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The transfer of maternal IgE and other immunoglobulins specific for *Trichostrongylus colubriformis* larval excretory/secretory product to the neonatal lamb

A. Pfeffer*, R.J. Shaw, R.S. Green, M.D. Phegan

AgResearch Ltd., Wallaceville Animal Research Centre, P.O. Box 40063, Ward Street, Upper Hutt, New Zealand

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Abstract

The transference of immunoglobulins from six New Zealand Romney ewes to their lambs was examined. Immunoglobulin levels were determined in ewe plasma, colostrum and lamb plasma shortly after birth and before the lambs fed, in lamb plasma 2 days after birth, and lamb plasma, ewe plasma and milk 30 days after parturition. Levels of total IgE, and IgE, IgG1, IgG2, IgM, and IgA with specificity for *Trichostrongylus colubriformis* third stage larval secretory/excretory products (TcL3E/S) were determined. Mean levels of total IgE were three times higher in colostrum than in parturient ewe plasma while only trace amounts were detected in milk at 30 days after birth (107.7 , 34.3 , and 0.2 U ml^{-1} , respectively, differences between means $P \leq 0.01$). Mean total IgE in lamb plasma rose from being undetectable before suckling to levels comparable to those of the ewes by 2 days after birth (21.7 U ml^{-1}) and then declined to low levels by 30 days (0.4 U ml^{-1}). Total IgE levels in lamb plasma were significantly correlated with levels in ewe plasma and colostrum ($r = 0.91$, $P \leq 0.01$; $r = 0.96$, $P \leq 0.003$, respectively). The transference of TcL3E/S-specific IgE, IgG1 and IgA was substantial with mean levels of these antibodies in lamb plasma at 2 days comparable to that in parturient ewe plasma (absorbance levels in lamb plasma of 0.283 , 0.537 , and 0.334 , respectively). Proportionally less maternal IgM and IgG2 appeared to be transferred to the lambs (absorbance of 0.112 and 0.081 , respectively). Levels of TcL3E/S-specific IgE and IgG1 in lamb plasma at 2 days were significantly correlated with levels in parturient ewe plasma and colostrum ($r = 0.89$ and 0.82 , 0.85 and 0.96 ; all $P \leq 0.05$, respectively). These results indicate that IgE is concentrated in ewe colostrum and that substantial amounts of maternal IgE are transferred to lambs via colostrum. Further, the results suggest that humoral immunity against gastro-intestinal nematode parasites and potentially other parasites in colostrum-fed lambs may approximate that of the ewe. The implications of the transference of humoral immunity through colostrum in ruminants for the passive protection and the development of active immunity against parasites remains to be fully explored.

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Keywords: Colostrum; Maternal immunoglobulins; IgE; *Trichostrongylus colubriformis*; Neonatal immunity; Sheep

* Corresponding author. Tel.: +64 4 5290315; fax: +64 4 5290380.

E-mail address: alex.pfeffer@agresearch.co.nz (A. Pfeffer).

1. Introduction

The transfer of factors from mammalian mothers that may confer passive immunity and influence the developing immunological capacity of foetuses and newborn is well recognised. While transferred cells and soluble factors potentially influence immunity in the neonate, transferred immunoglobulins have received the most attention (Butler, 1999). The extent of transfer of immunoglobulins to the foetus varies with species and is related to the type of placentation and species-related differences are also apparent in the amounts of different immunoglobulin types in the colostrums and milk. In ruminants, it is generally believed that no antibody is transferred from the mother to the foetus while successful transfer via the colostrum in the immediate period after birth is vitally important for the survival of the neonate (Campbell et al., 1977; Butler, 1999). IgG is the dominant immunoglobulin in colostrum of ruminants with lesser quantities of IgM and IgA. The amount of IgG1 substantially exceeds that of IgG2, is predominantly derived from the maternal circulating pool and is selectively concentrated in ruminant colostrum (Campbell et al., 1977; Butler, 1999). The transfer of IgG1 across the mammary epithelium into ruminant colostrum appears to be mediated by the neonatal Fc receptor (FcRn) (Mayer et al., 2002). IgA, and possibly IgM, are transferred to colostrum via the polymeric immunoglobulin receptor (secretory component) and local synthesis of these antibodies in the mammary gland may substantially contribute to the colostrum pool (Butler, 1999). Following the early neonatal period in ruminants, the non-specific pinocytotic absorption of antibodies from the intestine diminishes rapidly and the levels of antibodies in milk decline (Butler, 1999; Mayer et al., 2002). However, some immunoglobulins, principally IgG1 and IgA, continue to be found in ruminant milk and may contribute to protection of the newborn within the lumen of the alimentary tract.

The extent of transfer of maternal IgE to the foetus and the neonate and the immunological consequences of this are less well understood in animals and man compared to the other major immunoglobulin classes. The possible transference of IgE from human mothers to their offspring has received attention in relation to the development of allergic (atopic) diseases. There

appears to be little transfer of maternal IgE to the foetus via the placenta (Delespesse et al., 1983). Recently, however, transfer of maternal IgE to the foetus and arming of CD23-bearing antigen presenting cells in the alimentary tract via foetal ingestion of amniotic fluid has been proposed (Thornton et al., 2003). Although strong correlations between IgE levels in maternal serum and colostrum has been demonstrated, human colostrum and milk contain only low levels of IgE (Turner et al., 1977; Duchon and Bjorksten, 1996). Overall, the available evidence indicates that IgE in the blood of newborn infants and during the early neonatal period is predominantly autogenous and may be produced in response to exposure of the foetus to environmental allergens in utero (Delespesse et al., 1983).

The transfer of maternal IgE to neonatal ruminants via colostrum has been recognised for some time. Early studies showed homocytotrophic antibodies of an 'immunoglobulin class analogous to human IgE' in bovine colostrum and transfer to neonatal calves (Hammer et al., 1971). Petzoldt and von Benton (1978) also demonstrated the acquisition by neonatal calves and lambs of homocytotrophic antibodies following ingestion of colostrum. Additionally evidence has been presented that skin mast cells of colostrum-deprived newborn calves lack surface-bound IgE (Mossmann et al., 1974) but are capable of binding IgE following intracutaneous injection (Hammer et al., 1971). More recently, serial blood sampling of calves showed substantial levels of IgE during the first week post partum; however, this quickly waned and then gradually rose again after 12 weeks of age (Thatcher and Gershwin, 1989). It was concluded that the initial levels of IgE were derived from colostrum and the later increase represented acquired immunological responses. IgE in colostrum of Australian Merino sheep has been measured using a specific anti-ovine IgE monoclonal antibody (Bendixsen et al., 2004).

The transference of maternal anti-nematode specific antibody to lambs was recorded by Filmer and McClure (1951) and has been noted in the course of subsequent studies (for example, Watson and Gill, 1991; McClure et al., 1998). However, in circumstances of natural infections, the possibility of a protective effect of maternally transferred antibodies against nematode parasites appears to have received little attention in sheep. Connan (1968) determined that there was no passive resistance to gastro-intestinal

parasites in colostrum-fed compare to colostrum-deprived lambs but acknowledged the absence of information on the level of anti-nematode antibodies in the colostrum in this study. Maternal antibodies transferred to the lamb potentially may also influence the development of acquired immunity to these parasites. The ability of neonatal lambs to mount immunological responses and resist gastro-intestinal parasites has been controversial (Watson and Gill, 1991, see Introduction in Emery et al., 1999). However, the ability of neonatal lambs to mount protective responses to *Trichostrongylus colubriformis* and *Haemonchus contortus* has been demonstrated (McClure et al., 1998; Emery et al., 1999, 2000). While the mechanisms of protection in the lambs were not identified, the authors discuss the potential importance of TH-2 type immunological responses during this age period and the tendency in the past for these immunological responses to be overlooked.

IgE plays a critical role in atopic diseases and in immunological responses to external and internal parasites. However, information remains limited on the extent of the transfer of IgE from the ewe and the consequences of this transfer for the lamb. In the present study, a quantitative assay was used to determine the levels of total IgE in serum and colostrum of New Zealand Romney ewes and in the serum of the lambs before and following colostrum intake and at 30 days of age. Additionally, the transfer of IgE specific for the gastro-intestinal nematode parasite, *T. colubriformis*, was compared to other immunoglobulin isotypes specific for this parasite.

2. Materials and methods

2.1. Sheep and experimental design

Mixed aged New Zealand Romney ewes judged close to parturition were moved to a small paddock for close surveillance. The teats of the ewes were covered with cotton swabs which were held in place with medical body stocking (Tubular-NET, size 7, Sutherland Medical Pty. Ltd., Caulfield South, Australia) that extended around the caudal body and udder. The ewes were monitored four times a day and the covering of the teats adjusted as necessary. After lambing, the coverings of each ewe's teats were examined and if it

was obvious that the lamb could not have suckled, blood samples from the ewe and one of her lambs were obtained. At the same time, 25 ml of colostrum was stripped from each teat of the ewe and pooled. The teats were then uncovered and monitoring continued to ensure the lamb bonded with the ewe and suckled. Forty-eight hours later, the lamb was blood sampled again. This procedure was repeated until six ewes and their lambs were sampled. Thirty days after birth, the lambs and their ewes were blood sampled again and approximately 50 ml of milk collected as for colostrum. In all cases, blood samples were obtained from the jugular vein using 6 ml evacuated tubes containing lithium heparin (Vacutainer[®], Becton Dickinson). The blood samples were centrifuged at $900 \times g$ for 15 min at 20 °C. The plasma was separated and, along with the colostrum and milk samples, stored at –20 °C until assayed.

2.2. Immunoglobulin assays

To determine total IgE in samples, the quantitative ELISA described by Shaw et al. (1997) was used. Colostrum and milk were initially diluted 1:1 in PBS. When samples following standard dilution gave results outside the upper range of the assay, they were further diluted and re-assayed. Results were expressed as units of IgE per milliliter of the undiluted sample based on comparison to a standard positive control (Shaw et al., 1997).

Semi-quantitative ELISAs were used to determine the level of activity of each immunoglobulin isotype specific for excretory/secretory antigens of *T. colubriformis* third stage larvae (TcL3E/S) in the various samples. IgE specific for TcL3E/S was assayed as described by Shaw et al. (1998). Plasma, colostrums, and milk samples were precipitated with 36% saturated ammonium sulphate. Sample supernatants were then diluted to one in 10 for assay. The other immunoglobulin isotypes specific for TcL3E/S were assayed as previously described (Douch et al., 1994). Samples were diluted 1:2000 for assay of IgG1 and IgM and 1:20 for IgG2 and IgA.

2.3. Statistical analysis

Data was log *e* transformed for statistical analysis. Significance of differences between immunoglobulin

levels in lambs and ewes and at different time points was determined using one-way analysis of variance followed by paired *t*-tests. The relationships between data sets were examined using Pearson's correlation.

3. Results

The mean level of total IgE in colostrum before lambs suckled was three-fold higher than in the plasma of the ewes at the same time (Table 1). In individual ewes, colostrum IgE levels ranged from 1.7 to 6 times higher than in plasma (data not shown). Thirty days after parturition, IgE levels in the ewe's plasma were not significantly different from that at parturition but levels in milk had fallen to very low levels. IgE was not detected in lamb plasma before suckling but had increased substantially by 2 days after birth to levels that were not significantly different from that in parturient ewe plasma (Table 1). By 30 days after birth, total IgE levels in lamb plasma had

declined again to very low levels. Total IgE levels in colostrum were significantly correlated with levels in ewe plasma at parturition and 30 days later (Table 2). Additionally, total IgE in plasma from 2 day old lambs was highly and significantly correlated to levels in colostrum and in ewe plasma at parturition and at 30 days.

Substantial mean levels of IgE specific for TcL3E/S were observed in colostrum and in parturient and 30 days plasma from ewes (Table 3). In 2-day old lambs, specific IgE in plasma had increased to a mean level that was not significantly different from that in parturient ewe plasma or colostrum. Only low levels of specific IgE were observed in milk and lamb plasma 30 days after parturition. Like total IgE, levels of specific IgE were significantly correlated in colostrum and ewe plasma at parturition and at 30 days (Table 4). Specific IgE levels in plasma from 2 days old lambs were significantly correlated with those in ewe plasma at parturition and in colostrum.

Table 1

Means levels of total IgE (U ml^{-1}) in colostrum, milk and plasma from ewes and plasma from their lambs before suckling, and 2 and 30 days after birth

	Ewes ($n = 6$)				Lambs ($n = 6$)		
	Parturient plasma	Colostrum	Thirty days plasma	Thirty days milk	Prefeed plasma	Two days plasma	Thirty days plasma
Mean	34.3 a, b	107.7 c	44.8 a	0.2 d	0.0 d	21.7 b	0.4 d
$\pm$ S.E.M.	26.9–43.8	74.4–155.9	34.5–58.3	0.1–0.3	–	14.5–32.6	0.3–0.5

Values are back-transformed from the log *e* transformed data used for statistical analysis. a–d, means with different letters were significantly different at $P \leq 0.01$.

Table 2

Correlations between total IgE levels in colostrum, milk and plasma samples from ewes and their lambs

		Ewes		
		Parturient plasma	Colostrum	Thirty days plasma
Ewes	Colostrum	0.91 ^a		
		0.01 ^b		
	Thirty days plasma	0.84	0.84	
		0.04	0.04	
Lambs	Two days plasma	0.91	0.96	0.81
		0.01	0.003	0.05

Note: IgE levels for milk at 30 days, and plasma from unsuckled and 30 days lambs were undetectable or very low and are not included here, see Table 1. In all comparisons $n = 6$ for each group.

^a Correlation coefficient.

^b Probability.

Table 3

Mean adsorbances of *T. colubriformis* L3E/S-specific immunoglobulin isotypes in colostrum, milk and plasma from ewes and their lambs

	Ewes (n = 6)				Lambs (n = 6)		
	Parturient plasma	Colostrum	Thirty days plasma	Thirty days milk	Prefeed plasma	Two days plasma	Thirty days plasma
IgE	0.385 ^a a,b 0.294–0.504 ^b	0.411 a,b 0.285–0.591	0.614 a 0.450–0.839	0.011 c 0.009–0.013	ND	0.283 b 0.192–0.418	0.011 c 0.011–0.012
IgG1	0.600 a 0.493–0.732	0.826 b 0.660–1.033	0.908 b 0.792–1.042	0.110 d 0.088–0.138	0.032 e 0.027–0.038	0.537 a 0.417–0.691	0.415 c 0.350–0.492
IgG2	0.167 a 0.115–0.240	0.043 b,d,e 0.025–0.069	0.126 c 0.086–0.182	0.006 d 0.003–0.010	0.038 e 0.029–0.050	0.081 a,b,c 0.061–0.108	0.048 e 0.041–0.055
IgM	0.195 a 0.169–0.225	0.183 a,b 0.156–0.216	0.253 b 0.228–0.279	0.058 e 0.055–0.061	0.084 d 0.079–0.090	0.112 c 0.102–0.122	0.063 e 0.058–0.069
IgA	0.185 a 0.192–0.324	0.331 a,b 0.286–0.479	0.743 b 0.545–0.766	0.269 a 0.203–0.280	0.095 c 0.082–0.123	0.334 a 0.241–0.414	0.075 c 0.055–0.080

ND = not done. Values are back transformed from the log *e* data used for statistical analysis. a–e, within rows, means with different letters were significantly different at $P \leq 0.05$.

^a Mean.

^b $\pm$ S.E.M.

TcL3E/S-specific IgG1, IgA, and IgM were also detected at substantial mean levels in colostrum while levels of IgG2 were low (Table 3). Levels of specific IgM and IgA were not significantly different in colostrum compared to parturient plasma while significantly higher levels of IgG1 and lower levels of IgG2 occurred in colostrum. Specific IgG1, IgM, and IgA levels increased significantly in plasma between parturition and 30 days, while IgG2 levels declined. In contrast, mean levels of IgG1 and IgM had declined substantially in milk at 30 days while IgA levels were not significantly different from that in colostrum. Before suckling, lamb plasma showed only low background levels of each immunoglobulin isotype. All isotypes had increased significantly in lamb plasma 2 days after birth with levels of IgG1, IgG2 and IgA not significantly different from those observed in ewe parturient plasma while the IgM level was significantly lower in the lambs. Mean levels of IgG1, IgG2, and IgA were significantly lower at 30 days compared to 2 days in lamb plasma with the most pronounced decline occurring in IgA.

Levels of specific IgG1 and IgG2 were significantly correlated in colostrum and ewe plasma at parturition and at 30 days (Table 4). IgG1 levels in lamb plasma at 2 and 30 days were significantly correlated with levels in colostrum and ewe plasma at parturition and 30

days while IgG2 levels in the lambs at these ages correlated significantly only with colostrum levels. Levels of specific IgG1, IgG2 and IgA in lamb plasma were significantly correlated at 2 and 30 days.

4. Discussion

The results presented here show that ovine colostrum can contain substantial quantities of total IgE. The only previous quantification of IgE in ruminant colostrum of which we are aware was in Australian Merino ewes where a range of 0.55–11.05 ng ml⁻¹ was reported (Bendixsen et al., 2004). The geometric mean level of IgE in the colostrum of the Romney ewes examined here was 107.7 U ml⁻¹ which approximates 93 μ g ml⁻¹ (Shaw et al., 1997). The much higher levels observed in our ewes are not readily explained, however, if absence of technical reasons is assumed, could be related to breed differences and levels of allergenic challenge particularly from gastro-intestinal nematode parasites. In the present study, mean IgE levels in colostrum were three and 2.5 times higher than in ewe plasma at parturition and 30 days later, respectively (Table 1). However, levels of IgE in milk were very low (Table 1). The degree of concentration of IgE in

Table 4

Correlations between adsorbances for immunoglobulin isotypes specific for *T. colubriformis* L3E/S in samples from ewes and their lambs

		Ewes			Lambs
		Parturient plasma	Colostrum	Thirty days plasma	Two days plasma
Ewes					
Colostrum	IgE	0.90 ^{a,*}			
	IgG1	0.94 [*]			
	IgG2	0.87 [*]			
	IgM	−0.09			
	IgA	0.58			
30 Days Plasma	IgE	0.71	0.85 [*]		
	IgG1	0.77	0.87 [*]		
	IgG2	0.99 [*]	0.82 [*]		
	IgM	0.91 [*]	0.18		
	IgA	0.72	0.35		
Lambs					
2 Days plasma	IgE	0.89 [*]	0.82 [*]	0.80	
	IgG1	0.85 [*]	0.96 [*]	0.93 [*]	
	IgG2	0.58	0.86 ^{b,*}	0.54	
	IgM	0.25	0.59	0.37	
	IgA	0.73	0.47	0.27	
30 Days plasma	IgE	0.51	0.28	0.46	0.64
	IgG1	0.88 [*]	0.97 [*]	0.86 [*]	0.98 [*]
	IgG2	0.66	0.86 ^{*,b}	0.63	0.98 ^{*,b}
	IgM	0.78	0.03	0.92 ^{*,b}	0.39
	IgA	0.48	0.23	0.08	0.88 ^{*,b}

Note: No significant correlations were observed between immunoglobulins in milk or unsuckled lamb plasma and other plasma or colostrum samples.

^a Correlation coefficient.

^b Indicated comparisons include consistently low absorbances for the immunoglobulins in lamb plasma at 2 and 30 days and the biological relevance of the observed correlations should be regarded with caution, see Table 3.

^{*} Statistically significant ($P \leq 0.05$).

colostrum suggests that IgE is selectively transferred into this compartment or locally synthesised in the mammary gland (Butler, 1999). Total IgE levels in colostrum were highly correlated with those in plasma (Table 2) which is compatible with the selective transfer of IgE from the circulating pool. Additionally, the increase in mean plasma IgE levels in the ewes 30 days after parturition (Table 1), although not statistically different, could represent a rebound of plasma IgE levels reminiscent of that reported for IgG1 (Cripps et al., 1976; Butler, 1999). However, the possibility cannot be excluded that some of the IgE in colostrum is locally produced in the mammary gland as shown for IgA (Butler, 1999). There is evidence that the mechanisms of transfer of IgG1 and IgA across the glandular epithelium of the ruminant mammary gland differ. IgG1 is thought to be selectively transferred by

FcRn (Mayer et al., 2002). IgA and potentially IgM are concentrated in colostrum through transfer via secretory component (Butler, 1999). In the case of IgE, a possible mechanism for transference into colostrum might involve CD23 (FcεRII, low affinity IgE Fc receptor) as this receptor has been implicated in transport of IgE (and antigen) across the intestinal epithelium of rats (Yang et al., 2000). The possibility that IgE is selectively concentrated in ovine colostrum and the mechanisms by which this may occur require more detailed study.

Levels of TcL3E/S-specific IgE in colostrum were also highly correlated with levels in ewe plasma (Table 3). However, the mean level in colostrum was not significantly higher than in ewe plasma at parturition or 30 days later. This discrepancy between total and TcL3E/S-specific IgE suggests that the IgE in

colostrum may not fully represent the circulating pool of IgE. Discrepancy between plasma and colostrum levels of total IgG4 and IgG4 specific to several antigens has been observed, and suggested for IgE and IgD, in human mothers (Keller et al., 1983). This was ascribed most likely to local production of antibody in the mammary gland.

In our ewes, the significant increase in plasma levels of specific IgM and IgA at 30 days post-partum compared to levels at parturition, and the similar trends in total and specific IgE levels, concur with the general concept of recovery of immunological responsiveness following the periparturient period (Tables 1 and 3). For sheep on pasture, antibody levels during the periparturient period may be influenced by hormonal factors, nutrition, levels of antigenic stimulation, and stress (Barger, 1993). While these factors may also affect the levels of IgG1, the depression of circulating levels of this isotype in periparturient sheep and cattle with recovery around 20 days post-partum is regarded as largely due to the very substantial transfer of this isotype to colostrum (Cripps et al., 1976; Butler, 1999). In contrast to the other isotypes, TcL3E/S-specific IgG2 levels declined significantly between parturition and 30 days post partum possibly reflecting a shift in the type of immunological response to nematode parasites during this period.

Our data show that substantial quantities of the colostral IgE were transferred to the lambs. Before feeding, IgE was undetectable in lamb plasma while 2 days after birth mean plasma level of total IgE and TcL3E/S-specific IgE were not significantly different from levels in parturient ewe plasma (Tables 1 and 3). The IgE levels in the lambs at this time were highly correlated with those in their mother's plasma and colostrum (Tables 2 and 4). IgE in the plasma of the lambs declined to very low levels by 30 days after birth. A previous study in cattle similarly showed high levels of IgE in the very young calves and a rapid decline thereafter until active immunity became established (Thatcher and Gershwin, 1989). The fate of the IgE during the period of rapid decline of circulating levels in the young ruminant is not known but it is clear that mast cells in skin, at least, are effectively armed for prolonged periods and this provides the necessary mechanism for immediate hypersensitivity responses (Hammer et al., 1971; Mossmann et al., 1974).

The transference of anti-nematode antibody in ewe colostrum has been on record for some time (Filmer and McClure, 1951), however, the subject has received limited specific study. Comparison of plasma levels before feeding and at 2 days of age in the lambs in the present study showed that substantial transfer of TcL3E/S-specific IgG1 and IgA occurred in addition to specific IgE. In plasma from 2 day old lambs, levels of IgG1 approximated, and levels of IgA exceeded, levels in parturient ewe plasma. Proportionally less specific IgG2 and IgM appeared to be transferred to the lambs (Table 3). IgG1 specific for TcL3E/S was the only isotype maintained at substantial levels until 30 days post-partum. Like IgE, IgA levels in lamb plasma were substantially reduced by 30 days.

The colostral transference of IgE, IgG1, and IgA and also lesser proportional amounts of IgG2 and IgM suggest that the humoral immunity of a lamb in early life may approximate that of its mother. However, if antibodies of particular antigen specificities are not transferred in proportion to those occurring in the ewe then potentially some difference in the responsiveness of the lamb may occur. The value of the transferred immunoglobulin in ruminants for protection against microbial infections during early life and interference with immunological responses to vaccines are well recognised. The magnitude of transference of IgE to the lamb shown in the present study and the documented arming of mast cells further suggest that this isotype may contribute to passive protective responses to parasites in lambs. Transferred IgE may provide initial protective functions through inciting avoidance behaviour in response to ectoparasites and resistance to establishment of both ectoparasites and internal parasites. Generally, investigation of a protective effect of colostrum-derived antibodies against parasites appears to have been limited. Convincing demonstrations of protection afforded by maternally-derived antibody under natural circumstances have been recorded for *Ascaris suum* in pigs and *Taenia ovis* in sheep (Kelley and Nayak, 1965; Rickard and Arundel, 1974) while other studies suggesting either protection or lack of protection are not conclusive (Connan, 1968; Kloosterman et al., 1980; Rajapakse et al., 1994). Additionally, the possibility that humoral immunity transferred to the lamb may influence the development of acquired immunity to parasites appears to have been neglected. The ability of neonatal lambs to develop

significant protection to gastro-intestinal nematodes has been demonstrated and it was considered that a TH-2 type bias early in life may contribute to this (McClure et al., 1998; Emery et al., 1999, 2000). The possibility that the transference of parasite-specific IgE and other antibody isotypes may influence acquisition of acquired immunity should also be considered. IgG and IgE have been shown to focus antigen to APCs and potentially such focusing may influence not only the degree of responsiveness but also whether the immune response is biased in a Th-1 or Th-2 direction (Anderson and Mosser, 2002; Thornton et al., 2003). Further, maternally derived IgE may contribute to skewing immune responses in the neonate in the Th-2 direction by facilitating activation of mast cells and basophils with consequent release of Th-2 type cytokines.

5. Conclusion

The present work has demonstrated a substantial transference of IgE from ewes to lambs via colostrum. Further studies are required to determine if IgE is selectively concentrated in colostrum and, if so, what mechanisms may be involved. In addition, further research seems warranted to elucidate the full implications of the transference of IgE and other antibody isotypes for passive protection and the development of naturally acquired immunity against parasites in the neonatal lamb.

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References

- Anderson, C.F., Mosser, D.M., 2002. Cutting edge: biasing immune responses by directing antigen to macrophage Fc gamma receptors. *J. Immunol.* 168, 3697–3701.
- Barger, I.A., 1993. Influence of sex and reproductive status on susceptibility of ruminants to nematode parasitism. *Inter. J. Parasitol.* 23, 463–469.
- Bendixsen, T., Windon, R.G., Huntley, J.F., MacKellar, A., Davey, R.J., McClure, S.J., Emery, D.L., 2004. Development of a new monoclonal antibody to ovine chimeric IgE and its detection of systemic and local IgE antibody responses to the intestinal nematode *Trichostrongylus colubriformis*. *Vet. Immunol. Immunopathol.* 97, 11–24.
- Butler, J.E., 1999. Immunoglobulins and immunocytes in animal milks. In: Ogra, P.L. (Ed.), *Mucosal Immunology*. 2nd ed. Academic Press, New York, pp. 1531–1554.
- Campbell, S.G., Siegel, M.J., Knowlton, B.J., 1977. Sheep immunoglobulins and their transmission to the neonatal lamb. *N.Z. Vet. J.* 25, 361–365.
- Connan, R.M., 1968. An attempt to demonstrate passive resistance in lambs to three species of gastro-intestinal nematodes as a result of suckling the ewe. *Res. Vet. Sci.* 9, 591–593.
- Cripps, A.W., Fulkerson, W.J., Griffiths, D.A., McDowell, G.H., Lascelles, A.K., 1976. The relationship between the transfer of immunoglobulins, sodium and potassium into mammary secretion of the parturient ewe. *Aust. J. Exp. Biol. Med. Sci.* 54, 337–348.
- Delespesse, G., Sarfati, M., Lang, G., Sehon, A.H., 1983. Prenatal and neonatal synthesis of IgE. *Mongr. Allerg.* 18, 83–95.
- Douch, P.G.C., Green, R.S., Risdon, P.L., 1994. Antibody responses of sheep to challenge with *Trichostrongylus colubriformis* and the effect of dexamethasone treatment. *Int. J. Parasitol.* 24, 921–928.
- Duchen, K., Bjorksten, B., 1996. Total IgE levels in human colostrums. *Pediatr. Allerg. Immunol.* 7, 44–47.
- Emery, D.L., McClure, S.J., Davey, R.J., Bendixsen, T., 1999. Induction of protective immunity to *Trichostrongylus colubriformis* in neonatal merino lambs. *Int. J. Parasitol.* 29, 1037–1046.
- Emery, D.L., McClure, S.J., Davey, R.J., 2000. Protection of Merino lambs against *Haemonchus contortus* by trickle infection of neonates. *Parasitol. Int.* 49, 165–170.
- Filmer, D.B., McClure, T.J., 1951. Anti-nematode antibody in ewe colostrums. *Nature* 168, 170.
- Hammer, D.K., Kickhofen, B., Schmid, T., 1971. Detection of homocytotropic antibody associated with a unique immunoglobulin class in the bovine species. *Eur. J. Immunol.* 1, 249–258.
- Keller, M.A., Heiner, D.C., Kidd, R.M., Myers, A.S., 1983. Local production of IgG4 in human colostrums. *J. Immunol.* 130, 1654–1657.
- Kelley, G.W., Nayak, D.P., 1965. Passive immunity to *Ascaris suum* transferred in colostrum from sows to their offspring. *Am. J. Vet. Res.* 26, 948–950.
- Kloosterman, A., Benedictus, J., Aghina, H., 1980. Colostral transfer of anti-nematode antibodies in cattle and its significance for protection. *Vet. Parasitol.* 7, 133–142.
- Mayer, B., Zolnai, A., Frenyó, L.V., Jancsik, V., Szentirmay, Z., Hammarström, L., Kacsokovics, I., 2002. Redistribution of the sheep neonatal Fc receptor in the mammary gland around the time of parturition in ewes and its localization in the small intestine of neonatal lambs. *Immunology* 107, 288–296.
- McClure, S.J., Emery, D.L., Bendixsen, T., Davey, R.J., 1998. Attempts to generate immunity against *Trichostrongylus*

- colubriformis* and *Haemonchus contortus* in young lambs by vaccination with viable parasites. *Int. J. Parasitol.* 28, 739–746.
- Mossmann, H., Meyer-Delius, M., Vortisch, U., Kickhofen, B., Hammer, D.K., 1974. Experimental studies on the bridging hypothesis of anaphylaxis: haptenic determinants required to elicit immediate-type reactions in calf skin by separate or concurrent sensitization with reagents of different specificity. *J. Exp. Med.* 140, 1468–1481.
- Petzoldt, K., von Benton, C., 1978. Passive allergisation of calves and lambs due to colostral antibodies. *Ann. Rech. Vet.* 9, 235–238 (review).
- Rajapakse, R.P.V.J., Lloyd, S., Fernando, S.T., 1994. *Toxocara vitulorum*: maternal transfer of antibodies from buffalo cows (*Bubalis bubalis*) to calves and levels of infection with *T. vitulorum* in the calves. *Res. Vet. Sci.* 57, 81–87.
- Rickard, M.D., Arundel, J.H., 1974. Passive protection of lambs against infection with *Taenia ovis* via colostrum. *Aust. Vet. J.* 50, 22–24.
- Shaw, R.J., McNeill, M.M., Gatehouse, T.K., Douch, P.G.C., 1997. Quantification of total IgE concentration using anti-ovine IgE monoclonal antibodies in an enzyme immunoassay. *Vet. Immunol. Immunopathol.* 57, 253–265.
- Shaw, R.J., Gatehouse, T.K., McNeill, M.M., 1998. Serum IgE responses during primary and challenge infections of sheep with *Trichostrongylus colubriformis*. *Int. J. Parasitol.* 28, 293–302.
- Thatcher, E.F., Gershwin, L.J., 1989. Colostral transfer of bovine immunoglobulin E and dynamics of serum IgE in calves. *Vet. Immunol. Immunopathol.* 20, 325–334.
- Thornton, C.A., Holloway, J.A., Popplewell, E.J., Shute, J.K., Boughton, J., Warner, J.O., 2003. Fetal exposure to intact immunoglobulin E occurs via the gastro-intestinal tract. *Clin. Exp. Allergy* 33, 306–311.
- Turner, M.W., McClelland, D.B.L., Medlen, A.R., Stokes, C.R., 1977. IgE in human urine and milk. *Scand. J. Immunol.* 6, 343–348.
- Watson, D.L., Gill, H.S., 1991. Post natal ontogeny of immunological responsiveness in Merino sheep. *Res. Vet. Sci.* 51, 88–93.
- Yang, P.-C., Berlin, M.C., Yu, L.C.H., Conrad, D.H., Perdue, M.H., 2000. Enhanced intestinal transepithelial antigen transport in allergic rats is mediated by IgE and CD23 (FcεRII). *J. Clin. Invest.* 106, 879–886.