Summary

A case of classical acute porphyria occurring in a West African negro is described. Post-mortem and biochemical findings are included. The literature is briefly quoted.

I am indebted to Dr. A. Kahan, under whose care the patient was admitted, for permission to publish the case and for his encouragement and advice; to Dr. N. Orchard for the post-mortem report and the preliminary detection of porphyrins; to Dr. L. Ellis, biochemist to the Lambeth Group Laboratory, for his report on the urine findings; and to Dr. J. Olu-Mabayojé, who had known the patient for many years, for his help with the history.

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FOLLOW-UP OF RHESUS-NEGATIVE PRIMIGRAVIDAE DEVELOPMENT OF RHESUS IMMUNIZATION

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Rhesus immunization in the first pregnancy has been found only very exceptionally, apart from patients who had previously received a transfusion of rhesus-positive blood. Few authentic cases of rhesus immunization of the first-born child have been mentioned in the literature (Boorman, Daley, and Dodd, 1947).

It has been suggested that the immunizing stimulus is provided during labour by a small "blood transfusion" given to the mother by the foetus through the breakdown of the syncytial placental layer. During the second pregnancy small "booster doses" of foetal blood reaching the maternal circulation stimulate antibody formation further, and the "full-blown" picture of rhesus immunization develops. The assumption that the first pregnancy or labour provides the first antigenic stimulus seems to be necessary to explain the development of antibody formation during the next pregnancy, in which presumably identical conditions obtain with regard to the placental barrier as in the first pregnancy.

Stratton (1943) has shown that the rhesus factor can be discovered on the foetal red blood cells at the eleventh week of development, but it seems improbable that such an immature foetus could provide enough antigenic

material to produce antibodies in the maternal serum. Occasionally, however, antibodies are discovered in the early weeks of a second pregnancy. The following case illustrates this point.

A married woman aged 25 had her first baby on February 23, 1948. The infant, of 30 weeks' gestation and weighing 2 lb. 15 oz. (1.33 kg.), was born spontaneously. Serological investigations were performed on the mother at the ninth and twenty-seventh weeks and eight days after delivery. The result of all three investigations was Group B rhesus-negative, the serum containing no anomalous antibodies.

The patient became pregnant again in September, 1948. The first specimen of blood investigated early in January, 1949, at 16 weeks' gestation, showed definite signs of rhesus immunization by containing blocking anti-rhesus antibodies of fairly high titre (1:32). Several repeat investigations gave essentially identical results, and on May 3 a baby suffering from haemolytic disease of the newborn was born. She weighed 4 lb. 7 oz. (2 kg.). Despite a blood transfusion of rhesus-negative blood, she died of kernicterus at the age of 7 days. The diagnosis was confirmed at necropsy (Dr. Baar).

It was thought advisable to follow up a number of primigravidae after delivery, for a comparatively long period, to see whether any antibody formation followed delivery and whether the antibody could be proved to be present by routine serological methods. If the assumption is correct, that the primary immunizing dose is given during labour or afterwards, one could hope to find antibodies in sera of exceptionally good reactors without a further stimulus having been applied.

The investigation was undertaken on 62 primigravidae who were all seen antenatally and delivered at Sorrento Maternity Hospital, Birmingham. They were also followed up post-natally there. The serological investigations covered determination of the blood group, rhesus type, and investigation for antibodies in the serum. The latter was done by means of saline- and albumin-suspended cells, ten of which were rhesus-positive and two rhesus-negative. All the sera were also tested by means of the indirect Coombs test. The cord blood was also investigated. This investigation included the group and rhesus type and, from 1948 onwards, the direct Coombs test. Consecutive rhesus-negative primiparae were selected, and only those excluded who produced a rhesus-negative infant. The post-natal investigations were undertaken at various intervals. In most, the second specimen was obtained about eight days after delivery, and in no case were anomalous antibodies found. Several patients were followed up further at intervals up to two years. Two patients developed anti-rhesus antibodies. Their clinical and serological details follow.

Case 1

A woman aged 24 was delivered of a healthy, normal, full-term baby on October 20, 1947. This baby showed no icterus or other sign of haemolytic disease. His blood type was Group A rhesus-positive.

Further specimens were investigated from the mother, and approximately two years later the following results were obtained: The cells were confirmed as Group O rhesus-negative, the serum agglutinated strongly rhesus-positive albumin-suspended cells and did not agglutinate rhesus-negative cells. An indirect Coombs test with rhesus-positive cells was positive. Three weeks later a further specimen gave identical results. The serum was tested with a large battery of fully typed cells and agglutinated every sample cell which contained the D antigen. The titre of the antibody was found to be fairly low (1:2) against CDe/CDe and cDe/cDe. At the same time a specimen of blood from the patient's husband was investigated and found to be Group A rhesus-positive (most likely genotype CDe/CDe).

It was obviously important to find out whether the patient had at any time between the delivery and the follow-up investigation been pregnant. This seemed impossible. She had attended a welfare centre regularly. Husband and wife confirmed the use of birth control (by male sheath) because they did not desire a second child until they no longer had to live in the same house as a relative suffering from pulmonary tuberculosis.

The patient gave a history of regular menses and had received no injections of any kind either ante- or post-natally, and had never received a transfusion.

Case 2

A woman aged 22 was delivered of a living healthy, full-term baby on September 19, 1948. The infant showed no signs of haemolytic disease of the newborn. The infant's blood type was Group A rhesus-positive.

The maternal serology antenatally was Group A rhesus-negative, the serum containing no anomalous antibodies. A specimen of blood obtained on the eighth day after delivery gave identical results. A further specimen, however, obtained on June 22, 1949, gave definite evidence of the presence of a potent anti-rhesus antibody, again acting more strongly on albumin-suspended rhesus-positive cells. The titre was moderately high (1:8). The serological behaviour of the antibody was typical, no reaction occurring unless the test cells contained the D antigen.

This patient had shown no sign of a further pregnancy, her menses having been regular since the cessation of lactation three months after delivery. She had received no injections ante- or post-natally or transfusions at any time of her life. Her husband was Group O rhesus-positive and most likely genotype CDe/cde.

Discussion

The serological findings in these two cases are clear-cut and indicative of rhesus immunization. The fact that the antibody reacted better with albumin- than with saline-suspended cells might perhaps be due to its comparatively low titre. We share with several other workers the experience that sometimes an "albumin" antibody can change into a saline agglutinating antibody just before delivery. The contention, therefore, that a blocking antibody is always a sign of hyperimmunization might perhaps be open to discussion.

It is difficult to understand why antibodies in these two patients developed so late after delivery. In both, the antigenic stimulus must have been the first pregnancy, and, so far as can be established, there was no further antigenic stimulus. That antibodies can develop to a stimulus a long time after its first application is a not uncommon experience in immunology—for example, undulant fever. Further investigations are in progress to elucidate this problem in greater detail. As a practical application of our findings, if they can be confirmed on a larger series, it might perhaps be advisable to investigate for the presence of anomalous antibodies the sera of all primiparae contemplating a second pregnancy.

Summary

In a follow-up of 62 rhesus-negative primiparae with rhesus-positive babies, two were found who, after intervals of two years and of nine months respectively, had developed anti-rhesus antibodies in their serum without a further intervening pregnancy or other antigenic stimulus.

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MONGOLISM IN ONE OF TWINS

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Graham (1950), reporting a case of mongolism in one of twins, drew attention to the comparative rarity of such cases in the British literature. The largest series so far published seems to be that of Warner (1949), who collected 101 cases from the literature and recorded one further case in which an older sib was also a mongol. Of these 102 sets of twins, one child was affected in 82 cases and both children in 20.

It is well recognized that there is a considerably increased incidence of congenital cardiac defect among mongols. Wylie (1949) quotes 22 examples in a series of 138 mongols (16%); Benda (1947) states that up to 75% of mongols dying in the first two years of life have a congenital cardiac defect, as have 35% of those surviving. Post-mortem records of the Hospital for Sick Children, Great Ormond Street, yielded evidence of congenital cardiac abnormality in 28 of 63 mongols (Evans, 1950). While various malformations are encountered, persistent ostium atrio-ventricular commune is especially apt to be associated with mongolism (Abbott, 1936). Robinson (1941), in a series of 39 cases of this defect collected from the literature, states that about one-half of these were in mongols. Taussig (1947) emphasizes the likelihood that a mongol presenting signs superficially resembling ventricular septal defect, and without cyanosis, is suffering from persistent atrioventricularis communis. There were, however, only four examples of this in Evans's series, the commonest anomaly being in fact ventricular septal defect.

Case Report

Helen B. was born on November 20, 1949, at full term, the first of twin girls. The mother was aged 35; her health was good during pregnancy, apart from a cystocele which was troublesome during the first trimester. The father's age was 36. The family and personal histories of both parents were, so far as is known, good. There are two older (normal) daughters, now aged 4 and 7 years. Helen was delivered as a vertex, and the second (normal) twin as a breech; each weighed approximately 5½ lb. (2.5 kg.) at birth. A suggestion of mongoloid physiognomy was noted in Helen at birth, but was discounted to some extent by the medical attendant because