vagal stimulation to the stomach in normal subjects and ulcer patients.

In the accompanying report,[2] Feldman et al. examining the effect of sham feeding in a group of patients who have undergone vagotomy, some with endoscopically documented recurrent ulcers and others presumably without ulcer recurrence (no symptoms but not endoscoped). Eleven of 15 patients with recurrent ulcers had ratios of sham acid output to peak pentagastrin-stimulated acid output (SAO/PAO) of 0.1 or greater, while 28 of 41 patients without ulcer recurrence had a SAO/PAO of less than 0.1. The authors conclude that a SAO/PAO ratio after vagotomy of <0.1 suggests complete vagotomy, with 95% confidence limits; while a ratio of greater than 0.1 suggests incomplete vagotomy.

Although sham feeding appears to be a satisfactory test for completeness of vagotomy, and is certainly safer than using either insulin-induced hypoglycemia of 2-deoxy-D-glucose, it has limited predictive value for identifying those individuals at increased risk for developing recurrent ulcer. If two assumptions are made: (a) The population studied by Feldman et al. represents a random sample of vagotomized patients with and without recurrent ulcer, and (b) none of the patients without symptoms has ulcer recurrence, the sensitivity (the proportion of patients with the disease that have a positive test) is 73%, the specificity (the proportion of patients without the disease that have a negative test) is 68%. However, the predictive value of a positive test (the proportion of patients with a positive test that have the disease) is only 46% and of a negative test (the proportion of patients with a negative test that do not have the disease) is 62%. Therefore, the finding of a positive or negative response to sham feeding has little predictive value regarding ulcer recurrence.

When should the sham feeding be used in postvagotomy patients? It would seem reasonable that sham feeding should supplant the use of insulin or 2-deoxy-D-glucose in examining postvagotomy patients who have an ulcer recurrence, since the secretory responses to sham feeding and insulin are comparable. Most importantly, however, a prospective long-term study of this test with serial endoscopic evaluations and serial secretory studies in postvagotomy patients is needed to establish its clinical usefulness. Perhaps it will develop into a test which will accurately discriminate patients with intact vagal innervation to the stomach from those with complete vagotomy. However, only by conducting prospective studies will this important question be directly addressed.

JON I. ISENBERG, M.D.
Head, Division of Gastroenterology
University Hospital
San Diego, California

References

1. Feldman M, Richardson CT, Fordtran JS: Effect of sham feeding on gastric acid Secretion in healthy subjects and duodenal ulcer patients: evidence for increased basal tone in some ulcer patients. Gastroenterology 79:796–800, 1980
2. Feldman M, Richardson CT, Fordtran JS: Experience with sham feeding as a test for vagotomy. Gastroenterology. 79:792–795, 1980
3. Knutson U, Olbe L: Gastric acid response to sham feeding before and after resection of antrum and duodenal bulb in duodenal ulcer patients. Scand J Gastroenterol 9:191–201, 1974
4. Stenquist B, Knutson U, Olbe L: Gastric acid responses to adequate and modified sham feeding and to insulin hypoglycemia in duodenal ulcer patients. Scand J Gastroenterol 13:357–362, 1978

Address requests for reprints to: Jon I. Isenberg, M.D., Head, Division of Gastroenterology, University Hospital, 225 Dickinson Street, San Diego, California 92103.

This paper was supported in part by National Institute of Arthritis, Metabolism and Digestive Diseases grant AM 17328 to the Center for Ulcer Research and Education.

I am grateful to Drs. Morton I. Grossman and Robert M. Donaldson, Jr. for their comments.

Gluten-Sensitive Diarrhea Without Enteropathy: Fact or Fancy?

Koch's law indicates that to establish the specificity of a pathogenic organism as the cause of a disease, the following must be satisfied: (a) The organism must be present in every case. (b) Pure cultures of the organism must cause the same disease when inoculated into animals. (c) The organism must be recovered from the same animals. (d) The organism must be propagated in pure culture when recovered from the animal.

It is only careful adherence of this law that allows us to distinguish without ambiguity, fact from fancy in microbiology. A similar approach should be taken by the scientist who wishes to implicate a food as the cause of a particular illness. Food can clearly cause disease in humans, and establishing the causal link may be simple if objective features are present which can be quantitated. For example, patients with soy protein allergy develop not only diarrhea,

but a flat small bowel mucosa which returns to normal on soy restriction.[1] Patients with fish or peanut allergy develop anaphylaxis with hypotension and wheezing after eating the offending agent. However, if subjective symptoms are the only manifestation of a food-related problem, double-blind challenge is the only way to provide evidence for a causal link. Thus, May studied 30 patients with asthma in whom attacks were thought to be associated with ingestion of certain foods.[2] Symptoms were provoked in only 11 of 38 patients, when studied by double-blind food challenges!

Gluten-sensitive enteropathy is a disease in which gluten damages the small intestinal mucosa, resulting in villus flattening, epithelial cell damage, and various signs and symptoms related to the ensuing malabsorption—mainly diarrhea, abdominal bloating, and weight loss. Dicke documented that gluten ingestion was the immediate cause of the disease.[3] Since then, numerous investigators have shown many objective features are present in patients who are ill—short or absent intestinal villi, increased plasma cells in the lamina propria, increased intraepithelial lymphocytes in the epithelial cell layer and steatorrhea,[4] to name a few. It has been shown, also, that Koch's law must be essentially fulfilled to establish the diagnosis in patients, especially if the patients are children.[5] Thus (a) the disease must be suspected on clinical grounds, (b) a small bowel biopsy must be obtained showing the typical lesion, (c) a gluten-free diet must be instituted after which clinical remission and improvement of biopsy morphology must occur, and finally (d) a gluten challenge must be done and objective features such as changes in the small bowel biopsy or onset of diarrhea with steatorrhea must be shown before definitive diagnosis can be accepted. In some instances, in vitro demonstration of gluten-induced toxicity may establish the diagnosis, obviating the need for further biopsy.[6] Failure to establish incontrovertibly the diagnosis results in the mistaken belief that the patient has gluten-sensitive enteropathy, causing him to maintain a life-long gluten-free diet with its attendant financial and social disability. Such mistakes in diagnosis occur and can be readily documented. For example, Packer et al. showed that 22% of patients previously diagnosed without fulfilling the above criteria, did not truly have the disease.[5]

Cooper et al. describe a new syndrome in this issue of GASTROENTEROLOGY.[7] The clinical features of the syndrome are diarrhea with a nocturnal component, abdominal distention, pain, weakness, and weight loss, all apparently induced by a sensitivity to gluten *without* the presence of an enteropathy, a fact which is admirably documented. In contrast to patients with gluten-sensitive enteropathy (celiac disease), their patients were all female, had normal villus architecture, did not bear an increased incidence of HLA-B8, and had no steatorrhea or evidence for immunological disturbances. Yet, all these patients are said to respond to gluten restriction, with disappearance of the features of the syndrome. The significance of this study is quite obvious, in that the presence of food-induced diarrhea has been suspected by clinicians. The description by Cooper et al. would amount to the first objective description of such a syndrome. However, the limitation of the study lies in the weakness of the documentation. The authors state that during some 8 yr, 17 patients were identified who had diarrhea and other symptoms without an obvious cause. Arbitrary use of a gluten-free diet resulted in permanent remission of symptoms in 9 patients ("responders"). Eight of these 9 patients were subsequently challenged and form the basis for the description of the new syndrome. The challenge studies were performed as follows:

1. The first challenge of 8 responders was done by removing gluten from the diet and subsequently giving 30 g of gluten. However, this maneuver was not performed double-blinded, so although the patient had dramatic symptoms 8–12 hr after challenge, the result cannot be interpreted. Furthermore, 30 g of gluten were administered in a single dose during this challenge. This is equivalent to the gluten in *30 slices* of bread, an amount which may produce symptoms nonspecifically.
2. The second challenge study was blind, but only single-blind. Twenty grams of gluten/day were given to 5 responders, and 4 of 5 had symptoms within 24 hr. Because it was single-blind, the challenge results are open to question.
3. A third challenge was an accidental one which occurred with the unknowing ingestion of gluten by 2 patients. Such a "challenge" is difficult to interpret.
4. The last challenge was finally a double-blind challenge in 6 patients designed with a randomized cross-over at 2 wk with a week separating the two challenge periods. Twenty grams of gluten or a gluten-free flour was used. (The authors do not define the nature of their gluten-free flour.) Although well-designed, this challenge, which is the most important of all and upon which the syndrome must stand, cannot be interpreted because only a summary of the data are presented. No information is given regarding whether the challenge induced diarrhea in any patient! Furthermore, 1 patient did not complete the challenge, but was nevertheless included in the analysis of the data.

Thus, although it is possible that gluten may cause intractable diarrhea, abdominal pain, and bloating *without enteropathy* in some patients, it remains for these and other investigators to carry out an adequate double-blind challenge study to prove this. Since the patients described clearly developed symptoms within 8–12 hr after ingestion of 30 g of gluten, it should be relatively simple to establish unequivocally, the presence of this proposed new syndrome.

Levitt believes that all normal people malabsorb wheat flour to a degree.[8] It is possible that "Cooper's syndrome," if it proves to be real, is caused by an excess malabsorption of wheat flour or gluten, allowing the substance to reach the colon where bacteria would act upon it with fermentation. If this were the case, flatus analysis should show increased concentrations of hydrogen and carbon dioxide.[9] Until further work is done, the limitations of Cooper et al.'s provocative and interesting study are such that acceptance of the syndrome of gluten-induced diarrhea in patients without enteropathy must await the future.

Z. MYRON FALCHUK, M.D.
Department of Medicine
Harvard Medical School and
Affiliated Hospitals Center, Inc.
Peter Bent Brigham Hospital Division
Boston, Massachusetts

References

1. Ament ME, Rubin CE: Soy protein-another cause of the flat intestinal lesion. Gastroenterology 62:277, 1972
2. May CD: Objective clinical and laboratory studies of immediate hypersensitivity reactions to foods in asthmatic children. J Allergy Clin Immunol 58:500, 1976
3. Dicke WK: Coeliac disease: investigation of harmful effects of certain types of cereal in patients with celiac disease. Thesis. The Netherlands, University of Utrecht, 1950
4. Falchuk ZM: Update on gluten-sensitive enteropathy. Am J Med 67:1058, 1979
5. Packer SM, Charlton V, Keeling JW, et al: Gluten challenge in treated coeliac disease. Arch Dis Childhood 53:449, 1978
6. Katz AJ, Falchuk ZM: Definitive diagnosis of gluten-sensitive enteropathy: use of an in vitro organ culture model. Gastroenterology 75:695, 1978
7. Cooper BT, Holmes GKT, Ferguson R, et al: Gluten-sensitive diarrhea without evidence of coeliac disease. Gastroenterology 79:801–806, 1980
8. Anderson I, Levine A, Levitt MD: Use of breath H_2 excretion to study absorption of wheat flour (abstr). Gastroenterology 78:1131, 1980
9. Levitt MD, Donaldson RM: Use of respiratory hydrogen excretion to detect carbohydrate malabsorption. J Lab Clin Med 75:937, 1970

Address requests for reprints to: Z. Myron Falchuk, M.D., Peter Bent Brigham Hospital, 721 Huntington Avenue, Boston, Massachusetts 02115.

Dr. Falchuk is a recipient of Research Career Development Award, AM00210 from the Public Health Service and is supported in part by NIH Grant AM17684 from the National Institutes of Arthritis, Metabolism and Digestive Diseases.

Guidelines for Subspecialty Training in Gastroenterology

Whether desirable or not, there seems little doubt that certification of subspecialty training programs in the various disciplines of internal medicine including gastroenterology will soon be required. Which organization or organizations will ultimately assume responsibility for such program certification is not yet clear. However, the members of the Governing Board and the members of the Committee on Training and Education of the American Gastroenterological Association consider it important and timely that guidelines for subspecialty training in gastroenterology be prepared and published. Accordingly, the following guidelines were prepared by the Subcommittee on Graduate Education of the American Gastroenterological Association's Committee on Training and Education.

A. *General Principles*
   1. Gastroenterology, a subspecialty of internal medicine, is concerned primarily with the digestive system, including the gastrointestinal tract, the hepatobiliary system, and the pancreas.
   2. A strong clinical training experience is mandatory; training in research is highly desirable.
   3. Clear-cut objectives for the training program must be established, documented, and stated in terms which permit evaluation of achievement of the objectives.

B. *General Objectives of Training in Gastroenterology*
   1. The training program must provide access to the *basic concepts* and *facts* necessary to practice good gastroenterology.
   2. The training program must be designed to teach *critical analysis* and *reasoning* relative to clinical and investigative problems in gastroenterology.
   3. The training program must be designed to teach the *technical aspects* and the *procedures* of gastroenterology.