42:364.

77. Smith, V. R., R. E. Reed and E. S. Erwin. 1964. Relation of Physiological Age to Intestinal Permeability in the Bovine. J. Dairy Sci. 47:923.

78. Soulsby, E. J. L. 1972. Immunity to Animal Parasites. Academic Press, Inc., New York.

79. Steinbach, G. and H. Meyer. 1965. The Effect of Feeding Silage to Pregnant Heifers on the Composition of Colostral Milk and on the Vitality of the Newborn Calves. Vet. Med. 20:87.

80. Stoddard, C. D. 1975. Vaccinating Cows Saves Calves from Salmonella. Hoard's Dairyman 120:223.

81. Stott, G. H., F. Wiersma, B. E. Menefee and F. R. Radwanski. 1975. Environment Affecting Passive Immunity in Dairy Calves. J. Dairy Sci. 58:767.

82. Tennant, B., D. Harrold, M. Reina-Guerra and R. C. Laben. 1969. Neonatal Alterations in Serum Gamma Globulin Levels of Jersey and Holstein-Fresian Calves. Amer. J. Vet. Res. 30:345.

83. United States Department of Commerce. 1975-1976. Local Climatological Data, Federal Building, Asheville, North Carolina.

84. Warner, R. G. 1970. Feeding and Management of Veal Calves. Hoard's Dairyman 115:819.