# THE VALUE OF THE DISSECTING MICROSCOPE IN THE DIAGNOSIS OF NONTROPICAL SPRUE

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Since the introduction of the peroral intestinal biopsy tube by Shiner [1] in 1956, histologic study of various diseases of the small intestine has become a routine procedure. Likewise, the appearance of the mucosa as seen by electron microscopy has been well described.[2-6] Recently, the usefulness of the dissecting microscope in examining tissue in nontropical sprue has been reported.[7-9] With this technique, the mucosal surface of the biopsy specimen can be viewed immediately. In the normal state, individual villi are seen as finger-like projections. In some individuals these are flattened from side to side, forming so-called "leaf forms"; these occasionally constitute the predominant form in the proximal intestine,[8-11] but are rare distally.[8-11] In nontropical sprue in our experience and in that of others [7-9] finger-like villi do not occur in the duodenum.

The appearance of the small bowel at various levels as observed in dissecting and conventional microscopy has been described in nontropical sprue.[7-9] However, to date there has been no comparison of the findings by these two methods at multiple levels in the same patient. The purpose of this report is to present the results in a patient so studied and to evaluate the use of the dissecting microscope in the diagnosis of nontropical sprue.

## Methods

The subject was a 44-year-old white man who had had nontropical sprue for several years, the diagnosis having been established previously by peroral intestinal biopsy. At the time of the study the patient had been in clinical remission for 8 months, following the institution of the gluten-free diet. A hydraulically operated suction biopsy tube [12] was passed, and reached the terminal ileum on the fourth day. Its position was determined by injecting Gastrographin through the tube and obtaining a roentgenogram of the abdomen (Fig. 1). A biopsy specimen was obtained in the terminal ileum, immediately delivered, and the tube was withdrawn approximately 3 cm. At this point another specimen was taken, and this procedure was repeated throughout the entire length of the small intestine. Twenty-four biopsy specimens were ob-

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tained over a period of 3½ hours. As the tissue was taken, it was hardened in 10 per cent formalin for 3 minutes. This facilitated the spreading of the specimen on the stage of the dissecting microscope. All tissues were examined within 5 minutes and were photographed under formalin with a Leitz photomacroscope using an electronic flash. Histologic sections were then prepared from each specimen in order to compare the two methods of examination.

## RESULTS

All 24 biopsy specimens were examined by dissecting and conventional microscopy; 6 were selected as representative of the changes seen at various levels of the small bowel. The length of tube withdrawal between the various specimens (Figs. 2 to 7) is shown in Table I.

TABLE I

| Figure no. | Centimeters of biopsy tube withdrawal between specimens * |
|---|---|
| | Terminal ileum |
| 2 | |
| 3 | 30 |
| 4 | 15 |
| 5 | 26 |
| 6 | 20 |
| 7 | 24 |

* Since the intestine tends to telescope itself along the biopsy tube, the number of centimeters withdrawn is not an accurate measure of the distance traversed by the capsule in the small bowel. Fluoroscopic observations of the capsule at fixed anatomic checkpoints is necessary for more accurate positioning.

A biopsy specimen from the terminal ileum showed the villi to be entirely normal (Fig. 2A). A histologic section of the same specimen also exhibited no abnormality of the mucosa (Fig. 2B). A preparation taken from about the midportion of the ileum exhibited flattening of the villi from side to side into early "leaf forms" (Fig. 3A). In the corresponding histologic section, the mucosa appeared to be essentially normal (Fig. 3B).

In the upper ileum, villi and "leaf forms" were closely intermingled, the latter predominating (Fig. 4A). Histologically these villi appeared to be of varying diameter (Fig. 4B). However, a comparison with Figure 4A indicates that the appearance of wider villi resulted from sectioning through the broad diameter of the "leaf forms."

In the jejunum the appearance was similar to that in the upper ileum except that some of the "leaf forms" were joined together into short ridges (Fig. 5A). The corresponding histologic section (Fig. 5B) exhibited thickening of the lamina propria, increase in the number of

glands, and what appeared to be irregularly shaped villi. In the distal duodenum a convoluted pattern was found to consist of a series of long ridges joined together at various points (Fig. 6A). No "leaf forms" or villi were present. The histologic section (Fig. 6B) revealed the appearance of partial atrophy and falsely suggested the presence of clubbed, blunted villi. In the proximal duodenum a flat mosaic pattern was characterized by subdividing grooves (Fig. 7A). Some elevation of the mucosa was observed about the mouths of the crypts and appeared as circular ridges. The histologic section at the same level (Fig. 7B) showed typical subtotal atrophy.

## Discussion

In 1961, Holmes, Hourihane and Booth,[7] using a dissecting microscope, described 4 characteristic patterns in the small intestine mucosa of patients with nontropical sprue: (a) a completely flat mucosa with no projections from the surface; (b) a similar flat pattern with the surface divided into a mosaic by deep grooves ("flat mosaic"); (c) a mucosa composed of adjacent ridges occasionally joined together, termed "convoluted" because of a resemblance to the surface of the human brain; and (d) a convoluted mucosa divided by deep grooves into a "convoluted mosaic pattern." True villi were absent in all 4 groups. These authors suggested that the strikingly different patterns might be gradations of the characteristic pathologic process in patients with nontropical sprue. The present study has indicated (Figs. 2 to 7) that these alterations may occur in a single patient, varying sequentially from one end of the small bowel to the other.

Comparison of the histologic features and the appearance with the dissecting microscope at various levels indicated best correlation between subtotal atrophy noted histologically and the "flat" mucosa observed with the dissecting microscope. Discrepancies between the appearance of the histologic section and that with the dissecting microscope were encountered in areas where the mucosa was less affected. An area containing what appeared to be broad stunted villi histologically (Fig. 6B) exhibited no villi whatsoever with the dissecting microscope (Fig. 6A). It was apparent that the finger-like projections observed in the histologic section represented ridges which had been cut in cross section. It is possible that routine histologic examination in such instances might be interpreted as normal. In a biopsy from the upper ileum (Fig. 4), the histologic appearance was normal, although there was a wide range in the diameter of villi. With the dissecting microscope, however, "leaf forms" were more numerous at this level than was usual in the normal,[9] while the true villi present exhibited

little variation in diameter. It would appear, therefore, that the thick villi observed histologically were, in fact, "leaf forms" cut along their broad axes.

## Summary

Serial biopsy specimens were procured at varying levels from the duodenum to the terminal ileum in a patient with nontropical sprue. These were examined histologically and with the dissecting microscope. The terminal ileum was found to be normal by both methods. With the dissecting microscope the mucosa became progressively more abnormal as one approached the proximal jejunum; it was completely flat and devoid of villi in the duodenum. This transition could not be readily appreciated in the histologic sections.

The results indicate that the dissecting microscope is not only a useful accessory but may be superior to conventional histologic examination in the diagnosis of nontropical sprue.

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Photomicrographs were prepared from sections stained with hematoxylin and eosin.

FIG. 1. Biopsy capsule in the terminal ileum.

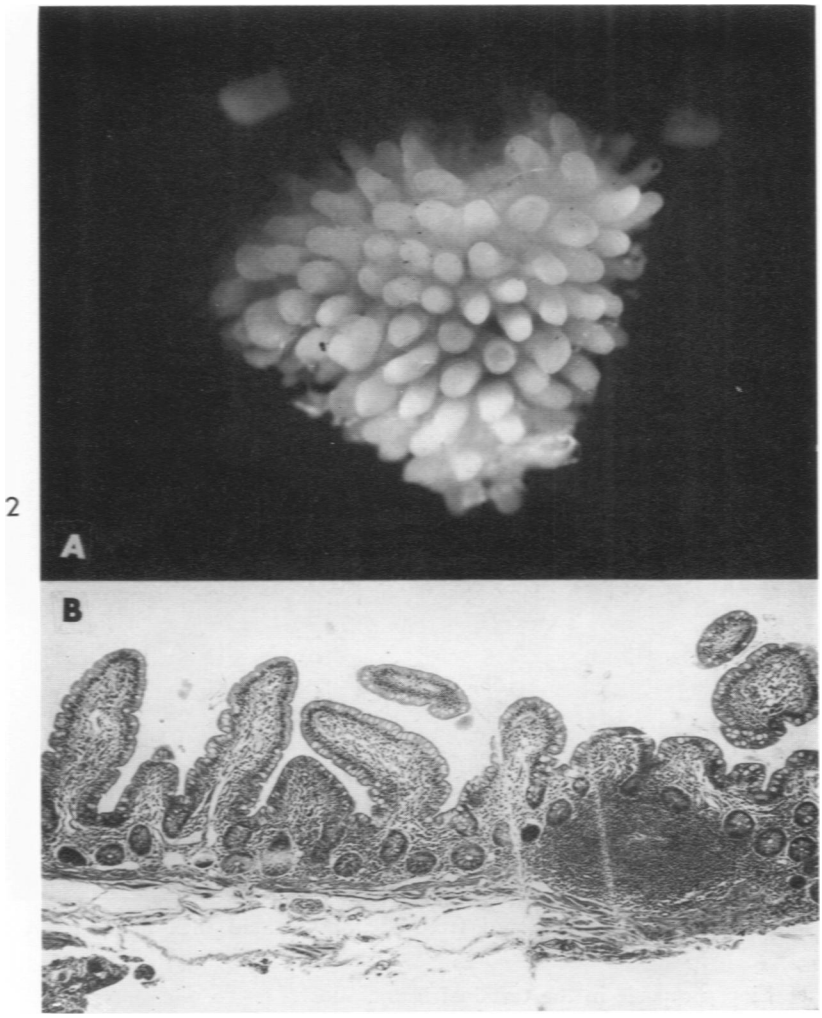


FIG. 2. A. Ileum. The mucosa is normal. × 17.
B. A conventional histologic section of the area shown in Figure 2A. × 64.

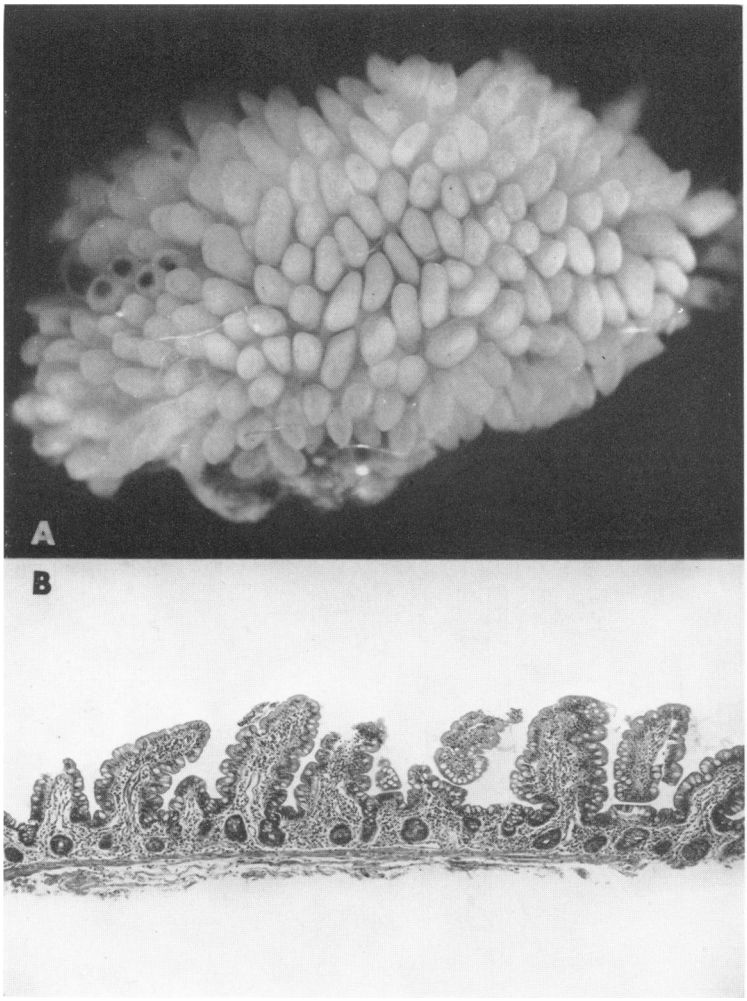


FIG. 3. A. At approximately midportion of the ileum. Many villi are flattened from side to side. × 17.

B. A histologic section of the specimen shown in Figure 3A. The mucosa appears essentially normal. × 64.

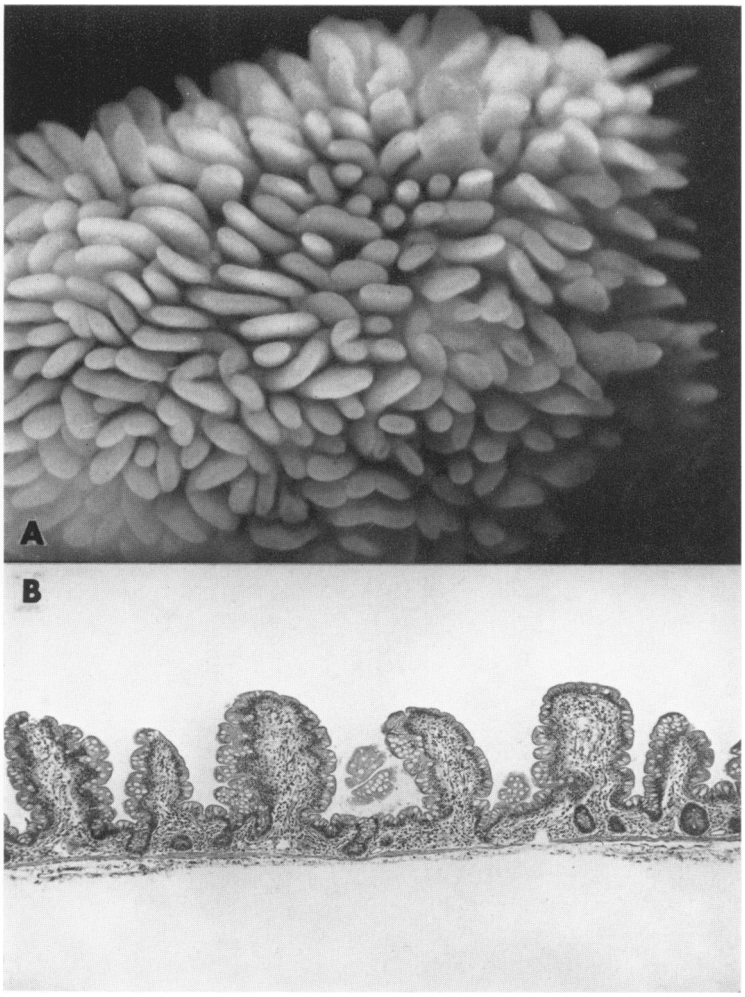


FIG. 4. A. Upper end of the ileum. Many "leaf forms" and a few normal villi are manifest. × 17.

B. A histologic section of the area shown in Figure 4A. Villi appear to vary widely in diameter. × 64.

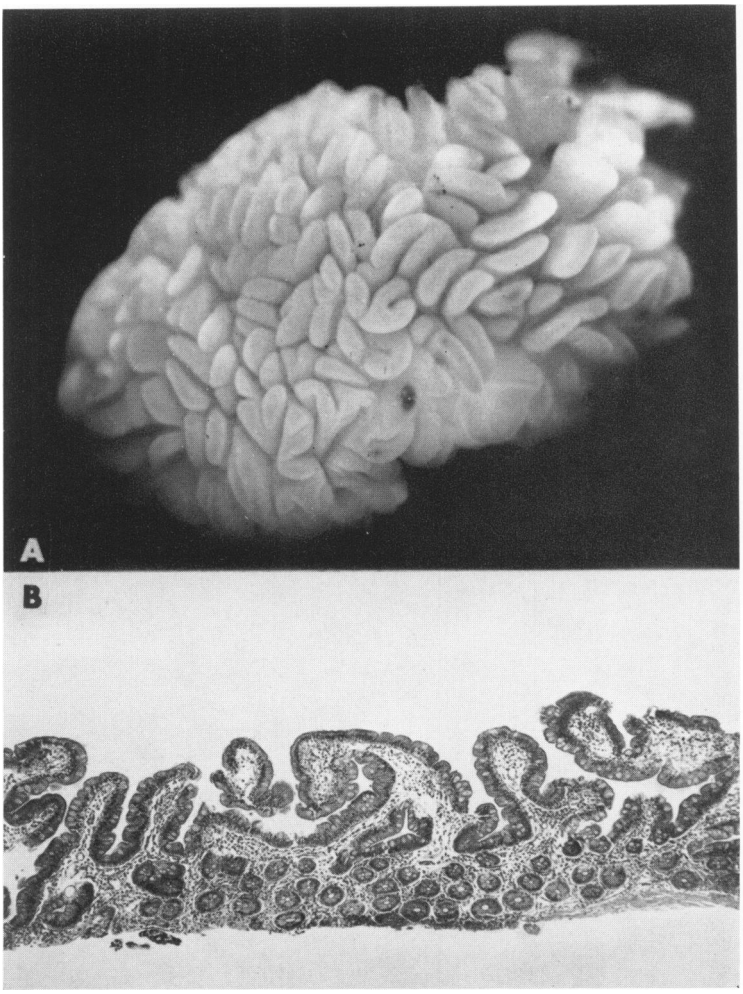


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FIG. 5. A. Jejunum. Many "leaf forms" are evident, and there is some ridge formation. × 17.

B. A histologic section of the area shown in Figure 5A. Villi appear to vary in diameter and lamina propria is thickened. × 64.

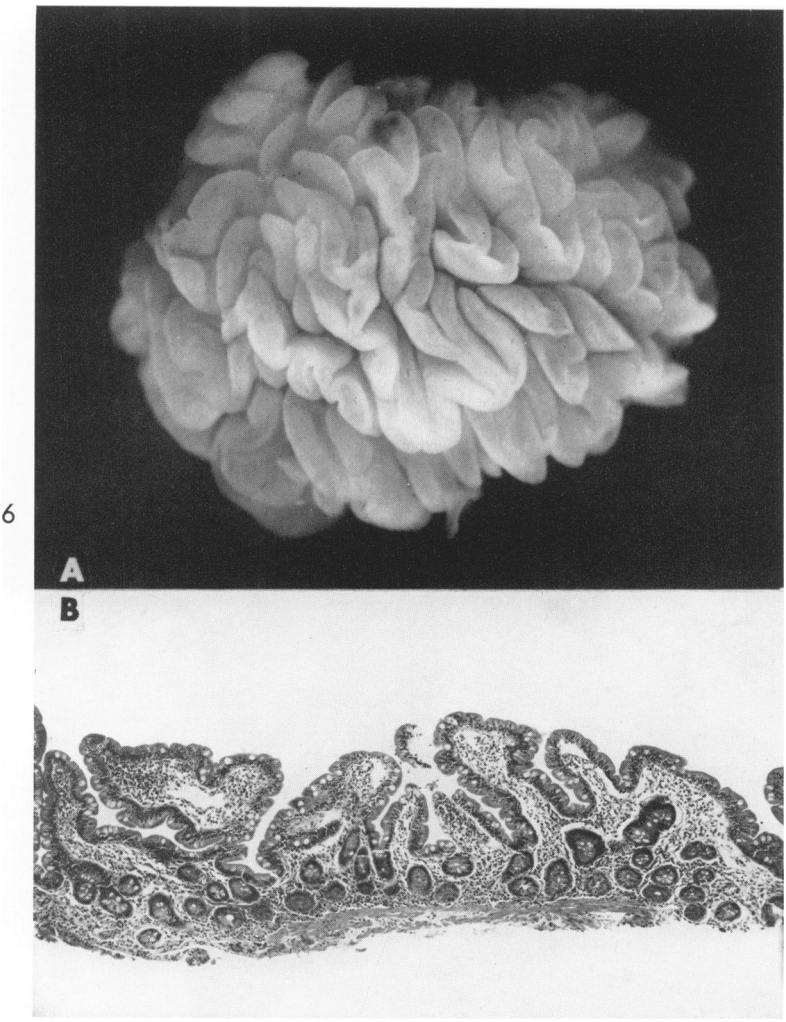


FIG. 6. A. In the distal duodenum the mucosa has a convoluted appearance. × 17.
B. Histologic appearance of area shown in Figure 6A. Blunted villi are falsely suggested. × 64.

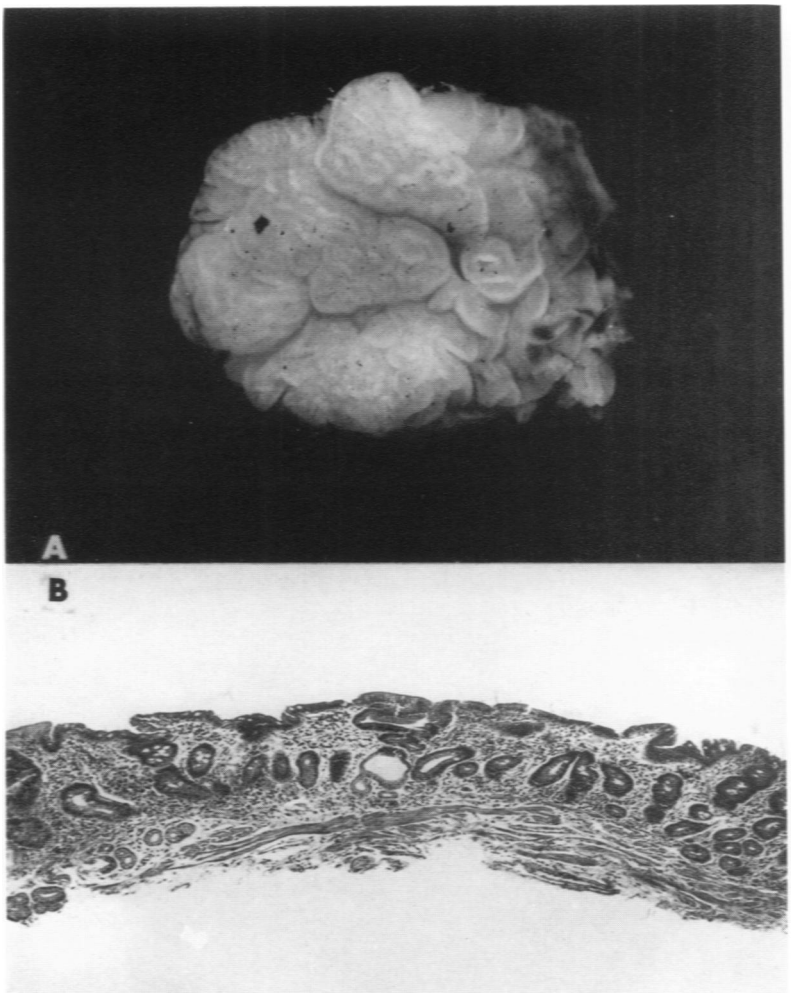


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FIG. 7. A. The duodenal mucosa is flat and exhibits a "mosaic" pattern. × 17.
B. A histologic section from the area shown in Figure 7A. The appearance is that of typical subtotal atrophy. × 64.