

## Structure and Biologic Functions of Human IgD

### II. Alteration of Serum IgD Levels During Pregnancy<sup>1</sup> (37672)

GERRIE A. LESLIE  
(Introduced by M. F. Shaffer)

*Department of Microbiology and Immunology, Tulane University School of Medicine,  
New Orleans, Louisiana 70112*

Normal adult human serum contains at least five classes of immunoglobulins, namely IgM, IgG, IgA, IgD and IgE. Considerable information is available on the biological properties of all classes with the notable exception of IgD, which despite its description more than 7 years ago (1) still lacks a defined biological function. It was recently suggested that IgD delta chains might possess one extra homology region, which in turn might reflect specialized function(s) for IgD (2).

Klapper and Mendenhall (3) demonstrated a significant elevation in IgD in the sera of women at the time of parturition. The purpose of the present study was to examine the serum of women at various times during gestation to ascertain if there was a particular period during pregnancy when IgD levels were different from other times. In addition, the effect of previous pregnancies on IgD levels was examined.

*Materials and Methods. Patients.* All of the patients for this study were Negro and most would be classified as of low socioeconomic status. Sera obtained from mothers at the time of delivery were collected at the Charity Hospital of New Orleans and the remaining sera were obtained at the facility of Family Planning, Inc. of New Orleans. Gestation times were determined by physicians of Family Planning, Inc.

*Quantification of IgD and IgM.* Serum was collected from peripheral venous blood and either assayed immediately or stored at  $-20^{\circ}$

until assaying.

IgD and IgM was quantified by single radial immunodiffusion. Each serum was assayed in duplicate using goat anti-IgD, guinea pig anti-IgD prepared in this laboratory, and goat anti-IgM and immunoglobulin standards from Meloy Laboratories (Springfield, Va.). Proof of specificity of these antisera has been discussed in detail elsewhere (4).

*Statistical analyses.* It has been repeatedly shown that serum immunoglobulin concentrations, in general, do not follow an arithmetic Gaussian distribution; therefore all data were subjected to a square root transformation for analysis. The details are given in *Results*.

*Results.* The women were divided into five groups, namely nonpregnant (controls), early pregnancy (up to 15 weeks), intermediate pregnancy (16–28 weeks), late pregnancy (29+ weeks), and in labor. The concentrations of IgD in the five groups are given in Table I. The data were found to have different variances in the respective groups. Using the transformation  $X = \sqrt{X_0 + 1}$  resulted in homoscedastic groups, as verified by Bartlett's test. A one-way analysis of variance was performed on the transformed data, resulting in an *F*-ratio which was significant at the 0.05 level. Subsequent use of Scheffe's method of multiple comparisons indicated that the only difference in means which was significant ( $\alpha = 0.05$ ) was between the levels in the control group and in the women in labor. There were no significant differences in IgD levels at any time during pregnancy prior to labor. Since the only

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TABLE I. The Effect of Gestation Time on Serum IgD Concentration.

| Group<br>(gestational<br>age) | Number of<br>specimens | Mean $\pm$ SD<br>( $\mu\text{g/ml}$ ) | Range <sup>a</sup><br>( $\mu\text{g/ml}$ ) |
|-------------------------------|------------------------|---------------------------------------|--|
| Control                       | 29                     | 33 $\pm$ 46                           | U-160                                      |
| <15 weeks                     | 38                     | 55 $\pm$ 54                           | U-205                                      |
| 16-28 weeks                   | 49                     | 59 $\pm$ 58                           | U-223                                      |
| 29+ weeks                     | 42                     | 55 $\pm$ 46                           | U-167                                      |
| In labor                      | 27                     | 89 $\pm$ 136                          | 15-900                                     |

<sup>a</sup> U = undetectable. The sensitivity of the method was 10  $\mu\text{g/ml}$  IgD.

significant differences seen was between the control group and women in labor, it was necessary to rule out generalized alterations in immunoglobulin metabolism and hemoconcentrations as factors contributing to elevated IgD at the time of labor. For this purpose IgM levels were measured. The mean IgM values for the control and women in labor groups were 1.66 and 1.76 mg/ml, respectively. There was no statistical difference between these two values.

To test if the IgD level was related to parity, three groups were set up: controls (nulliparous), women with no history of previous pregnancy, and women with one or more previous pregnancies. Sera from women in labor were excluded from these calculations. The mean IgD values for the control, no previous pregnancy, and one or more previous pregnancy, groups were 33  $\mu\text{g/ml}$ , 49  $\mu\text{g/ml}$ , and 61  $\mu\text{g/ml}$ , respectively (Table II). Statistical treatment similar to that outlined above indicated that the mean of the controls was different from the mean of the one or more previous pregnancies group, and also that the mean of the control group was different from the combined mean of the other two groups. The result of the *F*-test in the analysis of variance was significant at the 0.01 level. Although there was no statistically significant difference between the IgD concentrations in women with no previous pregnancies and those that were pregnant one or more times previously, the mean IgD concentration of the latter group was 24% greater than the former. These data would suggest that women who have had multiple pregnancies have more IgD than those who

have not previously been pregnant.

Klapper and Mendenhall (3) reported that less than 10% of normal women have greater than 80  $\mu\text{g/ml}$  of IgD in contrast with the 41% seen at the time of delivery. These data are in accord with the present observations of 10% for controls, 18% for up to 15 weeks, 26% for 16-28 weeks, 21% for 29+ weeks, and 30% at the time of delivery. In addition, of the 185 sera examined, only 2 had IgD concentrations greater than 500  $\mu\text{g/ml}$ . Both of these were in the sera of women at the time of delivery.

*Discussion.* The sera of primiparous and multiparous women often contains antibodies against leukocytes (5, 6) although the reasons for this are not really clear (7). The serum of some pregnant women presumably contains IgM or IgA anti-trophoblastic antigen (8). Furthermore, an immunohistological survey of full-term human placentas revealed deposits of IgG and IgM on the trophoblast basement membrane of placental villi (9). A recent study of IgG, IgA, and IgM in the serum of women at various stages of pregnancy has revealed that IgG was lower than normal postpartum, IgA was elevated postpartum and no changes were observed in group IgM concentrations during pregnancy (10). Unfortunately the above studies along with many others that demonstrated immunologic perturbation during pregnancy have either been inconclusive regarding IgD or IgD was not assayed.

In view of the present findings and those of Klapper and Mendenhall (3) on elevated serum IgD in pregnancy, it would appear that

TABLE II. The Effect of Parity on Serum IgD Concentration.<sup>a</sup>

| Group (no.<br>of preg-<br>nancies) | Number of<br>specimens | Mean $\pm$ SD<br>( $\mu\text{g/ml}$ ) | Range <sup>b</sup><br>( $\mu\text{g/ml}$ ) |
|------------------------------------|------------------------|---------------------------------------|--|
| Control                            | 29                     | 33 $\pm$ 46                           | U-160                                      |
| No previous                        | 44                     | 49 $\pm$ 56                           | U-223                                      |
| One or more<br>previous            | 84                     | 61 $\pm$ 51                           | U-221                                      |

<sup>a</sup> Sera from women in labor were excluded from these calculations.

<sup>b</sup> U = undetectable. The sensitivity of the method was 10  $\mu\text{g/ml}$  IgD.

an evaluation of the immunoglobulin class distribution of antibodies vs leukocytes and antitrophoblastic antigen may reveal that some of the IgD has an antibody function. It has been difficult previously to convincingly demonstrate antibody activity for IgD in any system. However, the study of Devey, *et al.* (11) would suggest that regular injection of antigens, possibly coupled with some "special" processing mechanism, may be required to stimulate IgD-producing cells. Pregnancy may well provide this type of prolonged regular stimulus in some way as may "self" antigens or closely related antigens.

Why then do many women have elevated IgD late during gestation? Either by chance or due to some selective pressures some women may have IgD receptors (lymphocyte antigen receptor) capable of recognizing the foreign leukocyte antigens (HLA?) expressed on the fetal leukocytes as a result of antigenic disparity between the mother and the father. This may also apply to other antigens such as the embryonic, trophoblastic, and erythrocyte antigens. Such antigens could stimulate IgD-antibody synthesis. Nonimmunologic changes that may occur during pregnancy such as altered immunoglobulin turnover and hemoconcentration could play a part in the observed changes in serum IgD reported here. However, the fact that IgM levels of these patients were almost identical to those of normal controls would eliminate generalized alteration in immunoglobulin turnover and hemoconcentration as factors in the observed elevation of IgD seen late during gestation.

*Summary.* Sera from 156 race-matched

New Orleans women at various stages of pregnancy were studied to determine the effect of gestation time on IgD concentration. A significant elevation in IgD was found in women at about time of delivery over concentrations observed at other times during pregnancy.

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