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IgD in Human Colostrum

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ABSTRACT. Simultaneous colostrum (C) and plasma samples (P) from 14 women, 1 to 5 days postpartum, were examined. Total IgD and specific IgD antibodies to β-lactoglobulin, bovine serum albumin, Bermuda grass, and α-gliadin were measured by solid phase radioimmunoassay. The geometric mean concentrations of IgD were 35.8 (range 2.2–410) μg/dl for colostrum and 591.3 (range 72–4100) μg/dl for plasma. Six subjects had a specific IgD antibody C/P ratio more than 10-fold greater than the total IgD C/P ratio, suggesting enhancement of antibody to a specific antigen in the mammary gland. All six had C/P ratios suggestive of local enhancement of IgD antibody to Bermuda grass, and two met this criterion for enhancement of IgD antibodies to β-lactoglobulin, bovine serum albumin, or α-gliadin. Specimens for these studies were obtained during the peak grass pollen season. Seventeen additional subjects were studied to compare total IgD in colostrum and plasma with total IgG and serum albumin. The mean C/P ratio for IgD (0.055 ± 0.015) exceeded the C/P ratio for total IgG (0.015 ± 0.003) or total albumin (0.020 ± 0.002). For 14 of 17 subjects the colostrum/plasma ratio for IgD exceeded the C/P ratio for albumin or IgG. Data were transformed logarithmically and correlation coefficients calculated. For albumin *versus* IgG in colostrum, there was a strong correlation, r = 0.865, $p = 0.001$. This was different from albumin *versus* IgD, r = 0.489, $p = 0.046$ and from IgD *versus* IgG, r = 0.556, $p = 0.020$. These analyses support a different mechanism of entry of IgD into milk compared to IgG or albumin. These studies also suggest that IgD antibodies may participate in responses of the mucosal immune system. (*Pediatr Res* 19: 122–126, 1985)

Abbreviations

C, colostrum
P, plasma
C/P, colostrum/plasma ratio
BG, Bermuda grass
BLG, β-lactoglobulin
BSA, bovine serum albumin

Recent interest in both animal and human breast milk immunology concerns homing of lymphoblasts from mucosal sites to the mammary gland with resultant local production of immunoglobulin in the mammary gland (1, 11, 23, 26). Evidence has been advanced for a common mucosal immune system involving the gastrointestinal tract, respiratory tract, salivary glands, lacrimal glands, and mammary glands (12, 18, 19, 27).

Although IgA is the principal immunoglobulin in human milk and is locally produced in the mammary gland (7, 20), data have also supported some local production of IgM (7, 20) and IgG_4 (13). IgD levels have been examined in human milk (2, 9, 24), and comparison of parallel milk and plasma IgD and IgE values suggest either selective transfer into colostrum or possible local production of these immunoglobulins in the mammary gland of individual subjects (2).

We wished to examine further the question of local mammary production of IgD and possible participation of IgD in a mucosal immune system. We examined paired colostrum and plasma samples for total IgD and IgD specific antibodies to BG, α-gliadin, BLG, and BSA to look for evidence of enhancement of specific IgD antibodies in human colostrum. These antigens were chosen as representative of antigens to which mucosal surfaces are exposed.

A second series of subjects was studied for IgD, albumin, and IgG in colostrum and plasma. The purpose of this study was to determine if total IgD was enhanced in colostrum compared to albumin and IgG, proteins which appear in the milk presumably by passive transfer from the serum.

MATERIALS AND METHODS

Informed consent was obtained from 31 postpartum women to obtain colostrum and peripheral blood specimens. Paired samples were obtained 1 to 5 days postpartum. Colostrum was obtained using either a hand pump (Lopuco, West Laurel, MD) or an electric pump (Egnell, Cary, IL). Blood samples were obtained at the time of colostrum collection by venipuncture and were heparinized using 10 units of heparin per ml.

Colostrum samples were centrifuged at 400 × *g* for 15 min to remove cells and were further clarified at 12,100 × *g* for 30 min after which they were frozen at −20° C until assayed.

Total IgD was determined using a paper disc solid phase radioimmunoassay (15) in which cyanogen bromide-activated paper discs were coated with rabbit anti-human IgD(Fc). Human IgD(Fc) was prepared and isolated by a method similar to that used previously to prepare IgE(Fc) (15) with the following modifications. Papain digestion of D-myeloma protein was shortened to 15 min in preparing IgD(Fc). Epsilon aminocaproic acid, 10 mM, was present in all reagents used during the isolation and digestion of D-myeloma protein and in all affinity chromatography and radioimmunoassays involving IgD. Rabbits were immunized with IgD(Fc) (16) and rabbit anti-IgD(Fc) was purified from rabbit antisera by fractional ammonium sulphate precipitation and by immunoadsorption of anti-IgD antibody to a second insolubilized D-myeloma protein followed by elution with 6 molar urea. This isolation by affinity chromatography also served to remove anti-idiotype antibodies.

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The product, when ^{125}I-labeled by the chloramine-T technique (16), showed 45% binding to a D-myeloma coated paper disc, indicating that at least 45% of the product was undenatured specific anti-IgD antibody. Less than 1% bound to discs coated with IgG. Inhibition of binding of ^{125}I-anti IgD to solid phase IgD was shown with D myeloma protein but not with IgG, IgA, IgM, or IgE myeloma proteins.

Anti IgD(Fc) was covalently bound to cyanogen bromide activated discs. Test samples were incubated with the discs. These assays were performed with 5 μl of plasma and 200 μl of 0.1 M phosphate buffer (20% unsuckled calf serum, 0.005 M epsilon aminocaproic acid, 0.02% sodium azide, and 0.05% tween 20). For colostrum studies (subjects 1 to 14) the volume of colostrum used (50 μl) was 10 times more than the volume of plasma used. The volume of buffer was decreased accordingly. In all assays, the total volume of specimen plus buffer was constant for both colostrum and plasma. This adjustment in volume was made since the total IgD content is lower in colostrum than in plasma. After washing, approximately 50,000 cpm of ^{125}I-labeled anti-IgD (specific activity 4 μCi/μg) were added. Counts per minute bound to each disc after removing unbound label were proportional to the total IgD in the test sample. Standard curve for percent bound radioactivity was drawn from the counts bound using dilutions of a known standard serum tested in the same assay. The standard curve ranged from 0.6 to 36,000 μg/dl. All assays were performed in duplicate and duplicate values did not deviate from the mean by more than 15%. All colostrum and plasma pairs were assayed simultaneously in the same assay.

For the second series of subjects (nos. 15 to 31), the IgD in plasma and colostrum samples was first assayed as above. One subject (no. 26) was noted to have less than 1 μg/dl IgD in both colostrum and plasma. This subject's IgD-deficient colostrum was then used to construct a separate IgD colostrum standard curve by adding 5 μl of serial dilutions of a control serum (36,000 μg/dl of IgD) to 150 μl of buffer plus 50 μl of IgD-deficient colostrum. Colostrum samples (nos. 15 to 31) (50 μl) plus 150 μl of buffer and 5 μl of a 1:100 dilution of serum without detectable IgD were then assayed for percentages of counts bound to the disc. IgD values were read from the colostrum curve and divided by 10 since 10 times more colostrum was added to the disc than control serum used for the standard curve. The assay was done in this way to control for differences in protein content of colostrum and plasma samples and possible effects of other colostrum constituents. The colostrum values for total IgD were lower when read from the colostrum curve compared to the plasma curve. It was not possible to reassay the first series of specimens (nos. 1 to 14) using a colostrum standard curve since the supply of IgD deficient colostrum had been exhausted.

Specific IgD. Specific IgD antibodies were measured using a solid phase radioimmunoassay technique, the basic steps for which were described previously (16), for subjects (nos. 1 to 14). Preparation of specific antigen coated discs was carried out by incubating 2 mg/ml of protein antigen with cyanogen bromide activated paper discs at 4° C for 72 h. BSA was obtained from Sigma (St. Louis, MO), BG from Hollister-Stier (Spokane, WA), α-gliadin from USDA Northern Utilization Research and Development Division (Peoria, IL), BLG from Pentex Research Products Division, Miles Laboratories, Inc., Kankakee, IL.

Either 5 μl plasma or 50 μl colostrum previously diluted with buffer to give a constant total volume of 100 μl was incubated with an antigen coated disc. Discs were washed with 0.1 M phosphate buffer containing 5% human serum albumin. ^{125}I-anti-IgD was then incubated with each disc and washed. The percentage of labelled anti-IgD bound to the disc was proportional to the amount of specific antibody present in the sample. All assays were performed in duplicate and duplicate values did not deviate from the mean by more than 15%. All colostrum and plasma pairs were assayed simultaneously in the same assay.

Standard curves were drawn for each antigen utilizing dilutions of known strongly positive sera each of which was assigned a value of 10,000 AU. Since the volume of colostrum used was 10 times greater than the volume of plasma, the sensitivity of the colostrum assays was 10 times greater than the plasma assays. An a-γ-globulinemic serum and a pooled serum from 12 healthy adults were also tested in each assay. It was not possible to reassay specific IgD antibody using a colostrum standard curve since the supply of IgD-deficient colostrum had been exhausted.

Serum albumin was assayed using radial immunodiffusion plates from Kallestad (Austin, TX). Low level albumin plates were used for colostrum. All measurements were done in duplicate and the mean value recorded. Total IgG was also assayed by radial immunodiffusion. Ultra low level plates from Kallestad were used for colostrum, and standard level plates (Meloy, Springfield, VA) were used for plasma values.

RESULTS

Data for subjects (nos. 1 to 14) are summarized in Table 1. Total IgD, specific IgD antibodies, geometric means, and colostrum/plasma ratios are listed for these antibodies. Specific antibody data for pooled normal serum and an agammaglobulinemic serum are also listed. The mean values for colostrum were considerably lower than mean values for plasma with the exception of BG data. The mean colostrum/plasma ratio (± SEM) for total IgD was 0.118 ± 0.049 while similar colostrum/plasma ratios for specific IgD antibodies were 0.168 ± 0.028 for BLG, 0.499 ± 0.124 for BG, 0.165 ± 0.031 for BSA, and 0.141 ± 0.028 for α-gliadin. For six subjects a specific IgD antibody colostrum/plasma ratio exceeded the comparison total IgD colostrum/plasma ratio by a factor greater than 10. These data demonstrate a marked enrichment of IgD antibodies of certain specificity in the colostrum and suggest the possibility of local production.

All six subjects with evidence of local antibody production had enrichment of anti-BG antibodies in colostrum. For each of the other three IgD antibodies assayed (BLG, BSA, α-gliadin), two subjects showed antibody enhancement. All these specimens were obtained from the end of March to the beginning of August 1978, a period of time which coincides with the peak season for grass pollen in the Los Angeles basin. Only one of the six subjects with enhanced anti-BG IgD antibodies in colostrum had an allergic history. This subject was allergic to a medication and possibly had hay fever symptoms.

The sign test (4) was used to compare the colostrum/plasma ratios for each of the specific IgD antibodies with the colostrum/plasma ratios for total IgD. The colostrum/plasma ratios for Bermuda grass specific IgD were significantly higher than the C/P ratios for IgD ($p < 0.01$). The ratios for BSA, BLG, and α-gliadin were not significantly higher than the IgD C/P ratios.

Data from Table 1 were transformed logarithmically and the Pearson correlation coefficient was calculated (3) for total colostrum IgD compared to specific IgD antibody in colostrum. There was no positive correlation between specific and total IgD in colostrum.

These data demonstrate that high specific IgD antibody in colostrum was not associated with high total IgD in colostrum and indicate that IgD antibodies of certain specificities are enhanced in colostrum.

In addition, the Pearson correlation coefficient was calculated comparing colostrum and plasma values for each specific IgD antibody. A positive correlation was found for BLG specific IgD in colostrum *versus* plasma ($r = 0.569$, $p = 0.034$) but not for BG, α-gliadin, or BSA in colostrum *versus* plasma. The lack of a positive correlation between colostrum and plasma values for BG, BSA, and α-gliadin specific IgD antibodies would further support an hypothesis that these antibodies were not passively transferred from the serum.

IgD, albumin, and IgG. Further information relating to the possible local production of specific IgD antibodies in colostrum was obtained by study of additional colostrum-plasma pairs for

Table 1. *Specific IgD antibodies and total IgD in colostrum and plasma from postpartum subjects**

	BG			BSA			α-Gliadin			BLG			Total IgD		
Subject	C	P	C/P	C	P	C/P	C	P	C/P	C	P	C/P	C	P	C/P
PS†		200			245			500			107			780	
Aγ‡		<10			<10			<10			<10			<0.6	
1	40	60	0.67	11	215	0.05	16	420	0.04	8.5	43	0.20	410	1400	0.29
2	24	275	0.09	24	140	0.17	38	420	0.09	<1.0	<10		21	340	0.06
3	53	72	0.74§	34	96	0.35	28	205	0.14	7.2	55	0.13	8.4	220	0.04
4	125	64	1.95§	47	100	0.47§	65	155	0.42§	7.0	52	0.14	2.2	72	0.03
5	47	158	0.30§	18	190	0.10	14	350	0.04	4.5	42	0.12	100	4100	0.02
6	4.7	50	0.09	12	105	0.11	21	140	0.15	3.5	54	0.07	92	140	0.67
7	24	90	0.27	22	130	0.17	44	210	0.21	3.3	25	0.13	30	400	0.08
8	20	100	0.20	17	170	0.10	31	450	0.07	5.8	21	0.28	49	840	0.06
9	48	133	0.36	18	160	0.11	30	155	0.19	8.4	150	0.06	120	560	0.21
10	60	125	0.48	22	120	0.18	36	250	0.14	5.4	45	0.12	58	730	0.08
11	36	100	0.36	12	130	0.09	33	400	0.08	11.4	32	0.36	56	1200	0.09
12	23	72	0.32§	15	135	0.11	26	780	0.03	15.0	62	0.24§	56	3200	0.02
13	27	46	0.59§	13	140	0.09	23	130	0.18	4.2	76	0.06	34	1000	0.03
14	17	30	0.57§	21	100	0.21§	35	175	0.20§	8.4	30	0.28§	3.5	280	0.01
Geometric mean	30.9	84.2		18.7	134.0		29.2	261.9		5.7	41.5		35.8	591.3	

* Specific antibodies are expressed in arbitrary units (AU) and IgD in μg/dl.

† Pooled normal serum.

‡ Serum from a-γ-globulinemic patient.

§ Indicates specific IgD colostrum/plasma ratio exceeded total IgD colostrum/plasma ratio by a factor > 10.

albumin, total IgD, and total IgG. Albumin and IgG were used as comparison proteins since presumably they are leaked from the plasma to milk and are not locally produced in the mammary gland. Values are shown in Table 2 with the geometric means. The colostrum/plasma ratios for albumin, IgD, and IgG are also illustrated in Figure 1.

The arithmetic mean colostrum/plasma ratio for IgD (0.055 ± 0.015) exceeded the mean colostrum/plasma ratio for albumin (0.020 ± 0.002) and for IgG (0.015 ± 0.003). For 14 of the 17 patients, the individual colostrum/plasma ratio for IgD exceeded the colostrum/plasma ratio for albumin, and for subject 19, the total IgD colostrum/plasma ratio was more than 10 times higher than the similar albumin ratio. The C/P ratio for IgD exceeded the ratio for IgG for all subjects except the IgD-deficient subject. The data for IgG are strikingly different since the C/P ratio was lower than the albumin C/P ratio for 16 of the 17 subjects studied. The sign test (4) was used to compare the colostrum/plasma ratios for IgD, IgG, and albumin. The IgD ratios were significantly higher than the IgG ratios ($p < 0.01$) or the albumin ratios ($p < 0.01$). In addition, the IgG ratios were significantly lower than the albumin ratios ($p < .01$). Both IgD (mol wt = 175,000) and IgG (mol wt = 150,000) have a higher molecular weight than albumin (60,000). One might expect more leakage from serum of the lower molecular weight albumin than either IgD or IgG. Yet IgD has the highest molecular weight and was enhanced in colostrum compared to IgG or albumin. Such data suggest enhancement of total IgD in colostrum, not a nonspecific transfer from serum.

The data in Table 2 were transformed logarithmically and correlation coefficients calculated. There was no correlation between plasma albumin and IgD or between plasma IgG and IgD. However, there was a strong correlation between albumin and IgG in colostrum ($r = 0.865$, $p = 0.001$) and weaker correlations for albumin *versus* IgD in colostrum ($r = 0.489$, $p = 0.046$) and IgG *versus* IgD in colostrum ($r = 0.556$, $p = 0.020$).

Correction for serum-derived antibody. The data for total albumin, IgG, and IgD were analyzed adapting the formula proposed by Donovan *et al.* (8) for local production of immunoglobulin in nasal polyps. $X = Ig_M - \left(\frac{Alb_M}{Alb_S} \times Ig_S\right)$. The quantity of Ig produced locally (x) is calculated from the observed Ig in the secretion (milk) by subtracting the Ig derived from serum. The ratio of albumin in the secretion to the albumin in the serum is used as the correction factor. Since the molecular weight of albumin is lower than that of immunoglobulins, leakage from serum may be higher for the albumin. Use of albumin in the above formula may result in an overcorrection for the serum contribution of immunoglobulins. Table 3 demonstrates the differences between locally produced IgD and IgG. Of 16 subjects (excluding the IgD-deficient subject), 14 showed evidence of mammary production of IgD. Only one of the 17 subjects had evidence of mammary production of IgG.

DISCUSSION

IgA and some IgM have been shown to be locally produced in the human mammary gland when both specific antibodies and mg of total antibody per gram of protein were considered (7, 20). Our previous work (13) suggests possible local mammary production of specific IgG_4 antibodies in colostrum of some women. In addition our data comparing total IgE and IgD (2) in human colostrum and plasma show that there may be enhancement of either of these immunoglobulins in the colostrum of individual subjects. In the current study we compared colostrum and plasma levels of total IgD with specific IgD antibodies to determine if evidence could be found to suggest local mammary production or selective enrichment of IgD in colostrum.

For the first series of subjects (Table 1), colostrum/plasma ratios for specific IgD antibodies to four antigens were compared to the colostrum/plasma ratio for total IgD. Such comparison serves to control for volume and protein variations of colostrum specimens. The finding of more than 10 times the expected colostrum/plasma ratio of specific IgD antibodies to either BLG, BSA, BG, or α-gliadin in specimens from six subjects suggested local production since selective transfer of IgD with a particular antibody specificity from serum into colostrum would be unlikely. It is also important to note that the subjects demonstrating colostrum enhancement of IgD specific antibodies (Table 1) were not restricted to those subjects with high total IgD in colostrum.

The observations in the initial group (Table 1) showing IgD antibodies to four mucosal antigens, BG, BSA, BLG, α-gliadin revealed a marked enhancement of BG-specific IgD antibody in

Table 2. *Colostrum and plasma values for albumin, total IgD, and total IgG*

Subject	Albumin (mg/dl)			Total IgD (μg/dl)			Total IgG (mg/dl)		
	C	P	C/P	C	P	C/P	C	P	C/P
15	54.5	2850	0.019	18.0	560	0.032	9.1	700	0.013
16	29.3	3400	0.009	14.0	600	0.023	1.6	510	0.003
17	37.6	3260	0.012	16.0	230	0.070	5.7	1120	0.005
18	66.3	2720	0.024	43.0	850	0.051	13.2	625	0.021
19	63.0	2350	0.027	180.0	640	0.281	34.3	900	0.038
20	88.0	2600	0.034	47.0	710	0.067	20.0	700	0.029
21	107.4	2975	0.036	30.0	980	0.031	20.4	680	0.030
22	30.8	2975	0.010	35.0	680	0.051	3.0	980	0.003
23	35.5	2600	0.014	20.0	1200	0.017	3.6	600	0.006
24	25.7	2950	0.009	19.0	1600	0.012	3.8	980	0.004
25	94.0	2575	0.037	44.0	1000	0.044	18.9	540	0.035
26	31.6	2825	0.011	<0.6	15	<0.037	3.3	620	0.005
27	42.0	2450	0.017	23.0	640	0.036	6.3	730	0.009
28	28.0	2325	0.012	16.0	1800	0.009	4.2	690	0.006
29	65.5	2450	0.023	32.0	980	0.033	10.0	640	0.016
30	53.4	2675	0.020	76.0	680	0.112	6.0	560	0.011
31	50.0	2025	0.025	26.0	850	0.031	17.9	740	0.024
Geometric mean	47.8	2685	0.018	24.2	628	0.039	7.7	707	0.011

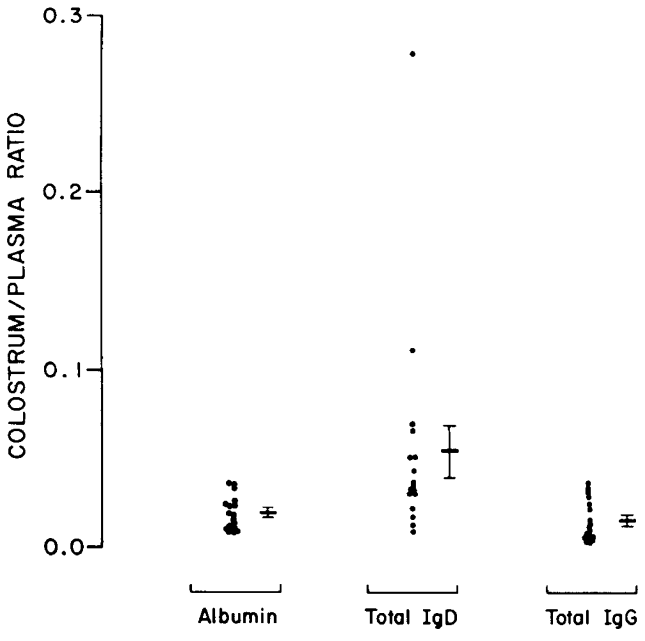

Fig. 1. The colostrum/plasma ratios for albumin, IgD, and IgG.

Table 3. *Local production of immunoglobulin*

$$Ig_M - \frac{Alb_M}{Alb_P} \times Ig_P^*$$

Subjects	IgD (μg/dl)	IgG (mg/dl)
15	7.4	−4.2
16	8.6	−3.0
17	13.2	−7.7
18	22.6	−1.8
19	162.7	10.0
20	22.9	−3.8
21	−5.3	−4.1
22	28.2	−6.8
23	3.2	−4.8
24	4.6	−5.0
25	7.0	−1.1
26	IgD deficient	−3.5
27	12.1	−6.1
28	−5.6	−4.1
29	5.5	−7.3
30	62.4	−5.2
31	4.7	−0.6

* Ig_M, immunoglobulin (μg/dl or mg/dl) in colostrum; Alb_M, albumin (mg/dl) in colostrum; Alb_P, albumin (mg/dl) in plasma; Ig_P, immunoglobulin (μg/dl or mg/dl) in plasma.

colostrum. At the time of this study, we had not considered that these specimens were obtained during the peak season for grass pollen allergy in our geographic locale. It was of interest that the only antigen presented to the respiratory tract mucosa stimulated the most impressive IgD antibody response. Subsequently, we have examined 18 colostrum-plasma paired specimens not obtained during the peak grass pollen season. This marked increase of BG specific IgD antibody was not found since only one of the 18 subjects had enhanced BG specific IgD in colostrum. Thus, there is a possibility that exposure of the respiratory mucosa to a pollen antigen may result in local production of IgD antibody to that antigen in the mammary gland.

Brantztaeg *et al.* (6) have examined IgD production by mucosal lymphocytes and have found striking differences at different mucosal surfaces. IgD producing lymphocytes appear to be very rare in the jejunal mucosa but are present in the nasal mucosa and parotid gland. Brandtzaeg *et al.* (5) recently examined immunoglobulin-producing cells in biopsies of two lactating human mammary glands. IgD immunocytes were found in the mammary glands in proportion (0.7 to 2.1%) comparable to what has been found in parotid (3.1%) and submandibular glands (1.6%). The percentage of IgD immunocytes in lacrimal glands (9.7%) was higher. The reasons for the observed differences at different mucosal sites is not clear but these investigators concluded that an IgA-producing capacity is not a requirement for homing to glandular sites. Brantztaeg *et al.* (6) also found that the presence of IgD producing lymphocytes in nasal, lacrimal, and parotid glands was markedly amplified in IgA-deficient patients. However, since IgD was not seen in the glandular epithelial cells, Brandztaeg *et al.* (6) did not believe that IgD is a secretory immunoglobulin. The recent work of Plebani *et al.* (22) examining IgD in saliva and nasal secretions of children with selective IgA deficiency did not show a compensatory increase in IgD as

was found for IgM. These authors failed to show a secretory role for IgD. Our current study suggests that IgD may be a participant in mucosal immunity and that respiratory tract exposure (BG) may be a particularly important determinant of the IgD composition of colostrum. Comparison of albumin colostrum/plasma ratios and total IgD colostrum/plasma ratios provide further evidence for an enhancement of IgD in colostrum compared to albumin. IgD was also enhanced in colostrum compared to IgG. The stronger correlation between albumin and IgG in colostrum than for albumin and IgD further suggests a different mechanism for entry of IgD into milk from that of IgG or albumin. Selective transport of IgD into colostrum could explain the enhancement of total IgD but could not explain specific antibody enhancement.

When colostrum concentrations of IgD were corrected for the serum contributions adapting the formula of Donovan *et al.* (8) for secretory antibody production, a strong enhancement of IgD was found in colostrum. This was not the case for IgG, providing additional support for possible local mammary production of IgD.

The physiological role of IgD is incompletely understood at present although evidence has accumulated suggesting an immunoregulatory role for this immunoglobulin. Skelly *et al.* (25) have shown that mice treated from birth with a monoclonal antibody to IgD develop reduced numbers of B cells in the spleen and lymph nodes whereas splenic lymphocytes expressing sIgM are increased. Finkelman *et al.* (10) have demonstrated polyclonal B cell activation of the murine immune system by an antibody to IgD. Kuritani and Cooper (14) have shown the enhancing effect of anti-IgD antibody in pokeweed mitogen-induced plasma cell differentiation. All of these studies support the concept that IgD may act as a receptor and may regulate B cell differentiation. Recent work by Xue *et al.* (28) demonstrated an enhanced 19S and 7S antibody response to keyhole limpet hemocyanin in mice bearing IgD-secreting plasmacytomas. The authors suggested the existence of an IgD responsive regulatory T cell.

The potential role of IgD as a mucosal immunoglobulin has been discussed by Olson and Leslie (21) based on their findings of an elevated IgD in rat milk. Our own studies provide support for a potential mucosal immunoglobulin role of IgD in humans although the mechanism regulating mammary IgD production and its function are still unknown.

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