

Cellular immunity in pregnancy: subpopulations of T lymphocytes bearing Fc receptors for IgG and IgM in pregnant women

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SUMMARY

Studies on the change of peripheral T and B lymphocytes and T cells bearing Fc receptors for IgG and IgM in pregnant women were performed by using rosette-formation tests. There was no significant difference in the proportion of T and B lymphocytes between pregnant and non-pregnant women. The percentage of T cells bearing Fc receptors for IgG in the T lymphocytes which are considered to have suppressive activity increased in the various stages of pregnancy and post-partum as compared with that in non-pregnant women. On the contrary, the percentage of T cells bearing Fc receptors for IgM in the T lymphocytes which have a helper function decreased in pregnant and post-partum women. The results of this investigation suggest that the depression of cell-mediated immunity during pregnancy depends on the qualitative change of T lymphocytes, i.e. increased suppressor and decreased helper T lymphocyte subpopulations.

INTRODUCTION

From an immunological point of view, pregnancy can be considered as an allotransplantation. It is proposed that cell-mediated immunity is depressed in pregnant women. Depressed lymphocyte function has been found with phytohaemagglutinin (PHA) induced transformation (Finn *et al.*, 1972; Prutilo, Hallgren & Yunis, 1972; Tomoda *et al.*, 1976; Gorai *et al.*, 1979) and with mixed leucocyte cultures (Kasakura, 1971; Inoue & Shiojima, 1972).

The present investigation was, therefore, designed to determine the changes in percentages of T and B lymphocytes and T cells bearing Fc receptors for IgG and IgM which are considered to have respectively suppressive and helper activity and to elucidate further the mechanisms of depressed lymphocyte function during normal pregnancy by using rosette tests.

MATERIALS AND METHODS

Blood samples. Heparinized peripheral venous blood (10 units of novo-heparin/ml of whole blood) was obtained from 114 normal pregnant women and eighteen women within 4 weeks post-partum. Control values were obtained from twenty-three healthy women of child-bearing age who had never been pregnant and were not taking oral contraceptives.

Cell separation. Peripheral blood lymphocytes (PBL) were isolated on a Ficoll-Hypaque

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gradient by centrifugation at 400 *g* for 30 min. Lymphocytes were obtained and washed twice with Hanks' balanced salt solution. The cells were adjusted with phosphate-buffered saline (PBS) at a concentration of 2×10^6 /ml.

Indicator cells. Unsensitized sheep erythrocytes were washed twice with gelatin veronal buffer (GVB) and twice with PBS. The cells were adjusted with foetal calf serum (FCS) at a concentration of 2×10^8 /ml. Sensitized chicken erythrocytes were supplied from the Department of Immunology, Toho University, Tokyo. The cells were washed with PBS and prepared at a concentration of 2×10^8 /ml. Ox erythrocytes (ORBC), preserved in Alsever's solution, were washed twice with GVB and resuspended at a concentration of 1×10^9 /ml. A purified IgM fraction from a rabbit anti-ORBC antiserum (Nihon-Kotai Kenkyujo Co., Takasaki, Japan) was diluted to an appropriate concentration which was selected after titration of IgM anti-ORBC antibody and indicated that ORBC agglutinated spontaneously. The ORBC were sensitized with IgM antibody at the appropriate concentration for 90 min at 37°C. The sensitized ORBC were resuspended at a concentration of 2×10^8 /ml in RPMI 1640 medium supplemented with 20% FCS.

T and B lymphocytes and T cells bearing Fc receptors for IgG. T lymphocytes, T cells bearing Fc receptors for IgG and B lymphocytes bearing receptors for IgG were determined simultaneously, using the same reagent by the double-rosette formation technique (Sandilands *et al.*, 1974; Shinbo *et al.*, 1977). PBL were placed overnight at 4°C in the mixture of chicken erythrocytes coated with rabbit IgG antibodies at a cell ratio of 1/100 to detect the presence of IgG Fc receptors. SRBC were incubated with PBL which had been treated with the chicken erythrocytes at a cell ratio of 1/100 for 24 hr at 4°C. Subsequently the pellet was gently resuspended and the proportion of the rosette-forming cells determined. T lymphocytes bearing Fc receptors for IgG were seen as a double-rosette-forming cell with chicken and sheep erythrocytes. T lymphocytes binding only SRBC and B lymphocytes making rosettes with chicken erythrocytes were both identified simultaneously.

T lymphocytes bearing Fc receptors for IgM. T lymphocytes which have receptors for IgM were determined by the method of Moretta *et al.* (1975) with minor modifications. T cell-enriched fractions were purified on density gradients after rosetting for 1 hr on ice with SRBC. The gradients were treated with 1/5 diluted PBS to lyse SRBC and used as an unfractionated T cell population. T cells were cultured overnight in IgM-free RPMI 1640 medium supplemented with 20% FCS. T cells bearing Fc receptors for IgM were determined after rosetting for 1 hr on ice with ORBC coated with rabbit IgM antibodies.

RESULTS

The results for the individuals are not given here (a total of 155 individuals), but the group means and ranges are shown in Figs 1 and 2 and Table 1.

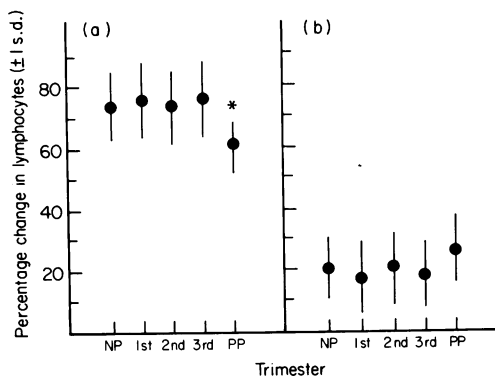


Fig. 1. Changes in percentages of lymphocyte subpopulations in pregnancy and post-partum. (*) Value significantly different ($P < 0.05$) from non-pregnant controls (Student's *t*-test). (a) T lymphocytes (%), (b) B lymphocytes (%).

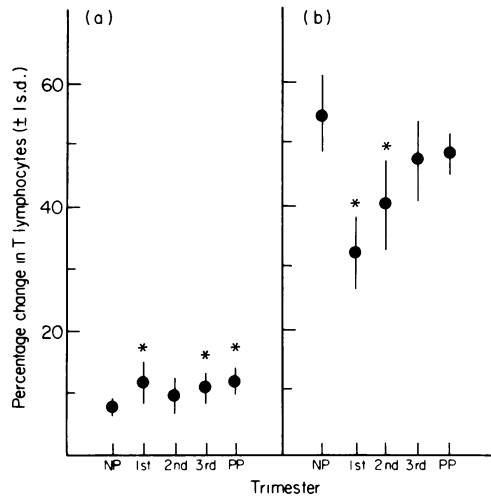


Fig. 2. Changes in percentages of T lymphocyte subsets in pregnancy and post-partum. (*) Value significantly different ($P < 0.05$) from non-pregnant controls (Student's *t*-test). (a) T cells bearing Fc-IgG receptors (%), (b) T cells bearing Fc-IgM receptors (%).

No obvious changes in the percentage of T and B lymphocytes were shown in pregnant women as compared with non-pregnant women. A decrease in the percentage of the T lymphocytes bearing Fc receptors for IgM was observed in pregnant women as compared with that in non-pregnant women, while an increase in the percentage of the T lymphocytes bearing Fc receptors for IgG in various stages of pregnancy and the post-partum period was recorded.

Table 1. Group means and ranges of 155 individuals studied for changes in T and B lymphocytes and T cells bearing receptors for IgG and IgM in pregnant and non-pregnant women*

Source of lymphocytes	Percentage change in lymphocytes		Percentage change in T lymphocytes	
	T cell	B cell	T cell bearing Fc-IgG receptor	T cell bearing Fc-IgM receptor
Non-pregnant	75.3 ± 12.1 <i>n</i> = 18	22.0 ± 11.1 <i>n</i> = 18	8.0 ± 3.2 <i>n</i> = 18	55.8 ± 12.6 <i>n</i> = 12
1st trimester	76.9 ± 12.8 <i>n</i> = 35	18.6 ± 12.6 <i>n</i> = 35	12.1 ± 7.0† <i>n</i> = 35	38.6 ± 12.5† <i>n</i> = 13
2nd trimester	75.6 ± 12.7 <i>n</i> = 36	22.5 ± 12.5 <i>n</i> = 36	10.4 ± 5.7 <i>n</i> = 36	41.3 ± 15.0† <i>n</i> = 15
3rd trimester	77.3 ± 13.5 <i>n</i> = 21	20.0 ± 12.2 <i>n</i> = 21	11.4 ± 5.5† <i>n</i> = 21	48.0 ± 12.8 <i>n</i> = 13
Post-partum	62.6 ± 8.9† <i>n</i> = 12	27.4 ± 12.0 <i>n</i> = 12	12.2 ± 4.9† <i>n</i> = 12	48.9 ± 7.6 <i>n</i> = 10

* Results expressed ± 1 s.d.

† $P < 0.05$ compared to the non-pregnant controls by Student's *t*-test.

n = Number of samples.

DISCUSSION

The depressed cell-mediated immunity found in pregnant women may play an important role in the protection of the foetus from rejection by the mother. This study was designed to detect the level of T and B lymphocytes including T lymphocytes bearing Fc receptors for IgG and IgM in an attempt to analyse the depressed cell-mediated immunity in pregnant women.

According to the previous reports quantitating T and B lymphocytes during pregnancy, whilst there was a decrease in T lymphocytes as compared with non-pregnant women, there was an increase in B lymphocytes (Nakakita *et al.*, 1973; Strelkauskas, Wilson & Dray, 1975; Clements *et al.*, 1976; Cornfield *et al.*, 1979). In this experiment, no significant change in the percentages of T and B lymphocytes was obtained and the same results have been reported by others (Gergely *et al.*, 1974; Baines, Pross & Millar, 1977; Birkeland & Kristoffersen, 1977; Scott & Feldbush, 1978).

Over the past few years, a number of reports have indicated that for the Fc portion of different classes of immunoglobulin receptors are found on the surface of human T lymphocytes (Ferrarini *et al.*, 1975; Moretta *et al.*, 1975; Lum *et al.*, 1979; Yodoi & Ishizaka, 1979). Studies by Moretta *et al.* (1977) demonstrated that the T lymphocytes bearing Fc receptors for IgG are suppressor cells and T lymphocytes bearing Fc receptors for IgM are helper cells for B cell differentiation *in vitro*. In addition, Moretta *et al.* (1976) have demonstrated differences in mitogen responsiveness between the Fc-IgG and Fc-IgM receptor bearing T lymphocytes.

In this study, we found a decrease in the percentage of T cells bearing Fc receptors for IgM (helper T cells), while there was an increase in those T cells bearing Fc receptors for IgG (suppressor T cells) in pregnant and post-partum women. These results imply that the depressed cell-mediated immunity in pregnancy may not depend on the quantitative alteration in the subpopulations of T and B lymphocytes but on the qualitative change in T lymphocytes, especially on an increase in the suppressor T cells and on a decrease in the helper T cells.

Phytohaemagglutinin (PHA) induced lymphocyte transformation was depressed in pregnant women as compared with that in non-pregnant controls (Finn *et al.*, 1972; Prutilo *et al.*, 1972; Tomoda *et al.*, 1976). Gorai *et al.* (1979) reported the depressed response of lymphocytes to PHA in pregnant women under conditions without the influence of maternal plasma proteins. The qualitative changes of T lymphocytes demonstrated in this study can be correlated with the depressed responses of lymphocytes to PHA in pregnant women.

The results of this study suggest that the qualitative changes in the T lymphocyte subsets play an important role in the depressed cell-mediated immunity during pregnancy.

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