

Haemoglobin M_{Iwate} in Cape Town

A Report of 2 Cases

P. B. HESSELING

SUMMARY

Two siblings had suffered from cyanosis since birth owing to the presence of Hb M_{Iwate}. The diagnosis was confirmed by electrophoresis, spectroscopy and peptide analysis. The benign nature of this unusual condition is stressed.

S. Afr. med. J., **56**, 1008 (1979).

Congenital cyanosis due to haemoglobin M is very uncommon in South Africa. In 1965 Swanepoel¹ reported Hb M_{Iwate} in an Indian boy from Durban. In 1967 Botha *et al.*² recorded 3 siblings with Hb M_{Saskatoon} in a Cape Coloured family. We now present 2 further cases of Hb M_{Iwate} in a Cape Coloured family.

CASE REPORTS

Case 1

The patient, now aged 2 years and 3 months, presented at our outpatient department with gastro-enteritis when he was 3 months old. Central cyanosis was noted, and according to the mother this had been present since birth. One older brother, of the same parents, was normal. The patient's weight, height and skull circumference were normal for age and no cardiac or respiratory abnormalities could be found on physical examination. Clubbing of the fingers was absent.

The haemoglobin value was 10,4 g/dl, the white cell count $10\,400 \times 10^9/l$ with a normal distribution, the platelet count $215\,000 \times 10^9/l$ and the reticulocyte count $400 \times 10^9/l$. A chest radiograph and the ECG were normal. The Po₂ with the patient breathing room air was 12 kPa. This increased to 34 kPa after inhalation of 100% oxygen. The blood had a very marked dark-brown colour. Intravenous administration of methylene blue did not correct the cyanosis. Spectroscopy of a blood haemolysate showed a spectrum similar to that of normal oxyhaemoglobin. A blood haemolysate treated with ferricyanide to oxidize all the haemoglobin to the ferric state had an absorption spectrum consistent with the diagnosis of Hb M.³ Haemoglobin electrophoresis on starch gel at pH 7,1 showed an abnormal fraction compatible with Hb M. Haemoglobin electrophoresis on cellulose acetate strips at pH 7,1 separated a fraction typical of

Hb M which constituted 26% of the total haemoglobin.

The abnormal haemoglobin was identified by peptide analysis and amino acid sequencing as Hb M_{Iwate} by Dr J. Clegg (Nuffield Department of Clinical Medicine, Radcliffe Infirmary, Oxford, UK).

Case 2

A male sibling with a birth weight of 2 910 g had been born 5 weeks previously, at 38 weeks' gestation. The Apgar rating was 8, 9 and 9 at 1 minute, 5 minutes and 10 minutes after birth respectively. Central cyanosis was present at birth.

The patient's Po₂ in room air was 8,8 kPa. At the age of 3 weeks the haemoglobin value was 17,5 g/dl, the white cell count $8\,600 \times 10^9/l$ with a normal distribution, and the reticulocyte count $88 \times 10^9/l$. The spectroscopic and electrophoretic findings were identical to those of the older sibling. The father, mother and other male sibling had normal results on spectroscopy and electrophoresis. No family history could be elicited and there was no consanguinity between the parents.

DISCUSSION

The existence of familial cyanosis with an autosomal dominant inheritance pattern has been recognized in Japan since 1800. This disorder, called 'kockikuru' (black mouth), was restricted to the prefecture of Iwate in Honshu.³ Various forms of Hb M may also arise as fresh mutations.⁴

Five different M haemoglobins with specific amino acid substitutions of the α or β chain have been reported.⁵ They are M_{Boston} (α_2^{58} His \rightarrow Tyr β_2), M_{Saskatoon} ($\alpha_2\beta_2^{63}$ His \rightarrow Tyr), M_{Milwaukee-1} ($\alpha_2\beta_2^{67}$ Val \rightarrow Glu), M_{Iwate} (α_2^{57} His \rightarrow Tyr β_2) and M_{Hyde Park} ($\alpha_2\beta_2^{32}$ His \rightarrow Tyr). The amino acid substitution causes structural and functional changes resulting in stabilization of the haem iron of the α or β chain in the ferric form; cyanosis results from the presence of methaemoglobin M. The low O₂ affinity of Hb M_{Iwate} at P₅₀ compensates functionally for the decreased Bohr effect and decreased haem-haem interaction, thus enabling the patient to lead a normal life. A patient with Hb M_{Iwate}, which is an α -chain variant, presents with cyanosis at birth, whereas patients with the β -chain variants present with cyanosis when the α chains of the Hb F are replaced by abnormal β chains after 3-4 months of age. Cyanosis may be easily missed in dark-skinned races.

The differential diagnosis rests between haemoglobin M and methaemoglobinaemia, which may be acquired through oxidant agents or may be congenital due to diaphorase I deficiency. Methaemoglobinaemia has a specific haemoglobin absorption spectrum and a normal

Department of Paediatrics, University of Stellenbosch and Tygerberg Hospital, Parowvallei, CP

P. B. HESSELING, M.MED. (PAED.)

Date received: 8 May 1979.

haemoglobin electrophoretic pattern, and improves clinically after the administration of methylene blue or ascorbic acid.

No treatment is indicated and the patient should be fully informed about the benign nature of the disorder. A Medic-Alert token may be useful to avoid unnecessary investigations and iatrogenic restrictions.

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The Action of Tetanus Toxin

A Case Report

D. T. FOURIE, B. GINSBERG

SUMMARY

A case of neonatal tetanus in an infant with myelomeningocele is described, and the possible action of tetanus toxin is discussed.

S. Afr. med. J., **56**, 1009 (1979).

Most of the research regarding the mode and site of action of tetanus toxin has been done on laboratory animals such as rats and cats. Infrequent reports on its action in human beings have been published.^{1,2} We have made observations which substantiate the results of the animal experiments.

CASE REPORT

A 10-day-old infant was brought to Ga-Rankuwa Hospital, Pretoria, with a 1-day history of convulsions. He had been born at home with the grandmother assisting. The umbilical cord had been cut with a non-sterilized pair of scissors, ligated with a piece of dress material, and covered with a layer of petroleum jelly. The birth weight had not been recorded. The mother noted a red swelling low down on the infant's back, and

since birth he had not been seen moving his lower limbs. He was breast-fed and sucked quite vigorously until the 9th day. When the convulsions started, he also started having difficulty sucking at the breast. The spasms involved his face and arms, but not his legs.

On examination he weighed 2.8 kg, his temperature was 35.9°C, the pulse rate was 180/min, and the respiratory rate was 36/min. The skull circumference was 37 cm (75th percentile). The trachea was central, but the entry of air was reduced in the right hemithorax, and no adventitious sounds could be heard. The umbilical stump appeared slightly septic. A type 1 myelomeningocele³ was present over the dorsum of the spine, with the upper border of the lesion at the level of L2. He had a total flaccid paralysis of both legs. There was one spontaneous spasm every 5 minutes, which was typical of tetanus with risus sardonicus, opisthotonus, and a rigid abdomen. Trismus and hypertonia were present between attacks. Spasms could also be started by stimulating the infant. Significantly, the upper limbs went into spasms, but not the lower limbs. Repeated tactile stimulation of the lower limbs did not result in spasms, but stimulation of the trunk and arms provoked it. The legs always remained flaccidly paralysed.

Although special investigations are not helpful in the diagnosis of tetanus, they do help to rule out other similar conditions. The results of investigations were as follows: the erythrocyte count was normal for age, and there was polymorphonuclear leucocytosis ($27.6 \times 10^9/l$). Blood chemical values were as follows: Na — 144 mmol/l, K — 4.6 mmol/l, Cl — 109 mmol/l, Mg — 0.83 mmol/l, and Ca — 2.32 mmol/l.

Department of Paediatrics, Medical University of Southern Africa and Ga-Rankuwa Hospital, Pretoria

D. T. FOURIE, M.B. CH.B., M.MED. (PAED.)
B. GINSBERG, M.B. B.CH.

Date received: 25 July 1979.