Intragastric Alkali Infusion

A Simple, Accurate Provocative Test for Diagnosis of Symptomatic Alkaline Reflux Gastritis

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Alkaline reflux gastritis is a disabling clinical syndrome, occurring most often after gastric surgery. It is characterized by abdominal pain and bilious vomiting, and, presumably, is due to gastric irritation by regurgitated duodenal contents. The only known effective treatment is by surgical diversion to prevent the duodenal reflux. Unfortunately, the clinical diagnosis is difficult to prove, and the results of surgery are too often disappointing because of inaccurate patient selection. This is a report of a new test for distinguishing patients with symptomatic bile reflux gastritis. The test consists of blind sequential infusion into the stomach, via nasogastric tube, of 20 ml of 0.1 N HCl, normal saline, 0.1 N NaOH, and the patient's own gastric contents. Each solution is given twice. A positive test is defined as reproduction of the patient's usual pain by NaOH, and/or gastric contents, but not by acid or saline. Fifteen of 21 patients with clinical symptoms and endoscopic findings suggesting bile gastritis had a positive alkali infusion test, while only one of 18 normal controls and none of 17 controls with other causes of abdominal pain had a positive test ($p < 0.001$). Of the 21 patients with clinical-endoscopic bile gastritis, 15 have had surgical treatment by Roux-en-Y gastrojejunostomy. Nine of ten patients with a positive test had excellent symptomatic relief after surgery. Zero of five patients with a negative test were relieved of pain after the operation. This simple test appears to be a sensitive, specific, and accurate means for selecting patients for surgical treatment of alkaline reflux gastritis.

ALKALINE REFLUX GASTRITIS, also commonly called bile gastritis, refers to the symptom complex of abdominal pain, nausea, and bilious vomiting most commonly recognized after operations which promote the regurgitation of duodenal contents into the stomach.[3,5,9,10,15,19,21,30,33] Most patients thought to have alkaline reflux gastritis have had a previous gastrectomy, gastrojejunostomy, or pyloroplasty, but the syndrome also occurs after cholecystectomy,[3,30,34] is accentuated by division of the sphincter of Oddi,[34] and may appear in occasional persons who have had no prior surgery.[15,30,33] The description of this syndrome was met with great enthusiasm, both as an explanation for that variety of postgastrectomy woes and as a beacon showing how to cure them by reoperation for diversion of duodenal contents away from the stomach. Series of surgically treated patients with excellent results accumulated rapidly.[10,15,19,25,30,33]

More recently, disillusionment with the results of surgical treatment has been growing as critical evaluations show failure to relieve symptoms in 30–50% of patients.[3,9] The symptoms of these patients not helped by diversion of duodenal contents, an operation which, in theory, ought to be completely effective, are ascribed to causes other than bile reflux, such as gastric motility disorders[9,32] or psychiatric abnormalities.[30,34]

A major difficulty has been the accurate selection of those individuals who truly have a gastric mucosal injury caused by reflux of duodenal contents. Endoscopic evaluation has been disappointing because there are inflammatory changes, at least in the region of the stoma, in most stomachs after gastric resection.[1,5,12] Even diffuse inflammatory changes may occur in asymptomatic patients, while patients with severe symptoms of bilious vomiting and pain may have minimal visible abnormality of the gastric mucosa.[16,17,34] Objective proof of gastritis by examination of a mucosal biopsy specimen has similarly failed to correlate with the presence or absence of symptoms of alkaline reflux gastritis.[1,3,16] Other tests recently proposed have included quantitation of bile reflux by measurement of bile acids[17,23,26] or by radionuclide scanning,[31] and provocation of symptoms by topical application of bile acids[23] or whole duodenal aspirates.[23] These approaches

Presented at the Annual Meeting of the American Surgical Association, Chicago, Illinois, April 22–24, 1981.

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0003-4932/81/0900/0297 $00.90

have, to date, proven unsuccessful because of overlapping of findings in symptomatic and nonsymptomatic patient groups, or remain unconfirmed in their accuracy for selecting symptomatic patients for successful surgical therapy.[18,23,26,31]

Using a concept akin to the Bernstein test for reflux esophagitis,[2] in which acid instilled into the esophagus reproduces the pertinent symptoms, we have developed a provocative test for alkaline reflux gastritis with alkali as the index. This report details the use of an alkali infusion test in persons with and without gastritis symptoms, and correlates the reproduction of pain and nausea with subsequent response to surgical diversion of duodenal contents.

Methods

Fifty-six subjects participated in this study and are divided into three categories: normal (n = 18), clinical/endoscopic diagnosis of alkaline reflux gastritis (n = 21), and other abdominal pain (n = 17). Informed consent was given by each patient according to protocols approved by the Subcommittee on Human Studies of the Massachusetts General Hospital.

Included in the normal group are six nonhospitalized volunteers and 12 patients who had a gastrostomy tube still in place after an abdominal surgical procedure. These latter patients were selected to exclude any active upper abdominal disease or symptoms; all were studied on the day prior to planned removal of the tube and discharge from the hospital.

The patients with putative alkaline reflux gastritis were referred for testing because of symptoms suggesting that diagnosis (upper abdominal pain, nausea, bilious vomiting, weight loss). Sixteen of the 21 patients had prior gastric surgery, and five had had cholecystectomies (three with transduodenal sphincteroplasties). All patients underwent gastroscopic examinations and were found to have abundant bile lakes in the stomach, mucosal staining with bile, and degrees of erythema and edema, varying from severe and diffuse to mild and confined to the peristomal region. All patients had gastric mucosal biopsies, which demonstrated a spectrum of changes from normal to severe gastritis, acute or chronic, some with intestinal metaplasia. The severity of histologic abnormality did not correlate well with the appearance of the mucosa by endoscopic examination by endoscopy. Upper gastrointestinal series in each patient revealed no other cause (such as recurrent ulcer or outlet obstruction) for the patient's presenting symptoms. Most were complex individuals who had undergone extensive medical and often psychiatric observation. Emotional and psychiatric factors were apparent in many and suspected in most.

Seventeen patients with chronic abdominal pain thought to be due to causes other than alkaline reflux gastritis served as a symptomatic control group. These included eight patients who had partial gastrectomies in the past, seven with endoscopic evidence of gastritis, seven with proven chronic pancreatitis, and two with proven duodenal ulcer. Some patients had more than one of these diagnoses. All the patients underwent gastroscopic examinations; with the exception of the postgastrectomy patients, none had abnormal amounts of bile reflux, bile lakes in the stomach, or mucosal staining by bile.

The usual symptoms of each patient were established by questioning. Each was then instructed that several test solutions were to be placed into his stomach and that any of these tests solutions might reproduce his usual symptoms, cause others, or cause no change. The subject was instructed to report any changes he felt and was questioned after each test solution had been instilled. The test was performed after an overnight fast by insertion of a nasogastric tube into the subject's stomach or by use of a previously placed gastrostomy tube. Aspiration of the stomach for five minutes emptied the stomach, provided gastric contents for observation of color and pH and for later reinstillation, and allowed the subject to accommodate to the test situation.

Without the subject knowing the order in which the test solutions were given, 20 ml aliquots of 0.1 N HCl, normal saline, 0.1 N NaOH, and the subject's own gastric contents were injected into the gastric tube by a hand-held syringe. The test solution was allowed to remain in the stomach for three minutes and then washed out with 20 ml of normal saline. The subject rested for five minutes before the next test solution was instilled. Each test solution was used twice, a total of eight test periods. If any test solution produced severe symptoms, as occasionally happened, only 10 ml of that solution was given the second time.

The responses to each test solution were recorded by the same nurse who performed all the tests and who was unaware of the category of the subject. Interpretation of the responses as positive or negative was made and recorded immediately, without reference to later clinical course or results of therapy.

Results

Interpretation of Test Results

Subjects commonly noted a sensation of coolness in the upper abdomen upon instillation of any of the test substances. This response was considered unimportant. Mild nausea also occurred with moderate frequency but without apparent meaningful pattern. Two

patients, known to have duodenal ulcers, had upper abdominal burning upon infusion of acid, a response considered specific but not pertinent. Two patients had extreme pain and nausea upon instillation of all test solutions, including normal saline; this excessive response was judged nonspecific and attributed to their known emotional lability. Thirty-seven patients had no significant symptoms during the test.

Sixteen patients had strong responses: 11 to alkali only, none to gastric contents only, but five to both alkali and gastric contents. The positive responses to these test solutions were upper abdominal pain in seven patients, severe nausea in one, and both pain and severe nausea/vomiting in eight.

On the basis of these findings, a positive alkali infusion test is considered to be upper abdominal pain (usually production of the patient's presenting complaint), with or without accompanying nausea upon intragastric infusion of alkali. There should be no significant response to acid or saline. Response to gastric content is suggestive in confirmation but not required.

Clinical Correlations with Test Results

The analysis of gastric aspirates for the 56 patients is shown in Table 1. In contrast to the normals and patients with other abdominal pain, bile was almost always obvious in gastric aspirates in patients thought to have bile gastritis. This, naturally, reflects both the high incidence of altered physiology due to prior surgery and to the process of selecting these patients for study because of bilious vomiting and endoscopic evidence of bile reflux. It is, therefore, not of further use in differential diagnosis.

Gastric pH was >6 in some patients in all groups, but most frequently in the patients who also had bile reflux. Conversely, gastric pH < 3 was found in 27/32 control patients, in five out of six of those patients referred for bile gastritis who turned out to have a negative alkali infusion test, but only two of the 13 with those who turned out to have a positive test. This observation suggests that gastric pH < 3 may be of some use as an index for screening out patients who are unlikely to have bile gastritis.

Based on the criteria defined in the preceding section, Table 2 shows the result of alkali infusion test in the study population. Of the 35 controls (normals and patients with other pain) only one test was considered positive: a female physician/volunteer with no abdominal complaints or prior surgery who had severe nausea upon infusion of alkali. Of the 21 patients with a clinical/endoscopic evidence of bile gastritis, 15 had a positive test ($p < 0.001$).

TABLE 1. *Baseline Gastric Analyses*

	Bile	pH > 6	pH < 3
Controls and other pain	12/32	2/32	27/32
Clinical alkaline reflux gastritis			
positive infusion test	12/13	10/13	2/13
negative infusion test	5/6	1/6	5/6

TABLE 2. *Intragastric Alkali Infusion Test*

Subjects	Positive	Negative
Normal controls	1	17
"Alkaline reflux gastritis"	15	6
Other abdominal pain	0	17

Sixteen of the 21 patients carrying the diagnosis of bile gastritis have now been operated on. The decision for surgery was made by each patient and his physician without regard for and usually without knowledge of the test results. Each patient has had construction of a long (usually 40–50 cm) Roux-en-Y gastrojejunostomy. Antrectomy, duodenal closure, and truncal vagotomy were added if not already performed. Fifteen of the 16 have been followed for 6–14 months after surgery. The surgery on the sixteenth patient was too recent to be evaluated.

Evaluation of the clinical response to the surgical diversion of duodenal contents from the stomach, made by the referring physicians without regard to knowledge of the test results is shown in Table 3. A good response means elimination of the patient's preoperative complaints of pain, nausea, bilious vomiting, and weight loss. Patients who had a positive test result were highly likely to benefit from surgical treatment directed at eliminating alkaline reflux, while those with a negative test uniformly derived no benefit from the surgery ($p < 0.001$).

TABLE 3. *Correlation of Intragastric Alkali Infusion Test and End-results of Surgical Treatment in Patients with Putative Alkaline Reflux Gastritis*

	Relief of Pain	No Improvement
positive test	9	1
negative test	0	5

Discussion

The initial enthusiasm which greeted the description of the alkaline reflux gastritis syndrome has cooled considerably as the complexities of this apparently simple entity have been delineated. A typical syndrome with characteristic features[5,30] has not emerged: bilious vomiting, once the hallmark, is no longer considered a necessary feature; the pain is steady and constant in some, episodic or worsened by eating in others; there may or may not be weight loss.[24] The time of appear-

ance of symptoms after surgery varies from weeks to years.[9,25,34] The susceptibility of a small minority of individuals to symptoms from alkaline reflux while most persons having the same reflux remain well has not been explained. Experimental models of alkaline reflux gastritis readily produce acute gastric mucosal changes, but this injury has been shown to heal in spite of continued alkaline reflux in chronic models.[6,7] The component or components of duodenal contents, such as bile acids, responsible for the gastric mucosal injury have not been identified.[4,11,14,26,28] The endoscopic appearance of the gastric mucosa does not at all correlate with the symptoms of alkaline reflux gastritis: not only are there inflammatory changes (at least in the region of the stoma) in most asymptomatic patients after gastrectomy,[1,12,17,32] but also the degree and extent of mucosal inflammation is highly variable in those patients who have symptoms ascribed to bile reflux.[3,9,13,17,34] The presence or absence of objective histologic changes is also inconstant, and fails to correlate either positively or negatively with symptoms.[3,9,13,16,26] Medical treatments aimed at binding bile salts with cholestyramine[22] and aluminum hydroxide,[20] or neutralizing acid with cimetidine[34] have failed. Surgical treatment to prevent duodenal contents from refluxing into the stomach fails in 30–50% of cases, according to recent reports.[3,9] If the symptoms and signs of this syndrome are variable, diagnostic tests nonexistent, and therapy both difficult and unreliable, it is no wonder that the very existence of alkaline reflux gastritis, at least as a useful clinical concept, is being challenged.[24]

In order to improve upon this situation, it will be necessary to improve the accuracy with which the diagnosis of alkaline reflux gastritis is made, to eliminate mimicking disorders such as gastric stasis[9] or dysmotility[32] and functional pain. One approach has been to quantitate bile reflux, on the assumption that either abnormal quantities of toxic (secondary or unconjudated) bile salts are present,[4,11,14,26,28] or that excessive total bile acid reflux is the cause of the syndrome.[17,26,31] Direct measurement of bile salts in gastric aspirates[17,23,26] have shown that some patients with the syndrome do have more reflux than normal persons, but in these studies there was considerable overlap between the groups of symptomatic and asymptomatic individuals. Tolin et al.[31] have recently reported the use of a radiolabelled marker and scintigraphic scanning to quantitate bile reflux. The amount of bile reflux in five patients thought to have symptomatic alkaline reflux gastritis was clearly greater than the bile reflux measured in eight asymptomatic postgastrectomy patients or in ten normal subjects. The study appears promising, but must be extended and confirmed by showing that symptomatic patients identified as having excessive bile reflux respond as uniformly to therapy.

Meshkinpour et al.[23] have attempted to reproduce the symptoms of alkaline reflux gastritis by administration of autologous upper intestinal contents into the stomachs of postgastrectomy patients with and without the syndrome. There were positive symptom responses to intestinal contents in ten of 11 symptomatic patients and only two of ten asymptomatic patients. This study is of great interest, but comprises a highly selected group of patients, intentionally skewed toward the most severe symptoms and stringent criteria. Sixteen additional symptomatic postgastrectomy patients were excluded from the study for not meeting all of these criteria. Such careful selection defines a group of patients at the extreme end of the spectrum who will probably demonstrate most clearly the abnormality sought.[9,16,26] Whether the results would be applicable and equally successful in a less selected group of patients, that is, whether the method has value in differential diagnosis, cannot be ascertained. Even in this selected group, the hypothesis would be strengthened by providing information on subsequent clinical course, including the results of surgical treatment.

Although Meshkinpour et al. found that bile acid concentrations were significantly greater in the upper intestinal contents of symptomatic patients than in those who were asymptomatic,[23] the same patients whose symptoms were provoked by the administration of intestinal contents were not bothered by infusion of artificial bile acid solutions into the stomach.[23] This important observation suggests that bile may be a valid marker for the presence and quantitation of enterogastric reflux, but not the cause of the gastric mucosal injury or at least of the clinical symptoms after injury.

Similarly, in the present study, infusion of gastric contents was much less likely to provoke symptoms than was alkali. This may be related to the fact that the pH of the endogenous gastric contents was near neutral, whereas that of the alkali was greater than 12. The alkali infusion test, as devised here, clearly exceeds physiologic or even the usual pathophysiologic conditions, and creates a specific form of stress.

The routine response to that stress was almost entirely limited to the group of patients for whom the diagnosis of alkaline reflux gastritis was being entertained. Furthermore, there was an excellent correlation between positive response to the test and relief of symptoms by appropriate surgery, and between negative response and failure of surgical treatment. This finding is all the more meaningful and practical in that it is derived from a group of patients *not* selected for

severity, but rather representative of a routine spectrum of patients suspected of having alkaline reflux gastritis. As judged by the end-results of surgery, it appears to have over 90% sensitivity, specificity, and accuracy, despite the emotional and psychiatric problems which becloud the clinical evaluation of these patients.

We are aware of the potential weakness that the scoring of the test results depends on subjective interpretation of subjective responses. We depend on the patient's blindness to the test solutions he is receiving, and upon both the magnitude and the specificity of the response to alkali. In addition, our minimum follow-up period after surgery may be too short to allow full subsidence of placebo effects, but the other failures were immediate and unequivocal. The acceptance of this test into clinical practice should still be provisional until its validity is confirmed by wider experience.

More questions are raised by these observations. Is alkali the primary cause of the gastric mucosal lesion in this syndrome, or is it only irritating tissue already injured by another agent? Bile salts are known to break the gastric mucosal barrier to back diffusion of acid[8,27,28] and cause morphologic injury, but alkali alone has also been shown to produce mucosal damage.[29] Both the failure of topical bile salts to cause symptoms in patients with alkaline reflux gastritis[23] and the failure of alkali to cause symptoms in patients with gastritis not caused by reflux are consistent with the possibility of a specific lesion caused by alkali in reflux gastritis. However, the alkali infusion test, itself, particularly because of the unphysiologic high pH of the infused alkali, should only be viewed as an acute provocative stress test. It does not provide information about pathogenesis.

We do not yet know whether the sensitivity to alkali infusion is the result of established mucosal injury or whether it is a permanent characteristic of that individual's stomach, existing before and after the period of alkaline reflux gastritis as well as during it. If it is a permanent characteristic, the alkali infusion test could be used in patients about to have a gastric operation or a cholecystectomy to evaluate their potential for developing alkaline reflux gastritis. In patients with a positive test, primary Roux-en-Y reconstruction after gastrectomy might be considered, and indications for cholecystectomy or sphincteroplasty should be more than casual. The prospective evaluation of alkali infusion would require testing thousands of patients, inasmuch as the syndrome occurs in only a small fraction of the population having a gastrectomy or cholecystectomy. We are, however, presently retesting those patients who had a positive test and subsequent Roux-en-Y gastrojejunostomy to see if the test remains positive after healing of the gastric mucosal lesion.

Acknowledgment

The author wishes to thank Judith Wilson, R.N. for the careful and thoughtful performance of the alkali infusion tests.

References

1. Berardi RS, Siroospour D, Ruiz R, et al. Alkaline reflux gastritis: a study in forty postoperative duodenal ulcer patients. Am J Surg 1976; 132:552.
2. Bernstein L, Fruin R, Pacini R. Differentiation of esophageal pain from angina pectoris. Role of acid perfusion test. Medicine 1962; 41:143.
3. Boren CH, Way LW. Alkaline reflux gastritis: a reevaluation. Am J Surg 1980; 140:40.
4. Brooks WS, Wenger J, Hersh T. Bile reflux gastritis. Analysis of fasting and postprandial gastric aspirates. Am J Gastroenterol 1975; 64:286.
5. Bushkin FL, Wickbom G, DeFord JW, et al. Postoperative alkaline reflux gastritis. Surg Gynecol Obstet 1974; 138:933.
6. Byers FM, Jordan PH. Effect of bile upon gastric mucosa. Proc Soc Exp Biol Med 1962; 110:864.
7. Cardoso de Oliveira M, Azevedo I. Long-term effects of bile on the gastric mucosa of the dog. World J Surg 1980; 4:471.
8. Davenport HW. Destruction of the gastric musocal barrier by detergents and urea. Gastroenterology 1968; 54:175.
9. Davidson ED, Hersh T. The surgical treatment of bile reflux gastritis. A study of 59 patients. Ann Surg 1980, 192:175.
10. Drapanas T, Bethea M. Reflux gastritis following gastric surgery. Ann Surg 1974; 179:618.
11. Gadacz TR, Zuidema GD. Bile acid composition in patients with and without symptoms of postoperative reflux gastritis. Am J Surg 1978; 135:48.
12. Geboes K, Rutgeerts P, Broeckaert L, et al. Histologic appearances of endoscopic mucosal biopsies 10-20 years after partial gastrectomy. Ann Surg 1980; 192:179.
13. Goldner FH, Boyce HW. Relation of bile in the stomach to gastritis. Gastrointest Endosc 1976; 22:197.
14. Harmon JW, Lewis CD, Gadacz T. Bile salt composition and concentration as determinants of canine gastric mucosal injury. Surgery 1981; 89:348.
15. Herrington JL Jr, Sawyers JL, Whitehead WA. Surgical management of reflux gastritis. Ann Surg 1974; 180:526.
16. Hoare AM, Jones EL, Williams JA, et al. Symptomatic significance of gastric mucosal changes after surgery for peptic ulcer. Gut 1977; 18:295.
17. Hoare AM, Keighley MRB, Starkey B. Measurement of bile acid in fasting gastric aspirates: an objective test for bile reflux after gastric surgery. Gut 1978; 19:166.
18. Hoare AM, McLeish A, Thompson H. Selection of patients for bile diversion surgery: use of bile acid measurement in fasting gastric aspirates. Gut 1978; 19:163.
19. Joseph WL, Rivera RA, O'Kieffe DA, et al. Management of postoperative alkaline reflux gastritis. Ann Surg 1973; 177:655.
20. Malagaleda JR, Phillips SF, Higgins JA. A prospective evaluation of alkaline reflux gastritis: bile acid binding agents and Roux-Y diversion. Gastroenterology 1979; 76:1192.
21. Menguy R, Chey W. Experiences with the treatment of alkaline reflux gastritis. Surgery 1980; 88:482.
22. Meshkinpour H, Elashoff J, Stewart H III, et al. Effect of cholestyramine on the symptoms of reflux gastritis. A randomized, double blind, crossover study. Gastroenterology 1977; 73:441.
23. Meshkinpour H, Marks JW, Schoenfield LJ, et al. Reflux gas-

tritis syndrome: mechanism of symptoms. Gastroenterology 1980; 79:1283.
24. Meyer JH. Reflections on reflux gastritis. Gastroenterology 1979; 77:1143.
25. Pyrtek LJ. Bartus SA. Reflux bile gastritis. Am J Surg 1973; 125:408.
26. Ritchie WP Jr. Alkaline reflux gastritis. An objective assessment of its diagnosis and treatment. Ann Surg 1980; 192:288.
27. Ritchie WP Jr. Bile acids, the "barrier", and reflux-related clinical disorders of the gastric mucosa. Surgery 1977; 82:192.
28. Ritchie WP Jr, Felger TS. Differing ulcerogenic potential of dihydroxy and trihydroxy bile acids in canine gastric musoca. Surgery 1981; 89:342.
29. Robert A, Nezamis JE, Lancaster C, et al. Cytoprotection by prostaglandins in rats. Prevention of gastric necrosis produced by alcohol, HCl, NaOH, hypertonic NaCl, and thermal injury. Gastroenterology 1979; 77:433.
30. Scudamore HH, Eckstam EE, Fencil WJ, et al. Bile reflux gastritis: diagnosis, medical and surgical therapy. Am J Gastroenterol 1973; 60:9.
31. Tolin RD, Malmud LS, Stelzer F, et al. Enterogastric reflux in normal subjects and patients with Billroth II gastroenterostomy. Measurement of enterogastric reflux. Gastroenterology 1979; 77:1027.
32. Toye DKM, Williams JA. Postgastrectomy bile vomiting. Lancet 1965; 2:524.
33. vanHeerden JA, Phillips SF, Adson MA, et al. Postpoerative reflux gastritis. Am J Surg 1975; 129:82.
34. Warshaw AL. Bile gastritis without prior gastric surgery: contributing role of cholecystectomy. Am J Surg 1979; 137:527.

Discussion

Dr. J. Lynwood Herrington, Jr. (Nashville, Tennessee): It has been my experience that patients with pronounced subjective symptoms of reflux, coupled with severe and widespread gastric mucosal inflammation, do gain benefit from the remedial operation. If these operative criteria are not rigidly met, the operative results are, indeed, disappointing. Satisfactory results have been obtained in approximately 80% of the patients in our series, which now totals 96 patients. Fifty-five of those patients obtained excellent results, and the conditions of 25% have improved.

Most of us will agree that severe reflux gastritis occurs more commonly after a Billroth II type reconstruction than after a Billroth I or a pyloroplasty, and it is virtually nonexistent after a proximal gastric vagotomy.

I present for your consideration, and I am not the first to suggest the use of, a Roux-en-Y diversion as a primary operation for duodenal ulcer, when proximal gastric vagotomy or a Billroth I type of reconstruction is not feasible. We are all aware that a Roux-en-Y diversion alone is ulcerogenic, but not so when accompanied by an adequate vagotomy and an adequate resection. The primary operation can then prevent the distressing complications of reflux gastritis that we so frequently encounter.

If we combine the resection with a selective gastric vagotomy, the possibility of severe postvagotomy diarrhea developing is, indeed, small. Furthermore, as you know, Dr. Edward Woodward has shown that a Roux-en-Y gastrojejunostomy empties slowly, and the dumping syndrome is, thus, diminished considerably. Emptying problems, however, can be of great concern in a small number of patients with Roux-en-Y diversions. Therefore, this primary operation could serve to diminish considerably the three distressing, long-range postgastrectomy problems that we face today.

In our series of 96 Roux-en-Y diversions, only two marginal ulcers have occurred, and each was due to incomplete vagotomy.

I congratulate Dr. Warshaw on a splendid presentation, and would like to have a later follow-up on a larger number of patients.

How do you explain the negative test response in your six patients with clinical symptoms and documented reflux? Did these six patients have severe and extensive mucosal changes?

Also, in your positive test cases, did the gross appearance of the gastric mucosa change on endoscopic study?

Dr. David Fromm (Syracuse, New York): Dr. Warshaw, I am left with more confusion than solution. The term alkaline is probably, as you admit, a misnomer. It is not, at least by current concepts, the alkalinity of the refluxed duodenal contents that is responsible for the symptoms. It is either the bile salts or bile acids or perhaps lysolecithin; it is the pH in the gastric lumen that is responsible for whether or not these agents cause mucosal alterations and symptoms.

I fail to understand how a solution of pH 13 can be responsible for symptoms, or responsible for an alkaline gastritis, if the patient's own gastric juice does not cause symptoms. Did you give any of your successfully treated patients your pH solution of 13 postoperatively to see if that correlated with their improvement?

Dr. A. Rahim Moossa (Chicago, Illinois): In the early 1950s (slide) Charles Wells of Liverpool suggested that bile acid reflux following a Billroth II gastrectomy is the result of an afferent loop syndrome. Intermittent emptying of bile from the afferent loop into the stomach, sometimes precipitated by eating, leads to alkaline gastritis/esophagitis and bilious vomiting. Because of this hypothesis we studied the problem using Tc-HIDA. This radiopharmaceutical agent is administered intravenously to the patient, and the abdomen is scanned. The liver parenchyma is first visualized followed by the appearance of isotope in the common bile duct and into the afferent loop (slide). The afferent loop is filled and distended; suddenly the afferent loop empties, especially in response to a meal, and the isotope refluxes into the stomach and sometimes into the esophagus. Bilious vomiting may occur at this stage.

This method was the most useful way of diagnosing bile acid reflux. Bile remains in the stomach and the afferent loop for quite a long time, even after 3 hours.

(slide) Following the Roux-en-Y diversion, repeat Tc-HIDA scan demonstrates bile coming into the afferent loop and bypassing the stomach without inducing the patient's symptoms.

In regard to the pain provocation tests suggested by Dr. Warshaw, I share the same reservations that Dr. Fromm mentioned, and I have two additional questions: 1) I am worried about the control group. I would have preferentially chosen as controls persons who have had a Billroth II gastrectomy but who have symptoms. 2) Have you tried using bile or a bile acid solution as the test solution?

We see a fair number of these patients referred to us with a provisional diagnosis of recurrent pancreatitis, because they often have elevated serum amylase levels during an attack of pain and vomiting.

Dr. Wallace P. Ritchie, Jr. (Charlottesville, Virginia): Stimulated by those who believe that alkaline reflux gastritis is a real entity, and not just a diagnosis in search of a disease, several fairly sophisticated methods have been developed to identify patients with excessive enterogastric reflux after gastrectomy. As Dr. Moossa has indicated, and in my opinion as well, the most specific and sensitive of these is gamma camera scintography, using tecnitium-labeled HIDA or PRIDA.

As Dr. Way and others have pointed out, none of these techniques is a reliable predictor of the clinical efficacy of remedial operative procedures, and therein, of course, lies the rub, and therein too, on the surface of it, lies the significance of Dr. Warshaw's contribution, a provocative test that, apparently, when positive predicts a 90% success rate, and that when negative predicts a 100% failure rate.