

# Endemic tropical sprue in Rhodesia

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**SUMMARY** The existence of tropical sprue in Africa is controversial. In this paper we present 31 cases seen in Rhodesia over a 15 month period. They have the clinical features, small intestinal morphology, malabsorption pattern, and treatment response of tropical sprue. Other causes of malabsorption, and primary malnutrition, have been excluded. The severity of the clinical state and intestinal malabsorption distinguish these patients from those we have described with tropical enteropathy. The previous work on tropical sprue in Africa is reviewed and it is apparent that, when it has been adequately looked for, it has been found. It is clear that the question of tropical sprue in Africa must be re-examined and that its existence may have hitherto been concealed by the assumption that primary malnutrition is responsible for the high prevalence of deficiency states.

The absence of tropical sprue in Africa has long been a source of surprise and controversy. Authorities on the disease and experienced workers in various parts of Africa (Trowell, 1960; Banwell *et al.*, 1967; Klipstein, 1968; Baker and Mathan, 1970; Foy and Kondi, 1971; Cook, 1974) have agreed that tropical sprue occurs extremely rarely, if at all, despite the presence of subclinical enteropathy.

During the past 65 years there have been isolated reports of a few possible cases from Malawi (Manson-Bahr, 1928), Zaire, (Begg, 1912; Limbos, 1956), Tanzania (Taute, 1919), Egypt (Salah, 1937), Rhodesia (Gelfand, 1947), Kenya (Harries, 1964), and Uganda (Banwell *et al.*, 1967). In South Africa Hift and Adams (1963) noted an association between megaloblastic anaemia and malabsorption. However, the data provided in these accounts were insufficient and the diagnosis of tropical sprue is in doubt. Recently Falaiye (1970) in Nigeria and Moshal *et al.* (1975) in South Africa have reported substantial series of patients with convincing evidence of tropical sprue, but have not observed their cases for evidence of a sustained response to treatment at long-term follow-up. Also in South Africa Keeton (1972) has documented two cases and Weir *et al.* (1972) a single patient whose condition is compatible with the diagnosis of tropical sprue.

In Rhodesia we have noticed a large group of undiagnosed megaloblastic anaemias, which were previously attributed solely to malnutrition. In 1968 Clain presented preliminary data on tropical

sprue in Rhodesia. We have now established the presence of subclinical tropical enteropathy in Rhodesia (Thomas *et al.*, 1976) and in this paper describe 31 cases of tropical sprue, 28 of which had megaloblastic anaemia and the remaining three gastrointestinal complaints and weight loss.

## Methods

During the periods February 1973 to January 1974 and November 1974 to January 1975, we investigated 48 African patients with megaloblastic anaemia, and three with diarrhoea and weight loss, but not megaloblastic anaemia. Only two megaloblastic anaemia patients seen during this period refused investigation. Twenty-eight with megaloblastic anaemia, and the three without, had tropical sprue and are the subject of this report.

A detailed history and examination were carried out on all patients. A dietary questionnaire was recorded from each patient and two controls per patient, matched for sex, age, and socioeconomic circumstances. Haematological and biochemical tests were performed according to standard laboratory methods. In addition, each patient had a bone marrow examination, serum B12 (Green *et al.*, 1974), serum folate (Waters and Mollin, 1961), red cell folate (Hoffbrand *et al.*, 1966), and a bromosulphthalein retention test.

Jejunal biopsies were obtained just distal to the ligament of Treitz using the Crosby capsule (Crosby and Kugler, 1957), which was positioned by the rapid method of Wicks and Clain (1972). The

specimens were examined immediately under a dissecting microscope, (Holmes *et al.*, 1961) and then fixed in 10% formalin for histology. Dissecting microscopy appearance was graded from 1 to 6 according to the predominant villous pattern: grade 1—fingers; 2—leaves; 3—joined leaves and short ridges; 4—long ridges; 5—convolutions; 6—flat. The criteria suggested by Schenk and Klipstein (1972) were used to grade histological sections for villous abnormalities and cellular infiltration. For villous appearance grade 0 is normal, grades 1—3 show progressive broadening and flattening of villi, and grade 4 is flat. For cellular infiltration, grade 0 is normal, grade 1 shows a mild increase, grade 2 a moderate increase, and grade 3 a marked increase. Histological sections were also measured using a calibrated micrometer eye piece (Shiner and Doniach, 1960). Villous height was taken from the base to the apex and width at the widest part of the villus. Mucosal thickness was assessed from the muscularis mucosa to the base of the villi and epithelial cell height was measured half way up the villus. At least 10 readings were recorded from each specimen.

Xylose excretion was determined after a 25 g dose and five hour urine collection (Roe and Rice, 1948). Faecal fat excretion was estimated (van de Kamer *et al.*, 1949) and expressed as the mean of a five day collection. Vitamin B12 absorption was measured using the plasma uptake method (Workman and Rusche, 1966), repeated with intrinsic factor when abnormal, and calculated as a percentage of the administered dose per litre of plasma. The normal value is defined as more than 0.75% of the administered dose per litre of plasma, which is the 95th percentile of a group of healthy Rhodesian African controls (Thomas *et al.*, 1976). Biopsies were obtained from the body of the stomach using a Quinton suction biopsy tube, and augmented histamine tests were performed (Kay, 1953). All gastrointestinal tubes were positioned fluoroscopically. Each patient had small intestinal radiology using non-flocculating barium. The jejunal aspirate, obtained at biopsy, the entero-test (Thomas *et al.*, 1974), and between three and six stools were examined for parasites.

During the period of investigation weights and reticulocyte counts were regularly checked to observe any response on the hospital diet. Treatment consisted of one of four regimens: (1) 12 patients had tetracycline 250 mg four times a day, folic acid 5 mg three times daily and vitamin B12 1000 µg monthly for six months; (2) nine had tetracycline alone for six months; (3) five had tetracycline alone for three weeks and folic acid and vitamin B12 added for six months; (4) four had vitamin B12 and

folic acid for six months and three of these subsequently had tetracycline for a further six months. One died after only three weeks' treatment with folic acid, vitamin B12, and tetracycline.

All patients were seen at monthly intervals for a minimum of six months up to 30 months. The 30 survivors were reinvestigated on completion of their treatment regimens. Eight were also reinvestigated after three weeks tetracycline alone, including the five who subsequently had folic acid and vitamin B12 added. Twenty-five jejunal biopsies and all abnormal gastric biopsies, gastric acid studies, and tests of absorption were repeated. Those who received only tetracycline had their haematological status reassessed on finishing treatment.

## Results

### SYMPTOMS AND SIGNS

The 31 patients consisted of 15 males and 16 females, only three of whom were post partum. Their ages ranged from 15 to 73 years with a mean of 37 years. Presenting complaints are listed in Table 1 in order

Table 1 *Presenting symptoms*

<i>Symptoms</i>	<i>%</i>	<i>Symptoms</i>	<i>%</i>
Weakness	83	Vomiting	10
Dyspnoea	77	Dizziness	10
Weight loss	71	Palpitations	10
Diarrhoea	48	Nausea	6
Abdominal pain	48	Abdominal distension	6
(exacerbated by food)	(10)		
Anorexia	48	Parasthaesia	6
Ankle swelling	16	Sore tongue	3

of frequency. Weakness, dyspnoea, weight loss, diarrhoea, abdominal pain, and anorexia were the most common. Twenty-four patients had gastrointestinal symptoms and seven symptoms of anaemia only.

Table 2 gives the physical signs in order of frequency. Twenty-five patients were clinically anaemic. Twenty-four had evidence of severe malnutrition, all with weight loss and some with signs of protein deficiency, avitaminosis, and dehydration.

Table 2 *Presenting signs*

<i>Signs</i>	<i>%</i>	<i>Signs</i>	<i>%</i>
Anaemia	81	Heart failure	6
Severe weight loss	55	Mental confusion	6
Moderate weight loss	23	Peripheral neuropathy	3
Oedema	26	Angular stomatitis	3
Pellagra skin changes	16	Glossitis	3
Adult kwashiorkor hair			
changes	13	Ascites	3
Dehydration	10	Tetany	3

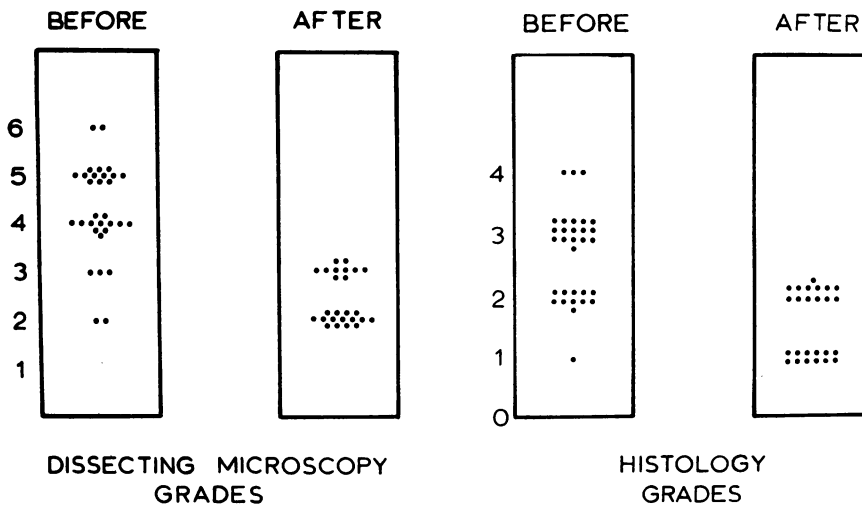


Fig. 1 Histological and dissecting microscopy grades of jejunal biopsies before and after treatment.

DIETS

The diets of individual patients, together with socioeconomic circumstances, varied considerably. The dietary fat content was impossible to determine but was certainly considerably less than that consumed in western society. Some ate first class protein and green vegetables daily, some on two days a week, and others as little as once a week. However, there was no statistical difference between the diets of patients with tropical sprue and those of healthy, non-anaemic matched controls.

INVESTIGATIONS

Haematology

The 28 patients with megaloblastic bone marrows had haemoglobins ranging from 2.7 g-11.7 g with a mean of 5.7 g. Seven had low serum vitamin B12 levels only (<400 pg); 11 had reduced serum folate (<3.0 ng) and or reduced red cell folate (<160 ng); and seven had abnormal levels of both vitamin B12 and folic acid. Three patients had received vitamin B12 and folic acid before they presented. The three with normoblastic bone marrows had haemoglobins of 9.5 g, 10.2 g, and 10.2 g. All three had subnormal serum or red cell folates but normal serum vitamin B12.

Biochemistry

Fourteen patients had hypokalaemia, five hyponatraemia, and three, who were severely dehydrated, a raised urea. One had the biochemical picture of osteomalacia and one had a low serum calcium only. The serum albumin was reduced to less than 30 g/l in 13 patients. Liver function tests, including bromsulphthalein retention, were normal in all 31.

Jejunal biopsies

Histological and dissecting microscopy grades before treatment are represented in the left hand columns of Fig 1. Histologically three were grade 4, 16 grade 3, 11 grade 2, and one grade 1; no biopsy was normal. Under the dissecting microscope two were grade 6, 12 grade 5, 12 grade 4, three grade 3, and two grade 2. Figures 2 and 3 show typical grade 3 and 4 histological sections. Figure 4 is a grade 5 dissecting microscopy specimen, photographed under the scanning electron microscope. Histological examination of all jejunal biopsies revealed no specific pathology such as intestinal tuberculosis or lymphoma. The range and mean measurements of villous height, villous width, epithelial cell height and mucosal thickness are given in Table 3; the three biopsies with histological grade 4 were too flat to measure. There was a dense infiltration of lymphocytes and plasma cells in the lamina propria of every specimen; 20 were grade 3 and 11 grade 2. The histological, dissecting microscopy and cellular infiltration grades ( $\chi^2$ ) and the histological measurements (Mann Whitney U test) were all significantly inferior to a group of healthy African controls (Thomas *et al.*, 1976) ( $P < 0.001$ ).

Table 3 Villous measurements before and after treatment

Treatment	No.	Villous height ( $\mu$ )	Villous width ( $\mu$ )	Epithelial cell height ( $\mu$ )	Mucosal thickness ( $\mu$ )
Before					
Mean	28	167	185	28.38	192
(range)		(123-227)	(151-209)	(24.13-32.18)	(93-315)
After					
Mean	25	259	137	31.68	144
(range)		(188-312)	(123-155)	(30.08-34.04)	(115-164)

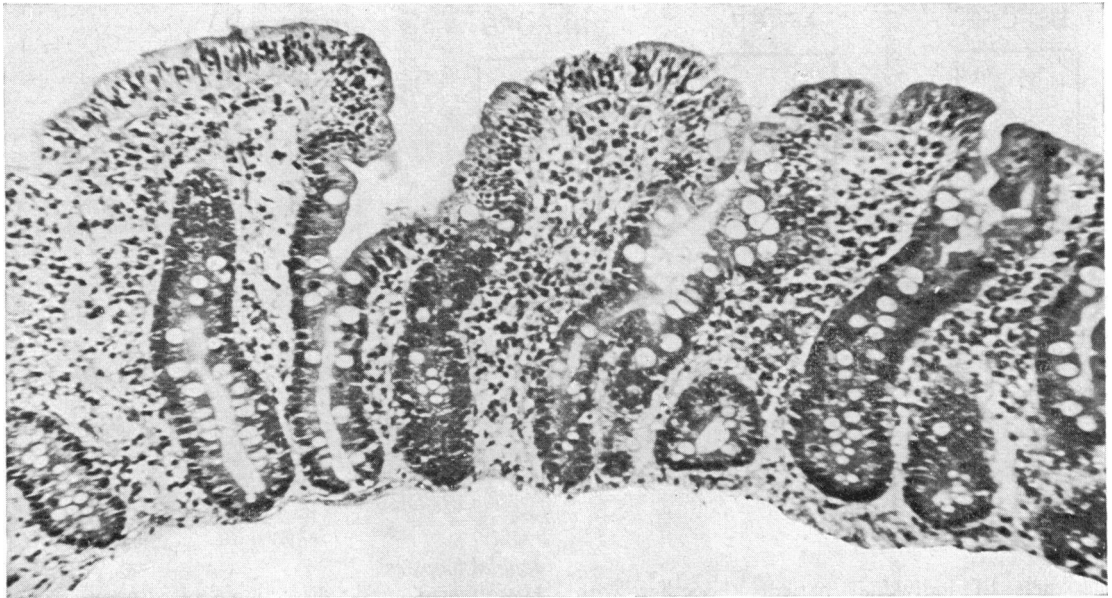


Fig. 2 Grade 3 histological section of a jejunal biopsy.

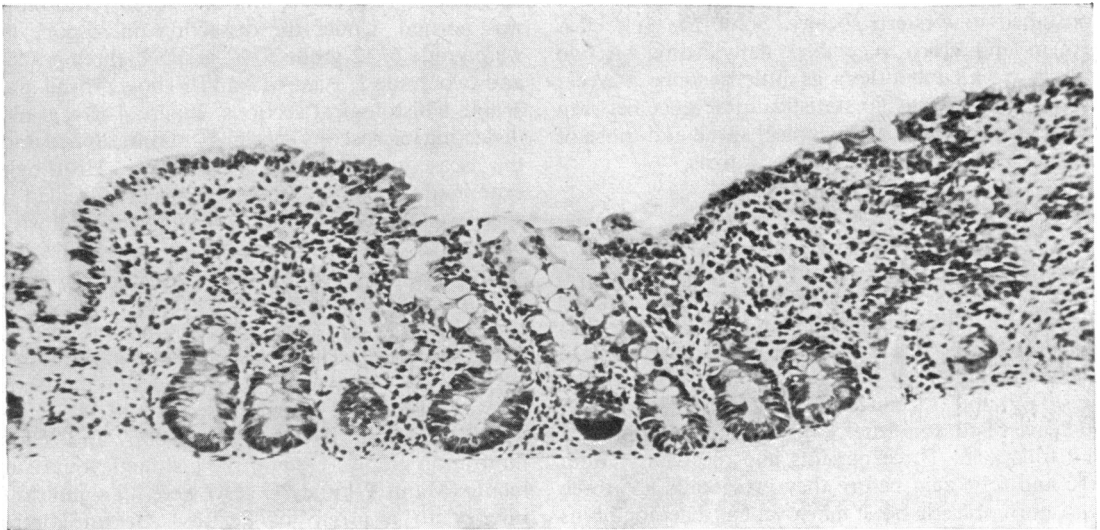


Fig. 3 Grade 4 histological section of a jejunal biopsy.

#### *Small intestinal absorption*

The left hand columns of Fig. 5 show the range of values and numbers of patients with abnormal fat, xylose and vitamin B12 absorption. Twelve (40%) of the 30 tested had steatorrhoea ( $>6.0$  g/24 hours). This is an underestimate, as the first 13 had faecal fats done while consuming ward diets containing 30-40 g of fat, and only one had steatorrhoea. The subsequent 17 had diets supplemented to contain

80-100 g of fat and 11 (65%) had steatorrhoea. Twenty-eight had xylose malabsorption ( $<5.0$  g) and all 31 had vitamin B12 absorption of less than 0.75%, the 95th percentile of our controls (Thomas *et al.*, 1976), despite added intrinsic factor. Xylose excretion and vitamin B12 absorption are significantly less than in a group of asymptomatic African controls (Thomas *et al.*, 1976) (Mann Whitney U test  $P < 0.001$ ).

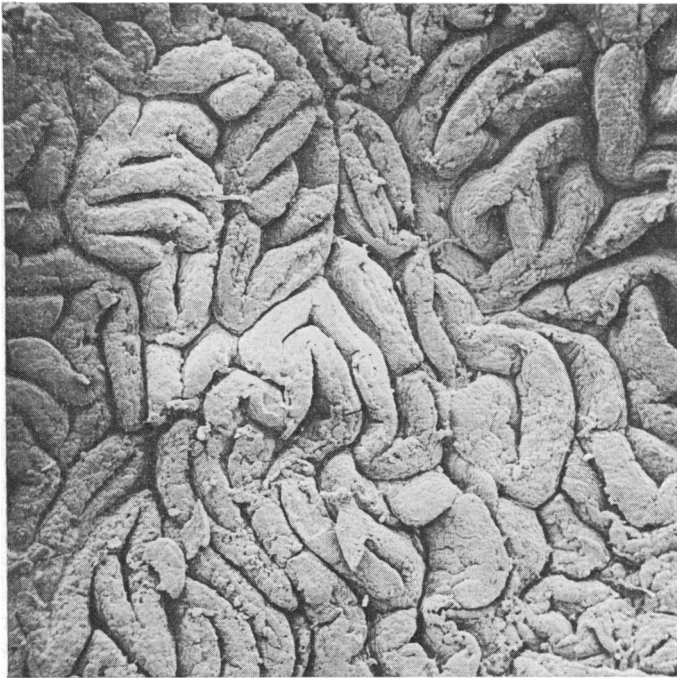


Fig. 4 A dissection microscopy grade 5 convoluted jejunal biopsy, photographed under a scanning electron microscope.

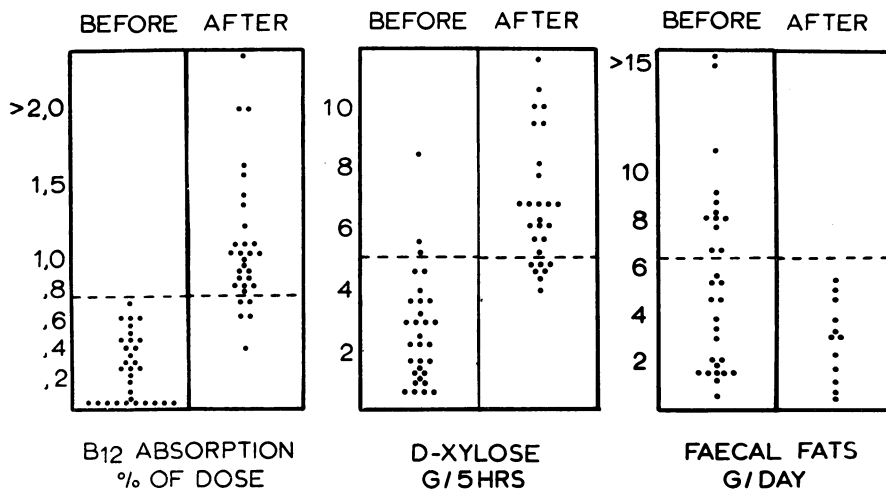


Fig. 5 Absorption of vitamin B<sub>12</sub>, xylose, and fat before and after treatment. The dotted lines signify normal limits.

**Barium studies**

Barium meal and follow-through revealed a mal-absorption pattern in 23 patients. Dilatation of at least 30 mm with flocculation or segmentation was considered abnormal. There was no evidence of intestinal lymphomas, tuberculosis, regional ileitis, fistulae, diverticulae, or blind loops.

**Gastric studies**

Gastric biopsies and acid studies were done on

30 patients. Seventeen had normal gastric histology, seven chronic superficial gastritis and six atrophic gastritis. Six had normal acid output, 14 hypochlorhydria (MAO < 8 mEq/l) and 10 histamine fast achlorhydria.

**Parasites**

*Giardia lamblia* was found in three patients. Trophozoites were demonstrated in the enterotest of all three and the Crosby capsule aspirate of two, and

cysts were excreted in the stools of two. *Giardia* were not seen in the jejunal biopsies. Two received no treatment for the parasite which was still present after full recovery from tropical sprue. In the third *Giardia lamblia* was eradicated by metronidazole. After no improvement was observed on reinvestigation at two weekly intervals for six weeks, she responded to treatment for tropical sprue. Had the parasite been responsible for malabsorption a response would have been observed within days of starting metronidazole therapy (Hoskins *et al.*, 1967). Three patients had hookworm in loads of less than 100 eggs per gram of stool which would not cause malabsorption (Banwell *et al.*, 1964; Mayoral *et al.*, 1967; Troncale *et al.*, 1967). *Schistosoma mansoni* was present in three but is not associated with malabsorption. Neither hookworm nor *S. mansoni* were treated and all three patients recovered.

#### COMBINED RESPONSE TO ALL TREATMENT REGIMENS

No patient gained weight or had a haematological response while under investigation for approximately three weeks on the hospital diet. In fact, one became frankly megaloblastic during this period and the haemoglobin fell by 3 g. One patient died in hospital on treatment after three weeks. Necropsy revealed no other cause of malabsorption, supporting the diagnosis of tropical sprue. The remaining 30 made a complete clinical recovery. All signs of malnutrition and anaemia disappeared. Weight gain ranged from 0.25 kg with a mean of 10.8 kg. The patient with biochemical evidence of osteomalacia achieved a normal calcium and phosphate on tetracycline alone. Eleven of the 13 with hypoalbuminaemia increased their serum albumins, nine by more than 10 g/l with no change in home diet.

#### Jejunal biopsies

The histological and dissecting microscopy grades of the 25 biopsies that were repeated after treatment are shown in the right hand columns of Fig. 1. Histologically they all improved by at least 1 grade and under the dissecting microscope all 25 were grade 2 or 3. These are highly significant improvements (Wilcoxon matched pairs signed-ranks test  $P < 0.001$ ). Table 3 indicates a similar improvement after treatment, in villous height, villous width, cell height and mucosal thickness ( $P < 0.001$ ). The chronic inflammatory cell infiltrate in the lamina propria improved by two grades in 7, one grade in 10, and remained unchanged in eight ( $P < 0.001$ ).

#### Small intestinal absorption

All abnormal tests of fat, xylose, and vitamin B12

absorption of the 30 survivors were repeated on completion of treatment. Figure 5 demonstrates the pretreatment results in the left hand columns and the values of those reinvestigated after treatment in the right hand columns for comparison. The 12 patients with steatorrhoea returned to normal, the 27 abnormal xylose tests improved, 20 to more than 5 g, and all 30 vitamin B12 absorptions improved, 25 to more than 0.75%, the 95th percentile of healthy African controls. The improvement in all three tests of absorption is highly significant (Wilcoxon matched pairs signed-ranks test  $P < 0.001$ ).

#### Gastric studies

Repeat gastric biopsies revealed no improvement in the six with atrophic gastritis, but four of the seven with chronic superficial gastritis became normal. This apparent recovery may, of course, merely indicate the patchy distribution of superficial gastritis (Joske *et al.*, 1955). The 10 with initial histamine fast achlorhydria had repeat acid studies. Six, who had atrophic gastritis, remained achlorhydric. One, with persistent superficial gastritis, improved but was still hypochlorhydric. Three achieved normal acid output and two of these had initially normal gastric biopsies.

#### INFLUENCE OF TETRACYCLINE ALONE

The nine patients treated for six months with tetracycline alone made complete clinical recoveries. The improvement of jejunal biopsies ( $\chi^2$ ), fat, xylose, and B12 absorption, and the mean weight gain (Mann Whitney U test), showed no statistical difference compared with those who had received additional folic acid and vitamin B12. Of six with megaloblastic and three with normochromic normocytic anaemias, all achieved normal haemoglobins. Four megaloblastic bone marrows became normoblastic and two had minor residual changes. Four of six low serum folates became normal and two improved. Six of eight low red cell folates regained normal levels and two improved. The two with subnormal vitamin B12 achieved normal values. Eight patients, reinvestigated after only three weeks tetracycline, already had significant weight gain and increase in xylose and B12 absorption (Wilcoxon matched-pairs signed-ranks test,  $0.01 > P > 0.001$ ). One of the four patients who received vitamin B12 and folic acid but not tetracycline, for six months, still had a severely abnormal biopsy and three had diminished xylose and B12 absorption. The addition of tetracycline for six months resulted in a greatly improved biopsy, normal intestinal absorption, and further weight increase.

## Discussion

The definition of tropical sprue proposed by Klipstein and Baker (1970) and Lindenbaum (1973) has been widely accepted. They suggest that tropical sprue should be diagnosed when there is symptomatic malabsorption of two or more unrelated substances, and other causes have been excluded. Non-specific jejunal abnormalities are almost invariably present. They emphasise that the clinical picture varies. Many patients present with chronic diarrhoea and evidence of extreme malnutrition, with or without megaloblastic anaemia, but a significant number have complaints relating only to severe anaemia.

The uncertainty concerning the differentiation of tropical sprue from tropical enteropathy can cause difficulty in applying this definition. Klipstein (1967) and Klipstein *et al.* (1969) suggest that their presence in the same populations, the tendency for the two conditions to overlap, and the improvement of tropical enteropathy on accepted treatment for tropical sprue indicate that they are at different ends of the same spectrum. Baker and Mathan (1972) argue that epidemiological evidence favours the existence of two separate entities. They point out the occurrence of tropical enteropathy in Africa where tropical sprue was thought to be absent; the frequency of enteropathy in children in whom tropical sprue is rare; and the regular recovery of tropical enteropathy on moving to a temperate climate, whereas tropical sprue may present for the first time after the patient has left the tropics.

The majority of subjects with tropical enteropathy have mild jejunal abnormalities and xylose malabsorption only. A minority have malabsorption of two unrelated substances and some have recurrent diarrhoea (Lindenbaum *et al.*, 1966a, b; Baker and Mathan, 1972; Klipstein *et al.*, 1972). It is therefore a simple matter to differentiate florid symptomatic tropical sprue from subclinical tropical enteropathy. However, it is difficult to categorise the few subjects with symptoms and malabsorption of one substance or malabsorption of two unrelated substances without symptoms. (Baker and Mathan, 1972; Klipstein *et al.*, 1968; Klipstein, 1970). This debate will be settled only when the aetiological agent(s) responsible for tropical sprue and tropical enteropathy are identified.

Tropical enteropathy in Rhodesia is ubiquitous but subclinical (Thomas *et al.*, 1976). All subjects studied were asymptomatic and had minor jejunal abnormalities, many had xylose malabsorption, but steatorrhoea and malabsorption of vitamin B12 were not seen.

The 31 patients described in this paper, of whom one died, had severe symptomatic tropical sprue.

This is confirmed by the high incidence of anaemia, gastrointestinal complaints, and malnutrition. Electrolyte depletion and hypoalbuminaemia occurred frequently, some patients were grossly dehydrated, and one had osteomalacia. Glossitis and stomatitis were observed only once each, contrasting with the high incidence reported from India (Jeejeebhoy *et al.*, 1968), South East Asia (O'Brien and England, 1971), and in Puerto Ricans (Klipstein, 1964).

Jejunal biopsies were all abnormal, demonstrating the non-specific villous stunting and chronic inflammatory cell infiltrate classically described in tropical sprue, (Baker *et al.*, 1962; Swanson and Thomassen, 1965; England and O'Brien, 1966; England, 1968; Schenk and Samloff, 1968).

Tests of absorption revealed malabsorption of two or more unrelated substances in all patients. Gastric involvement consisting of atrophic or chronic gastritis, achlorhydria, or hypochlorhydria occurred in 75%, which is similar to levels in other series (Floch *et al.*, 1963; Vaish *et al.*, 1965; Baker and Mathan, 1971). The relatively low overall incidence of steatorrhoea (40%) is explained by the inadequate fat content of the diets early in the study. In those patients whose diets were subsequently supplemented to contain 80-100 g of fat the incidence of steatorrhoea rose to 65%, which is probably a more realistic figure.

Klipstein (1968) doubts whether a normal xylose excretion is ever seen in tropical sprue and confirms this to be so in the West Indies. Experience in India is different. Jeejeebhoy *et al.* (1966) report 26% and Baker and Mathan (1971) 6% with normal xylose excretion. Three of our patients (9%) had a normal xylose, but had steatorrhoea and vitamin B12 malabsorption. All three were symptomatic and recovered on treatment. One was admitted emaciated, weighing 25 kg, and gained 20 kg in weight during recovery. There is no doubt that these three patients had tropical sprue.

Tropical sprue is above all a diagnosis of exclusion (Klipstein and Baker, 1970). We have excluded coeliac disease, intestinal tuberculosis, lymphomas, parasites, and other small intestinal pathologies, by clinical investigation, histology, radiology, and response to treatment. Primary malnutrition can be ruled out for three reasons. Firstly, the diets of our patients were no different from those of matched healthy controls. Secondly, there was no clinical or haematological improvement on the hospital diet. Thirdly, we have shown clinical and haematological recovery, with increases of serum albumin, folic acid, and vitamin B12, on tetracycline alone with no change of home diet. Finally, the recovery of these patients after treatment with six months

regimens of a combination of tetracycline, folic acid, and vitamin B12 or tetracycline alone is the expected response of tropical sprue (Guerra *et al.*, 1965; Klipstein and Falaiye, 1969; Rickles *et al.*, 1972). There has as yet been no incidence of relapse on prolonged follow-up after completing treatment.

Megaloblastic anaemia is not an invariable complication of tropical sprue (Klipstein *et al.*, 1966; Jeejeebhoy *et al.*, 1968; Klipstein, 1970), and occurs secondary to malabsorption at a relatively late stage (Klipstein, 1970; Baker and Mathan, 1971). Our selection of patients from a group of megaloblastic anaemias has therefore ensured that the majority of our cases are chronic endemic tropical sprue. Three patients in the present series, however, presented with weight loss and diarrhoea without megaloblastic anaemia, and we have recently investigated three more. Our hospital is the major referral centre for a vast area and only the very sick reach us. It is probable therefore that early tropical sprue is being missed at outside clinics. It is hoped that, as the existence of tropical sprue in Rhodesia becomes more widely accepted, the diagnosis will be made sooner and information on the earlier form will become available.

The absence of convincing reports of tropical sprue in European expatriates has always been a powerful argument against its existence in Africa. Tomkins *et al.* (1974) saw three Europeans in London with tropical sprue who had travelled only in Africa. Many of the early descriptions of possible cases in Africa were Europeans (Begg, 1912; Taute, 1919; Manson-Bahr, 1928; Gelfand, 1947; Limbos, 1956). We have recently investigated a European female with malabsorption who, after exclusion of other causes, has shown recovery of absorption and jejunal morphology on long-term folate and tetracycline. Tropical sprue may therefore occur in Europeans in Africa, but certainly not in the large numbers seen in India, South East Asia, and the West Indies, (Leishman, 1945; Keele and Bound, 1946; O'Brien and England, 1971; Sheehy *et al.*, 1965). There is no obvious explanation for this and clarification may await the discovery of aetiological factors.

The search for tropical sprue in indigenous Africans has been sporadic. Banwell *et al.* (1967) observed the pattern of malabsorption in Uganda. Most of their 45 cases were pancreatic, but two had tropical sprue. They studied only patients with faecal fats of more than 7 g, on a diet containing an average of 39.6 g of fat per day. We have found it necessary to supplement the ward diet to include 80-100 g of fat daily to obtain an accurate assessment of steatorrhoea. From our unit Wicks and Clain (1975) recorded a mean of 9.5 g for faecal fat

excretion in a group with pancreatic steatorrhoea, which is higher than the mean of 5.4 g in our tropical sprue. Steatorrhoea is often absent in tropical sprue (Jeejeebhoy *et al.*, 1968; Cowan *et al.*, 1968; Gardner, 1956; Klipstein, 1968) and the design of the Ugandan study was biased towards gross steatorrhoea and pancreatic disease. It is therefore possible that other cases of tropical sprue were missed.

Foy and Kondi (1971) report a strange series of megaloblastic anaemias from Kenya which they claim not to be due to tropical sprue. They state that the diets of their subjects were adequate and not different from non-anaemic controls. These patients were well nourished with no evidence of weight loss. Investigations for malabsorption were incomplete. All 29 had xylose excretion estimated and the mean value was 19%, but we are not told how many were subnormal. Only 16 had faecal fats done, six vitamin B12 absorption, and six folate absorption. Sixteen had jejunal biopsies and 15 are said to have had normal histology. This is surprising, as the high prevalence of tropical enteropathy in other parts of Africa (Cook, 1974) leads us to expect the same in Kenya. These patients were not treated with antibiotics but Foy *et al.* (1951) had previously shown a response to penicillin. The evidence in favour of a nutritional cause and against tropical sprue is therefore inconclusive and tropical sprue certainly could have been missed in this study.

Cook (1974) has never seen a case of tropical sprue while working in Nigeria, Uganda and Zambia, but has not published a study where he had specifically looked. He describes 85 Zambian megaloblastic anaemias, mostly in females, of whom only one male had malabsorption. No details of the investigations for malabsorption are given. Foster (1968) reports a series of nutritional megaloblastic anaemias from Mombasa, Kenya. Eighty-nine per cent were female and 94% of these were pregnant or post partum. He looked only at people with haemoglobins of less than 5.5 g, but Turner (1962), from the same hospital, found 34% males when he studied patients with haemoglobins up to 8 g. Neither group of patients was adequately investigated for malabsorption. If they had studied more people with milder anaemia, malabsorption might have been revealed. In this context it is interesting that we have yet to see a convincing nutritional megaloblastic anaemia in a non-pregnant adult.

Foster (1968), Foy and Kondi (1971), and Cook (1974) observe a seasonal variation in megaloblastic anaemias. The peak occurs when fruit and vegetables, and therefore dietary folate, are scarce and they suggest this favours a primary nutritional cause. Klipstein and Corcino (1974), however,



have noticed that the majority of tropical sprue patients in Puerto Rico become symptomatic and present at hospital between successive periods of maximum rainfall. In India Leishman (1945) and Keele and Bound (1946) have also observed a peak incidence of tropical sprue at the end of the dry season and during the first month of the monsoon. In Rhodesia, during one complete year, 64% of our patients presented during the rains, having become symptomatic during the dry season, which may indicate a seasonal trend.

When a specific search, using adequate investigations, has been made for tropical sprue in Africa, it has been found. Falaiye (1970) in Lagos, Nigeria, and Moshal *et al.* (1975) in Durban, South Africa, have reported nine and 24 cases respectively. Those observed by Falaiye were atypical in having normal serum vitamin B12s and only minor jejunal damage. A large proportion of those seen by Moshal *et al.* were female and post partum. The cases recorded in this paper are alone from Africa in their close similarity to chronic endemic tropical sprue in India, South East Asia, and the Caribbean. The absence of consistent reports of sprue in European expatriates and the variation in the pattern of the disease in the continent must leave some doubts as to whether the disease seen in Africa is totally identical to classical tropical sprue described elsewhere. However, the condition observed in this study fits the definition of the disease and, unless different aetiological factors are found, it must be classified as tropical sprue.

Falaiye (1970) and Moshal *et al.* (1975) suggest that the occurrence of tropical sprue in Lagos and Durban may be influenced by the hot, humid coastal climate, which is similar to that of other endemic areas. Salisbury, however, is at 5 000 feet and tropical sprue has long been recognised in mountainous regions of the Indian subcontinent (Bahr, 1915; Stefanini, 1948; Mathan and Baker, 1968). It is therefore important that the search in Africa should not be confined to humid coastal areas but should encompass the whole continent.

The precise geographical distribution of tropical sprue in Africa and elsewhere in the tropics is uncertain, because it has not been adequately researched. A more accurate pattern will unfold as more sophisticated gastroenterology units are established. The whole question of tropical sprue in Africa should be re-examined. The assumption that primary malnutrition is responsible for most deficiency states should be challenged. It may well be that this assumption has hitherto concealed the existence of tropical sprue in Africa.

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