FOETOMATERNAL TRANSFUSION AS A CAUSE OF NEONATAL ANAEMIA*

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After Levine, Burnham, Katzin and Vogel (1941) had described iso-immunization to the Rh factor, they postulated that sensitization might occur by passage of foetal red cells into the maternal circulation. Wiener (1948) first reported such a clinical example. Later Chown (1954) presented convincing evidence that foetomaternal transfusion was a definite entity.

Chown (1955) utilized three methods in his case for demonstrating passage of foetal cells into the maternal circulation. First he observed an elevated level of foetal type haemoglobin in the mother's blood. Second, by differential serum agglutination, he showed that red cells with foetal type antigen were present in the maternal circulation. Third, he observed a progressive rise in anti-D indirect Coombs titre in the mother.

Since Chown's proof of foetomaternal transfer, Colebatch, Pitt and Maddison (1956), Borum, Loyd and Talbot (1957), Gunson (1957), Shiller (1957), Goodall, Graham, Miller and Cameron (1958), McGovern, Driscoll, DuToit, Grove-Rasmussen and Bedell (1958), and Pearson and Diamond (1959) have reported further examples. Chown's case report is the only one thus far in which all three methods enumerated above were used to prove that foetomaternal transmission had taken place.

The case reported here includes proof of such foetomaternal red cell transfer by determination of elevated levels of foetal haemoglobin, by a rising anti-D titre and by detection of infant's cells in the mother's circulation using differential agglutination. The observations are submitted to confirm those of Chown.

Case History

Infant Q. was born on November 28, 1958. No signs of foetal or maternal distress had been noted. At delivery, however, the infant was pale and listless.

On examination, except for the marked pallor and listlessness, the infant was normal (length 18 in., head circumference 12½ in., weight 6 lb. 8 oz.). The liver was palpable 2 cm. below the costal margin. The spleen was not palpable. No petechiae were noted. There were no signs of foetal distress at this time.

Haemoglobin by skin prick shortly after birth was 6.7 g. %. The direct Coombs test was negative. There were 108 normoblasts per 100 white cells. Total bilirubin was 0.4 mg. %. The infant's blood cells were O (Rh+).

Because of the pallor and anaemia, the infant received 54 ml. of group O (Rh-) blood which was well tolerated. The haemoglobin on the second day of life was 11.8 g. %. Subsequent growth and development of the infant have been normal.

Maternal History. The pregnancy had been normal. One previous pregnancy had resulted in a normal infant who was Coombs negative and had a haemoglobin of 18.5 g. % at birth. The mother was group A Rh negative and no anti-D (Rh₀) had been found during either pregnancy. She had no postpartum complications and specifically did not have any fever or chills or other signs of blood incompatibility. Blood samples from the mother were available on days 1, 10, 17, 22, 40, 60 and 88 postpartum.

Evidence of Transfer of Foetal Cells into Maternal Circulation

Foetal Haemoglobin. The amount of foetal haemoglobin noted in the maternal circulation is shown in Fig. 1. The specimen obtained on the first postpartum day contained 6.6% of foetal haemoglobin. Thereafter there was a gradual decline to the normal range of 0.5% at 60 days postpartum. The infant's foetal haemoglobin at birth was 61%.

The methods used in this laboratory were those of Singer, Chernoff and Singer (1951). The range in the normal postpartum period for foetal haemoglobin was 0.5-1.0%.

Indirect Coombs Titre. The mother was group A Rh negative. Serum from day 1 revealed no antibodies to D antigen or to any other of a group of 22 antigens with which this serum was tested. However, subse-

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quently, as shown in Fig. 1, there was a definite rise in anti-D titre by the indirect microscopic Coombs test. This rise from zero on day 1 to 1:8 on day 8 and to 1:128 in 60 days is characteristic of events following the introduction of a large amount of antigen. No other antibodies were found in any of the later specimens.

FIG. 1.—Indirect Coombs titre and foetal haemoglobin from mother.

Differential Agglutination Studies. The infant's blood group was O D_{Ce}/d_{Ce}; Fy^a+; M+ N+; K-. The mother was group A d_{Ce}/d_{Ce}; Fy^a+; M+ N+; K-.

Therefore, direct differential agglutination was done by addition of anti-D serum to an aliquot of the mother's cells. By this method the infant's cells were agglutinated. The difference between the number of cells originally present and those cells remaining after addition of anti-D was considered to represent the cells of the infant.

The direct agglutination method, when first done, revealed that approximately 11% of the cells were of the Rh positive type. The percentage of the cells that were of the infant's type decreased gradually during the next 60 days to 3% at 30 days and 0 at 88 days.

Later, the indirect agglutination method was used. In this method the mother's cells, group A, were agglutinated by addition of anti-A serum and this left only the infant's cells, group O. By this method, cells that were antigenically like the infant's were identified in the maternal circulation. The percentage of surviving infant's cells, as determined by differential agglutination, parallels the foetal haemoglobin but at a slightly higher level.

Discussion

This article supports the thesis that foetal red cells can pass the placental barrier and enter the maternal circulation. The finding of infant's red cells, foetal type haemoglobin and a significant rise in anti-D titre in the blood of the mother indicates that a foetomaternal transfusion had occurred. These findings confirm those of Chown (1954) and others.

Recognition of the entity of foetomaternal trans-

fusion provides a basis for the abnormal clinical condition existing in the infant. Furthermore, knowledge that foetomaternal transfusion can occur provides an understanding of a mechanism for iso-immunization.

Levine *et al.* (1941) and Wiener (1948) had postulated that infant's red cells escaped into the maternal circulation. Until the entity of foetomaternal transfusion had been established the placental passage of foetal red cells had been considered impossible.

Physiological data now indicate that the foetal venous pressure is higher than that in the intervillous space. This pressure differential provides an explanation for the expulsion of infant's cells into the maternal system after a breach in the placental barrier has occurred.

The problem remains to determine how often and to what extent foetomaternal transfusion occurs. In answer to the problem, several methods have been devised.

Foetal type haemoglobin has been measured by O'Connor, Shields, Kohl and Sussman (1957) in mothers whose infants had cord blood haemoglobin levels below normal. Foetal haemoglobin was above average in these women. It was concluded that the anaemia of their babies was due to transfusion of foetal cells into the mother.

Another study by Creger and Steele (1957) has indicated that foetal red cells of group O infants are significantly increased in the circulation of group A women. For controls the unagglutinable cell counts in women of group A who had infants of group A were used.

A fuller understanding of the placental dysfunction that allows these transfusions to occur may evolve a means of preventing the clinical disease of erythroblastosis foetalis.

Summary

A case report of foetomaternal transfusion is presented.

Positive identification of the infant's cells in the mother's circulation was made by direct agglutination technique.

An increased level of foetal haemoglobin was noted in the maternal circulation.

A rising titre of anti-D was observed in the maternal circulation.

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