admitted more than eight weeks after injury and the danger period was considered to be passed; one suffered multiple trauma (head injury plus compound fractures of three limbs); one had such a transient and subjective neurological disturbance that it was thought that the dangers of therapy outweighed the advantages; and one who had a severe head injury with a pulsating exophthalmos together with a C3 fracture and amputation of one limb died after a week before therapy could be instituted. We used phenindione as we had most experience with this drug and did not think it necessary to begin anticoagulants rapidly by using heparin.

Owing to the fact that all patients with spinal injuries are admitted to another hospital after injury, there is an unavoidable delay in starting therapy, in contradistinction to Sevitt and Gallagher (1959), who worked in a receiving hospital; they showed that up to 50% of these patients developed deep venous thrombosis within a week of injury, and we realize that we may have been instituting therapy at a later stage than was ideal.

We controlled the therapy by the thrombotest reagent, as this was in use in the laboratory. We kept the level between 7 and 40%. We realize that the upper limit is slightly higher than recommended. If the level fell below 10% we had frequent bleeds, particularly from the bladder; however, it did not interfere with treatment in any way. Fifteen patients were in fact circumcized while under treatment (normal practice to reduce urinary infection and to facilitate the wearing of a urinal), nor did we find any ascent of the spinal lesion due to bleeding into or around the cord. One patient (an asthmatic) was sensitive to both phenindione and warfarin and developed bleeding from the bladder and mouth, so the treatment was discontinued. Of greater theoretical interest is the observation that there appears to be a greater incidence of ectopic ossification around the hips in patients on treatment (Silver, 1969), possibly owing to bleeding into the adductor muscles.

The regimen of general management has not substantially changed over the past four years, and, while we realize the pitfalls of retrospective comparisons, the fact that no patient has had pulmonary embolus since the institution of this prophylactic regimen in contrast to the previous period quoted, would indicate that this treatment is effective. The observation that four of the six patients who developed pulmonary emboli had thoracic lesions is of great interest since Walsh and Tribe (1965) and Watson (1968) observed the highest incidence in this group of patients (17·1% and 7% respectively).

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# *Medical Memoranda*

## Acute Sprue in Britain

*British Medical Journal*, 1970, **2**, 340–341

"Sprue" normally describes a classical clinical picture occurring within certain defined geographical regions. The following case is reported because we believe that sprue may occur in Britain and go unreported because of the difficulty of offering a satisfactory diagnosis.

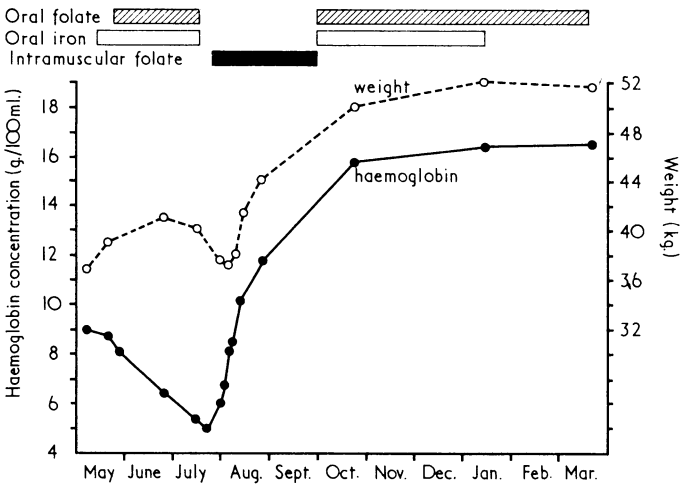
### CASE REPORT

A woman aged 34 developed diarrhoea, anorexia, and vomiting in April 1968. She had no history of any previous gastrointestinal disorder, and no one else in the family was affected. She lived in poor circumstances in central Birmingham and had never been abroad. She used lard for cooking, and there had been no recent change in her eating habits. Vomiting stopped after a week, but she remained weak and profoundly anorexic and diarrhoea persisted, accompanied by flatulence, distension, and central abdominal pain. After three weeks she developed a sore tongue, ulcers on the lips, and crusting of the eyelids, and had lost about 6 kg. in weight. She was treated by her family doctor with a kaolin mixture and topical gentian violet, but no antibiotics.

Examination showed a thin, depressed, apathetic woman of small stature (which was familial). There was a low-grade pyrexia. The tongue was bright red and atrophic, and ulceration of the lips, angular stomatitis, blepharitis, and pyoderma of several fingers were also present. The appearance of the mouth suggested candida infection, but this could not be confirmed. Abdominal examination was negative. The stools were profuse, pale, and unformed, and the fat content on a poor dietary intake averaged 10 g./day. Sigmoidoscopy showed a reddened mucosa with a few white granules suggestive of candidiasis, but no other abnormality. Rectal biopsy showed nothing abnormal. Eye swabs grew *Staphylococcus aureus*, but repeated stool examinations showed no staphylococci, fungi, giardia, or other pathogens.

*Investigations.*—Haemoglobin 9·0 g./100 ml.; M.C.H.C. 32%; W.B.C. 6,500, normal differential; normochromic blood film with anisocytosis, macrocytosis, and nuclear hypersegmentation of polymorphs. E.S.R. 57 mm. in one hour (Westergren); serum folate 0·3 ng./ml.; vitamin $B_{12}$ 170 pg./ml. Blood urea, liver function tests, and electrolytes normal. Serum albumin 4·0 g. and globulin 2·1 g./100 ml., with a normal electrophoretic pattern. Urine analysis and chest *x*-ray picture normal. Xylose absorption test showed 8·5% excretion of a 5-g. dose in five hours. Resting gastric juice *p*H 6·4. Jejunal biopsy specimen showed finger-like and leaf-like villi in about equal proportions, many of the leaves being broad. Microscopy showed mild villous atrophy with irregular shortened villi, pronounced shedding of the surface epithelium, and a moderate pleomorphic infiltrate in the lamina propria.

Initial treatment consisted of bed rest, normal diet, folic acid 5 mg. by mouth three times a day, and topical neomycin to skin and eyelids. The stools became semi-formed, but were still pale, and the skin sepsis cleared. The patient felt better and slowly gained 3 kg. in weight, but her mouth and tongue were still sore. By 28 May the haemoglobin had fallen to 8·1 g./100 ml. Oral ferrous fumarate was added to the folic acid and she was allowed home. A barium series in June showed normal transit time in the small intestine and no local intestinal lesion, but there was slight coarsening of the folds and widening of the lumen of the lower jejunum (33 mm. diameter). A barium enema was negative. The patient lost weight again and anaemia increased (see Chart).




Changes in body weight and haemoglobin concentration, showing specific response to parenteral folate.

She was readmitted on 17 July with severe anaemia, weakness, and pyrexia. The mouth and tongue had numerous aphthous ulcers, the tongue being red and atrophic, and there was a small boil on the face. The motions were bulky and semiformed, two or three times daily, and contained 9 g. of fat a day. The xylose absorption test was again abnormal (five-hour excretion 19%). Oral folic acid and iron were continued under supervision in hospital, in spite of which the haemoglobin fell from 5·1 to 4·8 g., with an M.C.H.C. of 33%, reticulocytes 1%, W.B.C. 3,500, and a partly macrocytic film as before. Bone marrow aspiration on 23 July showed frank megaloblastosis. Serum vitamin $B_{12}$ was 150 pg./ml., folic acid 0·8 ng./ml., and iron 188 µg./100 ml. (40% saturation).

On 19 July she was given a single intravenous infusion of 35 ml. of chelated iron (Imferon). There was no reticulocyte response and no rise in haemoglobin. On 24 July the daily intramuscular injection of 15 mg. of folic acid was started. There was a maximal reticulocyte response of 36% and the haemoglobin rose rapidly (see Chart). A dramatic immediate improvement in her well-being occurred, her appetite improved, and a week after starting the injections she began to gain weight. At the same time the continuous mild pyrexia settled to normal, abdominal discomfort disappeared, and the bowels became regular.

Further recovery was uninterrupted. The patient was discharged in mid-August, twice-weekly injections of folic acid being continued for a month. She was then given a course of oral ferrous sulphate for a month and oral folic acid for six months. All therapy was dicontinued in March 1969, when her haemoglobin was 16·4 g./100 ml. and her weight had risen by 16 kg. In May 1969 the faecal fat averaged 2·2 g./day and the five-hour excretion of xylose was 33·5%. In July 1969 her weight and haemoglobin remained steady and she said "it was lovely to feel so well."

### Comment

The traditional diagnostic features of tropical sprue include glossitis and stomatitis, diarrhoea and steatorrhoea, abdominal discomfort, anorexia, wasting, and anaemia. To these in the light of modern investigations may be added folic acid deficiency and a variable degree of jejunal mucosal abnormality which falls short of total atrophy. Unexplained pyrexia is not uncommon. There is a dramatic amelioration of symptoms and of anaemia by parenteral folic acid therapy, with a more gradual and variable improvement in malabsorption, though this also may resolve promptly in the acute case.

On all these counts the above case is a classical one of acute tropical sprue. In view of the fact that the patient had lived all her life in Britain an alternative diagnosis was sought, but the evidence was against gluten-induced enteropathy, abdominal reticulosis, or acute infective enteritis. Further, the patient had no iron deficiency or hypoalbuminaemia to suggest long-standing malnutrition. The complete lack of response to oral folic acid in this case is remarkable, and might be due to biological interference by abnormal flora in the small bowel.

In this general hospital, which includes a regional communicable diseases unit, we have investigated numerous cases of malabsorption following diarrhoea of acute onset that resembled infective enteritis. Most of these cases proved to be either Crohn's disease or gluten-induced enteropathy, but in a few instances no underlying lesion was found, and both the symptoms and the malabsorption resolved spontaneously after several months. Until the aetiology of acute sprue is clarified it is perhaps unjustifiable to claim that sojourn in a known endemic area is a prerequisite for the diagnosis.

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# Fulminating Hyperpyrexia during Anaesthesia in a Member of a Myopathic Family

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Rapidly rising body temperature resistant to treatment and usually ending fatally has been described on several occasions during the course of surgical anaesthesia (Saidman *et al.*, 1964; Thut and Davenport, 1966; Stephen, 1967; Wilson *et al.*, 1967; *British Medical Journal*, 1968; Hawthorne *et al.*, 1968). It has been called fulminating hyperpyrexia. The cause of the condition is not known, nor has it yet been possible to forecast its development in patients who have been affected. A sensitivity to succinylcholine has been postulated, and myopathy, infection, and enzymatic aberrations have all been suggested as aetiological factors. A further case is reported here with a possible myopathic association.

### Case Report

A youth of 16 was admitted to hospital on 10 July 1968 at 2.30 p.m. with a history and signs suggestive of acute appendicitis. On examination he was of full adult stature and strikingly muscular build. His temperature was 100·2°F. (37·9°C.), pulse regular at 84/minute, and blood pressure 130/90. The heart and lungs were clinically normal.

After premedication with atropine 0·6 mg. and pethidine 100 mg. anaesthesia was induced at 10.15 p.m. with thiopentone 400 mg. followed by suxamethonium 50 mg. An unusually pronounced muscular twitching for about 10 seconds occurred after the suxamethonium. It was noted that his mouth did not open easily, though intubation was not difficult. He was ventilated with oxygen and nitrous oxide, and spontaneous respiration returned. Tubocurarine 30 mg. was then given, but relaxation was poor, though no abnormal resistance to intermittent positive-pressure ventilation was noticed. He became cyanosed within 30 seconds of being disconnected from the anaesthetic machine for transfer to the adjacent theatre. After this a high oxygen percentage was needed to