

#41
Cop-2

Ref: - Ann. of Internal Med. v. 65 (C)
Dec. 1966

Malabsorption and Jejunitis in American Peace Corps Volunteers in Pakistan

JOHN LEVINSBAUM, M.D., THOMAS H. KENT, M.D., and HELMUTH SPRINZ, M.D., F.A.C.P.
Dacca, East Pakistan, and Washington, D. C.

TROPICAL SPRUE, a syndrome of unknown cause characterized by diarrhea, weight loss, malabsorption, and changes in small intestinal morphology, occurs in both native residents and visitors to tropical countries. The syndrome has been frequently described in European and American military personnel stationed in Asia (1, 2) or Puerto Rico (3, 4). During the past year, 10 cases of severe symptomatic sprue have been observed in Peace Corps Volunteers in East Pakistan, and several cases have been seen among Volunteers in Venezuela (5).

Recent studies from Thailand, India, Pakistan, Puerto Rico, and Haiti have shown a high prevalence of malabsorption and abnormalities of jejunal morphology in asymptomatic native-born individuals (6, 7). The impairment of absorption and abnormality of small-bowel appearance in these "normal" persons may often be similar in degree to that seen in patients with severe clinical sprue (7). Since, in accordance with the philosophy of the Peace Corps, Volunteers live in a manner as similar as possible to that of the indigenous population, it would be of interest to know whether Volunteers develop similar abnor-

malities of small-intestinal function and structure. Therefore, a study of Peace Corps members living in Pakistan was undertaken in order to answer this question.

METHODS AND MATERIALS

Studies of intestinal absorption were performed on three groups of adult subjects living in Pakistan during the period 1964 through 1965: [1] 114 Peace Corps volunteers,* 47 residing in West and 67 in East Pakistan; [2] 31 Americans and Europeans employed by various assistance and research organizations, who will be referred to as "protected" Westerners in view of their tendency to live in air-conditioned homes, eat imported commissary food, and avoid Pakistani eating places, resulting in minimal contact with the tropical environment; [3] 106 Pakistani employees of the Pakistan-SEATO Cholera Research Laboratory.

Subjects included in the study were selected only on the basis of willingness to cooperate in the study. The number of Peace Corps volunteers included comprised 61% of the total Volunteer population resident in Pakistan at the time of the study. The findings in the Pakistani employee group will be reported in greater detail in a separate communication (9).

The absorption tests were performed in the hospital or at the Peace Corps dormitories under the supervision of a specially trained nurse to insure completeness of urine and stool collections. The 5-hr urinary excretion of d-xylose

* Study subjects from among Peace Corps Volunteers are designated "volunteers."

Received June 15, 1966; accepted for publication August 24, 1966.

From the Pakistan-SEATO Cholera Research Laboratory, Dacca, East Pakistan, and the Walter Reed Army Institute of Research, Washington, D. C. This work was supported in part by research grant 196802 between the National Institutes of Health, Bethesda, Md., and the Pakistan-SEATO Cholera Research Laboratory.

Requests for reprints should be addressed to John Levinsbaum, M.D., First Medical Division, Bellevue Hospital, 462 1st St. Ave., New York, N. Y. 10016.

TABLE 1. Xylose Absorption in Subjects Living in Pakistan

	Subjects	Mean Xylose Excretion*	SD	Range	Subjects Excreting <5.0 g Xylose
	no.	g		g	no.
Peace Corps volunteers	114	5.32	1.81	1.0-9.4	45 (39.5%)
"Protected" Americans and Europeans	31	7.10	1.19	4.6-9.1	1 (3.3%)
Pakistani employees	106	5.35	1.57	0.5-9.3	42 (39.6%)

* Normal range 5.0 to 10.0 g.

after a 25-g oral dose was measured according to the method of Roe and Rice (12). Twenty-four-hour urinary excretion of ^{14}C vitamin B₁₂ after an oral dose of 1 μg of the labeled vitamin given with intrinsic factor was estimated following the method of Schilling (13). Fecal fat was measured on 72- to 96-hr collections (14, 15). Jejunal biopsies were obtained with the Crosby-Kugler capsule (16) and examined under the dissecting and light microscopes.

RESULTS

STUDIES OF XYLOSE ABSORPTION

Forty-five (39.5%) of the 114 Peace Corps volunteers had subnormal xylose absorption when first studied after 6 months to 2 years' residence in Pakistan (Table 1). The prevalence was similar in volunteers from the east and west wings of Pakistan. The incidence of xylose malabsorption and the mean xylose excretion were similar to those in the Pakistani employee group but differed significantly from those in the "protected" Europeans and Americans ($P < 0.0001$). The xylose tests were repeated one

or more times in 39 volunteers who were still in Pakistan 1 to 8 months after the initial study. Fifteen who originally had normal values remained normal; eight subjects with low initial xylose excretion again had low levels. In another nine who were originally low, absorption returned to normal. Seven who were initially normal developed xylose malabsorption during a period of several months' observation.

The presence of malabsorption of xylose did not appear to be related to duration of residence in Pakistan. The incidence

TABLE 3. Relation of Xylose Absorption to Symptoms in Peace Corps Volunteers in Pakistan

	Peace Corps Volunteers with Xylose:	
	<5.0 g	5.0 g or >
Lost weight while in Pakistan	72%	78%
Mean weight loss	12.3 lb	8.8 lb
Episodes of diarrhea while in Pakistan:		
Less than once/month	29%	23%
1-2 times/month	25%	43%
More than twice/month	46%	34%
Within 2 weeks before xylose test	53%	51%
Gastrointestinal symptoms after eating Pakistani food	37%	40%
Parasites present in stool* (on any of 6 to 12 concentrated specimens)	41%	43%

* The parasites most commonly found on stool examinations in both groups were *Entamoeba histolytica* and *Ascaris lumbricoides*.

TABLE 2. Xylose Absorption and Length of Residence of Peace Corps Volunteers in Pakistan

Number of Subjects	Length of Residence in Pakistan, Months			
	0-6	7-12	13-18	19-24
Total	17	17	35	74
With xylose <5.0 g	8	7	9	31
Percent with xylose <5.0 g	47	41	27	42

of malabsorption was similar in subjects studied after 6 months' residence and in those who had been in Pakistan 18 to 24 months at the time of study (Table 2). In addition, two of six volunteers studied within 6 weeks of arrival in Pakistan failed to absorb xylose normally.

Impairment in xylose absorptive capacity also did not correlate well with the presence or absence of symptoms. Thus, the incidence of weight loss, frequent or infrequent episodes of diarrhea, diarrhea during

the 2-week period immediately before the absorption study, and gastrointestinal intolerance to Pakistani food was similar in the groups of volunteers with and without malabsorption (Table 3). It should be noted that the incidence of these symptoms was rather high in both groups. While weight loss was more common in the group with malabsorption, the mean weight loss was greater in this group (12.3 lb) than in that with normal absorption (8.8 lb; $P > 0.08$). The incidence of in-

TABLE 4. Peace Corps Volunteers—Absorption Studies and Biopsies

Subject	Time in Pakistan	Symptoms	Weight Loss	Xylose	Schilling Test	Fecal Fat	Jejunal biopsy	
							Dissecting Microscope*	Histology†
	months		lb	g	%	g/day		
Volunteers with normal xylose								
K. C.	6	Minimal diarrhea	0	5.1	11.5	1.3	L > F, R	Normal
J. F.	6	Diarrhea	0	6.7	5.5	5.4	L > F	Mild
	11	None	Gained	5.4	10.8	3.2	L >> R, F	Moderate
S. E.	6	Diarrhea	22	5.9	9.2	5.0	L = F	Mild
	11	Diarrhea	26	4.2	2.6		R + L, rare F	Moderate
L. E.	17	Diarrhea	43	5.8	2.9	2.6	L >> F, R	Mild
F. W.	19	Diarrhea	20	7.9	8.8		L >> F, R	Normal
D. P.	19	Diarrhea	5	8.6	9.7			
T. B.	19	Diarrhea	18	5.8	2.3			
J. A.	19	Diarrhea	0	6.7	13.7			
W. S.	19	Diarrhea	7	5.2	8.8			
G. L.	19	Diarrhea	40	6.1	11.4			
D. S.	23	Diarrhea	5	6.0	5.1		L > R, C, rare F	Moderate
J. R.	23	Diarrhea	5	5.3	15.4	2.0	L >> R, C, rare F	Mild
W. M.	23	Minimal diarrhea	5	6.7	14.7	3.6	L > R, C, F	Mild
Volunteers with abnormal xylose								
H. T.	6	Diarrhea	0	3.8	4.5	2.2	L > F, C, R	Moderate
D. N.	6	Diarrhea	0	2.6	4.7		L >> F	Moderate
M. D.	6	None	Gained	1.4	5.9	2.9		
E. H.	7	Diarrhea, flatulence	2	4.3	0.8	6.2	L > F	Mild
M. B.	11	Severe diarrhea, abdominal pain, flatulence	40	2.4	3.1		L >> F	Moderate
	18	None (tetracycline treatment)	Gained	8.2	2.0		L > F, C	Mild
N. A.	14	Diarrhea	10	4.1	11.5			
K. H.	16	Severe diarrhea, weakness	35	2.0	0.6	10.2	L > F, R	Mild
W. C.	19	Diarrhea	30	4.3	7.6		F = L, R, C	Moderate
F. R.	19	Diarrhea	40	2.6	0.7			
D. B.	19	Diarrhea	25	3.4	8.8			
Normal values				5-10	8-26	<6.0		

* L = leaves, F = fingers, R = ridges, C = convolutions.

† See text.

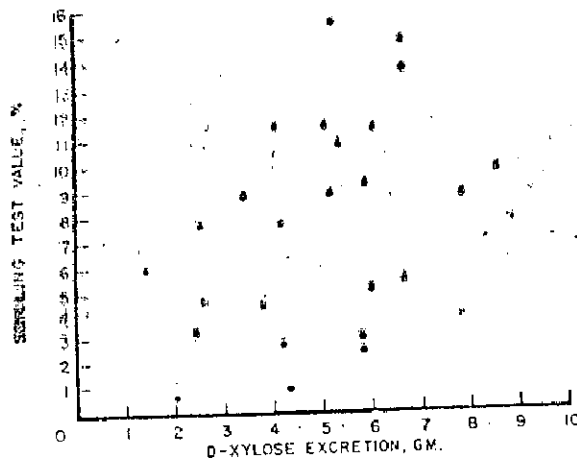


FIGURE 1. Correlation between xylose and Schilling tests in Peace Corps volunteers. The tests were performed within 1 to 2 days of each other in each subject.

testinal parasites was similar in the two groups, and the specific parasites found in each group were also similar. None of the subjects were anemic or had glossitis.

Most of the volunteers in both groups had intermittent episodes of diarrhea, most commonly passing three or four soft or watery stools for periods of 1 to 3 days several times a month. Two, however, had severe diarrhea associated with numerous bulky, light-colored stools, progressive weight loss, and malabsorption (patients M. B. and K. H., Table 4). In one, dramatic improvement occurred during a 3-week course of tetracycline; in the other, there were equivocal symptomatic responses to courses of tetracycline and folic acid.

VITAMIN B₁₂ ABSORPTION

The Schilling test was performed on 23 volunteers (Table 4). There was malabsorption of vitamin B₁₂ in 12 (52%). There was a general correlation between xylose and cyanocobalamin absorption (Figure 1; $r = 0.49$, $P < 0.01$). Thus, of 10 volunteers with low xylose values, 8 had low B₁₂ absorption; however, 4 of 13 volunteers with normal xylose absorption had low Schilling test values. Seven subjects who initially had low B₁₂ absorption were restudied 1 to 6 months later. In one the values had re-

turned to normal, but in six they were still low. Two of the latter group had B₁₂ absorption values in the low-normal range when studied for the third time 6 months after the original Schilling test.

FECAL FAT

Of 11 volunteers studied, only 2 had elevated fecal-fat excretion (9.0 and 6.2 g/day) (Table 4). Both of these individuals also had malabsorption of xylose and B₁₂. In both, the fecal-fat excretion later returned to normal (in one, after antibiotic therapy; in the other, spontaneously).

While impairment of absorption of xylose was usually paralleled by malabsorption of vitamin B₁₂, fecal-fat excretion was normal in several individuals with poor absorption of xylose or cyanocobalamin or both. Similar findings have been noted in our Pakistani employees (9). Since fat intake was not controlled in these studies the failure to demonstrate elevated fecal lipid levels may be due to the generally reduced intake of fat in tropical diets.



FIGURE 2. Patient K. H., a volunteer with severe diarrhea and malabsorption. Dissecting microscope appearance of jejunal mucosa. Most villi are leaf-like. A few round, finger forms are present, as well as elongated ridges such as those that can be seen near the bottom of the field. ($\times 50$)



FIGURE 3. Jejunal biopsy from Volunteer F. W., who had mild diarrhea but normal absorption of xylose and B₁₂ at the time of biopsy. The histologic appearance is normal. The normal scalloping of the villus borders (probably due to contraction after contact with the fixative) is present. Under the dissecting microscope there were more leaf-shaped than finger-like villi. (Hematoxylin and eosin, $\times 80$.)

JEJUNAL BIOPSIES

Seventeen biopsies of the upper jejunum were obtained from 14 volunteers, 10 of whom had evidence of malabsorption (Table 4). Under the dissecting microscope, none of the biopsies showed the predominantly finger-like villose architecture said to be normal for American subjects living in the United States. Two had equal numbers of leaf-like and finger-like villi; in the remaining 15, the majority of the villi were leaf-like. In 11 subjects in whom leaf-like villi predominated, some ridge-like villi were seen (Figure 2), and in 6 of this group convoluted forms were seen as well. In five of the individuals with ridge-like villi, results of xylose and B₁₂ absorption studies were normal during the days immediately before the biopsy (Table 4); the remaining six had impaired absorption.

Histologically, two of the specimens of jejunal mucosa were considered to be normal (Figure 3); eight were judged to have "mild" and seven, "moderate" enteritis. The

mild enteritis was characterized by slight lengthening of crypts and increased numbers of chronic inflammatory cells in the lamina propria (Figure 4). Increased numbers of lymphocytes infiltrating the villus epithelium were present in some. In the biopsies with moderate enteritis, there was a conspicuous layer of approximately 112. Irregular distended villi with dense chronic inflammatory cell infiltrate in the lamina propria, variable numbers of lymphocytes in the epithelium, and mild cuboidal change in the epithelium at the tips of some villi (Figure 5). Enlargement of epithelial cell nuclei such as has been described in advanced tropical sprue was not apparent. The histologic abnormalities were generally less severe than those present in the average "normal" Pakistani (9), and in none of the subjects (including



FIGURE 4. Jejunal biopsy from Volunteer E. H., who had diarrhea and malabsorption. Histologically, this was considered to be "mild" enteritis. Increased inflammatory-cell infiltrate in the lamina propria, slightly elongated and hyperplastic crypts, and increased numbers of lymphocytes infiltrating the surface epithelium are present. There is decrease in scalloping of the villus borders due to mild inflammatory distention of the villi. The villi were predominantly leaf-shaped under the dissecting microscope. (Hematoxylin and eosin, $\times 80$.)



FIGURE 5. Jejunal biopsy from Volunteer H. T., who had diarrhea and malabsorption. "Moderate" enteritis is present. The crypt-to-villus ratio varies from 1:3 to 1:1.5. There is dense chronic inflammatory cell infiltrate in the lamina propria. Under the dissecting microscope a mixture of leaves, fingers, ridges, and convolutions was observed. (Hematoxylin and eosin, $\times 80$.)

two volunteers with marked diarrhea and weight loss) were the changes severe or comparable to those seen in classic celiac disease or nontropical sprue.

Absorption of xylose was normal in the two volunteers with normal histologic findings and in six of the eight with mild enteritis. Malabsorption was present at the time of biopsy in five of the seven volunteers with moderate changes.

DISCUSSION

The Peace Corps represents a radical and often successful social experiment in which Americans live abroad in a manner as similar as possible to the indigenous population, while performing often highly demanding and challenging tasks. It must be recognized, however, that such an attempt at more or less total assimilation of the ways of a tropical country, in which stand-

ards of sanitation may be very low and diseases to which Americans may be immunologically unfamiliar are rife, may involve a certain risk to health. Because of this risk, the Peace Corps has instituted a carefully planned health program for its Volunteers including immunizations, instructions with regard to preparation of food and water in tropical countries, and periodic health checkups. Nonetheless a certain minimal, probably irreducible, risk remains. For example, the Peace Corps Volunteer may well insult his hosts if, on invitation into a local home, he refuses generously offered food on the grounds that it has been prepared without the benefit of modern sanitation and stored without refrigeration.

The findings of the present study indicate that one of the risks to which a Peace Corps Volunteer is exposed is the tropical malabsorption syndrome. About 40% of Volunteers stationed in Pakistan during the period of this report were found to have malabsorption. Since xylose is predominantly absorbed in the duodenum and upper jejunum (17) and B₁₂ in the ileum (18, 19) and since malabsorption of both substances was common, a lesion involving the entire small bowel is implicated. Ileal biopsies, however, were not obtained in the present study.

When jejunal biopsies obtained from volunteers were viewed under the dissecting microscope, in every instance leaf-shaped villi were found in equal or more often, greater numbers than the finger-like forms said to be characteristic of normal individuals residing in the United States. We have observed similar findings in native-born Pakistanis, since in none of more than 200 biopsies examined to date from 86 Pakistani subjects have finger-like villi predominated. Others have reported the occurrence of predominantly leaf-shaped villi in patients with idiopathic steatorrhea after successful treatment with a gluten-free diet (20) and in jejunal biopsies obtained

distal to the gastrojejunal anastomosis in patients who have undergone gastrectomy (21). Several workers have suggested that leaf-shaped villi represent the earliest stage of mucosal abnormality or are a transitional stage between normal and abnormal (20, 21). If this concept is correct and if further studies in other Volunteers bear out our initial findings, at least minimal bowel damage may be present in all Volunteers living in Pakistan. Prospective studies are needed of the appearance of the jejunal mucosa in North Americans before and after residence in a tropical environment. Furthermore, no detailed studies of the dissecting microscope appearance of small-intestinal mucosa in a large series of normal North Americans are available for comparison.

Malabsorption was commonly present in Volunteers within 6 months of arrival in Pakistan and its prevalence was no greater after 18 to 24 months' residence in the country. The onset of a tropical malabsorption syndrome within a few months (or even weeks) after arrival has frequently been reported in military personnel stationed in tropical countries (2-4, 22).

In recent years, reports from a number of tropical countries have indicated a high prevalence of bowel damage in supposedly normal members of the indigenous population. Studies of Thai army recruits (6), control South Indian subjects (7), rural inhabitants of Haiti (11), Puerto Rican villagers and army recruits (10), West Pakistani prison inmates (8), and East Pakistani laboratory employees (9) have shown a high prevalence of malabsorption and chronic enteritis in mucosal biopsies from asymptomatic native-born individuals. It is against this background that the development of similar though generally less marked changes in Peace Corps Volunteers living under conditions closely approximating those of the indigenous Pakistani population must be viewed. The rapid development in Volunteers of small-bowel disease

similar to that present in virtually all East Pakistanis (9) suggests that the small-intestinal damage observed in asymptomatic residents of tropical countries is on an acquired basis, due to an environmental rather than a genetic influence. It is noteworthy that the prevalence of malabsorption was negligible in the control group of "protected" Americans and Europeans, living in comfortable air-conditioned homes, eating predominantly imported food prepared under more sanitary conditions, and rarely or never eating in Pakistani homes or roadside restaurants.

The cause of the abnormalities in bowel function and structure among indigenous subjects and Volunteers in Pakistan is obscure. The possible contribution of infection or changes in gut bacterial flora requires further study. The occurrence of sprue in epidemic form in various parts of the Indian subcontinent has been repeatedly reported (2, 22-24), and responses to antibiotic therapy have been observed in sprue cases from Hong Kong (25), Malaya (25), Puerto Rico (26-28), and Pakistan (9). Attempts to isolate a causative viral or bacterial agent have so far been unsuccessful (11, 28-31).

It is possible that some of the histologic abnormalities found on jejunal biopsy represent adaptive changes in response to an increased variety and quantity of organisms ingested by the Volunteers under field conditions. Similar changes, such as inflammatory infiltrate and crypt lengthening, are seen in germ-free animals after exposure to normal bacterial flora (32) and may not necessarily represent "disease" in the sense of something harmful to the host organism. On the other hand, the presence of malabsorption in approximately half of the volunteers studied indicates that there was reduced functional capacity of the intestine in addition to the structural changes.

Transient malabsorption, usually without associated symptoms, is a common sequela to acute small-bowel infection and

2. STEFANINI, M.: Clinical features and pathogenesis of tropical sprue. *Medicine (Balt)* 27: 379, 1948.
3. CAMBER, F. H.: A malabsorption syndrome in military personnel in Puerto Rico. *Arch. Intern. Med. (Chicago)* 98: 44, 1956.
4. SULLIVY, T. W., COHEN, W. C., WALLACE, D. K., LACTUS, L. J.: Tropical sprue in North Americans. *JAMA* 191: 1069, 1965.
5. SMITH, R.: Personal communication.
6. SPRINZ, H., SPINNEHART, R., CHANTRONG, F., JIJANAJIT, B., KUNDEL, D., HAUSMAN, S.: Biopsy of small bowel of Thai people. With special reference to recovery from Asiatic cholera and an intestinal malabsorption syndrome. *Amer. J. Clin. Path.* 38: 43, 1962.
7. BAKER, S. J., IGNATIUS, M., MATHAN, V. I., VAISH, S. K., ZIACKO, C. C.: Intestinal biopsy in tropical sprue. in *Intestinal Biopsy*, Ciba Foundation Study Group no. 14, edited by WOLSTENHOLME, G. E. W., CAMERON, M. P. Little, Brown and Co., Boston, 1962, p. 81.
8. RUSSELL, P. K., AZIZ, M. A., AHMED, N., KENT, T. H., GANGAROSA, E. J.: Enteritis and gastritis in young asymptomatic Pakistani men. *Amer. J. Dig. Dis.* 11: 296, 1966.
9. LINDENBAUM, J., ALAM, A. K. M. J., KENT, T. H.: Subclinical small intestinal disease in East Pakistan. *Brit. Med. J.* In press.
10. ANGEL, C. R., GUERRA, R., MARTINEZ, J., PLOUGH, L. C.: Malabsorption of xylose in Puerto Rico (abstract). *Ped. Proc.* 22: 530, 1963.
11. KUEHN, F. A., SAMOFF, I. M., SCHENK, E. A.: Tropical sprue in Haiti. *Ann. Intern. Med.* 63: 373, 1966.
12. RICE, J. H., RICE, E. W.: Photometric method for determination of free pentoses in animal tissues. *J. Biol. Chem.* 173: 507, 1948.
13. SCHILLING, R. F.: Intrinsic factor studies. II. The effect of gastric juice on the urinary excretion of radioactivity after the oral administration of radioactive vitamin B₁₂. *J. Lab. Clin. Med.* 42: 860, 1953.
14. VAN DE KAMER, J. H., BOKKEL HUININK, H., WEYERS, H. A.: Rapid method for the determination of fat in feces. *J. Biol. Chem.* 177: 347, 1949.
15. JOYER, A., GORDON, R. S.: Procedure for quantitative analysis of feces with special reference to fecal fatty acids. *J. Lab. Clin. Med.* 59: 878, 1962.
16. CROSBY, W. H., KUGLER, H. W.: Intraluminal biopsy of the small intestine. *Amer. J. Dig. Dis.* 2: 235, 1957.
17. FORDTRAN, J. S., SOERGEL, K. H., INGELFINGER, F. J.: Intestinal absorption of D-xylose in man. *New Eng. J. Med.* 267: 274, 1962.
18. BOOTH, C. C., MOLLIN, D. L.: The site of absorption of vitamin B₁₂ in man. *Lancet* 1: 18, 1959.
19. RONNOV-JESSEN, V., HANSEN, J.: The site of absorption of Co⁵⁷-labelled vitamin B₁₂ in man. An investigation made by intestinal intubation with polyethylene glycol as a marker substance. *Blood* 25: 224, 1965.
20. BOOTH, C. C., SUTWART, J. S., HOLLERS, R., BRACKENBURY, W.: Dissecting microscope appearance of intestinal mucosa. *Intestinal Biopsy*, Ciba Foundation Study Group no. 14, edited by WOLSTENHOLME, G. E. W., CAMERON, M. P. Little, Brown and Co., Boston, 1962, p. 2.
21. KENT, T. H., WILSON, S. J., HAN, C. C.: Comparison of jejunal mucosa in postresection states, idiopathic steatorrhea, and controls using the dissecting microscope and conventional histological methods. *Gut* 5: 553, 1964.
22. LEISHMAN, A. W. D.: Thoughts on sprue. After experience in India. *Lancet* 2: 818, 1945.
23. AYREY, F.: Outbreaks of sprue during the Burma campaign. *Trans. Roy. Soc. Trop. Med. Hyg.* 41: 377, 1948.
24. BAKER, S. J., MATHAN, V. I., JOSEPH, J.: The epidemiology of tropical sprue. in *Malabsorption Syndromes*, Symposium of the Second World Congress of Gastroenterology, Karger, New York, 1963, p. 4.
25. FRENCH, J. M., GADDIE, R., SMITH, N. A.: Tropical sprue. A study of seven cases and their response to combined chemotherapy. *Quart. J. Med.* 25: 333, 1956.
26. SULLIVY, T. W., PEREZ-SANTIAGO, E.: Antibiotic therapy in tropical sprue. *Gastroenterology* 41: 208, 1961.
27. KLIPSFEIN, F. A.: Tropical sprue in New York City. *Gastroenterology* 47: 457, 1964.
28. GUERRA, R., WHEBY, M. S., BAYLESS, T. M.: Long-term antibiotic therapy in tropical sprue. *Ann. Intern. Med.* 63: 619, 1965.
29. MILANES, F., CURBELO, F., RODRIGUEZ, A., KOURI, P., SPIES, T. D.: A note on bacteriological and parasitic studies of the intestinal contents of patients with sprue. *Gastroenterology* 7: 306, 1946.
30. NADEL, H., GARDNER, F. H.: Bacteriological assay of small bowel secretion in tropical sprue. *Amer. J. Trop. Med. Hyg.* 5: 686, 1956.
31. BAYLESS, T. M., GUARDIOLA-ROTCER, A., WHILLY, M. S.: Tropical sprue: viral cultures of rectal swabs. *Gastroenterology* 51: 32, 1966.
32. SPRINZ, H., KUNDEL, D. W., DAMMIN, G. J., HOROWITZ, R. E., SCHNEIDER, H., FORMAL, S. B.: The response of the germ-free guinea pig to oral bacterial challenge with *Escherichia coli* and *Shigella flexneri*. *Amer. J. Path.* 39: 681, 1961.
33. LINDENBAUM, J.: Malabsorption during and after recovery from acute intestinal infection. *Brit. Med. J.* 2: 326, 1965.
34. LINDENBAUM, J.: Unpublished observations.
T. H.: Staphylococcal enterotoxin gastroenteritis in Rhesus monkeys. *Amer. J. Path.* 70: 1066, 1966.