TABLE II.—*Urinary Excretion Test Following an Oral Dose of ^{60}Co Vitamin B₁₂ With Varying Amounts of Animal Intrinsic Factor and Human Gastric Juice*

	Percentage Oral Dose Excreted	
	0-24 Hours	0-48 Hours
Animal intrinsic factor:		
Nil	3	3
50 mg.	1	2
50 mg.	Nil	1
200 mg.	3	—
Human gastric juice:		
50 ml.	9	12
100 ml.	12	31

Discussion

The investigation of this patient confirms the observation of Schwartz *et al.* that the effectiveness of animal intrinsic factor may be reduced in pernicious anaemia patients who have been treated orally with preparations containing intrinsic factor and vitamin B₁₂. This phenomenon presents certain difficulties in the interpretation of vitamin B₁₂ absorption tests in the diagnosis of pernicious anaemia. If failure to absorb radioactive vitamin B₁₂ when given with animal intrinsic factor occurs in a patient previously treated orally, it would be advisable to repeat the test, using human gastric juice. It seems possible that other patients reported in the literature as having a selective malabsorption to the vitamin B₁₂-intrinsic factor complex may also be identified as having pernicious anaemia when reinvestigated using pooled human gastric juice.

It is not yet known how often or how rapidly this phenomenon occurs in such patients. Mollin and Ross (1954) noted in a pernicious anaemia patient on continuous oral therapy with bifacton tablets that the serum vitamin B₁₂ level fell after approximately six months. In a patient of Schwartz *et al.* the values for the haemoglobin and red-cell count, while never normal during the successful period of oral therapy, began to fall after about eight months. In our patient, bifacton tablets were taken for a period of eight weeks.

In the treatment of pernicious anaemia patients, whether in a state of relapse or remission, it appears that parenteral therapy with vitamin B₁₂ is undoubtedly the more certain method and is therefore to be preferred.

Summary

The results of radioactive vitamin B₁₂ absorption tests using hog stomach and pooled human gastric juice as sources of intrinsic factor are presented in a pernicious anaemia patient previously treated with bifacton tablets. It was shown that potent animal intrinsic factor did not increase vitamin B₁₂ absorption in this patient. However, normal absorption occurred when human gastric juice was used as the source of intrinsic factor.

The implication of this phenomenon in the future investigation and management of pernicious anaemia patients is discussed.

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Addendum

Dr. Ellenbogen supplied a more highly purified hog intrinsic factor preparation for trial on the patient. 5 mg. of this material is at least as potent as 50 mg. of Batch 186-1 in potentiating the absorption of radioactive vitamin B₁₂ in patients with pernicious anaemia. The urinary excretion test was repeated on the patient, using the purified intrinsic factor, and was still abnormal. After an oral dose of 0.6 $\mu\text{g.}$ of ^{60}Co vitamin B₁₂ and 5 mg. of the purified material, 6% of administered radioactivity appeared in the urine in 48 hours. Three patients with pernicious anaemia in relapse excreted between 23% and 30% of administered

radioactivity when tested with the same dose of purified intrinsic factor.

To investigate the possibility that the patient's gastric juice contained a substance inhibitory to hog intrinsic factor, 75 ml. of gastric juice was mixed with 5 mg. of purified intrinsic factor. This was administered to a patient with known pernicious anaemia in remission, together with 0.6 $\mu\text{g.}$ ^{60}Co vitamin B₁₂. The pernicious anaemia patient excreted 15% of the radioactivity in the urinary excretion test. When the radioactive vitamin B₁₂ was given without intrinsic factor the urinary radioactivity in this patient was 2%.

Immunological studies using the patient's serum and hog intrinsic factor have not demonstrated the presence of circulating antibody.

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Medical Memoranda

Infected Facial "Cysts" and Sinuses of Dental Origin

An acute pulp infection of a tooth or root fragment is usually a painful event that demands urgent relief. Occasionally, however, the pulp undergoes a slow and silent degeneration without symptoms and without producing any visible change in the mouth. There is only an apparently sound and filled tooth, or a gap where a tooth was extracted months or even years ago, and a forgotten root fragment has become infected. In either case it would pass unnoticed at a routine dental examination unless a dental x-ray film was taken, where it would be clearly revealed.

After a variable period of chronic infection pus discharges through the thin outer alveolar plate into the mouth, or through into the soft tissues of the cheek. There is then left an established sinus from the infected tooth or retained root, either into the mouth or into the soft tissues. In the latter case a cystic swelling appears in the cheek, which can persist for weeks or months and is similar in appearance to a low-grade infection in a sebaceous cyst. Often it is treated as a simple cyst, by excision, and is followed by a chronic discharging sinus. The communicating track between the cystic swelling and the primary focus of infection is not necessarily the shortest distance between the two, and an oblique or variable course of the communicating track can be a misleading feature.

These cases generally come to us because we are expected to deal with the presenting facial lesion with the minimum of scarring, not because of the dental condition, as this has been overlooked. Obviously, any attempt to treat the facial lesion without first removing the dental focus is a waste of time. Sometimes we are able to deal with both the dental and the facial conditions simultaneously, although occasionally it is advisable to clear the dental focus before tidying the face.

FIG. 1.—Chronic infected facial cyst.

A TYPICAL CASE HISTORY

A perfectly fit schoolgirl aged 14 developed a small cystic swelling on the outside of her right cheek six months previously (Fig. 1). It had been painless throughout, and after its initial appearance had remained fairly constant in size. She was seen by a consultant, who considered it to be a sebaceous cyst and treated it with carbon dioxide

FIG. 2.—X-ray appearance of root infection.

snow. She was referred for plastic-surgical opinion. Examination within the mouth revealed a communicating track between the cyst and the alveolus of the upper six tooth. The teeth themselves appeared healthy, and the upper six had a filling which had been put in a year previously. There was no history of toothache. X-ray examination showed a quite definite root infection (Fig. 2).

Treatment.—Under general anaesthesia the upper six tooth was extracted; the photograph shows the chronic pulp infection with a large granuloma on the palatal root (Fig. 3). The cyst was incised and found to contain necrotic granulation tissue. Between the cyst and the alveolus was a well-defined track, and a probe inserted through the cheek presented in the base of the tooth socket. Culture of the cyst content was sterile. The facial wound healed in three days.

FIG. 3.—Showing chronic pulp infection.

Comment.—Although this condition is commonplace in plastic surgery units, experience of our own cases has shown that many doctors are unaware that a silent dental infection can produce this type of lesion; hence many unsuccessful operations, aimed

only at the external end of the trouble, are carried out. A dental opinion and x-ray examination should be a routine in all doubtful cases.

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Agranulocytosis following Dapsone Therapy

Dapsone (diaminodiphenyl-sulphone, D.A.D.P.S.) has been extensively used in the treatment of leprosy, and to-day it is considered to be the drug of choice for this disease. It was not until as recently as 1950 that Esteves and Brandão drew attention to the beneficial effects of dapsone in the treatment of dermatitis herpetiformis. Since their original publication many observers, including Cornbleet (1951), Kruizinga and

Hamminga (1953), Calnan (1954), Anning (1954), Vickers (1954), and Alexander (1955), have confirmed their findings, and dapsone is now recognized as a most valuable agent in the treatment of dermatitis herpetiformis.

The dosage of dapsone recommended has been variable, ranging from 50 mg. daily to 200 mg. daily. However, all are agreed that the dosage should be related to the clinical response, and when this has been achieved it should be replaced by a maintenance dose sufficient to suppress the clinical manifestations of the dermatosis.

The side-effects have been collected and are recorded in Table I.

Detailed investigations of the white-cell series in relation to the use of dapsone are few, and this has been confirmed by a personal communication with the manufacturers. It seems surprising that such an investigation has not appeared as a step in the preliminary therapeutic trials of this drug, which is closely related chemically to the sulphonamides. Calnan (1954) mentions agranulocytosis as a definite indication for cessation of therapy, but does not elaborate by a case history report. Fernandez *et al.* (1948) studied the effect on the cells of the white-cell series when dapsone was used in the treatment of leprosy, and found that the leucocyte count was either normal or indicated an increased granulopoiesis in the bone marrow. Lowe and Davey (1951) in a four-year therapeutic trial of the sulphone drugs, also in the treatment of leprosy, noted as the only white-cell abnormality an initial polymorphonucleosis, latterly mononucleosis, and other features suggestive of a sulphone-induced glandular fever.

Since no previous instance of agranulocytosis has been reported, we put the following case on record.

CASE REPORT

A single woman of 62 was referred to the Department of Dermatology, Western Infirmary, Glasgow, on March 19, 1956, suffering from dermatitis herpetiformis of three years' duration involving the arms, legs, back, and shoulders.

Treatment with dapsone, 50 mg. daily, was prescribed, and the patient was instructed to increase the dosage to 100 mg. in a week's time. She was seen again on April 4, and, although there was a definite clinical response, the condition was not yet under control, and the dosage was increased to 125 mg. daily.

On or about April 16, whilst on holiday, the patient developed an "influenza-like illness," and from that date until her admission to hospital two weeks later she was subject to listlessness, anorexia, periodic vomiting, sore throat, and night-sweating. A blood examination on April 16 (Royal Alexandra Infirmary, Paisley) revealed Hb. 12.2 g. per 100 ml. (84%); P.C.V., 36%; M.C.H.C., 33%; and the peripheral blood film showed no abnormality. On returning home her family doctor stopped dapsone therapy (total dosage, 4.2 g.) because of her general condition and also because a blood count carried out by him revealed a picture suggestive of agranulocytosis. She was admitted to Professor Wayne's wards, Western Infirmary, Glasgow, on April 30, where the diagnosis was confirmed.

On admission she was a rather drowsy woman showing the clinical features of dermatitis herpetiformis, and her temperature was 103° F. (39.4° C.) and B.P. 120/45. Purpuric lesions were present over the shoulders and arms, and the mucosae were uniformly pale. Bilateral ankle oedema and exertional dyspnoea were the only other features noted on examination of the cardiovascular and respiratory systems. The liver, spleen, and lymph nodes were not demonstrably enlarged.

Investigations.—The blood findings are recorded in Table II. The peripheral blood films showed severe leucopenia with the neutrophils virtually absent. The red cells were of normal size and well stained, while the platelets were not obviously deficient in numbers and no primitive cells of either the white or red cell series were present. The direct Coombs test was negative; blood cultures were negative; the augmented histamine test meal showed free acid to be