

joint capsules, ligaments, and dura mater in all 27 cases. In some of the 27 there was extensive bruising and destruction of the spinal cord, haemorrhage into the media of the vertebral arteries, and occlusion of a vertebral artery by thrombus. Such damage to vertebral arteries could impair circulation to the brain stem and cerebellum. Towbin (1969) found spinal cord and brain stem injury in more than 10% of all newborn infants at necropsy, the common sites of spinal injury being cervical and upper thoracic spine. Some factors that could have contributed to spinal injury in addition to birth trauma were: prematurity, intrauterine malposition, dystocia, and precipitate delivery.

Severe birth trauma to vital centres in the upper cervical cord and brain stem may lead to death shortly after birth. Infants who survive with spinal injury may have permanent neurological abnormalities due to damage to the spinal cord or vertebral arteries. The present case illustrates that spinal cord injury due to birth trauma can produce a paraplegia. Though there are recent reports of spinal cord injury due to birth trauma (Melchior and Tygstrup, 1963; Jones, 1970; Shulman *et al.*, 1971), such injury in the newborn asphyxiated infant may be overlooked, attention being primarily directed to cerebral lesions. Thus, some cases of paraplegia and quadriplegia attributed to cerebral palsy may be suffering from the after-effects of spinal cord damage.

### Summary

A neurologically abnormal infant who died at the age of 8 weeks was found to have spinal cord atrophy involving about 2.5 cm in the midcervical region. He was asphyxiated during birth and was delivered by breech extraction. Spinal cord injury was probably related to trauma associated with breech extraction. Asphyxiated babies are usually hypotonic and therefore may be particularly liable to sustain spinal injury.

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## Congenital erythroid hypoplastic anaemia in mother and daughter

Pure red cell anaemia, congenital erythroid hypoplastic anaemia, the syndrome of Diamond and Blackfan (1938) was first described briefly by Josephs (1936). Despite the many reports and reviews since then, there are only 9 familial occurrences of well-documented overt disease recorded, all in sibs (Burgert, Kennedy, and Pease, 1954; Diamond, Allen, and Magill, 1961; Förare, 1963; Seligmann *et al.*, 1963; Mott, Apley, and Raper, 1969). Nevertheless, the two separate and unusual families reported by Förare (1963) and Mott *et al.* (1969), where step-sibs, progeny of the same father by different mothers, suffered the anaemia, suggest that congenital erythroid hypoplastic anaemia can be transmitted in a mendelian-dominant fashion. This report documents definite vertical transmission of the disease from mother to daughter.

### Case reports

**Mother.** Born of unrelated parents on 7 November 1945, after a term normal pregnancy. Birthweight 2270 g, blood group B, Rhesus negative. She presented at 21 months with pallor and listlessness, Hb 4.7 g/100 ml, normal red cell morphology, white cell count 9400/mm<sup>3</sup>, and normal differential count for her age. She had a urinary infection and was treated with alkali and oral iron. Hb rose to 10.2 g/100 ml over 2 months. At 3 years severe anaemia recurred, Hb 4.9 g/100 ml, white cell count 3700/mm<sup>3</sup>, reticulocytes 8%, the marrow showing selective erythroid hypoplasia. Investigations excluded haemolysis, mucoviscidosis, and malabsorption, and Hb rose with iron, liver extract, and folic acid to 10.9 g/100 ml over 6 months. Convalescence was

complicated by acute otitis media and she underwent tonsillectomy. Aged 4 to 7 years, recurrent episodes of anaemia were treated with blood transfusion, two marrow examinations confirming erythroid hypoplasia. Aged 7 to 10 years, she had psychomotor epilepsy with a temporal lobe focus demonstrable by EEG; fits ceased with phenobarbitone and did not recur on discontinuing therapy. During this period her Hb was stable at 11 g/100 ml and she required no haematinics until at age 10 years severe anaemia recurred. Cortisone was given for the first time and though rapid withdrawal led to a fall in Hb, more cautious dose reduction was successful and with oral iron alone Hb remained between 10.5 and 11.7 g/100 ml for 5 years. Menarche was at 14½ years; 6 months later Hb had fallen to 5 g/100 ml and blood film for the first time showed microcytosis and hypochromia accompanied by a micronormoblastic hypoplastic marrow. Prednisolone and intravenous iron administration was followed by a brisk erythropoietic response, reticulocyte peak of 20%, and Hb reaching 8.7 g/100 ml. Fluoxymesterone 5 mg/day and prednisolone 5 mg/day stabilized the Hb at 11.2 g/100 ml, a value maintained on discontinuing the androgen after 6 months. Hb remained satisfactory over the years while she received intermittent courses of oral iron until her pregnancy at the age of 21½ years.

*Course of pregnancy.* At 4 weeks Hb was 11.1 g/100 ml, reticulocytes 1.8%, and she was taking prednisolone 5 mg/day and oral iron. A pathological fall in Hb occurred which, by 28 weeks, was 5.9 g/100 ml. She received 4 units red cell concentrate, folic acid supplements (serum folate 2.6 ng/ml), oral iron, and prednisolone was increased to 10 mg/day. She required another 4 units red cell concentrate at 32 weeks, but apart from some albuminuria she remained well until the spontaneous onset of labour at the 38th week. Delivery by elective low-cavity forceps was uneventful. 5 weeks after birth Hb was 5.7 g/100 ml and she received 6 units red cell concentrate. Subsequently serum iron was high, 200 µg/100 ml, and iron therapy was stopped, folic acid and prednisolone were continued, and the oral contraceptive Minovlar (norethisterone 1 mg and ethinyl oestradiol 0.05 mg) was started. One year later (aged 23) she again required transfusion. The red cells were for the first time macrocytic despite folate therapy and a normal serum B<sub>12</sub> of 460 pg/ml. Because of facial mooning and epigastric discomfort, prednisolone was reduced and oxymetholone introduced, the dosage gradually being reduced from 50 mg per day to 50 mg twice a week. She had also developed amenorrhoea while on Minovlar, and in view of the uncertain long-term effects of various steroid preparations, as well as for eugenic reasons, contraception was effected by her husband having a vasectomy. During this 2½-year period on the contraceptive pill, serum B<sub>12</sub> progressively fell to 160 pg/ml by *Lactobacillus leichmanii* assay. She was given hydroxocobalamin 100 µg/month, folic acid 5 mg/day, prednisolone 5 mg/day, and oxymetholone 50 mg twice-weekly, and as anaemia recurred when her periods started again, oral iron. She continues at present on this

haematinic cocktail and is aged 27 years, clinically well with Hb 10.7 g/100 ml, and reticulocyte count 2 to 5%. She has large numbers of fetal cells (by the acid elution technique) present in the peripheral blood, but Hb electrophoresis shows no increase in Hb A<sub>2</sub>. No serum antigastric or anti-intrinsic factor antibodies are detectable and at no time has anthranilic acid been detected in her urine.

**Daughter.** The child of unrelated parents, born on 9 January 1968 at 38 weeks' gestation, birthweight 2215 g, blood group O, Rhesus negative. On the first day of life Hb was 17 g/100 ml, reticulocytes 7.4%, white cell count 9370/mm<sup>3</sup>. She was physically normal and progress was uneventful. By 7 weeks Hb was 12 g/100 ml, weight 2400 g. At 12 months she was admitted with a history of irritability for 2 months and recurrent coughs and colds. Hb was 3.7 g/100 ml, red cells normocytic and normochromic, reticulocytes 4%. White cell count, differential and platelet count were normal. Serum iron 110 µg/100 ml, total iron binding capacity 375 µg/100 ml. Tibial marrow aspirate was highly cellular, erythropoiesis scanty but normoblastic. Extracellular but no intracellular iron was demonstrable, other marrow elements were normal. No anthranilic acid was detected by paper chromatography. Despite transfusion and prednisolone, anaemia recurred within 2 months and oxymetholone 3 mg/kg was introduced. But within 4 months the child had become conspicuously Cushingoid, with marked vulvar hair growth, clitoral enlargement, and labial scrotalization. Oxymetholone was discontinued, whereupon Hb fell from 14 g/100 ml to 8.6 g/100 ml. Prednisolone was increased to 10 mg/day maintaining Hb between 11 to 12 g/100 ml. Over the next 2 years prednisolone 2.5 to 5 mg/day kept her Hb stable, but aged 3½ years she had otitis media and mastoiditis requiring drainage. Recently, at age 4½ years, anaemia has recurred necessitating blood transfusion and increased prednisolone and cautious reintroduction of oxymetholone 0.8 mg/kg. Hb has risen to 13.8 g/100 ml, with a reticulocytic peak of 18%. Some 13% of red cells are fetal by acid elution staining. She has considerable macrocytosis of the red cells, despite a serum B<sub>12</sub> of 440 pg/ml, and serum folate 5.4 ng/ml. Her height is within 1 SD for her age, her weight follows the 10th centile growth curve.

### Discussion

The clinical course of both mother and child conforms well with the classical descriptions of congenital erythroid hypoplasia (Allen and Diamond, 1961; Diamond *et al.*, 1961). The onset in early infancy rather than in the neonatal period of a progressive anaemia with poor reticulocyte count and no disturbance of white cells nor platelets is well seen. Their disease is relatively mild and fairly well controlled with small doses of steroids, though occasionally the dose required induces unacceptable side effects and transfusion is needed. While steroids have lessened the severity of the anaemia

they have not induced a complete remission and cautious use of the synthetic androgen oxymetholone may reduce still further the need for blood transfusions. Fortunately, despite long-term glucocorticoid therapy, stunting of growth has not been troublesome.

In the previously reported familial cases of congenital erythroid hypoplastic anaemia, transmission of the disease has been apparently through father to offspring. Diamond *et al.* (1961) noted secondary sexual maturation to be retarded, particularly in the female. However, as treatment becomes more effective it is likely that the excess mortality and morbidity from the disease in girls compared with boys will decline, and more cases of transmission through the mother, as in this instance, will be seen.

### Summary

Erythroid hypoplastic anaemia in mother and daughter is described, thus supporting evidence of autosomal dominant transmission of the disease.

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