ACUTE ENTERITIS WITH TEMPORARY INTESTINAL MALABSORPTION

BY

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Increased clinical interest and improved methods of study have demonstrated in recent years that defects in alimentary absorption may occur in patients who do not present the clinical picture of advanced alimentary insufficiency represented by the sprue syndrome. It has also been shown that these defects may be found to a greater or less degree in a variety of diseases, which include biliary obstruction, pancreatic insufficiency, abdominal reticuloses, mesenteric vascular disease, and enteropathies such as regional enteritis and coeliac disease. It would seem reasonable that impairment of small-bowel function might occur in association with acute gastro-enteritis, but this has not been fully documented and few reports of such cases could be found in the literature available to us.

The occurrence of potassium depletion after diarrhoea has been reported by several observers, and it has also been shown that increased faecal loss of potassium is frequent in the malabsorption syndrome (Comfort *et al.*, 1953; Cooke, 1957). These observations refer to chronic alimentary insufficiency with prolonged diarrhoea, but there are also occasional case reports suggesting it may complicate acute episodes. Achor and Smith (1955) reported the case of a man aged 51 who developed hypokalaemia and muscle degeneration after an acute episode of diarrhoea and vomiting. Investigation of this case revealed steatorrhoea and oral and intravenous glucose-tolerance tests suggesting impaired alimentary absorption. These returned to normal on his eventual recovery. Achor and Smith could find no such case in the literature, though the one described by Ariel (1954) might possibly have been similar. Two other relevant cases have both been associated with some congenital abnormality of the spleen. Alexander (1958) described the case of a man aged 72 with congenital absence of the spleen who developed chronic enterocolitis with steatorrhoea after an infection with *Salmonella tennessee*, and Zelman and Lewin (1958) reported the case of a 25-year-old man with intestinal malabsorption, hypogammaglobulinaemia and multiple congenital anomalies, including a right-sided spleen. In this patient the radiological appearances of the bowel became normal after cessation of the diarrhoea.

In children, fat-absorption amounts to 85–90% of the oral intake, and this figure may fall to 60% or less in the presence of diarrhoea. There is also evidence that amino-acid absorption curves show temporary depression in infants after acute gastro-enteritis (Bate and James, 1956).

Mention must also be made of the experimental studies of Reynell and Spray (1958), who found that rats

with an enteritis due to castor oil or mercuric chloride solution had defective absorption of glucose and iodide by the small intestine, independent of changes in motility.

The present paper reports two cases which provide some evidence that severe acute enteritis in adults may be followed by a transient phase of intestinal malabsorption of considerable clinical significance. The laboratory methods used have been discussed elsewhere and do not require further description (Benson *et al.*, 1957; Pitney and Stokes, 1958; Joske and Blackwell, 1959).

Case 1

A farmer aged 66 was admitted to hospital on November 19, 1958, disorientated and in a state of circulatory collapse. He lived alone and had been well until five days previously, when he had a rapid onset of copious diarrhoea. At this time he was seen by his physician, who prescribed sulphonamides. His initial response to treatment was good and the diarrhoea ceased, so that he was not seen again for four days, when he was found collapsed and semicomatose, and was at once referred to hospital.

He was inaccessible on examination, but responded to painful stimuli. There was marked dehydration, with peripheral cyanosis and stasis indicative of circulatory failure. His blood-pressure was 120/60 mm. Hg and his heart moderately enlarged. Respirations were periodic at a rate of eight a minute. His abdomen was rigid but without distension or detectable tenderness. He was incontinent of faeces.

Initial investigations confirmed the clinical impression of infection and fluid and electrolyte depletion: haemoglobin, 13.8 g./100 ml.; white-cell count, 21,100/c.mm., with a polymorphonuclear leucocytosis; serum Na, 107 mEq/l.; serum K, 4.9 mEq/l.; blood sugar, 136 mg./100 ml.; blood urea 268 mg./100 ml.; serum albumin, 2.8 g./100 ml.; serum globulin, 2.7 g./100 ml. Stool cultures at this time grew a *Salmonella* group B organism.

Treatment was begun on admission with intravenous fluid and electrolyte replacement and parenteral tetracycline, 250 mg. six-hourly. Despite intensive therapy, however, adequate hydration was not achieved for two days. During this time he remained disorientated, with slow irregular respirations, and an area of gangrene developed on the tip of his tongue. Five days after admission he experienced abdominal distension and retention of urine: his serum potassium was found to be only 2.9 mEq/l. Parenteral potassium supplements were increased to 200 mEq daily, and thereafter he slowly but steadily improved. After three weeks in hospital he was rational and continent and was eating well. No pathogenic organisms were found on faecal culture, and all antibiotic therapy was stopped. He had, however, some diarrhoea and his weight fell from 150 lb. (68 kg.) on November 29 to 138 lb. (62.6 kg.) on December 13 despite a normal ward diet. A barium meal on December 11 showed no abnormality of the stomach or duodenum, and there was a normal rate of small-bowel transit, but with some segmentation of barium in the ileum. His final discharge from hospital was delayed for social reasons until January 12, 1959, at which time his weight was 146 lb. (66.2 kg.).

He has since been seen periodically in the out-patient clinic, and has remained well. At his last visit on September 30, 1959, he was well and had no diarrhoea or other alimentary symptoms. Clinical examination showed no significant abnormality. His blood-pressure was 160/100 mm. Hg and his weight 157 lb. (71.2 kg.). A barium meal at this time showed a normal small-bowel pattern.

Further Investigations

This patient was well, without symptoms of alimentary disease and maintaining a constant weight, until he had an acute illness with diarrhoea followed by circulatory collapse.

At this time *Salmonella* group B organisms were recovered from his faeces. There is thus strong clinical and bacteriological evidence that he was suffering from acute bacillary dysentery. After this acute illness he continued to have some diarrhoea and to lose weight, while a barium meal showed a "malabsorption pattern" in his small bowel. Further investigations of alimentary function were therefore undertaken during his convalescence, and these provided additional evidence of a temporary absorption defect with eventual recovery. Some of the results of these investigations are shown in Table I.

TABLE I.—*Biochemical Results from Case 1, Showing Temporary Depression of Protein, Lipid, and Calcium Levels, With Later Return to Normal*

Date	Serum Albumin (g./100 ml.)	Serum Globulin (g./100 ml.)	Plasma Carotene (μg./100 ml.)	Serum Cholesterol (mg./100 ml.)	Blood Urea (mg./100 ml.)	Serum Calcium (mg./100 ml.)	S.G.O.T. (Units)	Serum Amylase (Units)
20/11/58	2.8	2.7	—	—	268	6.6	—	420
24/11/58	2.4	3.0	87	136	310	—	53	227
23/12/58	2.4	3.5	—	—	43	9.2	41	196
15/12/58	2.5	3.8	79	—	—	8.9	—	—
29/12/58	2.9	3.5	—	—	32	9.9	—	307
8/1/59	3.2	3.3	—	—	—	10.5	13	207
28/1/59	4.1	3.6	200	—	—	—	—	227
24/3/59	4.2	3.5	166	256	40	—	—	—

Electrolyte Metabolism.—The initial electrolyte picture was of gross electrolyte depletion with acidosis. Treatment of this brought a progressive fall in serum potassium from 4.9 mEq/l. on admission to 2.7 mEq/l. five days later. However, as the patient was incontinent of urine and faeces, no measurements of electrolyte content of urine or faeces were possible. The high blood urea which returned rapidly to normal was probably also a manifestation of fluid and electrolyte depletion (Table I).

Haematological Studies.—Defective absorption of vitamin B₁₂ was demonstrated on two occasions. With an oral dose of 0.6 μg. ⁵⁵Co-vitamin B₁₂ (Pitney and Stokes, 1958) there was a urinary excretion of 1.4% of the ingested dose on December 19, 1958, and of 2.4% on January 6, 1959. When the tests were repeated with 50 mg. of intrinsic factor, the corresponding results were 19.3% and 27.6% respectively, which are within the normal range.

These results show an intrinsic-factor deficiency of the pernicious-anaemia type, and their explanation is uncertain. It may be either that the patient had in fact subclinical pernicious anaemia or that the results represent the absorptive defect which may follow severe infection of any type.

Fat Absorption.—Defective fat-absorption was shown by a six-day fat balance from December 13 to 18. With a fat intake of 80 g. daily, faecal excretion was 5.8 g./day as stearic acid. There were also low plasma levels of carotene and cholesterol, which returned to normal during succeeding months (Table I).

Protein Absorption.—Abnormal protein absorption was suggested by a low serum albumin level on admission with a later return to normal (Table I). There is no evidence of whether this represents a true absorptive defect or an acute protein-losing enteropathy associated with the acute enteritis (Gordon, 1959).

Carbohydrate Absorption.—The D-xylose absorption test was performed on three occasions before the patient was discharged from hospital. On two of these, five-hour urinary excretion figures of 1.1 and 1.9 g. indicated impaired carbohydrate absorption. The other test gave a normal five-hour urinary excretion of 5.8 g.: the explanation of this result is unknown.

Other Data.—There was a low serum-calcium level on admission (Table I), which was accompanied by a serum inorganic phosphate of 15.2 mg. P/100 ml. Both of these rapidly returned to normal, and were therefore regarded as a reflection of disturbed renal function rather than of alimentary disorder. Conventional liver-function tests were

normal on all occasions. Transient increases in serum amylase and glutamic oxalo-acetic transaminase probably reflected temporary pancreatic damage during the acute phase of the illness.

Case 2

A male pensioner aged 75 was admitted to hospital on September 25, 1958, for investigation of generalized muscular weakness. He had been well until two weeks previously, when he developed diarrhoea which had persisted until two days before admission. This was not excessive, however, and he did not seek medical advice at this time. On the day of admission he suddenly became unable to move his legs or to sit up in bed. Because of these symptoms he consulted his family physician, who referred him immediately to hospital.

Examination showed him to be an elderly man with an obvious Parkinsonian tremor. His temperature was normal and his blood-pressure 170/100 mm. Hg. His heart was slightly enlarged, with a grade 1 systolic ejection murmur at the apex, and his peripheral vessels were somewhat thickened and tortuous. His abdomen was grossly distended but soft and not tender to palpation, and occasional high-pitched borborygmi were audible. Examination of the nervous system showed gross diminution of muscular power and tone, with absent deep tendon reflexes in the legs. The plantar responses were both flexor. There was some weakness of the muscles of the back. In the upper limbs power was moderately diminished and the tone increased. The tendon reflexes were present, equal, and brisk. Cranial nerves and sensory system showed no abnormality.

Initial investigations showed severe hypokalaemia: haemoglobin, 13.4 g./100 ml.; white-cell count, 11,200/c.mm., with a polymorphonuclear leucocytosis; serum Na⁺, 140 mEq/l.; serum K⁺, 1.9 mEq/l.; serum Cl⁻, 94 mEq/l.; serum HCO₃⁻, 30 mEq/l.; blood urea, 240 mg./100 ml.; serum albumin, 2 g./100 ml.; serum globulin, 4.4 g./100 ml. Electrocardiogram; prolongation of the P-R interval, depression of the ST segments, and a well-defined U wave, consistent with hypokalaemia. A plain x-ray film of the abdomen revealed gross gaseous distension of small and large bowel, with fluid levels; and a barium enema

FIG. 1.—Case 2. Barium enema shortly after admission, showing gross dilatation of small and large bowel.

showed the opaque material to enter the dilated loops of colon with ease, excluding a low intestinal obstruction (Fig. 1). Faecal cultures taken at this time grew no pathogenic organisms, but a later specimen showed a moderate growth of *Staphylococcus aureus*, which was treated with antibiotic therapy.

A diagnosis was therefore made of hypokalaemia with neuropathy and paralytic ileus. Treatment was begun with intravenous fluid and electrolyte with added potassium chloride. A total of 980 mEq of potassium was given during the first 40 hours, after which his serum K level was 2.9 mEq/l. These measures were accompanied by clinical improvement, so that further potassium supplements were given orally. However, his diarrhoea recurred two weeks later, and further intravenous therapy was necessary to correct a serum K⁺ level of 2.1 mEq/l. He was eventually maintained on an oral dose of 160 mEq daily as potassium chloride.

During convalescence further investigation of the cause of his hypokalaemia was undertaken. Radiological and biochemical evidence of intestinal malabsorption was obtained. A barium meal on November 6, 1958, showed the typical flocculation and alterations in luminal calibre of the malabsorption syndrome (Fig. 2). The biochemical

FIG. 2.—Case 2. Barium meal after recovery from the acute phase, showing irregularity of calibre of the small bowel with flocculation of barium sulphate medium.

findings are discussed below. He was finally discharged from hospital on November 29, at which time his weight was 120 lb. (54.4 kg.).

He has been seen since in the out-patient clinic. At his first visit on December 11 he still had some diarrhoea and his weight was unchanged. Treatment was therefore begun with prednisone, 30 mg. daily, and further supplements of potassium chloride. On January 6, 1959, he was well and symptom-free; the dose of steroid was therefore reduced, and it was discontinued at the end of the month. When last seen on May 5 he was free of symptoms and his weight was 163 lb. (73.9 kg.).

Further Investigations

These are presented as in the previous case.

Electrolyte Metabolism.—The clinical picture in this case was that of potassium depletion, and there is considerable evidence that this was due to excessive loss of potassium

in the faeces. When on oral potassium chloride supplements the patient had a persistently low urinary potassium excretion from 7 to 25 mEq daily. Faecal potassium excretion was measured on two occasions, values of 120 mEq/day and 110 mEq/day being obtained on October 15 and November 19 respectively. The normal faecal potassium is of the order of 10 mEq/day. Faecal potassium losses of the order of 100 mEq/day in the presence of normal or low serum and urinary levels are strong presumptive evidence of intestinal malabsorption (Cooke, 1957). As in the previous case, the initial elevation of the blood urea is thought to be due to electrolyte depletion and hypokalaemia.

Haematological Studies.—Defective absorption of vitamin B₁₂ was present in this patient. On November 14, 1958, a urinary excretion test using 0.6 µg. of ⁵⁸Co vitamin B₁₂ gave a figure of 6.5% of the ingested dose. When this was repeated with 50 mg. of intrinsic factor a value of 14.1% indicated that absorption was still subnormal.

This patient also had a histamine-fast achlorhydria, shown by biopsy to be the result of atrophic gastritis.

Fat-Absorption.—No fat balance was possible in this case, but depressed fat-absorption was suggested by the low levels of plasma carotene and serum cholesterol and total lipids (Table II), all of which increased during the period of observation, though the carotene at no stage reached the lower limit of the normal range (70 µg./100 ml.).

TABLE II.—Biochemical Results from Case 2, Showing a Depression of Albumin, Cholesterol, and Total Lipid Values Returning to Normal, and a Persistently Low Plasma Carotene Level

Date	Serum Albumin (g./100 ml.)	Serum Globulin (g./100 ml.)	Plasma Carotene (µg./100 ml.)	Serum Cholesterol (mg./100 ml.)	Total Plasma Lipids (mg./100 ml.)	Blood Urea (mg./100 ml.)	Serum Calcium (mg./100 ml.)	Serum Phosphate (mg./100 ml.)
30/9/58	2.0	4.4	—	168	—	241	—	—
6/10/58	2.3	4.0	—	—	—	92	8.7	3.3
13/10/58	2.6	5.2	—	—	—	32	9.4	—
21/10/58	2.4	4.1	—	—	—	151	—	—
11/11/58	2.8	4.2	14	215	310	44	9.5	—
17/11/58	2.8	4.1	—	—	—	—	—	—
11/12/58	4.1	3.8	43	—	—	90	—	—
13/5/59	3.4	3.7	27	253	910	35	9.2	3.3

Protein Absorption.—As in the previous case, there was an initial hypoalbuminaemia, with a later return to normal levels (Table II).

Carbohydrate Absorption.—A D-xylose absorption test on November 13 showed a urinary excretion of only 1.4 g. in five hours, indicating carbohydrate malabsorption.

Other Data.—There was a slight hypocalcaemia on admission but no change in serum inorganic phosphate. Liver-function tests, serum amylase, and glutamic oxaloacetic transaminase were normal on all occasions. Plasma magnesium on one estimation was depressed to a value of 1.5 mEq/l., the normal value for this hospital being 1.9 to 2.5 mEq/l.

Assay of the urine for aldosterone did not show this to be increased.

Discussion

The sequence of events in these patients was similar. Both were well, with no abdominal symptoms and maintaining a steady weight, until the occurrence of an acute episode with the clinical features typical of acute enteritis occurred, leading to an illness severe enough to warrant admission to hospital. In both patients an organism which may cause acute enteritis was cultured from the faeces. This acute diarrhoeal illness was followed by a prolonged period of debility and progressive loss of weight, and laboratory investigations at this stage were highly suggestive of intestinal malabsorption. In Case 1 this was shown by abnormal radiological appearances of the small bowel,

hypokalaemia, impaired vitamin B₁₂ absorption, steatorrhoea, hypoalbuminaemia, and depressed xylose absorption. In Case 2 similar radiological appearances occurred, but the clinical picture was dominated by excessive loss of potassium in the faeces, with resultant hypokalaemia. Absorption of vitamin B₁₂ and xylose was also impaired, and there was hypoalbuminaemia. Steatorrhoea was not demonstrated in this patient, but the illness was accompanied by low serum cholesterol and plasma carotene levels.

Both patients made a complete clinical recovery and when last seen were without symptoms and had regained their normal weight. In Case 1 this was accompanied by a return to normal of the biochemical parameters, but in Case 2, in which the period of observation was shorter, these improved, but without a complete return to within normal limits.

It is suggested, therefore, that these two patients suffered from a severe acute enteritis which caused enough damage to the small bowel to result in a temporary phase of malabsorption before eventual recovery occurred.

One other possibility must be mentioned—that these patients had latent malabsorption before the acute illness which led to detailed investigation. This cannot be fully excluded; but several facts are against it, notably the patients' apparent state of good health beforehand and the progressive clinical and biochemical recovery which followed the acute diarrhoea. On the other hand an acute enteritis complicating a latent atrophic jejunitis might well explain the clinical and biochemical severity of the illness in our present cases.

If in fact an acute enteritis led to a prolonged phase of intestinal malabsorption, the mechanism of this is uncertain. A similar sequence may follow acute ischaemic episodes in man (Joske *et al.*, 1958), though Cameron and Khanna (1959) have shown experimentally that regeneration of intestinal villi after extensive mucosal infarction is extremely rapid in the rat. It would follow, therefore, that structural mucosal integrity alone is insufficient for normal alimentary function, and that more subtle concepts of tissue organization must be considered. The recent work of Gordon (1958) is relevant to this, and suggests that this post-infectious state may be due to an acute exudative enteropathy rather than to a primary absorptive defect. It is unlikely that the results observed are due to altered intestinal motility, for the available evidence provides little evidence relating absorption to motility. Cummins and Almy (1953) found hypermotility to be associated with increased absorption. Further speculation, however, is not within the province of the present paper.

Summary

Two cases are reported which provide evidence that severe acute enteritis in adults may be followed by a temporary phase of intestinal malabsorption before recovery.

A man aged 66 developed acute bacillary dysentery, and after the acute episode was found to have impaired absorption of fat, carbohydrate, protein, and vitamin B₁₂. This was accompanied by diarrhoea and loss of weight. Both clinical and laboratory abnormalities returned to normal during the succeeding five months, and he has since remained well.

A man aged 75 presented with hypokalaemic neuropathy after an acute episode of dysentery. Investigation showed gross elevation of faecal potassium, and a defective absorption of fat, carbohydrate, protein, and vitamin B₁₂. After the acute episode there was progressive clinical and laboratory improvement.

Since mucosal regeneration in the small bowel is rapid, and prolonged defects of function followed an acute episode, it is suggested that mucosal integrity also is insufficient for normal small-bowel function.

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VOMITING BY OUT-PATIENTS AFTER NITROUS OXIDE ANAESTHESIA

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This is an investigation into some of the factors relating to the occurrence of vomiting after the administration of nitrous oxide and oxygen in the casualty department at Hillingdon Hospital. We kept records of 3,000 consecutive anaesthetics given by anaesthetists of not less than registrar status. The patients were not premedicated and no supplementary drugs of any kind were given: the same intermittent-flow apparatus was used throughout. Whenever possible, patients were instructed to attend at least four hours after their last meal.

The following details were recorded: age and sex of the patient; type of operation done; time since the last meal; time of an accident when one occurred; duration of the anaesthetic, from the start of induction until the nitrous oxide was turned off; presence or absence of vomiting within the first quarter of an hour after operation; and the nature and quantity of the vomitus. (For the purpose of this investigation those patients who retched were recorded as having vomited.)

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