Carcinoma of the Stomach

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The first surgical attack on carcinoma of the stomach was performed by Theodore Billroth in 1881. Although his patient survived this first gastric resection for cancer, rapid “recurrence” soon followed. Today, despite improved therapeutic success with gastric cancer due largely to the availability and feasibility of more radical and thorough resectional procedures, the overall control rates remain quite low. Indeed reduced mortality from this disease in the United States has been more affected by a progressively declining incidence rate than by radical surgical procedures. (Fig. 1.)

For completely unknown reasons the incidence of carcinoma of the stomach in both men and women in the United States has continued to decline over the past 30 years. In 1930, carcinoma of the stomach was the most frequent cause of death from cancer in the United States. Comparison of the two-year U.S. cancer mortality figures for 1950-1952 and 1965-1967 demonstrates a 46 percent decline in incidence in males and a 49 percent decline in females. Nonetheless, gastric cancer will cause an estimated 15,000 deaths in the United States this year. It is usually more common in males than in females (two to one), in blacks than in whites and in patients between 50 and 70 years of age.

The changing incidence of carcinoma of the stomach is not a world-wide phenomenon. Certain countries, particularly Japan, Chile, Iceland and Finland, have a higher incidence of gastric carcinoma than the United States. More than half of the male cancer deaths in Japan are due to gastric cancer and the disease occurs at a much younger age than generally seen in this country.

Dietary habits may well be an important factor since countries with a high incidence of gastric carcinoma have different diets from our own. Most countries with a high incidence of gastric cancer consume large amounts of smoked food (particularly fish and mutton) which contain potential carcinogens, but specific causative factors are not yet defined. It has also been suggested that the decreasing incidence of gastric cancer in the United States may be related to the widespread consumption of wheat cereals rich in antioxidants and the extensive use of food antioxidant preservatives; antioxidants prevent carcinogenesis in mice, possibly by decreasing the attachment of the carcinogen to DNA. Gastric carcinoma is more frequent in the northern United States than in the south which may be related to differing dietary habits or preservatives, or to the higher proportion of foreign-born people in the northern states. It has

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also been shown that socioeconomic status has a definite relationship to the incidence of carcinoma of the stomach in the United States, Denmark, England and Wales but the reasons are unclear. Some investigators have suggested that the type of soil has bearing on incidence and that gastric cancer is more frequent in regions where crops are raised in peat soil than in sandy soil. This is a nebulous area, and it is most difficult to prove these possible etiologic relationships.

It is well known that carcinoma of the stomach is more frequent in certain families—the family of Napoleon Bonaparte is often cited in this regard—and in people with blood type group A, but several studies tend to discount the significance of these factors.

There is also some concern about the relationship between carcinoma of the stomach and potential premalignant lesions. In contrast to the possible relationship between adenomatous polyps and colon cancer, the adenomatous polyp of the stomach occurs too infrequently to be considered a significant potential precursor of gastric cancer.
the patient with gastric carcinoma, the common denominator is atrophic gastric mucosa (or "atrophic gastritis"). As might be anticipated, atrophic gastritis is usually seen in patients in older age groups. When severe changes occur, achlorhydria may develop resulting in complete atrophy of the fundal mucosa and pernicious anemia. Patients with achlorhydria are 4.5 times more likely to have carcinoma of the stomach than patients of the same age group with normal gastric acid production; patients with achlorhydria and pernicious anemia have 18 times the anticipated incidence. Although the atrophic gastric membrane is associated with both gastric polyps and carcinoma, the atrophic change is probably the true precursor lesion.

In terms of gross pathology, carcinoma of the stomach presents a number of gross configurations ranging from a large bulky polypoid mass bulging into the lumen of the stomach, to the infiltrating, poorly defined, anaplastic lesion that may not cause visible alterations on the mucosal surface. (Fig. 2.) Other neoplastic lesions which present as chronic ulcers in the stomach are occasionally difficult to differentiate from benign gastric ulcers, even under direct vision, and still other lesions present as various combinations of these gross types. The wide range of pathologic presentations may actually have etiologic implications. Other malignant neoplasms of the stomach, particularly the sarcomas, can occur but more than 95 percent of gastric cancers are carcinomas.

**Clinical Diagnosis**

The history and physical examination of patients with curable gastric cancer often reveal nonspecific findings which may make diagnosis difficult. We found vague symptoms of "indigestion" in over 80 percent of patients in our series; the typical "ulcer syndrome" or periodic pain relieved by food intake was discovered much less frequently—10 to 12 percent. Nausea and vomiting, fullness after meals, weight loss, hematemesis, melena or even free perforation on occasion are other common symptoms of gastric cancer. Dysphagia is often the presenting complaint in patients with lesions of the cardia. Only five to six percent of patients in our series had no gastrointestinal symptoms; in this group, unexplained weight loss or severe anemia from blood loss prompted a gastrointestina work-up. Some patients with gastric cancer who have a mass in the upper portion of the abdomen—a finding that implies a lower chance of resectability—are still in a curable stage of disease.

There are rather characteristic findings in the patient with metastatic disease. The most frequent sites of metastases are the cervical lymph nodes (Virchow's nodes), peritoneum (as manifested by ascites and/or Blumer's shelf), and the liver. The patient with unequivocal evidence of such metastases prior to laparotomy is usually considered "inoperable." Ovarian metastases (Krukenberg tumors) can be large, and occasionally a pelvic mass is the initial finding.
Fig. 2. Variations in the gross pathology of carcinoma of the stomach

2a. Polypoid carcinoma (Borrmann, Group I)

2b. "Ulcerocancer" (Borrmann, Group II)

2c. Ulcerating, infiltrating carcinoma (Borrmann, III)

2d. Anaplastic, infiltrating carcinoma (Borrmann, IV)
Lung, brain, skin, bone or bone marrow metastases can occur, but the clinical evidence of metastatic disease in these sites should generally lead one to suspect the validity of the diagnosis of gastric cancer. Despite the clinical rarity of lung metastases, autopsy studies revealed an unexpectedly high incidence of such metastases (25 percent) at the time of death. \(^{11}\)

Since history and physical examination are rarely rewarding unless the patient has advanced disease the classic method for diagnosing gastric carcinoma is radiologic. Radiologic techniques for identifying small inconspicuous lesions of the stomach have been improved, a factor that may lead to the "earlier" diagnosis of gastric carcinoma or premalignant lesions and might improve the high mortality. (Fig. 3.) No concerted effort has been made in this country to accomplish earlier radiologic identification of potential cancers, but refinements of radiologic and endoscopic techniques for identifying asymptomatic gastric lesions have been made in Japan where there is a high incidence of this disease. These technical developments may have a favorable influence in the United States.

The increasingly widespread use of gastric cytology as part of the routine evaluation of upper gastrointestinal symptoms is a favorable trend in the diagnosis of potentially curable gastric cancer.\(^{12,13}\) In our experience, careful cytologic study has detected un-
suspected neoplasms in a number of patients with minimal symptoms and questionable radiographic abnormalities. (Fig. 4.) Occasionally, cytologic findings indicate the need for surgical exploration of the stomach that appears radiographically to house a benign ulcer. Although the absence of cancer cells in a gastric aspirate obviously does not guarantee the absence of cancer, cytology is an extremely valuable tool for increasing the collective accuracy of radiography and endoscopy and should now be used in the diagnostic evaluation of all patients with suspicious gastric lesions.

Another advance is the fiberoptic gastroscope, an instrument that has revolutionized gastric endoscopy by making it easier on both the patient and the operator. The added value of easily visualizing (and photographing) gross pathology in the stomach has led to the use of endoscopy in patients with symptoms and radiographic findings that were considered, in the past, too insignificant to merit the rigor of endoscopy with the then available equipment. (Fig. 5, p. 292.) Thorough evaluation of gastric lesions does not always require gastroscopy, but evaluation of the poorly defined lesion or the gastric ulcer that will be managed without operation will be strengthened by endoscopic study.

In addition to radiology, endoscopy and cytology, we have a new tool that may eventually prove useful in the selection of patients for aggressive work-up: carcinoembryonic antigen (CEA), a tumor-associated antigen initially found in the serum of patients with carcinoma of the colon. As experience with this type of assay is accumulated, it becomes evident that the patient with other cancers, particularly those in the gastrointestinal tract, may have elevated levels of this antigen. Although still under study, the use of CEA to screen asymptomatic populations may eventually result in earlier diagnosis. A disturbing finding thus far is the direct relationship between the amount of circulating antigen and the bulk of the neoplasm, but the true potential for this immunologic assay must still be determined.

Fig. 4 Cytologic study of gastric aspirate demonstrating carcinoma.
The presence of an ulcerating lesion in the stomach is a most troublesome diagnostic problem. Much controversy has been generated over the diagnostic and therapeutic management of the patient with a gastric "ulcer" on radiologic examination. Carcinoma of the stomach can masquerade as a benign lesion radiologically, and although cytologic examination or gastroscopy may reveal malignancy, subsequent negative findings on such supplementary examinations are not absolute insurance that the lesion is benign. Many physicians generally use an intense therapeutic trial with careful follow-up examination as a further diagnostic method. Neither the relief of symptoms nor radiologic "improvement" is a true guarantee that the underlying lesion is not an "ulcer-cancer," but significant improvement on radiologic examination is usually reliable and persistently negative cytologic studies give additional confidence. In certain clinical situations, such as in the young patient with free acid on gastric analysis or in the patient with medical contraindications for surgery, such a nonoperative approach outweighs the danger of overlooking a gastric cancer. However, the significant incidence of carcinoma in these benign-appearing lesions (usually reported as 10 to 20 percent) and the high incidence of later complications from benign gastric ulcers that eventually require operative therapy have led many surgeons to advise surgery for all gastric ulcers where there is any doubt of the diagnosis and any delay in response to medical therapy.

Fig. 5. An endoscopic photograph of a gastric cancer by means of the fiberoptic gastroscope.
Other gastric abnormalities such as benign neoplasms, syphilis or tuberculosis of the stomach, bezoar, congenital hypertrophic stenosis in adults and functional pyloric abnormalities may also be difficult to differentiate from carcinoma on radiologic study. Surgical exploration is often required for definitive diagnosis in many of these situations, although other diagnostic measures may give additional information.

Treatment of Gastric Cancer

At the present time, surgery provides the only satisfactory curative treatment of gastric cancer. However, the end results of treatment of "resectable" lesions are affected more by the pathologic findings than by the surgeon's skill. Many clinical pathologic reviews have clearly shown that the salvage of patients with anaplastic, infiltrative lesions (which progress to a "leather bottle" stomach) is extremely low while patients with polypoid carcinomas or "ulcerocancers" have a reasonable prognosis after surgical resection. (Fig. 6, p. 294.) It is also clear that the presence or absence of regional lymph node metastasis is the most significant prognostic feature in patients with "curable" lesions at the time of surgical exploration: 45 percent to 50 percent five-year survival if regional lymph nodes do not contain metastasis.18

Choice of Operation

All patients with gastric cancer, except those with definite evidence of peritoneal metastasis (ascites containing malignant cells or "rectal shelf"), documented liver metastases or proven distant metastases should be subjected to exploratory celiotomy in order to select potentially "curable" patients. If a regionally localized process is found at the time of exploration, adequate resection of the primary neoplasm, as well as actual and potential lymphatic extensions, is required.

What is "adequate" resection? At one time the use of total gastrectomy for patients with small gastric cancers was advanced by Lahey and Marshall15,16 on the theoretical basis that removal of the entire organ of origin and its regional lymphatic bed would increase cure rates. Retrospective evaluation of our clinical experience has not supported this approach for cancer of the distal half of the stomach; these lesions can usually be adequately resected, including potential lymphatic extensions, by distal radial subtotal resection.18 In addition, liberal use of total gastrectomy for distal half lesions did not favorably affect survival rates. Larger lesions of pars media of the stomach and lesions of the proximal stomach, usually close to the esophagogastric junction, require the proximal line of resection to be through the distal esophagus. Since the esophageal anastomosis is the major added hazard of either proximal or total gastrectomy, we prefer total gastrectomy rather than proximal subtotal resection of the stomach for lesions requiring resection of the cardia. The established risk of an esophageal anastomosis is not avoided by retaining the distal portion of the stom-
ach and the functional value of the small, distal gastric remnant after adequate proximal gastrectomy is often inferior to other possible means of "reservoir" construction.

Although a careful exploration is intended to prevent a radical operation when cure is not possible, it is also important to confirm the diagnosis of cancer under certain circumstances. For instance, if a typical gastric cancer is observed grossly, it may not always seem essential to obtain a positive biopsy prior to surgery, particularly if the procedure is less radical than total gastrectomy. However, a gastric ulcer with an associated mass may mimic a malignant process and a total gastric resection may
be overly aggressive treatment for this patient from the standpoint of both morbidity and potential increase in mortality. Therefore, gastrotomy and biopsy are often indicated to definitely diagnose gastric cancer in questionable cases prior to performing radical resections, particularly total gastrectomy. Every effort should be made to avoid the spillage of gastric content and tumor cells during these operative biopsy procedures.

Since the presence of microscopic spread beyond the gross margins of the tumor is commonly found, the removal of a generous margin of normal stomach around the carcinoma is the major principle of gastric resection for malignant lesions of all sites. In distal gastric lesions, generous resection of the first portion of the duodenum is required; in proximal lesions, the removal of a generous margin of distal esophagus is necessary. Failure to control a potentially curable cancer by not achieving adequate gross margins around the primary neoplasm is a serious, avoidable error.

Lymphatic Spread

In designing a radical gastrectomy for patients with “curable” gastric cancer, one must consider the removal of potential regional lymphatic extensions. Although the incidence of regional lymphatic spread varies with different gross and histologic types of cancer, the overall incidence of lymphatic spread from carcinoma of the stomach is high: approximately 60 percent. In addition, gross observations do not reveal whether or not regional metastases are present. Frozen section examination of isolated nodes is not of real benefit except in the evaluation of nodes outside the anatomic boundary of a feasible “en bloc” resection. Potential areas of lymphatic spread must always be considered in the design of radical gastrectomy since the true status of the regional lymphatics can only be determined after treatment has been completed.

Since regional lymphatics accompany the blood vessels on both the lesser and greater curvatures of the stomach, lymphatic spread of gastric cancer also warrants consideration. (Fig. 7.) Detailed autopsy studies, and studies of cleared surgical specimens after total gastrectomy and distal pancreatectomy, have demonstrated many instances of regional spread to this group of lymph nodes. Since the finding of metastasis to lymph nodes in the splenic hilum is always accompanied by metastasis in the more proximal nodes along the body and tail of the pancreas, it is reasonable to assume that these hilar nodes are an extension of lymphatic metastases occurring initially in the retrogastric portion of the splenic artery chain (pancreatolienal nodes). That this area of spread is still within the limits of “curative” resection is shown by the long-term survival of several of our patients following resection of involved pancreatolienal nodes. However, liberal clinical trial of this approach at Memorial Hospital for Cancer and Allied Diseases in New York has led to no clear-cut increase in
the overall salvage of gastric cancer patients but rather to a definite increase in both morbidity and mortality. The extent of resection of the "gastric bed" of lymphatic bearing tissues obviously varies with the location and size of the lesion and the general status of the patient. Radical distal subtotal gastrectomy (Fig. 8, p. 298) does not include resection of the nodes adjacent to the cardia of the stomach, the pancreatico-glandular nodes along the splenic artery, or the lymph nodes in the splenic hilum. However, both logic and prior studies of operative specimens have shown that these lymph node groups are not in-

Fig. 7. Lymphatic drainage of the stomach.
volved in patients with cancers of the distal third of the stomach, except when nonresectable areas of lymphatic spread in the region of the head of the pancreas have already developed. Regional lymphatic spread to these sites has been demonstrated in potentially curable cancers of the pars media and proximal stomach—a major theoretical reason for considering total gastrectomy or even extended total gastrectomy (distal pancreas and spleen) for such cancers. (Fig. 9, p. 299.) Nevertheless, high subtotal gastrectomy appears to be a reasonable approach to the treatment of a small lesion in the pars media, particularly if a generous margin around the gross tumor can be removed. The resectional proce-
ature should always include perigastric tissues containing potential lymphatic extensions as an "en bloc" procedure, but the extent of lymphatic resection must vary. Because of the relatively limited gains with the extended procedures, the patient’s age and medical disability must be carefully weighed before deciding on the extent of resection.

Combined Organ Resections

Some otherwise resectable gastric cancers are adherent not only to the pancreas or spleen but also to the transverse mesocolon and the midcolic vessels. There should be no hesitation about division of the mesocolon, leaving adherent tissue attached to the surgical specimen. Adequate collateral blood supply of the transverse colon may allow sacrifice of the midcolic vessels without resection, but any question of the adequacy of the blood supply should prompt colon resection along with gastric resection. The left lobe of the liver, which is occasionally adherent to a proximal gastric
cancer, can also be resected in continuity with the gastrectomy under these circumstances. Resection of adjacent adherent organs prevents "violation" of the surgical margins, but local invasion of adherent structures may be difficult to demonstrate histologically. Of course, invasion of adjacent structures causes concern, but it is probably associated with a better prognosis than lymphatic spread.

Resection of a segment of transverse colon, the body and tail of the pancreas, the spleen, or a portion of the liver combined with resection for gastric carcinoma can provide benefits; however, whether combined organ resection is applicable to the head of the pancreas is difficult to answer. Pancreatoduodenectomy is a truly major extension of gastrectomy and vital structures in this area, particularly the superior mesenteric artery and portal vein, reduce the anatomic possibility of an en bloc resection. In addition, most gastric cancers involving the head of the pancreas to this extent,
also involve other structures in the porta hepatis or elsewhere, categorizing the patient as "incurable." The data of Berry and Rottschafer give no support for this approach. 20 It is conceivable that pancreateoduodenectomy could be advisable as a "curative operation," but there are no reported clinical data demonstrating benefits from this approach. Personal experience is limited to three patients in whom pancreateoduodenectomy seemed the logical approach: two developed recurrent carcinoma within 12 months and the third patient was operated on less than one year ago.

After distal subtotal gastrectomy, the restoration of continuity should always be accomplished by gastrojejunostomy rather than gastroduodenostomy. This procedure avoids the problem of gastric outlet obstruction in patients who develop recurrent carcinoma following attempted "curative" resection. Gastric cancer recurs in the region of the pancreas ("gastric bed") and a gastroduodenostomy would be more likely to be involved in this regrowth of cancer than a gastrojejunostomy.

Variations in the method of restoring continuity after total gastrectomy are many. Our preference is a double lumen jejunal pouch with a distal Roux-y anastomosis which creates a reservoir to substitute for the resected stomach. 21, 22 It is constructed to prevent reflux of duodenal secretions into the esophagus, and the Roux-y anastomosis tends to reduce the rate of outflow of foodstuff from the reservoir area. (Fig. 10.) This type of reconstruction is easily accomplished and it has been generally associated with good nutritional condition.

Palliative Surgery

A significant proportion of patients will have operative findings, such as tiny serosal implants, a solitary liver metastasis, an ovarian metastasis or metastatic disease in lymph nodes outside the range of "en bloc" dissection, denoting incurability. A palliative procedure is then planned or the abdomen is closed without further surgery, based on the appropriate biopsy confirmation of these findings.

We prefer palliative resection (without major attention to regional node areas) if the procedure can be accomplished without total gastrectomy, transection of gross tumor at the site of the planned anastomosis or major hazard to the patient. If these conditions are met, palliative resection can give significant relief of symptoms in the majority of patients and prolong survival. If these conditions cannot be met in the incurable patient, we prefer to close the abdomen without performing gastrojejunostomy, gastrostomy or jejunostomy which rarely relieve symptoms or prolong life expectancy.

Recurrent Gastric Carcinoma

A few patients who survive a considerable period after partial gastrectomy develop evidence of cancer in the gastric remnant. Since margins around the primary lesion are usually adequate at the
site of proximal transection of the stomach, the likelihood that "late recurrence" may be a new second primary gastric cancer must be considered. Whatever the mechanism, occasionally in a few selected patients, a second resection for neoplasms in the gastric remnant seems justified and offers some hope for "cure." Secondary operations under these circumstances usually entail a resection of the remaining stomach along with the spleen and body and tail of the pancreas (due to adherence of these structures).
Nonsurgical Palliation

Radiation therapy and systemic drug therapy are available in the treatment of patients with incurable gastric carcinoma. Neither modality can greatly prolong life, particularly in the patient who has widespread metastasis. If a large tumor dose can be achieved, radiation therapy usually has definite therapeutic benefit in patients with adenocarcinomas. However, in practice radiation therapy is rarely indicated since most patients with incurable gastric carcinoma do not have a localized lesion and it is difficult to achieve a high tumor dose under these circumstances. On the other hand, radiation therapy has been useful in chronically bleeding gastric cancers and in relieving localized areas of obstruction, particularly in the region of the cardia.

Although systemic cancer chemotherapy has been less effective in patients with gastric cancer than in those with colorectal cancer (probably because of the relatively rapid clinical course in most patients not effectively treated by gastric resection), the pattern of metastasis usually makes systemic chemotherapy rather than radiotherapy a more appropriate form of treatment. Many chemotherapeutic agents have been employed with generally disappointing results; the antimetabolite, 5-FU, is the most effective agent thus far. Approximately 15-20 percent of patients treated with this agent have demonstrated objective improvement for limited periods. There are at present no data to support chemotherapy as an effective adjuvant to the surgical treatment of gastric cancer.

End Results

Survival curves are a good indication of the results of therapy for all types of patients with gastric carcinoma. \(^{10}\) (Fig. 11.) These curves demonstrate that the five-year period is an excellent yardstick for evaluating treatment methods since a majority of patients who develop further difficulty do so within three years of the primary surgical treatment. Following resection, 90 percent of those patients in our series surviving five years without clinical evidence of residual cancer have remained free of disease.

The overall outlook for patients with gastric carcinoma remains poor since two thirds of patients have either physical or operative findings at the time of diagnosis that completely eliminate the possibility of surgical "cure"; no more than one third of those patients considered candidates for curative resection live five or more years after treatment. This surgical salvage of only 10 percent of all patients with the diagnosis of carcinoma of the stomach is discouraging. The decreasing incidence of carcinoma of the stomach is one of the few bright spots in the story.

Conclusion

Two factors emerge from this unhappy series of statistics and comments. The first consideration is the emerging possibility that more favorable lesions,
or even precancerous states, may be treated more vigorously as a result of improved diagnostic methods or increased diagnostic vigor. The second is the realization that we will continue to have a significant number of patients with gastric carcinoma who require thoughtful palliative management, certainly a larger group of patients than we can reasonably hope to "cure."

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**Fig. 11.** Survival curves for carcinoma of the stomach.
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The Patrons of Medical Research

The patrons of medical research survive in memory for centuries as benefactors of mankind. Medical research has this interesting facet: If treatment of value to mankind is discovered, it is not only of value to those hundreds of thousands of sufferers alive today, but it will aid human beings forever, or until it vanishes from the knowledge of the race.—Charles Huggins, M.D., quoted in Hughes, Robert J.: "Discovery Is Our Business." Chicago Today 4: 8-19, 1967. P. 16.