GASTRIC ACIDITY BEFORE AND AFTER OPERATIVE PROCEDURE WITH SPECIAL REFERENCE TO THE RÔLE OF THE PYLORUS AND ANTRUM*

A PRELIMINARY REPORT OF A CLINICAL AND EXPERIMENTAL STUDY

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THIS STUDY has as its objective definition of what operative procedure, upon the stomach, accomplishes in the management of duodenal and gastric ulcer. This effort represents an attempt to assay the effects of the commonly practiced operative procedures such as gastro-enterostomy, antral excision and extensive gastric resection upon gastric acidity, and to correlate these findings with the effect of these same operations upon gastric evacuation. The effects of tubular resection with and without gastrojejunostomy and the Schmilinsky operation, in which provision for complete intragastric regurgitation of duodenal content is effected, together with antral excision, upon gastric acidity and evacuation will be reported as well.

Despite studies made upon the physiology of gastric secretion, the factor or factors which determine whether the parietal cells of the acid secreting area of the stomach will or will not secrete free hydrochloric acid remain an enigma still. The importance of acid in the genesis of ulcer has been established definitely by the experiments of Mann and Williamson, and Dragstedt and his associates. Mann and Ivy and their associates, though stressing the importance of the acid factor in the genesis of ulcer, have pointed out repeatedly the importance of the mechanical factor. Moreover, the experiments of Matthews and Dragstedt may be construed to suggest that acid is *the* factor or common denominator of ulcer. The larger number of observers and experimenters are in agreement with Ochsner and his associates that acid is only an important factor in the genesis of ulcer. Other items, such as trauma, the nervous factor and deficiency states, are believed to play a significant rôle.

The operative procedures performed by surgeons for relief of uncomplicated chronic duodenal and gastric ulcer causing pain have largely an empiric

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basis. Through what agency the beneficial effects of operation upon the stomach for ulcer are mediated is still a matter of some speculation and considerable difference of opinion. It is not without interest that the favorable influence of gastro-enterostomy upon a duodenal ulcer has been ascribed successively through the years to: (1) Physiologic rest for the ulcer; (2) improved drainage from the stomach (decreased gastric evacuation time); (3) increased intragastric regurgitation affording opportunity for greater dilution and neutralization of the acid gastric content; and (4) effective reduction of gastric acidity.

Those who advise or practice gastric resection for ulcer set as their objective the attainment of achlorhydria in the residual gastric segment. If the weight of evidence were to be evaluated from the literature in terms of expressions from persons interested and experienced in the field, one would be forced to conclude that the "small gastric resection" (partial), whether performed by the Billroth I or II plan, is an eminently satisfactory operation, insuring achlorhydria—not always but usually achieving this effect through sacrifice of the pylorus and antrum, sometimes described as the acid regulator, awakener or titillator of the acid secreting glands in the corpus and fundus. A large number of surgeons favor the "small gastric resection" (partial) for ulcer. Among others are Friedmann, Fromme, Goetze, Haberer, Hoffman, Könnecke, Lorenz and Schur, Rieder, Rienhoff, and Smidt.

There are, of course, dissenting opinions to this expression. On the one hand, there are those who insist that, whereas antral excision will not insure achlorhydria, a more aggressive excision of the acid secreting area of the stomach will (Finsterer). On the other hand, there are those who suggest that excision of increasingly larger segments of the stomach ("subtotal resection") is not more likely to succeed in making the stomach achlorhydric than is the small gastric resection (partial), and that an extensive gastric resection is just as likely to be followed by an anastomotic ulcer (Shapiro and Berg, and Lewis). The dissenters in this latter group from extensive gastric resection disapprove of the operation for two different reasons: The one, because they feel that the stomach cannot be made achlorhydric as long as any gastric tissue remains; the other, because they feel that gastric resection *per se* is the wrong approach to the whole problem, believing that acid, after all, plays only a small, if any, part in the origins of ulcer (Emery). Others approve of extensive gastric resection for ulcer, but do not believe that gastric acidity *per se* has much to do with the etiology of ulcer (Konjetzny, Mizoguti, and Tomoda and Aramaki). An increasing number of surgeons have found that extensive gastric resection, though not affording the patient absolute protection against recurrent ulcer, is more likely to exhibit fewer failures (A. A. Berg, Finsterer, Graham, Klein, Lahey, Lewisohn, Ogilvie, and Strauss).

Were one of us to set ourselves the laudable task of reading all that has been written upon the mechanism of gastric secretion, the genesis of ulcer and its treatment, a long life of ardent study would not suffice to encompass

the entirety of these intimately related subjects. Moreover, it is even more significant that crucial experiments to secure direct and final answers to these issues have not yet been devised. Ivy, an experienced and successful experimentalist in the field of gastric physiology, said (1931) in a moment of discouragement, "I have been working on the question of ulcer for about 12 years, and I am about to give it up . . . , for the simple reason that I know of no way of producing a pylorospasm or reflex nervous disturbance in a dog, as they are known to occur in man, due to emotions and anxiety with their associated motor and secretory disturbances."

It is obvious that the stomach is a very complex and intricate organ, the functions and mechanisms of which are not wholly understood.

The Edkins' Hypothesis.—One of the chief objectives of this study has been to investigate the validity of the Edkins' hypothesis. Pavlov, it is to be remembered, divided gastric secretion into three phases: (1) The psychic or cephalic phase, in which sight, smell or taste of food set up impulses which reach the stomach by way of the vagi nerves, causing a flow of gastric juice. On sham-fed esophagotomized dogs, Pavlov was able to show that vagotomy inhibited psychic secretion of gastric juice. (2) The gastric phase, contingent upon the presence of food in the stomach—elicited by a large variety of foods including water. Whether hydrochloric acid, secreted in response to the presence of food in the stomach, is excited through a secretagogue or hormonal effect is not known. (3) The intestinal phase occasioned by the digestion of food in the intestine and its absorption.

When surgeons adapted gastric resection, which Billroth executed successfully for the removal of gastric cancer, to the surgery of ulcer, it is natural that the same pattern of excision of gastric tissue should have been employed for the management of gastric ulcer. With elaboration of Edkins' hypothesis that gastrin, a pyloric and antral hormone, regulated and controlled the gastric phase of gastric secretion, sufficient justification seemed to have been found for the surgeon's practice of excision of the pylorus and antrum to reduce gastric acidity—a practice which came to be applied later, with even more vigor in certain quarters to the treatment of duodenal ulcer.

The validity of the Edkins' hypothesis of pyloric hormonal control of the gastric phase of gastric secretion is still a matter of no general agreement. Ivy (1930) reviewed the experimental data for and against pyloric hormonal control of the gastric phase of gastric secretion, and concluded that the question could not be answered definitely and finally until it could be determined whether or not purified preparations of gastrin from the antral mucosa were chemically identical with histamine. On the experimental side, too, there is considerable disagreement as to the effect of removal of the pylorus and antrum upon gastric secretion. Among those who insist that results of the sacrifice of the pylorus and antrum in the dog (antral excision plus gastrojejunostomy) uphold the Edkins' hypothesis are Smidt (1923), who observed a shortening of the gastric phase of gastric secretion and a lowering of acidity, and Wilhelmj, and O'Brien and Hill (1936), who observed definite lowering

of gastric acidity. Priestley and Mann (1932), while reporting somewhat inconstant results, concluded that the pyloric mucosa played only a minor rôle in the regulation of gastric acidity. Lewis (1938) excised the antral mucosa, leaving the musculature of this gastric segment intact. He observed marked reduction in gastric acidity, but the response to the histamine test remained normal. Enderlen and Zukschwerdt (1931) demonstrated lowering of gastric acidity in Pavlov pouches in dogs after antral excision, but observed that, in time, the acidity returned to normal. London (1925) has noted this same occurrence.

Portis and Portis (1926), employing a Pavlov pouch, were unable to detect any significant difference in the secretion of the pouch after antral excision. The residual stomach anastomosed to the jejunum they found to be consistently achlorhydric. Shapiro and Berg (1934) confirmed these findings, failing, however, to observe achlorhydria consistently in the residual portion of the stomach anastomosed to the jejunum. The observations of Steinberg, Brougher and Vidgoff (1927) are in general agreement with those of Portis and Portis, and Shapiro and Berg—all of which tend to discredit the Edkins' hypothesis, as well as the practice of antral excision, as an effective means of reducing gastric acidity in the management of ulcer.

On the clinical side, however, as indicated above, expressions from those who have applied the Edkins' hypothesis to ulcer management suggest quite strongly that antral excision is an effectual and satisfactory means of reducing gastric acidity.

The Authors' Approach to the Problem.—In essaying to evaluate the accomplishments of operation in the management of ulcer, as well as the manner in which the effects of operation are mediated, we have regarded surgical therapy as an experimental approach to the ulcer problem. A most conservative attitude regarding the rôle of surgery in the management of ulcer has been entertained by both internists and surgeons in the clinics of the University Hospital. Up until recently, gastro-enterostomy was the commonly practiced operative procedure in those patients presenting classic and somewhat pressing indications for operations, save for the gastric ulcer which was suspected of being malignant. Gastric resection has been performed regularly for gastric ulcer when the roentgenographic defect persisted despite rigidly controlled dietary management and bed rest. With some mutual misgivings, entertained by both internists and surgeons over the accomplishments of gastro-enterostomy and with the consent of the Department of Medicine, the surgical staff, while still adhering strictly to orthodox indications for operation, chose to vary the type of surgical procedure, with the consideration in mind of garnering useful information concerning the rôle of various operations in the management of ulcer, as well as the manner in which such influence is mediated.

In addition, in the laboratory a variety of experimental procedures have been carried out, largely upon the dog, in an attempt to assay further the validity of the Edkins' hypothesis. These experiments will be cited briefly

here, together with some work still in the process of prosecution which lends increased credence to the significance of acid as a most important factor in the genesis of ulcer, as suggested in the experiments of Mann and Williamson, and Matthews and Dragstedt.

The Clinical Data.—It was the occurrence of gastrojejunal ulcer in two patients, subjected to antral resection because of continued bleeding from a duodenal ulcer, that suggested this study. Both patients (Cases 1 and 2, Table II) had had a previous gastro-enterostomy, and when the antral resection was performed, no evidence of a gastrojejunal ulcer was observed in either instance. In both patients, gastrojejunal ulcer followed antral excision within a few months.

Sixty patients having the following types of operative procedure were available for study:

Group I: Twenty-nine cases gastrojejunostomy—retrocolic.

Group II: Six cases antral excision, with complete terminolateral anastomosis (Pólya).

Group III: Ten cases extensive gastric resection including pylorus and antrum, with either partial (Hofmeister) or complete retrocolic terminolateral anastomosis (Pólya). Entero-anastomosis was performed in some; in others it was omitted.

Group IV: Six cases antral exclusion, with extensive gastric resection (Finsterer's operation) accompanied either by partial (Hofmeister) or complete retrocolic terminolateral anastomosis (Pólya). Entero-anastomosis was more often performed than omitted. This operation was undertaken in instances of duodenal ulcer with choledochoduodenal fistula and in other instances of duodenal ulcer in which there was a good deal of induration of the duodenum, extending in a few instances into the prepyloric region. The segment of stomach remaining proximal to the pylorus followed in all instances Finsterer's admonition of leaving not more than two fingers' breadth of gastric tissue.

Group V: Three cases—provision for complete intragastric regurgitation for gastrojejunal ulcer following antral excision (Schmilinsky operation). Cases 1 and 2 of this group appear also in Group II.

Group VI: Five cases tubular excision (fundus and corpus) with gastrojejunostomy, leaving the antrum and pylorus intact.

Group VII: Three cases tubular excision (fundus and corpus) without gastrojejunostomy, leaving the antrum and pylorus intact.

In those instances operated upon within the last year, careful note was made of the amount of gastric tissue excised at operation. In the earlier cases, extensive gastric resection was performed for high-lying gastric ulcer; in duodenal ulcer, gastro-enterostomy was the common operative procedure. Antral excisions were done for bleeding duodenal ulcer and the occasional gastric ulcer situated near the pylorus.

In all patients, carefully controlled postoperative studies of gastric acidity have been made. In most patients, including all the resections, such preoperative data are available. The postoperative observations made upon these patients include: (1) Studies of gastric acidity; (2) gastric emptying time, employing the neutralization test (introduction of 150 cc. of 0.4 per cent HCl into the stomach); and (3) gastric evacuation time, determined fluoroscopically, after the patient swallowed 150 cc. of a thin barium mixture. The emptying time for barium was 83 minutes in a small group of normal persons (Bergh).

The gastric acidity was determined by the usual colorimetric titration, employing Töpfer's reagent as the end-point for free hydrocholoric acid and phenolphthalein as the end-point for the total acid.

Gastric acidity was determined regularly in the morning, the patient having had no breakfast. A No. 14F. duodenal tube with four perforations at the tip was introduced through the nose into the stomach, and periodic aspirations were made as follows: (1) Fasting; (2) 30 minutes after intragastric instillation of alcohol (50 cc. of 7 per cent solution); and (3) 30, 60 and 90 minutes after 0.5 mg. of histamine hydrochloride.* In the "neutralization test," acid was introduced into the fasting stomach and aspirations were made at subsequent intervals of 15, 30, 45, 60, 75 and 90 minutes. The figures in the table indicate the amount of acid "neutralized or lost" in one hour. In the graphic sketches of the results of this test, we have employed the normal standard described by Elman. This test is probably described more accurately as a test of the gastric evacuation time. Control studies with barium suggest a fairly close parallelism between the ability of the stomach to "neutralize" acid and rapid evacuation. That is, a stomach that emptied rapidly with barium also showed a great capacity to "neutralize" acid introduced. We have come to speak, therefore, of acid loss, through rapid gastric emptying rather than neutralization.

We have chosen to put a good deal of emphasis upon the results of the histamine (maximal) stimulation, feeling that these findings are most significant. It is to be admitted freely that histamine, in a sense, is not a physiologic activator of gastric secretion. That is, histamine does not give a maximal stimulus alike to the secretion of pepsin and mucus, as it does to hydrochloric acid. Yet, the subcutaneous injection of histamine evokes the maximal known stimulation of acid secretion from the gastric glands and constitutes, therefore, a real test of the ability of operative procedures to make the stomach achlorhydric. It might reasonably be asked whether one should not regularly expect evidence of active secretion of hydrochloric acid after histamine, as long as any normal gastric tissue remained, no matter what type of operative procedure had been performed. Interestingly enough, however, as the data will indicate, the procedure and the amount of tissue removed have an important answer to give to this question.

* One-half milligram of histamine hydrochloride represents 0.3 mg. of histamine base.

The data are summarized briefly in tables corresponding in number to the groups listed above.

TABLE I

PATIENTS HAVING GASTROJEJUNOSTOMY

Name Hosp. No. Age—Diag. Oper.— Date	Date of Analysis	Fasting Free Acid	Maximum Free with Histamine	Maximum Total with Histamine	Volume of Secretion ½ hr. (in Cc.)	Acid Output Mg. ½ hr.		Acid Neutralized % Acid Loss	Motility Emptying Time —Ba.
						Free	Total		
(1) Mrs. L. L.* 685777 59—D.U. G.J.—9/6/20	10/24/39	0	0	32	12.0	0	14.0	93	
(2) Mr. H. H. 690290 40—D.U. G.J.—1927	1/23/40	20	8	32	18.0	5.0	21.0	94	195 min.
(3) Mr. A. S. 656876 55—G.U. and D.U. G.J.—1927	3/18/40	0	84	102	9.0	27.6	32.2		60 min.
(4) Mr. E.F. 617977 54—D.U. G.J.—8/28/33	2/27/40	32	34	54	11.0	13.6	21.6	90	
(5) Mrs. J. R. 606079 62—D.U. G.J.—3/23/34	2/6/40 4/17/40	14 40	80 57	96 67	3.5 4.7	10.3 9.0	12.3 10.0	94	30 min.
(6) Mr. R. Z. 674760 60—D.U. G.J.—4/1934	2/32/40	12	56	74	18.0	36.8	48.6	93	60 min. 15 min.
(7) Mr. V. C. 624155 67—D.U. G.J.—7/25/34	1/22/34 1/27/34 11/10/39 2/8/40	51 12 + 60	 50 0 37.5	 66 28 77.5	 9.0 4.6	 0 6.3	 18.4 13.5	 100 98	
(8) Mrs. A. S. 630909 38—P.U.† G.J.—10/12/34	9/8/34 11/12/39 2/29/40 4/4/40 4/27/40	0 0 0 0 0	 0 0 0 0†	 28 36 20 40‡	 13.4 2.7 2.0 1.2	 0 0 0 0	 13.5 3.6 1.46 	 88 79 	 40 min.
(9) Mr. H. M. 617859 31—J.U. G.J.—1/2/35	11/7/39	0	50	62	14.3	25.5	31.0		

TABLE I (*Continued*)

Name Hosp. No. Age—Diag. Oper.— Date	Date of Analysis	Fasting Free Acid	Maximum Free with Histamine	Maximum Total with Histamine	Volume of Secretion ½ hr. (in Cc.)	Acid Output Mg. ½ hr. Free	Acid Output Mg. ½ hr. Total	Acid Neutralized % Acid Loss	Motility Emptying Time —Ba.
(10) Mrs. J. F. 641350 71—D.U. G.J.—10/15/35	2/21/40	13.5	50	60	22.0	40.0	48.0	86	115 min.
(11) Mrs. R. S. 620111 66—D.U. G.J.—10/18/35	3/6/40	0	62	72	7.0	15.6	18.4	87	80 min. (95%) empty
(12) Mr. F. M. 645426 69—G.U. G.J.—7/28/36	2/21/40 4/4/40 4/17/40	0 0 24	0 50 34*	22 62 44‡	9.8 6.2 13.0‡	0 11.2 16.2	7.8 15.0 21.0	98	60 min.
(13) Mrs. C. H. 652147 55—G.U. G.J. 9/30/36	1/15/36 5/9/38 2/6/40	0 0 50	62 78 98	80 98 110	13.0 6.0 14.0	29.4 17.1 50.2	37.8 21.6 56.0	69	60 min.
(14) Mr. W. P. 655113 42—D.U. G.J.—1/11/37	3/25/40	62	116	132	17.0	72.0	82.0		95 min.
(15) Mr. J. J. 656061 32—D.U. G.J.—6/9/37	2/20/37 2/26/40	0 24	0 46	12 58					
(16) Mr. F. W. 661275 40—D.U. G.J.—6/1937	2/29/40 4/9/40	0 50	0 72	100 80	0.5 30.0	0 78.4	1.8 87.4	98	95 min.
(17) Mr. W. P. 659592 50—D.U. G.J.—8/18/37	2/19/40 4/26/40	15 0	32 50	44 60	5.0 28.0	5.8 51.0	8.0 61.0		15 min.
(18) Mr. O. W. 661145 60—D.U. G.J.—9/9/37	2/19/40	60	82	98	26.0	78.0	93.2		
(19) Mr. C. W. 659895 56—G.U. G.J.—9/9/37	6/24/37 12/8/39 2/8/40	20 0 64	36 40	68 56	3.1 4.0	3.8 5.8	7.5 8.1	97 93	12 min. 15 min. 14 min.

TABLE I (*Continued*)

Name Hosp. No. Age—Diag. Oper.— Date	Date of Analysis	Fasting Free Acid	Maximum Free with Histamine	Maximum Total with Histamine	Volume of Secretion ½ hr. (in Cc.)	Acid Output Mg. ½ hr. Free	Acid Output Mg. ½ hr. Total	Acid Neutralized % Acid Loss	Motility Emptying Time —Ba
(20)									
Mr. J. K.	2/16/38	0	20	30	9.0	6.5	9.2		
666254	11/8/39	12	74	92	14.0	37.6	30.0	89	
58—D.U.									
G.J.—3/3/38									
(21)									
Mr. M. B.	2/8/40	48	50	68	14.0	25.5	34.6	92	3 hr. 30 min. (65% empty)
636231									
55—D.U.									
G.J.—11/25/38									
(22)									
Mr. R. M.*	2/21/40	0	0	16	3.0	0	1.75	96	30 min.
637026									
39—D.U.									
G.J.—12/1938									
(23)									
Mr. L. J.	2/7/40	68	84	94	16.0	49.0	54.0	86	40 min.
672742									
30—D.U.									
G.J.—12/28/38									
(24)									
Mr. A. W.	5/12/36	37							
648654	1/29/38	21	71	80	17.0	44.0	49.5		
54—D.U.	4/25/39	0	8	18					
Perf. sutured	11/8/39	38	28	44	47.0	47.0	75.0		
7/28/37	3/5/40	18	0	18	11.0	0	7.2	100	85 min.
G.J.—1/31/39									
(25)									
Mr. O. N.	5/8/38	24							
668719	6/22/39	0							
73—G.U.	10/24/39	0	0					94	
G.J.—7/13/39	12/28/39	0	0	55	1.9	0	3.0	97	30 min.
	3/29/40	0	0	22	4.1	0	3.2		80 min.
	4/16/40	0	32‡	40‡	7.2	8.3	10.4		
(26)									
Mr. R. E.	2/19/40	0	10	18	12.0	4.4	7.9	96	1 hr.
672523	4/15/40	22	76*	92*	10.0	27.0	33.0		
29—D.U.									
G.J.—10/25/39									
(27)									
Mr. W. W.*	10/31/39	28	86	100	67.0	210.0	248.0	42	
686536	11/20/39	0	0	25	10.6	0	9.2	97	
51—G.U.	11/22/39	0							
G.J.—11/6/39	11/25/39		0	40	67.0	0	97.0		
(28)									
Mr. H. E.	12/21/39	64	96	110	15.0	52.0	61.0	90	
688048	1/20/40	0	25	55	4.6	4.7	10.2	83	
38—D.U.	1/22/40	12	38	78	7.0	9.6	20.0	96	
G.J.—12/21/39									

TABLE I (*Continued*)

Name Hosp. No. Age—Diag. Oper. Date	Amount Resected (in sq. cm.)	Date of Analysis	Fasting Free Acid	Maximum Free with Histamine	Maximum Total with Histamine	Volume of Secretion ½ hr. (in Cc.)	Acid Output (Histamine) Mg. ½ hr. Free	Acid Output (Histamine) Mg. ½ hr. Total	Acid Neutralized % Acid Loss	Motility Emptying Time —Ba.
(29)										
Mrs. D. V.	12/31/39	20	65	73	18.0		42.0	48.0	77	
686531	1/2/40	0								
50—D.U.	2/5/40	0	38	62	20.0		27.4	45.0	86	
G.J.—12/22/39	4/26/40	16	22‡	32†	18.0		14.4	21.0		

* Not available for verification with triple histamine.
† Possibly luetic gastritis.
‡ Specimens taken 30 minutes after three successive injections of 0.5 mg. of histamine.
Abbreviations: G.U. = gastric ulcer.
D.U. = duodenal ulcer.
P.U. = pyloric ulcer
G.J. = gastrojejunostomy

RESULTS

GROUP I—GASTROJEJUNOSTOMY

It is to be noted that the reduction in gastric acidity after gastrojejunostomy is slight. There are a few patients who have been achlorhydric, at least on one occasion. However, *not a single patient* with a well-authenticated record of ulcer has been achlorhydric after the administration of 1.5 mg. of histamine in triple doses of 0.5 mg. given one-half hour apart. These findings confirm the statement of Holman and Sandusky, who found that achlorhydria was a rare occurrence after gastrojejunostomy for ulcer.

That a number of patients having gastrojejunostomy became free of symptoms is well known and suggests that the operation has some virtue. The rapid loss of hydrochloric acid from the stomach in the neutralization test and the decreased emptying time with barium suggest that the value of gastrojejunostomy lies in the more rapid emptying of the stomach (Fig. 1).

GROUP II—EXCISION OF ANTRUM AND PYLORUS

There are six patients in this group. Without exception, all these patients had their operation for massive hemorrhage from duodenal ulcer. In four instances, a preliminary gastrojejunostomy was performed. In all instances, save the first, the interval between gastrojejunostomy and excision of pylorus and antrum was only a few days to a few weeks or months. In the first patient in the group, the interval between gastrojejunostomy and excision of the pylorus and antrum was more than 12 years. In this patient, unfortunately, no studies of gastric acidity were made until several months after the Schmilinsky operation had been performed for gastrojejunal ulcer occurring after antral excision.

This patient has exhibited achlorhydria occasionally after histamine. As recently as September, 1939, almost four years after the Schmilinsky operation, he was still not achlorhydric on histamine stimulation. After the administration of triple doses of 0.5 mg. of histamine given at intervals of half an hour, gastric analysis showed free hydrochloric acid to be present. One other

TABLE II

PATIENTS HAVING EXCISION OF ANTRUM AND PYLORUS*

Small Gastric Resection

All Complete Terminolateral Anastomoses—No Entero-anastomoses

Name Hosp. No. Age—Diag. Oper. Date	Amount Resected (in sq. cm.)	Date of Analysis	Fasting Free Acid	Maximum Free with Histamine	Maximum Total with Histamine	Volume of Secretion ½ hr. (in Cc.)	Acid Output (Histamine) Mg. ½ hr. Free	Acid Output (Histamine) Mg. ½ hr. Total	Acid Neutralized % Acid Loss	Motility Emptying Time —Ba.
(1)										
Mr. F. F.†		5/29/34	7	8	16					
627911		4/19/35	16	70	82	67.0	175.0	198.0		
49—D.U.		12/31/36	0	0	23					
G.J.—1918.		9/5/39	0	9	39	12.0	5.9	26.0		
Ant. Resect.		3/11/40	0	0	30	16.0	0	13.0		160 min.
4/20/35.										
Schmilinsky										
1/8/36										
(2)										
Mr. C. M.		1/20/34	0	53	63					
623906		11/11/36	0	0	32	20.0	0	23.2		
49—D.U.		11/14/36	13	0	20	1.5	0	2.11	100	
G.J.—11/14/38		2/26/40	0	34	52	13.0	15.0	25.0	95	30 min.
Ant. Resect.		4/4/40	30	68	72	.31	7.7	8.1		
12/17/38	138									
(3)										
Mr. L. K.‡		5/25/38	30							
669044		6/13/38		80	100					
24—D.U.		4/18/39	52							
G.J.—2/14/39		5/8/39	0	38	50	9.0	12.3	16.4		
Ant. Resect.		5/15/39	31							
2/21/39.										
Schmilinsky		6/28/39	24							
with excision		8/29/39	0	26	40	15.0	14.3	22.0		
of a portion										
of fundus										
5/15/39	110									
(4)										
Mr. L. W.		8/29/39	24	**	71					
643715		11/8/39	0	0	60	2.0	0	4.3	58	
50—D.U.‖		2/21/40	0	18	36	11.0	7.24	14.3	79	155 min.
9/3/39	130	4/10/40	0	0	24	12.0				
		4/22/40	0	18§	65§	1.7	1.1	4.0		
(5)										
Mr. C. B.		7/10/39	27	**	**					
642665		11/14/39	24	56	88	3.7	7.0	11.8	82	40 min
41—D.U.		2/15/40	20	56	64	22.0	45.0	51.0	84	
G.J.—3/20/39.										
Ant. Resect.	143									
7/10/39										
(6)										
Mr. G. A.		6/28/39	15	82	91	12.0				
661081		9/30/39	0	62	78	35.0	79.0	100.0	72	310 min.
56—D.U.		11/7/39	0	40	116	90.0	135.0	384.0	18	145 min.
9/18/39	117	4/23/40	66	100	122	12.0	43.8	53.0		

* All patients in this group were operated upon for massive hemorrhage from duodenal ulcers.

† Case 1, Table IV.

‡ Case 2, Table V.

§ Specimens taken 30 minutes after three successive injections of 0.5 mg. of histamine.

‖ This patient has also a stricture of the lower esophagus from "acid ulceration" of the esophagus.

** Operated upon as an emergency for massive hemorrhage threatening life. No preoperative determinations of acid were made.

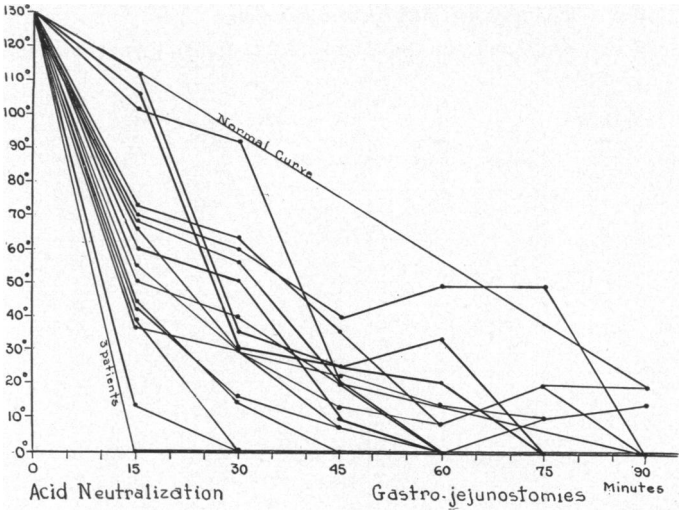


FIG. 1.—Decreased evacuation time of the stomach occurring after gastrojejunostomy, as indicated by the ability of the stomach to "neutralize" acid. The straight line of the normal curve is that previously employed by Elman (1929).

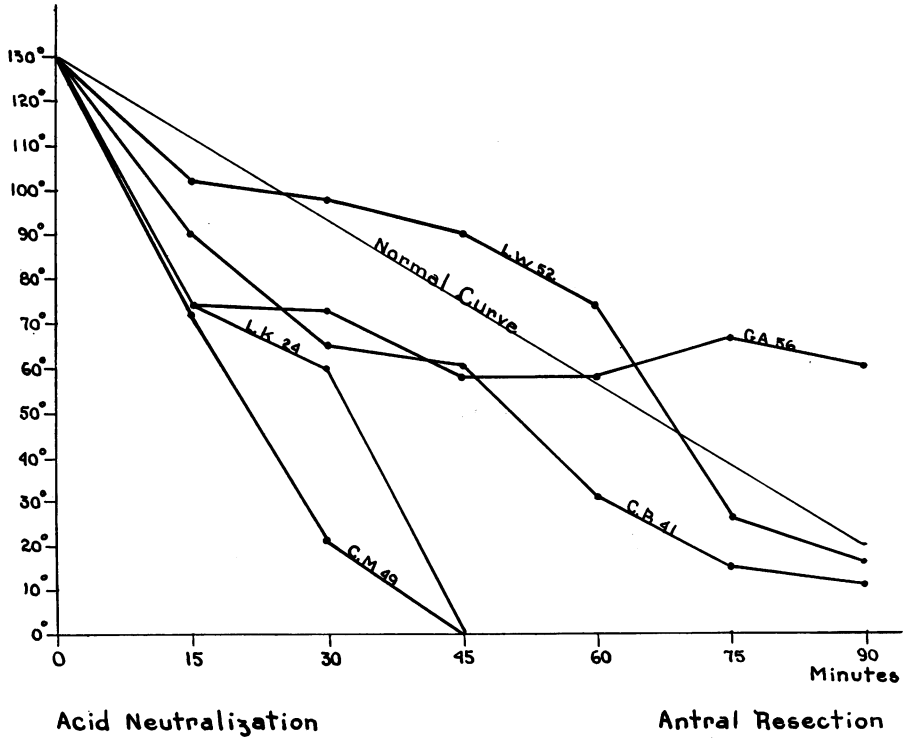


FIG. 2.—Gastric evacuation time as indicated by acid neutralization after antral resection.

TABLE III

EXTENSIVE GASTRIC RESECTION INCLUDING EXCISION OF PYLORUS AND ANTRUM*

Name Hosp. No. Age—Diag. Oper. Date	Amount Resected (in sq. cm.)	Date of Analysis	Fasting Free Acid	Maximum Free with Histamine	Maximum Total with Histamine	Volume of Secretion ½ hr. (in Cc.)	Acid Output (Histamine) Mg. ½ hr. Free	Acid Output (Histamine) Mg. ½ hr. Total	Acid Neutralized. % Acid Loss	Motility Emptying Time —Ba.
(1)										
Mr. G. T.		6/15/29	26							
48237		6/24/29	26							
58—G.U.		11/9/39	0	0	38	11.0	0	15.0	90	
7/3/29										
(2)										
Mrs. A. K.		4/10/40	0	0	12	3.2	0	1.4		
53599										
63—G.U.										
4/21/30										
(3)										
Mr. A. F.		1/25/32	49	77	93	78.0	219.0	264.0		
604349		3/14/40	0	0	22	17.0	0	13.6		155 min.
42—D.U.										
G.J.—1916.										
Reop. G.J.—1929										
2nd G.J.—1930										
2/29/32										
(4)										
Mr. M. S.		3/20/34	41	37	51					
625719		6/11/35	44	30	54	5.0	5.44	9.9		
44—G.U.		10/24/39	0	0	36	22.0	0	28.9	90	45 min.
and D.U.		3/18/40	0	84	102	9.0	27.0	33.0		
6/18/35		4/27/40	0	0†	30†	1.1	0			
(5)										
Mr. W. R.		5/5/38	20	45	52	15.0	17.5	35.0		
654309		4/3/39	0	20	24	8.0	5.8	7.0		
49—G.U.		5/23/39	0	0	8					
3/24/39	200	6/6/39	0	0	18	8.0	0	5.2	93	
		10/18/39	8	0	20	5.0	0	2.9	94	10 min.
		2/20/40	0	0	16	3.0	0	1.75	94	
		4/11/40	0	15†	45†	2.5	1.35	4.1		
(6)										
Mr. W. S.		12/30/39	26	36	63	19.5	26.0	46.0	54	
586233		1/3/40	0	14	32	18.0	9.2	21.0	100	
67—G.U.		1/17/40	0	0	20	12.7	0	9.0	96	
1/4/40	178	4/11/40	0	0	37.5	4.4	0	5.9		5 min.
(7)										
Mr. H. P.		2/1/40	0	0	14					
691274		3/8/40	0	0	32	9.0	0	10.5		
53—G.U.		4/11/40	0	0†	32†	7.5	0	8.7		9 min.
2/27/40	295									
(8)										
Mrs. E. F.		3/25/40	0	0	37.5	0.15	0	0.19		
693430		4/8/40	0	0†	40†	0.5	0	0.7		Unable
57—D.U.		4/24/40	0	0	40	3.0	0	4.3		to tolerate
and G.J.U.										
G.J.—20 yrs. ago										150 cc.
3/13/40	201§									Stomach empties immediately

TABLE III (*Continued*)

Name Hosp. No. Age—Diag. Oper. Date	Amount Resected (in sq. cm.)	Date of Analysis	Fasting Free Acid	Maximum Free with Histamine	Maximum Total with Histamine	Volume of Secretion ½ hr. (in Cc.)	Acid Output (Histamine) Mg. ½ hr. Free	Acid Output (Histamine) Mg. ½ hr. Total	Acid Neutralized. % Acid Loss	Motility Emptying Time —Ba.
(9)										
Mr. F. V.‡		4/11/40	32	72	92	33.0	85.4	111.0		
694465		4/22/40	0	0	58	7.5	0	16.0		
68 G. U.										
4/12/40	274									
(10)										
Mr. M. M.		4/14/40	0	94	122	132.0	413.6	539.0		
694565		2/26/40	0	16	32	15.0	8.7	17.5		
45—prepyloric ulcer										
4/18/40	310									

* Cases 1, 2, 3, 4, 5 and 6 had complete terminolateral anastomoses.
Cases 7, 8, 9 and 10 had partial inferior terminolateral anastomoses.
Cases 1, 3, and 4 had no entero-anastomosis. All other cases had entero-anastomoses.
† Specimens taken 30 minutes after three successive injections of 0.5 mg. of histamine.
‡ This patient had two lesions: An ulcer on the lesser curvature and a small carcinoma in the pyloric region. The lesions were definitely independent of one another.
§ Area determined after the specimen had been in the refrigerator for a few hours—this measurement, therefore, does not take into account the contraction that occurred. Patient operated upon as an emergency for acute, massive hemorrhage from gastrojejunal ulcer—consequently no preoperative determinations of gastric acidity.

patient in this group (Case 4) has been achlorhydric, even to histamine stimulation. After three doses of 0.5 mg. of histamine given consecutively over half-hour intervals, however, free hydrochloric acid appeared in the gastric secretion. None of the other patients in the group are achlorhydric to histamine, though Case 6 has been achlorhydric, fasting. It is apparent that removal of the antrum and pylorus is an unsatisfactory operation to reduce gastric acidity (Fig. 2). The rapid emptying observed after gastrojejunostomy was noted also in this group. Two of these six patients (Cases 1 and 3) also developed gastrojejunal ulcer, which neither patient had after gastrojejunostomy alone. With the exception of the patients who developed gastrojejunal ulcer, the others are well. The two who developed gastrojejunal ulcer (Cases 1 and 3) will be discussed again under Group V.

GROUP III—EXTENSIVE GASTRIC RESECTION INCLUDING EXCISION OF ANTRUM AND PYLORUS

There are ten patients in this group. The matter of the size of the resection will be discussed in a separate section. All patients in this group have been achlorhydric to histamine at times. However, none have been consistently achlorhydric. The lapse of time is apparently a factor in establishing achlorhydria (Cases 5 and 6). In the first four cases in the group, the first analysis of gastric acidity after operation, made after the lapse of months or years, demonstrated achlorhydria regularly. We have since learned that it is im-

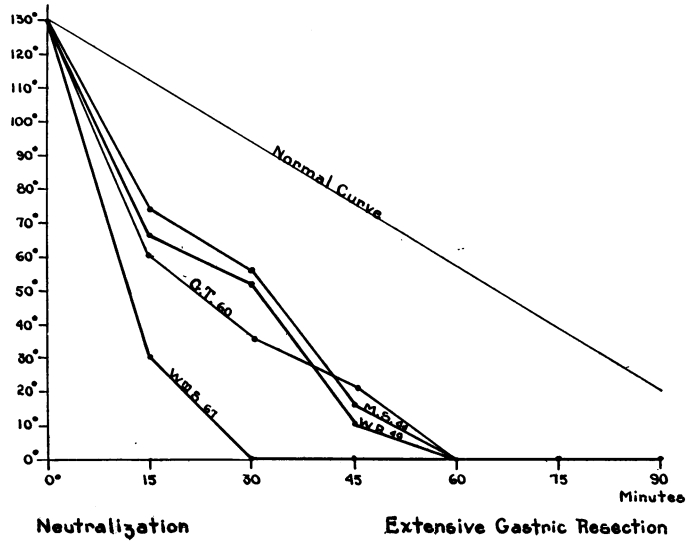


FIG. 3.—Gastric evacuation time as indicated by acid neutralization after extensive gastric resection (Cases in Group III).

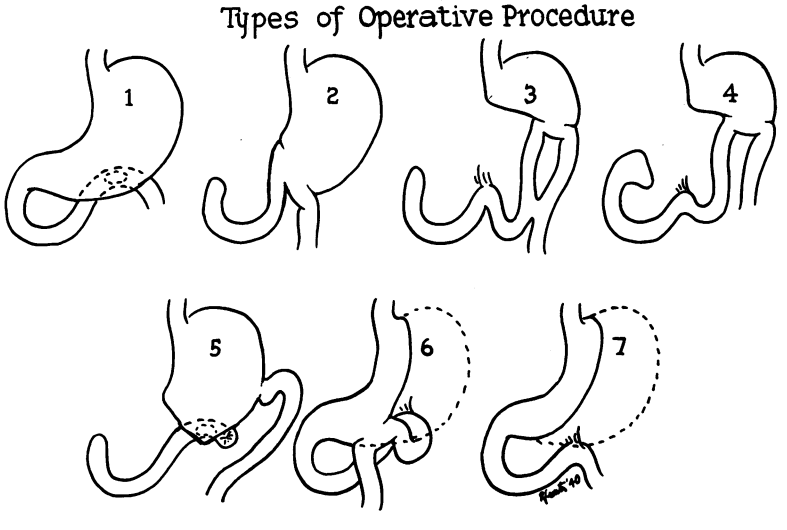


FIG. 4.—Various types of operative procedures employed in the cases listed in the tables:

1. Gastrojejunostomy.
2. Antral resection.
3. Extensive gastric resection. Some patients had entero-anastomosis—others did not.
4. Extensive gastric resection accompanied by antral exclusion (Finsterer). Some patients had entero-anastomosis—others did not.
5. Schmilinsky procedure providing total intragastric regurgitation.
6. Tubular resection with gastrojejunostomy, leaving pylorus and antrum intact.
7. Tubular resection without gastrojejunostomy, leaving pylorus and antrum intact.

TABLE IV

EXTENSIVE GASTRIC RESECTION LEAVING THE PYLORUS AND A SMALL SEGMENT OF THE ANTRUM*

Antral Exclusion Operation of Finsterer

Name Hosp. No. Age—Diag. Oper. Date	Amount Resected (in sq. cm.)	Date of Analysis	Fasting Free Acid	Maximum Free with Histamine	Maximum Total with Histamine	Volume of Secretion ½ hr. (in Cc.)	Acid Output (Histamine) Mg. ½ hr. Free	Acid Output (Histamine) Mg. ½ hr. Total	Acid Neutralized % Acid Loss	Motility Emptying Time —Ba.
(1)										
Mr. P. M.		4/20/37	14							
658072		6/6/39	0	0	18	10.0	0	6.5	98	10 min.
38—D.U.		2/14/40	0	0	16	3.5	0	2.1	97	
G.J.—5/1933										
5/13/37										
(2)										
Mrs. M. B.		10/14/39	54							
686389		2/18/40	42							
36—G.U.		3/7/40	0	0	44	4.3	0	6.9		30 min.
2/26/40	225	4/16/40	0	30†	40†	11.0	12.0	16.0		
(3)										
Mr. J. E.		3/2/40	50	64	84	55.0	138.0	168.0		
684691		3/19/40	0	26	32	30.0	28.0	28.6		
38—D.U.		4/9/40	8	0	20	11.0	0	8.0		120 min.
3/8/40	258									
(4)										
Mr. E. H.		2/27/40	0	0	28	2.6	0	2.6	80	
685488		3/27/40	90	122	128	30.0	124.0	140.0		
40—D.U.		4/15/40	12	38	58	19.0	26.0	40.2		60 min.
4/3/40	301	4/22/40	0	56	144	2.6	5.3	13.6		
(5)										
Mr. C. S.		4/2/40	36	86	94	12.0	37.5	41.0		
694074		4/20/40	0	0	24	11.0	0	9.6		35 min.
24—D.U.		4/22/40	0	17.5	42.5	5.0	3.0	7.8		
4/11/40	244									
(6)										
Mr. T. B.		3/29/40	14							
694134		3/30/40	8							
40—D.U.		3/31/40	44							
4/15/40	224	4/11/40	93							
		4/15/40	106							
		4/22/40	40	70	100	18.0	46.0	62.0		
		4/26/40	36	72	94	51.0	133.0	174.0		

* Complete terminolateral anastomoses in Cases 1 and 2. Partial, inferior terminolateral in the others. Entero-anastomoses in all but Case 1.

† Specimens taken 30 minutes after three successive injections of 0.5 mg. of histamine.

portant to make observations beginning early in the recovery period to determine when achlorhydria supervenes. Now, save with employment of triple 0.5 mg. doses of histamine, all but the last patient in the series (Case 10) is achlorhydric to the usual 0.5 mg. dose of histamine.

The emptying of the stomach in this group, in all instances in which the examination has been made, is very rapid (Fig. 3). All patients in the group are symptomatically well. There have been no gastrojejunal ulcers.

GROUP IV—EXTENSIVE GASTRIC EXCISION WITH EXCLUSION OF THE PYLORUS AND ANTRUM (FINSTERER OPERATION)

This type of operation is indicated particularly in duodenal ulcer complicated by choledochoduodenal fistula, or when there is considerable edematous induration of the duodenum, pylorus and antrum. The admonition, of Finsterer, to leave only a portion of the antrum, lest the acid secreting cells

TABLE V

PATIENTS HAVING THE SCHMILINSKY OPERATION FOR GASTRO-JEJUNAL ULCER

(Provision for Complete Intragastric Regurgitation)

Name Hosp. No. Age—Diag. Oper. Date	Amount Resected (in sq. cm.)	Date of Analysis	Fasting Free Acid	Maximum Free with Histamine	Maximum Total with Histamine	Volume of Secretion ½ hr. (in Cc.)	Acid Output (Histamine) Mg. ½ hr. Free	Acid Output (Histamine) Mg. ½ hr. Total	Acid Neutralized % Acid Loss	Motility Emptying Time —Ba.
(1)										
Mr. F. F.		5/29/34	7	8	16					
627911		4/19/35	16	70	82	67	175.0	198.0		
49—D.U.		12/31/36	0	0	23					
G.J.—1918.		9/5/39	0	9	39	12	5.9	26.0		
Ant. Resect. 4/20/35.		3/11/40	0	0	30	16	0	13.0		160 min.
Schmilinsky 1/8/36										
(2)										
Mr. L. K.*		5/25/38	30							
669044		6/13/38		80	100					
24—D.U.		4/18/39	52							
G.J.—2/14/39.		5/8/39	0	38	50	9	12.3	16.4		
Ant. Resect. 2/21/39.		5/15/39	31							
Schmilinsky with excision of a portion of fundus 5/15/39	110	6/28/39	24							
		8/29/39	0	26	40	15	14.3	22.0		
(3)										
Mr. A. S.†		9/5/35	69							
641802		4/7/39	27							
35—D.U.		4/14/39	89							
G.J. 1/1938.		4/24/39	16	22	40	25	20.0	36.5		
Excision of gastrojejunal ulcer and exclusion of greater curvature 4/14/39.	214	5/24/39	32							
		6/22/39	0	56	60	6	12.2	13.0		
		7/15/39	0	42	94	11	16.8	37.6		
		9/28/39	5	0	21	52	0	39.9		
Schmilinsky with excision of a portion of fundus and antrum 8/14/39	125									

* Died at home, suddenly, 9/16/39, four months after the Schmilinsky operation of perforation of a new, acute gastrojejunal ulcer in the new stoma. Autopsy courtesy Dr. B. O. Mork, Jr., Worthington, Minn.

† Died in hospital, 10/8/39, 52 days after the performance of Schmilinsky operation, of uncontrollable gastric hemorrhage. A large, shallow autolytic ulcer of the stomach was found—gastrojejunal ulcer healed.

of the corpus be allowed to remain behind distal to the site of section and inversion of the stomach, has been observed. The upper site of section remains the same as for the ordinary extensive gastric resection described in Group III.

Though there are only six patients in the entire group, the last four have been operated upon since April 1, 1940. After the findings in Group VI had been reviewed (tubular excision of corpus and fundus with gastrojejunostomy —leaving the antrum intact), it became apparent that the performance of a few Finsterer antral exclusion operations accompanied by extensive resection of the acid secreting area, for duodenal ulcer presenting satisfactory indications for operation, would shed additional enlightenment upon the validity of the Edkins' hypothesis in man. As remarked above, under the discussion in Group III, the time element plays an important rôle in making patients achlorhydric after histamine. The first two patients operated upon in this group are achlorhydric to single doses of histamine. The antral exclusion operation is illustrated, together with the other operative procedures, in Figure 4.

GROUP V—THE SCHMILINSKY OPERATION (PROVISION FOR COMPLETE INTRAGASTRIC REGURGITATION FOR GASTROJEJUNAL ULCER DEVELOPING AFTER ANTRAL EXCISION)

Three patients have been operated upon according to this plan of operation. The first patient in the group, operated upon now more than four years ago, has done fairly well. It is to be noted that his emptying time with barium is still extraordinarily slow and he has not been consistently achlorhydric to histamine. Symptomatically, he does quite well. He has been referred to already as Case 1 in Group II.

The experience with the other two patients in this group suggests that the operation shold never be performed. Neither patient became achlorhydric, and in both instances the termination was disastrous. In Case 2, perforation of an acute gastrojejunal ulcer in the new efferent loop caused death in a few hours—the perforation occurring four months after performance of the Schmilinsky operation. The old gastrojejunal ulcer healed (ref. footnote, Table V). The other patient developed a large, shallow gastric ulcer which involved a good portion of the residual stomach, and died of uncontrollable gastric hemorrhage, 52 days after performance of the Schmilinsky operation. The old gastrojejunal ulcer healed. The effect of this operative procedure upon the gastric secretory mechanism will be discussed again below under the heading of "Intragastric Regurgitation."

GROUP VI—TUBULAR EXCISION OF CORPUS AND FUNDUS WITH GASTROJEJUNOSTOMY (LEAVING THE ANTRUM AND PYLORUS INTACT)

This operation, in principle, is the same as that of the Connell fundusectomy, save that a much larger area of the acid secreting area is excised and with the addition of provision for partial intragastric regurgitation of duodenal content by a coincident gastrojejunostomy. There are five patients in this group. All had duodenal ulcer, and two of the group had both duodenal

and gastric ulcer (Cases 3 and 4). All are now achlorhydric to histamine.* Several are achlorhydric to triple doses of histamine given subcutaneously. It is to be noted, again, that in two patients in this group (Cases 2 and 5) the lapse of time played an important factor in establishing achlorhydria to histamine stimulation. It should be noted further that the emptying time in this group of patients was not as rapid as in the patients having extensive gastric resection after the Billroth II pattern of operation with terminolateral anasto-

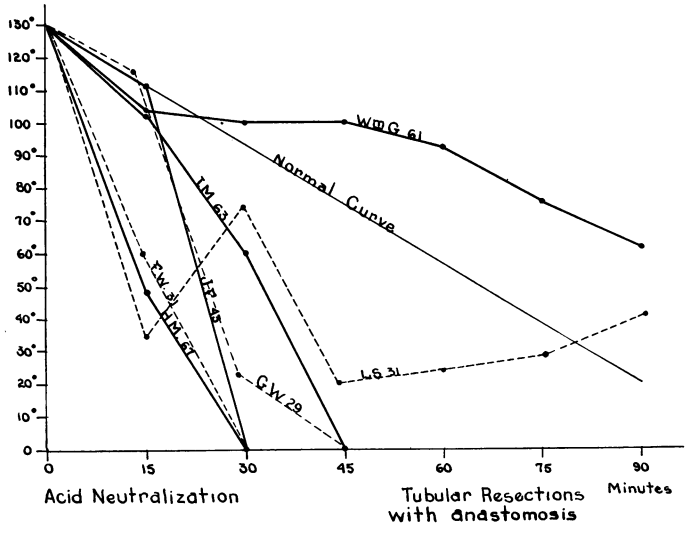


FIG. 5.—Gastric evacuation time after tubular resection with gastrojejunostomy, as indicated by the acid neutralization test.

mosis with the jejunum. No entero-anastomoses were made in this group. The amount of gastric tissue excised, paralleled closely that removed in the extensive gastric resections of Groups III and IV. All are symptomatically well. Roentgenologic examination fails to disclose any evidence of active ulcers. In no instance was the ulcer removed. Roentgenographically, distortion of the duodenal cap as a result of scarring is still present.

GROUP VII—TUBULAR EXCISION OF CORPUS AND FUNDUS WITHOUT GASTROJEJUNOSTOMY (LEAVING THE ANTRUM AND PYLORUS INTACT)

Only three patients have been operated upon by this plan. All three were young men with chronic duodenal ulcer causing severe pain and great disability. Massive hemorrhage had not occurred in any of the three cases. None have been achlorhydric, consistently, fasting or after histamine, though one patient was found to be achlorhydric on one occasion to histamine after operation. Significantly, the largest excisions of gastric tissue in the series have been in this group, but without producing achlorhydria. The emptying time in all three patients of this group is rapid. All are symptomatically well.

* Case 5 was not achlorhydric at the time of the most recent examination.

TABLE VI

PATIENTS HAVING TUBULAR EXCISION OF CORPUS AND FUNDUS WITH GASTROJEJUNOSTOMY

Leaving the Antrum and Pylorus Intact—No Entero-anastomosis

Name Hosp. No. Age—Diag. Oper. Date	Amount Resected (in sq. cm.)	Date of Analysis	Fasting Free Acid	Maximum Free with Histamine	Maximum Total with Histamine	Volume of Secretion ½ hr. (in Cc.)	Acid Output (Histamine) Mg. ½ hr. Free	Acid Output (Histamine) Mg. ½ hr. Total	Acid Neutralize. % Acid Loss	Motility Emptying Time —Ba.
(1)										
Mr. I. M.		3/2/39	12							
677903		3/12/39	12							190 min.
63—D.U.										
3/24/39	180	3/23/39	22							
		3/24/39	28							
		4/3/39	0	10	22	7.0	2.5	5.6		
		5/18/39	0	20	30					
		8/17/39		16	28					
		2/13/40	0	0	32.5	4.7	0	5.0		
		4/18/40	0	0	17					
(2)										
Mr. R. S.		4/18/39	33	62	74	18.0	22.0	49.0		
658862		4/29/39	0	15	30	10.0	5.4	10.9		
31—D.U.		8/29/39	0	0	14	15.0	0	7.7		
4/19/39	263	11/14/39	0	0	48	3.0	0	5.0		
		2/6/40	0	0	48	3.1	0	5.3		
(3)										
Mr. J. F.		11/4/37	0	36	40					
663579		3/28/39	0	30	42					
43—G.U.		5/1/39	0	0	24	5.0	0	4.4		30 min.
4/20/39	244	2/20/40	0	0	30	2.0	0	2.18		40 min.
		3/8/40	0						96	
		4/16/40	0	0*	8*	3.8	0	1.0		
(4)										
Mr. H. M.		5/10/39	35	54	68	24.0	47	60.0		
672813		5/17/39	0	0	14	6.0	0	3.0		
67—G.U.† and D.U.										
5/11/39	262									
(5)										
Mr. W. G.		9/5/39	41							
677176		9/14/39	0	108	116	11.0	42	46.0		
61—D.U.		9/29/39	24	30	60	18.0	19.8	39.4	86	
9/19/39	245	10/5/39	22	42	64	16.3	25	38.0	32	
		3/11/40	0	0	30	5.5	0	6.0		70 min.
		4/24/40	60	76*	116*	2.6	7.2	10.9		

* Specimens taken 30 minutes after three successive injections of 0.5 mg. of histamine.
† Gastric ulcer at the esophagogastric juncture on the lesser curvature—benign on biopsy.

In Case 1 of this group, the left vagus nerve was cut beside the subdiaphragmatic esophagus. In Case 2, both the vagi were divided below the diaphragm but without any special effect upon gastric secretion.

In young persons, in their twenties, who have chronic duodenal ulcer and present good indications for operation, without a history of massive hemorrhage, this operation has its best indication. Until it is demonstrated definitely

TABLE VII

PATIENTS HAVING TUBULAR EXCISION OF CORPUS AND FUNDUS WITHOUT ANASTOMOSIS

Leaving the Antrum and Pylorus Intact

Name Hosp. No. Age—Diag. Oper. Date	Amount Resected (in sq. cm.)	Date of Analysis	Fasting Free Acid	Maximum Free with Histamine	Maximum Total with Histamine	Volume of Secretion ½ hr. (in Cc.)	Acid Output (Histamine) Mg. ½ hr. Free	Acid Output (Histamine) Mg. ½ hr. Total	Acid Neutralize. % Acid Loss	Motility Emptying Time —Ba.
(1)										
Mr. F. W.		12/27/37	63							
664758		3/3/39	88	135	143	49.0	244.0	261		
31—D.U.		10/4/39	70						34	
10/9/39	270	10/6/39	82	114	130	62.0	257.0	293	7	
		10/21/39	0	20	38	46.0	33.0	63	96	
		10/24/39	0							
		11/1/39	—	49	86	14.0	25.0	43	89	8 min.
		12/8/39	0	60	90	17.0	37.2	55	85	
		4/10/40	58	92	106	14.0	47.2	54		
(2)										
Mr. L. S.		1/17/40	34	76	94	19.0	55.0	65	42	
688933		1/30/40	0	10	28	25.0	4.5	25	78	
31—D.U.		3/5/40	26	34	52	19.0	23.5	36	62	6 min.
1/18/40	299	4/23/40	7.5	60	100	9.5	20.8	34.6		25 min.
(3)										
Mr. W. G.		2/6/40	64	74	88	26.0	68.0	83	77	
691263		2/26/40	0	30	74	24.0	26.0	64		70 min.
29—D.U.		4/9/40	0	0	24	4.5	0	4		
2/23/40	359									

that extensive gastric resection performed according to the Billroth II method will insure achlorhydria with regularity, under all circumstances, an operative procedure of this kind will have its place.

Comment.—A few facts in this study stand out prominently:

(1) Extensive gastric resection *per se* does not produce achlorhydria to maximal stimulation (histamine), even when combined with bilateral subdiaphragmatic vagotomy (Group VII).

(2) Extensive gastric resection, when combined with gastrojejunostomy providing opportunity for partial intragastric regurgitation of duodenal content, will produce achlorhydria to maximal stimulation (histamine) usually. The lapse of time is an important factor in the development of such achlorhydria.

(3) Excision of the antrum and pylorus (the small or partial gastric resection) fails to make the residual gastric segment achlorhydric to maximal stimulation.

(4) Allowing the antrum and pylorus to remain, as is indicated particularly by the cases in Group VI, does not militate against securing an achlorhydric stomach to maximal (histamine) stimulation, granted that an extensive gastric resection of the acid secreting area is performed. The cases in Group IV will, with the lapse of more time, shed additional light upon this important issue.

(5) Gastrojejunostomy is not accompanied by achlorhydria to maximal stimulation.

(6) The emptying time is decreased considerably in: (a) All anastomotic operations upon the stomach, Groups I, II, III and IV; (b) after extensive resection of the stomach without anastomosis (Group VII). When the intragastric regurgitation of the duodenal content is complete, as it is in Group V, the emptying time is prolonged (barium evacuation time).

The Size of the Gastric Resection.—The size of the gastric segment excised has been measured carefully in all patients submitted to operation during the past year. After excision, the surgical pathologist* tacks the opened specimen on a board under a very slight stretch, which fails to straighten out the rugae of the mucosa and determines the square area, in centimeters, of the excised specimen. This measurement, to be certain, is considerably less than the true area of gastric mucosa removed, into which reckoning account must be taken of the area of the multiple gastric rugae.

In the antral excision series (Group II), the area of the excised gastric tissue varied between 110 and 143 sq. cm., measured as described above—the average for the group was 124 sq. cm. In Group III, in those instances in which the area of the excised tissue was determined, this measurement varied between 178 and 295 sq. cm., the average being 243 sq. cm. For Group IV, the area of the excised gastric tissue varied between 224 and 301 sq. cm., the average being 250 sq. cm. In Group VI, the amount of excised tissue averaged 283 sq. cm. In the successive cases in the group, the respective areas of the excised gastric tissue measured 180, 263, 244, 262 and 244 sq. cm. In the three cases in Group VII, the excised gastric tissue varied between 270 and 359 sq. cm.—averaging 309 sq. cm.

A survey of the data in these groups suggests that excision of 200 sq. cm., or more, of tissue, from the corporic and fundic zones of the stomach of average size, when combined with gastrojejunostomy, after a lapse of time of three to six months after performance of the operation, usually results in an achlorhydric residual gastric pouch to histamine (0.5 mg.). Some remain achlorhydric after the triple dose described above. By dividing the gastric tissue, under scrutiny, into squares and triangles, as illustrated in Figure 6, the surgeon may readily determine, in an approximate manner, the extent of the area to be removed. The senior author, who has performed the gastric resections reported here on man, has found that by employing the scheme depicted in Figure 6, he may excise the desired amount of gastric tissue within a margin of error usually not exceeding 5 to 10 per cent. The errors of measurement, with the stomach *in situ*, but devascularized for resection and anastomosis, are usually those of underestimation—that is, the excised specimen, when opened up and tacked down as described above, exhibits an area exceeding that determined at operation by 10 to 20 sq. cm.

In deciding upon the necessary extent of the excision, the surgeon must, of course, be guided by the relative size of the stomach. When the stomach is large and dilated, it is necessary to remove a correspondingly larger segment

* The writers gratefully acknowledge the helpful interest of Doctor Hebbel, Instructor in Pathology, in many new phases of the problem.

than 200 sq. cm.—which measurement may be suggested as the *minimal* amount to be removed, to secure achlorhydria in the stomach of average size. The senior author has the impression that duodenal ulcers are more likely to have large stomachs than gastric ulcers (excluding, of course, the pyloric ulcer). An ulcer on the lesser curvature causes shortening, frequently with a resultant smaller stomach. Duodenal ulcer, on the contrary, is more likely to be attended by obstruction and gastric enlargement.

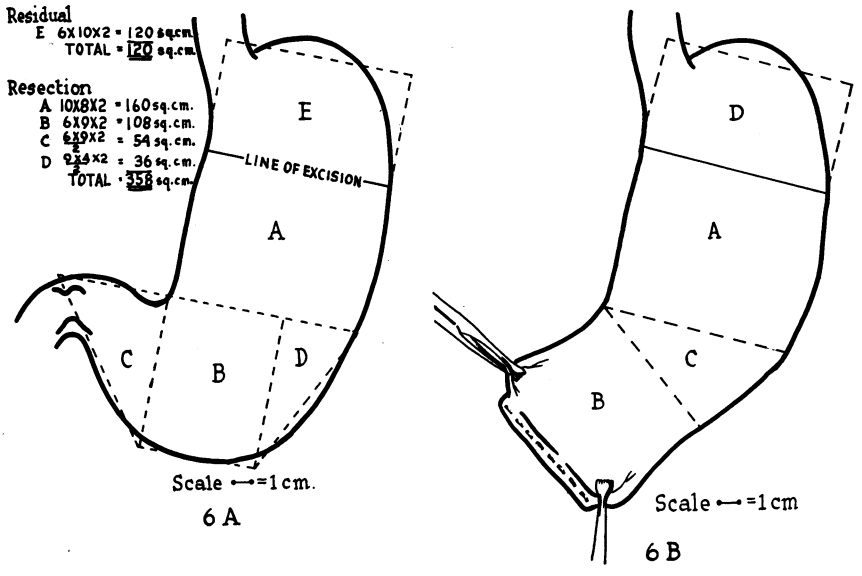


FIG. 6.—Proposed scheme for determining the surface area of the stomach at operation. It may be done as indicated in 6 A or 6 B, or by some variant thereof.

In order to procure achlorhydria with a high degree of regularity, it is necessary to sacrifice 66 to 80 per cent of the gastric tissue. In the literature, one hears much of small (partial) and extensive (subtotal) resections. Finsterer (1923), who has been an ardent advocate of extensive excision, has insisted the line of division of the stomach should be vertical to the axis of the body. We have enlarged Finsterer's illustration of the proposed segment for removal three times, employing small cardboard plaques cut to pattern, and have weighed these out on a fine balance scale. Figure 7 indicates the per cent of the total gastric tissue removed by Finsterer's plan (52 per cent) and confirms the impression, that in allowing so great a length of the greater curvature to remain, it is not likely that the surgeon can excise two-thirds to three-fourths of the stomach. In the diagram, indicating the manner in which the gastric tissue is triangulated and squared-off for excision, is illustrated also the usual extent of the excision as well as the usual size of the residual segment. This type of resection, when accompanied by gastrojejunostomy, is, in the course of a few months, likely to be accompanied by achlorhydria even to histamine stimulation. We have no case with total anacidity. In Case 5

in Group III, at least 95 per cent of the stomach was removed, the lesion being at the esophagogastric juncture on the lesser curvature. The lesion which was believed to be carcinoma proved to be benign. Unfortunately only one preoperative gastric analysis was made.

The Rôle of the Stoma in the Production of Achlorhydria.—From inspection of the tables it is apparent that extensive gastric resection *per se* cannot produce achlorhydria, nor can gastrojejunostomy alone. A number of years ago, Harvey (1907) examined the gastric mucous membrane in the vicinity of gastro-enterostomy stomata in dogs, some months after performance of the operation. He observed disappearance of parietal cells from the gastric tubules—cells responsible for the secretion of hydrochloric acid. Since gas-

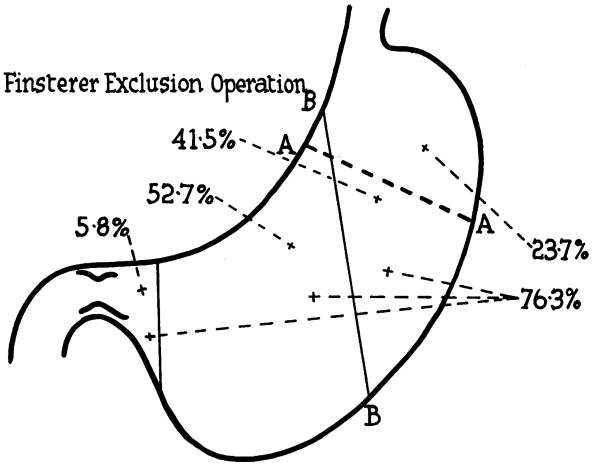


FIG. 7.—Finsterer's (1923) "subtotal" gastric resection with pyloric exclusion. The actual area removed is 52.7 per cent of the total. By elevating the line of excision on the greater curvature to a higher level, more than 70 per cent of the stomach may be removed.

troscopy has come into quite general use, atrophy and edema of the mucous membrane are not uncommon endoscopic observations upon the operated stomach. Of the present series, the larger number have been subjected to gastroscopic examination. Those findings, however, must await further analysis.

Inasmuch as the time factor appears to be an important item in the establishment of achlorhydria following extensive gastric resection and gastrojejunostomy, it is not unlikely that regurgitated duodenal contents impair the capacity of the parietal cells to secrete hydrochloric acid.

The relatively high total acidities, exhibited by some cases in Tables III and VI, free hydrochloric acid being absent, suggest that hydrochloric acid is either being secreted at a slower rate (most likely) or that with the establishment of the gastrojejunal stoma, more mucus is, through one agency or another (gastric, biliary, duodenal and jejunal), made available to combine with the free acid. It is not unlikely, when ulcer occurs spontaneously in man or is produced experimentally in the cat by intragastric instillation of

acid or the subcutaneous implantation of histamine (see below), that the rapid flow of hydrochloric acid (or secretion as a result of histamine stimulation) over the gastric mucosa washes mucus, the normal buffer for acid, away. When the rate of secretion of hydrochloric acid is slowed up by extensive gastric resection and gastrojejunostomy, enough mucus becomes available to neutralize hydrochloric acid as it is secreted by the gastric glands.

The mechanism by which achlorhydria occurs following excision of gastric tissue and the establishment of gastrojejunostomy, it must be said, is not wholly clear. It is not unlikely that it may be found to be a problem in colloid adsorption chemistry. The manner of adsorption of acid by protein (mucus) in the presence of bile and pancreatic juice on gastric and jejunal mucosal surfaces may have to be studied to solve the problem.

With the cooperation of Dr. Wallace D. Armstrong, associate professor of physiological chemistry, at the University of Minnesota, we recently undertook verification of the values titrated as total acid as being largely hydrochloric acid combined with protein, in patients and dogs in whose gastric contents, after extensive gastric resection and gastrojejunostomy no free hydrochloric acid was found. Much to our surprise, we found considerably less acid in these gastric contents than our titration figures for total acidity (in the absence of free HCl) had suggested. In explanation of this occurrence, Doctor Armstrong says: "The combined acid of gastric juice as determined by the difference between the results of analysis for free acid and total acid has usually been considered to represent, in greatest part, hydrochloric acid combined with protein. It appears very probable that the combined acid should not be interpreted to indicate only hydrochloric acid combined with protein, but also, in addition, the base combining ability of the protein. Proteins, on the alkaline side of their isoelectric point, possess the ability to act as an acid and so combine with base. In general, the base combining power of a protein increases as the p_H of the medium is raised above the isoelectric point of the protein. Since the end-point of the titration of total acid has arbitrarily been fixed at the p_H required to color phenolphthalein (p_H 8.3), it seems certain that a good deal of the alkali used in the titration of total acid is really used in the neutralization of the base combining groups of the protein of the fluid. Thus, the determined value for combined acid represents the alkali required to neutralize the hydrochloric acid combined with proteins plus that needed to neutralize the buffering ability of the protein. The relative proportions of the two will be expected to vary with circumstances depending upon the total hydrochloric acid and protein contents of the fluid."

In this connection, it may not be amiss to discuss briefly the commonly expressed belief that a gastric ulcer becomes achlorhydric more readily after the same type of operative procedure than does duodenal ulcer (Perman, 1935, and Walters, 1937). It is known also that patients with duodenal ulcer tend, in the main, to have higher acid values than gastric ulcer. This may in part be a matter of the size of the stomach as suggested above. However, a gastric ulcer in its typical location, on the mid lesser curvature, with

the frequent attendant indurative edema, radiating several centimeters in each direction into the acid secreting area of the stomach, is likely to injure somewhat the capacity of the stomach to secrete hydrochloric acid.

The Amount of Intragastric Regurgitation.—In this connection, the Schmilinsky operation affords an opportunity to evaluate the effect of total intragastric regurgitation of the duodenal content. Up until now, the beneficial effects of intragastric regurgitation accompanying anastomotic types of operation, such as gastrojejunostomy, have been attributed to neutralization and dilution of the acid secretions of the stomach. From the few experiences reported here with the Schmilinsky procedure, it is apparent that it is a highly undesirable type of operation. In this connection, it is to be remembered that McCann reported, in 1929, the development of ulcers at the new gastric outlet in 80 per cent of a series of 26 dogs, when the total duodenal secretions were drained back into the gastric fundus. Ivy and Fauley (1931), Weiss, Graves and Gurriaran (1932), and Graves (1935) repeated the McCann experiment, draining the duodenal secretions back, however, into the gastric antrum instead of into the fundus as McCann did. Except for Ivy and Fauley, who noted the occurrence of gastrojejunal ulcers twice at the new gastric outlet, no ulcers were obtained by the other observers. Maier and Grossman (1937) repeated the McCann experiment very much in the manner that McCann performed it initially, but only two dogs out of 12 developed gastrojejunal ulcers. We, too, have eight dogs with the McCann application of the Schmilinsky procedure; in four animals the duodenal content was drained back into the fundus, and in the remaining four into the antrum. All appear well. Four (two of each) have been reexplored after the lapse of at least four months' time in each instance, but no ulcers have been observed. Still our meager but unfortunate experience with the Schmilinsky procedure confirms McCann's observations and stamps total intragastric regurgitation of the duodenal contents as undesirable. An additional dog has been kept under observation in the experimental laboratory for more than a year, with the Schmilinsky operation performed as illustrated in Figure 4 (Group V). The pylorus and antrum have been removed and the dog is not achlorhydric despite total intragastric regurgitation of the duodenal content (ref. Table VIII).

What may be the explanation of this unusual behavior? To the senior author, only one explanation appears plausible, namely, provision for complete intragastric regurgitation protracts, interminably, the second phase (gastric) of gastric secretion and probably intensifies the intestinal phase as well. That is, the acid secreting cells in the residual gastric pouch are constantly stimulated. In time, with the lapse of years, as in Case 1 in Groups II and V, a relative achlorhydria may occur, ultimately, granted that the sequelae of gastric autolysis or perforation of a new gastrojejunal ulcer does not occur in the meanwhile.

The Size of the Stoma and the Question of Entero-anastomosis.—The ideal length of the gastrojejunal stoma is not known. In the earlier group

of cases, operated upon after the Billroth II plan of operation, a complete terminolateral (Pólya) anastomosis was made. Latterly, an incomplete (inferior) terminolateral (Hofmeister) anastomosis 5 cm. in length has been made. In a number of these an entero-anastomosis has been made also. The results of the Schmilinsky procedure suggest, quite definitely, that complete intragastric regurgitation is an undesirable feature. In the main, the large stomata (complete terminolateral anastomosis) empty unusually rapidly ("dumping stomachs"). Whether there is more or less intragastric regurgitation with a large or small stoma is difficult to ascertain definitely.

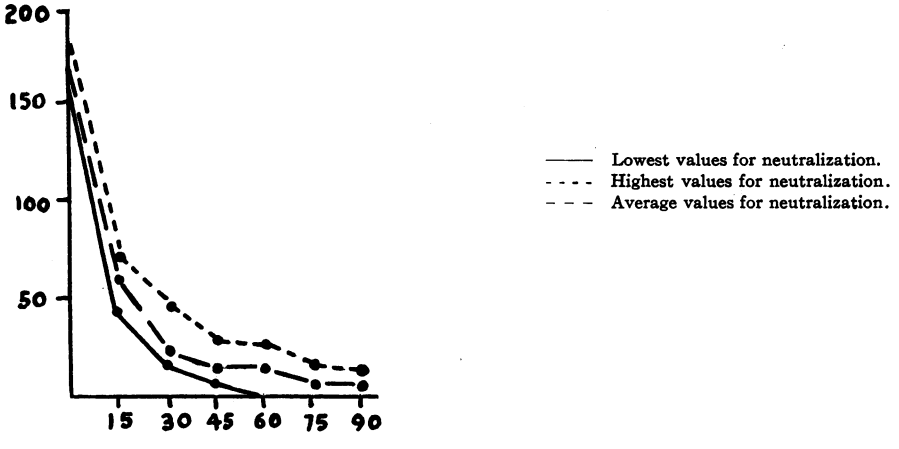
TABLE VIII

GASTRIC ACIDITY IN DOG'S STOMACH AFTER ESTABLISHMENT OF COMPLETE INTRAGASTRIC REGURGITATION OF DUODENAL CONTENT INTO THE FUNDUS

Schmilinsky Operation

Dog No. 3—Blackie:
Procedures and Dates
Antral resection 3/20/39
Duodenogastrostomy 5/17/39
(Schmilinsky)

Dates of Analysis	Fasting Free Acid	Alcohol Free Acid	Histamine Free Acid			Histamine Total Acid			Milligrams HCl with Histamine (Average)	
			Max.	Av.	Min.	Max.	Av.	Min.	Free	Total
4/11/39.....	0	12		73			88		113.4	138.0
4/12/39.....	0	11		24			104		17.6	76.0
4/13/39.....	0	23		24			48		12.2	24.4
4/24/39.....	0	25.5		34			58		17.45	12.8
2/14/40.....	0	0	62	32	0	86	62	50	31.5	60.4
2/15/40.....	0	0	14	4	0	57	46	40	5.6	18.6
4/25/40.....	0	12	56	37	0	64	44	10	26.8	32.3



Dr. George S. Bergh, of this department, and Drs. Curtis Nessa and Solveig Bergh, of the Department of Roentgenology, have studied intragastric

regurgitation occurring through gastrojejunostomy stomata by injecting barium and phenolsulphonphthalein in small amounts through a duodenal tube, the tip of which lies well into the duodenum. The amounts of intragastric regurgitation are variable. In the main, regurgitation to the extent of 33 per cent is common in the supine position—a figure which is considerably larger than when the patient stands erect.

In the antral excisions (Group II—six cases) a complete terminolateral anastomosis was made in all instances; achlorhydria to histamine (maximal) stimulation in this group was rare. In the extensive resections (Group III—ten cases) a complete terminolateral anastomosis was made in six patients and an entero-anastomosis was made also six times; in four of the patients with incomplete terminolateral anastomosis and in two of the others. In the antral exclusions (Group IV—six cases) complete terminolateral anastomosis was made only twice and an entero-anastomosis was made in five instances. In the tubular resections (Group VI—five cases) no entero-anastomoses were made.

It is difficult to draw any pertinent conclusions from the gastric acidities exhibited by these variants in the operative procedure. Yet, it does appear that an entero-anastomosis, if small (3.5 to 4 cm. in length) and placed near the gastrojejunal stoma, may be a helpful procedure, in that, while permitting intragastric regurgitation, it prevents undue prolongation of the gastric phase of gastric secretion by reducing the amount of the duodenal content regurgitated into the stomach. It seems worth while to determine the validity of this premise. It is to be understood clearly, however, that these latter remarks have *no meaning* for any other operation than extensive gastric resection, of the extent herein described.

Gastrojejunal Ulcer.—Bergh, Hay and Trach found in studying 138 patients having gastrojejunostomy, available for examination in the University Out-Patient Clinic, that 14 of the group had gastrojejunal ulcer (10.1 per cent). However, only 100 of the group had their gastrojejunostomy operation performed at the University Hospital; five of these had gastrojejunal ulcer (5 per cent). Yet others in the group may still develop gastrojejunal ulcer. Case 8 in Group III, upon whom emergency operation was performed for massive gastric hemorrhage, developed gastrojejunal ulcer (the cause of the bleeding) 20 years after gastrojejunostomy for obstructive duodenal ulcer.* In the experience of Church and Hinton (1940), gastrojejunal ulcer is a far more common sequel to gastrojejunostomy than is generally believed.

Two of the six patients in Group II (these patients appear again in Group V, Cases 1 and 2) with excision of antrum and pylorus developed gastrojejunal ulcer (33 per cent). Klein and his associates (1933) have reported previously an incidence of gastrojejunal ulcer following partial gastric resection of 8.5 per cent, and Lahey and Swinton (1935) noted this as a not infrequent complication of partial gastrectomy for ulcer.

* A patient who developed gastrojejunal ulcer 28 years after gastro-enterostomy was observed recently.

The only other gastrojejunal ulcer in this group of resections is Case 3 in Group V. He came with a gastrojejunal ulcer and when it was excised a portion of the greater curvature was excised, establishing a new gastrojejunostomy stoma in the line of excision. The stomach was extraordinarily large and the excision of 214 sq. cm. of gastric tissue was inadequate to make the patient achlorhydric.

No recurrent ulcers have been observed in any of the other group of patients.

Starlinger (1930) conducted a written inquiry on the incidence of gastrojejunal or recurrent ulcer after various types of gastric resection. Among 25,121 cases, constituting the basis of his report, only 169 patients were reported as having gastrojejunal or recurrent ulcer (0.7 per cent)—certainly a very conservative estimate (an unsatisfactory manner, however, in which to study its incidence).

Finsterer (1934) admits an incidence of gastrojejunal ulcer of 6.1 per cent after his operation of antral exclusion accompanied by gastric resection. As pointed out above, Finsterer, in insisting on a line of division of the stomach parallel to the vertical axis of the body, must of necessity leave more greater curvature than he is warranted in doing, mindful of the importance of extensive excision of gastric tissue to insure achlorhydria.

TABLE IX

EFFECT OF ANTRAL EXCISION IN STAGES UPON GASTRIC ACIDITY

(Pavlov Pouch and Residual Stomach)

PREOPERATIVE DETERMINATIONS

Dog No. 92—Johnny

	STOMACH SECRETION		
	No. of Determinations—2		
	Degrees of Free Acid		
	Maximum	Average	Minimum
Fasting—1 hr.:			
Free	48	39	29
Total	55	47	38
Alcohol—½ hr.:			
Free	80	72	64
Total	87	79	70
Histamine—½ hr.:			
Free	91	89	87
Total	101	99	90
Histamine—1 hr.:			
Free	109	106	102
Total	115	113	110
Histamine—1½ hr.:			
Free	69	69	69
Total	76	76	76

(See insert for continuation of Table IX)

TABLE IX (*Continued*)

(A) AFTER ESTABLISHMENT OF PAVLOV POUCH

Operation, October 2, 1939

	RESIDUAL STOMACH — No. of Determinations—3									PAVLOV POUCH — No. of Determinations—12								
	Degrees of Acid			Volume—Cc.			Milligrams HCl			Degrees of Acid			Volume—Cc.			Milligrams HCl		
	Max.	Av.	Min.	Max.	Av.	Min.	Max.	Av.	Min.	Max.	Av.	Min.	Max.	Av.	Min.	Max.	Av.	Min.
Fasting—1 hr.																		
Free	0	0	0	2.5	1.4	0.0	0.0	0.0	0.0	20	2	0	4.3	1.6	0.0	3.1	0.1	0.0
Total	47	32	16				4.3	1.6	0.0	150	52	0				23.5	3.0	0.0
Veal meal—½ hr.																		
Free										56	8	0	6.6	2.1	0.4	13.5	0.6	0.0
Total										93	66	33				22.4	5.0	0.0
Alcohol—½ hr.																		
Free	22	10	0	3.4	2.6	2.0	2.7	1.0	0.0	132	83	0	15.0	9.2	1.9	72.4	31.4	0.0
Total	39	36	32				5.0	3.4	2.3	130	114	60				71.2	38.4	0.0
Histamine—½ hr.																		
Free	76	31	0	6.5	3.6	1.7	18.0	4.1	0.0	140	119	76	23.8	14.0	2.7	120.4	61.0	7.5
Total	88	56	32				21.0	7.3	2.0	154	139	110				136.7	71.1	10.9
Histamine—1 hr.																		
Free	45	34	24	4.5	3.6	2.3	7.4	3.7	2.0	146	130	110	25.0	11.7	1.0	132.9	50.8	4.0
Total	76	62	44				12.5	6.9	3.7	168	144	114				153.2	60.2	4.2
Histamine—1½ hrs.																		
Free	34	11	0	5.3	3.2	1.7	6.6	1.3	0.0	128	75	40	4.3	1.6	0.2	20.0	4.4	0.3
Total	60	45	20				11.6	5.3	0.0	172	142	100				27.1	8.3	0.7

(B) AFTER ANTRAL EXCLUSION

Operation, November 13, 1939

	No. of Determinations—5									No. of Determinations—9								
Fasting—1 hr.																		
Free	20	4	0	7.5	5.3	1.0	5.5	0.8	0.0	40	4	0	1.5	0.8	0.4	2.2	1.2	0.0
Total	54	33	20				14.3	6.5	0.7	135	110	80				7.4	3.2	1.3
Veal meal—½ hr.																		
Free	0	0	0	4.6	3.7	2.9	0.0	0.0	0.0	0	0	0	0.8	0.3	0.1	0.0	0.0	0.0
Total	78	72	68				13.2	8.1	5.4	150	94	50				4.4	1.1	0.2
Alcohol—½ hr.																		
Free	0	0	0	22.8	11.2	2.3	0.0	0.0	0.0	114	76	36	11.1	7.1	2.2	45.9	22.5	2.9
Total	72	60	44				58.8	24.2	3.7	134	104	66				54.4	26.9	5.3
Histamine—½ hr.																		
Free	22	13	0	25.0	12.8	6.2	20.0	6.1	0.0	146	134	120	17.0	12.5	8.1	90.2	61.3	35.5
Total	66	49	19				60.2	36.9	4.3	162	147	135				100.5	67.6	38.4
Histamine—1 hr.																		
Free	20	10	0	24.5	12.7	2.0	17.9	4.6	0.0	150	141	133	17.5	12.6	2.1	86.1	64.9	9.2
Total	80	37	15				71.5	17.2	2.0	180	155	144				114.8	70.2	11.0
Histamine—1½ hrs.																		
Free	0	0	0	17.4	7.2	2.5	0.0	0.0	0.0	135	121	80	6.5	2.4	1.0	32.1	10.6	2.9
Total	52	35	15				33.0	8.1	1.4	180	141	106				42.7	12.2	3.9

(C) AFTER ISOLATION OF ANTRAL POUCH

Operation, January 11, 1940

	RESIDUAL STOMACH — No. of Determinations—2									PAVLOV POUCH — No. of Determinations—4									ANTRAL POUCH — No. of Determinations—4								
	Degrees of Acid			Volume—Cc.			Milligrams HCl			Degrees of Acid			Volume—Cc.			Milligrams HCl			Degrees of Acid			Volume—Cc.			Milligrams HCl		
	Max.	Av.	Min.	Max.	Av.	Min.	Max.	Av.	Min.	Max.	Av.	Min.	Max.	Av.	Min.	Max.	Av.	Min.	Max.	Av.	Min.	Max.	Av.	Min.	Max.	Av.	Min.
Fasting—1 hr.																											
Free	0	0	0	15.0	8.2	1.4	0.0	0.0	0.0	103	75	30	3.0	1.5	0.4	11.4	4.1	0.4	52	21	0	7.0	2.9	1.2	13.3	2.3	0.0
Total	57	53	48				31.3	15.9	2.5	173	109	55				18.9	6.0	0.8	112	59	28				28.8	6.2	1.2
Veal meal—½ hr.																											
Free	0	0	0	2.0	2.0	2.0	0.0	0.0	0.0	110	100	90	1.5	1.3	1.0	6.1	4.8	3.3	64	28	0	4.0	2.6	1.4	9.3	1.4	0.0
Total	120	120	120				3.8	8.8	8.8	115	108	100				6.4	5.1	3.7	120	83	43				17.5	8.1	2.2
Alcohol—½ hr.																											
Free	20	10	0	4.2	3.5	2.7	3.1	1.3	0.0	140	96	52	12.5	8.4	3.0	64.0	29.4	5.7	124	67	0	12.5	7.1	3.0	56.4	17.4	0.0
Total	43	42	40				6.7	5.4	4.0	150	118	64				68.7	36.1	7.0	144	101	26				65.4	26.2	2.9
Histamine—½ hr.																											
Free	20	17	14	5.5	4.2	2.8	4.0	2.6	1.4	152	142	124	18.5	13.8	11.0	102.8	71.2	50.0	138	117	80	17.5	13.9	11.0	88.2	59.5	32.0
Total	32	29	26				6.4	4.4	2.7	160	151	132				107.8	75.8	53.0	154	137	96				98.5	67.2	38.5
Histamine—1 hr.																											
Free	40	35	30	11.0	8.3	5.5	16.0	10.7	6.0	150	149	148	21.0	18.1	14.0	114.8	99.3	75.2	164	148	140	28.0	21.5	14.0	168.0	114.9	71.6
Total	52	51	50				21.0	15.5	10.0	168	159	154				128.4	105.0	79.0	170	159	152				175.0	124.8	77.6
Histamine—1½ hrs.																											
Free	32	16	0	4.2	3.7	3.1	4.9	2.1	0.0	150	143	140	11.8	6.3	2.7	64.6	32.5	13.8	136	132	128	16.0	7.7	2.7	78.8	35.0	10.0
Total	64	44	23				9.8	6.1	2.5	172	156	140				73.4	36.0	13.8	160	150	144				93.0	84.4	14.1

(D) AFTER EXCISION OF ANTRAL POUCH

Operation, April 10, 1940

	No. of Determinations—3									No. of Determinations—3								
Fasting—1 hr.																		
Free	0	0	0	3.8	2.0	1.6	0.0	0.0	0.0	60	20	0	3.4	1.2	0.1	7.4	0.9	0.0
Total	36	28	20				4.9	2.0	1.2	68	59	50				8.4	2.6	0.2
Meat—½ hr.																		
Free	0	0	0	7.5	7.5	7.5	0.0	0.0	0.0	0	0	0	0.0	0.0	0.0	0.0	0.0	0.0
Total	26	26	26				7.1	7.1	7.1									
Alcohol—½ hr.																		
Free	0	0	0	11.0	7.4	3.8	0.0	0.0	0.0	112	89	75	5.2	3.4	3.0	21.1	11.1	8.2
Total	28	23	18				11.2	6.2	2.5	120	193	90				23.8	12.8	9.9
Histamine—½ hr.																		
Free	10	3	0	6.5	5.2	3.8	2.4	1.0	0.0	142	135	128	17.0	15.0	13.0	87.2	74.0	60.8
Total	24	21	14				5.7	4.0	1.9	150	141	134				93.1	77.6	63.9
Histamine—1 hr.																		
Free	0	0	0	7.9	5.3	2.9	0.0	0.0	0.0	146	146	146	12.0	10.4	8.8	58.7	55.3	46.6
Total	32	23	14				8.2	4.5	1.5	152	151	150				66.8	54.0	48.0
Histamine—1½ hrs.																		
Free	0	0	0	12.0	9.2	6.1	0.0	0.0	0.0	157	135	100	1.6	1.0	0.7	9.3	4.9	2.6
Total	20	16	10				8.8	5.4	2.2	171	152	133				10.0	5.5	3.4

Balfour (1928) relates that 26 per cent of gastrojejunal ulcers coming under his observation have achlorhydria. It is very unlikely, however, that any patient with a well authenticated ulcer or gastrojejunal ulcer has a true achlorhydria—that is, is persistently achlorhydric after maximal stimulation with histamine. We have seen no such cases.

The absence of ulcer in patients with pernicious anemia (Kahn, 1937) having achlorhydria, and the absence of stomach ulcers in patients having gastric resection with gastrojejunostomy for cancer, bespeak the importance of acid in the genesis of ulcer, as does also the occurrence of an ulcer in Meckel's diverticulum where only a small fragment of gastric mucosa may cause ulceration with perforation or severe hemorrhage.

Among those who employ gastrojejunostomy for ulcer, the first and most positive indication for the operation is duodenal ulcer with obstruction. In this connection, the experience of those who have practiced the Eiselberg operation of gastrojejunostomy with pyloric exclusion is most important. It is generally conceded that the incidence of gastrojejunal ulcer after the Eiselberg operation is approximately 25 per cent. Only reopening of the pylorus when gastrojejunostomy is undertaken for obstructive ulcer can save the patient from running a similar risk of this dreaded complication. Moreover, Dublin and his associates, of the Metropolitan Life Insurance Company, in speaking of the risks of patients with ulcer, state that recurrent ulcer is the most important factor in mortality of patients who have been operated upon for ulcer.

Graham and Lewis (1935) state that they performed the Devine exclusion operation (transverse division of the stomach at the incisura without excision of gastric tissue) five times, and gastrojejunal ulcer developed at the stoma in all five patients.

Night Secretion.—Pavlov believed that fasting was attended by absence of gastric secretion in the dog. Carlson (1916) showed quite definitely, however, for man that the secretion of hydrochloric acid was continuous, and observers since (Polland and Bloomfield) have come to speak of a basal secretion of hydrochloric acid. Winkelstein believed that secretion of free hydrochloric acid at night occurred only in patients with ulcer and was absent in patients with a normal gastric secretory response without ulcer.

Our findings (Mears and Hay) on this score confirm the previous observations of Carlson, Polland and Bloomfield, and Hellebrandt, Tepper, Grant and Catherwood. In the main, however, patients with ulcer secrete more hydrochloric acid at night than do patients with normal stomachs. Undoubtedly, this item of night secretion, which will receive but bare mention here, is an important element in the dietary control of ulcer, and probably one of the most important items causing failure of such management. If some manner of suppressing night secretion adequately or controlling it continuously could be evolved, the necessity for surgery in the management of ulcer would diminish considerably. Measures such as suggested by Sand-

weiss (1939) and Brunschwig and his associates (1940) may, some day, make the rôle of the surgeon less prominent in dealing with the ulcer problem.

During the time that the work described above has been under way in the clinic, a broad approach to the ulcer problem has been made in the laboratory. Only a few observations, bearing somewhat intimately upon the questions described above, will be recited here.

Pouch Experiments in the Dog and the Edkins Hypothesis.—The validity of the Edkins' hypothesis was put to experimental test in the dog, employing methods very similar to those described previously by Smidt, Portis and Portis, Priestley and Mann, Enderlen and Zukschwerdt, and Shapiro and Berg.

Method.—A preliminary assay of the gastric secretory response was first made on the intact stomach. Then, either a Pavlov or a Heidenhain pouch was made of the proximal half of the greater curvature of the stomach and

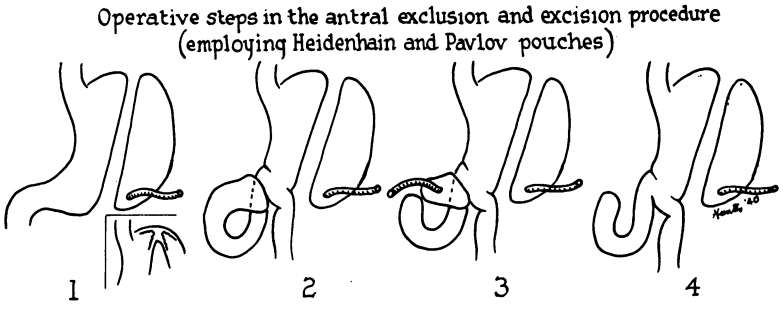


FIG. 8.—The various operative steps carried out in trying to evaluate the Edkins hypothesis experimentally by antral excision:
1. Establishment of a Heidenhain or Pavlov pouch.
2. Antral exclusion—the line of division being made in the acid secreting area of the stomach.
3. Isolation of the antral pouch.
4. After excision of the antral pouch.

the fundus. After complete recovery of the animal, the gastric response in both the residual stomach and the pouch was determined again. Later, an antral exclusion operation was performed, dividing the stomach transversely, the site of section being at or slightly above the incisura. The upper segment of the stomach was then anastomosed to a loop of jejunum. Determinations were made of the gastric secretory response in (1) the residual stomach; (2) the antral pouch; and (3) the Pavlov or Heidenhain pouch. Finally, the antral pouch was excised and the effect of its excision noted upon the gastric secretory response in the residual stomach and the Heidenhain or Pavlov pouch.

A number of such experiments have been completed. Excision of the antral pouch has been completed only recently in the majority. Nevertheless, our experiments indicate quite definitely that excision of the antrum and pylorus has no effect upon the secretory response in Pavlov or Heidenhain pouches in the fundus.

Portis and Portis, and Shapiro and Berg, while noting the absence of effect of antral excision upon the behavior of Pavlov pouches in the fundus of the dog's stomach, described also complete achlorhydria in the residual gastric segment (Portis and Portis), or a distinct lowering of acidity in the residual gastric segment (Shapiro and Berg). However, no special significance was attributed to this occurrence. Yet this is a *most* significant item. Our experiments still fail to indicate whether this is a regurgitation phenomenon (impaired function of acid secreting cells in response to intragastric regurgitation of duodenal contents as consequence of gastric resection and gastrojejunostomy) or whether sacrifice of the antrum and pylorus reduces the ability of the residual gastric pouch to sustain the initial capacity for secretion of hydrochloric acid. Reasoning by analogy, having in mind the absence of effect of antral excision upon the secretory capacity of Pavlov or Heidenhain pouches (also see Table X), one might say logically, it must be the regurgitation factor. Factual information can be obtained on this point in the dog which will eliminate the potential errors of apparently sound logic.

Summarizing data are given in Table IX on one such dog after: (1) Establishment of a Pavlov pouch; (2) antral exclusion; (3) isolation of

TABLE X

GASTRIC ACIDITY IN LARGE GASTRIC POUCH AND IN SMALL RESIDUAL STOMACH (AFTER GASTROJEJUNOSTOMY) FOLLOWING ESTABLISHMENT OF SUBTOTAL GASTRIC POUCH

Dog No. 9—Tony:
Procedures and Dates
Subtotal gastric pouch 5/26/39
Residual stomach approx. 20%

	Residual Stomach					Subtotal Pouch				
	Degrees			Mg. HCl in	Mg. HCl in	Degrees			Mg. HCl in	Mg. HCl in
	Free Acid	Total Acid	Volume Cc.	Free Acid	Total Acid	Free Acid	Total Acid	Volume Cc.	Free Acid	Total Acid
5/12/39 Preoperative Determinations:										
Fasting—1 hr.	24	46								
Veal broth—1 hr.	25	48								
Alcohol—½ hr.	66	80								
Histamine—½ hr.	76	90								
Histamine—1 hr.	16	32								
Histamine—1½ hr.	15	33								
3/1/40 Postoperative Determinations*										
Fasting—1 hr.	0	36	2.7	0	3.55	40	72	3.5	5.08	9.13
Veal meal—½ hr.	0	56	14	0	28.6	132	146	13	63.0	69.0
Alcohol—½ hr.	0	28	10	0	10.2	146	158	15	79.6	86.5
Histamine—½ hr.	0	60	17	0	37.2	144	156	13	68.0	74.2
Histamine—1 hr.	0	60	20	0	43.8	152	164	12	66.8	72.0
Histamine—1½ hr.	0	48	9	0	15.8	152	162	14	77.6	82.8

* In three subsequent determinations the residual stomach was achlorhydric to these stimuli. Achlorhydria in the residual gastric pouch on histamine stimulation since 8/31/39.

antrum as a pouch; and (4) excision of antral pouch and pylorus. Our antral pouches, as we had anticipatel, contained, quite uniformly, a fragment of the acid secreting area on the upper end. We wanted to be certain, when the antral pouch was removed, that no antral mucosa remained. The secretion from these antral pouches was, therefore, acid in reaction.

In another dog with a subtotal gastric pouch (isolation of entire stomach save for a small remnant of the fundus), a jejunofundic anastomosis was made. It is to be observed (Table X) that the isolated stomach secretes hydrochloric acid actively. The small residual stomach between esophagus and jejenum, however, has, with the lapse of time, become achlorhydric.

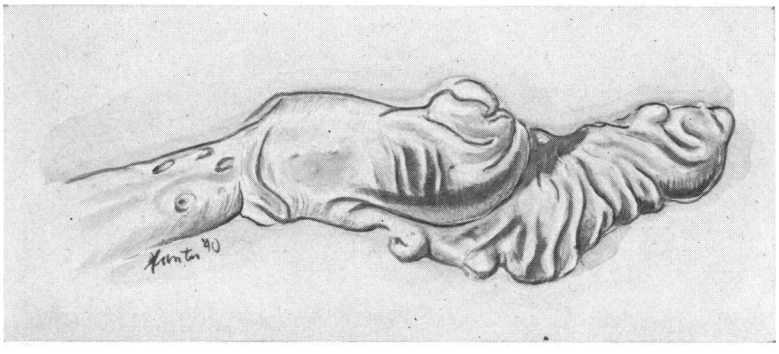


FIG. 9.—Drawing of ulcers produced by subcutaneous implantation of histamine in cat.

Acid Instillation.—Hydrochloric acid (0.4 per cent) was instilled (Walpole) over an interval of 15 to 46 days in four dogs, 82 to 108 cc. per hour being allowed to run into the fasting stomach by the drip gravity method through a gastrostomy opening. The instillations were made daily for six and a half to seven hours. The animals were fed late in the day, after the instillation was discontinued. No ulcers occurred in dogs. Samples removed periodically for titration indicated that during the time of acid installation an average acidity of 73 degrees of free hydrochloric acid was maintained in the stomach.

In three of four cats, similarly treated, but given only 40 to 50 per cent as much acid, ulcers were produced in four to 11 days. One cat pulled the gastrostomy tube out on the third day and presented no changes in the stomach, duodenum or esophagus. Ulceration in the cardiac esophagus, fundus, antrum and duodenum was a common finding in the other animals. This finding will be described in greater detail at a later date.

The Production of Ulcers by Subcutaneous Implantation of Histamine in Beeswax.—Dr. Charles F. Code, Assistant Professor of Physiology at the University of Minnesota, whose studies on histamine assays in body fluids are well known, wished to study the effects of subcutaneous implantation of histamine in beeswax upon the gastric secretory mechansm in dogs. The results of this study will be reported later (Code and Varco). This type of histamine poisoning succeeds in pouring out extraordinary quantities of a

highly concentrated acid. A concentration of 170 degrees (0.62 per cent HCl) has been maintained in the secretion of a Pavlov pouch more than one hour, and a liter of N/10 HCl will be secreted in 24 hours by such a pouch under the powerful stimulus of gradual liberation of histamine.

Histamine in beeswax (20 mg. of the base, equivalent to three times this amount of histamine as ergamine acid phosphate) was implanted into the back muscles at several sites in five cats (Walpole). Ulcers occurred in all in three to nine days—large and small erosions as well as perforating ulcers were observed (Fig. 9).

Antral and Fundic Extracts and Their Effect upon the Gastric Secretory Mechanism.—The gastric theory of gastric secretions rests on Edkins' work with pyloric and fundic extracts of gastric mucous membrane and their effect upon the secretory capacity of the cat's stomach. Much work has been done on this phase of the problem by many observers. One of us (Trach), working in collaboration with Dr. C. F. Code, of the Department of Physiology, has prepared histamine-containing and histamine-free extracts of the antral and fundic mucous membrane of both dog and man. In the main, these observations suggest that the histamine-containing extracts, whether from the antrum or the fundus, of both dog and man, exert a stimulating effect upon the secretory capacity of Pavlov and Heidenhain pouches in dogs, as well as upon the intact stomach of the dog. Histamine-free preparations were without effect. These findings will be reported in greater detail at a later date.

Code has determined the histamine content, per gram of antral and fundic mucosa, in both dog and man. He found a larger content of histamine, per unit of mucosal weight, in the fundus for both man and dog. Code also found that the dog's gastric mucosa contains considerably more histamine, per unit of weight, than does man's gastric mucosa. Code's observations on the histamine content of the gastric mucosa of dogs confirm the observations of Gavin, McHenry and Wilson, who found that 80 per cent of the total histamine is to be found in the fundus.

Gastric tissue, it is to be remembered, unlike intestinal mucosa which contains both histamine and histaminase, contains no histaminase. It has already been suggested (Dragstedt, C. A., and associates, 1940) that alcohol mediates its stimulating effect upon gastric secretion by the liberation of histamine. We, too, have noted that alcohol, when instilled into jejunostomy, enterostomy, cecostomy, or colostomy openings in man, exerts a stimulating effect upon gastric secretion in responsive stomachs in man. Similarly, we observed that veal broth instilled into jejunostomies in man excites the gastric secretory mechanism.

Responsiveness of Antral, Fundic (Pavlov and Heidenhain) Pouches and the Residual Stomach (after Establishment of Gastro-intestinal Continuity) to Introduction of Alcohol.—Sawitsch and Zeliony (1913) observed that a greater secretion of hydrochloric acid was obtained from the stomach when food came in contact with antral mucosa. Lim, Ivy and McCarthy

(1925) confirmed this observation and state that antral mucosa is definitely more sensitive in evoking the stimulus for hydrochloric acid secretion than is contact of food with fundic mucosa. These conclusions constitute a bit of evidence which lends tenable support to the Edkins' hypothesis. We have seven dogs with antral and fundic pouches in addition to the residual stomach. Into these pouches 25 cc. of a 7 per cent solution of alcohol has been introduced. Our experiments are incomplete. On surveying our data, we were inclined, at first, to believe that the observations of Sawitsch and Zeliony, and Lim, Ivy and McCarthy were supported by our findings. A typical response is indicated in Table XI. It is to be noted that a greater secretion was obtained from the Pavlov pouch. But there is no evidence of stimulation *over* the secretion obtained in the fasting state. It is to be remembered, further, that the amount of acid secreting tissue in our antral pouches is

TABLE XI

RESPONSE OF ANTRAL AND FUNDIC POUCHES TO INTRODUCTION OF ALCOHOL

Dog No. 108—Oscar:
Procedures
Antral and Pavlov pouches

	Residual Stomach					Antral Pouch				
	Degrees			Mg. HCl in	Mg. HCl in	Degrees			Mg. HCl in	Mg. HCl in
Date of Gastric Analysis	Free Acid	Total Acid	Volume Cc.	Free Acid	Total Acid	Free Acid	Total Acid	Volume Cc.	Free Acid	Total Acid
4/22/40										
Fasting—1 hr.	0	8	4.0	0	1.17	0	8	1.0	0	0.29
Fasting—2 hrs.	0	42	5.5	0	8.4	0	33.3	0.9	0	1.09
25 cc. 7% alcohol placed in Pavlov pouch—½ hr.	18	36	13.0	8.54	17.0	0	43	0.7	0	1.09
1 hr.	0	32	3.2	0	3.7	0	100	0.3	0	1.09
								Pavlov Pouch		
4/23/40										
Fasting—1 hr.	0	40	10.5	0	15.3	43	150	0.9	1.41	4.9
25 cc. 7% alcohol placed in antral pouch— ½ hr.	0	10	8.0	0	2.92	30	40	1.2	1.31	1.75
1 hr.	0	23	4.8	0	3.27	50	60	0.7	1.28	1.52

relatively small. It may be pointed out here that instillation of alcohol into the residual gastric pouch (ref. Table IX, under item IV) elicited a good response from the Pavlov pouch. In the light of the greater histamine content of fundic mucosa, one could expect, reasonably, a greater response upon the residual stomach from instillation of alcohol into fundic rather than antral pouches.

The responsiveness of the antral and fundic mucosa to contact with alcohol or food, with reference to the secretion of acid, is an important item. Should the antral mucosa prove to be definitely more sensitive, one bit of evidence would continue to support the Edkins' hypothesis.

SUMMARY.—These observations are not intended as suggestions upon which the indications, for the various gastric operations for the relief of

ulcer, should be formulated. Many items enter into consideration which determine choice of operative procedures, and, frequently, standardized indications fail to meet optimally the requirements of a given patient. However, the observations related here have some importance in determining what may be expected reasonably of certain types of operative procedures.

Satisfactory operations for ulcer insure: (1) Achlorhydria to maximal stimulation (histamine); and (2) decreased emptying time. Operations which fail to afford real promise of achlorhydria leave too much to chance and hold out too great a risk of gastrojejunal or recurrent ulcer, to stamp them as satisfactory operations to be invoked frequently for the surgical relief of ulcer. Gastrojejunostomy and excision of the pylorus and antrum fall into this class.

Gastrojejunostomy (and probably also, gastroduodenostomy and pyloroplasty) exerts its value through quickening of the gastric evacuation time. Removal of the pylorus and antrum whether by the Billroth I or II plan is probably of no great consequence) is attended by true achlorhydria only occasionally. The virtue of this procedure lies largely, also, in diminution of the emptying time.

Extensive gastric resection when accompanied by gastrojejunostomy is attended usually by achlorhydria to histamine stimulation. When, however, three successive doses of histamine are given, some such gastric pouches, previously achlorhydric, may secrete free hydrochloric acid. True achlorhydria is reported after extensive gastric resection, tubular resection of the corpus and antrum, accompanied by gastrojejunostomy leaving the pylorus and antrum intact), and after the antral exclusion resection save for the recent cases).

The items necessary to afford real promise of achlorhydria are (1) extensive excision of the acid secreting area; and (2) provision for gastrojejunostomy. Occasionally true achlorhydria follows performance of operation directly; in a number of instances a few months must elapse before achlorhydria occurs. Operations which delay the gastric evacuation time (such as provision for complete intragastric regurgitation) are not likely to be followed by achlorhydria and may, like anastomotic operations which lower gastric evacuation time without lowering gastric acidity, be followed by a high incidence of recurrent ulcer.

It is pointed out that the size of the resection is an important item in determining whether true achlorhydria will occur. The term "subtotal gastric resection"* has been applied by many experienced gastric surgeons, when their own diagrams indicate that they excise in the vicinity of 50 per cent of the total gastric tissue. The surgeon, intent on affording his patient maximal protection against recurrent ulcer, must take more serious account of the amount of gastric tissue which he removes. The minimal amount necessary to excise to afford real promise of achlorhydria is not known. Excision of

* A satisfactory definition of "subtotal" is a little less than all. No resections of less than 80 per cent can be described reasonably as "subtotal."

66 to 80 per cent usually suffices. Whether achlorhydria *per se* carries special risks for the patient remains to be seen.

On the clinical side, the data reported herein appear to indicate that the Edkins hypothesis, of control of the gastric phase of gastric secretion by a pyloric and antral hormone, is invalid. The essence of this proof lies in two occurrences: (1) The consistent production of true achlorhydria in five patients having duodenal ulcer after tubular resection of the corpus and fundus attended by gastrojejunostomy), leaving the pylorus and antrum intact (Group 6). (2) Failure to produce true achlorhydria in patients with excision of the pylorus and antrum (Group 2). Another item bearing directly upon the point in question, but upon which our evidence is not yet complete, is the group of patients in which extensive gastric resection has been performed, but in which the pylorus and a small fragment of the antrum are left (Group 4).

The importance of "night secretion" in this relatively long fasting period is pointed out. It often breaks the effectiveness of dietary control of the ulcer regimen.

On the experimental side, it is indicated that sacrifice of the pylorus and antrum does not diminish the secretory activity of fundic (Pavlov and Heidenhain) pouches. In time, the residual gastric pouch, after antral excision, tends to become achlorhydric. Whether this occurrence is owing largely to impaired gastric secretory capacity, consequent upon gastric resection and provision for intragastric regurgitation, or whether the occurrence is influenced significantly by sacrifice of the antrum, cannot be stated definitely.

On the item of the relative responsiveness of antral and fundic mucosa to the presence of alcohol, our findings are incomplete and inconclusive. Previously recorded data on this score suggest a greater sensitivity of the antral mucosa—an observation which would lend at least partial support for the Edkins' theory of gastric secretion.

The experimental production of ulcer (exogenous) in cats by the introduction of 0.4 per cent acid is reported. (See Walpole et al.) Similarly, the intramuscular implantation of histamine in beeswax (Code) is followed by maximal stimulation of hydrochloric acid secretion, and ulcer can be produced regularly in cats by this method (endogenous). These latter observations lend increased significance to the acid factor in the genesis of ulcer.

Extracts of gastric mucosa, prepared from the stomachs of dog and man, which contain histamine stimulate the secretion of hydrochloric acid in dogs with fundic pouches. Such activity was demonstrated in the extracts prepared from both antral and fundic mucosa. The mucosa of the fundic zone contains more histamine, per unit of weight (per gram), than does antral mucosa (Code) and the dog's gastric mucosa contains more histamine, per unit of weight, than does the gastric mucosa of man.

CONCLUSIONS

(1) Anastomotic operations performed for ulcer fail to produce achlor-

hydria. The virtue of such operative procedures is mediated through lessening of the gastric evacuation time.

(2) Extensive gastric resection *per se* is not followed by achlorhydria, but when accompanied by gastrojejunostomy, achlorhydria follows, usually with the lapse of time.

(3) Provision for complete intragastric regurgitation lengthens the gastric phase of gastric secretion and is undesirable.

(4) Excision of the pylorus and antrum in man for ulcer is rarely attended by achlorhydria.

(5) Achlorhydria may accompany extensive gastric resection for ulcer, when the pylorus and antrum remain.

(6) The Edkins' hypothesis on the clinical side, on the basis of our observations, appears to be invalid. On the experimental side, our observations are still incomplete, save that excision of the pylorus and antrum does not decrease the secretory capacity of fundic pouches.

(7) The importance of the acid factor in ulcer is emphasized in the occurrence of ulcers in cats after intragastric instillation of 0.4 per cent HCl and after subcutaneous intramuscular implantation of histamine in beeswax.

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DISCUSSION.—DR. LESTER R. DRAGSTEDT (Chicago, Ill.): Doctor Wangensteen and his associates deserve our congratulations and thanks for their extensive and painstaking study of the effects of various operative procedures on the physiology of the stomach. It is the kind of information that should have been available many years ago and would have made unnecessary many a surgical experiment on patients with gastric and duodenal ulcer. I do not share the pessimistic view of the ulcer problem expressed by Doctor Ivy in 1931. The vast amount of work done on the lower animals in a large number of laboratories during the past few years has so greatly clarified and extended our knowledge in this field that there are few diseases where our information is more complete.

A typical, chronic progressive ulcer can be produced at will in the dog and the factors necessary for its production are fairly well understood. Pure undiluted gastric juice has the capacity to digest away all living tissue, including the wall of the stomach itself, and an ulcer may be expected whenever opportunity for prolonged contact between such a secretion and the mucosa occurs. The normal stimulus for gastric secretion is the ingestion of food, and this food promptly reduces the acidity and pepsin concentration of the fundus secretion. In many ulcer patients, however, copious secretions of gastric juice occur without the stimulus of food, often during the night, and large amounts of pure gastric juice remain in contact with the gastric and duodenal mucosa for long periods. Solution of the clinical problem would seem to depend upon the discovery of the nature of this abnormal stimulus for gastric secretion.

The interpretation of Doctor Wangensteen that reduction of the acidity of the gastric content following partial gastrectomy, gastrojejunostomy, gastroduodenostomy, and similar procedures, is due to lessening of the gastric phase of secretion through more rapid emptying of the stomach seems well justified by the evidence presented. The new procedures of attempting to reduce the acidity by actual removal of large areas of the acid-secreting fundus are interesting, and it is important that they should be explored by investigators like Doctor Wangensteen and his associates, who are willing, also, to study the effects of these operations on gastric physiology.

The fact that subtotal gastrectomy is occasionally necessary to cure the disease does not indicate that this procedure is the solution to the problem, but it is only a confession of our inability in many cases to control the excessive gastric secretion by less radical measures.

DR. ROSCOE GRAHAM (Toronto, Can.): Gastro-enterostomy has been followed by relief of symptoms of duodenal ulcer in spite of the operation. A restudy of a series of our patients has shown of those symptom-free, 47 per cent had malfunctioning stomata.

Doctor Wangensteen's contribution is excellent, but it is doubtful whether the relation of acid to recurrent ulceration is still settled. While we have deleted the necessity of operation from the treatment of an uncomplicated duodenal ulcer, we are adding further confusion. Such confusion arises because in reports of operated cases there is not an accurate description of the extent of the resection and the type of reconstruction of the gastro-intestinal tract. Our clinical experience has borne out Doctor Wangensteen's statement —"If we must operate upon patients suffering from complicated duodenal ulcer, such operation should be a radical gastric resection." Doctor Dragstedt says it is an admission of defeat. It is! It is an unphysiologic compromise, which, however, if applied to properly selected cases, produces a happy result, and until we can determine accurately the cause of ulcer, must be an acceptable therapeutic procedure. May we, as a group, in reporting the results of our gastric resections for duodenal ulcer, state accurately the extent of the resection and the method of reconstruction. This, I trust, will avoid many years of confusion and error in arriving at an accurate evaluation of surgical therapy for duodenal ulcer.

DR. J. SHELTON HORSLEY (Richmond, Va.): Studies of the kind that Doctor Wangensteen and his associates have reported are always interesting. Much gastric surgery has been performed without the proper consideration of the underlying biologic principles. Physiologists have shown that in experimental animals a large portion, often more than 75 per cent, of normal kidney tissue can be removed, if undertaken in different stages, with no apparent permanent interference with the function of the kidney. The same is true of the liver. If more than this maximum amount is excised there may not be enough tissue left to undergo sufficient hyperplasia, and function may, therefore, be permanently affected. It would seem probable that this general law of compensation applies to the stomach, and doubtless accounts for the disappointing late results that follow many operations of so-called fundectomy, or excision of a large quantity of the acid-bearing region of the stomach.

The efficacy of operations on the stomach cannot always be evaluated by the amount of hydrochloric acid in the gastric contents. It is not as simple as that. If, for instance, the estimation of acid in the gastric contents is made before there is opportunity for hyperplasia of the acid-forming cells of the remaining portion of the stomach, naturally the acid will be low or absent. In Doctor Wangensteen's cases there was, I believe, achlorhydria, at some stage, in all of the cases that he reported. Then, too, it is probable that some individuals will have a tendency to compensate for the destruction of the acid-bearing part of the stomach more readily than others. Almost any subtotal resection would leave approximately at least one-fourth of the acid-secreting portion, and, as an analogy between this and the experimental work on the kidneys and liver, it would seem that the remaining portion is capable by hyperplasia of eventually restoring practically the full amount of acid. Other features that enter into the results of gastric operations are the

type of operation performed, and the portion of the intestinal tract into which the gastric contents empty. If, for instance, a Billroth II type of operation is undertaken and an entero-enterostomy performed, much of the alkaline contents of the duodenum is diverted and does not reach the gastric anastomosis. This is, in a sense, the duodenal drainage of Mann and Williamson, which has been found experimentally to result in an ulcer at the site of the anastomosis in almost every instance. Of course the entero-enterostomy does not necessarily drain off all of the alkaline contents, so that the analogy is not complete, but it, at least, takes away some of it and so weakens the resistance of the gastric anastomosis to the acid that is left.

It has been shown by physiologists that the sensitivity of the intestinal mucosa to the acid of the stomach increases from the duodenum down to and including the large intestine. The duodenum ulcerates more frequently because it bears the first brunt of the impact of the acid from the stomach, but an anastomosis with the jejunum, even when there is no entero-enterostomy, entails a greater probability of ulceration from the acid of the stomach than would occur with the same amount of gastric acid emptying into the duodenum.

DR. OWEN H. WANGENSTEEN (Minneapolis, Minn., closing): In my presentation, I had no opportunity to allude to the experimental production of ulcer. During the past year, my colleagues and I, with the cooperation of Dr. C. F. Code, Assistant Professor of Physiology, have been exploring some phases of this problem. The daily instillation of 0.4 per cent hydrochloric acid in fairly large amounts over a period of some hours into the stomach of the dog was not followed by the occurrence of ulcer. When, however, similar instillations, but in less amounts, were made into the stomachs of cats, ulcers were produced quite uniformly. Employing a suggestion of Doctor Code that histamine be embedded in beeswax, to permit constant liberation of the histamine, and implanted intramuscularly, ulcers were uniformly produced in cats as well as in the two dogs upon which the experiment has been tried to date. Doctors Cole and Varco have studied the effect of such gradual liberation of histamine upon the secretory capacity of gastric pouches. The effect is profound, high concentrations of hydrochloric acid (0.6 per cent) being poured out in large amounts. I have the impression that we may be able to produce ulcer experimentally by this method in every animal whose stomach secretes hydrochloric acid. We propose to probe this problem further. For therapeutic reasons, it is most important to know whether acid is *the* factor or only *an important* factor in the spontaneous occurrence of ulcer in man.

Mind you, it takes only a little wisp of actively secreting gastric mucosa to produce an ulcer. We need only recall what may happen in Meckel's diverticulum, where a bit of gastric mucosa, no larger in area than the thumbnail, may produce hemorrhage or perforation, as is seen more frequently in duodenal or gastric ulcer.

Doctor Horsley referred to the regeneration of gastric mucosa. The regenerative property and capacity of gastric mucosa is well known. When I stated that we removed *by measurement* 66 to 80 per cent of the stomach, I admit freely that this measurement probably does not constitute this same fraction of the gastric mucosa. As you know, the mucosa of the upper portion of the stomach is considerably more rugated than the antral portion. When, at operation, one leaves a small residual gastric pouch which would hold approximately four ounces of fluid (120 cc.) and a few months later, one sees that small residual gastric pouch expanded into a stomach of much

larger proportions, I like to think that the following has happened: Smooth muscle has an enormous capacity for adjusting itself to various degrees of stretch (one need think only of what happens quite normally in the stomach, bowel and bladder); the small residual gastric pouch, even in the absence of obstruction, enlarges to the extent that the mucosa and submucosa will permit the smooth muscle of the stomach to stretch.

So that whereas excision of the amount of stomach described in this presentation appears large, it is to be remembered that the same percentage of the gastric mucosa is not sacrificed.

Patients who have been achlorhydric to histamine, persistently during the early months after operation, have not in our experience exhibited free hydrochloric acid later. The use of continuous suction rather than intermittent aspiration diminishes the possibility of not getting *true* acid values from the gastric juice. Even with the employment of suction it is clear that all the gastric juice cannot be aspirated—hence the weakness of single aspirations.

It is interesting that provision for *some* intragastric regurgitation must be made to produce achlorhydria to histamine stimulation after gastric resection. It would appear that total intragastric regurgitation of the duodenal content is undesirable. *How much* intragastric regurgitation is optimal is not yet apparent. It may prove that the intragastric regurgitation which an ordinary stoma provides is optimal. We have been exploring this query in part by adding entero-anastomoses to some of the extensive gastric resections. An advantage of entero-anastomosis is that it does away with the mechanical derangements at the stoma after gastrojejunal anastomosis—disturbances which are familiar to everyone. I must emphasize, however, that I do not suggest that entero-anastomosis be performed in the ordinary small gastric resection. My colleagues and I do not feel that our findings should be interpreted as indications for choice of operative procedure. What we do mean to point out is what the surgeon may reasonably anticipate from alternative types of operation.

It is extraordinarily interesting that the residual stomach may become persistently achlorhydric to histamine stimulation after gastric resection and gastrojejunal anastomosis of the extent which I have described, for, after all, a sizable fragment of gastric mucosa remains still. Dr. Maurice Visscher, Professor of Physiology, with whom I have had many profitable discussions upon the ulcer problem, asked if it was reasonable to believe that one could make the stomach achlorhydric to maximal stimulation (histamine) as long as gastric mucosa remained. It appears that we can.

The surgeon, when operating for ulcer, must be studious in his effort not to inflict upon the patient a worse disorder than that with which the patient came to him. The operation which fails to reduce gastric acidity leaves a great deal to chance and invites the possibility of a recurrent ulcer.