# An Unusual Case of Nutritional Megaloblastic Anaemia

BY

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Nutritional megaloblastic anaemia is a condition of moderate rarity in the African in the Wankie district of Southern Rhodesia. When it does occur it is usually found in pregnant women, although cases occur in adolescent males. The precise aetiology of the condition is not yet fully agreed owing to the multiplicity of possible causative factors in both Asiatics and Africans, amongst whom the disease is most commonly found. Yet there is general acceptance of the characteristic features of the disease and that a folic acid deficiency is one of the principal factors in its causation. Both blood and marrow studies show a picture almost identical with that of pernicious anaemia and the clinical symptoms of the two conditions, being those of any severe anaemia, bear a close resemblance. The two most striking differences are in the presence of free acid in the gastric juice and neurological manifestations.

In pernicious anaemia absolute achlorhydria is the rule, and the symptoms of a subacute-combined-degeneration of the cord are an inevitable concomitant sooner or later during the course of the untreated illness. In nutritional megaloblastic anaemia free HCL is present in the great majority of cases and, as far as the writer knows, neurological symptoms and signs have very rarely been described. The generally accepted therapeutic difference is the specific response of pernicious anaemia to vitamin $B_{12}$ or liver, and the specific response of nutritional megaloblastic anaemia to folic acid. Megaloblastic anaemias in both African and Asiatic have been described which have responded to vitamin $B_{12}$, marmite, high protein diet, penicillin and crude liver, and in many of these cases a dietetic cause has been postulated. However, there seems to be fairly general agreement that in the classical nutritional megaloblastic anaemia folic acid is usually specific.

The case to be described, a fifteen-year-old married African girl, showed some marked differences to the conventional pattern. Her anaemia presumably had its origin during pregnancy, but when seen some three months after the birth of the child her condition had obviously been deteriorating. She had a complete histamine fast achlorhydria which disappeared during the third week of treatment, and she exhibited neurological signs, notably loss of reflexes and vibration sense, which returned whilst under treatment.

## Case Report

*History.*—An African girl, the wife of a colliery company employee, was admitted to Wankie Hospital complaining of diarrhoea and vomiting of 17 days' duration. She was accompanied by her small healthy baby, who had been born some three months previously. She had no other symptoms, but on being carefully questioned, admitted to increasing tiredness, numbness and a feeling of cold in the feet and legs. She insisted that she had been taking a full diet with plenty of meat and vegetables. History-taking in the primitive African is a matter of difficulty, and the patient's statements on all matters except the presenting symptoms must be treated with reserve.

*Clinical Examination.*—The girl was undernourished, with paper-white mucous membranes. Tongue was clean, moist and normal in appearance. There was no abnormal pigmentation of the skin, no hyperkeratosis and no cheilosis. There was no conjunctival abnormality. Gums were healthy. Moderate oedema of the ankles was present. The lungs were clear. Temperature was 100° F. and there was a resting tachycardia of 130. The apex beat was diffuse. There was no clear evidence of cardiac enlargement and no bruits could be heard on auscultation. The abdomen was slightly distended and the liver enlarged some two fingers. The spleen was palpable, hard, and one finger enlarged.

Examination of the central nervous sytem in the African patient cannot be carried out with quite the same certainty as in the European, and interpretation of one's results has to be guarded. On examination of this patient there did not appear to be any sensory impairment, but although the majority of the spinal reflexes could be readily elicited, neither knee jerks nor abdominal reflexes could be demonstrated.

The plantar responses were absent, but these signs are normally difficult to elicit in the African owing to the thickness and insensitivity of the skin on the sole and edge of the foot. Vibration sense was absent. A histamine fast achlorhydria was present. Stool and urine examinations revealed no abnormality nor evidence of infestation.

*Haematological Findings.*—Haemoglobin 3 grammes; r.b.c. 820,000 per c.cm.; colour index 1.4; w.b.c. 1,200; p.c.v. 10; m.c.v. 122; m.c.h. 37; m.c.h.c. 30 per cent.; reticulocyte count 1.2 per cent.

*Blood Film.*—Fairly well marked anisocytosis, slight poikilocytosis, slight polychromasis. Macrocytes present. No nucleated red cells. Platelets abundant. No malaria parasites seen. Kahn test negative.

*Bone Marrow Film.*—Increased cellularity. Predominant cells; metamyelocytes and megaloblasts. Giant metamyelocytes present. Granulocytes of all types. Metamyelocytes increased. Normoblasts present. Mature lymphocytes and monocytes present. Increased plasma cells. Many mitotic cells present, mainly early or intermediate stage megaloblasts.

The marrow picture was that of a typical megaloblastic anaemia.

A provisional diagnosis of nutritional megaloblastic anaemia was made and the patient placed on 30 mg. folic acid daily. The reticulocyte response proved maximal.

| *Day of Treatment.* | *Reticulocyte Response.* |
|---|---|
| 1st day | 1.2% |
| 3rd day | 5.2% |
| 6th day | 37.4% |
| 8th day | 52.8% |
| 10th day | 54% |

On the tenth day of treatment the haemoglobin was 4.8 grammes and the red cell count 1,200,000. On clinical examination the striking finding was a return of the knee jerks, which were now very brisk. The abdominal reflexes could just be elicited, but were extremely sluggish. Vibration sense was still absent. Ankle oedema had disappeared and the resting pulse was 88. On the twentieth day of treatment the red cell count was 2,400,000, Hb 6.95 grammes and the reticulocyte count 20 per cent. Gastric analysis still revealed an absolute achlorhydria. She was now placed on a daily dose of 50 microgrammes of vitamin $B_{12}$. Two days later the reticulocyte count had fallen to 7 per cent. On clinical examination of the central nervous system the patient was able to detect vibration in both tibiae with the tuning fork test. She was questioned very closely as to whether she had not, in fact, felt a similar sensation in previous tests, but had failed to report it. She was quite emphatic that this was not so. On the twenty-fourth day of treatment gastric analysis revealed free hydrochloric acid in the fasting juice. On the twenty-eighth day of treatment the haemoglobin value was 7.75 grammes and the red cell count 3,140,000 per c.cm. The reticulocyte count had dropped to 3 per cent. Four days previous to this the dosage of vitamin $B_{12}$ had been raised to 100 microgrammes daily. Unfortunately the patient, who had been feeling increasingly restive at prolonged hospitalisation, discharged herself before treatment could be completed or a final investigation of the bone marrow made.

## DISCUSSION

It seems from the haematological and clinical findings, and the specific response to folic acid therapy, that this case can rightly be classified as a nutritional megaloblastic anaemia. It fits quite closely the pattern described by Wills and Mehta (1930). After the peak of the reticulocyte response had passed, vitamin $B_{12}$ was given to see if a double response could be elicited. As there was no trace of a second response even on a dosage of 100 microgrammes daily, the reversal of the achlorhydria and the reversal of the neurological signs to normal could not be attributed to the $B_{12}$. It is fully appreciated that it is a matter of great difficulty to be quite certain that a primitive African can understand what is meant by a sensory phenomenon such as vibration sense. The tests were, however, repeated several times at each examination, using first the fork at rest and then vibrating. Whereas at the first two examinations there was a blank denial of any change in feeling, at the third test there was an equally positive assurance that there was a difference, although she was unable to give a verbal description of the difference, but fluttered her hand in illustration.

The fact that both liver and spleen were enlarged may have some bearing on the aetiology. Enlargement of the liver is a common clinical finding in the Africans in the Wankie area and, in some, may quite possibly be nutritional in origin. Splenomegaly, in an area where malaria is endemic, is almost certainly caused by that disease. In this connection it is of interest to note the link between chronic malaria with splenomegaly and macrocytic anaemia of pregnancy described by Gavrilski and Tedzer.

It is possible to postulate in this case an absence of intrinsic factor pointing to the absolute achlorhydria as a sign of failure of gastric secretion. This in turn would lead to the development of an anaemia of the pernicious anaemia pattern. Even accepting this, it is difficult to explain the reversal of early neurological signs on therapy with folic acid and the failure to obtain any sign of a double reticulocyte response with vitamin $B_{12}$.

## SUMMARY

A case is described of nutritional megaloblastic anaemia in a young African mother, showing before treatment an absolute histamine fast achlorhydria and early neurological signs of the pattern found in pernicious anaemia. Both the achlorhydria and the neurological signs disappeared under treatment with folic acid and there was complete failure to elicit a double reticulocyte response with vitamin $B_{12}$.

## REFERENCES

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