

Giant Gastric Ulcers *

ISIDORE COHN, JR., M.D., JACK SARTIN, M.D.

*From the Department of Surgery, Louisiana State University, School of Medicine,
New Orleans, Louisiana*

THE frequently expressed opinion that the larger a gastric ulcer, the more likely it is to be malignant has been disputed in recent years. As recently as 1953, there appeared in the literature⁹ the well entrenched diagrams comparing the size of an ulcer to its malignant potential, showing that of ulcers the size of a quarter (2.4 cm.) 25 per cent are malignant, of those the size of a half-dollar (3 cm.) 60 per cent are malignant, of those a dollar (3.7 cm.) 80 per cent are malignant, and of those over a dollar 100 per cent are malignant. Others^{20, 26} have indicated that the very large ulcers are exclusively benign.

Two experiences in a short period of time with large gastric ulcers that were found to be histologically benign (Fig. 1 and 2) have caused us to re-examine the total experience with giant gastric ulcers at a large general hospital. It was hoped that this would give some idea of the characteristics of, and the current incidence of malignancy in giant ulcers. Since there is no specific description in the literature for a giant gastric ulcer, a minimum diameter was arbitrarily chosen which would provide a suitable number of cases in the size range where previous reports have indicated cancer would predominate over benign disease.

With these thoughts in mind, a review was undertaken of all gastric ulcers seen at the Charity Hospital of Louisiana at

New Orleans from June 1950 to June 1956. Only those cases which included the pathologist's measurement of a gastric ulcer with a minimum diameter of 2.5 cm. were studied, and measured size was the only criterion for selection. Thirty-five cases found in the files for this six-year period form the basis for this study. Thirty-two were benign ulcers and three were malignant ulcers.

Interest in this study centered upon the differentiation of benign and malignant gastric ulcers, rather than upon a differentiation of gastric ulcers and obvious gastric carcinomas. The polypoid, fungating, or large invasive lesions which do not cause clinical confusion with benign ulcers have not been considered. This review deals exclusively with frank ulcers where the clinician, the radiologist, the gastroscopist, the surgeon, and even the pathologist would have some difficulty in distinguishing benign from malignant lesions.

History and Physical Findings

The age ranged from 24 to 80, as shown in Figure 3. Almost half of the entire group were between the ages of 50 and 69 but giant ulcers were found in both extremes of the usual age range for gastric ulcer disease. The ratio of 27 males to eight females emphasizes the usual sex incidence for gastric ulcers (Table 1). This is a surprisingly large group of females for such extensive gastric ulcer disease. Slightly more than half the group were white, which would tend to suggest the greater frequency of

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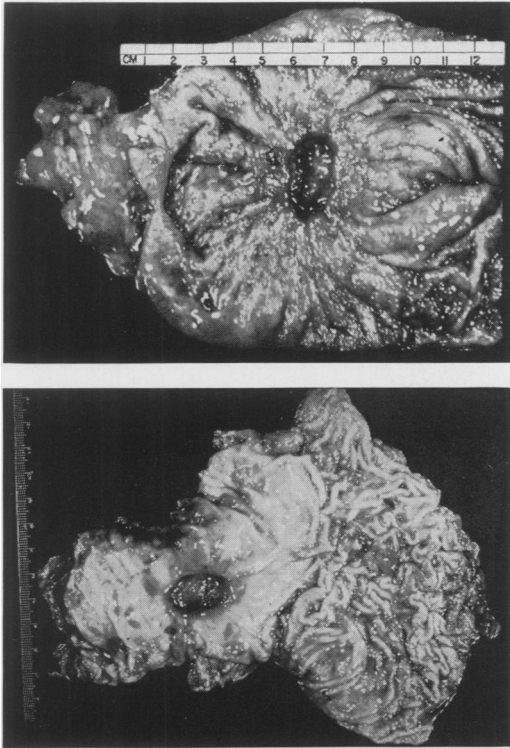


FIG. 1 (above), 2 (below). Resected specimens of two giant gastric ulcers which originally aroused interest in this subject. Both of these were benign lesions.

giant gastric ulcers in the white race since only 30 per cent of all hospital admissions during this period were white. Among the giant ulcer patients there were the same number of white and colored females and a similar but not identical distribution among the males.

The long duration of symptoms (Table 2) indicates the chronicity of the process in most patients. Almost half had symptoms for over one year, and eight had symptoms for ten to 34 years.

Epigastric pain, the most common chief complaint, was noted by 25 patients (Table 3). Vomiting and hematemesis were each the presenting complaint of five patients. Nausea, vomiting, melena, and hematemesis were each found in well over half the patients. In view of the size of the ulcer it was unexpected that 12 ob-

tained relief from milk. Perhaps even more significant was the presence of night pain in only five patients. Weight loss, noted by 13 patients, ranged from 10 to 50 pounds and averaged 24.6 pounds in the seven patients who mentioned a specific loss.

Previous treatment of gastro-intestinal disease, reported by 18 patients, included three patients with previous perforations, one of whom was readmitted with a second perforation, and ten with symptoms suggestive of obstruction due to cancer.

Physical findings were generally of no specific help, except in those admitted with either an acute perforation or massive bleeding. Epigastric tenderness was present in 16, liver enlargement in four, and dehydration in one.

An abdominal mass was palpated in three patients. The preoperative and operative diagnoses in each of these was carcinoma though each was found to have a benign giant gastric ulcer. One was a male with a 4.5 cm. ulcer adherent to the pancreas. The other two were women, each of whom had an intra-abdominal malignancy unassociated with their giant gastric ulcer.

Preoperative Study

Gastric analysis was performed on only 13 patients. Total acid ranged between six and 72 units, with a median value of 58 units. Free acid ranged from 0 to 52 units, with a median value of 20 units. Only one patient with a proven malignancy had a gastric analysis—the free and total values being 45 and 70 units.

Gastro-intestinal x-ray studies were obtained on 24 patients. Five patients did not have barium studies because of perforation, and six did not because of bleeding.

The confusion between the roentgenologic and the correct diagnoses can be seen from Figure 4. The over-all accuracy of radiologic diagnosis was 33 per cent. This low rate of accuracy is undoubtedly due in

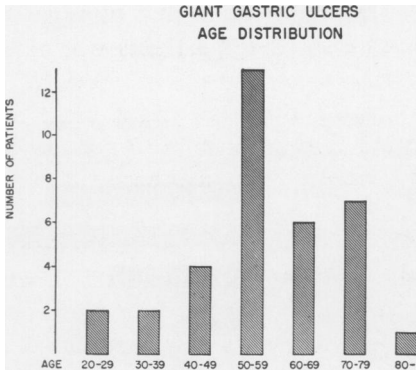


FIGURE 3

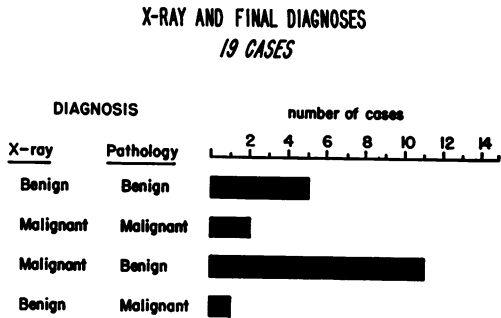


FIGURE 4

a large measure to the general impression that giant ulcers are malignant.

Since the radiologist would not be expected to miss lesions of this size, the five cases in which the ulcer was not reported have been reviewed. The properly diagnosed presence of a phytobezoar in one patient and a carcinoma in another patient probably attracted so much attention that the giant ulcers were missed. One 2.8 cm. lesion in the antrum was missed because an attempt at x-ray was "unsuccessful." X-ray reported no intrinsic pathology, but thought a metastasis from a known carcinoma of the cervix was present in one patient with a 3.0 cm. lesion on the greater curvature. The fifth lesion that was entirely missed was the 4.0 cm. ulcer in the fundus on the anterior surface of the lesser curvature. The location of this lesion probably accounts for its being missed.

Gastroscopy was accomplished in four patients. A correct diagnosis was reached in one with a 4.5 cm. ulcer, an incorrect

diagnosis was reached in one 3.5 cm. ulcer, and two ulcers—2.5 and 3.0 cm.—were not visualized.

Chest x-ray studies revealed no evidence of metastasis in the 28 patients who were specifically studied for this.

Medical therapy was tried in 13 patients. There was no improvement in 12 and slight improvement in one. Twelve patients did not have any trial of ulcer therapy because of perforation or bleeding and ten had no trial of medical therapy because a diagnosis of carcinoma was made.

Diagnosis and Therapy

The difficulty in arriving at a correct diagnosis in the 32 patients with histologically benign ulcers is obvious from a comparison of preoperative and operative diagnoses (Fig. 5). Similar confusion existed in the three patients with malignant ulcers. The over-all accuracy of diagnosis was 31.4 per cent at the time of operation. The poor diagnostic record of the surgeon,

TABLE 1. Giant Gastric Ulcers

	Male	Female	Total
White	16	4	20
Colored	11	4	15
Total	27	8	35

TABLE 2. Duration of Symptoms

1 month or less	6
1-6 months	7
6-12 months	5
1-5 years	7
Over 5 years	10

like that of the radiologist, can probably be traced to the commonly held belief that all giant ulcers are malignant.

Because of the confusion at operation, biopsy and frozen-section diagnosis was requested in several cases. Regional nodes were correctly diagnosed as benign disease in four patients with ulcers ranging from 2.5 to 7.0 cm. Three patients, including two of those with biopsies of regional nodes, also had biopsies of the ulcer, with the correct diagnosis of benign disease. However, the frozen-section diagnosis was benign for the lymphomatous lesion and for one adenocarcinoma, showing the danger of selecting a single location for frozen section of a gastric ulcer.

The operative procedures were dictated to a certain extent by the confusion surrounding the correct diagnoses in many of these cases, and therefore more radical procedures were done than was justified by the final diagnosis (Table 4). The surgeons' notes indicate a considerable uncertainty in a number of cases, and the performance of five radical subtotal gastric resections (included in the 25 subtotal resections), three that were considered palliative resections, one total gastrectomy, and the number of resections of other organs speaks for the clinical impression of an extensive malignancy at the time of operation. In the patients who did have a malignancy, a gastroenterostomy was done in one because of extensive disease, and two had subtotal resections for what were thought to be benign lesions. Thus the lack of correlation be-

TABLE 3. *Symptoms*

Nausea	31
Vomiting	31
Epigastric pain	30
Melena	21
Hematemesis	19
Weight loss	13
Milk relief	12
Massive G.I. bleeding	10
Night pain	6

PREOPERATIVE AND OPERATIVE DIAGNOSES 32 BENIGN LESIONS

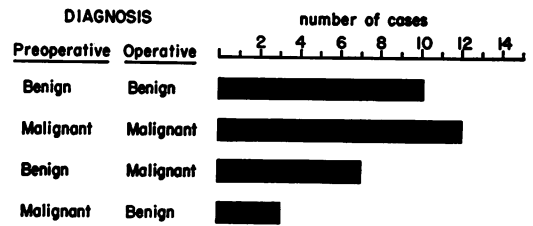


FIGURE 5

tween final diagnosis and operative findings is repeatedly underscored in the way the cases were handled.

Postoperative Course

In spite of the extensive procedures in patients with long-standing disease and altered nutritional state, there were 24 patients in whom no postoperative complications occurred. The complications occurring in the remaining patients varied from atelectasis and thrombophlebitis to the severe complications which led to the four deaths in the series.

The four deaths occurred in males admitted with a major complication of their disease—three with massive bleeding and one with a perforation. One 70-year-old male with cirrhosis continued to bleed following operation, and died on the third postoperative day with hepatic failure and aspiration pneumonia. The second death occurred in a 78-year-old male who eviscerated twice in the three weeks between the emergency gastrectomy and death, and at autopsy was found to have a generalized peritonitis from a breakdown of the gastrojejunostomy. The third patient with massive bleeding and subsequent death was a 59-year-old male who had a stormy postoperative course and died approximately four months after operation. Autopsy showed bronchopneumonia, subhepatic abscess, and thrombosis of the pancreatic ar-

LOCATION OF 35 GIANT GASTRIC ULCERS

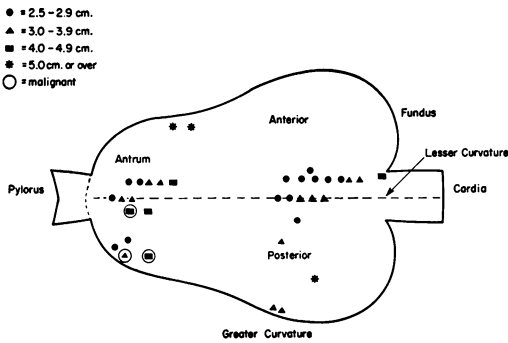


FIGURE 6

GASTRIC ULCER

SIZE OF ULCER IN RELATION TO MALIGNANCY

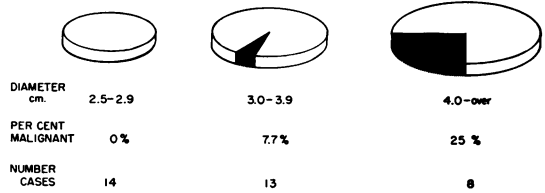


FIGURE 7

tery. The fourth death occurred on the first postoperative day following a severe transfusion reaction in a patient with a perforated ulcer.

Following discharge from the hospital, 19 of the 31 patients have remained asymptomatic, six have had mild dumping, two have had continued distress, one continued to lose weight, and three were lost to follow up. In view of the duration of symptoms prior to operation, these results speak for themselves.

Pathologic Study

The majority of the ulcers were located on or near the lesser curvature (Fig. 6). All of the malignant lesions were in the antrum, and two were on the greater curvature. The three largest lesions were on the anterior and posterior surfaces of the stomach. Only one lesion was in the fundus.

TABLE 4. Operative Procedures

Subtotal gastrectomy	25
Radical subtotal combined with:	
Splenectomy	4
Splenectomy, wedge resection liver	1
Splenectomy, pancreatectomy	1
Partial resection transverse colon	1
Total gastrectomy	1
Sleeve resection	1
Closure perforation	1
Gastroenterostomy	1

Location on or near the lesser curvature has been the common site in two other major series,^{5, 27} while the posterior surface of the stomach has been noted by several who have also noted the frequency of attachment to the pancreas.^{6, 20, 26}

The ulcers were adherent to adjacent viscera in 12 cases, most commonly to the pancreas (Table 5). The larger lesions were more frequently adherent to adjacent viscera than were the smaller lesions, six of the 12 adherent ulcers being found in the eight cases with ulcers 4.0 cm. or larger.

Two lesions were found in seven patients: an ulcer and a phytobezoar, a carcinoma and an unrelated ulcer, and five with multiple ulcers. The major ulcer varied in size from 2.5 cm. to 7 cm. and the secondary ulcers varied from 1 cm. to 6 cm.

Massive Bleeding

Six patients were operated upon primarily because of massive gastro-intestinal bleeding. Five were males. The ages ranged from 24—the youngest in the entire series—to 78, with an average age of 55. Vomiting or vomiting blood was the chief complaint of four and pain was the presenting complaint of the other two. Symptoms were recorded as being present from three weeks to four years, but it seems likely that this referred to the presence of abdominal

TABLE 5. *Attachment of Ulcer Base*

Pancreas	4
Liver	2
Pancreas, liver	1
Pancreas, spleen	1
Pancreas, transverse colon	1
Pancreas, liver, mesentery, transverse colon	1
Gastro-hepatic ligament	1
Transverse colon	1

pain rather than the current bleeding episode. Nausea, vomiting, and hematemesis were reported by all and melena had been noted by four. Weight loss was reported by two. Three had been seen previously for gastro-intestinal disturbances, one of whom had had a previous massive hemorrhage. Physical examination was not remarkable except for evidences of bleeding, and the presence of an enlarged liver in two. Four ulcers were less than 3.0 cm. in diameter, and one each was 3.0 and 4.0 cm. All were histologically benign. Four were in the body of the stomach, and two were in the antrum, but all were on the lesser curvature.

The greater severity of disease in these patients is shown by the fact that only one had an uneventful postoperative course. Two died during their hospitalization and one died on a subsequent admission after a prolonged and complicated postoperative course. One patient bled postoperatively, and also had atelectasis and jaundice. The sixth patient was still complaining of distress two years after surgery.

Perforation

Perforation was the immediate cause of surgery in six patients, all of whom had benign lesions. All were males, and they were evenly divided between white and colored patients. The age range was from 37 to 77, with an average of 55 years. Abdominal pain was the presenting complaint of five, and vomiting blood was the chief complaint of the sixth who had simultaneous massive bleeding and perforation. The total duration of symptoms was from

the day of admission to 15 years. Symptoms included vomiting and melena in all, and nausea and hematemesis in five each. One had perforated a year previously, one had bled two and one-half years before, and two had been treated for unspecified gastro-intestinal disease in the past. All had the usual physical findings associated with a perforated ulcer, and four had x-ray evidence of free air under the diaphragm. Four ulcers were on the lesser curvature, and two were on the anterior surface of the antrum. The marked preponderance of bleeding and perforating lesions on the lesser curvature is noteworthy.

Only one had a preoperative diagnosis of carcinoma in contrast to the operative diagnosis of perforated carcinoma in four, and a histologic diagnosis of benign disease in all. One had a closure of the perforation, but required re-exploration and subtotal gastrectomy to control postoperative bleeding, after which he made an uneventful recovery. The other five were treated with immediate subtotal gastrectomy. One died on the first postoperative day of a transfusion reaction and four had an uneventful recovery.

Carcinoma

Three patients had a malignant ulcer. All were white. One was a 29-year-old female with symptoms for one year, and two were 58- and 70-year-old males. The chief complaint of each was pain, but the five and one-half and 14 year duration of pain in the two males places them among those with the longest histories in the series. Nausea and vomiting were present in all, two noted weight loss, and one had perforated six months previously. Melena and night pain were each present in a single patient. Since response to therapy is often used as one indication of the type of ulcer present, it is of importance to note that two of the patients with cancer had relief from milk. X-ray study was suggestive of an an-

TABLE 6. Incidence of Cancer in Collected Series of Giant Gastric Ulcers

	Author	Size Range	Total Cases	Number Malignant	Per Cent Malignant
2.0-3.0 cm.	Denkewalter & Watman ⁸	2.0 cm. & over	40	17	42
	Boudreau, Harvey & Robbins ⁴	2.1 to 3.0 cm.	33	9	27
	Present Series	2.5 to 2.9 cm.	14	0	0
	Caruolo, Hallenbeck & Dockerty ⁶	2.6 to 3.0 cm.	9	2	22
	Total		96	28	29
2.5-5.0 cm.	Hayes ¹²	2.5 to 5.0 cm.	85	27	32
	Caruolo, Hallenbeck & Dockerty ⁶	3.0 to 3.5 cm.	3	0	0
	Present Series	3.0 to 3.9 cm.	13	1	8
	Boudreau, Harvey & Robbins ⁴	3.1 to 4.0 cm.	23	9	39
	Caruolo, Hallenbeck & Dockerty ⁶	3.6 to 4.0 cm.	8	0	0
	Total		132	37	28
2.5 cm. & over	Allen & Welch ¹	2.5 cm. & over	21	14	67
	Branwood ⁵	2.5 cm. & over	21	0	0
	Gott, Shapiro & Kelty ¹⁰	2.5 cm. & over	16	0	0
	Kirsh ¹⁴	2.5 cm. & over	33	9	27
	Marshall ^{21, 22}	2.5 cm. & over	108	32	30
	Paris & Theron ²⁴	2.5 cm. & over	13	0	0
	Grimes & Bell ¹¹	3.0 cm. & over	32	7	22
	Jennings & Richardson ¹³	3.0 cm. & over	11	1	9
	Ledoux-Lebard <i>et al.</i> ^{15, 16}	3.0 cm. & over	11	3	27
	Lumsden ¹⁷	3.0 cm. & over	11	4	36
	Petit-Dutaillis ²⁵	3.0 cm. & over	7	1	14
	Marshak, Yarnis & Friedman ²⁰	3.5 cm. & over	7	0	0
	Boudreau, Harvey & Robbins ⁴	4.0 cm. & over	53	33	62
	Present Series	4.0 cm. & over	8	2	25
	Caruolo, Hallenbeck & Dockerty ⁶	4.1 cm. & over	8	1	12
	Hayes ¹²	5.0 cm. & over	15	6	40
Shoulders & Lischer ²⁶	6.0 cm. & over	7	0	0	
Mathieu & Moutier ²³	12. cm. & over	3	0	0	
	Total		385	113	29
Grand Total			613	178	29

tral malignancy in one (correct), showed only pyloric obstruction in one, and made the correct diagnosis of a gastric lymphoma in the third. Frozen-section diagnosis was benign ulcer in the two patients so studied. In mid-1957, four years and three months after operation, the patient with the lymphoma had no evidence of recurrence. One of the patients with carcinoma died of widespread metastases three months after operation, and the other had evidence of dissemination when last seen in mid-1957, one and one-half years after operation.

Discussion

The theory that a large gastric ulcer is almost certain to be carcinomatous is not supported by these studies, for even the largest ulcers have only a 25 per cent incidence of malignancy in this series (Fig. 7). The finding that large gastric ulcers are more frequently benign than malignant is a significant deviation from the usually accepted reports. Accordingly, the literature was surveyed for articles that dealt with the diagnosis of gastric ulcers in relation to their size to determine if the small size

of this series had unduly weighted it in favor of benign disease.

From a review of the literature we have tabulated all reported series of gastric ulcers which met the following criteria: (1) minimum size of 2.0 cm., (2) histologic report available from either surgical or autopsy specimen, (3) the report include both benign and malignant disease unless case selection was made on the basis of size alone. Some authors, particularly the French, rely on response to therapy for final diagnosis, and in such articles only those cases with histologic proof of the diagnosis have been included.

The collected series have been classified into three major groups according to ulcer size (Table 6). Since different authors used varying dimensions for their own classification, there is some size overlap from one major group to another.*

The results of this survey confirm the results obtained in our own series. The tabulated series of 613 giant gastric ulcers shows an over-all incidence of malignancy of only 29 per cent. Since the collected series included cases from many parts of the world and cases collected from either surgical or autopsy files, or combinations of these, some explanation must be sought for the differences between these results and the figures so often repeated in the literature.

A careful review of the articles which are uniformly referred to whenever this subject is discussed reveals some of the problems which have led to the present confusion. The basic article by Alvarez and MacCarty² analyzed 638 gastric lesions. Other articles by MacCarty^{18, 19} and a later article by Comfort and Butsch⁷ provide a series of significant proportions on which the conclusions of these and subsequent authors

have been based. The basic difficulty with these papers is the failure to differentiate between malignant ulcers of the stomach and malignancy of the stomach in general. As one analyzes their reports it becomes obvious that they are distinguishing between benign ulcers and gastric cancers in general rather than between benign and malignant gastric ulcers. For this reason we have not included the figures from these papers in our collected series. There is no argument with their conclusion that the majority of all gastric lesions over 4.0 cm. in diameter are likely to be malignant, but we do disagree with their conclusions that all gastric *ulcers* over this size are likely to be malignant. More recent reports from the same institution^{6, 27} indicate that benign giant gastric ulcers are more commonly found there now. Thus changing times and differences in the basis for comparison explain the differences between the originally reported incidence of cancer in giant gastric ulcers and that reported here.

There is no characteristic picture which will serve to differentiate these lesions from other gastric lesions. A specific diagnosis cannot be made on the basis of age, sex, color, x-ray, gastroscopy, gastric analysis, location of the ulcer, or complications, since the same difficult differential diagnostic problems that exist with all gastric lesions are repeated here. The confusion in each means of diagnosis underlines the difficulty in making a correct diagnosis prior to histologic study of the specimen.

Most giant ulcers occur beyond the middle span of life. Indeed, the long history of most of these patients requires that they no longer be in the young age group. The preponderance of males is in agreement with the usual sex distribution of gastric ulcer disease.

The majority of the lesions were located along the lesser curvature. About half the ulcers were in the antrum and half in the body. This is in agreement with the loca-

* The largest ulcers cannot be determined from a chart such as used here, but ulcers have been reported which were the size of the palm of the hand,²⁵ 12 × 7 cm.,³ and 14 × 8 cm.²³

tion of gastric ulcers in general, and further complicates the diagnostic problems in these cases.

The frequency of massive bleeding and perforation indicates that giant ulcers are not immune to the usual complications of gastric ulcer disease.

The concept that giant gastric ulcers are most often benign presents the patient with an altered prognosis, and makes even more important an aggressive surgical attitude toward such a lesion. Delay in seeking surgical care is to be discouraged because of the poor response to medical management. Undue delay in exploration is no longer justified in a giant ulcer simply because of fear that an inoperable carcinoma will be found. On the contrary, all such patients should be subjected to exploration as soon as possible with the expectation that beneficial results may be obtained in a large percentage of these patients.

Summary

A review of all gastric ulcers observed at Charity Hospital during a six-year period revealed 35 cases with ulcers which had a minimum diameter of 2.5 cm. Thirty-two were benign ulcers.

Review of the literature disclosed 613 giant gastric ulcers, 71 per cent of which were benign.

There is no characteristic clinical picture for a giant gastric ulcer.

Clinical, x-ray, gastroscopic, and even operative diagnoses emphasize the difficulty in making a correct diagnosis prior to histologic section.

Giant gastric ulcers are subject to the same complications as gastric ulcers in general.

The response to surgical management suggests that early operation is the best therapy for such lesions.

Giant gastric ulcers are more often benign than malignant.

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DISCUSSION

DR. WALTMAN WALTERS: When Dr. Cohn wrote asking me to open the discussion of his and Dr. Sartin's paper, I thought the least I could do was review the papers by my colleagues to which they had referred in their text. Appended to this discussion, therefore, is the list of the papers which I have reviewed and on which I want to comment in order to emphasize some of the points made by Drs. Cohn and Sartin.

First of all, Drs. Cohn and Sartin studied 35 cases of gastric ulcer with a minimal diameter of 2.5 cm. and they found that the ulcers were benign in 32 and malignant in three. They comment that the high incidence of malignancy in "large" ulcerating gastric lesions reported by others is based on data which include all malignant gastric lesions which are 2.5 cm. or more in diameter.

The studies my colleagues have made at the Mayo Clinic indicate a need for defining the size of a "giant gastric ulcer," for among ulcers more than 4 cm. in diameter the possibility of an ulcer's being malignant is many times that of its being benign. Drs. Comfort, Priestly, Dockerty and co-workers,¹ in a study of 779 patients with benign and 226 with malignant gastric lesions removed surgically at the Mayo Clinic in the years 1940 through 1945, commented as follows: "It is seen that the frequency of benign gastric ulcer declines markedly when the diameter of a given gastric lesion exceeds 2 centimeters, and drops to a small percentage when the diameter exceed 4.0 centimeters." In a later paper Drs. Turner, Dockerty, Priestly and Comfort² considered in the category of "large gastric ulcers" only those with the diam-

eter of 4.0 centimeters or more, for which gastric resection had been performed at the Mayo Clinic. In the 15-year period from 1940 through 1954, 100 cases met the aforementioned requirements. Ulcer of this "large size" occurred in only 4.1% of all cases of benign gastric ulcer treated surgically during this time.

Drs. Cohn and Sartin have titled their paper "Giant Gastric Ulcers" to include ulcers more than 2.5 cm. and they studied 35 gastric ulcers in this category. If they were to confine their study, as Turner, Dockerty, Priestly and Comfort² did, to ulcers measuring more than 4 cm. in diameter, then a better comparison could be made. In the comparative study of the benign gastric ulcers and gastric carcinomas by my colleagues, only 2.1% of their 795 benign gastric ulcers were more than 4 cm. in diameter, whereas 75.5% of the 924 carcinomas were more than 4 cm. in diameter.

In commenting on the reports of Alvarez and MacCarty, of Comfort and Butsch, and more recently of Comfort, Priestley, Dockerty and associates,¹ Drs. Cohn and Sartin state as follows: "The basic difficulty of these papers is the failure to differentiate between malignant ulcers of the stomach and malignancy of the stomach in general." Caruolo, Hallenbeck and Dockerty³ in studying a group of posterior penetrating gastric ulcers found that of 91 patients operated on for posterior penetrating gastric ulcer during the 6-year period of 1944 through 1949, only 3.3% had malignant ulcers. However, in this series of cases only 28% of the ulcers were more than 2.5 cm. in diameter, and only 8% more than 4 cm. in diameter. Here is an example of the selected group of cases of posterior penetrating gastric ulcers. They