the sugar, which was initially less than 5 mg./100 ml., rose to 72 mg./100 ml. Again no serious side-effects were noted.

In spite of the apparent good initial response to

Penbritin, the patient subsequently died. At autopsy he was found to have a pocket of pus in his posterior fossa from which the organism was isolated.

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PERNICIOUS ANAEMIA IN A YOUNG ADULT

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PERNICIOUS ANÆMIA is rare in young adults. Davis (1944) reviewed six large series of patients diagnosed as pernicious anæmia and, out of a total of 1,532, only four were below the age of 20 years; the inadequacy of data necessary for a diagnosis of Addisonian anæmia in most of the cases previously described in young patients was noted. Wilkinson (1949) found an incidence of 2.8% of patients less than 30 years of age among 1,600 when first diagnosed; only one patient was under 21 years, and 67% were over the age of 50 years. Davidson (1952) in his Edinburgh series of 135 patients (1944-48) recorded 42% between the ages of 60 and 80 years when diagnosed. He later (1957) gave an incidence of over 50% occurring over 60 years of age in 100 cases (1950-56). Lambert, Prankerd and Smellie (1961) reviewed earlier publications on pernicious anæmia in childhood. They considered malabsorption of importance in the differential diagnosis and observed that fat-balance tests had been carried out in very few cases; the demonstration of intrinsic-factor deficiency is essential for the true diagnosis of pernicious anæmia, and they noted that in previous reports this examination had very rarely been carried out; in only four cases amongst those previously recorded was there adequate evidence of absence of intrinsic factor together with a satisfactory response to anti-pernicious anæmia therapy. They reported three recent cases diagnosed by modern techniques using labelled vitamin B₁₂. The authors similarly investigated two further cases of juvenile pernicious anæmia in siblings, and referred to a further similar report on two siblings by Leikin (1960).

Recently, Metz, Randall and Kniep (1961) described three cases of pernicious anæmia in young Bantu females.

Owing to the rarity of this condition in the young and the importance of precise diagnosis it was considered worthwhile to record the following case; according to our records this is the first such case below the age of 25 years to be admitted to this hospital during the last 14 years.

Case Report

N.M., an unmarried Irish woman aged 24 years, was admitted to this hospital in December 1960 with weakness of the legs and difficulty in walking. She had been a barmaid until one year before; her alcoholic intake had been 'several shorts on two or three nights a week' and she usually smoked 20 to 30 cigarettes a day. Her father died at 42 years of age of diabetes mellitus and a paternal aunt also had diabetes mellitus. There was no family history of anæmia.

During the last year she had noticed shortness of breath on exertion with slight swelling of the ankles in the evenings; there was also a cough with a little yellow sputum. Her appetite was poor, there was no indigestion but she complained of increased thirst.

Three months before admission she saw her doctor with backache and painful frequent micturition; this was treated firstly with sulphonamides and finally responded fully to injections of streptomycin for 12 days.

One month before she had gone to bed with 'flu'; she had pyrexia, backache and aching all over. There was no further frequency of micturition but she thought her urine was cloudy and 'chocolate' coloured, and this appearance gradually cleared after about two weeks. One week after being in bed she stated that she suddenly became numb from the waist downwards and could not walk properly—she fell twice and felt as though

FIG. 1.—Gastric biopsy showing characteristic atrophy.

drunk. Both legs felt weak especially the left, her finger-tips felt numb and she found difficulty in holding objects.

During the last few months her weight had fallen by 15 lb. to 87 lb.

Examination revealed an ill, rather pale girl with dyed hair. The mucous membranes showed slight pallor and the tongue appeared normal.

She seemed mentally depressed but was co-operative. The cranial nerves were normal. The limbs were generally wasted and hypotonic; there was marked ataxia, especially in the legs. Power was reduced, especially in the legs, and there was left foot drop. The limb and abdominal reflexes were absent and the plantar responses were flexor. Her calves were tender on pressure; vibration sense was absent in the hands and below the knees; sensation to pin prick and cotton wool were diminished at the same sites. The Romberg test was positive. The cardiovascular, respiratory and alimentary systems were normal.

Investigations. Blood examination showed a slight macrocytic anaemia. Hb. 10.2 g./100 ml. (69%); r.b.c., 3,160,000/c.mm.; colour index, 1.0; average mean cell diameter (halömeter), 7.7 μ ; P.C.V., 33%; M.C.H.C., 31%; M.C.V., 97 c. μ ; the red cells showed marked anisocytosis, moderate polychromasia and slight poikilocytosis; occasional cells were macrocytic. W.b.c., 6,700/c.mm. (neutrophils 53%, eosinophils 2%, basophils 1%, monocytes 4%, lymphocytes 40%). Platelets, 267,000/c.mm.; reticulocytes 4%.

Sternal marrow aspiration showed a normal incidence of total nucleated cells; erythropoiesis was active and partially megaloblastic, haemoglobinization of the nucleated red cells was normal; granulopoiesis and platelet formation appeared normal. The serum vitamin B₁₂ level

was 24 μ g./ml. (*Lactobacillus leichmannii* method); this was abnormally low. The gastric juice showed no free acid by the standard histamine test meal and also by the augmented histamine test meal (0.04 mg. histamine/kg. with 100 mg. anthesin i.m. 40 minutes before). The Schilling test using ⁵⁸Co showed 1% excretion of the administered radioactive vitamin B₁₂, and this rose to 12% in a subsequent test repeated with 40 mg. intrinsic factor. Total faecal fat was 22% of the dry weight of the stools and 80% was split; a three-day collection of faeces contained 9 g. of fat; ¹³¹I labelled triolein uptake from the gut was normal as reflected by normal faecal activity and peak blood levels. A barium meal flowed normally through the small bowel, and there was no evidence of diverticula or flocculation of the barium. A jejunal biopsy was considered within normal limits.

Repeated tests showed no evidence of porphyrinuria; there was slight proteinuria with the presence of scanty red cells and a few pus cells; *B. coli* and *Strep. faecalis* were grown.

Normal results were obtained in the glucose tolerance and liver function tests, the blood and cerebrospinal fluid Wassermann reactions, and chemistry and cytology of the cerebrospinal fluid.

A chest radiograph appeared normal.

Course. There was an excellent clinical and haematological response to intramuscular vitamin B₁₂ therapy; reticulocytes reached 10% on the eighth day and by two months her haemoglobin level rose to 15.5 g./100 ml. (105%). With intensive physiotherapy walking rapidly improved, and four months after therapy commenced she could walk and dance in high-heeled shoes and the sensation had returned to her legs.

Discussion

The outstanding clinical feature on admission was that of a neurological disturbance, and the signs were predominantly those of a severe polyneuritis accompanied by evidence of posterior column involvement with no indication of affection of the lateral columns.

The initial history suggested the possibilities of porphyrinuria, diabetes mellitus or alcoholism, but subsequent detailed investigations showed her to have the characteristic features of Addisonian anaemia. The family history of diabetes mellitus is of interest since a close familial association has been recorded by Joslin, Root, White and Marble (1959), who noted that in 1,500 consecutive cases of diabetes, pernicious anaemia was present in a parent or sibling in 15 instances.

Of the few cases in childhood and young adults, in the past diagnosed as pernicious anaemia it is likely that most were true megaloblastic anaemias but few were true Addisonian anaemias.

In young patients with megaloblastic anaemia it is essential to rule out malabsorption as the cause. In a leading article (*Lancet*, 1961), it is stated that 'the commonest cause of megaloblastic anaemia in childhood is overt or latent steatorrhoea'. Fat absorption tests in our patient were normal and further confirmation was obtained by the ¹³¹I labelled triolein uptake. Barium meal follow-through and a jejunal biopsy were also normal.

The exact diagnosis is of considerable importance as such patients, in accordance with our existing knowledge, will need lifelong substitutional therapy.

Recent investigations have added to our means of establishing the true diagnosis of pernicious anæmia. Until recently the cardinal laboratory features in pernicious anæmia were the characteristic blood picture, megaloblastic marrow and histamine-fast achlorhydria.

The serum vitamin B₁₂ level in our patient was abnormally low; this estimation may bring to light examples of neurological disease due to vitamin B₁₂ deficiency: this is amplified by the clinical picture resembling that of the patients reported by Jewesbury (1954).

Absolute achlorhydria was confirmed by the augmented histamine test meal, and the most important feature, absence of intrinsic factor production, was confirmed by the Schilling test carried out before and after giving the patient intrinsic factor.

The patient responded fully to vitamin B₁₂ therapy.

Summary

Pernicious anæmia is recorded in a patient aged 24 years, presenting chiefly with neurological manifestations.

The rarity of this disease in young patients is pointed out and reference is made to the literature. The importance of precise diagnosis aided by newer techniques is stressed owing to the necessary life-long substitution therapy required.

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HYPERTROPHIC PULMONARY OSTEOARTHROPATHY ASSOCIATED WITH PULMONARY METASTASES REMOVED SURGICALLY

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CLUBBING of the fingers and toes of the most advanced type, associated with thickening of the bones of the carpus and tarsus, painful swollen joints, and with periosteal thickening of the long bones of the limbs, is a well-recognized complication of many chest diseases. This degree of clubbing or, as it is more usually called, hypertrophic pulmonary osteoarthropathy (H.P.O.A.), is found most commonly in cases of bronchial carcinoma,

where the incidence in a large series was up to 2% (Semple and McCluskie, 1955). H.P.O.A. has also been observed in association with pulmonary metastases of many kinds arising from primary neoplasms outside the chest. Metastases in the lungs arising from primary osteogenic sarcomata are more often accompanied by the development of H.P.O.A. than is spread from other non-pulmonary primaries (Mendlowitz, 1942; Gibbs, Schiller and Stovin, 1960).

The case to be described is that of a young girl

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