

Rh Blood Group of Grandmother and Incidence of Erythroblastosis

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Ramos de Almeida, J. M., and Rosado, L. (1972). *Archives of Disease in Childhood*, **47**, 609. **Rh blood group of grandmother and incidence of erythroblastosis.** Maternal red cells may cross the placental barrier and enter the fetal circulation, and this transfer may cause primary sensitization in Rh-negative girls born to Rh-positive mothers.

60 families were studied. Each family consisted of the grandmother, her Rh-negative daughter, and the Rh-positive grandchildren. Only families with ABO compatibility in the three generations, and where the mothers had never been transfused or had never received blood intramuscularly, were selected.

The families were divided into 2 groups: the group of the Rh-positive grandmothers, group (+), which consisted of 40 families, and the group of Rh-negative grandmothers, group (—), which consisted of 20 families.

The 2 groups were analysed as to the presence of affected grandchildren in any pregnancy. There were 35 (87·5%) affected grandchildren in group (+), and 15 (75%) affected children in group (—).

In group (+) the number of mothers with 3 or more Rh-positive pregnancies was 16, and of these, 4 (25%) had only unaffected children. In group (—) 15 mothers had 3 or more Rh-positive pregnancies, and of these, 4 (27%) had only unaffected children.

There was a striking similarity in the percentage of affected children between the 1st birth in group (+), 20%, and the 2nd birth in group (—), 20%; the 2nd birth in group (+), 38%, and the 3rd birth in group (—), 30%; the 3rd birth in group (+), 28%, and the 4th birth in group (—), 25%.

It was concluded that (1) an Rh-positive grandmother acts similarly to the antigenic stimulation caused by pregnancy and the birth of an Rh-positive fetus; (2) it might be advisable to inject all Rh-negative newborn females, born to Rh-positive mothers, with anti-D γ -globulin, soon after birth; (3) prediction of the risk of erythroblastosis, especially in the case of primigravidae or mothers with one non-affected Rh-positive child, requires the investigation of the blood group of the grandmother on the mother's side.

Every woman who has had one or more pregnancies has been in physiological connexion with an alien circulation through the placenta ($x+1$) times, x being the number of her own pregnancies, and 1 her own gestation, when she was connected to the maternal circulation while in her mother's uterus (Fig.). In both instances the two circulations may not be completely separated from one another. During pregnancy, and especially after delivery, fetal red cells frequently are to be found

in the maternal circulation (Woodrow and Donohoe, 1968). This transfer of cells can also occur in the opposite direction, maternal red cells being found in the fetal circulation (Zarou, Lichtman, and Hellman, 1964).

Since the stimulus to Rh immunization is the introduction of Rh-positive erythrocytes into an Rh-negative recipient, haemolytic disease due to Rh incompatibility occurs whenever an Rh-negative woman has become sensitized to the antigens present in the transfused red cells which she may have acquired, either from her own mother during

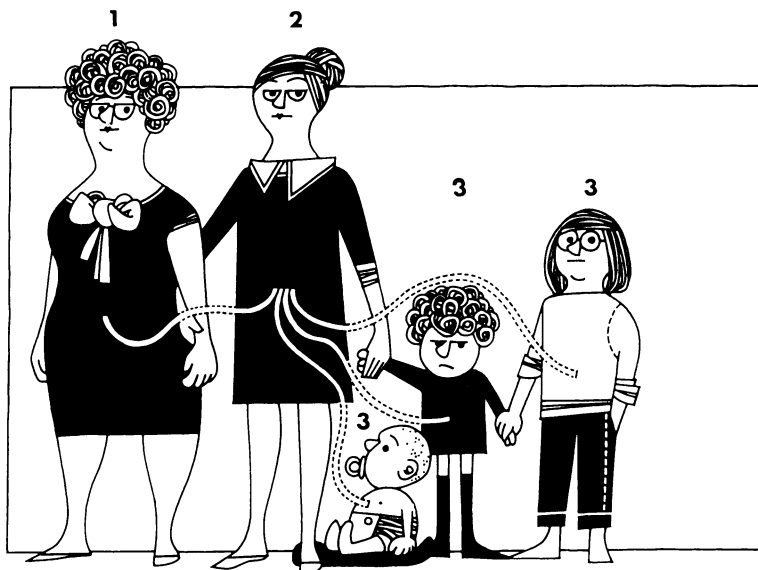


FIG.—Erythroblastotic saga. A mother may be immunized by receiving blood transferred across the placenta from her own mother, as well as from her own offspring. 'On the side of the mother-in-law there is reluctance to give up the possession of her daughter, distrust of the stranger to whom she is to be handed over, an impulse to retain the dominating position which she has occupied in her own house.' Sigmund Freud, *Totem and Taboo*.

gestation and at birth, or later on from her fetuses during her own pregnancies. In the first of these two situations this transfer of maternal cells into the fetal circulation may theoretically cause primary sensitization in an Rh-negative girl born to an Rh-positive mother.

This investigation was aimed at determining the influence of a grandmother's Rh blood group on her Rh-positive grandchildren, by studying (1) the incidence of erythroblastosis, and (2) the birth order of the first affected child.

Clinical Material

Sixty families were studied. Each family consisted of the grandmother, her Rh-negative daughter, and the Rh-positive grandchildren. So 60 nonrelated grandmothers, their 60 Rh-negative daughters, and their Rh-positive children were studied. Since, in the presence of ABO incompatibility, transfused red cells are destroyed before they can stimulate the production of Rh antibodies, only families with ABO compatibility in the three generations were selected. The families were all either A or O, 27 families being A and 33 families being O.

Furthermore, only families with mothers who had declared they had never had a miscarriage, nor had been transfused or injected intramuscularly with blood, were selected. The 60 families were divided into 2 groups: the group of Rh-positive grandmothers, group (+), which consisted of 40 families, and the group of

Rh-negative grandmothers, group (—), which consisted of 20 families.

In group (+) there were 6 Rh-negative grandchildren, and in group (—) there were 4. These pregnancies and these children were not taken into account for our data. The diagnosis of erythroblastosis was based on clinical evidence, on the presence of antibodies in the mother's serum, and on a positive antiglobulin test in the infant's cells.

Results

The analysis of the 2 groups as to the presence of affected grandchildren in any pregnancy is shown in Table I. There is no significant difference between the 2 groups ($\chi^2 = 0.39$).

TABLE I
Number of Mothers in Two Groups Who Have Had Any Erythroblastotic Children

	No. in Group	No. with Erythroblastotic children
Rh-positive grandmothers (Group +)	40	35 (87.5%)
Rh-negative grandmothers (Group —)	20	15 (75%)
Total	60	50

Table II shows the number of mothers in each group with 3 or more Rh-positive, ABO compatible

pregnancies, and of these, the numbers who had any affected children and who had only unaffected children.

In Table III the 2 groups are compared as to the birth order of the first affected sib.

TABLE II
Number of Mothers with 3 or More Rh-positive, ABO Compatible Pregnancies

Rh-positive grandmothers (40) (Group +)	16 (40%)	Mothers with affected children	12
		Mothers with no affected children	4 (25%)
Rh-negative grandmothers (20) (Group -)	15 (75%)	Mothers with affected children	11
		Mothers with no affected children	4 (26.6%)

Note: In both groups, 1 mother had 2 pregnancies of unaffected Rh-positive children.

TABLE III
Birth Order of First Affected Child

Birth Order	1	2	3	4
Rh-positive grandmothers (Group +)	8 (20%)	15 (37.5%)	11 (27.5%)	1
Rh-negative grandmothers (Group -)	0	4 (20%)	6 (30%)	5 (25%)

Discussion

The data in Table I show a very large percentage of affected children compared to the usual figures. While the possibility of undeclared previous pregnancies cannot be ruled out, probably a more important fact is that our series included only families with ABO compatibility between children and their mothers.

The data also show that Rh-positive grandmothers do not cause in their families an excessive number of grandchildren affected by erythroblastosis. This is in conflict with Taylor's (1967) results which showed an increased number of mothers with affected children in families with Rh-positive grandmothers. The explanation may be that in our series 83% of the mothers went on having children until they had an affected child. In fact, at the time the data were collected the average number of children per family was 2.5 in group (+) and 3.2 in group (-).

This is also shown in Table II. In group (-) the percentage of mothers with 3 or more Rh-positive, ABO compatible pregnancies was significantly larger than in group (+).

Since 3 is the number of stimulations by pregnancy required for the majority of women who have affected children (Taylor, 1967), we studied the percentage of mothers with 3 or more unaffected Rh-positive children. The percentages in the 2 groups were similar (Table II). Probably these mothers (in both groups) belonged to the type of Rh-negative persons who, though receiving Rh-positive blood, never produce antibodies (Allen and Diamond, 1958).

In Table III the very striking similarity in the percentage of affected children between the 1st birth in group (+) and the 2nd in group (-), the 2nd birth in group (+) and the 3rd in group (-), the 3rd birth in group (+) and the 4th in group (-), suggests that an Rh-positive grandmother acts similarly to the antigenic stimulation caused by pregnancy and the birth of an Rh-positive fetus.

Conclusion

It is often said that pregnancy alone usually leads to no significant transfer of red cells from the fetus into the mother, and that delivery is the main cause of important transplacental haemorrhage, so that immunization rarely develops in the course of a first pregnancy.

Our results suggest that primary Rh-immunization may precede the first pregnancy, due to maternofetal transfer of Rh-positive red cells during the birth of an Rh-negative girl to an Rh-positive mother.

If maternofetal transfer of cells takes place mainly during delivery, as is the case in fetomaternal transfer of cells, it would perhaps be advisable to inject with anti-D γ -globulin soon after birth all Rh-negative newborn females born to Rh-positive mothers.

Finally, for proper prediction of the risk of sensitization in an Rh-negative woman, especially in the case of primigravidae or mothers of a first Rh-positive child, the Rh blood group of the grandmother on the mother's side should always be investigated. Engaged couples should inquire about each other's blood group, and the man should always question his fiancée as to her mother's blood group. The combination of an Rh-positive mother-in-law with a homozygotic Rh-positive son-in-law is particularly hazardous.

We thank Mr. J. Abel Manta for drawing the Figure.

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