diagnostic skin tests. All parasites may not necessarily produce as intense or as long-lasting an immediate hypersensitivity as does *T. canis* (Wiseman and Woodruff, 1970), and any trial of an antigen in subjects with different known infections should preferably include a direct comparison with their response to homologous antigen. This response cannot be predicted reliably from the presence of infection or on the evidence of the eosinophil count or serum IgE level.

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MEDICAL MEMORANDA

Duodenal Diverticulosis and Chronic Diarrhoea

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Two patients presented with persistent diarrhoea in association with vitamin-B₁₂ deficiency and duodenal diverticulosis. They are of practical interest in that the diarrhoea was greatly improved by parenteral vitamin-B₁₂ therapy alone, and are also of theoretical interest in that they throw further light on the mechanism of malabsorption that operates in the blind-loop syndrome.

Case 1

A man aged 61 suffered several attacks of pancreatitis over a two-year period and then had intermittent diarrhoea for the next five years. This progressed to continuous diarrhoea for two years, during which time he lost 30 lb (13.6 kg) in weight. The stools were pale, bulky, and offensive. The first attack of pancreatitis was confirmed by laparotomy. Subsequently, three episodes were diagnosed clinically. These were relatively mild, and on two occasions the patient was managed at home. Examination showed nothing abnormal apart from generalized wasting. Haemoglobin was 12.0 g/100 ml, and initial investigation revealed a megaloblastic anaemia. Serum vitamin-B₁₂ concentration was 55 pg/ml; serum folate 4.0 ng/ml; and red cells folate 190 ng/ml. The total fasting fatty acid concentration in the serum was 194 mg/100 ml. The levels after a fatty test meal were 176 mg/100 ml at two hours and 208 mg/100 ml at four hours. After two intramuscular injections of 1 mg of cyanocobalamin the diarrhoea gradually ceased and the haemoglobin rose to 14.3 g/100 ml. Four months later the diarrhoea returned, but responded to weekly injections of 1 mg of cyanocobalamin. After eight weeks the injections were reduced to once a month, but a further relapse occurred. Before treatment the serum proteins were 5.8 g/100 ml; after treatment they had risen to 6.5 g/100 ml. He returned to weekly injections and has remained well for six months.

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Comment.—Free acid in the stomach together with the absence of parietal cell antibodies in the serum excluded the diagnosis of pernicious anaemia. A "blind-loop syndrome" was suggested by the radiological finding of a large diverticulum arising from the descending duodenum (Fig. 1). Despite the history of recurrent pancreatitis a pancreozymin-secretrin test was negative. The stomach and intestines at the time of laparotomy were reported to be normal. The subsequent attacks consisted of pain in the right hypochondrium associated with generalized abdominal discomfort and diarrhoea. Pancreatitis is a known complication of duodenal diverticulosis.

Case 2

A woman aged 73 had passed up to 12 semiformed stools a day for 20 years. The diarrhoea was of a sudden onset and a diagnosis of colitis had previously been made. Her admission to hospital was precipitated by the loss of 14 lb (6.4 kg) in weight in association with anorexia, nausea, abdominal discomfort, and occasional

FIG. 1—Case 1. Radiological view of solitary duodenal diverticulum.

vomiting over a period of two weeks. She also complained of increasing giddiness. The severity of her diarrhoea was reflected in a serum potassium concentration of 2.7 mEq/l. On examination she appeared pale and dehydrated. The tongue was smooth and sore. No other abnormalities were detected. The sternal marrow was megaloblastic and the haemoglobin was 8.5 g/100 ml. Serum vitamin B₁₂ was 70 pg/ml; serum folate 3.5 ng/ml; and red cell folate 46 ng/ml. Three-day faecal fat excretion (free diet) was 3.2 g/day. Xylose tolerance test yielded 2.5 g in the urine within five hours after a 25-g oral dose.

Treatment was started with intramuscular cyanocobalamin 1 mg weekly and oral folic acid 15 mg daily. Four weeks later the haemoglobin had risen to 14 g/100 ml and the diarrhoea had ceased. After her discharge she continued to have injections of cyanocobalamin 1 mg monthly. A year later her weight had increased by 22 lb (9.9 kg) and the haemoglobin was 17.5 g/100 ml. The serum proteins before treatment were 5.6 g/100 ml; after treatment they had risen to 7.4 g/100 ml. As her bowels were now costive she took magnesium hydroxide mixture regularly.

Comment.—Despite the normal faecal fat content a malabsorptive basis of the diarrhoea was suggested by the Schilling and xylose tolerance tests (Table I). The results of the lactose and galactose-glucose tests indicated an associated hypolactasia (Table II). Radiological examination of the small bowel

mechanism of steatorrhoea and vitamin-B₁₂ deficiency in the blind-loop syndrome is incomplete. Badenoch *et al.* (1955) suggested that bacterial colonization of a blind-loop results in bacterial overflow, with subsequent steatorrhoea resulting in

FIG. 2—Case 2. Two duodenal diverticula viewed radiologically.

TABLE I—Results of Schilling Test Expressed as Percentage of Original Dose of ⁵⁴Co. Figures in Parentheses Denote Results after Treatment

Case No.	24-hour Urinary Excretion		9-day Whole-body Retention	
		+ Intrinsic Factor		+ Intrinsic Factor
1 ..	3.8 (4.0)	8.5 (—)	17.0 (11.0)	32.5 (—)
2 ..	2.8 (5.0)	4.5 (—)	15.0 (16.0)	17.5 (—)

TABLE II—Blood Glucose Values (in mg/100 ml) after Galactose-Glucose and Lactose Tolerance Tests

Case No.	Time (min)	Galactose-Glucose Tolerance Test (25g each, by Mouth)	Lactose Tolerance Test (50g)	
			Before Treatment	After Treatment
1	0	63	58	72
	30	72	65	82
	60	65	67	70
	90	57	60	62
	120	64		69
2	0	63	70	75
	30	97	75	95
	60	95	79	81
	90	75	78	82
	120	58	77	72

All tests in Case 1 were carried out 6 weeks after treatment started, and in Case 2 18 months after treatment started.

showed two duodenal diverticula (Fig. 2). This, with the sudden onset of the diarrhoea, supports the diagnosis of blind-loop syndrome (Badenoch *et al.*, 1955). An associated lack of intrinsic factor remains a possibility in view of the histamine-fast achlorhydria. Parietal cell antibodies were not, however, found in the serum.

Discussion

Badenoch *et al.* (1955) first drew attention to the fact that the radiological demonstration of a duodenal diverticulum might be the only apparent manifestation of extensive upper intestinal diverticulosis, which may result in megaloblastic anaemia and/or steatorrhoea. Our understanding of the

vitamin-B₁₂ malabsorption. Booth (1965) pointed out that malabsorption of vitamin B₁₂ is not dependent on pre-existing steatorrhoea. Donaldson (1968) provided experimental evidence that the steatorrhoea in the blind-loop syndrome resulted from bacterial deconjugation of the bile salts, resulting in free bile acids. It is not clear whether the free bile acids act directly by impairing the mucosal function or by impairing micelle formation.

It is not to be expected that all cases of steatorrhoea and megaloblastic anaemia in association with duodenal diverticulosis will respond completely to vitamin B₁₂ alone. If the major cause of the diarrhoea is bacteria-induced steatorrhoea little or no improvement may occur with parenteral vitamin B₁₂. In Case 1 no lasting result was achieved with normal doses of vitamin B₁₂, and treatment with a course of antibiotics was considered. In view, however, of a rather dramatic response initially to vitamin B₁₂ larger doses (1 mg weekly) were administered and almost complete freedom from diarrhoea was achieved. At present this response to vitamin B₁₂ is inexplicable within the terms of current hypotheses. A parallel situation is seen in some cases of tropical sprue in relation to folic acid requirements (Avery Jones *et al.*, 1968).

Where the major cause of diarrhoea is vitamin-B₁₂ deficiency a definite improvement can be expected with parenteral vitamin B₁₂ in normal dosage such as occurred in Case 2. The variable response of different patients to vitamin B₁₂ shows the essential interaction of several different components in the production of the malabsorption syndrome.

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