# NOTES ON THE RHESUS FACTOR

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It had long been suspected that a number of transfusion reactions was due to some specific difference in blood other than the ABO system, for in spite of careful laboratory technique, reactions continued to occur in some cases. Another distinct clinical condition which baffled clinicians was that which affected the infant of parents both of whom were healthy and showed no sign of disease. These two problems were solved when in 1939 LEVINE observed a severe reaction following a transfusion to a woman recently delivered of a macerated foetus. He discovered that the mother's serum agglutinated the cells of only 85% of ABO compatible bloods. It was suggested that the foetus inherited a dominant factor from the father which was absent from the mother, with resulting immunization of the mother to this factor. The factor was designated "the Rhesus factor" since it was similar to that produced by immunization of rabbits with the cells of Rhesus monkeys. Individuals reacting with the serum were designated Rhesus positive, the remainder, Rhesus negative.

Isoimmunization may be defined as the formation of immune anti-bodies by a member of a given species against some antigen absent from its own body but present in that of another member of the same species. In practice it can occur in one of two ways; either by introducing the antigen by transfusion of blood, or by its passage from foetus to mother through the placenta. The fundamental difference between the ABO and Rh systems is that, whereas in the ABO system antibodies are naturally occurring, in the Rhesus system they are only found following immunization.

## CLINICAL ASPECTS

I. *BLOOD TRANSFUSION.* Any Rh negative person may form antibodies following the transfusion of Rh positive blood. The response to such a stimulus varies in different individuals, and, whereas some may show no response, others may form antibodies after a single stimulus. One large transfusion may not be a stronger stimulus than several small ones; in fact, spaced transfusions, whether large or small, are more potent stimuli, so that when the antibody production is of sufficient strength, a further transfusion will result in a haemolytic reaction of varying severity ranging from a mild and almost inapparent reaction to the severe ones the features of which include haemoglobinuria, collapse, and renal failure.

II. *PREGNANCY.* Two factors determine the degree of isoimmunization. Firstly, a number of previous pregnancies are usually required before sufficiently potent antibodies can be found in the mother to affect her foetus. It must be remembered that an Rh — ve mother who has had a blood transfusion of Rhesus positive blood may not require these extra stimuli from pregnancy and in her instance a first-born may be affected with haemolytic disease.

Secondly, there is an unknown factor governing the degree of susceptibility of the mother to a stimulus. Some do not react at all, even after many pregnancies, while others respond more quickly so that even a second infant may be affected. Once isoimmunization starts, however, the potency of the antibody increases with each subsequent stimulus and the condition becomes more severe at each pregnancy. Fortunately it is unusual for the first two infants to be affected, although it should

be remembered that abortions are a potential source of stimulation.

The method of forcasting whether a foetus whose mother has anti-bodies in her serum is likely to be affected by haemolytic disease is by titration of the antibodies during pregnancy. When occurring for the first time, antibody is not detected before the fifth month at the earliest; should it be found earlier the inference is that a previous pregnancy or transfusion has stimulated it, and a rising titre or antibody towards the end of the pregnancy would suggest that the foetus is immunizing the mother. Should the titre remain unchanged throughout the pregnancy the probability would be that the foetus, like the mother is Rhesus negative, the father being heterozygous. The importance of routine ante-natal serological tests should not be overlooked.

The effect of sensitization of the mother is shown by damage to the Rhesus positive cells of the foetus. The clinical effect will be either hydrops foetalis usually with intra-uterine death or icterus gravis neonatorum in which the infant is born at term but shows the effects of varying degrees of haemolysis. The main clinical features are enlargement of the spleen and liver, jaundice and anaemia, while the blood smear will show a number of immature cells. Increase in jaundice will lead to kernicterus which if not fatal, will cause irreversible cerebral damage. The final diagnosis is clinched by the Coomb's Test which is specific and establishes whether the infant's cells are coated with antibodies.

The *treatment of haemolytic disease of the newborn* is based on prematurity, strength of Coomb's reaction, presence of immature cells, a history of severe haemolytic disease in a previous sibling and the cord haemoglobin concentration. This last is probably the safest factor to go on, and an infant with a haemoglobin of 16G per 100cc is less likely to require treatment than is one with a haemoglobin of 11G. A sample of cord blood should be taken in all cases in which there is any suspicion that an infant may be affected.

Treatment of choice is Exchange Transfusion in selected cases, the volume of blood given is 60cc per lb. of loosely packed cells.