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A Quantitative Study of the Transfer of Colostral Immunoglobulins to the Newborn Calf

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Summary. The transfer of colostral IgM and IgG to newborn calves was studied quantitatively. Both IgM and IgG were absorbed equally well from the gastro-intestinal tract of the calf. However, the degree of globulin absorption and hence the serum immunoglobulin concentrations varied considerably from calf to calf. Three of the ten calves remained virtually agammaglobulinaemic despite the ingestion of colostrum. The significance of failure to absorb colostral immunoglobulins (especially IgM) is discussed in relation to the pathogenesis of neonatal septicaemias of the newborn calf.

INTRODUCTION

In most species of domestic animals maternal immunoglobulins are transferred to the offspring via the colostrum, during the immediate post-natal period (Brambell, 1958). In contrast, the human foetus acquires maternal globulins *in utero*. Transplacental transport of these proteins is a selective process, since only IgG, and not IgM or IgA, cross the placental barrier (Freda, 1962).

The information available on the types of immunoglobulins absorbed from the intestinal tract of the newborn in lower animals is confusing. The experiments of Halliday and Kekwick (1960) in the rat and those of Locke, Segre and Myers (1964) in the newborn pig, suggested that IgG globulins were absorbed more efficiently than IgM. On the other hand, Pierce and Feinstein (1965) reported that the newborn calf was able to absorb all of the immunoglobulins found in colostrum, without any indication of selectivity.

The present study was designed to evaluate the transfer of colostral IgM and IgG to the newborn calf and to characterize the process on a quantitative basis.

MATERIALS AND METHODS

Experimental animals

The cows and calves used in this study were part of the dairy herd of the Department of Dairy Science, Oklahoma State University, consisting of pure bred animals of the Holstein–Friesian, Guernsey and Ayrshire breeds.

Calves were allowed to suckle their dams within 1–1½ hours of birth, and they remained with the cow for 12–18 hours.

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For the next 3 days the calves were fed maternal colostrum from a nipple bucket, twice daily. This amounted to approximately 4 litres of colostrum per day. Subsequently they received whole milk.

Collection of samples

Each calf was bled as soon as possible after birth and before it suckled the cow. At the same time blood and colostrum samples were obtained from the cow. The calf was subsequently bled at 1, 2, 4 and 7 days of age. Sera and colostrum were stored at −20° until all the samples for each cow–calf pair were assayed for immunoglobulins at the same time.

Separation of colostral whey

Colostrum samples were centrifuged to remove the lipid portion and the remainder was acidified to pH 4·5 to precipitate the casein. Following a second centrifugation the whey was brought back to its original pH. In the following discussion the term 'colostrum' will be used instead of 'colostral whey', for the sake of brevity.

Immunoglobulin determinations

Samples were assayed for IgM and IgG concentrations by means of the radial gel diffusion test of Fahey and McKelvey (1965). The isolation of bovine IgM and IgG and the application of the radial diffusion test have been described in detail previously (Klaus and Jones, 1968).

Each serum or colostrum sample was assayed in triplicate for IgM and IgG, and the values presented here are the means of these determinations.

RESULTS

MATERNAL SERUM AND COLOSTRAL IMMUNOGLOBULIN LEVELS

The concentrations of IgM and IgG in the sera and colostrum of the ten cows are shown in Tables 1 and 2. The mean serum immunoglobulin levels were similar to those reported by Klaus and Jones (1968) in weaned calves. One of the cows (No. 291) had an

TABLE 1

IgM CONCENTRATIONS (mg/ml) IN THE SERA AND COLOSTRUM OF THE COWS AND IN THE SERA OF THEIR CALVES DURING THE 1ST WEEK OF LIFE

Cow No.	Cow serum	Colostrum	Calf				
			Day 0	Day 1	Day 2	Day 4	Day 7
623	3·6	3·7	0·1	2·1	2·1	1·3	–
679	4·1	4·5	0·1	1·9	1·9	1·5	1·8
291	2·5	2·7	0·1	0·8	0·7	0·5	0·5
662	2·7	2·5	0·2	0·7	0·5	0·4	0·3
722	2·0	1·8	0·1	2·1	2·1	Died	–
756	1·8	1·7	0·1	1·3	1·1	0·85	0·6
681	2·9	3·1	0·1	3·1	2·6	1·9	1·1
611	2·2	7·4*	0·04	0·06	0·1	–	0·3
674	1·5	1·5	0·1	0·3	0·3	0·2	0·2
691	2·7	3·0	0·2	0·2	0·2	0·2†	–
$\bar{X}$ (all animals)	2·6±0·8	3·2±1·7	0·1±0·0	1·26±1·0	1·16±0·9	0·9±0·6	0·7±0·6
$\bar{X}$ Calves absorbing IgM			0·1±0·0	1·7±0·8	1·6±0·8	1·1±0·6	0·9±0·6
$\bar{X}$ Calves not absorbing IgM			0·1±0·1	0·2±0·1	0·2±0·1	0·2	0·3

$\bar{X}$, Mean. Day 0, Day of birth: sample obtained prior to suckling.
* Cow 611 had mastitis soon after calving.
† This calf developed severe enteritis.

TABLE 2

IgG CONCENTRATIONS (mg/ml) IN THE SERA AND COLOSTRUM OF THE COWS AND IN THE SERA OF THEIR CALVES DURING THE 1ST WEEK OF LIFE

Cow No.	Cow Serum	Colostrum	Calf				
			Day 0	Day 1	Day 2	Day 4	Day 7
623	17·2	53·0	1·3	27·6	29·4	25·0	–
679	22·5	50·0	0·5	19·6	20·5	19·0	19·0
291	57·6	70·7	2·0	21·3	20·2	23·8	16·0
662	16·7	32·6	1·3	19·2	18·0	15·6	14·1
722	20·6	31·7	1·6	45·0	38·2	Died	–
756	21·1	44·7	1·6	39·3	39·4	30·6	29·1
681	26·4	33·3	1·2	44·8	55·2	42·3	34·4
611	20·1	35·0	0·7	0·9	1·1	–	2·1
674	23·0	26·3	1·4	3·1	2·8	2·3	3·5
691	39·0	56·0	0·8	1·8	1·3	2·3	–
$\bar{X}$ (all animals)	26·4 ± 12·6	43·3 ± 14·0	1·2 ± 0·5	22·3 ± 17·0	22·6 ± 18·2	20·1 ± 13·6	16·9 ± 12·0
$\bar{X}$ Calves absorbing IgG			1·4 ± 0·5	31·0 ± 11·8	31·6 ± 13·6	26·1 ± 9·5	22·5 ± 8·8
$\bar{X}$ Calves not absorbing IgG			1·0 ± 0·4	1·9 ± 1·1	1·7 ± 0·9	2·3	2·8

$\bar{X}$, Mean. Day 0, Day of birth: sample obtained prior to suckling.

unusually high IgG concentration (Table 2). This cow was the only older animal (8½ years old) in the group. The ages of the others ranging from 2 to 4½ years. However, it is doubtful that these values are representative of normal adult cattle, since a physiological hypogammaglobulinaemia accompanies parturition in the cow (Dixon, Weigle and Vasquez, 1961).

Colostral IgM levels were similar to the serum concentrations, except in one animal (No. 611) (Table 1). This cow had clinical signs of mastitis during the course of the study. In all of the cows except No. 674, colostral IgG levels were considerably higher than the corresponding serum value (Table 2). This difference was significant ($P = 0{\cdot}05$).

IMMUNOGLOBULIN LEVELS IN NEWBORN CALVES

The pre-suckling sera of all ten calves contained low levels of both IgM and IgG (Tables 1 and 2).

In most of the calves the ingestion of colostrum led to a rapid increase in serum IgM and IgG concentrations within 24 hours, and these reached a peak within the first 48 hours of life. Subsequently the serum concentration of both immunoglobulins fell (Tables 1 and 2, Fig. 1).

In three of the calves (those of cows Nos. 674, 611 and 691). IgM levels remained below 0·5 mg/ml and IgG levels below 4·0 mg/ml throughout the period of study. One of these calves (cow No. 691) developed enteritis of undetermined aetiology.

The maximum serum concentrations of IgM and IgG in the calves were calculated as percentages of the corresponding colostral concentration, to provide an estimate of the 'efficiency of absorption' of colostral proteins. This method of analysis has obvious limitations, particularly since it does not allow for possible variation dependent on the amount of colostrum ingested by each calf. However, it provides a convenient method for comparing the uptake of the two immunoglobulins.

The mean serum IgM concentration was 49 per cent of the colostral level, with a range of from 4 to 118 per cent. The mean for IgG was 60 per cent with a range of 6–166 per cent. Five of the calves had IgG levels equal to or exceeding that of the maternal serum. There was a complete lack of correlation between calf serum and colostral immunoglobulin

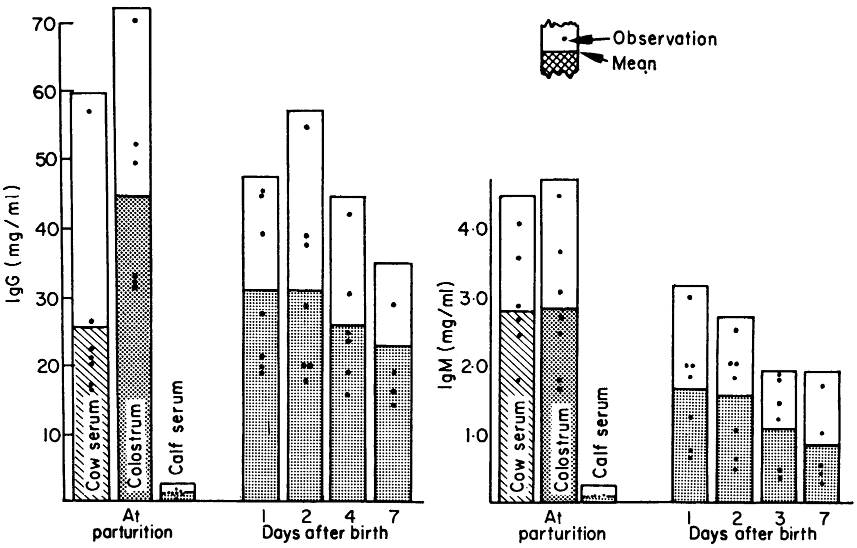

Fig. 1. Immunoglobulin concentrations in the sera and colostrum of cows at the time of parturition and in the sera of their calves which absorbed immunoglobulins during the 1st week of life.

levels (Tables 1 and 2), from which it is apparent that the hypogammaglobulinaemia observed in the three calves mentioned previously was not associated with low colostral immunoglobulin levels.

The 'percentage uptake' of IgM and IgG were plotted together (Fig. 2). The relationship obtained ($r = 0{\cdot}94$) was significant ($P = 0{\cdot}001$) indicating that both IgM and IgG were absorbed from the intestinal tract of the calf with equal efficiency.

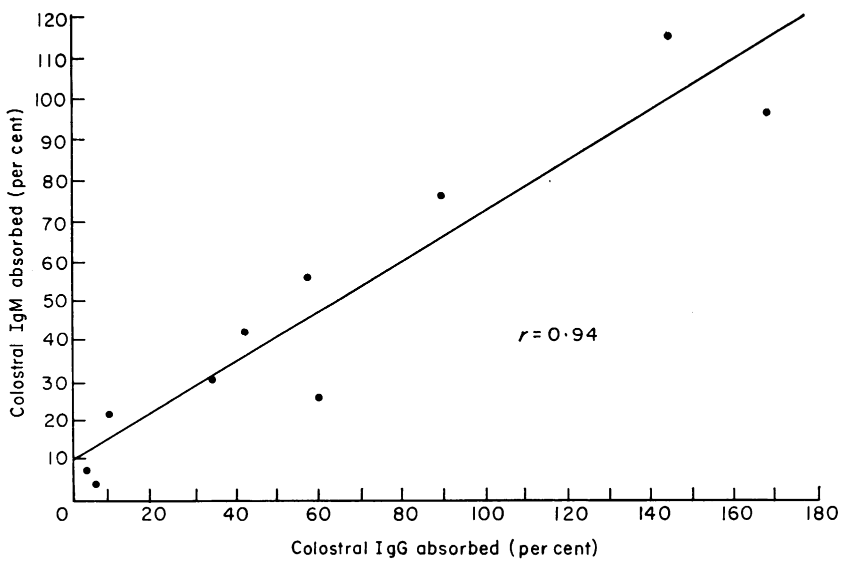

Fig. 2. Relation of absorption of colostral IgM to colostral IgG by newborn calves. Maximal serum concentrations of IgM and IgG in the calves were expressed as percentages of the corresponding colostral concentration.

DISCUSSION

It is apparent from the present study, and from that of Pierce (1955), that the calf is not totally agammaglobulinaemic at birth (Tables 1 and 2). Perhaps small amounts of immunoglobulins are synthesized by the bovine foetus, as has been found in human (Van Furth, Schuit and Hijmans, 1965), rat and chicken embryos (Reade, Jenkin and Turner, 1965).

The bovine mammary gland selectively secretes serum γ-globulins during all phases of lactation, but especially during the period of colostrum synthesis, when the colostral γ-globulin level may exceed that of the serum by five times (Dixon *et al.*, 1961). This secretory selectivity has been further characterized by Murphy, Aalund, Osebold and Carroll (1964) and Pierce and Feinstein (1965). They found that although bovine colostrum contains IgM, IgA and electrophoretically fast IgG, slow IgG is virtually absent, and thus does not appear in the serum of the suckling calf.

The present experiments have confirmed the observation of Dixon *et al.* (1961), that colostral IgG levels are considerably higher than those of the maternal serum, although the differences observed here (Table 2) were not as striking as those reported by Dixon *et al.* (1961). It is of considerable interest that there were no differences between colostral and serum IgM levels (Table 1).

The absorption of colostral immunoglobulins from the gut of the newborn calf appears to be a non-selective process. Indeed, under the conditions of this experiment, the 'degree of uptake' of IgM and IgG seems to be related (Fig. 2). Pierce and Feinstein (1965) and earlier workers, have also concluded that the intestinal tract of the newborn calf absorbs various proteins indiscriminately. This is in direct contrast with the evidence cited earlier, that in the newborn rat (Halliday and Kekwick, 1960) and pig (Locke *et al.*, 1964) IgG globulins are absorbed more efficiently than IgM.

The wide range in the percentage of colostral globulins appearing in the serum of the calves in this experiment may be related to differences in the amount of colostrum ingested by each calf during the first 36 hours of life. However, this would not account for the marked hypogammaglobulinaemia in three of the calves, nor for the lack of correlation between colostral and calf serum immunoglobulin levels.

A number of investigators have noted wide variations in serum γ-globulin levels, and frank hypogammaglobulinaemia, in calves that had received colostrum (Fey and Margadant, 1961; Smith, 1962; Smith, O'Neill and Simmonds, 1967).

Fey and Margadant (1961) found hypogammaglobulinaemia in 10 per cent of their group of 'normal' calves, and in twenty-one out of twenty-two calves dying of colibacillosis due to *Escherichia coli*. They suggested that hypogammaglobulinaemia was an important pathogenetic factor in colibacillosis. This is undoubtedly true, since *E. coli* septicaemia in the calf is a common sequel to colostrum deprivation (Smith, 1962). However, in the light of more recent knowledge on the functional heterogeneity of the immunoglobulins, this concept can be modified somewhat.

There is evidence that antibodies to the lipopolysaccharide O-antigens of Gram-negative enteric bacteria are predominantly IgM in nature (LoSpalluto, Miller, Dorward and Fink, 1962; Weidanz, Jackson and Landy, 1964; Pike and Schulze, 1964). Furthermore, the experiments of Robbins, Kenny and Suter (1965) with *Salmonella typhimurium* indicated that these IgM antibodies were more efficient in complement-mediated bacteriolysis and as opsonins than IgG antibodies. Hill and Robbins (1966) found that the mouse-protective activity of IgM anti-pneumococcal antibodies was some 100,000 times greater than that of IgG.

From this one can infer that effective passive immunity to enteric (and possibly other) bacteria in the newborn is intimately related to the efficient transfer of specific IgM antibodies from the maternal circulation. Thus Ellis and Smith (1966) have suggested that the impermeability of the human placenta to IgM antibodies may be a pathogenetic factor in the development of bacterial septicaemias of the infant. Analogous mechanisms may operate in colibacillosis in calves that either do not receive colostrum, or fail to absorb colostral globulins.

Clearly this postulate only affords a partial explanation for the pathogenesis of colibacillosis in the calf. Many other factors are no doubt involved such as the exposure of the calf to serotypes to which the dam is not immune, dietary and other environmental influences.

The defect underlying the failure of colostral globulin absorption by some calves is obscure. It is known that during the period of intestinal permeability whole proteins are absorbed by a process of pinocytosis through the intestinal epithelium (Lecce, 1966). It is difficult to envisage a defect in such a universal, basic cellular function. Premature development of the intestinal enzyme system or closure of the permeability period are both possible, though unsubstantiated explanations.

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