BRIEF REPORT

Intrinsic Factor in Tropical Sprue

By Munsey S. Wheby and Theodore M. Bayless

GASTRIC INFLAMMATION and atrophy associated with diminished production of hydrochloric acid are common in patients with tropical sprue.1,2 After a simple, in vitro assay for intrinsic factor was described,3,4 the present study was done to determine if intrinsic factor secretion is impaired in tropical sprue.

MATERIALS AND METHODS

Criteria used to establish the diagnosis of tropical sprue were previously published.5 Twenty-one of the patients with sprue and four of the normal subjects were Puerto Rican. The patients with sprue ranged in age from 15 to 74 and the normal groups from 25 to 56. Treated patients were receiving folic acid orally, 5 mg. daily. Gastric juice was collected before and for 90 min. after subcutaneous injection of histamine phosphate 0.01 mg./Kg. body weight. After the pH of the gastric juice was measured with a Beckman pH meter, it was depepsinized,5 brought to pH 7. and stored at −20 C. or lower until assayed. Intrinsic factor was assayed by the method of Gottlieb et al.,4 except for the use of 10 ng. 57cobalt vitamin B12 instead of 7.5 ng. of 60cobalt vitamin B12. This method is based on the observation that protein-coated charcoal adsorbs free B12 but not B12 combined with binding substances in gastric juice, thus allowing measurement of the unsaturated B12-binding capacity. By blocking binding of B12 to intrinsic factor with an antibody to intrinsic factor,6 the percentage of the total gastric juice B12 binding capacity due to intrinsic factor is assayed.

RESULTS

Table 1 contains the results of the intrinsic factor assays. Three of fourteen patients with untreated sprue, three of nine patients with treated sprue, and five of five patients with pernicious anemia had abnormally low intrinsic factor activity. When the total volume of gastric juice was taken into consideration, the results were the same. In addition, there was no correlation between duration of disease and inadequate secretion of intrinsic factor.

Of the six patients with sprue and a low intrinsic factor assay, only one failed to develop a gastric juice pH of less than 3 following the submaximal stimulating dose of histamine.
Table 1.—Intrinsic Factor Assays and pH Measurements on Gastric Juice from Normal Subjects, Patients with Tropical Sprue, and Patients with Pernicious Anemia

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Age</th>
<th>PH</th>
<th>Intrinsics Factor</th>
<th>% of Total 57Co B12 Binding Due to IF* After Histamine</th>
<th>Percentage of Total Binding Due to IF*</th>
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*Percentage of total 57Co B12 binding by gastric juice due to intrinsic factor.
†Based on our five normal subjects and Ref. 4.

**DISCUSSION**

Intestinal malabsorption and megaloblastic anemia associated with deficiencies of folic acid and vitamin B12 are the outstanding features of tropical sprue. While abnormalities of the small intestinal mucosa underlie the malabsorption, the inflammatory lesion is not limited to this site. Several recent re-
ports have emphasized involvement of the stomach with varying degrees of gastritis and depression of gastric acid secretion. Floch et al. found that ten of eighteen patients with untreated tropical sprue had diminished hydrochloric acid secretion, and fourteen of twenty-one gastric biopsies showed either atrophic gastritis (10) or gastritis (4). Vaish et al., using the augmented histamine test, found significant decrease in gastric acid secretion in patients with tropical sprue, while gastric biopsies showed either gastritis (10) or atrophic gastritis (17) in twenty-seven of thirty patients. Although these gastric lesions could result in inadequate secretion of intrinsic factor, this point was not studied owing to the complicating effect of the intestinal lesion. In tropical sprue, despite prolonged treatment with folic acid and vitamin B₁₂, there is usually persistent malabsorption of vitamin B₁₂ unless long-term antibiotic therapy is used; thus, radioactive vitamin B₁₂ absorption tests have been of no value in assaying intrinsic factor in these patients.

The development of an in vitro assay for intrinsic factor has greatly facilitated the detection of coexistent intestinal malabsorption and inadequate gastric intrinsic factor. Prior to the in vitro assay, the method of determining presence of intrinsic factor was to show that the gastric juice under study enhanced vitamin B₁₂ absorption in patients with pernicious anemia. Using this method, Sheehy et al. found intrinsic factor activity in the gastric juice of some patients with tropical sprue. The results of the present study support the finding of adequate intrinsic factor activity in gastric juice of most patients with tropical sprue. However, six of twenty-three patients had decreased gastric intrinsic factor activity measured with an in vitro assay. This deficiency could result in persistent inadequate absorption of vitamin B₁₂ in approximately 25 percent of patients with tropical sprue even if the intestinal lesion is corrected.

The incidence of decreased gastric intrinsic factor activity is lower than that previously reported for gastritis or atrophic gastritis. Although gastric biopsies were not part of the current study, our patients are comparable to those reported by Floch et al. since they were drawn from the same population and similar criteria were used to establish the diagnosis. Whether tropical sprue is responsible for the gastritis and decreased intrinsic factor is uncertain since the frequency of these changes in the Puerto Rican population is unknown.

**Summary**

Using an in vitro assay for gastric intrinsic factor, it was shown that seventeen of twenty-three patients with treated and untreated tropical sprue have adequate intrinsic factor in their gastric juice.

**SUMMARIO IN INTERLINGUA**

Per medio de un methodo de essayage in vitro, il esseva monstrate que dece-septe de vinti-tres patientes con tractate o non-tractate sprue tropic habeva adequate quantitates de factor intrinsec in lor succo gastric.

**ACKNOWLEDGMENTS**

We are indebted to Miss Aimee Rodriguez for her technical assistance.
REFERENCES


Brief Report: Intrinsic Factor in Tropical Sprue

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