Anastomotic Ulceration

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ANASTOMOTIC ULCER PROVIDES THE CLINICIAN with an even greater therapeutic challenge than primary peptic ulcer. Not only has the original operation failed to cure the patient's ulcerative diathesis, but subsequent management has been complicated by alterations in the physiology and anatomy of the upper gastrointestinal tract. It is therefore hardly surprising that there is a high mortality and morbidity associated with this complication. Although anastomotic ulcers have been studied since the first quoted case of Braun[5] in 1891 there is still insufficient information to guide the clinician in his management of this complication.

In the period 1957–1968, 331 patients with anastomotic ulcer were admitted to the Vancouver General or Shaughnessy Veteran's Hospital. This includes patients treated medically as well as surgically and enables a comparison to be made of the results of treatment after conservative as well as surgical therapy. The primary operation for peptic ulcer was carried out in the two hospitals in 44%. In all but 11% of the total series, the original case records were available. This information was supplemented over the years by more detailed case studies at the Gastrointestinal Clinic of the University of British Columbia. We do not know the size of the original "pool" of primary peptic ulcer patients.

Etiological Factors

We found certain factors important in the development of recurrent ulcers. Patients with a recurrent ulcer often developed further recurrence following therapy. Most of the patients developed recurrent ulcers following operation for duodenal ulcer, but some developed recurrence following operation for other varieties of peptic ulcer. As a group, the patients with recurrent ulcer were drug abusers. Patients with anastomotic ulcer tended to belong to blood group "O". There was a relatively high incidence of women with recurrent ulcer compared to the incidence found in primary peptic ulcer. In post-gastrectomy anastomotic ulcer, only a few recurrences were attributable to retained antra. Post-Billroth I recurrent ulcer patients had a lesser gastric resection than post-Billroth II anastomotic ulcer patients.

Distribution

Fifty-one of the 331 patients developed recurrent ulcers after surgical treatment and six of these developed a third recurrent ulcer. One patient went on to have a fourth and fifth anastomotic ulcer after surgical treatment. There were therefore 390 anastomotic ulcers in 331 patients (Table 1).

The follow-up varied from one to 14 years, half being followed six years or more. Only 20% of 331 patients were regular clinic attenders, and the other patients were followed-up by questionnaire or interview in 1971. Of the 331 patients, 22% were untraced but many of these had been previously followed-up for several years, 16% of the 74 untraced patients having been followed for six years or more.

Site of the Primary Ulcer

This reflects the usual finding that the primary operation was for duodenal ulcer in the majority of cases, 88% in our study (Table 2).

Submitted for publication April 10, 1973.

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TABLE 1. *Distribution of Anastomotic Ulcers by Primary Operation*

Primary Operation	No. with one Anastomotic Ulcer	No. with Two Anastomotic Ulcers	No. with Three Anastomotic Ulcers	No. with Five Anastomotic Ulcers
Billroth I	48 (90.6)	5 (9.4)		
Billroth II	124 (88.6)	15 (10.7)	1 (0.7)	
Vagotomy and Pyloroplasty	30 (85.7)	4 (11.4)	1 (2.9)	
Vagotomy and Gastroenterostomy	6 (66.7)	3 (33.3)		
Vagotomy and Partial Gastrectomy	14 (93.3)	1 (6.7)		
Gastroenterostomy	58 (73.4)	17 (21.5)	3 (3.8)	1 (1.3)
Total	280 (84.6)	45 (13.6)	5 (1.5)	1 (0.3)

Figures in parentheses are percentages

Results of Primary Operation

The immediate post-operative results of surgery for primary peptic ulcer disease were satisfactory in all but 19% of operations (Table 3). The early results of gastric surgery therefore gave no prediction of the eventual outcome in terms of ulcer recurrence. The excellent immediate results of simple gastroenterostomy (79%) are of particular interest.

Drug Habits

The incidence of tobacco smoking, and ingestion of aspirin products, alcohol and coffee and tea were studied in the anastomotic ulcer patients. Of the 331 patients 28% smoked more than one package of cigarettes per day. More than five cups of tea or coffee per day were drunk by 11% of the patients. Aspirin products were ingested every day for weeks at a time by 15% of patients, 11% took aspirin products more than once a week, and the rest avoided aspirin products or took them rarely. More than eight fluid ounces of spirits or the equivalent amount of alcohol per day was drunk by 19%, 14% were regular drinkers and the rest avoided alcohol or drank it rarely

These results are startlingly different from a similar survey by Small[21] in 1964, who found no aspirin ingestion in his series of 83 patients with jejunal ulcer, but a higher proportion of tobacco smoking than in our series.

Blood Group

The blood group was recorded in 324 of the 331 patients with anastomotic ulcer: 55% belonged to Blood Group O. In a study of blood groups of more than 15,000 donors at randomly selected clinics in the greater Vancouver area, the frequency of Blood Group O was found to be 44%. The increased frequency of Blood Group O in anastomotic ulcer has been noted in the past but the reason for this finding is still unclear.

TABLE 2. *Site of Ulcers at Primary Operations*

Primary Operation	One Duodenal	Two Duodenal	Duodenal & Gastric	Duodenal & Pyloric	Pyloric	Pyloric & Gastric	Gastric	Not Known
Billroth I	32 (60.4)		2 (3.8)		11 (20.7)		7 (13.2)	1 (1.9)
Billroth II	117 (83.6)	3 (2.1)	7 (5.0)	2 (1.4)	3 (2.1)		7 (5.0)	1 (0.7)
Vagotomy and Pyloroplasty	28 (80.0)	1 (2.9)	1 (2.9)		3 (8.6)	2		
Vagotomy and Gastroenterostomy	8 (88.9)				1 (11.1)			
Vagotomy and Partial Gastrectomy	13 (86.7)		1 (6.7)				1 (6.7)	
Gastroenterostomy	75 (94.9)				3 (3.8)			1 (1.3)
Total	273 (82.5)	4 (1.2)	11 (3.3)	2 (0.6)	21 (6.3)	2 (0.6)	15 (4.5)	3 (0.9)

Figures in parentheses are percentages

TABLE 3. *Visick Grading after Primary Operation. (In this, and the Tables Following, Grade I, II and IIIS are Considered Satisfactory Results. Grades IIIU and IV are Unsatisfactory)*

Primary Operation	Not Known	I	II	IIIS	IIIU	IV
Billroth I	1	20	15	3	1	13
	(1.9)	(37.7)	(28.3)	(5.7)	(1.9)	(24.5)
Billroth II		40	63	9	7	21
		(28.6)	(45.0)	(6.4)	(5.0)	(15.0)
Vagotomy and		5	3	1		
Gastroenterostomy		(55.6)	(33.3)	(11.1)		
Vagotomy and Pyloroplasty	1	16	10	2	2	4
	(2.9)	(45.7)	(28.6)	(5.7)	(5.7)	(11.4)
Vagotomy and Partial		1	3	2	6	3
Gastrectomy		(6.7)	(20.0)	(13.3)	(40.0)	(20.0)
Gastroenterostomy	1	62	7	2	1	6
	(1.3)	(78.5)	(8.9)	(2.5)	(1.3)	(7.6)
Total	3	144	101	19	17	47
	(0.9)	(43.5)	(30.5)	(5.7)	(5.1)	(14.2)

Figures in parentheses are percentages

Sex Incidence

In this study 21% of the patients were females. We have no means of ascertaining the size of the population from which these patients were drawn but there does seem to be a higher percentage of females than one could expect from the relative frequency of surgical intervention for primary peptic ulcer disease which is 15% for women in the Vancouver General Hospital. A possible explanation for this is that surgeons tend to be more conservative in the surgery of women both in terms of gastric resection and a tendency to carry out a Billroth I anastomosis rather than a Billroth II type.

Retained Antrum in the Duodenal Stump Following Partial Gastrectomy

The pathology reports from the original operation were available for most of the gastrectomy specimens. Many of the reports did not mention the presence or absence of duodenal mucosa in the excised specimen but it was possible to exclude antral tissue in the duodenum in 67% of Billroth II gastrectomies. Of the remaining 46 post Billroth II anastomotic ulcer patients, re-operation was carried out in 34 and the duodenal stump was examined in 31 of these, 16 of whom had a biopsy or excision done: six of these patients were found to have retained antra. Twelve patients were treated medically and we have no histologic evidence in 11 of these, but one autopsy showed no retained antrum in the duodenal stump. In the remaining patients we have no clinical evidence of retained antra but this has not been checked by histology or at operation. In summary, of the total 140 Billroth II gastrectomies retained antral tissue was present in the duodenal stump in six (4%) and there is good evidence that there was no retained antrum in the remaining 96%. This is a much lower incidence of retained antrum than that found by Boles[4] and his colleagues in 1960 who reported retained antra in 14 of 36 patients. This indicates improvement of surgical technique in this respect in the last 20 years due to awareness of this problem.

Of the six patients with retained antra, three had retained antra detected at their first anastomotic operation and three had the retained antra detected only after developing a second anastomotic ulcer. Table 4 summarizes the treatment of the patients in this group. One of the six patients has had an ulcer recurrence demonstrated at operation since removal of retained antrum.

Adequacy of Partial Gastrectomy

The adequacy of gastrectomy in terms of percentage of stomach resected must always be a compromise between prevention of anastomotic ulcer and the increased incidence of malnutrition, malabsorption and tuberculosis which follows a high gastrectomy. On the basis of the surgeon's estimate of percentage of stomach resected, 76% had a resection of 66% or more and only 3% had a resection of less than 50% of the stomach (Table 5). It may be important, however, to note that resection for a Billroth I was significantly less than resection for a Billroth II. This was presumably due to the fear of the surgeon that insufficient gastric remnant would be available for anastomosis to the duodenum without tension. This may be one of the reasons why Billroth I gastrectomy is more liable to result in recurrent ulceration.

Clinical Characteristics

We must stress that the clinical characteristics are still the best single method of diagnosing anastomotic ulcer. We found that haemorrhage was a prominent symptom of most of the patients with anastomotic ulcer. The site of the ulcer was influenced by the type of antecedent operation. The age of development of anastomotic ulcer varied with the type of antecedent

TABLE 4. *Retained Antrum in the Duodenal Stump. Summary of the Clinical Course in the Six Patients with Retained Antra Following Billroth II Gastrectomy.*

Sex	Date of Birth	Antecedent Operations	Findings	Follow-up
M	1897	1964, 60% BIIA for D.U. of 13 years duration. Oct. 1965, 75% BIIA for massive haemorrhage, 3 ulcers present, (2 stomal and 1 gastric).	Nov. 1965, retained antrum and 60 ml. blood in stomach. No bleeding point found. Antrum excised and anastomosis revised as Roux-en-Y.	1966, haemorrhage. Jejunal ulcer at operation and vagotomy with 85% BIIA. 1971, Visick I on F.U.
M	1905	1962, 70% BIIR and vagotomy for D.U. of 1 year duration. 1963, prandial pain. 1963, efferent jejunal ulcer, 90% BII and Roux-en-Y. 1964, pain and vomiting.	1966, retained antrum and efferent jejunal ulcer. Antrum excised and 95% BIIR.	1971, Visick I on F.U.
M	1926	1957, 66% BIIR and Roux-en-Y for D.U. of 7 years duration. 1958, pain and haemorrhage.	1961, stomal ulcer and retained antrum. Antrum excised and vagotomy.	1971, Visick II on F.U.
F	1924	1956, 66% BIIR for D.U. of 17 years duration. 1958, prandial pain.	1961, jejunal ulcer and retained antrum. Antrum excised and vagotomy.	1962, repeated episodes of bleeding oesophageal varices. On portogram pressure in portal vein was 340 mm Hg. Lost to follow-up.
F	1942	1962, 66% BIIA for D.U. of 12 years duration. 1965, pain and vomiting.	1968, distended afferent loop with jejunal ulcer on afferent side and retained antrum. Antrum excised and 75% BIIA.	1970, prandial pain and vomiting. 1971, Barium meal showed stomal ulcer crater.
M	1932	1968, V. and P. for D.U. of 1 year duration. 1968, prandial pain. 1969, 50% BIIA for perforated D.U. 1969, pain and haemorrhage.	1970, retained antrum—no ulcer found. Antrum excised and 66% BI with vagotomy	1971, Visick II on F.U.

operation as did the interval between antecedent operation and definitive treatment of recurrent ulcer.

Symptoms

The pattern of symptoms of anastomotic ulcer was similar to that of the primary operation. Post-prandial pain occurred in 74% of the patients, 24% had no pain and there was insufficient information concerning symptoms in 2%.

Twelve patients had diarrhoea and weight loss and seven of these were found to have gastro-jejuno-colic fistula. These symptoms of diarrhoea and weight loss were therefore considered to be highly suggestive of the diagnosis of gastro-jejuno-colic fistula. There were only 2% gastro-jejuno-colic fistulae in this study, indicative of the decreasing frequency of this dangerous complication in recent studies.

It is noteworthy that 56% of the 390 anastomotic ulcer patients had one or more episodes of haemorrhage. There was a perforation of an anastomotic ulcer in 5% and this is a standard observation. The incidence of stenosis was 9%.

Site of Anastomotic Ulcers

Table 6 shows the site of the 390 anastomotic ulcers. Clearly the site at which an anastomotic ulcer develops depends partly on the primary operation. The ulcers seen at operation were chronic in 91%, 7% were acute, and 2% were suture ulcers.

TABLE 5. *Percentage of Stomach Resected (Estimated) at the Primary Operation*

Antecedent Operation	Not Known	1/3 P. G.	1/2 P. G.	2/3 P. G.	3/4 P. G.	S. T.
Billroth I	1 (1.9)	1 (1.9)	28 (52.8)	18 (34.0)	5 (9.4)	
Billroth II		5 (3.6)	9 (6.4)	116 (82.9)	10 (7.1)	
Vagotomy and Partial Gastrectomy			6 (40.0)	7 (46.7)	1 (6.7)	1 (6.7)
Total	1 (0.5)	6 (3.0)	43 (20.5)	141 (67.5)	16 (8.0)	1 (0.5)

P. G.—Partial gastrectomy
S. T.—Subtotal gastrectomy
Figures in parentheses are percentages

TABLE 6. *Site of Anastomotic Ulcers*

Antecedent Operation (s)	Gastric	Stomal	Jejunal Efferent	Jejunal Afferent	Duodenal	Jejunal & Gastric	Jejunal & Duodenal	Not Known
Billroth I	11 (19.6)	20 (35.7)	0 (0)	0 (0)	15 (26.8)	0 (0)	0 (0)	10 (17.9)
Billroth II	14 (8.2)	36 (21.1)	74 (43.3)	1 (0.6)	0 (0)	3 (1.7)	0 (0)	43 (25.1)
Vagotomy and Pyloroplasty	7 (19.4)	0 (0)	0 (0)	0 (0)	18 (50.0)	0 (0)	0 (0)	11 (30.6)
Vagotomy and Gastroenterostomy	1 (9.1)	3 (27.3)	4 (36.4)	0 (0)	0 (0)	0 (0)	0 (0)	3 (27.3)
Vagotomy and Partial gastrectomy	6 (16.7)	8 (22.2)	10 (27.8)	0 (0)	2 (5.6)	0 (0)	0 (0)	10 (27.8)
Gastroenterstomy	17 (31.2)	10 (12.5)	32 (40.0)	0 (0)	6 (7.5)	0 (0)	3 (3.8)	12 (15.0)
Total	56 (14.4)	77 (19.7)	120 (31.1)	1 (0.3)	41 (10.5)	3 (0.7)	3 (0.7)	89 (22.8)

Figures in parentheses are percentages

Gastric ulcer was significantly commoner after gastroenterostomy alone than after Billroth II gastrectomy when numbers observed were compared to numbers expected by chance alone. A possible reason for this is that the area of the stomach at risk is larger in gastroenterostomy alone than after Billroth II gastrectomy. However, when the site of recurrence after Billroth I was compared to that after vagotomy with pyroroplasty there was no difference in the rate of gastric ulceration. Golligher[10] has noted increased frequency of development of gastric ulcer following the Billroth I procedure and considers this operation may predispose to the development of gastric ulceration. However, in our series, the vagotomy with pyloroplasty group has been followed for a much shorter time than the Billroth I group and the incidence of gastric ulcer after vagotomy and pyloroplasty procedures may rise as the results become available for long term follow-up. Another factor might be that the mean age following gastroenterostomy (61 ± 14) is higher than after the Billroth II operation (50 ± 11) and the mean age of the patients with a Billroth I procedure (52 ± 11) is not significantly higher than that of the vagotomy with pyloroplasty group (48 ± 13). It is known that gastric ulcers are more freqeunt in the elderly and this would explain our findings.

Age at Operation for First Anastomotic Ulcer

This was calculated only for those undergoing surgical treatment. The age of the patients with anastomotic ulceration following gastroenterostomy alone (61 ± 14) is greater on average than the patients with anastomotic ulceration following other procedures (54 ± 11). This reflects the changing fashion in surgical operations over the last 20 years and the decline in frequency of gastroenterostomy as a routine treatment of duodenal ulcer.

Interval Prior to Treatment of Anastomotic Ulcer

The interval between the primary operation of peptic ulcer and year of treatment of anastomotic ulcer varied markedly depending on the type of antecedent operation (Table 7). Although there is general agreement that after gastroenterostomy an anastomotic ulcer can occur many years after the initial treatment, it has been held that after gastrectomy an anastomotic ulcer tends to recur much earlier. Our study shows a long interval after gastrectomy does not convey immunity from subsequent anastomotic ulcer. We would suggest that this is due to the late results of gastrectomy now becoming available and predict that the present short intervals prior to the development of anastomotic ulcer following the vagotomy procedures will prove artifactual, and as long term studies become available more and more patients will be found to develop anastomotic ulcer at long intervals after these procedures.

Diagnostic Procedures

We define anastomotic ulcer as a benign peptic ulcer which develops after definitive gastric surgery. Two

TABLE 7. *Interval between Primary Operation and Operation for First Anastomotic Ulcer*

Antecedent Operation	No.	Interval—Mean & S.D. (In Years)	Range in years
Billroth I	53	5.40 ± 5.60	0–33
Billroth II	140	3.39 ± 3.04	0–24
Vagotomy and Pyloroplasty	35	1.48 ± 0.77	0–4
Vagotomy and Gastroenterostomy	9	3.56 ± 2.30	0–7
Vagotomy and Partial gastrectomy	15	2.78 ± 2.91	0–10
Gastroenterostomy	79	17.27 ± 11.18	0–40

hundred and forty-four of the 390 anastomotic ulcers in the series were visualized at operation or autopsy. An ulcer crater was detected on barium meal examination in a further 64 instances. An ulcer was seen on gastroscopy in 15, and in 67 remaining cases, the diagnosis was made on clinical grounds alone. Acid secretory tests, both maximal acid secretion and Hollander tests, were of value.

Barium Meal X-Ray

The diagnostic value of this test was low. In 331 barium meal examinations, 52% showed an ulcer crater. We consider the results indefinite in a further 19% since distortion or spasm were the only abnormalities demonstrated. No abnormality was demonstrated in the remaining 29%. These results agree with the findings of Walters and Chance[27] in 1955.

Gastroscopy

Gastroscopy proved disappointing in determining the presence of an anastomotic ulcer. Of 72 gastroscopies, an ulcer crater was seen in 37%. In a further 25%, spasm or irritability of the anastomosis or inflammation around the anastomosis was noted which would have given rise to suspicion of an ulcer beyond the range of the gastroscope. However, it must be noted that the gastroscopies performed in this series were carried out prior to the use of fiberoptic endoscopy in our department. It is probable therefore that with the use of the more modern instruments now available, the incidence of positive diagnosis will improve.

Maximal Acid Secretory Studies

The peak acid output in response to Histalog* or more recently Pentagastrin was measured in 142 of the anastomotic ulcers. We found that the peak acid output measurement in patients after partial gastrectomy with or without vagotomy, was of some value in discriminating between patients with anastomotic ulcer and controls. More than 95% of the control values (110 controls) were below 12 mEq. acid output in the peak post-stimulation hours and more than 40% of the anastomotic ulcers had acid secretory results above this value.

Hollander Test

This proved most valuable in the post-vagotomy with pyloroplasty group. Insulin testing was carried out in 22 of these patients, and the test was positive on Hollander's criteria in 21 of these, indicating an incomplete vagotomy. The solitary negative test occurred in a patient with a gastric anastomotic ulcer, but was not repeated prior to reoperation.

* Eli Lilly and Co.

Serum Gastrin

Serum gastrin estimations should now be available for every patient with anastomotic ulcer, using either radio-immune assay[14] or, if not available, bioassay.[6,25] This would serve the two-fold purpose of excluding the Zollinger-Ellison syndrome, and excluding the possibility of retained antra in the duodenal stump of post gastrectomy patients. Although we have been carrying out radio-immune assay and bioassay of gastrin for the last year, we do not yet have the serum gastrin levels for the patients in this study.

Therapy Employed

The effectiveness of treatment of anastomotic ulcer is usually judged by the mortality rate from the operation or treatment and the recurrent ulcer rate. In this study we have included deaths due to ulcer and deaths due to operation in each group. For medical treatment the mortality rate is deaths due to ulcer, and deaths from other causes are not included. Following surgical treatment, the deaths represent the operative mortality, and after the first month deaths from incidental causes are not included. The period of follow-up is critical to any assessment of the results. When our results were grouped into follow-up periods of five years or less and follow-up periods of six years or more there was a significantly higher recurrence rate in the group with longer follow-up. Of the 194 patients followed for five years or less, 18 had one recurrent ulcer (9%). Of the 137 patients followed six years or more, 27 had one recurrent ulcer and six had two or more recurrent ulcers (24%). In the further discussion of the results of treatment therefore, our results have been broken down into follow-up periods of greater than one year to permit comparison with the results of other studies, and six years or more to give the recurrence rate on long term follow-up.

Post-Gastrectomy Anastomotic Ulcer

These ulcers should be treated by transabdominal vagotomy. Seventy-one patients in our study were treated in this way with no operative deaths, seven proven recurrent ulcers and seven suspected recurrent ulcers (Tables 8–10). A further ten patients required some modification of the anastomosis in addition to vagotomy and of these patients there were no operative deaths. One had a recurrent ulcer and one had a suspected recurrent ulcer. A more proximal or higher gastrectomy was carried out in 78 patients, 40 of whom had a vagotomy in addition to the gastrectomy. Compared to vagotomy alone, there was no improvement in the recurrence rate which was 15 with recurrent ulcer, five with suspected recurrent ulcer, but there was a higher death rate. Six of the 71 patients died as a result of complications of the gastrectomy.

A study of the literature confirms our views on the treatment of this group of ulcers. The death rate following vagotomy alone as a treatment for post-partial gastrectomy anastomotic ulcers is less than 1%, while no other current treatment is below 5% (Table 11). The recurrence rate on short-term follow-up is less than 16% and on long-term follow-up less than 19% (Table 12). Only vagotomy with partial gastrectomy has a lower

TABLE 8. *Treatment of the Complete Series of Anastomotic Ulcers Followed from one to 14 Years*

Antecedent Operation	Treatment of Anastomotic Ulcer	Related Death	Unrelated Death	I	II	IIIS	IIIU	IV	Recurrent Ulcer	Lost	Total
					(Visick Grade)						
BI	Med Rx	1	1	4	1	0	4	1	0	4	16
	2nd op—BI	0	0	0	0	0	1	0	0	0	1
	—BII	2	2	2	2	2	0	1	4	3	18
	—Vag	0	0	3	4	2	0	0	0	2	11
	—V & PG	0	2	2	3	0	1	0	0	1	9
	—Other	0	0	0	0	0	0	0	1	0	1
	Total	3	5	11	10	4	6	2	5	10	56
BII	Med Rx	2	6	11	8	1	3	1	0	14	46
	2nd op—BI	0	0	0	0	0	0	0	1	0	1
	—BII	2	1	4	0	2	1	0	7	1	18
	—Vag	0	4	15	9	3	6	1	7	15	60
	—V & O	0	0	4	2	1	1	0	1	1	10
	—V & PG	2	1	14	3	1	1	0	3	6	31
	—Other	0	0	0	1	0	0	0	3	1	5
	Total	6	12	48	23	8	12	2	22	38	171
V & Pyl	Med Rx	0	1	5	3	2	0	0	0	2	13
	2nd op—BI	0	0	0	0	0	0	0	1	0	1
	—BII	0	1	4	3	0	1	0	3	1	13
	—Vag	0	0	2	1	0	0	0	1	1	5
	—V & O	0	0	0	0	0	0	0	0	0	0
	—V & PG	0	0	3	0	0	0	0	0	0	3
	—Other	0	0	0	0	0	0	0	0	1	1
	Total	0	2	14	7	2	1	0	5	5	36
V & G-E	Med Rx	0	3	0	0	0	0	0	0	0	3
	2nd op—BI	0	0	0	0	0	0	0	1	0	1
	—BII	0	1	3	0	0	0	0	1	0	5
	—V & PG	0	0	0	0	0	0	0	1	0	1
	—Other	0	0	0	0	0	0	0	0	1	1
	Total	0	4	3	0	0	0	0	3	1	11
V & PG	Med Rx	0	1	1	2	3	1	0	0	3	11
	2nd op—BII	0	1	2	1	1	0	0	3	1	9
	—Vag	0	1	2	1	2	0	0	0	1	7
	—V & O	0	0	1	0	0	0	0	0	0	1
	—V & PG	0	0	1	1	0	1	1	0	0	4
	—Other	0	0	4	0	0	0	0	0	0	4
	Total	0	3	11	5	6	2	1	3	5	36
G-E	Med Rx	7	6	0	0	1	1	0	0	4	19
	2nd op—BI	1	0	0	0	0	0	0	1	1	3
	—BII	2	10	6	1	1	0	0	17	8	45
	—Vag	0	0	0	0	1	0	0	2	0	3
	—V & O	0	0	2	2	1	0	0	0	0	5
	—V & PG	0	0	1	1	0	0	0	0	1	3
	—Other	1	0	0	0	0	0	0	1	0	2
	Total	11	16	9	4	4	1	0	21	14	80

Med Rx—Treated medically only
BI—Partial gastrectomy of the Billroth I type
BII—Partial gastrectomy of the Billroth II type
Vag—Vagotomy only
Vag & PG—Vagotomy combined with partial gastrectomy
O—Other operations (Non-definitive surgical procedures such as closure of perforation, undersewing of bleeding vessel, laparotomy, any excision or take-down of anastomosis)
Related deaths—Those occuring in the immediate postoperative period or, when following medical treatment, caused by complications of a persistent ulcer
Unrelated deaths—From causes unrelated to the ulcer or its surgical or medical treatment

recurrence rate than this and that is only on short-term follow-up.

Exceptionally, additional surgery may be required. Only six of our patients required excision of the retained antra in the duodenal stump and every effort should be made to exclude this condition pre-operatively rather than subject the patient to unnecessary exploration. Stenosis of the anastomosis is rare, but this may require treatment by excision and reconstitution of the anastomosis.

Post-Gastroenterostomy Anastomotic Ulcer

This group should be treated by two-thirds partial gastrectomy. Our results for all forms of treatment were unsatisfactory in this group of patients. Forty-eight patients were treated with two-thirds partial gastrectomy and three died. The cause of death in these three patients was, however, from embolism in two and pneumonia in the other, and we feel that this is more a reflection on the age and debility of the patients than on the choice of operation. The recurrence was high, with 18 patients having a proven recurrent ulcer and none suspected of recurrence. Only eight patients were treated by vagotomy, but five of these required some reconstruction of the anastomosis. There were no deaths but two patients developed recurrent ulcers (Table 8). Our views agree with those in the literature. The mortality rate for partial gastrectomy is the same as that following vagotomy for post-gastroenterostomy ulcers (Table 13). The rate of ulcer recurrence following partial gastrectomy is less than half that of vagotomy alone in that group (Table 13 and 14). Curiously, the addition of vagotomy to the gastrectomy in post-gastroenterostomy ulcers appears to result in an increased operative mortality in the literature, although we ourselves have had no deaths in this group in our study.

TABLE 9. *Late Results of Treatment of Anastomotic Ulcer, Including Only the Patients Followed for Six Years or More*

Antecedent Operation	Treatment of Anastomotic Ulcer	Related Death	Unrelated Death	I	II	IIIS	IIIU	IV	Recurrent Ulcer	Lost	Total
					(Visick Grade)						
BI	Med Rx	1	0	2	1	0	4	1	0	1	10
	2nd op—BI	0	0	0	0	0	1	0	0	0	1
	—BII	0	0	2	1	1	0	1	2	2	9
	—Vag	0	0	2	0	0	0	0	0	0	2
	—V & PG	0	0	0	1	0	0	0	0	0	1
	Total	1	0	6	3	1	5	2	2	3	23
BII	Med Rx	1	3	8	8	1	2	1	0	4	28
	2nd op—BI	0	0	0	0	0	0	0	1	0	1
	—BII	0	0	3	0	1	0	0	4	0	8
	—Vag	0	0	5	3	0	2	0	5	3	18
	—V & O	0	0	2	0	0	0	0	1	0	3
	—V & PG	1	1	6	1	1	1	0	3	0	14
	—Other	0	0	0	0	0	0	0	3	0	3
	Total	2	4	24	12	3	5	1	17	7	75
V & Pyl	Med Rx	0	0	1	1	0	0	0	0	0	2
	2nd op—BII	0	0	0	0	0	1	0	1	0	2
	Total	0	0	1	1	0	1	0	1	0	4
V & G-E	Med Rx	0	1	0	0	0	0	0	0	0	1
	2nd op—BI	0	0	0	0	0	0	0	1	0	1
	—BII	0	0	2	0	0	0	0	0	0	2
	Total	0	1	2	0	0	0	0	1	0	4
V & PG	Med Rx	0	1	0	1	2	1	0	0	0	5
	2nd op—BII	0	1	1	1	0	0	0	3	0	6
	—V & PG	0	0	0	0	0	1	0	0	0	1
	—Vag	0	0	1	1	0	0	0	0	0	2
	—Other	0	0	2	0	0	0	0	0	0	2
	Total	0	2	4	3	2	2	0	3	0	16
G-E	Med Rx	6	3	0	0	0	1	0	0	3	13
	2nd op—BI	0	0	0	0	0	0	0	1	0	1
	—BII	1	2	6	0	1	0	0	13	2	25
	—Vag	0	0	0	0	1	0	0	0	0	1
	—V & O	0	0	2	0	0	0	0	0	0	2
	—V & PG	0	0	0	0	0	0	0	0	1	1
	—Other	0	0	0	0	0	0	0	1	0	1
	Total	7	5	8	0	2	1	0	15	6	44

TABLE 10. *Deaths due to Operation or Ulcer*

A. Immediate Post-operative Deaths (10 Patients)

Age (Years)	Antecedent Operation (s)	Operation for Anastomotic ulcer	Cause of Death	Contributing Cause
71	BI	BII	Duodenal fistula	None
70	BI	BII	Anastomotic dehiscence	None
45	BI & BII	V & PG	Peritonitis	None
75	BII	BII	Cardiac arrest	Long operation
55	BII	V & PG	Anastomotic dehiscence	None
67	G-E	BI	Pneumonia	Emergency operation for haemorrhage
53	G-E	BII	Pulmonary embolus	None
70	G-E	Closure	Cardiac arrest	Perforated ulcer, 18 hours
69	G-E & BII	BII	Anastomotic dehiscence	Perforated ulcer
71	G-E	BII	Pulmonary embolus	None

B. Late Deaths (10 Patients)

Age (Years)	Antecedent Operation (s)	Treatment	Interval from antecedent Operation to death (years)	Cause of Death
49	BI	Medical	1	Haemorrhage
81	BII	Medical	4	Haemorrhage
75	G-E	Medical	10	Haemorrhage
79	G-E	Medical	37	G-J-C fistula
74	G-E	Medical	22	Haemorrhage
63	G-E	Medical	27	Haemorrhage
70	G-E	Medical	32	Haemorrhage
78	G-E & BII	Medical	3	Haemorrhage
72	G-E	Medical	20	Haemorrhage
76	G-E	Medical	29	Haemorrhage

The cause of death in those treated medically was haemorrhage, except for one patient with a gastro-jejunocolic (GJC) fistula.

Treatment of Post-Vagotomy and Drainage of Anastomotic Ulcers

We would suggest repeat transabdominal vagotomy alone for this group. This is probably the most difficult group to make a decision on as such small numbers are involved in our study and in other series. Five patients were treated with vagotomy in our study and there were no deaths and one recurrence on short-term follow-up. Of 20 patients treated with partial gastrectomy, there were no deaths but six patients developed recurrent ulcers on short-term follow-up.

Review of the literature confirms that vagotomy is the operation of choice. There was a mortality rate of one percent following vagotomy and the recurrence rate was approximately 26% on short-term follow-up (Table 15). Following partial gastrectomy, the death rate was 6% and the recurrence rate 24%.

Two-thirds of the deaths following gastrectomy were in the post-vagotomy and pyloroplasty group, although less than half of the patients had had a vagotomy and pyloroplasty. This would tend to indicate that gastrectomy is particularly dangerous as a treatment for post-vagotomy and pyloroplasty anastomotic ulcers. The mortality rate in the literature of gastrectomy for ulcer following vagotomy with pyloroplasty is 9% (six deaths in 63 procedures). This high death rate may be caused by the difficulty in closing the duodenal stump in patients who have a pyloroplasty and a recurrent ulcer. As most of the pyloroplasties in the literature were of the Heineke Mikulicz type, a Finney or Jaboulay pyloroplasty may have an even higher mortality when a gastrectomy is carried out as a second operation.

Experience of anastomotic ulcer following vagotomy and drainage is at the present time limited, but we would expect as found by Fawcett and his colleagues,[9] that the success rate of vagotomy would be much lower in this group of recurrent ulcers than when vagotomy was carried out for primary peptic ulcer. We feel it is wrong, however, to suggest gastrectomy as a routine procedure for ulcers following vagotomy and drainage because gastrectomy is attended by an increased mortality rate and also because there is no advantage to be shown for gastrectomy in terms of prevention of ulcer recurrence compared with vagotomy. In a patient in whom satisfactory closure of the duodenal stump could be assured, it would be logical to suggest vagotomy and gastrectomy, but if these conditions cannot be met our first choice would remain vagotomy alone. Jejunal, stomal, or gastric ulceration after gastroenterostomy with vagotomy may meet these conditions. The mortality rate in the literature is 4% (three deaths out of 77 patients) for gastrectomy for recurrent ulcer following vagotomy with gastroenterostomy, but it might be possible to reduce this mortality by selection of patients with easily closed duodenal stumps.

TABLE 11. *Summary of the Literature Regarding the Results of Treatment of Post Partial Gastrectomy Ulcer*

Operation	Result	Present Study	Literature	Total Per cent
More proximal Gastrectomy	Excellent	15 (30)	98 (143)	65.3
	Recurrent Ulcer	12 (30)	40 (143)	30.1
	Dead	4 (38)	10 (161)	7.0
Vagotomy alone	Excellent	40 (54)	215 (291)	73.9
	Recurrent Ulcer	7 (54)	47 (291)	15.7
	Dead	0 (71)	3 (301)	0.8
Vagotomy and Other	Excellent	7 (9)	1 (3)	—
	Recurrent Ulcer	1 (9)	0 (3)	—
	Dead	0 (10)	0 (3)	—
Vagotomy and Partial Gastrectomy	Excellent	26 (31)	66 (86)	78.6
	Recurrent Ulcer	3 (31)	11 (86)	12.0
	Dead	2 (40)	5 (94)	5.2
Other	Excellent	1 (5)	4 (14)	—
	Recurrent Ulcer	4 (5)	9 (14)	—
	Dead	0 (6)	3 (16)	—
Medical Treatment	Excellent	32 (41)	16 (36)	62.3
	Recurrent Ulcer	9 (41)	20 (36)	37.7
	Dead	3 (62)	2 (35)	5.2

Note: Lost patients are included in the operative mortality statistics, but excluded from all other statistics in this and subsequent tables. Patients who died of unrelated causes are included as excellent results if the treatment controlled their ulcer disease and if ulcer disease did not contribute to their deaths.

Follow-up period varied 0–16 years. [1–4,7,8,12,13,15–18,21,22,24,28–30]

Figures in parentheses are the number of patients in each group.

Post-Vagotomy and Partial Gastrectomy

We recommend repeat transabdominal vagotomy in this group. It is essential to screen patients with ulcer following vagotomy with gastrectomy for ulcer diathesis due to endocrine tumours or retained antrum in the duodenum. Although none of our patients had a non-beta cell tumour of the pancreas, nor a parathyroid tumour, two of our 36 patients had retained antra in the duodenal stump. In both patients excision of the antral tissue (with more proximal gastrectomy in one) cured the ulcers. It has been the experience of others too that this group of patients tends to have an appreciable incidence of high gastrin-secreting or parathormone-secreting conditions. Of 12 patients with ulceration after gastric resection and vagotomy, performed separately, Wychulis[30] found two patients with multiple endocrine adenomas. Of 14 patients with ulceration after gastric resection and vagotomy (ten were one stage and four were two stage procedures) Stuart[23] found two patients with the Zollinger-Ellison syndrome. Only 13 of 1600 patients with a one stage vagotomy and antrectomy procedure developed recurrent ulcers in Scott's[19] study, but three of the 13 had a Zollinger-Ellison syndrome. The Zollinger-Ellison syndrome requires a total gastrectomy to control the ulcer diathesis.

If an ulcer diathesis such as an endocrine adenoma or retained antrum can be excluded, it is our experience that the anastomotic ulcer following vagotomy with gastrectomy is a benign disease attended by no deaths and a low recurrence rate. Treatment by repeat vagotomy gave excellent results: there was no mortality, and six traced patients of the seven who had a vagotomy all had excellent results on follow-up. Study of the literature shows few reports of repeat vagotomy for this type of ulcer (Table 16) although Jaffe[11] had excellent results in the three patients who had vagotomy in his study.

Reresection gave worse results in our hands; three of the eight patients followed had ulcer recurrence. There are more reports available for this operation and these show a recurrence rate in line with our results.

Even medical treatment in 11 patients in our study gave reasonable results with only one of the eight patients

TABLE 12. *Results of Treatment of Post Partial Gastrectomy Ulcers in the Literature on Follow-up of Five Years or More*[1,3,13,18]

Operation	Result	Present Study	Literature	Total Per cent
More proximal Gastrectomy	Excellent	8 (17)	19 (27)	61.4
	Recurrent Ulcer	7 (17)	8 (27)	34.1
Vagotomy alone	Excellent	10 (17)	58 (71)	77.3
	Recurrent Ulcer	5 (17)	11 (71)	18.2
Vagotomy and Partial Gastrectomy	Excellent	10 (14)	—	—
	Recurrent Ulcer	3 (14)	—	—
Other	Excellent	0 (3)	0 (1)	—
	Recurrent Ulcer	3 (3)	1 (1)	—
Medical Treatment	Excellent	23 (31)	2 (9)	—
	Recurrent Ulcer	8 (31)	7 (9)	—

Figures in parentheses are the number of patients in each group.

followed having a suspected persistent ulcer. We do not, however, recommend medical treatment for the definitive treatment of this, or any other type of anastomotic ulcer at this time.

Repeat vagotomy with more proximal gastrectomy was carried out in four patients, and excellent results were found in two on follow-up, with unsatisfactory results in the other two, although there were no proven recurrences. We feel that more proximal gastrectomy adds little to revagotomy for this type of ulcer. If there is no ulcer diathesis, more proximal gastrectomy is probably unnecessary and adds additional risk for no proven gain. If there is an ulcer diathesis, then the operation is inadequate to control the disease.

Deaths

Sixty-two patients are known to have died. All the ten patients who died in the immediate post-operative period had an autopsy, and in many cases autopsy was carried out in those who died of incidental causes. Autopsy information on the cause of death and the presence or absence of stomal ulceration is available in 41 of the 62 patients. Forty patients died of incidental causes and are judged to have good results following their gastric surgery since no evidence of recurrence was noted clinically or at autopsy in these patients, and their gastric surgery was adequate to last them until the end of their natural life span.

TABLE 13. *Summary of the Literature Regarding the Results of Treatment of Post Simple Gastroenterostomy Ulcers*[1–4,7,8,11,13,15–18,21,22,24,28–30] *(Follow-up Period 0–16 Years)*

Operation	Result	Present Study	Literature	Total Per cent
Partial Gastrectomy	Excellent	18 (36)	543 (664)*	80.1
	Recurrent Ulcer	18 (36)	98 (664)	16.6
	Dead	3 (48)	18 (773)	2.7
Vagotomy alone	Excellent	1 (3)	51 (87)	57.8
	Recurrent Ulcer	2 (3)	34 (87)	40.0
	Dead	0 (3)	2 (85)	2.3
Vagotomy and Other	Excellent	5 (5)	0 (2)	—
	Recurrent Ulcer	0 (5)	2 (2)	—
	Dead	0 (5)	0 (2)	—
Vagotomy and Partial Gastrectomy	Excellent	2 (2)	25 (34)	75.0
	Recurrent Ulcer	0 (2)	4 (34)	11.1
	Dead	0 (3)	4 (38)	9.8
Other	Excellent	0 (1)	24 (102)	23.3
	Recurrent Ulcer	1 (1)	76 (102)	74.8
	Dead	1 (2)	14 (108)	13.6
Medical Treatment	Excellent	7 (15)	14 (81)	21.9
	Recurrent Ulcer	8 (15)	67 (81)	78.1
	Dead	7 (19)	11 (78)	18.6

* Three patients also had vagotomy.
Figures in parentheses are the number of patients in each group.

TABLE 14. *Summary ofthe Literature Regarding Results of Treatment of Post Gastroenterostomy Ulcers on Follow-up of Five Years or More*[1,13,13,18]

Operation	Result	Present Study	Literature	Total Per cent
Partial Gastrectomy	Excellent	9 (23)	184 (239)	73.6
	Recurrent Ulcer	14 (23)	55 (239)	26.4
Vagotomy alone	Excellent	1 (1)	10 (20)	—
	Recurrent Ulcer	0 (1)	10 (20)	—
Other	Excellent	0 (1)	14 (81)	17.1
	Recurrent Ulcer	1 (1)	67 (81)	82.9
Medical Treatment	Excellent	3 (10)	3 (36)	13.0
	Recurrent Ulcer	7 (10)	33 (36)	87.0

Figures in parentheses are the number of patients in each group

Post-operative Deaths

During the post-operative period seven patients died following a partial gastrectomy; two died following a partial gastrectomy with vagotomy and one died during closure of a neglected perforated jejunal ulcer. The cause of death following re-gastrectomy for a post-gastrectomy anastomotic ulcer differed from the cause of death following gastrectomy for a post-gastroenterostomy anastomotic ulcer. Of the six patients with post-gastrectomy ulcers, five died due to intra-abdominal sepsis and one died of cardiac arrest during a prolonged and difficult gastrectomy. On the other hand, the deaths in the three patients with post-gastroenterostomy ulcers were due to pulmonary embolus in two and pneumonia in one, the anastomosis being sound in all these patients. This would confirm the clinical impression that in stomal ulcer patients gastrectomy is much more difficult technically in a patient with a previous gastrectomy.

Late Deaths

All these ten patients were on medical treatment. We found that these patients had died of complications of anastomotic ulcer, six months to seven years after treat-

TABLE 15. *Summary of the Literature Regarding the Results of Treatment of Post Vagotomy with Drainage*[8,9,11,12,17,20–23,30] *(Follow-up Period 0–16 Years)*

Operation	Result	Present Study	Literature	Total Per cent
Partial Gastrectomy	Excellent	12 (19)	56 (82)	67.3
	Recurrent Ulcer	6 (19)	18 (82)	23.8
	Dead	0 (20)	9* (123)	6.3
Vagotomy alone	Excellent	3 (4)	44 (65)	68.1
	Recurrent Ulcer	1 (4)	17 (65)	26.1
	Dead	0 (15)	1 (88)	1.1
Vagotomy and Other	Excellent	—	1 (1)	—
	Recurrent Ulcer	—	0 (1)	—
	Dead	—	0 (4)	—
Vagotomy and Partial Gastrectomy	Excellent	3 (4)	2 (2)	—
	Recurrent Ulcer	1 (4)	0 (2)	—
	Dead	0 (4)	0 (2)	—
Other	Excellent	—	2 (2)	—
	Recurrent Ulcer	—	0 (2)	—
	Dead	0 (1)	0 (11)	—
Medical Treatment	Excellent	14 (14)†	3 (11)	—
	Recurrent Ulcer	0 (14)	8 (11)	—
	Dead	0 (14)	0 (11)	—

* Six of these deaths followed vagotomy with pyloroplasty ulcers. The mortality rate for gastrectomy was 9.5 per cent if a pyloroplasty was the drainage procedure, and 3.9 per cent if gastroenterostomy was the drainage operation.

† Three dead of related causes.

Figures in parentheses are the number of patients in each group.

ment of their anastomotic ulcer. In all of these a clear history of anastomotic ulcer symptoms was available, and medical treatment was employed with varying degrees of vigour. At the time of initial assessment, the clinicians chose medical treatment either because the clinical diagnosis was not supported by barium meal examination, or because of the advanced age of the patients.

In one further patient an unhealed anastomotic ulcer was found at autopsy, but this had not contributed to the patient's death of pulmonary edema at the age of 86 years.

Summary

Three hundred and thirty-one patients were treated for 390 episodes of anastomotic ulceration at two Vancouver hospitals. These patients were followed and the recurrence rate after varying treatment for their anastomotic ulceration was evaluated in terms of mortality and recurrence rate. The overall death rate from ulcer or its treatment was 6% of the 331 patients, and 15% had a further ulcer recurrence after surgical treatment. After surgical treatment of the second anastomotic ulcer, 12% of that group went on to develop a third ulcer. One patient developed a fourth and fifth anastomotic ulcer.

Barium meal was effective in diagnosing 51% of the 321 anastomotic ulcers in which this examination was carried out. Peak acid output studies were most useful in the post-gastrectomy with or without vagotomy groups: a level of over 12 mEq. was diagnostic of hypersecretion and was present in 40% of these anastomotic ulcers. Gastroscopy gave a positive result in only 33% of the 72 instances in which it was employed; this was in the pre-fiber-optic era.

TABLE 16. *Summary of the Literature Regarding Results of Treatment of Post Vagotomy with Gastrectomy Ulcers* [2,11,21–23,30] *(Follow-up Period 0–16 Years)*

Operation	Result	Present Study	Literature	Total
Partial Gastrectomy	Excellent	5 (8)	14 (26)	19 (34)
	Recurrent Ulcer	3 (8)	8 (26)	11 (34)
	Dead	0 (9)	1 (28)	1 (37)
Vagotomy alone	Excellent	6 (6)	3 (3)	9 (9)
	Recurrent Ulcer	0 (6)	0 (3)	0 (9)
	Dead	0 (7)	1 (4)	1 (11)
Vagotomy and Other	Excellent	1 (1)	—	1 (1)
	Recurrent Ulcer	0 (1)	—	0 (1)
	Dead	0 (1)	—	0 (1)
Vagotomy and Partial Gastrectomy	Excellent	2 (4)	1 (1)	3 (5)
	Recurrent Ulcer	0 (4)	0 (1)	0 (5)
	Dead	0 (4)	0 (2)	0 (6)
Other	Excellent	4 (4)	—	4 (4)
	Recurrent Ulcer	0 (4)	—	0 (4)
	Dead	0 (4)	1 (1)	1 (5)
Medical Treatment	Excellent	7 (8)	—	7 (8)
	Recurrent Ulcer	1 (8)	—	1 (8)
	Dead	0 (11)	—	0 (11)

Figures in parentheses are the number of patients in each group.

Of the patients with anastomotic ulcer, 74% had prandial pain and 56% had one or more episodes of haemorrhage. Perforation of an anastomotic ulcer was present in 5%, 9% had obstructive symptoms and 2% had gastro-jejuno-colic fistulae. We found no patients with secreting tumours of the pancreas or parathyroid. Of 140 Billroth II anastomotic ulcers, 6% had retained antrum in the duodenal stump.

After comparison of the mortality and recurrence rate of the various treatment options available in this and other studies, we conclude that vagotomy is the treatment of choice for post-gastrectomy anastomotic ulcer, for post-vagotomy and drainage anastomotic ulcer and for post-gastrectomy with vagotomy anastomotic ulcer. We also conclude that partial gastrectomy alone is the treatment of choice for post-gastroenterostomy anastomotic ulcer.

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