IDIOPATHIC TROPICAL STEATORRHEA

A REPORT OF SIXTY CASES

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For many years the occurrence of steatorrhea in “tropical sprue” has been well recognised, especially among Europeans, (Manson\textsuperscript{1}, Fairley\textsuperscript{2}) but the minor forms of this syndrome have not been so well recognised. Recently, the routine investigation and evaluation of fat absorption in patient with chronic diarrhea, and other unexplained gastro-intestinal disorders, has brought to light a surprising number of patients who, in the past, would not have been suspected of having steatorrhea. It is the purpose of this communication to present the results of clinical and biochemical investigation of the first 60 patients who were found to have an abnormal fat absorption, and in whom no organic gastro-intestinal disease such as stricture, tumor, pancreatitis, jaundice, etc. could be found.

MATERIAL

The cases investigated were drawn from the patients attending the medical and surgical departments of this hospital, some being themselves members of the hospital staff. Those investigated were a proportion of the people who complained of chronic diarrhea, or vague abdominal pain or discomfort, or who presented with one of the complications which we later learnt were often associated with this abnormality. Only a proportion of cases could be investigated owing to lack of sufficient facilities, but the cases for study were chosen more or less at random, except that preference was given to those who were more seriously ill and who, therefore, urgently needed hospitalisation, and also to those who were anemic, as we were interested in studying these for another purpose.

METHODS

Fat balance.—The patients were put on a diet containing a known constant intake of fat (usually 50 G. per day). Specimens were discarded for the first three days, and then all stools passed were kept, and the total fat content determined daily, for a minimum period of three days. The fat estimations were done by a modified “wet” method similar to that of van den Kamer et al\textsuperscript{10}.

Oral Glucose Tolerance Test.—After the patient had fasted overnight, a specimen of blood was taken. Fifty grams of glucose dissolved in water was then given to the patient to drink, and venous blood samples taken at half hourly intervals thereafter for two hours. Blood sugar estimations were carried out by the method of Folin and Wu\textsuperscript{8} modified to give true glucose values.

Hematology.—Standard hematological techniques as described by Dacie\textsuperscript{4} were employed.

RESULTS

Age, Sex and Race of the patients.—The sex and presumptive age of the patients, are set out in figure 1. Males preponderated over females in the ratio of 7 : 3. The out-patient attendance at this hospital

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is also weighted in favour of males, but in the ratio of 5.7 : 4.3. All children below the age of twelve are treated in the pediatric department, and no systematic investigation of patients in this age group has been made.

Social status.—The majority of the patients were villagers from neighbouring areas, who worked as unskilled or semiskilled labour, and earned from ten to fifty rupees per month. However, twelve patients were landlords or shop owners, and four were relatively well to do Europeans. This socio-economic distribution is much the same as that of the general hospital admissions.

Duration of Symptoms.—The interval between the onset of symptoms and the time the patients first sought treatment, ranged from two weeks to twelve years, with the great majority (80 per cent) within the first twelve months (figure 2).

Clinical Picture.—Soon after the beginning of this investigation, it became apparent that steatorrhea was occurring in a wide variety of patients ranging from those with symptoms of a severe fully developed "clinical sprue", to those with almost no symptoms. Three representative case history summaries are appended.
Case Reports.—

Case 59.—A twelve year old boy had been quite well until about twelve months previously, when he developed nausea and anorexia which persisted and gradually became worse. Eight months prior to admission he began to suffer from diarrhea, which gradually increased in severity until the month before admission when he was passing 10-15 pale, frothy, bulky, offensive, watery stools per day. Occasionally, for some 30 minutes before the passage of stool, there was colicky lower abdominal pain. For three months he had noticed, in addition, swelling of the ankles, increasing dyspnea on exertion, and soreness of the tongue, and of the angles of the mouth.

Examination showed a thin emaciated boy, with moderate conjunctival and mucosal pallor, pitting edema of the dependent parts, a well marked glossitis and cheilosis, and early pellagroid dermatitis. Observation in hospital confirmed his remarks about the number and character of stools passed. Stool examination showed hookworm ova, but no other abnormal features except for the frequent presence of large amounts of clear mucus. The hemoglobin was 7 G. per cent and the bone marrow was megaloblastic.

Fat balance studies showed a marked steatorrhea with excretion of 25-30 grams of fat a day, a very flat oral glucose tolerance curve (maximum rise 4 per cent) and low total serum proteins (4.5 G. per cent) with a reversal of the albumin-globulin ratio.

Comment.—This patient might well be considered as showing the fully developed picture of "classical sprue".

Case 22.—A 40 year old male farmer came to hospital complaining only of bleeding and prolapsing hemorrhoids. Otherwise he insisted that he was quite well, and that his bowel habit was quite normal, or if anything slightly constipated. He was seen by the surgeon who planned a hemorrhoidectomy, and asked for a hemoglobin estimation as a routine preoperative measure. He was found to have a hemoglobin of 10 G. per cent and the blood film showed a moderate degree of macrocytosis of the red cells. Sternal biopsy showed a megaloblastic change in the developing red cells. Careful observation of his stool habits showed that he was passing 1-2 stools per day most of which were unformed. A fat balance showed a daily average excretion of 15 grams of fat. A glucose tolerance test showed a rise of only five mg. per cent in the level of the blood sugar, and roentgenogram of the small intestine showed clumping and flocculation of the opaque medium together with thickening of the mucosal folds.

Comment.—This patient typifies the symptomless or almost symptomless cases of steatorrhea which are detected only because of the presence of some complication.

Case 1.—An eighteen year old housewife had been quite well until one and a half months before admission when she noticed the gradual onset of anorexia and asthenia. Some ten days later she began to suffer from attacks of colicky lower abdominal pain accompanied by loud borborygmi. This would last half to one hour and be relieved by the passage of a loose watery motion. This occurred three to five times a day, and persisted daily until her admission.

Examination at the time of her admission showed a normally built woman who had obviously lost weight, and had some pitting edema of her ankles. She had a mild iron deficiency anemia with a hemoglobin of 10 G. per cent, and a fat balance test showed an average excretion of 8 grams of fat a day. Repeated stool examinations for parasites showed no abnormality, but fat globules were present in every specimen.

Comment.—This case is representative of a very large group of cases which are intermediate in severity between the two extremes illustrated by the previous two case histories.
SYPMTOMS.—The frequency of occurrence of the various presenting symptoms, and of those elicited by questioning, is set out in figure 3.

1. Bowel habit.—Twenty four patients (40 per cent) volunteered a history of altered bowel habit, and a further thirty two patients (53 per cent) either admitted it after direct questioning, or were found to have an abnormal bowel habit after admission to hospital. The commonest symptom was diarrhea which was present in forty six patients (76 per cent). The severity of the diarrhea varied from the passage of one loose stool, up to fifteen or so per day, but most frequently four to six, loose or semiformal stools were passed per day. Occasionally there was constipation (four patients, 7 per cent) or attacks of diarrhea alternating with periods of constipation (six patients, 10 per cent). In four cases (7 per cent) the bowel habit as stated by the patient, and as confirmed by observation in hospital was normal.

The stools were usually liquid, or soft and mushy, and frequently the bulk of stool was increased considerably. In one case over two litres of stool was passed per day. Only in the more severely affected cases could the stool be described as "bulky, frothy, and offensive". Usually the stools were passed at varying times throughout the day, but in a few the diarrhea was worse in the morning, particularly up to about 11 a.m., after which no further stools would be passed until next morning. Three patients complained of nocturnal diarrhea, with relatively few symptoms in the day time.

It was noted that the history, no matter how expertly taken, was particularly inaccurate on the question of bowel habits, and the amount and character of stool passed in a day. Frequently the statement was made that one normal stool a day was passed, but time and again this was disproved by observation and collection of the stools in hospital.

Passage of mucus in the stools was the chief presenting symptom in four patients (7 per cent) but on direct questioning twenty one patients (35 per cent) admitted noticing it, and a further eight patients (14 per cent) were found to have mucus when the stools were examined. On the other hand blood in the stool was only noticed by two patients, and both of these had bleeding hemorrhoids.

2. Pain.—Thirty eight (63 per cent) of the patient in the present series suffered from abdominal pain or discomfort at some time or other; of these it was a presenting symptom in eighteen patients (30 per cent). This "pain" was of three main types.

(a) Intestinal pain, usually intermittent, or "colicky" in nature, but occasionally more constant. This occurred at some time or other in thirty (50 per cent) of the patients. It was usually felt either in the upper or lower part of the abdomen, presumably depending on whether or not it arose from the small or large intestine. It was usually not very severe, and the occurrence of severe pain was often, but not always, associated with some other disease. There was no relationship to food in the majority of cases, though occasionally eating brought on the pain. When the pain was in the lower abdomen it was frequently relieved by the passage of flatus, or of stool, and when in the upper abdomen by belching or vomiting. The frequency with which the pain was experienced varied considerably. A few patients had this type of pain for the greater part of each day whereas others experienced it only occasionally.
(b) A feeling of fulness in the abdomen often associated with attacks of actual distension occurred in twenty four cases (40 per cent). In a few cases marked distension occurred, and in one case distension of the abdomen up to the size of a seven month pregnancy would occasionally develop rapidly over a period of an hour or so, stay a number of hours, and then disappear as quickly as it had come. This distension appeared to be gaseous in origin since it was frequently relieved by the passage of flatus, and roentgenogram at the time of distension showed dilated loops of air-containing intestine.

(c) A burning sensation retrosternally, and diffusely throughout the abdomen, was present in ten patients (17 per cent). Although apparently never severe it caused some of the patients a lot of worry.

(d) In five cases (8 per cent) there was rectal and perianal pain of a burning nature, especially after defecation.

(3. Nausea and Vomiting.)—Nausea and vomiting were present in some degree in thirty nine patients (66 per cent) and very prominent in nine patients (15 per cent). Nausea alone was the main complaint in five cases (8 per cent). Vomiting in most cases was only of moderate severity, but in four patients it was so severe that pyloric stenosis or intestinal obstruction was simulated, especially when the vomiting was accompanied by colicky abdominal pain and visible peristalsis.

Case Report.—

Case 31.—A 27 year old tailor had been quite well until seven weeks before admission, when he noticed the onset of nausea which was accompanied by colicky upper abdominal pain. At first these symptoms occurred only once in two or three days, but later they increased in frequency and severity until they were occurring four or five times a day. The symptoms were precipitated by eating or drinking, and relieved by vomiting, and could be almost prevented by starving. No other symptoms were elicited, and he stated that his bowel habit was normal.

Examination revealed a man with a moderate degree of emaciation and dehydration. On observing the abdomen for some time well marked gastric peristalsis was seen. A barium meal showed a twenty-four hour residue in the stomach with what was thought to be spasm or stenosis of the pylorus. Some loops of small intestine were dilated, but the significance of this was not appreciated at the time.

A diagnosis of pyloric stenosis was made, and after suitable preparation, laparotomy was performed. At operation apart from some dilatation of the stomach and intestine, no abnormality was found. Postoperatively a more carefully taken history elicited the fact that for some two or three months he had been suffering from lack of energy, and had been passing two or three loose stools per day. Further investigation showed that the patient had a well marked steatorrhea excreting an average of 13 grams of fat per day, a flat oral glucose tolerance curve (maximum rise 5 mg. per cent) and definite abnormalities in the small intestinal roentgenograms not only dilatation of loops but also slow transit time and thickened mucoiJ folds.

He was subsequently treated symptomatically, and he recovered slowly, regaining his usual health after a period of three months.

4. Anorexia.—This symptom was present in forty five patients (75 per cent). In fifteen patients it was the first symptom to appear, and in eleven was throughout the most prominent one.

5. Loss of weight.—Thirty six patients (60 per cent) admitted of some loss of weight. In the more severely affected patients, anorexia combined with nausea,
vomiting and diarrhea led to gross weight loss and emaciation. In general, emaciation was commoner among the poorer patients who lived on an inferior diet even before the onset of their illness.

6. Asthenia.—In six patients (10 per cent), who were among the more observant in the series, the first complaint was one of marked asthenia. This asthenia was noticed even before the development of any alteration in bowel habit. Further nineteen (32 per cent) admitted noticing it when questioned directly.

7. Excessive Borborygmi.—Distressingly loud borborygmi were noticed by twenty three patients (37 per cent), and in three patients this was their chief complaint. Occasionally the occurrence of these loud borborygmi was associated with the presence of colicky abdominal pain, but more often there was no direct relationship between the two.

8. Other symptoms.—These include the symptoms of anemia and cardiac failure, such as breathlessness on exertion and swelling of the ankles (eight cases), of vitamin deficiency such as glossitis (nine cases) and stomatitis (five cases), and of pigmentation of the skin (three cases).

Case Report.—

Case 48.—A 45 year old farmer was well until three months before admission when he noticed gradually increasing pigmentation of the skin especially over the dorsal aspect of the hands and forearms. He complained of no other symptoms, but on direct questioning regarding his appetite, he admitted to having suffered from a mild degree of anorexia and nausea off and on for the previous two months.

Examination revealed a well nourished middle aged man with marked deep-brown pigmentation of the skin, maximal on the exposed parts, and particularly on the dorsum of the hands, and over the flexures. A similar but less marked pigmentation was also present on the buccal mucosa and tongue.

The hemoglobin was 6.0 G. per cent, and the blood film macrocytic. A sternal puncture showed a megaloblastic marrow. The glucose tolerance curve was flat with a maximum rise of 20 mg. per cent. Fat balance study over a ten day period showed an average excretion of 9 grams of fat per day.

Comment.—This case exemplifies in a striking way the pigmentation which may be seen in patients with this syndrome.

Previous History.—In only one patient was there any history of prolonged intestinal disorder suggestive of possible celiac disease in childhood. However, in most cases it was not possible to interview the parents of the patients, so no independent account of early childhood was available.

Five patients had had similar attacks two to seven years previously, but in all the others there was no previous history of diarrhea.

In six patients (10 per cent) the onset of symptoms was associated with an attack of what was diagnosed elsewhere as amebiasis, but which responded only temporarily or not at all, to antiamebic treatment.

In one case the onset of symptoms was associated with the ingestion of a broad spectrum antibiotic for the treatment of a severe respiratory tract infection.

Family History.—Two cases in the present series were husband and wife, and in both the symptoms commenced at about the same time. Apart from this one instance there was no evidence of a familial incidence.

Physical Examination.—As in the clinical symptoms, so on phy-
sical examination, there was a complete range from the patient with no apparent abnormality, to the one with a fully developed "text book" picture of "classical sprue".

**Wasting.**—As already mentioned under symptoms, varying degrees of wasting and emaciation were present in different patients.

**Edema.**—Edema of the dependent parts was present in twenty three patients (38 percent) and was commoner in the more anemic and hypoproteinemic cases. In eight cases it was associated with congestive heart failure secondary to a severe anemia.

In three severely ill patients, generalised edema was present in the absence of congestive heart failure, gross anemia or hypoproteinemia. The cause of this edema was not clear, but may have been related to fluid and electrolyte imbalance following chronic diarrhea.

**Skin and mucous membranes.**—Obvious pallor of the mucosae due to anemia was present in 21 cases. Loss of elasticity and dryness of the skin was present in twenty patients (33 per cent) and was usually associated with some degree of dehydration. In two patients there was frank pellagroid dermatitis. Excessive melanin deposition in the exposed parts, especially on the face and hands, and in the buccal mucosa was found in nine cases (figure 4). In five cases (8 per cent) there were shallow painful ulcers in the mouth which had a tendency to heal and recur.

**Signs of vitamin deficiency.**—Clinical evidence of vitamin A deficiency was present in thirty cases (50 per cent), but whether or not this was related to the intestinal disorder is doubtful, as there is also a very high incidence of vitamin A deficiency in the general population.

Glossitis of varying degrees was present in nineteen cases (32 per cent) and angular stomatitis in ten cases (16 per cent). One patient had diminished knee and ankle jerks and obvious muscle tenderness, which responded rapidly to injections of vitamin B1.

**Abdomen.**—Examination of the abdomen often showed no abnormality, but in twenty four patients (40 per cent) there was gaseous distension, and a "doughy" feeling on palpation. In four cases this distension was very marked.

In five cases (8 per cent) visible peristalsis was seen (2 cases of gastric, and 3 cases of small intestinal origin). This combined with colicky pain, vomiting, abdominal distension and fluid levels seen in the plain roentgenogram of the abdomen on occasion simulated intestinal obstruction.

Moderate enlargement of the liver was present in 18 cases (30 per cent)—eight of these were associated with congestive cardiac failure, three with cirrhosis of the liver and the rest with anemia of varying degrees of severity.

Splenic enlargement was present in five cases; in three the splenomegaly was associated with cirrhosis of the liver proven by biochemical tests and liver biopsy, and in two no definite cause was found. In no case were there any other palpable masses felt.

In seven patients free fluid was present in the peritoneal cavity, but in each case it was associated either with the presence of cirrhosis of the liver, congestive cardiac failure due to gross anemia, or with severe hypoproteinemia.

**Associated Diseases.**—Three patients, in addition to their bowel
disorder, suffered from cirrhosis of the liver with hepatosplenomegaly and portal hypertension, and two had a duodenal ulcer. In eight patients congestive cardiac failure was present on admission; in each case this was associated with a severe anemia.

**Special Investigations.—Stool Examination.**—In fifty six cases (93 per cent) the bulk of the stool passed in twenty four hours was increased. In each case the stools were watery, soft and mushy, or at best semifurmed. Mucus was present in the stool in 63 per cent of the cases at some time or other during their hospital stay, and in a few cases there was a large amount of mucus passed.

Every patient had at least six stool examinations for amebae, cysts, bacillary exudate and ova. In only five patients were *Entamoeba histolytica*, either vegetative forms or cysts, found, and in each of these antiamoebic treatment failed to improve the symptoms. Hookworm ova were found in twenty patients, round worm ova in five, and *Giardia lamblia* in two. This frequency of parasitic infection corresponds approximately to the findings in a general cross-section of the hospital population.

**Fat excretion.**—Fat balance studies in fifteen control subjects showed an excretion of one to four and a half grams of fat per day (91-98 per cent absorption). The sixty patients studied, excreted from six to twenty three grams of fat per day (54-58 per cent absorption). In some patients continuous fat balance studies were done, and, as found by others, there was a considerable day to day variation in fat excretion. Even when this was smoothed out by taking a three day running mean, there were still considerable fluctuations from time to time.

The finding of fat globules in the stool on microscopic examination was highly suggestive of steatorrhea, but the absence of such globules by no means excluded the diagnosis.

Comparing patient with patient, there was little apparent correlation between the degree of fat malabsorption, and the clinical state of the patient, or the number of stools passed per day. However, in a given patient, reduction in the amount of fat excreted often coincided with onset of clinical improvement. There was also some correlation in a given patient between the total bulk of the stool passed, and the degree of abnormality in the fat balance—in general the bulkier the stool the more the fat excretion, and vice versa.

In ten cases the ratio of split to unsplit fat was estimated, and in each the ratio was normal or increased. In the same ten patients fecal trypsin activity was estimated and found to be normal.

**Duodenal Enzymes.**—In ten cases duodenal intubation was performed and lipase and trypsin content of the duodenal juice estimated. In each case lipase and trypsin were present in normal amounts.

**Gastric Acidity.**—Histamine test meals were performed in thirty patients. Five patients had a histamine fast achlorhydria, and in fifteen the test meal was normal. In ten there was hypochlorhydria, but as has been shown by numerous authors the latter is of doubtful significance. (Jones).

**Glucose absorption.**—Oral glucose tolerance tests were done in all patients, and in fifty two (87 per cent) the rise of blood sugar was less than 40 mg. per cent and in twenty (33 per cent) it was less than 15 mg. per cent. There was no correlation between the severity of the
condition as judged by clinical findings and the degree of abnormality in the glucose tolerance test.

_Sigmoidoscopy._—Sigmoidoscopy was performed in fifteen cases, and in four of these there was hyperemia of the colonic mucosa, and in three of the four, the mucosa was friable and bled easily when it was traumatized. No other sigmoidoscopic abnormalities were noticed.

_Roentgenology of the Small Intestine._—In the majority of the cases (90 per cent) there were demonstrable abnormalities in the roentgenological appearances of the small intestine. The commonest abnormalities were dilatation of loops of small intestine, either jejunum or ileum, or both, and coarsening of the mucosal pattern. Other abnormalities found frequently were flocculation of the opaque medium when barium sulphate was used, and even sometimes when so-called non-flocculating barium suspensions were employed, and alterations in transit time, either slow, or less frequently, rapid passage through the small intestine. The roentgenological findings are described in greater detail elsewhere (Paterson and Baker¹⁸). It is important to note, however, that in six cases (10 per cent) there was no demonstrable radiological abnormality of the gastrointestinal tract.

_Serum proteins._—Serum protein estimation was performed in all cases. In twelve cases (20 per cent), the total protein was less than 5 G. per cent, the lowest being 2.9 G. per cent. In eight (13 per cent) there was reversal of the albumin-globulin ratio. There was some correlation between the presence of edema and the degree of wasting, and the level of the total serum proteins and the albumin globulin ratio. In general the more severe the clinical condition, the lower the total proteins and the lower the albumin globulin ratio.

_Hematology._—Thirty five cases (58 per cent) had a hemoglobin of less than 10 grams per cent. A recent survey in this locality²⁹ indicates that this incidence of anemia is greater than in the general population. Bone marrow studies were undertaken in nearly every case of anemia, and sixteen patients (27 per cent) were found to have a megaloblastic bone marrow, and the remainder to have a fairly typical picture of iron deficiency anemia. As already pointed out the incidence of anemia in this series may be unusually high, as the selection of cases for admission was biased in favour of those with anemia.

In general, iron deficiency anemia, when present, responded to the oral administration of iron as ferrous sulphate tablets, or ferric and ammonium citrate mixture. In four cases, however, there was no response to oral iron, and these patients were given intravenous iron to which they responded adequately.

Fifteen of the sixteen patients with megaloblastic anemia responded well to vitamin B₁₂ therapy (100 µg. by injection once a week). The remaining one did not respond to vitamin B₁₂, but did respond to folic acid therapy.

Sometimes patients who originally had a megaloblastic anemia developed iron deficiency while under treatment, and then needed to have iron therapy as well. A detailed analysis of the cases of megaloblastic anemia will be published elsewhere (Baker¹).

The relationship of the iron deficiency anemia to the disease is difficult to determine. In those cases who failed to respond to oral iron, there was presumably failure of absorption of the iron, and this was presumably due to disease of the intestinal wall. However, in the others who responded to oral iron, it is not possible to apportion the
blame. Iron deficiency is very common in the general population, and it may be that these subjects were suffering from iron deficiency even before developing the intestinal disease. However, it is also possible that disease of the intestinal wall interfered with normal iron absorption, when iron was taken in the amounts present in the diet, but that the effects of this absorption defect could be overcome by the administration of the relatively large amounts of iron used therapeutically.

Diet.—In every case an extensive dietary history was obtained as accurately as possible, including an account of the number of meals eaten per day, the type of food stuff eaten, and the amount of money spent by the family, per head, for food. Prior to the onset of symptoms fifteen patients (25 per cent) were judged to be living on a definitely inadequate diet. Thirty eight (63 per cent) were judged to be taking a ‘fair’ to ‘adequate’ diet, and seven (12 per cent) were considered to be eating a ‘good’ or ‘very good’ diet. This corresponded approximately with dietary histories taken on a random selection of surgical patients.

Complications.—Anemia and various vitamin deficiencies were the commonest complications, but these have already been discussed.

Heart failure secondary to the anemia was seen in eight patients. One patient with typical symptoms, but not included in the series because an adequate fat balance study could not be done, came to hospital with severe cardiac failure and a hemoglobin of approximately one gram, and a packed cell volume (P.C.V.) of 6 per cent. An attempt was made to transfuse him with packed cells, but he collapsed and died after receiving about 50 ml. of blood. Permission for autopsy was refused.

Fluid and electrolyte balance may be upset due to the chronic diarrhea, especially when this is associated with anorexia and vomiting. In four cases who were suffering in this way from gross fluid and electrolyte imbalance paralytic ileus developed. Two of the patients died in this state in spite of gastric suction, and what appeared to be adequate fluid and electrolyte replacement therapy. One of the other patients who appeared to be just as ill, recovered after treatment by gastric suction and fluid and electrolyte replacement, and in the fourth, who was deteriorating in spite of suction, and fluid and electrolyte replacement, dramatic improvement followed the use of prednisolone.

One patient, while in the ward, suddenly developed acute abdominal pain, and at laparotomy was found to have extensive mesenteric thrombosis with gangrene of the intestine. He died under anesthesia. Autopsy failed to show any cause for the thrombosis.

Three patients in this series who, when first seen, had normal chest roentgenograms, developed pulmonary tuberculosis while under observation. One of these developed extensive involvement and cavitation of the left upper lobe, and had a severe bout of hemoptysis which necessitated emergency lobectomy. The patient made a good recovery.

Treatment.—Frequently bed rest alone brought about considerable symptomatic improvement, and reduced the amount of stool passed and the frequency of evacuation. Without any other treatment some cases went into spontaneous remission with disappearance of symptoms and return of the fat balance to normal (figure 4). Some of these have not relapsed for periods of up to twelve months. It is, therefore, particularly difficult to assess the value of any specific therapy.

We have employed folic acid orally and parenterally in a total of twenty cases, but have been unable to show any definite response. Some
people given folic acid improved, but it was our impression that they would have done so anyway, and certainly in those where folic acid has been discontinued there has been no relapse. One patient had been receiving large amounts of folic acid daily for five months prior to consulting us, but there had been no significant improvement, and the fat balance still showed an average daily excretion of 18 grams of fat. Withdrawal of the folic acid made no difference. More recently patients have been studied by the continuous fat balance technique, and as yet we have not been able to demonstrate any case in which folic acid treatment decreased the degree of fat excretion during the period of observation.

Folic acid was, however, of undoubted therapeutic value in the patient suffering from a folic acid deficiency anemia. With the administration of the drug the sense of well being was increased, the marrow reverted to normoblastic pattern, and the anemia was cured, but the level of fat excretion remained unchanged (figure 5.)

The same is true of vitamin B₁₂. In the absence of vitamin B₁₂ deficiency, the use of this vitamin has been without demonstrable effect on the course of the disease. In patients with a B₁₂ deficiency anemia and a low serum B₁₂ concentration, administration of B₁₂ has cured the anemia, but in no case has there been a clear cut effect on the fat balance. Four cases who were treated with B₁₂ have been followed up for periods of 8-12 months. Of these two now appear normal, with normal bowel habits, a normal 3 day fat balance, a normal glucose tolerance test and no anemia. The other two have no anemia and a normal serum B₁₂ concentration, but still pass 2-3 loose stools per day and still have an abnormal fat balance.

Our standard regime of treatment, once the diagnosis was confirmed, was to endeavour to control the diarrhea and abdominal pain by the use of bismuth, or, especially when there was colicky pain, the use of a mixture of tincture of opium minims ten, and tincture belladonna minims ten, suitably flavoured and made up to half an ounce. This was given three or four times a day and the dose adjusted as necessary to suit the needs of the individual patient.

Any vitamin deficiency was corrected either by oral, or preferably, parenteral administration of the appropriate vitamin. The anemia was corrected by administration of the appropriate hematinic. In cases of iron deficiency, iron was given by mouth, and if this was unsuccessful due to defective absorption, it was given parenterally. In cases of megaloblastic anemia due to vitamin B₁₂ deficiency, vitamin B₁₂ was given by injection, and in the one case of folic acid deficiency anemia, injections of folic acid were given.

In patients where there had been gross weight loss and reduction in serum proteins, a high protein diet was employed. Fats were usually allowed according to the desire of the patient except when fat balance studies were in progress. However, in those cases where fats were restricted in quantity, there was no demonstrable difference in the clinical course. Some patients found that hot foods and fibrous vegetables aggravated their symptoms but others found that they made little difference.

One co-operative and intelligent patient was given an extended trial of a gluten-free diet for 8 months. During this time she improved considerably, and her fat balance returned to normal, but on stopping the
gluten-free diet she did not relapse, so that the evidence for any benefi-
cial effect of the gluten-free diet was rather slender.

A few patients have been tried on oral chemotherapy with alternate
courses of chloramphenicol, streptomycin, sulphaguanidine and
tetracycline. Some of these showed no improvement, others showed
temporary improvement as judged by the fat balance and the number
of stools passed per day, but relapsed when the chemotherapy was stop-
ped, and others appeared to show more lasting improvement. Further
work on the use of antibiotics is in progress.

Prednisolone in divided daily doses of 40-50 mg. per day was tried
in four cases, for periods up to 15 days, but in no case was any effect
demonstrable on the excretion of fat, although all the patients noticed
marked subjective improvement while taking the drug. In one case,
already mentioned, where the patient was desperately ill with gross fluid
and electrolyte imbalance associated with paralytic ileus, the adminis-
tration of 50 mg. of prednisolone daily in divided doses, produced dra-
matic improvement in the general condition, and was probably life
saving.

**Discussion**

*Differential Diagnosis.—* Before the full recognition of the clinical
manifestations of this syndrome, a large number of cases were being
misdiagnosed as suffering from abdominal tuberculosis. Clinically there
may be very little difference between them. Evidence of tuberculosis
elsewhere may possibly favour a diagnosis of intestinal tuberculosis, but
it must be remembered that patients with steatorrhea may be particu-
larly prone to secondary tuberculous infection. In the absence of tuberc-
ulous ascites, careful radiological examination of the small intestine
may often be the only way of diagnosing tuberculous enteritis. (Pat-
erson and Baker). The points which should be particularly looked for
are: (a) the presence of strictures, or of localised constant dilated loops
due to a distal stricture, (b) fixation of the loops of small intestine, and
(c) the presence of mucosal ulceration. The presence of any or all of
these radiological findings, makes the diagnosis of idiopathic steatorrhea
improbable.

Other things beside tuberculous enteritis may present a similar cli-
nical and biochemical picture, especially regional enteritis, and other
diseases which produce strictures in the small intestine. Again adequate
roentgenological examination may be the only means short of laparotomy
whereby these conditions can be diagnosed.

**Case History.—** A twenty-eight year old labourer had been quite well until two
months before admission when he noticed the onset of vague central abdominal
pain, together with attacks of abdominal distension and occasional attacks of
diarrhoea, with the passage of 4 to 6 watery stools per day.

On examination he was emaciated and dehydrated and had moderate pallor
of the mucous membranes. Abdominal and rectal examination revealed no abnor-
mality. His hemoglobin was 9 grams per cent, and examination of a blood film
showed an iron deficiency type of anemia.

Barium meal examination done without films, for the sake of economy, showed
coarsening of the mucosal pattern, some clumping of the barium suspension, and
dilatation of loops of intestine.

A fat balance study revealed an excretion of an average of thirteen grams
of fat per day, and a flat glucose tolerance curve.

A provisional diagnosis of idiopathic steatorrhea was made and treatment insti-
tured. About two weeks after the first roentgenray, it was decided to repeat the barium meal examination. This time films were taken and a stricture was clearly demonstrated in the upper jejunum.

Subsequently laparotomy was performed, the presence of the above stricture confirmed, and in addition twenty three other smaller strictures were found. The most severely affected portion of the intestine was resected, and the patient made a good recovery.

Histological examination of the affected areas showed a chronic inflammatory process resembling Crohn's disease.

Other gastrointestinal disorders such as carcinoma of the stomach or esophagus, pyloric stenosis and peptic ulcer may sometimes be simulated. One case had actually been referred to the thoracic surgeon as a case of carcinoma of the esophagus for resection, and only when roentgenology revealed a normal esophagus was any other diagnosis entertained. However, by careful history taking and examination, combined with good roentgenology, the correct diagnosis can usually be arrived at, and this can be confirmed by fat balance studies, because patients suffering from these other diseases will not usually have steatorrhea.

The combination of asthenia, pigmentation, vomiting and diarrhea, fluid and electrolyte imbalance and a flat glucose tolerance curve may sometimes simulate Addison’s disease of the suprarenals. The situation may further be complicated by the finding of a positive Klepler test, and a low 17-ketosteroid excretion such as occurred in two cases of this series, and has been noted by others (Rivas et al¹⁹). In such cases the diagnosis of idiopathic steatorrhea will often be suggested by the fact that the bowel disturbances start early in the clinical course of the disease, and will be supported by the presence of steatorrhea, which is said not to occur in Addison’s disease, and by clinical improvement without specific hormonal therapy. Moreover, in this part of the world this syndrome is very much more common than is Addison’s disease.

Complaints of asthenia, anorexia and nausea, with or without vague abdominal discomfort and diarrhea, may sometimes be wrongly attributed to psychoneurosis. A carefully taken history may help to differentiate between the two. Roentgenology and fat balance tests may also help. In psychoneurosis increased motility may be demonstrable on barium meal examination (Golden⁹), but mucosal changes do not seem to occur (Paterson¹⁷). In our experience steatorrhea does not occur in cases of psychological disorder of intestinal function (Baker⁹).

Differentiation from other causes of chronic diarrhea is important. The presence of blood in the stools suggests that the diagnosis is not that of idiopathic steatorrhea, and usually indicates that the patient is suffering from amebic dysentery, ulcerative colitis or colonic neoplasm. In only 2 of our cases was blood present in the stools and in each case the patient had hemorrhoids. It must, however, be remembered that bleeding from the intestine has been described in cases of non-tropical “idiopathic steatorrhea” (Cook et al⁸) and it may, therefore, be expected to occur occasionally in these cases.

In the absence of blood in the stools it may be difficult to distinguish chronic amebic dysentery from cases of this syndrome. In each instance repeated careful stool examinations should be made for the presence of amebae and cysts, but even if they are present the amebae may not be the cause of the symptoms. Treatment and eradication of the amebae will be rapidly effective in bringing symptomatic relief in cases of amebiasis, but this is not so in cases of steatorrhea. Three of our cases
were made semi-invalids by having been given excessive antiamebic therapy elsewhere because they had failed to respond symptomatically to adequate antiamebic treatment. In each case their symptoms were those due to the disorder of the small intestine and not to amebiasis.

Other causes of steatorrhea such as intestinal short circuits, biliary obstruction, fibrocytic disease, and pancreatitis can usually be excluded by careful history taking and adequate roentgenological examination. Occasionally duodenal intubation may be necessary to ensure the presence of normal amounts of pancreatic enzymes. Whipple’s disease, lymphosarcoma, and other disorders affecting the intestinal lymphatics may be undiagnosable without the aid of a laparotomy (Saint et al\(^20\)), and this may on occasion be justifiable, if cases which appear to be suffering from idiopathic steatorrhea fail to respond to conservative treatment.

Prognosis.—Since a number of patients come from a distance, and since, if patients are well, it is hard to persuade them to return to hospital, it has only been possible to follow up eighteen cases (30 per cent). Of these, the majority have been in complete remission for periods of two to twelve months after leaving the hospital. However, five patients, although improved, still have symptoms, and in three of these in whom it was possible to repeat the tests, steatorrhea still persisted after 6, 9 and 13 months respectively. One patient appeared to be cured, but relapsed six months later.

The fact that most patients seem to recover without specific therapy, and the fact that the great majority of patients present with a history of less than twelve months duration, suggests that this is probably a self-limiting disease. If it were often a chronic disease, one would not expect so many patients to recover spontaneously, and one would expect a very much greater proportion of patients to have had symptoms for more than a year before coming to hospital. It is, therefore, obvious that any “cures” must be very carefully evaluated in the light of this tendency to spontaneous remission.

Etiology.—The etiology of this disease is, like that of “tropical sprue”, quite unknown. As already pointed out, it may well be that this is a syndrome rather than a disease entity, and consequently it may be found that there are a number of etiological agents which can produce or initiate this disorder. At various times it has been suggested that “tropical sprue” may be due, among other things, to bacterial or virus infection (Keele and Bound\(^11\)) (Manson-Bahr\(^12\)), food allergy (French\(^2\)) dietary deficiency (McCarrison\(^15\)) and folic acid deficiency (Spies, et al\(^21\)). Of these, as pointed out already, folic acid deficiency does not appear to play any part in our cases. Similarly we could adduce no evidence that dietary deficiency played an etiological role, since the syndrome was found in well nourished patients living on a very good diet. and there was moreover, no detectable difference between the diets of affected individuals and those of a control group of hospital patients with other diseases. So far we have not been able to obtain any conclusive evidence for or against the infective or the allergic theories, but further studies are in progress and will be reported later.

Several cases in this series had amebiasis, or had a history of having been treated for amebiasis in the recent past. It is possible that amebiasis may be a precipitating factor, but it is difficult to conceive of the small intestine being involved in what is thought to be a purely large intestinal infection.
The onset of symptoms in one case followed the use of a broad spectrum antibiotic. Further cases of post-antibiotic diarrhea must be studied before the significance of this association can be assessed.

Terminology.—It is difficult to know what to call these cases. Some of the more severely affected ones conform to the fully developed classical picture of “tropical sprue,” as described by Fairley, Manson Bahr and others, but a large number of the milder ones do not, and there are all clinical and biochemical gradations between the mildest and the most severe.

The more severely affected cases of this series could certainly be labelled “tropical sprue”, as has been done in the past. However, to separate these cases from the others is not justified on the basis of our present knowledge, since this study has shown that no clear cut distinction between the “mild” and “severe” cases is possible; also many of the criteria used in the past for the diagnosis of sprue, such as the presence of anemia and vitamin deficiencies, are in fact secondary to the intestinal disease and are not primary.

On the other hand to call all these cases “sprue” may be misleading, as the term “sprue” conveys a definite clinical picture to some people. The term “parasprue” as applied by Napier to somewhat milder cases may likewise be misleading, and again no clear cut distinction between “sprue” and “parasprue” is possible (Stefanini).

It is also likely that we are dealing not with one disease entity, but with a variety of conditions which have certain features in common and hence may be looked upon as a syndrome which may occur in all grades of severity. This syndrome may be defined as a disorder, occurring in the tropics, in which there is steatorrhea associated with other biochemical and/or roentgenological evidence of intestinal dysfunction, but in which there is no evidence of pancreatic or biliary disease, and no evidence of known organic lesions of the intestine such as regional ileitis, tuberculous enteritis, etc. We have called this syndrome tropical idiopathic steatorrhea.

This is a non-specific descriptive term and, therefore, appears preferable to “sprue” or “parasprue” which often convey the idea of a disease entity, and which mean different things to different people.

Relationship to “non-tropical sprue”.—This syndrome often bears close resemblance to idiopathic steatorrhea as seen in non-tropical regions and it may be that it is one and the same syndrome. There are, however, certain differences, such as the relative frequencies of B₁₂ and folic acid deficiencies—the former apparently being relatively much more frequent in the tropical variety and vice versa in the non-tropical cases. However, the exact relationship between the two will not be clear until we have further information regarding the etiology and pathology of both syndromes.

Frequency of occurrence.—We have been surprised by the number of patients who present with this syndrome. In a medical out-patient clinic we have found that cases of idiopathic steatorrhea are as common as cases of peptic ulcer of which there is a high incidence in South India. The great importance of recognising the clinical features of this disorder is, therefore, obvious.

It has been said in the past that “sprue” is a disease occurring only, or chiefly, in Europeans, and Napier states that “it is very rare in dark southern and eastern Indians”, but this study has shown that this is by
no means the case. In fact, if our experience is at all representative, this is a very common disorder, and a large number of the indigenous population of South India must suffer from it at some time or other. The importance of determining the etiology, and hence the best methods of treatment and prevention is, therefore, self evident.

**Summary**

The clinical and biochemical findings in a group of 60 patients with idiopathic steatorrhea, are reviewed.

Clinically there was a complete gradation of cases, from those who were almost symptom free and practically normal on physical examination, to those with the classical symptoms and signs of fully developed "sprue".

It is suggested that this may not be a well defined disease entity but rather a symptom complex, or syndrome, characterised by steatorrhea and other evidence of intestinal dysfunction. For this reason the designation "tropical idiopathic steatorrhea" has been suggested for use until such time as the etiology is determined.

Contrary to experience elsewhere, folic acid and vitamin B₁₂, apart from their effect on hemopoiesis, did not produce any demonstrable improvement, but the use of antispasmodic drugs often gave marked symptomatic relief. Over a period of weeks or months the disease tended to go into spontaneous remission.

Common complications of this disorder are loss of weight, vitamin deficiencies, and anemia, and less commonly gross fluid and electrolyte imbalance.

The etiological factors which cause this syndrome remain unknown.

The frequency with which this syndrome occurs among the Indian population makes its recognition and investigation a matter of great importance.

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**References**


Vitamins in Infectious Diseases.—"The influence of vitamin nutrition on resistance to specific infections in the human subject remains largely unknown. There is considerable evidence that infections, and other stress situations, influence the requirement or utilization of certain vitamins, but there are few, if any, data regarding exact requirements in specific pathologic states. The therapeutic value of administration of large doses of vitamins in infection has not been appraised critically." . . .—G. A. Goldsmith: New Eng. J. Med. 254: 164, 1956.

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Beneficial Concussion.—"Did I have a time with my wife!" related Meyerhoff. "Such a grand lady, she had to go to a hotel that charges 40 dollars a day! Yesterday she went horseback riding. Right away she fell from the horse, hit her head, and knocked herself out. The doctor says she will be unconscious three weeks." "Unconscious three weeks?" echoed Myron. "What are you going to do?" His friend shrugged philosophically. "Why—move to a cheaper hotel, of course!"—The Bright Side, J.A.M.A. 162: 11, 98, 1956.