proliferation *in vivo* and so it can be argued that such lymphoid proliferation has no effect on the existence of a specific tolerant state. There are two possible reasons for this. One is that whatever proliferation there may be involves only lymphoid cells not directly involved in the immune response or, alternatively, does not involve the lymphoid stem cells concerned with tolerance and its loss. Alternatively, the explanation that we favour suggests that tolerance is the absence of competent cells and disappears only when new cells are produced by a source organ such as the thymus, a time dependent process not affected by PHA.

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Immunological Factors in Human Placentation

A CONSIDERABLE volume of evidence from animal experiments suggests that mammalian placentation is under some kind of immunological control. In the mouse, for example, it has been shown that placental size[1,2] and, indirectly, foetal size and length of gestation[3] can be influenced by the materno-foetal immunological relationship. An increase in placental weight with birth order has been described in several species (mouse[4], rat[5], guinea-pig[6] and man[7,8]) and this may represent an immunological effect.

In an attempt to detect an immunological influence on normal placental development in man, a pilot study has been carried out, utilizing retrospective data on maternal blood groups and placental weights. It is known that the AB antigens participate in transplantation immunity and that the ABO blood group system can be utilized in histocompatibility studies[9]. Despite the fact that the presence of AB antigens on trophoblast is in dispute[10,11], there is no doubt that an interchange of these group substances takes place across the placenta and may result in isoimmunization. Although there is therefore obviously a large background of genetic dissimilarity between mother and foetus, the ABO groups can be used as a convenient parameter for the study of histo-compatibility differences between these two individuals.

Data have been studied retrospectively from 3,688 consecutive confinements. This total excludes cases of multiple pregnancy, diabetes mellitus and rhesus isoimmunization, for in these conditions the placental weight is known to be abnormal. Mean placental weights were calculated in each of the maternal blood groups and the results are shown in Table 1. Although the mean placental weight increases progressively in the blood group order O–A–B–AB, the differences are not statistically significant. Comparison of placental weight for group O mothers ($629 \pm 3{\cdot}1$ g) and for groups A, B and AB combined ($639 \pm 3{\cdot}1$ g), however, revealed a significant difference (*S.E.* of difference $\pm$ 4·2). The mean gestation periods for each blood group did not differ significantly from each other.

Table 1. MEAN PLACENTAL WEIGHT ACCORDING TO MATERNAL ABO BLOOD GROUP

Maternal blood group	No. of cases	Mean placental weight (g)	*S.E.*
O	1,869	629	± 3·1
A	1,382	636	± 3·5
B	331	645	± 7·4
AB	106	656	± 14·9

Blood group data were not available for the children, but the expected proportion of ABO incompatible (heterospecific) pregnancies for each maternal group was calculated from the AB gene frequencies[12] in the population. The proportion of ABO heterospecific pregnancies in group O mothers would be expected to be 32 per cent; in group A, 6 per cent; in group B, 26 per cent; and in group AB, 0 per cent. The relative heterospecificity of unions involving group O women compared with those involving other groups is apparent.

These results suggest that immunological disparity of mother and foetus is associated with a relatively smaller placenta and vice versa. This agrees with observations made on human trophoblastic tumours, which by their unusual biological behaviour provide interesting material for the investigation of immunological aspects of placentation. The epidemiology of these tumours has been studied and a shift of blood group distribution away from group O towards A, B and AB has been demonstrated in patients with choriocarcinoma[13,14]. Furthermore, data from the Near East[15,16] suggest an association of choriocarcinoma with consanguinity of reproductive partners. On the basis of this preliminary evidence therefore the behaviour of these tumours in man implies that abnormal trophoblastic invasion is associated with increased genetic compatibility of mother and foetus.

While the evidence on normal and abnormal development in man is complementary, it is at variance with the experimental evidence presented by Billington[1] when he demonstrated increased placental growth with genetic disparity in the mouse. One theory which can be advanced to explain these discordant findings is that trophoblastic development is greater when the foetus "recognizes" foreign antigens in the mother (personal communication from D. R. S. Kirby). This explanation, however, is not supported by James's demonstration[2] that the increase in placental size may be an expression of maternal response to foreign antigens in the foetus.

It may be some time before discrepancies between animal and human studies can be resolved. In the meantime there is an evident need for the collection and study, in man, of genetic data in relation to trophoblastic development, both normal and abnormal.

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