

A FAMILIAL CRISIS IN CONGENITAL ACHOLURIC JAUNDICE

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A familial crisis in congenital acholuric jaundice involving several members of a family within a short space of time is an unusual occurrence. Nine further instances are reported by Barber (1934), Scott (1935), Murray-Lyon (1935), Dedichen (1937), Dameshek (1941), Lyngar (1942), Horne, Lederer, Kirkpatrick and Leys (1945), Owren (1948) and Marson, Meynell and Tarbush (1950). In the histories given below crises of varying severity are shown affecting five members of a family of seven. The family pedigree is illustrated in Fig. 1.

Case Reports

Case A. Beverley A, aged 4 years, was admitted to the Children's Hospital, Leicester Royal Infirmary, on September 27, 1950. The history showed that her illness began suddenly on September 21 when she vomited twice, became pale and listless, went off her food, became constipated, and complained of abdominal pain. On examination, besides the extreme pallor being noted, the child appeared listless and irritable. There was no jaundice. Her temperature was normal, pulse 100 and respirations 20. Small, shotty glands were palpable in the neck, axilla and groins, and the spleen was palpable two finger breadths below the costal margin; otherwise nothing abnormal was found.

On the day of admission a blood count showed Hb. 28% (4.5 g. %), red cells 1,800,000, colour index 0.78, white cells 18,500 (polymorphonuclears 90%, lymphocytes 8%, monocytes 2%). A blood film showed marked anisocytosis, spherocytosis and a large number of reticulocytes with occasional nucleated red blood cells.

Sternal puncture revealed a hyperplastic and normoblastic marrow.

Urine showed no haemoglobin, but *Bact. coli* was grown from a catheter specimen.

Her blood group was AII, Rh negative, and a transfusion of 170 ml. of packed cells was given at once in view of the severe anaemia. This raised the haemoglobin to 77% (12.32 g. %) and the red cells to 3,950,000. The urinary infection was treated with sulphamezathine and rapidly cleared.

When she had fully recovered from the crisis, on March 8, 1951, a blood count showed Hb. 67% (9.9 g. %),

packed cell volume 29% (69% of normal), mean corpuscular diameter 6.4 μ , mean corpuscular average thickness 3.1 μ . A blood film showed marked spherocytosis. Total white cells, 10,800. A blood fragility test showed haemolysis beginning at 0.72% saline and complete at 0.32% saline (control beginning at 0.65% saline and complete at 0.36% saline). The serum bilirubin level was 1.4 mg. per 100 ml.

On examination at this time the child was well, she had a very slight icteric tinge to the sclera, and the spleen was palpable two to three finger breadths below the costal margin.

Case B. Anthony A, aged 3 years, was admitted to the Children's Hospital, Leicester Royal Infirmary, on October 5, 1950. The history revealed that eight days previously, that is eight days after the onset of illness in Case A, he had developed a cold and become listless. He had gone off his food and was thought to be fretting for his sister (Case A). The symptoms increased in severity and he became very pale, had no strength to play, complained of headaches and tiredness.

On examination the positive findings were: temperature 99.6° F., pulse 120, respiration 20, sclera slightly icteric and mucous membranes pale. There was generalized shotty enlargement of the lymph nodes. The spleen was palpable three finger breadths below the costal margin, and the liver one finger breadth.

The blood picture on October 6 showed Hb. 26% (4.16 g. %), red cells 1,750,000, colour index 0.74, white cells 11,000.

A blood film showed marked microcytosis and spherocytosis and small numbers of nucleated red blood cells. His blood group was AII Rh negative, and a transfusion of 200 ml. of packed cells was given. Afterwards the Hb. was 80% (11.9 g. %), red cells 4,180,000, colour index 0.97.

A full blood count was carried out on March 8, 1951, and found to be Hb. 59% (8.9 g. %), packed cell volume 27% (59% of normal), mean corpuscular volume 101 μ , mean corpuscular diameter 6.5 μ , mean corpuscular average thickness 2.9 μ , white cells 3,900. Marked microcytosis and spherocytosis were seen in the blood film. The serum bilirubin level was 1 mg. per 100 ml. The urine showed no abnormality.

The blood fragility curve was typical of acholuric jaundice, haemolysis beginning at 0.88% saline and

complete at 0.28% saline (control 0.60% saline -0.32% saline).

On examination at this time the child's general condition was very good. The spleen was palpable two finger breadths below the costal margin.

As a result of a second case in the same family, the remainder of the family were sent for, and laboratory investigations gave the following results.

Family History

Case C. Martin A., aged 2 years, was not admitted to hospital, but about the time his sister and brother were admitted he was noticed to be pale and off colour. He was off his food and showed no interest in his toys. On examination he looked pale, but was well nourished. He seemed listless and tired. The only positive finding was that the tip of the spleen was palpable below the costal margin. A blood count on October 7 showed Hb. 40% (6.4 g. %), red cells 3,320,000, colour index 0.61, mean corpuscular diameter 6.43μ, white cells 6,600.

The blood fragility curve was typical of acholuric jaundice, haemolysis beginning at 0.88% saline and complete at 0.28% saline (control 0.60% saline -0.32% saline).

When he was seen on March 8, 1951, his general condition had much improved. He was lively and active and ate his meals well. On examination the mucous membranes were a very much better colour but the tip of the spleen was still palpable.

Case D. Mr. T. A. (father of Cases A, B, C and E) was a butcher. He gave a history of being subject to attacks of general malaise and had noticed that his eyes were frequently yellow-tinged. This had been recurring since he was a child, but the symptoms had never been severe enough to cause him to seek medical advice. At the time of the children's illness he noticed that the yellow tinge in his eyes had deepened. When seen on October 12, 1950, he was feeling quite well, but the sclera was markedly icteric. Apart from this nothing abnormal was found on examination, and the spleen was not palpable.

A blood count on October 7 showed Hb. 77% (12.32 g. %), red cells 4,450,000, colour index 0.88, packed cell volume 36%, mean corpuscular volume 81 cμ, mean corpuscular haemoglobin concentration 34%, mean corpuscular diameter 6.33μ, mean corpuscular average thickness 2.59μ.

The blood fragility curve showed haemolysis beginning at 0.84% saline and complete at 0.28% saline (control 0.60% saline -0.32% saline). The serum bilirubin level was 2.4 mg. per 100 ml.

Case E. Barry A., aged 7 years, was fit and well and did not complain of ill health during the time the other members of the family were ill. There was slight pallor of the mucous membranes, but no evidence of icterus and the spleen was not palpable.

A blood count on October 7, 1950, showed Hb. 62% (9.92 g. %), red cells 3,230,000, colour index 0.97, white cells 7,100. On March 8, 1951, Hb. 84% (12.4 g. %), packed cell volume 40% (95% of normal),

mean corpuscular diameter 6.5μ, white cells 7,300. The blood film, however, showed no spherocytosis. The blood fragility curve showed haemolysis beginning at 0.88% saline and complete at 0.28% saline (control 0.64% saline -0.32% saline). The serum bilirubin level was less than 1 mg. per 100 ml. In view of the fact that no spherocytes were present in the blood film, the child must be considered a doubtful case of acholuric jaundice, but the family history, a slight degree of anaemia at the time when other members of the family suffered a crisis, small mean corpuscular diameter and slight increased fragility suggested that he might be a mild case.

As shown in Fig. 1 no evidence of acholuric jaundice was found in the other members of the family, and at the time of the familial crisis all were fit and well.

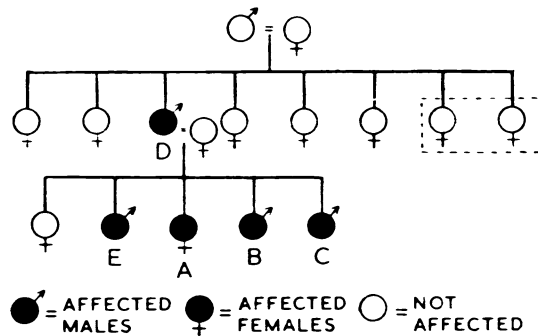


FIG. 1.—Pedigree of affected family. Siblings encircled in dotted lines had no symptoms. There are no records of them.

Discussion

Recently Marson *et al.* (1950) reviewed the literature and reported a family of seven in which four members underwent haemolytic crises within a short period. Two theories were put forward concerning the aetiology. The first was advocated by Owren (1948), who concluded that the crisis was due to a maturation arrest in the bone marrow causing aplasia, which, combined with the abnormal congenital condition of spherocytosis and thus a 14-day life span of the red cell (Dacie and Mollison 1943), caused the crisis. The second theory, that the crisis was due to the combination of a marked exaggeration of the usual haemolytic mechanism with arrested maturation of red cells in the bone marrow induced by a pathologically hyperactive spleen, was supported by Dameshek and Bloom (1948). Whichever aetiology is accepted some trigger mechanism is required to bring it into operation. In the case of familial crisis an infection would seem to be a possibility as it affects members living in close proximity and in the same environment. Dedichen (1937) has reported a series in

which a contagious respiratory infection was thought to be responsible. Horne *et al.* (1945) placed a ferret in the home in which a family crisis occurred and later the ferret died with symptoms of nasal catarrh and conjunctivitis. In the other cases reported infection was not a prominent feature, and emotion, as advocated by Piney (1931), appeared to have some association in three of the cases in Scott's (1935) series.

In this family no obvious infection was present. In Case A *Bact. coli* was present in the urine, but the child was afebrile and had no urinary symptoms. In Case B coryza was present at the onset, but the temperature was not raised above 99° F., and the degree of anaemia was thought sufficient to account for this. Indeed, in this case the mother felt the illness was due to the child fretting for his sister. The other members of the family had no obvious infection.

Recently Davidson, Duthie, Girdwood and Sinclair (1951) have shown that A.C.T.H. lowers the serum bilirubin level in congenital anaemia, and although clinical trials have not cured the condition, it is possible that the trigger mechanism may be associated with the reaction of the tissues to an antigen, and thus may be another disease associated in the stress syndrome.

Summary

A familial crisis affecting five members of a family with congenital acholuric jaundice is described. Consideration of this and other reported families does not support the view that infection is the trigger mechanism concerned.

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