FOETO-MATERNAL TRANSFUSION

A Cause of Anaemia at Birth

CAROL J. JACCARINI

M.D. (MALTA), D.C.H. (LONDON), M.R.C.P. (U.K.)

and

PAUL VASSALLO AGIUS

M.D. (MALTA), D.C.H. (LONDON), M.R.C.P. (LONDON)

Lecturer in Medicine, Royal University of Malta.

SUMMARY

Two cases of foeto-maternal transfusion are described. The clinical picture, diagnosis and treatment are given in some detail. Other causes of anaemia at birth are also mentioned.

It has been estimated that the passage of foetal erythrocytes into the maternal circulation (foeto-maternal transfusion) occurs normally in about 50% of all pregnancies (Cohen *et al.* 1964). This is the mechanism underlying Rh-isoimmunisation of the newborn and except in these cases it is usually of no consequence because the majority of such haemorrhages are small. In some cases, however, the bleed is of sufficient degree to cause anaemia, shock or even stillbirth. This was first suggested by Weiner in 1948 and in 1954 Chown was able to demonstrate the presence of foetal RBCs in the maternal circulation thus confirming Weiner's hypothesis. We report here two such cases and discuss the condition and other causes of anaemia occurring *at birth.*

Case I

Baby I.B. A male infant born on 24. 10. 69 at Westowcroft Nursing Home, was a second child born after a normal pregnancy and delivery at 38 weeks. The placenta and vessels looked normal. Birth weight: 5lbs. 5oz. The Apgar score at 1 min.. was 8 but the baby was noticed to be pale and Hb estimation on the Haldane apparatus was found to be 77% (11 G%). He was given Synkavit 1 mg IM and at 4½ hrs. of age was admitted to the Special Care Baby Unit at Fulford Hospital, York. On examination he was a small-for-dates baby with pallor, grunty respirations, and a tachycardia of 180/min. There was no obvious external source of bleeding, no jaundice, no petechiae and no hepatosplenomegaly. Investigations carried out were as follows: Both mother and baby were group O Rh positive. Direct Coombs test — negative. Kleihauer test on the mother's blood showed a strongly positive result with more than 20 mls of foetal blood present.

He was given 70 mls of packed RBCs via the umbilical vein and prophylactic Ampicillin and Cloxacillin intramuscularly. A repeat Hb done the next day was 16.2 G %. The respiratory distress was treated successfully with intravenous Sodium Bicarbonate and Dextrose-Saline together with antibiotics. Routine check examination prior to his discharge revealed a marked pansystolic heart murmur consistent with ventricular septal defect, and a Hb of 15.7 G%. He was subsequently put on oral iron.

Case II

Baby S.S. The second baby of an Rh negative mother, she was a full term normal delivery at St. Luke's Hospital on 18.2.70 following an uneventful pregnancy. No Rh antibodies were detected at term. The baby cried well at birth after simple resuscitative measures. Birth weight was 7 lbs. 7 oz. Vaginal blood loss

during delivery was assessed as 6 ounces. She was noted to be pale soon after delivery. There was no jaundice and no petechiae, the liver and spleen were just palpable and the umbilical cord was not stained. The placenta and cord vessels were normal. There was no abnormality in the heart or lungs. Investigations on Cord Blood showed Hb. 8.8 G %, Serum Bilirubin 1.3 mg %. Van den Bergh reaction indirect. Haemoglobin F = 69 %; Haemoglobin A_2 1.4%. Screening test for G-6PD: negative; Blood Group A Rh positive. Direct Coombs test negative. Mother's blood group A Rhesus negative. Kleihauer test at 18 hrs — 10.4% of erythrocytes contained foetal Hb. On 20.2.70: Hb electrophoresis on the mother showed Hb F 2.4% A_2 2.7%; on 4.3.70: Hb F 3.3% and A_2 2.0%, Kleihauer Test was again positive. The baby was transfused with 80 mls packed RBC. Repeat Hb was 12.5 G %. Her subsequent progress has remained uneventful. She was later put on oral iron.

Discussion

It is now well recognised that significant foeto-maternal haemorrhage may present at birth in two ways. More commonly, the bleeding is acute. In such cases the infant shows the picture of oligaemic shock with severe pallor, tachycardia, weak or absent peripheral pulses and rapid, shallow and often irregular respirations. The Apgar Score at 1 minute is characteristically high in contrast with the low score found in asphyxia pallida, with which it may be confused. This differentiation is of vital importance for the severely asphyxiated neonate needs urgent respiratory resuscitation — a procedure which, with the exposure, handling and possible trauma which it may entail, may make matters worse in cases of neonatal shock due to acute blood loss.

If the haemorrhage has been prolonged or repeated during the course of the pregnancy, the foetus has a chance to adjust haemodynamically and anaemia only develops slowly. Such an infant born after chronic haemorrhage presents with unexplained anaemia at birth — an anaemia which is commonly missed. Rarely there may be added signs of congestive heart failure.

Estimation of the infant's Hb at birth may show only a slight reduction in its level if the bleeding has occurred shortly before birth. This is because of the initial haemo-concentration and as restoration of the blood volume and heamodilution takes place over the next 12 - 24 hrs serial Hb estimations will reveal a fall.

It should be emphasised that the capillary Hb level may be also spuriously high in cases of severe shock because of peripheral circulatory stasis and for this reason one should always test venous (e.g. antecubital or umbilical vein) rather than capillary (e.g. heel-prick) blood.

In acute haemorrhage the RBCs in the peripheral film will be normocytic and normochromic, while in chranic blood loss a hypochromic microcytic picture may be seen. Other evidence of iron deficiency — low serum iron level and no stainable iron in the bone marrow — have also been demonstrated in the latter cases (Eshaghpour *et al.* 1966).

Proof that the foetus bled into the mother can be obtained with certainty only by demonstrating the presence of foetal red cells in the maternal circulation. This can be done by one of several techniques including direct differential agglutination (Jones and Silver 1958), fluorescent antibody techniques (Cohen *et al.* 1960), examination of the buffy coat for foetal RBCs (Goodall *et al.* 1958); the alkali denaturation method (Singer *et al.* 1951) and the acid elution method of staining for cells containing foetal Hb (Kleihauer *et al.* 1957).

The simplest and most widely used of these is the Kleihauer test in which methanol-fixed maternal blood films are treated with an acid buffer at pH 3.4. Foetal RBCs resist lysis by the buffer solution so that they subsequently react with the ordinary Hb stains, whereas the adult maternal RBCs are lysed and appear as "ghosts". The foetal erythrocytes are then counted and a rough calculation is made as to the degree of haemorrhage that has

taken place. The result may be conveniently reported as the ratio of foetal to maternal RBCs expressed as a percentage. The Kleihauer technique can be relied upon with certainty for diagnosis only when other conditions capable of producing a rise in maternal Hb F levels (e.g. thalassaemia minor, sickle cell anaemia) are absent. In such cases the tests based on differential agglutination should be performed.

Diagnosis of foeto-maternal transfusion may be missed in cases where the mother and infant are ABO incompatible. Here, the baby's A or B cells are rapidly cleared from the mother's circulation by maternal anti-A or anti B, and thus are not available for staining by the Kleihauer technique. This test should therefore bedone as early as possible after birth.

The exact mechanism by which the foetal blood enters the maternal circulation is obscure and in most cases there are no gross placental abnormalities. The placenta should be examined carefully because the haemorrhage from the infant may not have entered the mother's circulation and instead may have accumulated in the substance of the placenta. (Chown 1955) or retroplacentally (Kevy 1962). Rarely, the placenta may be damaged during high rupture of the membranes (Apley *et. al.* 1961) and in one case the condition was associated with a chorion-carcinoma (Benson *et al.* 1962).

The differential diagnosis of anaemia at birth is not usually difficult and a list of causes is shown in Table 1. There are two main groups of conditions causing obvious anaemia *at birth.* The first and by far the commonest is haemolytic anaemia due to Rh, ABO or other rare group incompatibility. The presence of Rh antibodies during pregnancy, direct Coombs test and serum bilirubin on cord blood, testing for incompatibility between mother's serum and baby's RBCs and blood film examination, are routinely undertaken to diagnose this group. Various infections are a less common cause of haemolytic anaemia at birth.

The second group is anaemia caused by intrauterine haemorrhage. Foetal haemorrhage should be suspected during labour or during the operation of artificial rupture of membranes if there is a sudden gush of bright red blood from the vagina. The foetal origin of the blood can be confirmed in the labour ward by testing for foetal Hb which resists denaturation with alkali (Apt test). The placenta should be examined to exclude rupture of anomalous vessels, retroplacental clot, etc. If there is no obvious source for the haemorrhage, foeto-maternal transfusion should be excluded by an immediate Kleihauer test. Pallor in one of a pair of monozygotic twins with relative polycythaemia in the other, points to twin-to-twin transfusion (Vassallo Agius 1967). Congenital hypoplastic anaemia is extremely rare and is confirmed by a low reticulocyte count and bone marrow studies.

Treatment depends on the degree of anaemia and the general condition of the baby. When the infant is in shock or if the pallor is very marked, plasma should be given rapidly initially (via an umbilical catheter) to expand the intravascular compartment. When blood becomes available a transfusion of 10 cc/lb (20 cc/kg) body weight packed cells should be given. Infants who are mildly anaemic and who show no distress do not require blood and should be given oral iron for three months to replenish the depleted iron stores. Iron is also needed for the infant who receives a blood transfusion because this is not generally sufficient to replace the iron lost from the haemorrhage. McGovern *et al.* (1958) reported iron deficiency anaemia in a three month old infant that had foeto-maternal haemorrhage and was transfused at birth.

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TABLE I
CAUSES OF ANAEMIA
AT BIRTH

A. INTRAUTERINE HAEMOLYSIS

1. ISO-IMMUNISATION (Erythroblastosis foetalis)
— Rh incompatibility
— ABO incompatibility
— Rare group incompatibility
2. INTRAUTERINE INFECTIONS
— Bacterial — Septicaemia
— Viral — Rubella; Cytomegalovirus
— Protozoal — Toxoplasmosis
— Spirochaetal — Syphilis

B. INTRAUTERINE HAEMORRHAGE

1. HAEMORRHAGE IS INVISIBLE
— Foeto-Maternal transfusion
— Twin-to-Twin tranfusion
2. HAEMORRHAGE IS USUALLY VISIBLE
— Incision of anteror placentia praevia at C.S.
— Placenta Praevia
— Abruptio Placentae
— Rupture of anomalous vessels
— Rupture of umbilical cord
— Damage to placental vessels at A.R.M.

C. IMPAIRED RBC PRODUCTION

Congenital Hypoplastic Anaemia
(Erythrogenesis imperfecta)

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