PROTEINS OF PREGNANCY

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1. PLASMA PROTEINS ASSOCIATED WITH IMMUNITY

The Female Defence Mechanism in Pregnancy

The reaction of a woman to pregnancy from an immunological point of view is similar to the unspecific immune response to noxious stimuli. This similarity was noted as long ago as 1836 by Cederschjöld. There is stress, histamine is released, 17-hydroxycorticosteroids are increased. The blood sedimentation rate rises, the relative leucocyte rises and there is a shift to the left in the Schilling index. The $\gamma_2$ globulin and $\beta$ globulin rise and albumin decreases. $\gamma$ globulin is unaltered or decreases. Serum lipoprotein is increased, as are the glyco and mucoproteins. The C-reactive or acute phase protein appears and ceruloplasmin, the copper binding protein, increases.

This unspecific response might well be expected to influence the effect of infection in the pregnant state. Reference to epidemic virus diseases showed the following:

**Influenza:** Pregnancy increases susceptibility. In the 1918 pandemic a total mortality of 27% among pregnant victims is reported. Half the cases developed pneumonia in which the mortality was 50%.

**Hepatitis:** Incidence lower than non-pregnant.

**Measles:** Prior to immune serum this was a serious disease in pregnancy. Mortality 14%.

**Mumps:** Rare in pregnancy.

**Chickenpox:** Rare in pregnancy.

**Smallpox:** Rare in pregnancy but high mortality.

**Poliomyelitis:** Pregnant more susceptible. Death rate 9.7% which is significantly higher than non-pregnant. Fifty per cent. of the deaths occurred in 3rd trimester.

**Rubella:** Not uncommon. Classical because of Gregg's (1941) discovery that rubella can cause malformation of child.

**Antibody titre in pregnancy**

Recently Malmnäs has shown that in the human during pregnancy the titre to Antistreptolysin (AST) Antistaphylolysin (ASTa) falls gradually, as does the agglutination titre to Bact. Coli (O and H antigens).

In toxaemia of pregnancy Malmnäs found a rise in AST titre, otherwise no great change.

**Source of antibody**

Gammaglobulin is the plasma protein chiefly concerned with immunity. Most of the antibodies are concentrated in $\gamma$ globulins and $\beta_2$ globulin.
The plasma cell is now generally recognised as the source of antibody and gammaglobulin. This theory was suggested in 1913 by Huebschmann, but first gained interest by the clinical observation that in plasma cell tumour (multiple myeloma) there was hypergammaglobulinaemia while in lymphatic leukaemia there was no rise in gammaglobulin. Tissue culture of the spleen showed most antibody production in the red pulp, which was rich in plasma cells. In the malpighian bodies rich in lymphocytes little antibody was produced. Antibody has been extracted from the adipose tissue in the renal sinus of hyperimmunised rabbits which shows massive plasma cell infiltration. No antibodies, on the other hand, could be detected in circulating lymphocytes of hyperimmunised rabbits.

Formerly, lymphatic tissue was held responsible for antibody production due largely to Murphy’s excellent paper on depression of antibody production by x-ray radiation of the lymph nodes, and to the observation that minced lymph nodes of immunised mice contain twice as much antibody as the blood serum. Prior to the lymphoid cellular theory came the reticuloendothelial cell theory. Metchinkoff in the 1880’s discovered phagocytosis by the macrophages and suggested that these cells which constitute part of Aschoff’s reticulo-endothelial system might produce antibody. This has long been a popular theory, largely because of the fact that injected dye particles are taken up by the system. Blockage of the system with colloidal iron or Indian ink depresses the production of antibodies. This is now assumed to be due to the role played by the macrophages in breaking down and preparing antigens to stimulate the plasma cells. Neither macrophages nor granulocytes have been shown to contain antibody.

Controls of antibody production

Antibody production appears to be under the control of the corticoids. Berglund in 1956 showed in rodents that cortisone depresses antibody formation, but does not effect passive immunisation. Antibodies, once produced, have a half life of 2-3 weeks in the circulation and are in a constant state of flux, as are the other plasma proteins. According to Ferrabee, the pregnant woman reacts to antigens of skin homotransplants as if she were full of cortisone.

It is interesting to note that production of antibody can take place locally in the tissues. Batty and Warrack in 1955 showed the local production of antitoxin to tetanus toxoid in many tissues including the rabbit uterus wall.

Burnet and Fenner in 1949 published a monograph on their adaptive enzyme theory of antibody production in which they postulated that all antigens coming in contact with the antibody system during its development would be tolerated. Thus the antigens of the host are tolerated, but foreign antigens are not. Although they failed in their experimental attempt to prove this theory many others have since succeeded by injecting antigen at the right time during development into a foetus or newborn animal. Antigen so injected is tolerated in adult life and, with reservations, antibody is not produced against it.

Feldon in 1949 reported that injection of large quantities of pneumo-