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Antral Exclusion with Vagotomy for Duodenal Ulcer: *

I. Acid Secretory Studies on 50 Patients

WILLIAM R. WADDELL, M.D., MARSHALL K. BARTLETT, M.D.

Boston, Massachusetts

From the Departments of Surgery, Massachusetts General Hospital and Harvard Medical School; and the Department of Nutrition, Harvard School of Public Health

DURING the past two and a half years the clinical and laboratory evaluation of a new operative procedure for the definitive surgical treatment of duodenal ulcer has been in progress. So far 100 patients have been operated upon. The purpose of this report is to describe the procedure and its physiologic basis and to present the results of acid secretory studies which allow preliminary evaluation of the effect of this operation on gastric acid secretory mechanisms.

The stimulus for this departure from accepted surgical treatment of duodenal ulcer resulted from dissatisfaction with the mortality and morbidity incident to dissection of the duodenum in performing gastrectomy and with the disagreeable and sometimes disabling side effects that follow the radical resections necessary to insure against recurrent ulceration. If subtotal gastrectomy, or any other procedure that involves dissection of the duodenum for its effectiveness is applied routinely there will be morbidity and mortality that cannot be neglected from such complications as pancreatitis, disruption of duodenal closure and injury to the common bile duct or other structures in the gastrohepatic ligament. In our experience these have been the chief sources of major or fatal complications directly attributable to the operative procedure. Staged gastrectomy as advocated by McKittrick, Moore and Warren [14] offers an alternative method of dealing with the difficult duodenum, but the necessity of two operations and the development of anastomotic ulceration after the first stage are hazards that prevent wide acceptance of this procedure.

The late complications of subtotal gastrectomy are related to the physiologic disturbances of digestion that result from removal of a large portion of the stomach. Several factors are involved in the "post-gastrectomy syndrome," the most conspicuous of which are inability to eat normally and absorption defects which contribute to loss of weight and lack of strength to work. The so-called dumping syndrome is some-

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times incapacitating and often annoying. These side effects of gastrectomy are in large part secondary to the elimination of the reservoir function of the stomach. Less radical resections minimize these difficulties,[8, 26] but under these circumstances the incidence of recurrent ulceration increases.

Vagotomy with posterior gastroenterostomy which avoids many of the above-mentioned complications has had a rather extensive clinical trial. The control of acid secretion after this operation is less than ideal and the incidence of recurrent duodenal or marginal ulcer is between two and five per cent.[2, 11, 17] The most attractive aspects of this procedure are the low operative mortality and the low incidence of serious nutritional disturbances.

The rationale for the use of antral exclusion and vagotomy for the treatment of patients with duodenal ulcer is based upon the premise that the cephalic phase of secretion must be minimized or abolished and that this is the *sine qua non* of successful duodenal ulcer surgery. The accomplishment of this is quite apparent in procedures involving vagotomy, such as the operation described here, but it is not generally appreciated that subtotal gastrectomy causes a similar effect.[9, 13, 15, 22] This is due in part to section of parasympathetic innervation of the parietal cell area in transecting the stomach and also to the effect of removing the antrum. It should be remembered that the ganglion cells of the intrinsic nerves of the stomach are concentrated in the antrum and along the lesser curvature.[1] Removal of this tissue probably leaves the proximal stomach partly denervated as far as parasympathetic innervation is concerned. Also it has been observed that removal of the excluded antrum after first stage gastrectomy lessens the response to central stimulation by insulin hypoglycemia and to local stimulation by histamine or food. This has been interpreted as indicating an influence of the antrum upon central reflex centers, the effects of which are mediated over the vagi.[22] The authors believe that the prevalent concept that subtotal gastrectomy is effective simply because of excision of the antrum and a portion of the parietal cell area should be modified and the additional factor of parasympathetic denervation of the residual gastric pouch recognized.

The second point of consideration concerns the mechanism by which the gastric antrum exerts its effect upon the gastric secretory processes. The function of the gastric antrum is not fully understood, but it seems reasonably clear that the stimulus for the major portion of the gastric or chemical phase of secretion is the contact of food or its breakdown products with the antral mucosa. Supposedly this causes the liberation of gastrin which is carried via the blood to exert its effect on the parietal cell area. The antrum also influences the response of the stomach to central stimulation and to direct stimulation by histamine. As mentioned above, these effects are believed to be due to the influence of the antrum on central reflex tone and the consequent release of acetylcholine at the secretory unit.[22] Disregarding these less well understood aspects of antral function it was reasoned that transection of the stomach and exclusion of the antrum would eliminate the contact of food with the antrum and thus eliminate the gastric phase of acid secretion. The extent to which this is true will be shown below.

TECHNIC

The technic of this operation is as follows. The abdominal cavity is entered through a midline incision extending from the umbilicus up to the xiphoid. If necessary the xiphoid is excised. After exploration of the abdomen three large gauze packs are introduced over the spleen, splenic flexure of the colon and fundus of the stomach. This aids exposure and will prevent injury to the spleen that sometimes results from traction on adhesions or ad-

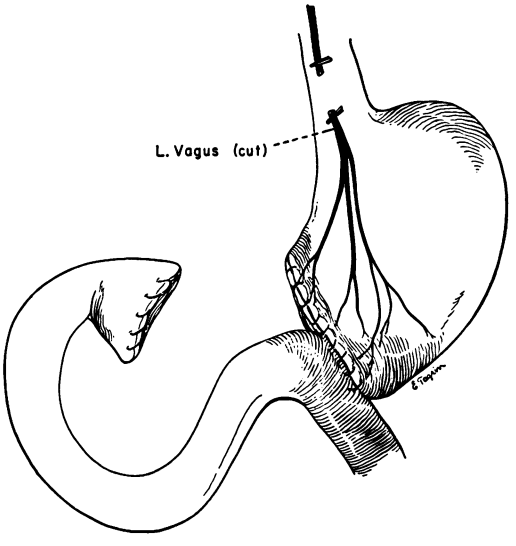

FIG. 1. Diagram of completed operation.

jacent viscera. The left triangular ligament of the liver is incised close to the liver to avoid the inferior phrenic vein, thus freeing the left lobe of the liver so that it can be folded back or retracted. The reflection of peritoneum over the cardia and lower esophagus is incised transversely and the areolar tissue surrounding the esophagus pushed away. The fundus and cardia are drawn down gently and by sharp and blunt dissection the crura of the diaphragm are dissected clean to the point where they meet anterior to the aorta. This portion of the operation is devoted only to exposure.

Following this maneuver and with the esophagus in its normal position the left and right vagi are *visualized.* Visual identification of these nerves is absolutely essential; it seems quite illogical to depend upon tactile identification as is sometimes done. It is our opinion that many of the incomplete vagotomies of the past can be attributed to inaccurate identification of the major trunks or large branches. Traction on the stomach and esophagus allows easy visualization of the left vagus since it is less yielding and causes a trough-like vertical indentation of the anterior wall of the esophagus. Once identified the nerve is elevated with nerve hooks and a 2 to 3 cm. segment excised following the application of dural clips for hemostasis. After section of the left vagus the esophagus is easily drawn down further. Retraction of the esophagus to the left allows visual identification and resection of the right vagus nerve. At this stage of the procedure the esophagus can be freed and drawn forward by tape or rubber wick. Division of both nerves allows 4 to 6 cm. of esophagus to be drawn into the abdomen. The adventitia, small nerve fibers and blood vessels are carefully divided and stripped away from a circular band about 1 cm. wide, leaving the muscle of the esophagus clean and clearly exposed. If a hiatus hernia is present, two or three heavy silk sutures are used to approximate the crura behind the esophagus. No attempt is made to reperitonealize the area.

The midpoint of the stomach, i.e. halfway between the fundus and pylorus, is located and the greater and lesser curvatures cleared. The stomach is transected at this level, leaving a proximal pouch of 50 per cent of the stomach. The distal portion is excised down to a point approximately 6 cm. from the pylorus. In this manner about half of the antrum is excised.*

The first loop of jejunum below the ligament of Treitz is brought anterior to the colon and anastomosed to the gastric remnant with an afferent loop 15 cm. in length brought to the lesser curvature. Either the Polya or Hofmeister method is used for this anastomosis. The wound is closed in layers

* In the first 50 patients the distal portion of the transected stomach was closed without removal of any tissue. This technic was modified after three patients developed a syndrome characterized by pain on eating. This is thought to have been due to intussusception of the antrum and was completely relieved by antrectomy. The resected antrums showed the mucosa in the region of the suture line to be hypertrophied, probably the leading point of the intussusceptum. None of the last 50 patients who had small sleeve resections have had any difficulty of this sort.

TABLE I. *Volume, Hydrogen Ion Concentration, Titrated Acidity and Total Chloride 75 Preoperative Patients with Duodenal Ulcer*

	Average Volume ml./Hour	Average pH			Average Free Acid		Average Total Chloride	
		Mean	Minimum	Maximum	mEq/Liter	mEq/Hour	mEq/Liter	mEq/Hour
Basal	96	1.8	1.3	2.8	41	4.3	108	10.6
Broth	144	1.4	1.1	1.9	68	10.8	126	18.8
Histamine	175	1.2	1.0	1.5	84	15.9	132	24.8
Insulin	129	1.3	1.0	2.2	73	10.7	134	18.1

with stay sutures passing beneath the fascial layer. Figure 1 is a diagram of the completed operation.

ACID SECRETORY STUDIES

For the evaluation of the secretory function of these patients the testing routine described by Smithwick and Kneisel [20] was adopted. This method was selected for several reasons. With their procedure the patients do not need hospitalization. Information is obtained concerning the secretory function during resting or basal conditions and after stimulation with broth (gastric phase), histamine, and insulin hypoglycemia (cephalic phase). This provides a thorough testing of the interdigestive phase of gastric secretory activity as well as the effect of central stimulation, the response to food and the more potent direct stimulation of histamine. Basal secretion measured over the period of one hour correlates with and gives the same type of information as the overnight secretory test used by Dragstedt and others.[21] The substantial body of data collected by Smithwick and his associates allows comparisons with other operative procedures that could not be made otherwise.

Briefly, the technic is as follows. After an overnight fast, a Levin tube is passed into the stomach and adjusted to aspirate freely. A small quantity of water is allowed during passage of the tube. After a 20 to 30 minute period of aspiration to allow subsidence of the stimulation of intubation, the collection of six ten minute samples is carried out using 1½ lbs. of suction. Following this, 80 ml. of peptone broth (reconstituted Difco bacteria media) is introduced through the tube which is then clamped for 20 minutes. The stomach is then emptied and six more ten minute collections made. After this 0.5 mg. of histamine diphosphate is administered subcutaneously and six additional ten minute samples collected. This concludes the first half of the tests. On another day the same procedure is repeated except that after the hour under basal conditions a three hour Hollander test is carried out.[12] Either 12 or 15 units of insulin are given intravenously depending upon the preceding dietary intake. Venous blood samples for sugar determination are obtained before the insulin is given and at 30 and 60 minutes thereafter.

In the testing reported here the blood sugar was reduced to 50 mg. or less in each instance. The patients expectorate all saliva throughout the collection periods. The volume of each sample of gastric juice was measured to the nearest milliliter. On each sample the pH was measured, and the free acidity titrated with 1/10 N NaOH. A Beckman calomel-glass electrode pH meter was used for the measurement of pH and for titration of free acid—end point 3.5. Total chloride concentration was also determined on each sample.[16] By multiplication of clinical units of free acid (milliequivalents per liter) by the volume of secretion in liters in each period the total milliequivalents of free acid were calculated. The same

TABLE II. *Volume, Hydrogen Ion Concentration, Titrated Acidity and Total Chloride 50 Patients, 6 to 12 Months After Antral Exclusion and Vagotomy*

	Average Volume ml./Hour	Average pH			Average Free Acid		Average Total Chloride	
		Mean	Minimum	Maximum	mEq/Liter	mEq/Hour	mEq/Liter	mEq/Hour
Basal	81	4.9	4.1	6.0	6	0.7	70	5.8
Broth	89	5.3	4.7	6.0	5	0.5	88	8.0
Histamine	79	4.1	3.2	5.4	10	0.9	92	7.5
Insulin	38	4.5	3.8	5.4	9	0.7	93	3.8

calculation was used to arrive at the total milliequivalents of chloride.

RESULTS AND DISCUSSION

In Tables I and II the summarized data on 75 preoperative patients and 50 patients who had antral exclusion and vagotomy are presented. All the patients studied preoperatively had active duodenal ulcers at the time the tests were carried out, usually during the period of hospitalization immediately prior to operation. The postoperative studies were carried out between six and 12 months after operation.

The results of the preoperative secretory tests on patients with active duodenal ulcers conform in general to those reported by Farmer *et al.*[7] and Edwards *et al.*[6] Certain differences, however, are apparent. Our patients secreted less volume of slightly higher acidity under basal conditions and appear to have been more responsive to stimulation of broth, histamine and insulin, again the main difference being in the hydrogen ion concentration. Whether this indicates a difference in the group of patients or simply normal variation cannot be stated at present, but it does illustrate differences that might influence subsequent tests and the outcome of operation.

After antral exclusion and vagotomy the secretion of acid was greatly depressed. This was apparent during the basal period and after stimulation with broth, histamine and insulin. The average volume per hour in the basal period was reduced to 81 ml. per hour as opposed to a preoperative level of 96 ml. per hour. In contrast to the preoperative responsiveness to stimulation there was essentially no increase over basal levels of volume after stimulation with either histamine or broth. After stimulation by insulin hypoglycemia the volume was approximately half of the basal period. Such reduction in volume is characteristic of all operative procedures that have proven satisfactory for the control of acid secretion and the clinical treatment of duodenal ulcer. A full discussion of this phenomenon is the subject of another report.[23] It is thought to reflect the imbalance between sympathetic and parasympathetic innervation of the gastric remnant after operation.

The hydrogen ion concentration is the most accurate measurement that can be made in studies such as these. In Tables I and II it can be seen that after operation the average hydrogen ion concentration was approximately one thousandth of the preoperative level. These average postoperative figures are well within the "safe" range as far as activation of peptic enzymatic digestion is concerned. However, it is obvious from these average figures that all patients were not achlorhydric. Of the 50 postoperative patients 60 per cent were completely achlorhydric during the two basal periods, 74 per cent after broth, 40 per cent after histamine and 52 per cent after insulin hypoglycemia. Forty per cent had no free acid in any of the 30 samples collected during the basal periods and after stimulation with broth, histamine or insulin hypoglycemia. Five patients had positive

Hollander tests, the maximal rise being between 20 and 50 units in each instance. Although control of acid-peptic digestion is crucial in the surgical treatment of duodenal ulcer there is as yet no conclusive evidence that complete achlorhydria is necessary or even a desirable objective. Such is not attained by any operation now accepted for duodenal ulcer. Indeed, there is considerable evidence that reduction of acid levels to the normal range gives reasonable protection in the majority of patient.[5, 10, 17, 18] On the basis of our own data and that from other sources,[6, 7, 21] we would like to clarify this concept of our objectives as far as acid secretion is concerned by pointing out that those operations that have proven satisfactory clinically are characterized not only by a reduction of acid concentrations but by a state of relative or absolute unresponsiveness on stimulation and particularly to nervous stimuli mediated over the vagi. In effect, if the mechanisms for strong activation of gastric secretion in response to parasympathetic stimulation are intact, one can predict a generally unsatisfactory result.

The secretion of pepsin is another factor which is obviously of great importance. In the few patients in whom we have measured this it was low. Inasmuch as the secretion of pepsin results from parasympathetic stimulation one would expect reduction of this enzyme in proportion to the reduction of acid secretion resulting from parasympathetic denervation.

The observations concerning the concentrations and total amounts of chloride recovered under various conditions are shown in Tables I and II. These results reflect the same reduction in gastric hydrochloric acid secretion as the direct measurement of acidity. It should be kept in mind that bile has a total chloride concentration of about 100 mEq. per liter and pancreatic juice contains 70 to 80 mEq. per liter. In the postoperative patients the modest rise in chloride concentration after stimulation by broth, histamine and insulin is probably due in part to stimulation of the outflow of bile and pancreatic juice and the regurgitation of a portion of it into the stomach. These chloride measurements were made in an effort to obtain some quantitative information concerning the relative importance of regurgitation of bile and pancreatic juice on the acidity of the mixed gastric contents recovered by tube. Comparison of the preoperative and postoperative results leaves little doubt that gastric acid secretion was greatly reduced as a result of operation. Otherwise one would not expect the reduction in total chloride as well as volume of secretion that was observed in the postoperative patients. If our interpretation of these data is correct, neither neutralization nor dilution by bile and pancreatic juice could account for more than a small fraction of the lessened acid concentrations that were observed.

The question then arises as to what significance can be attached to these data. If one accepts the concept of acidity and acid-peptic digestion as the most important factors in the etiology of duodenal and jejunal ulcer, data such as these should allow a reasonably accurate prediction of the expected incidence of recurrent ulceration. Further, by comparison of a set of figures such as these with similar data obtained after other operative procedures it should be possible to assess the relative worth of different operations in controlling the tendency to ulcer formation. It is only in regard to the control of recurrent ulceration that measurements such as presented above have any clinical significance.

There are several reasons for believing that antral exclusion and vagotomy will insure against recurrent ulceration. The principal theoretical objection to this operation centers about the degree to which the gastric or chemical phase of digestion is controlled by exclusion of the antrum. After stimulation by peptone broth the pH rose above the basal level, the total milliequiva-

lents of acid decreased and there was only a slight increase in volume (Table II). Comparison of these results with those obtained by Farmer *et al.*[7] on 10 cases of posterior gastroenterostomy with vagotomy indicates a more effective control of acid secretion following antral exclusion and vagotomy. The same is true of secretion following histamine. In the basal period the acidity was not greatly different but the total amounts of acid were less due to lessened volume in the antral exclusion, vagotomy group. This comparison leads us to believe that the control of ulcer-forming tendency will be more effective than after vagotomy with posterior gastroenterostomy.

It is also possible to compare the effect of this operative procedure on acid secretion with that produced by subtotal gastrectomy and by hemigastrectomy with vagotomy.[6, 7] It seems evident that acid secretion is further depressed by both these procedures than by antral exclusion and vagotomy except in the case of histamine stimulation. Whether these small increments will eventually justify the liabilities imposed by removing the antrum will probably require long periods of careful follow up of sizeable groups of patients. To date there have been no anastomotic ulcers in the antral exclusion vagotomy group or reported in the hemigastrectomy vagotomy patients being followed in other clinics.[3, 6, 7, 11]

Finally, the problem of incomplete vagotomy and regeneration of the vagus nerves deserves brief mention. The entire problem of "incomplete vagotomy" needs clarification, particularly the significance of a positive secretory response to the stimulation of insulin hypoglycemia. For example, during the performance of standard three hour Hollander tests on patients who had undergone extensive esophagectomy with mobilization and transplantation of the stomach into the chest, acid secretory curves indicative of significant parasympathetic innervation have been obtained.[24] These patients unquestionably had complete vagisection and the positive response to insulin hypoglycemia obviously does not indicate incomplete vagotomy. It is presumed that residual sympathetic nerves entering the stomach may carry sufficient parasympathetic fibers to activate secretion in these instances. As a matter of fact Dr. Hollander never concluded that a positive insulin secretory test proved incomplete vagotomy but only some parasympathetic connection with the central nervous system.[12] Recent observations on the effect of separation of the antrum from the fundus and body of the stomach indicate that the functional status of the intrinsic nerve plexus of the stomach has an important influence upon the response to stimulation by hypoglycemia.[25] Because of our incomplete understanding of the physiologic significance of positive or negative response to the stimulation of insulin hypoglycemia it seems unjustifiable to be more than cautious in interpreting the results obtained by this method. We are skeptical in accepting a slightly positive Hollander test as evidence of incomplete vagotomy.

If, during the performance of vagotomy, because of inadequate anatomical definition of the nerves, poor anesthesia, trouble with hemostasis or any other cause, there is uncertainty about the thoroughness of the division of both nerves, this maneuver should not be relied upon to control acid secretion. Under these circumstances some other procedure that does not depend for its success on vagotomy should be applied. It is our belief that if this plan is adopted there will be little, if any, clinically significant postoperative vagal function and consequently no failures on the basis of incomplete vagotomy.

In regard to the question of regeneration of vagus nerves the above considerations are pertinent. Actually, the observations of Brooks and Moore constitute the principal evidence that return of vagal function does occur.[2] There are other studies that have led to the opposite conclusion.[4, 19] Further-

more, it should be noted that in the report of Brooks and Moore the patients who had evidence of return of vagal function had had only vagotomy which leaves the intrinsic innervation intact and perhaps capable of responding to minimal stimulation from other sources, e.g. parasympathetic fibers carried along with the splanchnic nerves or antral stimulation secondary to retention.

The clinical status of this group of patients who had antral exclusion and vagotomy has been closely followed. Immediately after operation side effects of operation such as dumping, weight loss, diarrhea, anorexia, and attacks of vomiting have been troublesome in a number of patients. The majority of these patients improved rapidly and in the remainder slow improvement continued for months. Of the 81 patients that have been followed for six months or longer, three stated that, although improved, they were not entirely satisfied with the operation. Four patients have diarrhea—two of them drink excessive quantities of alcohol, one has chronic salmonella infection and pinworm infestation, the fourth has ulcerative colitis, possibly on the basis of amoebic infection. None of these patients is incapacitated by the diarrhea, three of them are working and the fourth is the patient currently being treated for ulcerative colitis. Six patients have mild dumping syndrome controlled by reduction of liquid volume and carbohydrate content of meals. Weight loss has been a problem in three patients and in all three there are other disease processes that probably account for failure to maintain weight. There have been no anastomotic ulcers. One patient had a perforation of his duodenum three months after operation. The exact mechanism leading to this accident was not established but presumably a deep penetrating ulcer failed to heal and finally ruptured at the superior junction of the duodenum and pancreas.

On the basis of our experience to date it appears that with respect to nutritional problems and unpleasant side effects of the operation, the behavior of this group of patients is similar to that of patients that have had vagotomy with posterior gastorenterostomy or limited gastric resections with vagotomy. It therefore seems that the success of antral exclusion and vagotomy as a procedure for the definitive treatment of duodenal ulcer will depend on whether or not the ulcer-forming tendency is controlled permanently. The preliminary evidence presented indicates that the control of acid secretion is satisfactory during the six to 12 month period after operation. The passage of time, further clinical observation and repeated secretory studies will eventually determine the place of this operation in the surgical therapy of duodenal ulcer.

SUMMARY

Acid secretory studies have been carried out on 75 preoperative ulcer patients and 50 patients who had antral exclusion with vagotomy for the definitive surgical treatment of duodenal ulcer. The preoperative studies revealed high acid concentration and large amounts of total acid. Stimulation by broth, histamine and insulin hypoglycemia caused further elevations in the concentration and rate of acid production. Following antral exclusion and vagotomy the secretion of acid was depressed and the gastric remnant became unresponsive to stimulation. The technic of the operation and the physiologic basis for it are briefly discussed.

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BIBLIOGRAPHY

1. Babkin, B. P.: Secretory Mechanism of the Digestive Glands, pp. 132–140. Paul B. Hoeber, Inc., New York. 2nd Edition, 1950.
2. Brooks, J. R. and F. D. Moore: Vagotomy for Duodenal Ulcer. A Final Survey After Ten Years. N. E. J. Med., **249**: 1089, 1953.

3. Buchanan, L. C., E. D. Grady, L. S. Riccardi and J. D. Martin, Jr.: Hemigastrectomy and Vagotomy. Preliminary Evaluation in the Treatment of Peptic Ulcer. Southern Med. Jour., **47**: 659, 1954.
4. Dragstedt, L. R., E. R. Woodward and E. H. Camp: Question of the Return of Gastric Secretion After Complete Vagotomy. Arch. Surg., **61**: 775, 1950.
5. Dragstedt, L. R. and E. R. Woodward: Appraisal of Vagotomy for Peptic Ulcer After Seven Years. J. A. M. A., **145**: 795, 1951.
6. Edwards, L. W. and J. L. Herrington, Jr.: Vagotomy and Gastroenterostomy—Vagotomy and Conservative Gastrectomy. Comparative Study. Ann. Surg., **137**: 873, 1953.
7. Farmer, D. A., C. W. Howe, W. J. Porell and R. H. Smithwick: The Effect of Various Surgical Procedures Upon the Acidity of the Gastric Contents of Ulcer Patients. Ann. Surg., **134**: 319, 1951.
8. Farmer, D. A. and R. H. Smithwick: Hemigastrectomy Combined with Resection of the Vagus Nerves. N. E. J. Med., **247**: 1017, 1952.
9. Glass, G. B. J. and S. Wolf: Hormonal Mechanisms in Nervous Mechanism of Gastric Acid Secretion in Humans. Proc. Soc. Exper. Biol. and Med., **73**: 535, 1950.
10. Grimson, K. S., C. R. Rowe, Jr. and H. M. Taylor: Results of Vagotomy During Seven Years. Clinical Observations and Tests of Gastric Secretions. Ann. Surg., **135**: 621, 1952.
11. Hoerr, S. O.: Preliminary Observations on Hemigastrectomy with Subdiaphragmatic Vagotomy for the Average Case of Chronic Duodenal Ulcer. Cleveland Clinic Quarterly, **22**: 172, 1955.
12. Hollander, F.: Laboratory Procedures in the Study of Vagotomy (with particular reference to insulin test). Gastroenterology, **11**: 419, 1948.
13. Linde, S.: Studies on the Stimulation Mechanism of Gastric Secretion. Acta Physiol. Scand. (supplement 74), **21**: 1, 1950.
14. McKittrick, L. S., F. D. Moore and R. Warren: Complications and Mortality in Subtotal Gastrectomy for Duodenal Ulcer. Report on a Two-Stage Procedure. Ann. Surg., **120**: 531, 1944.
15. Noring, O.: The Cephalic Phase of Gastric Secretion Following Partial Gastrectomy. Gastroenterology, **19**: 118, 1951.
16. Peters, J. P. and D. D. VanSlyke: Quantitative Clinical Chemistry: Volume II (Methods). Williams and Wilkins, Baltimore, 1932.
17. Report of Committee on Surgical Procedures of the National Committee on Peptic Ulcer of the American Gastroenterological Association. Gastroenterology, **22**: 295, 1952.
18. Pollock, A. V.: Vagotomy in the Treatment of Peptic Ulceration. Review of 1524 Cases. Lancet, **2**: 795, 1952.
19. Rowe, C. R., Jr., K. S. Grimson, B. H. Flowe, C. K. Lyons, F. H. Longino and H. M. Taylor: Early and Late Effects of Vagotomy on Gastric Secretions and Motility. Surgery, **32**: 226, 1952.
20. Smithwick, R. H. and J. J. Kneisel: The Effect of Resection of the Sympathetic and Parasympathetic Innervation of the Stomach Upon Gastric Acidity. Rev. of Gastroenterology, **17**: 439, 1950.
21. Stein, I. F., Jr. and K. A. Meyer: Studies on Vagotomy in the Treatment of Peptic Ulcer. III. Physiological Aspect. Surg., Gynec. & Obstr., **87**: 188, 1948.
22. Waddell, W. R.: Physiologic Significance of Retained Antral Tissue After Partial Gastrectomy. Ann. Surg., **143**: 520, 1956.
23. Waddell, W. R.: Acid Secretory Response to Histamine and Insulin Hypoglycemia After Various Operations on the Stomach. Surgery (In press).
24. Waddell, W. R.: Unpublished observations.
25. Waddell, W. R.: The Effect of Antrum Exclusion on Gastric Secretion. J. Applied Physiol., **9**: 222, 1956.
26. Wallensten, S. and L. Gothman: An Evaluation of the Billroth I Operation for Peptic Ulcer. Surgery, **33**: 1, 1953.