FIG. 2. Follow up X-ray showing pneumopericardium and a cavity in right lung adherent to pericardium.

He was then given emetine by injection, with chloroquin and di-iodohydroxy quinoline. His condition improved, but he developed cardiac tamponade again intermittently, and had to be subjected to paracentesis on three more occasions. Further X-rays showed a very large quantity of air

in the pericardium, which could not have been accidentally introduced during tapping. In one, a very interesting feature was noted. There was a cavity with fluid level in lower segment of right lung, filling the right cardiophrenic angle (Fig. 2). This explained the air in the pericardium. The recurring cardiac tamponade was in part due to this excessive air under pressure, having entered the pericardium from the involved lung segment.

The patient made an uneventful recovery and was followed for a period of 16 months, when a chest X-ray revealed normal cardiac silhouette. There was no clinical, radiological or ECG evidence of constrictive pericarditis.

Acknowledgment

We wish to thank the Director General of the Armed Forces Medical Services, India, for permission to publish this case since it was treated by the authors while in the Army Medical Corps.

References

- GERMILLON, W. (1899) These, Paris. Quoted by Fiegel (1959).
- LAMONT, N.M.E. & POOLER, N.R. (1958) Hepatic amoebiasis—a study of 250 cases. *Quarterly Journal of Medicine*, **27**, 389.
- MACLEOD, I.N., WILMOT, A.J. & POWELL, S.J. (1960) Amoebic pericarditis. *Quarterly Journal of Medicine*, **33**, 293.
- NORRIS, D.L. & BEEMER, A.M. (1956) Amoebic pericarditis: report of a case with brief review of literature. *Journal of Tropical Medicine and Hygiene*, **59**, 188.
- PAULLEY, J.W. (1961) Amoebic liver abscess in Great Britain. *British Medical Journal*, **1**, 462.
- ROUS (1860) Mentioned by Vergoz and Hermenjat Gerin (1932).
- TAKARA, T. & BOND, W.M. (1958) Pleuropulmonary, pericardial and cerebral complication of amoebiasis. *Surgery, Gynecology and Obstetrics*, **107**, 209.

Temperate sprue

M. J. KENDALL

T. J. BAYLEY

Queen Elizabeth Hospital, Birmingham B15 2TH

FOLIC acid deficiency and megaloblastic anaemia may occur in malabsorptive states. Some patients with tropical sprue respond to folic acid therapy even in small doses (O'Brien & England, 1964), and although not yet adequately explained the anaemia, malabsorption and abnormal jejunal mucosa may all return to normal in some cases treated in this way. Thus, it seems that folic acid deficiency may result from, or may play some part in, causing malabsorption. Tropical sprue has a striking geographical and local distribution, occurring all over the Far East but not in Africa, in some Caribbean islands

but not in Jamaica, and it may occur in particular areas of a country and in epidemic form (Stefanini, 1948; Baker, Mathan & Joseph, 1962). Cooke and his colleagues (1963) have described a syndrome called 'temperate sprue', two of their patients having steatorrhoea which improved with folic acid therapy. A further patient with malabsorption which responded to parenteral folic acid has recently been described (Drummond & Montgomery, 1970) in whom steatorrhoea disappeared rapidly with treatment. The patient reported here shared many of the features seen in tropical sprue, particularly as seen

in those living temporarily in the tropics, namely weight loss, glossitis, stomatitis, anaemia and steatorrhoea, which responded to folic acid therapy, but he has always lived in England.

Case report

A 56-year-old man, a bakelite worker, who has lived all his life in Birmingham, was admitted to hospital for investigation of anaemia. He had consulted his family doctor on account of symptoms of urinary frequency and dysuria. He was thought to have a urinary infection and treated with ampicillin for 4 days. The doctor thought he was pale and a blood count revealed a macrocytic anaemia.

He admitted that he had been unwell for 6 months with anorexia, especially for fish and meat, and epigastric discomfort related to meals. His dietary intake had been adequate and he had lost only a little weight. He said that his tongue had been sore for 2 months and that during this time there had been cracking of the skin at the corners of his mouth. His bowels were open twice daily, and although the stools were occasionally loose, their colour had not changed nor were they particularly offensive. He had also noted a reversal of the normal diurnal variation in urine volume. His wife said that there had been some mental changes during this illness and that whereas he was normally a quiet, rather withdrawn man, he had become more outspoken, frankly aggressive and forgetful.

On examination he was clinically anaemic and had stomatitis and cheilosis. He was, however, well nourished and had a healthy appearance due to pigmentation of the face and all exposed areas. There were plaques of heavy pigmentation in the buccal mucosa but the skin pigmentation was not pronounced in the flexural areas. The BP 120/80 mmHg and there was no postural hypotension. The spleen was easily palpable as was the liver which was firm and smooth. No other abnormalities were found on physical examination.

Investigations: Hb 7.1 g/100 ml, MCV 96 μ , WCC 5000/mm³ (normal distribution), platelets 65,000/mm³, ESR 43 mm in 1 hr (Wintrobe). The bone marrow was frankly megaloblastic. Serum folate was low, 1.1 ng/ml, vitamin B₁₂ was in the normal range, 180 pg/ml. Urinary folic acid excretion after oral and parenteral administration was similar, the ratio of excretion after oral dosage/parenteral dosage was normal, 0.93 (Girdwood, 1953). Absorption of vitamin B₁₂ with and without intrinsic factor was normal.

Faecal fat excretion was 9.9 g/day. The GTT showed a slow rise (Fig 1), and jejunal function as judged by xylose absorption was abnormal, only 1.04 g being excreted in the urine within 5 hr of an oral dose of 5 g (20.8%). The small bowel appeared

FIG. 1. Glucose tolerance before (—) and after (---) folic acid therapy.

normal on barium follow-through examination. Peroral jejunal biopsy was normal both under the dissecting microscope and histologically. Liver biopsy was histologically normal.

He was initially treated with cyanocobalamin 1000 μ g daily, but there was no reticulocyte response to this therapy. Treatment with folic acid, 15 mg/day by mouth, caused a reticulocytosis to a peak of 10% and a rise in haemoglobin. On the fourth day of folic acid therapy there was marked weight gain and dependent oedema, which had disappeared spontaneously by the tenth day of treatment. By the time of discharge the haemoglobin had risen to

FIG. 2. Changes in faecal fat, xylose absorption, and haemoglobin during the period of study.

11.4 g/100 ml, daily faecal fat excretion had fallen to 5.7 g and he was feeling well. The tongue was no longer sore, though cheilosis and skin pigmentation were unchanged.

He was re-admitted for assessment 2 months later. During this time he had felt well and continued to take folic acid 15 mg/day. His wife also reported that his mental changes had disappeared. There were no changes on physical examination, pigmentation persisted and splenomegaly was again noted. Haemoglobin had now risen to 16.9 g/100 ml. Faecal fat excretion was 3.9 g/day and xylose excretion had increased though it was still below the normal range (Fig. 2). Jejunal biopsy was repeated and again found to be histologically normal. The GTT was now normal (Fig. 1). Folic acid therapy was stopped and the patient has remained well since.

Discussion

Although folic acid deficiency is not a recognized cause of malabsorption in temperate countries, folate is essential for normal cellular metabolism and its deficiency might be expected to influence the function of the small bowel, where cell turnover is rapid (Lablond & Meisser, 1958; Creamer, Shorter & Bamforth, 1961), as it affects the erythroblast. Histological abnormalities of the jejunum in the form of partial villous atrophy (Forshaw, 1968) and megaloblastic changes (Bianchi *et al.*, 1970) have been noted in patients with folate deficiency. 'Anti-folic' drugs, such as methotrexate, lessen or abolish mitotic activity of intestinal cells and may cause marked alteration in the mucosa (Philips & Thiersch, 1949; Trier, 1962).

The similarities of the reported case to tropical sprue are several. The early stage of tropical sprue is manifested by asthenia, fatigue and variable diarrhoea. Malabsorption is usually present and though nutritional deficiency may appear slight, there is invariably evidence of folic acid deficiency at this stage (O'Brien & England, 1964). At the onset of the disease jejunal biopsies may show remarkably little change (Shechy, Cohen & Brodsky, 1963). There is usually defective proximal bowel function with failure of absorption of glucose, xylose and folic acid. Fat absorption is variable and steatorrhoea is often mild. In all these respects our patient presents similar clinical, pathological and functional features with the exception of defective folic acid absorption. The folic acid absorption test was, however, performed after folic acid therapy had been instituted and may possibly have been abnormal if performed earlier.

The dietetic requirements for folic acid have been variously estimated but seem to be of the order of 50–150 µg/day. The dietary history of our patient did not suggest that his folate intake was low. Folic acid

deficiency with impaired xylose absorption but without steatorrhoea or other evidence of proximal small bowel dysfunction has been described in an alcoholic female (Forshaw, 1969) and in two patients with malabsorption associated with anticonvulsant therapy (Reynolds *et al.*, 1965). Our patient seems to have been abstemious and there was no history of drug therapy of any kind immediately preceding or during his illness.

Defective proximal small bowel function with malabsorption of xylose is seen in true pernicious (Addison-Biermer) anaemia, and absorption of vitamin B₁₂ may also be impaired (Carmel & Herbert, 1967; Forshaw, 1969). Minor histological changes in the jejunum have been reported (Foroozan & Trier, 1967). By analogy with the blood it might be expected that deficiency of essential factors for cell multiplication, such as vitamin B₁₂ and folic acid, would slow down the rate of division of 'regeneration zones' in the crypts of Lieberkühn from which the epithelium of the villi is replaced every 2 days. Although the intestinal mucosa would seem to be more resistant to lack of these essential factors, no detailed studies of the mucosa in deficiency states have been made and in particular cell-turnover rates have not been estimated. Mucosal changes elsewhere are more obvious, particularly in the tongue, as glossitis, a common and diagnostic feature in such deficiencies. The tongue epithelium also has a rapid cell-turnover rate, but is slow by comparison with that of the small bowel. It may be that the mucosal changes are analogous to the changes in the red cell population where anaemia can be brought about by marrow failure, a maturation arrest in the marrow, or increased destruction. Thus a defective mucosa could result from failure of cell-production from the crypts with a reduction of mitotic rate as seen in patients with chronic or malignant diseases (Creamer, 1964) or maturation arrest. Alternatively there may be increased cell desquamation which occurs when the contents of the bowel lumen are altered chemically or bacteriologically. A combination of all three could explain the mucosal and functional changes in the alimentary tract in vitamin B₁₂ and folate deficiency.

Acknowledgment

We would like to thank Dr A. Brian Taylor for permission to report this case.

References

- BAKER, S.J., MATHAN, V.I. & JOSEPH, I. (1962) Epidemic tropical sprue. *American Journal of Digestive Diseases*, **7**, 959.
- BIANCHI, A., CHIPMAN, D.W., DRESKIN, A. & ROSENWEIG, N.S. (1970) Nutritional folic acid deficiency with megaloblastic changes in the small bowel epithelium. *New England Journal of Medicine*, **282**, 859.

- CARMEL, R. & HERBERT, V. (1967) Correctable intestinal defect of vitamin B₁₂ absorption in pernicious anaemia. *Annals of Internal Medicine*, 67, 1201.
- COOKE, W.T., FONE, D.J., COX, E.V., MEYNELL, M.J. & GADDIE, R. (1963) Acute folic acid deficiency of unknown aetiology: temperate sprue. *Gut*, 4, 292.
- CREAMER, B., SHORTER, R.G. & BAMFORTH, J. (1961) The turnover and shedding of epithelial cells. *Gut*, 2, 110.
- CREAMER, B. (1964) Malignancy and the small intestinal mucosa. *British Medical Journal*, 2, 1435.
- DRUMMOND, M.B. & MONTGOMERY, R.D. (1970) Acute sprue in Britain. *British Medical Journal*, 2, 340.
- FOROOZAN, P. & TRIER, J.S. (1967) Mucosa of the small intestine in pernicious anaemia. *New England Journal of Medicine*, 277, 553.
- FORSHAW, J. (1968) Faecal fats and the coeliac syndrome. *Lancet*, 1, 1204.
- FORSHAW, J. (1969) Effect of vitamin B₁₂ and folic acid deficiency on small intestinal absorption. *Journal of Clinical Pathology*, 22, 551.
- GIRDWOOD, R.H. (1953) A folic acid excretion test in the investigation of intestinal malabsorption. *Lancet*, ii, 53.
- LABLOND, C.P. & MEISSER, B. (1958) Renewal of chief cells and goblet cells as shown by radioautography after injection of thymidine-H³ into mice. *Anatomical Records*, 132, 247.
- O'BRIEN, W. & ENGLAND, M.J.W. (1966). Military tropical sprue from South East Asia. *British Medical Journal*, 2, 1157.
- PHILLIPS, F.S. & THIERSCH, J.B. (1949). Studies of the action of 4-aminopteroylglutamic acid in rats and mice. *Journal of Pharmacology*, 95, 303.
- REYNOLDS, E.H., HALLPIKE, J.F., PHILLIPS, B.M. & MATHEWS, D.M. (1965) Reversible absorptive defects in anticonvulsant megaloblastic anaemia. *Journal of Clinical Pathology*, 18, 593.
- SHECHY, T.W., COHEN, W.H. & BRODSKY, J.P. (1963) Intestinal lesions in the initial phase of tropical (military) sprue. *American Journal of Digestive Diseases*, 8, 826.
- STEFANINI, M. (1948) Clinical features and pathogenesis of tropical sprue. *Medicine (Baltimore)*, 27, 379.
- TRIER, J.S. (1962) Morphological alterations induced by methotrexate in the mucosa of human proximal intestine. *Gastroenterology*, 42, 295.

Active chronic hepatitis and haemolytic anaemia associated with Rh-specific antibodies

C. D. R. PENGELLY
M.D., F.R.C.P., F.R.C.P.E.

Consultant Physician

R. C. JENNINGS
M.D., F.R.C.Path.

Consultant Pathologist

Wythenshawe and North Cheshire and South Cheshire Hospitals

ACTIVE chronic hepatitis, a disease also known by the synonyms lupoid hepatitis, plasma cell hepatitis, chronic juvenile hepatitis and by a number of others, is now recognized as a not uncommon condition (Sherlock, 1968). None of these synonyms is entirely satisfactory but the name lupoid hepatitis has been used because in 15% of patients disturbance of the immunity mechanisms gives rise to a positive LE-cell test. Another manifestation of auto-immunity may be the development of a positive Coombs' test, or even a frank haemolytic anaemia (Read, Harrison & Sherlock, 1963), but this appears to be a rare complication of the disorder and these authors report only one case. We have been unable to find any references to patients with specific antibodies on the red cells or in the serum.

Case history

Mrs E. F., aged 62 years, without any previous illness of note, was referred to one of us (CDRP) on 22 February 1969. She had become jaundiced about 6 weeks previously. Her stools had been pale and urine dark. The illness had consisted of vague

upper abdominal pain, nausea, heartburn and a little dysphagia referred to the lower end of the oesophagus. There was no history of alcoholism or of the taking of drugs. She had had two normal pregnancies and no miscarriages, and she had never received any blood transfusions or injections of blood. The illness was accepted by her general practitioner as being an example of ordinary viral hepatitis and the jaundice apparently improved, but had become worse a few days before 22 February. Liver function tests had shown the following results: bilirubin 3.6 mg/100 ml; alkaline phosphatase 34 KA units/100 ml; thymol turbidity 6.5 units; SGOT 148 IU/l at 25° C; SGPT 168 IU/l at 25° C; total protein 8.7 g/100 ml; albumin 3.2 g/100 ml; globulin 5.5 g/100 ml; electrophoresis showed marked increase in gamma-globulin.

On examination she looked generally well and was moderately jaundiced. Her liver was only slightly enlarged but very easily palpable and firm. Urine contained both bile and an excess of urobilinogen but was otherwise normal. There were no clinical signs of liver failure, no spider naevi and no palmar erythema. Her spleen was not palpable. Her blood pressure was 160/90 mmHg. She was admitted

Requests for reprints to C. D. R. Pengelly, 62 Manchester Road, Altrincham, Cheshire.