CONTROL OF ACID SECRETION IN THE SURGERY OF DUODENAL ULCER

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While the basic derangements responsible for peptic ulceration are not understood, the chronicity and recurrence of these ulcers appear to depend on the amount of acid that the stomach of the patient with gastric or duodenal ulcer produces. Treatment of a chronic peptic ulcer is therefore directed towards reducing the patient's acid secretion to a level where the ulcer will heal, and maintaining it at the level to prevent a recurrence of the ulcer itself or the development after operative treatment of a new one at the stoma.

The most effective and certain cure of an ulcer is bed rest; such treatment almost never fails to heal a benign lesion and its efficacy is based on regular frequent meals as a means of neutralizing acid as much as on mental and physical rest. An ulcer so treated heals 'as fast as epithelium can epithelialize'.[1] Unfortunately few people are able or willing, for economic reasons, to undertake a thorough regime of rest, and the history of most patients with chronic ulcer reveals repeated half-hearted attempts at such a cure over a number of years. Even a thoroughly supervised course of treatment which temporarily heals the ulcer is not always sufficient to protect the patient against a recurrence. Some patients are fortunate and attacks may not recur for a number of years; but where an individual becomes incapacitated every few months it becomes economically impossible to repeat further 4-6 week periods in bed.

The ambulant treatment of chronic peptic ulcer is often unsatisfactory, yet a certain proportion of patients remain well despite disregard of strict medical orders. Dietary regimes with milk as a mainstay, antacids and stopping smoking (and substituting food) help to neutralize the excess acid but do not reduce the amount secreted. Anticholinergic drugs are more successful in reducing acid experimentally than clinically.

There are few reports of psychotherapeutic cure of duodenal ulcer. Hurst's hypothesis of an ulcer diathesis and the relationship between stress and emotional factors to the genesis of the disease have been attractive theories, but there is little scientific support for such causal relationships. There is contradictory evidence in the literature concerning the influence of emotional and unhappy childhood experiences in the development of duodenal ulcer, although it is common experience that emotional crises do cause exacerbation of ulcer symptoms. On the known facts the development of an ulcer and excess secretion of acid are more closely allied to irregular eating habits, dietary deficiency or excess, and constitutional factors. These undoubtedly play a major role in the pathogenesis of the lesion. No social class is exempt; lorry drivers and business executives, labourers and doctors are alike affected. While all these patients are common prey to frustration and emotional tension, a more direct and clear insult to a stomach bathed in continuous secretion of acid is the occasional snack or quick cup of tea taken at irregular intervals. The high incidence of ulcer in the rural South Nigerian[2] and the peasant of South India, and the contrast between the frequent ulcer occurrence among Europeans and Indians in Natal compared with the African population, seem to indicate the importance of dietary factors. The increasing incidence among the latter cannot be explained simply as due to the increasing tensions of city living but is probably as closely related to changes in diet and habits of eating.

Constitutional factors have recently received emphasis by the demonstration of a significantly higher proportion of duodenal ulcer patients with group 'O' blood types than is found in normal control samples of the population;[3, 4] an equally striking demonstration of the familial trend is the evidence that there is a distinct pattern of duodenal ulcer in both patients and their relatives. A smilar correlation is found with gastric ulcer patients.[5]

The general aim of surgical treatment is to reduce the individual's acid-pepsin secretion to a low level. Surgical fashions have tempted the operator to apply a standard treatment to all patients with duodenal ulcer or gastric ulcer, with the exception of the very old and the very young. This has its advantages and disadvantages. On the one hand a surgical routine provides a technically better operative result; but some of the poor end-results of surgical treatment spring from the use of a single ablative technique for a disease with as wide a variation in degree and severity as such endocrine and autonomic disturbances as thyrotoxicosis and hypertension.

The proper aim of surgical treatment should be to reduce the acid-pepsin factor not according to a formula generally applied to all patients, but in proportion to the output of the individual patient. This places a considerable emphasis on the acid-secreting capacity of the stomach but, in the light of our present knowledge of the physiology of gastric secretion, it represents one measurable factor which can guide the extent and scope of operative treatment. It is therefore necessary to have a standard measurement of the acid output and a means of measuring it. There are at least 4 operations which will achieve a reduction in acid to a greater or lesser degree and the particular one chosen should be based on the acid output of the resting and active stomach, the length of history of the disease and the age and the sex of the patient.

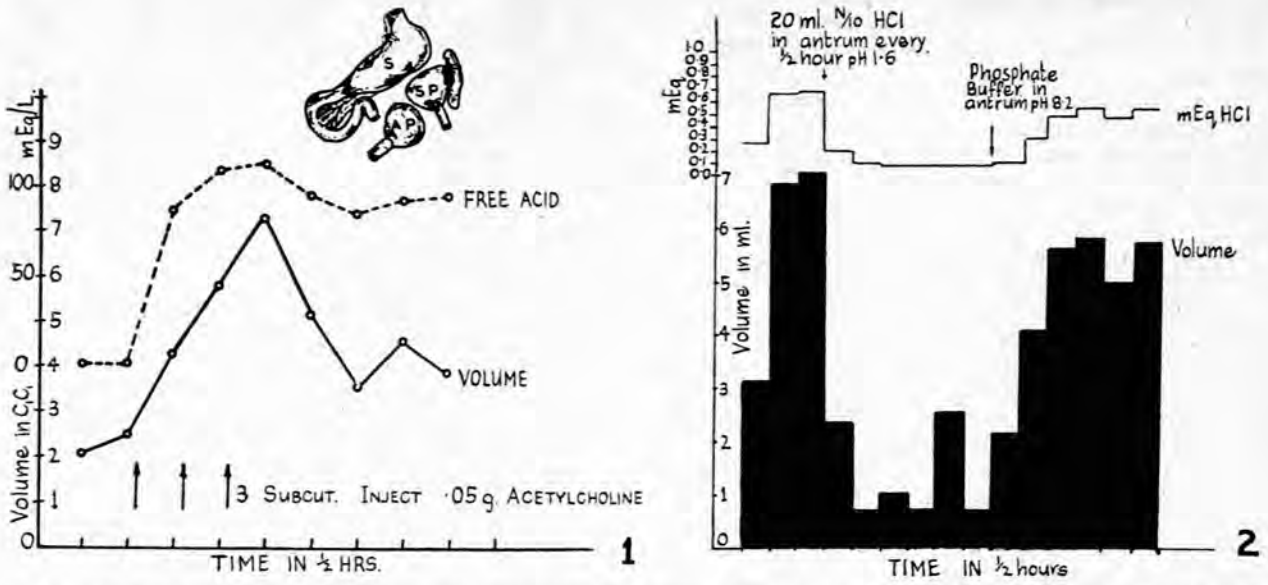


Fig. 1. Effect on acid secretion of acetylcholine in an exteriorized antrum pouch (Heidenhain pouch preparation). (The drawing at top applies also to Fig. 2.) *Fig.* 2. Effect on acid secretion of pH change in an exteriorized antrum pouch, indicating the inhibitory effect of acid in the antrum.

EXPERIMENTAL EVIDENCE

The experimental findings affording a rationale for the surgical reduction of acid production are based on Pavlov's concept of the 3 phases of gastric secretion:

1. *The cephalic phase*, mediated through the vagus nerve. Overwhelming evidence has been accumulated by Dragstedt[6-8] and his co-workers that in dogs abolition of this phase leads to a 60% or more reduction in the secretion of free hydrochloric acid. In man the quantity of acid reduction is not so predictable, since the human stomach is not dependent upon sudden outpourings of juice to deal with a large bolted meal, and secondly because night secretion (the interdigestive secretion) is not necessarily only vagal in origin. Yet marked reduction of the 12-hour night-secretion measurement following vagotomy is proof that this mechanism plays a predominent role in the hypersecretion found in duodenal ulcer patients. Three hundred duodenal ulcer patients with an average night secretion of 60 mEq. had, after vagotomy, an average free hydrochloric acid output of 5 mEq. in 12 hours. This reduction appears to be a permanent one.[7] An alternate mechanism for the hypersecretion of acid independent of the vagus nerve pathway has been suggested whereby stress phenomena cause the pituitary to secrete ACTH, liberating cortisone, which in turn stimulates an increase in acid and pepsin. Zubiran *et al.*[18,19] have shown that both ACTH and cortisone produce a sustained increase of free HCl in stomach pouches with and without vagal nerve supply. Since hypersecretion is abolished clinically and experimentally by vagotomy, it is clear that the excess secretory impulses are produced over the vagus nerves and not *via* the adrenal glands.

There is some experimental evidence that the vagus in fact plays a part in initiating the hormonal phase of secretion,[9] although other workers have failed to confirm this.[10] However, clinical data suggest that vagal and antral control of secretion forms part of an interrelated reflex arc and some of the value of removal of these nerves depends on this factor.[11]

2. *Gastric phase:* Gregory and Ivy[12] witnessed secretion from a stomach pouch transplanted to the submammary region when food was placed in the main stomach. Distension of the antrum was shown to produce secretion from such a transplant and procaine applied topically to the antrum prevented this response. This conclusively proved that the antral part of the stomach produces a hormone, 'gastrin', first postulated by Edkins in 1906.

Experimentally the stimuli for the production of 'gastrin' are food (particularly proteins), mechanical distension,[13] and acetylcholine. The latter affords presumptive evidence that cholinergic nerve endings are the trigger for the mechanism (Fig. 1). Dragstedt *et al.*[14] produced remarkable evidence of the power of the antrum to stimulate secretion when an antral pouch is transplanted to the colon, resulting in the application of constant *in vivo* distension stimulus.

On the other hand there is a growing body of evidence that the antrum not only produces a hormone which stimulates acid secretion, but that it acts as an inhibitor of acid as well.[15] Thus it is able to 'turn off the tap' of acid secretion in certain circumstances. Experimentally, inhibition of acid secretion from a Heidenhain pouch can be produced by a strongly acid solution placed in the exteriorized antrum (Fig. 2). Similarly the hypersecretion produced by an antral transplant to the colon is reduced if a portion of the antrum is left in its normal position exposed to an acid environment. There is no information of the relative importance in man of the antral and hormonal phases of secretion. The interrelation is too close for experimental separation; all that can be said is that in the experimental animal removal of each factor separately causes a profund drop in acid secretion.

3. *The intestinal phase* of secretion plays a relatively

small role and, despite earlier promising work with the hormone enterogastrone, little of clinical value has been achieved.

THE MEASUREMENT OF ACID OUTPUT

The strength of acid is measured by titrating a sample of gastric juice against 1/10 N NaOH. This gives the concentration of acid present. By measuring the total volume of gastric juice secreted in 12 hours, the final result is expressed as mEq/L of gastric juice. This provides a quantitative measurement of the output of acid.[7]

A multi-hole Levin tube is placed in the dependent part of the stomach and checked by screening to ensure that the tip lies in the antrum. Continuous suction with a low-pressure pump is maintained for 12 hours starting 4 hours after tea and a slice of toast, the patient being in a side ward or screened bed away from the sight and smell of food and with a sedative to ensure sleep. A sample is then titrated and the milli equivalents of acid estimated. This 12-hour secretion represents the acid output of a resting stomach.

For many years fractional test meals have been used and while they give a picture of the rise and fall of acidity and demonstrate definite differences between ulcer and normal patients, nevertheless in practice they are of little value in assessing the degree of acid production in an individual.

Histamine stimulation of secretion is more informative. Histamine is a specific stimulant of the gastric cells and there is evidence to support the view that it is identical with the hormone secreted by the stomach, if not the hormone itself. Unfortunately the size of the dose usually used, 0·5-1 mg., is not sufficient to produce more than a sudden sharp rise of acid secretion. Recently Kay[17] has shown that the side-effects produced by larger doses can all be overcome by an antihistaminic such as anthisan, which does not, however, affect the action of acid stimulation. This remarkable feature has no adequate explanation. Using this technique a true achlorhydria is only found in cases of pernicious anaemia.

It can be shown in experimental animals that repeated doses of histamine will produce a steady increase in acid output until the curve flattens out and the stomach is no longer able to produce more (Fig. 3). This supports Card's concept that the stomach can be stimulated to a maximum

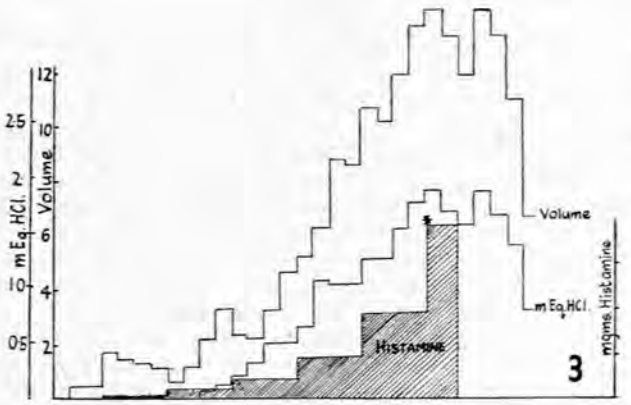


Fig. 3. Experiment showing the maximal output of acid by repeated and increasing doses of histamine (Heidenhain pouch).* The maximal acid output in this experiment was produced by 1·6 mg. of histamine.

capacity, and the rate and amount of secretion obtained is an index of the total number of parietal cells of the stomach.[16] Such tests on patients, using large doses in proportion to the patient's weight (0·04 mg./kg.) give an indication of the maximal total response of the stomach over three 20-minute periods and measured in mg. HCl or mEq represents the output of this 'parietal cell mass'.

The amount of acid secreted in 12 hours has been found, in a series of normal Indian and African patients, to be within a range of 5-20 mEq/L. This is in conformity with other workers' normal range with an upper limit of 20 mEq/L. Dragstedt[7] states that the average duodenal ulcer patient secretes 60 mEq/L, but analysis of a series of patients (to be published) shows that the range is wide, varying from just above the normal limit of 20 mEq/L to 100 or more mEq/L. It is reasonable to assume that a patient secreting 90 mEq/L in 12 hours, with a high level of secretion produced by maximal histamine stimulation and indicating a large total parietal cell mass, presents a different problem from one with 25 mEq/L output in 12 hours and a considerably smaller parietal cell mass that nevertheless responds to excessive stimuli by ulcer formation. An arbitrary dividing line at 60 mEq/L has been chosen between moderately high acid secretors and very high acid secretors. Such a distinction is felt to be of value in choosing an appropriate surgical procedure as indicated below.

SURGICAL APPROACH TO REDUCTION OF ACID

There are 4 approaches to the surgery of duodenal ulcer:

1. By-passing the ulcer by a gastro-enterostomy.
2. Wide surgical removal of acid secreting tissue by partial or subtotal gastrectomy.
3. Removal of the cephalic phase of secretion by vagotomy, together with drainage by gastro-enterostomy or pyloroplasty to obviate the mechanical side-effects.
4. Removal of the hormonal and cephalic phases of gastric secretion by antrectomy and vagotomy.

The removal of the acid secreting tissue is still the most widely used procedure. However, it is becoming increasingly apparent both experimentally and clinically that the effect produced by such a sledge-hammer approach, while usually meeting with 80-90% success, can in a majority of cases be at least rivalled by less radical procedures which attack the focal points of the pathological process of duodenal ulcer and with fewer resultant post-operative disabilities.

1. *Gastro-enterostomy*

Gastro-enterostomy was first performed in 1881 by Wolfler, using an anterior-long-loop antiperistaltic gastro-jejunostomy. This operation was modified by the use of a posterior loop and Petersen finally devised the posterior-no-loop procedure which Moynihan and Mayo advocated. Today there is generally a compromise between this and the original long-loop operation.

From 1900 to 1935 this procedure was the one of choice for duodenal ulcer. The operation apparently has little physiological basis and there is little if any reduction in acid output. In fact, experimentally it has been shown that there may under certain conditions be a rise in acid output.[46] In the 1920s, despite the continued popularity of the procedure amongst British and American surgeons, Finsterer and Eiselsberg in Europe had abandoned it in favour of partial

gastrectomy. By 1928 these surgeons were achieving mortality rates of under 3%.

There is little dispute that gastro-enterostomy will be followed by healing of almost every duodenal ulcer. The operation has however slowly fallen into disrepute as more and more evidence has accumulated that the rate of secondary ulceration is high. Sherren,[20] in the 1930s, is widely quoted as saying that non-recurrence after 2 years indicated a permanent cure. But the nature of this disease is such that recurrence in many cases only occurs after 2 or 3 years. The lack of a standard follow-up period is an unsatisfactory feature of most reports; these should be approached in the same way as malignancy reports by using definitive 5 or 10 year periods. It is the range in time of appearance of recurrence that explains some of the widely varying opinions of this operation.[23-29]

Patterson[21] in 1910 commented: 'The fear of recurrence casts a faint shadow over the otherwise admirable results of the operation' and he quoted a 2% recurrence rate. Bland-Sutton[22] was among the first in 1916 to indicate his objection by stating: 'With an unobstructed pylorus gastro-enterostomy cannot be relied on to cure the chronic duodenal ulcer and as it exposes it to regurgitant vomiting and jejunal ulcer I have gradually abandoned it as a routine method'. Yet Moynihan in his 12-year study gave his recurrence rate as 1·8%. The results of these surgeons in the early years of this century indicate how effective and flattering the immediate results sometimes are[25, 28] (Table I). But few patients in these years were consistently re-examined by X-ray and many of the post-operative symptoms, such as bleeding and dyspepsia, arouse the suspicion that some of these clinical syndromes were in fact recurrences.

TABLE I. RECURRENT ULCER FOLLOWING GASTROJEJUNOSTOMY

Author	*Year*	*No. of cases*	*Follow-up (years)*	*Recurrent Ulcers*		
				% Proven ulcers	*% Clinical ulcers*	*Total*
Lewisohn	1925	136	5—9	34	20	54
Luff	1929	744	6	2·8	6	8·8
Walton	1934	893	—	3·2	—	3·2
Wright	1935	17—30	5	4	4	8
Ogilvie	1935	—	—	20	—	15—20
Priestley	1948	—	—	—	—	15
Lahey	1945	—	—	—	—	15—20

TABLE II. TIME OF RECURRENCE OF ULCER SYMPTOMS AFTER OPERATION

Author	*Year*	*No. of cases*	*Symptom-free Interval (years)*	*Interval from 1st to 2nd operation (years)*	*Original operation*
Edwards *et al.*	1956	18	5·2	8	Gastro-enterostomy
			2·2	3·9	Gastric resection
Walters *et al.*	1955	301		11·2	Gastro-enterostomy
				3·7	Gastric resection
Everson *et al.*	1955	48	2	2	Gastro-enterostomy
			1	1	Gastric resection
Priestley *et al.*	1948	244	3·7	66% 10 yrs. later.	Gastro-enterostomy
			1·7	70% less than 5 yrs.	Gastric resection
Thompson	1956	63		60% 10 yrs. later.	Gastro-enterostomy
				66% in 5 yrs.	Gastric resection

A most interesting feature of these and other series, followed up over many years, is the comparison between the symptom-free interval following gastrojejunostomy and that following gastrectomy.[28, 30, 66-68] This symptom-free period is twice as long after the former operation and consequently the time of the second operation is delayed (Table II) for twice as long. Luff[24] in 1929 showed that of recurrent ulcers following gastrojejunostomy 68% delayed their appearance until a period of between 2 and 6 years had elapsed.

It will be seen that the rate of proven secondary ulceration ranges between 3-34% over large series of cases, many of which were followed up for 5 or more years. Priestley and Gibson,[28] reviewing the literature in 1948, state that the average incidence reported is 15%. Luff found a still higher recurrence rate following anterior gastrojejunostomy, the figure approaching 28% when an entero-anastomosis was added. Ogilvie's cynical view that the operation produces a patient 'who may be happy but is not safe' is a not unfair reflection.[27]

More recent results with a longer follow-up show clearly the trend towards late recurrence after gastrojejunostomy. Of a series of cases of proven gastrojejunal ulceration, the majority follow this operation. Marshall[31] found 77% of 172 cases followed gastrojejunostomy and 23% followed gastric resection. These figures, however, probably represent the end-result of many more gastrojejunostomies done in former years. The site of secondary ulceration is usually at the stoma or in the efferent jejunal loop (Thompson).[68]

2. *Gastric Resection*

Billroth laid the foundations for this type of operation. Other early surgeons concerned with this pioneer work were Rydygier in Poland (1881) and Braun (1892) who introduced afferent and efferent loop anastomosis. Kappeler in 1898 described a suspension method whereby the afferent limb is fixed above the stoma and the efferent limb into which the stomach empties—the forerunner of the Hofmeister valve.

The Billroth I operation was originally used for carcinoma and the anastomosis may be either end to end, with duodenum to greater curvature (Billroth-Finochietto), or with duodenum to lesser curvature (Horsley), or side of jejunum to stomach (von Haberer-Finnery).

Moloney[41] and Kanar *et al.*[38] recommend the Billroth I procedure for the following reasons: The operation is usually easier technically and the danger of leakage from a duodenal stump is removed. On the basis of the work showing that duodenal mucosa is more resistant to acid secretions than the jejunal mucosa, it is reasonable to assume that gastro-duodenal anastomosis is preferable to a gastrojejunal one. The nutritional state of the patients after the Billroth I procedure is considerably better, weight loss being present in only 10% as opposed to nearly 50% in Billroth II patients. The Billroth I operation presents fewer post-cibal symptoms and these tend to wear off with the passage of time. Serious nutritional deficiency following a Billroth II operation has been dealt with by a subsequent operation restoring gastro-duodenal continuity; Perman, quoted by Kanar,[38] reported 57 such successful conversions and Capper[34] states that 51 such operations from collected British sources were successful out of 60 cases.

Most authors agree that where less than 70% of stomach

is removed in duodenal ulceration there is a recurrence rate of nearly 10% (plus a 4% suspected recurrence) (Table III). With adequate high resection between 4 and 8%

TABLE III. RESULTS FOLLOWING BILLROTH I GASTRECTOMY

Author	Year	No. of cases	Follow-up (years)	% Mortality	% Recurrence
Horsley	1956	110	0–29	11	6
Walters *et al.*	1956	32	6–15	1·2	9
Capper *et al.*	1954	1000+			8·2 ≤70% resection 0·9 ≥70% resection
Goligher	1956	80	3–4	4	13·7
Wallensten	1954	159	4–20		7·5
Ordahl *et al.*	1955	35	3+		28·6
Kanar *et al.*	1956	248	1–8	3·1	3·5
Moore	1953	104	1–4	3·8	0
Harkins *et al.*	1954	266	1–6	2·6	1·3

develop stomal ulceration, a rate higher than that following the Billroth II operation.[32-40] This figure might still be the result of removing less than is excised in a Billroth II operation because of technical difficulty in bringing the cut end of the stomach to the duodenum.

The reduction of acid is said to approach anacid levels when 75% of the stomach is removed. Walters,[33] in 2 separate analyses, showed that approximately 40% of Billroth I patients developed achlorhydria, while 72-81% of Billroth II patients achieved this.

On the other hand, experimental work indicates that the Billroth I anastomosis is less likely to be followed by stomal ulceration than Billroth II operation. Kanar *et al.*,[38] in a series of experiments using hypersecreting gastric pouches after the method of Dragstedt, showed that there was a greater rise of acid secretion with the Billroth II anastomosis and that a larger number of animals died from stomal ulceration following Billroth II procedure.

The *Billroth II operation* is probably the most commonly used procedure today. The technique has become fairly standardized and many surgeons use the Hofmeister valve (Table IV). Unless 70% of the stomach is removed in cases

TABLE IV. RESULTS FOLLOWING BILLROTH II GASTRECTOMY

Author	Year	No. of cases	Follow-up (years)	% Mortality	% Recurrence
Walters *et al.*	1957	729	5–10	1·7	3·7
Wallensten	1954	322	4–20		2·5
Goligher	1956	106	3+	4·5	1·0
Ordahl	1955	64	3+	0·5	6
Moloney	1954	49			2
Moore *et al.*	1953	135	1–4	7·4	2·5
Thompson	1954	399	2–16	4·7	4·5

of duodenal ucler, the recurrent ulcer rate rises prohibitively.[34] When this is done it is generally agreed that the recurrence rate is distinctly lower than that following a Billroth I.[35-37,40-42,68] There is little to choose in the mortality figures, which range between 2 and 6%. Satisfactory results are obtained in 85-90% of patients and the operation has in this respect stood the test of 25 years practice. There is however a higher rate of minor, and sometimes disabling, digestive symptoms following a high subtotal gastrectomy, and persistent inability to gain weight is frequent.

3. *Vagotomy and Gastro-enterostomy*

This approach was first widely used by Dragstedt when in 1944 he introduced vagotomy alone. This soon proved an inadequate procedure as the end-results showed a high percentage of recurrent ulcers and many patients had a prolonged unpleasant convalescence. It was soon appreciated

TABLE V. RESULTS FOLLOWING VAGOTOMY AND GASTROENTEROSTOMY

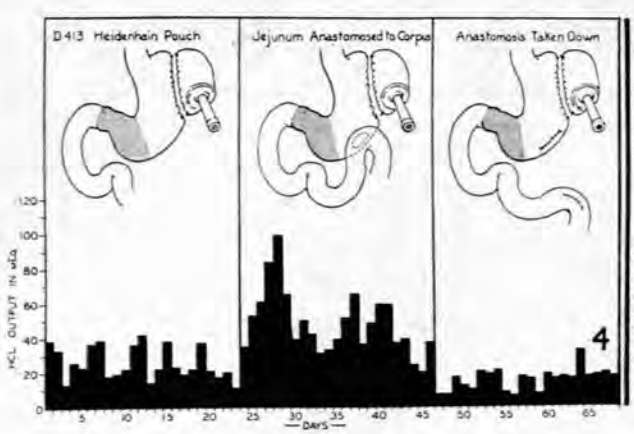
Author	Year	No. of cases	Follow-up (years)	% Mortality	% Recurrence	% Good results
Tanner	1951	116	1–3½	0	3·6	88
Jordan	1952	460		1·4	6·0	93
Hoerr *et al.*	1953	147	2–4	0·5	6·0	90
Johnson *et al.*	1954	324	1–8	2	0	
Holt *et al.*	1954	243	1–7	0·5	1	97
Henson *et al.*	1955	89	2–3	1	12·4	
Dragstedt	1955	487	2–10	1·2	5·8	82
McEvedy	1955	184	3–6	1·1	1	94
Lloyd-Davies	1956	366	5–7	1·5	5	92·4
Crile *et al.*	1956	600	5–9	0·3	4·5	
McKelvie	1957	298	1–9	2·7	2	90
Hindmarsh	1957	197	2–8	0·5	2	90
Everson *et al.*	1957	178	3–11	1·1	7·6	82

that drainage of the stomach by a gastro-enterostomy overcame the unpleasant immediate side-effects and considerably lowered the recurrence rate. Thus vagotomy and gastro-enterostomy have now been widely practised for some 10 years and it is possible to begin to give an estimate of the end-results over the past decade (Table V).[48, 54-65]

Initially the objection was raised that the gastro-enterostomy in itself cured many ulcers and that doing this together with a vagotomy would not provide a fair reflection of the efficacy of vagotomy alone. This argument is a specious one, for the end-results of the procedure in terms of the patient's benefit is the proper criterion.

The reasons for the failure of the operation of vagotomy alone can be duplicated experimentally. A marked and continued hypersecretion of acid occurs after vagotomy in animals in which a pyloric obstruction has been produced, indicating that the excess secretion is of humoral origin.[43] Similarly vagotomy produces an increase in acid secretion from a Heidenhain pouch suggesting that distension, resulting from the reduced stomach mobility, stimulates acid secretion. This rise in secretion is effectively abolished by gastro-jejunostomy drainage.[44]

There are 2 aspects of the operation essential in providing a satisfactory result. Firstly, the vagotomy must be complete. This, to a large extent, is dependent on the experience of the operator. While the variations in the anatomy of the vagus nerves have been adequately described, in the vast majority of cases an anterior and posterior trunk are present and the latter is the more elusive. Unless these 2 large trunks are found beyond doubt the completeness of the operation is in question. Twigs must be looked for around the full circumference of the oesophagus and they are, when present, big enough to be obvious. Burge[45] has recently described an electrical aid to ensure the completeness of the vagotomy; he stresses that many vagotomies reported in the past were incomplete and this aid is an additional safeguard if required. There is an undoubted correlation between the number of recurrent ulcers and the number of incomplete vagotomies. With increasing experience of the operator the recurrences in a large series diminish to a level of between 2 and 6%. In 10 of 14 recurrent ulcers in an early series of 158 cases where vagotomy alone was used, there was a positive post-operative insulin response indicating incomplete vagotomy.[48] However, it should be stressed that when a post-operative insulin test is obtained this is not always the result of inadequate division



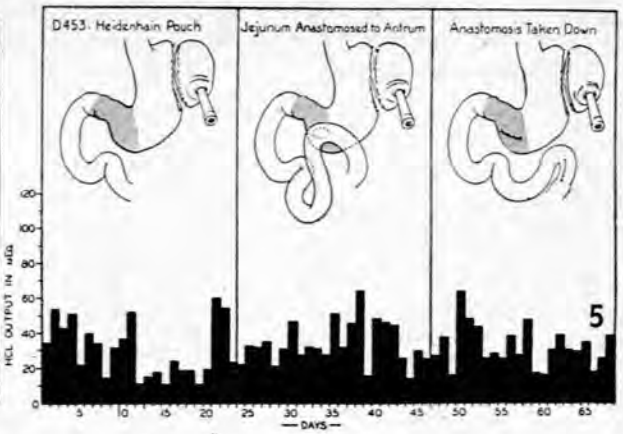


Fig. 4. The effect on acid secretion of gastrojejunostomy stoma in the fundus. *Fig.* 5. The effect on acid secretion of gastrojejunostomy stoma in the antrum.

of the vagus nerves. A positive response following oesophagectomy has been obtained where there has been no doubt about the complete anatomical removal of all vagal nerve supply. Presumably some parasympathetic fibres are still carried by sympathetic fibres to the stomach.

Secondly, the site of the stoma is of importance. It has been well demonstrated that the stoma placed in the fundus of the stomach produces an increase in acid secretion.[46] This work has been extended and confirmed (Figs. 4-6*); the stoma should be placed in the antrum as close to the pylorus as possible.

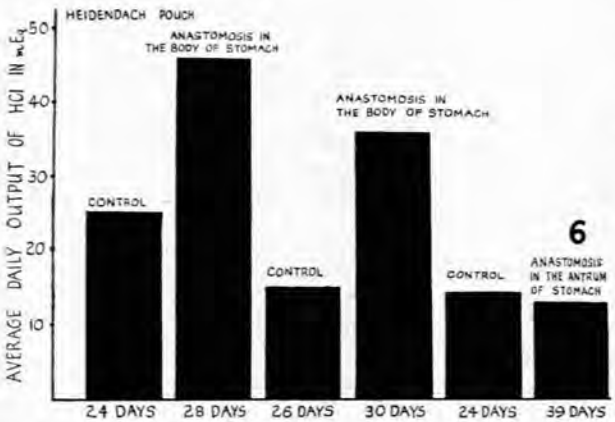


Fig. 6. The effect on acid secretion of varying the position of the stoma.

In 8 of 28 recurrent ulcers in a series of 487 cases, the stoma was found to be at the level of the mid-fundus, so allowing stasis in the antrum and producing hypersecretion.[48] It is of interest to note that in this later series the number of incomplete vagotomies fell to 11 in 400—3%.

Woodward[47] has recently shown that the size of the gastro-enterostomy stoma influences the level of acid secretion in dogs. When the size of the stoma was made larger than 4·5 cm. in diameter a threefold increase in acid secretion occurred, whereas small stomata produced no such increase.

Post-operative treatment following vagotomy and gastro-enterostomy is of importance, for there is always some degree of gastric paralysis. Gastric drainage by a Ryle's tube should be continued for at least 3-4 days and 12-hour gastric balances should be undertaken before finally dispensing with the tube. Perhaps the commonest post-operative complication of this operation is some degree of left basal congestion, and active breathing exercises and movement should be encouraged from the start.

A comparative series (Table V) shows that the operation of vagotomy and gastro-enterostomy takes its place as an effective surgical procedure in the treatment of duodenal ulcer. The mortality is under 1%, a significant reduction in comparison to any form of gastric resection. The recurrence rate is probably a little higher than large series of gastric resections indicate, but there are 3 further advantages which should be borne in mind: (*a*) The patient retains his stomach and therefore suffers less from dietary upsets, (*b*) weight loss is uncommon and considerably less than after any resection, (*c*) dumping and anaemia are seen less often.

A point of doubtful logic is frequently made—that one of the few indications for a vagotomy arises in cases of gastrojejunal ulcer. If, therefore, the surgeon is wedded to high gastrectomy as the operation of choice, the omission of such a relatively straightforward additional manoeuvre as vagotomy seems to be contrary to the patient's best interests.

4. *Vagotomy and Antrectomy*

The hormonal mechanism of the antrum has been adequately confirmed experimentally. The hypersecretion of acid in animals due to a high-lying gastro-enterostomy stoma, or from a Heidenhain pouch after vagotomy of the main stomach, is completely abolished by subsequent removal of the antrum.[43,46] Clinical confirmation of the importance of this source of acid stimulus is seen in the observation that failure to remove all antral tissue in a partial gastrectomy is followed by a high rate of recurrent stomal ulceration. The Finsterer-Devine exclusion operation, with its prohibitive recurrent ulcer rate, was a clinical experiment testifying to this.

Waddell,[49] in a clinical study on patients having a 2-stage gastric resection, has ably demonstrated the active role of the residual antral tissue. He showed that the response of the remaining stomach to all stimuli (histamine, insulin, broth) is still present, although reduced because the antrum is

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excluded from the main food stream. Removal of the remaining antrum almost completely abolishes response to any stimuli. Waddell postulates that the reason for the low acid production from the stomach remnant, after gastrectomy with vagal fibres intact, is the interruption of a reflex mechanism. This consists normally of afferent impulses sent from the antrum which maintain the tonic state of the vagal reflex centres; a constant stream of efferent cholinergic impulses to the parietal cells is then carried by the vagus nerves. Interruption of either limb of this reflex by antrectomy or vagotomy diminishes the effect of the remaining source of acid stimulus.

Removal of the vagal and antral source may be obtained either by vagotomy and antrectomy or by vagotomy and antral exclusion. Both these are logical procedures based on physiological principles. Furthermore, they both preserve the main body of the stomach and in consequence avoid the physiological disturbances of digestion seen after removing wide areas of the stomach. These sequelae (weight loss, dumping, anaemia and inability to eat normally) are much less commonly seen when vagotomy is combined with antrectomy, antral exclusion or gastro-enterostomy than after removal of 70% of the stomach.

Edwards *et al.*[50] have followed 294 patients over a period of 1-10 years after vagotomy and antrectomy with a Billroth I or II reconstruction. No recurrent ulcer among these patients has so far occurred. Crile[51] and Farmer and Smithwick[52] report results more satisfactory than with gastric resection alone and Harkins, quoted by Edwards, in 68 cases over 4 years has had no recurrent ulceration.

The reconstitution following the limited 30-40% resection of the distal stomach lends itself to a gastroduodenal anastomosis. The method used in this department over the past 2 years has been the Horsley modification of the Billroth I, where the duodenum is joined to the lesser curvature of the stomach.[53] There must be few, if any, cases in which limited resection by such a technique is not possible.

There is in the minds of many surgeons considerable uneasiness at leaving a duodenal ulcer *in situ*. Extensive experience by many operators has shown that leaving such ulcers behind in difficult gastrectomies has very rarely led to any ill effect. Such excluded ulcers heal rapidly; vagotomy and gastro-enterostomy, by definition, leaves the original ulcer behind and the recurrent ulcer that may occur is a stomal one, not a recrudescence of the original ulcer.

Nevertheless, removal of the ulcer represents a technical danger, and anxiety over the duodenal stump after difficult dissections is a constant reminder of this. To obviate this danger Waddell *et al.*[49] has described the operation of vagotomy and antral exclusion which fulfils the physiological desiderata and excludes the risk of duodenal dissection. The distal half of the antrum is cut across and closed, a third to a half distal gastrectomy performed, and reconstitution is made by a Polya-Hofmeister anastomosis.

This operation retains the technical advantages of vagotomy and gastro-enterostomy and early follow-up reports indicate that the acid reduction and response to stimulation are satisfactorily depressed.

There are 2 clinical and experimental observations that are theoretically in conflict with the principle of this operation. The Devine exclusion procedure has fallen into disuse because of the high recurrence rate. The Waddell procedure differs in the addition of vagotomy and it remains for a long-term follow-up to see whether the reduction of the cephalic phase, and its interference with the hormonal phase, will permanently overcome the presence of retained and potentially functioning antral tissue. Secondly, experimental evidence is conclusive that an acid environment in the antrum inhibits acid secretion while an alkaline environment does not (Fig. 2). In the antral exclusion operation the antrum is constantly exposed to alkaline secretions from both the duodenum and its own mucosa. Harrison *et al.*,[15] on the basis of their experimental work, postulate that the antrum in an acid medium acts by producing an acid inhibitor rather than by simply stopping gastrin release. Whether the antrum in a permanently alkaline medium is of physiological significance is not yet known clinically. Woodward,[69] however, has shown that such an operation in dogs prepared with a Heidenhain pouch produces persistent hyperfunction, probably on the basis of a reflux of food and alkaline juices into the excluded antrum without the inhibitory effect of acid.

SUMMARY

The aim of surgical treatment of duodenal ulcer is to reduce the hypersecretion of the acid-pepsin factor of gastric juice; no operation, short of total gastrectomy, produces complete abolition. Successful surgical results depend not only on this low level of acid-pepsin reduction but also on a greatly diminished response to nervous stimulation *via* the vagus nerves.

The best means of assessing the activity of the stomach is the measurement of free HCl output under resting conditions for a period of 12 hours and under maximum stimulation by large doses of histamine. Using mEq. as the unit of measurement, it is possible to grade the level of acid output into high and very high secretors. The upper limit of normal acid output is 20 mEq/L; a figure of 20-60 mEq/L has been arbitrarily taken for a high secretor and above 60 mEq/L for a very high secretor.

The experimental work on the physiology of gastric secretion is reviewed; these observations have clarified the role of the vagus nerves in maintaining the hypersecretion of acid and the hormonal mechanism of the antrum of the stomach.

The differing surgical approaches to treatment of duodenal ulcer are reviewed and comparative figures in a series of cases from many sources over a long period of time are quoted. The reasons for the long-term failure of gastro-enterostomy as a definitive operation are indicated.

Wide removal of acid-secreting tissue by a Billroth II operation is a very successful procedure; but it is too radical an approach to apply to all grades of severity of this disease. The Billroth I operation is in some hands equally successful; but most authors show a higher recurrence rate, despite the less frequent occurrence of digestive and nutritional disturbances.

The operation of vagotomy and gastro-enterostomy is an established and successful procedure with a mortality rate significantly lower than that of partial gastrectomy and with less disturbances of digestion and nutrition resulting from it. Two essential features of the operation—complete section of the vagus nerves and the optimum position of the stoma in the antrum—are emphasized. Neglect of either of these aspects considerably increases the risk of stomal ulceration.

Extensive information has been gathered in the last 10 years for comparison of the relative merits of the two Billroth

operations and vagotomy and gastro-enterostomy, each of which interrupts part of a complex neurophysiological mechanism of acid secretion. A more fruitful approach is the application of the physiological principles of gastric secretion. Where the aim of an operation is marked reduction of acid secretion in terms both of quantity and of response to nervous stimuli, then vagotomy is obligatory as an adjunct to any such surgical procedure.

The problem of *which* suitable surgical procedure to adopt may be re-stated in terms of a choice between a vagotomy with a high gastrectomy, vagotomy with a low gastric resection (antrectomy), vagotomy with gastro-enterostomy, or vagotomy with antral exclusion.

The surgical ideal is to remove the ulcer, interrupt completely the vagal nerve supply and remove the antrum, leaving the patient with an amount of stomach adequate in capacity and digestive function.

Vagotomy and antrectomy appear to represent the closest approximation to this ideal surgical procedure for the majority of patients with moderately high acid secretion. For a very high acid secretor a vagotomy and high partial gastrectomy is indicated, with a Billroth I reconstitution by preference, or a Billroth II anastomosis.

Where extensive and difficult duodenal dissection is necessary a vagotomy and gastro-enterostomy is indicated, but with a very high secretor the difficulties of duodenal dissection must be weighed against the probability of recurrent stomal ulcer.

A vagotomy and gastro-enterostomy is indicated for young patients, particularly women, for thin patients who have been unable to put on weight for many years, and for elderly patients from whom a high morbidity rate is expected after major surgery.

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