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Colostral Transfer of Bovine Immunoglobulin E and Dynamics of Serum IgE in Calves

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ABSTRACT

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The role of IgE in protective immunity is becoming understood, therefore the colostral transfer of IgE and the age-dependent changes of IgE levels may be important for neonatal immunity. To investigate this question, serum samples were collected from range-fed Hereford cows and their calves from birth through 9 months of age. The sera were assayed for total IgE by enzyme-linked immunosorbent assay (ELISA). Calves were found to have significant levels of IgE during the first week postpartum, indicating colostral transfer of IgE. Thereafter, serum levels declined rapidly within 3 weeks from birth. The IgE levels began to increase after 12 weeks of age, and in some cases reached adult levels. The passive transfer of maternal IgE through colostrum may be important in providing early protection from disease, especially against intestinal parasites.

INTRODUCTION

It is well known that the newborn calf has no serum antibodies and obtains neonatal humoral protection from the transfer of immunoglobulins from colostrum. This transfer generally occurs within the first 24 h after birth, although some factors, such as low ambient temperature (Fisher, 1965), may decrease this period to as low as 6 h. The amount of IgG, IgM, and IgA transferred have been quantitated and their relative importance has been long established (Hansen and Phillips, 1947; Pierce, 1955; Smith et al., 1967; Penhale et al., 1973). IgM is important in providing protection from septicaemia (Bywater and Logan, 1974) and both IgM and IgG may prevent but not cure enteric infections (Logan et al., 1974b,c). Although the role of IgA in the very young calf is not well established, IgA is actively absorbed and then passed back into the intestinal lumen through external secretions (Porter, 1973); this suggests that IgA may be selectively protective against bacteria. Protection against enteric viral infections is provided by a continual supply of specific

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antibodies, primarily IgG_1, to the gut lumen via the ingestion of colostrum and milk (Crouch, 1985; Saif and Smith, 1985). Finally, it should be noted that colostral transfer of lymphocytes may also have some protective influences (Parmely and Beer, 1977; Schollenberger et al., 1986). In contrast to these data, relatively little is known about the dynamics of IgE in neonatal calves. Bovine IgE was first described by Hammer et al. (1971), and although much has been reported about the role of IgE in parasitic and allergic diseases in some other species, only a paucity of information is known about its role in cattle. Previously, serum levels of IgE for weaned calves and adult cows have been reported (Gershwin and Dygert, 1983), and IgE responses to specific antigens have been studied (Gershwin and Olsen, 1984a,b; Gershwin and Friebertshauser, 1987). The purpose of this report is to describe the dynamics of IgE levels in newborn calves.

MATERIALS AND METHODS

Animals

Fifty-nine pairs of range-fed Hereford cows and their calves were used in this study. The animals were from two pasture groups kept in the Sierra foothills. The calves were reared at pasture and weaned at approximately 6 months of age. Serial serum samples were collected from these cows and their calves within 10 days postpartum, during fall calving between late October through early December. A second set of samples was collected from the calves in mid-December; a third set, in mid-February; a fourth set, in early May; and a fifth set collected from heifers only, in early August. Thus the time periods of roughly less than 1 week, 2 months, 4 months, 7 months, and 9 months of age were represented. Due to the range of birth dates, these times represent rough approximations of age. All samples were stored at −20°C until assayed.

ELISA for total bovine IgE

A standardized reagent consisting of a previously defined mixture of mouse monoclonal antibodies specific for bovine epsilon chain, E2, E21, E29, E32 (Thatcher and Gershwin, 1988) was used for plate sensitization, at 1 mg/ml protein. This reagent was then diluted 1:200 in carbonate buffer (pH 9.6) and used to sensitize Probind microtiter plates (Falcon), using 100 μl per well by overnight incubation at 4°C. Rabbit serum albumin (100 μl of 1% solution in carbonate buffer) was then added to block any remaining combining sites in the wells. The plates were incubated at 37°C for 1 h, and then stored frozen at −20°C until needed. The plates were soaked for 20 min in phosphate-buffered saline (pH 7.4) with 0.05% Tween-20 (PBS-T), followed by five washes with PBS-T. Control and test sera were diluted in PBS-T and added to the plates

in duplicate, using 100 μl per well. Positive control bovine serum containing IgE, which was previously standardized (Gershwin and Dygert, 1983), was diluted 1:2, 1:4, 1:8, ..., 1:64. Fetal calf serum diluted 1:2 served as the negative control. Test sera were diluted 1:4. Plates were incubated at 37°C for 1 h, followed by a soak and wash cycle. Horseradish peroxidase-conjugated rabbit anti-bovine IgG (heavy and light chain) (Antibodies, Inc., Davis, CA) was diluted 1:1500 in PBS-T and 100 μl was added to each well, then incubated at 37°C for 2 h. After a soak and wash cycle, 200 μl of 55 m*M* O-phenylenediamine (Sigma) in 0.02% hydrogen peroxide-citrate buffer (pH 4.5) was added to each well and incubated at room temperature for 10 min. Absorbence values of the wells were read on a Dynatech ELISA plate reader set at reference $\lambda = 570$ and test $\lambda = 490$. Standard curves were made from the positive pool values as previously described (Gershwin and Dygert, 1983) and unit values assigned to the test sera from these curves. The lower limit of the standard curve was 0.4 IgE Units/ml and the upper limit was 50 IgE U/ml. After calculating values for

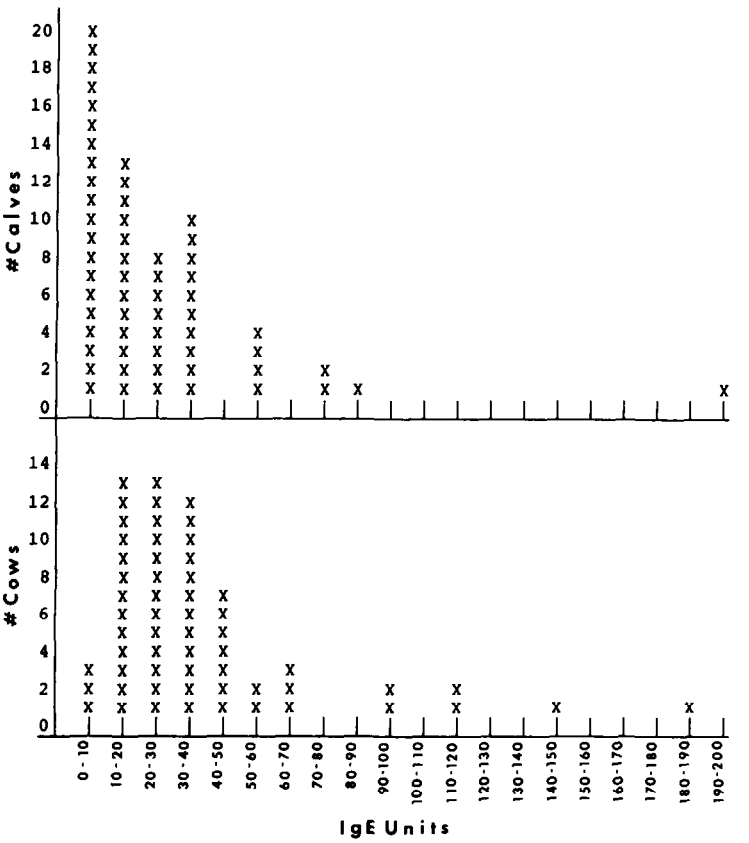

Fig. 1. Histogram illustrating distribution of serum IgE levels of 59 calves and their dams 0-10 days postpartum.

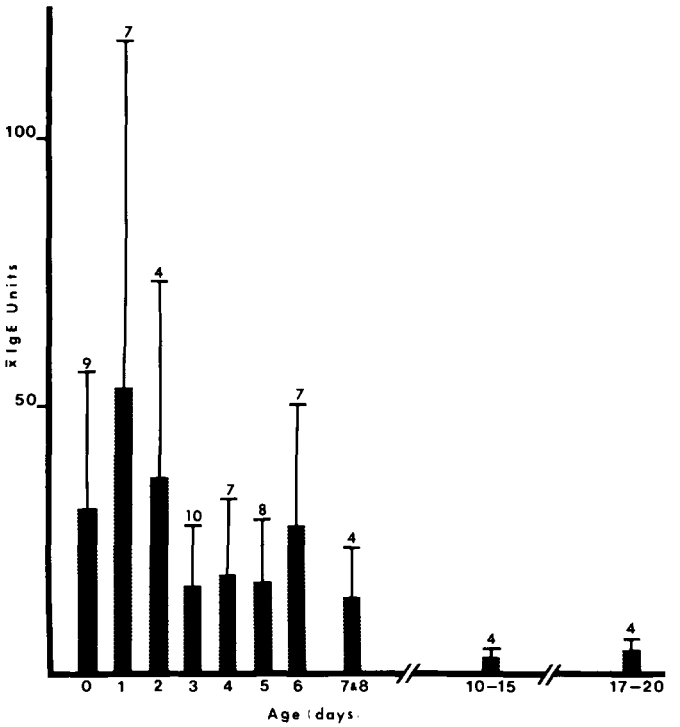

Fig. 2. Mean serum IgE levels for neonatal calves grouped by age at time of first sampling. Number per age group indicated at the top of each standard deviation bar.

test sera and multiplying by the dilution factor of 4, the limits for samples were 1.6 to 200 IgE U/ml.

Statistical analysis

Statistical analysis was done using the NCSS computer program (Hinze, Kaysville, UT). Variability was graphically displayed as standard deviation rather than standard error, to demonstrate the degree of variation between animals within a group. In analyzing the association of age with IgE levels, the Pearson product moment correlation coefficient (r) was used. The null hypothesis was $\rho = 0.00$ and Student's t-test was used to test for significance.

RESULTS

Calves less than 10 days old had a mean serum IgE level of 25.96 IgE U/ml, whereas the mean level for calves 11–60 days old was 2.82 IgE U/ml, nearly a ten-fold decrease. The cows' mean level was 39.76 IgE U/ml at 0–10 days post-

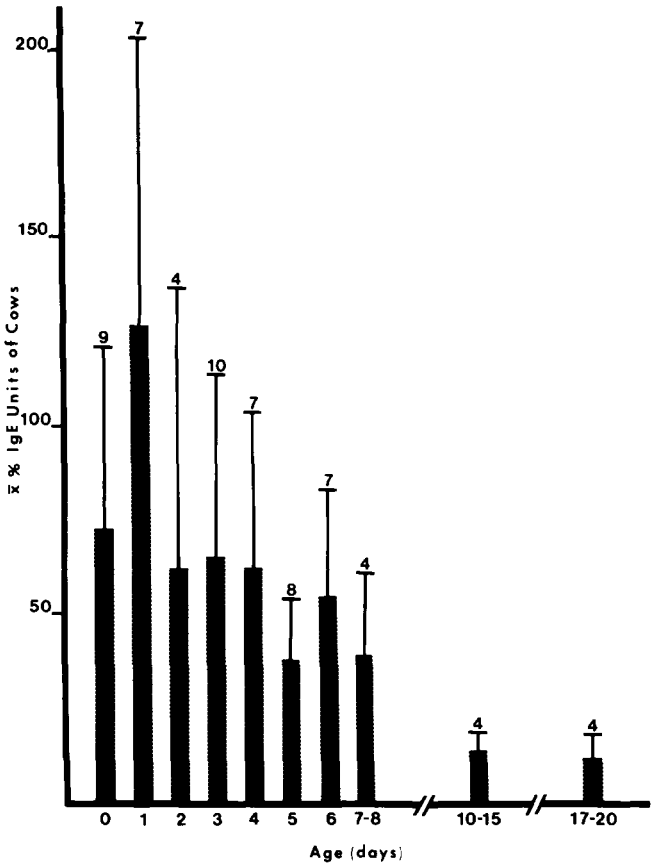

Fig. 3. Mean percent (calf [IgE U]/ cow [IgE U] × 100) serum IgE levels for neonatal calves grouped by age at time of first sampling. Number per age group indicated at the top of each standard deviation bar.

partum and 37.39 IgE U/ml at 11–60 days postpartum, which was not significantly different. At the first sampling, 55% of the calves had levels <20 U/ml, whereas only 27% of the cows had levels <20 U/ml. The distribution of the histogram shown in Fig. 1 is very similar to that of the larger sample group reported earlier (Gershwin and Dygert, 1983). With the calves grouped by age at the time of sampling, there was a marked rapid decline of IgE levels, beginning after the first 24 h and continuing through the third week of life, reaching a mean low of 2.65 IgE U/ml (Fig. 2). When the calf serum IgE levels were calculated as a percentage of the cows' IgE levels (Fig. 3), the decline was even more striking.

The initial serum IgE levels of the calves were strongly related to the IgE levels of their mothers and to the time elapsed postpartum before samples were

TABLE 1

Correlations of age with IgE levels

I.	Age vs. IgE U	
	0–10 days $r=-0.235$	$P=0.078$
II.	Age vs. $\bar{x}$ IgE U	
	0–8 days $r=-0.606$	$P=0.11$
	0–20 days $r=-0.746$	$P=0.013$
III.	Age vs. %IgE U	
	0–10 days $r=-0.343$	$P=0.013$
IV.	Age vs. $\bar{x}$ %IgE U	
	0–8 days $r=-0.699$	$P=0.05$
	0–20 days $r=-0.803$	$P=0.005$
Cow vs. calf at 1st bleed $r=0.398$		$P=0.002$

I: ungrouped, IgE levels (IgE U); II: grouped, mean IgE levels ($\bar{x}$ IgE U); III: ungrouped, IgE levels expressed as percentages of dams' levels (% IgE U); IV: grouped, mean IgE levels expressed as percentages of dams' levels ($\bar{x}$ %IgE U).

collected (see Table 1). When the calves' IgE levels were correlated without grouping by age at the time of sampling up to 10 days, the correlation coefficient (r) equalled -0.235, showing a weak trend of declining IgE levels with increasing age. By grouping the calves by age and correlating the mean IgE levels over a period of days, this trend became more obvious. To minimize the influence of the individual cows' IgE levels, the calf levels were calculated as percentages of their dams' IgE levels and correlations to age were made both ungrouped and grouped as above. This method gave $r=-0.803$ for grouped mean IgE levels up to 20 days old with a significance of $P=0.005$. There was a positive correlation of the calves' initial IgE levels compared with their dams' IgE levels, with $r=0.398$ ($P=0.002$). Due to the lack of multiple samples over a short period of time from individual calves, the half-life of IgE in serum could not be calculated. Based on the initial IgE levels of the calves and the decline after 24 h, the results suggested colostral transfer of IgE to the calves and absorption across the intestinal lumen within approximately the first 24 h.

Following the decline of serum IgE levels, increased levels began to appear in calves as early as 86 days old, with more individuals having higher values after 160 days old (Fig. 4). All but one of the calves sampled showed an autogenous IgE response some time after 12 weeks of age. The highest response found in this group of calves was 40 IgE U/ml. Of calves 12–18 weeks of age, 12% had levels > 7.5 U/ml; of calves 23–29 weeks old, 61% had levels > 7.5 U/ml and 22% of these had levels > 15 U/ml. Following this sampling, all calves were wormed with Tramisol. The lowered IgE levels of the heifers in the final

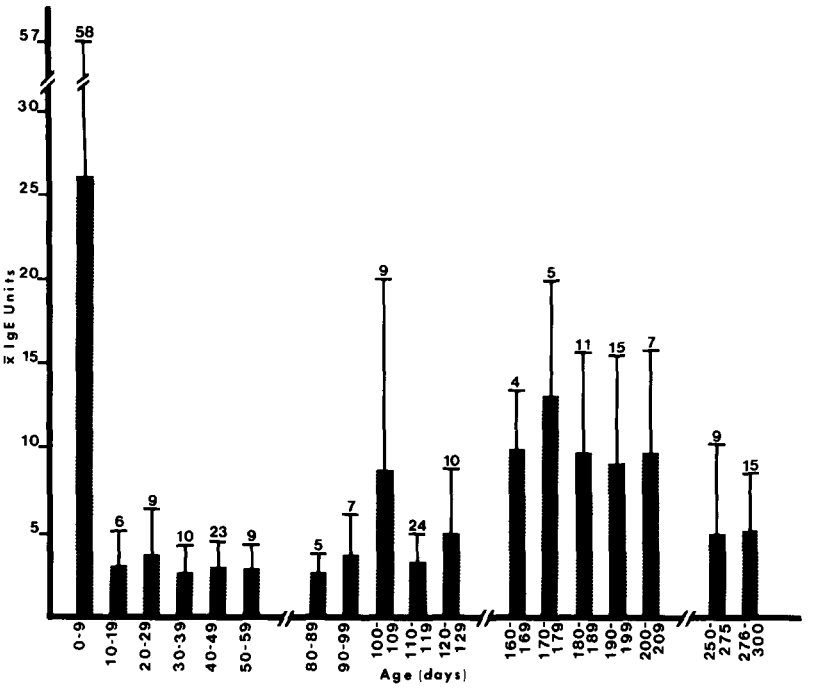

Fig. 4. Mean serum IgE levels of calves grouped by age at all sampling times. Number per group indicated at the top of each standard deviation bar.

sampling was probably due to the decreased worm burden. No correlation between initial levels and later response levels was demonstrated.

In comparing bull and heifer calves, no difference in IgE levels was noted at any sampling time up to 29 weeks of age. The differences between the two pasture groups were minor. Although there was no difference between the groups with regard to the serum IgE levels of the cows or the calves at the first three samplings, a significant difference in serum IgE levels occurred at the fourth sampling when the calves were between 22 and 29 weeks of age. One group had a mean IgE level of 11.61 IgE U/ml (S.D. = 5.76) and the other group had a mean level of 3.84 IgE U/ml (S.D. = 2.45), with the significance between the groups being $P = 0.0001$. As these two groups were maintained in separate pastures and the difference between the groups disappeared after worming, the most probable explanation would be differences in intestinal parasite exposure.

DISCUSSION

The apparent period of absorption of IgE from the colostrum of approximately the first 24 h is in agreement with reported periods of absorption of the

other immunoglobulins (Penhale et al., 1973). Indeed up to 40% of the immunoglobulin mass present in the intravascular space during the first 24 h is transferred to the extravascular space (Roy, 1980). This and the fact that the half-life of IgE in serum is quite short (Siraganian, 1983) would explain the rapid decline of the IgE levels in the neonatal calves. It is likely that much of the IgE becomes bound to Fc epsilon receptors on mast cells and basophils, which have very high binding constants, as well as to macrophages, eosinophils, T and B lymphocytes, and platelets (Capron et al., 1982, 1984; Huff et al., 1984; Joseph et al., 1986).

Calves normally begin to produce IgG after 4 weeks of age, although hypogammaglobulinaemic calves have been reported with autogenous IgG after only 7 days from birth (Logan et al., 1974a). Autogenous IgE appeared after 12 weeks of age in these calves, although IgE responses to soybean protein have been reported in the pre-ruminant calf (Kilshaw and Sissons, 1979).

The later response to a natural exposure of antigens is probably due to an initial passive protection of maternal IgE. The half-life of radio-labeled human myeloma IgE on mast cells is 8–14 days (Ishizaka and Ishizaka, 1971) and mast cell bindings of IgE has been reported to persist for 6–12 weeks in some species studied (Ishizaka and Ishizaka, 1971; Mendoza and Metzger, 1976). This passive immunity is probably important in protection against intestinal parasites in the neonatal calf. In one study of calves reared from birth at pasture, egg counts of trichostrongyles increased until 13 weeks of age, then the rate of increase slowed until 21 weeks of age, and after 21 weeks of age the egg count fell (Roy, 1964). It is well known that an immune response restricts egg production (Taylor, 1961). In fact, some 8-month-old calves in pasture exposure experiments have had very elevated IgE responses (Gershwin and Dygert, 1983), and this study demonstrates the ability of calves reared at pasture to respond after 12 weeks of age. Although the role of IgE in parasitic diseases is somewhat better described, IgE may also be involved in some bacterial and viral diseases (Bloch, 1967; Welliver et al., 1981; Gershwin and Friebertshauser, 1987).

The source of IgE in the colostrum is unknown at this time. It may be sequestered from the serum, as is the case for IgG and IgM (Rowland et al., 1953; Newby and Bourne, 1977), or it may be produced locally in the udder tissue, as is the case for IgA (Newby and Bourne, 1977). The answer to this question, as well as determination of IgE levels of serum and colostrum in cows prepartum and postpartum, is currently being pursued.

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