There is no evidence that the condition is giant-cell arteritis, a name which should be reserved for cases showing pathological proof of this condition.

The syndrome resembles the prodromal symptoms of rheumatoid arthritis more than other disorders and has an excellent prognosis.

Salicylate therapy was adequate in nearly all patients.

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BONE-MARROW HYPOPLASIA IN THE COURSE OF HAEMOLYTIC DISEASE OF THE NEWBORN

BY

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Haemolytic anaemia due to incompatibility in Rh blood groups of mother and foetus affects 0.5% of newborn babies (Walker and Mollison, 1957). That the bone-marrow may not respond to this anaemia by increased red-cell production has been pointed out by Gasser (1955), Giblett, Varela, and Finch (1956), and Lindquist and Ryttinger (1959). Smith (1949) reported a case of pure red-cell hypoplasia in an infant, probably following haemolytic disease of the newborn, and a further case of proved haemolytic disease of the newborn in which there was some evidence of marrow hypofunction. Diamond (1948) suggested that most cases of haemolytic disease of the newborn show marrow hypoplasia at 2 or 3 weeks of age. Dillon and Krivit (1959), however, in a study of serial marrow specimens, could find no convincing cases of hypoplasia among 14 affected infants. They stated that in general the marrow shows increased erythroid cellularity in proportion to the severity of the anaemia. The case reported below showed marrow erythroid hypoplasia and persistence of Rh antibody in the infant's serum.

Case Report

The child was referred to Hammersmith Hospital 18 hours after birth, following the onset of cardiac failure after exchange transfusion. He was born to a 37-year-old Englishwoman who had had three previous pregnancies. Her blood group was A Rh-negative (*cde/cde*) and that of her husband O Rh-positive (*CDe/cde*). Her first two children were unaffected, but the third is recorded as showing slight jaundice during the neonatal period, although requiring no treatment. During the present pregnancy Rh antibodies were detected in the mother's serum at 34½ weeks' gestation at a titre of 32. The titre rose to 256 at 36½ weeks and to 2,000 at 38½ weeks, all these figures being obtained using an albumin technique.

At 38½ weeks labour began spontaneously and a male infant, weighing 3,060 g., was born. He was jaundiced at birth and the spleen was palpable. Investigations on the cord blood gave the following results. Haemoglobin, 6.7 g./

100 ml. Blood film, 207 normoblasts per 100 white cells. Direct antiglobulin (Coombs) test, strongly positive. Group, A Rh-positive (*CDe/cde*). Serum bilirubin, 5.6 mg./100 ml.

An exchange transfusion was performed four and half hours after birth, using 450 ml. of packed red cells, group A Rh-negative. The infant developed heart failure, which responded to treatment with digoxin.

By the third day the serum bilirubin level had risen to 28.9 mg./100 ml. However, since the indirect-reacting fraction never exceeded 18.3 mg./100 ml., and it was realized that the jaundice was partly of the obstructive type (Oppé and Valaes, 1959), further exchange transfusion was not thought necessary.

After the original exchange transfusion the cord haemoglobin was 18.3 g./100 ml. (see Chart). Subsequent skin-prick blood samples showed a steady fall of haemoglobin, and after four weeks the following values were found: haemoglobin, 7 g./100 ml.; packed cell volume, 21.5%; red cells, 2,600,000/c.mm.; white cells, 5,000/c.mm.; platelets, 300,000/c.mm.; reticulocytes, nil. Rh antibody titre (indirect Coombs method), 32. Direct Coombs test,

negative (indicating that only Rh-negative cells—that is, donor cells—were present in the circulation).

Examination of the tibial marrow at this time (4 weeks) revealed red-cell hypoplasia (see Table).

Bone-marrow Findings

	4 Weeks	13½ Weeks
Erythroid cells (%)	7	31
Myeloid cells (%)	23	5
Lymphoid cells (%)	63	60
Reticulum cells, plasma cells, and monocytes (%)	7	4
Peripheral blood haemoglobin (g./100 ml.)	7.0	7.8
Reticulocytes (%)	0	8

At 4½ weeks of age the infant was given two further transfusions of 55 ml. and 75 ml. of fresh group-A-Rh-negative blood. The haemoglobin rose to 12.4 g./100 ml., but by 10½ weeks it had again fallen to 7 g./100 ml. Reticulocytes were first seen in the peripheral blood at 5 weeks (0.2%). The percentage remained less than 1 until 10 weeks, and at 11 weeks reached a peak of 17.2%. During the period of reticulocytosis (at 13 weeks), when the haemoglobin was 7.8 g./100 ml., a further marrow specimen showed active erythropoiesis.

At 12 weeks, for the first time since the exchange transfusion, Rh-positive cells appeared in the blood and the direct Coombs test was strongly positive. Rh antibody was present in the serum at a low titre (2) but had disappeared by 14½ weeks, when the direct Coombs test was also negative.

From the time of appearance of Rh-positive cells in the circulation the haemoglobin slowly rose until, at 21 weeks, it was 12.4 g./100 ml. The baby himself progressed normally after control of the initial heart failure and appeared to be normal in every way when last seen at the age of 21 weeks.

Discussion

Gairdner, Marks, and Roscoe (1952) point out that normally, from the age of 1 week, the marrow shows little activity until at 8 weeks the haemoglobin has fallen to about 11.5 g./100 ml., when it shows an increase in erythroid cells. They also show that the marrow of an infant of any age begins to increase red-cell production when the haemoglobin falls to between 11 and 12 g./100 ml. The fact that in the case reported here erythroblasts constituted only 7% of the nucleated cells in the marrow at 4 weeks, despite a circulating haemoglobin of 7 g./100 ml., is good evidence of hypoplasia. It will be noted that the marrow at 13 weeks was also obtained while the haemoglobin was about 7 g./100 ml. The specimen showed erythroid hyperplasia, which is the expected response to anaemia of a normal marrow.

The absence of circulating reticulocytes for the first five weeks may have been due to the persistence of a powerful Rh antibody which was destroying them, as well as more mature cells (Gasser, 1955). It was suggested by Giblett *et al.* (1956) that such an antibody may also depress marrow function. However, in the present case the florid erythroblastosis in the cord blood, when presumably the antibody was at its greatest concentration, does not suggest marrow depression. Lindquist and Ryttinger (1959) suggest that excessive marrow activity, in foetal and early neonatal life, may "exhaust" the marrow. They make a comparison with the aplastic crisis that may occur during the course of hereditary spherocytosis (Owren, 1948).

The concept of marrow exhaustion has little to support it when one considers the course of haemolytic anaemias in general. Many cases show persistent severe haemolysis continuing for many years, as is evident by

reticulocyte counts in the region of 50%, without developing hypoplasia. An acquired deficiency of some factor necessary for erythropoiesis is proposed as a cause of the "exhaustion," but there is no evidence of a lack of any of the known haematinic substances. It is well known that haemolytic anaemia may cause a deficiency of folic acid, but in the case recorded here the hypoplastic marrow at 4 weeks showed no sign of megaloblastosis. In fact, the bone-marrow seems to withstand the strain of haemolysis better than that of blood loss, as the products of haemolysis are retained in the body and are available for making fresh cells. It may be that the foetal marrow is enabled to respond vigorously to haemolysis by the erythropoietic hormone of the mother and that at birth the supply of this substance ceases. It is an attractive speculation that the infant is at first unable to make enough erythropoietin to maintain red-cell production at the *in utero* level, but later the manufacture of this substance increases. Parallels may be drawn with many physiological processes which are poorly developed at birth and gradually become more efficient with time.

As an explanation of the findings under discussion this hypothesis is obviously incomplete, since the infant's marrow remained hypoplastic despite a haemoglobin well below 10 g./100 ml. It would seem that the hypoplasia is related in some way to the persistence of antibody although the marrow is probably not affected directly by it for the reasons given. However, a depression of the formation of erythropoietin below the normal physiological level while circulating antibody is present might be expected to cause hypoplasia. Whatever the reason, it seems significant that while the haemolysis was most severe—that is, *in utero*—the foetal marrow was working at its best. Only after removal from the maternal environment, and when the antibody titre was declining, did the marrow become unresponsive.

With reference to the persistence of Rh antibody in Rh-positive infants, Ramaekers (1954) records that antibody could be detected for between four and nine weeks after exchange transfusion in 14 affected infants. Occasionally antibody persists for longer periods, as in the case reported by Lindquist and Ryttinger (1959) in which it persisted for between 11 and 13 weeks. Mollison and Cutbush (1949) report that the direct antiglobulin test may remain positive for more than 90 days after the simple transfusion of Rh-positive blood to severely affected infants. Antibody was present in the case recorded here for between 11 and 14 weeks, and it is interesting to consider that it probably caused both a haemolytic and a hypoplastic anaemia.

As regards the jaundice, the neonatal liver does not conjugate bilirubin efficiently by adult standards (Vest and Streiff, 1959). Thus the infant with haemolytic disease retains a high concentration of toxic indirect-reacting bilirubin in the blood. Occasionally such infants are able to conjugate larger amounts of bilirubin from birth and an obstructive type of jaundice may supervene. It has been suggested that a high bilirubin level *in utero* encourages the early development of the conjugating mechanism. In this instance anaemia was, from first to last, a greater problem than jaundice, as is often the case when the infant is very severely affected at birth.

Summary

A case of haemolytic disease of the newborn is presented showing bone-marrow hypoplasia and persist-

ence of Rh antibody after exchange transfusion. The literature is reviewed and the mechanism of these phenomena discussed.

We would like to thank Dr. J. Davis, who was in charge of the case, and Professor J. V. Dacie for much helpful advice.

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Medical Memoranda

Abdomino-scrotal Hydrocele

Abdomino-scrotal hydrocele is an uncommon condition, and case reports, usually solitary, have appeared at intervals since Dupuytren first described it in 1834. In the following report the condition presented as an acute abdomen.

CASE REPORT

A man aged 28 was admitted to hospital as an "acute" case on May 19, 1960. An indirect right inguinal hernia had been repaired at the age of 15. Within a year a swelling appeared in the right side of the scrotum and had increased slowly in size. Increasing prominence of the lower abdomen had been noticed over a period of six months. On the day of admission he awoke with pain in the right side of the scrotum. It radiated to the right lower quadrant of the abdomen and settled there as a constant ache. Nausea and vomiting were not symptoms and the bowels and micturition were normal. A similar episode had occurred two months previously.

Examination revealed a healthy young man with a normal temperature and pulse rate. The right side of the scrotum contained a cystic swelling of some 6-oz. (170-ml.) capacity, extending up into the inguinal canal via the external ring. The testicle could not be identified on that side, although on the left side it was normal. Transillumination was present. A large smooth swelling could be palpated in the right iliac fossa extending upward as far as the umbilicus, medially to the midline, and laterally into the flank. The swelling was moderately tender. The rest of the abdomen was soft and normal bowel sounds were present. No firm pre-operative diagnosis was made, but it was felt that the abdominal swelling was extraperitoneal.

Operation.—An incision was made in the right groin, excising the scar of the previous hernia repair. The external oblique was opened and later the internal oblique and transversus muscles had to be divided at the apex of their arch. A large bilocular hydrocele was found. The smaller loculus lay in the scrotum and the larger accompanied the cord through the posterior wall of the inguinal canal into the abdomen, where it rested in the extraperitoneal tissues behind the muscles of the anterior abdominal wall. It contained more than 50 oz. (1.4 litres) of clear straw-

coloured fluid. The sac was delivered through the inguinal canal, emptied, and most of the wall excised. The residue was everted around the cord and haemostasis obtained. The presence of so large a sac passing through the internal ring with the cord had disrupted the posterior wall of the inguinal canal almost completely, and it was repaired with a tantalum gauze implant. The wounds were closed without drainage.

Post-operative Course.—A haematoma collected in the undrained scrotum in spite of careful haemostasis, and although it was evacuated on the third post-operative day an area of scrotal wall sloughed, followed later by the right testis. Both eventually had to be excised. After this unfortunate sequel recovery was uneventful, and at follow-up three months later the right inguinal region was sound.

COMMENT

The presentation was that of an acute abdomen with considerable pain. The cause of this pain was obscure, as no other structure was being interfered with and haemorrhage had not occurred into the sac, nor into the surrounding tissues. A common physical sign is reported to be an impulse felt in the scrotum on coughing, together with a transmitted thrill between the two loculi. This sign was absent, and it is thought that the neck of the sac had become obstructed temporarily with the production of pain, presumably from overdistension.

The operative procedure was not particularly difficult, apart from the problem of the large defect in the posterior wall of the inguinal canal which remained. In fact, the posterior wall was virtually destroyed. The tantalum gauze implant which was used here has functioned well during the two-year follow-up period and did not become infected in spite of the subsequent scrotal complications. A better material now would probably be a plastic filigree, but it is felt that some such method is required in these circumstances rather than relying upon natural structures, especially when preservation of the testis is intended.

The importance of draining scrotal wounds is appreciated. Although the greatest care was taken with haemostasis, a large and very tense haematoma developed in the scrotum. This was evacuated; but too late, for it was so tense that a portion of scrotal wall became gangrenous and had to be excised. At the completion of the primary operation the testicular vessels were pulsating normally and the cord had not been damaged, so that the testicular necrosis is attributed to the same cause—namely, pressure from the undrained haematoma.

Thanks are due to Mr. F. R. R. Martin, consultant surgeon, Royal Infirmary, Bradford, under whose care the patient was.

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The Oxford Committee for Famine Relief has allocated £5,000 to the Ministry of Agriculture of the Tanganyika government for the control of sleeping sickness in the refugee resettlement area at Ngara. Large stocks of chemicals for use against the tsetse fly have been acquired by the Regional Tsetse Officer and are being used for the elimination of tsetse in the area, where sleeping sickness is endemic. The Oxfam grant covers the cost of clearing 4,500 acres.