ABSORPTION OF COLOSTRAL IMMUNOGLOBULINS BY THE NEWBORN CALF

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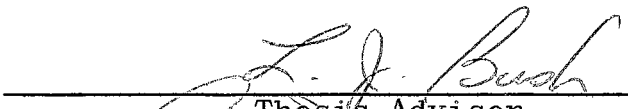

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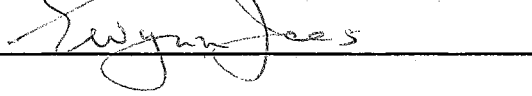

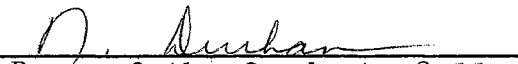

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CHAPTER I

INTRODUCTION

The transfer of maternal antibodies to the newborn ungulate was recognized as early as 1892 by Ehrlich, according to Sarwar (1964). The concept that the colostrum has special properties, distinct from those of normal milk, was developed in 1912 by Famulener, who remarked on the high concentration of immune bodies in the early milk.

Under natural conditions, bovine colostrum confers immunity to the newborn calf at the critical period when defense mechanisms are hypoplastic. At this time, calves are sometimes fed colostrum too haphazardly, which may account to some extent for the high incidence of infections in newborn calves. These infections result in morbidity and mortality which are responsible for heavy economic losses in dairy operations every year.

In ruminants, placental transmission of immunoglobulins does not occur and calves are born with serum protein profiles low or practically devoid of immunoglobulins (Lecce, 1966). Shortly after ingesting colostrum rich in immunoglobulins, increased amounts of these proteins occur in the calf's serum. The rapid postnatal elevation in serum protein concentration results from the absorption of large

amounts of presumably unaltered proteins from colostrum (Brambell, 1958).

In newborn calves, the absorption of colostral immunoglobulins occurs largely in the jejunum, entering the circulation via the lymphatics (El-Nageh, 1967a). Various estimates of the time that this absorption occurs are as follows: first 24 hours (Deutsch and Smith, 1957), 24-30 hours (Smith et al., 1964), 36 hours (Lecce, 1966). Factors which influence and terminate this absorptive mechanism have yet to be fully established. However, El-Nageh (1967b) has stated that immunoglobulin absorption in calves ceases because the aptitude for pinocytosis for proteins is lost after one or two replacements of the intestinal epithelium.

Marked variability in the level of passively acquired immunoglobulins in young calves has been demonstrated by Smith et al. (1967), and this is presumed to result from variation of the colostral intake. However, evidence has been reported suggesting that malabsorption of immunoglobulins may occur (Klaus et al., 1969).

The objective of this work was to determine the effect of the amount of colostral immunoglobulin ingested by newborn dairy calves on the amount absorbed.

CHAPTER II

REVIEW OF LITERATURE

Passive Immunity in Mammals

Passive immunity is that immunity acquired in an individual by immunoglobulins derived from another by transplacental, peroral, or parenteral transfer. It is only temporary and lasts for a few weeks or months (Carpenter, 1965).

According to Brambell et al. (1951), the resistance of the young mammal to disease during early life is contingent upon passive immunity derived from the mother. Antibodies produced by the mother and present in her circulation are transmitted to the young with resulting neonatal serum concentrations approximately equivalent to those of the mother. The transfer of maternal antibodies to offspring may occur before and/or after birth, as shown by the following table (page 4) by Brambell (1958). In man, the guinea pig, and rabbit, the transmission of immunoglobulins occurs in utero (Brambell, 1958). Ruminants, horse, and pig do not acquire immunoglobulins via the placenta and are born with just traces of serum antibodies (Brambell, 1958). In these species, immunoglobulins are therefore derived from initial

feedings of colostrum which is rapidly absorbed from the gut of the newborn animal. Absorption of colostrum is so rapid that within a few hours after birth serum gammaglobulin concentrations have reached values approximating those of maternal serum (Brambell, 1969). However, in these animals the capacity to absorb protein macromolecules from the gut is lost (closure) within 36 hours of birth (Lecce, 1966).

TABLE I

TRANSMISSION OF PASSIVE IMMUNITY

Species	Prenatal	Postnatal
Ox, goat, sheep	0	+++ (36 hrs)
Pig	0	+++ (36 hrs)
Horse	0	+++ (36 hrs)
Dog	+	++ (10 days)
Mouse	+	++ (16 days)
Rat	+	++ (20 days)
Guinea-Pig	+++	0
Rabbit	+++	0
Man	+++	0

Small, but significant, amounts of maternal antibodies occur in the serum of newborn animals such as rat, mouse, dog, and probably cat, prior to nursing. The passive immunization in these animals is both pre and postnal, and they continue to absorb antibodies from the gut for much longer periods than do ruminants. Most maternal antibody is

derived from colostrum and milk, and the intestinal closure occurs at 20, 16, and 10 days in the rat, mouse and dog, respectively (Brambell, 1958).

Bovine Immunoglobulins

General Characteristics

Within recent years it has become apparent that antibody activity is associated with a heterogeneous group of proteins known as immunoglobulins. Immunoglobulin is a general term which is applied to a group of high molecular weight proteins sharing common physico-chemical characteristics and common antigenic determinants. These compounds having gamma or slow beta electrophoretic mobility, occur in the blood serum and other body fluids in the animal body. This group of protein includes all molecules with antibody activity, as well as other chemically related normal or pathological proteins. Although certain types of antibody activity are associated with particular classes of immunoglobulins their classification is not based on antibody specificity but on antigenic and physico-chemical characteristics. All immunoglobulins appear to be either monomers or polymers of a 4-chain molecule consisting of two light polypeptide chains (L-chains) with 20,000 molecular weight and two heavy polypeptide chains (H-chains) with molecular weight varying from 50,000 to 70,000 for the different immunoglobulin classes (Butler, 1969).

At present, several types of immunoglobulins have been

recognized in man. These are IgGK, IgGL, IgMK, IgML, IgAK, IgD, and IgE (Martin, 1969), according to the recommended nomenclature (Bulletin World Health Organization, 1964). In the cow, three antigenically distinct classes of immunoglobulins have been identified. IgG and IgM occur in serum and lacteal secretions and IgA occurs mainly in lacteal secretions (Murphy et al., 1964a).

The bovine IgG immunoglobulins are divided into two subclasses, IgG1 and IgG2. IgG1 is selectively transported from the blood circulation to the lacteal secretion by mechanisms yet to be elucidated, and is the principal immunoglobulin for passive immunization of newborn calf (Micusan, 1965). Although there is normally no significant difference between the serum concentrations of IgG1 and IgG2, IgG1 is the principal immunoglobulin of the lacteal secretion (Kickofen et al., 1968). The two subclasses differ antigenically, and in amino acid composition, and both possess a sedimentation coefficient of approximately 7S (expressed in Svedberg units).

Bovine IgG has been isolated from blood serum, milk, and colostrum of the cow. It is also the most abundant immunoglobulin known in cow. Klaus et al. (1969) stated that at least 85 to 90 percent of blood serum and colostral whey immunoglobulins are of this class.

The homology of bovine IgG to the other species is suported by the findings that human gamma chains share antigenic determinants with bovine, caprine and ovine gamma

chains (Aalund et al., 1965).

Bovine IgM, an antigenically distinct macroglobulin, occurs in blood serum, colostrum and milk, comprising less than 10 percent of serum and colostral immunoglobulins. It is important in primary immune responses, complement fixation, and as an agglutinating antibody for serum, and has a sedimentation coefficient of 19S (Murphy et al., 1964b). Although similar to the IgM of other species, bovine IgM may be more electrophoretically heterogeneous (Murphy et al., 1964b).

Bovine IgA occurs as secretory IgA in milk and colostrum and its exact role is poorly understood in all species. It possesses a sedimentation coefficient of 10 to 12S (Svedberg units) for the lacteal form (Gough et al., 1966).

Colostrum in the Passive Immunity of Calves

During foetal life, all mammals are totally dependent on their mother, for nutrients, temperature control, and protection against injury and infections. At birth, this protection is terminated (Hafez, 1968). At this time, colostrum plays a very important role in ungulates providing nutrients and protection against infections, until they are able to produce their own immunity.

The first drawn milk after parturition is known as colostrum and milk is usually not considered normal until about the fifth day after calving (Turner, 1930). During

this period the total solids, especially the globulins and other proteins, are high, whereas the lactose content is lower than in normal milk. Even greater differences between normal milk and colostrum lies in their antibody titers (Smith, 1948). The blood serum of newborn calves contains practically none of the gamma globulins, which means that the newborn calf is highly susceptible to pathogenic organisms unless given the colostrum milk, from which it quickly absorbs the disease-resisting principle. Changes in colostral protein composition after parturition are presented in the following table, with data obtained from Allen and Jacobson (1956) and Jennes and Patton (1959).

TABLE II

COMPOSITION OF COLOSTRUM OF THE COW

	Days after calving		
Constituents: Proteins	0	3	5
	%		
Casein	5.9	3.1	3.1
Albumin	2.2	0.5	0.5
Globulin	4.5	0.4	0.3
Total Dry Matter	28.6	13.0	13.0

The use of radioactive isotypes has indicated that

colostral immunoglobulins are not synthesized in the udder, but in the reticuloendothelial system. These are passed from the blood serum into the udder. Therefore, prior to parturition, there is a decrease in serum globulin fraction (Dixon et al., 1961). The physiological changes which permit an influx of these globulins into the udder near parturition are unknown (Larson, 1958). Larson and Gillespie (1957) have shown that the immunoglobulins and milk albumin have properties identical to the protein of blood. These proteins apparently pass unchanged from the blood stream into milk. The gamma casein is similar in nature to the globulins and occurs in high levels in colostrum, which suggested that this protein also may enter the udder performed from the blood. Extensive studies by Dixon et al. (1961) have clearly shown a concentrating mechanism present in the alveolar cells of the mammary gland in the cow responsible for the transfer of large amounts of immunoglobulins from serum to colostrum and milk.

During the early phase when macromolecules can be absorbed, presumably the neonate's intestinal epithelium is not yet mature and absorption takes place by a primitive mechanism similar to that found in macrophages, planaria and amoeba (Chapman-Adresen, 1964). This mechanism is called pinocytosis, that is, cell drinking, accomplished by the folding and interiorizing of the cell's surface membrane.

The place where the maternal immunoglobulins are absorbed in the newborn calf is the mucosa of the small

intestine (jejunum, the last portion of duodenum, and the beginning of the ileum) and the channels of absorption of such proteins are the lymphatics of those regions (El-Nageh, 1967a). It is also well known (Smith, 1948) that the globulins ingested and absorbed by the newborn calf have mobility of the same order as serum gamma globulins and originate from serum proteins of the dam. Pierce and Feinstein (1965), and earlier workers, have also concluded that the intestinal tract of the newborn calf absorbs various types of protein indiscriminately.

Bangham et al. (1968) studied the absorption of ^{131}I labeled serum and colostral proteins from the gut of the young calf by tracer and electrophoretic techniques to find out whether the calf's gut has any selectivity for its mother's proteins. Several proteins present in the labeled serum and colostrum appeared to be absorbed with equal facility. There was no evidence that the calf's gut had any selectivity in the absorption of proteins such as is known to occur in the newborn rat (Halliday and Kekwick, 1960) and pig (Locke et al., 1964). Similarly, Klaus et al. (1969) found that the correlation coefficient of percent colostral IgM and percent of colostral IgG absorbed was 0.94, meaning that there was no selectivity in absorption of these proteins.

The maternal antibodies which ultimately enter the colostrum are elicited by the antigenic environment, with the immunoglobulins synthesized being specific for these

immunogens (Reisinger, 1965). It is, therefore, readily understandable why the maternal colostrum protects the young calf during the first hours of life.

Factors Affecting Immunoglobulin Absorption in Newborn Calves

Several factors are involved in this respect. Age of the calf is probably one of the most significant factors influencing absorption of immunoglobulins from the gut. It is well accepted at the present time that the gut permeability for immunoglobulins and other protein molecules in newborn calves lasts for a limited period. Deutsch and Smith (1957) have shown that permeability of the calf gut is maintained for approximately 24 hours following birth. Smith et al. (1964) studied the relation of physiological age to intestinal permeability in the bovine and found that this ability to absorb whole proteins is limited to the calf's first 24 to 30 hours of life. Thereafter, even if immunoglobulin is fed, no measurable increase can be detected in the calf's serum gammaglobulin. In some cases, however, this limit may be over estimated, as Gay et al. (1965) found in some calves that the capacity to absorb globulins from colostrum was lacking by four to six hours after birth. Leece (1966) stated that this unique capacity to absorb macromolecules ceases after approximately the first 36 hours of life. El-Nageh (1967a) found in three experiments that the intestinal absorption of colostrum

globulins occurred mainly during the first and to a lesser extent during the second day of life; however, some absorption was detectable in certain calves aged 52 to 53 hours.

The reason for the impermeability of the intestine (closure) of the calf to whole protein after the first few hours of life has not been definitely determined. El-Nageh (1967b) offered an explanation concerning cessation of absorption of immunoglobulins and other macromolecules in newborn calves, saying that the aptitude for pinocytosis of protein is probably lost after one or two replacements of the intestinal epithelium. Hill (1956) suggested that the cessation of intestinal absorption of immune proteins from colostrum by the newborn of several species coincides with the development of gastric protein digestion. One explanation of this relationship is that after gastric digestion is initiated colostral proteins are digested.

Deutsch and Smith (1957) reported results of several attempts to increase the period of gut permeability in the newborn calf. Administration of diethylstilbestrol and progesterone singly and in combination with each other did not alter intestinal permeability to immune proteins. Nor was permeability affected by cortisone or ACTH injections via several routes. Since the fetus was known to consume quantities of amniotic fluid during the latter part of gestation, the possibility of a permeability factor in the fluid was considered. Feeding amniotic fluid to calves failed to extend the time of intestinal permeability to

immune proteins (Deutsch and Smith, 1957). Also, inhibitors of deoxyribonuclease were administered to check whether deoxyribonucleic acids were influential in maintaining permeability of the gut, but the inhibitors had no effect in delaying permeability.

In other studies, Deutsch and Smith (1957) treated newborn calves with $Al(OH)_3$ gel to inhibit gastric activity and prevent gastric digestion of immune proteins. The treatment did not lengthen the time of intestinal permeability. These same workers also investigated the possibility of the immune protein being degraded by gastric and intestinal enzymes. Forty-eight-hour-old calves failed to absorb immune proteins when colostrum was infused directly into the duodenum (Smith and Erwin, 1959). The importance of calves receiving colostrum as early as possible after birth is obvious. Even so, two of seven calves that were given their first feed of colostrum with two hours of birth had very low immunoglobulin levels (Smith et al., 1967). Eight of the 80 calves that were seen to suckle within a few hours of birth also had very low levels of immunoglobulins in their blood serum. It is thus probable that, other factors apart, the serum immunoglobulin levels in neonatal calves kept under ordinary conditions are determined to a considerable extent by the ability of their alimentary tract to absorb immunoglobulins from colostrum or inability to digest them. Calves vary greatly in this respect.

Other factors affecting immunoglobulin absorption that

deserve some attention. Smith et al. (1967) stated that after examination of the blood serum immunoglobulin levels of hundreds of calves in different farm operations, the calves that received all their colostrum by bucket had, in general, lower values than those for the calves nursing the cow. Additional studies of a more detailed nature, however, are clearly necessary before any conclusions can be drawn as to the influence the method of administration of colostrum may have on immunoglobulin levels.

Another factor that could influence colostral immunoglobulin absorption is the presence of large amounts of amniotic fluid in the abomasum of the newborn calf at birth. This may retard the passage of colostrum to the small intestine and, hence, reduce the absorption of the immunoglobulins (El-Nageh, 1967a).

Hardy (1969) studied the influence of specific chemical factors on the absorption of macromolecular substances from the small intestine of the newborn calf and found that lactate, pyruvate, and salts of certain lower volatile fatty acids resemble factors in colostral whey in their facilitation of the absorption of gammaglobulins. However, these active compounds were not found in colostrum in significant quantities. Potassium isobutyrate was the most effective of the compounds tested, and generally accelerated absorption to a greater degree than did colostral whey itself.

Several other factors could impair absorption of immunoglobulins such as: weak animals at birth, early

infection of the calf, mastitis of the cow (Blood and Henderson, 1963), inherited traits (difference between breeds), individual variability, enzyme systems from the calf's gut, hormones, lactation of the cow, cow's age, type of ration used, concentration of immunoglobulins in colostral whey, proportion of the different components in colostrum and unknown factors that could come from the mother, from the calf, the colostrum, or the environment.

Effect of Deficiency of Gammaglobulins in Newborn Calves

Recent studies (Gay et al., 1965; Smith et al., 1967) have re-emphasized the importance of the role of maternally derived immunoglobulins in maintaining the health of newborn calves. Jones (1967) tried to detect IgG postpartum in calves to see whether this variation in absorption of immunoglobulins from colostrum is critical. In this report he stated that only three of twelve calves apparently absorbed maternally derived IgG, the rest of the calves remaining free of IgG. Electrophoretic studies of all the colostrum samples did not indicate any material difference in the amount of IgG available for absorption. These findings were similar to the results of Klaus et al. (1969) where of 10 calves, three remained virtually agammaglobulinemic.

Fey and Margadent (1962) demonstrated a relationship between agammaglobulinaemia and colisepticaemia, while Gay et al. (1965) also demonstrated a relationship between

death from causes other than colisepticaemia and the concentration of gammaglobulin in the serum. In their studies, low concentrations of gammaglobulin in calf sera were associated often with death from diarrhea. They also observed that low levels of immunoglobulins were much more common in calves born in winter and spring than at other times of the year. They were of the opinion that the seasonal variations in immunoglobulin levels might offer some explanation for the seasonal differences in calf mortality.

One of the classical symptoms of deficiency of immunoglobins in calves is the high susceptibility to infections and the most common among them is scours (Marsh, 1968). Calf scours, a common problem during the first few days of life, is frequently fatal. Reisinger (1965) attributed 90 percent of all dairy calf diarrhea mortalities to this disease complex. Ensminger et al. (1955) ranked calf scours second in over-all importance (without regard to ages) among beef cattle diseases. Early calving in unsanitary corrals and sheds in inclement weather has increased the problem in some range areas. Blood and Henderson (1963) have stated that the incidence of this disease decreases as husbandry methods are intensified, and colostrum is administered as soon as the newborn calf is able to suckle.

Gay et al. (1965) studied the immunoglobulin level of 178 newborn calves at 4 days of age that were treated on regular farm management procedures. Fifty-three (29.8%) were markedly or absolutely deficient in sera gammaglobulins

and 33 (18.5%) possessed low globulin levels. A total of 31 calves died with colisepticaemia and 11 from other causes. All but one of the deaths from colisepticaemia were in calves whose sera were markedly deficient and the majority of these deaths were in calves considered absolutely deficient in immunoglobulins. Smith (1962) found a great variation in the levels of immunoglobulins in the blood serum of 52 calves that had spent the first two days of life with their dams, and which would have had access to colostrum. Of six of these calves with very low or no immunoglobulins, three died from bacteriemia. Very low levels of immunoglobulins also were found by Fey and Margadent (1962) in the blood serum of five out of 46 calves that had received maternal colostrum. These workers showed that 21 of 22 calves that have received colostrum, but had died of Escherichia coli bacteriemia, had no or only small amounts of immunoglobulins in their serum. However, results obtained by Dam (1968) have shown a somewhat lower average gammaglobulin level in calves which later succumbed to colisepticaemia, but 25 percent of the surviving calves had a percentage of gammaglobulin lower than the average for the calves that succumbed to septicaemia, and 35 percent had a lower content of gammaglobulin. It was concluded that although hypogammaglobulinaemia may well be of the main factors in colisepticaemia, it is hardly of as great importance as environmental factors such as housing, feeding, and management.

CHAPTER III

MATERIALS AND METHODS

Experimental Plan

In this experiment 27 cows and their calves were chosen at random from the dairy herd at Oklahoma State University.

All cows were bled immediately after parturition and all calves were bled at the following times: immediately after birth (pre-nursing) and at 3, 12, 24, 48, 96, and 168 hours after birth. The blood samples taken were examined for serum total proteins and immunoglobulin concentration.

Sufficient colostrum was milked by hand immediately after parturition to feed the calf and to provide a colostral sample. Subsequently, cows were machine milked at 12, 24, and 36 hours. Colostrum obtained at each milking time was fed to the appropriate calves by means of nippled pail. The amount of colostrum fed was 2.5% of the calf's body weight at 0 and 12 hours after birth, and 3.75% of the original body weight at 24 and 36 hours. From 48 hours on, milk from other cows was fed at the rate of 5% of birth weight every twelve hours until they were 15 days old. Colostrum samples taken at 0, 12, and 24 hours after parturition were assayed for total protein, immunoglobulin and percentage of colostral whey.

Experimental Animals

The cows and calves used in this study were part of the dairy herd of the Department of Animal Sciences and Industry at Oklahoma State University, consisting of pure breed animals of the Holstein-Friesian, Guernsey, Jersey and Ayrshire breeds. Age, breed, type of parturition, lactation number, general health and number of each cow was recorded at parturition (Table IV, Appendix).

Breed, weight, temperature, diarrhea rating, general health and death losses were recorded for calves throughout the experiment (Table V, Appendix).

Collection of Samples

The blood samples were obtained by jugular venipuncture with hypodermic needle (caliber 18), one and one-half inches long. The 5 to 8 ml. of blood obtained were stored in clean sterile 10 ml. glass vials at 5°C for not longer than 12-14 hours. The samples were free of anticoagulants or any kind of chemicals.

Colostral samples were collected by mixing the total amount obtained from the four quarters of the udder and pouring 40 to 45 ml. into a clean plastic container of 50 ml. capacity. Afterwards, the samples were frozen at -20° C and kept until sufficient samples were accumulated to perform the laboratory procedures on a group of samples.

Laboratory Procedures

Blood serum was separated by centrifugation at 2,100 rpm for 15 minutes. The serum was removed with a clean pippete and transferred to a properly labeled new glass tube, and either processed immediately or stored at -20°C until more samples were obtained.

The frozen colostral samples were allowed to thaw at room temperature and then mixed gently. A 10 ml. aliquot was taken from each sample and centrifugated at 2,100 rpm for 15 minutes to separate the fat from the colostrum, leaving colostral whey which included casein. The colostral whey samples were then transferred to tubes of 10 ml. capacity and acidified to pH 4.6 with concentrated HCl to precipitate the casein. The samples were centrifugated at 2,100 rpm for 5 minutes to separate the casein from the rest of the sample. The supernatant, colostral whey, was removed and adjusted to pH 7, by adding 6N NaOH. These samples were either processed at this point or stored at -20°C.

The percentage of colostral whey was measured to determine the amount of immunoglobulins accurately in every sample of colostrum. An aliquot of 1 ml. was taken from the original sample and centrifugated at 2,100 rpm for 15 minutes in Wintrobe Hematocrit tubes. Subtraction of the fat percentage from the total gave the percent of colostral whey-casein of the samples.

Sample Determinations

a) Total Protein

The total protein of collected sera was determined with a Bansch and Lomb refractometer, prior to storage at -20°C, using the method described by Lecoq (1962). Samples were then stored at -20°C until more samples were obtained, before proceeding to the next steps.

The total protein of colostrum was determined using the same method. Samples were frozen upon collection and processed to recover colostral whey and then total protein was measured. The samples were diluted if necessary to approximate the protein concentration of normal serum.

b) Immunoglobulins

Essentially the same process was used for both blood serum and colostral whey samples. The samples stored at -20°C were thawed at room temperature and electrophoresis was performed using the MicroZone system, which was fully described by Elliott (1966). The method separates each protein fraction according to the migration rate of different molecules in an electric field. The fraction of concern here was the gamma-fraction (gammaglobulins), because most immunoglobulins possess gamma mobility on electrophoresis (Carpenter, 1965).

The actual immunoglobulin concentration in both blood serum and colostral whey was calculated as percentage of

gammaglobulin times the grams of total protein in the sample. This is expressed in grams per 100 ml of sample.

Statistical Analysis

Several estimations were made, describing relationships between amount of immunoglobulins consumed and level of concentrations reached in the blood serum of calves at different hours after birth. Both linear and quadratic regression equations were calculated and analyses of variance were performed to determine which equation was more appropriate for defining the relationships observed.

CHAPTER IV

RESULTS AND DISCUSSION

Serum immunoglobulin concentrations of cows, calves, and colostral whey are summarized in Table III. The immunoglobulin concentration is given in grams per 100 ml. of sample and the figures shown are means, standard deviations, and ranges of groups of samples obtained at designated periods during the experiment.

It is apparent that the mean immunoglobulin concentration of maternal serum is significantly higher than that of the calves at any time during the experiment, an observation comparable with that of Smith et al. (1967). However, some individual calves did have serum immunoglobulin concentrations in excess of that of their respective dams. The rather wide variation in blood serum immunoglobulin concentration of the cows did not appear to be associated with breed or age in this experiment. The causes of this variation are largely unknown and represent an area that could possibly be elucidated in further work involving a large number of animals.

There is some question about the efficacy of immunoglobulin concentration in blood serum of calves in relation to protection against infectious agents. Since a

TABLE III

IMMUNOGLOBULIN CONCENTRATION IN THE SERA OF COWS AND CALVES AND IN COLOSTRAL WHEY

Item	No. of samples	Time of sampling after parturition	Immunoglobulin Concentration Mean*	Range
		(hrs.)	------(gm./100 ml.)-----	
Cow blood serum	27	0	2.30 ± 0.80	1.27 - 4.27
Colostral whey	27	0	12.93 5.03	3.1 - 20.5
	27	12	9.78 4.53	2.8 - 20.0
	24	24	5.75 2.73	2.0 - 13.5
Calf blood serum	27	0	0.29 0.16	0.0 - 0.85
	27	3	0.69 0.40	0.32 - 2.23
	27	12	1.31 0.59	0.50 - 3.03
	27	24	1.55 0.58	0.36 - 2.87
	27	48	1.38 0.58	0.51 - 2.65
	26	96	1.29 0.53	0.43 - 2.26
	26	168	1.13 0.42	0.30 - 1.78

*Mean ± standard deviation.

physiological hypogammaglobulinaemia accompanies parturition in the cow (Dixon et al., 1961), and since the maximal neonatal serum immunoglobulin concentrations are significantly lower than those of their dams in the majority of calves, the efficiency of transfer of maternal anitbody to the neonate may well be questioned.

Colostral samples tend to have several times more immunoglobulin concentration than maternal serum at any particular time. Such observation is generally accepted by other workers (Blakemore and Garner, 1965; Pierce and Feinstein, 1963; Dixon et al., 1961).

Figure 1 indicates serum immunoglobulins concentrations of cows, calves and colestral whey samples obtained throughout the experiment. As expected, calves had very low serum immunoglobulin concentrations prior to nursing, but in most calves the concentration increased after the ingestion of colostrum. There was a wide range in the serum immunoglobulins concentration at each time of sampling; however, on the average, a peak was reached at 24 hours (ranging from 12 to 48 hours) after birth. Thereafter, immunoglobulin concentrations tended to decrease until 168 hours, when the last samples were taken. It should be recognized that the results shown were obtained under conditions where colostrum feeding was restricted to 2.5% body weight at 0 and 12 hours after birth. There is a possibility that the peak would occur at a different time after birth if colostrum feeding were unrestricted.

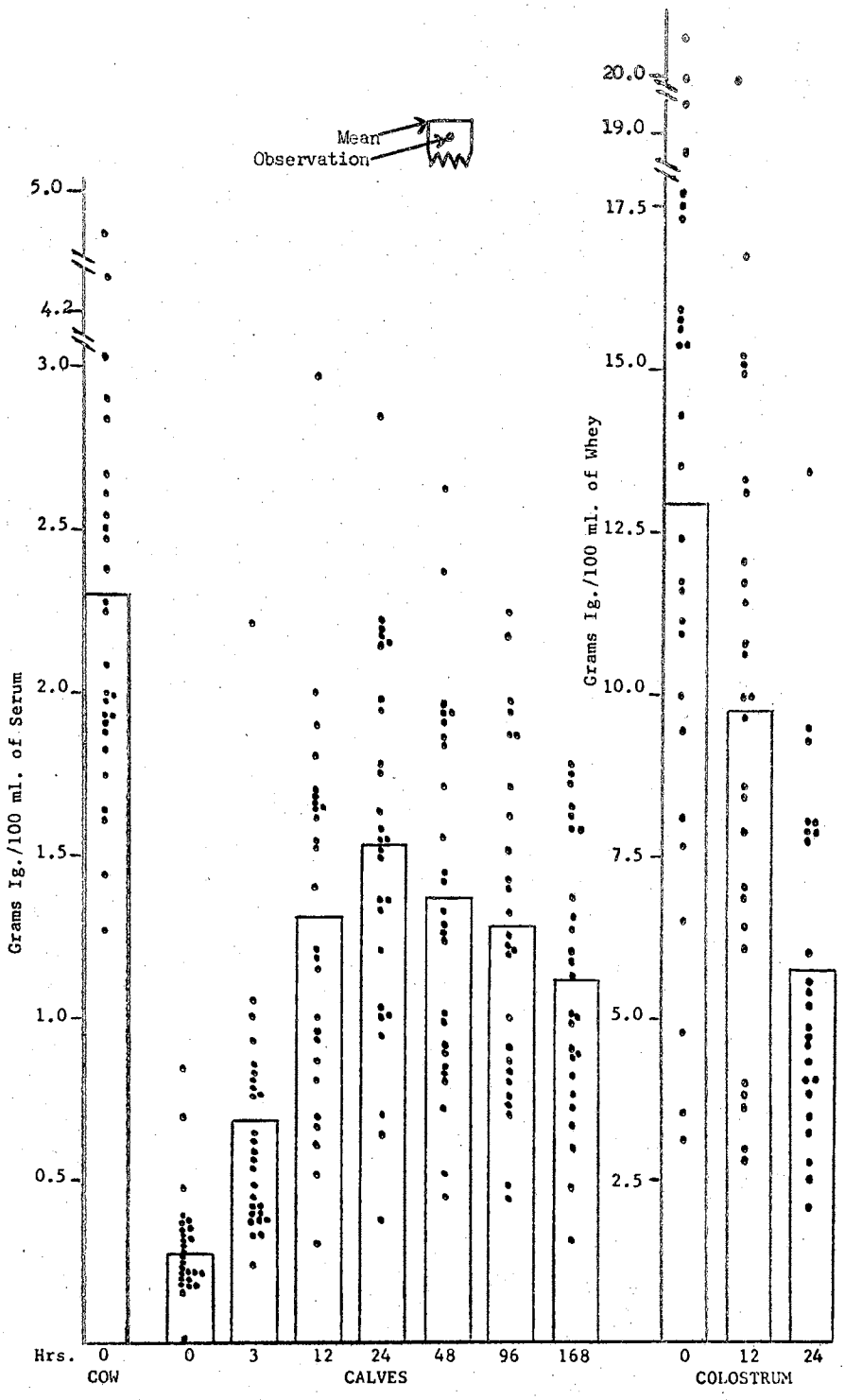

Figure 1. Grams of Immunoglobulin Concentration in Sera of Cows, Calves, and Colostral Whey.

It is apparent from the present study and those of Pierce (1955) and Klaus et al. (1969), that the calf is not totally agammaglobulinaemic at birth. Perhaps small amount of immunoglobulins are synthesized by the bovine foetus, as has been found in human foetus (Van Furth et al., 1965) and in rat and chicken embryos (Reade et al., 1965).

In seven out of 27 calves, serum immunoglobulin concentration remained below 1.0 gm./100 ml. of blood serum throughout the period of study (Figure 1). Hence, approximately 30% of the calves studied remained hypogammaglobulinaemic, a finding consistent with results obtained by Fey and Margadent (1961), Smith (1962), Smith et al. (1967), and Klaus et al. (1969). However, it appears that low serum immunoglobulin levels result mainly from inadequate immunoglobulin consumption rather than malabsorption.

The decline of serum immunoglobulin concentration in most calves from 24 hours after birth is presumably due to the intesinal "closure" at 24 to 48 hours after birth (Deutsch et al., 1957; Smith et al., 1964; Lecce, 1966).

Some cows had a comparatively low level of immunoglobulin in their colostral whey at parturition, in contrast to other cows (i.e., the range was 3.1 to 20.5 gm./100 ml.). The over-all correlation between blood serum values in cows and colostral whey concentrations at parturition was 0.43, meaning that a relatively small amount of the variation in colostral whey values could be accounted for by differences in blood levels. However, it is recognized that breed

interaction may have existed, tending to invalidate the over-all correlation. Observations on larger numbers of animals of each breed would be needed to establish this point.

In most cases, the maximal immunoglobulin concentration of the colostral whey occurred at parturition. There was a rapid decline of immunoglobulin concentrations by 12 and 24 hours postpartum (Figure 1). Therefore, one cannot underestimate the importance of the first feeding time relative to the amount of immunoglobulins ingested by the calf.

Regression analyses were conducted to study the effect of the amount of colostral immunoglobulin ingested by the newborn dairy calves on the blood sera levels. The regression between the amount of colostral immunoglobulin consumed at 0 hours (initial feeding) per 50 kilograms of body weight and the blood serum immunoglobulin concentration obtained at 3 hours after parturition is shown in Figure 2. A straight line fits the data well and shows that immunoglobulin serum concentration at 3 hours is very little affected by the colostral immunoglobulin consumed at 0 hours. These observations suggest that significant absorption requires larger than 3 hours after the initial feeding.

There was a positive linear relationship between colostral immunoglobulin consumption per 50 kg. of body weight at 0 hours and the serum immunoglobulin concentration obtained at 12 hours after birth (Figure 3). A statistically significant ($P < .05$) reduction in the sum of squares of

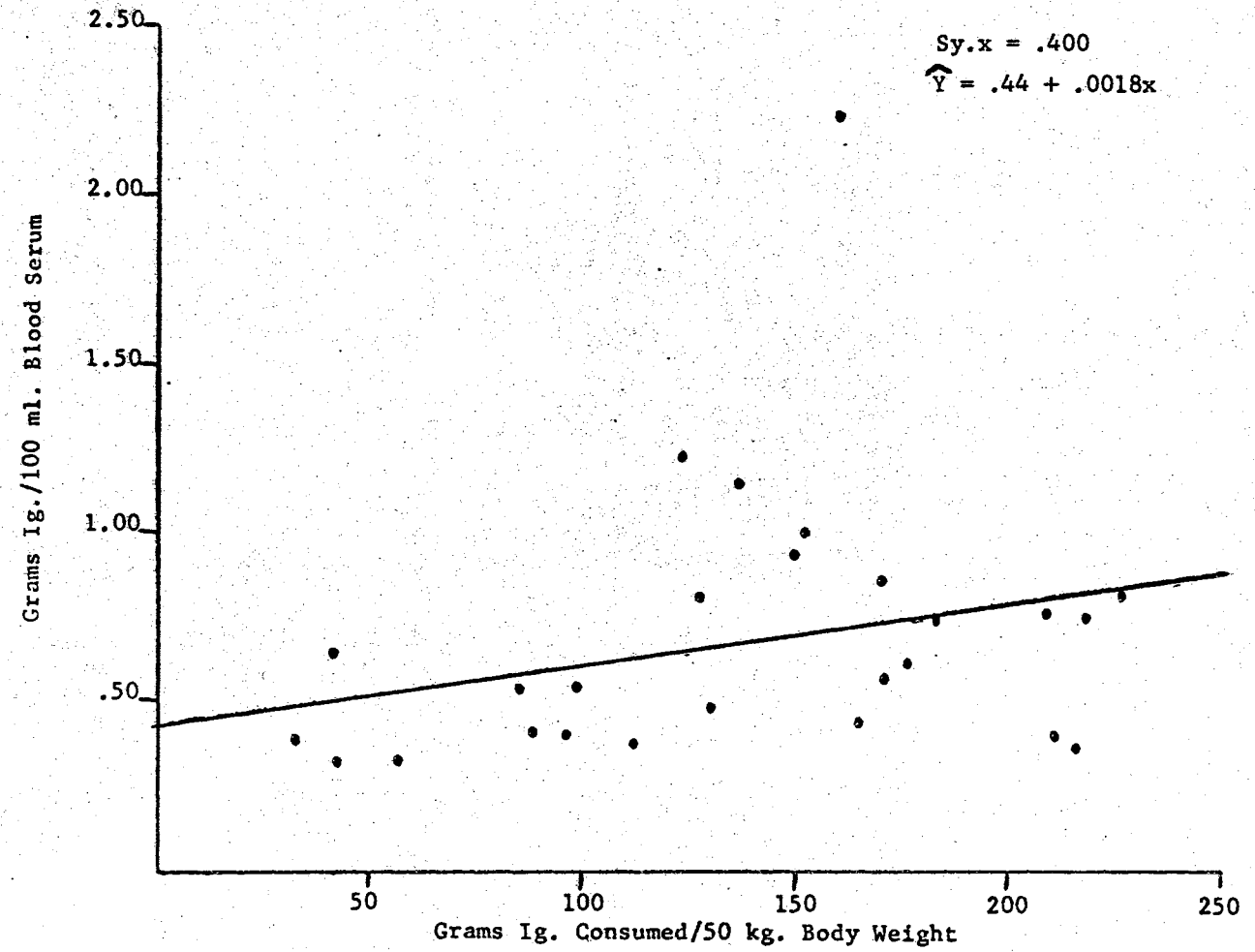

Figure 2. Relationship Between Immunoglobulin Consumption Immediately After Birth and Blood Serum Concentration at Three Hours

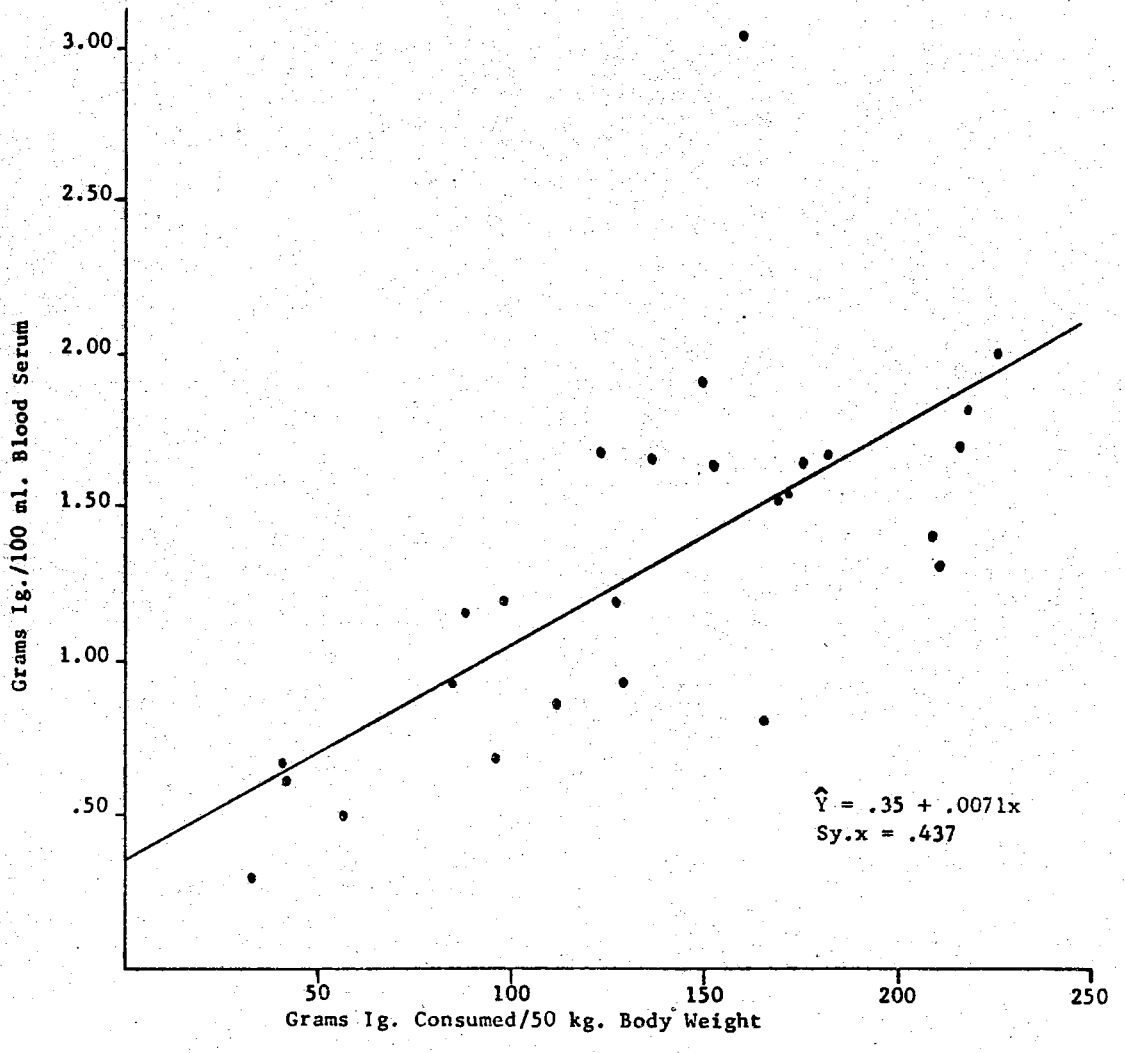

Figure 3. Relationship of Immunoglobulin Consumption Immediately After Birth to Blood Serum Concentration at 12 Hours

deviations was obtained by fitting the straight regression line. Moreover, the correlation between amount of immunoglobulin consumed per 50 kg. of weight and blood level of immunoglobulin was .70. The fraction of the variation in blood values due to changes in amount consumed (i.e., r^2) was .49. Thus, about 50% of the variation in blood values were not attributable to differences in the amount of immunoglobulin consumed, and, therefore, could be due to differences in absorption efficiency or other factors.

A positive relationship was found between colostral immunoglobulin consumption per 50 kg. of body weight immediately after birth plus that at 12 hours to blood serum immunoglobulin concentration observed in calves at 24 hours after birth (Figure 4). Again, a straight regression line resulted in a significant ($P < .05$) reduction in the sum of squares, meaning that there is a direct relationship of dependency on levels of immunoglobulin consumption to serum concentration obtained at 24 hours. The correlation between amount of immunoglobulin consumed per 50 kg. of body weight and blood level of immunoglobulin was .74, and r^2 was = 55. As with the blood values at 12 hours, an appreciable part, i.e., approximately 45%, of the variation at 24 hours was apparently due to differences in absorption efficiency or other factors.

Jones (1967), Klaus et al. (1969), Gay et al. (1965), Fey and Margadent (1962), Smith (1962), and Smith et al. (1967) found that some calves absorbed very little colostral

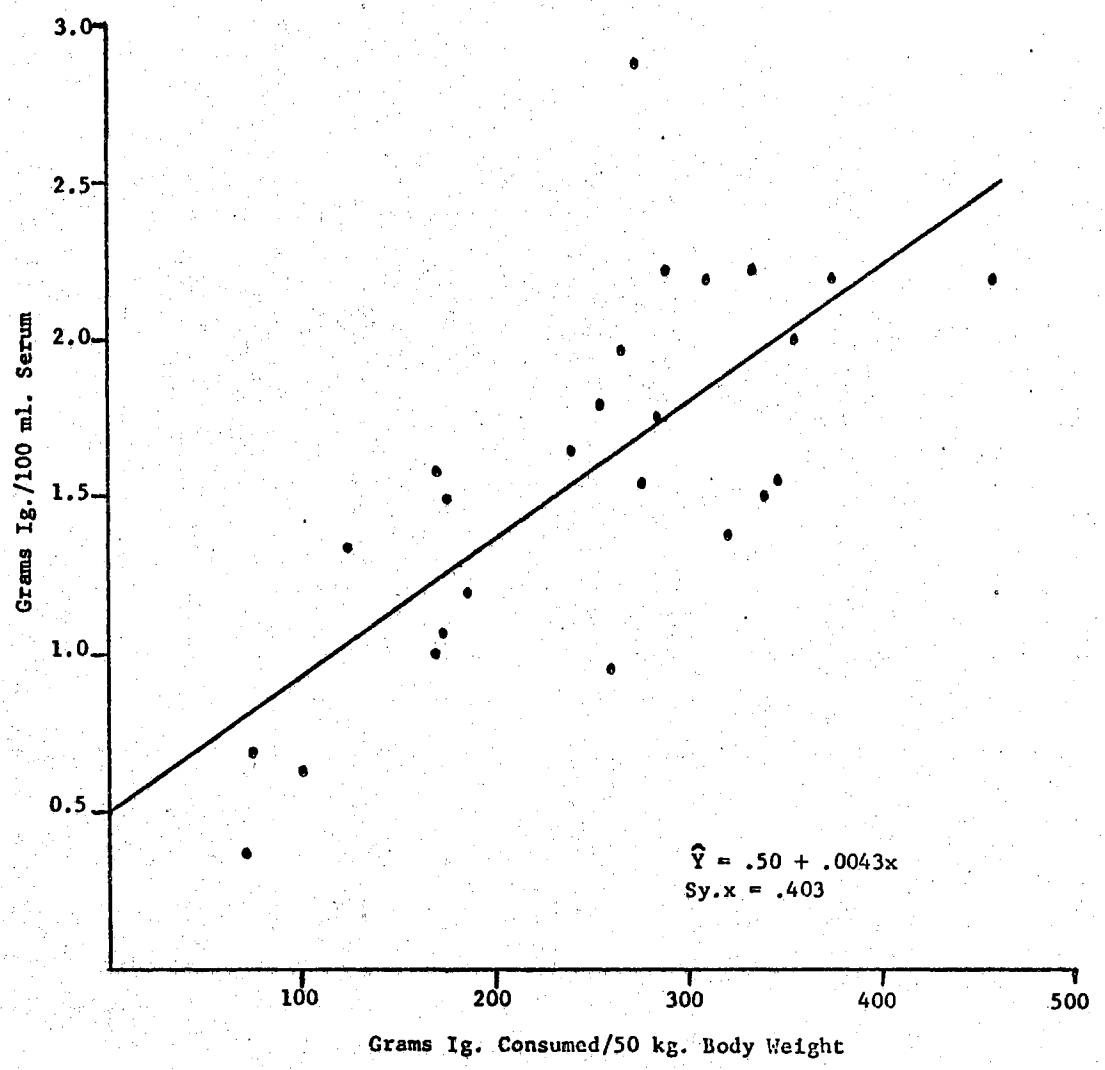

Figure 4. Relationship of Ig. Consumption Immediately After Birth and at 12 Hours to Blood Serum Concentration at 24 Hours

immunoglobulins regardless of supposedly enough quantities of immunoglobulins fed in colostrum. Those results are in agreement with the results of this study, but there may be some variation due to the different techniques, scientific approach and experimental procedures used in each experiment. Besides that, some experiments were performed on specific immunoglobulins. For instance, the work of Jones (1967) on absorption of IgG specifically, Klaus et al. (1969) on IgG and IgM. Gay et al. (1965), Fey and Margadent (1962), Smith (1962), and Smith et al. (1967), on the other hand observed immunoglobulin as a group.

There was a positive relationship between the immunoglobulin concentration in colostrum at parturition and maximum immunoglobulin concentration in blood serum of calves (Figure 5). This relationship was expected in view of the foregoing and the fact that differences in concentration of immunoglobulin in colostral whey accounted for most of the variation in amount of immunoglobulin consumed by the calves per unit of body weight (Figure 6).

Maximum blood serum immunoglobulin concentration in the calves and incidence of diarrhea did not seem to be related in this experiment (Table VI, Appendix), in contrast to reports by Fey and Margadent (1962), Gay et al. (1965), and Smith (1962). The three calves which died during this experiment had maximum immunoglobulin concentrations of 1.72, 1.39, and 1.00 gm./100 ml., respectively, while the range for all the calves was 0.44 to 3.30 gm./100ml. Since

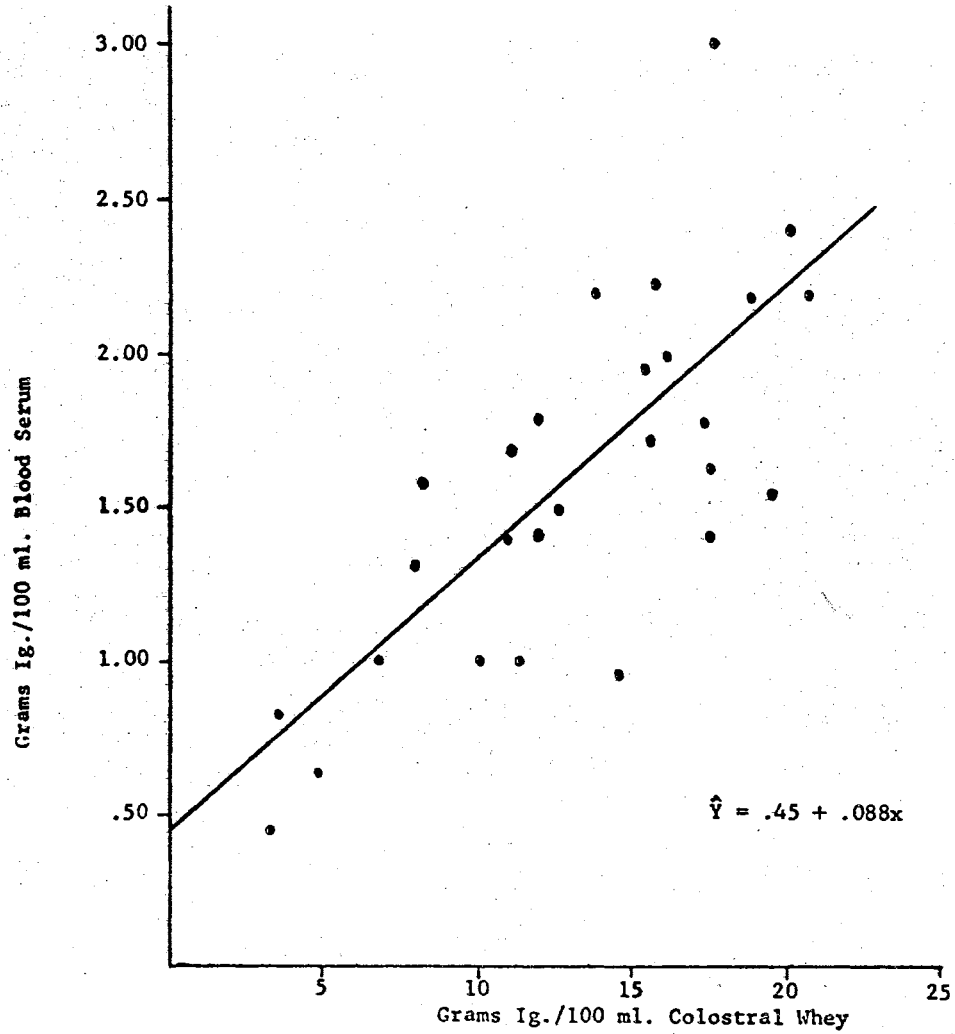

Figure 5. Relationship Between Immunoglobulin Concentration in Colostrum at Parturition and Maximum Ig. Concentration in Serum of Calves

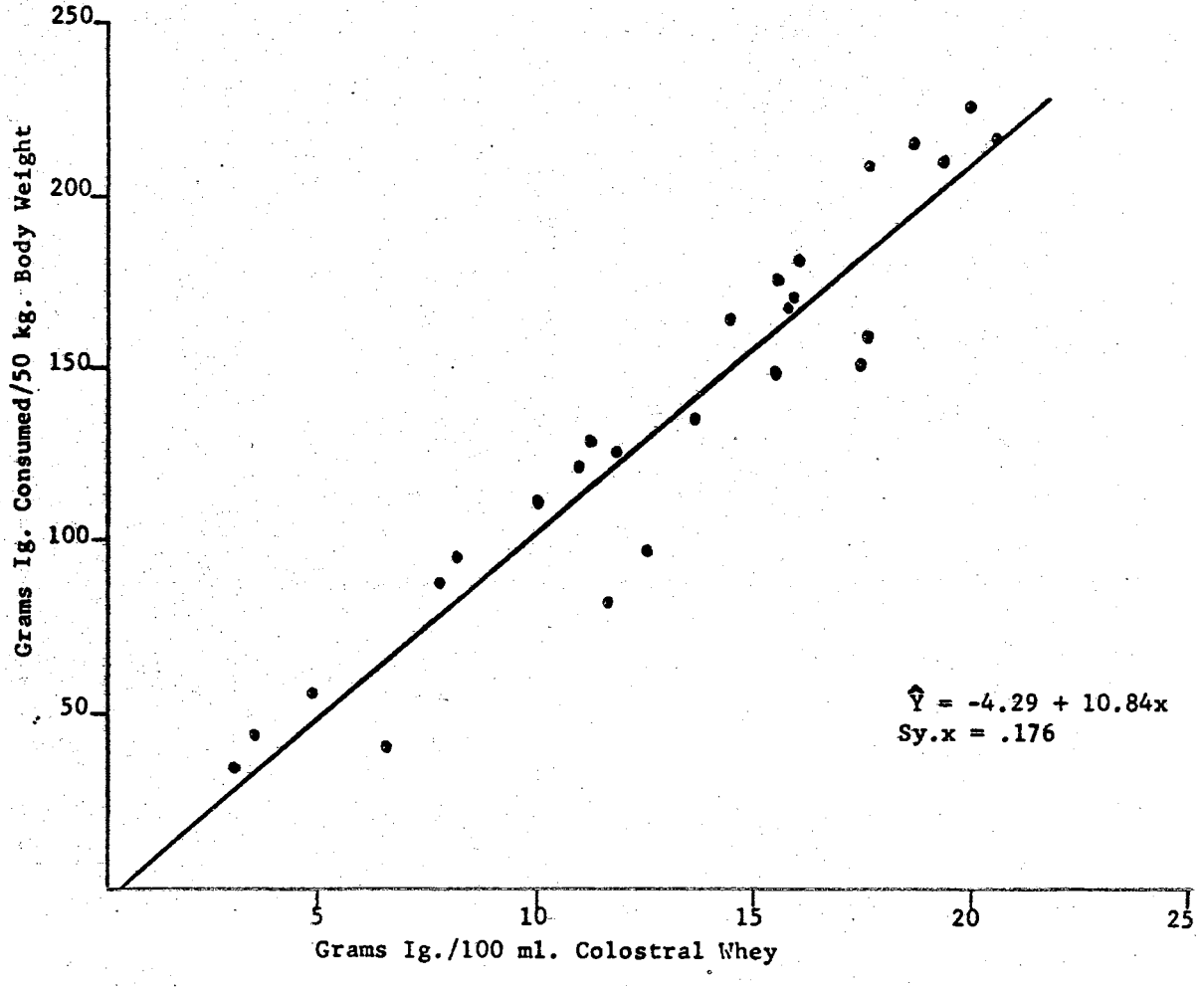

Figure 6. Relationship of Immunoglobulin Concentration to Consumption Immediately After Birth

the number of experimental units involved in this experiment was small and the exposure to pathogenic organisms was not controlled in any way, these results are not considered conclusive in terms of the relationship of blood serum levels of immunoglobulins to disease resistance.

CHAPTER V

SUMMARY AND CONCLUSIONS

The transfer of immunoglobulins from colostrum to the blood of newborn calves was measured in 27 cow-calf pairs. Concentration of globulin was determined in blood and colostrum taken immediately after calving and in colostrum at 12 and 24 hours thereafter. Blood concentration in calves was determined immediately after birth (before nursing) and at 3, 12, 24, 48, 96, and 168 hours thereafter. Each calf was fed colostrum from its dam at the daily rate of 5 and 7.5% of body weight during the first and second days, respectively. Afterwards, whole milk was fed at the daily rate of 10% of initial weight. Concentration of immunoglobulins in blood serum and colostral whey was determined by electrophoresis. The following conclusions were made from the results of this experiment:

1. The average blood serum immunoglobulin concentration in calves was significantly lower than that of their respective dams.
2. Most calves reached a peak of immunoglobulin concentration in the blood serum at 24 hours after birth.

3. Hypogammaglobulinaemia, defined as blood serum levels below 1.0 gm./100ml., remained in 7 out of 27 calves in the experiment.

4. There was a positive linear relationship between colostral immunoglobulin consumption per unit of body weight and the blood serum immunoglobulin concentration attained in the calves. Approximately 50% of the variation in blood values was accounted for by differences in amount of immunoglobulin consumed, leaving nearly one-half of the variation attributable to other factors. Hence, a significant part of the variations in blood immunoglobulin levels could have been due to differences in efficiency of immunoglobulin absorption.

5. There was a positive relationship between the maximum immunoglobulin concentration in colostrum (at parturition) and the maximum immunoglobulin concentration attained in blood serum of calves after ingestion of the colostrum.

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APPENDIX

TABLE IV

GENERAL INFORMATION ABOUT THE COWS, THEIR BLOOD SERUM AND COLOSTRAL IMMUNOGLOBULIN CONCENTRATIONS

No. of cow	Breed	No. of lactation	Ig. in cow blood serum	Ig. in colostral whey at the following hours after parturition			Remarks
				0	12	24	
			gm./100 ml.	--- gm./100 ml.---			
818	Hol.	2	2.00	15.9	16.9	13.5	
745	Hol.	3	2.10	4.8	3.9	4.0	
725	Hol.	3	2.50	11.7	9.7	7.9	
563	Ayr.	5	1.64	17.5	10.7	9.3	Dystocia
718	Hol.	3	2.63	9.5	6.9	2.7	Dystocia
962	Jer.	1	1.62	16.0	8.6	4.3	
942	Ayr.	1	1.85	8.1	8.5	4.6	
998	Hol.	1	2.52	20.5	20.0	9.5	
866	Hol.	2	2.69	15.8	13.4	3.8	
967	Hol.	1	4.27	3.5	2.8	2.5	Dystocia
941	Ayr.	1	1.27	7.7	2.9	2.0	
829	Ayr.	2	1.90	11.2	3.8	3.4	
953	Guer.	1	2.00	15.5	15.1	8.0	
951	Ayr.	1	2.27	6.5	6.4	4.7	

TABLE IV (Continued)

No. of cow	Breed	No. of lactation	Ig. in cow blood serum	Ig. in colostral whey at the following hours after parturition			Remarks
				0	12	24	
			gm./100 ml.	--- gm./100 ml. ---			
749	Ayr.	3	1.84	19.9	6.1	8.0	
001	Ayr.	1	3.13	12.7	15.2	4.0	
995	Jer.	1	1.76	11.0	10.0	4.8	
958	Ayr.	1	4.90	3.1	3.6	3.2	
864	Hol.	2	2.39	11.8	11.5	7.7	Dystocia
983	Ayr.	1	2.28	13.6	15.3	5.2	
943	Ayr.	1	1.99	15.5	10.8	5.4	
936	Guer.	1	2.56	19.3	11.8	-	
979	Guer.	1	1.91	17.4	13.2	-	
938	Guer.	1	1.94	17.6	12.1	5.5	
792	Hol.	3	2.93	12.5	10.0	7.9	
014	Guer.	1	1.94	14.4	7.9	6.0	Yield insufficient colostrum
875	Ayr.	2	1.44	10.0	7.0	-	
Mean			2.3062	12.9259	9.7814	5.7458	
Standard Deviation			.7952	5.0323	4.5346	2.7327	
Standard Error			.1530	.9684	.8726	.5577	

TABLE V

GENERAL INFORMATION ABOUT THE CALVES USED IN THE EXPERIMENTS

Animal No.	Birth Weight (-kg.-)	Breed	Sex	Date of Birth	Remarks
214	49.8	Hol.	M	2-23-69	
193	54.2	Hol.	F	3-31-69	
289	47.1	Hol.	M	4-26-69	
200	35.6	Ayr.	F	4-30-69	Weak at Birth; was Pulled.
210	53.3	Hol.	F	6-29-69	Last to long to born. Died.
004	18.7	Jer.	M	8-23-69	
001	27.8	Ayr.	M	8-24-69	
002	40.9	Hol.	M	8-27-69	
226	39.1	Hol.	F	8-28-69	
228	42.7	Hol.	F	8-31-69	Was Pulled.
008	34.7	Ayr.	M	9- 2-69	
229	33.3	Ayr.	F	9- 3-69	
012	31.1	Guer.	M	9- 4-69	
010	34.7	Ayr.	M	9- 4-69	
015	35.6	Ayr.	M	9- 5-69	
017	36.4	Ayr.	M	9- 5-69	
016	20.0	Jer.	M	9- 6-69	
231	26.7	Ayr.	F	9- 7-69	

TABLE V (Continued)

Animal No.	Birth Weight (-kg.-)	Breed	Sex	Date of Birth	Remarks
045	40.0	Hol.	M	9- 9-69	Was Pulled (one of twins).
018	24.8	Ayr.	M	9- 9-69	
009	32.0	Ayr.	M	9-12-69	
956	36.4	Guer.	M	9-15-69	
247	30.7	Guer.	M	9-15-69	
663	39.1	Guer.	M	9-25-69	
238	50.2	Hol.	F	10- 1-69	
287	32.9	Guer.	M	10-15-69	Insufficient colostrum from cow.
241	35.6	Ayr.	F	10-15-69	

TABLE VI

PERFORMANCE OF CALVES

No. of Calf	Body Weight Birth	8-day	15-day	Time of Maximum Ig. Level	Maximum Ig. Level in Blood	Diarrhea Rating*	Remarks
	(-------kg.--------)			(---hrs.--)	(gm./100 ml.)		
200	35.6	35.6	37.8	12	3.03	2.6	Treated, sulfas (1 day)
015	35.6	37.3	41.8	48	2.39	1.4	Treated, sulfas (2 day)
226	39.1	43.1	45.3	24	2.23	1.1	
002	40.9	43.6	49.8	24	2.19	1.0	
017	36.4	37.3	39.6	24	2.17	1.1	
214	49.8	51.1	52.0	24	1.99	2.2	Treated, sulfas (2 day)
009	32.0	34.2	33.8	24	1.96	1.1	
045	40.0	40.4	38.2	24	1.78	1.1	
004	18.7	20.4	23.1	24	1.77	1.0	
012	31.1	33.3	-	48	1.72	1.0	Died
016	20.0	22.7	26.7	12	1.68	1.2	
247	30.7	34.2	35.6	12	1.63	1.0	
001	27.8	26.7	31.1	24	1.58	1.0	
956	36.4	39.6	41.3	24	1.55	1.0	
238	50.2	55.1	58.7	24	1.51	1.0	
663	39.1	40.9	43.1	12	1.40	1.6	

TABLE VI (Continued)

No. of Calf	Body Weight Birth	8-day	15-day	Time of Maximum Ig. Level	Maximum Ig. Level in Blood	Diarrhea Rating*	Remarks
	(-------kg.---------)			(---hrs.--)	(gm./100 ml.)		
210	53.3	-	-	24	1.39	2.2	Difficult birth: dies soon afterwards
008	34.7	36.4	40.4	24	1.34	1.0	
289	47.1	47.6	60.0	48	1.33	2.3	Treated sulfas (2 day)
241	35.6	37.3	40.0	24	1.09	1.3	
229	33.3	35.6	39.6	24	1.00	1.0	
010	34.7	36.0	37.8	24	1.00	1.1	Died
287	32.9	33.3	38.2	24	0.94	1.2	
228	42.7	44.4	52.4	48	0.84	1.0	
193	54.2	55.6	57.8	24	0.63	2.7	Treated sulfas (5 days)
231	26.7	30.2	34.7	48	0.44	1.8	

*Diarrhea Rating:
1. Firm
2. Soft
3. Loose
4. Watery

TABLE VII

IMMUNOGLOBULIN CONCENTRATION IN BLOOD SERUM OF CALVES AT DIFFERENT HOURS (gm./100 ml.)

Calves No.	0 hrs.	3 hrs.	12 hrs.	24 hrs.	48 hrs.	96 hrs.	168 hrs.
214	0.36	0.58	1.55	1.99	1.97	1.88	1.59
193	0.27	0.32	0.50	0.63	0.51	0.48	0.46
289	0.22	0.53	0.93	1.21	1.33	1.20	1.09
200	0.47	2.23	3.03	2.87	2.65	2.19	1.76
210	0.36	0.39	1.00	1.39	died	-	-
004	0.18	0.75	1.67	1.77	0.89	1.42	1.20
001	0.19	0.39	0.68	1.58	0.81	0.70	0.66
002	0.26	0.75	1.82	2.19	1.93	1.72	1.63
226	0.21	0.85	1.54	2.23	1.95	1.95	1.73
228	0.19	0.32	0.61	0.69	0.84	0.75	0.59
008	0.00	0.40	1.15	1.34	0.72	0.71	0.72
229	0.29	0.48	0.96	1.00	0.99	0.81	0.82
012	0.20	0.62	1.64	1.50	1.72	1.63	1.12
010	0.31	0.63	0.66	1.00	0.91	0.90	0.99
015	0.29	0.82	2.07	2.21	2.39	2.26	1.78
017	0.34	0.37	1.70	2.17	1.87	1.98	1.58
016	0.85	1.23	1.68	1.64	1.45	1.33	0.88

TABLE VII (Continued)

Calves No.	0 hrs.	3 hrs.	12 hrs.	24 hrs.	48 hrs.	96 hrs.	168 hrs.
231	0.21	0.38	0.29	0.36	0.44	0.43	0.30
045	0.34	0.81	1.19	1.78	1.56	1.41	1.28
018	0.37	1.15	1.66	2.17	1.95	1.88	1.66
009	0.68	0.93	1.91	1.96	1.86	1.52	1.37
956	0.33	0.40	1.31	1.55	1.43	1.25	1.31
247	0.15	1.04	1.63	1.55	1.28	1.09	1.04
663	0.23	0.77	1.40	1.37	1.27	1.21	0.88
238	0.18	0.55	1.20	1.51	1.25	1.20	1.18
287	0.18	0.44	0.80	0.94	0.82	0.83	0.76
241	0.17	0.37	0.86	1.09	1.04	0.86	0.89
Mean	.28629	.6896	1.3125	1.5440	1.378076	1.291923	1.125769
Standard Deviation	.16314	.4028	.5854	.5785	.577428	.527636	.424604
Standard Error	.03139	.0775	.11266	.1113	.113243	.103477	.083271

TABLE VIII

TOTAL PROTEIN CONCENTRATION IN BLOOD SERUM OF CALVES AT DIFFERENT HOURS (gm./100 ml.)

Calves No.	0 hrs.	3 hrs.	12 hrs.	24 hrs.	48 hrs.	96 hrs.	168 hrs.
214	4.2	4.2	5.3	5.8	5.9	5.8	5.6
193	4.2	4.0	4.2	4.7	4.3	4.3	4.1
289	4.5	4.5	4.8	5.2	5.5	5.4	5.4
200	4.6	6.5	7.4	7.2	7.1	6.8	6.0
210	3.9	3.9	4.5	5.1	-	-	-
004	4.3	3.7	6.0	6.2	5.4	5.8	5.8
001	4.7	4.4	5.0	6.0	4.7	4.4	4.4
002	4.7	5.0	6.2	6.8	6.3	5.9	6.0
226	4.7	5.1	6.3	6.5	6.2	6.4	6.1
228	4.4	4.5	4.7	5.0	5.0	5.2	4.6
008	4.0	4.3	5.4	5.4	5.2	5.1	5.5
229	4.3	4.6	5.6	5.4	5.7	5.6	5.0
012	4.2	4.4	5.3	5.4	5.7	5.5	5.6
010	4.3	4.6	4.3	5.0	5.3	5.3	5.3
015	4.3	4.2	6.2	6.3	6.1	6.8	5.8
017	5.1	5.0	6.3	6.9	6.5	7.0	6.4
016	5.4	5.5	6.1	6.3	6.1	6.0	5.8

TABLE VIII (Continued)

Calves No.	0 hrs.	3 hrs.	12 hrs.	24 hrs.	48 hrs.	96 hrs.	168 hrs.
231	4.0	4.2	4.2	4.4	4.5	4.4	4.1
045	4.5	4.7	5.1	5.8	5.9	5.7	5.7
018	4.3	5.3	5.8	6.5	6.7	6.2	6.2
009	5.2	5.2	6.5	6.5	6.3	6.0	5.6
956	4.3	4.2	5.3	5.9	5.4	5.4	5.6
247	4.4	5.0	5.6	5.7	6.0	6.1	6.3
663	4.1	4.5	5.2	5.1	5.3	5.5	5.1
238	4.3	4.3	5.3	5.8	5.5	5.3	5.9
287	4.1	4.2	4.8	5.1	5.0	5.3	5.4
241	4.0	3.7	4.8	5.0	5.2	5.1	5.3

TABLE IX

TOTAL PROTEIN CONCENTRATION IN BLOOD SERUM AND COLOSTRAL WHEY AT THE FOLLOWING HOURS

No. of cow	Cow serum 0 hrs.	Colostral whey 0	12	24
818	6.4	22.0	23.0	19.0
745	6.4	8.0	6.7	6.7
725	7.5	16.8	12.8	10.8
563	7.4	22.0	14.8	12.0
718	6.6	14.0	11.2	5.0
962	6.9	22.4	13.2	7.6
942	7.0	10.8	12.0	7.5
998	7.1	25.0	25.0	14.0
866	7.2	20.0	18.4	6.6
967	9.2	6.0	5.6	4.2
941	6.2	10.0	4.8	3.0
829	6.9	16.0	5.6	6.0
953	6.1	22.0	20.0	11.5
951	7.3	10.0	9.9	7.5
749	6.6	27.0	11.7	11.5
001	8.4	24.0	20.8	5.4
995	6.2	15.5	15.0	7.8

TABLE IX (Continued)

No. of cow	Cow serum 0 hrs.	Colostral whey 0	12	24
958	9.5	4.7	6.0	4.6
864	6.8	17.6	17.0	12.0
983	7.0	18.5	20.0	7.8
943	6.6	20.0	13.5	7.5
936	7.5	24.2	16.0	-
979	6.5	25.0	17.1	-
938	6.4	23.0	17.0	9.2
792	7.8	17.1	15.0	11.4
014	6.3	20.0	12.0	8.0
875	6.1	-	-	-

TABLE X

PERCENTAGE OF COLOSTRAL WHEY IN COLOSTRUM

No. of cow	Colostral whey at the following hours after parturition		
	0	12	24
818	86.0	87.0	94.0
745	94.5	92.5	92.0
725	58.0	82.5	93.5
563	73.0	85.0	92.0
718	-	-	-
962	91.0	95.0	98.0
942	94.5	70.0	86.0
998	85.0	96.0	90.0
866	85.5	99.0	97.0
967	96.0	98.0	99.0
941	92.0	98.0	85.0
829	93.0	78.0	63.0
953	91.0	87.0	87.0
951	50.0	91.5	93.5
749	91.0	81.0	70.0
001	92.5	83.0	89.0
995	90.0	94.0	95.0
958	85.5	87.5	87.0
864	86.0	88.5	92.5
983	80.0	91.0	88.0
943	77.0	86.0	85.0
936	87.5	91.0	-
979	70.0	75.5	-
938	95.0	74.0	89.0
792	62.5	62.0	61.0
014	92.0	96.0	96.0
875	90.0	68.5	85.0

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