

This Week's Citation Classic

Rubin C E, Brandborg L L, Phelps P C & Taylor H C. Studies of celiac disease, 1. The apparent identical and specific nature of the duodenal and proximal jejunal lesion in celiac disease and idiopathic sprue. *Gastroenterology* 38:28-49. 1960. [Univ. Washington Sch. Med., Seattle. WA]

From infancy to old age abnormalities of villous architecture were found in duodenojejunal biopsies from all patients with celiac disease or idiopathic sprue. Such abnormalities were not seen in normals or in patients with a wide variety of other types of malabsorption. Heal mucosal morphology was normal in two celiac sprue patients with abnormal duodenojejunal mucosa. [The SC[®] indicates that this paper has been cited over 320 times since 1961.]

Cyrus E. Rubin
Department of Medicine RC:20
University of Washington
Seattle, WA 98195

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"Our research on celiac sprue began accidentally when we were studying the gastric mucosa of some of Dr. Louis Diamond's patients with juvenile pernicious anemia. Before that time we'd never performed a small bowel biopsy, but we wanted to see whether the intestinal mucosa was normal in these patients, because a duodenal abnormality had just been reported in one type of malabsorption — celiac disease. With Dr. Harry Schwachman's encouragement and help, we not only biopsied our study patients but also several of his celiacs. The findings were so fascinating that completion of our studies of juvenile pernicious anemia had to wait eight years while we pursued celiac sprue.

"The research reported in this paper probably made the Plenary Session of the 'Young Turks' because it contained

quantitative data to prove a histologic difference between normal controls and celiac sprue that was *visually obvious*. The presentation was almost entirely morphologic and so distractingly beautiful that the audience failed to notice the paucity of precise measurements.

"This study raised several questions: Was the lack of correlation between the severity of malabsorption and the severity of the duodenal and proximal jejunal mucosal abnormality somehow explained by the normal ileal mucosa? Actually it was: our subsequent studies of the whole length of the small bowel of patients with celiac sprue showed that the severity of malabsorption correlated with the length of bowel lined by abnormal mucosa, i.e., if the ileum and distal jejunum were normal, malabsorption was milder than if they were involved. If we had hypothesized correctly that the mucosal lesion of celiac sprue was pathognomonic, why was the lesion indistinguishable from that seen in tropical sprue? We now know that our hypothesis was wrong because several other rare illnesses cause the same lesion, although only celiac sprue responds to a glutenfree diet. The presence of the identical proximal intestinal lesion in children with celiac disease, and in adults with idiopathic sprue, suggested that they were the same disease and that is why we call the illness celiac sprue; a hypothesis that is now generally accepted.

"In retrospect the main contribution of this paper was to make morphologic research a respectable scientific pursuit for gastroenterologists; this was accomplished by demonstrating the validity of blind review for testing subjective histologic criteria, by emphasizing the need for orientating biopsies precisely before fixation and by sectioning them serially to obtain maximal information."