2

The Gastrointestinal System and the Elderly

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2.1. Introduction

Gastrointestinal diseases increase with age, and their clinical presentations are often confused by functional complaints and by pathophysiologic changes affecting the individual organs and the nervous system of the gastrointestinal tract. Hence, the statement that diseases of the aged are characterized by chronicity, duplicity, and multiplicity is most appropriate in regard to the gastrointestinal tract. Functional bowel distress represents the most common gastrointestinal disorder in the elderly. Indeed, over one-half of all their gastrointestinal complaints are of a functional nature. In view of the many stressful situations confronting elderly patients, such as loss of loved ones, the fears of helplessness, insolvency, ill health, and retirement, it is a marvel that more do not have functional complaints, become depressed, or overcompensate with alcohol. These, of course, make the diagnosis of organic complaints all the more difficult in the geriatric patient. In this chapter, we shall deal primarily with organic diseases afflicting the gastrointestinal tract of the elderly. To do otherwise would require the creation of a sizable textbook.

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2.1.1. Pathophysiologic Changes

Age leads to general and specific changes in all the organs of the gastrointestinal tract.[1] Invariably, the teeth show evidence of wear, discloration, plaque, and caries. After age 70 years the majority of the elderly are edentulous, and this may lead to nutritional problems. Dry mouth (xerostomia) is a frequent complaint and results from decreased salivary and parotid secretions and from mouth breathing. A dry mouth makes it difficult to retain dentures. The endentulous state also leads to a change in the bacterial flora of the mouth from predominantly anaerobic to aerobic and indirectly influences the type of bacterial aspiration encountered in older patients. Taste declines owing to a substantial loss of taste buds.[2] The order of loss is salt, sweet, sour, and bitter, with the latter two persisting long after the disappearance of the former. This has a twofold effect. Food tastes bitter and becomes undesirable, or it is tasteless, which leads some patients to use salt excessively. Taste is also impaired by congestive heart failure and, of course, by zinc deficiency. The ability to smell decreases significantly after age 40. The elderly require threshold concentrations for food odors 11 times greater than the young. Loss of smell is thought to account for the high incidence of domestic gas poisoning in the elderly.

2.1.2. Achlorhydria

Achlorhydria assumes importance. The absence of hydrochloric acid leads to impaired solubilization of iron and thus to impaired iron absorption. It also makes the older achlorhydric individual more susceptible to bacterial infections of the gastrointestinal tract such as *Shigella* and *Cholera* infections. Small bowel motility may decrease in elderly patients to the point that bacterial overgrowth leads to malabsorption in the absence of organic disease. Small as well as large bowel transit times are also altered in patients with the irritable bowel syndrome. Liver size, blood flow, and metabolism all decline with age. Flatulence and constipation become more frequent. Diverticulosis and colonic polyps increase with age. Overshadowing these physiologic changes, and in some cases accentuating them, are the major diseases that afflict the gastrointestinal tract of the elderly, which we shall now discuss, starting with the esophagus.

2.2. Esophagus

Age alone does not seriously impair the physiologic activity of the esophagus. Normally food is transported through this organ by peristaltic waves. "Primary" peristalsis occurs with the initiation of swallow-

ing. "Secondary" peristalsis develops when the upper portion of the esophagus is distended locally by balloon or by reflux of gastric material. Reflux from the stomach into the esophagus is prevented by the lower esophageal sphincter. This physiologic zone has a higher resting pressure than either the adjacent stomach or the esophagus. Its activity, however, may be affected by disease or altered by drugs. Previously, it was thought that the elderly person often developed a senile condition known as "presbyesophagus" which altered peristalsis and delayed esophageal emptying. This is no longer a valid concept. Nor does age, *per se,* alter the esophageal "swallowing time," which ranges from 9 to 12 sec. However, the organ is affected by several disorders that stem from deterioration of its neurologic elements, e.g., "diffuse esophageal spasm" and "cricopharyngeal dysfunction." These swallowing disorders are common among the elderly as well as a cause of considerable discomfort and diagnostic concern.

2.2.1. Dysphagia

Esophageal disorders result from alterations of motility, from infections, and from tumors. Unlike the young, the geriatric patient with dysphagia is usually suffering from organic disease. In this respect, there are two types of organic dysphagia: (1) preesophageal and (2) esophageal.[1] Both are further subdivided into motor (neuromuscular) and structural (intrinsic and extrinsic) lesions.[3]

2.2.2. Preesophageal Dysphagia

Preesophageal dysphagia (PED) usually implies neuromuscular disease and it may be caused by pseudobulbar palsy, multiple sclerosis, amyotrophic lateral sclerosis, tetanus, bulbar poliomyelitis, lesions of the glossopharyngeal nerve, myasthenia gravis, muscular dystrophies, and Parkinson's disease. Pharyngitis secondary to herpes or moniliasis may also induce PED, as may obstructions of the oropharynx by abscess, neoplasm, or diverticulum. With PED there is an inability to initiate swallowing; hence food cannot escape from the oropharynx into the esophagus. This makes it more difficult to swallow liquids than solids. Such patients sputter and cough during attempts to swallow and may suffer from nasal regurgitation or aspiration.

2.2.2.1. Dysfunction of the Cricopharyngeus Muscle

Dysfunction of the cricopharyngeus muscle is a common cause of PED in the aged.[4] This muscle acts as an upper esophageal sphincter. With dysfunction, attempts to swallow give the patient the sensation of

an obstruction in the throat. If the cricopharyngeus muscle relaxes too slowly, food cannot pass freely into the esophagus. If it relaxes promptly but closes too quickly, food is trapped at the entrance to the esophagus. Such patients can swallow solids more easily than liquids. In a study to determine whether cricopharyngeus dysfunction is common in the elderly, Piaget and Fouillet studied cricopharyngeal function in 100 symptomless individuals over age 65 years.[5] Thirty-eight percent of the men and 15% of the women had evidence of neurologic dysfunction.

2.2.2.2. Diagnosis and Complications

A history of inability to drink fluids readily (85%), excessive expectoration of saliva (30%), weight loss (50%), and heartburn (50%) should arouse one's suspicion for cricopharyngeal dysfunction, particularly in a patient with diabetes mellitus. Usually, diagnosis can be confirmed by cineroentgenography. If the cricopharyngeal muscle fails to relax, there is puddling of the contrast material in the valleculae and pyriform sinuses. Hypopharyngoscopy and esophagoscopy are necessary to exclude other diseases.

Complications include chronic irritation of the larynx, aspiration, and the development of a Zenker's diverticulum (Fig. 1). Eventually, repeated aspirations cause many patients to develop chronic bronchitis or bronchiectasis.

2.2.2.3. Treatment

Treatment for cricopharyngeal dysphagia consists of cricopharyngeal myotomy. Usually this procedure results in prompt relief whereas bouginage is seldom helpful.[6–10] Such surgery also corrects one of the major complications of cricopharyngeal dysphagia, namely, Zenker's diverticulum. Formerly, a Zenker's diverticulum had to be removed surgically. This is no longer necessary. Even in the advanced stage, older patients with severe obstruction responded successfully to myotomy alone. Once the obstruction is relieved by myotomy, the diverticulum begins to involute.[8] The advantages of this approach are (1) a shorter operating time, (2) ability to resume oral feedings promptly, (3) elimination of the need for a Levine tube, (4) a decreased risk of suture line leakage and stricture formation, and (5) no need for antibiotics.[8]

2.2.3. Esophageal Dysphagia

Initially, esophageal motor disorders cause greater dysphagia for liquids than solids, whereas structural lesions create more difficulty in

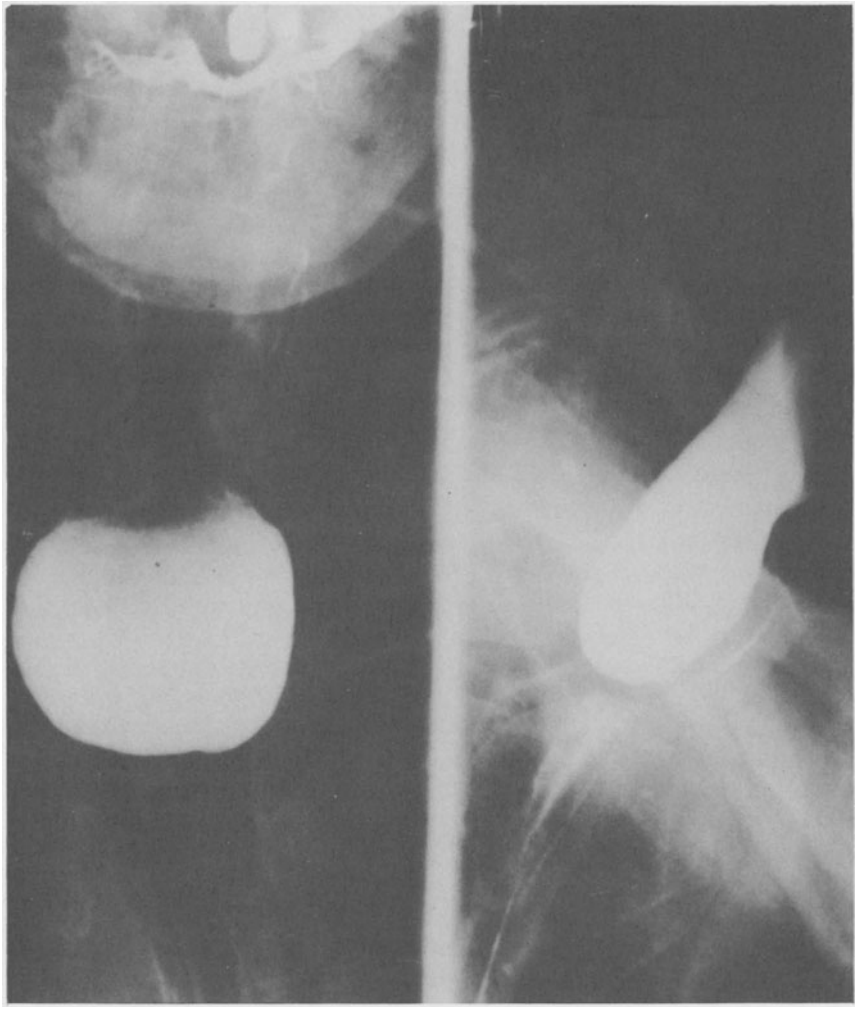

Figure 1. Zenker's diverticulum—anterior and lateral views.

swallowing solids. Motor abnormalities leading to dysphagia in the geriatric patient include achalasia, diffuse esophageal spasm, and neuropathies secondary to diabetes, alcoholism, and so forth. Temporary dysphagia is also fairly common (14%) following vagotomy procedures.[11] In this section we shall discuss achalasia, diffuse esophageal spasm, and reflux esophagitis, three common esophageal entities causing dysphagia in the elderly.

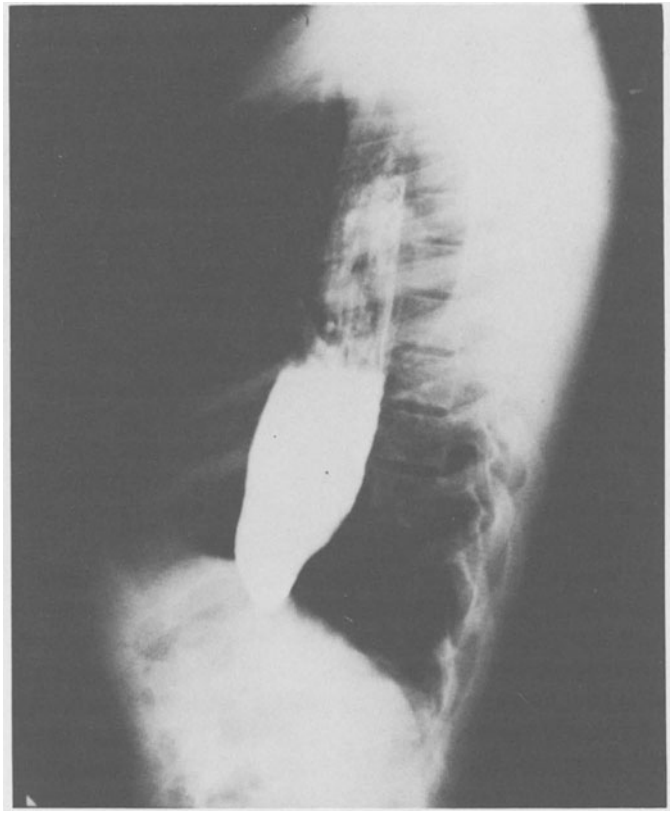

Figure 2. Achalasia. Note the markedly dilated body of the esophagus.

2.2.3.1. Achalasia of the Lower Esophagus

In this disorder, the muscular wall of the distal esophagus is narrow while the proximal esophagus is dilated and tortuous (Fig. 2). Achalasia has been attributed to degeneration of neural elements. In the early years of this disorder, the most consistent neuropathologic lesion is ganglion cell loss or degeneration within the esophageal myenteric plexus, the vagus nerve, and the dorsal motor nucleus of the vagus nerve.[12] Qualman *et al.* compared the neuropathologic features in the esophageal ganglionic plexuses of eight patients with achalasia and 22 patients with Parkinson's disease of whom three had dysphagia. Lewy bodies, a classic pathologic finding in the cortex of patients with parkinsonism, were observed in the esophageal ganglionic cells of two of the patients with achalasia and two of the three parkinsonian patients with dysphagia.[13]

The exact importance of this finding remains to be ascertained. Whatever the basic lesion, the eventual result is an increase in lower esophageal spasm (LES) pressure with incomplete relaxation of the sphincter and absence of effective esophageal peristalsis during the swallowing act. Stasis results, leading to inflammation of ulceration of the mucosal lining.

2.2.3.2. Clinical Findings

Achalasia occurs in 1 per 100,000 population per year and it is more common in middle than old age. Symptomwise, afflicted patients complain of progressive dysphasia. Early, they have more difficulty swallowing liquids than solids. Later, they tend to regurgitate undigested foods. Since bile is absent, the regurgitated food does not have a bitter taste. Nocturnal aspiration, however, is common and often leads to spasms of coughing and sometimes to aspiration and penumonia. Odynophagia occurs with ingestion of hot or cold beverages or food. This pain is often severe. It is localized to the substernum and it may radiate to the shoulders or back and even down the arms, mimicking angina. Eventually, as a result of complete motor failure, the esophagus dilates and loses its capability to propel food into the stomach.

2.2.3.3. Diagnosis

Achalasia is easily identified by an upper gastrointestinal series with barium sulfate. Characteristically, the bulk of the esophagus is dilated, but the distal end is smoothly tapered and narrow. Its beaklike distal end helps to differentiate achalasia from the more ragged mucosal appearance of carcinoma. Manometric studies of the esophagus are essential. The principal findings are (1) absence of peristalsis in the body of the esophagus, (2) incomplete relaxation of the lower esophageal sphincter, (3) a hypertensive LES manifested by elevated manometric pressure, and (4) an elevated resting intraesophageal pressure. Presumably, the elevated pressures prevent normal relaxation of the sphincter that usually occurs with swallowing and in conjunction with the neural changes inhibit or eliminate peristalsis. Mecholyl (acetyl–beta-methyl choline–chloride) is a valuable aid to diagnosis. Five to ten grams given subcutaneously increases the baseline lower esophageal pressure in 80% of patients with achalasia and keeps it elevated for 5 to 10 minutes.[15] Normally, Mecholyl does not increase baseline esophageal pressure. If Mecholyl causes severe chest pain, the administration of atropine sulfate usually relieves it.

2.2.3.4. Treatment

Treatment is directed toward reducing the elevated resting pressure of the LES. This can be accomplished by forceful pneumatic dilatation or by surgical myotomy. Symptomatic improvements occur with either procedure, if it succeeds in reducing the LES resting pressure. Unfortunately, neither treatment leads to a return of normal esophageal peristalsis. At present, most gastroenterologists favor pneumatic dilatation as the primary method of treatment[16,17]; however, pneumatic dilatation carries a 2 to 6% chance of perforation. This and the discomfort associated with pneumatic dilatation have led a number of investigators to seek a medical means of providing relief. Bortolotti and Labo found the calcium antagonist nifedipine (10 to 20 mg every 6 hr) decreased LES tone significantly and led to noticeable clinical improvement in patients with mild to moderate achalasia.[18]

2.2.4. Diffuse Esophageal Spasm

Formerly, presbyesophagus was thought to be an age-induced condition.[19] Later, Castell *et al.* showed that most of the patients studied originally for presbyesophagus actually had some type of neuropathic condition to account for their abnormal esophageal motility. We now know that esophageal motility is not impaired by age alone.[20]

Diffuse esophageal spasm (DES) has long been considered the classic type of motility disorder. It arises from neuromuscular abnormality due either to deterioration of Auerbach's plexus or to Wallerian degeneration of the vagal nerve branches. Radiographically, DES yields the so-called "curling" or the "corkscrew or rosary bead" esophagus seen on barium swallow (Fig. 3). The symptoms associated with DES are usually intermittent and consist of progressive dysphagia and mild to severe chest pain. Dysphagia tends to occur after swallowing, and it may be worse on attempts to swallow hot or cold beverages. Severe chest pain may awaken patients from their sleep. The pain radiation pattern simulates angina pectoris, and like anginal pain, it is often relieved by sublingual nitroglycerin. Figure 4 shows the location of chest pain in 51 patients with esophageal abnormalities along with their concept of the pain's location. Fifty-one of the sixty-five patients (80%) in this study had chest pain, 35 (54%) had dysphagia for solid foods, 26 (40%) had dysphagia for liquids, 31 (48%) had heartburn, and 36 (55%) had regurgitation.[21] Neither the severity of their chest pain nor the prevalence of heartburn correlated with the severity of their manometric contraction abnormalities. The cause of chest pain in DES remains unsolved. Recently, Richter and his associates found that baloon distention of the

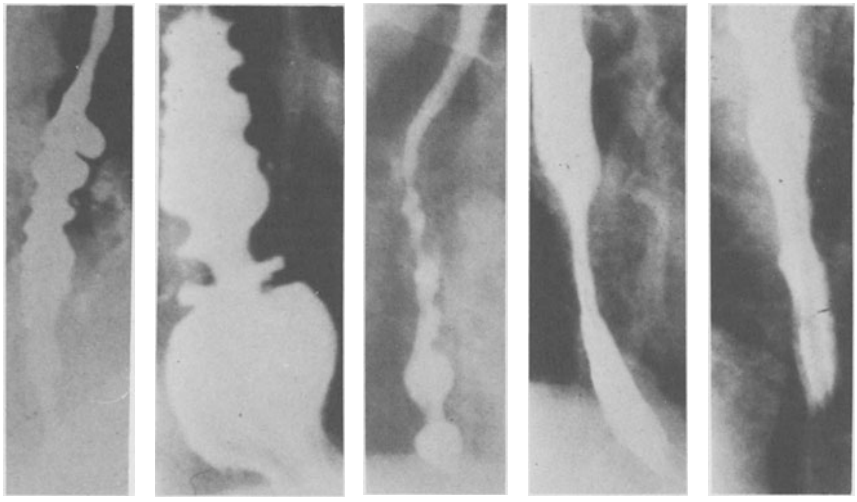

Figure 3. Diffuse esophageal spasm. This composite shows spasm of varying degrees from left to right. The second radiogram from the left also shows a prominent hiatal hernia. The first radiogram on the left is more characteristic of the so-called "curling" or "rosary-bead" esophagus. (Courtesy of Dr. Robert L. Slaughter.)

esophagus replicated the chest pain of DES, but at balloon volumes (8 mm) below those required to produce similar chest pain in normal individuals.[22] These investigators believed the chest pain of DES is due to enhanced sensitivity to esophageal distention, as a result of lower visceral pain thresholds. A similar conclusion was reached by Ritchie and others in regard to the origin of the abdominal pain observed in patients with

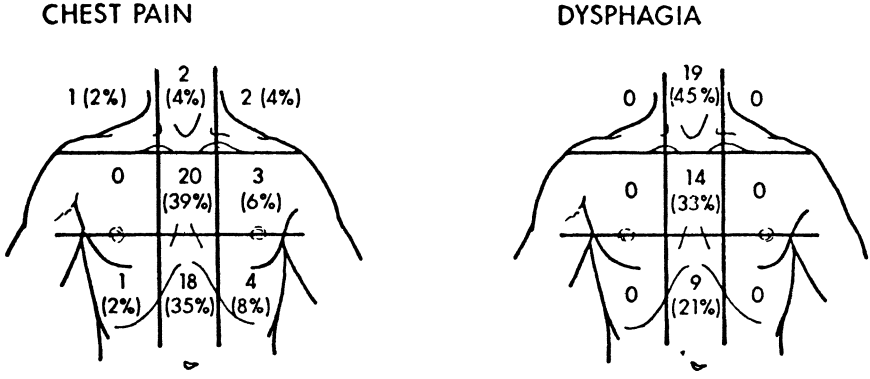

Figure 4. Various locations of chest pain in diffuse esophageal spasm. (Courtesy of Dr. Ray E. Clouse and Plenum Publishing Corporation).

irritable bowel.[23,24] Among the latter patients, lower abdominal pain could be replicated by rectal balloon volumes not even perceived by normal volunteers.

2.2.4.1. Diagnosis

Diagnosis is aided by both manometric and radiologic studies of the esophagus. Originally, DES was characterized manometrically by simultaneous, nonperistaltic continuous waves with an amplitude greater than 35 mm Hg, with appropriate relaxation of the LES on swallowing. Subsequently, technical improvements in manometry led to the discovery that other types of contraction abnormalities may be associated with the clinical manifestations of DES. In 1979, Benjamin *et al.* described the "nutcracker esophagus."[25] Clinically, their patients had symptoms of chest pain and dysphagia identical to those of classical DES, but manometrically they exhibited peristaltic waves of excessively high amplitude (200 to 300 mm Hg) and/or prolonged duration (> 6 sec). In 1985, Narducci *et al.* reported a patient with "nutcracker esophagus" who developed manometric transition to classic DES over the course of 1 year.[26,27] Reidel and Clouse suggested these were closely associated motor abnormalities after observing that only 9 of 75 of their symptomatic DES patients had classical manometric findings, whereas the reamining 66 symptomatic patients had a variety of manometric abnormalities. Among the latter, contraction abnormalities were (1) an increase in mean distal wave amplitude ("nutcracker"), (2) a prolonged mean distal wave duration, (3) an increased number of motor responses, and (4) the presence of triple-peak waves. These individual abnormality patterns could exist alone or in combination with one or more of the other manometric abnormalities. They also found that acid instillation (Bernstein test) reproduced chest pain in 35% of their patients with chest pain and in 48% of those with heartburn. Five of the latter patients had hypertensive LES pressures. They concluded that esophageal symptoms *per se* were poor predictors of manometric findings in patients with motility disorders. Castell found the prevalence of esophageal motility disorders in patients with noncardiac chest pain to be achalasia (5 to 10%), DES (0 to 24%), nutcracker esophagus (28 to 45%), hypertensive lower esophageal sphincter (0 to 23%), and nonspecific esophageal motility disorder (23 to 55%).

The differentiation of angina pectoris from esophageal-induced chest pain is difficult but immensely important. Manometric advances have aided us in this respect. In an analysis of 910 patients with noncardiac chest pain, Castell and his associates found 255 (28%) had abnormal baseline esophageal motility. The manometric patterns observed were

classified as (1) nutcracker esophagus, 122 (48%); (2) nonspecific esophageal motility disorder, 91 (36%); (3) diffuse esophageal spasm, 25 (10%); (4) hypertensive LES, 11 (4%); and (5) achalasia, 6 (2%). Provocative tests were positive in an additional 27% of their patients. Chest pain was reproduced in 48 during the Bernstein test while 125 patients had replication of their chest pain following a bolus of edrophonium (Tensilon), 80 μg/kg. Using manometric and provocative tests, approximately one-half of their patients had substantial evidence for chest pain of esophageal origin. Another aid to diagnosis is the esophageal radionuclide test. It is more physiologic and more sensitive than barium swallow and involves less radiation exposure. Moreover, the results correlate well with manometry.[28]

2.2.4.2. Treatment of Diffuse Esophageal Spasm

Three forms of treatment are available: (1) medical, (2) dilatation, and (3) surgery.[29] Medical therapy is beneficial in 50% of patients with gastric reflux. Sublingual nitroglycerin, 1/200 grains, is given 15 to 20 min before meals. If this is successful, long-acting nitrates, such as isosorbide dinitrate, are substituted for more prolonged relief.[30] In the absence of gastric reflux, anticholinergic agents are often helpful. A number of new studies dealing with the use of calcium channel blocking agents are underway. Both nifedipine and diltiazem have been used because of their smooth muscle relaxing action. Initial observations suggest that nifedipine is superior to diltiazem. Nifedipine decreases the amplitude of esophageal contractions by more than 50% in patients with the nutcracker esophagus.

Bouginage, with a 50 French dilator, is reserved for extremely symptomatic patients. Pneumatic dilatation of the lower esophageal sphincter is reserved for patients with associated achalasia and elevated lower esophageal sphincter pressures. Esophageal myotomy is used when symptoms are severe or incapacitating.[31] In the Mayo Clinic series, two-thirds of patients treated surgically had good results.[32]

Other causes of dysphagia are relatively common in the aged and must be considered. These include esophageal carcinoma, peptic or caustic esophageal structures, an enlarged left atrium, an aortic arch aneurysm (dysphagia aorticum), an aberrant subclavian artery (dysphagia lusoria), metastatic carcinoma, and benign esophageal tumors.

2.2.5. Esophagitis

Esophagitis may develop secondary to infections, tumor, corrosives, or from the reflux of acid or bile. Infections are a rare cause of

esophagitis today, and when infection does occur, it is predominantly due to herpes simplex or to *Candida albicans.*[33] These infections are more common in the immunocompromised host. Herpetic esophagitis is characterized by volcano ulcers on endoscopy or by the presence of discrete shallow ulcers on double-contrast barium esophagrams.[34]

2.2.5.1. Reflux Esophagitis—Pathogenesis

Reflux esophagitis is defined as esophageal inflammation caused by reflux of acid or bile or a combination of both into the esophagus without inducing vomiting or belching. It is a multifactorial condition related to changes in the antireflux mechanisms, including LES pressure, the volume and composition of the refluxate, the efficiency of esophageal acid clearance, and tissue resistance.[35/37] A brief look at each of these factors shows the following.

2.2.5.1a. Lower Esophageal Sphincter. The intrinsic tone of the LES pressure, a major factor in preventing gastroesophageal reflux (GR), is maintained by neural hormonal and myogenic factors.[38,39] When the LES pressure falls to 10 mm Hg or less, the sphincteric action is probably impaired sufficiently to allow reflux. Patients with severe esophagitis usually have lower LES pressures than patients with mild reflux esophagitis.[40] Foods such as fat, chocolate, peppermint, and alcohol aggravate this condition because they lower the LES pressure sufficiently to increase GR.[41,42]

Until recently, it was assumed that when the LES pressure fell to 10 mm Hg or less, reflux occurred. Recently, Dodds *et al.* claimed that episodes of GR in asymptomatic healthy individuals were related to transient complete relaxation of the LES.[37] Their patients with reflux esophagitis had more episodes of reflux than controls (35 ± 15 versus 9 ± 8 in 12 hr) and their LES pressure was lower than that of controls (13 ± 8 mm Hg versus 29 ± 9 mm Hg). These authors postulated that reflux occurred by three different mechanisms, namely, (1) transient complete relaxation of the LES, (2) a transient increase in intraabdominal pressure, and (3) spontaneous free reflux associated with a low resting pressure of the LES. Among their patients, reflux was associated with transient sphincter relaxation in 65%, with increased intraabdominal pressure in 17%, and with spontaneous free reflux in 18%. In controls, reflux episodes were caused predominantly by transient sphincter relaxation. Gill and his associates also believe the physiologic adaptive response of the LES to increased intraabdominal pressure is deficient in GR. Their patients with GR had diminished amplitude and duration of peristaltic contractions at all levels of their esophagus, a decreased velocity of peristalsis, and an increased incidence of aperistalsis—in other words, severe motor incoordination. A modified Nissen procedure re-

stored both the mean amplitude of peristaltic contractions as well as the LES pressure to normal, presumably by creating a physiologiclike sphincter.[43]

2.2.5.1b. Gastric Volume. A large gastric volume increases both the chances for and the amount of refluxate. In turn, the gastric volume is directly related to the quantity of food and drink ingested, the rate of gastric secretion and gastric emptying, and the frequency of reflux. An abnormality of any one of these facfors leads to an excessive gastric volume that favors reflux and the development of esophagitis.

2.2.5.1c. Refluxate. The refluxate composition is also related to tissue injury. Even a small amount of the enzyme pepsin in an acid milieu (i.e., pH of 2 or less) is capable of inducing severe esophagitis.[44] Conjugated bile salts appear to damage the esophageal mucosa at an acid pH, whereas deconjugated bile salts and the enzyme trypsin are more injurious at a neutral pH. Bile acids also increase the permeability of the esophageal mucosa to hydrogen ions.

2.2.5.1d. Esophageal Clearance. The esophageal clearance of acid from the lumen after acid reflux is obviously an important defense against esophagitis. It is enhanced by gravity, by peristalsis, and by saliva. Peristalsis appears to be the primary force behind esophageal clearance, while the presence of saliva is important in maintaining the luminal pH above 3. Helm *et al.* found that an injection (15-ml bolus) of 0.1 NHC1 acid into the normal esophagus produced a transient increase in pressure and an immediate peristaltic sequence that almost cleared the bolus from the esophagus.[45] However, the pH did not begin to rise within the esophagus until the first swallow, 30 sec later. The over clearance time to a pH of 4 required 284 sec. When saliva production was stimulated by sucking on a lozenge, the clearance time of the bolus was reduced to one-half. This shows the importance of the combination of both peristalsis and swallowed saliva in maintaining an esophageal pH of 4. A loss of or abnormality in either of these mechanisms impairs esophageal motility and the clearance time and favors the development of reflux esophagitis. Patients with reflux esophagitis are more likely to have nocturnal symptoms because the effect of gravity is lost in the recumbent position and salivation ceases or decreases entirely at night.[36] Sleep also tends to reduce the frequency of swallowing and to increase the clearance time, thus favoring the evolution of reflux esophagitis. These factors combine to lower tissue resistance.

2.2.5.2. Clinical Findings

Patients with GR complain of either heartburn or chest pain. The former may be worsened by eating, by hot drinks, or during sleep. Many regurgitate food into their mouths with deep bending or during the

night. The chest pain may simulate angina pectoris, and commonly it occurs at night. It may give the sensation of squeezing, crushing, or burning pain. Its radiation patterns may be similar to those of angina pectoris.

2.2.5.3. Diagnosis

Esophagram should be obtained to rule out neoplasms and other lesions. Double-contrast radiography is often helpful in making a diagnosis of GR. The distensibility of the distal esophagus is increased in reflux esophagitis. Usually, it is greater than 25 mm in diameter in symptomatic patients. The esophageal radionuclide transit test correlates well with the manometric findings in revealing esophageal reflux.[28] The sensitivity and reliability of the acid perfusion (Bernstein test) have been improved by the addition of taurine bile salt conjugate to the 0.1 NHC1.[46]

Endoscopy allows identification of mucosal lesions and permits mucosal biopsy. In this disorder, the mucosa is often disclored, and ulcers, exudates, and luminal narrowing may be observed visually. Histologically, the mucosa is infiltrated with polymorphonuclear or mixed polymorphonuclear esosinophils and plasma cells. Usually, there is evidence of erosion or ulceration. The histologic findings are essential for diagnosis. Occasionally at endoscopy, there may be no visible evidence of esophagitis. In these patients, microscopic examination of the biopsy may reveal the diagnosis.

2.2.5.4. Treatment

Symptomatic therapy consists of advising the patient (1) to avoid certain foods and eating before bedtime and to refrain from substances that lower esophageal sphincter pressure, such as caffeine, alcohol, chocolate, and peppermint; (2) to lose weight if he is overweight, since obesity is associated with increased reflux; (3) to elevate the head of the bed on 4-in. blocks for gravity effect; (4) to use drugs such as antacids, 30 ml 1 hr after meals and at bedtime, or Bethanechol, 10 to 25 mg, cimetidine, 300 mg, or metoclopramide, 10 mg, given on a schedule similar to that of antacids. Ranitidine, 150 mg, is given bid. The H_2 antagonists inhibit basal, nocturnal, and stimulated gastric secretion.[47,48] Koeltz *et al.* found the most important factor in the healing of esophagitis is related to the extent of erosions found at endoscopy.[49] Lesions that involve the entire circumference of the esophagus healed much slower than isolated superficial lesions. After 6 weeks of ranitidine therapy, 150 mg bid, only 6 of 26 patients with large circumferential lesions had healed, whereas 78% of patients with smaller erosions healed

within the same period. Age, sex, body weight, the duration of symptoms, and alcohol consumption had no effect on healing. In a second double-blind maintenance study with ranitidine, 61 patients with healed esophagitis were given placebo versus ranitidine at bedtime. After 6 months, approximately one-third of the patients in each group had had a recurrence. Patients who had had the most pronounced daytime symptoms at the time of initial healing had the highest relapse rate. Endoscopy is a valuable diagnostic as well as prognostic tool in dealing with reflux esophagitis.

Omeprazole is a new type of inhibitor of gastric acid secretion. It works as the H^+,K^+-ATPase level in the parietal cell. Dent *et al.* treated eight patients with ulcerative peptic esophagitis with 30 mg of Omeprazole daily for 8 weeks. Seven of the eight patients had resolution of their heartburn within 2 weeks; by 4 weeks, six of the patients had endoscopic evidence of complete healing, while the remaining two patients had substantial improvement. After 8 weeks, only one patient had persistent evidence of a tiny area of esophageal ulceration. Omeprazole effectively blockaded acidification, but did not alter the manometric findings of these patients.[50]

About 75% of patients with GR respond to antacid therapy. Ninety percent of the 25% who do not respond to antacids usually respond to treatment with cimetidine or anitidine. For those who develop scarring or cicatricial lesions of the esophagus, dilatation is required.

If medical therapy fails, antireflux surgery may be necessary. One of the most popular surgical procedures for reflux esophagitis is the Nissen gastroplasty. Henderson and Harryatt followed 335 consecutive patients for 6 years after they had undergone a Nissen gastroplasty for intractable GR.[51] All were extensively studied preoperatively and postoperatively. The postoperative results were impressive; 93% ate normally and had no investigative evidence of a recurrence of their GR, 4% had mild residual symptoms, and 3% had persistent or recurrent symptoms. Sometimes a reoperation may be necessary for individuals with recurrent GR following antireflux procedures. Maher *et al.* reviewed the results of 55 patients who had failed surgery for reflux esophagitis and underwent reoperation. Overall, 80% claimed satisfactory results following their second operation. The mortality in this group, however, was 4%.[52]

2.3. Stomach

Achylorhydria is a relatively common occurrence in the elderly, the incidence increasing from 10% at age 45 to approximately 20% by age 75 years. Both basal and maximal gastric secretion decline with age,

particularly in women. This decrease tends to correlate with the development of chronic atrophic gastritis. Loss of acid production indirectly influences iron absorption and pepsin activity by altering the gastric pH. Other aged-induced physiologic changes occur in the elderly upper gastrointestinal tract but they are less dangerous than disease *per se,* most notably peptic ulcer disease, cancer, and bleeding.

2.3.1. Upper Gastrointestinal Bleeding

The major causes of upper gastrointestinal bleeding (UGIB) have not changed significantly over the past 25 years. Table I lists the etiology and the mortality observed in 633 older patients with upper gastrointestinal bleeding over a 5-year period (1975–1980).[53] The results are comparable to those observed in other large studies of middle-aged patients[54–56] (Table II). Age appears to favor UGIB. Forty-eight percent of Allen's patients with UGIB were over age 60, and 40% of the men and 60% of the women in Schiller's series were 68 years of age or older. In the national survey of the American Society of Gastroenterology, the average age of patients with UGIB was 57 years ± 17.5 years.[57] A few other studies of UGIB in the elderly are available.[58,59] Chang and his associates studied 66 patients over age 65 with massive UGIB. Thirty had duodenal ulcers, 17 gastric ulcers, seven gastritis, seven esophageal varices, two marginal ulcers, and three had an un-

Table I. Etiology and Mortality of Upper Gastrointestinal Tract Hemorrhage in 633 Patients[a]

	Number (%)	Deaths	Alcoholic liver disease (%)
Duodenal ulcer	122 (19.3)	4	18.1
Gastritis	107 (16.9)	4	23.6
Esophageal varices	72 (11.4)	14	98.6
Mallory–Weiss tear	53 (8.4)	6	96.2
Gastric ulcer	45 (7.1)	4	15.7
Esophagitis	25 (3.9)	—	19.3
Duodenitis	21 (3.3)	—	30.3
Gastric carcinoma	10 (1.6)	—	10.0
Stomal ulcer	10 (1.6)	—	20.0
Warfarin	24 (3.8)	—	13.0
Unknown	26 (4.1)	5	19.2
Multiple lesions	118 (18.6)	14	57.5
	633	51	

[a]All patients had endoscopy, upper-gastrointestinal series, or both studies within the initial 36 hr of admission.

Table II. Causes of Upper Gastrointestinal Bleeding

	ASGE (1981)[a]		Palmer (1970)		Thomas-Rees (1954)		BVAMC[a]	
	%	No.	%	No.	%	No.	%	No.
Duodenal ulcer	24.3	(541)	27.1	(406)	32.6	(157)	24.6	(157)
Gastric erosions	23.4	(521)	12.8	(193)			20.3	(129)
Gastric ulcer	21.3	(474)	12.4	(186)	17.3	(84)	7.7	(49)
Varices	10.3	(229)	19.6	(295)	3.5	(17)	17.3	(111)
Mallory–Weiss tear	7.2	(160)	4.8	(77)			10.7	(68)
Esophagitis	6.3	(141)	7.2	(109)			4.2	(27)
Erosive duodenitis	5.8	(128)					3.5	(22)
			0.5	(7E)[a]				
Neoplasm	2.9	(64)	1.4	(21G)[c]	5.1	(25)	1.6	(10)
Stomal ulcer	1.8	(41)	3.1	(47)	2.9	(14)	1.6	(10)
Esophageal ulcer	1.7	(37)	0.7	(10)				
Osler's disease	0.5	(11)	0.5	(8)				(3)
Warfarin							3.7	(24)
Other	6.3	(139)	6.9	(141)	38.4	(186)	4.1	(26)
Total		2486		1500		483		636
Multiple lesions	32.2	(696)[b]	38.6	(530)			18.6	(118)

[a]ASGE, American Society Gastroendoscopy (Survey); BVAMC, Birmingham Veterans Administration Medical Center.
[b]Two lesions, 532; three lesions, 126; four lesions, 38.
[c]E, esophagus; G, gastric.

determined bleeding site. Seventy percent experienced hypovolemic shock, yet with early endoscopic diagnosis and appropriate surgery the mortality among the 39 surgically treated patients was only 5%. Surgical morbidity was high, however, because of associated diseases, such as diabetes, pulmonary disease, hypertension, and atherosclerosis.[58]

Yao and Wang treated 100 consecutive patients over age 60 years with active UGIB.[59] Among their patients, as in our series of 633 older patients with UGIB, peptic ulcer disease was the most common cause of bleeding. Twenty-two of their patients also bled from esophageal ulcers. The incidence of malignant disease in this series was 23%. This is considerably higher than the incidence reported from England and the United States.[60]

2.3.1.1. Endoscopy

Most agree that UGIB is a common event in the elderly, and that gastroendoscopy provides a higher diagnostic yield (50 to 95%) than upper gastrointestinal radiologic studies (50 to 70%) even with double-

contrast barium examination (65 to 80%).[53–58] However, there is considerable disagreement on the need for early endoscopy, i.e., within the first 12 to 24 hr of UGIB. Some believe that early endoscopy fails to decrease mortality or to shorten hospital stay and therefore is not necessary.[61–63] Since many patients, perhaps 70 to 85%, stop bleeding within 24 to 48 hr, these authors suggest that endoscopy can be done later when the patient is stabilized. One investigator even questions the need to treat alcoholic cirrhotics who are bleeding because of the cost and frequent lack of compliance of alcoholics.[64] For several reasons the latter is not well accepted. The study of Peterson *et al.* is often given as a reference for the nonessentiality of early endoscopy. These investigators evaluated the need for early endoscopy randomly in 202 patients with UGIB.[62] However, randomization was carried out after their patients stopped bleeding; 32 of the 102 nonendoscoped patients rebled, and these patients had to undergo subsequent endoscopy to establish a diagnosis so that definitive treatment could be undertaken. Patients who stop bleeding and then rebleed in the hospital have a high mortality. In these patients, endoscopy becomes even more crucial to both diagnosis and treatment.

Proponents of early endoscopy believe it ensures a more accurate diagnosis, leads to early appropriate therapy, and permits selection of patients with a high rebleeding risk. Bleeding that recurs after hospitalization is associated with a 12-fold increase in mortality.[65] Early endoscopy allows identification of certain stigmata, such as the "visible vessel" or "adherent clot" in an ulcer that helps to identify most ulcer patients who are likely to rebleed and therefore are at greater risk of death.[66–68] A visible vessel refers to a raised red or blue lesion within the ulcer. Vigorous washing of the ulcer bed may be necessary to remove nonadherent material covering the vessel. Endoscopy can be carried out on patients too ill to be moved to a radiologic suite. It also permits identification of the highly lethal lesions that are often missed by upper gastrointestinal barium studies, namely, esophageal varices, multiple lesions, and Mallory–Weiss tears.[53] A recent prospective reappraisal of emergency endoscopy for patients with portal hypertension showed that (1) bleeding from esophageal varices was often intermittent; (2) coexisting lesions capable of bleeding were common (39 of 90 patients) but seldom bled (5 of 90 patients); (3) active bleeding often occurred later (61%); and (4) repeated endoscopy was necessary to assess subsequent variceal hemorrhages. Intermittent bleeding of this type could only be diagnosed by endoscopy.[69]

Between 1968 and 1977, national mortality from UGIB decreased. Early endoscopy and more effective immediate treatment, e.g., sclerotherapy for varices, lowered mortality from UGIB from 8–10% to 5–

6%.[70] Mortality was even lower (2.4 to 4.4%) when variceal bleeding was excluded from Hunt's series and our own.[70,71] In Hunt's study of 2377 patients, mortality decreased despite a significant rise in the number of elderly patients. Improved survival was attributed to early endoscopy, sclerosis of bleeding esophageal varices, improved resuscitation, and postoperative care.[71]

Unfortunately, the use of propranolol in the management of esophageal varices had not proven to be a major factor.[72,73] This drug lowers portal pressure, reduces liver blood flow, decreases the cardiac index, and increases sodium excretion in cirrhotic patients after an acute sodium load. The mechanism underlying its ability to reduce portal pressure is not entirely clear. Initially, LeBrec *et al.* reported that patients with bleeding esophageal varices treated with propranolol, sufficient to reduce their pulse rate by 25%, had a lower incidence of bleeding from esophageal varices.[74] Using a dosage of 2 mg/kg twice daily, Sogaard claimed that after 18 months all of his propranolol-treated patients were alive and none had rebled.[75] Placebo-treated patients fared poorly. Eight died from variceal bleeding and four others rebled. Burroughs *et al.*, in a prospective randomized trial of 48 patients with cirrhosis and esophageal varices, found no difference in recurrent variceal bleeding among propranolol-treated patients (12 of 26) and controls (11 of 22) over a follow-up period of up to 21 months.[72] The contrast between LeBrec's and Burroughs' reports may have been due to the inclusion in the latter study of patients with more severe liver disease. More recent data suggest propranolol is not effective in patients with Child's class III and IV cirrhosis.[73] Propranolol has some serious side effects. It may induce portal–systemic encephalopathy, and it may interfere with the diuretic treatment of ascites.[73]

Vasopressin is another drug capable of reducing portal pressure. Systemic vasopressin infusion may stop variceal bleeding by decreasing portal venous flow and reducing portal vascular resistence. Unfortunately, it does not improve survival. One toxic side effect, peripheral vasoconstriction, can be reduced or prevented by use of sublingual nitroglycerin or isosorbide dinitrate.[76]

2.3.1.2. Therapeutic Endoscopy

Therapeutic endoscopy is now a common practice as well as a subject of intense study. Bipolar electrocoagulation and neodymium–yttrium aluminum Garnet (ND–YAG) laser photocoagulation are both effective procedures for the treatment of solitary bleeding gastrointestinal lesions such as peptic ulcers.[77,78] Kiefhaber *et al.* claim that when the results of ND–YAG laser therapy are compared with surgery, the

mortality rate is reduced for acute bleeding ulcers from 58 to 23%, and for chronic bleeding ulcers from 25% for resection and 15% for vagotomy to 0%.[77] Today more than 200 medical centers are using lasers for treatment of UGIB. The recent approval by the U.S. Food and Drug Administration of lasers for this purpose indicates laser therapy is safe and effective for UGIB and that it is no longer considered an investigational device. Recent data suggest the "heater probe" may be better than the laser for UGIB. It is also less expensive than the laser unit and more readily transported. O'Brien *et al.* compared the use of the small bipolar probe (heater probe) in 204 patients with bleeding peptic ulcers.[78] Patients were randomized to electrocoagulation (101) or supportive therapy (103). Fewer patients in the treated group continued to bleed or rebled (17) than in the control group (34). The small (7 Fr.) bipolar probe used in this study passes through the biopsy channel of a standard endoscope. Active bleeding does not hinder the effectiveness of the probe. Indeed, those with active bleeding in O'Brien's study had the greatest benefit. Mortality related to bleeding was also lower in the treated patients. The authors indicate the probe is fragile and easily broken and they emphasize that inexperience on the part of the endoscopists may be hazardous to the patient.[78]

Terblanche *et al.* revitalized the use of sclerotherapy for esophageal variceal bleeding.[79] In an early study, they were able to eradicate varices in 95% of their 37 patients with sclerotherapy. Unfortunately, varices recurred in over one-half after 21 months. Recent studies that have provided additional information concerning sclerotherapy are numerous. Witzel *et al.* compared prophylactic sclerotherapy in 56 patients with cirrhosis and varices who had never bled from their varices with 53 similar patients treated conservatively. Prophylactic sclerotherapy diminished the frequency of variceal bleeding and overall mortality. Over a 2-year follow-up, bleeding occurred in 9% of the sclerotherapy patients compared to 57% in the control group. Mortality rates in the groups were 23% and 55%, respectively.[80] Terblanche's current treatment policy for suspected acute variceal bleeding includes vasopressin infusion and emergency endoscopy. Sengstaken balloon tube tamponade is reserved for patients with active variceal bleeding at the time of emergency endoscopy.[81] Bornman *et al.* followed 66 patients with 127 active bleeding episodes for 1 year after balloon tamponade and injection sclerotherapy were used to control the bleeding. Bleeding was staunched with one or two injections during 75 admissions with a mortality rate of 21%. Unfortunately, the mortality rate increased to 66% for those requiring three or four injections during a single hospitalization and reached 89% when patients with Child's category A disease were excluded.[82] Spence *et al.*, too, found patients with Child's categories B

and C did poorly.[83] Patients requiring repeated sclerotherapy for eradication of all their varices appear to do better if their sclerotherapy treatment is given once a week rather than every 3 weeks. Sarin *et al.* found weekly sclerotherapy obliterated the varices earlier ($p < 0.01$) and reduced the rebleeding rate. However, those receiving weekly variceal injection developed more local ulcers ($p = 0.01$). Other complications of sclerotherapy, namely strictures, dysphagia, retrosternal pain, and fever, were the same in groups sclerosed at 1- and 3-week intervals, as was the mortality rate.[84] In recent studies, sclerotherapy patients had fewer recurrent bleeding episodes than controls, and the majority of rebleeds occurred before variceal eradication was complete and they are mild. Control of hemorrhage is achieved in 70 to 86% of patients with one or two injections of the sclerosant. Unfortunately, no difference in survival has been observed between sclerosed and nonsclerosed patients.

In essence, injection sclerotherapy effectively controls hemorrhage from bleeding esophageal varices in most patients, but it is no longer the panacea predicted earlier. Repeat sclerotherapy is usually necessary for eradication, and the chemical esophagitis may impair esophageal motility or induce esophageal ulcers, reflux esophagitis, and/or esophageal stricture.[85]

At present, patients with massive UGIB and characteristic orthostatic changes should be placed in an intensive-care unit and undergo early endoscopy. This is particularly true for older patients. These measures and supportive treatment and/or surgery optimize the chances of the elderly bleeder for survival. Of course, the presence of severe cardiac or respiratory disease, metastatic cancer, or renal failure alters the prognosis greatly and may force the geriatrician and the family to accept less aggressive therapy.

2.3.2. Peptic Ulcer Disease

Age does not decrease the incidence or dim the suffering caused by ulcer disease. Many patients experience the disease for the first time after age 60.[86,87] Among older patients, the disease is more serious and complications are more frequent. Gastric ulcers and duodenal ulcers are referred to, herein, as peptic ulcer disease (PUD). However, each has its own clinical and pathophysiologic characteristics.

2.3.2.1. Incidence

About 4 million Americans are afflicted by PUD in the course of 1 year. Even so, the incidence and virulence of PUD have been declining for several decades. Similarly, the number of surgical operations for PUD has

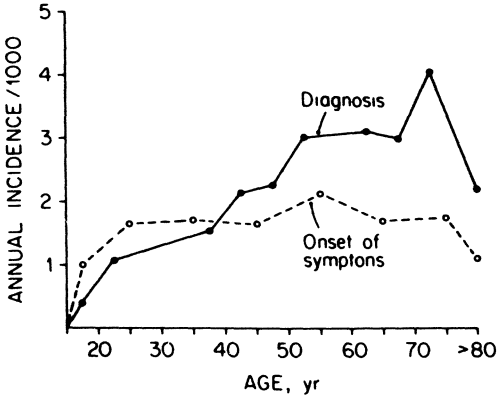

Figure 5. Incidences of new cases of duodenal ulcer in men according to age of onset of symptoms and age at time of diagnosis. Incidence by onset of symptoms reaches plateau at age 25, but incidence by time of diagnosis keeps increasing to age 75. (Adapted from Grossman,[88] through courtesy of Yearbook Publishers Inc.)

decreased. In the United States the death rate due to duodenal ulcer for men in their fifth decade fell from 40 per million in 1921 to 7 per million in 1976 and in England from 104 per million in 1930 to 16 per million in 76. A similar decrease was observed for duodenal ulcer disease in women and for gastric ulcers in both men and women. PUD is prevalent among the elderly. Between 1970 and 1978, the percentage of persons over age 60 in the United States increased from 14 to 15% while the number of people this age who were hospitalized for duodenal ulcers (DU) rose from 27 to 36% and for gastric ulcer from 40 to 48%.[86–90] Figure 5 shows the incidence of DU by onset of symptoms and diagnosis. Incidence of symptoms reaches a plateau by age 25 years, whereas the incidence by diagnosis increases steadily to age 75. The incidence for gastric ulcer is low before age 40 years and peaks between 40 and 65 years.[87–91] Gastric ulcers constitute 30 to 50% of ulcers in patients 65 years of age and 85% of ulcers in patients requiring surgery after age 75 years. Although PUD does not affect life expectancy, unless complications occur, the death rate due to PUD increases with age. In 1977 in the United States, it rose from 1 per 100,000 at age 45 to 48 per 100,000 at age 85.[87]

2.3.2.2. Etiology

The etiology of PUD is probably multifactorial. The previous concept that duodenal ulcers are solely the result of increased acid secretion is no longer valid. Hydrochloric acid and pepsin are essential to the development of duodenal ulcer but not necessarily to the evolution of a gastric ulcer. Heredity plays a role. One-half of all patients with DU have hyperpepsinogenemia I, as the result of an autosomal dominant trait.[92] Pepsin's role in the etiology of peptic ulcer disease has been under in-

creasing investigation. Pepsinogen I contains at least five electrophoretically discrete bands. The role of pepsin I may be important in ulcerogenesis. It is increased in peptic ulceration, and its activity extends over a wide range, i.e., from pH 1 to pH 5. Some have suggested increased secretion of pepsin I may be the cause of peptic ulcer. This subject was reviewed recently.[92,93] DU is more common in "individuals with blood group 0 and in 'secretors,' i.e. individuals who secrete blood group substances into their saliva and gastric juice."[92,93] Since ulcer disease is not explained by simple Mendelian genetics, two theories, the "polygenic" and the "heterogeneity" concept have been proposed as explanations.[94]

Other factors related to etiology include smoking, aspirin use, and long-term corticosteroid usage. Smoking is associated with an increased incidence for PUD and with delayed ulcer healing. Excessive aspirin ingestion doubles one's chance for acquiring a gastric but not a duodenal ulcer. Contrary to popular opinion, stress, occupation, and personality type are no longer considered risks for ulcer disease.[95]

Patients with DU are hypersecretors of acid. They have the capacity to produce more gastric acid and pepsin than normal individuals. Their parietal cell mass is greater; the response of these cells to pentagastrin, gastrin, and histamine is increased and gastrin release is thought to be greater than normal following ingestion of food. DU patients often have elevated plasma levels of pepsin I presumably as the result of a greater number of pepsinogen I-producing cells. Because of heterogeneity, however, not all these changes are found in every ulcer patient. Patients with PUD frequently have defective mechanisms for protecting the mucosa from acid and pepsin.

Much excitement has been generated by the recent finding of a strong correlation between the presence of *Campylobacter pyloridis* on the gastric epithelial cells and histologically confirmed gastritis, duodenitis, and peptic ulcer disease. This spiral bacteria colonizes the gastric antrum in 90 to 100% of patients with duodenal ulcer, over 70% of those with gastric ulcer, and one-half or more of those with nonulcer dyspepsia.[96–98]

C. pyloridis is unique in that it is able to move freely in the viscid mucus layer covering gastric epithelial cells. Here, it is protected from both acid and alkaline gastric secretions and free to induce ultrastructural changes such as the destruction of the epithelial cell microvilli and intracellular edema.[99] Other findings supportive of a pathogenetic role for *C. pyloridis* in the upper gastrointestinal tract include (1) its ability to produce an acute dyspeptic syndrome in a volunteer who swallowed a culture of the organism in an attempt to fulfill Koch's postulate,[100] (2) the finding of high serum IgA and IgG titers to *C. pyloridis* in patients

with gastritis,[101] (3) histologic improvement and eradication of the organism from the gastric mucosa of patients treated orally with bismuth salicylate but not with placebo or erythromycin ethylsuccinate,[102] (4) the ability of metranidazole to destroy *C. pyloridis* in patients with DU and to induce clinical improvement, and (5) the observation that bismuth subcitrate lowers the rate of ulcer recurrence better than acid-reducing agents.[102–104]

Proponents of an etiologic role for *C. pyloridis* in peptic ulcer disease have shown the organism infests islands of metaplastic gastric epithelium in the duodenum. Here, presumably, it causes a breakdown in mucosal integrity, thereby abetting back-diffusion of H^+ ions and causing mucosal ulceration.[104] If *C. pyloridis* does have an etiologic role in PUD, the new urea nucleotide breath test may prove to be a valuable diagnostic tool. This organism has a high endogenous urease content, and Graham found the ^{13}C urea test picked up evidence of *C. pyloridis* in 10 of 48 volunteers, one of four patients with nonulcer dyspepsia, and 10 of 12 patients with PUD.

Figure 6. Large, benign, penetrating gastric ulcer. Benign ulcers usually have a depth that is greater than their width, rugae radiating from the ulcer base, an incisura opposite the crater (not seen in this case), and a Hampton's line—a line of decreased desnity surrounding the ulcer and representing the margin of normal mucosa at the ulcer's edge.

2.3.2.3. Diagnosis

One feature unique to PUD is the unreliability of the history. Less than 50% of patients with a history suggestive of PUD have endoscopic evidence of ucler. In the elderly, epigastric ulcer pain is less common and often bears no temporal relation to meals. Eating may actually make the pain worse. Symptoms are likely to be vague with no pattern of pain relief following eating. Often, there is a substantial loss of weight and a loss of appetite. Ninety percent have nocturnal pain, but such pain is common to other chronic abdominal disorders in the aged, as is relief by antacids.[105]

Despite the unreliability of the history and a paucity of physical findings in ulcer disease, both are essential to determine the elderly patient's health status. It is important to know whether the patient has an ulcer history, is taking medications that can induce a gastric ulcer, and has other diseases, e.g., cardiovascular, renal, or pulmonary disease. The best ways to diagnose PUD is by upper gastrointestinal radiologic study or endoscopy (Fig. 6). Endoscopy is more accurate but it is more expensive.[105] In older patient with gastric ulcers, endoscopy is essential to rule out malignancy. Six to eight biopsies are taken from the ulcer side and one or two are taken from the ulcer base at the time of endoscopy. Brush cytology of the ulcer is also mandatory before initiating treatment for gastric ulcer.

2.3.2.4. Clinical Course

More than one-half of patients over 60 years with ulcer disease experience the disease for the first time. The elderly ulcer patient suffers a disproportionate number of serious complications, and the ulcer disease is often masked by the presence of other serious illnesses. Diagnosis is often delayed by the belief that ulcer is uncommon among the aged.[90,91]

The aged with symptomatic ulcer disease usually have a serious course. Only one in four can be expected to become asymptomatic. About one-half develop major complications as the first sign of their ulcer. Twenty percent will be hospitalized with a bleeding complication sometime in the course of the disease.[90,91] Many obtain relief only with surgery. Although patients over 60 constitute only 15% of the ulcer population, they account for 80% of all ulcer deaths.[106]

2.3.2.5. Treatment of Ulcer Disease

Considerable advances have been made in the therapy of ulcer disease over the last 20 years. Initially, antacids were the mainstay of treat-

ment. Then, the H_2 antagonists became available, and now a newer group, the benzimidazole agents, appear to be even more efficacious in their healing properties.

Antacids are still useful therapeutic agents, particularly for the relief of pain. Thirty milliliters of a potent antacid, given 1 to 3 hr after meals and at bedtime, promotes healing of duodenal ulcers within 4 to 8 weeks.[107,108] Hypersecretors require about 80 mEq/hr of neutralizing capacity. Fortunately, high-potency antacids, like Mylanta II, Gelusil II, and Maalox Therapeutic Concentrate, provide 120 mEq/30 ml. The abundant therapeutic literature relative to antacid use in duodenal ulcer stands in striking contrast to the ability of antacids to heal gastric ulcers. In fact, until recently, no clinical trials were available to show that antacids were superior to placebo in healing gastric ulcers.

Sucralfate, a sulfated disaccharide (1 g before each meal and at bedtime), is also effective in the short-term healing of duodenal and gastric ulcers.[109] Relapse is common after either short-term cimetidine or sucralfate therapy, but the duration of remission is longer after sucralfate, 7.3 versus 4.6 months.[110]

Both cimetidine and ranitidine are effective in promoting the healing of duodenal ulcers. Cimetidine (200 to 300 mg) taken with meals and at bedtime (300 to 400 mg) or Rantidine (150 mg bid) leads to healing of 73 to 85% of duodenal and 65 to 88% of gastric ulcers within 4 to 6 weeks.[106,107] Ranitidine appears to heal even ulcers resistant to Cimetidine and antacids. Furthermore, its side effects are relatively few. Duodenal ulcers, however, recur within a year in 80 to 90% of patients treated initially with H_2 antagonists. Relapse may be lower after treatment with other ulcer-healing drugs, notably certain bismuth preparations.[111]

Pain relief occurs earlier and more frequently than ulcer healing with H_2 antagonists and antacids, a fact revealed by serial endoscopic examinations.[112,113] In one study, 75% of duodenal ulcer patients treated with cimetidine were asymptomatic by the fourth week of treatment, but only 30% had endoscopic evidence of ulcer healing. Many of these same patients later developed asymptomatic recurrences of their ulcers.

Both vitamin A, 50,000 units tid, and tricyclic antidepressants (TCA) aid ulcer healing. In combination with antacid therapy, vitamin A improves the healing rate of gastric ulcers significantly.[114] *In vivo,* TCAs decrease gastric acid secretion, while *in vitro* they are potent H_1 and H_2 receptor blocking agents.[115,116]

Omeprazole, a substituted benzimidazole, is a new potent, long-acting antisecretory drug. It interferes with the proton pump in the secretory membrane of the gastric pareital cell and H^+,K^+-ATPase, an enzyme unique to gastric mucosa. It is the only antisecretory drug capable of reducing day and night gastric acid by 100% and 85%, respec-

tively. Omeprazole given orally, 40 mg, is rapidly absorbed from the gastrointestinal tract of the elderly with a T_{max} of 15.4 ± 5 min. Oral omeprazole, 20 mg (57 patients) or 30 mg (55 patients), given once daily to these patients with duodenal ulcer led to endoscopic evidence of healing in 79 and 96%, respectively, after 2 and 4 weeks of therapy. Other studies have shown a 30-mg oral dose is just as effective in healing gastric ulcers within 4 weeks. In the German multicenter trial, omeprazole, 20 mg daily, led to a higher healing rate than ranitidine (150 mg bid). In the Danish multicenter trial, 46% of ulcer patients given cimetidine and 73% of those given omeprazole had ulcer healing after 2 weeks of therapy. By 4 weeks, 74% and 92% of each group had healed ulcers.[117,118] As Walan notes: "The effect of omeprazole on ulcer healing and symptom relief has been of a magnitude never seen before. The action of the drug is so rapid and pronounced that it is not yet possible to determine the lowest dose which should be recommended to achieve an optimal effect."[118] Omeprazole is also more efficacious in the treatment of the Zollinger–Ellison (Z–E) syndrome than H_2 antagonists. In both the European study, which involved seven patients, and the NIH study, which included 11 patients with Z–E syndrome, omeprazole, 60 and 70 mg daily, respectively, led to a dramatic and stable reduction of gastric acid secretion. At present, omeprazole is the most valuable alternative to total gastrectomy in patients with the Z–E syndrome, especially those resistant to H_2 antagonists.[119]

2.3.2.6. Long-Term Therapy with Cimetidine and Ranitidine

The safety of long-term therapy with H_2 antagonists has been studied carefully. Both cimetidine and ranitidine are relatively safe and prevent duodenal and gastric ulcer recurrence. Over a 12-month follow-up, the recurrence rate fell from 80% to less than 20%.[109] In one study, ranitidine given at bedtime for 3 years did not cause significant side effects.[120] Long-term therapy is particularly valuable for elderly ulcer patients when the risk of surgery is unacceptable because of disease.

2.3.2.7. Side Effects

Diarrhea is common with antacids containing magnesium hydroxide. Aluminum hydroxide preparations tend to cause constipation. Older patients with hypertension or borderline cardiac failure should be given a low-sodium antacid, e.g., Riopan. Commerical antacid preparations containing calcium, e.g., Tums and Rolaids, are dangerous to the elderly, particularly those with renal dysfunction. These agents can induce the milk–alkali syndrome or cause acid rebound.

Sucralfate is practically nonabsorbable. It acts locally at the ulcer site to block the errosive effects of acid, pepsin, and bile.[109,110] Its most notable side effect to date is constipation. Side effects due to cimetidine include gynecomastia, agranulocytosis, and mental confusion. Confusion occurs more commonly in the elderly, particularly in those with hepatic or renal disease and higher-than-normal blood levels. Somnolence is common in the old, and drugs like Librium and Valium increase it. Cimetidine inhibits the hepatic microsomal enzyme metabolism of chlordiozepoxide (Librium) and diazepam (Valium) but not oxazepam (Serax) or lorazepam (Ativan).[121,122] It also slows the metabolism of theophylline and propanolol hydrochloride (Inderal) and potentiates the hypoprothrombinemic effect of warfarin.[122–126] It may lead to elevation of serum transaminase (SGOT, SGPT) levels but rarely causes clinical hepatitis. In general, reactions are relatively rare and usually are short term. Side effects are fewer with ranitidine because cimetidine binds at other sites in the body. Unlike cimetidine, ranitidine does not bind cytochrome P-450 at androgen receptor sites or at certain brain sites. Prolactin levels increase after intravenous boluses of cimetidine but not ranitidine. Ranitidine does not affect the drug blood levels of agents metabolized by hepatic microsomal enzymes, but it may induce hepatotoxicity and has caused hepatitis on occasion. It also crosses the cerebrospinal barrier and may cause mental confusion, somnolence, depression, vertigo, and other central nervous system reactions. Ranitidine has also been observed to induce both tachycardia and bradycardia. In 11 of 18 prospective randomized studies, the monthly relapse rate following ulcer healing and cessation of therapy was 16.9 ± 4% for cimetidine and 8.1 ± 3% for comparative agents.

The side effects secondary to omeprazole have not been fully characterized to date. Solvell analyzed its side effects in 2500 volunteers and patients.[127] Most of them had peptic ulcer disease, but 72 had Z–E syndrome that was H_2-blocker resistant; 45% of the latter were treated for up to 1 year with 60 mg/day. No significant hematologic, renal, electrolyte, glucose, triiodothyronine, or thyroxine abnormalities occurred. Four of the 2500 patients developed rashes, one a deep-vein thrombosis, one vertigo, one diarrhea. and one had leukopenia before the study. Omeprazole does not appear to interact with anticoagulants, although it does seem to inhibit the elimination of diazepam. To date, no specific pattern of reactions to the drug has been detected. They appear to be relatively few.

Five factors are known to affect ulcer healing. In order of importance, they are as follows: (1) sex (women heal more rapidly than men); (2) alcohol (small doses (20 mg/day) may actually improve healing); (3) smoking (impairs healing); (4) age (the elderly heal more slowly); and (5)

antacids, sucralfate, H_2 antagonists (cimetidine–ranitidine), and omeprazole potentiate healing.[121]

2.3.2.8. Complications

Major complications of duodenal ulcer in the elderly are similar to those found in the young, namely, bleeding, perforation, obstruction, and intractability.

Bleeding, the most common complication, accounts for over one-half of all fatal ulcer cases. One-half of all patients with bleeding ulcers are over age 50 years and their chances for bleeding are twice that of younger ulcer patients. Table II shows the incidence of bleeding ulcers in several large series of patients with massive UGIB. Recently, a common criterion was proposed for massive bleeding. Specifically, a patient suffering from shock who needs more than 1000 ml of blood or plasma expander by rapid transfusion within 1 hr, or more than 2000 ml within the initial 24 hr, to stabilize the circulation and in whom the hemoglobin level is 8.0 g/dl or less "is considered to have massive bleeding." Ulcer disease is still the most common cause of UGIB. After age 70, the risk of bleeding in a duodenal ulcer patient increases 7% yearly.[90] Bleeding also accounts for 80% of the complications of gastric ulcer after age 70 years.[105,128] At this age, massive bleeding is common. In the study of Brooks and Eraklis, it was the first sign of disease in 80% of fatal cases.[129] Mortality ranges from 3 to 11% for duodenal and 8 to 30% for gastric ulcer bleeding. When older patients require surgery for uncontrolled bleeding, the mortality approaches 50%. Forty percent of exsanguinating hemorrhages after age 65 are due to gastric ulcers. Death from bleeding gastric ulcers is twice that from bleeding duodenal ulcers.[128]

Mortality increases considerably with ulcer rebleeding, and the risk of rebleeding is doubled in the elderly patient who has bleeding at the first sign of ulcer disease.[90] Twenty to thirty percent of patients with bleeding duodenal ulcers and 30 to 40% of patients with bleeding gastric ulcers rebleed after hospitalization. A substantial number of these patients require emergency surgery.[128] Under these circumstances, mortality often exceeds 50%. As mentioned earlier, endoscopy is extremely valuable in detecting patients who will rebleed.[130,131] Factors predisposing to recurrent hemorrhage should be looked for carefully. These include age, hypotension, massive bleeding, increased transfusion requirements, and certain endoscopic observations.[130,131] In a prospective study of 177 patients with acute UGIB due to PUD, rebleeding occurred in 2 (2%) of 114 without shock, in 7 (18%) of 38 with a pulse rate above 100 beats/min, and in 12 (48%) of 25 with shock (systolic blood pressure

less 100 mm Hg). A similar gradient was found with the presence of endocopic signs above. Rebleeding occurred in 4 (5%) of 79 without endoscopic signs, in 11 (23%) of 48 with a clot, and in 5 (50%) of 10 with a visible vessel. When the evidence of rebleeding was assessed in shock patients, it was significantly higher in those with endoscopic signs. Shock in patients with a visible vessel or clot led to rebleeding in 11 (79%) of 14 patients, whereas only 1 (9%) of 11 patients with no endoscopic signs rebled.[132] Thus, the presence of shock in a patient with a positive endoscopic finding is a stronger prediction for rebleeding than the presence of either of these parameters alone.

2.3.2.8a. Diagnosis. Diagnosis usually entails procedures such as nasogastric aspiration (NGA), endoscopy, or barium sulfate roentgenography. NGA for blood or heme-positive material is a simple and accurate means of localizing UGIB. Less than 1% of patients with UBIG have negative NGAs. A linear correlation also exists between the color of the NGA and active UGIB.[130] Forty-eight percent of patients with a bloody NGA have active bleeding or at least oozing lesions at endoscopy.

The color of the NGA and stools is also related to mortality. Bleeding patients with a clear NGA and brown stool have a mortality of 7.9%. When both are bloody, mortality is about 28%.[130] Red or maroon stools in ulcer patients are associated with increased mortality, transfusion requirements, complications, and the need for surgery.

Barium studies of the UGI tract miss or lead to misdiagnosis of duodenal ulcers in 20 to 40% of bleeding patients. In contrast, endoscopy reveals up to 95% of the lesions responsible for UGIB.[130] Although double-contrast barium studies are superior diagnostically to routine barium studies in patients with UGIB, few hospitals provide this service. All agree that endoscopy is the best method to make the diagnosis of bleeding ulcers, and the elderly including octagenarians tolerate it well. Eschar *et al.* carried out 104 gastrointestinal endoscopies on 75 patients 80 to 90 years old. Seventy-three were upper (29 emergency) endoscopies. In 24 patients, diagnoses were not made radiologically. These authors concluded that the safety and accuracy of endoscopy in the elderly did not differ from those in the young.[133] Since mortality is so high in the elderly, endoscopy should be carried out promptly without regard to the controversies concerning the value of early endoscopy. In the elderly diagnosis is critical—so endoscopy should be mandatory. The urgency of the situation in the elderly dictates that early management be instituted promptly, taking full advantage of the newer techniques to control bleeding. The high mortality associated with gastric ulcer bleeding makes it imperative to consider surgery early in the course of bleeding from a gastric ulcer.

2.3.2.8b. Treatment of Bleeding Ulcers. Mortality from peptic ulcer bleeding has not changed significantly over the past 40 years. Resuscitative and supportive measures constitute the initial therapeutic steps in management of UGIB. Volume replacement, particularly blood, is crucial, indeed often essential for survival. Four double-blinded control studies have shown that neither H_2 antagonists nor antacids stop bleeding.[134–138] Conversely, examination of the data from 27 randomized trials involving 2500 patients with UGIB suggests that treatment with H_2 antagonists may reduce the rates of rebleeding, surgery, and death.[139] However, in elderly patients the only significnat benefit appeared to be confined to the reduction of rebleeding from gastric ulcers. Somatostatin, a potent inhibitor of pentagastrin, stimulated hydrochloric acid, and pepsin secretion may have a therapeutic role. One recent randomized study showed 8 of 10 bleeding patients responded to an intravenous bolus of somatostatin (250 μg) followed by 250 μg every hour for 48 to 120 hr. In contrast, cimetidine was ineffective in 8 of 10 patients.[137] If supportive measures fail, the newer endoscopic techniques such as laser photocoagulation and electrocoagulation are beneficial and have been discussed. When these fail, surgery becomes necessary.

High-risk factors associated with UGIB due to PUD include age (>60 years), six or more blood transfusions, absence of a preoperative diagnosis, a systolic blood pressure under 100 mm Hg, a history of cardiac, respiratory, renal, or hepatic disease, or the presence of congestive heart failure.[139]

2.3.2.8c. Perforation and Penetration. The incidence of peptic ulceration declined in both the United States and Great Britain after 1940 and for years remained steady between 20 and 23 per 100,000. After age 45 years, the risk of perforation doubles and almost triples by age 65 years. Since 1979, however, the rates in older (>65 years) women in Great Britain, but not older men, have increased significantly, climbing from 13.8 to 42.5/100,000 per year in Scotland and from 8.3 to 20.8/100,000 per year in England and Wales. In contrast, the rate of perforation in younger men and women continues to decline.[140] Perforation is the first sign of disease in 20% of older patients with duodenal ulcer and in 11% of those with gastric ulcers. One in ten of these patients bleed from their perforating ulcer. Perforation accounts for 25% of all ulcer-related deaths, the mortality rate increasing sharply with age.[141,142] The increase in ulcer perforation in the United Kingdom may be due to a sharp rise in the use of nonsteroidal and antiinflammatory drugs by the elderly.[143] Factors affecting the outcome of perforation and associated with increased morbidity and mortality in-

clude (1) age—the chance of dying from any cause within the next year increases 60% between the ages of 65 and 70; (2) delay in diagnosis, i.e., greater than 48 hrs; (3) recent onset of ulcer symptoms before perforation; (4) presentation with gastrointestinal bleeding, (5) concurrent medical disease, and (6) shock.[141,142]

Perforation in the elderly leads to two clinical patterns. In the first there is a typical history for ulceration: sudden onset of severe abdominal pain accompanied by marked rigitidy of the abdominal muscles and radiologic evidence of air under the diaphragm. Early recognition and surgical treatment lead to a low mortality. In the second, the history of ulcers is vague or unreliable; signs and symptoms associated with perforation are atypical and abdominal pain is mild or absent. Often the patient is confused, complains of malaise, or has nausea and vomiting. The significant clinical features associated with admission to medical or surgical wards are listed in Table III. As shown, in patients admitted to the surgical service diagnosis is usually clear, whereas the diagnosis is seldom obvious in patients admitted to the medical service.

Surgery is essential to treatment. Simple closure of the perforation is still effective and is prefrred by many surgeons. Others prefer partial gastric vagotomy.[144,145]

2.3.2.8d. Giant Duodenal Ulcer. Giant duodenal ulcer is in effect a posterior penetrating lesion, 3 to 6 cm in size. These ulcers are encountered predominantly in the elderly. The mean age in Nussbaum and Schusterman's study of 32 patients was 59 years (range 30 to 81 years).[146] These ulcers are associated with a high complication rate. Usually the diagnosis is delayed. Only 11 of the 34 cases reported by Lumsden *et al.* were diagnosed radiologically, because the entire duodenal bulb was eroded and gave the appearance radiologically of a badly scarred duodenal bulb or a duodenal diverticulum.[147] Similar erosion was found in 18 of 26 patients studied by Eisenberger and his co-workers.[148] Because of the propensity of giant ulcers to penetrate posteriorly, their base is often composed of necrotic pancreatic tissue. Perforation is much less common than bleeding, which occurs in 50 to 75% of patients with giant ulcers. Seventy-five percent of 32 patients in the Nussbaum-Schusterman series presented with UGIB and 9% with perforation. Mortality is high (40 to 50%), and emergency surgery is often necessary. Treatment with cimetidine was shown to be effective in over one-half of 26 patients with giant ulcers in Klamer and Mahr's series.[149] Only two died. Nussbaum and Schusterman believe these lesions should be managed surgically and that an acid-reducing procedure should be carried out during primary surgery. Two of twenty-four patients whom they managed medically (mean length 41 months) had hemorrhage (two deaths) and 22 had recurrence, requiring subsequent surgery. The com-

Table III. Clinical Features Observed in Patients with Perforated Duodenal Ulcers[a]

		Medical admissions (14)	Surgical admissions (24)
Confusion	(+)	4	0
	(−)	10	24
Guarding	(+)	3	18
	(−)	11	6
Rigidity	(+)	3	19
	(−)	11	5

[a]From Coleman and Denham.[142]

bination of UGIB and posterior penetration should always raise the possibility of giant duodenal ulcer, particularly in an elderly person.

2.3.2.8e. Obstruction. Overall, the incidence of obstruction is 4% in the young and 10% in the elderly.[129] Patients with obstructions usually have a history of long-standing ulcer disease. Edema and spasm of the bulb secondary to ulcer disease are usually responsible for the blockage. Nasogastric suction in conjunction with fasting and parenteral fluid support usually provides temporary relief. Effectiveness of this therapy can be checked by use of the "saline-load test," which is used to assess the degree of obstruction. Symptoms are similar to those found in the young, but weight loss can be marked and in older patients suggests the possibility of cancer.[134]

2.3.2.9. Surgery

Surgery for ulcer disease in the elderly carries a significant risk and considerable morbidity. In the Framingham study, surgical mortality was 10% for patients under age 60 years with bleeding duodenal ulcers and was 25% for those over 60 years of age.[89] Since the course of ulcer disease in the elderly is unpredictable, most patients were treated medically at onset. Patients with massive bleeding from gastric ulcers with exposed blood vessels need YAG laser hemostasis or ethanol injection as soon as possible, since 30 to 40% will rebleed within 72 hr with conventional drug therapy.[150]

The indications for surgery are intractability, recurrent bleeding, obstruction, and perforation. About 20% of Americans with duodenal ulcers require surgery. Five percent of these are incapacitated by surgery and even more (10 to 40%) develop chronic ill effects.[89] Hence, the decision to operate should not be taken lightly. Surprisingly, most opera-

tions are carried out for intractable disease rather than bleeding, perforation, or obstruction. Not surprisingly, these patients have a higher risk of postoperative complications than patients who have bled, perforated, or obstructed.

About 30% of patients with a bleeding ulcer have a second hemorrhage within 5 years. Chances for rebleeding a third time approach 60%. Since each episode carries a 7% chance for death, recurrent bleeding is a serious condition and demands prompt attention.

In the past, simple closure of ulcer perforations was the treatment of choice. However, over one-half of patients treated in this manner require definitive surgery within 10 years. For this reason, many surgeons now carry out more definitive surgery at the time of perforation, especially in patients with a long history of ulcer disease.[140,142,151]

Certain differences between duodenal and gastric ulcer lead to different surgical approaches. When surgery is necessary for duodenal ulcers, the preferred treatment is hyperselective vagotomy. At present, proximal truncal (parietal cell) vagotomy is the operation of choice for severe or intractable duodenal ulcer disease.[152–154] Among 233 patients with intractable disease subjected to this operation at the Mayo Clinic, there was no mortality. Postoperative symptoms such as nausea and diarrhea occurred in less than 3%, and the recurrence rate was 4.9%. The recurrence rate was higher (12.3%) among 154 duodenal ulcer patients treated with vagotomy and pyloroplasty at the same institution. Diarrhea and dumping occurred in 16.2% and 7.8% of these patients, respectively.[139] A 5- to 10-year follow-up of parietal cell vagotomy at the Lahey Clinic showed that 2 of 25 patients (8%) operated for intractability, 3 of 19 treated for obstruction, and two of seven operated on for bleeding had a recurrence of ulcers.[155] In another 36-month follow-up, after highly selective vagotomy, 9% of 174 patients had symptomatic ulcers and another 9% had asymptomatic ulcers found endoscopically; 30% also had duodenitis.[156] This high recurrence rate may lead to more radical surgery in the future.

In a 10-year review, Atkins initially treated 135 of 163 gastric ulcers medically and 28 with surgery. Medical therapy was successful in 58 patients. Forty of the remaining 77 patients required surgery; the remaining 37 continued on medical therapy.[157] The appropriate surgical procedure for the complications of gastric ulcer disease remains a matter of individual choice. The end results of gastric resection with vagotomy versus oversewing the bleeding point of the gastric ulcer together with a vagotomy plus a drainage procedure do not appear to differ significantly. The risk of cancer with gastric ulcer, although relatively low, often leads to quicker surgical intervention than for duodenal ulcer.[158]

2.3.3. Gastritis

Acute (AG) and chronic (CG) gastritis are common afflictions of the elderly. Achlorhydria in the elderly is usually due to CG. The frequency of achlorhydria rises steadily with age. About 30% are afflicted by age 70 years.[159,160]

2.3.3.1. Etiology

AG has usually been associated with viral enteritis, food poisoning, and bacterial toxins and has a rapid onset. Recently, Marshall *et al.* have shown that *Campylobacter pyloridis* (CP) appears to be an important factor in the origin of dyspeptic disease, gastritis, and peptic ulcers.[98,100] They have suggested that CP—which is seldom detected in normal gastric mucosa—is a cause of AG and that infection with CP can lead to CG.[96] In an effort to fulfill Koch's postulate, Marshall ingested a culture of CP and developed acute gastritis, but gastroscopically his antral mucosa appeared to be normal.[100] Since then Salmeron *et al.* reported a 28-year-old woman with acute AG who on gastroscopy had a purulent antral gastritis.[161] Microbiologic examination of biopsy tissue smears revealed *Campylobacter*—like gram-negative curved rods among mucus and in polymorphonuclear neutrophils. Oral erythromycin (1 g daily × 10) led to resolution of symptoms within 24 hr. Fifteen days after the end of antibiotic treatment the antral mucosa appeared to be normal and no evidence of CP was evident on microscopic examination.

Tobacco, alcohol, salicylates, hot drinks, iron deficiency, pernicious anemia, bile reflux, and allergy have all been associated with CG.[160,162] Atrophic gastritis develops in the wake of superficial gastritis. The mean transition time is about 17 years.[159] Atrophic gastritis is common in the sixth and seventh decades.[163]

2.3.3.2. Clinical Findings

In AG, symptoms vary considerably owing to differing etiologies. They include anorexia, nausea, vomiting, epigastric fullness, and pain. If infection is the cause, fever, headache, diarrhea, and flulike symptoms may develop. Dehydration and prerenal azotemia are common in the aged if vomiting or diarrhea is severe.

In CG, symptoms are usually vague and nondescript and may consist of epigastric tenderness or flatulence. Clinical findings are usually unremarkable unless other disease, e.g., gastric ulcer or carcinoma, is present. CG is never diagnosed until other possibilities are eliminated.

2.3.3.3. Diagnosis

Diagnosis of both AG and CG requires invasive procedures. Endoscopy revealed the acute purulent gastritis described above and considered the result of CP invastion. In CG, radiographic studies may show thinning of the gastric folds. Endoscopically, the mucosa appears thin. Visible mucosal capillaries and superficial erosions are seen easily.[162] Biopsy is confirmatory, revealing glandular atrophy and infiltration of the lamina propria with lymphocytes and plasma cells. Hypochlorhydria in CG is associated with a raised fasting serum gastrin level and gastrin cell hyperplasia.[159]

2.3.3.4. Treatment

There is no specific treatment for AG. Treatment is mainly supportive. It consists of replenishing fluid, maintaining electrolyte balance, and refraining from solid food during the acute episode. Removal of aggravating factors such as alcohol, salicylates, nonsteroidal antiinflammatory drugs, and caffeine is important. If CP is responsible, erythromycin appears to be therapeutic. Vitamin B_{12} improves the chronic gastritis associated with pernicious anemia, but once atrophic gastritis develops, the lesion is usually irreversible.[163]

2.4. Hepatobiliary Disease

By age 65, the liver mass has decreased from 2.5 to 1.5% of total body mass while hepatic blood has decreased by 40%. Even so, there is sufficient liver mass to allow normal liver function and bile salt production. The hepatobiliary system of the geriatric patient is subject to the same diseases as in the young. Cirrhosis is common, with its peak incidence at 60 to 65 years of age. Alcoholism is a major cause in the elderly as in the young, reportedly accounting for 7 to 17% of so-called "senile cirrhosis" patients. In the elderly, ascites, portal encephalopathy, hepatic coma, and other hepatic complications differ little in their clinical presentation or treatment. All of these have been the subject of recent reviews.[164–167]

2.4.1. Viral Hepatitis

All four forms of viral hepatitis (A, B, non-A–non-B, and delta) occur in the elderly but none occur with the frequency seen in youth. Clinical manifestations, laboratory abnormalities, and other features of

the disease are essentially the same, but morbidity and mortality are greater in the aged. In the older patients, congestive heart failure may occasionally mimic acute viral hepatitis.[168]

2.4.2. Chronic Acitve Hepatitis

2.4.2.1. Etiology

In the past, chronic active hepatitis (CAH) was thought to result from an altered immune response to viral hepatitis B or drugs such as methlydopa, isoniaziad, oxyphenisatin, and nitrofurantoin.[169] Now we know that hepatitis B, hepatitis non-A–non-B (NANB), superinfection of hepatitis B virus with delta agent can all lead to CAH. Many drugs, too, are capable of the same. Presumably, the etiologic agent alters the hepatocyte membrane in such a manner that the immune system no longer recognizes it as self and produces antibodies against the patient's liver cells.[170] "D" (delta) hepatitis is a defective virus composed of a delta antigen core encapsulated by an HBsAG coat and requiring the help of hepatitis B virus to support its replication and expression.[171,172] Since "D" hepatitis is dependent on HBsAG synthesis for its assembly, it can only infect HBsAG-positive individuals. The duration of the HB virus infection determines the duration of delta infection; hence patients with chronic hepatitis B infection can support delta virus replication indefinitely. Patients with simultaneous acute hepatitis B and D infection tend to have fulminant hepatitis. Indeed, about one-third of patients with fulminant hepatitis B have serologic evidence of simultaneous delta infection. In patients with simultaneous infection, liver damage appears to be caused by the direct cytopathic effect of the delta agent rather than an immunologic mechanism. HBsAG-positive patients with delta infections also appear to have a high frequency (60 to 80%) of antibody to hepatitis "e" antigen. Previously up to 20% of CAH patients were thought to harbor NANB hepatitis virus.[172,173] Many of these may have delta infections instead of NANB hepatitis.

NANB hepatitis is transmitted predominantly by transfusion or percutaneous inoculation. Evidence to date suggests there are two different types of blood-borne NANB hepatitis agents, in addition to an enterically transmitted NANB agent. NANB hepatitis accounts for approximately 90% of transfusion-associated hepatitis and for about 15 to 30% of sporadic cases of hepatitis. Clinically, the features of percutaneously acquired NANB hepatitis resemble those of hepatitis B but are less severe during the acute phase of illness. Transfusion-acquired NANB hepatitis is more likely to lead to chronic hepatitis. Chronic hepatitis has not been identified following the epidemic type of NANB hepatitis.

2.4.2.2. Clinical Findings

CAH is a late complication of hepatitis B or NANB infection. Superimposed D virus can transform a mild chronic hepatitis to a severe form of CAH. The patient with CAH is often symptom free, the only evidence of disease being abnormal liver function studies. Symptomatic patients usually complain of fatigue, anorexia, weakness, and malaise. Later, they may develop the signs and symptoms of cirrhosis or those of its complications. Diagnosis requires biochemical (SGOT–SGPT elevations) and histologic evidence of liver disease 6 months after an attack of acute viral or drug-induced hepatitis. Histologic evidence consists of infiltration of the parenchyma and portal zones by plasma cells and lymphocytes, piecemeal necrosis, and formation of intralobular septa.

The natural course of CAH varies considerably. For patients who fail to improve with treatment, the course is one of progressive deterioration. About two-thirds of CAH patients die within 5 years of onset of symptoms.

2.4.2.3. Treatment

Over the past several years a clearer perspective of the natural course of chronic hepatitis B virus (HBV) infection has been developed. When viral replication is ongoing, the patient is infectious and has progressive liver disease. When viral replication ceases, the liver disease becomes inactive and the hepatitis B surface antigen (HBs) is positive owing to integration of viral genes within the patient's genome. Fortunately, these two phases can be identified by HBe antigenemia and anti-HBe, respectively. During active viral replication, the patient's serum is positive for HBeAg and HB-DNA. During this phase the patient is highly infectious. However, spontaneous clearance of HBe antigenemia occurs in 5 to 15% of patients annually. Antiviral agents such as vidarabine acclerate this process. Conversion from the infectious to the noninfectious state also increases with age. As the hepatic disease becomes inactive, patients are likely to be serum anti-HBe positive and HBV-DNA negative.[174] Management for the HBeAg positive, HBV-DNA positive patient differs from that of the patient who is anti-HBe positive and HBV-DNA negative.

Previously, steroids and azathioprine were the mainstays of therapy for CAH. Then, Lam and his associates suggested prednisone hastened relapse and increases complications in CAH.[175] There is suggestive evidence, too, that azothiaprine therapy was harmful in CAH^+ HBsAG patients. Therapeutically, transfer factor and levamisole did not prove efficacious. Available data for antiviral chemotherapy, however, are somewhat promising.

Current studies have indicated that corticosteroids enhance viral replication, while withdrawal leads to rebound immune stimulation with temporary loss of HBe antigen. Perrillo and his colleagues took advantage of this and treated their CAH patients with prednisone, 40 mg daily for 8 weeks; then they stopped the drug and treated the patients with vidarabine phosphate for 4 weeks. Seventy-three percent of their patients had clearance of HBe antigen positivity.[177] In another study six of nine patients treated with a combination of steroids and vidarabine phosphate had a loss of HBe antigen.[178]

Anti-HBVe positive patients are usually older and have more advanced liver disease than those who are HBeAg positive. If they are symptomatic and are HBV-DNA positive, antiviral therapy may be tried. Those who are HBV-DNA negative but anti-HBVe positive may have an immunologic component to their liver disease. If they are symptomatic and their liver biopsy is compatible with CAH, a cautious trial of prednisone therapy may be helpful, at a dose of 30 mg daily for 1 week followed by 10 to 15 mg daily for 3 months.[176]

2.4.3. Cholelithiasis

2.4.3.1. Incidence

The true incidence of cholelithiasis is unknown. It varies among nations and races and it increases with age. The highest incidence is found in Sweden and the lowest among the Masai of Africa. In Sweden, 70% of women over age 70 and 50% of men in the 90s have gallstones.[179] In England 30% of the women over age 70 and 15% of the men have gallstones. The percentage rises with age.[180] About 20,000,000 Americans have gallstones, and each year, 500,000 to 700,000 undergo a cholecystectomy.[181] In the Framingham study, the incidence was 8% over a 10-year period. Gallstones are more common in women than in men in this country. They occur more frequently in multiparous women. Most Americans have cholesterol stones (80%), 10% have mixed stones containing cholesterol and pigment, and 10% pure pigmented stones.[182]

2.4.3.2. Etiology

The high prevalence rate in Western countries has been attributed to a high consumption of refined carbohydrates, which induce lithogenic bile formation.[179] However, the micellar theory of stone formation is no longer unchallenged. Fasting bile is usually supersaturated with cholesterol according to the mixed micelle theory. Yet, it does not readily nucleate. Biliary nucleation is essential to stone formation. The crucial element for nucleation is still unknown. Pattinson and Chapman

claim that biliary cholesterol is transported as a mixed micelle and nonmicelle complex. The latter predominates during the fasting period when the bile acid concentration is lowest.[183] The rich fasting cholesterol is largely in a stable vesicular form in association with phospholipids but not bile acid. The importance of sex hormones in cholesterol gallstone formation has also come to light via the demonstration of estrogen and progesterone receptors in the human gallbladder. It will be interesting to see how these new concepts evolve over the next few years.

Other factors associated with increased prevalence of gallstones are obesity, cirrhosis, and Crohn's disease. Vegetarians rarely, if ever, develop gallstones.[183] The incidence is doubled in cirrhosis and increased two- to fivefold in Crohn's disease. Hemolysis is responsible in cirrhosis and impaired absorption of bile salts in ileitis. Age and drugs (e.g., oral contraceptives and clofibrinate) are other factors.[182,184] Cholesterol stones develop if bile salt production is altered due to (1) defective bile synthesis, (2) a decrease in the enzyme necessary for bile synthesis (cholesterol 6-alpha-hydroxalase) or (3) an increase in cholesterol production secondary to an increase in the hepatic enzyme (hydroxymethylglutaryl coenzyme-A reductase) necessary for cholesterol synthesis.[185,186] The kinetics of biliary lipid secretion and gallbladder storage of bile have been reviewed recently by Mok *et al.*[187] Pigmented stones are usually associated with hemolysis, alcoholic liver disease, biliary tract infection, and advanced age.

2.4.3.3. Prognosis

Patients with gallstones are grouped into four categories: (1) asymptomatic (50%), (2) symptomatic (30%), (3) dyspeptic (15%), and (4) surgical (5%).[188] Previously, it was reported that 50% of symptomatic patients would undergo cholecystectomy within 5 years owing to recurrent symptoms, ductal obstruction, or pancreatitis. Over the same period a similar percentage of asymptomatic patients become symptomatic. Twenty percent of the dyspeptics develop cholecystitis or biliary colic within a decade. Results of the National Cooperative Gallstone Study, in which 305 patients were followed for 24 months and given only placebo, were not as distressing. The probability of patients in this study having biliary tract pain during the 2 years of follow-up was significantly increased only if the patient had a history of such pain in the preceding year. Stone growth (>0.5 cm) was observed in 38%, but stone volume decreased spontaneously in 18%. Despite the high incidence of biliary pain, only 4% required nonelective surgery over the 24-month period.[189]

Gallstones are the cause of jaundice in about one-third of the elderly. Croker reviewed seven different series of elderly patients with

jaundice reported between 1962 and 1979.[190] Primary extrahepatic malignancy and metastatic carcinoma were responsible for jaundice in about 50% of all patients (range 31 to 62%), stones were responsible in 27% (range 12 to 50%), drugs in 6 to 20%, liver disease *per se* in 11 to 48%, and hemolysis in 2 to 5%.[190]

Gallstones are common in the elderly, but they are frequently overlooked because in most they are silent or their presentation is atypical. The usual clinical presentations found in association with stones, i.e., acute cholecystitis, biliary colic, or Charcot's triad (right-upper-quadrant pain, fever, and jaundice), are usually absent.

Fortunately, diagnosis has been aided by the availability of ultrasonography and endoscopic retrograde cholangiopancreatography (ERCP). While stones may only be demonstrated in 50% of patients by ultrasonography, a normal-sized duct and the presence of normal liver function tests are proof that there is little chance of stones and that ERCP is unnecessary.[191]

2.4.3.4. Treatment

Many surgeons consider the presence of gallstones a mandate for cholecystectomy. Their reasoning is based on three observations; namely, (1) 50% of patients become symptomatic with age, (2) the elderly tolerate surgery less readily, and (3) they account for 70% of the deaths associated with acute cholecystitis.[181] Cholecystectomy is also advocated for patients with diabetes mellitus, stable angina pectoris, and gallbladder stones. These conditions increase complications and the surgical risk. Still, most prefer to treat asymptomatic patients over 65 years of age conservatively, particularly those with renal or liver disease. In this respect, ERCP has proven helpful both diagnostically and therapeutically in the aged. It may also be used to eliminate gallstone obstruction at the time of diagnosis. Since 1973, bile duct stones have been extracted by endoscopic papillotomy (EPT). Success has been achieved in almost 90% of patients, but there are complications in 7 to 10% of patients undergoing EPT. Hemorrhage is the most frequent complication (30%), but only one in three requires surgery. EPT is associated with a 1% mortality rate. Extracorporeal lithotripsy or gallstone dissolution may be necessary if EPT fails.[192]

2.4.3.5. Gallstone Dissolution

Earlier it was hoped that advances in gallstone dissolution might prove a boon for the aged with cholesterol gallstones. Effective dissolution is limited to cholesterol stones and this type of stone is found in

about 80% of American patients. Cholesterol gallstone dissolution has been used for both gallbladder stones and common-bile-duct stones. Two basic radiologic criteria are essential before patients are considered for dissolution therapy, namely, the presence of radiolucent (cholesterol) stones and a functioning gallbladder. Stones with a rim of calcification are usually cholesterol stones, but odds are 4 to 1 they are pigment stones if the calcification is central.

In the National Cooperative Gallstone Study (NCGS), 900 patients with cholesterol stones were treated with chenodeoxycholic acid (CA). Only 13.5% of those taking 750 mg daily of CA had complete stone dissolution; 27% had partial dissolution of their stones. Among those taking 375 mg daily, only 5.2% had complete stone dissolution.[193] The latter dosage is now considered to be inadequate.[194] The recommended oral dose is now 15 mg/kg per day for 2 years. Slim patients achieve better results and women respond to treatment better than men. Chemical analysis of stones later removed surgically from CA-treated patients who had participated in the NCGS study showed a significant difference in the surface calcium of their stones. It was greater than 1% in 48% of stones taken from the CA-treated group whose stones did not dissolve but greater than 1% in only 16% of the placebo-treated patients. Rings of increased calcium concentration on the gallstone surface may impair gallstone dissolution by CA.[195]

Ursodeoxycholic acid (UDCA) is superior to CA for stone dissolution.[194] It is essentially free of the major side effects of chenodeoxycholic acid, i.e., nausea, vomiting, diarrhea, and transient elevation of serum transaminase and cholesterol levels, without a decrease in cholelitholytic power. These two agents also differ in their mode of cholesterol solubilization. CA is more effective than UDCA in bringing cholesterol into micellar solution, but it has less ability to transport cholesterol in a liquid crystalline form (mesophase). UDCA decreases cholesterol absorption more effectively than CA but does not suppress bile acid synthesis as effectively as CA.[196]

As experience has been gained, we have learned that prolonged therapy fails to increase the rate of stone dissolution; calcification of undissolved stones occurs in 20%, and complications requiring cholecystectomy are relatively common. Even when partial stone dissolution occurs, continued CA treatment fails to yield complete dissolution in one-third. Recurrence rates rising from 22% from 1 year after cessation of therapy to 53% after 2 years have been observed. Thus medical dissolution of gallstones appears to be of limited value.[196,197] At present, it is indicated for aged patients with radiolucent stones and functioning gallbladders who are poor surgical candidates and who lack immediate surgical indications for cholecystectomy.

Experience with CA and UDCA has led to studies of other agents. One of these, methyl tertiary butyl ether (MTBE), has been found to dissolve cholesterol gallstones both *in vitro* and *in vivo*. *In vitro* it dissolved human cholesterol gallstones within 60 to 100 min versus 50 hr for monooctanoin. Preliminary studies in humans have shown MTBE rapidly dissolved cholesterol gallstones without causing serious side effects. However, MTBE is a potent lipid solvent, and intravascular or intrahepatic infusion could lead to hemolysis or necrosis. In one recent study, the drug was administered by percutaneous transhepatic puncture of the gallbladder.[198] This would not be feasible in patients with acute biliary tract infection. MTBE effectively dissolved the gallstones of these two patients. In another, MTBE was infused after surgery for retained common bile duct stones via a teflon catheter inserted through the postoperative T tube. MTBE failed to dissolve the radiolucent stones of all three patients in this study.[199] The different results contained with MTBE in these two studies are attributed to contact. Within the gallbladder, MTBE had direct and persistent contact with the gallstones. In the common bile duct, persistent contact is not as efficacious because of MTBE leakage from the common bile duct into the duodenum. Thus, the usage of MTBE will probably be for stones confined to the gallbladder.[199]

Biliary Tract Stones. In most instances, the treatment of choice for choledocholithiasis is cholecystectomy with T-tube insertion and drainage. Two to six percent of such patients are found to have common duct stones postoperatively. These stones may be removed by a basket inserted through the T-tube sinus tract or by endoscopic sphincterotomy. As an alternative, attempts have also been made to dissolve stones through the T tube left in place following cholecystectomy. Originally, surgeons used saline or heparin T-tube lavage to flush out retained stones. Later sodium cholate was used but without great success.[197] More recently monooctanoin (Capmul 8210) was introduced for this purpose. Monooctanoin is a digestion product of medium-chain triglycerides.[200,201] *In vitro,* it dissolves mixed cholesterol stones twice as fast as sodium cholate solutions. Initially monooctanoin (Capmul 8210), infused at a rate of 3 to 10 ml/hr via a T tube, was claimed to dissolve 90% of retained bile duct over a 4- to 21-day period.[201,202] The duration of treatment was dependent on the size and number of stones. Recent reports vary; e.g., Palmer and Hofmann found monooctanoin effective in only 26% of cases, but in another 21% of their patients the stones became smaller but did not pass.[202] However, in 90% of the patients it facilitated successful endoscopic treatment. In the remainder it was ineffective or was stopped because of side effects. In contrast, Abate and Moore reported dissolution of 50 to 75% of gallstones with use of monooctanoin.[203] This drug is

relatively safe, but toxicity results from absorption of the drug or tissue infiltration. Gastrointestinal side effects include nausea, vomiting, abdominal pain, and diarrhea. Previously, we mentioned the value of MTBE in gallstone dissolution.

Ultrasonic fragmentation of gallstones has also been carried out successfully *in vitro* using the Wolf ultrasonic lithotrite. Average fragmentation time is about 20 sec compared to a minimum dissolution time of 4 days with monooctanoin. Moreover, ultrasonic fragmentation does not depend on the cholesterol content of stones. Ultrasonics may assume an important role in the future therapy of biliary gallstones.[204]

2.4.4. Acute Cholecystitis

The major complication of cholelithiasis, "acute cholecystitis," is a serious and often fatal illness of the aged.[181] In this group, emergency cholecystecomy carries a higher mortality (11 to 17%) than for the young (1 to 3%). Indeed, 70% of all deaths from acute cholecystitis occur in the elderly.[181] About 50% of those who die have other concomitant illnesses.

2.4.4.1. Etiology

Gallstones are the major cause of acute cholecystitis. With cystic duct blockage, bile accumulates, leading to a chemical irritation of the mucosal lining and to inflammation of the gallbladder wall. With continued obstruction, bacterial invasion occurs via the lymphatics. *Escherichia coli* and enterococci are the most common aerobic agents. *Clostridium perfringens* and *Bacteroides fragilis* are the dominant anaerobic bacteria associated with acute cholecystitis.[205] Emphysematous cholecystitis is associated with infection by clostridia and certain types of *E. coli.* Usually, it occurs in patients with diabetes mellitus.

Acalculous cholecystitis refers to acute cholecystitis in the absence of gallstones. Usually it results from the bacteremia associated with extensive wounds or severe burns.[206]

2.4.4.2. Clinical Findings

The study by Marrow *et al.* of 88 elderly patients with acute cholecystitis exemplifies the problem in the aged.[207] All but one of their patients experienced some type of abdominal pain but only 34 had temperature elevations above 37.8°C. Patients were divided into two groups: those who required emergency surgery (group I) and those who underwent elective surgery (group II). Twenty (74%) of the thirty-nine patients in group I had abdominal tenderness. Less than one-half had

peritoneal signs. Sixteen (41%) had peritonitis and 11 (28%) had jaundice. A mass was palpated in seven (18%). Absence of overt right-upper-quadrant peritonitis led to a delay in diagnosis of longer than 24 hr in one-third.

Leukocytosis occurred in 65% of acutely ill patients (group I); total bilirubin and alkaline phosphatase levels were increased in 60%, and SGOT and SGPT levels were elevated in 62%. Bactobilia was present in 70%. It was also found in 38% of elective surgery (group II) patients. Among group I patients, 17 had acute cholecystitis, nine had empyema, three gangrenous cholecystitis, four perforated gallbladder, six subphrenic abscess, and six had common bile duct stones. Among group II, four had acute cholecystitis, two empyema, one gangrenous cholecystitis, one a perforated gallbladder, and seven had common duct stones. None of the patients who had elective surgery (group II) developed a subphrenic abscess. The obvious complications in both groups were empyema, gangrene, and perforation. These complications occur in 15 to 40% of the aged with acute cholecystitis. Gangrenous cholecystitis arises from ischemic necrosis of the gallbladder wall. It results in a 22% mortality rate.

In older patients, emergency surgery is often necessary because the diagnosis is masked by a deceptively benign presentation. Many, including those with gallstones, have none of the classical symptoms or signs associated with acute cholecystitis. Instead, they may only show evidence of physical deterioration or increasing dementia.[208] Associated diseases such as coronary artery disease (30%), severe pulmonary disease (25%), hypertension (15%), and diabetes mellitus (13%) may further obscure the diagnosis.

2.4.4.3. Diagnosis

A plain film of the abdomen may reveal gallstones or a dilated or emphysematous gallbladder. Oral cholangiography and intravenous cholangiography are helpful in nonjaundiced patients. Ultrasonography is the most useful examination. This test has a specificity of 97% and a sensitivity of 88% in patients with acute biliary tract disease.[209]

2.4.4.4. Treatment of Acute Cholecystitis

Initial therapy consists of bed rest, nasogastric suction to decompress the stomach, and intravenous fluid replacement. Pain can be relieved by meperidine hydrochloride or by intravenous indomethacin.[210] Indomethacin inhibits prostaglandin synthesis, thereby reducing intraluminal pressure and relieving biliary pain. Antibiotics are

useful. Kefzolin, 1 g intravenously every 6 hr or Ampicillin, 500 mg intravenously or intramuscularly every 6 hr is usually preferred. This approach successfully relieves symptoms in 90% of patients within 72 to 96 hr.

In the past, a "cooling-off" period was often allowed so that surgery could be performed safely at a later time. Now, cholecystectomy is advocated within 24 to 72 hr of hospitalization to decrease both morbidity (15 to 45%) and mortality (3 to 10%) in the aged.[211,212] These high rates were attributed to surgical delay, to the wrong diagnosis, to cardiopulmonary problems, or to difficulty stabilizing the patient for operation. The overall mortality in patients over 64 years of age was found to be 3.3% in a recent British prospective study of 151 elective operations. It rose to 19% (4 of 21) when emergency surgery was necessary. The present and future views of gallstone disease were recently assessed at the Ninth International Bile Acid Conference in Basel.[191]

2.4.5. Choledocholithiasis

Fifteen percent of patients undergoing cholecystectomy have bile duct stones. Ultrasonography or computerized tomography readily reveals impacted stones or the presence of dilated bile ducts which suggests their presence. Percutaneous transhepatic cholangiography is also effective for localizing obstructing stones. This test should be done on the day of operation even though the Chiba (skinny) needle decreases bile leakage from the liver.[213] Operative cholangiography is another important advance. Like cholecystoscopy with a Stor–Hopkins choledocoscope, it allows visualization of the entire biliary tree.

2.5. Acute Pancreatitis

After age 70 there is a decrease in the weight of the normal pancreas from an average of 60 ± 20 g to 40 g or less by age 85 years. Diffuse atrophy of the gland occurs as the gland ages. It becomes harder and smaller and assumes a yellowish-brown hue. Pancreatic secretory capacity is maximal around the fourth decade in humans and declines thereafter. In contrast, enzymatic output declines linearly with age, peaking at about age 15.[214] Since 20% of the dry weight of the pancreas consists of enzymes, their decrease as well as acinar cell atrophy probably contributes to the loss of weight that occurs with age. The enormous proteolytic and lipolytic activity of the pancreas makes it a potentially lethal organ. This amazing gland requires only 1 or 2 min to synthesize isotopically administered amino acids into digestive enzymes and less

than 1 hr for then labeled enzymes to appear in pancreatic juice. The pancreas (0.1% body weight) has 13 times the protein-producing capacity of the liver and reticuloendothelial system combined. In a 24-hr span it secretes up to 6 g of protein, mostly as enzymes.

2.5.1. Incidence

The incidence of acute pancreatitis (AP) increases with age. Corfield *et al.*, in a study of 650 patients with AP, found the mean age for the first attack was 60 years. Mortality was 28% for those over 60 and 9% for those less than 60 years. Regional surveys from England and the United States suggest an annual incidence of 4.7 to 11 per 100,000 population per year.[215] AP is the most important nonsurgical cause of the acute abdomen in the elderly. Although there are many causes of AP (Table IV), 75 to 80% of patients have either gallstone (GSP) or alcoholic pan-

Table IV. Etiology of Pancreatitis[a]

Alcohol
Gallstones
Drugs
Thiazides
Steroids
Other
Hereditary
Traumatic
Postsurgical
Posttraumatic
Infection, viral
Metabolic
Hyperparathyroidism
Hyperlipemia
Hypercalcemia
Hemochromatosis
Diabetes
Pregnancy
Porphyria
Uremia
Idiopathic
Odd
Scorpion venom
Vascular disease
Peptic ulcer
Liver disease
Cirrhosis
Small-bowel disease

[a]From Ranson.[214]

creatitis (AAP).[213] In an analysis of 5019 patients reported by 12 different authors, Ranson found cholelithiasis was responsible for 27% and alcohol for 55%; all other causes together accounted for the remaining 19% of cases of acute pancreatitis.[214] Seligson claims that in Scandinavia, alcholol is the most common cause of AP irrespective of age or sex and that chronic pancreatitis is almost invariably caused by alcohol.[216]

Four kinds of pancreatitis have been recognized: AP, recurrent AP, recurrent chronic pancreatitis, and chronic pancreatitis.[217] Both AAP and GSP are found in the elderly, the latter being more common because many patients with AAP die before they reach 60 years of age.

The risk for alcoholic pancreatitis increases linearly as a function of the quantity of alcohol and protein consumed. For every additional 20-g intake of alcohol, the risk is multiplied by a factor of 1.4. Fat consumption correlates quadratically with risk. It is increased by ingestion of both a low-lipid diet (<85 g/day) and a high-lipid diet (>110 g/day).[218,219]

2.5.2. Alcoholic Pancreatitis

Alcoholic pancreatitis is common among the elderly. Fifty-two of our 200 patients with alcoholic pancreatitis were over age 55. AAP usually evolves after 5 to 20 years of heavy drinking. Occasionally, however, acute hemorrhagic necrotizing pancreatitis can occur after only 7 to 10 days of drinking 100 to 450 g of alcohol daily. Alcohol increases the protein content of pancreatic juice five- to sixfold, leads to protein precipitation within the intracalated ducts, and induces "lactoferrin" formation.[220] Protein precipitates present in the pancreatic juice of alcoholics and of patients with chronic calcific pancreatitis are immunologically identical with the "stone protein" that is believed to be the matrix for pancreatic stones.[221] The consumption of 80 g or more of alcohol daily also leads to fat accumulation within pancreatic acinar cells and to ultrastructural changes similar to those described in the liver cells of alcoholics. Alcohol has certain actions that make it a likely causal factor for AP. It is believed to (1) cause an increase in gastric secretion, (2) stimulate secretion production, (3) stimulate an increase in sphincter of Oddi pressure, (4) lead to a rise in intrabiliary pressure, and (5) stimulate an increase in intraductal pressure up to 40 mm Hg. Ninety percent of patients with AAP are classified as having "chronic recurrent pancreatitis."

2.5.3. Gallstone Pancreatitis

In contrast to AAP, which involves small ductules, GSP involves the large pancreatic ducts. Eighty-five to ninety percent of GSP patients have gallstones in their stools.[222,223] GSP may arise as a result of a

common channel with bile reflux, an obstructed or compressed bile duct, or edema and inflammation secondary to passage of a stone through the ampulla of Vater.

2.5.4. Diagnosis

The clinical presentation of AP varies in the elderly. Often, the history is noncontributory. In most clinical series, pain is the predominant symptom (Table V). Initially, the pain may be mild. Gradually, it increases until it peaks, where it remains for hours or days. Occasionally, pain is abrupt in onset and initially is of severe quality. It may cause the patient to seek relief by sitting bent forward with knees flexed. The location of pain and its radiation pattern changes with the site of injury, i.e., head versus pancreatic tail. This, too, tends to make diagnosis more difficult. Radiation to the back occurred in 36% of our patients with AP. Pain radiating straight through to the back, however, is more characteristic of hemorrhagic pancreatitis than pancreatic carcinoma. Nausea and vomiting are almost always present; the exception is the mild attack. Vomiting usually begins after onset of the pain, but it may precede the pain. Mild attacks often induce abdominal distention, whereas paralytic ileus is more characteristic of the severe attack. Physical findings, with the exception of tachycardia, upper abdominal pain, and guarding, are nonspecific[219] (Table VI). Severe pancreatitis causes hemodynamic changes similar to sepsis, i.e., a rise in cardiac index, a fall in peripheral

Table V. Acute Alcoholic Pancreatitis—Symptoms[a] (200 Cases)

	%
Nausea and vomiting	96
Pain	100
Location	
Generalized	26
Midepigastrium	46
Right upper quadrant	8
Left upper quadrant	4
Lower quadrants	4
Periumbilical	10
Subxiphoid	2
Radiation	
Back	48
Shoulders	18
Postural relief	10

[a]Duration of symptoms after therapy—61 hr.

Table VI. Acute Alcoholic Pancreatitis—Physical Findings (200 Cases)

	%
Jaundice	8
Hypotension—postural	12
Hypertension—diastolic < 110	14
Abdominal	
Tenderness	74
Guarding	34
Rebound	10
Hepatomegaly	6
Bowel sounds	6
Distended	2
Pleural effusion	6
Other	
Bronchitis	10
Melena	4
Hematemesis	8
DTs	16
Pallor (2° anemia)	8

vascular resistance, and an elevation of pulmonary capillary wedge pressure.[224] Hypotension, tachycardia, and shock may result from fluid loss and/or hemorrhage. The proteolytic enzymes released during AP chemically burn the omental fat and intestinal and peritoneal tissue, leading to significant fluid and protein loss. Abdominal tenderness is common. About 10% have rebound tenderness and 30% have guarding. As muscle spasm and abdominal tenderness decline, 10 to 20% of patients have a palpable mass. This may represent a pseudocyst, a swollen inflamed pancreas, or a distended stomach. Cutaneous signs such as Cullen's and Grey–Turner's are late signs of hemorrhage. Nodular fat necrosis affects about 3% of patients. These lesions can appear anywhere on the trunk or extremities.

Clinically, the most important factor is to differentiate AP from other causes of an acute abdomen. About 96% of older patients have an elevated serum amylase secondary to AP; other causes of an acute abdomen lead to elevated levels in 5% of the elderly.[225,226] Sixty percent of patients with GSP and 10 to 30% with AAP have jaundice. Serum bilirubin levels are increased two- to threefold. Hypercalcemia is more common with acute hemorrhagic pancreatitis. The amylase/creatinine ratio is not a specific indicator for acute pancreatitis. Lactoferrin is increased in the duodenal and pancreatic juices of patients with alcoholic,

idiopathic, hereditary, and chronic pancreatitis and in a small number of normal individuals.[227] C-reactive protein has proven useful in determining the severity of pancreatic inflammation in AP and its progress. A C-reactive protein level greater than 100 mg/liter at the end of the first week of illness is associated with increased risk for pancreatic complications.[228] Age, sex, and serum values for alkaline phosphatase, aminotransferases, amylase, and bilirubin together help significantly in differentiating GSP and AAP.[228]

Other helpful diagnostic tests include the following: (1) A flat plate of the abdomen to determine whether pancreatic calcification is present; it may also reveal calcified gallstones, air in the biliary tract with emphysematous cholecystitis, organ displacement, a pseudocyst, a colon cutoff sign, or obliteration of the iliopsoas shadow. (2) Intravenous cholangiography to help determine the presence or absence of biliary tract disease in the nonjaundiced patient. (3) Ultrasonography in jaundiced individulas to assess the presence of cholelithiasis. It is useless, however, when the bowel is distended with gas or the patient is markedly obese. Sequential sonographic studies may detect liquefication and pseudocyst formation in alcoholic pancreatitis. (4) Computerized tomography (CT) is of little help in identifying gallstones, but it may reveal intrahepatic and common duct dilatation as well as changes in pancreatic and peripancreatic tissues. CT also aids in differentiating chronic pancreatitis from carcinoma of the pancreas in jaundiced patients. (5) Chiba needle cholangiography allows differentiation of acute pancreatitis from acute biliary disease with hyperamylasemia.[229] (6) Endoscopic retrograde cholangiography is an excellent way to visualize the pancreatic ducts but it may induce pain identical to that experienced during attacks of pancreatitis. Recently, Anderson and his associates reported indium III autologous leukocyte imaging was as accurate as Ranson's prognostic factors in grading the severity of AP and that the technique could be used to separate mild from severe acute pancreatitis. A positive image was thought to imply substantial fat necrosis.[230]

2.5.5. Prognosis

Fortunately, acute pancreatitis is self-limiting in 95% of patients and acute hemorrhagic necrotizing pancreatitis only develops in 5%, although 40 to 80% of the latter die.[231] Acute hemorrhagic necrotizing pancreatitis usually occurs (90%) with the first attack of pancreatitis and its prognosis is poor. The mortality for hemorrhagic pancreatitis is 28% versus 7% for acute edematous pancreatitis. Hence, early diagnosis is imperative for survival. Acute hemorrhagic necrotizing pancreatitis is also highly unpredictable. This led Ranson *et al.* to search for prognostic

Table VII. Early Prognostic Signs in Acute Pancreatitis That Correlate with Serious Illness or Death[a]

Admission
Age: over 55 years
WBC: over 16,000
Glucose: over 200 mg%
LDH: over 350 1 units
SGOT: over 250 SF
During first 48 hr
Hct: decrease of 10%
BUN: rise over 5 mg%
Ca^{2+}: below 8 mg%
P_aO_2: below 60 mm Hg
Base deficit over 4 meq/liter
Estimated fluid sequestration over 6 liters

[a]From Ranson et al.[232]

signs, and 11 were found to be helpful[232] (Table VII). Among 79 patients with less than three positive signs, mortality was 3%, whereas it was 62% in the 21 patients with three or more positive signs. It was obvious that mortality increased in proportion to the number of positive criteria. The value of Ranson's prognostic criteria has been confirmed repeatedly.

2.5.6. Treatment—Medical

By the time acute pancreatitis is diagnosed, autodigestion of the organ is well advanced in the severe attack. At present, direct inhibition of intrapancreatic enzyme activation or the process of autodigestion is still not feasible. So, treatment is predominantly supportive and directed toward preventing or treating complications. However, the effectiveness of many of the past measures is still not proven. Recently, Lange and Pederson randomly treated their patients with either nasogastric suction and intravenous fluids or with oral intake of clear fluids.[233] No significant difference was found between the two groups in abdominal symptoms, degree of hyperamylasemia, and hospital stay. Mortality and complications, such as pseudocyst and pancreatic abscess, were equal in both groups. Nasogastric suction and intravenous fluids appeared to offer no advantage over simple oral fluids. To date, four controlled studies have failed to demonstrate the benefit of nasogastric suction in mild or moderately severe pancreatitis. Patients with acute necrotizing pancreatitis may require nasogastric suction because of bowel distention or paralytic ileus. No one questions the value of intravenous fluid replacement and

monitoring of the pulmonary artery and capillary wedge pressures, electrolytes and fluid intake, and output in management of severe pancreatitis. Hyperalimentation along with calcium and magnesium administration can be crucial. Pulmonary blood gases are drawn frequently. These usually become abnormal about 24 hr before the onset of acute respiratory distress developing in the patient with severe AP. Questions have been raised about other measures. Lankisch, in a discerning review, has pointed out that the use of cimetidine in AP is contradictory in both animal and human studies; that glucagon, calcitonin, and somatostatin, all hormonal inhibitors of pancreatic secretion, have not been beneficial in human studies; and that attempts to use inhibitors of autodigestive enzymes have been adjudged negatively, as controversial, or have not been evaluated in humans.[234]

Pain relief is often necessary, for the pain may be excruciating. Intravenous procaine hydrochloride is helpful in many. This agent inhibits phospholipase A, the enzyme held responsible for parenchymal necrosis. Meperidine is also effective as an analgesic. Prophylactic antibiotics have not proven helpful in stemming infections or the evolution of pancreatic abscess formation. Wall (1965) first recommended peritoneal lavage (PL) (dialysis) for acute necrotizing pancreatitis.[234a] Balldin and Ohlsson, in an uncontrolled study of 60 patients with AP, also recommended PL.[235] Ranson *et al.* retrospectively compared PL against early surgical drainage in 103 patients and recommended PL as a means of decreasing both morbidity and mortality.[232] Mayer *et al.*, in a more recent prospective randomized study of 91 patients with severe acute peritonitis, concluded differently. Of the 46 patients subjected to PL, 13 (28%) died and 16 (35%) developed major complications. There were 12 (27%) deaths and 17 (38%) major complications among the controls. All but one of the patients who died was over 50 years of age. PL did not modify the length of survival, the incidence of major complications, or the plasma amylase concentration. Occasionally, PL injured abdominal viscera and impaired ventilation. This group concluded that PL did not modify the outcome of severe acute pancreatitis.[236]

2.5.7. Treatment—Surgical

The exact role of surgery in acute alcoholic pancreatitis is not clear. Martin *et al.* state, "The results of such treatment [surgical] have been detrimental in collected series. The overall mortality for patients with acute pancreatitis increased with an increase in operative rate, regardless of the proportion of the series related to alcohol or biliary causes."[237] Overall mortality for pancreatic resection in eight reports dealing with 291 patients was 33%. Aldridge and his associates have reviewed pan-

creatic resection for acute pancreatitis in detail.[238] They note there are major problems in the application of radical surgery to acute necrotizing pancreatitis, including definition of the pathologic processes, identification of patients who will benefit from surgery, the timing, and the extent of surgery. Aldridge has identified two broad groups of patients of AP who benefit from surgery: (1) Fulminant—these patients have multisystem failure of rapid onset and deteriorate quickly. They die unless the pancreas is removed. Essentially, the pancreas is dead, and liquefaction occurs and the retroperitoneum fills with slough and pus. (2) Delayed—After a severe attack of acute pancreatitis these patients fail to thrive. Their pancreas is still partly alive and continues to secrete, leading to peripancreatic necrosis. In some the diagnosis is obvious, they have fever, retroperitoneal sepsis, and intestinal malfunction. In others the diagnosis may be difficult to make for they are clinically well. These patients improve only with removal of the necrotic tissue. These authors did not consider phlegmons or the pseudocysts in this group.

Unfortunately, no diagnostic test is available to predict the presence or absence of necrosis preoperatively, and clinical indications are the only guide to the need for surgery. So, surgeons vary in their approach. Some advocate early surgery, i.e., on the second day of the attack; others wait for 8 to 12 days. The latter hold that time allows demarcation between viable and dead tissue and thus decreases the amount of pancreas removed in many patients. They also believe that early operative intervention for AAP is dangerous and leads to an increase in intraabdominal sepsis, pancreatic abscess, and the severity of respiratory complications.[239] The answers to the major problems mentioned earlier, including the timing of surgery, are not yet available.

The issue is even more controversial for GSP. Early operative intervention for GSP carries a mortality of 5 to 25%; nonoperative mortality is higher.[240,241] Postoperative complications occur in 5 to 10%.[242–244] More impacted gallstones are found in patients operated on within 48 hr of their attack than in patients operated on after 4 days. Acosta *et al.* advocate operative intervention for GSP within 24 to 48 hr of onset of symptoms.[223] They believe early decompression decreases the chance of edematous pancreatitis progressing to hemorrhagic pancreatitis. Ranson *et al.* advocate supportive treatment for GSP until the acute symptoms have subsided and then operate.[232] Heij and his associates found that early surgery in acute biliary pancreatitis is not harmful but also that it does not improve survival.[243] All agree that biliary tract pathology must be eliminated. Otherwise, 10 to 50% of these patients sustain repeated bouts of pancreatitis.[240,241] Semel *et al.* propose a more flexible surgical approach, believing an absolute approach to GSP treatment is neither

necessary nor desirable.[245] Martin *et al.* believe surgical intervention is indicated when (1) there is uncertainty about the diagnosis, (2) the patient is getting worse despite medical treatment. (3) gallstones are present, or (4) an abdominal abscess is suspected. In their opinion, the first three conditions are indications for early operation.[237]

Since there is considerable debate concerning the timing of surgery, other approaches have been tried. Recently, Rosseland and Solhaug performed endoscopic papillotomy (EPT), within 48 hr of the onset of clinical symptoms of GSP. EPT was well tolerated and carried out without serious complications. It provided effective drainage and relieved the acute symptoms due to GSP.[246]

2.5.8. Complications

Patients with GSP survive the fluid loss associated with acute necrotizing hemorrhagic pancreatitis better than those with AAP. Hence more survive to develop pancreatic abscesses and pancreaticoenteric fistulae.[247] In contrast, pseudocysts, pancreatic ascites, thrombotic vein thrombosis, and chronic pancreatitis are more commonly associated with alcoholic pancreatitis.[248]

Hyperglycemia occurs in 50% of patients with AAP. Parathyroid hormone inactivation or parahormone deficiency is thought to be responsible for hypocalcemia.[249] Hyperlipidemia is common in alcoholics with types I, IV, and V hyperlipoproteinemia.

Respiratory complications are frequent in AP. Respiratory insufficency may result from pleural effusion, fluid overload, pneumonitis, or pulmonary infarction. Mild to moderate hypoxia occurs in 60% of patients with AP during the first 48 hr of their attack. Nonspecific factors contributing to pulmonary distress include pulmonary capillary damage, surfactant impairment, and altered respiratory muscle coordination. Respiratory distress usually develops after 4 to 5 days of illness.[250] Fortunately, arterial blood gases are more predictive of an evolving acute respiratory distress syndrome (ARDS) than the chest x-ray. Usually they become abnormal 24 hr prior to clinical onset of ARDS.

Pseudocysts occur in 5 to 20% of patients with acute pancreatitis. In most, a simple pseudocyst occurs, but about 15% of patients develop multiple pseudocysts. Serial ultrasound studies are especially helpful in early detection and for observing the spontaneous resolution of acute pseudocysts.[251] Overall mortality associated with the surgical drainage of persistent pseudocysts is 6 to 8%. Ten to fifteen percent recur following surgery and 5% rupture.[252] Pseudocyst growth depends on the continued existence of a fistula linking the cyst with the pancreatic duct.[253]

If the inflammatory resection fails to seal off the retroperitoneal space, fluid drains anteriorly, causing pancreatic ascites. If the inflammatory reaction directs the leak posteriorly, fluid seeps upward into the pleural cavity, yielding massive pleural effusions.[253,254] This type of effusion is not to be confused with the small pleural effusions seen early in an acute attack.

2.6. Appendicitis

June 1986 marked the 100th anniversary of the recognition of the appendicitis syndrome.[255] Appendicitis is a disease of the young, only 5% of all cases occurring in the elderly. However, the majority of deaths due to this lesion occur in the geriatric group. Prior to the antibiotic era, appendicitis caused mortality rates of 13 to 15% in patients over 65 years. Mortality rates still range from 2 to 14%. The elderly have a 15-fold greater chance for death from appendicitis than the young.

The causes for higher mortality among the elderly are similar to those responsible for the higher mortality rates associated with acute cholangitis and acute cholecystitis, namely, (1) delay in diagnosis and in surgery, (2) atypical symptoms in the elderly, (3) complicating diseases, and (4) postoperative complications. Many clinicians believe acute appendicitis seldom occurs in the elderly or are unaware that it often presents atypically; still others are reluctant to operate on the elderly patient.

Yet, it is essential to recognize, to diagnose, and to remove the inflamed appendix early. Otherwise, a relatively minor acute illness can progress to a lethal complication such as perforation, peritonitis, or abscess. The accuracy of diagnosis has a direct linear correlation with appendiceal perforation. In an analysis of 14,000 patients, the study with the highest perforation rate (29%) had the best diagnostic accuracy (89%) for appendicitis. The lowest perforation rate (14%) was found in the study with the worst accuracy (67%). Delays in diagnosis lead to complications.[256]

Once the diagnosis of appendicitis is made, prophylactic antibiotics, usually a combination of pencillin, gentamicin, and clindamycin, are given to protect against the possibility of appendiceal rupture prior to operation. No one can guarantee in advance of surgery that the organ is intact. Gaffney reported that the combination of antibiotics listed led to prevention of wound sepsis in 99% of 100 patients; none of his 47 patients with a perforated appendix developed subsequent sepsis.[257] Today, amputation of the appendix with ligation of the stump is the preferred method of surgery for a nonperforated inflamed appendix.

2.7. Colon

2.7.1. Diverticulosis

2.7.1.1. Incidence

It was not until the advent of contrast radiology that the frequency of diverticulosis was appreciated. Now we know diverticulosis is the most common pathologic lesion of the colon, the incidence increasing from 5% to age 40 to 50% in the ninth decade[258–260] (Table VIII). Only 1 in 70 of these patients will need hospitalization and only 1 in 200 will require surgery for diverticular disease. In Britain this amounted to 16,000 admissions in 1975.[261] In 1982, 1221 patients, (289 men and 932 women) died from diverticular disease in the United Kingdom. After age 60, the incidence of diverticular disease is considerably higher in women than men.

2.7.1.2. Etiology

The cause of diverticulosis is not known. Until recently, it was believed that diverticula resulted from either continued ingestion of a low-fiber diet, an abnormality of the muscularis propria, or an abnormality of colonic motility.[262] A lack of dietary bulk was thought to cause partitioning of the colon into partially obstructed compartments with high intraluminal pressure. Presumably the high pressure caused the mucosal lining to herniate along vascular channels through the bowel wall. A strong argument against this concept was the discovery of high intraluminal pressures in patients with the irritable bowel syndrome and following food ingestion or the administration of morphine or parasympathomimetic drugs.[263,264] Early enthusiasm for the high-fiber diets as a means of preventing diverticulosis has waned as reports appear claiming a high-fiber diet merely acts as a stool softener.[264] To date, dietary fiber has not been proven beneficial in the prevention of diverticulosis.[265]

Table VIII. Incidence of Diverticuli

Year		Percent	Number of patients	Number examined
1930	Mayo[258]	5.7	1819	31,838
1930	Rankin and Brown[417]	5.6	1398	24,620
1935	Oschner and Bargen[418]	7.0	Not given	2,747
1936	Willard and Bockus[419]	8.2	38	463
1953	Allen[420]	30		2,000
1939	Smith and Christensen[421]	22		1,016

The abnormal motility concept evolved after Barling (1926) reported that spasm of the colon observed at laparotomy produced tiny saccules along the longitudinal muscle bands.[266] Since then it has been learned that patients with asymptomatic diverticulosis and an irritable bowel syndrome have normal colonic motility whereas symptomatic patients with these diseases have abnormal motility indexes.[267] Some claim diverticulosis is a concomitant part of aging, and that it is a degenerative change. Others believe it results from progressive elastosis that may result from (1) early weaning from breast feeding, (2) the Western diet, (3) atherogenesis, and so forth. All these factors are discussed in recent reviews.[262,268] Still others maintain the disease is basically the result of a primary defect in the muscularis propria which leads to muscular thickening. Supporting this concept is the observation by Hodgson that teniamyotomy tends to a return to normal colon length and luminal caliber.[269]

2.7.1.3. Clinical Findings

Most patients with diverticulosis have few symptoms. Some complain of constipation, others of abdominal distention, and some of severe cramping pain. Constipation is more common than diarrhea and may alternate with it. The physical examination is not characteristic. Laboratory studies are also nonspecific. The barium enema is diagnostic, but in some patients only muscular thickening and luminal narrowing of the sigmoid are found on barium contrast study. In 90% of patients, the disease involves the sigmoid colon. In 45 to 60%, it is the only area involved.

2.7.1.4. Prognosis

At one time, it was thought that the greater the number of diverticula, the greater the chance for complications. This concept has never been proven. In two-thirds of patients, the disease remains relatively quiescent.[267] The other one-third develop diverticulitis, which implies inflammation or perforation of diverticulum. Of those treated medically for this condition, one-third have a recurrence within 5 years.[270,271]

2.7.2. Diverticulitis

2.7.2.1. Etiology

Diverticulitis results from micro- or macroperforation of a diverticulum. With rupture of the mucosa, bacteria escape into the limiting serosa, yielding peridiverticular infection. With rupture through the

serosa, bacteria escape into the peritoneium, yielding peritonitis. Usually both occur on the left side of the colon and lead to localized or generalized peritonitis.

2.7.2.2. Clinical Findings

Diverticulitis is characterized by pain or tenderness to deep palpation in the left lower quadrant and a change in bowel habits. Occasionally there is rebound tenderness. About one-fourth of patients have a tender palpable mass in the left lower quadrant. If septicemia develops, chills and fever become prominent. The degree of fever depends on the severity and extent of the inflammation. In the elderly, leukocytosis is often absent. The only indication of infection may be an increase in the number of immatue neutrophils. Sigmoidoscopy may disclose an edematous reddened mucosa proximal to the rectosigmoid area. About 50 to 60% of patients have diverticular involvement of the sigmoid colon. With perforation, upright films may reveal air under the diaphragm or dilatation of the colon, suggesting possible obstruction. Barium contrast study may reveal the site of diverticular rupture or the presence of one or more fistulae. This examination can be done during an acute episode of diverticulitis, but must be done cautiously and without excess pressure. With precaution, complications seldom ensue.[272] Differential diagnosis include Crohn's disease, ischemic colitis, carcinoma of the colon, and the irritable bowel syndrome.

2.7.2.3. Treatment

There are no good control studies for the treatment of acute diverticulitis. Mild attacks manifested by constipation and left-lower-quadrant pain without fever tend to respond to a soft or liquid diet. Antibiotics are seldom required in this situation. In the severely ill patient with fever, chills, abdominal pain, and leukocytosis, adequate fluid replacement and antibiotics are essential. A nasogatric tube is placed if nausea and vomiting are present. The choice of antibiotics is questionable. It is wise to use a combination of antibiotics that will destroy colonic flora. Many prefer Gentamicin, 1.0 mg/kg every 8 hr, in combination with Clindamycin, 600 mg every 6 to 8 hr. Medical therapy is effective in two-thirds and ameliorates the need for surgery.[273]

2.7.2.4. Complications

Paracolic abscesses rarely perforate into the abdominal cavity, but tend to localize. As they enlarge, they tend to encroach on the lumen,

causing progressive narrowing and giving rise to a filling defect on barium sulfate examination of the colon. The bowel wall becomes rigid, and as the lesion grows it may resemble a malignancy. At this stage, the presence of normal mucosal pattern on the radiologic films is of paramount importance.

Paracolic or peridiverticular abscess leads to localized abdominal pain and occasionally to rectal pain. Occasionally, these abscesses are palpable on abdominal or pelvic examination. Fever, chills, weight loss, and pain are the predominant clinical symptoms. Such lesions may be identified by barium enema, by sonography, by CT scan, and by gallium-67 scans. However, in some patients all these diagnostic tests may be negative and the diagnosis becomes a clinical one. Diverticulitis is also the most common primary disease resulting in the formation of fistula.[274] Fistulae develop in 12 to 25% of patients. The most common type is the enterovesicle fistula; other types are colovaginal, coloileal, or colocutaneous.

Diverticulitis is the most common cause of lower gastrointestinal bleeding. Unlike other complications it arises from an uninflamed diverticulum. Spontaneous cessation of bleeding tends to occur after a slow, but considerable blood loss. If conservative management and transfusion fail to control bleeding, vasopressin (0.2 units/min) leads to temporary control in 90% of patients. About 25% will have recurrence, and surgery is often necessary for those who continue to bleed. Bleeding from diverticula does not recur as often as from angiodysplasia but it is more severe. Other causes of lower intestinal bleeding must be considered. In the study by Boley *et al.* of 99 elderly patients with lower gastrointestinal bleeding, 43 had diverticulosis, 20 angiodysplasia, nine colonic carcinoma, six radiation proctitis, and four ischemic proctitis.[275]

Surgery is frequently necessary for complicated diverticulitis. A recent survey of 140 patients at the Lahey Clinic revealed that 86 had resection with primary anastomosis with a 1% mortality and 18% morbidity rate; 13 had resection with anastomosis and creation of a proximal colostomy with no deaths but a 22% morbidity rate; 19 had a colostomy with mucous fistula with a 16% mortality and 23% morbidity rate; and 22 had a traditional three-stage operation with a 14% mortality and 24% morbidity rate. Hospital stays averaged 21 days for patients who had the one-stage procedure, 31 and 39 days for those who had a two-stage procedure, and 52 days for those who had the three-stage procedure.[276]

2.7.3. Polyposis

2.7.3.1. Incidence

Colonic polyps are a danger at all ages. They may cause bleeding, obstruction, and intussusception. They are also one of the three major

colonic lesions predisposing to cancer, along with familial polyposis and ulcerative colitis.[277,278]

Although the true incidence of colonic polyps is not certain, polyps become more frequent with advancing age, and in the elderly they are more likely to be multiple. About one-half of individuals over 50 years of age have one or more polyps. Men are afflicted with colonic polyps more frequently than women and whites have polyps more often than blacks. Morson and Bussey followed 1001 patients who presented with one or more adenomatous polyps for 1 to 15 years. The cumulative risk of developing further adenomas and cancer over this 15-year period is almost linear. The risk for the development of additional adenomas was 1 in 5 at 5 years, 1 in 2.5 at 10 years, and 1 in 2 at 15 years. The risk for cancer was less, reaching 1 in 40 at 5 years, 1 in 25 at 10 years, and almost 1 in 15 at 15 years. The cumulative risk of developing cancer in a patient with a single adenoma was 1 in 100 at 5 years, one in 50 at 10 years, and 1 in 20 at 15 years.[279]

2.7.3.2. Etiology

The cause of colonic polyps is unknown. Genetics and familial predisposition play roles in the familial polyposis syndromes but not in the evaluation of solitary polyps.[280,281] Sixty percent of adenomatous polyps are found in the rectum and sigmoid colon. The remainder are scattered from the transverse colon to the cecum.[282] Colonic crypt production is increased in familial polposis and ulcerative colitis, but the triggering mechanism for increased crypt replication is not known.[283] Pedunculated polyps are attached to the mucosa via a stalk; sessile polyps rest on the mucosa and have a broad base. Adenomas have been classified into three histologic types: (1) adenomatous polyp (tubular adenoma), (2) tubulovillous adenomas, and (3) villous adenomas (villous papilloma). The tubulovillous adenoma is a mixed type of tumor.[284] Previously adenomas were thought to rise from crypt epithelium and villous adenomas from surface epithelium. Whitehead believes all polyps are of the same origin, i.e., a neoplastic proliferation of colonic epithelium that produces different varieties of growth patterns.[285,286]

Villous adenomas comprise 5% of all large bowel polyps. Although considered benign, they have a strong tendency toward malignancy, transformation occurring in from 40 to 60%. Usually, villous adenomas are large (i.e., over 6 cm in diameter), shaggy, and sessile. Occasionally, they may have stalks. Since they are soft and have the same consistency as bowel tissue, they are not easily palpable.

Other forms of colonic polyps include myomas arising from smooth muscles, fibromas originating from supporting tissue, lipomas from fatty tissue, hemangiomas, and lymphoid polyps.

2.7.3.3. Clinical Findings

Both adenomatous polyps and villous adenomas may give rise to vague abdominal discomfort or they may be completely asymptomatic. Rectal bleeding is common to both. Large polyps with stalks may also cause intussusception or obstruction.

Villous adenomas usually occur in patients over age 50 years. Since they have large numbers of goblet cells, as they grow, they tend to secrete copious amounts of salty mucus. Sometimes they give rise to watery diarrhea, salt depletion, and dehydration. Fluid losses of 2 to 4 liters and salt joss of 8 to 10 g daily have been reported. Protein-losing enteropathy may also develop.

Simple skin tags reportedly serve as a cutaneous marker for the presence of adenomatous polyps of the colon. Chobanian and his colleagues studied 100 patients (61 men and 39 females) referred for colonoscopy.[287] The average age of this group was 54 years. Adenomatous polyps were found and removed in 41 patients. Skin tags (acrochordons), 2 mm in height and diameter, were identified in 47 patients. The skin tags were found most often in the axillae, in the groin, under the breasts, or on the neck. The association between skin tags and colonic polyposis was significant ($p > 0.001$).[298] "The odds of having a polyp were nearly sevenfold greater in patients with skin tags than in those without them."

2.7.3.4. Treatment

Villous adenomas should not be biopsied. They must be removed in one piece by local excision. If this is not possible, then part of the colon must be removed. These steps are necessary because of the tendency of this tumor to recur and to be malignant. Villous adenomas must also be distinguished from polypoid carcinoma of the colon and rectum, although differentiation is almost academic. Both must be removed surgically.

This is not the case, however, for the benign adenoma. Several factors are related to the cancer potential of an adenomatous polyp. These include a stalk, polyp size, the degree of histologic change, age, and sex. A stalk suggests the lesion is benign. Adenomas less than 1 cm in diameter are usually benign. Five percent of those with a diameter of 1 to 2 cm and 10% of those 2 cm in diameter contain invasive carcinoma.[286] Polyps over 2 cm engender a 50% chance of malignancy. Polyps greater than 1 cm in size, regardless of their location, should be removed. Today, colonoscopy usually permits removal of small adenomatous polyps for diagnosis. Histologic examination is essential for

further decision. Penetration of malignant cells beyond the muscularis mucosa is believed to be a prerequisite for metastases. This concept is based on the finding that lymphatics in the polyp extend up the stalk to the undersurface of the muscularis mucosa. Once malignant cells penetrate the muscularis mucosa, they have access to these lymphatics and can disseminate easily. Polypoid carcinoma that has not extended beyond the muscularis mucosa at the time of resection offers the chance for an almost 100% cure rate.[288] Today, most agree that adenomatous polyps are a premalignant lesion. If there is no invasion beyond the muscularis mucosa, the lesion is benign and no further surgery is necessary. If invasion is beyond the muscularis mucosa, a colonic resection is indicated.[286] If the entire polyp cannot be removed at colonoscopy, an open operation is necessary. Williams, in a pilot study of 300 patients, found age to be an important risk factor for the development of cancer in a polyp. Patients over age 60 were at a "higher risk" than patients under 60 years of age. Male sex appeared to double the risk for future cancer development. The highest-risk patients were elderly men with multiple polyps.[289]

Follow-up of patients undergoing polypectomy is essential. Colonoscopy studies have shown the expected annual rate for the discovery of new adenomas is 30 to 50% in those who had one polyp removed. All patients should have a follow-up colonoscopy after 1 year. Another reason for follow-up colonoscopy is the 10% chance of having missed a significantly sized polyp at the time of initial polypectomy. Colonoscopy has certain limitations. Williams, in a review of 300 patients subjected to both colonoscopy and x-ray, found 14 adenomas over 7 mm in size missed by the endoscopist and subsequently shown on double-contrast barium enema.[289] If no polyp is found after 1 year, colonoscopy should be repeated every 3 years if a single adenoma was removed originally and every 2 years if several were removed initially.[290]

2.7.4. Superior Mesenteric Artery Occlusion

2.7.4.1. Incidence

Acute occlusion of the superior mesenteric artery (SMA) is relatively common among the elderly, but the true incidence is unknown. Death from intestinal ischemia rises fourfold in men and almost 14-fold in women between the ages of 50 and 80 years. Acute occlusion of the SMA has an appallingly high mortality rate (85 to 100%). It is higher with thrombotic occlusion (96%) than with emoblic occlusion (66%) or with nonocclusive ischemia (66%).[291,292]

2.7.4.2. Etiology

Occlusion of either the SMA or inferior mesenteric artery (IMA) may result from arteriosclerosis, thrombosis, vasculitis, embolism, surgical ligation, or adhesions. Mesenteric embolism, however, is relatively infrequent except in patients with left-sided valvular lesions of the heart or arrhythmias. Proximal acute occlusion of the SMA is 5 times more common than distal occlusion.[293] With main-trunk occlusion, collateral linkages are usually inadequate to prevent ischemic infarction of the entire midgut loop. With distal occlusion, however, chances for survival are better because the collateral network usually guarantees the ischemic area will recover or, at worst, the infarction will be limited. With healing, these areas frequently develop strictures that may ultimately lead to bowel obstruction.

2.7.4.3. "Nonocclusive" Disease

"Nonocclusive" disease (NOD) of the SMA and the IMA has been associated with diabetes, rheumatoid arthritis, collagen vascular disease, disseminated intravascular coagulation, hypovolemia, cardiac failure, arrythmias, alcohol, and digitalis glycosides, like digoxin. In accordance with its name, there is no discrete evidence of thrombosis or embolus of the mesenteric arteries at autopsy or surgery, but marked luminal narrowing of vessels occurs due to prominent intimal fibromuscular proliferation, medial hypertrophy, transmural elastosis, and focal periarteric fibrosis.[294] NOD may be precipitated by a sudden fall in cardiac output due to arrhythmias, myocardial infarction, pericardial tamponade, decompensated heart failure, infection, or surgery. The syndrome is common in patients with a mesenteric ischemia. One recent study of 20 patients with SMA syndrome revealed NOD was more common than thrombotic disease.[293] Another, involving 136 patients with mesenteric infarction, reported that approximately 50% had NOD.[295]

2.7.4.4. Clinical Findings

These are not very helpful,[293–295] yet early diagnosis is essential to survival. Potential clues are a past history of embolization or of heart valve replacement or the presence of heart failure, auricular fibrillation, or alcoholism (Table IX). The classical description of acute SMA occlusion is acute onset of abdominal pain, usually confined to the central abdominal area or upper epigastrium, followed by the passage of mucus or blood rectally. However, pain tends to occur late in the critical period. Then, it is usually excruciating and may even exceed the pain associated

Table IX. Underlying Conditions in Bowel Infarction and in Diseases Mimicking Bowel Infarction[a,b]

	Bowel infarction (n = 20)	No bowel infarction (n = 7)
Cardiovascular disease	13	3
Atherosclerosis	10	2
Atrial fibrillation	4	1
Congestive heart failure	3	1
Digoxin therapy	3	1
History of embolization	1	0
History of thrombosis	1	0
Acute myocardial infarction	1	0
Noncardiac disease	18	6
Alcoholism	8	5
Abdominal pain of more than 1 month's duration	6	1
Diabetes	2	0
Cancer	2	0
Hip fracture	1	0
Drug overdose	1	0

[a]No $p < 0.2$ using Fisher's exact test.
[b]With permission of Drs. M. Cooke and M. A. Sande.[293]

with myocardial infarction. Nausea and vomiting followed by watery diarrhea results from forceful gastrointestinal emptying. Severe abdominal pain (70 to 100%) has been found in several studies; abdominal tenderness occurs in 75% of patients, and abdominal distention is found in a similar number. The occurrence of abdominal pain in old atherosclerotic patients with congestive heart failure or atrial fibrillation and the absence of significant abdominal signs constitute a triad once considered classical for SMA. More recent studies, however, show that the presentation of bowel infarction is nonspecific (Table X). Peritoneal aspiration will yield blood-stained peritoneal fluid in over 50% of these patients.

Laboratory findings are also nonspecific. As intestinal ischemia increases, metabolic acidosis occurs yielding arterial blood gas changes, electrolyte alterations, and increases in the serum amylase and alkaline phosphatase levels. Early abdominal x-rays are of little help. Colonoscopy is helpful.[295] Lateral aortography provides precise information about the takeoff of the superior mesenteric artery. If the stem is patent, the distal portions and collaterals are easily scanned. In general, emboli are located distally beyond the origin of the middle colic artery, while thrombi are found within the first few centimeters of the SMA. Viability

Table X. Symptoms and Signs in Bowel Infarction and in Disease Mimicking Bowel Infarction[a,b]

	Bowel infarction (n = 20)	No bowel infarction (n = 7)
Symptoms		
Abdominal pain	15	6
Collapse	9	4
Vomiting	8	3
Shortness of breath	8	1
Diarrhea	7	2
Confusion	6	1
Bloody diarrhea	5	2
Hematemesis	4	2
Signs		
Temperature (°F; mean ± SD)	97.6 ± 6.1	97.2 ± 4.7
Systolic blood pressure below 100 mm Hg	12	4
Abdominal tenderness	15	7
Abdominal distention	15	3
Occult blood in stool	13	6
Occult blood in nasogastric aspirate	11	3
Absent bowel sounds	7	1
Abdominal rigidity	3	1

[a]No $p < 0.02$ using Fisher's exact test.
[b]With permission of Drs. M. Cooke and M. A. Sande.[293]

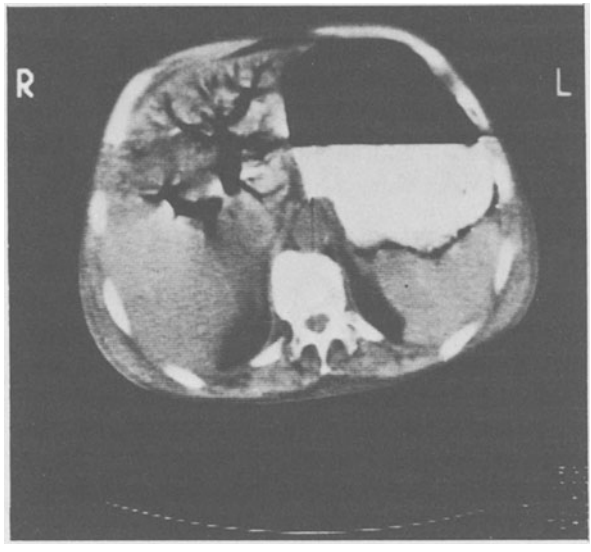

Figure 7. Mesenteric infarction. The computerized tomography scan shows air in the portal circulation.

of the involved intestine can be assessed accurately through use of the Doppler ultrasonic flowmeter. It provides useful presurgical knowledge of the involved circulation.[296] CT scans may show air in the peritoneal cavity or in the portal vein, as shown in Figure 7.

2.7.4.5. Prognosis

Occlusion of the SMA has a grim prognosis. Following infarction, intestinal ileus, abdominal distention, and bloody diarrhea ensue. Serosal leakage of bacteria leads to peritonitis and eventually to vascular collapse. Unfortunately, in 40 to 80% of patients, the diagnosis is not made until vascular collapse occurs.

NOD disease is equally common in the elderly and just as deadly in the absence of aggressive therapy. The average age is 61 years.[297] Unlike acute SMA occlusion, NOD may involve any part of the gastrointestinal tract. In one series of patients with NOD, 48 had only small bowel involvement, 35 had involvement of the small intestine and colon, and six had involvement of the stomach and small intestine.[297] Both types of infarction have a poor prognosis; mortality remains around 90%.

2.7.4.6. Treatment

Surgical restoration of arterial circulation within the "critical period," i.e., the first 6-hr period after occlusion, may be curative and obviate the need for extensive bowel resection. Beyond this time, however, management becomes more difficult and mortality rises briskly. Unfortunately 6 of 10 patients have a delay in diagnosis beyond 12 hr and over 50% have another 12-hr delay between the time of diagnosis and laparotomy.[293,297] In part, this is due to the reticence of older patients concerning hospitalization, to dementia, or to proscrastination by the family or physician. Surgery at the takeoff of SMA is technically complex, and several approaches have been used with varying success. Embolectomy is accomplished more easily in distal areas. In three of four patients, the embolus is found at the junction of the SMA and the middle colic artery.[298] The arterial procedure of choice depends on individual findings and the surgeon's preference. The surgical management of SMA occlusion has been reviewed in detail by Ottinger and Austen.[295] Even if surgery is successful, it is often followed by massive fluid and plasma loss into the bowel lumen, a decrease in cardiac output, and the appearance of vasoactive polypeptides. Metabolic acidosis and hyperkalemia ensue as the result of "acute intestinal failure." Vasopressors are contraindicated for the resulting hypotension because they cause splanchnic and portal venous vasoconstriction, further reducing the

mesenteric blood supply. Vasodilators have been used as part of the aggressive treatment of NOD. Their judicious use in some patients may improve survival and decrease the amount of bowel removed. Boley infused the mesenteric vasodilator papaverine directly into mesenteric arteries in patients with NOD as well as embolic mesenteric ischemia, thereby reducing mortality after surgery to 40% and 45%, respectively. Experimental use of the new intravenously selective mesenteric vasodilator "urotensin I" in animals with NOD returned mesenteric circulation without the systemic effects associated with papaverine given intravenously.[299]

2.7.5. Ischemic Colitis

2.7.5.1. Etiology

Ischemic colitis is much more common than ischemic enteritis. In the elderly patient it is also more common than inflammatory bowel disease. The latter is a disease of the young and middle-aged.

Like ischemic enteritis, ischemic colitis results from occlusive disease involving the IMA and is usually related to arteriosclerosis. Nonocclusive colitis may be related to diabetes mellitus, collagen vascular disease, disseminated intravascular coagulation, hypovolemia, cardiac failure, arrhythmias, and digoxin. It can lead to antithrombin III deficiency and subsequent deep-vein thrombosis.[300] Ischemic colitis may also develop following abdominal perineal resection (2%) or after aortoiliac surgery.[296] A fall in the intramural pH of the colon below normal limits (pH 6.8) has been used on the day of abdominal aortic operation as a prognostic test for development of ischemic colitis. In one study, 6 of 25 patients developed pH evidence of ischemia on the day of aortic surgery. All six subsequently had transient episodes of guaiac-positive diarrhea and four developed physical signs consistent with ischemic colitis and died. None of the 19 patients without a fall in intramural pH developed ischemic colitis.[301]

Marston classified ischemic colitis into three types, depending on the end result of ischemic episodes, namely, acute transitory colitis, acute nongangrenous, and gangrenous colitis.[302] The nongangrenous variety is 10 times more common than the gangrenous type.

2.7.5.2. Acute Transitory Colitis

The victims of ischemic colitis are usually aged with a history of heart failure and atherosclerosis. Often their attacks follow decompensated congestive heart failure, myocardial infarction, or arrhythmia, notably articular fibrillation. Saegesser believes that episodes of ischemic

colitis that do not culminate in necrosis of the colonic wall are caused more frequently by hemodynamic disorders than by vascular occlusion.[298] Here, the crisis is often mitigated by the development of collateral circulation. This leaves the involved area vulnerable to subsequent changes in cardiac output and to subsequent stricture formation and, in turn, obstruction.

2.7.5.3. Acute Nongangrenous (Strictural) Colitis

Patients with acute nongrangrenous ischemia usually have a history of left-sided lower abdominal pain which is easily confused with diverticulitis. Usually, they have no prior history of bowel disease. Abdominal pain tends to follow passage of loose stools containing bright or dark-red blood. Fever, tachycardia, left-sided abdominal tenderness, and guarding are evident. Bowel sounds are usually present, and occasionally a mass is palpable. Rectal examination usually reveals dark-red blood.

Differential diagnosis includes infective dysentery, diverticulitis, immunopathic proctocolitis, Crohn's disease, ulcerative colitis, volvulus, and carcinoma of the bowel.

2.7.5.4. Gangrenous Colitis

These patients tend to have a short history and to expire within the first 24 to 48 hr of illness. Abdominal pain is severe and generalized. Diarrhea is common, but rectal bleeding is seldom present. Most patients are in a state of collapse at the time of diagnosis due to generalized peritonitis and/or hypovolemia. The diagnosis is rarely made preoperatively unless the rectum and sigmoid areas are involved. Only 3% of patients with gangrenous colitis have involvement of these areas.

Gangrenous colitis arises from a combination of occlusive vascular damage and a fall in cardiac output. The mucosa of the large intestine is more sensitive to hypoxia and contains far more bacteria than the small intestine. The abundant bacterial flora rapidly invade any ulcerated or edematous mucosal lesion, leading to localized infection and penetration of the ischemic area. In the elderly, fever, pain in the left side of the colon, bloody diarrhea, and tenesmus are more likely to be caused by ischemic colitis than by ulcerative colitis or regional enteritis.

2.7.5.5. Diagnosis

Leukocytosis is usually present. The serum alkaline phosphate, amylase, and transaminase levels become elevated in the course of an evolving metabolic acidosis.

Plain x-ray films of the abdomen often show a narrowed splenic flexure, thumbprinting, and occasionally streaks of gas in the bowel wall. The barium enema may be diagnostic. It is not contraindicated in patients with acute ischemic colitis, but it must be done carefully. The most likely sites of ischemia are the splenic flexure (35 to 40%), the descending colon (30 to 35%), and the sigmoid area (10 to 20%). Involved segments are narrow and show thumbprinting. Serial double-contrast barium enema examinations performed on patients with nongangrenous colitis revealed thumbprinting in 30 of 40 (75%) patients (15 with stricture and 25 with transient ischemic colitis). Thumbprinting appeared within 9 days of onset of illness in those with strictures and within 6 days in those with transient ischemic colitis.[302] Thumbprinting disappeared from barium enema examination about 10 days after it was first recognized. Longitudinal ulcers are found in 60% of the patients. These ulcers heal faster in patients with transient ischemic colitis (9 days) than in those with strictures (20+ days). The double-contrast barium study is particularly useful for visualization of linear ulcers. Angiography may disclose areas of vascular stenosis and occlusion. Colonoscopy reveals three states of involvement: (1) an acute stage, earmarked by petechiae, mucosal pallor, or hyperemia; (2) a subacute state, characterized by ulceration and exudation; and (3) a chronic stage, recognizable by stricture, haustral markings, and mucosal granularity.[303] A nonspecific prostatitis is found in 5 to 10% of patients during proctoscopy. Since ischemic colitis is limited to the submucosa, biopsy at the time of colonoscopy or proctoscopy is usually diagnostic. As mentioned previously, patients subjected to abdominal aortic repairs, particularly those undergoing repair of a ruptured aortic aneurysm, must be watched very carefully postoperatively. Aortic rupture may also lead to tissue hypoperfusion and mesenteric ischemia in those with preexistent occlusive disease. Colonoscopy may be helpful in the early postoperative period, for symptoms may develop insidiously when tissue damage is limited to the mucosal layer.

2.7.5.6. Treatment

When gangrenous colitis is suspected, the hypovolemia must be corrected immediately and laparotomy undertaken as soon as possible in order to evaluate the extent of the disease and to ascertain the possibilities for appropriate surgical correction.

2.7.6. Constipation

Constipation has been defined as "infrequent or difficult evacuation of feces." To some, constipation means infrequent bowel movements or

difficulty in passing stools, painful stools, or increasing stool hardness. To others, it is no more than the sense of abdominal discomfort. One recent definition takes two of these aspects into consideration and defines constipation as "straining at stool for more than 25% of the time and/or two or fewer stools per week."[304] In Britain, less than 1% and in the United States about 4% of the population claim that they have less than two stools per week.[305] Among the aged, constipation is the most common disorder of the gastrointestinal tract.[306] One in five complain of constipation and over 40 to 50% take laxatives routinely even if they have a daily bowel movement. Many elderly patients believe it is essential that they have at least one bowel movement daily. They are unaware that in 90% of adults, the frequenty of bowel movements ranges from twice daily to three times a week. This pattern is not changed by age.[307] Similarly, the intestinal transit times of the active older individual are comparable to those of the active young, i.e., 1 to 2 days. However, when the elderly individual becomes bedfast, intestinal transit becomes prolonged and may range up to 1 week or more.[307] Constipation, too, prolongs intestinal transit in some. Ritchie found that barium sulfate given orally reached the rectum within 12 to 15 hr in 56% of patients with normal bowel habits but in only 33% of patients wtih constipation.[308]

2.7.6.1. Primary Constipation

Primary constipation results from one or more of the following motility, hygienic, or dietary problems: (1) delayed transit time, (2) incomplete bowel emptying, (3) diminished bowel awareness, (4) neglect of call to stool, a common problem in patients with dementia and cortical degeneration, and (5) deficient intake of food, particularly fiber and fluids. In Western societies a lack of exercise, stress, and a sedentary way of life are also important factors. Other causes are listed in Table XI.

Changes in intestinal transit time are usually due to alterations in colonic motility. There are three types of colonic motor activity (motility): (1) nonpropulsive (segmental), (2) propulsive over short segments, and (3) mass propulsion. Colonic motor activity can be effected by myogenic, neurogenic, or hormonal influences. Nonpropulsive motility (rhythmic segmentation), or to-and-fro motion, is responsible for mixing the colonic contents. It predominates in the colon and moves fecal material from one haustral segment to another, thereby increasing water and electrolyte absorption and preventing rapid movement of feces through the bowel. Nonpropulsive motility is enhanced by narcotics and is inhibited by epinephrine and prostaglandins.

Mass propulsive motility may be peristaltic or antiperistaltic. It is under humoral rather than neuronal control and is responsible for mass

Table XI. Causes of Constipation[a]

Dietary habits	Endocrine—Metabolic
Ignoring urge to defecate	Diabetes mellitus
Inadequate dietary bulk	Hypothyroidism
Laxative abuse	Pheochromocytoma
Lack of exercise	Hypopituitarism
Motility disorders	Hypercalcemia
Idiopathic slow transit	Hypokalemia
Idiopathic megacolon	Uremia
Diverticulum disease	Neurologic
Irritable bowel	Hirschsprung's disease
Inadequate bulk in diet	Cerebral tumors
Drugs	Parkinsonism
Opiates	Paraplegia
Diuretics	Multiple sclerosis
Analgesics	Bowel disorders
Anticholenergics	Neoplasm
Antidepressants	Anal fissure
Anticonvulsants	Intussusception
Antiparkinsonians	Rectal procidentia
	Rectocele
	Prolapsed hemorrhoids

[a]Adapted from Nivatvongs and Hooks.[312]

movement of fecal material. The "gastrocolic reflex" is the best example of mass propulsion. It is responsible for the mass movement of fecal material from the cecal area to the sigmoid colon, a distance of approximately 75 cm. Most individuals experience a gastrocolic reflux several times daily, usually at mealtime. When the elderly individual becomes bedfast, mass propulsion decreases significantly. If the call to defecation is not forthcoming, many soon lose the desire to defecate and develop what Brocklehurst and Kahn call "the terminal reservoir syndrome" and others, the "institutional colon."[309] These individuals fill their cecum and soon their entire colon with feces. Subsequently, some develop a megacolon with or without fecal incontinence.

A disparity between the separate propulsive activities of the colon leads to bowel dysfunction. An excess of mass propulsion leads to diarrhea while an excess of nonpropulsive activity causes constipation. Abnormal colonic activity confined solely to the colon leads to "chronic idiopathic constipation" (CIC). This condition usually begins in childhood, is painless in contrast to irritable bowel, and is a lifelong condition. Connell *et al.* were the first to recognize that contraction of the pelvic colon was increased in CIC.[306] Subsequently, it was recognized that constipation in some patients was the result of a colonic motility disor-

der. When it was found that motility patterns were variable, it was suggested that CIC was a heterogeneous disorder and that the colonic transit time in CIC may be decreased or normal. Later, the physiologic importance of anorectal function was recognized during studies of colonic transit studies using radiopaque markers. With colonic inertia, the opaque markers accumulated throughout the colon, but with colorectal disorders the markers accumulated on the left side of the colon and in the rectum. Anorectal (outlet) obstruction was found to be a cause of CIC in some patients. Marzio *et al.* recently found anorectal function in CIC was markedly different from normal. There was an increase in the threshold of rectal distending volume necessary to induce the rectoanal inhibitory reflex (RAIR), a prolonged duration of the RAIR, and a decrease in the volume of rectal distention necessary to obtain constant relaxation. In 30% of the CIC patients the maximum resting pressure in the anal canal was elevated. In adults, CIC, anorectal motility, and rectal sensitivity are altered. In some a high-fiber diet corrects the motor abnormalities but not the sensitivity changes.[310]

Some patients with CIC show a paradoxic increase in puborectalis muscle activity (myographically) on straining and cannot expel a water balloon. Surgical subdivision of this muscle rarely relieves constipation but frequently leads to incontinence for mucus, liquid feces, and flatus.[311]

In patients with diabetic autonomic neuropathy-associated constipation, the usual increase in colonic motor activity after a meal is decreased even though the colon is normally responsive to prostigmine. Destruction of the parasympathetic outflow of S2, S3, or S4 by tumor or disease causes severe constipation with loss of rectal sensation, abnormal motor function of the left side of the colon, and increased distensibility of the colon.

These disturbances may be identified by giving the patients radiopaque markers and studying their passage by abdominal x-ray films. With hindgut inertia, the markers accumulate on the left side of the colon and in the rectum, whereas in patients with colorectal inertia, the markers accumulate throughout the colon.[312]

2.7.6.2. Secondary Constipation

Secondary constipation is due to drugs such as analgesics, diuretics, laxatives, calcium and aluminum salts, opiates, anticholinergics, anticonvulsants, and antiparkinsonian drugs, or diseases such as bowel cancer, hyperthyroidism, hypothyroidism, hypercalcemia, diverticulosis, anorectal lesions, dementia, and depression[313] (Table XI).

2.7.6.3. Diagnosis

A thorough history and a careful review of medications and physical examination are essential for diagnosis. Perineal disease must be ruled out by rectal and pelvic examination. A distended abdomen requires study for evidence of a megacolon or the terminal reservoir syndrome. Radiographic sigmoidoscopic or colonoscopic examinations may be necessary. If back neurologic findings are evident, tumor invasion or neurologic disease must be considered. Endocrinologic abnormalities such as hyper- and hypothyroidism, too, should not be overlooked as potential causes of both constipation and/or diarrhea.

2.7.6.4. Treatment

Chronic constipation is a distressing problem for many patients, a fact consistent with huge expenditures for laxatives, $368 million in 1982 in the United States, and the list of 55 laxatives included in the *Physicians' Desk Reference* for 1986. It is imperative that whenever possible the cause of constipation be identified. Effective treatment may require alteration of bowel habits, daily activity, dietary management, breaking the laxative habit, and treatment of remedial conditions. Obese or sedentary but mobile healthy patients should be assured that constipation is not life-threatening and the physiology of defecation explained to them. They should attempt to defecate at the slightest urge and for 5 min at the same time every day. They must be encouraged to avoid laxatives. Since the elderly tend to lose their thirst sensation, they often drink less fluids than they need. Therefore, it is necessary to ensure an adequate fluid intake. Prescribe a glass or two of water on rising and one with every meal and at bedtime. Bran-containing cereals or the addition of Miller's bran (15 g) to cereal provides a high-fiber diet. Six to twelve teaspoonsful of unprocessed bran daily along with adequate hydration and exercise often improves the patient's constipation, unless he has a terminal reservoir syndrome. Bran makes this condition worse. If unprocessed bran is used, start with 1 teaspoonful daily and gradually increase the amount every third day. When large doses are given initially, they often cause abdominal cramps and gaseousness. In a recent study of 33 institutionalized demented elderly patients, high-bran bread proved efficacious in increasing both the number and volume of daily bowel movements, and decreased total laxative consumption by 93%.[314] A soy polysaccharide (20 to 22 g daily) has also been added to elemental liquid diets to increase stool bulk. Given to constipated tube-fed, and nonambulant mentally retarded patients, it increased stool size and improved stool consistency, but did not change the transit time of 5 to 6

days.[315] Hydrophilic substances such as Metamucil or psyllium seed preparations also increase stool bulk. But if fluids are not taken in adequate amounts, these preparations are ineffective. Osmotic laxatives, such as magnesium sulfate, or sodium phosphate is occasionally helpful.

For the immobile patient, stool softeners such as diocytl sodium sulfosuccinate (Colase) are reportedly useful in preventing constipation. These emollient laxatives are wetting agents that break up feces by allowing water to penetrate into it. Irritant purgatives or surface-acting agents such as bisacodyl (Ducolax) or standardized senna (Senokot) stimulate the myenteric plexus of the colon, increase bowel motility, and inhibit mucosal transfer of fluids. Bisacodyl has the capacity to induce progressive peristaltic waves in patients with relative inactivity of the colon or so-called "slow-transit" constipation.[316] Prolonged use of anthracene purgatives should be avoided for they may cause degeneration of the myenteric plexus and lead to melanosis coli (Fig. 8). Badiali *et al.* found melanosis of the rectum in 74% of their patients consuming anthracene laxatives.[317] If stool softeners fail, however, these agents may be temporarily helpful.[312] Bulk producers, like bran, methycellulose, or psyllium, should not be used in the severely constipated, immobilized patient. They may compound the problem by increasing the bulk in an

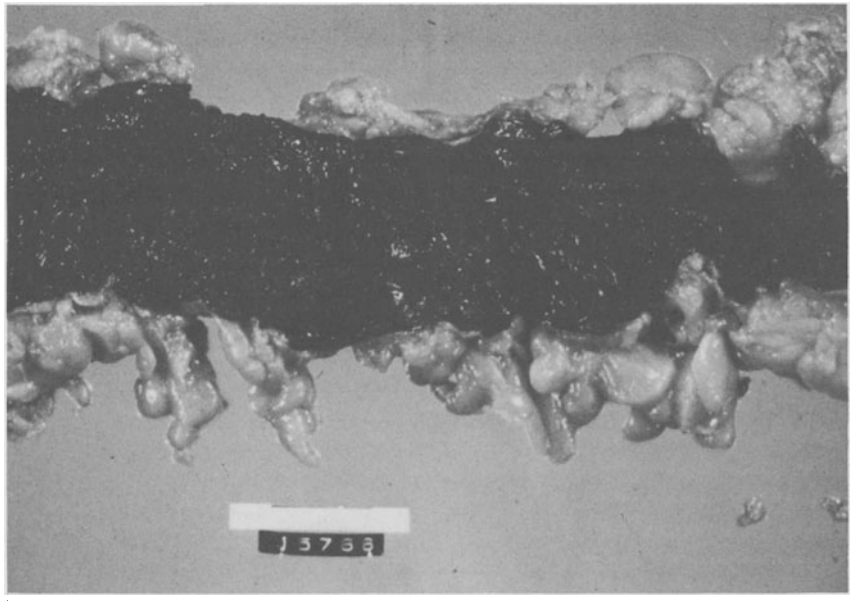

Figure 8. Melanosis coli, secondary to prolonged use of anthracene purgatives. (Courtesy of Dr. Jack Geer.)

already distended colon and/or lead to intestinal obstruction. Mineral oil is not recommended because it may cause anal seepage and lipoid pneumonia in the elderly with impaired gag reflexes. It also interfers with vitamin D absorption and reportedly causes lymph node enlargement in the mesenteric and biliary areas. Recently, Smith and his associates found that saline infused into the stomach through a nasogastric tube over a period of several hours promptly relieves severe constipation. Furosemide is given to patients prone to congestive heart failure.[318]

2.7.6.5. Fecal Impaction

Fecal impaction can be serious and may lead to sudden death, to acute organic brain syndrome, or to cerebral vascular accidents due to straining at stool by cardiovascular patients. Undiagnosed fecal impaction has been associated with confusion, disorientation, and agitation in the elderly as well as tachycardia, abdominal distention, temperature elevations to 101°F, ureteral obstruction, intestinal obstruction, hepatic encephalopathy, and stercomatous perforation.[319–321] Over 90% of fecal impactions occur in the rectum or sigmoid colon, the storage area of the colon. Usually, an x-ray of the abdomen will show massive fecal retention throughout the colon. Stercomas account for 20% of colonic perforations and are a common cause of colonic bleeding. These complications are associated with a 50% mortality in the debilitated elderly patient.

The treatment of fecal impaction is related to the extent of the impaction, its duration, and the presence of megacolon or organic disease. Stool softeners such as dioctyl sodium sulfosuccinate, 50 mg every 8 hr, are usually sufficient for mild impactions. For more severe impactions, hypertonic phosphate or olive oil enemas in combination with syrup of dioctyl sodium sulfosuccinate are often effective. If manual removal is required, it should follow the enema. If manual removal is extremely painful, anesthesia may be necessary. If a megacolon develops, surgery with stripping of the longitudinal muscle from the distal colon may be necessary to overcome sphincter resistance and to relieve the impaction.[322]

2.7.6.6. Fecal Incontinence

Etiology. Fecal incontinence (FI) poses a devastating social, psychologic, and hygienic problem for any person and becomes a distasteful, burdensome chore for those nursing the incontinent patient. Tobin and Brocklehurst found FI occurred at least once weekly among 10% of the elderly in 30 homes for the aged.[323] Recently, Schiller reviewed the

causes of FI in an elegant treatise. He and others have stressed the importance of the anatomy of the pelvic area and the anal canal in the maintenance of continence.[324] The coordinated interrelation of the anal sphincters, internal (IAS) and external (EAS), along with the puborectalis muscle is essential in preventing FI. The IAS maintains a basal tone that ensures closure of the anal canal. This pressure is maintained even when the EAS is paralyzed by pudendal block. The tone of the IAS is maintained via the intrinsic and extrinsic autonomic nerves.[325] Relaxation of the IAS is missing in Hirschsprung's disease owing to absence of the intrinsic neural plexus. Diabetic incontinence is usually due to involvement of the IAS. The EAS is supplied by the pudendal nerve. Rectal distention leads to IAS relaxation and to reflex contraction of the EAS, yielding lower-anal-canal contraction and continence. Loss of EAS function leads to incontinence for solid and liquid stools. The puborectalis muscle (PRM) is tonically active and is under conscious as well as reflex control. Its tension increases with increased intraabdominal pressure. Normally, the sling above the anal canal formed by the PRM is contracted and maintains a 90° angulation between the axis of the rectum and that of the anal canal. When the PRM relaxes, the angle becomes obtuse, thereby straightening the rectoanal canal and allowing the passage of feces. Abnormal PRM function is thought to be responsible for "idiopathic fecal incontinence"—due in many patients to denervation of the PRM and EAS.[326] This condition may also be found in patients with the perineal descent syndrome. Such patients strain at stool and often feel they do not have complete evacuation of the rectum. Continued straining leads to weakness of the PRM muscles because the motor nerves to the pelvic floor muscles and the EAS run on their surface. Stretching the muscle damages the nerves and eventually leads to denervation—muscle weakness, and incontinence. Dysfunction of either the IAS, the EAS, or the PRM or loss of rectal compliance and accommodation may lead to FI.[324]

2.7.6.7. Diagnosis

Diagnosis requires a careful history and physical examination. The clinician must be aware that fecal incontinence is often mistaken for chronic diarrhea. Specific questions concerning soilage of underclothing, bedding, straining at stool, a feeling of incomplete evacuation, urgency, and so forth may reveal the presence of FI. The cause of incontinence is the next objective. Does the patient have diabetes mellitus, a neurologic disease, a history of pelvic trauma or surgery, perineal tears from childbirth, inflammatory bowel disease? Physical examination should include visual and digital examination of the rectoanal

canal for hemorrhoids, proctitis, rectal prolapse, and an intact cutaneorectal reflex.[327] The PRM should be palpated posteriorly. Its effectiveness can be gauged by pulling the examining finger posteriorly. Weakness of the PMR leads to gaping of the anus. A large number of physiologic tests are available to help determine the cause of FI. In the review mentioned previously, Schiller examines these procedures in detail.

2.7.6.8. Treatment

In general, treatment is supportive. The avoidance of stool straining may help in patients with suspected "perineal descent syndrome." Removal of a fecal impaction may eliminate the diarrhea associated with this condition. Lomotil or loperamide (Immodium) may help. The latter (4 mg tid) slows intestinal motility and inhibits peristaltic activity. It is more effective than lomotil in reducing the frequency of incontinent episodes and frequency.[328] Biofeedback training reportedly is effective in reducing FI in over one-half of patients. The value of surgery in control of FI depends on its etiology. Recently, the use of a pelvorectal sling has been advocated as effective (60%) in the treatment of rectal prolapse and FI.[329]

2.7.7. Diarrhea

Diarrhea is one of man's oldest known and most distressing illnesses. In Third World countries it remains a major cause of death and/or malnutrition. Estimates of the former range from 5 to 18 million annually in Africa, South America, and Asia. Fortunately, in the United States diarrhea is usually self-limiting. Even here, however, diarrhea can quickly lead to dehydration, severe electrolyte imbalance, and death for the elderly. Diarrhea lasting more than 3 weeks is either the result of a serious disorder or a functional state known as "irritable colon."

Diarrhea has been defined as a change in the frequency, fluidity, or volume of stool[330] (Fig. 9). Clinically, it may be "functional" or "organic." Functional diarrhea is characterized by an increase in bowel movements during the day and an absence of blood, pus, or visible fat in the stools. There are no constitutional symptoms such as weight loss or fever.

Organic diarrhea is characterized by a loss of synchronization of bowel movements with the clock. Patients may have nocturnal diarrhea and/or be awakened from sleep by the urge or need to defecate. Blood, pus, and fat may be found in the stool. Systemic findings such as anemia, finger clubbing, arthritis, and weight loss are often present.

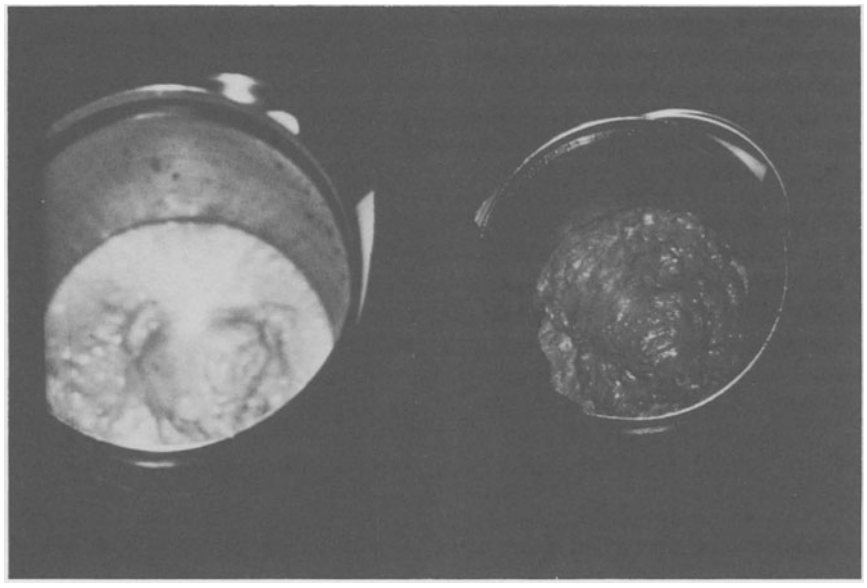

Figure 9. The voluminous stool encountered in celiac disease.

2.7.7.1. Bowel Fluid and Electrolyte Absorption and Secretion with Diarrhea

Since the water and electrolyte content of the stool is generally increased or altered in diarrhea, knowledge of the normal contents is essential to an understanding of the diarrheal state.

2.7.7.1a. Water. Increased stool water content is the *sine qua non* of diarrhea. This increase results either from impaired fluid absorption or from increased mucosal secretion into the lumen. In our society, the mean daily stool weight varies from 100 to 200 g, of which 60 to 80% is water. With diarrhea, stool water increases to 70 to 90% of overall weight.[331] In essence, diarrhea is a form of water malabsorption. An excess of 100 or 200 ml of daily fecal water, or about 1 to 3% of the total fluid handled daily by the gastrointestinal tract, is enough to alter both the frequency and consistency of stools.

Figure 10 shows the approximate volumes of fluid entering and leaving the lumen of the gastrointestinal tract daily. Only a relatively small volume of chyme, 0.8 to 1.0 liter daily, of the 8 to 10 liters entering the bowel, passes beyond the ileocecal valve. Seventy-five percent of fluid entering the bowel is absorbed during passage through the small bowel to the ileocecal valve.

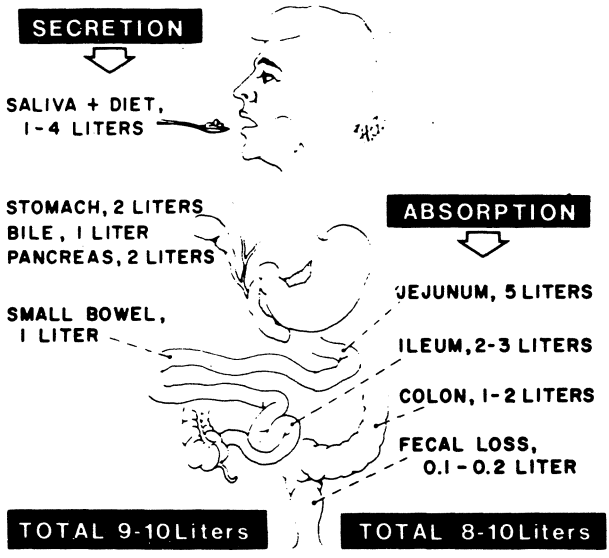

Figure 10. Fluid secretion and absorption in the normal alimentary canal.

Normal stool contains only 0.1 to 0.2 liter of water, yet over a liter reaches the large bowel. Therefore, the colon must be a net absorber of water. Even so, an active bidirectional flux of water occurs in the colon; i.e., both fluid absorption and secretion occur simultaneously. Fluid absorption, however, exceeds secretion, thereby allowing concentration of colonic luminal fluid. Actually, the colon can absorb up to 2 liters of fluid within 24 hr. When this limit is exceeded, stool water increases and diarrhea ensues.

2.7.7.1b. Electrolytes. Electrolytes, too, are both absorbed and excreted by the small bowel and the colon (Fig. 11). Intestinal fluid entering the colon contains about 125 meq/liter of sodium, 9 meq/liter of potassium, 60 meq/liter of chloride, and 74 meq/liter of bicarbonate. Colonic sodium and chloride absorption is so efficient that stool electrolyte concentrations are reduced to 40 meq/liter of sodium, 2 meq/liter of chloride, and 30 meq/liter of bicarbonate. Ordinarly, stool sodium (40 meq/liter) is less than the plasma sodium concentration, whereas stool potassium (90 meq/liter) greatly exceeds plasma levels. With diarrhea, high stool potassium levels are the result of rapid water absorption and active potassium secretion by the colon. In this condition, stool sodium and chloride concentrations tend to increase while potassium levels fall. Stool bicarbonate is low in diarrheal patients who eat, but high if the patient fasts.

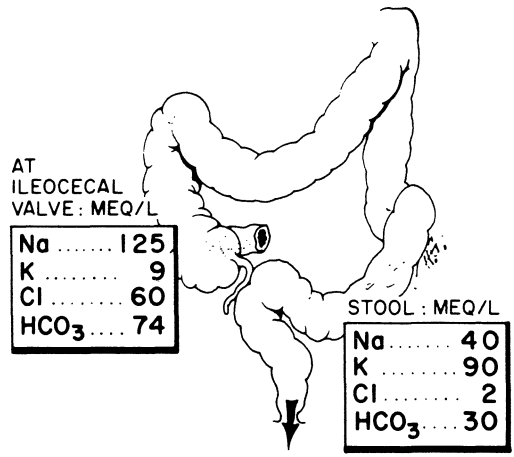

Figure 11. Electrolyte concentration on entry and exit from normal colon.

2.7.7.2. Etiology

In the elderly, diarrhea results from infection, fecal impaction, drugs, and diseases such as cancer, inflammatory bowel disorders, and ischemic colitis.[331–334] Utilizing new bacteriologic and viral techniques, Jewkes *et al.* were able to identify the cause of acute diarrhea in 58% of 106 adult patients.[335] The bacterial infections most often identified were *Salmonella, Campylobacter,* and *Shigella. Clostrioium difficile,* toxigenic *Escherichia coli,* and *Vibrio parahaemolyticus* were relatively rare. Rotavirus and Norwalk-type viruses were recovered in 8%. *Giardia lamblia* and *Candida albicans* infections were detected in 4%. Antibiotic diarrhea characterized by sudden onset, bloody stools, colicky abdominal pain, and a rapid resolution occurred in 10%. Laxatives were responsible in 5%. Although no cultural organisms were found in 40%, Jewkes *et al.* suspected an infection that alluded their capabilities for culture and identification. His prediction shows promise of early fulfillment. Recent studies suggest that *Aeromonas,* previously considered a harmless pathogen, may be a common cause of bacterial diarrhea. At the Wadsworth VA Hospital, George *et al.* found *Aeromonas* to be the most common fecal isolate in adults with diarrhea, but only after they began using special culture media. Most of their patients had diarrhea of less than 30 days' duration.[336] In 73 of 80 adults with diarrhea, *Aeromonas* was the only potential bacterial or parasitic pathogen isolated from their feces. Sixteen percent (13/80) had evidence of colitis during sigmoidoscopy. Antibiotic therapy was successful in terminating 8 of 15 episodes of *Aeromonas* diarrhea and led to improvement in two others. The genus *Aeromonas* consists of three motile species—*A. caviae, A. hydrophilia,* and

A. sobria—and one nonmotile species—*A. Salmonicidia.* The reported incidence of asymptomatic intestinal carriage varies from 0 to 3.2%. This facultative gram-negative bacillus is cultured best on ampicillin blood agar (BAA 30). Sixteen patients of Jewkes *et al.* had organic disease such as ulcerative colitis, regional enteritis, fecal impaction, pancreatic steatorrhea, irritable bowel, postvagotomy diarrhea, Stevens–Johnson syndrome, and gram-negative septicemia.

Changes occur in the elderly bowel that may facilitate the development of certain types of diarrhea. Intestinal bacteria are usually inhibited by gastric acid. Hence, older patients with hypochlorhydria are more susceptible to infection with *Salmonella, Shigella, E. coli, Vibrio cholerae,* and others. Bowel motility also decreases in some older individuals, and this may lead both to bacterial overgrowth and to malabsorption in an otherwise normal small bowel.[337] Intestinal immunity also declines in some of the elderly. How this affects the small bowel's ability to resist colonization by bacteria or protozoa or its susceptibility to viral infections is not clear. Such changes could explain why some volunteers infected with Norwalk agent develop long-term immunity to that virus while others develop repeated clinical infections with every challenge. Travelers' diarrhea, too, may lead to chronic diarrhea or may unmask celiac disease or some other preexistent asymptomatic gastrointestinal disorder.

2.7.7.3. Pathogenesis of Diarrhea

There are five major types of diarrhea: (1) osmotic, (2) secretory, (3) impaired ion absorption, (4) mucosal permeability defects, and (5) motility defects.[338,339] Their pathogenesis and treatment have been reviewed extensively in a recent symposium on diarrhea.[340]

Osmotic diarrhea results from the ingestion of poorly soluble substances, e.g., laxatives, or from maldigestion, e.g., lactase deficiency due to obstruction of the microvilli in viral gastrointestinal infections or sprue. Nonabsorbable water-soluble molecules create an osmotic lumenal drag that causes a net movement of water from the plasma into the lumen.

If diarrhea continues after fasting for 12 to 24 hr, the fasting bowel is in a secretory state due to a defect in mucosal membrane transport of water and electrolytes. Secretory diarrhea results from (1) increased tissue pressure, e.g., hypervolemia, (2) decreased intestinal absorption associated with a high rate of normal intestinal secretion, and (3) active ion secretion by mucosal cells. Cholera is the classic example of secretory diarrhea. The cholera enterotoxin stimulates production of the enzyme adenylcyclase, which converts an adenosine triphosphate to cyclic 3′5′-adenosine monophosphate, which stimulates marked secretion.[340,341] The molecular structure of the cholera toxin has been studied intensely.

It consists of two active subunits labeled "A" and "B." In each unit there is a single A subunit and five B subunits. The latter are responsible for binding the toxin to specific membrane receptors on the microvilli of the epithelial cell. The A subunit enters the crypt cell and is split into two parts, A1 and A2. The A1 activates adenylate cyclase and leads to cell secretion and inhibition of villous absorption.[342] Toxigenic *E. coli* causes another type of secretory diarrhea; however, the mechanisms whereby *E. coli* cause diarrhea vary. The enteroinvasive forms of *E. coli* invade and damage the intestinal cell without producing an enterotoxin. The enterotoxic *E. coli* (EEC) elaborate a toxin that causes a secretory diarrhea but does not cause histologic evidence of cellular damage.[343] The EEC strains adhere to the epithelial cells but do not invade it. Instead, the heat-labile toxin of EEC, which is structurally and genetically almost identical to the cholera toxin, acts similarly on the cells' adenylate cyclase. Our knowledge of infectious, especially bacterial, diarrhea has advanced rapidly in the past decade. *E. coli* sero groups that produce shiga toxin are recognized as the cause of the hemolytic–uremia syndrome, while *E. coli* 157 can cause an acute hemorrhagic colitis.[344]

A mucosal permeability defect is best exemplified by celiac disease (Fig. 12). Here, extensive mucosal surface loss leads to impaired absorption of many substances and to steatorrhea. Malabsorption of bile salts,

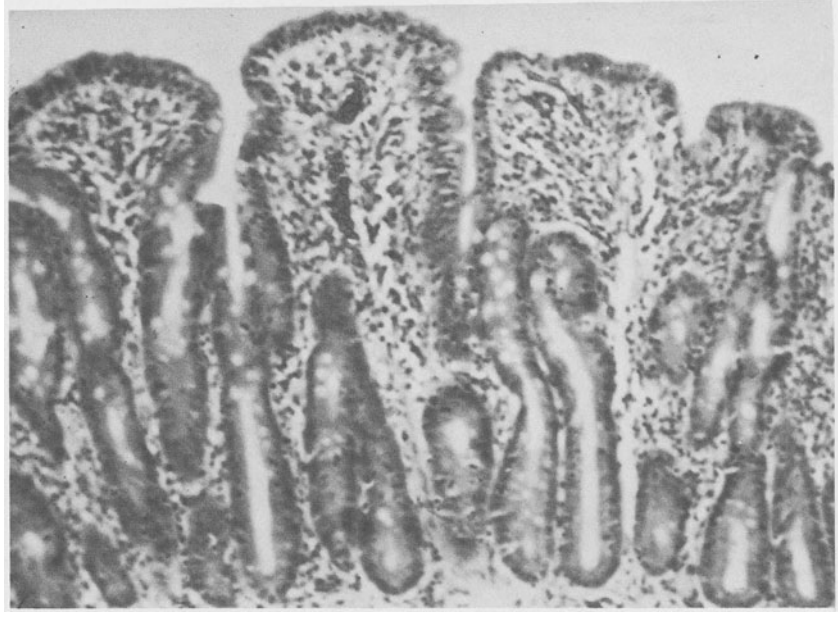

Figure 12. Abnormal intestinal mucosa in celiac disease. There is a marked loss of surface area owing to blunting of the villi: note the inflammatory infiltrate in the lamina propria.

either idiopathic or resulting from surgical resection or disease of the distal ileum, too, may cause chronic diarrhea. In diabetic diarrhea and in the afferent loop syndrome, decreased motility promotes stasis and leads to bacterial overgrowth. The irritable colon syndrome is considered by some a good example of altered intestinal motility.

2.7.7.4. Diagnosis

A good history and physical are essential. The history may provide clues such as antibiotic or laxative use or previous bowel surgery, or it may suggest organic bowel disease. The physical examination may indicate hyperthyroid or hyperparathyroidism, or other diseases.

Often, the stool examination is the key to diagnosis. The presence of blood or pus rules out the diagnosis of "psychogenic" diarrhea immedi-

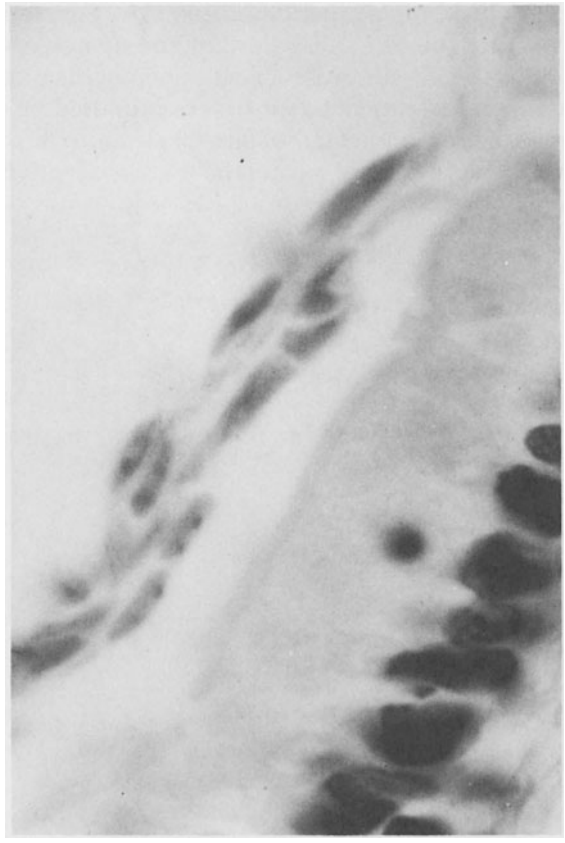

Figure 13. *Giardia lamblia.* Trophozoites overlying the intestinal epithelium.

ately. Stools should be examined for pH, color, odor, leukocytes, and blood. The foul odor of fat-containing stools is well known. A low pH (5.0) suggests a fermentation diarrhea due to bacterial overgrowth or lactase deficiency. Oil droplets are easily identified microscopically with Sudan III stains. Leukocytes, bacteria, and fungi can be seen with a Wright's stain stool preparation. The presence of granulocytes in the stool points to bacterial infection or inflammatory bowel disease. Stool cultures should be obtained when leukocytes are seen. Duodenal aspiration may be necessary for the diagnosis of *G. lambdia* (Fig. 13). Proctoscopy is done if the diarrhea fails to subside within 4 days or immediately if there is bloody diarrhea. Preparatory enemas should be avoided. They obscure fine mucosal detail, decrease the chance of isolating parasites, and increase mucous secretion. Rectal swabs for culture are helpful in preparing slides for microscopic examination and for streaking culture plates for bacterial isolation. If a viral isolation laboratory is available, viral cultures should be taken in the absence of stool leukocytes. Rectal biopsy is indicated when stool leukocytes are seen. It may reveal ulcerative colitis, amebiasis, granulomatous colitis, or carcinoma. If inflammatory bowel disease or cancer is suspected, a barium enema and upper gastrointestinal series with a small bowel follow-through should be obtained. Other tests may be necessary, e.g., T_3 and T_4 levels if thyroid disease is suspected, or a secretin test is pancreatic disease is considered. Small bowel biopsy may reveal evidence of sprue, *Strongyloides,* hookworm, cryptosporosis, and other diseases capable of causing diarrhea. Certain isotope tests may be helpful, e.g., the oral administration of 23-Selena-25-homocholyltaurine (75SeHCAT) is a highly specific (100%) and sensitive (94%) test for detecting bile acid loss as a cause of diarrhea.[345]

2.7.7.5. Treatment

Treatment of acute diarrhea in the elderly is primarily dietary and supportive. They should stop eating solid foods or milk for 24 hr and drink lots of fluids to improve hydration and replace lost electrolytes. Since thirst sensation and total body fluid are decreased by age, hydration and electrolyte replacement are essential if the diarrhea is severe or protracted. The World Health Organization's oral rehydration solution or a similar commercial preparation may effectively accomplish both. Once the diet is resumed, have the patient eat small portions frequently and omit stimulants like caffeine. Antibiotics may be necessary for the treatment of certain bacterial diarrheas, e.g., *Salmonella* septicemia. For shigellosis, Ampicillin, 100 mg/kg per day for 5 days, is often effective, but resistance to this drug varies geographically, ranging from 7% in

Dacca to 87% in Thailand. Similarly, resistance to tetracycline varied from 11% in Sri Lanka to 91% in Mexico and to trimethoprim–sulfamethoxazole from 0% in 1980 to 55% in 1984.[346] Resistance to *Salmonella* strains showed similar variability to antibiotics whereas few strains of *E. coli* were resistant (10%) to trimethoprim–sulfamethoxazole. The use of antibiotics in shigellosis is still debatable. Diphenxylate hydrochloride (Lomotil) is contraindicated in bacterial diarrhea because it prolongs the course of the disease. Bismuth subsalicylate (Pepto-Bismol) is helpful in secretory diarrhea induced by *E. coli.*[347] Giardiasis responds readily to quinacrine hydrochloride (Atabrine), 100 mg thrice daily for 5 days, or to metronidazole (Flagyl), 2 g with breakfast for 3 successive days.

Lactose intolerance may be inherited. Over 90% of Orientals and 40 to 60% of blacks have lactase deficiency. Cessation of lactose intake, which includes wheat flour and cordials, leads to cessation of this type diarrhea. Lactose intolerance may also be acquired temporarily following acute viral gastroenteritis or with giardiasis. The former leads to microvillus changes and to temporarily impaired disaccharidase production. Elimination of milk for 2 to 4 weeks may be necessary for the former while chemotherapeutic treatment for giardiasis eliminates the latter. Yogurt is tolerated reasonably well by lactase-deficient individuals. Levitt showed nonpasteurized yogurt provides its own lactase, which is activated at body temperature and at the pH of the jejunal lumen. Celiac sprue responds to a gluten-free diet; pancreatic steatorrhea often improves significantly with enzyme therapy, e.g., pancreatin (Viokase), 2 g orally thrice daily. Sulfasalazine (Azulfidine) and corticosteroids may be helpful for ulcerative colitis. Cholestyramine will often give immediate relief of the diarrhea associated with bile acid loss. Surgery may be necessary if carcinoma or regional enteritis is responsible for intractable diarrhea. Fecal evacuation is necessary when fecal incontinence due to a fecal impaction causes diarrhea.

2.7.8. Flatus

The elderly often complain of excessive belching, abdominal bloating, or excessive passage of rectal gas. Indeed, the complaint of "passing too much gas" is one of their most frequent and most embarrassing. Unfortunately, gaseous problems grow worse with age. Contrary to popular belief, "bloating and distention" are not due to excessive gas. Such patients have the same volume and composition of bowel gas as controls.[309,347] Their problem should not be equated with chronic eructation. Usually, this results from a nervous habit in which air is sucked into the esophagus. Bloating and distention are often associated with the

irritable bowel syndrome. Excessive flatus results from bacterial gas production within the colon. Normally, our intestinal tract contains between 100 and 200 ml of gas and man expels flatus an average of 14 times daily. Patients afflicted with significant flatus expel gas 25 to 40 times daily.[347,348] Ninety percent of this consists of five gases: nitrogen, oxygen, hydrogen, carbon dioxide, and methane, with nitrogen predominating. Of these, only oxygen and nitrogen are present in air; the remainder originate in the bowel where they can be produced in large volumes. Odoriferous gases, i.e., indoles, skatoles, mercaptans, and hydrogen sulfide, account for the remainder of gases as well as for the odor of flatus.

2.7.8.1. Etiology

Excessive intestinal gas may result from air swallowing, intraluminal gas production, or diffusion from blood into the lumen. Chronic repetitive belching is usually due to air swallowing. Each belch is preceded by a swallow of air, which then passes about halfway down the esophagus before regurgitation.[348] Belching is frequently the result of a nervous habit, hence medications such as antacids and anticholinergics are not indicated. Hydrogen, carbon dioxide, and methane are produced by bacterial fermentation of carbohydrates and proteins in the colon. One of these, methane, is produced by a specific type of anaerobic bacteria. About one-third of mankind are methane producers. This is not a hereditary condition; rather the methane-producing bacteria are acquired through close contact, such as with parents. Unlike H_2-producing bacteria, which require a substrate of carbohydrates, methane-producing bacteria use substratees endogenous to the gut. Man's maximal rate of methane production is about 1 liter/day.[349] Methane excretion is twice as common in patients with colonic cancer as in the general population (see Section 2.8.4). Clinically, hydrogen and methane in proper mixture are explosive. Colons have been exploded in subjects ill prepared for bowel procedures involving electrocautery.

Hydrogen production is negligible in the fasting state, but increases rapidly when nonfermentable carbohydrates are ingested and pass unabsorbed from the small intestine into the colon, the only known site of hydrogen production. Hydrogen is rapidly absorbed from the colon and about 14% is expired through the lungs. This is the basis for the hydrogen breath test for lactose intolerance.[340,350] Recent studies using hydrogen breath analysis have shown that up to 20% of dietary starch is not absorbed by normal individuals. Whether or not age increases starch malabsorption is unknown. It is known, however, that in the colon some bacteria make H^+ while other bacteria consume it, thus maintaining a

balance. The concentration of hydrogen is higher in the bowel lumen than in blood, so it diffuses into the bloodstream and then to the lungs for excretion. The H^+ breath excretion correlates with H^+ gut production.[349,350]

The presence of carbon dioxide in flatus also results from colonic bacterial metabolism and from the interaction of bicarbonate and hydrogen ions in the duodenum and colon. The neutralization of 1 meq of bicarbonate by 1 meq of HCl yields 22.4 ml of CO_2. The combination of pancreatic bicarbonate with HCl in the duodenum is thus one source of CO_2. Luminal production of carbon dioxide depends on the type of food ingested. The ingestion of legumes (beans, peas, lentils) increases carbon dioxide production from a normal 1 ml to an abnormal 80 ml/hr.[350] This increase is due to the presence of oligosaccharides in beans (flatulence factor) that are neither digested nor absorbed from the small intestine. These pass to the colon where they are fermented, with the resultant production of hydrogen and carbon dioxide.[351] Gas production can alo result from chemical interactions. A 30-g fat meal releases about 100 meq of fatty acids. If this amount of fatty acid reacts with HCO_3, about 1800 ml of carbon dioxide is formed.[352]

Intestinal gases, like hydrogen, carbon dioxide, and methane, diffuse back and forth between the intestinal lumen and the blood. The direction of diffusion is related to partial pressure. Thus, gases can escape the gut lumen through the gastrointestinal epithelium or remain and be expelled as flatus. The peculiar breath of certain animals and humans is in part due to gases produced and absorbed in the colon and excreted by the lungs. The odor of garlic on the breath 24 hr after its ingestion is due to its absorption from the bowel and its excretion in the breath.[353,354] The clinical gas syndromes have been described in detail by Levitt. His articles are worth reading by the practioner who encounters gas problems frequently among his patients.

2.7.8.2. Diagnosis

Gas syndromes frequently induce pain sufficient to mimic angina pectoris, cholelithiasis, reflux esophagitis, and even peptic ulcer disease. Organic disease however must always be ruled out before flatulence can be considered a primary disorder. Lactose malabsorption can be discerned by history or by use of a lactose tolerance test. In this test, the blood sugar curve is flat. Two hours after taking the oral lactose load, the blood glucose level has risen less than 20 mg% above the fasting glucose level. Lacaste like sucrase deficiency can also be determined by assaying its content within the jejunal brush border or by the hydrogen breath test.

2.7.8.3. Treatment

Patients should be made aware that belching is accompanied by air swallowing. Aerophagia is often due to anxiety, and treatment of the latter may lead to remission. Anticholinergic drugs may also help to decrease aerophagia by reducing saliva production. Bloating is considered a motor disorder and few drugs are helpful, although metoclopramide is believed to aid motility coordination and has been credited as effective in Europe. Since flatulence is the result of gas production, treatment consists in restricting the quantity of carbohydrate ingested, notably legumes and wheat, decreasing the intake of carbonated beverages, and avoidance of chewing gum. Charcoal and simethicone are sometimes helpful. If lactase intolerance is suspected, a lactose-free diet should be tried.

2.7.9. Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) refers to a group of chronic symptoms including recurrent cramping abdominal pain, flatulence, and altered bowel habits in the absence of underlying disease. It is one of the most common bowel disorders in developed countries and reportedly accounts for 40 to 70% of gastroenterologic consultation. Its exact incidence is unknown, but estimates as low as 1.5 million to as high as 22 million Americans have been rendered.[355]

2.7.9.1. Etiology

The cause of IBS is not certain, but most authorities believe it has a multifactorial etiology. It has been regarded as a psychosomatic disorder, as a bowel motility disorder, and as the result of food intolerance. Depression is more common in IBS patients than in matched controls.[356] The panic syndrome, too, has been described in patients with IBS, leading to the suggestion that some patients suffer from a primary anxiety disorder.[357] Seventy-two percent of office patients with IBS have psychiatric illnesses, in contrast to 18% of controls.[358] However, 30% of presumably normal individuals may have an irritable bowel-like syndrome.[359]

Almy and Tulin first noted that painless diarrhea was associated with decreased colonic motility whereas IBS was associated with increased sigmoid motility.[360] Subsequently, the hypomotility pattern was also found in patients with ulcerative colitis while the hypermotility pattern was found in patients with diverticulitis and constipation.[361] Almy and Tulin now believe the altered motility patterns observed in IBS

"represent a qualitative or merely a quantitative departure from the psychophysiologic reactions in healthy persons."[362] The cramping abdominal pain of IBS coincides with colonic hypermotility while "gas" pains are due to abnormal jejunal motility.[363,364] More recently, IBS patients with diarrhea were found to have "small bowel transit times" significantly shorter than normal while IBS patients who complained predominantly of constipation or abdominal pain or distention had longer small bowel transit times than normal. Thus, IBS apparently effects both small and large bowel motility.[365] The gastric emptying rates of IBS patients, however, do not differ from those of controls.

About 41% of IBS patients have an abnormal duodenal loop versus 18% of patients with Crohn's disease. Food-provoked pain occurs more often in patients with an abnormal duodenal loop than in IBS patients with a normal duodenal loop. An abnormal duodenal loop may contribute to abnormal pain in the IBS.[366] Food intolerance, too, is found in IBS. Alun-Jones *et al.* found that 14 of 21 patients with IBS had a clearing of their symptoms following dietary management. Wheat, corn, dairy products, coffee, tea, and citrus fruits were common food offenders, and removal of one or more from the diet led to relief of symptoms.[367] Kruis and his colleagues found wheat bran (15 g/day) gave better symptomatic relief than mebeverine.[368] Cann *et al.* found the low levels of rectal prostoglandin E_2 present in fasting patients rose significantly after the administration of test foods and remained elevated for 24 hr. Unlike patients with intestinal allergy to wheat, however, the IBS patients did not have an increase in hydrogen production following wheat ingestion.[369]

2.7.9.2. Clinical Findings

The IBS is four times more common in women than men. Women with IBS tend to be constipated whereas men tend to have a mucous-type diarrhea. Constipation, diarrhea, dyspeptic symptoms, abdominal pains, and varying degrees of anxiety or depression are frequent findings. Constipation often alternates with diarrhea. Since the diarrhea is functional, it occurs during the day. The abdominal pain is poorly localized and lasts from minutes to hours. Sometimes it is relieved by flatus, by bowel movements, or by enema. The splenic flexure syndrome is believed to be a variant of the IBS.

2.7.9.3. Diagnosis

IBS is one of the most difficult conditions to diagnose and the disorder remains an expensive diagnosis of exclusion. Sigmoidoscopy, colonoscopy, barium enema, fecal examination for ova and parasites, bacterial cultures, lactose tolerance tests, ultrasonography of the liver,

bladder, and pancreas, and CT scan of the abdomen are recommended to rule out organic disease. This expensive, extensive, and invasive work-up led Krivis and his associates to devise a diagnostic score for IBS to be used for diagnosis, to reduce costs and to save the elderly and others from unnecessary invasive diagnostic and sometimes dangerous procedures.[370] It is based on seven patient questions and eight physician findings. This diagnostic scale had a specificity of 97% and a sensitivity of 83%. It incorporates features of the patient's history, physical examination, and basic laboratory studies, including a complete blood count and erythrocyte sedimentation rate. Kyosola believes the value of the Krivis scoring system can be improved further by rectal mucosal biopsy and fluorescence histochemical analysis. Glyoxylic acid allows easy identification of adrenergic nerves and enterochromaffin cells in mucosal biopsies. In IBS the number of enterochromaffin cells is increased significantly while adrenergic nerves are difficult to find. Inverse changes are found in ulcerative colitis. Kyosola states, "The explosive increase in the amount of bright yellow fluorescing enterochromaffin cells are easily recognized by even the inexperienced microscopist."[371] This scoring system should be of great value to physicians trying to rule out IBS in elderly patients who cannot stand invasive studies.

2.7.9.4. Treatment

Treatment is empiric. An adequate fluid intake is essential, and laxatives are to be avoided. Few drugs are of proven efficacy. In general, if constipation is the primary complaint, regular dietary habits, adequate sleep, and exercise are to be encouraged. A high-fiber diet is helpful if constipation is the primary complaint. However, those with diarrhea, urgency, and abdominal pain are made worse by bran.[372] Metamucil is sometimes useful, as are combination drugs that include an anxiolytic and anticholinergic agent. Exclusion of certain foods as noted by Alun-Jones is worth a try if other measures fail. For diarrhea, it may be necessary to try diphenoxylate hydrochloride or codeine. If anxiety and depression are present, they should be treated appropriately. Reassurance and therapeutic intervention help at least 75% of patients with IBS. The remainder often require psychotherapy, stress management care, or hypnotherapy.

2.8. Lower Gastrointestinal Bleeding

2.8.1. Etiology

After age 60, vascular ectasias, diverticulosis, malignancy, and polyps, in that order, are the primary causes of major lower gastrointestinal bleeding (LGIB),[373,374] while diverticulosis, polyps, cancer, and hemor-

rhoids, in that order, are the primary causes of minor LGIB. Introduction of selected angiography led to recognition of angiodysplasia (vascular ectasia) as an important and common cause of LGIB.[374] Actually, in one recent study, angiodysplasia was the cause of LGIB in 43 of 72 patients and was more common than diverticular bleeding, which occurred in only 29 patients.[375]

2.8.2. Vascular Ectasias (Angiodysplasias)

These are small (<5 mm), degenerative arteriovenous malformations that occur with aging. They are not to be confused with congenital telangiectasia,[376] for they are acquired and usually restricted to the cecum and proximal descending bowel. They are not found in the upper gastrointestinal tract. Vascular ectasias are usually multiple and are rarely diagnosed without angiography.

LGIB due to ectasias is recurrent and usually mild, but 15% of patients may have massive hemorrhage. The nature and variation in the type of bleeding are due to characteristics of the ectasias. They are the result of repeated, partial, intermittent, low-grade obstruction of submucosal veins by colonic muscular contractions.[373] Eventually, the dilated submucosal veins lead to retrograde congestion of the hexagonal capillary rings surrounding the mucosal crypts. When the competency of the precapillary sphincters is lost, the result is a small arteriovenous communication. Eventually a maze of distorted dilated vascular channels may almost replace the mucosa. Bleeding varies with the stage of evolution. Since bleeding is from veins or capillaries, it is less severe than the arterial bleeding encountered in diverticulosis.[374,375] Boley *et al.* reviewed the etiology, evolution, and progress of vascular ectasias in detail. About 40% of older patients who have never experienced LGIB also have vascular ectasias.[377]

2.8.3. Diverticulosis

Diverticular bleeding is usually experienced after age 50. This is the second most common cause of LGIB. Over one-half of patients have their bleeding lesions in the right colon. Bleeding from diverticulosis is more severe than from vascular ectasia and does not recur as often. In most instances (75%), the bleeding stops spontaneously.

2.8.4. Cancer

Cancer of the colon is the most common cause of malignancy in old age and the third cause of major LGIB. Its prevalence rate is 3% after age 70.[373]

2.8.5. Diagnosis

Colonoscopy is extremely valuable for localizing sites of LGIB. The flexible sigmoidoscope with a 5.0-mm suction port permits aspiration of 500 ml of fluid per minute; hence active bleeding can be evaluated. Vascular ectasias are more readily seen when they are actively bleeding. Otherwise, they are very difficult to visualize at colonoscopy. If endoscopy is unsuccessful in localizing a bleeding site, a technetium 99 mm scan may be helpful in identifying the site of bleeding.[378] If both colonoscopy and scintigraphic studies are negative and bleeding continues, emergency angiography is the next step. However, the rate of bleeding must be at least 1.5 ml/min. At this rate, localization of the bleeding site is possible in 60% of patients with LGIB.[379] Unfortunately, angiography is not as accurate for vascular ectasias as it is for other causes of LGIB.

2.8.6. Treatment

Treatment is directed at locating the site of bleeding and stopping it. Vasopressin effusions through an angiographic catheter or intravenously are effective in stopping hemorrhage in 70 to 80% of the cases.[373] If vasopressin therapy is unsuccessful, transcatheter embolization may prove efficacious. Occasionally, this procedure leads to colonic infarction or stricture formation. If surgery becomes necessary, standard procedures are available for removal of malignancies, polyps, and other lesions. Segmental resection for bleeding diverticulosis is highly successful. Angiographically identified ectasias, too, can be removed successfully in 80% of patients.[373,374]

2.9. Cancer

The incidence of cancer rises with age. Cancer of the gastrointestinal tract accounts for one-third of the annual mortality due to cancer. In 1976, 169,000 of the 675,000 newly reported cancers and 102,000 of the 370,000 cancer deaths were due to malignancies of the gastrointestinal tract.[380] Cancers of the colon and rectum are the most common enteric cancers, followed in order by cancer of the pancreas, stomach, hepatobiliary system, and esophagus. With the exception of the esophagus and anus, most gastrointestinal tract cancers are adenocarcinomas. Their spread is usually by progressive local invasion with subsequent embolization of either the lymphatics or blood vessels.

2.9.1. Cancer of the Esophagus

This is a cancer of the aged and it is more common in men than in women (4 : 1). Almost one-half of patients are over age 60 years and approximately 25% are over age 70 years.[381] Esophageal cancers are more common among the less affluent. A striking rise in the incidence has been observed among nonwhites in this country over the past several decades.[382] Morbidity is high. Among the 7500 new cases reported annually, there are 6600 fatalities.

2.9.1.1. Etiology

Etiology is unknown, but smoking, alcoholism, malnutrition, poor oral hygiene, esophageal diverticuli, Barrett's esophagus, and lye strictures are associated with an increased incidence.[382] Patients with sideropenia tend to develop cancer of the middle esophagus. Esophageal carcinoma is seven times greater in patients with achalasia than in the general population. The rich capillary beds of the mucosa and submucosa and lack of a serosal layer allow easy dissemination to the mediastinum.

2.9.1.2. Clinical Findings

The clinical findings are vague in general, the most common being dysphagia (90%).[383] Initially, this is usually painless; later, it is associated with difficulty in swallowing solid foods. Other presenting complaints include weight loss (84%), odynophagia (29%) vomiting/regurgitation (24%), cough (10%), and hoarseness (6%). The mean duration of symptoms before presentation is about 2 to 4 months. Almost one-half of patients have their lesions in the lower third of the esophagus, and close to another one-third in midesophagus. The remainder have lesions in the upper third or at the gastroesophageal junction.

Barium radiography reveals 90% of esophageal carcinomas (Fig. 14). Still, esophagoscopy is necessary to establish a tissue diagnosis and to evaluate the extent of the disease. If the gastroesophageal junction is involved, bronchoscopy is indicated to determine whether the tracheal bronchial tree is also involved.

2.9.1.3. Treatment

Surgery is the principal form of therapy. Esophagogastrectomy with or without interposition of a segment of colon is the usual procedure. Unfortunately, surgery is difficult (the operative mortality ranging from 15 to 30%) and prognosis is poor. The 5-year survival rate is less than

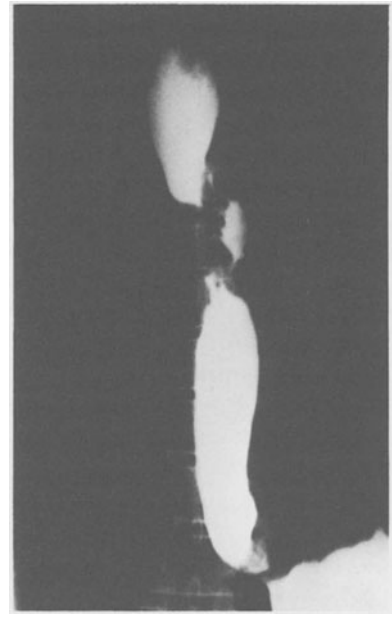

Figure 14. Cancer of the esophagus. A large filling defect is present in the middle third of the esophagus.

10%. In a recent review of 51 patients, the mean survival for the entire group was only 5.5 months. This review confirms the dismal results of surgical therapy for esophageal carcinoma.

Radiation therapy is also disappointing. The survival rate for this form of treatment is generally less than 5%.[384] Chemotherapy offers little therapeutic hope. In most instances, the therapeutic responses are brief and last less than 2 to 3 months.

Palliation and improved swallowing are often possible with placement of an esophageal prosthesis made from polyvinyl tubing. The prosthesis can be placed periorally within a stenosing carcinoma and may remain patent until death.[385] It reduces the incidence of aspiration pneumonia. Overall, despite our ability to diagnose esophageal cancer with relative ease, attempts at therapy are inadequate.

2.9.2. Cancer of the Stomach

This form of cancer is decreasing in the United States. It is rare before the age of 40, the highest incidence occurring in the sixth or seventh decades. Although gastric cancer may develop in any part of the stomach, it is more likely to occur in the pyloric and antral regions.[378]

2.9.2.1. Etiology

Etiology is unknown. The incidence is increased in individuals with relatives who have gastric cancer, with blood type A, achlorhydria, atrophic gastritis with pernicious anemia, and in older males.

2.9.2.2. Clinical Findings

Ming classified gastric carcinoma into two types: (1) the expanding type, wherein the carcinoma cells grow en masse, and (2) the infiltrative type, wherein the cancer cells invade the stomach wall individually or in small clusters.[387] Patients with the expanding type are usually older and have less lymph node involvement than those with the infiltrative type.[388]

The primary manifestations are often vague and may include epigastric pain and uneasiness following meals, anorexia, early satiety, weight loss, weakness, and blood loss. By the time the diagnosis is made, most patients have some pain. Often it is comparable to that of peptic ulcer disease and may be relieved by fluid or antacids.

The mainstays of diagnosis are radiography, endoscopy, and cytology. Contrast roentgenography is extremely useful because it allows assessment of gastric mobility, distention, and wall flexibility. The diagnostic accuracy for endoscopy with biopsy is high, ranging from 85 to 99%.[389]

2.9.2.3. Treatment

Surgery is the preferred approach. The type of operation is related to tumor location and the surgeon's expertise. Results are related to the state of the tumor. The 5-year survival rate at the New York Memorial Hospital study was 57% when the neoplasm was confined to the stomach. It was only 5% when regional nodes were involved.[390] The 5-year survival rate following surgery is better in patients with expanding-type tumor (45%) than in those with infiltrating tumor (27%).[391] Gastric surgery can lead to successful results in the elderly and long-term survival is possible. Some patients live to be 80 or 90 years of age without evidence of recurrence.[391]

Radiation therapy alone is not effective therapeutically. In conjunction with chemotherapy, however, objective responses may be obtained. Combination chemotherapy is superior to single-drug therapy for gastric carcinoma. Among drugs known to be chemotherapeutically active, 5-fluorouracil yields a response rate of about 25%. Doxorubicin reportedly yields a 40% overall response and nitrosourea BCNU an 18% response.[392] There is no combination of chemotherapeutic agents that leads to remarkable success.

2.9.3. Colorectal Cancer

Colorectal cancer is the commonest malignancy of the aged. The incidence increases significantly after age 45. Each decade thereafter it increases by a factor of 2 until it peaks at age 75. Unfortunately, more than one-half of all patients who develop large bowel cancer die from it. In 1976, there were over 100,000 new cases of colorectal cancer in this country with 38,900 deaths from colon cancer and 10,3000 deaths from rectal cancer.[386] It was estimated that 130,000 new cases with 59,400 deaths would occur in 1984. About 5 to 10% of the population over 40 will have one or more adenomas. Fortunately most of these are noninvasive when detected. Their removal reduces the risk of cancer to about 15% of the expected rate.

2.9.3.1. Etiology

While etiology is unknown, certain environmental factors have been associated with the disease. A high-fiber diet is thought to reduce the incidence of colorectal cancer by inducing rapid transit and reducing mucosal contact time with potential carcinogens. Its protective effect has been shown in rats fed a highly carcinogenic substance. In contrast, a high animal fat intake and a high meat intake have the opposite effect and appear to have carcinogenic potential for colon cancer. Bile acids, too, have been implicated. Several studies comparing postcholecystectomy patients with controls have shown an increased relative risk for large bowel cancer following cholecystectomy.[393–395] Linos *et al.* found the relative risk for colonic cancer following cholecystectomy was increased significantly only in females; Rundgren and Mellstrom found the relative risk increased in both sexes between 70 and 75 years of age, while Vernick and Kuller, in an age-sex-race-matched study, found a relative risk of 1.77 compared to controls. Similar findings have been found in cholecystectomized mice. Colonic carcinoma evolved in 70% of the cholecystectomized mice but in only 16% of the control animals.[396] Cholecystectomy alters bile metabolism and the composition of the bile acid pool. Presumably bacterial alteration of bile acid and cholesterol creates a carcinogenic milieu in the large bowel. In contrast, Garland *et al.* found an inverse relationship between dietary intake of vitamin D and calcium and the incidence of colorectal cancer. Here, the carcinogenic potential of fatty acids and free bile salts is believed to be negated by their conversion to insoluble calcium soaps. Colorectal cancer is also increased in patients with polyposis, regional enteritis, and ulcerative colitis. More recently, methane excretion was reported to be twice as common in British patients with colonic cancer as in controls.[397] Methane excretion is these studies was defined as a concentration in

breath greater than 1 ppm above ambient air. Pique *et al.* found such concentrations in 91% of 47 untreated patients. Resection of the tumor in 36 patients led to a return to normal, whereas methane excretion continued above normal in six of seven patients with unresectable tumors.[398] Perman believes the methane excretion test may offer the potential for noninvasive, readily available surveillance for colonic cancer in premalignant conditions.[399]

Most cancers of the colon appear to rise from adenomas and the risk of having cancer in an adenoma in about 5%. It is estimated that a period of from 5 to 15 years is required for the growth and transformation of a small adenoma into an invasive cancer. The risk of having cancer in an adenoma increases with the number of adenomas, is higher in adenomas of a villous type, and is markedly increased in adenomas of 2 cm or more.

2.9.3.2. Diagnosis

The onset of colorectal cancer varies considerably depending on the age of the individual and the location and type of cancer. In the elderly, onset may be insidious or acute. Recognition may come only after increasing apathy, fatigue, or the symptoms and signs of anemia become prominent or after the cancer proclaims its presence by causing rectal bleeding, abdominal pain, or bowel obstruction or by infiltrating other organs. Edwards and his associates found patients with the more acute presentations were generally admitted to surgery, whereas those with less fulminant but generally more advanced disease were admitted to medical wards. Consequently, the operative rate was higher and the mortality rate lower on the surgical service.[400]

None of the screening tests devised for early detection of colorectal carcinoma have been shown to reduce mortality effectively by control studies. These tests include fecal occult blood tests, proctosigmoidoscopy, double-contrast barium enemas, and colonoscopy. The latter is the most effective means for diagnosing colorectal cancer. Recognition, too, has been increased by the increasing use of the flexible fiberoptic sigmoidoscope (FS) by clinicians. The diagnostic yield with this instrument was 30% versus 6.5% in the same patients subjected to both FS and rigid sigmoidoscopy.[401] Furthermore, it permits biopsy and even removal of some lesions. Pelvic CT has proven very helpful in staging rectal cancer. One recent study showed that CT and surgical and/or pathologic staging agreed in 18 of 23 patients.[402] In two others, the pelvic extent of disease was correctjy assessed, but small liver implants were not recognized. CT also influenced the extent of treatment in almost 50% of these patients.[402] Carcinoma embryonic antigen is not

a specific test for colorectal cancer. It may be elevated in inflammatory bowel disease, pancreatitis, and alcoholic liver disease. The sensitivity of the simple, easy, and cheap Hemoccult test varies from 37 to 97%, but specificity ranges from 89 to 99%. False positive reactions may occur with a red-meat diet, vitamin C, and delay in developing slides.[403] Ornithine decarboxylase, the rate-limiting enzyme essential to colonic mucosal proliferation, is greatly increased in polyps from patients with familial polyposis. Studies are underway to evaluate its potential for predicting the presence of colonic cancer.

2.9.3.3 Treatment

Surgery, again, is the primary mode of therapy. The survival rate after appropriate elective surgery depends on the extent of the cancer at the time of operation. Advanced age is not a major detriment to surgery. Patients over 70 years tolerate colon resection better when the surgery is elective.[404] Five-year survival rates approach 80% when only the mucosa is involved (Duke's stage A); it is 60% with involvement of the muscularis mucosa (Duke's stage B) and about 40% when there is extension through the serosa or involvement of the nodes (Duke's stage C).[405] The 10-year survival rate is better for patients with tumors originating in the right and transverse colon than for those whose tumors originate in the left colon.[406] A collaborative prospective study involving 2524 patients in the United Kingdom showed that curative resection depends on both clinical and pathologic factors. Factors that influenced long-term survival were, in order of importance, lymph node status, tumor mobility, number of lymph nodes positive for tumor, presence of bowel obstruction, and depth of primary tumor invasion. Factors that influenced in-hospital mortality were cardiopulmonary complications, intraabdominal sepsis, bowel obstruction, and age. Preliminary experience with 1262 patients showed 103 died within 3 months. Of the remaining 1159, 623 who were discharged from the hospital were alive after 3 years.[407] Since surgery for biopsy-proven adenocarcinoma of the rectum carries a mortality rate of 2 to 10%, which tends to be higher in the elderly, Gingold believes local treatment may be a more realistic therapeutic approach in some of the aged.[408] He considers electrocoagulation therapy for this type of cancer superior to the results of radical surgery.

Combination chemotherapy is more effective than single-drug therapy. The best combination at present consists of 5-fluorouracil and methyl-CCNU (semustine). It is superior to regimens combining three or four chemotherapeutic agents. Even so, the response rate is low (12%) and its duration is limited to months.[409]

2.9.4. Cancer of the Pancreas

A total of 22,000 new cases of pancreatic cancer are reported annually in the United States. The incidence increases with age. Average age at onset is 56 years. For men over age 75 years the risk of developing pancreatic cancer is 10 times that of the general population. Etiologically, the cause is unknown, but factors associated with the increased incidence of pancreatic carcinoma include pancreatitis, diabetes mellitus, alcoholism, and cigarette smoking.

2.9.4.1. Clinical Findings

In 50 to 60% of patients, the tumor involves the head of the pancreas, in 15 to 20% it involves the body or tail, in 10 to 15% the ampulla of Vater, and in 8 to 10% the terminal bile duct. Tumors close to the common bile duct have the highest rate of resectability. Twenty to forty percent of patients with cancer of the head or body have an audible abdominal bruit. Classical findings include pain, particularly epigastric pain radiating through the back and relieved by forward bending. The pain has been described as boring, dull, steady, and piercing and it may become intractable. Progressive fatigue, dyspepsia, early satiety, weight loss, and progressive jaundice are common. The jaundice may begin before or after onset of the pain and may lead to severe pruritus. Fever in the presence of jaundice may be a sign of cholangitis in patients with bile duct obstruction. Twenty to forty percent of the patients have associated diabetes mellitus.

2.9.4.2. Diagnosis

Cancer of the pancreas is one of the most difficult tumors to diagnose. Furthermore, there are no specific tests, although endoscopic retrograde cholangiopancreatography has improved diagnostic accuracy tremendously through direct visualization, biopsy, and aspiration for cytologic material.[410] Diagnostic sensitivity is about 92% and specificity is 90%. Ultrasound is helpful if there is sufficient obstruction of the common duct to cause dilatation. It is more useful for following progressive changes than for early diagnosis. Computerized transaxial tomography is the most effective noninvasive test.[411] Percutaneous needle aspiration is difficult to perform and has been associated with clinical pancreatitis following biopsy. According to the National Cancer Institute study of 184 patients with cancer of the pancreas, computerized axial tomography, celiac angiography, serum alkaline phosphatase levels, pancreatic scan, and ultrasonography, in that order, gave the greatest percentage of direct diagnosis.[412]

2.9.4.3. Treatment

A variety of surgical procedures are available, including radical pancreaticoduodenectomy (Whipple's procedure). Even in the best hands, however, surgical mortality is high and the 5-year survival rate is low, ranging from 7 to 15%. Radiation and chemotherapy have not proven very successful.[382] There is no curative therapy.

Supportive therapy, too, may be difficult because of the severe pain encountered by some patients, which often leads to a demanding addiction, neuropsychiatric symptoms, and even suicide. The itching may be controlled by use of a biliary stent positioned by endoscopy or via the percutaneous transhepatic route. Sometimes, grounding the patient via an electrocardiographic lead will reduce some of the static electricity created by itching and allow some relief.

2.9.5. Hepatoma

2.9.5.1. Etiology

Hepatic neoplasms arise either from the hepatic parenchymal cells or from biliary ductules. Primary hepatoma, a tumor of parenchymal cells, is extremely common in the Orient where the liver fluke, *Clonorchis sinensis,* is believed to be an etiologic factor. In the United States, about 4% of patients with cirrhosis develop hepatomas. The relationship between alcoholism and hepatoma is not clear. Exposure to aflatoxin, a substance derived from peanuts infected with *Aspergillus flavus,* and infections with hepatitis B virus have also been suggested as etiologic possibilities.[413] Hepatitis B antigen is present in the liver cells of 74% of patients with cirrhosis and hepatoma.[414]

2.9.5.2. Clinical Findings

Onset is usually insidious and symptoms often attributed to cirrhosis. Cachexia, weakness, and weight loss are common. Malnutrition and hepatomegaly occur as the tumor expands. Sudden onset of hypotension or abdominal pain may occur secondary to massive hemorrhage into the tumor or the peritoneal cavity. Hypercalcemia, hyperglycemia, polycythemia, the carcinoid syndrome, and porphyria are some of the paraneoplastic syndromes associated with hepatoma.[414] Hepatoscans, angiography, needle biopsy, and peritoneoscopy are helpful diagnostic aids. The test for $alpha_1$-fetoprotein is positive in 30 to 50% of patients.

2.9.5.3. Treatment

In some instances, surgical resection of the involved lobe leads to relatively prolonged survival. In most instances, however, surgical resec-

tion is impossible because of advanced cirrhosis or diffuse tumor involvement.

Systemic chemotherapy is not highly successful. In those who respond to treatment, survival ranges from 7 to 9 months. Regional chemotherapy, using the Seldinger approach, or by placement of a catheter into the tumor at laporotomy, also fails to yield significant survival.[415]

2.9.6. Cancer of the Gallbladder

Cancer of the gallbladder usually occurs in older women; the male-to-female ratio is 5 : 1. Usually, the tumor is an adenocarcinoma. Metastases occur via submucosal lymphatics or by direct extension to surrounding nodes and organs. Median survival time is 3 months. Obstruction of the biliary tree by malignancy leads to jaundice, which in turn may lead to recurrent ascending cholangitis, unremitting pruritus, nutritional deficiencies, and progressive hepatic failure.

2.9.6.1. Clinical Findings

Symptoms of gallbladder cancer are similar to those found with cholecystitis or cholelithiasis and consist of right-upper-quadrant pain, nausea, vomiting, and weight loss. Common-duct obstruction leads to jaundice.

Calcification of the wall of the gallbladder may serve as an indicator of tumor. With obstruction of the biliary tree by malignancy due to pancreatic or bile duct carcinoma or metastatic lesions to the hilum from the stomach, colon, or other organs, initial symptoms and others encountered are primarily related to the obstruction. Pruritus in these patients may be devastating.

2.9.6.2. Treatment

Surgery offers the only chance for cure of cancer of the gallbladder *per se*. The obvious link between cholelithiasis and gallbladder carcinoma has led some to suggest that elective cholecystectomy be advised to prevent further cancer. The large number of patients with gallstones in this country and the relative paucity of gallbladder carcinoma (6000 patients annually) have led others to question the need for prophylactic therapy.[382] Palliative surgical procedures for jaundiced patients with malignant obstruction of the biliary tree secondary to cancer of the bile duct, pancreas, or metastatic lesions include choledochojejunostomy, cholecystojejunostomy, choledochoduodenostomy, and hepaticojejunostomy. Insertion of various internal stents, T-tube placement through the

tumor with internal drains, and percutaneous insertion of a permanent prosthesis in the biliary tract have all been employed for relief of malignant obstructive jaundice in relation to its etiology.

2.9.7. Summary

Cancer of the gastrointestinal tract is still undefeated. Surgery and radiation have not improved prognosis in the last 20 years. None of the single chemotherapeutic agents used to treat malignant tumors of the gastrointestinal tract gives an overall response greater than 30%. Moreover, none of the multidrug regimens has consistently produced response in more than 50% of patients.[416]

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