The presence of iron-deficiency anemia in men and of occult blood in the stool in both sexes mandates a search for an occult gastrointestinal tract lesion. A careful assessment is of particular importance in patients with atrophic gastritis or pernicious anemia. Unusual clinical features associated with gastric adenocarcinomas include migratory thrombophlebitis, microangiopathic hemolytic anemia, diffuse seborrheic keratoses (so-called Leser-Trélat sign), and acanthosis nigricans.

Diagnosis The use of double-contrast radiographic examinations has been supplanted by esophagogastroscopy and CT scanning for the evaluation of patients with epigastric complaints.

Gastric ulcers identified at the time of such endoscopic procedure may appear benign but merit biopsy in order to exclude a malignancy. Malignant gastric ulcers must be recognized before they penetrate into surrounding tissues, because the rate of cure of early lesions limited to the mucosa or submucosa is >80%. Because gastric carcinomas are difficult to distinguish clinically or endoscopically from gastric lymphomas, endoscopic biopsies should be made as deeply as possible, due to the submucosal location of lymphoid tumors.

The staging system for gastric carcinoma is shown in Table 109-4.

TABLE 109-4 STAGING SYSTEM FOR GASTRIC CARCINOMA

Stage	TNM	Features	Data from ACS in the United States	
			No. of Cases, %	5-Year Survival, %
0	$T_{is}N0M0$	Node negative; limited to mucosa	1	90
IA	T1N0M0	Node negative; invasion of lamina propria or submucosa	7	59
IB	T2N0M0 T1N1M0	Node negative; invasion of muscularis propria	10	44
II	T1N2M0 T2N1M0	Node positive; invasion beyond mucosa but within wall	17	29
		or		
	T3N0M0	Node negative; extension through wall		
IIIA	T2N2M0 T3N1-2M0	Node positive; invasion of muscularis propria or through wall	21	15
IIIB	T4N0-1M0	Node negative; adherence to surrounding tissue	14	9
IIIC	T4N2-3M0	>3 nodes positive; invasion of serosa or adjacent structures		
	T3N3M0	7 or more positive nodes; penetrates wall without invading serosa or adjacent structures		
IV	T4N2M0	Node positive; adherence to surrounding tissue	30	3
		or		
	T1-4N0-2-M1	Distant metastases		

Abbreviations: ACS, American Cancer Society; TNM, tumor, node, metastasis.

TREATMENT GASTRIC ADENOCARCINOMA

Complete surgical removal of the tumor with resection of adjacent lymph nodes offers the only chance for cure. However, this is possible in less than a third of patients. A subtotal gastrectomy is the treatment of choice for patients with distal carcinomas, whereas total or near-total gastrectomies are required for more proximal tumors. The inclusion of extended lymph node dissection in these procedures appears to confer an added risk for complications without providing a meaningful enhancement in survival. The prognosis following complete surgical resection depends on the degree of tumor penetration into the stomach wall and is adversely influenced by regional lymph node involvement and vascular invasion, characteristics found in the vast majority of American patients. As a result, the probability of survival after 5 years for the 25–30% of patients able to undergo complete resection is ~20% for distal tumors and <10% for proximal tumors, with recurrences continuing for at least 8 years after surgery. In the absence of ascites or extensive hepatic or peritoneal metastases, even patients whose disease is believed to be incurable by surgery should be offered resection of the primary lesion. Reduction of tumor bulk is the best form of palliation and may enhance the probability of benefit from subsequent therapy. In high-incidence regions such as Japan and Korea, where the use of endoscopic screening programs has identified patients with superficial tumors, the use of laparoscopic gastrectomy has gained popularity. In the United States and western Europe, the use of this less invasive surgical approach remains investigational.

Gastric adenocarcinoma is a relatively radioresistant tumor, and the adequate control of the primary tumor requires doses of external-beam irradiation that exceed the tolerance of surrounding structures, such as bowel mucosa and spinal cord. As a result, the major role of radiation therapy in patients has been palliation of pain. Radiation therapy alone after a complete resection does not prolong survival. In the setting of surgically unresectable disease limited to the epigastrium, patients treated with 3500–4000 cGy did not live longer than similar patients not receiving radiotherapy; however, survival was prolonged slightly when 5-fluorouracil (5-FU) plus leucovorin was given in combination with radiation therapy (3-year survival 50% vs 41% for radiation therapy alone). In this clinical setting, the 5-FU likely functions as a radiosensitizer.

The administration of combinations of cytotoxic drugs to patients with advanced gastric carcinoma has been associated with partial responses in 30–50% of cases; responders appear to benefit from treatment. Such drug combinations have generally included cisplatin combined with epirubicin or docetaxel and infusional 5-FU or capecitabine, or with irinotecan. Despite the encouraging response rates, complete remissions are uncommon, the partial responses are transient, and the overall impact of multidrug therapy on survival has been limited; the median survival time for patients treated in this manner remains less than 12 months. As with adenocarcinomas arising in the esophagus, the addition of bevacizumab (Avastin) to chemotherapy regimens in treating gastric cancer appears to provide limited benefit. However, preliminary results utilizing another antiangiogenic compound—ramucirumab (Cyranza)—in the treatment of gastric cancer are encouraging. The use of adjuvant chemotherapy alone following the complete resection of a gastric cancer has only minimally improved survival. However, combination chemotherapy administered before and after surgery (*perioperative treatment*) as well as postoperative chemotherapy combined with radiation therapy reduces the recurrence rate and prolongs survival.

PRIMARY GASTRIC LYMPHOMA

Primary lymphoma of the stomach is relatively uncommon, accounting for <15% of gastric malignancies and ~2% of all lymphomas. The stomach is, however, the most frequent extranodal site for lymphoma, and gastric lymphoma has increased in frequency during the past