THE TREATMENT OF PEPTIC ULCER

Present Status, Including Vagotomy

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"RECENT measures advocated for the treatment of peptic ulcer range from pituitary 'snuff' to fresh cabbage juice! To these can be added mucin, protein hydrolysates, amino acids, resins, certain detergents and what have you." This quotation is from an article by George B. Eusterman in the 1949 Year Book of Medicine. The number of treatments for peptic ulcer are indeed unlimited.

Although each patient presents an individual problem, all clinicians are agreed that first attention should be given to the patient's general health, including his hygienic needs such as living habits, physical and mental rest, and proper nutrition.

The methods employed in treating peptic ulcer at Cleveland Clinic depend primarily upon the location of the ulcer. Analysis of our records show that 85 per cent of patients having duodenal ulcers make satisfactory progress on medical management alone. Most of the other 15 per cent, having intractable duodenal ulcers and/or complications, have been benefited by bilateral vagus resections plus gastroenterostomy. Gastric resection is being employed in most patients having gastric ulcer.

This discussion is divided into three parts: first, gastric ulcer and the complications of peptic ulcer in general; second, the medical management in patients having uncomplicated duodenal ulcers, and finally, a 2 year follow-up study of our first 100 consecutive patients with complicated duodenal ulcers who have had bilateral vagotomies plus gastroenterostomy or pyloroplasty. During the past 4 years 495 patients have had bilateral vagotomies.

Part I

Gastric Ulcer

When an ulcerating carcinoma of the stomach is demonstrated by roentgen and/or gastroscopic examination, gastric resection obviously is indicated. However, the problem of whether or not the gastric ulcer is benign or malignant is frequently encountered. When it is in the distal third of the stomach we believe that gastric resection is indicated, even though the ulcer may prove to be benign. Malignant lesions are most common in this area.

Unlike duodenal ulcer, gastric resection for a benign gastric ulcer is rarely, if ever, followed by the formation of a jejunal ulcer. The results are usually excellent.

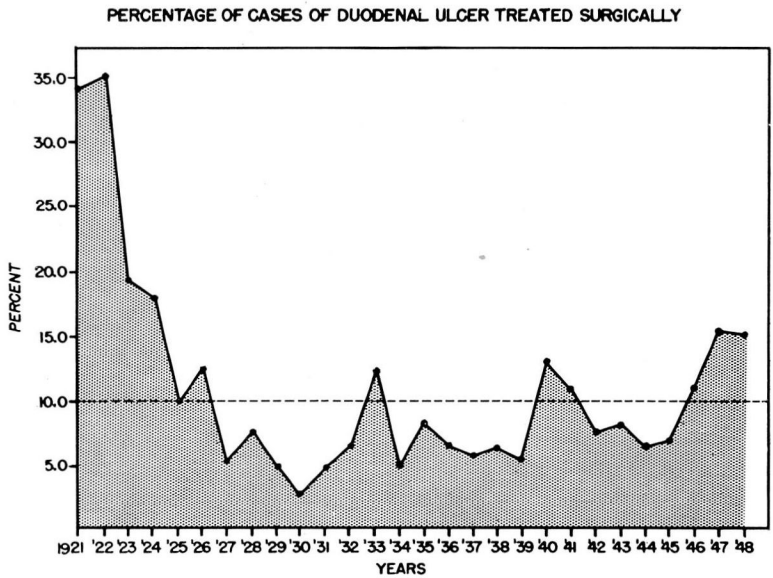
When the ulcer is on the lesser curvature in the pars media of the stomach and the patient presents a history of attacks characteristic of benign ulcer which have recurred for years, and when the roentgenologist and gastroscopist agree that the ulcer is benign, we may advise strict medical management provided re-check examinations are made in 1 month.

We have seen a number of instances where the roentgen and gastroscopic findings were questionable, and where at operation the surgeon believed the gastric ulcer benign as did the pathologist. Frozen sections disclosed no evidence of a malignant process but paraffin sections following gastric resection revealed a malignant disease. We re-emphasize our conviction that, in most instances, gastric resection is the treatment of choice for gastric ulcer.

Dr. George Crile, Jr. observes that, when dealing with a high gastric ulcer a centimeter or two from the esophagus, a more conservative procedure than total gastrectomy should be considered, such as excision of the ulcer coupled with gastroenterostomy, or gastroenterostomy with vagotomy. It is assumed that no cancer cells are found in the frozen biopsy specimen.

Duodenal Ulcer

The accompanying graph shows trends we have experienced in the surgical treatment of duodenal ulcer. It will be observed that in 1921, 35 per cent of patients had operations, i. e. gastroenterostomies. This period was followed by one of gastric resections (at that time the curve was as low as 5 per cent), and now, with the advent of bilateral vagotomy plus gastroenterostomy or pyloroplasty, the curve has risen to 15 per cent. It should be emphasized that surgery is employed for duodenal ulcer only when complications are present



such as acute perforation, two or more massive hemorrhages, or pyloric obstruction due to true cicatricial narrowing. It is indicated also for patients who continue to have intractable symptoms while on strict medical management.

Acute Perforation

Regardless of its location an acute perforation should, of course, have simple closure as soon as possible. It is a lifesaving procedure. A gastroenterostomy is combined with simple closure only if the ulcer is in the pyloric canal or associated with pyloric obstruction.

In recent years, since antibiotics and sulfonamides have become available, we occasionally see a patient on whom surgery is not performed immediately. Sometimes a patient is not observed until 24 hours or more following a small perforation by which time a "walling off process" has occurred. Constant Wangensteen suction, the use of 100,000 units of penicillin every 2 hours with or without intravenous sodium sulfadiazine and with parenteral fluid therapy, has resulted in postponement of surgery until an elective type of operation, such as vagotomy and gastroenterostomy, could be performed. Colonel Seeley and associates[1] at Fort Sam Houston, Texas, treated 34 cases of perforated duodenal ulcers in a similar manner without operations and without a single death.

In most cases we still believe prompt closure of the perforation to be the preferred treatment.

Massive Hemorrhage

Our present treatment of massive hemorrhage is influenced by the age of the patient, evidence of definite arteriosclerosis, and the immediate response to medical management. If operation during the massive hemorrhage is indicated, it should be performed preferably during the first 48 hours, in combination with a continuous "drip method" of blood transfusions. Although we believe this complication to be primarily a medical problem at the time of the hemorrhage, a surgeon familiar with all the details should be in constant attendance, prepared to operate at a moment's notice.

In this issue of the *Cleveland Clinic Quarterly* Dr. Stanley O. Hoerr has given our criteria for emergency operation. "The crux of the matter is the rapidity of the bleeding." Each patient presents an individual problem. It is commonly stated that young patients rarely require surgery at the time of active bleeding. However we have found that occasionally a patient below the age of 50 may continue to bleed while on medical management, while a patient of 70 years may have a sudden cessation of hemorrhage.

Medical management includes immediate sedation, such as sodium phenobarbital, gr. 1 or 2, and atropine sulfate, gr. 1/100, given hypodermically and repeated every 2 or 4 hours, in quantity sufficient to allay apprehension and to keep the patient drowsy. Morphine may increase the tendency to nausea and vomiting. Feedings of a bland type, including ground meat, are

given immediately at 2 hour intervals, and antacids are given between feedings; the antacids are repeated during the night hours.

Dr. Hoerr has summarized our convictions relative to blood transfusions. Although blood counts, including hematocrit readings, are made daily in an attempt to determine the *rapidity of bleeding*, most reliance is placed on efficient nursing care, the general condition of the patient, frequent determinations of the quality and rapidity of the pulse, and blood pressure determinations. Due to factors of dehydration and hemoconcentration, the blood counts may rise during active bleeding and fall when dehydration has been corrected and active bleeding has ceased.

Daily blood urea determinations have proved significant from the standpoint of prognosis. A high initial reading is associated with shock, with diminished flow of blood through the kidneys, as well as absorption of blood from the intestinal tract. If the blood urea level returns to normal in 2 or 3 days the patient obviously is not in immediate danger; if it continues to rise surgical intervention is strongly indicated. The color of the stools and tests for occult blood are observed daily but may not become negative until 10 days following the cessation of bleeding; thus stool examinations are valueless in determining immediate treatment, although reassuring when negative.

Surgeons prefer to operate when the massive hemorrhage has subsided, the lesion is localized, and the patient is in good condition. If the patient gives a history of two or more massive hemorrhages, we believe surgery should be employed regardless of age, and preferably when the bleeding has ceased and the patient is completely rehabilitated.

Pyloric Obstruction

Brilliant results follow the use of gastroenterostomy alone when the patient is 70 years old and the obstruction is due to a cicatrix of a healed ulcer. However, a patient 30 years of age, observed at the time of his first pyloric obstruction when undergoing considerable dilatation of the stomach due to an active duodenal ulcer, may overcome the symptoms and signs within a few days on medical management. In this instance the obstruction may be due to spasm or inflammatory edema. In the event of recurrent obstruction, surgery is unquestionably indicated.

Criteria which establish the diagnosis of true pyloric stenosis due to cicatricial narrowing should include observation on adequate medical management during a period of at least 5 days.[2] The same method is followed in preparing the patient for surgical treatment, so that no time is lost. Decompression of the stomach by daily gastric aspirations and continuous suction, at least during the night hours, are extremely important. Utilization of a new plastic tube has proved a more comfortable procedure than the older Levine rubber tubes. It is necessary to obtain an accurate record of the fluid intake and output, as well as to re-establish normal chemical balance.

We find that the determinations of the 24 hour urinary excretion of chlorides are particularly important.[3] The urinary chloride excretion is a simple

procedure and is more significant than the blood chloride determination. Haden has observed that the plasma chloride content is preserved at the expense of the tissue chloride, so that the amount of chloride in the blood may be normal when the tissue chlorides are depleted. The purpose of parenteral fluid therapy is to maintain a daily urinary output of 1500 cc. with an excretion of at least 5 Gm. of sodium chloride.

Foods which, in our experience, pass through the pylorus most easily are: strained cereals with sugar and cream, plain malted milk, chocolate malted milk, eggnog (nonalcoholic), plain ice cream, junket, plain gelatins with cream, strained cream soups, cocoa made with half milk and half cream, coffee with sugar and cream from which the caffeine has been removed.

Feedings from this selection are given every 2 hours throughout the day, the last at 6 p.m. Additions are made to the diet as rapidly as tolerated. Parenteral vitamins are given as indicated by clinical evidence of deficiency and the history of dietary inadequacy. Parenteral antispasmodics are prescribed similar to those given to patients with massive hemorrhage.

Since these patients commonly have alkalosis when first observed, the preferred antacid is aluminum hydroxide gel combined with magnesium trisilicate. The antacid is given every 2 hours, alternating with feedings except at the time when gastric suction is being employed. In none of our patients has there been a disturbance of the acid base or urinary complications attributable to this preparation.

If the obstruction is relieved within a period of 5 days, and medical management is continued, treatment is simplified and the ambulatory management for uncomplicated ulcer is instituted.

Part II

Medical Management of Uncomplicated Duodenal Ulcer

As previously mentioned, at least 85 per cent of our patients having duodenal ulcers make satisfactory progress on medical management. If this is prescribed adequately early in the course of the disease, and the patient cooperates, few complications occur.

Since the cause of peptic ulcer is unknown, measures have been used in its treatment based on the hygienic needs of the patient. The work of B. W. Sippy, published in 1915, is familiar to all clinicians. Extensive experimental work since that time, summarized by Walter L. Palmer,[4] has confirmed the value of antacid therapy.

Approximately 13 years ago we observed a number of patients with peptic ulcers who also had renal calculi or other renal complications. As the urologists wished to maintain an acid reaction in the urine, aluminum hydroxide gel was substituted in these cases for the usual Sippy powders.[5] These patients made satisfactory progress, even though the number of interval feedings and doses of antacid per day were reduced. Since that time aluminum hydroxide in combination with magnesium trisilicate or other nonabsorbable antacids have been used routinely, and the results of this therapy have proved as satis-

factory as those obtained formerly with the more rigid original Sippy treatment.

Evaluation of any treatment is difficult in a disease of unknown cause subject to spontaneous remission. However, as shown on the graph, the trends in surgical treatment of duodenal ulcer did not change when nonabsorbable antacids were substituted for the usual Sippy powders.

In treating these ulcers we attempt to effect more than the immediate relief of the symptoms. Satisfactory response to medical treatment is evidenced when ulcer craters disappear by progress roentgen examination as well as by gastroscopy in patients having gastric or anastomotic ulcers. These examinations are regulated according to the severity of the initial problem; even though they appear favorable, medical management is continued. However, the patient is advised to have further check-up examinations during the first year's treatment and at least annually during the next several years.

It is now generally agreed that adequate antacid therapy does not require complete neutralization of gastric acidity. The purpose is to keep the level of free acidity low enough to prevent activation of pepsinogen, the proteolytic neutralization point emphasized by Hollander.[6] Eyerly and Breuhaus[7] demonstrated by repeated electrometer readings, checked by repeated examinations of aspirated material over a 3 hour test period, that boiled egg white failed to digest when the stomach contents were maintained at a pH of 3.5 or higher.

James Flexner and his associates,[8] using a method for the continuous recording of gastric pH in situ (which included a pumping system to maintain circulation of the mixture around the glass electrode), studied the efficacy of numerous antacids and found that aluminum hydroxide gel had a prolonged antacid effect when prescribed in suitable dosage. The Komarovs[9] and Schriffrin and Komarov[10] demonstrated the precipitation and inactivation of pepsin in vitro and in vivo in dogs by the alumina gels without excessive reduction of acidity.

The intensity of our present therapy naturally varies with the severity of the disease and with the patient. Although details vary, standard medical management for uncomplicated duodenal ulcer during the first 6 weeks includes the use of a "smooth diet" and a glassful of milk or food every 2 hours while awake.

Diet

The diet has been liberalized in many instances. Vegetables and fruit are not pureed but in all instances the patient is advised to avoid seeds, skins and coarse fibers as long as he lives. While most patients with peptic ulcer like milk the most important feature is not how much they consume per day, but how often.

During the first week all foods except vegetables and fruit are allowed. Cooked vegetables and fruits are added during the second week. During the third week, and thereafter, the patient is on a well-balanced diet, including raw vegetables and fruits and juices.

Antacids

We have tested many antacids, detergents, mucin-combinations and other preparations by doing hourly aspirations and titrations of the patient during several 24 hour periods; in many instances with each substance. Beckman pH determinations using tenth normal hydrochloric acid with various "anti-ulcer" substances also have been made in vitro.

Nonabsorbable antacids, chiefly aluminum hydroxide, have been used in the Clinic during the past 13 years. In addition to their antacid property, aluminum hydroxide preparations have astringent, adsorptive, bactericidal, and demulcent properties, and they inactivate pepsin without excessive reduction of gastric acidity. Also, they can be prescribed without danger to the acid-base balance of the patient or of urinary complications. Formerly, milk of magnesia was added to prevent the constipating effect of aluminum hydroxide, but this is rarely needed now because we use aluminum hydroxide with magnesium trisilicate preparations.

The liquid forms are preferable and are used while the patient is in the hospital or around home. The dosage varies according to the gastric acidity but averages 2 teaspoonfuls (stirred in a third of a glass of water) every 2 hours during waking hours throughout the first 6 weeks of treatment, and 1 ounce on retiring. If the patient has had night pain he is advised to set his alarm clock and take 1 ounce at midnight and at 3 a.m. during the first week. In other words, during the first stage of the treatment the patient takes milk or food one hour and antacid the next, thereby alternating the two every waking hour. If he continues to work, tablets are substituted for the liquid when away from home for the sake of convenience. Antispasmodics and/or mild sedatives are used during the first 3 weeks' treatment.

We call the above treatment "minimal therapy." If the patient does not experience immediate and complete relief of symptoms, we conclude that the diagnosis was wrong or that a "surgical ulcer" exists. However, even though the patient has had complete relief of symptoms, we always advise progress roentgen examinations (and gastroscopic examination if the patient has a gastric ulcer), at the end of 6 weeks. Management is adjusted according to all details but he is advised to take milk or food at least once between meals and an antacid at least 4 times daily as long as he lives, as a means of preventing recurrence. Should the symptoms recur he must at once revert to the original schedule.

Roentgen Therapy

Palmer and his associates[11] at the University of Chicago have reported their results in 800 cases of peptic ulcer studied from 1936 to 1947. The optimum depth dose was found to vary from 1600 to 2500 r in 12 days. Ulcer pain disappeared and healing occurred uniformly during periods of achlorhydria. However, the duration of achlorhydria was unpredictable. It varied from a few days to as long as 8 years, the average being several months.

We have used radiation therapy in rare instances, particularly in patients with intractable symptoms who refused operation. The immediate results were

usually favorable but invariably the patients developed recurrent ulcers within a few months.

Protein Hydrolysates

Protein hydrolysates have been used in the treatment of peptic ulcer since 1942, when Levy and Siler[12] reported a noticeable buffering action on gastric acidity. For several months we substituted various forms of protein hydrolysates for our usual antacid therapy but the patients objected to the taste of the medicine as well as to the cost. Inasmuch as progress x-ray examinations were also unfavorable, its use was abandoned.

When, in 1945, Co Tui and his associates[13] at New York University reported favorable results in a small group of patients given protein hydrolysate and dextrimaltose, we tried this form of treatment but were again disappointed in the results.

Woldman and his associates,[14] working at St. Luke's Hospital in Cleveland, found there was a sharp rise in the free acidity in the stomach after the period of neutralization with protein hydrolysate. Multiple doses of 25 Gm. every hour ceased to neutralize free hydrochloric acid in the stomach; in fact the continuous drip of a 10 per cent solution failed to neutralize the acid. Although the ulcer pain continued for from 24 to 72 hours at the beginning of this treatment, it disappeared immediately in the patients receiving aluminum hydroxide gel. Recurrence of the ulcer within a short period after treatment was more common during treatment with protein hydrolysate, and this included such complications as hemorrhage and perforation. It was concluded that protein hydrolysate is valuable as a food, but has little value as a therapeutic agent in peptic ulcer.

Enterogastrone

Enterogastrone, an extract of hog-intestinal mucosa, depresses the secretion of acid by the gastric glands when administered intravenously to dogs. According to Ivy and associates[15] at the University of Illinois, enterogastrone extracts prevent postoperative jejunal ulceration in a high percentage of dogs with the Mann-Williamson operation, in 98 per cent of which ulcer ordinarily develops. They note as remarkable the fact that the anti-ulcer effect extends well beyond the period of administration of the extract; in most instances at least several years.

In the human subject intramuscular injections are given 6 times a week for 1 year. The recorded results to date are not better than antacid therapy. The cost of treatment and the inconvenience to the patient are important items. We have had no clinical experience with enterogastrone.

Banthine

Since January 1, 1950, we have used Banthine* (a drug with anticholinergic effects) in 20 patients having complicated duodenal ulcer. The initial response

Generously supplied by the Searle Company.

to the use of this drug has been favorable. Several physicians requested the use of Banthine before resorting to vagotomy with gastroenterostomy, and they have obtained satisfactory results without surgery. A long-term "follow-up" study will be required before evaluating this or any other form of treatment for peptic ulcer.[16,17]

Part III

Bilateral Vagotomy

The extensive work pertaining to this subject by Lester Dragstedt and his associates is well known. Members of our medical division have welcomed bilateral vagotomy in patients having intractable pain or complicated duodenal ulcers because they have witnessed the immediate relief of pain; the morbidity, as well as the mortality rate, has been lower in these patients than in those having gastroenterostomies or gastric resections alone. Many surgeons now agree that bilateral vagotomy is the procedure of choice in patients having jejunal ulcers following gastric resections. Dr. Dragstedt has reiterated, "Since we are agreed that bilateral vagotomy is the treatment of choice for jejunal ulcer, why does not this procedure apply to other simpler forms of peptic ulcer?"

Since January, 1946, 495 bilateral vagotomies have been performed at the Clinic. Vagotomy has passed through several stages in our experience. The transthoracic approach was used first. Thereafter the transabdominal approach without drainage was employed unless there was obvious pyloric stenosis. For a time gastric ulcers were treated by this procedure.

At the present time, as stated previously, gastric resection is the surgical treatment of choice in gastric ulcer. Vagotomy is not done at the time of a massive hemorrhage for any form of peptic ulcer. Vagotomy plus gastroenterostomy or pyloroplasty is the treatment of choice for complicated duodenal ulcer. The mortality rate for vagotomy with gastroenterostomy has been under 1 per cent.

Transabdominal vagotomies with or without revisions of the stoma in 31 patients with proved cases of marginal ulcers have given the following results: 21 excellent, 5 satisfactory, 2 improved, and 3 failures.

Results of 2 year follow-up studies of the first 100 patients having bilateral vagotomies plus gastroenterostomies or pyloroplasties for complicated duodenal ulcers follow:

Bilateral vagotomy plus gastroenterostomy . . 73 patients
Bilateral vagotomy plus pyloroplasty . . . . . 27 patients
(Operations performed by the late Dr. T. E. Jones and Dr. George Crile, Jr.)

Complications prior to operation:

Pyloric obstructions	24
Massive hemorrhages	21
multiple	9
Acute perforations	10
multiple	2

Twenty of the 24 patients having pyloric obstructions had 50 to 100 per cent gastric retention in 6 hours, as evidenced by roentgen examination. More than half of the patients in this series had intractable pain, including night pain, and medical management was ineffective.

The sex and age distribution and the duration of symptoms follow:

100 consecutive patients having complicated duodenal ulcers

Sex . . . . . 85 men 15 women

Age . . . . . Average—47 years

Duration of ulcer symptoms (prior to vagotomy)—average 12.6 years

Results of Follow-up Studies

Results to date are known in 97 of the first 100 consecutive patients. One patient died in the hospital and 1 died 6 months after operation of an unrelated disease. We were unable to trace 2 patients. Another patient had obtained an excellent result at the end of 9 months, but we have not seen him recently. Therefore, the present follow-up study concerns 95 patients who have been followed for an average of 2 years.

Insulin tolerance tests, unless positive, have not proved reliable in determining the completeness of the vagotomies in this investigation because of regurgitation of duodenal contents. Drainage studies have proved important, and postoperative roentgen examinations equally so.

In an attempt to appraise the results in 95 patients having follow-up studies over a period of 2 years, the following criteria were used:

Excellent . . . 100 per cent normal health from gastrointestinal standpoint.

Satisfactory . . No ulcer distress; gastrointestinal symptoms so mild that they do not interfere with work; no special diet or medication used.

Improved . . . No ulcer distress; fewer gastrointestinal symptoms than before operation, but diet and/or medication have been used to control symptoms.

Failure . . . . Persistence of ulcer-like distress or development of other gastrointestinal symptoms sufficiently severe to constitute disability.

	Excellent	Satisfactory	Improved	Failure
Cases	62	20	10	3

Excellent plus satisfactory—86 per cent. (Patients with complicated duodenal ulcer).

Three of the 95 patients were considered to be in the failure group. One patient developed a jejunal ulcer. At a subsequent operation he was found to have had an incomplete vagotomy. The other 2 patients continue to have intermittent ulcer-like distress but progress roentgen examinations have revealed no evidence of ulcer craters. Motility studies of these patients were normal; stomas functioned normally. One patient, a retired physician, has symptoms referable to many parts of the body, particularly the cardiovascular

system. The other patient is a 28-year-old registered nurse who had epigastric burning at times, as well as intermittent diarrhea not exceeding 4 stools in any 24 hour period. Although her roentgen examination demonstrated an excellent result from the operation, she has used antacids at times and is therefore considered a failure.

The patients who are placed in the excellent and satisfactory groups are following no special diet, taking no medicine, and have no significant symptoms. This is in contrast to the patients having partial gastrectomies or gastroenterostomies without vagotomy, where intensive postoperative medical management, including the use of antacids, is usually advised. It will be noted that 92 patients included in the first three categories are free of ulcer distress and are in much better health than before operation. Only 3 of the 95 are classified as failures.

Comment

The present report deals with the first 100 consecutive patients having bilateral vagotomies combined with gastroenterostomies or pyloroplasties for complicated duodenal ulcers. Of these we were able to follow 95 over an average period of 2 years.

Renshaw and Beck[18] reviewed 25 years' experience of our staff with conventional surgery, i. e. gastric resection or gastroenterostomy alone. The greatest percentage of recurrences occurred within the first year after operation.

The patients in the group reported here have obtained better results than comparable series of patients having conventional surgery followed over a similar period of time. The mortality rate was 1 per cent. One patient developed a jejunal ulcer with obstruction. At a subsequent operation he was found to have had an incomplete vagotomy. Otherwise no patient in this series has developed roentgen evidence of recurrent ulcer, and no patient has had a recurrence of obstruction, hemorrhage, or perforation.

At the present time, when elective surgery is indicated for complicated duodenal ulcer, our group favors bilateral vagotomy plus gastroenterostomy or pyloroplasty.

The final evaluation of any form of treatment for peptic ulcer must, of course, be based on years of experience, always bearing in mind that this disease is characterized by spontaneous remissions.

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