

THE EFFECT OF DEFINITIVE SURGERY ON DUODENAL ULCER DISEASE

A COMPARATIVE STUDY OF SURGICAL AND NON-SURGICAL MANAGEMENT
IN 997 CASES*

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WITH FEW EXCEPTIONS, the natural history of a malignant process terminates in the death of the host; the success of treatment would not appear difficult to assess. In the older age group any attempt to evaluate surgery surprisingly belies this simplicity, since death from other causes may remove the statistical unit from the scene before it can be classified. Despite this difficulty, the statistical problem in malignancy is a relatively simple one because of the high mortality and readily demonstrable evidence of recurrent disease. Much surgical thought has been influenced by our habitual concept of success in malignancy: survival is the objective. We search for operative survivals or for "cure rates," often considering that after five years survival and cure are synonymous.

In dealing with a benign process such as duodenal ulcer, the vast majority of patients may be expected to succumb to other causes; the natural history of the disease terminates as a cause of death in only a small (but significant) number of patients, and some sort of symptomatic or economic criterion must be used for success with the remainder. Although it is common knowledge that duodenal ulcer is a life-long recurrent disease, and although this statement is repeatedly made in the literature, there are surprisingly few facts available which prove that any form of treatment has altered this life-long history.

In medicine generally and in the medical treatment of ulcer in particular, a life-long rapport between patient and physician is necessary to realize the best results. A physician counts his work well done if, with little risk, the patient has been saved from the surgeon's scalpel or from the autopsy table; but he should remain a patient. The concept of discharge is indistinctly seen on the distant horizon.

The surgeon's objective, by assuming a much greater immediate risk, is to free the patient from the physician and from the surgeon alike, and cast

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him loose again into the main stream of society well, as a citizen rather than as a patient. This difference in viewpoint has been fruitful of much controversy and it must be bridged in order to bring the total problem into focus and discover whether either the physician or the surgeon accomplishes his objective.

Despite the fact that the doctor treating duodenal ulcer is trying to intervene in a disease which has a long and complicated life history, attention in the literature has remained focussed on technics in all fields of therapy. Whether the physician uses alkalis, midnight aspirations or enterogastrone is a source for discussion exactly akin to the question of whether the surgeon shall do his anastomosis anterior or posterior to the colon or whether he shall do a vagotomy with his gastro-enterostomy. Such questions of technic have important short-term significance, particularly in surgery, where they may influence the mortality. As the years go by their importance shrinks and a more fundamental problem begins to emerge which can be stated as follows: "Has the doctor's treatment altered the life history of the patient's disease or has it been merely an episode in a long series of remissions and exacerbations?" Such was the genesis of this study.

It is our purpose to record a statistically significant group of cases taken from this hospital, followed up by the same method, and success judged by the same criteria in both medically and surgically treated patients. Since conditions in hospitals differ, each clinic must turn the mirror upon itself to establish norms, and lay down the criteria by which improvements in method may be judged.

In this study we have sought several objectives:

1. To examine a sizable group of ulcer patients regardless of the mode of treatment or the nature of the complications, so as to discern the outcome of the disease process.
2. To apply to all cases the same criteria of success and failure.
3. To discern within a single frame of reference whether the doctor improves the outlook of the patient or indeed alters in any way the course of the disease.

MATERIALS AND METHODS

A. Clinical Selection. To accomplish the purpose of this study, an unselected group of duodenal ulcer patients was needed, recent enough in date to include present methods of treatment, old enough to be viewed in perspective and to give some duration for follow-up. All patients with a proved duodenal ulcer or with ulcer deformity of the duodenum demonstrated by roentgenogram (with or without a crater) seen in the wards or Out-patient Department of the Massachusetts General Hospital in the years 1942 to 1946 inclusive formed the material of this research. It then remained to discover the source of these patients and evaluate their course subsequent to the 1942-46 episode (or episodes) at the Massachusetts General Hospital.

Gastric ulcers were excluded from the study. Patients suspected of duodenal ulcer by symptom, unproved by roentgen ray, were excluded; patients

entering for other complaints and found to have duodenal ulcer incidentally were included in the study, although they are few in number. Thirty-eight patients with gastro-jejunal ulcer are included without separate classification, providing the jejunal ulcer developed after surgery for duodenal ulcer. If jejunal ulcer arose under other circumstances it was excluded from the study. Private patients were excluded.

B. Origin and Subsequent Course. This group of patients numbered 1246. Their origins could be described in general as a graded series of case histories ranging from those few patients who had no gastro-intestinal symptoms and only a roentgenographic finding of ulcer, through the group entering the hospital at the time of their first symptoms (not infrequently hemorrhage or perforation), and progressing on to that large group of patients who had been suffering ulcer symptoms for years, often with complications, and in a few cases with previous attempts at definitive surgery.

While under care at the Massachusetts General Hospital during the 1942-46 period, their courses were equally divergent. At the one extreme were those patients treated not at all for ulcer because of other more important disease, although hardly one escaped without an admonition to follow an "ulcer diet." Many patients were treated as out-patients; a large number entered the hospital for one admission and were then followed in the out-patient department. At the other extreme of therapeutic endeavor lay those many patients having multiple house admissions, intensive treatment, consultation with gastro-intestinal specialists, psychiatric interviews, and finally definitive surgery. A small number died of their ulcers while in the hospital.

Subsequent to their therapeutic adventures in the 1942 to 1946 period under study, a variety of fates awaited this group of patients. It is the detailed consideration of this subsequent fate which permits the classification as to success or failure as described below. Some patients were "lost," meaning that they either died of other causes before progress could be evaluated or that insufficient data were accumulated. A number died of ulcer at other hospitals and many were lost track of by hospital record but were readily uncovered by follow-up letters. Not a few of these had undergone definitive surgery elsewhere. Then, finally, there was that large group of faithful patients whose courses right up to the time of evaluation could be ascertained from a complete hospital follow-up record, together with an interview at an outpatient visit.

C. Methods of Follow-up Study. Had we confined our evaluation of events since the 1942-46 period entirely to the hospital record, much of interest would have been lost. It soon became apparent that in dealing with duodenal ulcer "no news is bad news."* Many whose hospital records ceased after an

* There is a point here of more general interest: physician and surgeon alike base an "impression" of result in personal cases on those followed in office or clinic. Such is a self-selected group and will invariably leave the doctor with a specious impression of success. The untraced 13.4 per cent in this series should accordingly be viewed with suspicion.

uneventful house admission and a few follow-up clinic visits were found to have had repeated exacerbations later, often with admissions to other hospitals for complications or surgery. A few had definitive surgery elsewhere and several of the "late ulcer deaths" in the non-operative group were uncovered only by personal follow-up and examination of official records at the State House.

In order to discover these facts, all patients were sent a letter with a questionnaire giving them (or their survivors) an opportunity to express an opinion as to progress and present status. To this information was added a personal interview whenever possible and the results of whatever other data (roentgenograms, clinic visits) could be brought to bear on the problem.

D. Categories Studied. All the cases were divided into four categories based on the predominant therapeusis carried out at the Massachusetts General Hospital in 1942-1946.

Category 1—Non-surgical Management. None of these patients received definitive surgery at the Massachusetts General Hospital in 1942-1946.

Category 2—Acute Perforation. Patients treated at the Massachusetts General Hospital for acute perforation in 1942-1946 were placed in this category. None in this category received definitive surgery at the Massachusetts General Hospital in 1942-1946, and for this reason the group is in many respects a subdivision of category 1.

Category 3—Subtotal Gastrectomy. Patients having subtotal gastrectomy at the Massachusetts General Hospital in 1942-1946 fell into this category.

Category 4—Vagus Resection. Vagotomy performed at the Massachusetts General Hospital in 1942-1946 determined placement in this group.

E. Terminology. The term "non-surgical management" is deliberately ambiguous. Of this large group only a few could be considered as having "ideal medical treatment" and hence avoidance of the latter term; the task of giving perfect medical management to this large group would have been overwhelming to the facilities available. So few received other than casual treatment or sporadic follow-up (even after an intensive hospital experience) that category 1 may approximate in its main features the natural history of duodenal ulcer disease.

The term "definitive surgery" denotes an operation undertaken to alter the development of the disease process. Subtotal gastrectomy and vagus resection were the only procedures used at the Massachusetts General Hospital in 1942-1946. Operation to close perforation does not fall into this category; operation to stop hemorrhage is classed as definitive, providing a procedure was carried out which at the same time satisfied the anatomic requirements of an elective subtotal gastrectomy. Just as the medical care of these patients should not be thought of as "ideal," so also the surgical operations should be regarded in the light of the fact that they were largely carried out by the resident staff. The hospital policy of presenting to young doctors

experience under supervision prevents the continuity of medical treatment or standardization of surgery found in private clinic or practice. It is the opinion of the authors that this factor operates to the detriment of long-term medical treatment more than it does in surgical care.

F. Classification of Results. Based on all the information available, the trend of the patient's disease since his Massachusetts General Hospital episode of 1942-1946 was classified. This required a subjective judgment on the part of the observer. The patient's own account of his degree of deficit or rehabilitation usually did not conflict with a physician's evaluation. When it did, a choice had to be made. Each result was independently rated by at least two observers, who based their estimates on the most recent 80 per cent of the follow-up period. Except for ulcer deaths, no result shorter than two years was rated; follow-up periods range from two to eight years in all categories. The following classification of results was used, employing four classes:

Class I. Excellent. The patient appears to be completely free of his disease, with no restrictions on his manner of living any more than if he had never had a duodenal ulcer at all; asymptomatic *without* ulcer regimen. Not a patient any more.

Class II. Good. The patient is able to qualify as having an excellent result only by observing some sort of ulcer regimen. This may vary from a rigid diet and medication to modification of smoking habits or the avoidance of certain foods. In other words, asymptomatic *with* ulcer regimen; still a patient, but well.

Class III. Fair. Though improved, the patient cannot or will not qualify as having an excellent or good result; improved but still symptomatic. An ailing patient. Two subgroups are used, which follow.

Class III (a). In this group are patients with mildly incapacitating symptoms, such as those causing the loss of an occasional day from work but not more than seven days in the most recent year. Symptoms due to unavoidable emotional stress or fatigue, mild "dumping" symptoms, and poor appetite also qualify for this group. *(b)* Patients who are somewhat underweight but not enough to interfere with their normal activities or to present a medical problem are considered as having a III b result. This group is small because even in the presence of a slight weight deficit, other factors are usually more important in determining the result.

Class IV. Poor. The patient's disease is unimproved, worse or fatal. This is a dissatisfied patient. Reasons for classification as Poor are seven, listed as seven subgroups: (a) Hospital death following a definitive ulcer operation or suture of a perforated ulcer at the Massachusetts General Hospital. (b) Death from ulcer or its complications other than the above. (c) Major ulcer complications not yet fatal, such as stomal ulcer, hemorrhage, obstruction, perforation or intractable pain, developing or continuing in spite of attempted treatment; subsequent definitive ulcer surgery. (d) Severely underweight,

in itself constituting a disability. (e) Ulcer symptoms producing economic incapacity amounting to the loss of more than 14 days' work in the most recent year. (f) Persistent distress or disability resulting from ulcer therapy, such as disabling unrepaired incisional hernia, painful scar, malfunctioning anastomosis, severe "dumping" syndrome amounting to a crippling disorder, neuritis, diarrhea, anemia, etc. (g) Definite dissatisfaction with the result on the part of the patient or the evaluators for some reason or combination of reasons not specified above.

It should be emphasized that the mere recurrence of a duodenal crater by roentgen ray is not taken as evidence of failure in medical management; such a criterion would confer an overwhelming incidence of failure in the non-surgical cases. An ulcer crater should rightly be accompanied by crippling or endangering manifestations to be indicative of medical failure. Recurrent ulcer or stomal ulcer is universally regarded as evidence of surgical failure and is so classed here regardless of other manifestations.

A word is necessary concerning our use of "subsequent definitive surgery" as a criterion of failure (Class IV c): if a patient had definitive surgery at the Massachusetts General Hospital in 1942-1946. This is not rated as a failure of *previous* medical or surgical treatment. If, on the other hand, he had either medical or surgical care at the Massachusetts General Hospital, 1942-1946, and *subsequently* required resection or re-resection, this is rated as a "Poor" (Class IV c) result of his 1942-1946 treatment. Similarly, perforations cared for at the Massachusetts General Hospital in 1942-1946 are not rated as failures of previous non-operative management. On the other hand a patient known to have duodenal ulcer in 1942-1946 and treated medically or surgically at the Massachusetts General Hospital who subsequently perforates, is rated as "Poor" (Class IV c). Finally, postoperative mortality is always listed as a surgical failure (IV a) regardless of how many years of non-surgical management contributed to the age and debility of the patient or the anatomic complexity of the procedure.

Classes I and II (Excellent and Good) are taken together as "Satisfactory Result"; classes III and IV (Fair and Poor) as "Unsatisfactory Result." Patients who died from other causes less than two years after their Massachusetts General Hospital 1942-1946 episode were excluded from classification as yielding insufficient data for classification.

A simple system of coding is possible within this framework, *e.g.*, a "3-IV c" result means that a patient having a subtotal gastrectomy at the Massachusetts General Hospital in 1942-1946 is rated as a poor result because of subsequent major ulcer complications or surgery.

G. Statistical Methods. The work of Hollander and Mage¹ and later of Cooper,² Heuer³ and others⁴⁻¹⁰ point up some of the pitfalls of statistical method in such a study. Since we are grading a set of results in four categories of patients treated concomitantly, differences in follow-up period

between the groups do not upset the comparative values. The follow-up period is two to seven years in all groups except the small and statistically insignificant vagotomy series, where it is two to five years. The doctrine of "once a failure always a failure" applies for Class IV a, IV b and IV c results (death, major ulcer complications, or subsequent definitive surgery); for other types of results the "most recent 80 per cent of the follow-up period (at least two years)" is used. Since this method is used on all cases it does not introduce any disparity between the series.

Our follow-up method, as mentioned previously, uncovered many failures not documented on the hospital record, thus disproving (if any further disproof were needed) the contention that "lost" cases may be assumed to have done as well as the traced cases.

The only statistical problem remaining is the comparison of percentages between two series of patients of differing numerical size. To establish significance between groups, the probability ratio was determined as follows:

$$\begin{aligned}
 s_1 &= \text{Standard deviation of a percentage} \\
 P_1 &= \text{Percentage in N, number of cases} \\
 \text{Then: } s_1 &= \sqrt{\frac{P_1 (100 - P_1)}{N_1 - 1}}
 \end{aligned}$$

For standard deviations (s_1 and s_2) of two series, the probability ratio (P.R.):

$$\text{P.R.} = \frac{P_1 - P_2}{\sqrt{s_1^2 + s_2^2}}$$

A P.R. of 2.6 or higher indicates a 99 per cent (or greater) probability that the difference in the percentages is a phenomenon due to factors other than chance.

The results so compared cannot be regarded in any sense as final for the series. In this group of patients suffering from a benign disease the final result cannot be tabulated until all 1246 patients have died.

RESULTS

A. Number of Patients Studied. The 1246 patients whose records were abstracted grouped themselves in the four categories of treatment as follows (Table I):

Category 1. Patients receiving no attempt at definitive surgical treatment at the Massachusetts General Hospital during 1942-1946—952 cases.

Category 2. Patients admitted to the Massachusetts General Hospital, 1942-1946, because of acute perforation of a duodenal ulcer—85 cases.

Category 3. Patients receiving subtotal gastrectomy at the Massachusetts General Hospital, 1942-1946—175 cases.

Category 4. Patients receiving vagus resection at the Massachusetts General Hospital, 1942-1946—34 cases. All of these were transthoracic operations without gastro-enterostomy.

B. Success of Follow-up. Although 1080 patients (86.6 per cent) of the 1246 cases were successfully traced, in only 997 cases (80 per cent) were sufficient data obtained to justify classification of the results in terms of ulcer treatment. Eighty-three patients died of other causes and 44 of these succumbed to other pathologic processes before a result in terms of ulcer care could be classified on the basis of two-year follow-up. Thirty-nine patients, although followed satisfactorily, could not be classified because of conflicting or incomplete information. Patients dying of duodenal ulcer were rated as deaths due to ulcer (Classes IV a or IV b) regardless of when they occurred.

C. Success of Treatment. In Tables II-A and II-B is shown a brief summary of the results obtained in the 997 classified patients. Of the entire group,

TABLE I.—*Duodenal Ulcer, 1942-1946. Cases Studied.*

Category	Total	Followed	Classified	Deaths	Ulcer Deaths
1 Non-surgical.....	952	807	738	82	15
2 Perforating.....	85	77	70	15	8
3 Subtotal gastrectomy.....	175	162	155	12	5
4 Vagus resection.....	34	34	34	2	0
Totals.....	1246	1080	997	111	28

Per cent followed, 86.6; per cent classified, 80.

Death rate in followed patients, 10.3 per cent; ulcer death rate in classified patients, 2.8 per cent; per cent of total deaths due to ulcer, 25.2.

Note: The 83 patients followed but not classified include 44 patients who died from other causes before an ulcer result could be classified on the basis of two years' follow-up and 39 followed patients in whom no valid judgment could be made as to result.

about one-half (51.4 per cent) had pursued a course since 1942-1946 which could be termed satisfactory, by which was meant that their results fell either into Class I or Class II. The remaining 48.6 per cent fell into Classes III or IV and must be termed unsatisfactory. In those patients in whom no definitive surgery was carried out (Category 1), 45.6 per cent achieved a satisfactory result and 15.1 per cent an excellent result. In those patients in whom subtotal gastrectomy was carried out, 76.1 per cent achieved a satisfactory result and 53.5 per cent an excellent result. This difference is significant statistically, with a probability ratio of 6.8.

D. General Mortality. Of the 1080 patients traced, 111 are known to be dead. Twenty-eight of these 111 deaths (25.2 per cent of the deaths) are known to have been due to duodenal ulcer or its complications and the remainder due to other causes. These 28 deaths represent an overall ulcer mortality of 2.8 per cent for the 997 cases in which the details are accurately known.

Among those patients who did not receive definitive surgical treatment (Category 1) there was an ulcer mortality of 2.03 per cent. None of the patients who died of perforation had received definitive surgical treatment and when

these two categories (1 and 2) are added, the total mortality in patients managed without definitive surgical treatment at the Massachusetts General Hospital, 1942-1946, is found to be 2.85 per cent. As will be described later, this figure should be revised downwards in the light of several of the case histories which included no opportunity for either medical care or definitive surgery.

Among the 175 subtotal gastrectomy patients, a hospital mortality of 2.86 per cent was encountered; none of the traced cases died subsequently of ulcer.

TABLE II-A.—*Duodenal Ulcer, 1942-1946, Total Results by Four Classifications.*

Category	Number Classified	Class I Excellent	Class II Good	Class III Fair	Class IV Poor
1 Non-surgical.....	738	111 15.1%	225 30.5%	161 21.8%	241 32.6%
2 Perforating.....	70	13 18.6%	21 30.0%	17 24.3%	19 27.1%
3 Subtotal gastrectomy....	155	83 53.5%	35 22.6%	18 11.6%	19 12.3%
4 Vagus resection.....	34	11 32.2%	13 38.3%	4 11.8%	6 17.7%
Totals.....	997	218 21.9%	294 29.5%	200 20.0%	285 28.6%

There were no deaths in the small series of vagotomies for duodenal ulcer, although two of the patients subsequently succumbed to other diseases.

The mortality of definitive surgery at the Massachusetts General Hospital, 1942-1946, is therefore 2.39 per cent of operations, 2.65 per cent of classified cases, or 2.86 per cent of subtotal gastrectomies.

Regardless of which basis is chosen for computing the ulcer deaths in the surgical cases as versus those patients who did not receive definitive surgery,

TABLE II-B.—*Duodenal Ulcer, 1942-1946, Total Results by Two Classifications.*

Category	Number Classified	Satisfactory Classes I and II	Unsatisfactory Classes III and IV
1 Non-surgical.....	738	336 45.6%	402 54.4%
2 Perforating.....	70	34 48.6%	36 51.4%
3 Subtotal gastrectomy....	155	118 76.1%	37 23.9%
4 Vagus resection.....	34	24 70.5%	10 29.5%
Totals.....	997	512 51.4%	485 48.6%

there is no statistically significant difference in mortality between the two groups. A comparison of the lowest non-surgical mortality (2.03 per cent in 738 cases) with the highest surgical mortality (2.86 per cent in 175 cases) yields a probability ratio of 0.6, which is far below the significance level.

PATTERNS OF FATALITY

Having examined the overall statistical results, it is worth-while turning our attention to the anatomy of failure. This can only be done by shifting from group statistics to a discussion of those individual cases who succumbed to this disease. We can then ascertain whether or not any consistent pattern emerges; these brief histories of fatal cases are of importance in discovering those sorts of phenomena which lead to death. The fatal cases will be discussed

in each category of treatment. Following each history a note as to interpretation is given; these notes are further clarified in the next section.

Category 1.—Patients who received no definitive surgery at the Massachusetts General Hospital, 1942–1946. There were 15 such deaths as follows:

Case 1.—D. C., 201,829, was a male, age 58, with an 18-year ulcer history, including perforation in 1926 and hemorrhage in 1931 and 1942. He died 1943 (Massachusetts General Hospital) of pyloric obstruction and pyelonephritis. Postmortem was obtained. (Preventable, salvageable).

Case 2.—J. M., 315,297, was a male, age 69, with a 35-year ulcer history, including pyloric obstruction in 1939, for which a posterior gastro-enterostomy was carried out at another hospital; jejunal ulcer was observed in 1942 and hemorrhage occurred. Subtotal gastrectomy was evidently not considered at this time, nor were the surgeons consulted. The patient died in 1944 (at another hospital) of perforated ulcer, intestinal obstruction, and pneumonia. (Preventable, salvageable).

Case 3.—E. M., 368,152, was a male, age 39, with a 7-year ulcer history, including two perforations in 1938 and 1941 respectively. He died in 1945 (at another hospital two years after Massachusetts General Hospital admission for ulcer), following operation for perforation and acute massive hemorrhage. No postmortem was obtained. While in this hospital under study the patient was admitted to the emergency ward, and despite two previous perforations, no concerted attempt was made to guide him into adequate treatment. (Preventable, salvageable).

Case 4.—E. C., 416,300, was a male, age 35, with an ulcer history of 4 years or more, including one perforation. He had suffered from pyloric and intestinal obstruction since his perforation. He was a chronic intestinal invalid, having had 8 laparotomies for ill-defined reasons. He died in 1947 (at another hospital) after operation to relieve obstruction. No postmortem was obtained. While in this hospital for study, the patient was extremely unco-operative and was discharged against advice. (Non-preventable, salvageable).

Case 5.—D. C., 384,256 was a female, age 76, with a history of duodenal ulcer with appropriate roentgen ray findings of long standing, concomitant chronic alcoholism, cirrhosis of the liver, arteriosclerotic heart disease and psychotic states. She died in 1949 (at another hospital) of peritonitis secondary to a perforated viscus. Clinical diagnosis was perforated ulcer. No postmortem was obtained. (Non-preventable, non-salvageable).

Case 6.—A. H., 391,873, was a male, age 86, with no history of duodenal ulcer. He died in 1943 (Massachusetts General Hospital) of hemorrhage, 28 days after admission to the hospital because of acute cardiac decompensation. Postmortem examination revealed a bleeding duodenal ulcer. Ten days previously a gastro-intestinal roentgenogram had been negative. (Non-preventable, non-salvageable).

Case 7.—H. M., 397,548, was a male, age 52, with a 5-year ulcer history. He died in 1943 (Massachusetts General Hospital), 5 days after a duodenectomy and pancreatectomy undertaken with the erroneous diagnosis of cancer of the second portion of the duodenum. Diagnosis on the surgical specimen: duodenal ulcer of the second portion of the duodenum with large inflammatory mass and penetration into the head of the pancreas. No postmortem was obtained. (Preventable, salvageable; a diagnostic error).

Case 8.—J. R., 394,893, was a male, age 42, with a 10-year ulcer history. He was hospitalized for bleeding at the Massachusetts General Hospital, at which time no surgical consultation was requested. He was discharged to the Out-patient Department on dietary

treatment. Three months later he suffered a perforation and died (at another hospital) of peritonitis. Postmortem examination was obtained. (Preventable, salvageable).

Case 9.—J. B., 457,012, was a male, age 74, with an ulcer history of unknown duration. He died in 1944 (Massachusetts General Hospital), one hour after admission. He was in shock due to acute massive hemorrhage on admission. Postmortem examination revealed a bleeding duodenal ulcer. (Non-preventable, non-salvageable).

Case 10.—D. S., 319,914, was a male, age 60, with an ulcer history of at least 3 years' duration. He underwent combined abdomino-perineal resection for carcinoma of the rectum 6 years previously, was treated at the Massachusetts General Hospital about one month previous to death, and had had previous acute massive hemorrhage. He died in 1947 (at home) of acute massive hemorrhage leading to hemiplegia and death. No postmortem examination was obtained. (Non-preventable, non-salvageable).

Case 11.—J. C., 425,641, was a male, age 77, with an ulcer history of 3 years' duration, including massive hemorrhage under very careful and persistent medical supervision. Throughout his illness, the patient was also suffering from arteriosclerotic heart disease. He died in 1949 (Massachusetts General Hospital) of acute massive hemorrhage. Generalized arteriosclerosis and senile dementia were present. No postmortem was obtained. (Non-preventable, non-salvageable).

Case 12.—G. G., 187,384, was a male, age 74, with no ulcer history, although he had previous appendicitis and cholecystitis. He died in 1945 (Massachusetts General Hospital), 3 days after admission for acute massive hemorrhage. The patient fainted when he began to bleed and sustained a fracture of the left side of his head and face as a complicating factor. Postmortem revealed a bleeding duodenal ulcer. (Non-preventable, salvageable).

Case 13.—H. M., 433,380, was a male, age 48, with an ulcer history of 7 years, with perforation 7 years previously. He died in 1945 (at another hospital) of ulcer, one year after the last Massachusetts General Hospital admission, at which time roentgen ray showed an active ulcer crater. No postmortem was obtained. (Preventable, salvageable).

Case 14.—D. Q., 174,017, was a male with a 13-year ulcer history, including hemorrhage 10 years previously. He died in 1945 (Massachusetts General Hospital) one day (age 72) after admission for acute massive hemorrhage. Postmortem revealed a bleeding ulcer, cardiac infarction, bronchopneumonia and pulmonary edema. (Preventable, non-salvageable).

Case 15.—P. C., 528,442, was a male, age 44, with a 6-year ulcer history, who died in 1946 (at home), 23 days after Massachusetts General Hospital admission. The Massachusetts General Hospital admission was for undiagnosed abdominal pain. The patient died of a perforated duodenal ulcer with peritonitis, proved by postmortem examination carried out in the patient's home. (Preventable, salvageable).

Category 2.—Patients who had received no definitive surgery at the Massachusetts General Hospital, 1942–1946, and who died at the Massachusetts General Hospital following acute perforation. There were eight such deaths as follows:

Case 16.—E. H., 401,617, was a male, age 72, who was admitted to the ward for arteriosclerotic heart disease, not in congestive failure. While on the ward the patient perforated and died in 2 days of generalized peritonitis. There was no operation. Postmortem revealed a perforated ulcer which had not been suspected prior to death. (Non-preventable, non-salvageable).

Case 17.—W. W., 276,099, was a male, age 82, with a one-year ulcer history, including hemorrhage on one occasion. He died (Massachusetts General Hospital), 12 hours after admission, of perforated duodenal ulcer with peritonitis. No operation was performed. Postmortem revealed perforated ulcer with peritonitis, coronary thrombosis, and an old inactive rheumatic endocarditis. The patient also had diabetes mellitus. (Preventable, non-salvageable).

Case 18.—E. C., 498,534, was a male, age 76, with a 20-year ulcer history, who died in 1945 (Massachusetts General Hospital), less than one day after admission, of perforated duodenal ulcer. No operation was performed. Postmortem revealed a perforated ulcer with peritonitis. The patient was admitted with perforation of 3 days' duration and in moribund condition. (Preventable and salvageable on the basis of history; a lost cause tactically in the final episode).

Case 19.—F. W., 43,804, was a male, age 47, with an 18-year ulcer history including admission 13 years previously for duodenal ulcer. He died in 1945 (Massachusetts General Hospital) 72 hours after suture of a perforated ulcer. The clinical episode suggested re-perforation, and for this reason re-exploration was carried out just before death. No postmortem was obtained. (Preventable, salvageable).

Case 20.—W. L., 221,452, was a male, age 54, with a 13-year ulcer history, including admission for ulcer one year previously. He died in 1947 (Massachusetts General Hospital) on the twelfth postoperative day, after suture of an acute perforation of duodenal ulcer. The patient also had pyloric obstruction, portal cirrhosis and ascites. No postmortem was obtained. (Preventable, non-salvageable).

Case 21.—E. T., 553,430, was a male, age 42, with no previous history of duodenal ulcer. He died on the sixth day after suture of perforation, of extending peritonitis and bronchopneumonia. Postmortem was obtained. (Non-preventable, salvageable).

Case 22.—M. C., 452,564, was a male, age 30, with a 15-year ulcer history complicating rheumatic heart disease. He died in 1944 (Massachusetts General Hospital), the sixth postoperative day after suture of perforation. Postmortem revealed peritonitis with bronchopneumonia and inactive rheumatic heart disease. (Preventable, salvageable).

Case 23.—H. L., 337,257, was a male, age 54, with an unknown duration of history. He died in 1942 (Massachusetts General Hospital), 7 days after operation for perforated viscus. The patient had been admitted the previous month because of active duodenal ulcer with bleeding. He was discharged home after 12 days' treatment and re-admitted within 4 days because of acute massive hemorrhage. Thirteen days after admission an acute perforation occurred which led to his death. Postmortem disclosed an active duodenal ulcer with perforation, and fecal impaction with necrosis of the bowel wall and simultaneous perforation of the sigmoid. The recently perforated duodenal ulcer had sealed over. (Preventable, salvageable).

Category 3.—Death following subtotal gastrectomy carried out at the Massachusetts General Hospital, 1942-1946. There were five such deaths as follows:

Case 24.—G. A., 384,686, was a male, age 49, with a 23-year ulcer history with very consistent medical treatment. Posterior gastro-enterostomy was carried out in 1929 at another hospital followed by the development of a jejunal ulcer. He died (Massachusetts General Hospital) 15 days after subtotal gastrectomy, of pulmonary embolus. No postmortem was obtained. (Preventable, salvageable).

Case 25.—J. D., 395,116, was a male, age 54, with a 13-year ulcer history with a gastro-enterostomy carried out in 1940 at another hospital. The patient also suffered

from chronic alcoholism and psychosis. Five months prior to that a volvulus of the small bowel occurred and small bowel was resected. One month later the patient was admitted for elective surgery. The old gastro-enterostomy, which turned out to have been a gastro-ileostomy, was taken down. Three months after this episode, the patient entered with acute massive hemorrhage from reactivated duodenal ulcer. A subtotal gastrectomy was carried out and the patient died of acute massive hemorrhage on the fifth postoperative day. The postmortem revealed bleeding duodenal ulcer, the ulcer crater having been left in at the time of the subtotal gastrectomy. (Preventable, salvageable).

Case 26.—G. F., 492,366, was a male, age 50, with a 3-year ulcer history. He entered with pyloric obstruction, and died in 1945 (Massachusetts General Hospital) ten days after subtotal gastrectomy. He died with an episode of vomiting and convulsions. The postmortem did not include the brain and revealed pulmonary edema. A cerebrovascular accident could have been a contributory cause of death; the patient's postoperative course was stormy and febrile with questionable patency of the operative stoma throughout. (Preventable, salvageable).

Case 27.—J. W., 555,507, was a male, age 60, with a 20-year ulcer history with massive hemorrhage, 12, 5 and 3 years prior to admission. He was admitted with pyloric obstruction. He died in 1946 (Massachusetts General Hospital) 27 days after subtotal gastrectomy, of peritonitis secondary to inadvertent operative interruption of the bile ducts in a difficult duodenal dissection. Postmortem was obtained. (Preventable, salvageable, and tactically would have been a simpler problem if surgery had been undertaken earlier in the history of the disease).

Case 28.—D. M., 14,717, was a male, age 76, with a 45-year ulcer history with 4 previous hemorrhages. He died in 1942 (Massachusetts General Hospital) following subtotal gastrectomy for duodenal obstruction, of bronchopneumonia and peritonitis. No postmortem was obtained. (Preventable, salvageable and tactically would have been a simpler problem if surgery had been undertaken earlier in the history of the disease).

Discussion of Deaths. From these 28 deaths two distinct patterns emerge—one takes the form of a young or middle-aged man in the prime of life, who succumbs to a complication of which his physicians have been forewarned by a long and virulent ulcer history. These deaths are preventable deaths in salvageable patients. The other pattern is that of an elderly male with a short or non-existent ulcer history often with complicating pathologic conditions in vital organs, a patient who, on the basis of other serious disease, may be regarded as non-salvageable.

Of the 15 deaths in patients of category 1 (no definitive surgery at the Massachusetts General Hospital, 1942-1946) seven (cases 1, 2, 3, 7, 8, 13 and 15) may be regarded as preventable deaths in patients whose general condition and lack of other pathologic changes made them salvageable. Five cases (cases 5, 6, 9, 10, 11) seem neither salvageable nor preventable; the remaining three were either non-preventable or non-salvageable.

Of the eight deaths in category 2 (acute perforation), four (cases 18, 19, 22 and 23) were salvageable and preventable, viewed in retrospect. Case 16 was neither salvageable nor preventable. Cases 17 and 20 were probably preventable but not clearly salvageable. Case 21 was salvageable, but because of lack of ulcer history, hardly preventable. These terms (preventable, salvage-

able) refer to the *history*, not to the immediate surgical problem of treating the perforation.

Thus of 23 deaths in the 808 classified patients who received no definitive surgery at the Massachusetts General Hospital in 1942-1946 (categories 1 and 2), 11 were pathologically salvageable and clinically preventable by proceeding with earlier definitive surgery, which with its inherent risk of 2.86 per cent would have claimed one patient or less of these 11 patients (on a statistical expectancy basis). Six of these patients (cases 1, 2, 3, 8, 13 and 15) had previous serious complications or previous Massachusetts General Hospital admissions to give additional warning of the presence of a progressive and virulent form of the disease. The other 12 deaths must be viewed as having clinical features making rescue unlikely or excessively hazardous.

All five deaths following subtotal gastrectomy were truly surgical deaths tactically salvageable if all details of the postoperative course had proceeded according to plan; there were no patients of such advanced age and infirmity that the surgeon could claim "calculated risk" or make out a case for surgery as a desperate measure for a patient in *extremis*. All five were both salvageable and preventable, viewed in the framework used in the foregoing paragraphs. Two of the five (cases 27 and 28) had such long and complicated histories that surgical approach at a younger age and with less advanced local pathology might have been expected to carry a lesser risk.

There were no vagotomy ulcer deaths.

The lack of late ulcer deaths in the category 3 and 4 cases (the 189 gastrectomies and vagotomies) is probably not significant, since time enough has not elapsed since operation.

PATTERNS OF FAILURE SHORT OF FATALITY

Although the 28 ulcer deaths in the series form a highly significant group, they do not have the statistical importance of those classified as Class IV (Poor) Results which include 28.6 per cent of the entire group of traced patients (285 individuals). An analysis of the reasons why these patients were classified as failures may lead us to a better understanding of the phenomena involved in the natural history of progressive duodenal ulcer disease. These will also be dealt with according to categories of treatment (Table III).

Category 1.—Patients in whom no definitive surgery was performed at the Massachusetts General Hospital, 1942-1946 (738 cases classified):

In the non-surgical group, 96 (13 per cent) were classified as poor results because of subsequent major complications or surgery (IV c); 79 (11 per cent) because of economic incapacity (IV e) (loss of more than 14 days in the past year because of ulcer difficulty) and 51 (7 per cent) were "dissatisfied for other reasons" (IV g). It will be profitable to examine these subcategories of poor results more closely.

1-IV c. There are 96 patients in category 1 who were classified as having a poor result because of subsequent major ulcer complications or surgery. Of

these, 25 had subsequent major hemorrhages, most of them treated in other hospitals. Six had subsequent perforations. A total of 58 had subsequent major surgery for their ulcers (definitive surgery) or for the complications of ulcer. Most of these definitive operations and ulcer complications requiring surgery occurred at outside hospitals, a few of them occurred at the Massachusetts General Hospital after 1946. The remaining seven patients had other major ulcer difficulties, including prolonged intractable pain and symptoms of obstruction. These 96 patients, then, had unequivocal evidence of failure of the regimen instituted.

1-IV e. There were 79 patients in category I who were classified as poor results because of economic handicap. Of these, 14 lost eight to 20 days' work,

TABLE III.—*Duodenal Ulcer, 1942-1946, Subclassification of Poor Results (Class IV).*

Category	Number Classified	Class IV*							Total IV
		IV a	IV b	IV c	IV d	IV e	IV f	IV g	
1 Non-surgical	738	0	15 2%	96 13%	0	79 11%	0	51 7%	241 32.6%
2 Perforating	70	5 7%	3 4%	6 9%	0	2 3%	0	3 4%	19 27.1%
3 Subtotal									
gastrectomy	155	5 3%†	0	5 3%	3 2%	0	3 2%	3 2%	19 12.3%
4 Vagus resection	34	0	0	6 18%	0	0	0	0	6 17.7%
Totals	997	10 1%	18 1.9%	113 11%	3 0.3%	81 8%	3 0.3%	57 6%	285 28.6%

* Class IV is sub-classified as follows:

- a — Postoperative death.
- b — Ulcer death.
- c — Major ulcer complication or subsequent definitive surgery.
- d — Severely underweight.
- e — Economic incapacity.
- f — Persistent disability as side-effect of treatment.
- g — Poor result for other reasons.

† The postoperative mortality in the 175 sub-total gastrectomies was 2.86 per cent (5 deaths in 175 resections).

28 lost 21 to 40 days' work and 37 lost over 41 days' work in the year prior to our most recent follow-up contact.

1-IV g. There were 50 patients in category I who were classified as poor results because of "other reasons." This polyglot group is best illustrated by a few examples:

Patient H., 131,186, was treated in the Out-Patient Department for duodenal ulcer in 1943 and has been seen at intervals since that time. He has occasional vomiting spells, lost eight days' work in the year prior to his questionnaire, and states that he is worse off than when first seen in the hospital.

Patient C., 444,457, a 44-year-old male, was first seen in the Massachusetts General Hospital, Out-Patient Department in 1944. He was placed on an ulcer regimen and has been followed since. He continues to have ulcer symptoms, lost time from work in 1948 because of them, and has an active ulcer crater on his last roentgen ray examination.

Patient Z., 349,200, a 39-year-old male first seen in 1946, continued to have symptoms on a good diet. He has had a recent hemorrhage and lost eight days' work in 1948.

Of the 738 patients in category 1, 329 or 44.6 per cent were hospitalized for ulcer on the wards of the hospital, and 409 (55.4 per cent) were treated only in the Out-Patient Department. The effect of this difference on results is not dramatic. The out-patients had a slightly lower incidence of failure than the house cases (29.1 per cent Class IV results as versus 37.1 per cent in the house cases) and a slightly higher incidence of excellent (Class I) results (16.4 per cent as versus 13.4 per cent). These minor differences might be predicted on the basis of the fact that the more severe cases are admitted to the hospital.

Category 2.—Patients who were treated at the Massachusetts General Hospital, 1942–1946, for acute perforation (70 classified cases):

In this group six patients (9 per cent) were classified as having a poor result because of subsequent major ulcer complications or surgery (2-IV c). Of these six patients, four had definitive surgery carried out later at an outside hospital, one re-perforated and one developed large painful hernias after two drainages of subhepatic abscess. Eight died of their perforation as recounted previously.

There were five other patients in category 2 who had poor results for a miscellany of reasons, including economic incapacity and dissatisfaction of the patient with his ulcer symptoms.

Category 3—Patients who had subtotal gastrectomy at the Massachusetts General Hospital, 1942–1946, (155 classified cases):

There are five patients in the gastrectomy group to whom poor results were assigned because of later major ulcer complications or surgery (3-IV c). Three of these patients developed proved jejunal ulcer and two had symptoms compatible with jejunal ulcer, a total incidence of five in the 155 followed cases (3 per cent). One case, N. S. (341,839), bled six years postoperatively and jejunal ulcer was proved by roentgen ray. Patient W. W., (320,712), perforated a stomal ulcer one year postoperatively and had a vagus resection carried out in another hospital. Patient H. D. (27,407), developed a stomal ulcer one year after a resection, had a re-resection and has been well since. J. S. (267,405), perforated an anastomotic ulcer two months after his resection and has been well since without management. Patient A. V. (427,309), bled massively two years after his resection, presumably from a jejunal ulcer, the presence of which was never established.

Three patients belong in category 3-IV d because of failure due to chronic malnourishment after subtotal gastrectomy. Two patients are underweight, (25 and 30 pounds respectively), one remained malnourished, required revision of his stoma, and died seven years later of pulmonary tuberculosis. There are no poor results due only to economic handicap (3-IV e) after resection.

Three patients after subtotal gastrectomy belong in the group of failures due to untoward side-effects (3-IV f). Of these, one had weakness in his legs

beginning two months after spinal anesthesia and persisting to follow-up five years later, one had a severe "dumping syndrome," not well controlled and causing periodic illness. One patient has a "dumping syndrome," well controlled by careful diet. This leaves us with an incidence of very severe "dumping syndrome" of about 1.6 per cent. It should be emphasized that this figure only includes patients in whom the "dumping syndrome" was of serious and continuing disabling significance. It has been our experience that symptoms characteristic of the "dumping syndrome"* occur transiently at some time after operation in about 30 per cent of individuals having subtotal gastrectomy if they are closely questioned.

The miscellaneous group of failures has three members from the resected patients as follows:

Patient E. (455,785), had a subtotal resection in 1944. He now has an incisional hernia which has not been repaired and which gives him symptoms.

Patient G. (257,637), a 57-year-old male, reports constant pain which requires the attention of his family physician. He is not working and has lost 10 pounds in weight.

Patient K., (12,449), is a 63-year-old man who was operated upon in 1945. He continues to report abdominal pain and has failed to regain normal weight.

Category 4—Patients undergoing vagus resection at the Massachusetts General Hospital, 1942–1946, (34 cases):

There were six failures in the vagus group, all of them falling into that classification assigned to major ulcer complications or surgery (4-IV c).

Patient G. B. (270,852), developed a recurrent ulcer crater about two years after vagotomy; he persistently denied symptoms but progressively lost weight. About a year later he developed a pulmonary carcinoma to which he subsequently succumbed.

Patient M. E. (433,311), was a patient with Raynaud's disease, esophageal ulcer, and duodenal ulcer. Four years following transthoracic vagotomy, she developed renewed esophageal and duodenal ulceration with obstruction at the lower end of the esophagus, requiring bouginage.

Patient J. P. (501,746), had had a subtotal gastrectomy at another hospital in which the antrum of the stomach was left in place (the "antral syndrome"). A vagotomy was carried out with the hope that the vagus governs the secretory function of the antral mucous membrane. This was not the case and removal of the retained gastric antrum was necessary to achieve healing. Strictly speaking, this is hardly a failure of vagotomy alone since it also involves an inadequate subtotal gastrectomy. Yet, by our criteria, as a patient undergoing vagotomy at the Massachusetts General Hospital in 1942–1946, subsequent major surgery was required and, therefore, the patient stands as a class 4-IV c failure.

Patient J. S. (413,140), required a subtotal gastrectomy two years after vagotomy for duodenal ulcer because of the presence of a large gastric ulcer.

* The term "dumping syndrome" is used quite specifically here to denote a feeling of faintness and warmth coming on soon after eating, with flushing, palpitation, varying degrees of abdominal pain and a desire to lie down. Other types of postprandial symptoms are not included; in case the incidence of dumping syndrome here seems low it should be pointed out that 10 of the 18 Class III results after subtotal gastrectomy were assigned because of dumping syndrome severe enough to give an "unsatisfactory" result but not severe enough to be assigned as a "poor" (Class IV) result.

Patient J. V. (456,917), required a subtotal gastrectomy two and a half years after vagotomy because of obstructive symptoms, markedly delayed gastric emptying and malnutrition.

Patient M. McN. (344,702), required a subtotal gastrectomy about three years after vagotomy because of a recurrent duodenal ulcer complicating her chronic diarrhea. It is of interest that this patient had a flat insulin test at this time, an experience which has been noteworthy in several other recurrent ulcers after vagotomy.

There were no vagotomy failures in any of the other subclassifications of Class IV.

Discussion of Failures. In the deaths previously noted, two distinct patterns were discernible, (1) the "preventable deaths" where readier recourse to definitive surgery resulting from a more realistic evaluation of the cause of progressive duodenal ulcer might have been helpful and (2) those non-preventable or non-salvageable deaths in which little forewarning was given of a fatal turn of duodenal ulcer disease, or where concomitant renal or cardiac disease made rescue impossible.

The pattern of failure short of fatality is in contrast quite consistent. The failures are all essentially the same whether the patient has had surgery or not. The only difference to be discerned is that there are about twice as many failures in the non-surgical group as in the surgical group. The outstanding failures in all instances are those described as class IV c, meaning subsequent major ulcer complications, or deterioration requiring definitive surgery.

This calls to mind the essential unity of duodenal ulcer disease. A spectrum of therapy ranging on the one hand from simple diet or the most casual type of conversational management to, on the other hand, extensive consultation by specialists, psychiatry and definitive surgery, has a pattern of failure which is the same throughout. This pattern is characterized by recurrence not only of the ulcer by roentgen ray but of the organic changes which the disease induces, culminating in hemorrhage, perforation, painful ulceration or obstruction. It is in this category also that vagotomy has its most egregious failure. Indeed, the percentage of class IV c results is higher in vagotomy than in any other group in the whole series, suggesting that the operation of vagotomy, whatever its other effects, certainly has not altered the essential characteristic of this disease, namely that of recurrence with anatomic complications due to digestion of tissue in the upper gastro-intestinal tract.

The predominant pattern of failure due to subsequent major ulcer complications, major ulcer surgery or complications of ulcer surgery, is broken at one point in the medical series. This alteration in pattern arises from the 11 per cent incidence of economic incapacity as a cause of failure in the non-surgically treated group. Although definitive surgery has in general the same type of failure shown by medical treatment, it has these failures at a much lower rate of incidence and is noteworthy because economic incapacity is practically removed from the scene.

PERFORATION

We are examining the history of a benign process whose most outstanding local anatomic characteristic is the digestion of tissue. It is therefore of interest to separate out from the group those cases where this digestion has occurred so rapidly and to such depth as to produce a free perforation into the peritoneal cavity. We may then discern whether or not this group of patients has any different make-up or any different prognostic significance from the rest of the patients.

TABLE IV.—*Duodenal Ulcer, 1942-1946, Incidence of Perforation.*

Classified patients.....	997
Previous perforations.....	62
Acute perforations.....	70
Subsequent perforations.....	14
Total perforations.....	146 (14.7%)

Incidence of Perforation. Of the 1246 patients whose records were abstracted, a total of 151 or 12 per cent had perforated sometime prior to admission to the Massachusetts General Hospital, but only 85 or 6.8 per cent presented the problem of acute perforation and were treated specifically for this perforation. Of this group of 85, two had previous perforations to their credit.

TABLE V.—*Duodenal Ulcer, 1942-1946, Subsequent Fate of Patients Suffering Perforation.*

A. <i>Acute perforation</i>	62 Survivors traced
Satisfactory (Class I and II).....	34 (54.7%)
Unsatisfactory (Class III and IV).....	28 (45.3%)
Poor results (Class IV).....	11 (17.8%)
B. <i>Previous perforation with present symptoms</i>	62 Traced
Satisfactory (Class I and II).....	9 (14.5%)
Unsatisfactory (Class III and IV).....	53 (85.5%)
Poor results (Class IV).....	51 (82.2%)
Dead of ulcer: 4.	
Subsequent definitive surgery: 37.	
Re-perforation: 2	
Other types of failure: 8.	

Of the 997 patients followed and classified, 62 had previous perforations, 70 had acute perforations and 14 had perforations after their 1942-1946 episode, giving an over-all figure of 14.7 per cent as a first approximation for the incidence of perforation in the total time span studied. Several had multiple perforations (Table IV).

Fate of Perforators. It has become evident that the prognosis following a single perforation is far better than that for a patient with perforation in the past who re-enters with renewed symptoms (Table V). Of 62 traced survivors of acute perforation at the Massachusetts General Hospital 1942-1946,

34 (54.7 per cent) went on to satisfactory results, and only 11 (17.8 per cent) had failures.

In contrast, the 62 traced patients with previous perforation and renewed symptoms showed only nine satisfactory courses (14.5 per cent) and 51 (82.2 per cent) failures of non-surgical management. Of these 51 failures, four died later of ulcer, 37 required definitive surgery and two re-perforated. This difference in failure rate is strongly significant with a probability ratio of 9.26.

It would appear from this that perforation may literally be a "meaningless accident" in duodenal ulcer disease; a recurrence of symptoms guarantees that it was no such accident.

The total mortality of perforation is impressive. Of 132 patients with past or present perforation who were classified, 12 died at the time of perforation or later from duodenal ulcer or its complications, a mortality of 9.1 per cent.

Of the 25 patients in category 1 (non-surgical treatment) who had previous perforations and who were followed up to classification, four or 16 per cent are now dead of ulcers and 12 or 48 per cent have had poor results. Of the 15 patients in the non-surgical group who died of ulcer or its complications, perforation played a role in the fatality of eight or 53 per cent. Four of the patients in category 1 who previously perforated (16 per cent) have had subsequent definitive surgery.

In category 3, the subtotal gastrectomies, 29 patients (16.5 per cent) had a history of previous perforation. There were no deaths in those patients who had had previous perforations, a striking contrast to the 16 per cent mortality in previously perforated patients who had no definitive surgery. Of these 29 cases with previous perforations who came to subtotal gastrectomy five had a poor (Class IV) result.

These data on perforation point to the fact that when perforation is later followed by relapse it leads to fatality, re-perforation, obstruction, lasting symptoms and the necessity for subsequent definitive surgery in a higher percentage of cases than in any other sub-group studied.

Perforation has often been considered as an acute problem, as a surgical emergency in which tactics are of importance only in producing survival. In addition, perforation may be an event in the life history of ulcer which should alter our strategy; if followed by even a single relapse it denotes a virulent form of the disease and unless dealt with by definitive surgery bodes ill for the prognosis of the patient. Perforation may come out of a clear sky and the sky may remain clear thereafter; when the sky does not remain clear thereafter, a very bad storm is brewing.

HEMORRHAGE

The incidence and prognostic significance of hemorrhage are a great deal more difficult to quantitate than is the case with perforation. Perforation is an "all or none" phenomenon, an indubitable event in the patient's history not subject to quantitative variation. Hemorrhage by contrast varies from a single

tarry stool to an exsanguinating hematemesis or melena. It would be valid to expect all duodenal ulcer patients to have occult blood in the feces on at least one occasion, when duodenal ulceration is actively occurring; hemorrhage is accordingly somewhat more common than perforation. An attempt to compare hemorrhage with perforation as a determinant of subsequent course has yielded the following facts:

Incidence of Hemorrhage. Of the 997 classified patients, 229 or 23 per cent had a history of previous hemorrhage of sufficient significance to play a prominent part in the history. Multiple previous hemorrhages were by no means rare.

Deaths from acute massive hemorrhage in the whole group were eight (cases 3, 6, 9, 10, 11, 12, 14, 25) of which seven were in the non-surgical category and one (case 25) was treated by subtotal gastrectomy.

Thirty-seven patients had subsequent hemorrhage serious enough to warrant a Poor classification on that account. This yields an overall figure of 274 cases or a 27.5 per cent incidence of significant hemorrhage, twice the 13.5 per cent incidence of perforation.

Fate of Bleeders. Of this entire group of 274, eight are now dead of hemorrhage and seven who had previous hemorrhage of significance in the history are dead of ulcer (cases 1, 2, 8, 17, 23, 27, 28) by mechanisms other than hemorrhage. This yields a mortality of 5.5 per cent, somewhat less than the ulcer mortality in patients with perforation as a feature in the history (9.1 per cent).

Of the 177 classified patients in category I (non-surgical) who had hemorrhage as a prominent symptom in history, 64 or 36 per cent have Poor results as contrasted with the 48 per cent Poor results in the small group of 25 non-surgically treated "previous perforators." The recurrent tendency of hemorrhage is much more striking than perforation. It will be recalled that two of the 85 acute perforators had previously perforated, and that two of the Poor results were due to re-perforation. In contrast, of the 177 classified patients in category I with *previous hemorrhage*, 23 (13 per cent) were classified as poor results because of subsequent non-fatal hemorrhages and eight (4.5 per cent) are dead of hemorrhage. Of the 554 classified patients in category I, with *no previous hemorrhage*, only 12 (2.16 per cent) were classified as Poor results because of subsequent hemorrhage and only four (0.73 per cent) died of hemorrhage.

In the subtotal gastrectomy cases hemorrhage played a role in the indication for surgery in 41 or 23.5 per cent. Of these 41 cases, one (case 25) died postoperatively and three others have Poor results, a total incidence of failure of 10 per cent.

Eleven of the 34 vagotomy patients had previous hemorrhages; none was operated upon for acute massive hemorrhage and none of these 11 had subsequent hemorrhages or class IV results—seemingly a category in which vagotomy was quite effective, although numbers are small.

“Significant hemorrhage” has been loosely applied here and means hemorrhage noticeable enough to be a distinct historical episode to the patient. This seems a reasonable definition for our present purpose, which is specifically to find clues as to ulcer prognosis. Used in this sense, hemorrhage is not as grave a prognostic index for failure or fatality as a perforation followed by ulcer symptoms. All will agree that acute massive hemorrhage in elderly individuals is peculiarly lethal as an ulcer complication and indeed our death list supports such a contention. Taking all hemorrhages rather than this one

TABLE VI.—*Duodenal Ulcer, 1942-1946, Sex Factors in Result.*

Category	Sex	Number Classified	Class I Excellent	Class II Good	Class III Fair	Class IV Poor
1 and 2 Non-surgical	M	628	102 16.2%	181 28.8%	118 18.8%	227 36.2%
1 and 2 Non-surgical	F	180	25 13.9%	60 33.4%	62 34.4%	33 18.3%
3 and 4 Def. surgery	M	166	80 48.3%	48 28.9%	16 9.6%	22 13.2%
3 and 4 Def. surgery	F	23	11 47.8%	5 21.8%	4 17.4%	3 13.0%
Total	M	794	182 22.9%	229 28.8%	134 16.9%	249 31.4%
Total	F	203	36 17.7%	65 32.0%	66 32.5%	36 17.8%
Total		997	218 21.9%	294 29.5%	200 20.0%	285 28.6%

unfavorable group, the long-term outlook is not quite as poor as with past perforation and present symptoms. Perforation is less common than hemorrhage, but if followed by renewed symptoms it is a more certain index of “virulence” of the ulcer process.

OTHER CORRELATIVE FACTORS

Sex. The largest difference between the two sex groups appears in the mortality rate. Although males outnumber females by more than four to one (1004-242) in the entire series, the difference in ulcer mortality was in the proportion of seven to one (3.4 per cent death rate in males, 27 in 794 males; 0.5 per cent death rate in females, one in 203 females). Another striking disparity is in the uneven distribution of the fair and poor results. Although the division of unsatisfactory results (fair or poor) was nearly identical, males had about twice as many poor and about half as many fair results as did females (Table VI).

Age of onset. The age of onset of symptoms was analyzed in this group of patients, but the results were not rewarding (Tables VII-A and VII-B). The age of onset appears to make surprisingly little difference with the possible exception of a tendency towards poorer results in the patients whose symptoms began before the age of 20 or after the age of 65. As is clear from the death list, there is a group of men who acquire a duodenal ulcer when of advanced age. They have a very poor prognosis because of their age and general condition.

Duration of History. The duration of ulcer history as measured from the onset of ulcer symptoms to the date of the follow-up observations is known in 945 cases (Table VIII). The death rate of 13.9 per cent for the ulcers of shortest duration is very interesting. This is given additional meaning when

TABLE VII-A.—*Duodenal Ulcer, 1942-1946, Effect of Onset Age on Result Achieved in Patients Without Definitive Surgery (Categories 1 & 2).*

Onset Age	Number Classified	Result			
		Class I Excellent	Class II Good	Class III Fair	Class IV Poor
10-20 years.....	58	10 17.2%	12 20.7%	14 24.1%	22 38.0%
21-30 years.....	158	19 12.0%	53 33.5%	28 17.7%	58 36.8%
31-40 years.....	209	28 13.4%	56 26.8%	55 26.3%	70 33.5%
41-50 years.....	165	24 14.5%	50 30.3%	34 20.6%	57 34.6%
51 and over.....	154	39 25.3%	52 33.7%	28 18.2%	35 22.8%

it is pointed out that these highly fatal ulcers of short duration are in old individuals who represent the group mentioned in the above paragraph. The consistent similarity of incidence of poor result (medical or surgical) regardless of duration of ulcer history in patients under 65 is quite clearcut.

TABLE VII-B.—*Duodenal Ulcer, 1942-1946, Effect of Onset Age on Result Achieved in Patients With Subtotal Gastrectomy (Category 3).*

Onset Age	Number Classified	Result			
		Class I Excellent	Class II Good	Class III Fair	Class IV Poor
10-20 years.....	22	11 50.0%	5 22.8%	3 13.6%	3 13.6%
21-30 years.....	36	20 55.6%	8 22.2%	4 11.1%	4 11.1%
31-40 years.....	33	18 54.6%	8 24.2%	4 12.1%	3 9.1%
1-50 years.....	37	19 51.5%	7 18.9%	5 13.5%	6 16.1%
1 and over.....	26	15 57.7%	7 27.0%	1 3.8%	3 11.5%

DEFINITIVE SURGERY

The nature and results of definitive surgery carried out at the Massachusetts General Hospital in 1942-1946 have been dealt with in other sections and will not be reviewed here. The definitive surgery carried out elsewhere or outside the 1942-1946 limit of classification will be mentioned briefly (Tables IX and X).

Previous Definitive Surgery. Of the 952 Category 1 (non-surgically treated) patients whose records were abstracted, 15 had previous posterior gastro-enterostomies, an incidence of 1.6 per cent previous attempts at definitive surgery by technical means now regarded as inadequate save in exceptional circumstances.

None of the acute perforating ulcers had previous definitive surgery.

Previously attempted definitive surgery characterized the history of 20 (11.4 per cent) of those patients undergoing subtotal gastrectomy at the Massachusetts General Hospital 1942-1946. Of these, the majority (16) were posterior gastro-enterostomies, the remainder divided between pyloroplasty (2) and subtotal gastrectomy (2).

In the vagotomy group five patients had previous definitive surgery (three gastrectomies, two gastro-enterostomies).

TABLE VIII.—*Duodenal Ulcer, 1942-1946, Effect of Duration of Symptoms on Mortality Rate in 945 Classified Cases Regardless of Treatment.*

Duration	Number Classified	Ulcer Deaths	
		No.	%
Under 2 years.....	72	10	13.9%
2 to 5 years.....	284	3	1.1%
6 to 10 years.....	318	8	2.5%
11 to 20 years.....	188	2	1.1%
Over 20 years.....	83	3	3.6%
Total.....	945	26	2.7%

Thus in 3.2 per cent of the 1246 records was there evidence of a previous operation planned to cure the patient. Many of these had failed by the criteria used herein. As pointed out in the section on "Materials and Methods," our effort has not been to classify previous treatment or treatment in other hospitals, and for this reason the failures of previous medical treatment and of these 40 previous surgical operations do not so appear in the results: they are a part of the history, not a feature of the treatment we are examining.

TABLE IX.—*Duodenal Ulcer, 1942-1946, Incidence of Previous Definitive Surgery.*

Category	Number Abstracted	Previous Definitive Surgery			Total %
		Pyloroplasty	Gastro-enterostomy	Gastrectomy	
1 Non-surgical.....	952	0	15	0	15 1.6%
2 Perforating.....	85	0	0	0	0 0.0%
3 Subtotal gastrectomy.....	175	2	16	2	20 11.4%
4 Vagus resection.....	34	0	2	3	5 14.7%
Totals.....	1246	2	33*	5*	40 3.2%

* In these 38 cases jejunal ulcer was present or suspected at the first Massachusetts General Hospital Admission.

In the 997 classified cases there were 18 instances where posterior gastro-enterostomy was followed later by subtotal gastrectomy for jejunal ulcer. The length of time intervening between the posterior gastro-enterostomy and the development of symptoms of jejunal ulcer (duration of relief from posterior gastro-enterostomy) shows two patterns. One-half the cases had relief ranging from zero to three years (average 1-3/12 years); the other half ranged from

three to 23 years (average 11-5/12 years with six cases over ten years of relief).

Subsequent Definitive Surgery. Subsequent to the 1942-1946 episode at the Massachusetts General Hospital there were 67 definitive surgical operations, all of which constitute *prima facie* evidence of failure of the 1942-1946 treatment (whether medical or surgical) by definition of Class IV c (poor result due to necessity for subsequent definitive surgery).

Of those subsequent operations, 14 were carried out at the Massachusetts General Hospital after 1946, 53 at outside hospitals. It is clear that a research method confined to record analysis would have overlooked 80 per cent of the subsequent surgery.

Five of the subsequent 67 operations were carried out on patients treated by definitive surgery at the Massachusetts General Hospital, 1942-1946. Two of the gastrectomies had to be re-operated upon (one by re-resection and one

TABLE X.—*Duodenal Ulcer, 1942-1946, Incidence of Definitive Surgery Subsequent to Admission in Classified Patients.*

Category	Number Classi- fied	Def. Surg. M.G.H. '42-'46	Definitive Surgery Subsequent to Discharge							Total	%
			M.G.H.		At Other Hospitals			Vagus	Unknown		
			Stg.	Pge.	Stg.	Pge.	Pge.				
1 Non-surgical.....	738	0	10	1	34	5	6	2	58	7.9%	
2 Perforating.....	70	0	1	0	1	1	1	0	4	5.7%	
3 Subtotal gastrectomy..	155	155	0	0	1	0	1	0	2	1.3%	
4 Vagus resection.....	34	34	2	0	1	0	0	0	3	8.8%	
Totals.....	997*	189	13	1	37	6	8	2	67	6.8%	

Total definitive surgery at Massachusetts General Hospital, 204 (20.4%).
 Total definitive surgery at other hospitals subsequent to M.G.H. admission, 53 (5.3%).
 Total definitive surgery subsequent to M.G.H. admission, 256 (25.7%).
 Per cent of definitive surgery carried out elsewhere, 20.6%.

by vagotomy); three of the vagotomies required re-operation, all by gastrectomy.

The remaining 62 operations were carried out on patients who received no definitive surgery at the Massachusetts General Hospital, 1942-1946, 58 in the category 1 patients and four in patients who perforated just prior to their Massachusetts General Hospital admission. In all these instances the progressing ulcer process required surgery despite attempts to control the situation non-surgically; this further event in the history of the disease took place at the Massachusetts General Hospital in 12 cases, elsewhere in 50.

In summary, of the 1246 patients whose records were abstracted, 40 had had previous definitive surgery; 189 had surgery at the Massachusetts General Hospital, 1942-1946; of the 997 classified patients, 67 had subsequent definitive surgery. *Leaving out repeated operations on the same individuals,* the total incidence of definitive surgery in the group studied is about 25 per

cent. This figure is a first approximation because of the heterogeneous group from which the percentages are taken. It is probably accurate to state that between 24 and 26 per cent of these patients had at one time or another up to completion of follow-up an attempted definitive operation.

DISCUSSION

Despite the unity of ulcer disease as demonstrated by the patterns of failure, there is clearly a spread in the intensity with which this disease may occur in individual patients. Certain evidences may suggest that the disease is capable of rapid and penetrating tissue digestion. Chief among these are perforation and bleeding. Persistent severe pain is apparently a manifestation of this progression, although more difficult to define statistically. The consistently better results obtained by subtotal gastrectomy and the lack of late ulcer deaths in those operated on in the Massachusetts General Hospital, 1942-1946, would argue strongly for the performance of this operation as soon as progressive ulcer disease can be diagnosed. Before embracing this conclusion wholeheartedly, we must point out that the subtotal gastrectomy group consisted largely of middle-aged patients, and that another ten or 20 years must pass before we can state that they have had a lower incidence of late ulcer deaths than the non-surgical patients. There is no question about their greatly improved results in terms of medical and economic rehabilitation; no further time is needed to establish a significant percentile difference here.

In reviewing the non-surgically treated patients, one is impressed by the large number of individuals who have ulcer symptoms on one or two occasions, sometimes even with hospital admissions, but who then undergo some change—organic, psychiatric, or environmental—which holds the ulcer diathesis in check for many years. It is significant that this benign form of the disease occurs much less commonly when a past perforation is followed by renewed symptoms, when hemorrhage is part of the history, when pain is not amenable to management and when onset is at the extremes of life. Males are universally less fortunate than females in this regard. When these ill omens are present we should make a new diagnosis, that of “progressive” or “virulent” ulcer disease. This diagnosis places the patient in the worst prognostic group of duodenal ulcer and serves as a guide to treatment.

In treating such a patient, definitive surgery appears about twice as likely to give a good result as does avoidance of that surgery; his likelihood of dying from ulcer has apparently diminished if he is given definitive surgery.

The patient with a recurrent ulcer without hemorrhage or perforation but with recurrent pain is the most difficult to classify. Whether he should or should not have definitive surgery is difficult to state categorically and most surgical pronouncements have been conservative on this score. Control of ulcer symptoms on “ideal hospital management” is useful diagnostically and as a preparation for surgery but has been a false idol in non-surgical management. The fact that a patient is well handled by the practice of physic on a

hospital ward does not signify satisfactory management when the same patient returns to home, family and business. He must live his life among the latter and it is to symptom-freedom in that environment that attention should be directed. If it cannot be secured in a reasonable time, surgery should be undertaken.

It should be mentioned that obstruction does not acquire much if any importance in this study. Obstruction due to "spasm" or "edema" is a symptom of acute activity. Cicatricial obstruction is a late result of an old organic disease and it has little prognostic significance since it is occurring at the end of the life history of a disease and in itself requires relief, wholly aside from any remaining ulcer activity. There have been no patients with persistent obstruction successfully carried on medical measures; this was attempted in some cases, the physicians being unaware of the continued presence of partial obstruction.

Finally, we would do well to omit the "intractable ulcer" from our vocabulary. What is meant is that the patient's disease is of the "progressive," or "virulent" variety, a diagnosis which can often be made long before enough therapeutic failures have accumulated to justify the term "intractable." The nicety of ulcer care in future years lies in the diagnosis of progressive or virulent ulcer disease and its appropriate treatment before failure has occurred to an extent which justifies the use of the term "intractable." At the time of this writing there is nothing to offer the patient that is effective, yet less radical than subtotal gastrectomy. More evidence by careful comparative follow-up must be accumulated on patients undergoing vagotomy or vagotomy with anastomotic combinations, before we can confidently eliminate gastrectomy as the most effective form of definitive treatment for progressive virulent duodenal ulcer.

FORMULATION

I. On the basis of these data it is possible to advance a set of primary and secondary criteria for the diagnosis of progressive or virulent ulcer disease:

A—Primary criteria

1. One perforation in the past, with present ulcer symptoms.
2. One acute hemorrhage requiring blood transfusion.
3. Progressive pain over a two-year period under a physician's care and advice in the patient's normal living environment, at work.

B—Secondary criteria

1. A male with duodenal ulcer symptoms under a physician's care.
2. A male with onset of symptoms prior to the age of 20 or subsequent to the age of 65.

II. If two of these criteria, at least one of which must be primary, are present, the diagnosis of progressive virulent ulcer disease may be considered established.

III. Once established, the outlook for a satisfactory result on non-surgical management is poor and the intrinsic mortality elevated.

IV. If surgical skill and facilities are available for accomplishing subtotal gastrectomy with a low mortality, the patient should be offered this procedure.

V. If three criteria are present, such surgery should be urged. Symptomatic alleviation under hospital conditions does not alter the importance of these criteria. Obstruction is an end-stage in the natural history of ulcer, and in itself requires operation for relief; it therefore does not appear amongst these diagnostic criteria.

VI.—If subtotal gastrectomy cannot be safely accomplished under the conditions available, we have no irrefutable evidence that other operations can replace it.

SUMMARY

1. The records of all the duodenal ulcer patients managed with or without surgery at the Massachusetts General Hospital during the years 1942-1946 have been abstracted and reviewed; 1246 such records were reviewed.

2. Nine hundred and ninety-seven of these patients have been followed to mid-1949 and enough data collected to form a valid clinical judgment as to the success of their regimens in 1942-1946 and thereafter.

3. These results have been classified by the same criteria whether the technics and skills of medicine or surgery formed the predominant feature in the management of the patient.

4. The concept of "progressive" or "virulent" duodenal ulcer disease emerges as expressing the outstanding feature of that fraction of the ulcer population who do poorly without definitive surgery.

5. The occurrence of a past perforation with present symptoms, an acute hemorrhage, progressive pain under a physician's care at home, or onset at the extremes of life in male patients are clues to this diagnosis.

6. The mortality from hemorrhage, perforation and late obstruction in non-operated patients appears to balance the intrinsic hospital mortality of definitive surgery.

7. Following definitive surgery only half as many patients have an unsatisfactory result in symptomatic or economic terms as do those managed without surgery.

8. One is led therefore to the conclusion that the diagnosis of "duodenal ulcer" is not enough. Once this general classification is made by the usual methods, the doctor must proceed to the consideration of a more important diagnosis: "progressive virulent ulcer disease."

9. When established, the diagnosis of progressive virulent ulcer disease is the key to the prognosis; a definite decision as to surgery should be made. Our data indicate that subtotal gastrectomy should be undertaken.

10. Such a conclusion can be acted upon conscientiously only when the surgical skill and facilities are available to permit performance of subtotal

gastrectomy with an acceptable mortality. A policy for each hospital can only be made after critical study of its own cases.

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