of Asian influenza virus. We also thank Dr. J. H. Bowie, Dr. R. A. Cumming, Dr. P. N. Edmunds, Dr. A. Joe, Dr. R. Lees, Dr. J. M. Murdoch, and Dr. R. E. Verney, for their co-operation in supplying the sera used for these tests. It is a pleasure also to mention the willingness with which the nursing staff volunteered their own sera for examination in this survey.

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GIANT INNOCENT GASTRIC ULCER ITS BEHAVIOUR AND TREATMENT

BY

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Various writers have drawn attention to the giant innocent gastric ulcer (Lumsden, 1950; Marshak *et al.*, 1953; Reid, 1954; Jennings and Richardson, 1954). They have reported series of cases refuting the previously held belief that most gastric ulcers with a diameter of 3 cm. or more are malignant. Avery Jones (1957) has gone further in stating that gastric ulcers of a diameter of more than 3 cm. radiologically are much more likely to be simple than malignant.

Present Investigation

FIG. 1.—Age incidence of 73 patients with giant gastric ulcers.

specimen, is 3 cm. or more. This series, the largest yet recorded, is from the Gastro-enterological Unit of Whittington Hospital, where the patients have been under the care of Mr. W. W. Davey and Dr. T. St. M. Norris, to whom I am indebted for permission to report these cases. The patients presented during the period 1950-7.

Sex and Age Incidence.—The series consists of 47 males and 26 females, a ratio of 1.8:1. This conforms

roughly with the ratio of 2:1 which applies to gastric ulcers in general (Illingworth, 1956). Fig. 1 shows the age incidence, being the age at which the patients presented at hospital with giant ulcers. It will be seen that the highest incidence is between 60 and 70, which is 20 years later than the highest incidence for gastric ulcers as a whole (Illingworth, 1953). The maximum incidence for males is also between 60 and 70, but that for females is between 70 and 80.

Size and Situation of Ulcers.—Table I shows the size of the ulcers, measured either radiologically or from the specimens. They have been situated mostly in

TABLE I

Size of Ulcers	Cases	
	Male	Female
3-3.9 c.m.	24	13
4-4.9 "	13	4
5-5.9 "	4	6
6-6.9 "	2	2
7-7.9 "	0	1
8-8.9 "	1	0
10-10.9 "	3	0
	47	26

relation to the lesser curve and the adjacent posterior wall of the stomach between the angulus and the cardia. In 80% of cases the ulcer penetrated the pancreas and in a further 10% it was adherent to it. Some ulcers have been entirely on the posterior wall and a few have been confined to the anterior wall. In a third of the cases the ulcer "saddled" the lesser curve. In the "saddle" type the anterior limb has frequently been adherent to the liver, while the posterior limb has penetrated the pancreas. Fig. 2 shows a large "saddle" ulcer which at operation measured 5 by 10 cm.

Length of Gastric History.

—Except in a few cases it has not been possible to determine how long the patient has had a giant ulcer and so decide whether it is a new one or merely the latest ulcer in a peptic ulcer history. An arbitrary division of the patients has been made into two groups: 29 (40%) had their gastric trouble for a year or less and 44 (60%) for over a year. The women were equally divided between the two groups, but two-thirds of the men had their gastric

FIG. 2.—Large "saddle" ulcer which measured 5 by 10 cm. at operation.

symptoms for more than a year and only one-third for less. Ten men had evidence of previous duodenal ulcers in addition to their giant gastric ulcers. Of these, nine were in the "over one year" group, suggesting that a duodenal ulcer was responsible for their early symptoms.

Factors of Possible Aetiological Significance

Jennings and Richardson (1954) mentioned possible aetiological factors in the production of giant ulcers,

including irritation of the colon by constipation and aperients, alcohol, smoking, psychological factors, and chronic bronchitis. There was no evidence in this series that constipation or regular excessive consumption of alcohol were causative factors.

Smoking.—Out of 66 patients for whom information is available, 11 may be classed as heavy smokers (25 or more cigarettes a day). The ulcer of the only woman in this group has remained healed for five years although she still smokes 20 cigarettes a day. A man whose ulcer has remained healed for four years smokes 40–50 cigarettes a day. Eight patients have been treated by surgery, and the eleventh in the group died from carcinoma of the larynx with his ulcer unhealed. No conclusions can be drawn from these figures regarding the effect of heavy smoking.

Psychological Factors.—Obvious abnormal psychological factors were present in 10 out of the 73 patients. Five had anxiety states and a sixth patient developed her ulcer five years after a leucotomy. In only one patient in this group has the ulcer remained healed.

Chronic Bronchitis.—Sixteen patients had chronic bronchitis. The ulcers of 11 were treated medically and seven of them healed, but only one (Case 51; Fig. 5) has remained healed.

Gastric Mucosa.—Tanner (1954) has pointed out that in cases of gastric ulcer the gastric mucosa is occasionally well developed but much more often it is thinner than normal. He said that it appears that gastric ulcer frequently arises in a diseased or degenerate mucosa. This does not seem to be true for the giant gastric ulcer. In 43 cases there are notes about the quality of the mucosa, seen either in the gastrectomy specimen or through the gastroscope. In only four cases (9%) was it noted to be atrophic, in 17 (40%) it was hypertrophic, and in 22 (51%) it was average in quality. These figures suggest that the giant gastric ulcer arises more often in a well-developed mucosa than in a degenerate one.

Modes of Presentation of the Giant Ulcer

Table II shows the mode of presentation of the 73 cases. It will be seen that 41 (56%) presented with pain as the principal symptom and 25 (34%) with haemorrhage.

TABLE II.—Modes of Presentation of the Giant Ulcer

Haemorrhage	25
Pain	27
Pain and vomiting	12
Pain and abdominal tumour	2
Vomiting from gastric retention	3
Perforation	1
Loss of appetite and anaemia	1

Site of Pain.—Pain was a symptom in 70 out of the 73 patients and information about its site is available in 68. Of these 68, 49 (72%) had pain somewhere in the area of the epigastrium, the lower retrosternal region, the left hypochondrium, and the left lower chest. Pain was confined to the left lower chest in three patients, to the left iliac fossa in three, to the right iliac fossa in two, and to the hypogastrium in six. Thus in 14 patients (20%) the pain was not in the usual gastric area. Its gastric origin may be still more difficult to recognize if there is no food relationship, as occurred in about 20% of patients in this series. Diagnosis is thereby delayed, possibly dangerously if a haematemesis provides startling evidence of the site of the lesion.

Back Pain.—As already noted, in 90% of cases the ulcer either penetrated the pancreas or was adherent to

it. In view of this it is surprising that only 34 (56%) out of 61 patients for whom there is information had back pain.

Complications of the Giant Gastric Ulcer

Haemorrhage

Of the 73 giant ulcers, 25 (34%) presented with haemorrhage; another patient, who had been treated medically, was readmitted for this reason. In addition, seven patients had severe degrees of anaemia. Of the 26 patients with haemorrhage, only five (20%) ceased bleeding under conservative treatment and 21 (80%) required emergency surgery. The proportion requiring emergency surgery is, of course, much higher than that for haemorrhage from gastric ulcers in general. A high proportion of these giant ulcers penetrate to outside the stomach wall, and when that happens violent bleeding can occur from involvement of the splenic or left gastric arteries or their main branches.

Surgical Treatment.—Table III shows the emergency operations that were done on the 21 patients whose haemorrhage was treated surgically. Two operations

TABLE III.—Emergency Operations for Haemorrhage

	Cases	Deaths
Partial gastrectomy	18	4
Laparotomy only	2	2
Gastrotomy and undersewing	2	1

were done on one patient. Her general condition permitted only gastrotomy and undersewing of the vessel at the first operation. Four days later, when further bleeding occurred, a gastrectomy was successfully performed. Her posterior ulcer measured 5 by 5 cm.

Mortality.—It will be seen that 7 out of 21 patients died following emergency surgery. In the partial gastrectomy group, two died from leaks of the anastomosis, one died two months after operation from bronchial carcinoma, and the fourth, a diabetic of 79, died suddenly five days after operation. Of the two patients who had laparotomy only, one had massive secondaries in the liver from a bronchial carcinoma and the other died at the end of an operation under local analgesia in which his ulcer was not found. He was extremely obese and his ulcer was situated 3 cm. from the oesophagus. The remaining death occurred after an unsuccessful attempt to save an exsanguinated woman of 74 by aortic transfusion and undersewing of the vessel. The true mortality from haemorrhage in this series was 27%—7 deaths out of 26 patients treated for it. Haemorrhage from a giant gastric ulcer is often an exceedingly dangerous complication, occurring as it does in elderly patients who are not infrequently in poor general condition. Referring to massive haemorrhage from ulcers, Tanner (1954) has said that in some cases death is almost certain unless a hazardous gastrectomy is performed on a near moribund patient. A high operative mortality must therefore be accepted if lives are to be saved.

Perforation

Perforation is uncommon, as only about one-third of the ulcers involve the anterior wall of the stomach. Five cases in the series perforated—an anterior ulcer in three and the anterior limb of a "saddle" ulcer in two. There was one death (Case 39, Fig. 3). As this patient's ulcer had caused gastric retention before perforating, an

emergency gastrectomy was done. He died at the end of the operation and the necropsy finding was coronary occlusion.

Gastric Retention

It is not generally realized that a large gastric ulcer situated low on the lesser curve can cause gastric retention with a big dilated stomach. The symptoms produced are similar to those of stenosing duodenal ulcer. Case 39 (Fig. 3), referred to above, is an example of this process.

There is a second way in which gastric retention occurs. Recurrent ulceration of the lesser curve causes progressive shortening of the lesser curve due to breakdown of tissue and healing by fibrosis. The length of the lesser curve between the oesophagus and the pylorus gets steadily less and there is relative elongation of the greater curve. As a result the stomach does not empty normally. Case 31 (Fig. 3) is an example of this process of shortening of the lesser curve.

Hour-glass Deformity

Two women and one man with giant ulcers developed hour-glass deformities of the stomach. It is unusual to get this deformity in a man.

FIG. 3.—Two giant ulcers that produced gastric retention. Case 39, a low lesser curve ulcer. Case 31, recurrent ulceration causing extreme shortening of the lesser curve.

Diagnosis

In addition to stating that gastric ulcers of more than 3 cm. radiological size are much more likely to be simple than malignant, Avery Jones (1957) has said that the gastric ulcer which projects clearly from the lesser curve between the angulus and the cardia is virtually never malignant. On the other hand, mentioning size as one of the points to be considered in deciding whether a gastric ulcer is simple or malignant, Cochrane Shanks and Kerley (1958) have written: "Any ulcer larger than 2.5 cm. in diameter should be suspected as malignant until it has been proved to be simple. The larger the ulcer the greater should be the suspicion. Many large ulcers will, in fact, turn out to be simple but the maxim is none the less a sound one." The maxim would not appear to be a sound one for ulcers between the angulus and the cardia, as the evidence of this series shows.

During the period in which these 73 cases of giant innocent gastric ulcers presented for treatment, only two giant malignant ulcers of the lesser curve were seen. One was diagnosed as a malignant ulcer by gastroscopy. The other was thought to be innocent on gastroscopy, but the correct diagnosis was made at immediate operation, made necessary by gastroscopic perforation of the stomach. It proved to be an ulcer-cancer.

In addition to history taking and physical examination, the methods used in investigating these ulcers have been the barium meal, fractional test meal, and gastroscopy. During treatment further evidence of innocence is provided by gain in weight and radiological and gastroscopic evidence of healing.

It is most important not to label a giant innocent ulcer as malignant. The great majority of these ulcers are innocent but require careful treatment. To regard a large ulcer like that of Case 2 (Fig. 4) as malignant and therefore beyond the reach of surgery is to expose the patient to the very serious risk of haemorrhage and death from an innocent condition. Fig. 4

FIG. 4.—Three giant innocent ulcers with radiological appearances that suggested malignancy.

shows the films of Cases 2, 60, and 65 in which the radiological appearances suggested malignancy but histological examination of the ulcers excised at operation showed them to be innocent.

Treatment

Fifty-two patients were treated by medical measures for varying lengths of time. All were treated in hospital, as it is thought that in-patient treatment at the start and for as long as the patient is content is the most satisfactory method of medical treatment. These are ill patients, in considerable risk of haemorrhage from their ulcers, and it is important that healing should start as soon as possible. The rate at which healing is occurring is observed by studying comparable radiological views of the ulcer, and a decision must be made whether elective surgery or medical treatment is indicated. However, it may not be possible to make this decision until the patient has been in hospital for about six weeks.

Elective Surgery

Elective surgery was regarded as the correct primary treatment for 13 patients—in two because of gastric retention, in one because of uncertainty about the character of the ulcer, and in 10 because of the length of gastric history. A preliminary course of medical treatment was given to all these patients. In addition to improving their nutrition, it is very desirable in certain cases with high ulcers to secure some healing of the ulcer before resorting to surgery, so that as much of the stomach as possible can be preserved.

A further 21 patients were treated by elective surgery because their ulcers either failed to heal under medical treatment or recurred after healing.

A Billroth I partial gastrectomy was the operation of choice and elective surgery was carried out on 34 patients without loss.

Medical Treatment

The principal item in the medical treatment of these patients is bed rest except for toilet purposes. A light nourishing diet with extra milk is given and suitable sedation and antacids are prescribed as required. A special effort is made to maintain the patient's morale and to secure his understanding and co-operation in the tedious treatment.

Differing opinions have been expressed about the value of medical treatment of these giant ulcers. Jennings and Richardson (1954) think it well worth while, but that dieting and rest are rarely necessary. Marshak *et al.* (1953) consider that medical measures have nothing to offer. Avery Jones (1957) has said that "a large gastric ulcer with a short history may heal completely and a medical trial is worth while, but the prognosis is poor if there are other associated illnesses."

Thirty-nine patients were treated medically with a view to getting the ulcer healed, but three ceased attending before healing occurred. The result of the primary medical treatment of the remaining 36 patients was: ulcers healed, 21; and ulcers failed to heal, 15.

Ulcers that Failed to Heal (15).—The ulcers of 15 patients (7 male, 8 female) failed to heal under prolonged medical treatment. One patient died of carcinoma of the larynx. Of the remaining 14, 13 were treated by elective gastrectomy and one by emergency gastrectomy for haemorrhage, which caused his readmission to hospital.

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Ulcers that Healed (21).—The ulcers of 21 patients (15 male, 6 female) healed under medical treatment. It is desirable to have final gastroscopic as well as radiological evidence of healing, because an ulcer can be so nearly healed that there is no longer a crater to fill with barium. However, the breach of mucosa can be seen with the gastroscope. At this stage the patient is symptom-free, so that the absence of symptoms is not proof of healing. The average time taken for these ulcers to heal was six and a half months. Five healed in under two months and eight in under three months. In this group that healed were two ulcers of 5 cm. in diameter and one of 6 cm. The latter required three and a half months' in-patient treatment and two and a half months' out-patient treatment to obtain radiological healing. Three months later symptoms recurred and a Billroth I gastrectomy was performed. The two ulcers of 5 cm. diameter also recurred.

Recurrences (14).—In 14 patients (12 male, 2 female) recurrent ulceration took place after healing of the original giant ulcer. In two cases the recurrence was associated with the patient's fatal illness from another cause; in a third case with the death of the patient's wife; in a fourth with the wife's illness; in a fifth with domestic disharmony; and in a sixth with whisky drinking. Thus in 6 out of the 14 cases there is a possible reason for the recurrence. Nine out of the 14 patients had their recurrence within six months of the date of healing and 12 within a year. This suggests a more hopeful outlook for those whose ulcers remain healed for over a year. In two patients recurrent ulcers have healed again and remained healed for about four years in each case. Of the remaining 12, eight have had partial gastrectomy, two have refused surgery, and two, as already mentioned, have died.

Ulcers that have Remained Healed (8).—The ulcers of eight patients (5 male, and 3 female) have remained healed for periods varying from two to five years. All of them have had barium meals within the past year, followed in some cases by gastroscopy. A ninth patient is placed in the "probably healed" category only because her last negative barium-meal examination was two years ago. Her giant ulcer healed two and a half years ago and she remains symptom-free.

In Fig. 5 is seen the giant ulcer of one of the eight patients in this group with long-term healing (Case 51). His ulcer, measuring 4 cm. in diameter, was gastroscopically healed after 15 weeks' treatment. It has remained healed for over two years, and he is the only patient with chronic bronchitis in the group with long-term healing.

FIG. 5.—Case 51. One of the eight successes of medical treatment.

Discussion

Table IV summarizes the results of treatment of the 73 patients in this series. It has been shown that these

TABLE IV.—*Summary of Results of Treatment of 73 Patients with Giant Gastric Ulcers*

Emergency surgery	..	..	..	..	..	22 (8 deaths)
Elective	..	..	..	..	..	34 (No deaths)
Ulcers remain healed	..	..	..	..	..	8
Ulcer probably remains healed	..	..	..	..	..	1
Recurrent ulcers	..	..	..	..	..	2
Defaulted	..	..	..	..	..	3
Died (other diseases)	..	..	..	..	..	3

giant ulcers can be healed, as, using strict criteria of healing, 8 (22%) out of 36 treated medically have remained healed for two years and upwards. These eight patients are our successes. Is there any way in which they could have been picked out of the original 36 and so avoided much time-consuming and unsuccessful medical treatment for the other 28? With this aim in view various factors have been analysed.

Sex.—Of 22 men and 14 women who were treated medically, five men and three women are in the group that remains healed. The sexes are thus represented in almost the same proportions in the two groups. Among the 14 patients whose ulcers recurred there are only two women and the recurrence of one was during her terminal illness. It may be that when a giant ulcer heals in a woman it is more likely to remain healed than in a man.

Length of History.—The group of eight who have remained healed are equally divided between those with a gastric history of up to one year and those with a history of over one year.

Size of Ulcer.—The average size of the ulcer is smallest (3.7 cm.) in the group that has remained healed. Of six ulcers treated medically whose diameters were 5 cm. or more, only three healed and they all recurred.

Duodenal Ulcer.—Four patients in the group treated medically had evidence of previous duodenal ulcers but in none of these has the gastric ulcer remained healed.

Effect of Treatment on Weight.—Avery Jones (1957) has said that patients who put on weight usually do well, but the figures for this series do not support that conclusion. Out of the group of eight, whose ulcers have remained healed, five (62%) put on weight (7–37 lb.; 3.2–16.8 kg.) during treatment. Information about weight increase is available for only 12 of the 15 whose ulcers failed to heal. Eight (66%) of these 12 patients put on weight (8–21 lb.; 3.6–9.5 kg.). Thus the proportions that put on weight in each group are similar.

A Possible Plan of Treatment

An effort has been made to find out what factors, if considered early in treatment, can enable one to select those whose ulcers are likely to heal and remain healed. It must be confessed that no obvious method of selection has been discovered, but the following points have been suggested by the investigation.

Surgical treatment is indicated for ulcers of 5 cm. diameter and upwards. If the ulcer heals, presumably the scar is a permanent site of lessened mucosal resistance (Illingworth, 1956). Chronic bronchitis seems to be another factor in favour of surgical treatment. During the initial period of in-patient treatment the rate of healing can be assessed and a decision made on whether treatment should be medical or surgical. If healing is likely to occur reasonably quickly, by which is meant in 8 to 10 weeks, and there are no factors apparent that are likely to cause a recurrence, then healing of the ulcer should be sought. Unfortunately in some patients the initial rate of healing is quite fast,

only to slow down and perhaps halt altogether. Finally, there is the attitude of the patient which is all important. Is he able and willing to undergo prolonged bed rest, preferably in hospital? This point will greatly influence the treatment given.

A high proportion of these patients will require surgical treatment either by emergency surgery for haemorrhage or by elective surgery after a preliminary period of medical treatment. In this series, which may be described as having been very conservatively treated, 77% of the patients have already had surgical treatment. If the series is looked at with hind sight it may be said that too much time has been spent on treating cases medically, but this has been a largely uncharted road and it has been necessary to explore the possibilities of medical treatment.

Summary

A series of 73 giant innocent gastric ulcers, measuring at least 3 cm. in diameter, is reported.

The age incidence of the patients, the size and situation of the ulcers, the length of gastric history, and factors of possible aetiological significance are given.

Pain was the principal symptom in 41 (56%) patients and haemorrhage in 25 (34%).

Emergency surgery was required for haemorrhage in 21 patients, of whom seven died. There were five perforations with one death.

The distinction between the giant innocent ulcer of the lesser curve and the malignant one is discussed. Two cases of giant malignant ulcer of the lesser curve are described.

Eight ulcers out of 36 treated medically have remained healed for two to five years.

Thirty-four patients were treated by elective partial gastrectomy without loss.

A method of selection for medical or surgical treatment is described.

It will be apparent how much the diagnosis and treatment of these patients has depended on the careful radiology which was carried out by Drs. G. Osborne, F. L. Rayner, and W. Stachurko. I am also grateful to Mr. W. W. Davey for much help in the preparation of this paper.

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In 1957 in England and Wales 9,273 sets of twins were born, 95 sets of triplets, and 3 sets of quadruplets. Of the quads, one set comprised 4 liveborn females, one set 2 liveborn males and 2 liveborn females, and one set 2 liveborn females and 2 stillborn males. The birth rate of 16.1 per thousand population was the highest since 1949 (though it was exceeded in 1958, when it was 16.4), and the number of divorces (23,785) was the lowest since 1945. In addition 462 marriages were annulled, also the lowest total since the war.—*Registrar-General's Statistical Review of England and Wales*, 1957, Part II, Tables, Civil. H.M.S.O., 11s. 6d. net.