Small intestinal deficit in pellagra[1]

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Pellagra is essentially a syndrome that occurs either as a result of maize eating or as a result of malabsorption or malnutrition. Gastrointestinal symptoms such as diarrhea, stomatitis, or glossitis are characteristic of patients with pellagra. Little attention has, however, been paid to the absorptive status of the small gut in pellagra, in spite of diarrhea. Van Heerden (1) showed that the fat absorption of a test dose of labeled triolein was not disturbed in pellagra, and even when severe diarrhea was induced, these patients failed to reveal any defect in their absorption of fat. In view of the paucity of the literature on small bowel status in patients with pellagra, we decided to study this aspect of the problem.

Material and methods

Twenty-four patients with pellagra, admitted to the Postgraduate Medical Institute Hospital, Chandigarh, India, were investigated. Most of the patients came from the dermatology service and some were from the psychiatric wards. The patients had varying dietary habits, half of them being predominantly maize eaters. Particular attention was given to the dietary history of the patients as, in this region, patients who develop pellagra secondary to malabsorption generally eat all cereals including wheat flour, which is the staple food.

Routine clinical examination, sigmoidoscopy, stool examination to exclude any parasitic infestation, routine hematological tests and barium meal, using a microsuspension of barium, were done in all cases to exclude diseases such as tuberculosis, regional enteritis, lymphoma, and tropical sprue. Small intestine functional studies were then carried out; the techniques have been reported earlier (2, 3).

Twenty-four-hour fecal fat estimations with a fat intake of 100 g for 7 days, urinary excretion of D-xylose after a 25-g dose, and an oral dose of radioactive B_{12} using 1 $\mu g/\mu Ci$ of $^{58}CO\text{-}B_{12}$ were performed on all 24 patients. In addition, we did bone marrow smear examinations and jejunal biopsies, using a Rubin's multipurpose capsule for the latter.

A repeat study of the absorption functions was done in six of these patients after treatment with nicotinic acid.

Results

Of the 24 patients, 15 were male and 9 were female; their age ranged between 20 and 60 years. The symptoms were generally of a short duration. One patient had symptoms for only 20 days, whereas the patient with the longest history had symptoms for 14 months. Fifty percent (12) of the patients were predominantly maize eaters and the rest ate maize intermittently along with wheat.

Clinically, all the patients exhibited typical cutaneous manifestations, a prerequisite for inclusion in the study (Fig. 1). Dermatitis varied from a mild to severe form. Psychiatric symptoms were seen in only three patients and these were 1^+ to 2^+ according to the grading of Shah and Singh (4). Only 10 of the 24 patients complained of diarrhea (3 to 10 movements per day). The rest of the patients were asymptomatic as far as the gastrointestinal tract was concerned.

Average hemoglobin was 9.25 $\pm$ (SD) 2.28 g/100 ml. Average total serum values

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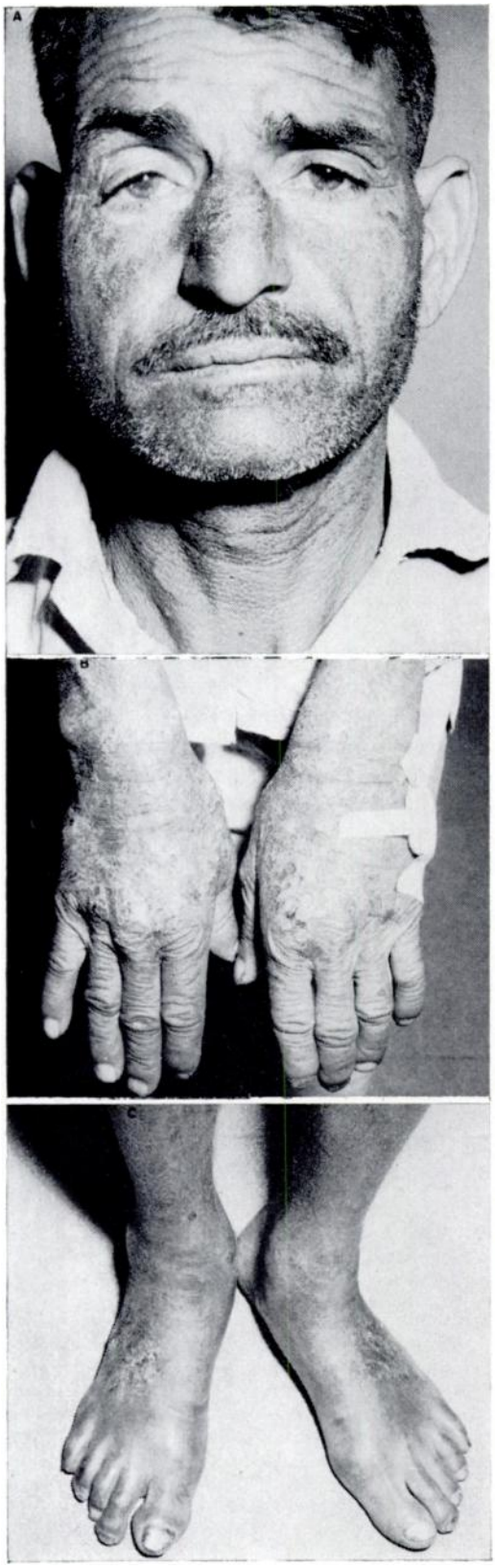

were: protein, 5.74 ± 0.65; albumin, 2.99 ± 0.59; and globulin, 2.79 ± 0.31 g/100 ml. There was an alteration of the A/G ratio with the lowering of serum albumin. Bone marrow examination was carried out in only 17 of the patients; 7 of them had recently received vitamin injections before coming to us and their bone marrow examinations could not have been pertinent to our data. Eleven of them had dimorphic anemia; one showed iron-deficiency anemia alone, whereas five were megaloblastic. Serum B_{12} determinations were done for 11 patients and folic acid estimations were done on 5 of them. The former was abnormal (<70 pg/ml) in eight and the latter was abnormal (<6 ng/ml) in two patients. The bone marrow smear revealed megaloblastic anemia in those patients whose serum vitamin levels were abnormal.

Stool fat estimation was carried out in all but two of the patients (91.6%). The mean fat excretion was 7.60 ± 4.10 g/24 hr. Steatorrhea was present in 14 cases (63.6%). It was mild (6.1 to 12 g/24 hr) in 11 and moderate (12.1 to 20 g/24 hr) in 3 cases. Urinary D-xylose excretion was studied in 23 patients and the average excretion on a 25-g dose was 3.10 ± 1.78 g; it was abnormal in 18 cases (78.6%). The disturbance was mild (3.1 to 4 g) in five, moderate (2.1 to 3 g) in five, and severe (2 or < 2 g) in eight cases. The Schilling test was performed on 18 of the 24 cases (75%); the mean value was 7.18 ± 5.12%; the excretion was abnormal in 10 patients (55.5%). Figure 2 shows the results of the patients' absorption tests.

All three absorption tests, i.e., 24-hr fecal fat excretion, D-xylose excretion, and Schilling test, were abnormal in six patients (25%); two tests were abnormal in eight (33.3%), and eight patients (33.3%) showed derangement of only one of three tests. The absorptive status was abnormal in two patients (8.3%).

In 10 of 11 patients who had jejunal biopsies, partial villous atrophy (PVA) was revealed. Nine patients with abnormal jejunal mucosa showed evidence of biochemical malabsorption as manifested by one or more abnormal absorption tests. One normal patient showed PVA on biopsy and another had a normal jejunal mucosa in spite of the abnormality of all the three absorption tests.

FIG. 1. Classical cutaneous features of pellagra.

Depending upon their staple food, maize or wheat, the subjects were classified into two groups of primary and secondary pellagra, respectively, with a view to separating the true cases of pellagra from the possible cases of tropical sprue. Twelve patients fell in each of these two groups. Comparing the two groups, it was noticed that nine out of twelve in the first group had derangement of two or three tests, whereas the remaining three had abnormality of one test only (Table 1). In the second group, however, two cases were completely normal, five had an abnormality of one test only, and five cases showed derangement of two or three absorptive functions.

The absorption tests were repeated in six pellagrins who showed malabsorption after adequate treatment with nicotinic acid (Fig. 3). Five showed complete recovery and one showed partial improvement (Table 2).

Discussion

Pellagra is etiologically related to excessive maize consumption as has been established experimentally by Goldberger and Wheeler (5). Zein, one of the proteins present in maize, is deficient in tryptophan, and, moreover, the niacin present in maize is in a bound form (4), resulting in the development of a nicotinic acid deficiency. Pellagra has also been etiologically related to excessive leucine in cereals (6). Our patients did not eat "Jowar" (*Sorghum vulgare*) and hence leucine did not seem to be responsible for the production of pellagra in these cases.

As far as we are aware, no detailed studies on the absorptive function in patients with pellagra have been reported. Manson-Bahr (7) recorded that the feces in the pellagrins could be pale, foul, milky, soapy, and at times steatorrheic. Mayer and Stare (8) observed that the stools were not abnormal and contained no excess fat. In an investigative study of fat absorption in the pellagrins reported by Van Heerden (1), it was observed that the fat absorption of a test dose of labeled triolein was normal and even the induction of severe diarrhea failed to reveal any defect in fat absorption.

Our observations in this regard have been different. Fourteen (63.6%) out of twenty-two patients were found to have either mild

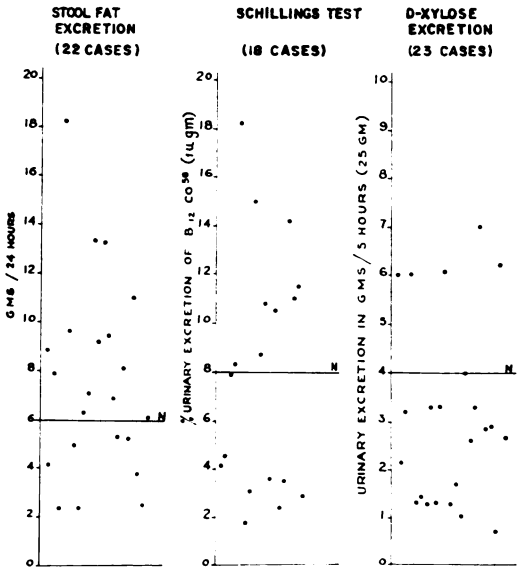

FIG. 2. Absorption studies in 24 cases of pellagra. Each dot represents the value obtained in a single patient. Normal stool fat excretion was <6g/24 hr, normal ^{58}Co-B_{12} excretion was >8%, and normal D-xylose excretion was >4g/5 hr.

or moderate steatorrhea. In seven patients (29.1%), this was associated with the presence of diarrhea. It is quite possible that many of the remaining patients failed to attach any importance to their bowel habits. Steatorrhea seems to have had a direct relationship to the development of pellagra as shown by the improvement in six patients in whom a repeat study was done after treatment with nicotinic acid (Table 2).

Urinary excretion of D-xylose was abnor-

TABLE 1
Comparison of absorptive function abnormality in primary and secondary pellagra

Name of test	Primary pellagra, group I[a]	Secondary pellagra, group II[b]
	No. of cases	No. of cases
Steatorrhea	8	6
Abnormal D-xylose excretion	11	7
Abnormal Schilling test	6	5
PVA	7	4
Normal	Nil	2

[a] Predominantly maize eaters. [b] Predominantly wheat eaters.

mal in 18 of the 23 patients (78.6%). The derangement was severe in eight (44.4%) and moderately severe in five cases (27.7%). The Schilling test was abnormal in 14 of the 18 patients (55.5%) who were tested.

Gillman and Gillman (9) reported that changes in the intestinal wall of adult pellagrins were usually minimal. We encountered partial villous atrophy in nine patients who had biochemical malabsorption of one, two, or all three tests. The jejunal mucosa was normal in one case with gross biochemical malabsorption and abnormal in another pellagrin who showed no biochemical abnormality. This result supports our earlier observations that the value of jejunal biopsy as a diagnostic technique in malabsorption has its limitations (3).

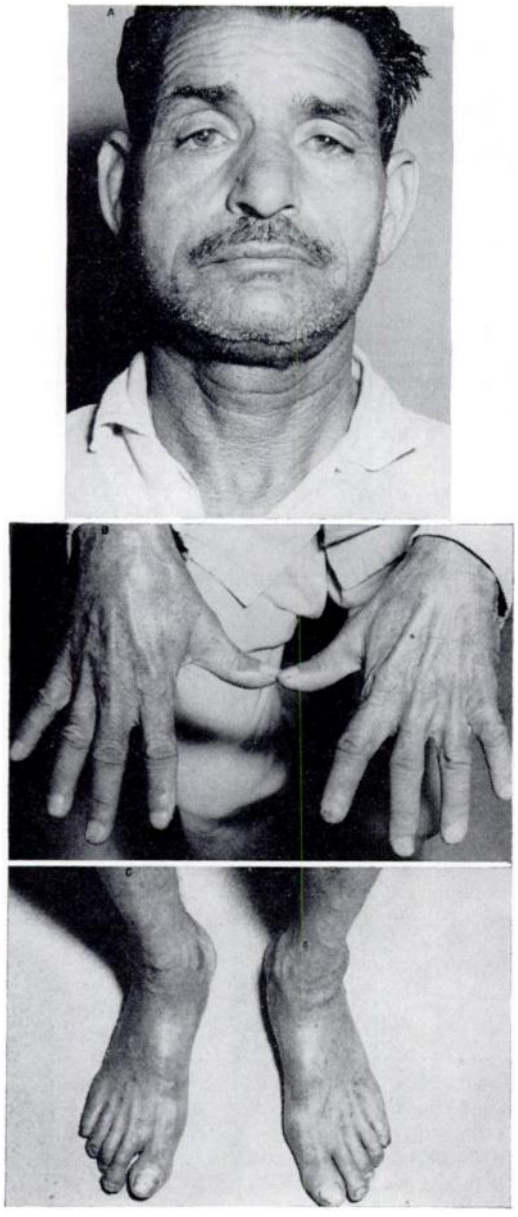

FIG. 3. Subject showing almost complete recovery after 6 weeks of treatment with nicotinic acid.

TABLE 2
Improvement in absorptive functions[a]

Case no.	Before therapy			After therapy		
	Fecal fat	D-Xylose excretion	Schilling test	Fecal fat	D-Xylose excretion	Schilling test
6	8.12	7.00	3.5	5.0	7.0	9
8	6.90	2.60	2.4	4.2	5.0	11
9	9.44	4.00	1.5	3.8	5.2	8
16	4.99	3.30	2.1	2.4	6.1	9.3
17	9.60	1.28	1.8	4.2	4.5	11.2
19	18.20			9.0		

[a] Data of six pellagrins after therapy.

Etiopathogenesis of malabsorption in pellagra seems to be multifactorial. The role of hypoproteinemia in the production of malabsorption in such cases is substantial. This was experimentally shown to be causing malabsorption (10, 11); intestinal malabsorption has also been shown in kwashiorkor and marasmus (12, 13).

With the frequent reports of tropical sprue from Northern India (2, 14–16), the differentiation between primary and secondary pellagra (due to tropical sprue) becomes difficult. We have tried to exclude patients with a long-standing history of diarrhea. A close scrutiny of their dietary habits revealed that in 12 predominantly maize eating patients (vide supra), nine had equivocal evidence of biochemical malabsorption (derangement of two or three absorptive tests) and three showed faulty absorption in one of the three tests. Out of the remaining twelve patients whose staple food was wheat flour, two showed no defect of absorption, five had only one test deranged, whereas in five others two of three tests were abnormal. Moreover, 6 out of the 14 cases (42.8%) recovered on nicotinic acid therapy, even when two or more

absorptive tests were abnormal. It is likely, therefore, that malabsorption serves to become an additional factor in the rapid deterioration and emaciation of some of these pellagrins.

The small intestine with a large absorptive cell surface probably reacts to a number of noxious factors by producing malabsorption. Malnutrition of protein and vitamins, bowel infection, and dietary factors may lead to the production of malabsorption and so the pellagrous patients could be no exception.

Summary

Twenty-four persons with pellagra were the subjects of absorption testing. Fourteen (58.3%) showed evidence of defective absorption of two or three absorption tests and eight showed (33.3%) abnormality of only one of the tests of absorption. Only two cases (8.3%) were found to be having completely normal absorptive status of the small bowel. Six of these fourteen (42.8%) cases recovered completely or partially on treatment with nicotinic acid. The etiopathogenesis of malabsorption in pellagra is discussed. Patients of both primary as well as secondary pellagra showed similar derangement of small intestinal functions.

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