CANCER OF THE STOMACH

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FOREWORD

THE PAUCITY of knowledge with respect to the etiology of malignant growths and the resultant absence of a completely effective therapeutic approach thereto has led to the avid search for early malignant lesions amenable to current methods of treatment. In the past 20 years significant advances have been made in the discovery of early cancers of various organs, with large series of possibly curable carcinomas being reported. Recent advances in gastric cytology show promise, but currently the diagnosis of gastric cancer is often made first in the pathology laboratory after removal of a lesion that is suspected of being malignant.

The aphorism, "there is no subject in medicine that will not bear reinvestigation," continues to be true. This is especially so with regard to gastric cancer. Cancer is a continuous challenge to the medical profession, and the responsibility of the profession cannot be lessened by overemphasis given to failure of the public to profit by an educational program directed toward the early investigation of those signs or symptoms that may herald the beginning of an actual or potential malignant process.

Twenty years ago the responsibility for allowing cancer of the stomach to reach an advanced stage before the first opportunity for treatment was made available was shown to be due to neglect, ignorance, or pessimism on the part of the public and incomplete examinations, erroneous interpretations of symptoms and findings, or even pessimism on the part of the medical profession. This continues to be true today, although to a somewhat less extent. There is a continuing challenge to surgeons and the surgical profession to strive toward reduction of the discrepancy between incidences and operability. The authors of this book have shown that in the experience of the Mayo Clinic a marked improvement in this direction has, indeed, taken place. They and their associates have shown that exhaustive concentration of effort is worth while.

The experience of the authors and their associates has been accumulated and evaluated with particular attention to the features of the disease

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that seem to offer, in their coordination, a plan by which the general management of the disease can be made more effective. The factors governing prognosis of cancer of the stomach are as varied as those in relation to cancer in any situation in the body, and since cancer lends itself to statistical investigation perhaps more readily than any other disease, careful study of these factors has unusual significance. If there is any value in such a detailed study of a large number of cases of a disease in which the manifestations are so variable as to make early detection difficult, a disease which also demands most exacting care in its surgical management, this monograph will serve a useful purpose.

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PREFACE

IN THE FOREWORD to the book "The Stomach and Duodenum" by Drs. G. B. Eusterman and D. C. Balfour and our colleagues at the Mayo Clinic in 1935, Drs. William J. and Charles H. Mayo commented as follows: "Here a group of men . . . have presented . . . not the general opinions of a number of men, but the opinion of a group who are working together as one man on the patient, in the attempt to give the patient the advantage of what is known. This book serves to present in coördinated form what we have learned in an important field of medicine." Happily this statement continues to apply to this book written by different members of the Staff of the Mayo Clinic in cooperation with Drs. ReMine, Priestley, and Berkson.

It is interesting to note that the percentage of patients with cancer of the stomach who undergo operations has increased and the proportion of those whose lesions were resected has increased also. The result is an increase of the over-all 5-year survival rate. It is interesting, too, that the ratio of total gastrectomies to partial gastrectomies performed at the Mayo Clinic during the last 15 years was approximately 1 to 5.5. Reports show a 10 per cent 5-year survival rate among the 242 patients who underwent total gastrectomy for carcinoma at the Mayo Clinic prior to 1957.

Improvement in results over the years has been attributed to the fact that more patients have undergone exploratory operations and resections and to the fact that more extensive operations, including the removal of lymph node-bearing tissues and portions of adjacent viscera, have been performed with lowered mortality rates. The decrease of the mortality rate has been due to improvements in preoperative and postoperative care and to the applicational refinements in anesthesia and in surgical technic. Total gastrectomy has been performed only in those cases in which subtotal gastrectomy would not remove the entire lesion.

It is rather significant that, while the mortality rates from cancer of the stomach in certain races, particularly the Japanese, is high and has increased somewhat in recent years, the death rate from cancer of the

stomach in the United States is relatively low and has been steadily declining for many years. This reduction might indicate that the incidence of cancer of the stomach has decreased in the United States, perhaps as a result of a change in the constitutional make-up of the present adult population related to the epochal lowering of death rates in the younger ages of life which has taken place in our time. It might, however, indicate that cancerous gastric lesions are being recognized earlier in the United States and that earlier and more extensive operations are being performed with less risk, resulting in a considerable increase in the 5-year survival rate of all patients with cancer of the stomach.

In addition to a thorough discussion of the diagnosis and treatment of malignant lesions of the stomach, the reader will find in this book the contributions of the many specialists participating in its preparation, and I believe it will serve to stimulate a broader understanding of the problem of gastric carcinoma and its treatment.

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CONTENTS

CHAPTER 1

Historical Review of Surgical Aspects of Carcinoma of the Stomach

WILLIAM H. ReMINE

AVICENNA first recognized and described the symptoms and findings in carcinoma of the stomach in the beginning of the eleventh century.[90, 96] Hippocrates and Galen had made previous references to what in retrospect may be interpreted as gastric malignancy. Among the numerous early references to and descriptions of carcinoma of the stomach in the literature were the excellent detailed descriptions by Aussant, Chardel, Laennec, and Otto that appeared in the first years of the nineteenth century. These, however, were for the most part without benefit of any scientific confirmation.

Merrem, in 1810, was the first to report experimental work that could be directed toward the alleviation of this disease. He reported successful pylorectomy on three dogs. He also alluded to similar experimental work carried on by other investigators.

Bayle published an entire book in 1839 dealing with the problem of gastric malignancy which was so far ahead of its time that little, if any, attention was paid to it. The description of the symptoms and the lesions was classic, and great stress was laid on the importance of early diagnosis.

The first attempt to distinguish between benign and malignant gastric ulceration and also to point out the presence of the benign lesion was that of Cruveilhier in 1830.

The first big impetus to the improvement of the diagnosis of cancer of the stomach was given in 1879 by von den Velden when he showed the value of gastric analysis in fairly advanced cases of the disease. The next big advance in methods of diagnosis came around 1910, when the German roentgenologists perfected the technic of roentgenoscopy.

INTRODUCTION OF PARTIAL AND TOTAL GASTRECTOMY

Seventy-one years after Merrem's work, Billroth,[6-9, 37, 38] in 1881, accomplished the first successful partial gastrectomy in the human. In this

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first procedure Billroth sutured the end of the stomach to the duodenum, decreasing the circumference of the stomach by sutures placed in the vicinity of the lesser curvature. A similar type of operation had been performed by Péan[6, 70, 71] previously, but as his patient failed to recover, his place as a pioneer surgeon frequently is overlooked. In view of the fact that Billroth a few years later abandoned this type of anastomosis for an indirect one of stomach to jejunum which has been called the "Billroth II operation,"[39] it might be well to call the Billroth I operation the "Péan-Billroth procedure."

Since this momentous break-through in 1881, extensive studies have been made on the surgical treatment of carcinoma of the stomach. The history of the development of gastric surgery is filled with the names of men who contributed to this area and to the general field of surgery as well.

Connor, in this country, made the first attempt at total gastrectomy in 1883. In his case the shock of the operation prevented anastomosis from being attempted.

Schlatter, in 1897, performed the first successful total gastrectomy on the human being. His patient survived 1 year and 53 days after gastrectomy and esophagojejunostomy. In this manner procedures were established which have formed the basis for all of our present-day surgical treatment of carcinoma of the stomach.

Brigham and MacDonald, in 1898, reported additional cases in which total gastrectomy was employed. Since that time an increasing number of reports on total gastrectomy have appeared in the literature. Moynihan, in 1903, reported a case. W. J. Mayo, in 1918, accomplished total gastric resection on a patient who survived for more than 4 years. It was not until Finney and Reinhoff, in 1929, collected 122 cases from the literature that the first adequate appraisal of the procedure could be made. In 67 of the 122 cases in their study, the operation was classified as a true total gastrectomy, in the remaining 55 cases a small portion of the stomach was left with which to make the anastomosis. Of the 67 patients treated by true and complete gastrectomy, 36 failed to survive the hospital stay, a mortality of 53.7 per cent.

FURTHER DEVELOPMENT OF SURGICAL PROCEDURES

During the early years of gastric surgery a number of procedures were developed which continue to be well known to us today. Among these was that of Schoemaker,[81, 82] who closed the lesser curvature portion of the stomach so that the remaining circumference of the stomach could be approximated to the cut end of the duodenum as in performing the Billroth I procedure. This was accomplished by the use of a special clamp devised by Schoemaker. C. H. Mayo and W. J. Mayo obtained the same

result by using two curved clamps across the lower half of the stomach; the second was placed almost at right angles to the first clamp to take out a portion of the lesser curvature.[90] (See also Chapter 8.) Horsley,[41] in 1923, suggested that the duodenum be sutured to the lesser curvature rather than to the greater curvature of the stomach. The difference in the circumferences of the two was compensated for by a longitudinal incision down the anterior wall of the duodenum; the greater curvature portion of the stomach was not included in the anastomosis and was closed by sutures. Von Haberer[35, 36] modified the procedure somewhat and described it in 1922 and again in 1933.

In 1888 von Eiselsberg first performed the modification now widely known as the Hofmeister[87] type of Billroth II operation. He described this modification in 1889 and advised closure of the upper portion of the cut end of the stomach and use of only the lower portion to establish continuity with the jejunum after gastric resection.

Pólya's[72] report in 1911 on the modification now bearing his name was widely recognized at the time. It has been said, however, that von Hacker[39] really first suggested the end-to-side gastrojejunostomy in 1885, and Krönlein[44] apparently was the first to perform this type of anastomosis in 1887. Pólya[73] readily admitted that he was perhaps not the first to utilize this method but was unable to find descriptions of it in the textbooks and journals which were accessible to him at the time. Pólya stated further, "The great majority of surgeons, however, did not know of the method at all until I called it to the attention of the surgical world, and especially to the attention of William Mayo who saw in it the operation of the future and whose endorsement helped make it the one most widely adopted."

In the Pólya modification the cut end of the duodenum is closed and a loop of jejunum is brought up through an opening in the mesocolon to form an end-to-side anastomosis with the cut end of the stomach. Balfour, in 1917, modified the procedure further. At this time he utilized a loop of jejunum which he brought up anterior to the colon. He also suggested the advisability of establishing entero-anastomosis at the dependent part of the afferent loop with the distal loop of jejunum.

Numerous other modifications of the original Billroth II procedure have been suggested, most of which have some merit. In most instances, however, the basic principle of the Billroth II procedure has been retained.

Livingston and Pack, in 1939, discussed the end results of treatment of gastric cancer and gave an analytical and statistical study of the experience to that date.

ANAPLASIA AND SPREAD

Von Hansmann,[90] around the turn of this century, carried on an extensive investigation and brought forth the concept of anaplasia. He

further suggested that noncancerous cells change to malignant cells by such a process. He observed that the greater the degree of anaplasia the greater the tendency to metastasize. He further noted that the degree of anaplasia was not the same in all tumors and that the degree of anaplasia in metastatically involved lymph nodes was the same or greater than that of the primary lesion but was never less.

Cunéo, in 1900, made the first extensive study of invasion of the gastric wall by carcinoma and reported the general tendency of carcinoma of the stomach to spread toward the lesser curvature and to involve the various groups of nodes. He also studied the gastric lymphatics and their influence on intramural spread of the malignant lesion of the stomach.

THE LYMPHATIC SYSTEM OF THE STOMACH

Jamison and Dobson, in 1907, published an extensive study of the lymphatic system of the stomach. They found an unexpected connection between the lymph vessels of the stomach and nodes which seemed from their position to be totally unconnected with it. They listed the various lymph node groups of the stomach as follows: (1) lower coronary, (2) upper coronary, (3) right paracardial, (4) left paracardial, (5) posterior paracardial, (6) splenic, (7) right gastroepiploic, (8) subpyloric, (9) suprapyloric, (10) suprapancreatic, and (11) celiac. The name "celiac nodes" is used loosely to define that row of lymph nodes which lies along the superior border of the pancreas. This group of nodes receives vessels from distinct areas of the stomach.

In 1913, Delamere, Poirier, and Cunéo described the gastric lymphatic system as consisting of two primary groups. The first group was the mucosal group and the submucosal network which in turn connects with the second primary group, the seromuscular network.

One of the best and more recent extensive studies of the perigastric lymphatic drainage was made in 1941 by Coller, Kay, and McIntyre. Rouviere, in 1938, published an anatomy of the human lymphatic system. Berry and Rottschafer, in 1957, also published an excellent study on lymphatic spread of cancer of the stomach seen in operative specimens.

The importance to the surgeon of familiarity with areas of lymphatic drainage cannot be overemphasized in the removal of gastric carcinoma as well as of most other malignant lesions.

PROGNOSTIC CRITERIA, OPERATIVE RESULTS AND RECOMMENDATIONS

Efforts to establish prognostic criteria by study of the gross and microscopic findings in surgical specimens of carcinoma of the stomach have been made by Broders, MacCarty and Mahle, Borrmann and Dochat

and Gray, among others. The prognostic significance for each classification has been sought.

In 1921, Broders published his work on the microscopic grading of squamous cell epithelioma of the lip. This grading was extended to carcinoma of the stomach by MacCarty and Mahle.

Borrmann, in 1926, reported a classification based on the gross appearance of malignant lesions of the stomach. The following is a summary of this classification which will be referred to later in the text:

Type 1: Polypoid carcinoma.

Type 2: Sharply defined ulcerating lesions surrounded by an elevated ridge.

Type 3: Sharply defined ulcerating lesions except that one edge blends with the surrounding mucosa and is diffusely infiltrated.

Type 4: Diffusely infiltrating carcinomas with no sharp limit.

Verbrugghen, in 1934, studied the intramural extension of gastric carcinoma with relation to prognosis. This investigator found the submucosa to be the favorite plane for lateral extension.

In 1934, Comfort and Vanzant among others investigated gastric acidity in carcinoma of the stomach. Comfort, Butsch, and Eusterman, in 1937, reported their observations on gastric acidity before and after development of carcinoma of the stomach.

Whipple and Raiford, in 1934, correlated the type and grade of gastric carcinoma in relation to operability and prognosis. These authors found that in 56 per cent of the cases in which resection was carried out the carcinoma had metastasized to the lymph nodes, but none of the 5-year survivors had nodal involvement.

Schindler and co-workers, in 1941, concluded that gross typing was more valuable to them than microscopic grading. Schindler again advocated gross typing in 1946.

Dochat and Gray, in 1943, studied prognosis of carcinoma of the stomach using a combination of Dukes' and Broders' methods of grading. They concluded that the use of the two methods together was superior to the separate use of either one.

Morton, in 1940, in an editorial suggested that since the results of surgical treatment of carcinoma of the stomach were so poor, perhaps total gastrectomy might be the operation of choice for all gastric carcinoma.

Coller and associates, in 1941, concluded that often the associated gastric nodes are inadequately excised because the lesion is extensive and only a palliative operation is done, because nodes are not palpable, or because the surgeon is not making a conscientious attempt at complete removal of the carcinoma. They concluded also that contiguous lymph nodes need not be involved in order to have distant lymphatic involvement. In the majority of their cases of carcinoma of the stomach in which regional nodes were not palpable or if palpable were not thought to be

suggestive of malignancy, the carcinoma was subsequently shown to have metastasized.

In 1942, Walters, Gray, and Priestley published an exhaustive study of carcinoma of the stomach. They found nodal metastasis in 53.6 per cent of cases.

In 1944, St. John, Swenson, and Harvey wrote that to that time in their hospital only four patients had survived for 5 years after resection of the stomach for carcinoma with nodal metastasis.

In 1948, Steiner and associates reported on 30 patients who had survived for 5 years after gastric resection for carcinoma. Six of these survivors were reported to have nodal metastasis. These authors concluded that involvement of regional lymph nodes should not obviate attempts at surgical care.

Also in 1948, Pack and McNeer[68] reported the results of a study in which 30.8 per cent of the long-term survivors had nodal metastasis.

At the same time, Hebbel and Gaviser studied the relationship between gross appearance of gastric carcinoma and anacidity. These authors concluded that there was a uniform association between carcinoma of Borrmann's type 1 and achlorhydria but there was no constant association between the gastric acids and types 2, 3, and 4.

In addition to these studies, numerous significant reports[27, 29, 32–34, 42, 46–49, 52, 56–58, 68, 69, 74, 83, 85, 91–93] appeared in the literature from 1940 to 1950.

McNeer and associates,[61] in 1951, reviewed 92 necropsy specimens after partial gastrectomy for carcinoma and found recurrence in the gastric remnant in half of the cases; in 14 per cent of such cases the recurrence was in the duodenum and in 22 per cent it was in the perigastric lymph nodes. These authors[60] later suggested that a more radical operation should be attempted and offered as the technic for such a procedure a radical total gastrectomy, partial pancreatectomy (tail), and splenectomy.

Allen, in 1951, discussed the problem of recurrences in the gastric remnant and suggested that frozen-section microscopic examination of the stomach at the edge of the resection at the time of operation would obviate the frequent finding of neoplasm in the gastric remnant. He did not think that total gastrectomy was the operation of choice for all carcinomas of the stomach. He said that it should be reserved for use in those cases in which it was necessary to get around the entire lesion.

In a study[76] at the Mayo Clinic, in 1952, the late results of total gastrectomy in 170 cases of carcinoma of the stomach were reviewed. Lymph nodes were involved in 78 per cent of the 170 patients; 18 per cent of the patients traced survived for 5 years. One patient out of 10 (10 per cent) who had a malignant lesion in the distal part of the stomach lived for 5 years after total gastrectomy. Lesions of grade 3 or 4 malignancy (Broders' classification) were found in 85 per cent of the 170 patients; yet none of the 5-year survivors had had lesions of grade 3 or

4 malignancy. The conclusion from this study was that total gastrectomy was not the operation of choice for all gastric carcinomas.

In a study reported[75] from the Mayo Clinic in 1953, great attention was paid to the lymph nodal involvement from carcinoma of the stomach. The distance of the involved lymph nodes from the nearest edge of the lesion and involvement of the subpyloric lymph nodes were found to be of great prognostic significance. (These factors will be discussed in detail later.)

Eker and Efskind, in 1960, carried out an extensive study on the pathology and prognosis of gastric carcinoma. Their study was based on 1314 cases in which partial resection was performed.

Many other well-known surgeons have made timely and substantial contributions to the literature and to the field of gastric surgery. Obviously, it is impossible to include all of these in a work of this kind since in many instances it is exceedingly difficult to separate the surgery of the stomach and duodenum for benign disease from that strictly related to carcinoma and other malignant lesions.

In more recent years the theory of biologic predeterminism in patients having gastric cancer has been discussed in the literature on several occasions. MacDonald and Kotin, in 1954, Blalock and Ochsner, in 1957, and Brown, Merlo and Hazard, in 1961, suggested that a long preoperative history affords as good or better prognosis than a short one.

COMMENT

That many patients have been cured of gastric carcinoma for 5, 10, 15 years or longer by appropriate surgical treatment is well attested by the literature.[14, 25, 30, 31, 50, 62, 66, 94] This is an important fact to remember since a defeatist attitude concerning gastric carcinoma is sometimes expressed in an unjustifiable manner.

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