Sprue in the Middle East: five case reports

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SUMMARY Tropical sprue is a well documented condition with a special geographical distribution. This paper describes five patients with unexplained malabsorption whose symptoms began during a period of residence in the Middle East or Mediterranean areas.

Tropical sprue was originally described in the English literature two centuries ago, by Hillary from the island of Barbados (Booth, 1964). It was subsequently recognized to be endemic in the West Indies, the Indian subcontinent, and South East Asia. The condition is now well documented in both indigenous inhabitants and expatriates from temperate zones resident in endemic areas. Although it has long been thought to have a special geographical distribution even within the tropics (Manson, 1972), the reported absence of the disease in some areas has not always been based on sound evidence (Wellcome Trust Collaborative Study, 1971). Thus, in recent years, tropical sprue has been shown to be present in areas of the western hemisphere from which it was previously thought to be absent. Affected patients include expatriates in the Dominican Republic and Guatemala (Klipstein and Falaiye, 1969) and residents of Haiti (Klipstein, Samloff, and Schenk, 1966), Venezuela (Beker, Valencia-Parparcen, Carbonnel, Bosch, de Bosch, and Moncada, 1961), and Colombia (Ghitis, Tripathy, and Mayoral, 1967).

Most authorities consider that there are no well documented reports of tropical sprue in Africa south of the Sahara (Foy and Kondi, 1971). Sprue-like disease has been described in Rhodesia and the Congo (Gelfand, 1947, 1967; Limbos, 1956), but other causes of malabsorption were not satisfactorily eliminated. More recently, however, Falaiye (1970) described Nigerian patients with chronic diarrhoea and malabsorption who may be suffering from tropical sprue.

The evidence for the occurrence of sprue in the Middle East and Mediterranean littoral is confined to isolated and incompletely documented observations made some years ago (Manson, 1972) when the distinction between sprue and gluten-in-

duced enteropathy could not reliably be made. This also applies to the vivid classical description by Aretaeus of Cappadocia, writing in Asia Minor in the second century AD (Major, 1948). Since this unit was opened in 1955, five patients have been seen with unexplained malabsorption indistinguishable from tropical sprue as defined by modern criteria (Baker and Mathan, 1970; Klipstein and Baker, 1970). Symptoms began during a period of residence in the Middle East or Mediterranean area. These cases are documented in detail.

Case 1

C.W. presented in 1956 when 26 years old. A regular soldier in the British Army, he enjoyed excellent health until his unit was posted to Cyprus. He arrived in January 1956 and remained well until July of that year, when he developed diarrhoea which failed to respond to simple remedies. This diarrhoea became more profuse over the next four weeks, with the passage of pale, offensive stools. It was associated with anorexia, abdominal distension, and the passage of considerable flatus. He lost weight and complained of increasing weakness and lassitude. In September 1956 a stool specimen was reported as showing a gross excess of fat and he was therefore repatriated to a military hospital in England. Following his return to this country his symptoms improved rapidly. The diarrhoea subsided, whilst his appetite and weight increased. By the time of his transfer to this unit he was largely asymptomatic.

PHYSICAL EXAMINATION

He was a healthy-looking individual with no clinical evidence of anaemia. The tongue was normal. He weighed 60 kg compared with his usual weight of 67 kg. Systematic examination revealed no abnormality other than signs of meralgia paraesthetica.

INVESTIGATIONS

Haematology

Haemoglobin 13.3 g/100 ml, PCV 40%, red cells 4.1×10^6 per mm^3 ; MCV $100 \mu^3$; white cells 6×10^3 per mm^3 ; ESR 2 mm fall in one hour. Serum iron 181 μg per 100 ml; serum vitamin B₁₂ 400 pg per ml. Figlu excretion following a single 20 g loading dose of histidine was at the upper limit of normal. Bone marrow was normoblastic.

Biochemistry

Urea and electrolytes normal; serum calcium 8.2 mg per 100 ml; serum inorganic phosphate 4.1 mg per 100 ml; serum magnesium 1.6 mg per 100 ml; alkaline phosphatase 8 KA units per 100 ml; total serum proteins 6.9 g per 100 ml (serum albumin 5.1 g per 100 ml).

Bacteriology

Repeated stool cultures grew no pathogenic organisms, and no ova, cysts, or parasites were seen on microscopy.

Intestinal function

Stool examination revealed semiformal motions (average volume 300 ml per day); mean fat excretion on admission of 20 g per day with a faecal nitrogen excretion of less than 2 g per day. Following 20 g of xylose, 11.2% of the dose was excreted in a five-hour period.

A glucose tolerance test showed a flat curve. Barium meal and follow-through examination showed an abnormal small intestinal pattern with clumping of barium and dilatation of intestinal loops.

Duodenal intubation showed normal concentrations of amylase, lipase, trypsin, and cholic acid in the duodenal aspirate. No organisms were cultured from the fluid. The dissecting microscope appearance of a jejunal biopsy was of finger-like villi, with only slight cellular infiltration histologically.

TREATMENT AND PROGRESS (FIG 1)

During a two-week baseline period the patient's weight rose steadily, although he continued to excrete, on average, 20 g of fat per day in the stool. In view of the normal haemoglobin level, and in the absence of evidence of folate deficiency, folic acid replacement therapy was not given. Instead, he received a 15-day course of chemotherapy, consisting of five days each of sulphasuxidine, chloramphenicol, and chlortetracycline. During this course the faecal fat excretion began to fall towards normal, although the levels were still elevated (mean 8.4 g per day) at discharge. When allowed home he was not receiving any medication.

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SECOND ADMISSION

C.W. was reassessed in 1957, 12 months after his first admission. He was asymptomatic. Physical examination was normal and he weighed 74 kg, 8 kg heavier than on discharge.

Haematology

Haemoglobin 15.3 g per 100 ml; PCV 46%; red cells 5.2×10^6 per mm^3 ; MCV $88 \mu^3$; WBC 6.5×10^3 per mm^3 ; ESR 2 mm fall in one hour.

Biochemistry

Total serum proteins 7.4 g per 100 ml (serum albumin 4.8 g per 100 ml; serum calcium 9.2 mg per 100 ml; serum magnesium 2.1 mg per 100 ml).

Intestinal function

Stools were formed and of normal colour. Stool volume averaged 80 ml per day. The fat content was 4 g per day with a faecal nitrogen excretion of 1.5 g per day.

Following a 25 g dose of xylose, 17% was excreted in five hours.

Fig 1 The clinical course of C.W., a British soldier serving in Cyprus in 1956.

Barium follow-through examination showed a normal mucosal pattern.

Progress (fig 1)

All results showed considerable improvement on his previous findings, although the xylose absorption test was still slightly abnormal. No further treatment was considered indicated and he was discharged.

Case 2

B.P., a British soldier, was posted to Cyprus in February 1960, when he was 20 years old. He remained in excellent health for four months but then developed nausea, malaise, and diarrhoea. Several pale, unformed, offensive stools were passed each day. Lethargy became a prominent symptom. The buccal mucosa became ulcerated and his weight fell by 7 kg in four weeks. Despite two courses of sulphaguanidine the diarrhoea persisted and he was transferred to Birmingham for investigation in August 1960.

Examination showed a fairly well nourished soldier of average height. He weighed 53 kg compared with his weight of 60 kg before his illness. No abnormality was detected on clinical examination.

INVESTIGATIONS

Haematology

Haemoglobin 13.0 g per 100 ml; MCHC 41%; WBC 8.5×10^3 per mm^3 ; normochromic blood film. ESR 2 mm fall in one hour. Serum iron 135 μg per 100 ml; serum vitamin B₁₂ 130 pg per ml. Figlu excretion, following a 20 g loading dose of histidine, was at the upper limit of the normal range.

Biochemistry

Urea and electrolytes normal. Serum calcium 9.1 mg per 100 ml; serum albumin 4.8 g per 100 ml; total serum proteins 7.5 g per 100 ml, with a normal electrophoretic strip. Twenty-four-hour urinary calcium excretion of 223 mg (mean of three readings).

Bacteriology

Repeated stool microscopy failed to reveal any ova, cysts, or parasites and no pathogenic organisms were cultured.

Intestinal function

Stools were profuse, pale, and unformed. During a three-week control period, the mean faecal fat excretion was 16.7 g per day and faecal nitrogen was 4.5 g per day. A xylose absorption test showed that 13.4% of a 5 g dose was excreted in five hours. Barium studies showed dilatation of the small

intestine with clumping of barium and alteration in the mucosal pattern.

Duodenal intubation

Culture of the duodenal aspirate grew enterobacteriaceae, diphtheroid organisms, and *Staphylococcus albus*. Estimation of duodenal trypsin, amylase, and lipase was normal. The dissecting microscope appearance of the jejunal biopsy was of mixed fingers and leaves and histologically there were some club-shaped villi and excessive infiltration with inflammatory cells.

TREATMENT AND PROGRESS (FIG 2)

On a normal ward diet, without additional therapy, his weight began to rise during the control period. Although there was no evidence of folate deficiency he was given intramuscular folic acid in a dose of 15 mg per day. The weight gain continued at the same rate but there was no decrease in faecal fat excretion. He was then treated with sulphasuxidine for four

Fig 2 The clinical course of B.P., a British soldier serving in Cyprus in 1960.

days, followed by chloramphenicol and streptomycin for a further four days. During the two-week period following the end of the chemotherapy course the mean faecal fat excretion fell to 4.8 g per day and the faecal nitrogen excretion to 2.6 g per day. A repeat xylose absorption test showed 29% excretion of a 5 g dose in five hours, while a repeat jejunal biopsy showed considerable improvement in the histological appearances.

In September 1961 B.P. was admitted for reassessment. He weighed 60 kg. Haemoglobin was 14.0 g per 100 ml. A xylose absorption test showed 37% excretion of a 5-g dose in five hours. The mean faecal fat excretion was 5.5 g per day. He remained well and was last seen in 1966 when his health was excellent.

Case 3

I.M., a British university student, presented in 1964 at the age of 20 years. His summer vacation was spent in Israel, travelling via Marseilles and Naples. He arrived in Haifa in mid-July 1964 and proceeded to Jerusalem where he remained for over two weeks. During that second week he developed a sore throat and cervical lymphadenopathy which lasted for 10 days. Moving on to a kibbutz in Galilee he felt nauseated and began to pass four to six loose motions each day. These symptoms completely subsided after three days. Four days later, he fainted following an episode of vomiting and this led to his investigation at Tel Hashomer Hospital where he was noted to have a cardiac bruit. The provisional diagnosis was one of mild myocarditis after an acute viral illness. He was allowed to travel to Elat but the visit was curtailed by a further fainting episode. He was flown back to Tel Aviv and remained in hospital for six days. During the six-week stay in Israel, he lost 12 kg in weight. He returned to England at the end of August 1964 but during the journey his diarrhoea recurred. Four weeks later he was investigated at a Coventry hospital and found to be folate deficient. Transfer to this unit took place in October.

Physical examination revealed a relatively fit young man, weighing 68 kg. There was no evidence of anaemia or glossitis. No significant abnormalities were present.

INVESTIGATIONS

Haematology

Haemoglobin 14.2 g per 100 ml; ESR 3 mm fall in one hour; serum iron 57 μ g per 100 ml; serum vitamin B₁₂ 148 and 260 pg per ml; serum folate 1.1 ng per ml (mean of three estimations).

Biochemistry

Urea and electrolytes normal. Serum calcium 9.6 mg per 100 ml; total serum proteins 6.8 g per 100 ml (serum albumin 4.2 g per 100 ml).

Bacteriology

Culture and microscopy of the stools was normal. The Widal reaction was negative and no malarial parasites were seen in the peripheral blood. The Paul-Bunnell test was negative.

Intestinal function

Stool volume on admission varied between 200 ml and 700 ml per day, with a mean faecal fat excretion of 20 g per day. The faecal nitrogen excretion was 5 g per day. The xylose absorption test showed that following a 5-g dose, only 8% was excreted in the first two hours and 20% over the total five-hour period. The Schilling test showed that the 48-hour excretion of ⁵⁸CoB₁₂ was 13% (normal range 15-30%). Barium studies showed dilatation of the small intestinal loops and clumping of barium.

Fig 3 The clinical course of I.M., a British student, who developed malabsorption on vacation in Israel in 1964.

Duodenal intubation

The concentrations of amylase, lipase, trypsin, and bile salts in the aspirate were all normal. No organisms were cultured from the fluid. Dissecting microscopy of the jejunal biopsy showed stunting of villi with broad leaves. Histologically there was partial villous atrophy and marked cellular infiltration.

TREATMENT AND PROGRESS (FIG 3)

He was initially treated with intramuscular folic acid in a dose of 5 mg per day. There was some subjective improvement and his weight increased by 6 kg over a four-week period. The steatorrhoea persisted, however, and he later received successive five-day courses of succinyl sulphathiazole, neomycin, and chloramphenicol. There followed a prompt fall in stool volumes to normal levels, with a mean fat excretion of 7 g per day and a faecal nitrogen excretion of 3 g per day. He was discharged in December 1964 on folic acid.

SECOND ADMISSION

Only four weeks after discharge the diarrhoea recurred. Generalized lethargy was a prominent feature. He was readmitted in March 1965. He looked well and there were no physical signs of significance. His weight had remained steady.

Haematology

Haemoglobin 15 g per 100 ml; ESR 2 mm fall in one hour. Serum folate 1.6 ng per ml. Impairment of folate absorption following a test meal was demonstrated.

Intestinal function

Stool volume was normal with a faecal fat excretion of 6 g per day and faecal nitrogen excretion of 3 g per day. Following a 5-g dose of xylose, 22.5% was excreted in the first two hours and 35% in the total five-hour period.

He was recommenced on oral folic acid therapy for a total of seven weeks and discharged.

THIRD ADMISSION

The course of folic acid was completed uneventfully but within two weeks of discontinuing folic acid he developed ulceration of the buccal mucosa. The ulcers disappeared just seven days after he restarted folic acid. He was re-investigated in July 1965.

INVESTIGATIONS

Haematology

Haemoglobin 14.8 g per 100 ml; serum folate 2 ng per ml.

Intestinal function

Stool volume 200 ml per day; faecal fat excretion 8.6 g per day over the duration of his inpatient stay; faecal nitrogen 3 g per day. Following a 5-g dose of xylose, 19.2% was excreted in the first two hours and 30% in the total five-hour period.

Progress

He was recommenced on folic acid, which produced a fall in faecal fat excretion to 5 g per day. He continued to take folic acid on a permanent basis and when last seen in October 1970 he was in excellent health. The serum folate level was 6.9 ng per ml.

Case 4

A.Y., a married Yemenite, was 55 years old when he first presented in May 1972. He had lived in England since 1947, but returned to the Yemen frequently. His last visit there had been in September 1970. Two months following his arrival in the Yemen he developed diarrhoea which did not become troublesome until after his return to Birmingham four weeks later. He then started passing profuse, pale, liquid motions, associated with central abdominal pain, distension, and borborygmi. Tiredness and soreness of the tongue developed insidiously. There was marked anorexia and he lost 19 kg in weight during the period of his illness.

Physical examination revealed a thin, small man who weighed 53.5 kg. His tongue was red and depapillated but there was no evidence of anaemia. No other abnormalities were found.

INVESTIGATIONS

Haematology

Haemoglobin 13.8 g per 100 ml; WBC 3.1×10^3 per mm³; ESR 10 mm fall in one hour; stained films showed some macrocytosis. Serum iron 132 µg per 100 ml; total iron-binding capacity 444 µg per 100 ml. Serum folate 1.6 ng per ml (mean of three estimations); serum vitamin B₁₂ 90 pg per ml.

Biochemistry

Urea and electrolytes normal. Serum calcium 9.1 mg per 100 ml; alkaline phosphatase 14 K-A u per 100 ml; 5-nucleotidase 10 IU per litre; total serum proteins 7.8 g per 100 ml (serum albumin 4.9 g per 100 ml).

Bacteriology

No pathogenic organisms were isolated on culture of the stools and no ova, cysts, or parasites were seen on microscopy.

Immunology

Quantitative immunoglobulin estimations were IgG 1970 mg per 100 ml; IgA 296 mg per 100 ml; IgM 35 mg per 100 ml. Parietal cell antibodies were not present.

Intestinal function

Stool volumes ranged up to 1 litre per day. The stool was yellow and semi-formed. On admission, the faecal fat excretion averaged 63 g per day with a mean faecal nitrogen excretion of 3.5 g per day. Following a 5-g dose of xylose only 1% was excreted in the first two hours, and 3.5% in the total five-hour period. The Schilling test gave recovery of $^{57}\text{CoB}_{12}$ with intrinsic factor 0.28%; recovery of $^{58}\text{CoB}_{12}$ without intrinsic factor 0.05%.

Duodenal intubation

Estimations of the trypsin, lipase, and cholic acid content of the aspirate were normal. A *Streptococcus viridans* was cultured from the fluid. The dissecting microscope appearance of the jejunal biopsy was of many flattened broad leaves and ridges and histologically there was severe partial villous atrophy (fig 4).

TREATMENT AND PROGRESS (FIG 5)

In view of his severe malabsorption of fat, xylose, and vitamin B₁₂, together with folic acid deficiency, he was started on intramuscular injections of folic acid, 15 mg per day. There was a dramatic response

Fig 5 The clinical course of A.Y., whose symptoms developed on return to his native Yemen in 1970.

Fig 4 Histological appearance of the jejunal biopsy obtained from A.Y., showing severe partial villous atrophy.

and his motions rapidly became formed, of normal volume, and with a fat content of 6 g per day. His weight increased by 5 kg in four weeks. The reticulocyte count rose to 7.4%. In view of his vitamin B₁₂ deficiency, he was also given intramuscular hydroxycobalamin. A repeat xylose absorption test 10 days after starting folic acid therapy showed that, following a 5 g dose, 8% was excreted in the first two hours and 21% in the total five-hour period. At discharge he was continuing to take folic acid 15 mg per day.

When seen for review one year later, he was asymptomatic. He weighed 64.5 kg. Repeat investigations were as follows: haemoglobin 15.3 g per 100 ml, MCV 86 μ^3 ; ESR 10 mm fall in one hour, urea and electrolytes normal; serum folate 4.7 ng per ml; xylose absorption showed 17.6% excretion of the 5-g dose in the first two hours and 36.5% excretion in the total five-hour period. He had discontinued folic acid therapy of his own accord some months earlier, and in view of the above results, treatment was not re-started.

Case 5

W.H., a widowed Englishwoman aged 64 years, was well until mid-October 1972. She travelled on holiday to the Middle East, visiting Egypt, Lebanon, and Israel. Her stay in Egypt was uneventful, but in Lebanon she developed a 36-hour episode of diarrhoea. This rapidly settled and she was able to move on to Israel for the remainder of her holiday. After seven days, however, diarrhoea recurred, with

the passage of profuse, bulky motions and associated vague abdominal pains. This again improved after three days and did not recur during the remainder of her tour. Ten days after her return to England the diarrhoea relapsed and continued intermittently for three months before her admission to hospital. During this period she lost 3 kg in weight despite a relatively normal appetite.

Physical examination revealed a well proportioned woman of normal external appearances. The tongue was normal. She was not anaemic and there were no abnormal physical signs.

INVESTIGATIONS

Haematology

Haemoglobin 13.7 g per 100 ml; PCV 41%; MCV 87 μ^3 ; WBC 8.8×10^3 ; ESR 25 mm fall in one hour. Serum iron 92 μg per 100 ml; total iron-binding capacity 330 μg per 100 ml. Serum vitamin B₁₂ 230 pg per ml; serum folate 1.2 ng per ml.

Biochemistry

Urea and electrolytes normal; serum calcium 9.5 mg per 100 ml; alkaline phosphatase 7 K-A u per 100 ml. Total serum proteins 7.4 g per 100 ml (serum albumin 4.3 g per 100 ml). Serum vitamin A 7.4 μg per 100 ml; serum orosomucoid 100 mg per 100 ml.

Bacteriology

No pathogens were cultured from the stools, and no ova, cysts, or parasites were seen on microscopy.

Fig 6 *Histological appearance of the jejunal biopsy obtained from W.H., showing partial villous atrophy with a marked increase in inflammatory cell infiltration.*

Immunology

Quantitative immunoglobulin estimations: IgG 1655 mg per 100 ml; IgA 610 mg per 100 ml; IgM 50 mg per 100 ml.

Intestinal function

Stool fat excretion was 7 g and 9 g per day during two successive five-day balance periods. Faecal nitrogen excretion was 2.5 g and 3.1 g per day over the same periods.

Glucose absorption (venous blood) was normal following 50 g of glucose, the blood glucose level rising from a fasting level of 85 mg per 100 ml to 148 mg per 100 ml at one hour. Xylose absorption: 11.6% of the 5 g dose was excreted in the first two hours and 18.4% in the total five-hour period. A double isotope Schilling test showed recovery of $^{57}\text{CoB}_{12}$ with intrinsic factor 27%; recovery of $^{58}\text{CoB}_{12}$ without intrinsic factor 28%.

Barium meal and follow-through examination showed a normal stomach, duodenum, and small intestine.

Culture of the duodenal aspirate grew no pathogenic organisms. The dissecting microscope appearance was of broad leaf-shaped and flattened villi; histologically the appearances were those of partial villous atrophy with marked increase in inflammatory cell infiltration (fig 6).

TREATMENT AND PROGRESS

During her stay in hospital she improved symptomatically on a ward diet. After two weeks the diarrhoea subsided rapidly and within a further two weeks the faecal fat excretion had returned to less

than 5 g per day. She was not therefore given folic acid or antibiotics, but reviewed frequently as an outpatient. At her most recent attendance in August 1973 the faecal fat excretion averaged 2 g per day over a five-day period. The serum folate was still low, however, at 2.2 ng per ml, and she has been put on folic acid therapy.

Discussion

In the absence of knowledge of the aetiology of tropical sprue, the condition can be defined only in clinical terms, by establishing the features of the syndrome and excluding other causes of intestinal malabsorption. Until recently, the criteria for diagnosis were generally considered to be the presence of chronic diarrhoea, megaloblastic anaemia, malabsorption of fat, xylose, and vitamin B_{12} , together with nonspecific intestinal morphological abnormalities (Perez-Santiago and Butterworth, 1957). Others, however, have frequently noted a whole spectrum of clinical presentations, with marked fluctuations in severity (Baker and Mathan, 1971). These variations are related, in part at least, to the duration of the disorder and the nutritional reserves of the individual. It is reasonable, if arbitrary, to restrict the application of the term tropical sprue to patients in certain areas who have demonstrable malabsorption of two or more unrelated substances, in whom all other known causes of malabsorption are excluded (Klipstein and Baker, 1970; Wellcome Trust Collaborative Study, 1971; Lindenbaum, 1973). On this basis, the clinical features seen in the five cases described from the Middle East (see table) are indistinguishable from

Case	Country Visited	Length of Stay before Onset of Symptoms	Duration of Symptoms before Diagnosis	Weight Loss (kg)	Haemoglobin	Figu Excretion	Serum Folate (N.R. 2.5-18 ng/ml)	Schilling Test	d-Xylose % Dose Excreted (2 hr/5 hr)	Faecal Fat Excreted (g/day)	Jejunal Biopsy	
											Dissecting Microscopy	Histology
1	Cyprus	6 months	3 months	7	13.3	Normal	—	—	—/11.2	20	Finger-shaped villi	Slight cellular infiltrate
2	Cyprus	4 months	2 months	7	13.0	Normal	—	—	—/13.4	16.7	Finger- and leaf-shaped villi	Considerable cellular infiltrate
3	Israel	3 weeks	2 months	12	14.2	—	1.1 (mean of two)	Malabsorption	6/20	20	Broad leaves	Partial villous atrophy
4	Yemen	2 months	18 months	19	13.8	—	1.6 (mean of three)	Gross malabsorption	1/3	63	Broad leaves and ridges	Severe partial villous atrophy
5	Egypt Lebanon Israel	2 weeks	3 months	3	13.7	—	1.7 (mean of two)	Normal	11/18	8	Broad leaves	Partial villous atrophy

Table Summary of the clinical features seen in the five cases described

cases of tropical sprue seen in the accepted endemic zones. The minor deviations from the 'classical' case are all well documented.

The absence of anaemia is understandable in relation to the short duration of symptoms before diagnosis, and the good nutritional stores of these individuals (O'Brien and England, 1971; Klipstein and Baker, 1970). The normal Figlu excretion seen in cases 1 and 2 is also a reflection of this short symptomatic period (O'Brien and England, 1971). Malabsorption of vitamin B₁₂ has been a variable feature in different series (Klipstein, 1970) and normal absorption, as seen in case 5, may occur in up to 30% of cases of short duration (Wellcome Trust Collaborative Study, 1971). The patients described in cases 3 and 5 spent only a relatively short period of two or three weeks in the Middle East. Sheehy, Cohen, Wallace, and Legtes (1965) recorded that in North Americans living in Puerto Rico who developed sprue, the symptoms in some instances occurred as soon as two weeks after arrival. Indeed, damage to intestinal mucosal cells can be seen by light and electron microscopy in specimens obtained as early as the first week (Chacko, 1970). Bacterial overgrowth in the jejunum was seen in cases 2 and 4, an occurrence well documented in sprue by Gorbach and other workers (Gorbach, Mitra, Jacobs, Banwell, Chatterjee, and Guha Mazumder, 1969; Banwell and Gorbach, 1969; Gorbach, Banwell, Jacobs, Chatterjee, Mitra, Sen, and Mazumder, 1970). The morphological appearance of the jejunal biopsy seen in all five cases conforms to the spectrum of characteristic but nonspecific changes seen in tropical sprue (Swanson and Thomassen, 1965; Schenk, Samloff, and Klipstein, 1968).

We have been unable to find any recent published data on sprue arising in the Middle East or Mediterranean area. Enright (*Lancet*, 1944) described prisoners-of-war captured in the Palestine campaign of 1918, who had offensive, copious, and 'porridgy' stools. In 1944, Howat reported cases of a sprue-like syndrome occurring in the Middle East as a sequel to chronic and relapsing dysentery of varied aetiology (Howat, 1944). Early cases were seen in malnourished Polish ex-prisoners (Howat, 1973) while later cases occurred in British soldiers on apparently normal diets. In many instances, the clinical picture was complicated by infestations with *Entamoeba histolytica*, *Giardia lamblia*, or *Shigella sonnei*. However, despite the appropriate therapy, there was little improvement in steatorrhoea. In a few patients, parenteral liver extract produced amelioration of the acute features. Bulic (1953) briefly described an epidemic of sprue in troops in Yugoslavia, under conditions of dietary deprivation. This epidemic ended with the introduction of fresh food supplies.

One patient in a large series of sprue affecting British servicemen in the Far East, appeared to develop the condition on board ship en route from the Persian Gulf to Singapore (O'Brien and England, 1971). Despite the rarity or absence of clinical sprue in the countries of the Middle East, a high incidence of subclinical enteropathy is reported in some areas (Dutz, Asradi, and Sadri, 1971). Creamer, Dutz, and Post (1970), reporting from Iran, documented small intestinal lesions in association with chronic diarrhoea and marasmus in children, a condition very similar to the syndrome of sprue in adults. Subclinical enteropathy is also known to occur in Egypt (Halsted, Sheir, and Sourial, 1969) and Liberia (Lindenbaum, Harmon, and Gerson, 1972; Rhodes, Shea, and Lindenbaum, 1971). The postulate that these subclinical enteropathies represent a mild form of tropical sprue (Klipstein, 1967) cannot be tested until the aetiology of sprue is known.

The relationship between the classic type of chronic sprue and more acute sprue syndromes also requires evaluation. It is recognized that a temporary phase of malabsorption may occur following acute gastrointestinal infections in Australian (King and Joske, 1960), Pakistani (Lindenbaum, 1965), and British patients (Montgomery, Beale, Sammons, and Schneider, 1973). Up to 50% of cases of tropical sprue may present with acute watery diarrhoea (Sheehy *et al*, 1965; Bayless, Wheby, and Swanson, 1968; Mathan and Baker, 1970; O'Brien and England, 1971). This tends to support the concept that an unknown transmissible agent is the initiating factor in tropical sprue (Mathan and Baker, 1971; Dean and Jones, 1972), while folate and vitamin B₁₂ deficiency play a part in perpetuation of the disease (Foroozan and Trier, 1967; O'Brien and England, 1971; Lindenbaum and Pezzimenti, 1972; Hermos, Adams, and Liu, 1972). Contamination of the jejunum by colonic bacteria may be a further perpetuating factor, but the role of this bacterial overgrowth is not completely understood (Banwell and Gorbach, 1969; Mollin and Booth, 1971). The 'classical' picture of tropical sprue described in the earlier literature is now recognized to be a late result of the disease process.

Despite evidence to the contrary, some authors considered, even in quite recent times, that tropical sprue occurred only in Europeans. This led some observers to assume that intestinal malabsorption in the local population was a different disease. The special geographical distribution of sprue may have resulted in cases in non-sprue areas being overlooked because of their sporadic nature. The five cases discussed in this article fulfil the criteria for the diagnosis of sprue as defined above. They are indistinguishable from cases of sprue seen in British

servicemen repatriated from Hong Kong and Malaya who were investigated in this Unit, using the same techniques in the same laboratories.

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