The Malabsorption Syndrome in Man

Clinical and Pathologic Aspects

DAVID ADLERSBERG, M.D.*

THE clinical features of primary malabsorption syndrome (non-tropical sprue) to be presented in this summary are based on a study of more tnan 100 patients with this disorder observed at the Mount Sinai Hospital over a period of many years. In all the diagnosis was established by clinical and laboratory evidence; and all or most of the typical features of this syndrome appeared in all subjects at some time. Absence of gross gastrointestinal disease was established by roentgenologic and other laboratory and clinical procedures. Most of the patients had prolonged follow-up periods, averaging over five years.

There was a predominance of women in the present series, as previously reported from this Hospital.[1,2] Only Manson-Bahr noted a larger number of women with tropical sprue; others found the sex incidence approximately equal.

The average age of the patients at the time of first observation was forty-five years, range sixteen to seventy-three. When the patients were first seen the duration of symptoms ranged from one month to fifty-two years, with an average of 7.2 years. The long duration of symptoms is caused by the insidious onset, the vagueness of symptoms in the initial phases and the tendency to spontaneous remissions.

SIGNS AND SYMPTONS

The symptoms are summarized in order of frequency Figure 1. The most frequent complaints were the combination of diarrhea, weakness and weight loss but the leading symptom of diarrhea was absent in 4.2 per cent of the patients, while 1.2 per cent were constipated. These patients had considerable steatorrhea, nevertheless, and they may fall into the group of atypical or incomplete sprue. Loss of weight may be considerable: maximum 60 pounds, average 25.3 pounds. Glossitis and stomatitis, vague abdominal discomfort, bleeding, tetany, paresthesias and bone pains have been seen in the described order. Severe mental changes were seen in approximately 10 per cent of the patients. These ranged from frank psychosis to varying degrees of depression, anxiety and character disorders.

The pathologic signs observed are summarized in order of frequency in Figure 2. Emaciation was the leading sign. The initial body weight ranged from 67 to 167 pounds, mean weight 104 pounds. A large number of patients showed marked abdominal distention and dependent edema. Hepatomegaly and mild splenomegaly were seen in 31 and 6 per cent, respectively. Hypotension with systolic blood pressures below 100 mm. Hg was seen in approximately one-third of the patients. Less common manifestations were clubbing of the digits, pigmentation, dryness of the skin and abnormal neurologic signs.

CLINICAL PICTURE

In the typical case of non-tropical sprue, the patient is a middle-aged person with a long history of intermittent diarrhea, periods of marked weight loss, weakness, sore mouth and tongue, and abdominal complaints such as flatulence, mild pain or other discomfort. Often hemorrhagic manifestations, paresthesias or tetany may be present. The patient is pale, in poor nutritional status and may have clubbing of the digits; the abdomen is distended; the blood pressure is low.

From The Mount Sinai Hospital and Columbia University, New York, New York.

* Deceased.

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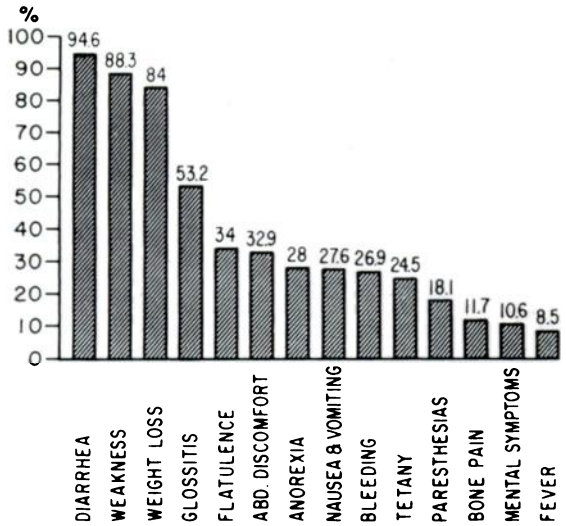


FIG. 1. Major symptoms observed in ninety-four patients with idiopathic sprue. (From: BOSSAK, E., WANG, C.-I. and ADLERSBERG, D. Clinical aspects of the malabsorption syndrome (idiopathic sprue): observations in 94 patients. *J. Mt. Sinai Hosp.*, 24: 286, 1957.)

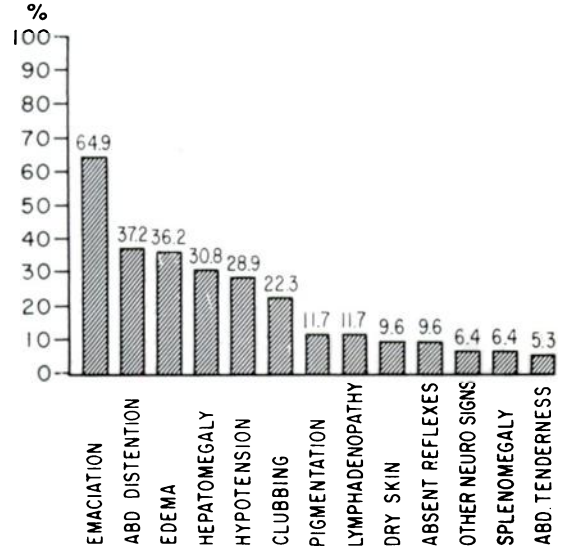


FIG 2. Major signs observed in same group of patients with idiopathic sprue as in Figure 1. (From: BOSSAK, E., WANG, C.-I. and ADLERSBERG, D. Clinical aspects of the malabsorption syndrome (idiopathic sprue): observations in 94 patients. *J. Mt. Sinai Hosp.*, 24: 286, 1957.)

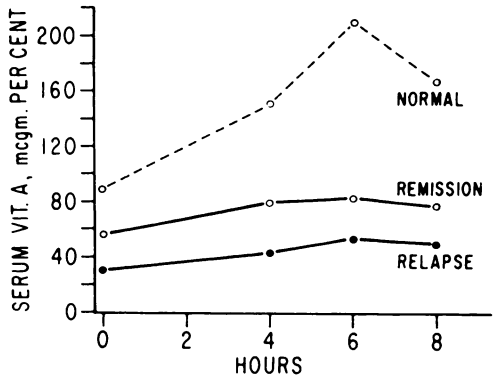


FIG. 3. The average vitamin A tolerance curve obtained in fifty-four patients with sprue in relapse compared with twenty-nine patients with sprue under clinical control. The normal absorption curve was the average of values obtained in ten healthy subjects. Note the progressive elevation of the serum vitamin A concentration after oral administration of the standard load of vitamin A with a gradual return toward normal levels; low fasting levels and flat curves in sprue in relapse and somewhat higher fasting levels but still flat character of the curve in sprue in remission. (From: ADLERSBERG, D., WANG, C.-I. and BOSSAK, E. Disturbances in protein and lipid metabolism in malabsorption syndrome. *J. Mt. Sinai Hosp.*, 24: 206, 1957.)

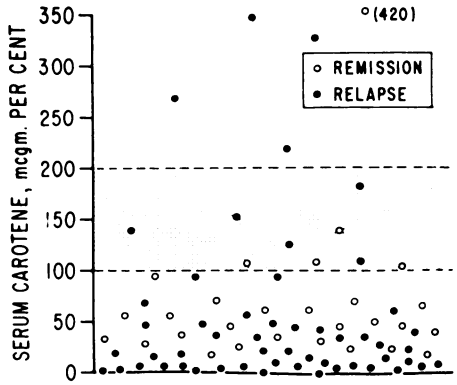
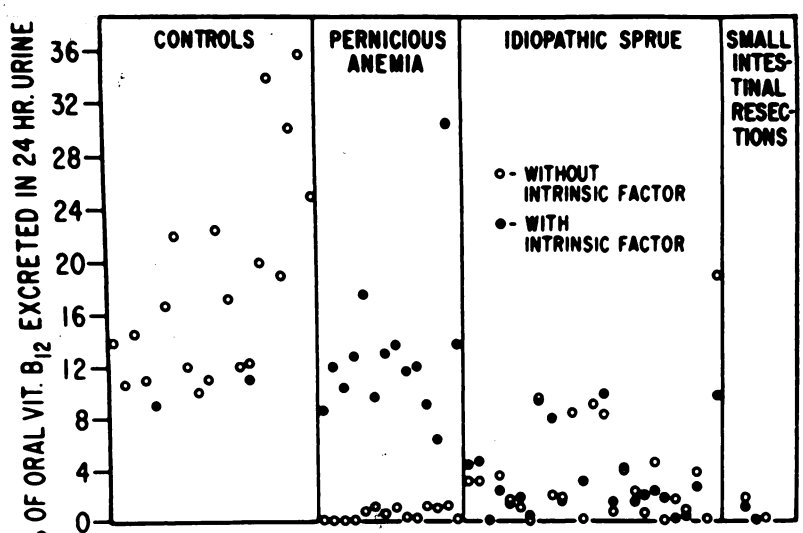


FIG. 4. Individual serum carotene levels in fifty-four patients with idiopathic sprue in relapse compared with twenty-eight patients with sprue under clinical control. The shaded area represents the range of normal serum carotene concentration. Note that the majority of patients with idiopathic sprue in relapse and in remission have serum carotene levels far below the normal range. (From: ADLERSBERG, D., WANG, C.-I., and BOSSAK, E. Disturbances in protein and lipid metabolism in malabsorption syndrome. *J. Mt. Sinai Hosp.*, 24: 206, 1957.)

Anemia is usually present and is often combined with a megaloblastic bone marrow in the presence of gastric acid. Serum albumin tends to be less than 3.5 gm./100 ml. and serum calcium less than 9 mg./100 ml. There is often an increase in alkaline phosphatase and a prolonged prothrombin time. All serum lipid



	CONTROLS	PERNICIOUS ANEMIA		IDIOPATHIC SPRUE		SMALL INTESTINAL RESECTIONS	
	NO I.F. (o)	NO I.F. (o)	I.F. (•)	NO I.F. (o)	I.F. (•)	NO I.F. (o)	I.F.(•)
AVERAGE	17.9	0.5	12.9	3.6	3.3	0.63	0.6
RANGE	9-36	0-1.2	6.3-30.5	0-19	0-10	0-1.8	0-1.1

FIG. 5. Scattergraph of urinary excretion tests in control subjects as well as in patients with pernicious anemia, idiopathic sprue and extensive intestinal resections. The open circles represent the excretion of labeled vitamin B_{12} given orally without intrinsic factor. The closed circles represent the excretion of labeled vitamin B_{12} given orally with intrinsic factor. Each test on the same patient is placed in vertical alignment. Note that the abnormally low excretion of vitamin B_{12} in patients with pernicious anemia can be reverted to normal by the addition of intrinsic factor (I.F.) whereas in patients with idiopathic sprue the excretion levels remain low with or without the addition of intrinsic factor. (From: OXENHORN, S., ESTREN, S., AND ADLERSBERG, D. *J. Mt. Sinai Hosp.*, 24: 232, 1957.[3])

fractions are low, along with low levels of serum vitamin A and carotene. Steatorrhea is present. On roentgenologic examination the bones are demineralized (osteomalacia and/or osteoporosis). There are evidences of diminished glucose and xylose absorption, of impaired fat, vitamin A and vitamin B_{12} absorption (Figs. 3, 4 and 5).[2,3] Other problems, such as the absorption of folic acid, iron, protein, water and electrolytes will not be discussed here.

Roentgenologic studies of the small bowel are mandatory in every patient with primary malabsorption syndrome. Organic changes of the gastrointestinal tract must be ruled out before the diagnosis of primary malabsorption syndrome is established. In the latter, characteristic changes of the pattern of the small bowel can be seen which consist of pronounced dilatation of small bowel loops, segmentation

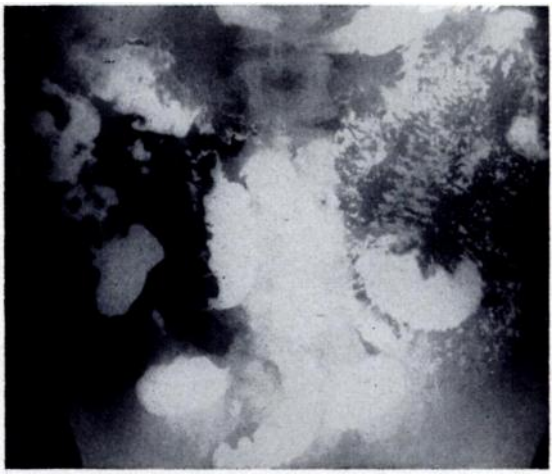


FIG. 6. Roentgenogram of the small bowel in a typical case of non-tropical sprue. The "sprue pattern" is characterized by considerable dilatation of the loops segmentation and evidences of hypersecretion. (From: ADLERSBERG, D., MARSHAK, R. H., COLCHER, H., DRACHMAN, S., FRIEDMAN, A. I. and WANG, C.-I. *Gastroenterology*, 26: 548, 1954.[4])

TABLE I

Comparison of Clinical and Laboratory Data in Puerto Rican and Non-Puerto Rican Patients with Sprue

Data	Non-Puerto Rican	Puerto Rican
Patients (no.)	71	23
Duration of symptoms (yr.)	8.8	2.3
Glossitis (%)	46.5	74.0
Bleeding (%)	33.8	8.7
Tetany (%)	29.6	8.7
Clubbing (%)	26.8	8.7
Hepatomegaly (%)	25.4	52.2
Paresthesias (%)	15.5	26.1
Splenomegaly (%)	2.8	17.4
Megaloblastic bone marrow (%)	9.5	89.0
Hemoglobin <5 gm. % (%)	7.0	34.8
Leukopenia (%)	24.6	74.0
Bone demineralization (%)	65.6	20.0
Calcium <7 mg. % (%)	38.9	5.9
Mortality (%)	26.7	4.5
Cured (%)	1.7	21.7

* From: BOSSAK, E., WANG, C.-I. and ADLERSBERG, D. Clinical aspects of the malabsorption syndrome (idiopathic sprue): observations in 94 patients. *J. Mt. Sinai Hosp.*, 24: 286, 1957.

resulting in "puddling" of the barium and evidence of excessive amounts of secretion in the small intestinal tract (Fig. 6). Approximately 90 per cent of the patients with primary malabsorption syndrome present the "sprue pattern" of the small bowel on roentgenographic examination.[4] Thus, this finding may represent an important diagnostic criterion.

Patients with milder or incomplete cases may present diagnostic difficulties. Steatorrhea without diarrhea as well as severe bleeding (hypoprothrombinemia), fractures (osteomalacia) and intractable edema (hypoproteinemia) may mask the basic disorder.

Puerto Rican patients with sprue (seen in New York) differ in several respects from non-Puerto Ricans with sprue. They have a higher incidence of glossitis and hepatomegaly and a lower incidence of bleeding, tetany and clubbing; a higher incidence of severe anemia, macrocytosis and leukopenia; higher levels of serum calcium and a lower incidence of bone demineralization. Since the majority of these patients had symptoms before emigrating to New York, they may be presenting the tropical variety of sprue (Table I).[5]

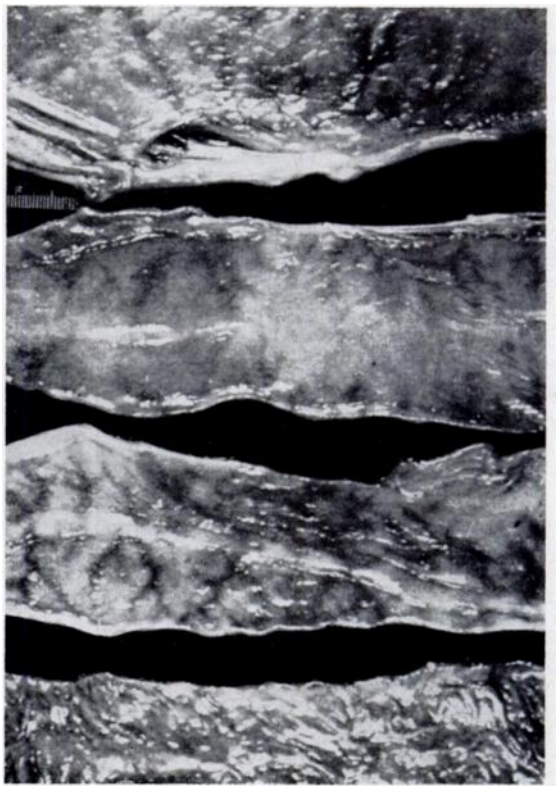


FIG. 7. Atrophy and thinning of wall of small bowel in a patient with nontropical sprue. (From: HIMES, H. W. AND ADLERSBERG, D. Pathologic studies in idiopathic sprue. *J. Mt. Sinai Hosp.*, 24: 251, 1957.)

HISTOLOGIC ASPECTS

Clinical evidence would suggest that the primary malabsorption syndrome is caused by a derangement or a defect in the small bowel. Since a number of patients with primary malabsorption syndrome present some morphologic change in the small bowel at autopsy and biopsy, it would appear that these changes are causally related to the clinical manifestations.[6] The pathologic changes in the small bowel seen in advanced cases are characterized macroscopically and microscopically by marked atrophy of the small intestinal mucosa (Fig. 7). In some instances, blunting and thickening of the villi, in others, almost complete atrophy of the villous layer, may be seen (Figs. 8 and 9). These changes obviously lessen the surface area available for absorption. The question of

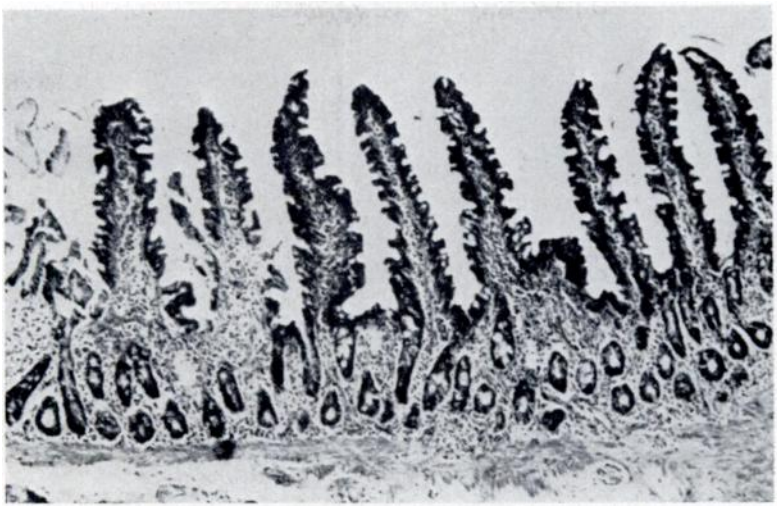


FIG. 8. Jejunal biopsy specimen from a normal control subject. Note finger-like appearance of normal villi. (From: HIMES, H. W. and ADLERSBERG, D. *Gastroenterology*, 35: 142, 1958.[6])

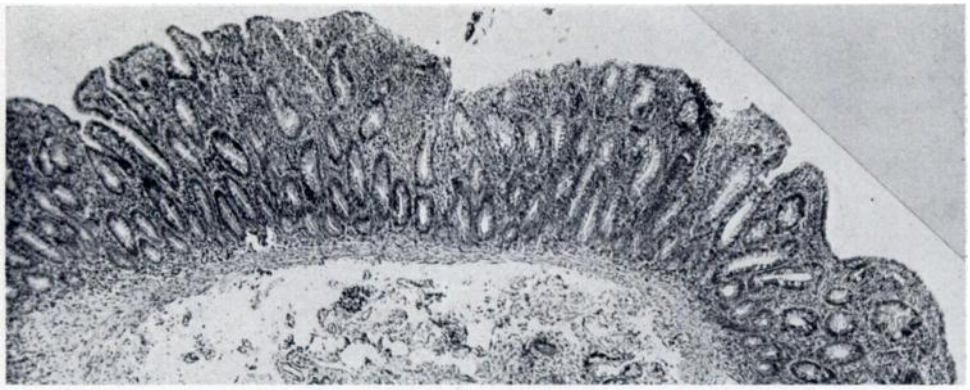


FIG. 9. Jejunal biopsy by the oral route in a patient with non-tropical sprue of long duration. Note atrophy of the mucosa with complete distortion of the villous layer.

the reversibility of these structural changes in sprue is still open. Interesting information concerning the ultimate structure of the jejunal mucosa is being obtained presently by electron microscopic studies.

The changes in the small bowel may be the result of alterations in small bowel motility, absorption of abnormal products or lack of specific nutritional factors such as vitamin B_{12}, folic acid and other as yet unidentified compounds. They may be the result of some deranged enzymatic mechanisms in the intestinal mucosa and thus be a part of the basic disturbance in malabsorption. Experience with small intestinal biopsies seems to indicate that the severe atrophy of the mucosa is, to a certain extent, characteristic of non-tropical sprue. In tropical sprue, the changes observed by others and us seem to be milder in character.

Patients with pernicious anemia, prolonged steatorrhea caused by pancreatic disease and with chronic diarrhea of various causes do not show the atrophy of the small intestinal mucosa seen in the primary malabsorption syndrome. The same degree of atrophy of the mucosa may be seen in patients with non-tropical sprue in full remission, normal nutritional status and in absence of steatorrhea. The question arises then, as to how normal absorption can be maintained during full remission despite severe atrophy of the mucosa. Whether atrophy of the small bowel mucosa

and malabsorption are actually causally related and whether the atrophy is at all reversible remain to be established.[7]

SUMMARY

Primary malabsorption syndrome includes several clinical entities which are probably varieties of the same inborn metabolic disorder. It is not clear at present whether the characteristic changes of atrophy of the small intestinal mucosa seen at autopsy and in biopsy specimen of patients with the primary malabsorption syndrome are due to a specific enzymatic or nutritional defect or whether they result from some toxic or other influences.

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