ALLO-IMMUNITY AND RECURRENT PREGNANCY LOSS

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Recurrent miscarriage, the loss of three or more consecutive pregnancies, affects 1% of couples trying to conceive. It is associated not only with a large financial burden for society but also significant psychological sequelae for the putative parents. Despite its importance in reproductive medicine - bridging the gap between infertility and later obstetric complications - the investigation and treatment of women with recurrent miscarriage has been based on anecdotal evidence, historical beliefs and the results of small uncontrolled studies. This has led to the situation where women have in some cases been subjected to treatments of no proven efficacy, some of which have subsequently been shown to be harmful.

The concept of the fetus as an allograft was first popularised by Peter Medawar in 1953 who posed the question as to 'how does the pregnant mother continue to nourish within itself for many weeks and months a fetus that is an antigenically foreign body?' Since this time the conventional view of reproductive immunology is to portray pregnancy as a battle or conflict between mother and fetus – miscarriage being due to immune rejection of the fetus by the mother. A more informed view is that a successful pregnancy represents a co-operative venture between mother and fetus.

One of the first alloimmune causes of pregnancy loss was said to be failure of the mother to mount a protective immune response in pregnancy due to increased sharing of HLA alleles between herself and her partner. Hence paternal white cell immunisation (Lymphocyte Immune Therapy) was introduced into clinical practice. However, increased HLA sharing between partners has been disproved. White cell immunisation has been demonstrated not to be of benefit and has been abandoned by the vast majority of practitioners. Similarly, increased sharing of the HLA DQ allele has been refuted as implicated in the causation of recurrent miscarriage.

Attention is currently focused on the role of Natural Killer (NK) cells in the pathogenesis of implantation failure after IVF-ET and of recurrent miscarriage. The role of both peripheral blood and uterine NK cell testing in the prediction of pregnancy loss will be discussed as well as that of the NK cell receptor repertoire. Finally, the role of immuno-modulation in particular the use of steroids, IVIG and Intralipid will be critically examined.