Addisonian Pernicious Anaemia in a Juvenile Bantu* 

J. B. WITCOMBE,† M.B. B.S., D.C.H. UNIV. LOND., J. RODD, M.B. B.CH. UNIV. RAND, Baragwanath Hospital and Department of Medicine, University of Witwatersrand, AND R. GREEN, M.B. B.CH. UNIV. RAND, Department of Haematology, South African Institute for Medical Research, Johannesburg

SUMMARY

Pernicious anaemia is commonly a disease of late middle age and only 2.6% of 2,413 cases quoted by Chanarin occurred before the age of 30 years. Pernicious anaemia presenting in the first two decades of life is extremely uncommon, and in 1965 McIntyre and his colleagues stated that only 26 definitely proved cases had been reported in the medical literature. No proved cases have previously been reported in the Bantu.

It is the purpose of this report to document pernicious anaemia occurring in a 15-year-old Bantu girl.


CASE REPORT

An intelligent Bantu female of pure Sotho extraction presented at the age of 15 years with symptoms of anaemia. She had never been pregnant, her diet had always been good and her previous health had been excellent; in particular there was no history of any gastro-intestinal disorders or parasitic infections. Both parents of the patient and her only sister were perfectly fit. On examination, marked pallor was obvious and a pulse-rate of 128/minute, a soft systolic ejection murmur and retinal haemorrhages, were noted. There were no positive neurological findings and no other abnormal features were present.

Investigation of Anaemia

As shown in Table I, the haemoglobin was 5.1 g/100 ml. Red-cell count 1,160,000/mm³. Mean corpuscular volume 132 μm³. Mean corpuscular haemoglobin 42.5 pg. Mean corpuscular haemoglobin concentration 31.5%. Platelet count 59,000/mm³.

A blood smear showed a macrocytic anaemia, and a sternal marrow examination showed classic features of megaloblastic maturation, affecting both the myeloid and erythroid elements. The erythroid series showed maturation arrest with gross megaloblastic change, while the granulocytic series showed a pronounced right shift and the presence of giant myelocytes.

The serum iron level was 122 μg/100 ml and the unsaturated iron-binding capacity 171 μg/100 ml (Table II).

| TABLE I. LABORATORY INVESTIGATIONS: HAEMATOLOGICAL DATA ON ADMISSION |
|-------------------|-------------------|-------------------|
| Haemoglobin       | 5.1 g/100 ml      |
| Red cell count    | 1,16 million/mm³  |
| Reticulocytes     | 4%                |
| Haematocrit       | 31.5%             |
| Mean corpuscular volume | 132 μm³ |
| Mean corpuscular haemoglobin | 42.5 pg |
| Mean corpuscular haemoglobin concentration | 31.5% |
| White cell count  | 3,3 thousand/mm³  |
| Platelet count    | 59,000/mm³        |
| Morphology        | Macrocytes and hypersegmented neutrophils |

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†Present address: Department of Radiology, Radcliffe Infirmary, Oxford, England.**
The serum folate was estimated by the microbiological method using *Lactobacillus casei* and was 17.2 ng/ml (Normal 5 - 18 ng/ml).

Vitamin 

 deficiency was confirmed by giving intramuscular physiological doses of 1 μg of cyanocobalamin each day. There was a successive reticulocyte response from 3.5% on the first day of therapy, to 22.5% on the sixth day (Fig. 1).

![Fig. 1. Haemoglobin and reticulocyte response.](image)

Vitamin 

 absorption was measured by the urinary excretion test of Schilling' with the use of "cobalt-labelled 

 ("Co 

) supplied by Radiochemicals, Amersham. Only 0.5% of the oral dose was excreted in the urine in the 24 hours following administration of the "Co 

 (normal > 5%). However, when the test was repeated with the addition of intrinsic factor concentrate, 18.7% of the "Co 

 was excreted in the urine in the subsequent 24 hours.

The augmented histamine test meal was carried out according to Kay,' and no free acid was demonstrated, the pH of the gastric juices remaining at 7.5 throughout the test.

A chest X-ray and barium meal with follow-through showed no abnormalities.

Gastroscopy was performed, and under direct vision biopsies taken from the gastric fundus and antrum. There was a slight reduction of the gastric rugae macroscopically, and on microscopy, although the antral biopsy was normal, the biopsy specimen from the fundus showed atrophic gastric mucosa. Inflammatory cells were absent from the lamina propria (Fig. 2).

Using the method of Gottlieb et al.,6 blocking antibodies to intrinsic factor were demonstrated in the patient's serum in the concentration of 7.1 units/ml of serum. The Coombs consumption test for gastric parietal cell antibodies was negative.

![Fig. 2. Biopsy of gastric fundus showing atrophic mucosa.](image)

**Other investigations**

Blood urea was 34 mg/100 ml; potassium 3.9 mEq/L; sodium 139 mEq/L; carbon dioxide 16 mEq/L; chloride 106 mEq/L; calcium 5.3 mEq/L; phosphate 4.9 mEq/L; alkaline phosphatase 9 IU; serum glutamic oxalo-acetic transaminase 43 units, serum glutamic pyruvic transaminase 10 units; and lactic dehydrogenase > 2000 units. Direct Coombs test was negative; and protein-bound iodine was 7.4 mg/100 ml. The tanned red cell test for thyroid antibodies was negative. Plasma proteins were normal. The average faecal fat excretion was 2.2 g in 24 hours. Urinary protein excretion was 92 mg/24 hours. No parasites were observed in the stools.

Following cyanocobalamin treatment, the serum folate fell to 11.2 pg/ml, and the serum iron to 52 μg/100 ml.

**Family Studies**

Genetic marker studies on the patient's family failed to show any evidence of Caucasian admixture. The haemoglobin and serum 

 values of the patient's parents and only sister were within the normal range. No antibodies to parietal cell or intrinsic factor were demonstrated in any of the patient's family.

**DISCUSSION**

To entertain the diagnosis of Addisonian pernicious anaemia, a megaloblastic anaemia due to vitamin 

 deficiency has to occur, and failure to absorb oral vitamin 

 with absence of gastric intrinsic factor, has to be demonstrated. The impaired vitamin 

 absorption will be corrected by oral intrinsic factor administration. Other causes of vitamin 

 deficiency, such as dietary deficiency, small bowel anomalies, fish tapeworm infestations, general malabsorption syndromes and the congenital specific vitamin 

 malabsorption described by Imerslund and Gräsbeck et al.' have to be excluded. We believe these criteria have been fulfilled in the case described.
In the United States pernicious anaemia in adults occurs much less frequently in Negroes (26 cases per 100000 Negro hospital admissions) than in Caucasians (77.8 cases per 100000 White admissions). However, adult pernicious anaemia has been described in the South African Bantu several times. In the largest Bantu series, a tendency to affect a younger age-group was noted, for 2 of the 10 cases reported were aged 30 years. In 1961, Metz et al. reported pernicious anaemia in 3 Bantu females aged 23, 28 and 34, respectively. He commented on the importance in this age-group of distinguishing pernicious anaemia from folate deficiency associated with pregnancy. It may be inferred from this article that pernicious anaemia has a tendency to affect young females among the Bantu. The case reported here would support this suggestion.

'Juvenile' pernicious anaemia is a well-known but imprecise term, which usually refers to two broad groups of disorders characterized by the absence of gastric intrinsic factor and vitamin B12 deficiency anaemia, presenting in the first two decades of life. In addition, the term is occasionally applied to the condition of specific vitamin B12 malabsorption described by Imerslund and Grässbeck et al. where there is intestinal failure to take up the vitamin B12 from the vitamin B12 intrinsic factor complex. Gastric histology and gastric secretions are normal in this condition and there is almost invariably an associated proteinuria. The term 'juvenile' pernicious anaemia is probably best not applied to this syndrome and reserved for the two main disorders where intrinsic factor is absent from the gastric secretions.

The more common of the two main types of 'juvenile' pernicious anaemia is caused by congenital intrinsic factor deficiency. Although intrinsic factor is absent from the gastric secretions there is no gastric atrophy and the gastric juice contains normal amounts of hydrochloric acid and pepsin. Gastric antibodies are not present in the blood and there is no associated proteinuria.

The second group of 'juvenile' pernicious anaemia which includes the case reported here, is less common and almost invariably presents in the second decade of life. Clinical features closely resemble those of the adult form, and gastric atrophy with a histamine-fast achlorhydria is present. Antibodies to intrinsic factor, and less commonly, gastric parietal cells, are found in a high proportion of these cases.

It is clear that the patient reported here must belong to this rare second type of 'juvenile' pernicious anaemia, for gastric atrophy, a histamine-fast achlorhydria and intrinsic factor antibodies, were demonstrated.

Three cases of congenital intrinsic factor deficiency have been previously described in American Negroes and, and 2 possible cases of the 'adult-form' of 'juvenile' pernicious anaemia have been described in the Bantu. However, in one of these Bantu cases no serum vitamin B12 estimation, gastric biopsy or histamine test meal were done, and in the other, there was no gastric atrophy, and a dose of oral vitamin B12 without intrinsic factor, produced a reticulocyte response. We believe, therefore, that the case reported here is the first definitely proved case of the 'adult form' of 'juvenile' pernicious anaemia to be described in a Negro, and the first case of either type of 'juvenile' pernicious anaemia to be described in the Bantu.

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REFERENCES