2 - Gastrointestinal Disorders

Chapter 7. Approach to the Patient With Upper GI Complaints

Introduction

Upper GI complaints include chest pain (see p. 2025), chronic and recurrent abdominal pain, dyspepsia, lump in the throat, halitosis (see p. 506), hiccups, nausea and vomiting, and rumination. Some upper GI complaints represent functional illness (ie, no physiologic cause found after extensive evaluation).

History: Using open-ended, interview-style questions, the physician identifies the location and quality of symptoms and any aggravating and alleviating factors. Psychologic stress factors must be specifically sought. Because a psychiatric disorder does not preclude physiologic disease, the significance of vague, dramatic, or bizarre complaints should not be minimized.

Patients report symptoms differently depending on their personality, the impact of the illness on their life, and sociocultural influences. For example, nausea and vomiting may be minimized or reported indirectly by a severely depressed patient but presented with dramatic urgency by a histrionic one.

Physical examination: Inspection of the abdomen with the patient supine may show a convex appearance when bowel obstruction, ascites, or, rarely, a large mass is present. Auscultation to assess bowel sounds and determine presence of bruits should follow. Percussion elicits hyperresonance (tympany) in the presence of bowel obstruction and dullness with ascites and can determine the span of the liver. Palpation proceeds systematically, beginning gently to identify areas of tenderness and, if tolerated, palpating deeper to locate masses or organomegaly. Digital rectal examination with testing for occult blood and (in women) pelvic examination complete the evaluation of the abdomen.

Testing: Patients with acute, nonspecific symptoms (eg, dyspepsia, nausea) and an unremarkable physical examination rarely require testing. Findings suggesting significant disease (alarm symptoms) should prompt further evaluation:

• Anorexia

• Anemia

• Blood in stool (gross or occult)

• Dysphagia

• Fever

• Hepatomegaly

• Pain that awakens patient

• Persistent nausea and vomiting

• Weight loss

Chronic or recurrent symptoms, even with an unremarkable examination, also warrant evaluation. Specific GI tests are discussed in Ch. 9.

Chronic and Recurrent Abdominal Pain

Chronic abdominal pain (CAP) persists for more than 3 mo either continuously or intermittently. Intermittent pain may be referred to as recurrent abdominal pain (RAP). Acute abdominal pain is discussed on p. 105. CAP occurs any time after 5 yr of age. Up to 10% of children require evaluation for RAP. About 2% of adults, predominantly women, have CAP (a much higher percentage of adults have

some type of chronic GI symptoms, including nonulcer dyspepsia and various bowel disturbances).

Nearly all patients with CAP have had prior medical evaluation that did not yield a diagnosis after history, physical, and basic testing.

Pathophysiology

Functional abdominal pain syndrome (FAPS) is pain that persists > 6 mo without evidence of physiologic disease, shows no relationship to physiologic events (eg, meals, defecation, menses), and interferes with daily functioning. FAPS is poorly understood but seems to involve altered nociception. Sensory neurons in the dorsal horn of the spinal cord may become abnormally excitable and hyperalgesic due to a combination of factors. Cognitive and psychologic factors (eg, depression, stress, culture, secondary gain, coping and support mechanisms) may cause efferent stimulation that amplifies pain signals, resulting in perception of pain with low level inputs and persistence of pain long after the stimulus has ceased. Additionally, the pain itself may function as a stressor, perpetuating a positive feedback loop.

In addition, menopause increases GI symptoms in several disorders including irritable bowel syndrome, inflammatory bowel disease, endometriosis, and nonulcer dyspepsia.

Etiology

Perhaps 10% of patients have an occult physiologic illness (see Table 7-1); the remainder have a functional process. However, determining whether a particular abnormality (eg, adhesions, ovarian cyst, endometriosis) is the cause of CAP symptoms or an incidental finding can be difficult.

Evaluation

History: History of present illness should elicit pain location, quality, duration, timing and frequency of recurrence, and factors that worsen or relieve pain (particularly eating or moving bowels). A specific inquiry as to whether milk and milk products cause abdominal cramps, bloating, or distention is needed, because lactose intolerance is common, especially among blacks.

Review of systems seeks concomitant GI symptoms such as gastroesophageal reflux, anorexia, bloating or "gas," nausea, vomiting, jaundice, melena, hematuria, hematemesis, weight loss, and mucus or blood in the stool. Bowel symptoms, such as diarrhea, constipation, and changes in stool consistency, color, or elimination pattern, are particularly important.

In adolescents, a diet history is important because ingestion of large amounts of cola beverages and fruit juices (which may contain significant quantities of fructose and sorbitol) can account for otherwise puzzling abdominal pain.

Past medical history should include nature and timing of any abdominal surgery and the results of previous tests that have been done and treatments that have been tried. A drug history should include details concerning prescription and illicit drug use as well as alcohol.

Family history of RAP, fevers, or both should be ascertained, as well as known diagnoses of sickle cell trait or disease, familial Mediterranean fever, and porphyria.

Physical examination: Review of vital signs should particularly note presence of fever or tachycardia.

General examination should seek presence of jaundice, skin rash, and peripheral edema. Abdominal examination should note areas of tenderness, presence of peritoneal findings (eg, guarding, rigidity, rebound), and any masses or organomegaly. Rectal examination and (in women) pelvic examination to locate tenderness, masses, and blood are essential.

Red flags: The following findings are of particular concern:

• Fever

• Anorexia, weight loss

• Pain that awakens patient

• Blood in stool or urine

• Jaundice

• Edema

• Abdominal mass or organomegaly

Interpretation of findings: Clinical examination alone infrequently provides a firm diagnosis.

Determining whether CAP is physiologic or functional can be difficult. Although the presence of red flag findings indicates a high likelihood of a physiologic cause, their absence does not rule it out. Other hints are that physiologic causes usually cause pain that is well localized, especially to areas other than the periumbilical region. Pain that wakes the patient is usually physiologic. Some findings suggestive of specific disorders are listed in Table 7-1.

Functional CAP may result in pain similar to that of physiologic origin. However, there are no associated red flag findings, and psychosocial features are often prominent. A history of physical or sexual abuse or an unresolved loss (eg, divorce, miscarriage, or death of a family member) may be a clue.

The Rome criteria for diagnosis of irritable bowel syndrome are the presence of abdominal pain or discomfort for at least 3 days/mo in the last 3 mo along with at least 2 of the following: (1) improvement with defecation; (2) onset (of each episode of discomfort) associated with a change in frequency of defecation; and (3) change in consistency of stool.

Testing: In general, simple tests (including urinalysis, CBC, liver tests, ESR, amylase, and lipase) should be done. Abnormalities in these tests, the presence of red flag findings, or specific clinical findings mandate further testing, even if previous assessments have been negative. Specific tests depend on the findings (see Table 7-1) but typically include CT of the abdomen and pelvis with contrast, upper GI endoscopy or colonoscopy, and perhaps small-bowel x-rays or stool testing.

The benefits of testing patients with no red flag findings are unclear. Those > 50 should probably have a colonoscopy; those ≤ 50 can be observed or have CT of the abdomen and pelvis with contrast if an imaging study is desired. Magnetic resonance cholangiopancreatography (MRCP), ERCP, and laparoscopy are rarely helpful in the absence of specific indications.

Between the initial evaluation and the follow-up visit, the patient (or family, if the patient is a child) should record any pain, including

[**Table 7-1.** Physiologic Causes of Chronic Abdominal Pain]

its nature, intensity, duration, and precipitating factors. Diet, defecation pattern, and any remedies tried (and the results obtained) should also be recorded. This record may reveal inappropriate behavior patterns and exaggerated responses to pain or otherwise suggest a diagnosis.

Treatment

Physiologic conditions are treated.

If the diagnosis of functional CAP is made, frequent examinations and tests should be avoided because they may focus on or magnify the physical complaints or imply that the physician lacks confidence in the diagnosis.

There are no modalities to cure functional CAP; however, many helpful measures are available. These measures rest on a foundation of a trusting, empathic relationship among the physician, patient, and family. Patients should be reassured that they are not in danger; specific concerns should be sought and addressed. The physician should explain the laboratory findings and the nature of the problem and describe how the pain is generated and how the patient perceives it (ie, that there is a constitutional tendency to feel pain at times of stress). It is important to avoid perpetuating the negative psychosocial consequences of chronic pain (eg, prolonged absences from school or work, withdrawal from social activities) and to promote independence, social participation, and self-reliance. These strategies help the patient control or tolerate the symptoms while participating fully in everyday activities.

Drugs such as aspirin, NSAIDs, H_2 receptor blockers, proton pump inhibitors, and tricyclic antidepressants can be effective. Opioids should be avoided because they invariably lead to dependency.

Cognitive methods (eg, relaxation training, biofeedback, hypnosis) may help by contributing to the patient's sense of well-being and control. Regular follow-up visits should be scheduled weekly, monthly, or bimonthly, depending on the patient's needs, and should continue until well after the problem has resolved. Psychiatric referral may be required if symptoms persist, especially if the patient is depressed or there are significant psychologic difficulties in the family.

School personnel should become involved for children who have CAP. Children can rest briefly in the nurse's office during the school day, with the expectation that they return to class after 15 to 30 min. The school nurse can be authorized to dispense a mild analgesic (eg, acetaminophen). The nurse can sometimes allow the child to call a parent, who should encourage the child to stay in school. However, once parents stop treating their child as special or ill, the symptoms may worsen before they abate.

Key Points

• Most cases represent a functional process.

• Red flag findings indicate a physiologic cause and need for further assessment.

• Testing is guided by clinical features.

• Repeated testing after physiologic causes are ruled out is usually counterproductive.

Dyspepsia

Dyspepsia is a sensation of pain or discomfort in the upper abdomen; it often is recurrent. It may be described as indigestion, gassiness, early satiety, postprandial fullness, gnawing, or burning.

Etiology

There are several common causes of dyspepsia (see Table 7-2).

Many patients have findings on testing (eg, duodenitis, pyloric dysfunction, motility disturbance, *Helicobacter pylori* gastritis, lactose deficiency, cholelithiasis) that correlate poorly with symptoms (ie, correction of the condition does not alleviate dyspepsia).

Nonulcer (functional) dyspepsia is defined as dyspeptic symptoms in a patient who has no abnormalities on physical examination and upper GI endoscopy.

Evaluation

History: History of present illness should elicit a clear description of the symptoms, including whether they are acute or chronic and recurrent. Other elements include timing and frequency of recurrence, any difficulty swallowing, and relationship of symptoms to eating or taking drugs. Factors that worsen

symptoms (particularly exertion, certain foods or alcohol) or relieve them (particularly eating or taking antacids) are noted.

Review of systems seeks concomitant GI symptoms such as anorexia, nausea, vomiting, hematemesis, weight loss, and bloody or black (melanotic) stools. Other symptoms include dyspnea and diaphoresis.

Past medical history should include known GI and cardiac diagnoses, cardiac risk factors (eg, hypertension, hypercholesterolemia), and the results of previous tests that have been done and treatments that have been tried. Drug history should include prescription and illicit drug use as well as alcohol.

Physical examination: Review of vital signs should note presence of tachycardia or irregular pulse.

General examination should note presence of pallor or diaphoresis, cachexia, or jaundice. Abdomen is palpated for tenderness, masses, and organomegaly. Rectal examination is done to detect gross or occult blood.

Red flags: The following findings are of particular concern:

[**Table 7-2.** Some Causes of Dyspepsia]

• Acute episode with dyspnea, diaphoresis, or tachycardia

• Anorexia

• Nausea or vomiting

• Weight loss

• Blood in the stool

• Dysphagia or odynophagia

• Failure to respond to therapy with H_2 blockers or proton pump inhibitors (PPIs)

Interpretation of findings: Some findings are helpful (see Table 7-2).

A patient presenting with a single, acute episode of dyspepsia is of concern, particularly if symptoms are accompanied by dyspnea, diaphoresis, or tachycardia; such patients may have acute coronary ischemia. Chronic symptoms that occur with exertion and are relieved by rest may represent angina.

GI causes are most likely to manifest as chronic complaints. Symptoms are sometimes classified as ulcer-like, dysmotility-like, or reflux-like; these classifications suggest but do not confirm an etiology. Ulcer-like symptoms consist of pain that is localized in the epigastrium, frequently occurs before meals, and is partially relieved by food, antacids, or H_2 blockers. Dysmotility-like symptoms consist of discomfort rather than pain, along with early satiety, postprandial fullness, nausea, vomiting, bloating, and symptoms that are worsened by food. Reflux-like symptoms consist of heartburn or acid regurgitation. However, symptoms often overlap.

Alternating constipation and diarrhea with dyspepsia suggests irritable bowel syndrome or excessive use of OTC laxatives or antidiarrheals.

[**Table 7-3.** Some Oral Drugs for Dyspepsia]

Testing: Patients in whom symptoms suggest acute coronary ischemia, particularly those with risk factors, should be sent to the emergency department for urgent evaluation, including ECG and serum cardiac markers.

For patients with chronic, nonspecific symptoms, routine tests include CBC (to exclude anemia caused by GI blood loss) and routine blood chemistries. If results are abnormal, additional tests (eg, imaging studies, endoscopy) should be considered. Because of the risk of cancer, patients > 45 and those with new-onset red flag findings should undergo upper GI endoscopy. For patients < 45 with no red flag findings, some authorities recommend empiric therapy for 2 to 4 wk with antisecretory agents followed by endoscopy in treatment failures. Others recommend screening for *H. pylori* infection with a C_{14}-urea breath test or stool assay (see p. 129). However, caution is required in using *H. pylori* or any other nonspecific findings to explain symptoms.

Esophageal manometry and pH studies are indicated if reflux symptoms persist after upper GI endoscopy and a 2- to 4-wk trial with a PPI.

Treatment

Specific conditions are treated. Patients without identifiable conditions are observed over time and reassured. Symptoms are treated with PPIs, H_2 blockers, or a cytoprotective agent (see Table 7-3). Prokinetic drugs (eg, metoclopramide, erythromycin) given as a liquid suspension also may be tried in patients with dysmotility-like dyspepsia. However, there is no clear evidence that matching the drug class to the specific symptoms (eg, reflux vs dysmotility) makes a difference. Misoprostol and anticholinergics are not effective in functional dyspepsia. Drugs that alter sensory perception (eg, tricyclic antidepressants) may be helpful.

Key Points

• Coronary ischemia is possible in a patient with acute "gas."

• Endoscopy is indicated for those > 45 or with red flag findings.

• Empiric treatment with an acid blocker is reasonable for those < 45 without red flag findings. Those who do not respond in 2 to 4 wk require further evaluation.

Hiccups

Hiccups (hiccough, singultus) are repeated involuntary spasms of the diaphragm followed by sudden closure of the glottis, which checks the inflow of air and causes the characteristic sound. Transient episodes are very common. Persistent (> 2 days) and intractable (> 1 mo) hiccups are uncommon but quite distressing.

Etiology

Hiccups follow irritation of afferent or efferent diaphragmatic nerves or of medullary centers that control the respiratory muscles, particularly the diaphragm. Hiccups are more common among men.

Cause is generally unknown, but transient hiccups are often caused by the following:

• Gastric distention

• Alcohol consumption

• Swallowing hot or irritating substances

Persistent and intractable hiccups have myriad causes (see Table 7-4).

Evaluation

History: History of present illness should note duration of hiccups, remedies tried, and relationship of

onset to recent illness or surgery.

Review of systems seeks concomitant GI symptoms such as gastroesophageal reflux and swallowing difficulties; thoracic symptoms such as cough, fever, or chest pain; and any neurologic symptoms.

Past medical history should query known GI and neurologic disorders. A drug history should include details concerning alcohol use.

Physical examination: Examination is usually unrewarding but should seek signs of chronic disease (eg, cachexia). A full neurologic examination is important.

Red flags: The following is of particular concern:

• Neurologic symptoms or signs

Interpretation of findings: Few findings are specific. Hiccups after alcohol consumption or surgery may well be related to those events. Other possible causes (see Table 7-4) are both numerous and rarely a cause of hiccups.

Testing: No specific evaluation is required for acute hiccups if routine history and physical examination are unremarkable; abnormalities are pursued with appropriate testing.

Patients with hiccups of longer duration and no obvious cause should have testing, probably including serum electrolytes, BUN and creatinine, chest x-ray, and ECG. Upper GI endoscopy and perhaps esophageal pH monitoring should be considered. If these are unremarkable, brain MRI and chest CT may be done.

[**Table 7-4.** Some Causes of Intractable Hiccups]

Treatment

Identified problems are treated (eg, proton pump inhibitors for gastroesophageal reflux disease, dilation for esophageal stricture).

For symptom relief, many simple measures can be tried, although none are more than slightly effective: $PaCO_2$ can be increased and diaphragmatic activity can be inhibited by a series of deep breath-holds or by breathing deeply in to and out of a paper bag. (CAUTION: *Plastic bags can cling to the nostrils and should not be used*.) Vagal stimulation by pharyngeal irritation (eg, swallowing dry bread, granulated sugar, or crushed ice; applying traction on the tongue; stimulating gagging) may work. Numerous other folk remedies exist.

Persistent hiccups are often recalcitrant to treatment. Many drugs have been used in anecdotal series. Baclofen, a γ-aminobutyric acid agonist (5 mg po q 6 h increasing to 20 mg/dose), may be effective. Other drugs include chlorpromazine 10 to 50 mg po tid as needed, metoclopramide 10 mg po bid to qid, and various anticonvulsants (eg, gabapentin). Additionally, an empiric trial of proton pump inhibitors may be given. For severe symptoms, chlorpromazine 25 to 50 mg IM or IV can be given. In intractable cases, the phrenic nerve may be blocked by small amounts of 0.5% procaine solution, with caution being taken to avoid respiratory depression and pneumothorax. Even bilateral phrenicotomy does not cure all cases.

Key Points

• The cause is usually unknown.

• Rarely, a serious disorder is present.

• Evaluation is typically unrewarding but should be pursued for hiccups of long duration.

• Numerous remedies exist, none with clear superiority (or perhaps even effectiveness).

Lump in Throat

Lump in the throat (globus sensation, globus hystericus) is the sensation of a lump or mass in the throat, unrelated to swallowing, when no mass is present. (If a mass is present, see p. 461.)

Etiology

No specific etiology or physiologic mechanism has been established. Some studies suggest that elevated cricopharyngeal (upper esophageal sphincter) pressure or abnormal hypopharyngeal motility occur during the time of symptoms. The sensation may also result from gastroesophageal reflux disease (GERD) or from frequent swallowing and drying of the throat associated with anxiety or another emotional state. Although not associated with stress factors or a specific psychiatric disorder, globus sensation may be a symptom of certain mood states (eg, grief, pride); some patients may have a predisposition to this response.

Disorders that can be confused with globus sensation include cricopharyngeal (upper esophageal) webs, symptomatic diffuse esophageal spasm, GERD, skeletal muscle disorders (eg, myasthenia gravis, myotonia dystrophica, polymyositis), and mass lesions in the neck or mediastinum that cause esophageal compression.

Evaluation

The main goal is to distinguish globus sensation from true dysphagia (see p. 120), which suggests a structural or motor disorder of the pharynx or esophagus.

History: History of present illness should elicit a clear description of the symptom, particularly as to whether there is any pain with swallowing, difficulty swallowing (including sensation of food sticking). Timing of symptoms is important, particularly whether it occurs with eating or drinking or is independent of those activities; association with emotional events should be queried specifically.

Review of systems seeks weight loss (as evidence of a swallowing disorder) and symptoms of muscle weakness.

Past medical history should include known neurologic diagnoses, particularly those causing weakness.

Physical examination: The neck and floor of the mouth are palpated for masses. The oropharynx is inspected (including by direct laryngoscopy). Swallowing (of water and a solid food such as crackers) should be observed. Neurologic examination with particular attention to motor function is important.

Red flags: The following findings are of particular concern:

- Neck or throat pain
- Weight loss
- Abrupt onset after age 50
- Pain, choking, or difficulty with swallowing
- Regurgitation of food
- Muscle weakness
- Palpable or visible mass
- Progressive worsening of symptoms

Interpretation of findings: Symptoms unrelated to swallowing, with no pain or difficulty with swallowing, or sensation of food sticking in the throat in a patient with a normal examination imply globus sensation. Any red flag findings or abnormal findings on examination suggest a mechanical or motor disorder of swallowing. Chronic symptoms that occur during unresolved or pathologic grief and that may be relieved by crying suggest globus sensation.

Testing: Those with findings typical of globus sensation need no testing. If the diagnosis is unclear or the clinician cannot adequately visualize the pharynx, testing as for dysphagia is done. Typical tests include plain or video esophagography, measurement of swallowing time, chest x-ray, and esophageal manometry.

Treatment

Treatment involves reassurance and sympathetic concern. No drug is of proven benefit. Underlying depression, anxiety, or other behavioral disturbances should be managed supportively, with psychiatric referral if necessary. At times, communicating to the patient the association between symptoms and mood state can be beneficial.

Key Points

- Globus symptoms are unrelated to swallowing.
- Tests are not needed unless symptoms are related to swallowing, examination is abnormal, or there are red flag findings.

Nausea and Vomiting

(For nausea and vomiting in infants and children, see p. 2746.)

Nausea, the unpleasant feeling of needing to vomit, represents awareness of afferent stimuli (including increased parasympathetic tone) to the medullary vomiting center. Vomiting is the forceful expulsion of gastric contents caused by involuntary contraction of the abdominal musculature when the gastric fundus and lower esophageal sphincter are relaxed.

Vomiting should be distinguished from regurgitation, the spitting up of gastric contents without associated nausea or forceful abdominal muscular contractions. Patients with achalasia or a Zenker's diverticulum may regurgitate undigested food without nausea.

Complications: Severe vomiting can lead to symptomatic dehydration and electrolyte abnormalities (typically a metabolic alkalosis with hypokalemia) or rarely to an esophageal tear, either partial (Mallory-Weiss) or complete (Boerhaave's syndrome). Chronic vomiting can result in undernutrition, weight loss, and metabolic abnormalities.

Etiology

Nausea and vomiting occur in response to conditions that affect the vomiting center. Causes may originate in the GI tract or CNS or may result from a number of systemic conditions (see Table 7-5).

The most common causes are the following:

- Gastroenteritis
- Drugs
- Toxins

Cyclic vomiting syndrome is an uncommon disorder characterized by severe, discrete attacks of vomiting or sometimes only nausea that occur at varying intervals, with normal health between episodes. It is most common in childhood (mean age of onset 5 yr) and tends to remit with adulthood. The condition may be associated with migraine headaches, possibly representing a migraine variant.

Evaluation

History: History of present illness should elicit frequency and duration of vomiting; its relation to possible precipitants such as drug or toxin ingestion, head injury, and motion (eg, car, plane, boat, amusement rides); and whether vomitus contained bile (bitter, yellow-green) or blood (red or "coffee ground" material). Important associated symptoms include presence of abdominal pain and diarrhea; the last passage of stool and flatus; and presence of headache, vertigo, or both.

Review of systems seeks symptoms of causative disorders such as amenorrhea, breast swelling (pregnancy); polyuria, polydipsia (diabetes); and hematuria, flank pain (kidney stones).

Past medical history should ascertain known causes such as pregnancy, diabetes, migraine, hepatic or renal disease, cancer (including timing of any chemotherapy or radiation therapy), and previous abdominal surgery (which may cause bowel obstruction due to adhesions). All drugs and substances ingested recently should be ascertained; certain substances may not manifest toxicity until several days after ingestion (eg, acetaminophen, some mushrooms).

Family history of recurrent vomiting should be noted.

Physical examination: Vital signs should particularly note presence of fever and signs of hypovolemia (eg, tachycardia, hypotension, or both).

General examination should seek presence of jaundice and skin rash.

On abdominal examination, the clinician should look for distention and surgical scars; listen for presence and quality of bowel sounds (eg, normal, high-pitched); percuss for tympany; and palpate for tenderness, peritoneal findings (eg, guarding, rigidity, rebound), and any masses, organomegaly, or hernias. Rectal examination and (in women) pelvic examination to locate tenderness, masses, and blood are essential.

Neurologic examination should particularly note mental status, nystagmus, meningismus (eg, stiff neck, Kernig's or Brudzinski's signs), and ocular signs of increased intracranial pressure (eg, papilledema, absence of venous pulsations, 3rd cranial nerve palsy) or subarachnoid hemorrhage (retinal hemorrhage).

Red flags: The following findings are of particular concern:

• Signs of hypovolemia

• Headache, stiff neck, or mental status change

• Peritoneal signs

• Distended, tympanitic abdomen

Interpretation of findings: Many findings are suggestive of a cause or group of causes (see Table 7-5). Vomiting occurring shortly after drug or toxin ingestion or exposure to motion in a patient with an unremarkable neurologic and abdominal examination can confidently be ascribed to those causes, as may vomiting in a woman with a known pregnancy and a benign examination. Acute vomiting accompanied by diarrhea in an otherwise

[**Table 7-5.** Some Causes of Nausea and Vomiting]

healthy patient with a benign examination is highly likely to be infectious gastroenteritis; further

assessment may be deferred.

Vomiting that occurs at the thought of food or that is not temporally related to eating suggests a psychogenic cause, as does personal or family history of functional nausea and vomiting. Patients should be questioned about the relationship between vomiting and stressful events because they may not recognize the association or even admit to feeling distress at those times.

Testing: All females of childbearing age should have a urine pregnancy test. Patients with severe vomiting, vomiting lasting over 1 day, or signs of dehydration on examination should have other laboratory tests (eg, electrolytes, BUN, creatinine, glucose, urinalysis, and sometimes liver tests). Patients with red flag findings should have testing appropriate to the symptoms (see Table 7-5).

The assessment of chronic vomiting usually includes the previously listed laboratory tests plus upper GI endoscopy, small-bowel x-rays, and tests to assess gastric emptying and antral-duodenal motility.

Treatment

Specific conditions, including dehydration, are treated. Even without significant dehydration, IV fluid therapy (0.9% saline 1 L, or 20 mL/kg in children) often leads to reduction of symptoms. In adults, various antiemetics are effective (see Table 7-6). Choice of agent varies somewhat with the cause and severity of symptoms. Typical use is the following:

• Motion sickness: Antihistamines, scopolamine patches, or both

• Mild to moderate symptoms: Prochlorperazine or metoclopramide

• Severe or refractory vomiting and vomiting caused by chemotherapy: 5-HT_3 antagonists

Obviously, only parenteral agents should be used in actively vomiting patients.

For psychogenic vomiting, reassurance indicates awareness of the patient's discomfort and a desire to work toward relief of symptoms, regardless of cause. Comments such as "nothing is wrong" or "the problem is emotional" should be avoided. Brief symptomatic treatment with antiemetics can be tried. If long-term management is necessary, supportive, regular office visits may help resolve the underlying problem.

Key Points

• Many episodes have an obvious cause and benign examination and require only symptomatic treatment.

• Physicians should be alert for signs of an acute abdomen or significant intracranial disorder.

• Pregnancy should always be considered in females of childbearing age.

Rumination

Rumination is the (usually involuntary) regurgitation of small amounts of food from the stomach (most often 15 to 30 min after eating) that are rechewed and, in most cases, again swallowed. Patients do not complain of nausea or abdominal pain.

[**Table 7-6.** Some Drugs for Vomiting]

Rumination is commonly observed in infants. The incidence in adults is unknown, because it is rarely reported by patients themselves.

Etiology

Patients with achalasia or a Zenker's diverticulum may regurgitate undigested food without nausea. In the majority of patients who do not have these obstructive esophageal conditions, the pathophysiology is poorly understood. The reverse peristalsis in ruminants has not been reported in humans. The disorder is probably a learned, maladaptive habit and may be part of an eating disorder. The person learns to open the lower esophageal sphincter and propel gastric contents into the esophagus and throat by increasing gastric pressure via rhythmic contraction and relaxation of the diaphragm.

Symptoms

Nausea, pain, and dysphagia do not occur. During periods of stress, the patient may be less careful about concealing rumination. Seeing the act for the first time, others may refer the patient to a physician. Rarely, patients regurgitate and expel enough food to lose weight.

Diagnosis

• Clinical evaluation

• Sometimes endoscopy, esophageal motility studies, or both

Rumination is usually diagnosed through observation. A psychosocial history may disclose underlying emotional stress. Endoscopy or an upper GI series is necessary to exclude disorders causing mechanical obstruction or Zenker's diverticulum. Esophageal manometry and tests to assess gastric emptying and antral-duodenal motility may be used to identify a motility disturbance.

Treatment

• Behavioral techniques

Treatment is supportive. Drug therapy generally does not help. Motivated patients may respond to behavioral techniques (eg, relaxation, biofeedback, training in diaphragmatic breathing [using the diaphragm instead of chest muscles to breathe]). Psychiatric consultation may be helpful.

Functional GI Illness

Often, no physiologic cause for GI complaints is found, even after extensive evaluation. Such patients are said to have functional illness, which accounts for 30 to 50% of referrals to gastroenterologists. Functional illness may manifest with upper and/or lower GI symptoms.

The reasons for functional symptoms are not clear. Some evidence suggests that such patients have visceral hypersensitivity, a disturbance of nociception in which they experience discomfort caused by sensations (eg, luminal distention, peristalsis) that other people do not find distressing. In some patients, psychologic conditions such as anxiety (with or without aerophagia), conversion disorder, somatization in depression, or hypochondriasis are associated with GI symptoms. Psychologic theories hold that functional symptoms may satisfy certain psychologic needs. For example, some patients with chronic illness derive secondary benefits from being sick. For such patients, successful treatment of symptoms may lead to development of other symptoms.

Many referring physicians and GI specialists find functional GI complaints difficult to understand and treat, and uncertainty may lead to frustration and judgmental attitudes. Physicians should avoid ordering repeated studies or multiple drug trials for the insistent patient with inexplicable complaints. When symptoms are not suggestive of serious illness, the physician should wait rather than embark on another diagnostic or therapeutic plan. In time, new information may direct evaluation and management. Functional complaints are sometimes present in patients with physiologic disease (eg, peptic ulcer, esophagitis); such symptoms may not remit even when a physiologic illness is addressed.

Chapter 8. Approach to the Patient With Lower GI Complaints

Introduction

Lower GI complaints include constipation, diarrhea, gas and bloating, abdominal pain (see also p. 105), and rectal pain or bleeding (see Ch. 21). As with upper GI complaints, lower GI complaints result from physiologic illness or represent a functional disorder (ie, no radiologic, biochemical, or pathologic abnormalities found even after extensive evaluation). The reasons for functional symptoms are not clear. Evidence suggests that patients with functional symptoms may have disturbances of motility, nociception, or both; ie, they perceive as uncomfortable certain sensations (eg, luminal distention, peristalsis) that other people do not find distressing.

No bodily function is more variable and subject to external influences than defecation. Bowel habits vary considerably from person to person and are affected by age, physiology, diet, and social and cultural influences. Some people have unwarranted preoccupation with bowel habits. In Western society, normal stool frequency ranges from 2 to 3/day to 2 to 3/wk. Changes in stool frequency, consistency, volume, or composition (ie, presence of blood, mucus, pus, or excess fatty material) may indicate disease.

Constipation

Constipation is difficult or infrequent passage of stool, hardness of stool, or a feeling of incomplete evacuation.

Many people incorrectly believe that daily defecation is necessary and complain of constipation if stools occur less frequently. Others are concerned with the appearance (size, shape, color) or consistency of stools. Sometimes the major complaint is dissatisfaction with the act of defecation or the sense of incomplete evacuation after defecation. Constipation is blamed for many complaints (abdominal pain, nausea, fatigue, anorexia) that are actually symptoms of an underlying problem (eg, irritable bowel syndrome [IBS], depression). Patients should not expect all symptoms to be relieved by a daily bowel movement, and measures to aid bowel habits should be used judiciously.

Obsessive-compulsive patients often feel the need to rid the body daily of "unclean" wastes. Such patients often spend excessive time on the toilet or become chronic users of cathartics.

Etiology

Acute constipation suggests an organic cause, whereas chronic constipation may be organic or functional (see
Table 8-1).

In many patients, constipation is associated with sluggish movement of stool through the colon. This delay may be due to drugs, organic conditions, or a disorder of defecatory function (ie, pelvic floor dysfunction). Patients with disordered defecation do not generate adequate rectal propulsive forces, do not relax the puborectalis and the external anal sphincter during defecation, or both. In IBS, patients have symptoms (eg, abdominal discomfort and altered bowel habits) but generally normal colonic transit and anorectal functions. However, IBS-disordered defecation may coexist.

Excessive straining, perhaps secondary to pelvic floor dysfunctions, may contribute to anorectal pathology (eg, hemorrhoids, anal fissures, and rectal prolapse) and possibly even to syncope. Fecal impaction, which may cause or develop from constipation, is also common among elderly patients, particularly with prolonged bed rest or decreased physical activity. It is also common after barium has been given by mouth or enema.

Changes with aging: Constipation is common among elderly people because of low-fiber diets, lack of exercise, coexisting medical conditions, and use of constipating drugs. Many elderly people have misconceptions about normal bowel habits and use laxatives regularly. Other changes that predispose the elderly to constipation include increased rectal compliance and impaired rectal sensation (such that larger rectal volumes are needed to elicit the desire to defecate).

Evaluation

History: A lifetime history of the patient's stool frequency, consistency, need to strain or use perineal maneuvers (eg, pushing on the perineum, gluteal region, or recto-vaginal wall) during defecation, and satisfaction after defecation should be obtained, including frequency and duration of laxative or enema use. Some patients deny previous constipation

[**Table 8-1.** Causes of Constipation]

but, when questioned specifically, admit to spending 15 to 20 min per bowel movement. The presence, amount, and duration of blood in the stool should also be elicited.

Symptoms of metabolic (eg, hypothyroidism, diabetes mellitus) and neurologic (eg, spinal cord injury) disorders and systemic symptoms (eg, weight loss) should also be sought. Prescription and nonprescription drug use should be assessed, with specific questioning about anticholinergic and opioid drugs.

Physical examination: A general examination is done to look for signs of systemic disease, including fever and cachexia. Abdominal masses should be sought by palpation. A rectal examination should be done not only for fissures, strictures, blood, or masses (including fecal impaction) but also to evaluate anal resting tone (the puborectalis "lift" when patients squeeze the anal sphincter), perineal descent during simulated evacuation, and rectal sensation. Patients with defecatory disorders may have increased anal resting tone (or anismus), reduced (ie, < 2 cm) or increased (ie, > 4 cm) perineal descent, and/or paradoxical contraction of the puborectalis during simulated evacuation.

Red flags: Certain findings raise suspicion of a more serious etiology of chronic constipation:

• Distended, tympanitic abdomen

• Vomiting

• Blood in stool

• Weight loss

• Severe constipation of recent onset/worsening in elderly patients

Interpretation of findings: Certain symptoms (eg, a sense of anorectal blockage, prolonged or difficult defecation), particularly when associated with abnormal (ie, increased or reduced) perineal motion during simulated evacuation, suggest a defecatory disorder. A tense, distended, tympanitic abdomen, particularly when there is nausea and vomiting, suggests mechanical obstruction.

Patients with IBS typically have abdominal pain with disordered bowel habits (see p. 162). Chronic constipation with modest abdominal discomfort in a patient who has used laxatives for a long time suggests slow-transit constipation. Acute constipation coincident with the start of a constipating drug in patients without red flag findings suggests the drug is the cause. New-onset constipation that persists for weeks or occurs intermittently with increasing frequency or severity, in the absence of a known cause, suggests colonic tumor or other causes of partial obstruction. Excessive straining or prolonged or unsatisfactory defecation, with or without anal digitation, suggests a defecatory disorder. Patients with fecal impaction may have cramps and may pass watery mucus or fecal material around the impacted mass, mimicking diarrhea (paradoxic diarrhea).

Testing: Testing is guided by clinical presentation.

Constipation with a clear etiology (drugs, trauma, bed rest) may be treated symptomatically without further study. Patients with symptoms of bowel obstruction require flat and upright abdominal x-rays, possibly a water-soluble contrast enema to evaluate for colonic obstruction, and possibly a CT scan or barium x-ray

of the small intestine (see also p. 116). Most patients without a clear etiology should have sigmoidoscopy or colonoscopy and a laboratory evaluation (CBC, thyroid-stimulating hormone, fasting glucose, electrolytes, and Ca).

Further tests are usually reserved for patients with abnormal findings on the previously mentioned tests or who do not respond to symptomatic treatment. If the primary complaint is infrequent defecation, colonic transit times should be measured with radiopaque markers or scintigraphy. If the primary complaint is difficulty with defecation, anorectal manometry and rectal balloon expulsion should be assessed.

Treatment

• Possibly discontinuation of causative drugs (some may be necessary)

• Increase in dietary fiber

• Possibly trial with a brief course of osmotic laxatives

Any identified conditions should be treated.

Agents used to treat constipation are summarized in Table 8-2. Laxatives should be used judiciously. Some (eg, phosphate, bran, cellulose) bind drugs and interfere with absorption. Rapid fecal transit may rush some drugs and nutrients beyond their optimal absorptive locus. Contraindications to laxative and cathartic use include acute abdominal pain of unknown origin, inflammatory bowel disorders, intestinal obstruction, GI bleeding, and fecal impaction.

Diet and behavior: The diet should contain enough fiber (typically 15 to 20 g/day) to ensure adequate stool bulk. Vegetable fiber, which is largely indigestible and unabsorbable, increases stool bulk. Certain components of fiber also absorb fluid, making stools softer and facilitating their passage. Fruits and vegetables are recommended sources, as are cereals containing bran. Fiber supplementation is particularly effective in treating normal-transit constipation but is not very effective for slow-transit constipation or defecatory disorders.

[**Table 8-2.** Agents Used to Treat Constipation]

Behavioral changes may help. Patients should try to move their bowels at the same time daily, preferably 15 to 45 min after breakfast, because food ingestion stimulates colonic motility. Initial efforts at regular, unhurried bowel movements may be aided by glycerin suppositories.

Explanation is important, but it is difficult to convince obsessive-compulsive patients that their attitude toward defecation is abnormal. Physicians must explain that daily bowel movements are not essential, that the bowel must be given a chance to function, and that frequent use of laxatives or enemas (> once/3 days) denies the bowel that chance.

Types of laxatives: Bulking agents (eg, psyllium, Ca polycarbophil, methylcellulose) act slowly and gently and are the safest agents for promoting elimination. Proper use involves gradually increasing the dose—ideally taken tid or qid with sufficient liquid (eg, 500 mL/day of extra fluid) to prevent impaction—until a softer, bulkier stool results. Bloating may be reduced by gradually titrating the dose of dietary fiber to the recommended dose, or by switching to a synthetic fiber preparation such as methylcellulose.

Osmotic agents contain poorly absorbed polyvalent ions (eg, Mg, phosphate, sulfate), polymers (eg, polyethylene glycol), or carbohydrates (eg, lactulose, sorbitol) that remain in the bowel, increasing intraluminal osmotic pressure and thereby drawing water into the intestine. The increased volume stimulates peristalsis. These agents usually work within 3 h.

In general, osmotic laxatives are reasonably safe even when used regularly. However, Na phosphate should not be used for bowel cleansing because it may rarely cause acute renal failure even after a single use for bowel preparation. These events occurred primarily in elderly patients, those with preexisting renal disease, and those who were taking drugs that affect renal perfusion or function (eg, diuretics, ACE

inhibitors, angiotensin II receptor blockers). Also, Mg and phosphate are partially absorbed and may be detrimental in some conditions (eg, renal insufficiency). Na (in some preparations) may exacerbate heart failure. In large or frequent doses, these drugs may upset fluid and electrolyte balance. Another approach to cleansing the bowel for diagnostic tests or surgery or sometimes for chronic constipation uses large volumes of a balanced osmotic agent (eg, polyethylene glycol-electrolyte solution) given orally or via NGT.

Secretory or stimulant cathartics (eg, phenolphthalein, bisacodyl, anthraquinones, castor oil, anthraquinones) act by irritating the intestinal mucosa or by directly stimulating the submucosal and myenteric plexus. Although phenolphthalein was withdrawn from the US market after animal studies suggested the compound was carcinogenic, there is no epidemiologic evidence of this in humans. Bisacodyl is an effective rescue drug for chronic constipation. The anthraquinones senna, cascara sagrada, aloe, and rhubarb are common constituents of herbal and OTC laxatives. They pass unchanged to the colon where bacterial metabolism converts them to active forms. Adverse effects include allergic reactions, electrolyte depletion, melanosis coli, and cathartic colon. Melanosis coli is a brownish black colorectal pigmentation of unknown composition. Cathartic colon refers to alterations in colonic anatomy observed on barium enema in patients with chronic stimulant laxative use. It is unclear whether cathartic colon, which has been attributed to destruction of myenteric plexus neurons by anthraquinones, is caused by currently available agents or other neurotoxic agents (eg, podophyllin), which are no longer available. There does not seem to be an increased risk of colon cancer with long-term anthraquinone use.

Enemas can be used, including tap water and commercially prepared hypertonic solutions.

Emollient agents (eg, docusate, mineral oil) act slowly to soften stools, making them easier to pass. However, they are not potent stimulators of defecation. Docusate is a surfactant, which allows water to enter the fecal mass to soften and increase its bulk.

Fecal impaction: Fecal impaction is treated initially with enemas of tap water followed by small enemas (100 mL) of commercially prepared hypertonic solutions (eg, Na phosphate). If these do not work, manual fragmentation and disimpaction of the mass is necessary. This procedure is painful, so perirectal and intrarectal application of local anesthetics (eg, lidocaine 5% ointment or dibucaine 1% ointment) is recommended. Some patients require sedation.

Key Points

- Drug causes are common (eg, chronic laxative abuse, use of anticholinergic or opioid drugs).
- Clinicians should be wary of bowel obstruction when constipation is acute and severe.
- Symptomatic treatment is reasonable in the absence of red flag findings and after excluding pelvic floor dysfunction.

Dyschezia

(Disordered Evacuation; Dysfunction of Pelvic Floor or Anal Sphincters; Functional Defecatory Disorders; Dyssynergia)

Dyschezia is difficulty defecating. Patients sense the presence of stool and the need to defecate but are unable. It results from a lack of coordination of pelvic floor muscles and anal sphincters. Diagnosis requires anorectal testing. Treatment is difficult, but biofeedback may be of benefit.

Etiology

Normally, when a person tries to defecate, rectal pressure rises in coordination with relaxation of the external anal sphincter. This process may be affected by one or more dysfunctions (eg, impaired rectal contraction, excessive contraction of the abdominal wall, paradoxic anal contraction, failure of anal relaxation) of unclear etiology. Functional defecatory disorders may manifest at any age. In contrast,

Hirschsprung's disease, which is due to an absent recto-anal inhibitory reflex, is almost always diagnosed in infancy or childhood.

Symptoms and Signs

The patient may or may not sense that stool is present in the rectum. Despite prolonged straining, evacuation is tedious or impossible, frequently even for soft stool or enemas. Patients may complain of anal blockage and may digitally remove stool from their rectum or manually support their perineum or splint the vagina to evacuate. Actual stool frequency may or may not be decreased.

Diagnosis

Rectal and pelvic examinations may reveal hypertonia of the pelvic floor muscles and anal sphincters. With bearing down, patients may not demonstrate the expected anal relaxation and perineal descent. With excessive straining, the anterior rectal wall prolapses into the vagina in patients with impaired anal relaxation; thus rectoceles are usually a secondary rather than a primary disturbance. Long-standing dyschezia with chronic straining may cause a solitary rectal ulcer or varying degrees of rectal prolapse or excessive perineal descent or an enterocoele. Anorectal manometry and rectal balloon expulsion, occasionally supplemented by defecatory or magnetic resonance proctography, are necessary to diagnose the condition.

Treatment

Because treatment with laxatives is unsatisfactory, it is important to assess anorectal functions in patients with refractory constipation. Biofeedback therapy can improve coordination between abdominal contraction and pelvic floor relaxation during defecation, thereby alleviating symptoms. However, pelvic floor retraining for defecatory disorders is highly specialized and available at select centers only. A collaborative approach (physiotherapists, dietitians, behavior therapists, gastroenterologists) is necessary.

Diarrhea

(See also Chs. 17 and 19. For diarrhea in children, see p. 2737.)

Stool is 60 to 90% water. In Western society, stool amount is 100 to 200 g/day in healthy adults and 10 g/kg/day in infants, depending on the amount of unabsorbable dietary material (mainly carbohydrates). Diarrhea is defined as stool weight > 200 g/day. However, many people consider any increased stool fluidity to be diarrhea. Alternatively, many people who ingest fiber have bulkier but formed stools but do not consider themselves to have diarrhea.

Complications: Complications may result from diarrhea of any etiology. Fluid loss with consequent dehydration, electrolyte loss (Na, K, Mg, Cl), and even vascular collapse sometimes occur. Collapse can develop rapidly in patients who have severe diarrhea (eg, patients with cholera) or are very young, very old, or debilitated. HCO_3 loss can cause metabolic acidosis. Hypokalemia can occur when patients have severe or chronic diarrhea or if the stool contains excess mucus. Hypomagnesemia after prolonged diarrhea can cause tetany.

Etiology

Normally, the small intestine and colon absorb 99% of fluid resulting from oral intake and GI tract secretions—a total fluid load of about 9 of 10 L daily. Thus, even small reductions (ie, 1%) in intestinal water absorption or increases in secretion can increase water content enough to cause diarrhea.

There are a number of causes of diarrhea (see Table 8-3). Several basic mechanisms are responsible for most clinically significant diarrheas: increased osmotic load, increased secretions, and decreased contact time/surface area. In many disorders, more than one mechanism is active. For example, diarrhea in inflammatory bowel disease results from mucosal destruction, exudation into the lumen, and from multiple secretagogues and bacterial toxins that affect

enterocyte function.

[Table 8-3. Some Causes of Diarrhea*]

Osmotic load: Diarrhea occurs when unabsorbable, water-soluble solutes remain in the bowel and retain water. Such solutes include polyethylene glycol, Mg salts (hydroxide and sulfate), and Na phosphate, which are used as laxatives. Osmotic diarrhea occurs with sugar intolerance (eg, lactose intolerance caused by lactase deficiency). Ingesting large amounts of hexitols (eg, sorbitol, mannitol, xylitol) or high fructose corn syrups, which are used as sugar substitutes in candy, gum, and fruit juices, causes osmotic diarrhea because hexitols are poorly absorbed. Lactulose, which is used as a laxative, causes diarrhea by a similar mechanism. Overingesting certain foodstuffs (see Table 8-4) can cause osmotic diarrhea.

Increased secretions: Diarrhea occurs when the bowels secrete more electrolytes and water than they absorb. Causes of increased secretions include infections, unabsorbed fats, certain drugs, and various intrinsic and extrinsic secretagogues.

Infections (eg, gastroenteritis; discussed in Ch. 16) are the most common causes of secretory diarrhea. Infections combined with food poisoning are the most common causes of acute diarrhea (< 4 days in duration). Most enterotoxins block Na^+-H^+ exchange, which is an important driving force for fluid absorption in the small bowel and colon.

Unabsorbed dietary fat and bile acids (as in malabsorption syndromes and after ileal resection) can stimulate colonic secretion and cause diarrhea.

Drugs may stimulate intestinal secretions directly (eg, quinidine, quinine, colchicine, anthraquinone cathartics, castor oil, prostaglandins) or indirectly by impairing fat absorption (eg, orlistat).

Various endocrine tumors produce secretagogues, including vipomas (vasoactive intestinal peptide), gastrinomas (gastrin), mastocytosis (histamine), medullary carcinoma of the thyroid (calcitonin and prostaglandins), and carcinoid tumors (histamine, serotonin, and polypeptides). Some of these mediators (eg, prostaglandins, serotonin, related compounds) also accelerate intestinal transit, colonic transit, or both.

Reduced contact time/surface area: Rapid intestinal transit and diminished surface area impair fluid absorption and cause diarrhea. Common causes include small-bowel or large-bowel resection or bypass, gastric resection,

[Table 8-4. Dietary Factors that May Worsen Diarrhea]

and inflammatory bowel disease. Other causes include microscopic colitis (collagenous or lymphocytic colitis) and celiac sprue.

Stimulation of intestinal smooth muscle by drugs (eg, Mg-containing antacids, laxatives, cholinesterase inhibitors, SSRIs) or humoral agents (eg, prostaglandins, serotonin) also can speed transit.

Evaluation

History: Duration and severity of diarrhea, circumstances of onset (including recent travel, food ingested, source of water), drug use (including any antibiotics within the previous 3 mo), abdominal pain or vomiting, frequency and timing of bowel movements, changes in stool characteristics (eg, presence of blood, pus, or mucus; changes in color or consistency; evidence of steatorrhea), associated changes in weight or appetite, and rectal urgency or tenesmus should be noted. Simultaneous occurrence of diarrhea in close contacts should be ascertained.

Physical examination: Fluid and hydration status should be evaluated. A full examination with attention to the abdomen and a digital rectal examination for sphincter competence and occult blood testing are important.

Red flags: Certain findings raise suspicion of an organic or more serious etiology of diarrhea:

• Blood or pus

• Fever

• Signs of dehydration

• Chronic diarrhea

• Weight loss

Interpretation of findings: Acute, watery diarrhea in an otherwise healthy person is likely to be of infectious etiology, particularly when travel, possibly tainted food, or an outbreak with a point-source is involved. Acute bloody diarrhea with or without hemodynamic instability in an otherwise healthy person suggests an enteroinvasive infection. Diverticular bleeding and ischemic colitis also manifest with acute bloody diarrhea. Recurrent bouts of bloody diarrhea in a younger person suggest inflammatory bowel disease. In the absence of laxative use, large-volume diarrhea (eg, daily stool volume > 1 L/day) strongly suggests an endocrine cause in patients with normal GI anatomy. A history of oil droplets in stool, particularly if associated with weight loss, suggests malabsorption.

Diarrhea that consistently follows ingestion of certain foods (eg, fats) suggests food intolerance. Recent antibiotic use should raise suspicion for antibiotic-associated diarrhea, including *Clostridium difficile* colitis.

The symptoms can help identify the affected part of the bowel. Generally, in small-bowel diseases, stools are voluminous and watery or fatty. In colonic diseases, stools are frequent, sometimes small in volume, and possibly accompanied by blood, mucus, pus, and abdominal discomfort. In irritable bowel syndrome (IBS), abdominal discomfort is relieved by defecation, associated with more loose or frequent stools, or both. However, these symptoms alone do not discriminate IBS from other diseases (eg, inflammatory bowel disease). Patients with IBS or rectal mucosal involvement often have marked urgency, tenesmus, and small, frequent stools (see p. 163).

Extra-abdominal findings that suggest an etiology include skin lesions or flushing (mastocytosis), thyroid nodules (medullary carcinoma of the thyroid), right-sided heart murmur (carcinoid), lymphadenopathy (lymphoma, AIDS), and arthritis (inflammatory bowel disease, celiac disease).

Testing: Acute diarrhea (< 4 days) typically does not require testing. Exceptions are patients with signs of dehydration, bloody stool, fever, severe pain, hypotension, or toxic features—particularly those who are very young or very old. These patients should have a CBC and measurement of electrolytes, BUN, and creatinine. Stool samples should be collected for microscopy, culture, fecal leukocyte testing, and, if antibiotics have been taken recently, *C. difficile* toxin assay.

Chronic diarrhea (> 4 wk) requires evaluation, as does a shorter (1 to 3 wk) bout of diarrhea in immunocompromised patients or those who appear significantly ill. Initial stool testing should include culture, fecal leukocytes (detected by smear or measurement of fecal lactoferrin), microscopic examination for ova and parasites, pH (bacterial fermentation of unabsorbed carbohydrate lowers stool pH < 6.0), fat (by Sudan stain), and electrolytes (Na and K). If no standard pathogens are found, specific tests for *Giardia* antigen and *Aeromonas*, *Plesiomonas*, coccidia, and microsporidia should be requested. Sigmoidoscopy or colonoscopy with biopsies should follow to look for inflammatory causes.

If no diagnosis is apparent and Sudan stain is positive for fat, fecal fat excretion should be measured, followed by small-bowel enteroclysis or CT enterography (structural disease) and endoscopic small-bowel biopsy (mucosal disease). If evaluation still yields negative findings, assessment of pancreatic structure and function (see p. 142) should be considered for patients who have unexplained steatorrhea. Infrequently, capsule endoscopy may uncover lesions, predominantly Crohn's disease or NSAID enteropathy, not identified by other modalities.

The stool osmotic gap, which is calculated 290 - 2 × (stool Na + stool K), indicates whether diarrhea is secretory or osmotic. An osmotic gap < 50 mEq/L indicates secretory diarrhea; a larger gap suggests osmotic diarrhea. Patients with osmotic diarrhea may have covert Mg laxative ingestion (detectable by stool Mg levels) or carbohydrate malabsorption (diagnosed by hydrogen breath test, lactase assay, and dietary review).

Undiagnosed secretory diarrhea requires testing (eg, plasma gastrin, calcitonin, vasoactive intestinal peptide levels, histamine, urinary 5-hydroxyindole acetic acid [5-HIAA]) for endocrine-related causes. A review for symptoms and signs of thyroid disease and adrenal insufficiency should be done. Surreptitious laxative abuse must be considered; it can be ruled out by a fecal laxative assay.

Treatment

• Fluid and electrolytes for dehydration

• Possibly antidiarrheals for nonbloody diarrhea in patients without systemic toxicity

Severe diarrhea requires fluid and electrolyte replacement to correct dehydration, electrolyte imbalance, and acidosis. Parenteral fluids containing NaCl, KCl, and glucose are generally required. Salts to counteract acidosis (Na lactate, acetate, HCO_3) may be indicated if serum HCO_3 is < 15 mEq/L. An oral glucose-electrolyte solution can be given if diarrhea is not severe and nausea and vomiting are minimal (see p. 2809). Oral and parenteral fluids are sometimes given simultaneously when water and electrolytes must be replaced in massive amounts (eg, in cholera).

Diarrhea is a symptom. When possible, the underlying disorder should be treated, but symptomatic treatment is often necessary. Diarrhea may be decreased by oral loperamide 2 to 4 mg tid or qid (preferably given 30 min before meals), diphenoxylate 2.5 to 5 mg (tablets or liquid) tid or qid, codeine phosphate 15 to 30 mg bid or tid, or paregoric (camphorated opium tincture) 5 to 10 mL once/day to qid.

Because antidiarrheals may exacerbate *C. difficile* colitis or increase the likelihood of hemolytic-uremic syndrome in *Shiga* toxin-producing *Escherichia coli* infection, they should not be used in bloody diarrhea of unknown cause. Their use should be restricted to patients with watery diarrhea and no signs of systemic toxicity. However, there is little evidence to justify previous concerns about prolonging excretion of possible bacterial pathogens with antidiarrheals.

Psyllium or methylcellulose compounds provide bulk. Although usually prescribed for constipation, bulking agents given in small doses decrease the fluidity of liquid stools. Kaolin, pectin, and activated attapulgite adsorb fluid. Osmotically active dietary substances (see Table 8-4) and stimulatory drugs should be avoided.

Key Points

• In patients with acute diarrhea, stool examination (cultures, ova and parasites, *C. difficile* cytotoxin) is only necessary for those who have prolonged symptoms (ie, > 1 wk) or red flag findings.

• Antidiarrheals should be used cautiously if there is a possibility of *C. difficile*, *Salmonella*, or shigellosis.

Gas-Related Complaints

The gut contains < 200 mL of gas, whereas daily gas expulsion averages 600 to 700 mL after consuming a standard diet plus 200 g of baked beans. About 75% of flatus is derived from colonic bacterial fermentation of ingested nutrients and endogenous glycoproteins. Gases include hydrogen (H_2), methane (CH_4), and carbon dioxide (CO_2). Flatus odor correlates with H_2 sulphide concentrations. Swallowed air (aerophagia) and diffusion from the blood into the lumen also contribute to intestinal gas. Gas diffuses between the lumen and the blood in a direction that depends on the difference in partial

pressures. Thus, most nitrogen (N_2) in the lumen originates from the bloodstream, and most H_2 in the bloodstream originates from the lumen.

Etiology

There are 3 main gas-related complaints: excessive belching, distention (bloating), and excessive flatus, each with a number of causes (see Table 8-5). Infants 2 to 4 mo of age with recurrent crying spells often appear to observers to be in pain, which in the past has been attributed to abdominal cramping or gas and termed colic. However, studies show no increase in H_2 production or in mouth-to-cecum transit times in colicky infants. Hence, the cause of infantile colic remains unclear (see p. 2725).

Excessive belching: Belching (eructation) results from swallowed air or from gas generated by carbonated beverages. Aerophagia occurs normally in small amounts during eating and drinking, but some people unconsciously swallow air repeatedly while eating or smoking and at other times, especially when anxious or in an attempt to induce belching. Excessive salivation increases aerophagia and may be associated with various GI disorders (eg, gastroesophageal reflux disease), ill-fitting dentures, certain drugs, gum chewing, or nausea of any cause.

Most swallowed air is eructated. Only a small amount of swallowed air passes into the small bowel; the amount is apparently influenced by position. In an upright person, air is readily belched; in a supine person, air trapped above the stomach fluid tends to be propelled into the duodenum. Excessive eructation may also be voluntary; patients who belch after taking antacids may attribute the relief of symptoms to belching rather than to antacids and may intentionally belch to relieve distress.

Distention (bloating): Abdominal bloating may occur in isolation or along with other GI symptoms in patients with functional disorders (eg, aerophagia, nonulcer dyspepsia, gastroparesis, irritable bowel syndrome) or organic disorders (eg, ovarian cancer, colon cancer). However, excessive intestinal gas is not clearly linked to these complaints. In most healthy people, 1 L/h of gas can be infused into the gut with minimal symptoms. It is likely that many symptoms are incorrectly attributed to "too much gas."

On the other hand, some patients with recurrent GI symptoms often cannot tolerate small quantities of gas: Retrograde colonic distention by balloon inflation or air instillation during colonoscopy often elicits severe discomfort in some patients (eg, those with irritable bowel syndrome) but minimal symptoms in others. Similarly, patients with eating disorders (eg, anorexia nervosa, bulimia) often misperceive and are particularly stressed by symptoms such as bloating. Thus, the basic abnormality in patients with gas-related symptoms may be a hypersensitive intestine. Altered motility may contribute further to symptoms.

Excessive flatus: There is great variability in the quantity and frequency of rectal gas passage. As with stool frequency, people who complain of flatulence often have a misconception of what is normal. The average number of gas passages is about 13 to 21/day. Objectively recording flatus frequency (using a diary kept by the patient) is a first step in evaluation.

Flatus is a metabolic byproduct of intestinal bacteria; almost none originates from swallowed air or back-diffusion of gases (primarily N_2) from the bloodstream. Bacterial metabolism yields significant volumes of H_2, CH_4, and CO_2.

H_2 is produced in large quantities in patients with malabsorption syndromes and after ingestion of certain fruits and vegetables containing indigestible carbohydrates (eg, baked beans), sugars (eg, fructose), or sugar alcohols (eg, sorbitol). In patients with disaccharidase deficiencies (most commonly lactase deficiency), large amounts of disaccharides pass into the colon and are fermented to H_2. Celiac disease, tropical sprue, pancreatic insufficiency, and other causes of carbohydrate malabsorption should also be considered in cases of excess colonic gas.

CH_4 is also produced by colonic bacterial metabolism of the same foods (eg, dietary fiber). However, about 10% of people have bacteria that produce CH_4 but not H_2.

CO_2 is also produced by bacterial metabolism and generated in the reaction of HCO_3^- and H^+. H^+ may come from gastric HCl or from fatty acids released during digestion of fats—the latter sometimes produces several hundred mEq of H^+. The acid products released by bacterial fermentation of unabsorbed carbohydrates in the colon may also react with HCO_3^- to produce CO_2. Although bloating may occasionally occur, the rapid diffusion of CO_2 into the blood generally prevents distention.

[Table 8-5. Some Causes of Gas-Related Complaints]

Diet accounts for much of the variation in flatus production among individuals, but poorly understood factors (eg, differences in colonic flora and motility) may also play a role.

Despite the flammable nature of the H_2 and CH_4 in flatulence, working near open flames is not hazardous. However, gas explosion, even with fatal outcome, has been reported during jejunal and colonic surgery and colonoscopy, when diathermy was used during procedures in patients with incomplete bowel cleaning.

Evaluation

History: Patients with belching should have the history directed at finding the cause of aerophagia, especially dietary causes.

In patients complaining of gas, bloating, or flatus, the relationship between symptoms and meals (both timing and type and amount of food), bowel movements, and exertion should be explored. Certain patients, particularly in the acute setting, may use the term "gas" to describe their symptoms of coronary ischemia. Changes in frequency and color and consistency of stool are sought. History of weight loss is noted.

Physical examination: The examination is generally normal, but in patients with bloating or flatus, signs of an underlying organic disorder should be sought on abdominal, rectal, and (for women) pelvic examination.

Red flags: The following findings are of concern:

• Weight loss

• Blood in stool (occult or gross)

Interpretation of findings: Chronic, recurrent bloating or distention relieved by defecation and associated with change in frequency or consistency of stool but without red flag findings suggests irritable bowel syndrome.

Long-standing symptoms in an otherwise well young person who has not lost weight are unlikely to be caused by serious physiologic disease, although an eating disorder should be considered, particularly in young women. Bloating accompanied by diarrhea, weight loss, or both (or only after ingestion of certain foods) suggests a malabsorption syndrome.

Testing: Testing is not indicated for belching unless other symptoms suggest a particular disorder. Testing for carbohydrate intolerance (eg, lactose, fructose) with breath tests should be considered particularly when the history suggests significant consumption of these sugars. Testing for small-bowel bacterial overgrowth should also be considered, particularly in patients who also have diarrhea, weight loss, or both, preferably by aerobic and anaerobic culture of small-bowel aspirates obtained during upper GI endoscopy. Testing for bacterial overgrowth with H_2 breath tests, generally glucose-H_2 breath tests, is prone to false-positive (ie, with rapid transit) and false-negative (ie, when there are no H_2-producing bacteria) results. New, persistent bloating in middle-aged or older women (or those with an abnormal pelvic examination) should prompt pelvic ultrasonography to rule out ovarian cancer.

Treatment

Belching and bloating are difficult to relieve because they are usually caused by unconscious aerophagia or increased sensitivity to normal amounts of gas. Aerophagia may be reduced by eliminating gum and carbonated beverages, cognitive behavioral techniques to prevent air swallowing, and management of associated upper GI diseases (eg, peptic ulcer). Foods containing unabsorbable carbohydrates should be avoided. Even lactose-intolerant patients generally tolerate up to 1 glass of milk drunk in small amounts throughout the day. The mechanism of repeated belching should be explained and demonstrated. When aerophagia is troublesome, behavioral therapy to encourage open-mouth, diaphragmatic breathing and minimize swallowing may be effective.

Sidebar 8-1 Essay on Flatulence

(First printed in the 14th Edition of *The Merck Manual*)

Flatulence, which can cause great psychosocial distress, is unofficially described according to its salient characteristics: (1) the "slider" (crowded elevator type), which is released slowly and noiselessly, sometimes with devastating effect; (2) the open sphincter, or "pooh" type, which is said to be of higher temperature and more aromatic; (3) the staccato or drumbeat type, pleasantly passed in privacy; and (4) the "bark" type (described in a personal communication) is characterized by a sharp exclamatory eruption that effectively interrupts (and often concludes) conversation. Aromaticity is not a prominent feature. Rarely, this usually distressing symptom has been turned to advantage, as with a Frenchman referred to as "Le Petomane," who became affluent as an effluent performer who played tunes with the gas from his rectum on the Moulin Rouge stage.

Drugs provide little benefit. Results with simethicone, an agent that breaks up small gas bubbles, and various anticholinergics are poor. Some patients with dyspepsia and postprandial upper abdominal fullness benefit from antacids, a low dose of tricyclic antidepressants (eg, nortriptyline 10 to 50 mg po once/day), or both to reduce visceral hypersensitivity.

Complaints of excess flatus are treated with avoidance of triggering substances (see Table 8-5). Roughage (eg, bran, psyllium seed) may be added to the diet to try to increase colonic transit; however, in some patients, worsening of symptoms may result. Activated charcoal can sometimes help reduce gas and unpleasant odor; however, it stains clothing and the oral mucosa. Charcoal-lined undergarments are available. Probiotics (eg, VSL#3) may also reduce bloating and flatulence by modulating intestinal bacterial flora. Antibiotics are useful in patients with documented bacterial overgrowth.

Functional bloating, distention, and flatus may run an intermittent, chronic course that is only partially relieved by therapy. When appropriate, reassurance that these problems are not detrimental to health is important.

Key Points

• Testing should be guided by the clinical features.

• Clinicians should be wary of new-onset, persistent symptoms in older patients.

Chapter 9. Diagnostic and Therapeutic GI Procedures

Introduction

Diagnostic tests and therapeutic procedures available for patients with GI disorders include acid-related tests, endoscopy, laparoscopy, manometry, nuclear scans, x-ray contrast studies, nasogastric or intestinal intubation, anoscopy and sigmoidoscopy, abdominal paracentesis, electrogastrography, and electrical impedance testing. CT, MRI, and ultrasonography are also commonly done for GI disorders, and sometimes angiography is used. The selection of procedures is discussed in subsequent chapters. ERCP, percutaneous transhepatic cholangiography, and liver biopsy are discussed in Ch. 24.

Acid-Related Tests

Acid-related tests are used to ascertain the effectiveness of acid-blocking drugs. All require nasogastric or nasoesophageal intubation. Complications are very rare. Patients must have nothing by mouth (npo) after midnight.

Ambulatory pH Monitoring

Ambulatory 24-h esophageal pH monitoring is currently the best available test for quantifying esophageal acid exposure. The principal indications are

• To document excessive acid exposure in patients without endoscopic evidence of esophagitis

• To evaluate the effectiveness of medical or surgical treatments

A thin tube containing a pH probe is positioned 5 cm above the lower esophageal sphincter. The patient records symptoms, meals, and sleep for 24 h. Esophageal acid exposure is defined by the percentage of the 24-h recording time that the pH is < 4.0. Values > 3.5% are considered abnormal. However, symptoms may not correlate with acid exposure or the presence of esophagitis. This may be because symptoms may result from nonacidic as well as acidic refluxate. Multichannel intraluminal impedance testing allows for recognition of major acid, minor acid, nonacid, and gas reflux, all of which can cause reflux symptoms.

Gastric Analysis

Samples of stomach contents obtained via NGT are used to measure gastric acid output in a basal and stimulated state. This information may be useful in a patient who develops a recurrent ulcer after surgical vagotomy for peptic ulcer disease. In this case, a positive acid response to stimulation (sham feeding) indicates an incomplete vagotomy. The test also is used to evaluate a patient with elevated serum gastrin levels. Hyperchlorhydria in the presence of elevated gastrin usually indicates Zollinger-Ellison syndrome. Hypochlorhydria in the presence of elevated gastrin indicates impairment of acid output, such as occurs in pernicious anemia, atrophic gastritis, and Menetrier's disease and after inhibition of gastric acid secretion by potent antisecretory drugs.

To do gastric analysis, an NGT is inserted and the gastric contents are aspirated and discarded. Gastric juice is then collected for 1 h, divided into four 15-min samples. These samples represent basal acid output.

Endoscopy

Flexible endoscopes equipped with video cameras can be used to view the upper GI tract from pharynx to upper duodenum and the lower GI tract from anus to cecum (and, sometimes, terminal ileum). Several other diagnostic and therapeutic interventions also can be done endoscopically. The potential to combine diagnosis and therapy in one procedure gives endoscopy a significant advantage over procedures that provide only imaging (eg, x-ray contrast studies, CT, MRI) and often outweighs endoscopy's higher cost and need for sedation.

Diagnostic procedures include the use of ultrasound-equipped endoscopes to evaluate blood flow or

provide imaging of lesions. Endoscopic ultrasound can provide information (eg, the depth and extent of lesions) that is not available via conventional endoscopy. Other diagnostic procedures include cell and tissue sample collection by brush or biopsy forceps.

Screening colonoscopy is recommended for patients at high risk of colon cancer and for everyone ≥ 50. Colonoscopy should be done every 10 yr for patients with no risk factors and with a normal initial colonoscopy. CT colonography (see p. 98) is an alternative to colonoscopy for screening for colonic tumors.

Therapeutic endoscopic procedures include removal of foreign bodies; hemostasis by thermal coagulation, laser photocoagulation, variceal banding, or sclerotherapy; debulking of tumors by laser or bipolar electrocoagulation; dilation of webs or strictures; stent placement; reduction of volvulus or intussusception; and decompression of acute or subacute colonic dilatation.

Absolute contraindications to endoscopy include

• Shock

• Acute MI

• Peritonitis

• Acute perforation

• Fulminant colitis

Relative contraindications include poor patient cooperation, coma (unless the patient is intubated), and cardiac arrhythmias or recent myocardial ischemia.

Patients taking anticoagulants or chronic NSAID therapy can safely undergo diagnostic endoscopy. However, if there is a possibility that biopsy or photocoagulation will be done, these drugs should be stopped for an appropriate interval before the procedure. Oral iron-containing drugs should be stopped 4 to 5 days before colonoscopy, because certain green vegetables interact with iron to form a sticky residue that is difficult to remove with a bowel preparation and interferes with visualization. The American Heart Association no longer recommends endocarditis prophylaxis for patients having GI endoscopy.

Routine preparations for endoscopy include no solids for 6 to 8 h and no liquids for 4 h before the procedure. Additionally, colonoscopy requires cleansing of the colon. A variety of regimens may be used, but all typically include a full or clear liquid diet for 24 to 48 h and some type of laxative, with or without an enema. A common laxative preparation involves having the patient drink a high-volume (4 L) balanced electrolyte solution over a period of 3 to 4 h before the procedure. Patients who cannot tolerate this solution may be given Mg citrate, Na phosphate, lactulose, or other laxatives. Enemas can be done with either Na phosphate or tap water. Phosphate preparations should not be used in patients with renal insufficiency.

Endoscopy generally requires IV sedation and, for upper endoscopy, topical anesthesia of the throat. Exceptions are anoscopy and sigmoidoscopy (see p. 98), which generally require nothing. The overall complication rate of endoscopy is 0.1 to 0.2%; mortality is about 0.03%. Complications are usually drug related (eg, respiratory depression); procedural complications (eg, aspiration, perforation, significant bleeding) are less common.

Video capsule endoscopy: In video capsule endoscopy (wireless video endoscopy), patients swallow a capsule containing a camera that transmits images to an external recorder. This noninvasive technology provides diagnostic imaging of the small bowel that is otherwise difficult to obtain. This procedure is particularly useful in patients with occult GI bleeding. Capsule endoscopy is more difficult in the colon; products and procedures are under development.

Laparoscopy

Diagnostic laparoscopy is a surgical procedure used to evaluate intra-abdominal or pelvic pathology (eg, tumor, endometriosis) in patients with acute or chronic abdominal pain and operability in patients with cancer. It also is used for lymphoma staging and liver biopsy.

Absolute contraindications include

- A coagulation or bleeding disorder
- Poor patient cooperation
- Peritonitis
- Intestinal obstruction
- Infection of the abdominal wall

Relative contraindications include severe cardiac or pulmonary disease, large abdominal hernias, multiple abdominal operations, and tense ascites.

CBC, coagulation studies, and type and Rh testing are done before laparoscopy. X-rays of the chest and abdomen (kidneys, ureters, and bladder) are also taken. Laparoscopy is done with sterile technique in an operating room or a well-equipped endoscopy suite. The patient is given local anesthesia plus IV sedation and analgesia with an opioid and short-acting sedative (eg, midazolam, propofol).

The procedure involves insertion of a pneumoperitoneum needle into the peritoneal cavity and infusion of nitrous oxide to distend the abdomen. After the opening is enlarged, a peritoneoscope is inserted into the abdomen and the abdominal contents are examined. Surgical instruments for biopsy and other procedures are inserted through separate openings. When the procedure is completed, the nitrous oxide is expelled by the patient with a Valsalva maneuver and the cannula is removed. Complications can include bleeding, bacterial peritonitis, and perforation of a viscus.

Manometry

Manometry is measurement of pressure within various parts of the GI tract. It is done by passing a catheter containing solid-state or liquid-filled pressure transducers through the mouth or anus into the lumen of the organ to be studied. Manometry typically is done to evaluate motility disorders in patients in whom structural lesions have been ruled out by other studies. Manometry is used in the esophagus, stomach and duodenum, sphincter of Oddi, and rectum. Aside from minor discomfort, complications are very rare. Patients must have nothing by mouth (npo) after midnight.

Esophageal manometry: This test is used to evaluate patients with dysphagia, heartburn, or chest pain. It measures the pressure in the upper and lower esophageal sphincters, determines the effectiveness and coordination of propulsive movements, and detects abnormal contractions. Manometry is used to diagnose achalasia, diffuse spasm, systemic sclerosis, and lower esophageal sphincter hypotension and hypertension. It also is used to evaluate esophageal function before certain therapeutic procedures (eg, antireflux surgery, pneumatic dilation for achalasia).

Gastroduodenal manometry: In this test, transducers are placed in the gastric antrum, duodenum, and proximal jejunum. Pressure is monitored for 5 to 24 h in both fasting and fed states. This test is used mainly in patients who have symptoms suggestive of dysmotility but normal gastric emptying studies.

Barostat: This is a pressure-sensing device that is placed in the stomach to measure gastric accommodation. The device consists of a plastic balloon and an electronic controller that varies the amount of air in the balloon to maintain constant pressure. This device is used mainly in research studies assessing sensory threshold and altered visceral perception, particularly in functional GI disorders.

Anorectal manometry: This test evaluates the anorectal sphincter mechanism and rectal sensation in

patients with incontinence (and sometimes constipation) by means of a pressure transducer in the anus. It can help diagnose Hirschsprung's disease and provide biofeedback training for fecal incontinence.

Nuclear Scans

Gastric emptying can be measured by having the patient ingest a radiolabeled meal (solid or liquid) and observing its passage out of the stomach with a gamma camera. Because this test cannot differentiate physical obstruction from gastroparesis, further diagnostic studies typically are done if emptying is delayed. The test also is useful in monitoring response to promotility drugs (eg, metoclopramide, erythromycin).

Bleeding scans use ^{99m}Tc-labeled RBCs, or occasionally ^{99m}Tc-labeled colloid, to determine the origin of lower GI hemorrhage before surgery or angiography. Active bleeding sites are identified by focal areas of tracer that conform to bowel anatomy, increase with time, and move with peristalsis. Bleeding scans are useful mainly for colonic bleeding in patients with significant hemorrhage and an unprepared bowel, in whom endoscopic visualization is difficult.

A **Meckel scan** identifies ectopic gastric mucosa (as in a Meckel's diverticulum) by using an injection of ^{99m}Tc pertechnetate, which is taken up by mucus-secreting cells of the gastric mucosa. Focal uptake outside of the stomach and in the small bowel indicates a Meckel's diverticulum.

X-Ray and Other Imaging Contrast Studies

X-ray and other imaging contrast studies visualize the entire GI tract from pharynx to rectum and are most useful for detecting mass lesions and structural abnormalities (eg, tumors, strictures). Single-contrast studies fill the lumen with radiopaque material, outlining the structure. Better, more detailed images are obtained from double-contrast studies, in which a small amount of high-density barium coats the mucosal surface and gas distends the organ and enhances contrast. The gas is injected by the operator in double-contrast barium enema, whereas in other studies, intrinsic GI tract gas is adequate. In all cases, patients turn themselves to properly distribute the gas and barium. Fluoroscopy can monitor the progress of the contrast material. Either video or plain films can be taken for documentation, but video is particularly useful when assessing motor disorders (eg, cricopharyngeal spasm, achalasia).

The main contraindication to x-ray contrast studies is suspected perforation, because free barium is highly irritating to the mediastinum and peritoneum; water-soluble contrast is less irritating and may be used if perforation is possible. Older patients may have difficulty turning themselves to properly distribute the barium and intraluminal gas.

Patients having upper GI x-ray contrast studies must have nothing by mouth (npo) after midnight. Patients having barium enema follow a clear liquid diet the day before, take an oral Na phosphate laxative in the afternoon, and take a bisacodyl suppository in the evening. Other laxative regimens are effective.

Complications are rare. Perforation can occur if barium enema is done in a patient with toxic megacolon. Barium impaction may be prevented by postprocedure oral fluids and sometimes laxatives.

An **upper GI examination** is best done as a biphasic study beginning with a double-contrast examination of the esophagus, stomach, and duodenum, followed by a single-contrast study using low-density barium. Glucagon 0.5 mg IV can facilitate the examination by causing gastric hypotonia.

A **small-bowel meal** is done by using fluoroscopy and provides a more detailed evaluation of the small bowel. Shortly before the examination, the patient is given metoclopramide 20 mg po to hasten transit of the contrast material.

Enteroclysis (small-bowel enema) provides still better visualization of the small bowel but requires intubation of the duodenum with a flexible, balloon-tipped catheter. A barium suspension is injected, followed by a solution of methylcellulose, which functions as a double-contrast agent that enhances visualization of the small-bowel mucosa.

A **barium enema** can be done as a single-or double-contrast study. Single-contrast barium enemas are used for potential obstruction, diverticulitis, fistulas, and megacolon. Double-contrast studies are preferred for detection of tumors.

CT scanning of the abdomen: CT scanning using oral and IV contrast allows excellent visualization of both the small bowel and colon as well as of other intra-abdominal structures.

CT enterography provides optimal visualization of the small-bowel mucosa; it is preferably done by using a multidetector CT (MDCT) scanner. Patients are given a large volume (1350 mL) of 0.1% barium sulfate before imaging. For certain indications (eg, obscure GI bleeding, small-bowel tumors, chronic ischemia), a biphasic contrast-enhanced MDCT study is done.

CT colonography (virtual colonoscopy) generates 3D and 2D images of the colon by using MDCT and a combination of oral contrast and gas distention of the colon. Viewing the high-resolution 3D images somewhat simulates the appearance of optical endoscopy, hence the name. Optimal CT colonography technique requires careful cleansing and distention of the colon. Residual stool causes problems similar to those encountered with barium enema because it simulates polyps or masses. Three-dimensional endoluminal images are useful to confirm the presence of a lesion and to improve diagnostic confidence.

CT enterography and CT colonoscopy have largely supplanted standard small-bowel series and barium enema examinations.

GI Procedures for the Generalist

Nasogastric or Intestinal Intubation

Nasogastric or intestinal intubation is used to decompress the stomach. It is used to treat gastric atony, ileus, or obstruction; remove ingested toxins, give antidotes (eg, activated charcoal), or both; obtain a sample of gastric contents for analysis (volume, acid content, blood); and supply nutrients.

Contraindications include

• Nasopharyngeal or esophageal obstruction

• Severe maxillofacial trauma

• Uncorrected coagulation abnormalities

Esophageal varices previously have been considered a contraindication, but evidence of adverse effects is lacking.

Several types of tubes are available. A Levin or Salem sump tube is used for gastric decompression or analysis and rarely for short-term feeding. A variety of long, thin, intestinal tubes are used for long-term enteral feeding (see p. 21).

For intubation, the patient sits upright or, if unable, lies in the left lateral decubitus position. A topical anesthetic sprayed in the nose and pharynx helps reduce discomfort. With the patient's head partially flexed, the lubricated tube is inserted through the nares and aimed back and then down to conform to the nasopharynx. As the tip reaches the posterior pharyngeal wall, the patient should sip water through a straw. Violent coughing with flow of air through the tube during respiration indicates that the tube is misplaced in the trachea. Aspiration of gastric juice verifies entry into the stomach. The position of larger tubes can be confirmed by instilling 20 to 30 mL of air and listening with the stethoscope under the left subcostal region for a rush of air.

Some smaller, more flexible intestinal feeding tubes require the use of stiffening wires or stylets. These tubes usually require fluoroscopic or endoscopic assistance for passage through the pylorus.

Complications are rare and include nasopharyngeal trauma with or without hemorrhage, pulmonary aspiration, traumatic esophageal or gastric hemorrhage or perforation, and (very rarely) intracranial or mediastinal penetration.

Anoscopy and Sigmoidoscopy

Anoscopy and sigmoidoscopy are used to evaluate symptoms referable to the rectum or anus (eg, bright rectal bleeding, discharge, protrusions, pain). There are no absolute contraindications. Patients with cardiac arrhythmias or recent myocardial ischemia should have the procedure postponed until the comorbid conditions improve; otherwise, patients will need cardiac monitoring. Per changes in American Heart Association guidelines, these procedures no longer require endocarditis prophylaxis.

The perianal area and distal rectum can be examined with a 7-cm anoscope, and the rectum and sigmoid with either a rigid 25-cm or a flexible 60-cm instrument. Flexible sigmoidoscopy is much more comfortable for the patient and readily permits photography and biopsy of tissue. Considerable skill is required to pass a rigid sigmoidoscope beyond the rectosigmoid junction (15 cm) without causing discomfort.

Sigmoidoscopy is done after giving an enema to empty the rectum. IV drugs are usually not needed. The patient is placed in the left lateral position. After external inspection and digital rectal examination, the lubricated instrument is gently inserted 3 to 4 cm past the anal sphincter. At this point, the obturator of the rigid sigmoidoscope is removed, and the instrument is inserted further under direct vision.

Anoscopy may be done without preparation. The anoscope is inserted its full length as described above for rigid sigmoidoscopy, usually with the patient in the left lateral position. Complications are exceedingly rare when the procedure is done properly.

Abdominal Paracentesis

Abdominal paracentesis is used to obtain ascitic fluid for testing. It also can be used to remove tense ascites causing respiratory difficulties or pain or as a treatment for chronic ascites.

Absolute contraindications include

- Severe, uncorrectable disorders of blood coagulation
- Intestinal obstruction
- An infected abdominal wall

Poor patient cooperation, surgical scarring over the puncture area, and severe portal hypertension with abdominal collateral circulation are relative contraindications.

CBC, platelet count, and coagulation studies are done before the procedure. After emptying the bladder, the patient sits in bed with the head elevated 45 to 90°. In patients with obvious and marked ascites, a point is located at the midline between the umbilicus and the pubic bone and is cleaned with an antiseptic solution and alcohol. In patients with moderate ascites, precise location of ascitic fluid by abdominal ultrasound is indicated. Under sterile technique, the area is anesthetized to the peritoneum with lidocaine 1%. For diagnostic paracentesis, an 18-gauge needle attached to a 50-mL syringe is inserted through the peritoneum (generally a popping sensation is noted). Fluid is gently aspirated and sent for cell count, protein or amylase content, cytology, or culture as needed. For therapeutic (large-volume) paracentesis, a 14-gauge cannula attached to a vacuum aspiration system is used to collect up to 8 L of ascitic fluid. Postprocedure hypotension caused by fluid redistribution is rare as long as interstitial (leg) edema is present.

Hemorrhage is the most common complication. Occasionally, with tense ascites, prolonged leakage of ascitic fluid occurs through the needle site.

Other Testing Procedures

Electrogastrography measures gastric electrical activity with adhesive cutaneous electrodes. This procedure is useful in patients with gastroparesis.

In **electrical impedance testing**, an electrical sensor is placed in the distal esophagus to assess nonacid reflux, which is common among patients receiving gastric antisecretory drugs and among infants with reflux disease.

Chapter 10. GI Bleeding

Introduction

GI bleeding can originate anywhere from the mouth to the anus and can be overt or occult. The manifestations depend on the location and rate of bleeding.

Hematemesis is vomiting of red blood and indicates upper GI bleeding, usually from an arterial source or varix. Coffee-ground emesis is vomiting of dark brown, granular material that resembles coffee grounds. It results from upper GI bleeding that has slowed or stopped, with conversion of red Hb to brown hematin by gastric acid.

Hematochezia is the passage of gross blood from the rectum and usually indicates lower GI bleeding but may result from vigorous upper GI bleeding with rapid transit of blood through the intestines.

Melena is black, tarry stool and typically indicates upper GI bleeding, but bleeding from a source in the small bowel or right colon may also be the cause. About 100 to 200 mL of blood in the upper GI tract is required to cause melena, which may persist for several days after bleeding has ceased. Black stool that does not contain occult blood may result from ingestion of iron, bismuth, or various foods and should not be mistaken for melena.

Chronic occult bleeding can occur from anywhere in the GI tract and is detectable by chemical testing of a stool specimen. Acute, severe bleeding also can occur from anywhere in the GI tract. Patients may present with signs of shock. Those with underlying ischemic heart disease may develop angina or MI because of hypoperfusion.

GI bleeding may precipitate portal-systemic encephalopathy (see p. 220) or hepatorenal syndrome (kidney failure secondary to liver failure—see p. 223).

Etiology

There are many possible causes (see Table 10-1), which are divided into upper GI (above the ligament of Treitz), lower GI, and small bowel.

Bleeding of any cause is more likely, and potentially more severe, in patients with chronic liver disease (eg, caused by alcohol abuse or chronic hepatitis), in those with hereditary coagulation disorders, or in those taking certain drugs. Drugs associated with GI bleeding include anticoagulants (eg, heparin, warfarin), those affecting platelet function (eg, aspirin and certain other NSAIDs, clopidogrel, SSRIs), and those affecting mucosal defenses (eg, NSAIDs).

Evaluation

Stabilization with airway management, IV fluids, or transfusions is essential before and during diagnostic evaluation.

History: History of present illness should attempt to ascertain quantity and frequency of blood passage. However, quantity can be difficult to assess because even small amounts (5 to 10 mL) of blood turn water in a toilet bowl an opaque red, and modest amounts of vomited blood appear huge to an anxious patient. However, most can distinguish among blood streaks, a few teaspoons, and clots.

Patients with hematemesis should be asked whether blood was passed with initial vomiting or only after an initial (or several) nonbloody emesis.

Patients with rectal bleeding should be asked whether pure blood was passed; whether it was mixed with stool, pus, or mucus; or whether blood simply coated the stool. Those with bloody diarrhea should be asked about travel or other possible exposure to GI pathogens.

[**Table 10-1.** Common Causes of GI Bleeding]

Review of symptoms should include presence of abdominal discomfort, weight loss, easy bleeding or bruising, previous colonoscopy results, and symptoms of anemia (eg, weakness, easy fatigability, dizziness).

Past medical history should inquire about previous GI bleeding (diagnosed or undiagnosed); known inflammatory bowel disease, bleeding diatheses, and liver disease; and use of any drugs that increase the likelihood of bleeding or chronic liver disease (eg, alcohol).

Physical examination: General examination focuses on vital signs and other indicators of shock or hypovolemia (eg, tachycardia, tachypnea, pallor, diaphoresis, oliguria, confusion) and anemia (eg, pallor, diaphoresis). Patients with lesser degrees of bleeding may simply have mild tachycardia (heart rate > 100). Orthostatic changes in pulse (a change of > 10 beats/min) or BP (a drop of ≥ 10 mm Hg) often develop after acute loss of ≥ 2 units of blood. However, orthostatic measurements are unwise in patients with severe bleeding (possibly causing syncope) and generally lack sensitivity and specificity as a measure of intravascular volume, especially in elderly patients.

External stigmata of bleeding disorders (eg, petechiae, ecchymoses) are sought, as are signs of chronic liver disease (eg, spider angiomas, ascites, palmar erythema) and portal hypertension (eg, splenomegaly, dilated abdominal wall veins).

A digital rectal examination is necessary to search for stool color, masses, and fissures. Anoscopy is done to diagnose hemorrhoids. Chemical testing of a stool specimen for occult blood completes the examination if gross blood is not present.

Red flags: Several findings suggest hypovolemia or hemorrhagic shock:

• Syncope

• Hypotension

• Pallor

• Diaphoresis

• Tachycardia

Interpretation of findings: The history and physical examination suggest a diagnosis in about 50% of patients, but findings are rarely diagnostic and confirmatory testing is required.

Epigastric abdominal discomfort relieved by food or antacids suggests peptic ulcer disease. However, many patients with bleeding ulcers have no history of pain. Weight loss and anorexia, with or without a change in stool, suggest a GI cancer. A history of cirrhosis or chronic hepatitis suggests esophageal varices. Dysphagia suggests esophageal cancer or stricture. Vomiting and retching before the onset of bleeding suggests a Mallory-Weiss tear of the esophagus, although about 50% of patients with Mallory-Weiss tears do not have this history.

A history of bleeding (eg, purpura, ecchymosis, hematuria) may indicate a bleeding diathesis (eg, hemophilia, hepatic failure). Bloody diarrhea, fever, and abdominal pain suggest ischemic colitis, inflammatory bowel disease (eg, ulcerative colitis, Crohn's disease), or an infectious colitis (eg, *Shigella*, *Salmonella*, *Campylobacter*, amebiasis). Hematochezia suggests diverticulosis or angiodysplasia. Fresh blood only on toilet paper or the surface of formed stools suggests internal hemorrhoids or fissures, whereas blood mixed with the stool indicates a more proximal source. Occult blood in the stool may be the first sign of colon cancer or a polyp, particularly in patients > 45 yr.

Blood in the nose or trickling down the pharynx suggests the nasopharynx as the source. Spider angiomas, hepatosplenomegaly, or ascites is consistent with chronic liver disease and hence possible esophageal varices. Arteriovenous malformations, especially of the mucous membranes, suggest

hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber syndrome). Cutaneous nail bed and GI telangiectasia may indicate systemic sclerosis or mixed connective tissue disease.

Testing: Several tests are done to help confirm the suspected diagnosis.

• CBC and often other laboratory studies

• NGT for all but those with minimal rectal bleeding

• Upper endoscopy for suspected upper GI bleeding

• Colonoscopy for lower GI bleeding (unless clearly caused by hemorrhoids)

CBC should be obtained in patients with occult blood loss. Those with more significant bleeding also require coagulation studies (eg, platelet count, PT, PTT) and liver function tests (eg, bilirubin, alkaline phosphatase, albumin, AST, ALT). Type and crossmatch are done if bleeding is ongoing. Hb and Hct may be repeated up to every 6 h in patients with severe bleeding. Additionally, one or more diagnostic procedures are typically required.

Nasogastric aspiration and lavage should be done in all patients with suspected upper GI bleeding (eg, hematemesis, coffee-ground emesis, melena, massive rectal bleeding). Bloody nasogastric aspirate indicates active upper GI bleeding, but about 10% of patients with upper GI bleeding have no blood in the nasogastric aspirate. Coffee-ground material indicates bleeding that is slow or stopped. If there is no sign of bleeding, and bile is returned, the NGT is removed; otherwise, it is left in place to monitor continuing or recurrent bleeding. Nonbloody, nonbilious return is considered a nondiagnostic aspirate.

Upper endoscopy (examination of the esophagus, stomach, and duodenum) should be done for upper GI bleeding. Because endoscopy may be therapeutic as well as diagnostic, it should be done rapidly for significant bleeding but may be deferred for 24 h if bleeding stops or is minimal. Upper GI barium x-rays have no role in acute bleeding, and the contrast used may obscure subsequent attempts at angiography. Angiography is useful in the diagnosis of upper GI bleeding and permits certain therapeutic maneuvers (eg, embolization, vasoconstrictor infusion).

Flexible sigmoidoscopy and anoscopy may be all that is required acutely for patients with symptoms typical of hemorrhoidal bleeding. All other patients with hematochezia should have colonoscopy, which can be done electively after routine preparation unless there is significant ongoing bleeding. In such patients, a rapid prep (5 to 10 L of polyethylene glycol solution delivered via NGT or by mouth over 3 to 4 h) often allows adequate visualization. If colonoscopy cannot visualize the source and ongoing bleeding is sufficiently rapid (> 0.5 to 1 mL/min), angiography may localize the source. Some angiographers first take a radionuclide scan to focus the examination, because angiography is less sensitive than the radionuclide scan.

Diagnosis of occult bleeding can be difficult, because heme-positive stools may result from bleeding anywhere in the GI tract. Endoscopy is the preferred method, with symptoms determining whether the upper or lower GI tract is examined first. Double-contrast barium enema and sigmoidoscopy can be used for the lower tract when colonoscopy is unavailable or the patient refuses it. If the results of upper endoscopy and colonoscopy are negative and occult blood persists in the stool, an upper GI series with small-bowel follow-through, small-bowel endoscopy (enteroscopy), capsule endoscopy, technetium-labeled colloid or RBC scan, and angiography should be considered.

Treatment

• Secure airway if needed

• IV fluid resuscitation

• Blood transfusion if needed

• In some, angiographic or endoscopic hemostasis

Hematemesis, hematochezia, or melena should be considered an emergency. Admission to an ICU, with consultation by both a gastroenterologist and a surgeon, is recommended for all patients with severe GI bleeding. General treatment is directed at maintenance of the airway and restoration of circulating volume. Hemostasis and other treatment depend on the cause of the bleeding.

Airway: A major cause of morbidity and mortality in patients with active upper GI bleeding is aspiration of blood with subsequent respiratory compromise. To prevent these problems, endotracheal intubation should be considered in patients who have inadequate gag reflexes or are obtunded or unconscious —particularly if they will be undergoing upper endoscopy.

Fluid resuscitation: IV fluids are initiated as for any patient with hypovolemia or hemorrhagic shock (see p. 2297): healthy adults are given normal saline IV in 500- to 1000-mL aliquots until signs of hypovolemia remit—up to a maximum of 2 L (for children, 20 mL/kg, that may be repeated once). Patients requiring further resuscitation should receive transfusion with packed RBCs. Transfusions continue until intravascular volume is restored and then are given as needed to replace ongoing blood loss. Transfusions in older patients or those with coronary artery disease may be stopped when Hct is stable at 30 unless the patient is symptomatic. Younger patients or those with chronic bleeding are usually not transfused unless Hct is < 23 or they have symptoms such as dyspnea or coronary ischemia.

Platelet count should be monitored closely; platelet transfusion may be required with severe bleeding. Patients who are taking antiplatelet drugs (eg, clopidogrel, aspirin) have platelet dysfunction, often resulting in increased bleeding. Platelet transfusion should be considered when patients taking these drugs have severe ongoing bleeding, although a residual circulating drug (particularly clopidogrel) may inactivate transfused platelets. Fresh frozen plasma should be transfused after every 4 units of packed RBCs.

Hemostasis: GI bleeding stops spontaneously in about 80% of patients. The remaining patients require some type of intervention. Specific therapy depends on the bleeding site. Early intervention to control bleeding is important to minimize mortality, particularly in elderly patients.

For peptic ulcer, ongoing bleeding or rebleeding is treated with endoscopic coagulation (with bipolar electrocoagulation, injection sclerotherapy, heater probes, or laser). Non-bleeding vessels that are visible within an ulcer crater are also treated. If endoscopy does not stop the bleeding, surgery is required to oversew the bleeding site. If medical management does not control gastric acid secretion, surgeons do acid-reduction surgery (see p. 136) at the same time.

Active variceal bleeding can be treated with endoscopic banding, injection sclerotherapy, or a transjugular intrahepatic portosystemic shunting (TIPS) procedure.

Severe, ongoing lower GI bleeding caused by diverticula or angiomas can sometimes be controlled colonoscopically by electrocautery, coagulation with a heater probe, or injection with dilute epinephrine. Polyps can be removed by snare or cautery. If these methods are ineffective or unfeasible, angiography with embolization or vasopressin infusion may be successful. However, because collateral blood flow to the bowel is limited, angiographic techniques have a significant risk of bowel ischemia or infarction unless super-selective catheterization techniques are used. In most series, the rate of ischemic complications is < 5%. Vasopressin infusion has about an 80% success rate for stopping bleeding, but bleeding recurs in about 50% of patients. Also, there is a risk of hypertension and coronary ischemia. Furthermore, angiography can be used to localize the source of bleeding more accurately. Surgery may be used in patients with continued bleeding (requiring > 4 units transfusion/24 h), but localization of the bleeding site is very important. Blind hemicolectomy (with no preoperative identification of the bleeding site) carries a much higher mortality risk than does directed segmental resection. However, assessment must be expeditious so that surgery is not unnecessarily delayed.

Acute or chronic bleeding of internal hemorrhoids stops spontaneously in most cases. Patients with refractory bleeding are treated via anoscopy with rubber band ligation, injection, coagulation, or surgery.

Geriatrics Essentials

In the elderly, hemorrhoids and colorectal cancer are the most common causes of minor bleeding. Peptic ulcer, diverticular disease, and angiodysplasia are the most common causes of major bleeding. Variceal bleeding is less common than in younger patients.

Massive GI bleeding is tolerated poorly by elderly patients. Diagnosis must be made quickly, and treatment must be started sooner than in younger patients, who can better tolerate repeated episodes of bleeding.

Key Points

• Rectal bleeding may result from upper or lower GI bleeding.

• Orthostatic changes in vital signs are unreliable markers for serious bleeding.

• About 80% of patients stop bleeding spontaneously; various endoscopic techniques are usually the first choice for the remainder.

Varices

Varices are dilated veins in the distal esophagus or proximal stomach caused by elevated pressure in the portal venous system, typically from cirrhosis. They may bleed massively but cause no other symptoms. Diagnosis is by upper endoscopy. Treatment is primarily with endoscopic banding and IV octreotide. Sometimes a transjugular intrahepatic portosystemic shunting procedure is needed.

Portal hypertension (see p. 218) results from a number of conditions, predominantly liver cirrhosis. If portal pressure remains higher than inferior vena caval pressure for a significant period, venous collaterals develop. The most dangerous collaterals occur in the distal esophagus and gastric fundus, causing engorged, serpentine submucosal vessels known as varices. These varices partially decompress portal hypertension but can rupture, causing massive GI bleeding. The trigger for variceal rupture is unknown, but bleeding almost never occurs unless the portal/systemic pressure gradient is > 12 mm Hg. Coagulopathies caused by liver disease may facilitate bleeding. NGT passage in a patient with varices has not been shown to trigger bleeding.

Symptoms and Signs

Patients typically present with sudden, painless, upper GI bleeding, often massive. Signs of shock may be present. Bleeding is usually from the distal esophagus, less often from the gastric fundus. Bleeding from gastric varices also may be acute but is more often subacute or chronic.

Bleeding into the GI tract may precipitate portal-systemic encephalopathy in patients with impaired hepatic function.

Diagnosis

• Endoscopy

• Evaluation for coagulopathy

Both esophageal and gastric varices are best diagnosed by endoscopy, which may also identify varices at high risk of bleeding (eg, those with red markings). Endoscopy is also critical to exclude other causes of acute bleeding (eg, peptic ulcer), even in patients known to have varices; perhaps as many as one third of patients with known varices who have upper GI bleeding have a nonvariceal source.

Because varices are typically associated with significant hepatic disease, evaluation for possible coagulopathy is important. Laboratory tests include CBC with platelets, PT, PTT, and liver function tests.

Bleeding patients should have type and crossmatch for 6 units of packed RBCs.

Prognosis

In about 80% of patients, variceal bleeding stops spontaneously. Nevertheless, mortality is high, often > 50%. Mortality depends primarily on severity of the associated liver disease rather than on the bleeding itself. Bleeding is often fatal in patients with severe hepatocellular impairment (eg, advanced cirrhosis), whereas patients with good hepatic reserve usually recover.

Surviving patients are at high risk of further variceal bleeding; typically, 50 to 75% have recurrence within 1 to 2 yr. Ongoing endoscopic or drug therapy significantly lowers this risk, but the overall effect on long-term mortality seems to be marginal, probably because of the underlying hepatic disease.

Treatment

• Fluid resuscitation

• Endoscopic banding (sclerotherapy second choice)

• IV octreotide

• Possibly a transjugular intrahepatic portosystemic shunting (TIPS) procedure

Management of hypovolemia and hemorrhagic shock is as described above and in Ch. 226. Patients with coagulation abnormalities (eg, elevated INR) should be given 1 to 2 units of fresh frozen plasma and 2.5 to 10 mg vitamin K IM (or IV if severe).

Because varices are invariably diagnosed during endoscopy, primary treatment is endoscopic. Endoscopic banding of varices is preferred over injection sclerotherapy. At the same time, IV octreotide (a synthetic analog of somatostatin, which may also be used) should be given. Octreotide increases splanchnic vascular resistance by inhibiting the release of splanchnic vasodilator hormones (eg, glucagon, vasoactive intestinal peptide). The usual dose is a 50 µg IV bolus, followed by infusion of 50 µg/h. Octreotide is preferred over previously used agents such as vasopressin and terlipressin, because it has fewer adverse effects.

If bleeding continues or recurs despite these measures, emergency techniques to shunt blood from the portal system to the vena cava can lower portal pressure and diminish bleeding. A TIPS procedure is the emergency intervention of choice. TIPS is an invasive radiologic procedure in which a guidewire is passed from the vena cava through the liver parenchyma into the portal circulation. The resultant passage is dilated by a balloon catheter, and a metallic stent is inserted, creating a bypass between the portal and hepatic venous circulations. Stent size is crucial. If the stent is too large, portal-systemic encephalopathy results because of diversion of too much portal blood flow from the liver. If the stent is too small, it is more likely to occlude. Surgical portacaval shunts, such as the distal spleno-renal shunt, work by a similar mechanism but are more invasive and have a higher immediate mortality.

Mechanical compression of bleeding varices with a Sengstaken-Blakemore tube or one of its variants causes considerable morbidity and should not be used as primary management. However, such a tube may provide life-saving tamponade pending decompression with a TIPS or surgical procedure. The tube is a flexible NGT with one gastric balloon and one esophageal balloon. After insertion, the gastric balloon is inflated with a fixed volume of air, and traction is applied to the tube to pull the balloon snugly against the gastroesophageal junction. This balloon is often sufficient to control bleeding, but if not, the esophageal balloon is inflated to a pressure of 25 mm Hg. The procedure is quite uncomfortable and may result in esophageal perforation and aspiration; thus, endotracheal intubation and IV sedation are often recommended.

Liver transplantation can also decompress the portal system but is a practical option only for patients already on a transplant list.

Long-term medical therapy of portal hypertension (with β-blockers and nitrates) is discussed elsewhere (see p. 219). Treatment of portal-systemic encephalopathy may be needed (see p. 220).

Vascular GI Lesions

Several distinct congenital or acquired syndromes involve abnormal mucosal or submucosal blood vessels in the GI tract. These vessels may cause recurrent bleeding, which is rarely massive. Diagnosis is by endoscopy and sometimes angiography. Treatment is endoscopic hemostasis; occasionally, angiographic embolization or surgical resection may be needed.

Vascular ectasias (angiodysplasias, arteriovenous malformations) are dilated, tortuous vessels that typically develop in the cecum and ascending colon. They occur mainly in people > 60 and are the most common cause of lower GI bleeding in that age group. They are thought to be degenerative and do not occur in association with other vascular abnormalities. Most patients have 2 or 3 lesions, which are typically 0.5 to 1.0 cm, bright red, flat or slightly raised, and covered by very thin epithelium. Vascular ectasias also occur in association with a number of systemic diseases (eg, renal failure, cirrhosis, CREST syndrome [calcinosis cutis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly, telangiectasias]—see p. 310) and after radiation to the bowel.

Gastric antral vascular ectasia (watermelon stomach) consists of large dilated veins running linearly along the stomach, creating a striped appearance suggestive of a watermelon. The condition occurs mainly in older women and is of unknown etiology.

Hereditary hemorrhagic telangiectasia (Rendu-Osler-Weber syndrome—see also p. 982) is an autosomal dominant disorder that causes multiple vascular lesions in various parts of the body, including the entire GI tract. GI bleeding rarely occurs before age 40.

Dieulafoy's lesion is an abnormally large artery that penetrates the gut wall, occasionally eroding through the mucosa and causing massive bleeding. It occurs mainly in the proximal stomach.

Arteriovenous malformations and **hemangiomas**, both congenital disorders of blood vessels, can occur in the GI tract but are rare.

Symptoms and Signs

Vascular lesions are painless. Patients often present with heme-positive stools or modest amounts of bright red blood from the rectum. Bleeding is often intermittent, sometimes with long periods between episodes. Patients with upper GI lesions may present with melena. Major bleeding is unusual.

Diagnosis

• Endoscopy

Vascular lesions are most commonly diagnosed endoscopically. If routine endoscopy is nondiagnostic, small-bowel endoscopy, capsule endoscopy, intraoperative endoscopy, or visceral angiography may be required. ^{99m}Tc-labeled RBC scans are less specific but may help localize the lesion enough to facilitate endoscopy or angiography.

Treatment

• Endoscopic coagulation

Endoscopic coagulation (with heater probe, laser, argon plasma, or bipolar electrocoagulation) is effective for many vascular lesions. Vascular ectasias often recur, although there is some evidence that oral estrogen-progesterone combinations may limit recurrence.

Mild recurrent bleeding can be treated simply with chronic iron therapy. More significant bleeding that is

unresponsive to endoscopic measures may require angiographic embolization or surgical resection. However, rebleeding occurs in about 15 to 25% of surgically treated patients.

Chapter 11. Acute Abdomen and Surgical Gastroenterology

Introduction

Acute abdomen refers to abdominal symptoms and signs of such severity or concern that disorders requiring surgery should be considered. The primary symptom is acute abdominal pain. Chronic abdominal pain is discussed in Ch. 7.

Acute Abdominal Pain

Abdominal pain is common and often inconsequential. Acute and severe abdominal pain, however, is almost always a symptom of intra-abdominal disease. It may be the sole indicator of the need for surgery and must be attended to swiftly: Gangrene and perforation of the gut can occur < 6 h from onset of symptoms in certain conditions (eg, interruption of the intestinal blood supply caused by a strangulating obstruction or an arterial embolus). Abdominal pain is of particular concern in patients who are very young or very old and those who have HIV infection or are taking immunosuppressants.

Textbook descriptions of abdominal pain have limitations because people react to pain differently. Some, particularly elderly people, are stoic, whereas others exaggerate their symptoms. Infants, young children, and some elderly people may have difficulty localizing the pain.

Pathophysiology

Visceral pain comes from the abdominal viscera, which are innervated by autonomic nerve fibers and respond mainly to the sensations of distention and muscular contraction—not to cutting, tearing, or local irritation. Visceral pain is typically vague, dull, and nauseating. It is poorly localized and tends to be referred to areas corresponding to the embryonic origin of the affected structure. Foregut structures (stomach, duodenum, liver, and pancreas) cause upper abdominal pain. Midgut structures (small bowel, proximal colon, and appendix) cause periumbilical pain. Hindgut structures (distal colon and GU tract) cause lower abdominal pain.

Somatic pain comes from the parietal peritoneum, which is innervated by somatic nerves, which respond to irritation from infectious, chemical, or other inflammatory processes. Somatic pain is sharp and well localized.

Referred pain is pain perceived distant from its source and results from convergence of nerve fibers at the spinal cord. Common examples of referred pain are scapular pain due to biliary colic, groin pain due to renal colic, and shoulder pain due to blood or infection irritating the diaphragm.

Peritonitis: Peritonitis is inflammation of the peritoneal cavity. The most serious cause is perforation of the GI tract (see p. 111), which causes immediate chemical inflammation followed shortly by infection from intestinal organisms. Peritonitis can also result from any abdominal condition that causes marked inflammation (eg, appendicitis, diverticulitis, strangulating intestinal obstruction, pancreatitis, pelvic inflammatory disease, mesenteric ischemia). Intraperitoneal blood from any source (eg, ruptured aneurysm, trauma, surgery, ectopic pregnancy) is irritating and results in peritonitis. Barium causes severe peritonitis and should never be given to a patient with suspected GI tract perforation. Peritoneo-systemic shunts, drains, and dialysis catheters in the peritoneal cavity predispose a patient to infectious peritonitis, as does ascitic fluid. Rarely, spontaneous bacterial peritonitis occurs, in which the peritoneal cavity is infected by blood-borne bacteria.

Peritonitis causes fluid shift into the peritoneal cavity and bowel, leading to severe dehydration and electrolyte disturbances. Adult respiratory distress syndrome can develop rapidly. Kidney failure, liver failure, and disseminated intravascular coagulation follow. The patient's face becomes drawn into the masklike appearance typical of hippocratic facies. Death occurs within days.

Etiology

Many intra-abdominal disorders cause abdominal pain (see

Fig. 11-1); some are trivial but some are immediately life threatening, requiring rapid diagnosis and surgery. These include ruptured abdominal aortic aneurysm (AAA), perforated viscus, mesenteric ischemia, and ruptured ectopic pregnancy. Others (eg, intestinal obstruction, appendicitis, severe acute pancreatitis) are also serious and nearly as urgent. Several extra-abdominal disorders also cause abdominal pain (see
Table 11-1).

Abdominal pain in neonates, infants, and young children has numerous causes not encountered in adults, including meconium peritonitis, pyloric stenosis, esophageal webs, volvulus of a gut with a common mesentery, imperforate anus, intussusception, and intestinal obstruction caused by atresia.

Evaluation

Evaluation of mild and severe pain follows the same process, although with severe abdominal pain, therapy sometimes proceeds simultaneously and involves early consultation with a surgeon. History and physical examination usually exclude all but a few possible causes, with final diagnosis confirmed by judicious use of laboratory and imaging tests. Life-threatening causes should always be ruled out before focusing on less serious diagnoses. In seriously ill patients with severe abdominal pain, the most important diagnostic measure may be expeditious surgical exploration. In mildly ill patients, watchful waiting may be best.

History: A thorough history usually suggests the diagnosis (see
Table 11-2). Of particular importance are pain location (see Fig. 11-1) and characteristics, history of similar symptoms, and associated symptoms. Concomitant symptoms such as gastroesophageal reflux, nausea, vomiting, diarrhea, constipation, jaundice, melena, hematuria, hematemesis, weight loss, and mucus or blood in the stool help direct subsequent evaluation. A drug history should include details concerning prescription and illicit drug use as well as alcohol. Many drugs cause GI upset. Prednisone or immunosuppressants may inhibit the inflammatory response to perforation or peritonitis and result in less pain and leukocytosis than might otherwise be expected. Anticoagulants can increase the chances of bleeding and hematoma formation. Alcohol predisposes to pancreatitis.

Known medical conditions and previous abdominal surgeries are important to ascertain. Women should be asked whether they are pregnant.

Physical examination: The general appearance is important. A happy, comfortable-appearing patient rarely has a serious problem, unlike one who is anxious, pale, diaphoretic, or in obvious pain. BP, pulse, state of consciousness, and other signs of peripheral perfusion must be evaluated. However, the focus

[**Fig. 11-1.** Location of abdominal pain and possible causes.]

[**Table 11-1.** Extra-Abdominal Causes of Abdominal Pain]

of the examination is the abdomen, beginning with inspection and auscultation, followed by palpation and percussion. Rectal examination and pelvic examination (for women) to locate tenderness, masses, and blood are essential.

Palpation begins gently, away from the area of greatest pain, detecting areas of particular tenderness, as well as the presence of guarding, rigidity, and rebound (all suggesting peritoneal irritation) and any masses. Guarding is an involuntary contraction of the abdominal muscles that is slightly slower and more sustained than the rapid, voluntary flinch exhibited by sensitive or anxious patients. Rebound is a distinct flinch upon brisk withdrawal of the examiner's hand. The inguinal area and all surgical scars should be palpated for hernias.

Red flags: Certain findings raise suspicion of a more serious etiology:

• Severe pain

• Signs of shock (eg, tachycardia, hypotension, diaphoresis, confusion)

• Signs of peritonitis

• Abdominal distention

Interpretation of findings: Distention, especially when surgical scars, tympany to percussion, and high-pitched peristalsis or borborygmi in rushes are present, strongly suggests bowel obstruction. Severe pain in a patient with a silent abdomen who is lying as still as possible suggests peritonitis; location of tenderness suggests etiology (eg, right upper quadrant suggests cholecystitis, right lower quadrant suggests appendicitis) but may not be diagnostic. Back pain with shock suggests ruptured AAA, particularly if there is a tender, pulsatile mass. Shock and vaginal bleeding in a pregnant woman suggest ruptured ectopic pregnancy. Ecchymoses of the costovertebral angles (Grey Turner's sign) or around the umbilicus (Cullen's sign) suggest hemorrhagic pancreatitis but are not very sensitive for this disorder.

History is often suggestive (see Table 11-2). Mild to moderate pain in the presence of active peristalsis of normal pitch suggests a nonsurgical disease (eg, gastroenteritis) but may also be the early manifestations of a more serious disorder. A patient who is writhing around trying to get comfortable is more likely to have an obstructive mechanism (eg, renal or biliary colic).

Previous abdominal surgery makes obstruction from adhesions more likely. Generalized atherosclerosis increases the possibility of MI, AAA, and mesenteric ischemia. HIV infection makes infectious causes and drug adverse effects likely.

Testing: Tests are selected based on clinical suspicion.

• Urine pregnancy test for all women of childbearing age

• Selected imaging tests based on suspected diagnosis

Standard tests (eg, CBC, chemistries, urinalysis) are often done but are of little value due to poor specificity; patients with significant disease may have normal results. Abnormal results do not provide a specific diagnosis (the urinalysis in particular may show pyuria or hematuria in a wide variety of conditions), and they can also occur in the absence of significant disease. An exception is serum lipase, which strongly suggests a diagnosis of acute pancreatitis. A bedside urine pregnancy test should be done for all women of childbearing age because a negative result effectively excludes ruptured ectopic pregnancy.

An abdominal series, consisting of flat and upright abdominal x-rays and upright chest x-rays (left lateral recumbent abdomen and anteroposterior chest x-ray for patients unable to stand), should be done when perforation or obstruction is suspected. However, these plain x-rays are seldom diagnostic for other conditions and need not be automatically done. Ultrasound should be done for suspected biliary tract disease or ectopic pregnancy (transvaginal

[**Table 11-2.** History in Patients with Acute Abdominal Pain]

probe). Ultrasound can also detect AAA but cannot reliably identify rupture. Noncontrast helical CT is the modality of choice for suspected renal stones. CT with oral contrast is diagnostic in about 95% of patients with significant abdominal pain and has markedly lowered the negative laparotomy rate. However, advanced imaging must not be allowed to delay surgery in patients with definitive symptoms and signs.

Treatment

Some clinicians feel that providing pain relief before a diagnosis is made interferes with their ability to evaluate. However, moderate doses of IV analgesics (eg, fentanyl 50 to 100 µg, morphine 4 to 6 mg) do not mask peritoneal signs and, by diminishing anxiety and discomfort, often make examination easier.

Key Points

• Life-threatening causes should be looked for first.

• Pregnancy should be ruled out in women of childbearing age.

• Signs of peritonitis, shock, and obstruction should be sought.

• Blood tests are of minimal value.

Acute Mesenteric Ischemia

Acute mesenteric ischemia is interruption of intestinal blood flow by embolism, thrombosis, or a low-flow state. It leads to mediator release, inflammation, and ultimately infarction. Abdominal pain is out of proportion to physical findings. Early diagnosis is difficult, but angiography and exploratory laparotomy have the most sensitivity; other imaging modalities often become positive only late in the disease. Treatment is by embolectomy, revascularization of viable segments, or resection; sometimes vasodilator therapy is successful. Mortality is high.

Pathophysiology

The intestinal mucosa has a high metabolic rate and, accordingly, a high blood flow requirement (normally receiving 20 to 25% of cardiac output), making it very sensitive to the effects of decreased perfusion. Ischemia disrupts the mucosal barrier, allowing release of bacteria, toxins, and vasoactive mediators, which in turn leads to myocardial depression, systemic inflammatory response syndrome (see p. 2299), multisystem organ failure, and death. Mediator release may occur even before complete infarction. Necrosis can occur as soon as 10 to 12 h after the onset of symptoms.

Three major vessels serve the abdominal contents: the celiac trunk, the superior mesenteric artery (SMA), and the inferior mesenteric artery (IMA). The celiac trunk supplies the esophagus, stomach, proximal duodenum, liver, gallbladder, pancreas, and spleen. The SMA supplies the distal duodenum, jejunum, ileum, and colon to the splenic flexure. The IMA supplies the descending colon and sigmoid colon and the rectum. Collateral vessels are abundant in the stomach, duodenum, and rectum; these areas rarely develop ischemia. The splenic flexure is a watershed between the SMA and IMA and is at particular risk of ischemia.

Etiology

Mesenteric blood flow may be disrupted on either the venous or arterial sides. In general, patients > 50 are at greatest risk and have the types of occlusions and risk factors shown in Table 11-3. However, many patients have no identifiable risk factors.

Symptoms and Signs

The early hallmark of mesenteric ischemia is severe pain but minimal physical findings. The abdomen remains soft, with little or no tenderness. Mild tachycardia may be present. Later, as necrosis develops, signs of peritonitis appear, with marked abdominal tenderness, guarding, rigidity, and no bowel sounds. The stool may be heme-positive (increasingly likely as ischemia progresses). The usual signs of shock develop and are frequently followed by death.

Sudden onset of pain suggests but is not diagnostic of an arterial embolism, whereas a more gradual onset is typical of venous thrombosis. Patients with a history of postprandial abdominal discomfort (which suggests intestinal angina) may have arterial thrombosis.

[**Table 11-3.** Causes of Acute Mesenteric Ischemia]

Diagnosis

• Clinical diagnosis more important than diagnostic tests

• Mesenteric angiography if diagnosis unclear

Early diagnosis is particularly important because mortality increases significantly once intestinal infarction has occurred. Mesenteric ischemia must be considered in any patient > 50 with known risk factors or predisposing conditions who develops sudden, severe abdominal pain.

Patients with clear peritoneal signs should proceed directly to the operating room for both diagnosis and treatment. For others, selective mesenteric angiography is the diagnostic procedure of choice. Other imaging studies and serum markers can show abnormalities but lack sensitivity and specificity early in the course of the disease when diagnosis is most critical. Plain abdominal x-rays are useful mainly in ruling out other causes of pain (eg, perforated viscus), although portal venous gas or pneumatosis intestinalis may be seen late in the disease. These findings also appear on CT, which may also directly visualize vascular occlusion—more accurately on the venous side. Doppler ultrasonography can sometimes identify arterial occlusion, but sensitivity is low. MRI is very accurate in proximal vascular occlusion, less so in distal vascular occlusion. Serum markers (eg, creatine kinase, lactate) rise with necrosis but are nonspecific findings that are seen later. Intestinal fatty acid binding protein in the urine may prove valuable in the future as an early marker.

Prognosis

If diagnosis and treatment take place before infarction occurs, mortality is low; after intestinal infarction, mortality approaches 70 to 90%. For this reason, clinical diagnosis of mesenteric ischemia should supersede diagnostic tests, which may delay treatment.

Treatment

• Surgical: Embolectomy, revascularization, or resection

• Angiographic: Vasodilators or thrombolysis

• Long-term anticoagulation or antiplatelet therapy

If diagnosis is made during exploratory laparotomy, options are surgical embolectomy, revascularization, and resection. A "second look" laparotomy may be needed to reassess the viability of questionable areas of bowel. If diagnosis is made by angiography, infusion of the vasodilator papaverine through the angiography catheter may improve survival in both occlusive and nonocclusive ischemia. A 60-mg bolus is given over 2 min, followed by an infusion of 30 to 60 mg/h. Papaverine is useful even when surgical intervention is planned and is sometimes given during and after surgical intervention as well. In addition, for arterial occlusion, thrombolysis or surgical embolectomy may be done. The development of peritoneal signs at any time during the evaluation suggests the need for immediate surgery. Mesenteric venous thrombosis without signs of peritonitis can be treated with papaverine followed by anticoagulation with heparin and then warfarin.

Patients with arterial embolism or venous thrombosis require long-term anticoagulation with warfarin. Patients with nonocclusive ischemia may be treated with antiplatelet therapy.

Acute Perforation

Any part of the GI tract may become perforated, releasing gastric or intestinal contents into the peritoneal space. Causes vary. Symptoms develop suddenly, with severe pain followed shortly by signs of shock. Diagnosis is usually made by the presence of free air in the abdomen on imaging studies. Treatment is with fluid resuscitation, antibiotics, and surgery. Mortality is high, varying with the underlying disorder and the patient's general health.

Etiology

Both blunt and penetrating trauma can result in perforation of any part of the GI tract (see Table 11-4). Swallowed foreign bodies, even sharp ones, rarely cause perforation unless they become

impacted, causing ischemia and necrosis from local pressure. Foreign bodies inserted via the anus may perforate the rectum.

Symptoms and Signs

Esophageal, gastric, and duodenal perforation tends to manifest suddenly and catastrophically, with abrupt onset of acute abdomen with severe generalized abdominal pain, tenderness, and peritoneal signs. Pain may radiate to the shoulder.

Perforation at other GI sites often occurs in the setting of other painful, inflammatory conditions. Because such perforations are often small initially and frequently walled off by the omentum, pain often develops gradually and may be localized. Tenderness also is more focal. Such findings can make it difficult to distinguish perforation from worsening of the underlying disorder or lack of response to treatment.

In all types of perforation, nausea, vomiting, and anorexia are common. Bowel sounds are quiet to absent.

Diagnosis

• Abdominal series

• If nondiagnostic, abdominal CT

An abdominal series (supine and upright abdominal x-rays and chest x-rays) may be diagnostic, showing free air under the diaphragm in 50 to 75% of cases. As time passes, this sign becomes more common. A lateral chest x-ray is more sensitive for free air than a posteroanterior x-ray. If the abdominal series is nondiagnostic, abdominal CT usually with oral and IV and/or rectal contrast may be helpful. Barium should not be used if perforation is suspected.

Treatment

• Surgery

• IV fluids and antibiotics

[Table 11-4. Some Causes of GI Tract Perforation]

If a perforation is noted, immediate surgery is necessary because mortality caused by peritonitis increases rapidly the longer treatment is delayed. If an abscess or an inflammatory mass has formed, the procedure may be limited to drainage of the abscess.

An NGT is inserted before operation. Patients with signs of volume depletion should have urine output monitored with a catheter. Fluid status is maintained by adequate IV fluid and electrolyte replacement. IV antibiotics effective against intestinal flora should be given (eg, cefotetan 1 to 2 g bid, or amikacin 5 mg/kg tid plus clindamycin 600 to 900 mg qid).

Appendicitis

Appendicitis is acute inflammation of the vermiform appendix, typically resulting in abdominal pain, anorexia, and abdominal tenderness. Diagnosis is clinical, often supplemented by CT or ultrasound. Treatment is surgical removal.

In the US, acute appendicitis is the most common cause of acute abdominal pain requiring surgery. Over 5% of the population develops appendicitis at some point. It most commonly occurs in the teens and 20s but may occur at any age.

Other conditions affecting the appendix include carcinoids, cancer, villous adenomas, and diverticula. The appendix may also be affected by Crohn's disease or ulcerative colitis with pancolitis.

Etiology

Appendicitis is thought to result from obstruction of the appendiceal lumen, typically by lymphoid hyperplasia, but occasionally by a fecalith, foreign body, or even worms. The obstruction leads to distention, bacterial overgrowth, ischemia, and inflammation. If untreated, necrosis, gangrene, and perforation occur. If the perforation is contained by the omentum, an appendiceal abscess results.

Symptoms and Signs

The classic symptoms of acute appendicitis are epigastric or periumbilical pain followed by brief nausea, vomiting, and anorexia; after a few hours, the pain shifts to the right lower quadrant. Pain increases with cough and motion. Classic signs are right lower quadrant direct and rebound tenderness located at McBurney's point (junction of the middle and outer thirds of the line joining the umbilicus to the anterior superior spine). Additional signs are pain felt in the right lower quadrant with palpation of the left lower quadrant (Rovsing sign), an increase in pain from passive extension of the right hip joint that stretches the iliopsoas muscle (psoas sign), or pain caused by passive internal rotation of the flexed thigh (obturator sign). Low-grade fever (rectal temperature 37.7 to 38.3° C [100 to 101° F]) is common.

Unfortunately, these classic findings appear in < 50% of patients. Many variations of symptoms and signs occur. Pain may not be localized, particularly in infants and children. Tenderness may be diffuse or, in rare instances, absent. Bowel movements are usually less frequent or absent; if diarrhea is a sign, a retrocecal appendix should be suspected. RBCs or WBCs may be present in the urine. Atypical symptoms are common among elderly patients and pregnant women; in particular, pain is less severe and local tenderness is less marked.

Diagnosis

• Clinical evaluation

• Abdominal CT if necessary

• Ultrasound an option to CT

When classic symptoms and signs are present, the diagnosis is clinical. In such patients, delaying laparotomy to do imaging tests only increases the likelihood of perforation and subsequent complications. In patients with atypical or equivocal findings, imaging studies should be done without delay. Contrast-enhanced CT has reasonable accuracy in diagnosing appendicitis and can also reveal other causes of an acute abdomen. Graded compression ultrasound can usually be done quickly and uses no radiation (of particular concern in children); however, it is occasionally limited by the presence of bowel gas and is less useful for recognizing nonappendiceal causes of pain. Appendicitis remains primarily a clinical diagnosis. Selective and judicious use of radiographic studies may reduce the rate of negative laparotomy.

Laparoscopy can be used for diagnosis as well as definitive treatment; it may be especially helpful in women with lower abdominal pain of unclear etiology. Laboratory studies typically show leukocytosis (12,000 to 15,000/µL), but this finding is highly variable; a normal WBC count should not be used to exclude appendicitis.

Prognosis

Without surgery or antibiotics, mortality is > 50%.

With early surgery, the mortality rate is < 1%, and convalescence is normally rapid and complete. With complications (rupture and development of an abscess or peritonitis), the prognosis is worse: Repeat operations and a long convalescence may follow.

Treatment

• Surgical removal

• IV fluids and antibiotics

Treatment of acute appendicitis is open or laparoscopic appendectomy; because treatment delay increases mortality, a negative appendectomy rate of 15% is considered acceptable. The surgeon can usually remove the appendix even if perforated. Occasionally, the appendix is difficult to locate: In these cases, it usually lies behind the cecum or the ileum and mesentery of the right colon. A contraindication to appendectomy is inflammatory bowel disease involving the cecum. However, in cases of terminal ileitis and a normal cecum, the appendix should be removed.

Appendectomy should be preceded by IV antibiotics. Third-generation cephalosporins are preferred. For nonperforated appendicitis, no further antibiotics are required. If the appendix is perforated, antibiotics should be continued until the patient's temperature and WBC count have normalized or continued for a fixed course, according to the surgeon's preference. If surgery is impossible, antibiotics—although not curative—markedly improve the survival rate. When a large inflammatory mass is found involving the appendix, terminal ileum, and cecum, resection of the entire mass and ileocolostomy are preferable. In late cases in which a pericolic abscess has already formed, the abscess is drained either by an ultrasound-guided percutaneous catheter or by open operation (with appendectomy to follow at a later date). A Meckel's diverticulum in a patient under the age of 40 should be removed concomitantly with the appendectomy unless extensive inflammation around the appendix prevents the procedure.

Hernias of the Abdominal Wall

A hernia of the abdominal wall is a protrusion of the abdominal contents through an acquired or congenital area of weakness or defect in the wall. Many hernias are asymptomatic, but some become incarcerated or strangulated, causing pain and requiring immediate surgery. Diagnosis is clinical. Treatment is elective surgical repair.

Abdominal hernias are extremely common, particularly among males, necessitating about 700,000 operations each year in the US.

Classification

Abdominal hernias are classified as either abdominal wall or groin hernias. Strangulated hernias are ischemic from physical constriction of their blood supply. Gangrene, perforation, and peritonitis may develop. Incarcerated and strangulated hernias cannot be reduced manually.

Abdominal wall hernias include umbilical hernias, epigastric hernias, Spigelian hernias, and incisional (ventral) hernias. Umbilical hernias (protrusions through the umbilical ring) are mostly congenital, but some are acquired in adulthood secondary to obesity, ascites, pregnancy, or chronic peritoneal dialysis. Epigastric hernias occur through the linea alba. Spigelian hernias occur through defects in the transversus abdominis muscle lateral to the rectus sheath, usually below the level of the umbilicus. Incisional hernias occur through an incision from previous abdominal surgery.

Groin hernias include inguinal hernias and femoral hernias. Inguinal hernias occur above the inguinal ligament. Indirect inguinal hernias traverse the internal inguinal ring into the inguinal canal, and direct inguinal hernias extend directly forward and do not pass through the inguinal canal. Femoral hernias occur below the inguinal ligament and go into the femoral canal.

About 75% of all abdominal hernias are inguinal. Incisional hernias comprise another 10 to 15%. Femoral and unusual hernias account for the remaining 10 to 15%.

Symptoms and Signs

Most patients complain only of a visible bulge, which may cause vague discomfort or be asymptomatic. Most hernias, even large ones, can be manually reduced with persistent gentle pressure; placing the patient in the Trendelenburg position may help. An incarcerated hernia cannot be reduced but has no

additional symptoms. A strangulated hernia causes steady, gradually increasing pain, typically with nausea and vomiting. The hernia itself is tender, and the overlying skin may be erythematous; peritonitis may develop depending on location, with diffuse tenderness, guarding, and rebound.

Diagnosis

• Clinical evaluation

The diagnosis is clinical. Because the hernia may be apparent only when abdominal pressure is increased, the patient should be examined in a standing position. If no hernia is palpable, the patient should cough or perform a Valsalva maneuver as the examiner palpates the abdominal wall. Examination focuses on the umbilicus, the inguinal area (with a finger in the inguinal canal in males), the femoral triangle, and any incisions that are present.

Inguinal masses that resemble hernias may be the result of adenopathy (infectious or malignant), an ectopic testis, or lipoma. These masses are solid and are not reducible. A scrotal mass may be a varicocele, hydrocele, or testicular tumor. Ultrasound may be done if physical examination is equivocal.

Prognosis

Congenital umbilical hernias rarely strangulate and are not treated; most resolve spontaneously within several years. Very large defects may be repaired electively after age 2 yr. Umbilical hernias in adults cause cosmetic concerns and can be electively repaired; strangulation and incarceration are unusual but, if happen, usually contain omentum rather than intestine.

Treatment

• Surgical repair

Groin hernias should be repaired electively because of the risk of strangulation, which results in higher morbidity (and possible mortality in elderly patients). Repair may be through a standard incision or laparoscopically.

An incarcerated or strangulated hernia of any kind requires urgent surgical repair.

Ileus

(Paralytic Ileus; Adynamic Ileus; Paresis)

Ileus is a temporary arrest of intestinal peristalsis. It occurs most commonly after abdominal surgery, particularly when the intestines have been manipulated. Symptoms are nausea, vomiting, and vague abdominal discomfort. Diagnosis is based on x-ray findings and clinical impression. Treatment is supportive, with nasogastric suction and IV fluids.

Etiology

In addition to postoperative causes, ileus also results from intraperitoneal or retroperitoneal inflammation (eg, appendicitis, diverticulitis, perforated duodenal ulcer), retroperitoneal or intra-abdominal hematomas (eg, ruptured abdominal aortic aneurysm, lumbar compression fracture), metabolic disturbances (eg, hypokalemia), or drugs (eg, opioids, anticholinergics, sometimes Ca channel blockers). Ileus sometimes occurs in association with renal or thoracic disease (eg, lower rib fractures, lower lobe pneumonias, MI).

Gastric and colonic motility disturbances after abdominal surgery are common. The small bowel is typically least affected, with motility and absorption returning to normal within hours after surgery. Stomach emptying is usually impaired for about 24 h or more. The colon is often most affected and may remain inactive for 48 to 72 h or more.

Symptoms and Signs

Symptoms and signs include abdominal distention, vomiting, and vague discomfort. Pain rarely has the classic colicky pattern present in mechanical obstruction. There may be obstipation or passage of slight amounts of watery stool. Auscultation reveals a silent abdomen or minimal peristalsis. The abdomen is not tender unless the underlying cause is inflammatory.

Diagnosis

• Clinical evaluation

• Sometimes x-rays

The most essential task is to distinguish ileus from intestinal obstruction. In both conditions, x-rays show gaseous distention of isolated segments of intestine. In postoperative ileus, however, gas may accumulate more in the colon than in the small bowel. Postoperative accumulation of gas in the small bowel often implies development of a complication (eg, obstruction, peritonitis). In other types of ileus, x-ray findings are similar to obstruction; differentiation can be difficult unless clinical features clearly favor one or the other. Water-soluble contrast studies may help differentiate.

Treatment

• NGT

• IV fluids

Treatment involves continuous nasogastric suction, npo status, IV fluids and electrolytes, a minimal amount of sedatives, and avoidance of opioids and anticholinergic drugs. Maintaining an adequate serum K level (> 4 mEq/L [> 4 mmol/L]) is especially important. Ileus persisting > 1 wk probably has a mechanical obstructive cause, and laparotomy should be considered. Sometimes colonic ileus can be relieved by colonoscopic decompression; rarely, cecostomy is required. Colonoscopic decompression is helpful in treating pseudo-obstruction (Ogilvie's syndrome), which consists of apparent obstruction at the splenic flexure, although no cause can be found by contrast enema or colonoscopy for the failure of gas and feces to pass this point. Some clinicians use IV neostigmine (requires cardiac monitoring) to treat Ogilvie's syndrome.

Intestinal Obstruction

Intestinal obstruction is significant mechanical impairment or complete arrest of the passage of contents through the intestine. Symptoms include cramping pain, vomiting, obstipation, and lack of flatus. Diagnosis is clinical, confirmed by abdominal x-rays. Treatment is fluid resuscitation, nasogastric suction, and, in most cases of complete obstruction, surgery.

Mechanical obstruction is divided into obstruction of the small bowel (including the duodenum) and obstruction of the large bowel. Obstruction may be partial or complete. About 85% of partial small-bowel obstructions resolve with nonoperative treatment, whereas about 85% of complete small-bowel obstructions require operation.

Etiology

Overall, the most common causes of mechanical obstruction are adhesions, hernias, and tumors. Other general causes are diverticulitis, foreign bodies (including gallstones), volvulus (twisting of bowel on its mesentery), intussusception (telescoping of one segment of bowel into another—see p. 2801), and fecal impaction. Specific segments of the intestine are affected differently (see Table 11-5).

Pathophysiology

In simple mechanical obstruction, blockage occurs without vascular compromise. Ingested fluid and food,

digestive secretions, and gas accumulate above the obstruction. The proximal bowel distends, and the distal segment collapses. The normal secretory and absorptive functions of the mucosa are depressed, and the bowel wall becomes edematous and congested. Severe intestinal distention is self-perpetuating and progressive, intensifying

[Table 11-5. Causes of Intestinal Obstruction]

the peristaltic and secretory derangements and increasing the risks of dehydration and progression to strangulating obstruction.

Strangulating obstruction is obstruction with compromised blood flow; it occurs in nearly 25% of patients with small-bowel obstruction. It is usually associated with hernia, volvulus, and intussusception. Strangulating obstruction can progress to infarction and gangrene in as little as 6 h. Venous obstruction occurs first, followed by arterial occlusion, resulting in rapid ischemia of the bowel wall. The ischemic bowel becomes edematous and infarcts, leading to gangrene and perforation. In large-bowel obstruction, strangulation is rare (except with volvulus).

Perforation may occur in an ischemic segment (typically small bowel) or when marked dilation occurs. The risk is high if the cecum is dilated to a diameter ≥ 13 cm. Perforation of a tumor or a diverticulum may also occur at the obstruction site.

Symptoms and Signs

Obstruction of the small bowel causes symptoms shortly after onset: abdominal cramps centered around the umbilicus or in the epigastrium, vomiting, and—in patients with complete obstruction—obstipation. Patients with partial obstruction may develop diarrhea. Severe, steady pain suggests that strangulation has occurred. In the absence of strangulation, the abdomen is not tender. Hyperactive, high-pitched peristalsis with rushes coinciding with cramps is typical. Sometimes, dilated loops of bowel are palpable. With infarction, the abdomen becomes tender and auscultation reveals a silent abdomen or minimal peristalsis. Shock and oliguria are serious signs that indicate either late simple obstruction or strangulation.

Obstruction of the large bowel usually causes milder symptoms that develop more gradually than those caused by small-bowel obstruction. Increasing constipation leads to obstipation and abdominal distention. Vomiting may occur (usually several hours after onset of other symptoms) but is not common. Lower abdominal cramps unproductive of feces occur. Physical examination typically shows a distended abdomen with loud borborygmi. There is no tenderness, and the rectum is usually empty. A mass corresponding to the site of an obstructing tumor may be palpable. Systemic symptoms are relatively mild, and fluid and electrolyte deficits are uncommon.

Volvulus often has an abrupt onset. Pain is continuous, sometimes with superimposed waves of colicky pain.

Diagnosis

• Abdominal series

Supine and upright abdominal x-rays should be taken and are usually adequate to diagnose obstruction. Although only laparotomy can definitively diagnose strangulation, careful serial clinical examination may provide early warning. Elevated WBCs and acidosis may indicate that strangulation has already occurred.

On plain x-rays, a ladderlike series of distended small-bowel loops is typical of small-bowel obstruction but may also occur with obstruction of the right colon. Fluid levels in the bowel can be seen in upright views. Similar, although perhaps less dramatic, x-ray findings and symptoms occur in ileus (paralysis of the intestine without obstruction—see p. 114); differentiation can be difficult. Distended loops and fluid levels may be absent with an obstruction of the upper jejunum or with closed-loop strangulating obstructions (as may occur with volvulus). Infarcted bowel may produce a mass effect on x-ray. Gas in the bowel wall (pneumatosis intestinalis) indicates gangrene.

In large-bowel obstruction, abdominal x-ray shows distention of the colon proximal to the obstruction. In cecal volvulus, there may be a large gas bubble in the mid-abdomen or left upper quadrant. With both cecal and sigmoidal volvulus, a contrast enema shows the site of obstruction by a typical "bird-beak" deformity at the site of the twist; the procedure may actually reduce a sigmoid volvulus. If contrast enema is not done, colonoscopy can be used to decompress a sigmoid volvulus but rarely works with a cecal volvulus.

Treatment

• Nasogastric suction

• IV fluids

• IV antibiotics if bowel ischemia suspected

Patients with possible intestinal obstruction should be hospitalized. Treatment of acute intestinal obstruction must proceed simultaneously with diagnosis. A surgeon should always be involved.

Supportive care is similar for small- and large-bowel obstruction: nasogastric suction, IV fluids (0.9% saline or lactated Ringer's solution for intravascular volume repletion), and a urinary catheter to monitor fluid output. Electrolyte replacement should be guided by test results, although in cases of repeated vomiting serum Na and K are likely to be depleted. If bowel ischemia or infarction is suspected, antibiotics should be given (eg, a 3rd-generation cephalosporin, such as cefotetan 2 g IV) before laparotomy.

Specific measures: Obstruction of the duodenum in adults is treated by resection or, if the lesion cannot be removed, palliative gastrojejunostomy (for treatment in children, see p. 2978).

Complete obstruction of the small bowel is preferentially treated with early laparotomy, although surgery can be delayed 2 or 3 h to improve fluid status and urine output in a very ill, dehydrated patient. The offending lesion is removed whenever possible. If a gallstone is the cause of obstruction, it is removed through an enterotomy, and cholecystectomy need not be done. Procedures to prevent recurrence should be done, including repair of hernias, removal of foreign bodies, and lysis of the offending adhesions. In some patients with early postoperative obstruction or repeated obstruction caused by adhesions, simple intubation with a long intestinal tube (many consider a standard NGT to be equally effective), rather than surgery, may be attempted in the absence of peritoneal signs.

Disseminated intraperitoneal cancer obstructing the small bowel is a major cause of death in adult patients with GI tract cancer. Bypassing the obstruction, either surgically or with endoscopically placed stents, may palliate symptoms briefly.

Obstructing colon cancers can often be treated by a single-stage resection and anastomosis. Other options include a diverting ileostomy and distal anastomosis. Occasionally, a diverting colostomy with delayed resection is required.

When diverticulitis causes obstruction, perforation is often present. Removal of the involved area may be very difficult but is indicated if perforation and general peritonitis are present. Resection and colostomy are done, and anastomosis is postponed.

Fecal impaction usually occurs in the rectum and can be removed digitally and with enemas. However, a fecal concretion alone or in a mixture (ie, with barium or antacids) that causes complete obstruction (usually in the sigmoid) requires laparotomy.

Treatment of cecal volvulus consists of resection and anastomosis of the involved segment or fixation of the cecum in its normal position by cecostomy in the frail patient. In sigmoidal volvulus, an endoscope or a long rectal tube can often decompress the loop, and resection and anastomosis may be deferred for a few days. Without a resection, recurrence is almost inevitable.

Intra-Abdominal Abscesses

Abscesses can occur anywhere in the abdomen and retroperitoneum. They mainly occur after surgery, trauma, or conditions involving abdominal infection and inflammation, particularly when peritonitis or perforation occurs. Symptoms are malaise, fever, and abdominal pain. Diagnosis is by CT. Treatment is with drainage, either surgical or percutaneous. Antibiotics are ancillary.

Etiology

Intra-abdominal abscesses are classified as intraperitoneal, retroperitoneal, or visceral (see Table 11-6). Many intra-abdominal abscesses develop after perforation of a hollow viscus or colonic cancer. Others develop by extension of infection or inflammation resulting from conditions such as appendicitis, diverticulitis, Crohn's disease, pancreatitis, pelvic inflammatory disease, or indeed any condition causing generalized peritonitis. Abdominal surgery, particularly that involving the digestive or biliary tract, is another significant risk factor: The peritoneum may be contaminated during or after surgery from such events as anastomotic leaks. Traumatic

[**Table 11-6.** Intra-Abdominal Abscesses]

abdominal injuries—particularly lacerations and hematomas of the liver, pancreas, spleen, and intestines—may develop abscesses, whether treated operatively or not.

The infecting organisms typically reflect normal bowel flora and are a complex mixture of anaerobic and aerobic bacteria. Most frequent isolates are aerobic gram-negative bacilli (eg, *Escherichia coli* and *Klebsiella*) and anaerobes (especially *Bacteroides fragilis*).

Undrained abscesses may extend to contiguous structures, erode into adjacent vessels (causing hemorrhage or thrombosis), rupture into the peritoneum or bowel, or form a cutaneous fistula. Subdiaphragmatic abscesses may extend into the thoracic cavity, causing an empyema, lung abscess, or pneumonia. An abscess in the lower abdomen may track down into the thigh or perirectal fossa. Splenic abscess is a rare cause of sustained bacteremia in endocarditis that persists despite appropriate antimicrobial therapy.

Symptoms and Signs

Abscesses may form within 1 wk of perforation or significant peritonitis, whereas postoperative abscesses may not occur until 2 to 3 wk after operation and, rarely, not for several months. Although manifestations vary, most abscesses cause fever and abdominal discomfort ranging from minimal to severe (usually near the abscess). Paralytic ileus, either generalized or localized, may develop. Nausea, anorexia, and weight loss are common.

Abscesses in Douglas' cul-de-sac, adjacent to the colon, may cause diarrhea. Contiguity to the bladder may result in urinary urgency and frequency and, if caused by diverticulitis, may create a colovesical fistula.

Subphrenic abscesses may cause chest symptoms such as nonproductive cough, chest pain, dyspnea, and shoulder pain. Rales, rhonchi, or a friction rub may be audible. Dullness to percussion and decreased breath sounds are typical when basilar atelectasis, pneumonia, or pleural effusion occurs.

Generally, there is tenderness over the location of the abscess. Large abscesses may be palpable as a mass.

Diagnosis

• Abdominal CT

• Rarely, radionuclide scanning

CT of the abdomen and pelvis with oral contrast is the preferred diagnostic modality for suspected abscess. Other imaging studies, if done, may show abnormalities; plain abdominal x-rays may reveal extraintestinal gas in the abscess, displacement of adjacent organs, a soft-tissue density representing the abscess, or loss of the psoas muscle shadow. Abscesses near the diaphragm may result in chest x-ray abnormalities such as ipsilateral pleural effusion, elevated or immobile hemidiaphragm, lower lobe infiltrates, and atelectasis.

CBC and blood cultures should be done. Leukocytosis occurs in most patients, and anemia is common.

Occasionally, radionuclide scanning with indium^{111}-labeled leukocytes may be helpful in identifying intra-abdominal abscesses.

Prognosis

Intra-abdominal abscesses have a mortality rate of 10 to 40%. Outcome depends mainly on the patient's primary illness or injury and general medical condition rather than on the specific nature and location of the abscess.

Treatment

• IV antibiotics

• Drainage: Percutaneous or surgical

All intra-abdominal abscesses require drainage, either by percutaneous catheters or surgery. Drainage through catheters (placed with CT or ultrasound guidance) may be appropriate given the following conditions: Few abscess cavities are present; the drainage route does not traverse bowel or uncontaminated organs, pleura, or peritoneum; the source of contamination is controlled; and the pus is thin enough to pass through the catheter.

Antibiotics are not curative but may limit hematogenous spread and should be given before and after intervention. Therapy requires drugs active against bowel flora, such as a combination of an aminoglycoside (eg, gentamicin 1.5 mg/kg q 8 h) and metronidazole 500 mg q 8 h. Single-agent therapy with cefotetan 2 g q 12 h is also reasonable. Patients previously given antibiotics or those who have hospital-acquired infections should receive drugs active against resistant aerobic gram-negative bacilli (eg, *Pseudomonas*) and anaerobes.

Nutritional support is important, with the enteral route preferred. Parenteral nutrition should begin early if the enteral route is not feasible.

Ischemic Colitis

Ischemic colitis is a transient reduction in blood flow to the colon.

Necrosis may occur but is usually limited to the mucosa and submucosa, only occasionally causing full-thickness necrosis necessitating surgery. It occurs mainly in older people (> 60) and is thought to be caused by small-vessel atherosclerosis.

Symptoms are milder and of slower onset than those of acute mesenteric ischemia and consist of left lower quadrant pain followed by rectal bleeding. Diagnosis is made by colonoscopy; angiography or magnetic resonance angiography is not indicated. Treatment is supportive with IV fluids, bowel rest, and antibiotics. Surgery is rarely required. About 5% of patients have a recurrence. Occasionally, strictures develop at the site of the ischemia several weeks later, necessitating surgical resection.

Chapter 12. Esophageal and Swallowing Disorders

Introduction

(See also Esophageal Cancer on p. 186 and Esophageal Atresia on p. 2975.)

The swallowing apparatus consists of the pharynx, upper esophageal (cricopharyngeal) sphincter, the body of the esophagus, and the lower esophageal sphincter (LES). The upper third of the esophagus and the structures proximal to it are composed of skeletal muscle; the distal esophagus and LES are composed of smooth muscle. These components work as an integrated system that transports material from the mouth to the stomach and prevents its reflux into the esophagus. Physical obstruction or disorders that interfere with motor function (motility disorders) can affect the system.

The patient's history suggests the diagnosis almost 80% of the time. The only physical findings in esophageal disorders are cervical and supraclavicular lymphadenopathy caused by metastasis, swellings in the neck caused by large pharyngeal diverticula or thyromegaly, and prolonged swallowing time (the time from the act of swallowing to the sound of the bolus of fluid and air entering the stomach—normally ≤ 12 sec—heard by auscultation with the stethoscope over the epigastrium). Watching the patient swallow may help diagnose aspiration or nasal regurgitation. Most esophageal disorders require specific tests for diagnosis.

Dysphagia

Dysphagia is difficulty swallowing. The condition results from impeded transport of liquids, solids, or both from the pharynx to the stomach. Dysphagia should not be confused with globus sensation (see p. 78), a feeling of having a lump in the throat, which is unrelated to swallowing and occurs without impaired transport.

Complications: Dysphagia can lead to tracheal aspiration of ingested material, oral secretions, or both. Aspiration can cause acute pneumonia; recurrent aspiration may eventually lead to chronic lung disease. Prolonged dysphagia often leads to inadequate nutrition and weight loss.

Etiology

Dysphagia is classified as oropharyngeal or esophageal, depending on where it occurs.

Oropharyngeal dysphagia: Oropharyngeal dysphagia is difficulty emptying material from the oropharynx into the esophagus; it results from abnormal function proximal to the esophagus. Patients complain of difficulty initiating swallowing, nasal regurgitation, and tracheal aspiration followed by coughing.

Most often, oropharyngeal dysphagia occurs in patients with neurologic conditions or muscular disorders that affect skeletal muscles (see Table 12-1).

Esophageal dysphagia: Esophageal dysphagia is difficulty passing food down the esophagus. It results from either a motility disorder or a mechanical obstruction (see Table 12-2).

Evaluation

History: History of present illness begins with duration of symptoms and acuity of onset. Patients should describe what substances cause difficulty and where they feel the disturbance is located. Specific concerns include whether patients have difficulty swallowing solids, liquids, or both; whether food comes out their nose; whether they drool or have food spill from their mouth; and whether they cough or choke while eating.

[**Table 12-1.** Some Causes of Oropharyngeal Dysphagia]

Review of symptoms should focus on symptoms suggestive of neuromuscular, GI, and connective tissue disorders and on the presence of complications. Important neuromuscular symptoms include weakness and easy fatigability, gait or balance disturbance, tremor, and difficulty speaking. Important GI symptoms include heartburn or other chest discomfort suggestive of reflux. Symptoms of connective tissue disorders include muscle and joint pain, Raynaud's phenomenon, and skin changes (eg, rash, swelling, thickening).

Past medical history should ascertain known diseases that may cause dysphagia (see Tables 12-1 and 12-2).

Physical examination: Examination focuses on findings suggestive of neuromuscular, GI, and connective tissue disorders and on the presence of complications.

General examination should evaluate nutritional status (including body weight). A complete neurologic examination is essential, with attention to any resting tremor, the cranial nerves (note the gag reflex may normally be absent; this absence is thus not a good marker of swallowing dysfunction), and muscle strength. Patients who describe easy fatigability should be observed performing a repetitive action (eg, blinking, counting aloud) for a rapid decrement in performance.

[**Table 12-2.** Some Causes of Esophageal Dysphagia]

The patient's gait should be observed, and balance should be tested. Skin is examined for rash and thickening or texture changes, particularly on the fingertips. Muscles are inspected for wasting and fasciculations and are palpated for tenderness. The neck is evaluated for thyromegaly or other mass.

Red flags: Any dysphagia is of concern, but certain findings are more urgent:

• Symptoms of complete obstruction (eg, drooling, inability to swallow anything)

• Dysphagia resulting in weight loss

• New focal neurologic deficit, particularly any objective weakness

Interpretation of findings: Dysphagia that occurs in conjunction with an acute neurologic event is likely the result of that event; new dysphagia in a patient with a stable, long-standing neurologic disorder may have another etiology. Dysphagia for solids alone suggests mechanical obstruction; however, a problem with both solids and liquids is nonspecific. Drooling and spilling food from the mouth while eating or nasal regurgitation suggests an oropharyngeal disorder. Regurgitation of a small amount of food on lateral compression of the neck is virtually diagnostic of pharyngeal diverticulum.

Patients who complain of difficulty getting food to leave the mouth or of food sticking in the lower esophagus are usually correct about the condition's location; the sensation of dysphagia in the upper esophagus is less specific.

Many findings suggest specific disorders (see Table 12-3) but are of varying sensitivity and specificity and thus do not rule in or out a given cause; however, they can guide testing.

Testing: A barium swallow (with a solid bolus, usually a marshmallow or tablet) should be done. If this test shows obstruction, endoscopy (and possibly biopsy) should be done to rule out malignancy. If the barium swallow is negative or suggestive of a motility disorder, esophageal motility studies should be done. Other tests for specific causes are done as suggested by findings.

Treatment

Treatment is directed at the specific cause. If complete obstruction occurs, emergent upper endoscopy is essential. If a stricture, ring, or web is found, careful endoscopic dilation is performed. Pending resolution,

patients with oropharyngeal dysphagia may benefit

[Table 12-3. Some Helpful Findings in Dysphagia]

from evaluation by a rehabilitation specialist. Sometimes patients benefit from changing head position while eating, retraining the swallowing muscles, doing exercises that improve the ability to accommodate a food bolus in the oral cavity, or doing strength and coordination exercises for the tongue. Patients with severe dysphagia and recurrent aspiration may require a gastrostomy tube.

Geriatrics Essentials

Chewing, swallowing, tasting, and communicating require intact, coordinated neuromuscular function in the mouth, face, and neck. Oral motor function in particular declines measurably with aging, even in healthy people. Decline in function may have many manifestations:

- Reduction in masticatory muscle strength and coordination is common, especially among patients with partial or complete dentures, and may lead to a tendency to swallow larger food particles, which can increase the risk of choking or aspiration.

- Drooping of the lower face and lips caused by decreased circumoral muscle tone and, in edentulous people, reduced bone support, is an aesthetic concern and can lead to drooling, spilling of food and liquids, and difficulty closing the lips while eating, sleeping, or resting. Sialorrhea (saliva leakage) is often the first symptom.

- Swallowing difficulties increase. It takes longer to move food from mouth to oropharynx, which increases the likelihood of aspiration.

After age-related changes, the most common causes of oral motor disorders are neuromuscular disorders (eg, cranial neuropathies caused by diabetes, stroke, Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis). Iatrogenic causes also contribute. Drugs (eg, anticholinergics, diuretics), radiation therapy to the head and neck, and chemotherapy can greatly impair saliva production. Hyposalivation is a major cause of delayed and impaired swallowing.

Oral motor dysfunction is best managed with a multidisciplinary approach. Coordinated referrals to specialists in prosthetic dentistry, rehabilitative medicine, speech pathology, otolaryngology, and gastroenterology may be needed.

Key Points

- All patients complaining of esophageal dysphagia should undergo upper endoscopy to rule out cancer.

- If the upper endoscopy is normal, biopsies should be obtained to rule out eosinophilic esophagitis.

- Treatment is geared toward the cause.

Cricopharyngeal Incoordination

In cricopharyngeal incoordination, the cricopharyngeal muscle (the upper esophageal sphincter) is uncoordinated. It can cause a Zenker's diverticulum (see p. 125). Repeated aspiration of material from the diverticulum can lead to chronic lung disease. The condition can be treated by surgical section of the cricopharyngeal muscle.

Obstructive Disorders

(See also Benign Esophageal Tumors and Esophageal Cancer on p. 186.)

Lower Esophageal Ring

(Schatzki's Ring, B Ring)

A lower esophageal ring is a 2- to 4-mm mucosal stricture, probably congenital, causing a ringlike narrowing of the distal esophagus at the squamocolumnar junction.

These rings cause intermittent dysphagia for solids. This symptom can begin at any age but usually does not begin until after age 25. The swallowing difficulty comes and goes and is especially aggravated by meat and dry bread. Symptoms usually occur only when the esophageal lumen is < 12 mm in diameter and never when it is > 20 mm. If the distal esophagus is adequately distended, barium x-rays usually show the ring. Instructing the patient to chew food thoroughly is usually the only treatment required in wider rings, but narrow-lumen rings require dilation by endoscopy or bougienage. Surgical resection is rarely required.

Esophageal Web

(Plummer-Vinson Syndrome; Paterson-Kelly Syndrome; Sideropenic Dysphagia)

An esophageal web is a thin mucosal membrane that grows across the lumen.

Rarely, webs develop in patients with untreated severe iron-deficiency anemia; they develop even more rarely in patients without anemia. Webs usually occur in the upper esophagus, causing dysphagia for solids. They are best diagnosed by barium swallow. Webs resolve with treatment of the anemia but can be easily ruptured during esophagoscopy.

Dysphagia Lusoria

Dysphagia lusoria is caused by compression of the esophagus from any of several congenital vascular abnormalities.

The vascular abnormality is usually an aberrant right subclavian artery arising from the left side of the aortic arch, a double aortic arch, or a right aortic arch with left ligamentum arteriosum. The dysphagia may develop in childhood or later in life as a result of arteriosclerotic changes in the aberrant vessel. Barium swallow shows the extrinsic compression, but arteriography is necessary for absolute diagnosis. Most patients require no treatment, but surgical repair is sometimes done.

Motility Disorders

Achalasia

(Cardiospasm; Esophageal Aperistalsis; Megaesophagus)

Achalasia is a neurogenic esophageal motility disorder characterized by impaired esophageal peristalsis, a lack of lower esophageal sphincter relaxation during swallowing, and an elevation of lower esophageal sphincter resting pressure. Symptoms are slowly progressive dysphagia, usually to both liquids and solids, and regurgitation of undigested food. Evaluation typically includes barium swallow, endoscopy, and sometimes manometry. Treatments include dilation, chemical denervation, and surgical myotomy.

Achalasia is thought to be caused by a loss of ganglion cells in the myenteric plexus of the esophagus, resulting in denervation of esophageal muscle. Etiology of the denervation is unknown, although a viral cause is suspected, and certain tumors may cause achalasia either by direct obstruction or as a paraneoplastic process. Chagas disease, which causes destruction of autonomic ganglia, may result in achalasia.

Increased pressure at the lower esophageal sphincter (LES) causes obstruction with secondary dilation of the esophagus. Esophageal retention of undigested food is common.

Symptoms and Signs

Achalasia occurs at any age but usually begins between ages 20 and 60. Onset is insidious, and progression is gradual over months or years. Dysphagia for both solids and liquids is the major symptom. Nocturnal regurgitation of undigested food occurs in about 33% of patients and may cause cough and pulmonary aspiration. Chest pain is less common but may occur on swallowing or spontaneously. Mild to moderate weight loss occurs; when weight loss is pronounced, particularly in elderly patients whose symptoms of dysphagia developed rapidly, achalasia secondary to a tumor of the gastroesophageal junction should be considered.

Diagnosis

• Barium swallow

• Esophageal manometry

The preferred test is barium swallow, which shows absence of progressive peristaltic contractions during swallowing. The esophagus is dilated, often enormously, but is narrowed and beaklike at the LES. If esophagoscopy is done, there is dilation but no obstructing lesion. The esophagoscope usually passes readily into the stomach; resistance raises the possibility of an inapparent cancer or stricture. To exclude cancer, a retroflexed view of the gastric cardia, biopsies, and brushings for cytology should be obtained. Esophageal manometry is usually done and typically shows aperistalsis, increased LES pressure, and incomplete sphincteric relaxation during swallowing.

Achalasia must be differentiated from a distal stenosing carcinoma and a peptic stricture, particularly in patients with systemic sclerosis (see p. 309), in whom esophageal manometry may also show aperistalsis. Systemic sclerosis is usually accompanied by a history of Raynaud's phenomenon and symptoms of gastroesophageal reflux disease (GERD), due to low or absent LES pressure.

Achalasia due to cancer at the gastroesophageal junction can be diagnosed by CT of the chest and abdomen or by endoscopic ultrasound.

Prognosis

Pulmonary aspiration and the presence of cancer are the determining prognostic factors. Nocturnal regurgitation and coughing suggest aspiration. Pulmonary complications secondary to aspiration are difficult to manage. Incidence of esophageal cancer in patients with achalasia may be increased; this point is controversial.

Treatment

• Balloon dilation of the LES

• Alternatively, botulinum toxin injection or surgical myotomy

No therapy restores peristalsis; treatment aims at reducing the pressure (and thus the obstruction) at the LES. Pneumatic balloon dilation of the LES is indicated initially. Results are satisfactory in about 85% of patients, but repeated dilations may be needed. Esophageal rupture and secondary mediastinitis requiring surgical repair occur in < 2% of patients. Nitrates (eg, isosorbide dinitrate 5 to 10 mg sublingually before meals) or Ca channel blockers (eg, nifedipine 10 mg po tid) are of limited effectiveness but may reduce LES pressure enough to prolong the time between dilations.

Achalasia can also be treated by chemical denervation of cholinergic nerves in the distal esophagus by direct injection of botulinum toxin type A into the LES. Clinical improvement occurs in 70 to 80% of patients, but results may last only 6 mo to 1 yr.

A Heller myotomy, in which the muscular fibers in the LES are cut, is usually reserved for patients who do not respond to dilation; its success rate is about 85%. It can be done via laparoscopy or thoracoscopy and may be a viable alternative to dilation as primary therapy. Symptomatic GERD occurs after surgery in

about 15% of patients.

Symptomatic Diffuse Esophageal Spasm

(Spastic Pseudodiverticulosis; Rosary Bead or Corkscrew Esophagus)

Symptomatic diffuse esophageal spasm is part of a spectrum of motility disorders characterized variously by nonpropulsive contractions, hyperdynamic contractions, or elevated lower esophageal sphincter pressure. Symptoms are chest pain and sometimes dysphagia. Diagnosis is by barium swallow or manometry. Treatment is difficult but includes nitrates, Ca channel blockers, botulinum toxin injection, and antireflux therapy.

Abnormalities in esophageal motility correlate poorly with patient symptoms; similar abnormalities may cause different or no symptoms in different people. Furthermore, neither symptoms nor abnormal contractions are definitively associated with histopathologic abnormalities of the esophagus.

Symptoms and Signs

Diffuse esophageal spasm typically causes substernal chest pain with dysphagia for both liquids and solids. The pain may waken the patient from sleep. Very hot or cold liquids may aggravate the pain. Over many years, this disorder may evolve into achalasia.

Esophageal spasms can cause severe pain without dysphagia. This pain is often described as a substernal squeezing pain and may occur in association with exercise. Such pain may be indistinguishable from angina pectoris.

Some patients have symptoms that combine those of achalasia and diffuse spasm. One such combination has been called vigorous achalasia because it features both the food retention and aspiration of achalasia and the severe pain and spasm of diffuse spasm.

Diagnosis

• Barium swallow

• Esophageal manometry

• Possibly testing for coronary ischemia

Alternative diagnoses include coronary ischemia. Definitive confirmation of an esophageal origin for symptoms is difficult. Barium swallow may show poor progression of a bolus and disordered, simultaneous contractions or tertiary contractions. Severe spasms may mimic the radiographic appearance of diverticula but vary in size and position. Esophageal manometry (see p. 96) provides the most specific description of the spasms. Contractions are usually simultaneous, prolonged or multiphasic, and possibly of very high amplitude ("nutcracker esophagus"). However, spasms may not occur during testing. Lower esophageal sphincter (LES) pressure elevation or impaired relaxation is present in 30% of patients. Esophageal scintigraphy and provocative tests with drugs (eg, edrophonium chloride 10 mg IV) have not proved helpful.

Treatment

• Ca channel blockers

• Botulinum toxin injection

Esophageal spasms are often difficult to treat, and controlled studies of treatment methods are lacking. Anticholinergics, nitroglycerin, and long-acting nitrates have had limited success. Ca channel blockers given orally (eg, verapamil 80 mg tid, nifedipine 10 mg tid) may be useful, as may injection of botulinum toxin type A into the LES.

Medical management is usually sufficient, but pneumatic dilation and bougienage, or even surgical myotomy along the full length of the esophagus, may be tried in intractable cases.

Esophageal Diverticula

An esophageal diverticulum is an outpouching of mucosa through the muscular layer of the esophagus. It can be asymptomatic or cause dysphagia and regurgitation. Diagnosis is made by barium swallow; surgical repair is rarely required.

There are several types of esophageal diverticula, each of different origin.

- Zenker's (pharyngeal) diverticula are posterior outpouchings of mucosa and submucosa through the cricopharyngeal muscle, probably resulting from an incoordination between pharyngeal propulsion and cricopharyngeal relaxation.

- Midesophageal (traction) diverticula are caused by traction from mediastinal inflammatory lesions or, secondarily, by motility disorders.

- Epiphrenic diverticula occur just above the diaphragm and usually accompany a motility disorder (achalasia, diffuse esophageal spasm).

Symptoms and Signs

A Zenker's diverticulum fills with food that might be regurgitated when the patient bends or lies down. Aspiration pneumonitis may result if regurgitation is nocturnal. Rarely, the pouch becomes large, causing dysphagia and sometimes a palpable neck mass.

Traction and epiphrenic diverticula are rarely symptomatic, although their underlying cause may be.

Diagnosis

All diverticula are diagnosed by videotaped barium swallow.

Treatment

- Usually none

- Sometimes surgical resection

Specific treatment is usually not required, although resection is occasionally necessary for large or symptomatic diverticula. Diverticula associated with motility disorders require treatment of the primary disorder. For example, case reports suggest doing a cricopharyngeal myotomy when resecting a Zenker's diverticulum.

Gastroesophageal Reflux Disease

Incompetence of the lower esophageal sphincter allows reflux of gastric contents into the esophagus, causing burning pain. Prolonged reflux may lead to esophagitis, stricture, and rarely metaplasia or cancer. Diagnosis is clinical, sometimes with endoscopy, with or without acid testing. Treatment involves lifestyle modification, acid suppression using proton pump inhibitors, and sometimes surgical repair.

Gastroesophageal reflux disease (GERD) is common, occurring in 30 to 40% of adults. It also occurs frequently in infants, typically beginning at birth.

Etiology

The presence of reflux implies lower esophageal sphincter (LES) incompetence, which may result from a generalized loss of intrinsic sphincter tone or from recurrent inappropriate transient relaxations (ie, unrelated to swallowing). Transient LES relaxations are triggered by gastric distention or subthreshold pharyngeal stimulation.

Factors that contribute to the competence of the gastroesophageal junction include the angle of the cardioesophageal junction, the action of the diaphragm, and gravity (ie, an upright position). Factors contributing to reflux include weight gain, fatty foods, caffeinated or carbonated beverages, alcohol, tobacco smoking, and drugs. Drugs that lower LES pressure include anticholinergics, antihistamines, tricyclic antidepressants, Ca channel blockers, progesterone, and nitrates.

Complications: GERD may lead to esophagitis, peptic esophageal ulcer, esophageal stricture, Barrett's esophagus, and esophageal adenocarcinoma (see p. 186). Factors that contribute to the development of esophagitis include the caustic nature of the refluxate, the inability to clear the refluxate from the esophagus, the volume of gastric contents, and local mucosal protective functions. Some patients, particularly infants, aspirate the reflux material.

Symptoms and Signs

The most prominent symptom of GERD is heartburn, with or without regurgitation of gastric contents into the mouth. Infants present with vomiting, irritability, anorexia, and sometimes symptoms of chronic aspiration. Both adults and infants with chronic aspiration may have cough, hoarseness, or wheezing.

Esophagitis may cause odynophagia and even esophageal hemorrhage, which is usually occult but can be massive. Peptic stricture causes a gradually progressive dysphagia for solid foods. Peptic esophageal ulcers cause the same type of pain as gastric or duodenal ulcers, but the pain is usually localized to the xiphoid or high substernal region. Peptic esophageal ulcers heal slowly, tend to recur, and usually leave a stricture on healing.

Diagnosis

• Clinical diagnosis

• Endoscopy for those not responding to empiric treatment

• 24-h pH testing for those with typical symptoms but normal endoscopy

A detailed history points to the diagnosis. Patients with typical symptoms of GERD may be given a trial of therapy. Patients who do not improve, or have long-standing symptoms or symptoms of complications, should be studied. Endoscopy, with cytologic washings and biopsy of abnormal areas, is the test of choice. Endoscopic biopsy is the only test that consistently detects the columnar mucosal changes of Barrett's esophagus. Patients with unremarkable endoscopy findings who have typical symptoms despite treatment with proton pump inhibitors should undergo 24-h pH testing (see p. 95). Although barium swallow readily shows esophageal ulcers and peptic strictures, it is less useful for mild to moderate reflux; in addition, most patients with abnormalities require subsequent endoscopy. Esophageal manometry may be used to guide pH probe placement and to evaluate esophageal peristalsis before surgical treatment.

Treatment

• Head of bed elevated

• Coffee, alcohol, fats, and smoking avoided

• Proton pump inhibitors

Management of uncomplicated GERD consists of elevating the head of the bed about 15 cm (6 in) and avoiding the following: eating within 2 to 3 h of bedtime, strong stimulants of acid secretion (eg, coffee, alcohol), certain drugs (eg, anticholinergics), specific foods (eg, fats, chocolate), and smoking.

Drug therapy is with a proton pump inhibitor. For example, adults can be given omeprazole 20 mg, lansoprazole 30 mg, or esomeprazole 40 mg 30 min before breakfast. In some cases, proton pump inhibitors may be given bid. Infants and children may be given these drugs at an appropriate lower single daily dose (ie, omeprazole 20 mg in children > 3 yr, 10 mg in children < 3 yr; lansoprazole 15 mg in children ≤ 30 kg, 30 mg in children > 30 kg). These drugs may be continued long-term, but the dose should be adjusted to the minimum required to prevent symptoms. H_2 blockers (eg, ranitidine 150 mg at bedtime) or promotility agents (eg, metoclopramide 10 mg po 30 min before meals and at bedtime) are less effective.

Antireflux surgery (usually via laparoscopy) is done on patients with serious esophagitis, large hiatal hernias, hemorrhage, stricture, or ulcers. Esophageal strictures are managed by repeated balloon dilation.

Barrett's esophagus may or may not regress with medical or surgical therapy. Because Barrett's esophagus is a precursor to adenocarcinoma, endoscopic surveillance for malignant transformation is recommended every 1 to 2 yr. Surveillance has uncertain cost-effectiveness in patients with low-grade dysplasia but is important in high-grade dysplasia in patients who are unable to undergo surgical resection. Alternatively, Barrett's esophagus may be treated with endoscopic mucosal resection, photodynamic therapy, cryotherapy, or laser ablation.

Hiatus Hernia

Hiatus hernia is a protrusion of the stomach through the diaphragmatic hiatus. Most hernias are asymptomatic, but an increased incidence of acid reflux may lead to symptoms of gastroesophageal reflux disease (GERD). Diagnosis is by barium swallow. Treatment is directed at symptoms of GERD if present.

Etiology

Etiology is usually unknown, but a hiatus hernia is thought to be acquired through stretching of the fascial attachments between the esophagus and diaphragm at the hiatus (the opening through which the esophagus traverses the diaphragm).

Pathophysiology

In a sliding hiatus hernia (the most common type), the gastroesophageal junction and a portion of the stomach are above the diaphragm. In a paraesophageal hiatus hernia, the gastroesophageal junction is in the normal location, but a portion of the stomach is adjacent to the esophagus in the diaphragmatic hiatus. Hernias may also occur through other parts of the diaphragm (see p. 2977).

A sliding hiatus hernia is common and is an incidental finding on x-ray in > 40% of the population; therefore, the relationship of hernia to symptoms is unclear. Although most patients with GERD have some degree of hiatus hernia, < 50% of patients with hiatus hernia have GERD.

Symptoms and Signs

Most patients with a sliding hiatus hernia are asymptomatic, but chest pain and other reflux symptoms can occur. A paraesophageal hiatus hernia is generally asymptomatic but, unlike a sliding hiatus hernia, may incarcerate and strangulate. Occult or massive GI hemorrhage may occur with either type.

Diagnosis

• Barium swallow

A large hiatus hernia is often discovered incidentally on chest x-ray. Smaller hernias are diagnosed with a barium swallow.

Treatment

• Sometimes a proton pump inhibitor

An asymptomatic sliding hiatus hernia requires no specific therapy. Patients with accompanying GERD should be treated with a proton pump inhibitor. A paraesophageal hernia should be reduced surgically because of the risk of strangulation.

Infectious Esophageal Disorders

Esophageal infection occurs mainly in patients with impaired host defenses. Primary agents include *Candida albicans*, herpes simplex virus, and cytomegalovirus. Symptoms are odynophagia and chest pain. Diagnosis is by endoscopic visualization and culture. Treatment is with antifungal or antiviral drugs.

Esophageal infection is rare in patients with normal host defenses. Primary esophageal defenses include saliva, esophageal motility, and cellular immunity. Thus, at-risk patients include those with AIDS, organ transplants, alcoholism, diabetes, undernutrition, cancer, and motility disorders. *Candida* infection may occur in any of these patients. Herpes simplex virus (HSV) and cytomegalovirus (CMV) infections occur mainly in AIDS and transplant patients.

Candida: Patients with *Candida* esophagitis usually complain of odynophagia and, less commonly, dysphagia. About two thirds of patients have signs of oral thrush (thus its absence does not exclude esophageal involvement). Patients with odynophagia and typical thrush may be given empiric treatment, but if significant improvement does not occur in 5 to 7 days, endoscopic evaluation is required. Barium swallow is less accurate.

Treatment is with fluconazole 200 mg po or IV for one dose, then 100 mg po or IV q 24 h for 14 to 21 days. Alternatives include the azoles (eg, itraconazole, voriconazole, ketoconazole) or echinocandins (eg, caspofungin). Topical therapy has no role.

HSV and CMV: These infections are equally likely in transplant patients, but HSV occurs early after transplantation (reactivation) and CMV occurs 2 to 6 mo after. Among AIDS patients, CMV is much more common than HSV, and viral esophagitis occurs mainly when the CD4+ count is < 200/µL. Severe odynophagia results from either infection.

Endoscopy, with cytology or biopsy, is usually necessary for diagnosis. HSV is treated with IV acyclovir 5 mg/kg q 8 h for 7 days or valacyclovir 1 g po tid. CMV is treated with ganciclovir 5 mg/kg IV q 12 h for 14 to 21 days with maintenance at 5 mg/kg IV 5 days/wk in immunocompromised patients. Alternatives include foscarnet and cidofovir.

Mallory-Weiss Syndrome

Mallory-Weiss syndrome is a nonpenetrating mucosal laceration of the distal esophagus and proximal stomach caused by vomiting, retching, or hiccuping.

Initially described in alcoholics, Mallory-Weiss syndrome can occur in any patient who vomits forcefully. It is the cause of about 5% of episodes of upper GI hemorrhage. Most episodes of bleeding stop spontaneously; severe bleeding occurs in about 10% of patients who require significant intervention, such as transfusion or endoscopic hemostasis (by injection of ethanol, polidocanol, or epinephrine or by electrocautery). Intra-arterial infusion of pitressin or therapeutic embolization into the left gastric artery during angiography may also be used to control bleeding. Surgical repair is rarely required.

Esophageal Rupture

Esophageal rupture may be iatrogenic during endoscopic procedures or other instrumentation or may be spontaneous (Boerhaave's syndrome). Patients are seriously ill, with symptoms of mediastinitis. Diagnosis is by esophagography with a water-soluble contrast agent. Immediate

surgical repair and drainage are required.

Endoscopic procedures are the primary cause of esophageal rupture, but spontaneous rupture may occur, typically related to vomiting, retching, or swallowing a large food bolus. The most common site of rupture is the distal esophagus on the left side. Acid and other stomach contents cause a fulminant mediastinitis and shock. Pneumomediastinum is common.

Symptoms and Signs

Symptoms include chest and abdominal pain, vomiting, hematemesis, and shock. Subcutaneous emphysema is palpable in about 30% of patients. Mediastinal crunch (Hamman's sign), a crackling sound synchronous with the heartbeat, may be present.

Diagnosis

• Chest and abdominal x-rays

• Esophagography

Chest and abdominal x-rays showing mediastinal air, pleural effusion, or mediastinal widening suggest the diagnosis. Diagnosis is confirmed by esophagography with a water-soluble contrast agent, which avoids potential mediastinal irritation from barium. CT of the thorax detects mediastinal air and fluid but does not localize the perforation well. Endoscopy may miss a small perforation.

Treatment

• Surgical repair

Pending surgical repair, patients should receive broad-spectrum antibiotics (eg, gentamicin plus metronidazole or piperacillin/tazobactam) and fluid resuscitation as needed for shock. Even with treatment, mortality is high.

Chapter 13. Gastritis and Peptic Ulcer Disease

Introduction

Acid is secreted by parietal cells in the proximal two thirds (body) of the stomach. Gastric acid aids digestion by creating the optimal pH for pepsin and gastric lipase and by stimulating pancreatic bicarbonate secretion. Acid secretion is initiated by food: the thought, smell, or taste of food effects vagal stimulation of the gastrin-secreting G cells located in the distal one third (antrum) of the stomach. The arrival of protein to the stomach further stimulates gastrin output. Circulating gastrin triggers the release of histamine from enterochromaffin-like cells in the body of the stomach. Histamine stimulates the parietal cells via their H_2 receptors. The parietal cells secrete acid, and the resulting drop in pH causes the antral D cells to release somatostatin, which inhibits gastrin release (negative feedback control).

Acid secretion is present at birth and reaches adult levels (on a weight basis) by age 2. There is a decline in acid output in elderly patients who develop chronic gastritis, but acid output is otherwise maintained throughout life.

Normally, the GI mucosa is protected by several distinct mechanisms: (1) Mucosal production of mucus and HCO_3 creates a pH gradient from the gastric lumen (low pH) to the mucosa (neutral pH). The mucus serves as a barrier to the diffusion of acid and pepsin. (2) Epithelial cells remove excess hydrogen ions (H^+) via membrane transport systems and have tight junctions, which prevent back diffusion of H^+ ions. (3) Mucosal blood flow removes excess acid that has diffused across the epithelial layer. Several growth factors (eg, epidermal growth factor, insulin-like growth factor I) and prostaglandins have been linked to mucosal repair and maintenance of mucosal integrity.

Factors that interfere with these mucosal defenses (particularly NSAIDs and *Helicobacter pylori* infection) predispose to gastritis and peptic ulcer disease.

NSAIDs promote mucosal inflammation and ulcer formation (sometimes with GI bleeding) both topically and systemically. By inhibiting prostaglandin production via blockage of the enzyme cyclooxygenase (COX), NSAIDs reduce gastric blood flow, reduce mucus and HCO_3 secretion, and decrease cell repair and replication. Also, because NSAIDs are weak acids and are nonionized at gastric pH, they diffuse freely across the mucus barrier into gastric epithelial cells, where H^+ ions are liberated, leading to cellular damage. Because gastric prostaglandin production involves the COX-1 isoform, NSAIDs that are selective COX-2 inhibitors have fewer adverse gastric effects than other NSAIDs.

Helicobacter pylori Infection

***H. pylori* is a common gastric pathogen that causes gastritis, peptic ulcer disease, gastric adenocarcinoma, and low-grade gastric lymphoma. Infection may be asymptomatic or result in varying degrees of dyspepsia. Diagnosis is by urea breath test and testing of endoscopic biopsy samples. Treatment is with a proton pump inhibitor plus two antibiotics.**

H. pylori is a spiral-shaped, gram-negative organism that has adapted to thrive in acid. In developing countries, it commonly causes chronic infections and is usually acquired during childhood. In the US, infection is less common among children but increases with age: by age 60, about 50% of people are infected. Infection is most common among blacks, Hispanics, and Asians.

The organism has been cultured from stool, saliva, and dental plaque, which suggests oral-oral or fecal-oral transmission. Infections tend to cluster in families and in residents of custodial institutions. Nurses and gastroenterologists seem to be at high risk because bacteria can be transmitted by improperly disinfected endoscopes.

Pathophysiology

Effects of *H. pylori* infection vary depending on the location within the stomach. Antral-predominant

infection results in increased gastrin production, probably via local impairment of somatostatin release. Resultant hypersecretion of acid predisposes to prepyloric and duodenal ulcer. Body-predominant infection leads to gastric atrophy and decreased acid production, possibly via increased local production of IL-1β. Patients with body-predominant infection are predisposed to gastric ulcer and adenocarcinoma. Some patients have mixed infection of both antrum and body with varying clinical effects. Many patients with *H. pylori* infection have no noticeable clinical effects.

Ammonia produced by *H. pylori* enables the organism to survive in the acidic environment of the stomach and may erode the mucus barrier. Cytotoxins and mucolytic enzymes (eg, bacterial protease, lipase) produced by *H. pylori* may play a role in mucosal damage and subsequent ulcerogenesis.

Infected people are 3 to 6 times more likely to develop stomach cancer. *H. pylori* infection is associated with intestinal-type adenocarcinoma of the gastric body and antrum but not cancer of the gastric cardia. Other associated cancers include gastric lymphoma and mucosa-associated lymphoid tissue (MALT) lymphoma, a monoclonally restricted B-cell tumor.

Diagnosis

• For initial diagnosis: Serologic tests

• For confirmation of cure: Urea breath test or stool antigen assay

Screening of asymptomatic patients is not warranted. Tests are done during evaluation for peptic ulcer and gastritis. Posttreatment testing is typically done to confirm eradication of the organism. Different tests are preferred for initial diagnosis and posttreatment.

Noninvasive tests: Laboratory and office-based serologic assays for antibodies to *H. pylori* have sensitivity and specificity of > 85% and are considered the noninvasive tests of choice for initial documentation of *H. pylori* infection. However, because qualitative assays remain positive for up to 3 yr after successful treatment and because quantitative antibody levels do not decline significantly for 6 to 12 mo after treatment, serologic assays are not usually used to assess cure.

Urea breath tests use an oral dose of ^{13}C- or ^{14}C-labeled urea. In an infected patient, the organism metabolizes the urea and liberates labeled CO_2, which is exhaled and can be quantified in breath samples taken 20 to 30 min after ingestion of the urea. Sensitivity and specificity are > 90%. Urea breath tests are well suited for confirming eradication of the organism after therapy. False-negative results are possible with recent antibiotic use or concomitant proton pump inhibitor therapy; therefore, follow-up testing should be delayed ≥ 4 wk after antibiotic therapy and 1 wk after proton pump inhibitor therapy. H_2 blockers do not affect the test.

Stool antigen assays seem to have a sensitivity and specificity near that of urea breath tests, particularly for initial diagnosis; an office-based test is under development.

Invasive tests: Endoscopy is used to obtain mucosal biopsy samples for a rapid urease test (RUT) or histologic staining. Bacterial culture is of limited use because of the fastidious nature of the organism. Endoscopy is not recommended solely for diagnosis of *H. pylori;* noninvasive tests are preferred unless endoscopy is indicated for other reasons.

The RUT, in which presence of bacterial urease in the biopsy sample causes a color change on a special medium, is the diagnostic method of choice on tissue samples. Histologic staining of biopsy samples should be done for patients with negative RUT results but suspicious clinical findings, recent antibiotic use, or treatment with proton pump inhibitors. RUT and histologic staining each have a sensitivity and specificity of > 90%.

Treatment

• Antibiotics (various regimens) plus a proton pump inhibitor

Patients with complications (eg, gastritis, ulcer, cancer) should have the organism eradicated. Eradication of *H. pylori* can even cure some cases of MALT lymphoma (but not other infection-related cancers). Treatment of asymptomatic infection has been controversial, but the recognition of the role of *H. pylori* in cancer has led to a recommendation for treatment. Vaccines, both preventive and therapeutic (ie, as an adjunct to treatment of infected patients), are under development.

H. pylori eradication requires multidrug therapy, typically antibiotics plus acid suppressants. Proton pump inhibitors suppress *H. pylori*, and the increased gastric pH accompanying their use can enhance tissue concentration and efficacy of antimicrobials, creating a hostile environment for *H. pylori*.

Triple therapy is recommended. Oral omeprazole 20 mg bid or lansoprazole 30 mg bid, plus clarithromycin 500 mg bid, plus amoxicillin 1 g bid (or, for penicillin-allergic patients, metronidazole 500 mg bid) for 14 days, cures infection in > 95% of cases. This regimen has excellent tolerability. Ranitidine bismuth citrate 400 mg po bid may be substituted for the proton pump inhibitor.

Quadruple therapy with a proton pump inhibitor bid, tetracycline 500 mg and bismuth subsalicylate or subcitrate 525 mg qid, and metronidazole 500 mg tid is also effective but more cumbersome.

Infected patients with duodenal or gastric ulcer require continuation of the acid suppression for at least 4 wk.

Treatment is repeated if *H. pylori* is not eradicated. If two courses are unsuccessful, some authorities recommend endoscopy to obtain cultures for sensitivity testing.

Gastritis

Gastritis is inflammation of the gastric mucosa caused by any of several conditions, including infection (*Helicobacter pylori*), drugs (NSAIDs, alcohol), stress, and autoimmune phenomena (atrophic gastritis). Many cases are asymptomatic, but dyspepsia and GI bleeding sometimes occur. Diagnosis is by endoscopy. Treatment is directed at the cause but often includes acid suppression and, for *H. pylori* infection, antibiotics.

Gastritis is classified as erosive or nonerosive based on the severity of mucosal injury. It is also classified according to the site of involvement (ie, cardia, body, antrum). Gastritis can be further classified histologically as acute or chronic based on the inflammatory cell type. No classification scheme matches perfectly with the pathophysiology; a large degree of overlap exists. Some forms of gastritis involve acid-peptic and *H. pylori* disease. Additionally, the term is often loosely applied to nonspecific (and often undiagnosed) abdominal discomfort and gastroenteritis.

Acute gastritis is characterized by PMN infiltration of the mucosa of the antrum and body.

Chronic gastritis implies some degree of atrophy (with loss of function of the mucosa) or metaplasia. It predominantly involves the antrum (with subsequent loss of G cells and decreased gastrin secretion) or the corpus (with loss of oxyntic glands, leading to reduced acid, pepsin, and intrinsic factor).

Erosive Gastritis

Erosive gastritis is gastric mucosal erosion caused by damage to mucosal defenses. It is typically acute, manifesting with bleeding, but may be subacute or chronic with few or no symptoms. Diagnosis is by endoscopy. Treatment is supportive, with removal of the inciting cause. Certain ICU patients (eg, ventilator-bound, head trauma, burn, multisystem trauma) benefit from prophylaxis with acid suppressants.

Causes of erosive gastritis include NSAIDs, alcohol, stress, and less commonly radiation, viral infection (eg, cytomegalovirus), vascular injury, and direct trauma (eg, nasogastric tubes).

Superficial erosions and punctate mucosal lesions occur. These may develop as soon as 12 h after the

initial insult. Deep erosions, ulcers, and sometimes perforation may occur in severe or untreated cases. Lesions typically occur in the body, but the antrum may also be involved.

Acute stress gastritis, a form of erosive gastritis, occurs in about 5% of critically ill patients. The incidence increases with duration of ICU stay and length of time the patient is not receiving enteral feeding. Pathogenesis likely involves hypoperfusion of the GI mucosa, resulting in impaired mucosal defenses. Patients with head injury or burns may also have increased secretion of acid.

Symptoms and Signs

Patients with mild erosive gastritis are often asymptomatic, although some complain of dyspepsia, nausea, or vomiting. Often, the first sign is hematemesis, melena, or blood in the nasogastric aspirate, usually within 2 to 5 days of the inciting event. Bleeding is usually mild to moderate, although it can be massive if deep ulceration is present, particularly in acute stress gastritis. Acute and chronic erosive gastritis are diagnosed endoscopically.

Diagnosis

Acute and chronic erosive gastritis are diagnosed endoscopically.

Treatment

• For bleeding: Endoscopic hemostasis

• For acid suppression: A proton pump inhibitor or H_2 blocker

In severe gastritis, bleeding is managed with IV fluids and blood transfusion as needed. Endoscopic hemostasis should be attempted, with surgery (total gastrectomy) a fallback procedure. Angiography is unlikely to stop severe gastric bleeding because of the many collateral vessels supplying the stomach. Acid suppression should be started if the patient is not already receiving it.

For milder gastritis, removing the offending agent and using drugs to reduce gastric acidity (see p. 136) may be all that is required.

Prevention

Prophylaxis with acid-suppressive drugs can reduce the incidence of acute stress gastritis. However, it mainly benefits certain high-risk ICU patients, including those with severe burns, CNS trauma, coagulopathy, sepsis, shock, multiple trauma, mechanical ventilation for > 48 h, hepatic or renal failure, multiorgan dysfunction, and history of peptic ulcer or GI bleeding.

Prophylaxis consists of IV H_2 blockers, proton pump inhibitors, or oral antacids to raise intragastric pH > 4.0. Repeated pH measurement and titration of therapy are not required. Early enteral feeding also can decrease the incidence of bleeding.

Acid suppression is not recommended for patients simply taking NSAIDs unless they have previously had an ulcer.

Nonerosive Gastritis

Nonerosive gastritis refers to a variety of histologic abnormalities that are mainly the result of *H. pylori* infection. Most patients are asymptomatic. Diagnosis is by endoscopy. Treatment is eradication of *H. pylori* and sometimes acid suppression.

Pathology

Superficial gastritis: Lymphocytes and plasma cells mixed with neutrophils are the predominant infiltrating inflammatory cells. Inflammation is superficial and may involve the antrum, body, or both. It is

usually not accompanied by atrophy or metaplasia. Prevalence increases with age.

Deep gastritis: Deep gastritis is more likely to be symptomatic (eg, vague dyspepsia). Mononuclear cells and neutrophils infiltrate the entire mucosa to the level of the muscularis, but exudate or crypt abscesses seldom result, as might be expected by such infiltration. Distribution may be patchy. Superficial gastritis may be present, as may partial gland atrophy and metaplasia.

Gastric atrophy: Atrophy of gastric glands may follow in gastritis, most often longstanding antral (sometimes referred to as type B) gastritis. Some patients with gastric atrophy have autoantibodies to parietal cells, usually in association with corpus (type A) gastritis and pernicious anemia.

Atrophy may occur without specific symptoms. Endoscopically, the mucosa may appear normal until atrophy is advanced, when submucosal vascularity may be visible. As atrophy becomes complete, secretion of acid and pepsin diminishes and intrinsic factor may be lost, resulting in vitamin B_{12} malabsorption.

Metaplasia: Two types of metaplasia are common in chronic nonerosive gastritis: mucous gland and intestinal.

Mucous gland metaplasia (pseudopyloric metaplasia) occurs in the setting of severe atrophy of the gastric glands, which are progressively replaced by mucous glands (antral mucosa), especially along the lesser curve. Gastric ulcers may be present (typically at the junction of antral and corpus mucosa), but whether they are the cause or consequence of these metaplastic changes is not clear.

Intestinal metaplasia typically begins in the antrum in response to chronic mucosal injury and may extend to the body. Gastric mucosa cells change to resemble intestinal mucosa—with goblet cells, endocrine (enterochromaffin or enterochromaffin-like) cells, and rudimentary villi—and may even assume functional (absorptive) characteristics. Intestinal metaplasia is classified histologically as complete (most common) or incomplete. With complete metaplasia, gastric mucosa is completely transformed into small-bowel mucosa, both histologically and functionally, with the ability to absorb nutrients and secrete peptides. In incomplete metaplasia, the epithelium assumes a histologic appearance closer to that of the large intestine and frequently exhibits dysplasia. Intestinal metaplasia may lead to stomach cancer.

Symptoms and Signs

Most patients with *H. pylori*-associated gastritis are asymptomatic, although some have mild dyspepsia or other vague symptoms.

Diagnosis

• Endoscopy

Often, the condition is discovered during endoscopy done for other purposes. Testing of asymptomatic patients is not indicated. Once gastritis is identified, testing for *H. pylori* is appropriate.

Treatment

• Eradication of *H. pylori*

• Sometimes acid-suppressive drugs

Treatment of chronic nonerosive gastritis is *H. pylori* eradication (see p. 130). Treatment of asymptomatic patients is somewhat controversial given the high prevalence of *H. pylori*-associated superficial gastritis and the relatively low incidence of clinical sequelae (ie, peptic ulcer disease). However, *H. pylori* is a class J carcinogen; eradication removes the cancer risk. In *H. pylori*-negative patients, treatment is directed at symptoms using acid-suppressive drugs (eg, H_2 blockers, proton pump inhibitors) or antacids.

Postgastrectomy Gastritis

Postgastrectomy gastritis is gastric atrophy developing after partial or subtotal gastrectomy (except in cases of gastrinoma).

Metaplasia of the remaining corpus mucosa is common. The degree of gastritis is usually greatest at the lines of anastomosis.

Several mechanisms are responsible: bile reflux, which is common after such surgery, damages the gastric mucosa; loss of antral gastrin decreases stimulation of parietal and peptic cells, causing atrophy; and vagotomy may result in a loss of vagal trophic action.

There are no specific symptoms of gastritis. Postgastrectomy gastritis often progresses to severe atrophy and achlorhydria. Production of intrinsic factor may cease with resultant vitamin B_{12} deficiency (which may be worsened by bacterial overgrowth in the afferent loop). The relative risk of gastric adenocarcinoma seems to increase 15 to 20 yr after partial gastrectomy; however, given the low absolute incidence of postgastrectomy cancer, routine endoscopic surveillance is probably not cost effective, but upper GI symptoms or anemia in such patients should prompt endoscopy.

Uncommon Gastritis Syndromes

Menetrier's disease: This rare idiopathic disorder affects adults aged 30 to 60 and is more common among men. It manifests as a significant thickening of the gastric folds of the gastric body but not the antrum. Gland atrophy and marked foveolar pit hyperplasia occur, often accompanied by mucous gland metaplasia and increased mucosal thickness with little inflammation. Hypoalbuminemia (the most consistent laboratory abnormality) caused by GI protein loss may be present (protein-losing gastropathy). As the disease progresses, the secretion of acid and pepsin decreases, causing hypochlorhydria.

Symptoms are nonspecific and commonly include epigastric pain, nausea, weight loss, edema, and diarrhea. Differential diagnosis includes (1) lymphoma, in which multiple gastric ulcers may occur; (2) mucosa-associated lymphoid tissue (MALT) lymphoma, with extensive infiltration of monoclonal B lymphocytes; (3) Zollinger-Ellison syndrome with associated gastric fold hypertrophy; and (4) Cronkhite-Canada syndrome, a mucosal polypoid protein-losing syndrome associated with diarrhea. Diagnosis is made by endoscopy with deep mucosal biopsy or full-thickness laparoscopic gastric biopsy.

Various treatments have been used, including anticholinergics, antisecretory drugs, and corticosteroids, but none have proved fully effective. Partial or complete gastric resection may be necessary in cases of severe hypoalbuminemia.

Eosinophilic gastritis: Extensive infiltration of the mucosa, submucosa, and muscle layers with eosinophils often occurs in the antrum. It is usually idiopathic but may result from nematode infestation. Symptoms include nausea, vomiting, and early satiety. Diagnosis is by endoscopic biopsy of involved areas. Corticosteroids can be successful in idiopathic cases; however, if pyloric obstruction develops, surgery may be required.

Mucosa-associated lymphoid tissue (MALT) lymphoma: This rare condition is characterized by massive lymphoid infiltration of the gastric mucosa, which can resemble Menetrier's disease.

Gastritis caused by systemic disorders: Sarcoidosis, TB, amyloidosis, and other granulomatous diseases can cause gastritis, which is seldom of primary importance.

Gastritis caused by physical agents: Radiation and ingestion of corrosives (especially acidic compounds) can cause gastritis. Exposure to > 16 Gy of radiation causes marked deep gastritis, usually involving the antrum more than the corpus. Pyloric stenosis and perforation are possible complications of radiation-induced gastritis.

Infectious (septic) gastritis: Except for *H. pylori* infection, bacterial invasion of the stomach is rare and mainly occurs after ischemia, ingestion of corrosives, or exposure to radiation. On x-ray, gas outlines the

mucosa. The condition can manifest as an acute surgical abdomen and has a very high mortality rate. Surgery is often necessary.

Debilitated or immunocompromised patients may develop viral or fungal gastritis with cytomegalovirus, *Candida*, histoplasmosis, or mucormycosis; these diagnoses should be considered in patients with exudative gastritis, esophagitis, or duodenitis.

Autoimmune Metaplastic Atrophic Gastritis

Autoimmune metaplastic atrophic gastritis (AMAG) is an inherited autoimmune disease that attacks parietal cells, resulting in hypochlorhydria and decreased production of intrinsic factor. Consequences include atrophic gastritis, B_{12} malabsorption, and, frequently, pernicious anemia. Risk of gastric adenocarcinoma increases 3-fold. Diagnosis is by endoscopy. Treatment is with parenteral vitamin B_{12}.

Patients with AMAG have antibodies to parietal cells and their components (which include intrinsic factor and the proton pump H^+,K^+-ATPase). AMAG is inherited as an autosomal dominant trait. Some patients also develop Hashimoto's thyroiditis and 50% have thyroid antibodies; conversely, parietal cell antibodies are found in 30% of patients with thyroiditis.

The lack of intrinsic factor leads to vitamin B_{12} deficiency that can result in a megaloblastic anemia (pernicious anemia—see p. 932) or neurologic symptoms (subacute combined degeneration—see p. 38).

Hypochlorhydria leads to G-cell hyperplasia and elevated serum gastrin levels (often >1000 pg/mL). Elevated gastrin levels lead to enterochromaffin-like cell hyperplasia, which occasionally undergoes transformation to a carcinoid tumor.

In some patients, AMAG may be associated with chronic *Helicobacter pylori* infection, although the relationship is not clear. Gastrectomy and chronic acid suppression with proton pump inhibitors cause similar deficiencies of intrinsic factor secretion.

The areas of atrophic gastritis in the body and fundus may manifest metaplasia. Patients with AMAG have a 3-fold increased relative risk of developing gastric adenocarcinoma.

Diagnosis is made by endoscopic biopsy. Serum B_{12} levels should be obtained. Parietal cell antibodies can be detected but are not measured routinely. The issue of surveillance endoscopy for cancer screening is unsettled; follow-up examinations are unnecessary unless histologic abnormalities (eg, dysplasia) are present on initial biopsy or symptoms develop. No treatment is needed other than parenteral replacement of vitamin B_{12}.

Peptic Ulcer Disease

A peptic ulcer is an erosion in a segment of the GI mucosa, typically in the stomach (gastric ulcer) or the first few centimeters of the duodenum (duodenal ulcer), that penetrates through the muscularis mucosae. Nearly all ulcers are caused by *Helicobacter pylori* infection or NSAID use. Symptoms typically include burning epigastric pain that is often relieved by food. Diagnosis is by endoscopy and testing for *H. pylori*. Treatment involves acid suppression, eradication of *H. pylori* (if present), and avoidance of NSAIDs.

Ulcers may range in size from several millimeters to several centimeters. Ulcers are delineated from erosions by the depth of penetration; erosions are more superficial and do not involve the muscularis mucosae. Ulcers can occur at any age, including infancy and childhood, but are most common among middle-aged adults.

Etiology

H. pylori and NSAIDs disrupt normal mucosal defense and repair, making the mucosa more susceptible to acid. *H. pylori* infection is present in 50 to 70% of patients with duodenal ulcers and 30 to 50% of patients with gastric ulcers. If *H. pylori* is eradicated, only 10% of patients have recurrence of peptic ulcer disease, compared with 70% recurrence in patients treated with acid suppression alone. NSAIDs now account for > 50% of peptic ulcers.

Cigarette smoking is a risk factor for the development of ulcers and their complications. Also, smoking impairs ulcer healing and increases the incidence of recurrence. Risk correlates with the number of cigarettes smoked per day. Although alcohol is a strong promoter of acid secretion, no definitive data link moderate amounts of alcohol to the development or delayed healing of ulcers. Very few patients have hypersecretion of gastrin (Zollinger-Ellison syndrome—see p. 200).

A family history exists in 50 to 60% of children with duodenal ulcer.

Symptoms and Signs

Symptoms depend on ulcer location and patient age; many patients, particularly elderly patients, have few or no symptoms. Pain is most common, often localized to the epigastrium and relieved by food or antacids. The pain is described as burning or gnawing, or sometimes as a sensation of hunger. The course is usually chronic and recurrent. Only about half of patients present with the characteristic pattern of symptoms.

Gastric ulcer symptoms often do not follow a consistent pattern (eg, eating sometimes exacerbates rather than relieves pain). This is especially true for pyloric channel ulcers, which are often associated with symptoms of obstruction (eg, bloating, nausea, vomiting) caused by edema and scarring.

Duodenal ulcers tend to cause more consistent pain. Pain is absent when the patient awakens but appears in mid-morning, is relieved by food, but recurs 2 to 3 h after a meal. Pain that awakens a patient at night is common and is highly suggestive of duodenal ulcer. In neonates, perforation and hemorrhage may be the first manifestation of duodenal ulcer. Hemorrhage may also be the first recognized sign in later infancy and early childhood, although repeated vomiting or evidence of abdominal pain may be a clue.

Diagnosis

• Endoscopy

• Sometimes serum gastrin levels

Diagnosis of peptic ulcer is suggested by patient history and confirmed by endoscopy. Empiric therapy is often begun without definitive diagnosis. However, endoscopy allows for biopsy or cytologic brushing of gastric and esophageal lesions to distinguish between simple ulceration and ulcerating stomach cancer. Stomach cancer may manifest with similar manifestations and must be excluded, especially in patients who are > 45, have lost weight, or report severe or refractory symptoms. The incidence of malignant duodenal ulcer is extremely low, so biopsies of lesions in that area are generally not warranted. Endoscopy can also be used to definitively diagnose *H. pylori* infection, which should be sought when an ulcer is detected.

Gastrin-secreting cancer and Zollinger-Ellison syndrome should be considered when there are multiple ulcers, when ulcers develop in atypical locations (eg, postbulbar) or are refractory to treatment, or when the patient has prominent diarrhea or weight loss. Serum gastrin levels should be measured in these patients.

Complications

Hemorrhage: Mild to severe hemorrhage is the most common complication of peptic ulcer disease. Symptoms include hematemesis (vomiting of fresh blood or "coffee ground" material); passage of bloody stools (hematochezia) or black tarry stools (melena); and weakness, orthostasis, syncope, thirst, and sweating caused by blood loss.

Penetration (confined perforation): A peptic ulcer may penetrate the wall of the stomach. If adhesions prevent leakage into the peritoneal cavity, free penetration is avoided and confined perforation occurs. Still, the ulcer may penetrate into the duodenum and enter the adjacent confined space (lesser sac) or another organ (eg, pancreas, liver). Pain may be intense, persistent, referred to sites other than the abdomen (usually the back when caused by penetration of a posterior duodenal ulcer into the pancreas), and modified by body position. CT or MRI is usually needed to confirm the diagnosis. When therapy does not result in healing, surgery is required.

Free perforation: Ulcers that perforate into the peritoneal cavity unchecked by adhesions are usually located in the anterior wall of the duodenum or, less commonly, in the stomach. The patient presents with an acute abdomen. There is sudden, intense, continuous epigastric pain that spreads rapidly throughout the abdomen, often becoming prominent in the right lower quadrant and at times referred to one or both shoulders. The patient usually lies still because even deep breathing worsens the pain. Palpation of the abdomen is painful, rebound tenderness is prominent, abdominal muscles are rigid (boardlike), and bowel sounds are diminished or absent. Shock may ensue, heralded by increased pulse rate and decreased BP and urine output. Symptoms may be less striking in elderly or moribund patients and those receiving corticosteroids or immunosuppressants.

Diagnosis is confirmed if an x-ray or CT shows free air under the diaphragm or in the peritoneal cavity. Upright views of the chest and abdomen are preferred. The most sensitive view is the lateral x-ray of the chest. Severely ill patients may be unable to sit upright and should have a lateral decubitus x-ray of the abdomen. Failure to detect free air does not exclude the diagnosis.

Immediate surgery is required. The longer the delay, the poorer is the prognosis. When surgery is contraindicated, the alternatives are continuous nasogastric suction and broad-spectrum antibiotics.

Gastric outlet obstruction: Obstruction may be caused by scarring, spasm, or inflammation from an ulcer. Symptoms include recurrent, large-volume vomiting, occurring more frequently at the end of the day and often as late as 6 h after the last meal. Loss of appetite with persistent bloating or fullness after eating also suggests gastric outlet obstruction. Prolonged vomiting may cause weight loss, dehydration, and alkalosis.

If the patient's history suggests obstruction, physical examination, gastric aspiration, or x-rays may provide evidence of retained gastric contents. A succussion splash heard > 6 h after a meal or aspiration of fluid or food residue > 200 mL after an overnight fast suggests gastric retention. If gastric aspiration shows marked retention, the stomach should be emptied and endoscopy done or x-rays taken to determine site, cause, and degree of obstruction.

Edema or spasm caused by an active pyloric channel ulcer is treated with gastric decompression by nasogastric suction and acid suppression (eg, IV H_2 blockers). Dehydration and electrolyte imbalances resulting from protracted vomiting or continued nasogastric suctioning should be vigorously sought and corrected. Prokinetic agents are not indicated. Generally, obstruction resolves within 2 to 5 days of treatment. Prolonged obstruction may result from peptic scarring and may respond to endoscopic pyloric balloon dilation. Surgery is necessary to relieve obstruction in selected cases.

Recurrence: Factors that affect recurrence of ulcer include failure to eradicate *H. pylori*, continued NSAID use, and smoking. Less commonly, a gastrinoma (Zollinger-Ellison syndrome) may be the cause. The 3-yr recurrence rate for gastric and duodenal ulcers is < 10% when *H. pylori* is successfully eradicated but > 50% when it is not. Thus, a patient with recurrent disease should be tested for *H. pylori* and treated again if the tests are positive.

Although long-term treatment with H_2 blockers, proton pump inhibitors, or misoprostol reduces the risk of recurrence, their routine use for this purpose is not recommended. However, patients who require NSAIDs after having had a peptic ulcer are candidates for long-term therapy, as are those with a marginal ulcer or prior perforation or bleeding.

Stomach cancer: Patients with *H. pylori*-associated ulcers have a 3- to 6-fold increased risk of gastric cancer later in life. There is no increased risk of cancer with ulcers of other etiology.

Treatment

• Eradication of *H. pylori* (when present)

• Acid-suppressive drugs

Treatment of gastric and duodenal ulcers requires eradication of *H. pylori* when present (see p. 130) and a reduction of gastric acidity. For duodenal ulcers, it is particularly important to suppress nocturnal acid secretion.

Methods of decreasing acidity include a number of drugs, all of which are effective but which vary in cost, duration of therapy, and convenience of dosing. In addition, mucosal protective drugs (eg, sucralfate) and acid-reducing surgical procedures may be used. Drug therapy is discussed on p. 136.

Adjuncts: Smoking should be stopped, and alcohol consumption stopped or limited to small amounts of dilute alcohol. There is no evidence that changing the diet speeds ulcer healing or prevents recurrence. Thus, many physicians recommend eliminating only foods that cause distress.

Surgery: With current drug therapy, the number of patients requiring surgery has declined dramatically. Indications include perforation, obstruction, uncontrolled or recurrent bleeding, and, although rare, symptoms that do not respond to drug therapy.

Surgery consists of a procedure to reduce acid secretion, often combined with a procedure to ensure gastric drainage. The recommended operation for duodenal ulcer is highly selective, or parietal cell, vagotomy (which is limited to nerves at the gastric body and spares antral innervation, thereby obviating the need for a drainage procedure). This procedure has a very low mortality rate and avoids the morbidity associated with resection and traditional vagotomy. Other acid-reducing surgical procedures include antrectomy, hemigastrectomy, partial gastrectomy, and subtotal gastrectomy (ie, resection of 30 to 90% of the distal stomach). These are typically combined with truncal vagotomy. Patients who undergo a resective procedure or who have an obstruction require gastric drainage via a gastroduodenostomy (Billroth I) or gastrojejunostomy (Billroth II).

The incidence and type of postsurgical symptoms vary with the type of operation. After resective surgery, up to 30% of patients have significant symptoms, including weight loss, maldigestion, anemia, dumping syndrome, reactive hypoglycemia, bilious vomiting, mechanical problems, and ulcer recurrence.

Weight loss is common after subtotal gastrectomy; the patient may limit food intake because of early satiety (because the residual gastric pouch is small) or to prevent dumping syndrome and other postprandial syndromes. With a small gastric pouch, distention or discomfort may occur after a meal of even moderate size; patients should be encouraged to eat smaller and more frequent meals.

Maldigestion and steatorrhea caused by pancreaticobiliary bypass, especially with Billroth II anastomosis, may contribute to weight loss.

Anemia is common (usually from iron deficiency, but occasionally from vitamin B_{12} deficiency caused by loss of intrinsic factor or bacterial overgrowth) in the afferent limb, and osteomalacia may occur. IM vitamin B_{12} supplementation is recommended for all patients with total gastrectomy but may also be given to patients with subtotal gastrectomy if deficiency is suspected.

Dumping syndrome may follow gastric surgical procedures, particularly resections. Weakness, dizziness, sweating, nausea, vomiting, and palpitation occur soon after eating, especially hyperosmolar foods. This phenomenon is referred to as early dumping, the cause of which remains unclear but likely involves autonomic reflexes, intravascular volume contraction, and release of vasoactive peptides from the small intestine. Dietary modifications, with smaller, more frequent meals and decreased carbohydrate

intake, usually help.

Reactive hypoglycemia or **late dumping** (another form of the syndrome) results from rapid emptying of carbohydrates from the gastric pouch. Early high peaks in blood glucose stimulate excess release of insulin, which leads to symptomatic hypoglycemia several hours after the meal. A high-protein, low-carbohydrate diet and adequate caloric intake (in frequent small feedings) are recommended.

Mechanical problems (including gastroparesis and bezoar formation—see p. 138) may occur secondary to a decrease in phase III gastric motor contractions, which are altered after antrectomy and vagotomy. Diarrhea is especially common after vagotomy, even without a resection (pyloroplasty).

Ulcer recurrence, according to older studies, occurs in 5 to 12% after highly selective vagotomy and in 2 to 5% after resective surgery. Recurrent ulcers are diagnosed by endoscopy and generally respond to either proton pump inhibitors or H_2 blockers. For ulcers that continue to recur, the completeness of vagotomy should be tested by gastric analysis, *H. pylori* eliminated if present, and Zollinger-Ellison syndrome ruled out by serum gastrin studies.

Drug Treatment of Gastric Acidity

Drugs for decreasing acidity are used for peptic ulcer, gastroesophageal reflux disease (GERD—see p. 125), and many forms of gastritis. Some drugs are used in regimens for treating *H. pylori* infection. Drugs include proton pump inhibitors, H_2 blockers, antacids, and prostaglandins.

Proton pump inhibitors: These drugs are potent inhibitors of H^+,K^+-ATPase. This enzyme, located in the apical secretory membrane of the parietal cell, plays a key role in the secretion of H^+ (protons). These drugs can completely inhibit acid secretion and have a long duration of action. They promote ulcer healing and are also key components of *H. pylori* eradication regimens. Proton pump inhibitors have replaced H_2 blockers in most clinical situations because of greater rapidity of action and efficacy.

Proton pump inhibitors include esomeprazole, lansoprazole, and pantoprazole, all available orally and IV, and omeprazole and rabeprazole, available only orally in the US (see Table 13-1). Omeprazole is available without a prescription in the US. For uncomplicated duodenal ulcers, omeprazole 20 mg po once/day or lansoprazole 30 mg po once/day is given for 4 wk. Complicated duodenal ulcers (ie, multiple

[**Table 13-1.** Proton Pump Inhibitors]

ulcers, bleeding ulcers, those > 1.5 cm, or those occurring in patients with serious underlying illness) respond better to higher doses (omeprazole 40 mg once/day, lansoprazole 60 mg once/day or 30 mg bid). Gastric ulcers require treatment for 6 to 8 wk. Gastritis and GERD require 8 to 12 wk of therapy; GERD additionally requires long-term maintenance.

Long-term proton pump inhibitor therapy produces elevated gastrin levels, which lead to enterochromaffin-like cell hyperplasia. However, there is no evidence of dysplasia or malignant transformation in patients receiving this treatment. Some may develop vitamin B_{12} malabsorption.

H_2 blockers: These drugs (cimetidine, ranitidine, famotidine, available IV and orally; and nizatidine available orally) are competitive inhibitors of histamine at the H_2 receptor, thus suppressing gastrin-stimulated acid secretion and proportionately reducing gastric juice volume. Histamine-mediated pepsin secretion is also decreased.

H_2 blockers are well absorbed from the GI tract, with onset of action 30 to 60 min after ingestion and peak effects at 1 to 2 h. IV administration produces a more rapid onset of action. Duration of action is proportional to dose and ranges from 6 to 20 h. Doses should often be reduced in elderly patients.

For duodenal ulcers, once daily oral administration of cimetidine 800 mg, ranitidine 300 mg, famotidine 40

mg, or nizatidine 300 mg given at bedtime or after dinner for 6 to 8 wk is effective. Gastric ulcers may respond to the same regimen continued for 8 to 12 wk, but because nocturnal acid secretion is less important, morning administration may be equally or more effective. Children ≥ 40 kg may receive adult doses. Below that weight, the oral dosage is ranitidine 2 mg/kg q 12 h and cimetidine 10 mg/kg q 12 h. For GERD, H_2 blockers are now mostly used for pain management. Gastritis heals with famotidine or ranitidine given bid for 8 to 12 wk.

Cimetidine has minor antiandrogen effects expressed as reversible gynecomastia and, less commonly, erectile dysfunction with prolonged use. Mental status changes, diarrhea, rash, drug fever, myalgias, thrombocytopenia, and sinus bradycardia and hypotension after rapid IV administration have been reported with all H_2 blockers, generally in < 1% of treated patients but more commonly in elderly patients.

Cimetidine and, to a lesser extent, other H_2 blockers interact with the P-450 microsomal enzyme system and may delay metabolism of other drugs eliminated through this system (eg, phenytoin, warfarin, theophylline, diazepam, lidocaine).

Antacids: These agents neutralize gastric acid and reduce pepsin activity (which diminishes as gastric pH rises to > 4.0). In addition, some antacids adsorb pepsin. Antacids may interfere with the absorption of other drugs (eg, tetracycline, digoxin, iron).

Antacids relieve symptoms, promote ulcer healing, and reduce recurrence. They are relatively inexpensive but must be taken 5 to 7 times/day. The optimal antacid regimen for ulcer healing seems to be 15 to 30 mL of liquid or 2 to 4 tablets 1 h and 3 h after each meal and at bedtime. The total daily dosage of antacids should provide 200 to 400 mEq neutralizing capacity. However, antacids have been superseded by acid-suppressive therapy in the treatment of peptic ulcer and are used only for short-term symptom relief.

In general, there are 2 types of antacids: absorbable and nonabsorbable. Absorbable antacids (eg, Na bicarbonate, Ca carbonate) provide rapid, complete neutralization but may cause alkalosis and should be used only briefly (1 or 2 days). Nonabsorbable antacids (eg, aluminum or Mg hydroxide) have fewer systemic adverse effects and are preferred.

Aluminum hydroxide is a relatively safe, commonly used antacid. With chronic use, phosphate depletion occasionally develops as a result of binding of phosphate by aluminum in the GI tract. The risk of phosphate depletion increases in alcoholics, undernourished patients, and patients with renal disease (including those receiving hemodialysis). Aluminum hydroxide causes constipation.

Mg hydroxide is a more effective antacid than aluminum but may cause diarrhea. To limit diarrhea, many proprietary antacids combine Mg and aluminum antacids. Because small amounts of Mg are absorbed, Mg preparations should be used with caution in patients with renal disease.

Prostaglandins: Certain prostaglandins (especially misoprostol) inhibit acid secretion by decreasing the generation of cyclic AMP that is triggered by histamine stimulation of the parietal cell, and enhance mucosal defense. Synthetic prostaglandin derivatives are used predominantly to decrease the risk of NSAID-induced mucosal injury. Patients at high risk of NSAID-induced ulcers (ie, elderly patients, those with a history of ulcer or ulcer complication, those also taking corticosteroids) are candidates to take misoprostol 200 µg po qid with food along with their NSAID. Common adverse effects of misoprostol are abdominal cramping and diarrhea, which occur in 30% of patients. Misoprostol is a powerful abortifacient and is absolutely contraindicated in women of childbearing age who are not using contraception.

Sucralfate: This drug is a sucrose-aluminum complex that dissociates in stomach acid and forms a physical barrier over an inflamed area, protecting it from acid, pepsin, and bile salts. It also inhibits pepsin-substrate interaction, stimulates mucosal prostaglandin production, and binds bile salts. It has no effect on acid output or gastrin secretion. Sucralfate seems to have trophic effects on the ulcerated mucosa, possibly by binding growth factors and concentrating them at an ulcer site. Systemic absorption of sucralfate is negligible. Constipation occurs in 3 to 5% of patients. Sucralfate may bind to other drugs and interfere with their absorption.

Chapter 14. Bezoars and Foreign Bodies

Introduction

Food and other ingested materials may collect and form solid masses within the GI tract.

Bezoars

A bezoar is a tightly packed collection of partially digested or undigested material that is unable to exit the stomach. It often occurs in patients with abnormal gastric emptying, especially those that have diabetic gastroparesis, as well as after gastric surgery. Many bezoars are asymptomatic, but some cause symptoms of gastric outlet obstruction. Some can be dissolved enzymatically, others removed endoscopically, and some require surgery.

Partially digested agglomerations of vegetable matter are called phytobezoars; agglomerations of hair are called trichobezoars. Pharmacobezoars are concretions of medication (particularly common with sucralfate and aluminum hydroxide gel). Many other substances have been found in bezoars.

Etiology

Trichobezoars, which can weigh several kg, most commonly occur in patients with psychiatric disturbances who chew and swallow their own hair. Phytobezoars often occur in patients who have undergone a Billroth I or II partial gastrectomy, especially when accompanied by vagotomy. Hypochlorhydria, diminished antral motility, and incomplete mastication are the main predisposing factors; these factors are more common among the elderly, who are thus at higher risk of bezoar formation. Others include diabetic gastroparesis and gastroplasty for morbid obesity. Consumption of persimmons (a fruit containing the tannin shibuol, which polymerizes in the stomach) has been known to cause bezoars that require surgery in > 90% of cases. Persimmon bezoars often occur in epidemics in regions where the fruit is grown.

Symptoms and Signs

Most bezoars cause no symptoms, although postprandial fullness, nausea and vomiting, pain, and GI bleeding may occur.

Diagnosis

• Endoscopy

Bezoars are detectable as a mass lesion on most tests (eg, x-ray, ultrasound, CT) that may be done to evaluate upper GI symptoms. They may be mistaken for tumors; upper endoscopy is usually done. On endoscopy, bezoars have an unmistakable irregular surface and may range in color from yellow-green to gray-black. An endoscopic biopsy that yields hair or plant material is diagnostic.

Treatment

• Observation

• Sometimes manual removal via endoscopy

• Sometimes enzymatic therapy

If initial diagnosis is made by endoscopy, removal can be attempted at that time. Fragmentation with forceps, wire snare, jet spray, or even laser may break up bezoars, allowing them to pass or be extracted. Metoclopramide 40 mg IV over 24 h or 10 mg IM q 4 h for several days may increase peristalsis and aid gastric emptying of fragmented material.

If endoscopy was not initially done, treatment is based on symptoms. Asymptomatic patients that have a

bezoar discovered incidentally during testing for other reasons do not necessarily require intervention. In some cases, a trial of enzymatic therapy can be attempted. Enzymes include papain (10,000 U with each meal), meat tenderizer (5 mL [1 tsp] in 8 oz of clear liquid before each meal), or cellulase (10 g dissolved in 1 L water, consumed over 24 h for 2 to 3 days). If enzymatic therapy is unsuccessful, or if patients are symptomatic, endoscopic removal may be tried. Rocklike concretions and trichobezoars usually require laparotomy.

Foreign Bodies

A variety of foreign bodies may enter the GI tract. Many pass spontaneously, but some become impacted, causing symptoms of obstruction. Perforation may occur. The esophagus is the most common (75%) site of impaction. Nearly all impacted objects can be removed endoscopically, but surgery is occasionally necessary.

Undigestible objects may be intentionally swallowed by children and demented adults. Denture wearers, the elderly, and inebriated people are prone to accidentally swallowing inadequately masticated food (particularly meat), which may become impacted in the esophagus. Smugglers who swallow drug-filled balloons, vials, or packages to escape detection (body packers or body stuffers) may develop intestinal obstruction. The packaging may rupture, leading to drug overdose.

Esophageal foreign bodies: Foreign bodies usually lodge in an area of esophageal narrowing such as at the cricopharyngeus or aortic arch or just above the gastroesophageal junction. If obstruction is complete, patients retch or vomit. Some patients drool because they are unable to swallow secretions.

Immediate endoscopic removal is required for sharp objects, coins in the proximal esophagus, and any obstruction causing significant symptoms. Also, button batteries lodged in the esophagus may cause direct corrosive damage, low-voltage burns, and pressure necrosis and thus require prompt removal.

Other esophageal foreign bodies may be observed for a maximum of 12 to 24 h. Glucagon 1 mg IV sometimes relaxes the esophagus enough to allow spontaneous passage. Other methods, such as use of effervescent agents, meat tenderizer, and bougienage, are not recommended. Endoscopic removal is the treatment of choice. Removal is best achieved using a forceps, basket, or snare with an overtube placed in the esophagus to prevent aspiration.

Sometimes, foreign bodies scratch the esophagus but do not become lodged. In such cases, patients may report a foreign body sensation even though no foreign body is present.

Gastric and intestinal foreign bodies: Foreign bodies that pass through the esophagus are asymptomatic unless obstruction or perforation occurs. Of the foreign bodies that reach the stomach, 80 to 90% pass spontaneously, 10 to 20% require nonoperative intervention, and ≤ 1% require surgery. Thus, most intragastric foreign bodies can be ignored. However, objects larger than 5 × 2 cm rarely pass the stomach. Sharp objects should be retrieved from the stomach because 15 to 35% will cause intestinal perforation, but small round objects (eg, coins and button batteries) can simply be observed. The patient's stools should be searched, and if the object does not appear, x-rays are taken at 48-h intervals. A coin that remains in the stomach for > 4 wk or a battery showing signs of corrosion on x-ray that remains in the stomach for > 48 h should be removed. A hand-held metal detector can localize metallic foreign bodies and provide information comparable to that yielded by plain x-rays.

Patients with symptoms of obstruction or perforation require laparotomy. Ingested drug packages are of great concern because of the risk of leakage and consequent drug overdose. Patients with symptoms of drug toxicity should have immediate laparotomy with interim medical management of symptoms (eg, benzodiazepines for cocaine toxicity). Asymptomatic patients should be admitted to the hospital. Some clinicians advocate oral polyethylene glycol solution as a cathartic to enhance passage of the material; others suggest surgical removal. The best practice is unclear.

Most foreign objects that have passed into the small intestine usually traverse the GI tract without problem, even if they take weeks or months to do so. They tend to be held up just before the ileocecal valve or at any site of narrowing, as is present in Crohn's disease. Sometimes objects such as toothpicks

remain within the GI tract for many years, only to turn up in a granuloma or abscess.

Rectal foreign bodies: Gallstones, fecaliths, and swallowed foreign bodies (including toothpicks and chicken and fish bones) may lodge at the anorectal junction. Urinary calculi, vaginal pessaries, or surgical sponges or instruments may erode into the rectum. Foreign bodies, sometimes bizarre and/or related to sexual play, may be introduced intentionally but become lodged unintentionally. Some objects are caught in the rectal wall, and others are trapped just above the anal sphincter.

Sudden, excruciating pain during defecation should arouse suspicion of a penetrating foreign body, usually lodged at or just above the anorectal junction. Other manifestations depend on the size and shape of the foreign body, its duration in situ, and the presence of infection or perforation.

Foreign bodies usually become lodged in the mid rectum, where they cannot negotiate the anterior angulation of the rectum. They can be felt on digital examination. Abdominal examination and chest x-rays may be necessary to exclude possible intraperitoneal rectal perforation.

If the object can be palpated, a local anesthetic is given by sc and submucosal injections of 0.5% lidocaine or bupivacaine. The anus is dilated with a rectal retractor, and the foreign body is grasped and removed. If the object cannot be palpated, the patient should be hospitalized. Peristalsis usually moves the foreign body down to the mid rectum, and the above routine can be followed. Removal via a sigmoidoscope or proctoscope is rarely successful, and sigmoidoscopy usually forces the foreign body proximally, delaying its extraction. Regional or general anesthesia is infrequently necessary, and laparotomy with milking of the foreign body toward the anus or colotomy with extraction of the foreign body is rarely necessary. After extraction, sigmoidoscopy should be done to rule out significant rectal trauma or perforation. Removal of a rectal foreign body may be of high risk and should be done by a surgeon or gastroenterologist skilled in foreign body removal.

Chapter 15. Pancreatitis

Introduction

Pancreatitis is classified as either acute or chronic. Acute pancreatitis is inflammation that resolves both clinically and histologically. Chronic pancreatitis is characterized by histologic changes that are irreversible and progressive and that result in considerable loss of exocrine and endocrine pancreatic function. Patients with chronic pancreatitis may have a flare-up of acute disease.

Pancreatitis can affect both the exocrine and endocrine functions of the pancreas. Pancreatic acinar cells secrete bicarbonate and digestive enzymes into ducts that connect the pancreas to the duodenum at the ampulla of Vater (exocrine function). Pancreatic β-cells secrete insulin directly into the bloodstream (endocrine function).

Acute Pancreatitis

Acute pancreatitis is inflammation of the pancreas (and, sometimes, adjacent tissues) caused by the release of activated pancreatic enzymes. The most common triggers are biliary tract disease and chronic heavy alcohol intake. The condition ranges from mild (abdominal pain and vomiting) to severe (pancreatic necrosis and a systemic inflammatory process with shock and multiorgan failure). Diagnosis is based on clinical presentation and serum amylase and lipase levels. Treatment is supportive, with IV fluids, analgesics, and fasting.

Etiology

Biliary tract disease and alcoholism account for ≥ 80% of acute pancreatitis cases. The remaining 20% result from myriad causes (see
Table 15-1).

Pathophysiology

The precise mechanism by which obstruction of the sphincter of Oddi by a gallstone or microlithiasis (sludge) causes pancreatitis is unclear, although it probably involves increased ductal pressure. Prolonged alcohol intake (> 100 g/day for > 3 to 5 yr) may cause the protein of pancreatic enzymes to precipitate within small pancreatic ductules. Ductal obstruction by these protein plugs may cause premature activation of pancreatic enzymes. An alcohol binge in such patients can trigger pancreatitis, but the exact mechanism is not known.

A number of genetic mutations predisposing to pancreatitis have been identified. One, an autosomal dominant mutation of the cationic trypsinogen gene, causes pancreatitis in 80% of carriers; an obvious familial pattern is present. Other mutations have lesser penetrance and are not readily apparent clinically except through genetic testing. The genetic abnormality responsible for cystic fibrosis increases the risk of recurrent acute as well as chronic pancreatitis.

Regardless of the etiology, pancreatic enzymes (including trypsin, phospholipase A_2, and elastase) become activated within the gland itself. The enzymes can damage tissue and activate complement and the inflammatory cascade, producing cytokines. This process causes inflammation, edema, and sometimes necrosis. In mild pancreatitis, inflammation is confined to the pancreas; the mortality rate is < 5%. In severe pancreatitis, there is significant inflammation, with necrosis and hemorrhage of the gland and a systemic inflammatory response; the mortality rate is 10 to 50%. After 5 to 7 days, necrotic pancreatic tissue may become infected by enteric bacteria.

[**Table 15-1.** Some Causes of Acute Pancreatitis]

Activated enzymes and cytokines that enter the peritoneal cavity cause a chemical burn and third spacing of fluid; those that enter the systemic circulation cause a systemic inflammatory response that can result in acute respiratory distress syndrome and renal failure. The systemic effects are mainly the result of

increased capillary permeability and decreased vascular tone, which result from the released cytokines and chemokines. Phospholipase A_2 is thought to injure alveolar membranes of the lungs.

In about 40% of patients, collections of enzyme-rich pancreatic fluid and tissue debris form in and around the pancreas. In about half, the collections resolve spontaneously. In others, the collections become infected or form pseudocysts. Pseudocysts have a fibrous capsule without an epithelial lining. Pseudocysts may hemorrhage, rupture, or become infected.

Death during the first several days is usually caused by cardiovascular instability (with refractory shock and renal failure) or respiratory failure (with hypoxemia and at times adult respiratory distress syndrome). Occasionally, death results from heart failure secondary to an unidentified myocardial depressant factor. Death after the first week is usually caused by multiorgan system failure.

Symptoms and Signs

An acute attack causes steady, boring upper abdominal pain, typically severe enough to require large doses of parenteral opioids. The pain radiates through to the back in about 50% of patients; rarely, pain is first felt in the lower abdomen. Pain usually develops suddenly in gallstone pancreatitis; in alcoholic pancreatitis, pain develops over a few days. The pain usually persists for several days. Sitting up and leaning forward may reduce pain, but coughing, vigorous movement, and deep breathing may accentuate it. Nausea and vomiting are common.

The patient appears acutely ill and sweaty. Pulse rate is usually 100 to 140 beats/min. Respiration is shallow and rapid. BP may be transiently high or low, with significant postural hypotension. Temperature may be normal or even subnormal at first but may increase to 37.7 to 38.3° C (100 to 101° F) within a few hours. Sensorium may be blunted to the point of semicoma. Scleral icterus is occasionally present. The lungs may have limited diaphragmatic excursion and evidence of atelectasis.

About 20% of patients experience upper abdominal distention caused by gastric distention or displacement of the stomach by a pancreatic inflammatory mass. Pancreatic duct disruption may cause ascites (pancreatic ascites). Marked abdominal tenderness occurs, most often in the upper abdomen. There may be mild tenderness in the lower abdomen, but the rectum is not tender and the stool is usually negative for occult blood. Mild-to-moderate muscular rigidity may be present in the upper abdomen but is rare in the lower abdomen. Rarely, severe peritoneal irritation results in a rigid and boardlike abdomen. Bowel sounds may be hypoactive. Grey Turner's sign (ecchymoses of the flanks) and Cullen's sign (ecchymoses of the umbilical region) indicate extravasation of hemorrhagic exudate.

Infection in the pancreas or in an adjacent fluid collection should be suspected if the patient has a generally toxic appearance with elevated temperature and WBC count or if deterioration follows an initial period of stabilization.

Diagnosis

• Serum markers (amylase, lipase)

• Once pancreatitis is diagnosed, CT usually done

Pancreatitis is suspected whenever severe abdominal pain occurs, especially in a patient with significant alcohol use or known gallstones. Conditions causing similar symptoms include perforated gastric or duodenal ulcer, mesenteric infarction, strangulating intestinal obstruction, dissecting aneurysm, biliary colic, appendicitis, diverticulitis, inferior wall MI, and hematoma of the abdominal muscles or spleen.

Diagnosis is made by clinical suspicion, serum markers (amylase and lipase), and the absence of other causes for the patient's symptoms. Thus, a broad range of tests is done, typically including CBC, electrolytes, Ca, Mg, glucose, BUN, creatinine, amylase, and lipase. Other routine tests include ECG and an abdominal series (chest, flat, and upright abdomen). A urine dipstick for trypsinogen-2 has sensitivity and specificity of > 90% for acute pancreatitis. Ultrasound and CT are not generally done specifically to diagnose pancreatitis but are often used to evaluate acute abdominal pain (see p.

108).

Laboratory tests: Serum amylase and lipase concentrations increase on the first day of acute pancreatitis and return to normal in 3 to 7 days. Lipase is more specific for pancreatitis, but both enzymes may be increased in renal failure and various abdominal conditions (eg, perforated ulcer, mesenteric vascular occlusion, intestinal obstruction). Other causes of increased serum amylase include salivary gland dysfunction, macroamylasemia, and tumors that secrete amylase. Both amylase and lipase levels may remain normal if destruction of acinar tissue during previous episodes precludes release of sufficient amounts of enzymes. The serum of patients with hypertriglyceridemia may contain a circulating inhibitor that must be diluted before an elevation in serum amylase can be detected.

Amylase:creatinine clearance ratio does not have sufficient sensitivity or specificity to diagnose pancreatitis. It is generally used to diagnose macroamylasemia when no pancreatitis exists. In macroamylasemia, amylase bound to serum immunoglobulin falsely elevates the serum amylase level.

Fractionation of total serum amylase into pancreatic type (p-type) isoamylase and salivary-type (s-type) isoamylase increases the accuracy of serum amylase. However, the level of p-type also increases in renal failure and in other severe abdominal conditions in which amylase clearance is altered.

The WBC count usually increases to 12,000 to 20,000/µL. Third-space fluid losses may increase the Hct to as high as 50 to 55%, indicating severe inflammation. Hyperglycemia may occur. Serum Ca concentration falls as early as the first day because of the formation of Ca "soaps" secondary to excess generation of free fatty acids, especially by pancreatic lipase. Serum bilirubin increases in 15 to 25% of patients because pancreatic edema compresses the common bile duct.

Imaging: Plain x-rays of the abdomen may disclose calcifications within pancreatic ducts (evidence of prior inflammation and hence chronic pancreatitis), calcified gallstones, or localized ileus in the left upper quadrant or the center of the abdomen (a "sentinel loop" of small bowel, dilation of the transverse colon, or duodenal ileus). Chest x-ray may reveal atelectasis or a pleural effusion (usually left-sided or bilateral but rarely confined to the right pleural space).

Ultrasound should be done if gallstone pancreatitis is suspected (and another etiology is not obvious) to detect gallstones or dilation of the common bile duct (which indicates biliary tract obstruction). Edema of the pancreas may be visualized, but overlying gas frequently obscures the pancreas.

CT with IV contrast is generally done to identify necrosis, fluid collections, or pseudocysts once pancreatitis has been diagnosed. It is particularly recommended for severe pancreatitis or if a complication ensues (eg, hypotension or progressive leukocytosis and elevation of temperature). IV contrast facilitates the recognition of pancreatic necrosis; however, it may cause pancreatic necrosis in areas of low perfusion (ie, ischemia). Thus, contrast-enhanced CT should be done only after the patient has been adequately hydrated.

If pancreatic infection is suspected, fluid obtained by percutaneous CT-guided needle aspiration of cysts or areas of fluid collection or necrosis may reveal organisms on Gram stain or culture. The diagnosis is supported by positive blood cultures and, particularly, by the presence of air bubbles in the retroperitoneum on abdominal CT. The advent of magnetic resonance cholangiopancreatography (MRCP) may make the selection of pancreatic imaging simpler.

Prognosis

In edematous pancreatitis, mortality is < 5%. In pancreatitis with necrosis and hemorrhage, mortality is 10 to 50%. In pancreatic infection, mortality is usually 100% without extensive surgical debridement or drainage of the infected area.

CT findings correlate with prognosis. If CT is normal or shows only mild pancreatic edema (Balthazar class A or B), the prognosis is excellent. Patients with peripancreatic inflammation or one area of fluid collection (classes C and D) have a 10 to 15% incidence of abscess formation; the incidence is over 60% in patients with two or more areas of fluid collection (class E).

Ranson's prognostic signs help predict the prognosis of acute pancreatitis. Five of Ranson's signs can be documented at admission:

• Age > 55 yr

• Plasma glucose > 200 mg/dL (> 11.1 mmol/L)

• Serum LDH > 350 IU/L

• AST > 250 UL

• WBC count > 16,000/µL

The rest of Ranson's signs are determined within 48 h of admission:

• Hct decrease > 10%

• BUN increase > 5 mg/dL (> 1.78 mmol/L)

• Serum Ca < 8 mg/dL (< 2 mmol/L)

• Pao_2 < 60 mm Hg (< 7.98 kPa)

• Base deficit > 4 mEq/L (> 4 mmol/L)

• Estimated fluid sequestration > 6 L

Mortality increases with the number of positive signs: If < 3 signs are positive, the mortality rate is < 5%; if ≥ 3 are positive, mortality is 15 to 20%.

The APACHE II index (see
Table 222-4 on p. 2248), calculated on the second hospital day, also correlates with prognosis.

Treatment

• Fluid resuscitation

• Fasting

• Drugs, including adequate analgesia and acid blockers

• Antibiotics for pancreatic necrosis

• Drainage of infected pseudocysts or areas of necrosis

Adequate fluid resuscitation is essential; up to 6 to 8 L/day of fluid containing appropriate electrolytes may be required. Inadequate fluid therapy increases the risk of pancreatic necrosis.

Fasting is indicated until acute inflammation subsides (ie, cessation of abdominal tenderness and pain, normalization of serum amylase, return of appetite, feeling better). Fasting can last from a few days in mild pancreatitis to several weeks. TPN should be initiated in severe cases within the first few days to prevent undernutrition.

Pain relief requires parenteral opioids, which should be given in adequate doses. Although morphine may cause the sphincter of Oddi to contract, this is of doubtful clinical significance. Antiemetic agents (eg, prochlorperazine 5 to 10 mg IV q 6 h) should be given to alleviate vomiting. An NGT is required only if significant vomiting persists or ileus is present.

Parenteral H_2 blockers or proton pump inhibitors are given. Efforts to reduce pancreatic secretion with drugs (eg, anticholinergics, glucagon, somatostatin, octreotide) have no proven benefit.

Severe acute pancreatitis should be treated in an ICU, particularly in patients with hypotension, oliguria, Ranson's score ≥ 3, APACHE II ≥ 8, or pancreatic necrosis on CT > 30%. In the ICU, vital signs and urine output are monitored hourly; metabolic parameters (Hct, glucose, and electrolytes) are reassessed every 8 h; ABG is determined as needed; central venous pressure line or Swan-Ganz catheter measurements are determined every 6 h if the patient is hemodynamically unstable or if fluid requirements are unclear. CBC, platelet count, coagulation parameters, total protein with albumin, BUN, creatinine, Ca, and Mg are measured daily.

Hypoxemia is treated with humidified O_2 via mask or nasal prongs. If hypoxemia persists or adult respiratory distress syndrome develops, assisted ventilation may be required. Glucose > 170 to 200 mg/dL (9.4 to 11.1 mmol/L) should be treated cautiously with sc or IV insulin and carefully monitored. Hypocalcemia generally is not treated unless neuromuscular irritability occurs; 10 to 20 mL of 10% Ca gluconate in 1 L of IV fluid is given over 4 to 6 h. Chronic alcoholics and patients with documented hypomagnesemia should receive Mg sulfate 1 g/L of replacement fluid for a total of 2 to 4 g, or until levels normalize. If renal failure occurs, serum Mg levels are monitored and IV Mg is given cautiously. With restoration of normal Mg levels, serum Ca levels usually return to normal.

Heart failure should be treated (see p. 2126). Prerenal azotemia should be treated by increased fluid replacement. Renal failure may require dialysis (usually peritoneal).

Antibiotic prophylaxis with imipenem can prevent infection of sterile pancreatic necrosis, although the effect on reducing mortality is unclear. Infected areas of pancreatic necrosis require surgical debridement, but infected fluid collections outside the pancreas may be drained percutaneously. A pseudocyst that is expanding rapidly, infected, bleeding, or likely to rupture requires drainage. Whether drainage is percutaneous, surgical, or endoscopic depends on location of the pseudocyst and institutional expertise. Peritoneal lavage to wash out activated pancreatic enzymes and inflammatory mediators has no proven benefit.

Surgical intervention during the first several days is justified for severe blunt or penetrating trauma or uncontrolled biliary sepsis. Although > 80% of patients with gallstone pancreatitis pass the stone spontaneously, ERCP with sphincterotomy and stone removal is indicated for patients who do not improve after 24 h of treatment. Patients who spontaneously improve generally undergo elective laparoscopic cholecystectomy. Elective cholangiography remains controversial.

Chronic Pancreatitis

Chronic pancreatitis is persistent inflammation of the pancreas that results in permanent structural damage with fibrosis and ductal strictures, followed by a decline in exocrine and endocrine function. It can occur as the result of chronic alcohol abuse but may be idiopathic. Initial symptoms are recurrent attacks of pain. Later in the disease, some patients develop malabsorption and glucose intolerance. Diagnosis is usually made by imaging studies such as ERCP, endoscopic ultrasound, or secretin pancreatic function testing. Treatment is supportive, with dietary modification, analgesics, and enzyme supplements. In some cases, surgical treatment is helpful.

Etiology

In the US, 70 to 80% of cases result from alcoholism, and 15 to 25% are idiopathic. However, recent data suggest that alcohol is becoming less of a cause. Less common causes include hereditary pancreatitis, hyperparathyroidism, and obstruction of the main pancreatic duct caused by stenosis, stones, or cancer. In India, Indonesia, and Nigeria, idiopathic calcific pancreatitis occurs among children and young adults (tropical pancreatitis).

Pathophysiology

Similar to acute pancreatitis, the mechanism of disease may be ductal obstruction by protein plugs. The protein plugs may result from excess secretion of glycoprotein-2 or a deficiency of lithostatin, a protein in pancreatic fluid that inhibits Ca precipitation. If obstruction is chronic, persistent inflammation leads to fibrosis and alternating areas of ductal dilation and stricture, which may become calcified. Neuronal sheath hypertrophy and perineural inflammation occur and may contribute to chronic pain.

After several years, progressive fibrosis leads to loss of exocrine and endocrine function. Diabetes develops in 20 to 30% of patients within 10 to 15 yr of onset.

Symptoms and Signs

Most patients present with episodic abdominal pain. About 10 to 15% have no pain and present with malabsorption. Pain is epigastric, severe, and may last many hours or several days. Episodes typically subside spontaneously after 6 to 10 yr as the acinar cells that secrete pancreatic digestive enzymes are progressively destroyed. When lipase and protease secretions are reduced to < 10% of normal, the patient develops steatorrhea, passing greasy stools or even oil droplets, and creatorrhea (the presence of undigested muscle fibers in the feces). Symptoms of glucose intolerance may appear at this time.

Diagnosis

• Clinical suspicion

• Abdominal CT

• Sometimes magnetic resonance cholangiopancreatography (MRCP), endoscopic ultrasonography, or ERCP

Diagnosis can be difficult because amylase and lipase levels are frequently normal because of significant loss of pancreatic function. In a patient with a typical history of alcohol abuse and recurrent episodes of acute pancreatitis, detection of pancreatic calcification on plain x-ray of the abdomen may be sufficient. However, such calcifications typically occur late in the disease and then are visible in only about 30% of patients. In patients without a typical history, pancreatic cancer must be excluded as the cause of pain: abdominal CT is recommended. CT can show calcifications and other pancreatic abnormalities (eg, pseudocyst or dilated ducts) but still may be normal early in the disease.

The primary options for patients with normal CT findings include ERCP, endoscopic ultrasonography, and secretin pancreatic function testing. These tests are quite sensitive, but ERCP precipitates acute pancreatitis in about 5% of patients. MRCP may prove an acceptable alternative.

Late in the disease, tests of pancreatic exocrine function become abnormal. A 72-h test for stool fat is diagnostic for steatorrhea but cannot establish a cause. The secretin test collects pancreatic secretions via a duodenal tube for analysis but is done in only a few centers. Levels of serum trypsinogen and fecal chymotrypsin and elastase may be decreased. In the bentiromide test and the pancreolauryl test, substances are given orally, and urine is analyzed for cleavage products generated by pancreatic enzymes. All such exocrine tests are less sensitive than ERCP or endoscopic ultrasonography early in the disease.

Treatment

• IV fluids

• Fasting

• Drugs, including adequate analgesia and acid blockers

• Pancreatic enzyme supplements

• Sometimes drainage of pseudocysts (surgical or endoscopic)

A relapse requires treatment similar to acute pancreatitis with fasting, IV fluids, and analgesics. When feeding resumes, the patient must eschew alcohol and consume a low-fat (< 25 g/day) diet (to reduce secretion of pancreatic enzymes). An H_2 blocker or proton pump inhibitor may reduce acid-stimulated release of secretin, thereby decreasing the flow of pancreatic secretions. Too often, these measures do not relieve pain, requiring increased amounts of opioids, with the threat of addiction. Medical treatment of chronic pancreatic pain is often unsatisfactory.

Pancreatic enzyme supplementation may reduce chronic pain by inhibiting the release of cholecystokinin, thereby reducing the secretion of pancreatic enzymes. Supplementation is more likely to be successful in mild idiopathic pancreatitis than in alcoholic pancreatitis. Enzymes are also used to treat steatorrhea. Various preparations are available, and a dose providing at least 30,000 U of lipase should be used. Non-enteric coated tablets should be used, and they should be taken with meals. An H_2 blocker or proton pump inhibitor should be given to prevent acid breakdown of the enzymes.

Favorable clinical responses include weight gain, fewer bowel movements, elimination of oil droplet seepage, and improved well-being. Clinical response can be documented by showing a decrease in stool fat after enzyme therapy. If steatorrhea is particularly severe and refractory to these measures, medium-chain triglycerides can be provided as a source of fat (they are absorbed without pancreatic enzymes), reducing other dietary fats proportionally. Supplementation with fat-soluble vitamins (A, D, K) should be given, including vitamin E, which may minimize inflammation.

Surgical treatment may be effective for pain relief. A pancreatic pseudocyst, which may cause chronic pain, can be decompressed into a nearby structure to which it firmly adheres (eg, the stomach) or into a defunctionalized loop of jejunum (via a Roux-en-Y cystojejunostomy). If the main pancreatic duct is dilated > 5 to 8 mm, a lateral pancreaticojejunostomy (Puestow procedure) relieves pain in about 70 to 80% of patients. If the duct is not dilated, a partial resection is similarly effective; either distal pancreatectomy (for extensive disease at the tail of the pancreas) or Whipple procedure (for extensive disease at the head of the pancreas) is done. Operative approaches should be reserved for patients who have stopped using alcohol and who can manage diabetes that may be intensified by pancreatic resection.

Some pseudocysts can be drained endoscopically. Endoscopic ultrasound-guided denervation of the celiac plexus with alcohol and bupivacaine may provide pain relief. If there is significant stricture at the papilla or distal pancreatic duct, ERCP with sphincterotomy, stent placement, or dilatation may be effective.

Oral hypoglycemic drugs rarely help treat diabetes caused by chronic pancreatitis. Insulin should be given cautiously because the coexisting deficiency of glucagon secretion by α-cells means that the hypoglycemic effects of insulin are unopposed and prolonged hypoglycemia may occur.

Patients are at increased risk of pancreatic cancer. Worsening of symptoms, especially with development of a pancreatic duct stricture, should prompt an evaluation for cancer. Evaluation may include brushing strictures for cytologic analysis or measuring serum markers (eg, CA 19-9, carcinoembryonic antigen).

Chapter 16. Gastroenteritis

Introduction

(See also Food Allergy on p. 1118 and Mushroom Poisoning on p. 3336.)

Gastroenteritis is inflammation of the lining of the stomach and small and large intestines. Most cases are infectious, although gastroenteritis may occur after ingestion of drugs and chemical toxins (eg, metals, plant substances). Symptoms include anorexia, nausea, vomiting, diarrhea, and abdominal discomfort. Diagnosis is clinical or by stool culture, although immunoassays are increasingly used. Treatment is symptomatic, although parasitic and some bacterial infections require specific anti-infective therapy.

Gastroenteritis is usually uncomfortable but self-limited. Electrolyte and fluid loss is usually little more than an inconvenience to an otherwise healthy adult but can be grave for people who are very young (see p. 2806), elderly, or debilitated or who have serious concomitant illnesses. Worldwide, an estimated 3 to 6 million children die each year from infectious gastroenteritis.

Etiology

Infectious gastroenteritis may be caused by viruses, bacteria, or parasites. Many specific organisms are discussed further in the Infectious Diseases section.

Viruses: The viruses most commonly implicated are

• Rotavirus

• Norovirus

Viruses are the most common cause of gastroenteritis in the US. They infect enterocytes in the villous epithelium of the small bowel. The result is transudation of fluid and salts into the intestinal lumen; sometimes, malabsorption of carbohydrates worsens symptoms by causing osmotic diarrhea. Diarrhea is watery. Inflammatory diarrhea (dysentery), with fecal WBCs and RBCs or gross blood, is uncommon. Four categories of viruses cause most gastroenteritis: rotavirus and calicivirus (predominantly the norovirus [formerly Norwalk virus]) cause the majority of viral gastroenteritis, followed by astrovirus and enteric adenovirus.

Rotavirus is the most common cause of sporadic, severe, dehydrating diarrhea in young children (peak incidence, 3 to 15 mo). Rotavirus is highly contagious; most infections occur by the fecal-oral route. Adults may be infected after close contact with an infected infant. The illness in adults is generally mild. Incubation is 1 to 3 days. In temperate climates, most infections occur in the winter. Each year in the US, a wave of rotavirus illness begins in the Southwest in November and ends in the Northeast in March.

Norovirus most commonly infects older children and adults. Infections occur year-round. Norovirus is the principal cause of sporadic viral gastroenteritis in adults and of epidemic viral gastroenteritis in all age groups; large waterborne and food-borne outbreaks occur. Person-to-person transmission also occurs because the virus is highly contagious. Incubation is 24 to 48 h.

Astrovirus can infect people of all ages but usually infects infants and young children. Infection is most common in winter. Transmission is by the fecal-oral route. Incubation is 3 to 4 days.

Adenoviruses are the 4th most common cause of childhood viral gastroenteritis. Infections occur year-round, with a slight increase in summer. Children < 2 yr are primarily affected. Transmission is by the fecal-oral route. Incubation is 3 to 10 days.

In immunocompromised patients, additional viruses (eg, cytomegalovirus, enterovirus) can cause gastroenteritis.

Bacteria: The bacteria most commonly implicated are

• *Salmonella*

• *Campylobacter*

• *Shigella*

• *Escherichia coli* (especially serotype O157:H7)

Bacterial gastroenteritis is less common than viral. Bacteria cause gastroenteritis by several mechanisms. Certain species (eg, *Vibrio cholerae*, enterotoxigenic strains of *E. coli*) adhere to intestinal mucosa without invading and produce enterotoxins. These toxins impair intestinal absorption and cause secretion of electrolytes and water by stimulating adenylate cyclase, resulting in watery diarrhea. *Clostridium difficile* produces a similar toxin when overgrowth follows antibiotic use (see p. 1292).

Some bacteria (eg, *Staphylococcus aureus*, *Bacillus cereus*, *Clostridium perfringens*) produce an exotoxin that is ingested in contaminated food. The exotoxin can cause gastroenteritis without bacterial infection. These toxins generally cause acute nausea, vomiting, and diarrhea within 12 h of ingestion of contaminated food. Symptoms abate within 36 h.

Other bacteria (eg, *Shigella*, *Salmonella*, *Campylobacter*, some *E. coli* subtypes) invade the mucosa of the small bowel or colon and cause microscopic ulceration, bleeding, exudation of protein-rich fluid, and secretion of electrolytes and water. The invasive process and its results can occur whether or not the organism produces an enterotoxin. The resulting diarrhea contains WBCs and RBCs and sometimes gross blood.

Salmonella and *Campylobacter* are the most common bacterial causes of diarrheal illness in the US. Both infections are most frequently acquired through undercooked poultry; unpasteurized milk is also a possible source. *Campylobacter* is occasionally transmitted from dogs or cats with diarrhea. *Salmonella* can be transmitted by undercooked eggs and by contact with reptiles. Species of *Shigella* are the 3rd most common bacterial cause of diarrhea in the US and are usually transmitted person to person, although food-borne epidemics occur. *Shigella dysenteriae* type 1 (not present in the US) produces Shiga toxin, which can cause hemolytic-uremic syndrome (see p. 961).

Several different subtypes of *E. coli* cause diarrhea. The epidemiology and clinical manifestations vary greatly depending on the subtype: (1) Enterohemorrhagic *E. coli* is the most clinically significant subtype in the US. It produces Shiga toxin, which causes bloody diarrhea (hemorrhagic colitis). *E. coli* O157:H7 is the most common strain of this subtype in the US. Undercooked ground beef, unpasteurized milk and juice, and contaminated water are possible sources. Person-to-person transmission is common in the day care setting. Hemolytic-uremic syndrome is a serious complication that develops in 2 to 7% of cases, most commonly among the young and old. (2) Enterotoxigenic *E. coli* produces two toxins (one similar to cholera toxin) that cause watery diarrhea. This subtype is the most common cause of traveler's diarrhea. (3) Enteropathogenic *E. coli* causes watery diarrhea. Once a common cause of diarrhea outbreaks in nurseries, this subtype is now rare. (4) Enteroinvasive *E. coli* causes bloody or nonbloody diarrhea, primarily in the developing world. It is rare in the US.

Several other bacteria cause gastroenteritis, but most are uncommon in the US. *Yersinia enterocolitica* can cause gastroenteritis or a syndrome that mimics appendicitis. It is transmitted by undercooked pork, unpasteurized milk, or contaminated water. Several *Vibrio* species (eg, *V. parahaemolyticus*) cause diarrhea after ingestion of undercooked seafood. *V. cholerae* sometimes causes severe dehydrating diarrhea in the developing world. *Listeria* causes food-borne gastroenteritis. *Aeromonas* is acquired from swimming in or drinking contaminated fresh or brackish water. *Plesiomonas shigelloides* can cause diarrhea in patients who have eaten raw shellfish or traveled to tropical regions of the developing world.

Parasites: The parasites most commonly implicated are

• *Giardia*

• *Cryptosporidium*

Certain intestinal parasites, notably *Giardia intestinalis* (*lamblia*—see p. 1371), adhere to or invade the intestinal mucosa, causing nausea, vomiting, diarrhea, and general malaise. Giardiasis occurs in every region of the US and throughout the world. The infection can become chronic and cause a malabsorption syndrome. It is usually acquired via person-to-person transmission (often in day care centers) or from contaminated water.

Cryptosporidium parvum causes watery diarrhea sometimes accompanied by abdominal cramps, nausea, and vomiting. In healthy people, the illness is self-limited, lasting about 2 wk. In immunocompromised patients, illness may be severe, causing substantial electrolyte and fluid loss. *Cryptosporidium* is usually acquired through contaminated water.

Other parasites that can cause symptoms similar to those of cryptosporidiosis include *Cyclospora cayetanensis* and, in immunocompromised patients, *Cystoisospora* (*Isospora*) *belli*, and a collection of organisms referred to as microsporidia (eg, *Enterocytozoon bieneusi*, *Encephalitozoon intestinalis*). *Entamoeba histolytica* (amebiasis) is a common cause of subacute bloody diarrhea in the developing world and occasionally occurs in the US.

Symptoms and Signs

The character and severity of symptoms vary. Generally, onset is sudden, with anorexia, nausea, vomiting, borborygmi, abdominal cramps, and diarrhea (with or without blood and mucus). Malaise, myalgias, and prostration may occur. The abdomen may be distended and mildly tender; in severe cases, muscle guarding may be present. Gas-distended intestinal loops may be palpable. Borborygmi are present even without diarrhea (an important differential feature from paralytic ileus). Persistent vomiting and diarrhea can result in intravascular fluid depletion with hypotension and tachycardia. In severe cases, shock, with vascular collapse and oliguric renal failure, occurs.

If vomiting is the main cause of fluid loss, metabolic alkalosis with hypochloremia can occur. If diarrhea is more prominent, acidosis is more likely. Both vomiting and diarrhea can cause hypokalemia. Hyponatremia may develop, particularly if hypotonic fluids are used in replacement therapy.

In viral infections, watery diarrhea is the most common symptom; stools rarely contain mucus or blood. Rotavirus gastroenteritis in infants and young children may last 5 to 7 days. Vomiting occurs in 90% of patients, and fever > 39° C (> 102.2° F) occurs in about 30%. Norovirus typically causes acute onset of vomiting, abdominal cramps, and diarrhea, with symptoms lasting only 1 to 2 days. In children, vomiting is more prominent than diarrhea, whereas in adults, diarrhea usually predominates. Patients may also experience fever, headache, and myalgias. The hallmark of adenovirus gastroenteritis is diarrhea lasting 1 to 2 wk. Affected infants and children may have mild vomiting that typically starts 1 to 2 days after the onset of diarrhea. Low-grade fever occurs in about 50% of patients. Astrovirus causes a syndrome similar to mild rotavirus infection.

Bacteria that cause invasive disease (eg, *Shigella*, *Salmonella*) are more likely to result in fever, prostration, and bloody diarrhea. Bacteria that produce an enterotoxin (eg, *S. aureus*, *B. cereus*, *C. perfringens*) usually cause watery diarrhea.

Parasitic infections typically cause subacute or chronic diarrhea. Most cause nonbloody diarrhea; an exception is *E. histolytica*, which causes amebic dysentery. Fatigue and weight loss are common when diarrhea is persistent.

Diagnosis

• Clinical evaluation

• Stool testing in select cases

Other GI disorders that cause similar symptoms (eg, appendicitis, cholecystitis, ulcerative colitis) must be excluded. Findings suggestive of gastroenteritis include copious, watery diarrhea; ingestion of potentially contaminated food (particularly during a known outbreak), untreated surface water, or a known GI irritant; recent travel; or contact with similarly ill people. *E. coli* O157:H7-induced diarrhea is notorious for appearing to be a hemorrhagic rather than an infectious process, manifesting as GI bleeding with little or no stool. Hemolyticuremic syndrome may follow as evidenced by renal failure and hemolytic anemia (see p. 961). Recent oral antibiotic use (within 3 mo) must raise suspicion for *C. difficile* infection (see p. 1292).

Stool testing: If a rectal examination shows occult blood or if watery diarrhea persists > 48 h, stool examination (fecal WBCs, ova, parasites) and culture are indicated. However, for the diagnosis of giardiasis or cryptosporidiosis, stool antigen detection using an enzyme immunoassay has a higher sensitivity. Rotavirus and enteric adenovirus infections can be diagnosed using commercially available rapid assays that detect viral antigen in the stool, but these are usually done only to document an outbreak.

All patients with grossly bloody diarrhea should be tested for *E. coli* O157:H7, as should patients with nonbloody diarrhea during a known outbreak. Specific cultures must be requested because this organism is not detected on standard stool culture media. Alternatively, a rapid enzyme assay for the detection of Shiga toxin in stool can be done; a positive test indicates infection with *E. coli* O157:H7 or one of the other serotypes of enterohemorrhagic *E. coli*. (NOTE: *Shigella* species in the US do not produce Shiga toxin.)

Adults with grossly bloody diarrhea should usually have sigmoidoscopy with cultures and biopsy. Appearance of the colonic mucosa may help diagnose amebic dysentery, shigellosis, and *E. coli* O157:H7 infection, although ulcerative colitis may cause similar lesions. Patients with recent antibiotic use should have a stool assay for *C. difficile* toxin.

General tests: Serum electrolytes, BUN, and creatinine should be obtained to evaluate hydration and acid-base status in patients who appear seriously ill. CBC is nonspecific, although eosinophilia may indicate parasitic infection.

Treatment

• Oral or IV rehydration

• Consideration of antidiarrheal agents if there is no suspicion of *C. difficile* or *E. coli* O157:H7 infection

• Antibiotics only in select cases

Supportive treatment is all that is needed for most patients. Bed rest with convenient access to a toilet or bedpan is desirable. Oral glucose-electrolyte solutions, broth, or bouillon may prevent dehydration or treat mild dehydration. Even if vomiting, the patient should take frequent small sips of such fluids: vomiting may abate with volume replacement. For patients with *E. coli* O157:H7 infection, rehydration with isotonic IV fluids may attenuate the severity of any renal injury should hemolytic-uremic syndrome develop. Children may become dehydrated more quickly and should be given an appropriate rehydration solution (several are available commercially—see also p. 2809). Carbonated beverages and sports drinks lack the correct ratio of glucose to Na and thus are not appropriate for children < 5 yr. If the child is breastfed, breastfeeding should continue. If vomiting is protracted or if severe dehydration is prominent, IV replacement of volume and electrolytes is necessary (see p. 2297).

When the patient can tolerate fluids without vomiting and the appetite has begun to return, food may be gradually restarted. There is no demonstrated benefit from restriction to bland food (eg, cereal, gelatin, bananas, toast). Some patients have temporary lactose intolerance.

Antidiarrheal agents are safe for patients > 5 yr with watery diarrhea (as shown by heme-negative stool). However, antidiarrheals may cause deterioration of patients with *C. difficile* or *E. coli* O157:H7 infection and thus should not be given to any patient with recent antibiotic use or heme-positive stool, pending specific diagnosis. Effective antidiarrheals include loperamide 4 mg po initially, followed by 2 mg po for each subsequent episode of diarrhea (maximum of 6 doses/day or 16 mg/day), or diphenoxylate 2.5 to 5 mg tid or qid in tablet or liquid form.

If vomiting is severe and a surgical condition has been excluded, an antiemetic may be beneficial. Agents useful in adults include prochlorperazine 5 to 10 mg IV tid or qid, or 25 mg per rectum bid; and promethazine 12.5 to 25 mg IM tid or qid, or 25 to 50 mg per rectum qid. These drugs are usually avoided in children because of lack of demonstrated efficacy and the high incidence of dystonic reactions.

Antimicrobials: Empiric antibiotics are generally not recommended except for certain cases of traveler's diarrhea or when suspicion of *Shigella* or *Campylobacter* infection is high (eg, contact with a known case). Otherwise, antibiotics should not be given until stool culture results are known, particularly in children, who have a higher rate of infection with *E. coli* O157:H7 (antibiotics increase the risk of hemolytic-uremic syndrome in patients infected with *E. coli* O157:H7).

In proven bacterial gastroenteritis, antibiotics are not always required. They do not help with *Salmonella* and prolong the duration of shedding in the stool. Exceptions include immunocompromised patients, neonates, and patients with *Salmonella* bacteremia. Antibiotics are also ineffective against toxic gastroenteritis (eg, *S. aureus*, *B. cereus*, *C. perfringens*). Indiscriminate use of antibiotics fosters the emergence of drug-resistant organisms. However, certain infections do require antibiotics (see Table 16-1).

The use of probiotics, such as lactobacillus, is generally safe and may have some benefit in relieving symptoms. They can be given in the form of yogurt with active cultures.

[**Table 16-1.** Selected Oral Antibiotics for Infectious Gastroenteritis*]

For cryptosporidiosis, nitazoxanide may be helpful in immunocompetent patients. The dose is 100 mg po bid for children 1 to 3 yr, 200 mg po bid for children 4 to 11 yr, and 500 mg po bid for children ≥ 12 yr and adults.

Prevention

A new oral pentavalent rotavirus vaccine is available that is safe and effective against the majority of strains responsible for disease. This vaccine is now part of the recommended infant vaccination schedule and is given at 2, 4, and 6 mo of age (see p. 2718).

Prevention of infection is complicated by the frequency of asymptomatic infection and the ease with which many agents, particularly viruses, are transmitted from person to person. In general, proper procedures for handling and preparing food must be followed. Travelers must avoid potentially contaminated food and drink.

Breastfeeding affords some protection to neonates and infants. Caregivers should wash their hands thoroughly with soap and water after changing diapers, and diaper-changing areas should be disinfected with a freshly prepared solution of 1:64 household bleach (one fourth cup diluted in 1 gallon of water). Children with diarrhea should be excluded from child care facilities for the duration of symptoms. Children infected with enterohemorrhagic *E. coli* or *Shigella* should also have two negative stool cultures before readmission to the facility.

Traveler's Diarrhea

(Turista)

Traveler's diarrhea is gastroenteritis that is usually caused by bacteria endemic to local water.

Symptoms include vomiting and diarrhea. Diagnosis is mainly clinical. Treatment is with ciprofloxacin or azithromycin, loperamide, and replacement fluids.

Etiology

Traveler's diarrhea may be caused by any of several bacteria, viruses, or, less commonly, parasites. However, enterotoxigenic *Escherichia coli* is most common. *E. coli* is common in the water supplies of areas that lack adequate purification. Infection is common among people traveling to developing countries. Norovirus infection has been a particular problem on some cruise ships.

Both food and water can be the source of infection. Travelers who avoid drinking local water may still become infected by brushing their teeth with an improperly rinsed toothbrush, drinking bottled drinks with ice made from local water, or eating food that is improperly handled or washed with local water. People taking drugs that decrease stomach acid (antacids, H_2 blockers, and proton pump inhibitors) are at risk of more severe illness.

Symptoms and Signs

Nausea, vomiting, borborygmi, abdominal cramps, and diarrhea begin 12 to 72 h after ingesting contaminated food or water. Severity is variable. Some people develop fever and myalgias. Most cases are mild and self-limited, although dehydration can occur, especially in warm climates.

Diagnosis

• Clinical evaluation

Specific diagnostic measures are usually not necessary. However, fever, severe abdominal pain, and bloody diarrhea suggest more serious disease and should prompt immediate evaluation.

Treatment

• Fluid replacement

• Sometimes antimotility drugs

• Rarely antibiotics (eg, ciprofloxacin, azithromycin)

The mainstay of treatment is fluid replacement and an antimotility drug such as loperamide 4 mg po initially, followed by 2 mg po for each subsequent episode of diarrhea (maximum of 6 doses/day or 16 mg/day), or diphenoxylate 2.5 to 5 mg po tid or qid in tablet or liquid form. Antimotility drugs are contraindicated in patients with fever or bloody stools and in children < 2 yr. Iodochlorhydroxyquin, which may be available in some developing countries, should not be used because it may cause neurologic damage.

Generally, antibiotics are not necessary for mild diarrhea. In patients with moderate to severe diarrhea (≥ 3 loose stools over 8 h), antibiotics are given, especially if vomiting, abdominal cramps, fever, or bloody stools are present. For adults, ciprofloxacin 500 mg po bid for 3 days or levofloxacin 500 mg po once/day for 3 days is recommended. Azithromycin 250 mg po once/day for 3 days or rifaximin 200 mg po tid for 3 days may also be used. For children, azithromycin 5 to 10 mg/kg po once/day for 3 days is preferred.

Prevention

Travelers should dine at restaurants with a reputation for safety and avoid foods and beverages from street vendors. They should consume only cooked foods that are still steaming hot, fruit that can be peeled, and carbonated beverages without ice served in sealed bottles (bottles of noncarbonated beverages can contain tap water added by unscrupulous vendors); uncooked vegetables should be avoided. Buffets and fast food restaurants pose an increased risk.

Prophylactic antibiotics are effective in preventing diarrhea, but because of concerns about adverse effects and development of resistance, they should probably be reserved for immunocompromised patients.

Drug- and Chemical-Related Gastroenteritis

Many drugs cause nausea, vomiting, and diarrhea as adverse effects. A detailed drug history must be obtained. In mild cases, cessation followed by reuse of the drug may establish a causal relationship. Commonly responsible drugs include antacids containing Mg, antibiotics, antihelminthics, cytotoxics (used in cancer therapy), colchicine, digoxin, heavy metals, laxatives, and radiation therapy. Use of antibiotics may lead to *Clostridium difficile*-induced diarrhea (see p. 1292).

Iatrogenic, accidental, or intentional heavy-metal poisoning frequently causes nausea, vomiting, abdominal pain, and diarrhea.

Laxative abuse, sometimes denied by patients, may lead to weakness, vomiting, diarrhea, electrolyte depletion, and metabolic disturbances.

Various plants and mushrooms cause a syndrome of gastroenteritis (see p. 3336).

Chapter 17. Malabsorption Syndromes

Introduction

Malabsorption is inadequate assimilation of dietary substances due to defects in digestion, absorption, or transport. Malabsorption can affect macronutrients (eg, proteins, carbohydrates, fats), micronutrients (eg, vitamins, minerals), or both, causing excessive fecal excretion, nutritional deficiencies, and GI symptoms.

Pathophysiology

Digestion and absorption occur in three phases: (1) intraluminal hydrolysis of fats, proteins, and carbohydrates by enzymes—bile salts enhance the solubilization of fat in this phase; (2) digestion by brush border enzymes and uptake of end-products; and (3) lymphatic transport of nutrients. Malabsorption occurs when any of these phases is impaired.

Fats: Pancreatic enzymes split long-chain triglycerides into fatty acids and monoglycerides, which combine with bile acids and phospholipids to form micelles that pass through jejunal enterocytes. Absorbed fatty acids are resynthesized and combined with protein, cholesterol, and phospholipid to form chylomicrons, which are transported by the lymphatic system. Medium-chain triglycerides are absorbed directly.

Unabsorbed fats trap fat-soluble vitamins (A, D, E, K) and possibly some minerals, causing deficiency. Bacterial overgrowth results in deconjugation and dehydroxylation of bile salts, limiting the absorption of fats. Unabsorbed bile salts stimulate the colon, causing diarrhea.

Carbohydrates: Enzymes on microvilli lyse carbohydrates and disaccharides into constituent monosaccharides. Colonic bacteria ferment unabsorbed carbohydrates into CO_2, methane, H_2, and short-chain fatty acids (butyrate, propionate, acetate, and lactate). These fatty acids cause diarrhea. The gases cause abdominal distention and bloating.

Proteins: Enterokinase, a brush border enzyme, activates trypsinogen into trypsin, which converts many pancreatic proteases into their active forms. Active pancreatic enzymes hydrolyze proteins into oligopeptides, which are absorbed directly or hydrolyzed into amino acids.

Etiology

Malabsorption has many causes (see Table 17-1). Some malabsorptive disorders (eg, celiac sprue) impair the absorption of most nutrients, vitamins, and trace minerals (global malabsorption); others (eg, pernicious anemia) are more selective.

[**Table 17-1.** Causes of Malabsorption]

Pancreatic insufficiency causes malabsorption if > 90% of function is lost. Increased luminal acidity (eg, Zollinger-Ellison syndrome) inhibits lipase and fat digestion. Cirrhosis and cholestasis reduce hepatic bile synthesis or delivery of bile salts to the duodenum, causing malabsorption. Other causes are discussed elsewhere in this chapter.

Symptoms and Signs

The effects of unabsorbed substances include diarrhea, steatorrhea, abdominal bloating, and gas. Other symptoms result from nutritional deficiencies. Patients often lose weight despite adequate food intake.

Chronic diarrhea is the most common symptom and is what usually prompts evaluation of the patient. Steatorrhea—fatty stool, the hallmark of malabsorption—occurs when > 7 g/day of fat are excreted. Steatorrhea causes foul-smelling, pale, bulky, and greasy stools.

Severe vitamin and mineral deficiencies occur in advanced malabsorption; symptoms are related to the

specific nutrient deficiency (see Table 17-2). Vitamin B_{12} deficiency may occur in blind loop syndrome or after extensive resection of the distal ileum or stomach.

Amenorrhea may result from undernutrition and is an important manifestation of celiac sprue in young women.

Diagnosis

• Diagnosis typically clinically apparent

• Blood tests to screen for consequences of malabsorption

• Stool fat testing to confirm malabsorption (if unclear)

• Cause diagnosed with endoscopy, contrast x-rays, or other tests based on findings

Malabsorption is suspected in a patient with chronic diarrhea, weight loss, and anemia. The etiology is sometimes obvious. For example, those with malabsorption due to chronic pancreatitis usually have had prior bouts of acute pancreatitis. Patients with celiac sprue can present with classic lifelong diarrhea exacerbated by gluten products and may have dermatitis herpetiformis. Those with cirrhosis and pancreatic cancer can present with jaundice. Abdominal distention, excessive flatus, and watery diarrhea occurring 30 to 90 min after carbohydrate ingestion suggest deficiency of a disaccharidase enzyme, usually lactase. Previous extensive abdominal operations suggest short bowel syndrome.

If the history suggests a specific cause, testing should be directed to that condition (see Fig. 17-1). If no cause is readily apparent, blood tests can be used as screening tools (eg, CBC, RBC indices, ferritin, vitamin B_{12}, folate, Ca, albumin, cholesterol, PT). These results may suggest a diagnosis and direct further investigation.

[**Table 17-2.** Symptoms of Malabsorption]

Macrocytic anemia should prompt measurement of serum folate and B_{12} levels. Folate deficiency is common in mucosal disorders involving the proximal small bowel (eg, celiac sprue, tropical sprue, Whipple's disease). Low B_{12} levels can occur in pernicious anemia, chronic pancreatitis, bacterial overgrowth, and terminal ileal disease. A combination of low B_{12} and high folate levels is suggestive of bacterial overgrowth, because intestinal bacteria use vitamin B_{12} and synthesize folate.

Microcytic anemia suggests iron deficiency, which may occur with celiac sprue. Albumin is a general indicator of nutritional state. Low albumin can result from poor intake, decreased synthesis in cirrhosis, or protein wasting. Low serum carotene (a precursor of vitamin A) suggests malabsorption if intake is adequate.

Confirming malabsorption: Tests to confirm malabsorption are appropriate when symptoms are vague and the etiology is not apparent. Most tests for malabsorption assess fat malabsorption because it is relatively easy to measure. Confirmation of carbohydrate malabsorption is not helpful once steatorrhea is documented. Tests for protein malabsorption are rarely used because fecal nitrogen is difficult to measure.

[**Fig. 17-1.** Suggested evaluation for malabsorption.]

[**Table 17-3.** Small-Bowel Mucosal Histology in Certain Malabsorptive Disorders]

Direct measurement of fecal fat from a 72-h stool collection is the gold standard for establishing steatorrhea but unnecessary with gross steatorrhea of obvious cause. However, this test is available routinely in only a few centers. Stool is collected for a 3-day period during which the patient consumes ≥

100 g fat/day. Total fat in the stool is measured. Fecal fat > 7 g/day is abnormal. Although severe fat malabsorption (fecal fat ≥ 40 g/day) suggests pancreatic insufficiency or small-bowel mucosal disease, this test cannot determine the specific cause of malabsorption. Because the test is messy, unpleasant, and time consuming, it is unacceptable to most patients and difficult to do.

Sudan III staining of a stool smear is a simple and direct, but nonquantitative, screening test for fecal fat. Acid steatocrit is a gravimetric assay done on a single stool sample; it has a reported high sensitivity and specificity (using 72-h collection as the standard). Near-infrared reflectance analysis (NIRA) simultaneously tests stool for fat, nitrogen, and carbohydrates and may become the preferred test in the future.

Measurement of elastase and chymotrypsin in the stool can also help differentiate pancreatic and intestinal causes of malabsorption; both are decreased in pancreatic exocrine insufficiency.

The D-xylose absorption test, if available, can be done if the etiology is not obvious. It is the best noninvasive test to assess intestinal mucosal integrity and differentiate mucosal from pancreatic disease. This test has a reported specificity of 98% and sensitivity of 91% for small-bowel malabsorption.

D-Xylose is absorbed by passive diffusion and does not require pancreatic enzymes for digestion. A normal D-xylose test in the presence of moderate to severe steatorrhea indicates pancreatic exocrine insufficiency rather than small-bowel mucosal disease. Bacterial overgrowth syndrome can cause abnormal results because the enteric bacteria metabolize pentose, thus decreasing the D-xylose available for absorption.

After fasting, the patient is given 25 g of D-xylose in 200 to 300 mL of water po. Urine is collected over 5 h, and a venous sample is obtained after 1 h. Serum D-xylose < 20 mg/dL or < 4 g in the urine sample indicates abnormal absorption. Falsely low levels can also occur in renal diseases, portal hypertension, ascites, or delayed gastric emptying time. This test is rarely used today. In addition, an abnormal D-xylose test will require an endoscopic examination with biopsies of the small-bowel mucosa. As a result, small-bowel biopsy has replaced this test to establish intestinal mucosal disease.

Diagnosing the cause of malabsorption: More specific diagnostic tests (eg, upper endoscopy, colonoscopy, barium x-rays) are indicated to diagnose several causes of malabsorption.

Endoscopy with small-bowel biopsy is done when mucosal disease of the small bowel is suspected or if the D-xylose test is abnormal in a patient with massive steatorrhea. Aspirate from the small bowel can be sent for bacterial culture and colony count to document bacterial overgrowth. Histologic features on small-bowel biopsy (see Table 17-3) can establish the specific mucosal disease.

Small-bowel x-rays (eg, small-bowel follow-through, enteroclysis) can detect anatomic conditions that predispose to bacterial overgrowth. These include jejunal diverticula, fistulas, surgically created blind loops and anastomoses, ulcerations, and strictures. Abdominal flat plate x-ray may show pancreatic calcifications indicative of chronic pancreatitis. Barium contrast studies of the small bowel are neither sensitive nor specific but may have findings suggestive of mucosal disease (eg, dilated small-bowel loops, thinned or thickened mucosal folds, coarse fragmentation of the barium column).

Tests for pancreatic insufficiency (eg, secretin stimulation test, bentiromide test, pancreolauryl test, serum trypsinogen, fecal elastase, fecal chymotrypsin—see p. 145) are done if history is suggestive but are not sensitive for mild pancreatic disease.

The ^{14}C-xylose breath test helps diagnose bacterial overgrowth. ^{14}C-xylose is given orally, and the exhaled $^{14}CO_2$ concentration is measured. Catabolism of ingested xylose by the overgrowth flora causes $^{14}CO_2$ to appear in exhaled breath.

The H_2 breath test measures the exhaled H_2 produced by the bacterial degradation of carbohydrates. In patients with disaccharidase deficiencies, enteric bacteria degrade nonabsorbed carbohydrates in the

colon, increasing exhaled H_2. The lactose-H_2 breath test is useful only to confirm lactase deficiency (see p. 158) and is not used as an initial diagnostic test in the work-up of malabsorption.

The Schilling test assesses malabsorption of vitamin B_{12}. Its 4 stages determine whether the deficiency results from pernicious anemia, pancreatic exocrine insufficiency, bacterial overgrowth, or ileal disease.

- Stage 1: The patient is given 1 µg of radiolabeled cyanocobalamin po concurrent with 1000 µg of nonlabeled cobalamin IM to saturate hepatic binding sites. A 24-h urine collection is analyzed for radioactivity; urinary excretion of < 8% of the oral dose indicates malabsorption of cobalamin.

- Stage 2: If stage 1 is abnormal, the test is repeated with the addition of intrinsic factor. Pernicious anemia is present if this normalizes absorption.

- Stage 3: Stage 3 is done after adding pancreatic enzymes; normalization in this stage indicates cobalamin malabsorption secondary to pancreatic insufficiency.

- Stage 4: Stage 4 is done after antimicrobial therapy with anaerobic coverage; normalization after antibiotics suggests bacterial overgrowth.

Cobalamin deficiency secondary to ileal disease or ileal resection results in abnormalities in all stages.

Tests for less common causes of malabsorption include serum gastrin (Zollinger-Ellison syndrome), intrinsic factor and parietal cell antibodies (pernicious anemia), sweat chloride (cystic fibrosis), lipoprotein electrophoresis (abetalipoproteinemia), and serum cortisol (Addison's disease).

Bacterial Overgrowth Syndrome

Small-bowel bacterial overgrowth can occur from alterations in intestinal anatomy or GI motility, or lack of gastric acid secretion. This condition can lead to vitamin deficiencies, fat malabsorption, and undernutrition. Diagnosis is by breath test or quantitative culture of intestinal fluid aspirate. Treatment is with oral antibiotics.

Under normal conditions, the proximal small bowel contains < 10^5 bacteria/mL, mainly gram-positive aerobic bacteria. This low bacterial count is maintained by normal peristalsis, normal gastric acid secretion, mucus, secretory IgA, and an intact ileocecal valve.

Etiology

Usually, bacterial overgrowth occurs when anatomic alterations promote stasis of intestinal contents. These conditions include small-bowel diverticulosis, surgical blind loops, postgastrectomy states (especially in the afferent loop of a Billroth II), strictures, or partial obstruction. Intestinal motility disorders associated with diabetic neuropathy, systemic sclerosis, amyloidosis, and idiopathic intestinal pseudo-obstruction can also impair bacterial clearance. Achlorhydria and idiopathic changes in intestinal motility may cause bacterial overgrowth in elderly people.

Pathophysiology

The excess bacteria consume nutrients, including vitamin B_{12} and carbohydrates, leading to caloric deprivation and vitamin B_{12} deficiency. However, because the bacteria produce folate, this deficiency is rare. The bacteria deconjugate bile salts, causing failure of micelle formation and subsequent fat malabsorption. Severe bacterial overgrowth also damages the intestinal mucosa. Fat malabsorption and mucosal damage can cause diarrhea.

Symptoms and Signs

Many patients are asymptomatic and present with only weight loss or nutrient deficiencies. Some have significant diarrhea or steatorrhea.

Diagnosis

• ^{14}C-xylose breath test or quantitative culture of intestinal aspirate

• Upper GI series with small-bowel follow-through

Some clinicians advocate response to empiric antibiotic therapy as a diagnostic test. However, because bacterial overgrowth can mimic other malabsorptive disorders (eg, Crohn's disease) and adverse effects of the antibiotics can worsen symptoms, establishing a definitive etiology is preferred.

The standard for diagnosis is quantitative culture of intestinal fluid aspirate showing bacterial count > 10^5/mL. This method, however, requires endoscopy. Breath tests, using substrates like glucose, lactulose, and xylose, are noninvasive and easy to do. The ^{14}C-xylose breath test seems to perform better than the other breath tests. In addition, an upper GI series with small-bowel follow-through should be done to identify predisposing anatomic lesions.

Treatment

• Oral antibiotics (various)

Treatment is with 10 to 14 days of oral antibiotics. Empiric regimens include tetracycline 250 mg qid, amoxicillin/clavulanic acid 250 to 500 mg tid, cephalexin 250 mg qid, trimethoprim/sulfamethoxazole 160/800 mg bid, and metronidazole 250 to 500 mg tid or qid. Antibiotics should be changed based on culture and sensitivity results. Underlying conditions and nutritional deficiencies (eg, vitamin B_{12}) should be corrected.

Carbohydrate Intolerance

Carbohydrate intolerance is the inability to digest certain carbohydrates due to a lack of one or more intestinal enzymes. Symptoms include diarrhea, abdominal distention, and flatulence. Diagnosis is clinical and by an H_2 breath test. Treatment is removal of the causative disaccharide from the diet.

Pathophysiology

Disaccharides are normally split into monosaccharides by disaccharidases (eg, lactase, maltase, isomaltase, sucrase [invertase]) located in the brush border of small-bowel enterocytes. Undigested disaccharides cause an osmotic load that attracts water and electrolytes into the bowel, causing watery diarrhea. Bacterial fermentation of carbohydrates in the colon produces gases (H_2, CO_2, and methane), resulting in excessive flatus, bloating and distention, and abdominal pain.

Etiology

Enzyme deficiencies can be congenital, acquired (primary), or secondary. Congenital deficiencies are rare.

Acquired lactase deficiency (primary adult hypolactasia) is the most common form of carbohydrate intolerance. Lactase levels are high in neonates, permitting digestion of milk; in most ethnic groups (80% of blacks and Hispanics, almost 100% of Asians), the levels decrease in the post-weaning period rendering older children and adults unable to digest significant amounts of lactose. However, 80 to 85% of whites of Northwest European descent produce lactase throughout life and are thus able to digest milk and milk products. It is unclear why the normal state of > 75% of the world's population should be labeled a "deficiency."

Secondary lactase deficiency occurs in conditions that damage the small-bowel mucosa (eg, celiac sprue,

tropical sprue, acute intestinal infections). In infants, temporary secondary disaccharidase deficiency may complicate enteric infections or abdominal surgery. Recovery from the underlying disease is followed by an increase in activity of the enzyme.

Symptoms and Signs

Symptoms and signs are similar in all disaccharidase deficiencies. A child who cannot tolerate lactose develops diarrhea after ingesting significant amounts of milk and may not gain weight. An affected adult may have watery diarrhea, bloating, excessive flatus, nausea, borborygmi, and abdominal cramps after ingesting lactose. The patient often recognizes this early in life and avoids eating dairy products. Symptoms typically require ingestion of more than the equivalent of 8 to 12 oz of milk. Diarrhea may be severe enough to purge other nutrients before they can be absorbed. Symptoms may be similar to and can be confused with irritable bowel syndrome (see p. 162).

Diagnosis

• Clinical diagnosis

• H_2 breath test for confirmation

Lactose intolerance can usually be diagnosed with a careful history supported by dietary challenge. Patients usually have a history of intolerance to milk and dairy foods. The diagnosis is also suggested if the stool from chronic or intermittent diarrhea is acidic (pH < 6) and can be confirmed by an H_2 breath or a lactose tolerance test.

In the H_2 breath test, 50 g of lactose is given orally and the H_2 produced by bacterial metabolism of undigested lactose is measured with a breath meter at 2, 3, and 4 h postingestion. Most affected patients have an increase in expired H_2 of > 20 ppm over baseline. Sensitivity and specificity are > 95%.

The lactose tolerance test is less specific. Oral lactose (1.0 to 1.5 g/kg body weight) is given. Serum glucose is measured before ingestion and 60 and 120 min after. Lactose-intolerant patients develop diarrhea, abdominal bloating, and discomfort within 20 to 30 min, and their serum glucose levels do not rise > 20 mg/dL (< 1.1 mmol/L) above baseline. Low lactase activity in a jejunal biopsy specimen is diagnostic, but endoscopy is needed to obtain a specimen and is not routine.

Treatment

• Dietary restriction

Carbohydrate malabsorption is readily controlled by avoiding dietary sugars that cannot be absorbed (ie, following a lactose-free diet in cases of lactase deficiency). However, because the degree of lactose malabsorption varies greatly, many patients can ingest up to 12 oz (18 g of lactose) of milk daily without symptoms. Yogurt is usually tolerated because it contains an appreciable amount of lactase produced by intrinsic *Lactobacilli*.

For symptomatic patients wishing to drink milk, lactose in milk can be predigested by the addition of a commercially prepared lactase, and pretreated milk is now available. Enzyme supplements should be an adjunct to, not a substitute for, dietary restriction. Lactose-intolerant patients must take Ca supplements (1200 to 1500 mg/day).

Celiac Sprue

(Nontropical Sprue; Gluten Enteropathy; Celiac Disease)

Celiac sprue is an immunologically mediated disease in genetically susceptible people caused by intolerance to gluten, resulting in mucosal inflammation, which causes malabsorption. Symptoms usually include diarrhea and abdominal discomfort. Diagnosis is by small-bowel

biopsies showing characteristic though not specific pathologic changes of villous atrophy that resolve with a strict gluten-free diet.

Etiology

Celiac sprue is a hereditary disorder caused by sensitivity to the gliadin fraction of gluten, a protein found in wheat; similar proteins are present in rye and barley. In a genetically susceptible person, gluten-sensitive T cells are activated when gluten-derived peptide epitopes are presented. The inflammatory response causes characteristic mucosal villous atrophy in the small bowel.

Epidemiology: Celiac sprue mainly affects whites of northern European descent. Prevalence estimates based on serologic screens (sometimes confirmed by biopsy) indicate the disorder is present in about 1/300 in Europe and perhaps 1/250 in the US overall (but there may be significant variation among regions in the US).

The disease affects about 10 to 20% of 1st-degree relatives. Female:male ratio is 2:1. Onset is generally in childhood but may occur later.

Symptoms and Signs

The clinical presentation varies; no typical presentation exists. Some patients are asymptomatic or have only signs of nutritional deficiency. Others have significant GI symptoms.

Celiac sprue can manifest in infancy and childhood after introduction of cereals into the diet. The child has failure to thrive, apathy, anorexia, pallor, generalized hypotonia, abdominal distention, and muscle wasting. Stools are soft, bulky, clay-colored, and offensive. Older children may present with anemia or failure to grow normally.

In adults, lassitude, weakness, and anorexia are most common. Mild and intermittent diarrhea is sometimes the presenting symptom. Steatorrhea ranges from mild to severe (7 to 50 g fat/day). Some patients have weight loss, rarely enough to become underweight. Anemia, glossitis, angular stomatitis, and aphthous ulcers are usually seen in these patients. Manifestations of vitamin D and Ca deficiencies (eg, osteomalacia, osteopenia, osteoporosis) are common. Both men and women may have reduced fertility.

About 10% have dermatitis herpetiformis, an intensely pruritic papulovesicular rash that is symmetrically distributed over the extensor areas of the elbows, knees, buttocks, shoulders, and scalp. This rash can be induced by a high-gluten diet. Celiac sprue is also associated with diabetes mellitus, autoimmune thyroid disease, and Down syndrome.

Diagnosis

• Serologic markers

• Small-bowel biopsy

The diagnosis is suspected clinically and by laboratory abnormalities suggestive of malabsorption. Family incidence is a valuable clue. Celiac sprue should be strongly considered in a patient with iron deficiency without obvious GI bleeding.

Confirmation requires a small-bowel biopsy from the second portion of the duodenum. Findings include lack or shortening of villi (villous atrophy), increased intraepithelial cells, and crypt hyperplasia. However, such findings can also occur in tropical sprue, severe intestinal bacterial overgrowth, eosinophilic enteritis, lactose intolerance, and lymphoma.

Because biopsy lacks specificity, serologic markers can aid diagnosis. Anti-tissue transglutaminase antibody (AGA) and anti-endomysial antibody (EMA—an antibody against an intestinal connective tissue protein) each have sensitivity and specificity > 90%. These markers can also be used to screen

populations with high prevalence of celiac sprue, including 1st-degree relatives of affected patients and patients with diseases that occur at a greater frequency in association with celiac sprue. If either test is positive, the patient should have a diagnostic small-bowel biopsy. If both are negative, celiac sprue is extremely unlikely. These antibodies decrease in titer in patients on a gluten-free diet and thus are useful in monitoring dietary compliance.

Other laboratory abnormalities often occur and should be sought. They include anemia (iron-deficiency anemia in children and folate-deficiency anemia in adults); low albumin, Ca, K, and Na; and elevated alkaline phosphatase and PT.

Malabsorption tests are not specific for celiac sprue. If done, common findings include steatorrhea of 10 to 40 g/day and abnormal results with D-xylose and (in severe ileal disease) Schilling tests.

Prognosis

Mortality is 10 to 30% without a gluten-free diet. With proper diet, mortality is < 1%, mainly in adults who have severe disease at the outset. Complications include refractory sprue, collagenous sprue, and intestinal lymphomas. Intestinal lymphomas affect 6 to 8% of patients with celiac sprue, usually manifesting after 20 to 40 yr of disease. The incidence of other GI cancers (eg, carcinoma of the esophagus or oropharynx, small-bowel adenocarcinoma) also increases. Adherence to a gluten-free diet can significantly reduce the risk of cancer.

Treatment

• Gluten-free diet

• Supplements to replace any serious deficiencies

Treatment is a gluten-free diet (avoiding foods containing wheat, rye, or barley). Gluten is so widely used (eg, in commercial soups, sauces, ice creams, hot dogs) that a patient needs a detailed list of foods to avoid. Patients are encouraged to consult a dietitian and join a celiac support group. The response to a gluten-free diet is usually rapid, and symptoms resolve in 1 to 2 wk. Ingesting even small amounts of food containing gluten may prevent remission or induce relapse.

Small-bowel biopsy should be repeated after 3 to 4 mo of a gluten-free diet. If abnormalities persist, other causes of villous atrophy (eg, lymphoma) should be considered. Lessening of symptoms and improvement in small-bowel morphology are accompanied by a decrease in AGA and EMA titers.

Supplementary vitamins, minerals, and hematinics may be given, depending on the deficiencies. Mild cases may not require supplementation, whereas severe cases may require comprehensive replacement. For adults, replacement includes ferrous sulfate 300 mg po once/day to tid, folate 5 to 10 mg po once/day, Ca supplements, and any standard multivitamin. Sometimes children (but rarely adults) who are seriously ill on initial diagnosis require bowel rest and TPN.

If a patient responds poorly to gluten withdrawal, either the diagnosis is incorrect or the disease has become refractory. Corticosteroids can control symptoms in the latter case.

Infection and Infestation

Acute bacterial, viral, and parasitic infections may cause transient malabsorption, probably as a result of temporary, superficial damage to the villi and microvilli. Chronic bacterial infections of the small bowel are uncommon, apart from blind loops, systemic sclerosis, and diverticula. Intestinal bacteria may use up dietary vitamin B_{12} and other nutrients, perhaps interfere with enzyme systems, and cause mucosal injury.

Intestinal Lymphangiectasia

(Idiopathic Hypoproteinemia)

Intestinal lymphangiectasia is obstruction or malformation of the intramucosal lymphatics of the small bowel. It primarily affects children and young adults. Symptoms include those of malabsorption, with edema and growth retardation. Diagnosis is by small-bowel biopsy. Treatment is usually supportive.

Malformation of the lymphatic system is congenital or acquired. Congenital cases usually manifest in children and young adults (mean age of onset: 11 yr). Males and females are equally affected. In acquired cases, the defect may be secondary to retroperitoneal fibrosis, constrictive pericarditis, pancreatitis, neoplastic tumors, and infiltrative disorders that block the lymphatics.

Impaired lymphatic drainage leads to increased pressure and leakage of lymph into the intestinal lumen. Impairment of chylomicron and lipoprotein absorption results in malabsorption of fats and protein. Because carbohydrates are not absorbed through the lymphatic system, their uptake is not impaired.

Symptoms and Signs

Early manifestations include massive and often asymmetric peripheral edema, intermittent diarrhea, nausea, vomiting, and abdominal pain. Some patients have mild to moderate steatorrhea. Chylous pleural effusions (chylothorax) and chylous ascites may be present. Growth is retarded if onset is in the first decade of life.

Diagnosis

• Endoscopic small-bowel biopsy

• Sometimes contrast lymphangiography

Diagnosis usually requires endoscopic small-bowel biopsy, which shows marked dilation and ectasia of the mucosal and submucosal lymphatic vessels. Alternatively, contrast lymphangiography (injection of contrast material via the pedal vein) can show abnormal intestinal lymphatics.

Laboratory abnormalities include lymphocytopenia and low levels of serum albumin, cholesterol, IgA, IgM, IgG, transferrin, and ceruloplasmin. Barium studies may show thickened, nodular mucosal folds that resemble stacked coins. D-Xylose absorption is normal. Intestinal protein loss can be shown by using chromium-51-labeled albumin.

Treatment

• Supportive care

• Sometimes surgical resection or repair

Abnormal lymphatics cannot be corrected. Supportive treatment includes a low-fat (< 30 g/day), high-protein diet containing medium-chain triglyceride supplements. Supplemental Ca and fat-soluble vitamins are given. Intestinal resection or anastomosis of the abnormal lymphatics to the venous channels may be beneficial. Pleural effusions should be drained by thoracentesis.

Short Bowel Syndrome

Short bowel syndrome is malabsorption resulting from extensive resection of the small bowel. Symptoms depend on the length and function of the remaining small bowel, but diarrhea can be severe, and nutritional deficiencies are common. Treatment is with small feedings, antidiarrheals, and sometimes TPN or intestinal transplantation.

Common reasons for extensive resection are Crohn's disease, mesenteric infarction, radiation enteritis, cancer, volvulus, and congenital anomalies.

Because the jejunum is the primary digestive and absorptive site for most nutrients, jejunal resection significantly reduces nutrient absorption. In response, the ileum adapts by increasing the length and absorptive function of its villi, resulting in gradual improvement of nutrient absorption.

The ileum is the site of vitamin B_{12} and bile acid absorption. Severe diarrhea and bile acid malabsorption result when > 100 cm of the ileum is resected. Notably, there is no compensatory adaptation of the remaining jejunum. Consequently, malabsorption of fat, fat-soluble vitamins, and vitamin B_{12} occurs. In addition, unabsorbed bile acids in the colon result in secretory diarrhea. Preservation of the colon can significantly reduce water and electrolyte losses. Resection of the terminal ileum and ileocecal valve can predispose to bacterial overgrowth.

Treatment

• TPN

• Eventual oral feeding if > 100 cm of jejunum remain

• Antidiarrheals, cholestyramine, proton pump inhibitors, vitamin supplements

In the immediate postoperative period, diarrhea is typically severe, with significant electrolyte losses. Patients typically require TPN and intensive monitoring of fluid and electrolytes (including Ca and Mg). An oral iso-osmotic solution of Na and glucose (similar to WHO oral rehydration formula—see p. 2809) is slowly introduced in the postoperative phase once the patient stabilizes and stool output is < 2 L/day.

Patients with extensive resection (< 100 cm of remaining jejunum) and those with excessive fluid and electrolyte losses require TPN for life.

Patients with > 100 cm of jejunum left can achieve adequate nutrition through oral feeding. Fat and protein in the diet are usually well tolerated, unlike carbohydrates, which contribute a significant osmotic load. Small feedings reduce the osmotic load. Ideally, 40% of calories should consist of fat.

Patients who have diarrhea after meals should take antidiarrheals (eg, loperamide) 1 h before eating. Cholestyramine 2 to 4 g taken with meals reduces diarrhea associated with bile acid malabsorption. Monthly IM injections of vitamin B_{12} should be given to patients with a documented deficiency. Most patients should take supplemental vitamins, Ca, and Mg.

Gastric acid hypersecretion can develop, which can deactivate pancreatic enzymes; thus, most patients are given H_2 blockers or proton pump inhibitors.

Small-bowel transplantation is advocated for patients who are not candidates for long-term TPN and in whom adaptation does not occur.

Tropical Sprue

Tropical sprue is an acquired disease, probably of infectious etiology, characterized by malabsorption and megaloblastic anemia. Diagnosis is clinical and by small-bowel biopsy. Treatment is with tetracycline and folate for 6 mo.

Etiology

Tropical sprue occurs chiefly in the Caribbean, southern India, and Southeast Asia, affecting both natives and visitors. The illness is rare in visitors spending < 1 mo in areas where the disease is endemic. Although etiology is unclear, it is thought to result from chronic infection of the small bowel by toxigenic strains of coliform bacteria. Malabsorption of folate and vitamin B_{12} deficiency result in megaloblastic anemia. The incidence of tropical sprue is decreasing, perhaps because of increasing use of antibiotics for acute traveler's diarrhea.

Symptoms and Signs

Patients commonly have acute diarrhea with fever and malaise. A chronic phase of milder diarrhea, nausea, anorexia, abdominal cramps, and fatigue follows. Steatorrhea is common. Nutritional deficiencies, especially of folate and vitamin B_{12}, eventually develop after several months to years. The patient may also have weight loss, glossitis, stomatitis, and peripheral edema.

Diagnosis

• Endoscopy with small-bowel biopsy

• Blood tests to screen for consequences of malabsorption

Tropical sprue is suspected in people who live in or have visited areas where the disease is endemic and who have megaloblastic anemia and symptoms of malabsorption. The definitive test is upper GI endoscopy with small-bowel biopsy. Characteristic histologic changes (see Table 17-3) usually involve the entire small bowel and include blunting of the villi with infiltration of chronic inflammatory cells in the epithelium and lamina propria. Celiac disease and parasitic infection must be ruled out.

Additional laboratory studies (eg, CBC; albumin; Ca; PT; iron, folate, and B_{12} levels) help evaluate nutritional status. Barium small-bowel follow-through may show segmentation of the barium, dilation of the lumen, and thickening of the mucosal folds. D-Xylose absorption is abnormal in > 90% of cases. However, these tests are not specific or essential for diagnosis.

Treatment

• Long-term tetracycline

Treatment is tetracycline 250 mg po qid for 1 or 2 mo, then bid for up to 6 mo, depending on disease severity and response to treatment. Folate 5 to 10 mg po once/day should be given for the first month along with vitamin B_{12} 1 mg IM weekly for several weeks. Megaloblastic anemia promptly abates, and the clinical response is dramatic. Other nutritional replacements are given as needed. Relapse may occur in 20%. Failure to respond after 4 wk of therapy suggests another condition.

Whipple's Disease

(Intestinal Lipodystrophy)

Whipple's disease is a rare systemic illness caused by the bacterium *Tropheryma whippelii*. Main symptoms are arthritis, weight loss, and diarrhea. Diagnosis is by small-bowel biopsy. Treatment is with a minimum 1 yr of trimethoprim/sulfamethoxazole.

Whipple's disease predominately affects white men aged 30 to 60. Although it affects many parts of the body (eg, heart, lung, brain, serous cavities, joints, eye, GI tract), the mucosa of the small bowel is almost always involved. Affected patients may have subtle defects of cell-mediated immunity that predispose to infection with *T. whippelii*. About 30% of patients have HLA-B27.

Symptoms and Signs

Clinical presentation varies depending on the organ systems affected. Usually, the first symptoms are arthritis and fever. Intestinal symptoms (eg, watery diarrhea, steatorrhea, abdominal pain, anorexia, weight loss) usually manifest later, sometimes years after the initial complaint. Gross or occult intestinal bleeding may occur. Severe malabsorption may be present in patients diagnosed late in the clinical course. Other findings include increased skin pigmentation, anemia, lymphadenopathy, chronic cough, serositis, peripheral edema, and CNS symptoms.

Diagnosis

• Endoscopy with small-bowel biopsy

The diagnosis may be missed in patients without prominent GI symptoms. Whipple's disease should be suspected in middle-aged white men who have arthritis and abdominal pain, diarrhea, weight loss, or other symptoms of malabsorption. Such patients should have upper endoscopy with small-bowel biopsy; the intestinal lesions are specific and diagnostic. The most severe and consistent changes are in the proximal small bowel. Light microscopy shows periodic acid-Schiff-positive macrophages that distort the villus architecture. Gram-positive, acid fast-negative bacilli (*T. whippelii*) are seen in the lamina propria and in the macrophages. Confirmation by electron microscopy is recommended.

Whipple's disease should be differentiated from intestinal infection with *Mycobacterium avium-intracellulare* (MAI), which has similar histologic findings. However, MAI stains positive with acid fast. PCR testing may be useful for confirmation.

Treatment

• Antibiotics

• Late relapse a possibility

Untreated disease is progressive and fatal. Many antibiotics are curative (eg, tetracycline, trimethoprim/sulfamethoxazole, chloramphenicol, ampicillin, penicillin, cephalosporins). Treatment is initiated with ceftriaxone (2 g IV daily) or with procaine (1.2 million units IM once/day) or penicillin G (1.5 to 6 million units IV q 6 h) plus streptomycin (1.0 g IM once/day for 10 to 14 days). This regimen is followed by a long-term course of trimethoprim/sulfamethoxazole (160/800 mg po bid for 1 yr). Sulfa-allergic patients may substitute oral penicillin VK or ampicillin. Prompt clinical improvement occurs, with fever and joint pains resolving in a few days. Intestinal symptoms usually abate within 1 to 4 wk.

Some authorities do not recommend repeat small-bowel biopsies because macrophages may persist for years after treatment. However, others recommend repeat biopsy after 1 yr. In the latter approach, electron microscopy is needed to document bacilli (not just macrophages). Relapses are common and may occur years later. If relapse is suspected, small-bowel biopsies should be done (regardless of affected organ systems) to determine presence of free bacilli.

Chapter 18. Irritable Bowel Syndrome

(Spastic Colon)

Irritable bowel syndrome (IBS) is characterized by abdominal discomfort or pain that is accompanied by at least two of the following: relief by defecation, change in frequency of stool, or change in consistency of stool. The cause is unknown, and the pathophysiology is incompletely understood. Diagnosis is clinical. Treatment is symptomatic, consisting of dietary management and drugs, including anticholinergics and agents active at serotonin receptors.

Etiology

The cause of IBS is unknown. No anatomic cause can be found on laboratory tests, x-rays, and biopsies. Emotional factors, diet, drugs, or hormones may precipitate or aggravate GI symptoms. Historically, the disorder was often considered as purely psychosomatic. Although psychosocial factors are involved, IBS is better understood as a combination of psychosocial and physiologic factors.

Psychosocial factors: Psychologic distress is common among patients with IBS, especially among those who seek medical care. Some patients have anxiety disorders, depression, or a somatization disorder. Sleep disturbances also coexist. However, stress and emotional conflict do not always coincide with symptom onset and recurrence. Some patients with IBS seem to have a learned aberrant illness behavior (ie, they express emotional conflict as a GI complaint, usually abdominal pain). The physician evaluating patients with IBS, particularly those with refractory symptoms, should investigate for unresolved psychologic issues, including the possibility of sexual or physical abuse. Psychosocial factors also affect the outcome in IBS.

Physiologic factors: A variety of physiologic factors seem to be involved in IBS symptoms. Factors include altered motility, visceral hyperalgesia, and various genetic and environmental factors.

Visceral hyperalgesia refers to hypersensitivity to normal amounts of intraluminal distention and heightened perception of pain in the presence of normal quantities of intestinal gas; it may result from remodeling of neural pathways in the brain-gut axis. Some patients (perhaps 1 in 7) have reported their IBS symptoms began after an episode of acute gastroenteritis (termed postinfectious IBS). A subset of patients with IBS has autonomic dysfunctions. However, many patients have no demonstrable physiologic abnormalities, and even in those that do, the abnormalities may not correlate with symptoms.

Constipation may be explained by slower colonic transit, and diarrhea may be explained by faster colonic transit. Some patients with constipation have fewer colonic high amplitude-propagated contractions, which propel colonic contents over several segments. Conversely, excess sigmoid motor activity may retard transit in functional constipation.

Postprandial abdominal discomfort may be attributed to an exaggerated gastro-colonic reflex (the colonic contractile response to a meal), the presence of colonic high amplitude-propagated contractions, increased intestinal sensitivity (visceral hyperalgesia), or a combination of these. Fat ingestion may exaggerate hypersensitivity.

Hormonal fluctuations affect bowel functions in women. Rectal sensitivity is increased during menses but not during other phases of the menstrual cycle. The effects of sex steroids on GI transit are subtle. The role of small-bowel bacterial overgrowth in IBS is controversial.

Symptoms and Signs

IBS tends to begin in the teens and 20s, causing bouts of symptoms that recur at irregular periods. Onset in late adult life is less common but not rare. Symptoms rarely rouse the sleeping patient. Symptoms are often triggered by food, particularly fats, or by stress.

Patients have abdominal discomfort, which varies considerably but is often located in the lower quadrant, steady or cramping in nature, and relieved by defecation. In addition, abdominal discomfort is temporally

associated with alterations in stool frequency (increased in diarrhea-predominant IBS and decreased in constipation-predominant IBS) and consistency (ie, loose or lumpy and hard). Pain or discomfort related to defecation is likely to be of bowel origin; that associated with exercise, movement, urination, or menstruation usually has a different cause. Although bowel patterns are relatively consistent in most patients, it is not unusual for patients to alternate between constipation and diarrhea. Patients may also have symptoms of abnormal stool passage (straining, urgency, or feeling of incomplete evacuation), pass mucus, or complain of bloating or abdominal distention. Many patients also have symptoms of dyspepsia. Extraintestinal symptoms (eg, fatigue, fibromyalgia, sleep disturbances, chronic headaches) are common.

Diagnosis

• Clinical evaluation, based on Rome criteria

• Screening for organic causes with basic laboratory tests and sigmoidoscopy or colonoscopy

• Other tests for patients with red flag findings (rectal blood, weight loss, fever)

Diagnosis is based on characteristic bowel patterns, time and character of pain, and exclusion of other disease processes through physical examination and routine diagnostic tests. Diagnostic testing should be more intensive when the following red flag findings are present either at initial presentation or at any time after diagnosis: older age, fever, weight loss, rectal bleeding, vomiting. Because patients with IBS can develop organic conditions, testing for other conditions should also be considered in patients who develop alarm symptoms or markedly different symptoms during the course of IBS. Common illnesses that may be confused with IBS include lactose intolerance, drug-induced diarrhea, post-cholecystectomy diarrhea, laxative abuse, parasitic diseases (eg, giardiasis), eosinophilic gastritis or enteritis, microscopic colitis, and early inflammatory bowel disease. However, uninflamed colonic diverticula do not cause symptoms, and their presence should not be considered explanatory.

The bimodal age distribution of patients with inflammatory bowel disease makes it imperative to evaluate both younger and older patients. In patients > 60 with acute symptoms, ischemic colitis should be considered. Patients with constipation and no anatomic lesion should be evaluated for hypothyroidism and hyperparathyroidism. If the patient's symptoms suggest malabsorption, tropical sprue, celiac disease, and Whipple's disease must be considered. Defecatory disorders should be considered as a cause of constipation in patients who report symptoms of difficult defecation. Rare causes of diarrhea include hyperthyroidism, medullary cancer of the thyroid, or carcinoid syndrome, gastrinoma, vipoma, and Zollinger-Ellison syndrome. However, secretory diarrhea caused by vasoactive intestinal peptide (VIP), calcitonin, or gastrin is typically accompanied by stool volumes > 1000 mL daily.

History: Particular attention should be given to the character of the pain, bowel habits, familial interrelationships, and drug and dietary histories. Equally important are the patient's overall emotional state, interpretation of personal problems and quality of life. The quality of the patient-physician interaction is key to diagnostic and therapeutic efficacy.

The **Rome criteria** are standardized symptom-based criteria for diagnosing IBS. The Rome criteria require the presence of abdominal pain or discomfort for at least 3 days/mo in the last 3 mo along with ≥ 2 of the following: (1) improvement with defecation, (2) onset (of each episode of discomfort) associated with a change in frequency of defecation, or (3) change in consistency of stool.

Physical examination: Patients generally appear to be healthy. Palpation of the abdomen may reveal tenderness, particularly in the left lower quadrant, at times associated with a palpable, tender sigmoid. A digital rectal examination, including a test for occult blood, should be done on all patients. In women, a pelvic examination helps rule out ovarian tumors and cysts or endometriosis, which may mimic IBS.

Testing: The diagnosis of IBS can reasonably be made using the Rome criteria as long as patients have no red flag findings, such as rectal bleeding, weight loss, and fever, or other findings that might suggest another etiology. Many patients with IBS are overtested; however, CBC, biochemical profile (including liver tests), ESR, stool examination for ova and parasites (in those with diarrhea predominance), thyroid-stimulating hormone and Ca for those with constipation, and flexible sigmoidoscopy or colonoscopy

should be done. During flexible fiber-optic proctosigmoidoscopy, introduction of the instrument and air insufflation frequently trigger bowel spasm and pain. The mucosal and vascular patterns in IBS usually appear normal. Colonoscopy is preferred for patients > 50 with a change in bowel habits, particularly those with no previous IBS symptoms, to exclude colonic polyps and tumors. In patients with chronic diarrhea, particularly older women, mucosal biopsy can rule out possible microscopic colitis.

Additional studies (such as ultrasound, CT, barium enema x-ray, upper GI esophagogastroduodenoscopy, and small-bowel x-rays) should be undertaken only when there are other objective abnormalities. Fecal fat excretion should be measured when there is a concern about steatorrhea. Testing for celiac sprue and small-bowel x-rays are recommended when malabsorption is suspected. Testing for carbohydrate intolerance should be considered in appropriate circumstances.

Intercurrent disease: Patients with IBS may subsequently develop additional GI disorders, and the clinician must not summarily dismiss their complaints. Changes in symptoms (eg, in the location, type, or intensity of pain; in bowel habits; in constipation and diarrhea) and new symptoms or complaints (eg, nocturnal diarrhea) may signal another disease process. Other symptoms that require investigation include fresh blood in the stool, weight loss, very severe abdominal pain or unusual abdominal distention, steatorrhea or noticeably foul-smelling stools, fever or chills, persistent vomiting, hematemesis, symptoms that wake the patient from sleep (eg, pain, the urge to defecate), and a steady progressive worsening of symptoms. Patients > 40 are more likely than younger patients to develop an intercurrent physiologic illness.

Treatment

• Support and understanding

• Normal diet, avoiding gas-producing and diarrhea-producing foods

• Increased fiber intake constipation

• Loperamide for diarrhea

• Possibly tricyclic antidepressants

Therapy is directed at specific symptoms. An effective therapeutic relationship is essential for effectively managing IBS. Patients should be invited to express not only their symptoms but also their understanding of their symptoms and the reasons prompting a visit to the health care practitioner (eg, fear of serious disease). Patients should be educated about the disorder (eg, normal bowel physiology and the bowel's hypersensitivity to stress and food) and reassured, after appropriate tests, about the absence of a serious or life-threatening disease. Appropriate therapeutic goals (eg, expectations regarding the normal course or variability in symptoms, adverse effects of drugs, the appropriate and available working relationship between the physician and the patient) should be established. Finally, patients can benefit by being actively involved in the management of their condition. When successful, this can enhance the patient's motivation to adhere to treatment, foster a more positive physician-patient relationship, and mobilize the coping resources of even the most chronically passive patients. Psychologic stress, anxiety, or mood disorders should be identified, evaluated, and treated. Regular physical activity helps relieve stress and assists in bowel function, particularly in patients with constipation.

Diet: In general, a normal diet should be followed. Meals should not be overly large, and eating should be slow and paced. Patients with abdominal distention and increased flatulence may benefit from reducing or eliminating beans, cabbage, and other foods containing fermentable carbohydrates. Reduced intake of sweeteners (eg, sorbitol, mannitol, fructose), which are constituents of natural and processed foods (eg, apple and grape juice, bananas, nuts, and raisins), may alleviate flatulence, bloating, and diarrhea. Patients with evidence of lactose intolerance should reduce their intake of milk and dairy products. A low-fat diet may reduce postprandial abdominal symptoms.

Dietary fiber supplements may soften stool and improve the ease of evacuation. A bland bulk-producing agent may be used (eg, raw bran, starting with 15 mL [1 tbsp] with each meal, supplemented with

increased fluid intake). Alternatively, psyllium hydrophilic mucilloid with two glasses of water may be used. However, excessive use of fiber can lead to bloating and diarrhea, so fiber doses must be individualized. Occasionally, flatulence may be reduced by switching to a synthetic fiber preparation (eg, methylcellulose).

Drug therapy: Drug therapy is directed toward the dominant symptoms. Anticholinergic drugs (eg, hyoscyamine 0.125 mg po 30 to 60 min before meals) may be used for their antispasmodic effects.

Serotonin receptor modulation may be of benefit. Tegaserod, a 5HT4 agonist, stimulates motility and alleviates constipation. In 2007, tegaserod was withdrawn from the market because, in clinical trials, it slightly increased the incidence of cardiovascular ischemic events (ie, MI, unstable angina pectoris, stroke) compared with placebo. Tegaserod has since been reintroduced under a restricted program. The chloride channel activator lubiprostone may help patients with constipation.

In patients with diarrhea, oral diphenoxylate 2.5 to 5 mg or loperamide 2 to 4 mg may be given before meals. The dose of loperamide should be titrated upward to reduce diarrhea while avoiding constipation. For many patients, tricyclic antidepressants (TCAs) help relieve symptoms of diarrhea, abdominal pain, and bloating. These drugs are thought to reduce pain by down-regulating the activity of spinal cord and cortical afferent pathways arriving from the intestine. Secondary amine TCAs (eg, nortriptyline, desipramine) are often better tolerated than parent tertiary amines (eg, amitriptyline, imipramine, doxepin) because of fewer anticholinergic, sedating antihistaminic, and α-adrenergic adverse effects. Treatment should begin with a very low dose of a TCA (eg, desipramine 10 to 25 mg once/day at bedtime), increasing as necessary and tolerated up to about 100 to 150 mg once/day. SSRIs are also useful, particularly for patients with anxiety or an affective disorder, but may exacerbate diarrhea. 5HT3 antagonists (eg, alosetron) may benefit female patients with severe diarrhea refractory to other drugs. Because alosetron is associated with ischemic colitis, its use is restricted.

Preliminary data suggest that certain probiotics (eg, *Bifidobacterium infantis*) alleviate IBS symptoms, particularly bloating. The beneficial effects of probiotics are not generic to the entire species but specific to certain strains. Certain aromatic oils (carminatives) can relax smooth muscle and relieve pain caused by cramps in some patients. Peppermint oil is the most commonly used agent in this class.

Psychologic therapies: Cognitive-behavioral therapy, standard psychotherapy, and hypnotherapy may help some IBS patients.

Chapter 19. Inflammatory Bowel Disease

Introduction

Inflammatory bowel disease (IBD), which includes Crohn's disease and ulcerative colitis (UC), is a relapsing and remitting condition characterized by chronic inflammation at various sites in the GI tract, which results in diarrhea and abdominal pain.

Inflammation results from a cell-mediated immune response in the GI mucosa. The precise etiology is unknown, but evidence suggests that the normal intestinal flora trigger an immune reaction in patients with a multifactorial genetic predisposition (perhaps involving abnormal epithelial barriers and mucosal immune defenses). No specific environmental, dietary, or infectious causes have been identified. The immune reaction involves the release of inflammatory mediators, including cytokines, interleukins, and tumor necrosis factor (TNF).

Although Crohn's disease and UC are similar, they can be distinguished in most cases (see Table 19-1). About 10% of colitis cases are considered indeterminate. The term colitis applies only to inflammatory disease of the colon (eg, ulcerative, granulomatous, ischemic, radiation-induced, infectious). Spastic (mucous) colitis is a misnomer sometimes applied to a functional disorder, irritable bowel syndrome (see p. 162).

Epidemiology: IBD affects people of all ages but usually begins before age 30, with peak incidence from 14 to 24. IBD may have a second smaller peak between ages 50 and 70; however, this later peak may include some cases of ischemic colitis.

IBD is most common among people of Northern European and Anglo-Saxon origin and is 2 to 4 times more common among Ashkenazi Jews than in non-Jewish whites. The incidence is lower in central and southern Europe and lower still in South America, Asia, and Africa. However, the incidence is increasing among blacks and Latin Americans living in North America. Both sexes are equally affected. First-degree relatives of patients with IBD have a 4- to 20-fold increased risk; their absolute risk may be as high as 7%. Familial tendency is much higher in Crohn's disease than in UC.

[**Table 19-1.** Differentiating Crohn's Disease and Ulcerative Colitis]

Several gene mutations conferring a higher risk of Crohn's disease (and some possibly related to UC) have been identified.

Cigarette smoking seems to contribute to development or exacerbation of Crohn's disease but decreases risk of UC. NSAIDs may exacerbate IBD.

Extraintestinal Manifestations

Crohn's disease and UC both affect organs other than the intestines. Most extraintestinal manifestations are more common in UC and Crohn's colitis than in Crohn's disease limited to the small bowel. Extraintestinal manifestations are categorized in 3 ways:

1. Disorders that usually parallel (ie, wax and wane with) IBD flare-ups. These disorders include peripheral arthritis, episcleritis, aphthous stomatitis, erythema nodosum, and pyoderma gangrenosum. Arthritis tends to involve large joints and be migratory and transient. One or more of these parallel disorders develops in more than one third of patients hospitalized with IBD.

2. Disorders that are clearly associated with IBD but appear independently of IBD activity. These disorders include ankylosing spondylitis, sacroiliitis, uveitis, and primary sclerosing cholangitis. Ankylosing spondylitis occurs more commonly in IBD patients with the HLA-B27 antigen. Most patients with spinal or sacroiliac involvement have evidence of uveitis and vice versa. Primary sclerosing cholangitis, which is a risk factor for cancer of the biliary tract, is strongly associated with UC or Crohn's colitis. Cholangitis may appear before or concurrently with the bowel disease or even 20 yr after colectomy. Liver disease (eg, fatty liver, autoimmune hepatitis, pericholangitis, cirrhosis) occurs in 3 to

5% of patients, although minor abnormalities in liver function tests are more common. Some of these conditions (eg, primary sclerosing cholangitis) may precede IBD by many years and, when diagnosed, should prompt an evaluation for IBD.

3. Disorders that are consequences of disrupted bowel physiology. These disorders occur mainly in severe Crohn's disease of the small bowel. Malabsorption may result from extensive ileal resection and cause deficiencies of fat-soluble vitamins, vitamin B_{12}, or minerals, resulting in anemia, hypocalcemia, hypomagnesemia, clotting disorders, and bone demineralization. In children, malabsorption retards growth and development. Other disorders include kidney stones from excessive dietary oxalate absorption, hydroureter and hydronephrosis from ureteral compression by the intestinal inflammatory process, gallstones from impaired ileal reabsorption of bile salts, and amyloidosis secondary to long-standing inflammatory and suppurative disease.

Thromboembolic disease may occur as a result of multiple factors in all 3 categories.

Treatment

• Supportive care

• 5-Aminosalicylic acid

• Corticosteroids

• Immunomodulating drugs

• Anticytokine drugs

• Sometimes antibiotics (eg, metronidazole, ciprofloxacin) and probiotics

Several classes of drugs are helpful for IBD. Details of their selection and use are discussed under each disorder.

5-Aminosalicylic acid (5-ASA, mesalamine): 5-ASA blocks production of prostaglandins and leukotrienes and has other beneficial effects on the inflammatory cascade. Because 5-ASA is active only intraluminally and is rapidly absorbed by the proximal small bowel, it must be formulated for delayed absorption when given orally. Sulfasalazine, the original agent in this class, delays absorption by complexing 5-ASA with a sulfa moiety, sulfapyridine. The complex is cleaved by bacterial flora in the lower ileum and colon, releasing the 5-ASA. The sulfa moiety, however, causes numerous adverse effects (eg, nausea, dyspepsia, headache), interferes with folate (folic acid) absorption, and occasionally causes serious adverse reactions (eg, hemolytic anemia or agranulocytosis and, rarely, hepatitis or pneumonitis). Reversible decreases in sperm count and motility occur in up to 80% of men. If used, sulfasalazine should be given with food, initially in a low dosage (eg, 0.5 g po bid) and gradually increased over several days to 1 to 2 g bid to tid. Patients should take daily folate supplements 1 mg po and have CBC and liver tests every 6 to 12 mo. Acute interstitial nephritis secondary to mesalamine occurs rarely; periodic monitoring of renal function is advisable because most cases are reversible if recognized early.

Newer drugs that complex 5-ASA with other vehicles seem almost equally effective but have fewer adverse effects. Olsalazine (a 5-ASA dimer) and balsalazide (5-ASA conjugated to an inactive compound) are cleaved by bacterial azoreductases (as is sulfasalazine). These drugs are activated mainly in the colon and are less effective for proximal small-bowel disease. Olsalazine dosage is 500 to 1500 mg po bid, and balsalazide is 2.25 g po tid. Olsalazine sometimes causes diarrhea, especially in patients with pancolitis. This problem is minimized by gradual escalation of dose and administration with meals.

Other forms of 5-ASA use delayed-release coatings. Asacol (typical dose 800 to 1200 mg po tid) is 5-ASA coated with an acrylic polymer whose pH solubility delays release of the drug until entry into the distal ileum and colon. Pentasa (1 g po qid) is 5-ASA encapsulated in ethylcellulose microgranules that release 35% of the drug in the small bowel. Two once/day formulations of mesalamine (Lialda, Apriso) are available; this less frequent dosing may improve adherence.

5-ASA is also available as a suppository (500 or 1000 mg at bedtime or bid) or enema (4 g at bedtime or bid) for proctitis and left-sided colon disease. These rectal preparations are effective for both acute treatment and long-term maintenance in proctitis and left-sided colon disease, and they have incremental benefit in combination with oral 5-ASA.

Corticosteroids: Corticosteroids are useful for acute flare-ups of most forms of IBD when 5-ASA compounds are inadequate. However, corticosteroids are not appropriate for maintenance. IV hydrocortisone 300 mg/day or methylprednisolone 60 to 80 mg/day by continuous drip or in divided doses is used for severe disease; oral prednisone or prednisolone 40 to 60 mg once/day may be used for moderate disease. Treatment is continued until symptoms remit (usually 7 to 28 days) and then tapered by 5 to 10 mg weekly to 20 mg once/day. Treatment is then further tapered by 2.5 to 5 mg weekly while instituting maintenance therapy with 5-ASA or immunomodulators. Adverse effects of short-term corticosteroids in high doses include hyperglycemia, hypertension, insomnia, hyperactivity, and acute psychotic episodes.

Hydrocortisone enemas or foam may be used for proctitis and left-sided colon disease; as an enema, 100 mg in 60 mL of isotonic solution is given once/day or bid. The enema should be retained in the bowel as long as possible; instillation at night, with the patient lying on the left side with hips elevated, may prolong retention and extend distribution. Treatment, if effective, should be continued daily for about 2 to 4 wk, then every other day for 1 to 2 wk, and then gradually discontinued over 1 to 2 wk.

Budesonide is a corticosteroid with a high (> 90%) first-pass liver metabolism; thus, oral administration may have a significant effect on GI tract disease but minimal adrenal suppression. Oral budesonide has fewer adverse effects than prednisolone but is not as rapidly effective and is typically used for less severe disease. Budesonide may be effective in maintaining remission for 3 to 6 mo but has not yet proved effective for long-term maintenance. Dosage is 9 mg once/day. It is also available outside the US as an enema.

Immunomodulating drugs: Azathioprine and its metabolite 6-mercaptopurine inhibit T-cell function. They are effective long-term and may diminish corticosteroid requirements and maintain remission for years. These drugs often require 1 to 3 mo to produce clinical benefits, so corticosteroids cannot be withdrawn until at least the 2nd month. Dosage of azathioprine is usually 2.5 to 3.0 mg/kg po once/day and 6-mercaptopurine 1.5 to 2.5 mg/kg po once/day but varies depending on individual metabolism. Signs of bone marrow suppression must be monitored with regular WBC count (biweekly for 1 mo, then every 1 to 2 mo). Pancreatitis or high fever occurs in about 3 to 5% of patients; either is an absolute contraindication to rechallenge. Hepatotoxicity is rarer and can be screened by blood tests every 6 to 12 mo. Newly available blood tests that measure the activity of one of the enzymes that metabolize azathioprine and 6-mercaptopurine and that directly measure metabolite levels may sometimes be helpful in ensuring safe and effective drug dosages.

Methotrexate 15 to 25 mg po or sc weekly is of benefit to many patients with corticosteroid-refractory or corticosteroid-dependent Crohn's disease, even those who have not responded to azathioprine or 6-mercaptopurine. Adverse effects include nausea, vomiting, and asymptomatic liver function test abnormalities. Folate 1 mg po once/day may diminish some of the adverse effects. Alcohol use, obesity, diabetes, and possibly psoriasis are risk factors for hepatotoxicity. Patients with these conditions should have a liver biopsy after a total dose of 1.5 g, but otherwise, concerns over hepatotoxicity are too often exaggerated. Pulmonary toxicity can also occur with methotrexate therapy.

Cyclosporine, which blocks lymphocyte activation, may benefit patients with severe UC unresponsive to corticosteroids and who may otherwise require colectomy. Its only well-documented use in Crohn's disease is for patients with refractory fistulas or pyoderma. Initial dose is 4 mg/kg IV in continuous infusion over 24 h; responders are converted to an oral dose of 6 to 8 mg/kg once/day with early introduction of azathioprine or 6-mercaptopurine. Long-term use (> 6 mo) is contraindicated by multiple adverse effects (eg, renal toxicity, seizures, opportunistic infections, hypertension, neuropathy). Generally, patients are not offered cyclosporine unless there is a reason to avoid the safer curative option of colectomy. If the drug is used, trough blood levels should be kept between 200 to 400 ng/mL and *Pneumocystis jirovecii* prophylaxis should be considered during the period of concomitant corticosteroid, cyclosporine, and

antimetabolite treatment. Tacrolimus, an immunosuppressant also used in transplant patients, seems as effective as cyclosporine.

Anticytokine drugs: Infliximab, certolizumab, and adalimumab are antibodies to TNF. These agents may be useful in Crohn's disease; additionally infliximab may be beneficial in UC for refractory or corticosteroid-dependent disease. Several anti-interleukin antibodies and interleukins may decrease the inflammatory response and are being studied for Crohn's disease. An antibody to leukocyte adhesion molecules (natalizumab) is approved as monotherapy for the most refractory cases of Crohn's disease; other analogs (eg, vedolizumab) are also being studied.

Infliximab is given as a single IV infusion of 5 mg/kg over 2 h. Monotherapy with infliximab is clearly effective for both induction and maintenance of remission, but some studies suggest better short-term results when infliximab is initiated in combination with a thiopurine (eg, azathioprine). Ideally, infliximab would eventually be stopped and patients would be maintained on the antimetabolite, but this strategy has not been validated in controlled studies. Corticosteroid tapering may begin after 2 wk. The initial infliximab infusion is usually followed by repeat infusions at weeks 2 and 6. Subsequently, it is given every 8 wk or at intervals determined by the patient's clinical course. Adverse effects during infusion (infusion reaction) include immediate hypersensitivity reactions (eg, rash, itching, sometimes anaphylactoid reactions), fever, chills, headache, and nausea. Delayed hypersensitivity reactions have also occurred. Anti-TNF drugs given subcutaneously (eg, adalimumab) do not cause infusion reactions, although they may cause local erythema, pain, and itching (injection site reaction). Patients who are intolerant or who have lost their initial response to infliximab may respond to adalimumab therapy.

Several patients have died of sepsis after infliximab use, so it is contraindicated when uncontrolled bacterial infection is present. Furthermore, TB reactivation has been attributed to this drug; therefore, screening by PPD and chest x-ray is required before its use. Lymphoma, demyelinating disease, and liver and hematologic toxicity are other potential concerns with anti-TNF antibody treatment. Other anticytokine, anti-integrin, and growth factors are under investigation, as is leukopheresis therapy to deplete activated immunocytes.

Antibiotics and probiotics: Antibiotics may be helpful in Crohn's disease but are of limited use in UC. Metronidazole 500 to 750 mg po tid for 4 to 8 wk may control mild Crohn's disease and help heal fistulas. However, adverse effects (particularly neurotoxicity) often preclude completion of treatment. Ciprofloxacin 500 to 750 mg po bid may prove less toxic. Many experts recommend metronidazole and ciprofloxacin in combination. Rifaximin, a nonabsorbable antibiotic, at a dose of 200 mg po tid is also being studied as treatment for active Crohn's disease.

Various nonpathogenic microorganisms (eg, commensal *Escherichia coli*, *Lactobacillus* species, *Saccharomyces*) given daily serve as probiotics and may be effective in preventing pouchitis (see p. 176), but other therapeutic roles have yet to be clearly defined. Therapeutic infestation with the parasite *Trichuris suis* has been tried in an effort to stimulate T2-helper cell immunity and may decrease disease activity in UC.

Supportive care: Most patients and their families are interested in diet and stress management. Although there are anecdotal reports of clinical improvement on certain diets, including one with rigid carbohydrate restrictions, controlled trials have shown no benefit. Stress management may be helpful.

Crohn's Disease

(Regional Enteritis; Granulomatous Ileitis or Ileocolitis)

Crohn's disease is a chronic transmural inflammatory disease that usually affects the distal ileum and colon but may occur in any part of the GI tract. Symptoms include diarrhea and abdominal pain. Abscesses, internal and external fistulas, and bowel obstruction may arise. Extraintestinal symptoms, particularly arthritis, may occur. Diagnosis is by colonoscopy and barium contrast studies. Treatment is with 5-aminosalicylic acid, corticosteroids, immunomodulators, anticytokines, antibiotics, and often surgery.

Pathophysiology

Crohn's disease begins with crypt inflammation and abscesses, which progress to tiny focal aphthoid ulcers. These mucosal lesions may develop into deep longitudinal and transverse ulcers with intervening mucosal edema, creating a characteristic cobblestoned appearance to the bowel.

Transmural spread of inflammation leads to lymphedema and thickening of the bowel wall and mesentery. Mesenteric fat typically extends onto the serosal surface of the bowel. Mesenteric lymph nodes often enlarge. Extensive inflammation may result in hypertrophy of the muscularis mucosae, fibrosis, and stricture formation, which can lead to bowel obstruction. Abscesses are common, and fistulas often penetrate into adjoining structures, including other loops of bowel, the bladder, or psoas muscle. Fistulas may even extend to the skin of the anterior abdomen or flanks. Independently of intra-abdominal disease activity, perianal fistulas and abscesses occur in 25 to 33% of cases; these complications are frequently the most troublesome aspects of Crohn's disease.

Noncaseating granulomas can occur in lymph nodes, peritoneum, the liver, and all layers of the bowel wall. Although pathognomonic when present, granulomas are not detected in about half of patients with Crohn's disease. The presence of granulomas does not seem to be related to the clinical course.

Segments of diseased bowel are sharply demarcated from adjacent normal bowel ("skip areas"); hence, the name regional enteritis. About 35% of Crohn's disease cases involve the ileum alone (ileitis); about 45% involve the ileum and colon (ileocolitis), with a predilection for the right side of the colon; and about 20% involve the colon alone (granulomatous colitis), most of which, unlike ulcerative colitis (UC), spare the rectum. Occasionally, the entire small bowel is involved (jejunoileitis). The stomach, duodenum, or esophagus is clinically involved only rarely, although microscopic evidence of disease is often detectable in the gastric antrum, especially in younger patients. In the absence of surgical intervention, the disease almost never extends into areas of small bowel that are not involved at first diagnosis.

There is an increased risk of cancer in affected small-bowel segments. Patients with colonic involvement have a long-term risk of colorectal cancer equal to that of UC, given the same extent and duration of disease.

Symptoms and Signs

The most common initial manifestation is chronic diarrhea with abdominal pain, fever, anorexia, and weight loss. The abdomen is tender, and a mass or fullness may be palpable. Gross rectal bleeding is unusual except in isolated colonic disease, which may manifest similarly to UC. Some patients present with an acute abdomen that simulates acute appendicitis or intestinal obstruction. About 33% of patients have perianal disease (especially fissures and fistulas), which is sometimes the most prominent or even initial complaint. In children, extraintestinal manifestations frequently predominate over GI symptoms; arthritis, FUO, anemia, or growth retardation may be a presenting symptom, whereas abdominal pain or diarrhea may be absent.

With recurrent disease, symptoms vary. Pain is most common and occurs with both simple recurrence and abscess formation. Patients with severe flare-up or abscess are likely to have marked tenderness, guarding, rebound, and a general toxic appearance. Stenotic segments may cause bowel obstruction, with colicky pain, distention, obstipation, and vomiting. Adhesions from previous surgery may also cause bowel obstruction, which begins rapidly, without the prodrome of fever, pain, and malaise typical of obstruction due to a Crohn's disease flare-up. An enterovesical fistula may produce air bubbles in the urine (pneumaturia). Draining cutaneous fistulas may occur. Free perforation into the peritoneal cavity is unusual.

Chronic disease causes a variety of systemic symptoms, including fever, weight loss, undernutrition, and extraintestinal manifestations (see p. 166).

The Vienna Classification and its recent Montreal modification categorize Crohn's disease into 3 principal patterns: (1) primarily inflammatory, which after several years commonly evolves into either (2) primarily stenotic or obstructing or (3) primarily penetrating or fistulizing. These different clinical patterns dictate

different therapeutic approaches. Some genetic studies suggest a molecular basis for this classification.

Diagnosis

• Barium x-rays of the stomach, small bowel, and colon

• Abdominal CT (conventional or CT enterography)

• Sometimes magnetic resonance (MR) enterography, upper endoscopy, and/or colonoscopy

Crohn's disease should be suspected in a patient with inflammatory or obstructive symptoms or in a patient without prominent GI symptoms but with perianal fistulas or abscesses or with otherwise unexplained arthritis, erythema nodosum, fever, anemia, or (in a child) stunted growth. A family history of Crohn's disease also increases the index of suspicion. Similar symptoms and signs (eg, abdominal pain, diarrhea) may be caused by other GI disorders. Differentiation from UC (see Table 19-1) may be an issue in the 20% of cases in which Crohn's disease is confined to the colon. However, because treatment is similar, this distinction is critical only when surgery or experimental therapy is contemplated.

Patients presenting with an acute abdomen (either initially or on relapse) should have flat and upright abdominal x-rays and an abdominal CT scan. These studies may show obstruction, abscesses or fistulas, and other possible causes of an acute abdomen (eg, appendicitis). Ultrasound may better delineate gynecologic pathology in women with lower abdominal and pelvic pain.

If initial presentation is less acute, an upper GI series with small-bowel follow-through and spot films of the terminal ileum is preferred over conventional CT. However, newer techniques of CT or MR enterography, which combine high-resolution CT or MR imaging with large volumes of ingested contrast, are becoming the procedures of choice in some centers. These imaging studies are virtually diagnostic if they show characteristic strictures or fistulas with accompanying separation of bowel loops. If findings are questionable, CT enteroclysis or video capsule enteroscopy may show superficial aphthous and linear ulcers. Barium enema x-ray may be used if symptoms seem predominantly colonic (eg, diarrhea) and may show reflux of barium into the terminal ileum with irregularity, nodularity, stiffness, wall thickening, and a narrowed lumen. Differential diagnoses in patients with similar x-ray findings include cancer of the cecum, ileal carcinoid, lymphoma, systemic vasculitis, radiation enteritis, ileocecal TB, and ameboma.

In atypical cases (eg, predominantly diarrhea, with minimal pain), evaluation is similar to suspected UC, with colonoscopy (including biopsy, sampling for enteric pathogens, and, when possible, visualization of the terminal ileum). Upper GI endoscopy may identify subtle gastroduodenal involvement even in the absence of upper GI symptoms.

Laboratory tests should be done to screen for anemia, hypoalbuminemia, and electrolyte abnormalities. Liver function tests should be done; elevated alkaline phosphatase and γ-glutamyl transpeptidase levels in patients with major colonic involvement suggest possible primary sclerosing cholangitis. Leukocytosis or increased levels of acute-phase reactants (eg, ESR, C-reactive protein) are nonspecific but may be used serially to monitor disease activity.

Perinuclear antineutrophil cytoplasmic antibodies are present in 60 to 70% of patients with UC and in only 5 to 20% of patients with Crohn's disease. Anti-*Saccharomyces cerevisiae* antibodies are relatively specific for Crohn's disease. However, these tests do not reliably separate the 2 diseases. They have uncertain value in cases of indeterminate colitis and are not recommended for routine diagnosis.

Prognosis

Established Crohn's disease is rarely cured but is characterized by intermittent exacerbations and remissions. Some patients have severe disease with frequent, debilitating periods of pain. However, with judicious medical therapy and, where appropriate, surgical therapy, most patients function well and adapt successfully. Disease-related mortality is very low. GI cancer, including cancer of the colon and small bowel, is the leading cause of excess Crohn's disease-related mortality.

Treatment

• Loperamide or antispasmodics for symptom relief

• 5-Aminosalicylic acid (5-ASA) or antibiotics

• Other drugs depending on symptoms and severity

• Sometimes surgery

Details of specific drugs and dosages are discussed on p. 167.

General management: Cramps and diarrhea may be relieved by oral administration of loperamide 2 to 4 mg or antispasmodic drugs up to 4 times/day (ideally before meals). Such symptomatic treatment is safe, except in cases of severe, acute Crohn's colitis, which may progress to toxic megacolon as in UC. Hydrophilic mucilloids (eg, methylcellulose or psyllium preparations) sometimes help prevent anal irritation by increasing stool firmness. Dietary roughage is to be avoided in stricturing disease or active colonic inflammation.

Mild to moderate disease: This category includes ambulatory patients who tolerate oral intake and have no signs of toxicity, tenderness, mass, or obstruction. 5-ASA (mesalamine) is commonly used as first-line treatment, although its benefits for small-bowel disease are modest at best. Pentasa is the most effective formulation for disease proximal to the terminal ileum; Asacol is effective in distal ileal disease. All formulations are roughly equivalent for Crohn's colitis, although none of the newer preparations rival sulfasalazine for efficacy on a dose-for-dose basis.

Antibiotics are considered a first-line agent by some clinicians, or they may be reserved for patients not responding to 4 wk of 5-ASA; their use is strictly empiric. With any of these drugs, 8 to 16 wk of treatment may be required.

Responders should receive maintenance therapy.

Moderate to severe disease: Patients without fistulas or abscesses but with significant pain, tenderness, fever, or vomiting, or those who have not responded to treatment for mild disease, require corticosteroids, either oral or parenteral, depending on severity of symptoms and frequency of vomiting. Oral prednisone or prednisolone may act more rapidly and reliably than oral budesonide, but budesonide has somewhat fewer adverse effects and is considered the corticosteroid of choice in many centers, especially in Europe. Patients not responding to corticosteroids, or those whose doses cannot be tapered, should receive azathioprine, 6-mercaptopurine, or possibly methotrexate. Infliximab is preferred by some as a second-line agent after corticosteroids, and even as a first-line agent in preference to corticosteroids, but it is contraindicated in active uncontrolled infection.

Obstruction is managed initially with nasogastric suction and IV fluids. Obstruction due to uncomplicated Crohn's disease should resolve within a few days and therefore does not require parenteral nutrition; absence of prompt response indicates a complication or another etiology and demands immediate surgery.

Fulminant disease or abscess: Patients with toxic appearance, high fever, persistent vomiting, rebound, or a tender or palpable mass must be hospitalized for administration of IV fluids and antibiotics. Abscesses must be drained, either percutaneously or surgically. IV corticosteroids should be given only when infection has been ruled out or controlled. If there is no response to corticosteroids and antibiotics within 5 to 7 days, surgery is usually indicated.

Fistulas: Fistulas are treated initially with metronidazole and ciprofloxacin. Patients who do not respond in 3 to 4 wk may receive an immunomodulator (eg, azathioprine, 6-mercaptopurine), with or without an induction regimen of infliximab for more rapid response. Cyclosporine is an alternative, but fistulas often relapse after treatment. Severe refractory perianal fistulas may require temporary diverting colostomy but almost invariably recur after reconnection; hence, diversion is more appropriately considered a

preparation for definitive surgery or at best an adjunct to infliximab rather than a primary treatment.

Maintenance therapy: Patients who require only 5-ASA or an antibiotic to achieve remission can be maintained on this drug. Patients requiring acute treatment with corticosteroids or infliximab generally require azathioprine, 6-mercaptopurine, methotrexate, or infliximab for maintenance. Systemically active corticosteroids are neither safe nor effective for long-term maintenance, although budesonide has been shown to delay relapse with fewer adverse effects. Patients who respond to infliximab for acute disease but who are not well maintained on antimetabolites may stay in remission with repeat doses of infliximab 5 to 10 mg/kg at 8-wk intervals. Monitoring during remission can be done by following symptoms and blood tests and does not require routine x-rays or colonoscopy (other than regular surveillance for dysplasia after 7 to 8 yr of disease).

Surgery: Even though about 70% of patients ultimately require an operation, surgery is always done reluctantly. It is best reserved for recurrent intestinal obstruction or intractable fistulas or abscesses. Resection of the involved bowel may ameliorate symptoms but does not cure the disease, which is likely to recur even after resection of all clinically apparent lesions. The recurrence rate, defined by endoscopic lesions at the anastomotic site, is > 70% at 1 yr and > 85% at 3 yr; defined by clinical symptoms, it is about 25 to 30% at 3 yr and 40 to 50% at 5 yr. Ultimately, further surgery is required in nearly 50% of cases. However, recurrence rates seem to be reduced by early postoperative prophylaxis with 6-mercaptopurine, metronidazole, or possibly infliximab or 5-ASA. Moreover, when surgery is done for appropriate indications, almost all patients have improved quality of life.

Ulcerative Colitis

Ulcerative colitis (UC) is a chronic inflammatory and ulcerative disease arising in the colonic mucosa, characterized most often by bloody diarrhea. Extraintestinal symptoms, particularly arthritis, may occur. Long-term risk of colon cancer is high. Diagnosis is by colonoscopy. Treatment is with 5-aminosalicylic acid, corticosteroids, immunomodulators, anticytokines, antibiotics, and occasionally surgery.

Pathophysiology

UC usually begins in the rectum. It may remain localized to the rectum (ulcerative proctitis) or extend proximally, sometimes involving the entire colon. Rarely, it involves most of the large bowel at once.

The inflammation caused by UC affects the mucosa and submucosa, and there is a sharp border between normal and affected tissue. Only in severe disease is the muscularis involved. In early cases, the mucous membrane is erythematous, finely granular, and friable, with loss of the normal vascular pattern and often with scattered hemorrhagic areas. Large mucosal ulcers with copious purulent exudate characterize severe disease. Islands of relatively normal or hyperplastic inflammatory mucosa (pseudopolyps) project above areas of ulcerated mucosa. Fistulas and abscesses do not occur.

Toxic or fulminant colitis occurs when transmural extension of ulceration results in localized ileus and peritonitis. Within hours to days, the colon loses muscular tone and begins to dilate. The terms toxic megacolon or toxic dilation are discouraged because the toxic inflammatory state and its complications can occur without frank megacolon (defined as transverse colon > 6 cm diameter during an exacerbation). Toxic colitis is a medical emergency that usually occurs spontaneously in the course of very severe colitis but is sometimes precipitated by opioid or anticholinergic antidiarrheal drugs. Colonic perforation may occur, which increases mortality significantly.

Symptoms and Signs

Bloody diarrhea of varied intensity and duration is interspersed with asymptomatic intervals. Usually an attack begins insidiously, with increased urgency to defecate, mild lower abdominal cramps, and blood and mucus in the stools. Some cases develop after an infection (eg, amebiasis, bacillary dysentery).

When ulceration is confined to the rectosigmoid, the stool may be normal or hard and dry, but rectal discharges of mucus loaded with RBCs and WBCs accompany or occur between bowel movements.

Systemic symptoms are absent or mild. If ulceration extends proximally, stools become looser and the patient may have > 10 bowel movements per day, often with severe cramps and distressing rectal tenesmus, without respite at night. The stools may be watery or contain mucus and frequently consist almost entirely of blood and pus.

Toxic or fulminant colitis manifests initially with sudden violent diarrhea, fever to 40° C (104° F), abdominal pain, signs of peritonitis (eg, rebound tenderness), and profound toxemia.

Systemic symptoms and signs, more common with extensive UC, include malaise, fever, anemia, anorexia, and weight loss. Extraintestinal manifestations (particularly joint and skin complications—see p. 167) are most common when systemic symptoms are present.

Diagnosis

• Stool cultures and microscopy (to exclude infectious causes)

• Sigmoidoscopy with biopsy

Initial presentation: Diagnosis is suggested by typical symptoms and signs, particularly when accompanied by extraintestinal manifestations or a history of previous similar attacks. UC should be distinguished from Crohn's disease (see Table 19-1) but more importantly from other causes of acute colitis (eg, infection; in elderly patients, ischemia).

In all patients, stool cultures for enteric pathogens should be done, and *Entamoeba histolytica* should be excluded by examination of fresh stool specimens. When amebiasis is suspected because of epidemiologic or travel history, serologic titers and biopsies should be done. History of prior antibiotic use or recent hospitalization should prompt stool assay for *Clostridium difficile* toxin. Patients at risk should be tested for HIV, gonorrhea, herpesvirus, chlamydia, and amebiasis. Opportunistic infections (eg, cytomegalovirus, *Mycobacterium avium-intracellulare*) or Kaposi's sarcoma must also be considered in immunosuppressed patients. In women using oral contraceptives, contraceptive-induced colitis is possible; it usually resolves spontaneously after hormone therapy is stopped.

Sigmoidoscopy should be done; it allows visual confirmation of colitis and permits direct sampling of stool or mucus for culture and microscopic evaluation, as well as biopsy of affected areas. Although visual inspection and biopsies may be nondiagnostic, because there is much overlap in appearance among different types of colitis, acute, self-limited, infectious colitis can usually be distinguished histologically from chronic idiopathic UC or Crohn's colitis. Severe perianal disease, rectal sparing, absence of bleeding, and asymmetric or segmental involvement of the colon indicate Crohn's disease rather than UC (see Table 19-1). Colonoscopy is usually unnecessary initially but should be done electively if inflammation has extended proximal to the reach of the sigmoidoscope.

Laboratory tests should be done to screen for anemia, hypoalbuminemia, and electrolyte abnormalities. Liver function tests should be done; elevated alkaline phosphatase and γ-glutamyl transpeptidase levels suggest possible primary sclerosing cholangitis. Perinuclear antineutrophil cytoplasmic antibodies are relatively specific (60 to 70%) for UC. Anti-*Saccharomyces cerevisiae* antibodies are relatively specific for Crohn's disease. However, these tests do not reliably separate the 2 diseases and are not recommended for routine diagnosis. Other possible laboratory abnormalities include leukocytosis, thrombocytosis, and elevated acute-phase reactants (eg, ESR, C-reactive protein).

X-rays are not diagnostic but occasionally show abnormalities. Plain x-rays of the abdomen may show mucosal edema, loss of haustration, and absence of formed stool in the diseased bowel. Barium enema shows similar changes, albeit more clearly, and may also show ulcerations, but the enema should not be done during an acute presentation. A shortened, rigid colon with an atrophic or pseudopolypoid mucosa is often seen after several years' illness. X-ray findings of thumbprinting and segmental distribution are more suggestive of intestinal ischemia or possibly Crohn's colitis rather than of UC.

Recurrent symptoms: Patients with known disease and a recurrence of typical symptoms should be examined, but extensive testing is not always required. Depending on duration and severity of symptoms,

sigmoidoscopy or colonoscopy may be done and a CBC obtained. Cultures, ova and parasite examination, and *C. difficile* toxin assay should be done when there are atypical features to the relapse or when there is an exacerbation after prolonged remission, during a contagious outbreak, after antibiotic exposure, or whenever the clinician is suspicious.

Fulminant symptoms: Patients require further evaluation during severe flare-ups. Flat and upright abdominal x-rays should be taken; they may show megacolon or intraluminal gas accumulated over a long, continuous, paralyzed segment of colon—a result of lost muscle tone. Colonoscopy and barium enema should be avoided because of the risk of perforation. CBC, ESR, electrolytes, PT, PTT, and type and crossmatch should be obtained.

The patient must be watched closely for progressive peritonitis or perforation. Percussion over the liver is important because loss of hepatic dullness may be the first clinical sign of free perforation, especially in a patient whose peritoneal signs are suppressed by high-dose corticosteroids. Abdominal x-rays are taken every 1 or 2 days to follow the course of colonic distention and to detect free or intramural air.

Prognosis

Usually, UC is chronic with repeated exacerbations and remissions. In about 10% of patients, an initial attack becomes fulminant with massive hemorrhage, perforation, or sepsis and toxemia. Complete recovery after a single attack occurs in another 10%.

Patients with localized ulcerative proctitis have the best prognosis. Severe systemic manifestations, toxic complications, and malignant degeneration are unlikely, and late extension of the disease occurs in only about 20 to 30%. Surgery is rarely required, and life expectancy is normal. The symptoms, however, may prove stubborn and refractory. Moreover, because extensive UC may begin in the rectum and spread proximally, proctitis should not be considered localized until it has been observed for ≥ 6 mo. Localized disease that later extends is often more severe and more refractory to therapy.

Colon cancer: The risk of colon cancer is proportional to the duration of disease and amount of colon affected, but not necessarily to the clinical severity of the attacks. Some recent studies suggest that sustained microscopic inflammation is a risk factor, and that use of aminosalicylate to control inflammation is protective. Cancer begins to appear by 7 yr from onset of illness in patients with extensive colitis. The cumulative likelihood of cancer is about 3% at 15 yr, 5% at 20 yr, and 9% at 25 yr, representing an annual risk of about 0.5 to 1% after the 10th yr. There is probably no higher absolute cancer risk among patients with childhood-onset colitis independent of the longer duration of disease. However, patients who have inflammatory bowel disease and primary sclerosing cholangitis are at a higher risk of cancer from the time of colitis diagnosis.

Regular colonoscopic surveillance, preferably during remission, is advised for patients with disease duration > 8 to 10 yr (except for those with isolated proctitis). Endoscopic biopsies should be taken every 10 cm throughout the colon. Newer techniques, especially chromoendoscopy, may better identify areas of suspicion in preference to totally random biopsies. Any grade of definite dysplasia within an area affected by colitis is liable to progress to more advanced neoplasia and even cancer and is a strong indication for total colectomy unless the dysplasia is strictly confined to a discrete, completely excisable polyp. It is important to distinguish definite neoplastic dysplasia from reactive or regenerative atypia secondary to inflammation. However, if the dysplasia is unequivocal, delaying colectomy in favor of repeated follow-up surveillance is a risky strategy. Pseudopolyps have no prognostic significance but may be difficult to distinguish from neoplastic polyps; thus, any suspect polyp should undergo excision biopsy.

The optimal frequency of colonoscopic surveillance has not been established, but some authorities recommend every 2 yr during the 2nd decade of disease and annually thereafter.

Long-term survival after diagnosis of colitis-related cancer is about 50%, a figure comparable to that for colorectal cancer in the general population.

Treatment

• Loperamide and dietary management for symptom relief

• 5-Aminosalicylic acid (5-ASA)

• Corticosteroids and other drugs depending on symptoms and severity

• Anticytokine drugs

• Sometimes surgery

Details of specific drugs and regimens are discussed on p. 167.

General management: Avoiding raw fruits and vegetables limits trauma to the inflamed colonic mucosa and may lessen symptoms. A milk-free diet may help but need not be continued if no benefit is noted. Loperamide 2 mg po bid to qid is indicated for relatively mild diarrhea; higher oral doses (4 mg in the morning and 2 mg after each bowel movement) may be required for more intense diarrhea. Antidiarrheal drugs must be used with extreme caution in severe cases because they may precipitate toxic dilation.

Mild left-sided disease: Patients with proctitis, or colitis that does not extend proximally beyond the splenic flexure, are treated with 5-ASA (mesalamine) enemas once/day or bid depending on severity. Suppositories are effective for more distal disease and are usually preferred by patients. Corticosteroid and budesonide enemas are slightly less effective but should be used if 5-ASA is unsuccessful or not tolerated. Once remission is achieved, dosage is slowly tapered to maintenance levels. Oral 5-ASA drugs theoretically have some incremental benefit in lessening the probability of proximal spread of disease.

Moderate or extensive disease: Patients with inflammation proximal to the splenic flexure or left-sided disease unresponsive to topical agents should receive an oral 5-ASA formulation in addition to 5-ASA enemas. High-dose corticosteroids are added for more severe symptoms; after 1 to 2 wk, the daily dose is reduced by about 5 to 10 mg each wk. Immunomodulater therapy with azathioprine or 6-mercaptopurine can be used in patients who are refractory to maximal doses of 5-ASA and would otherwise need long-term corticosteroid therapy. Additionally, infliximab is beneficial in some patients and may be considered for those refractory to immunomodulator or corticosteroid therapy as well as those who are corticosteroid dependent.

Severe disease: Patients with > 10 bloody bowel movements per day, tachycardia, high fever, or severe abdominal pain require hospitalization to receive high-dose IV corticosteroids. 5-ASA may be continued. IV fluids and blood transfusion are given as needed for dehydration and anemia. The patient must be observed closely for the development of toxic megacolon. Parenteral hyperalimentation is sometimes used for nutritional support but is of no value as primary therapy; patients who can tolerate food should eat.

Patients who do not respond within 3 to 7 days should be considered for IV cyclosporine or infliximab or else for surgery. Patients who do respond to a corticosteroid regimen are switched within a week or so to prednisone 60 mg po once/day, which may be gradually reduced at home based on clinical response. Patients who are started on IV cyclosporine and respond to therapy are switched to oral cyclosporine and concomitant azathioprine or 6-mercaptopurine. Oral cyclosporine is continued for about 3 to 4 mo, during which time corticosteroids are tapered and cyclosporine levels are closely monitored. Some clinicians recommend prophylaxis against *Pneumocystis jirovecii* pneumonia during the interval of overlapping treatment with corticosteroids, cyclosporine, and an antimetabolite.

Fulminant colitis: If fulminant colitis or toxic megacolon is suspected, the patient should (1) stop all antidiarrheal drugs; (2) take nothing by mouth and have inserted a long intestinal tube attached to intermittent suction; (3) receive aggressive IV fluid and electrolyte therapy with 0.9% NaCl, and potassium chloride and blood as needed; (4) be treated with high-dose IV corticosteroid or cyclosporine; and (5) receive antibiotics (eg, metronidazole 500 mg IV q 8 h and ciprofloxacin 500 mg IV q 12 h).

Having the patient roll over in bed from the supine to prone position every 2 to 3 h may help redistribute colonic gas and prevent progressive distention. Passage of a soft rectal tube may also be helpful but

must be done with extreme caution to avoid bowel perforation.

If intensive medical measures do not produce definite improvement within 24 to 48 h, immediate surgery is required or the patient may die of sepsis caused by bacterial translocation or even perforation.

Maintenance therapy: After effective treatment of a flare-up, corticosteroids are tapered based on clinical response and then stopped because they are ineffective as maintenance. Patients should remain on 5-ASA drugs indefinitely—oral or rectal, depending on location of disease—because stopping maintenance therapy often allows disease relapse. Dosage intervals for rectal preparations may be gradually lengthened to every 2nd or 3rd day.

Patients who cannot be withdrawn from corticosteroids should be given azathioprine or 6-mercaptopurine. Also, infliximab is becoming more widely accepted as maintenance therapy for UC as well as for Crohn's disease.

Surgery: Nearly one third of patients with extensive UC ultimately require surgery. Total proctocolectomy is curative: Life expectancy and quality of life are restored to normal, the disease does not recur (unlike Crohn's disease), and the risk of colon cancer is eliminated.

Emergency colectomy is indicated for massive hemorrhage, fulminating toxic colitis, or perforation. Subtotal colectomy with ileostomy and rectosigmoid closure or mucous fistula is usually the procedure of choice because most critically ill patients cannot tolerate more extensive surgery. The rectosigmoid stump may be electively removed later or may be used for ileoanal anastomosis with a pouch. The intact rectal stump should not be allowed to remain indefinitely because of the risk of disease activation and malignant transformation.

Elective surgery is indicated for cancer, symptomatic strictures, growth retardation in children, or, most commonly, intractable chronic disease resulting in invalidism or corticosteroid dependence. Colectomy is also done for high-grade and perhaps even low-grade mucosal dysplasia confirmed on pathologic consultation, unless the dysplasia is limited exclusively to a completely excisable polyp. Severe colitis-related extraintestinal manifestations (eg, pyoderma gangrenosum), now better controlled by intensive medical therapies, are only rarely indications for surgery.

The elective procedure of choice in patients with normal sphincter function is restorative proctocolectomy with ileoanal anastomosis. This procedure creates a pelvic reservoir or pouch from distal ileum, which is connected to the anus. The intact sphincter allows continence, typically with 8 to 10 bowel movements/day. Pouchitis is an inflammatory reaction occurring after this procedure in about 50% of patients. It is thought to be related to bacterial overgrowth and is treated with antibiotics (eg, quinolones). Probiotics may be protective. Most cases of pouchitis are readily controlled, but 5 to 10% prove refractory to all medical therapy and require conversion to a conventional (Brooke) ileostomy. For a minority of patients who are older, who have well-established families and lifestyles, who have poor sphincter tone or cannot tolerate frequent bowel movements, or who are simply unable or unwilling to face the consequences of frequent or chronic pouchitis, the Brooke ileostomy remains the procedure of choice.

In any event, the physical and emotional burdens imposed by any form of colon resection must be recognized, and care should be taken to see that the patient receives all the instructions and all the medical and psychologic support that is necessary before and after surgery.

Chapter 20. Diverticular Disease

Introduction

Diverticula are saclike mucosal outpouchings that protrude from a tubular structure. True diverticula contain all layers of the parent structure. False or pseudodiverticula are mucosal projections through the muscular layer. Esophageal (see p. 125) and Meckel's diverticula are true diverticula. Colonic diverticula are pseudodiverticula; they cause symptoms by trapping feces and becoming inflamed or infected, bleeding, or rupturing.

Diverticulosis

Diverticulosis is the presence of multiple diverticula in the colon, probably resulting from a lifelong low-fiber diet. Most diverticula are asymptomatic, but some become inflamed or bleed. Diagnosis is by colonoscopy or barium enema. Treatment varies depending on manifestation.

Diverticula occur anywhere in the large bowel—usually in the sigmoid but rarely below the peritoneal reflection of the rectum. They vary in diameter from 3 mm to > 3 cm. Patients with diverticula usually have several of them. Diverticulosis is uncommon in people < 40 but becomes common rapidly thereafter; essentially every 90-yr-old person has many diverticula. Giant diverticula, which are rare, range in diameter from 3 to 15 cm and may be single.

Pathophysiology

Diverticula are probably caused by increased intraluminal pressure leading to mucosal extrusion through the weakest points of the muscular layer of the bowel—areas adjacent to intramural blood vessels. Diverticula are more common among people who eat a low-fiber diet; however, the mechanism is not clear. One theory is that increased intraluminal pressure is required to move low-bulk stool through the colon. Another theory is that low-stool bulk causes a smaller diameter colon, which by Laplace's law would have increased pressure.

The etiology of giant diverticula is unclear. One theory is that a valvelike abnormality exists at the base of the diverticulum, so bowel gas can enter but escapes less freely.

Symptoms and Signs

Most (70%) diverticula are asymptomatic, 15 to 25% become painfully inflamed (diverticulitis), and 10 to 15% bleed painlessly. The bleeding is probably caused by erosion of the adjacent vessel by local trauma from impacted feces in the diverticulum. Although most diverticula are distal, 75% of bleeding occurs from diverticula proximal to the splenic flexure. In 33% of patients (5% overall), bleeding is serious enough to require transfusion.

Diagnosis

• Usually colonoscopy

Asymptomatic diverticula are usually found incidentally during barium enema or colonoscopy. Diverticulosis is suspected when painless rectal bleeding develops, particularly in an elderly patient. Evaluation of rectal bleeding typically includes colonoscopy, which can be done electively after routine preparation unless there is significant ongoing bleeding. In such patients, a rapid preparation (5 to 10 L of polyethylene glycol solution delivered via NGT over 3 to 4 h) often allows adequate visualization. If colonoscopy cannot visualize the source and ongoing bleeding is sufficiently rapid (> 0.5 to 1 mL/min), angiography may localize the source. Some angiographers first do a radionuclide scan to focus the examination.

Treatment

• High-fiber diet

• Sometimes angiographic or endoscopic treatment of bleeding

Treatment of diverticulosis aims at reducing segmental spasm. A high-fiber diet helps and may be supplemented by psyllium seed preparations or bran. Low-fiber diets are contraindicated. The intuitive injunction to avoid seeds or other dietary material that might become impacted in a diverticulum has no established medical basis. Antispasmodics (eg, belladonna) are not of benefit and may cause adverse effects. Surgery is unwarranted for uncomplicated disease. Giant diverticula, however, require surgery.

Diverticular bleeding stops spontaneously in 75% of patients. Treatment is often given during diagnostic procedures. If angiography was done for diagnosis, ongoing bleeding can be controlled in 70 to 90% of patients by intraarterial injection of vasopressin. In some cases, bleeding recurs within a few days and requires surgery. Angiographic embolization effectively stops bleeding but leads to bowel infarction in up to 20% of patients and is not recommended. Colonoscopy allows heat or laser coagulation of vessels or injection of epinephrine. If these measures fail to stop bleeding, segmental resection or subtotal colectomy is indicated.

Diverticulitis

Diverticulitis is inflammation of a diverticulum, which can result in phlegmon of the bowel wall, peritonitis, perforation, fistula, or abscess. The primary symptom is abdominal pain. Diagnosis is by CT. Treatment is with antibiotics (ciprofloxacin, or a 3rd-generation cephalosporin plus metronidazole) and occasionally surgery.

Diverticulitis occurs when a micro or macro perforation develops in a diverticulum, releasing intestinal bacteria. The resultant inflammation remains localized in about 75% of patients. The remaining 25% may develop abscess, free intraperitoneal perforation, bowel obstruction, or fistulas. The most common fistulas involve the bladder but may also involve the small bowel, uterus, vagina, abdominal wall, or even the thigh.

Diverticulitis is most serious in elderly patients, especially those taking prednisone or other drugs that increase the risk of infection. Nearly all serious diverticulitis occurs in the sigmoid.

Symptoms and Signs

Diverticulitis usually manifests with pain or tenderness in the left lower quadrant of the abdomen and fever. Peritoneal signs (eg, rebound or guarding) may be present, particularly with abscess or free perforation. Fistulas may manifest as pneumaturia, feculent vaginal discharge, or a cutaneous or myofascial infection of the abdominal wall, perineum, or upper leg. Patients with bowel obstruction have nausea, vomiting, and abdominal distention. Bleeding is uncommon.

Diagnosis

• Abdominal CT

• Colonoscopy after resolution

Clinical suspicion is high in patients with known diverticulosis. However, because other disorders (eg, appendicitis, colon or ovarian cancer) may cause similar symptoms, testing is required. Abdominal CT with oral and IV contrast is preferred, although findings in about 10% of patients cannot be distinguished from colon cancer. Colonoscopy, after resolution of the acute infection, is necessary for definitive diagnosis.

Treatment

• Varies with severity

• Liquid diet, oral antibiotics for mild disease

• IV antibiotics, npo for more severe disease

• CT-guided percutaneous drainage of abscess

• Sometimes surgery

A patient who is not very ill is treated at home with rest, a liquid diet, and oral antibiotics (eg, ciprofloxacin 500 mg bid amoxicillin/clavulanate 500 mg tid plus metronidazole 500 mg qid). Symptoms usually subside rapidly. The patient gradually advances to a soft low-fiber diet and a daily psyllium seed preparation. The colon should be evaluated after 2 to 4 wk with a colonoscopy or barium enema. After 1 mo, a high-fiber diet is resumed.

Patients with more severe symptoms (eg, pain, fever, marked leukocytosis) should be hospitalized, as should patients taking prednisone (who are at higher risk of perforation and general peritonitis). Treatment is bed rest, npo, IV fluids, and IV antibiotics (eg, ceftazidime 1 g IV q 8 h plus metronidazole 500 mg IV q 6 to 8 h).

About 80% of patients can be treated successfully without surgery. An abscess may respond to percutaneous drainage (CT guided). If response is satisfactory, the patient remains hospitalized until symptoms are relieved and a soft diet is resumed. A colonoscopy or barium enema is done ≥ 2 wk after symptoms have resolved.

Surgery: Surgery is required immediately for patients with free perforation or general peritonitis and for patients with severe symptoms that do not respond to nonsurgical treatment within 48 h. Increasing pain, tenderness, and fever are other signs that surgery is needed. Surgery should also be considered in patients with any of the following: ≥ 2 previous attacks of mild diverticulitis (or one attack in a patient < 50); a persistent tender mass; clinical, endoscopic, or x-ray signs suggestive of cancer; and dysuria associated with diverticulitis in men (or in women who have had a hysterectomy), because this symptom may presage perforation into the bladder.

The involved section of the colon is resected. The ends can be reanastomosed immediately in healthy patients without perforation, abscess, or significant inflammation. Other patients have a temporary colostomy with anastomosis carried out in a subsequent operation after inflammation resolves and the patient's general condition improves.

Meckel's Diverticulum

Meckel's diverticulum is a congenital sacculation of the distal ileum occurring in 2 to 3% of people. It is usually located within 100 cm of the ileocecal valve and often contains heterotopic gastric tissue, pancreatic tissue, or both. Symptoms are uncommon but include bleeding, bowel obstruction, and inflammation (diverticulitis). Diagnosis is difficult and often involves radionuclide scanning and barium studies. Treatment is surgical resection.

Pathophysiology

In early fetal life, the vitelline duct running from the terminal ileum to the umbilicus and yolk sac is normally obliterated by the 7th wk. If the portion connecting to the ileum fails to atrophy, a Meckel's diverticulum results. This congenital diverticulum arises from the antimesenteric margin of the intestine and contains all layers of the normal bowel. About 50% of diverticula also contain heterotopic tissue of the stomach (and thus contain parietal cells that secrete HCl), pancreas, or both.

Only about 2% of people with Meckel's diverticulum develop complications. Although diverticula are equally common among males and females, males are 2 to 3 times more likely to have complications. Complications include the following:

• Bleeding

• Obstruction

• Diverticulitis

• Tumors

Bleeding is more common among young children (< 5 yr) and occurs when acid secreted from ectopic gastric mucosa in the diverticulum ulcerates the adjacent ileum. Obstruction can occur at any age but is more common among older children and adults. In children, obstruction is most likely caused by intussusception of the diverticulum. Obstruction may also result from adhesions, volvulus, retained foreign bodies, tumors, or incarceration in a hernia (Littre's hernia). Acute Meckel's diverticulitis can occur at any age, but its incidence peaks in older children. Tumors, including carcinoids, are rare and occur mainly in adults.

Symptoms and Signs

In all ages, intestinal obstruction is manifested by cramping abdominal pain, nausea, and vomiting. Acute Meckel's diverticulitis is characterized by abdominal pain and tenderness typically localized below or to the left of the umbilicus; it is often accompanied by vomiting and is similar to appendicitis except for location of pain.

Children may present with repeated episodes of painless, bright red rectal bleeding, which is usually not severe enough to cause shock. Adults may also bleed, typically resulting in melena rather than frank blood.

Diagnosis

• Based on symptoms

• Radionuclide scan for bleeding

• CT for pain

Diagnosis is difficult, and tests are chosen based on presenting symptoms. If rectal bleeding is suspected to originate from a Meckel's diverticulum, a ^{99m}Tc pertechnetate scan may identify ectopic gastric mucosa and hence the diverticulum. Patients presenting with abdominal pain and focal tenderness should have a CT scan with oral contrast. If vomiting and signs of obstruction are predominant, flat and upright x-rays of the abdomen are done. Sometimes diagnosis is made only during surgical exploration for presumed appendicitis; whenever a normal appendix is found, Meckel's diverticulum should be suspected.

Treatment

• Surgery

Patients with intestinal obstruction caused by Meckel's diverticulum require early surgery. For detailed treatment of intestinal obstruction, see p. 117.

A bleeding diverticulum with an indurated area in the adjacent ileum requires resection of this section of the bowel and the diverticulum. A bleeding diverticulum without ileal induration requires only resection of the diverticulum.

Meckel's diverticulitis also requires resection. Small, asymptomatic diverticula encountered incidentally at laparotomy need not be removed.

Diverticular Disease of the Stomach and Small Bowel

Diverticula rarely involve the stomach but occur in the duodenum in up to 25% of people. Most duodenal

diverticula are solitary and occur in the second portion of the duodenum near the ampulla of Vater (periampullary). Jejunal diverticula occur in about 0.26% of patients and are more common among patients with disorders of intestinal motility. Meckel's diverticulum occurs in the distal ileum.

Duodenal and jejunal diverticula are asymptomatic in > 90% of cases and are usually detected incidentally during radiologic or endoscopic investigation of the upper GI tract for an unrelated disease. Rarely, small-bowel diverticula bleed or become inflamed, causing pain and nausea. Some even perforate. For poorly understood reasons, patients with periampullary diverticula are at increased risk of gallstones and pancreatitis. Treatment is surgical resection; however, the clinician should be cautious of recommending surgery for patients with a diverticulum and vague GI symptoms (eg, dyspepsia).

Chapter 21. Anorectal Disorders

Introduction

(See also Foreign Bodies on p. 139 and Anorectal Cancer on p. 195.)

The anal canal begins at the anal sphincter and ends at the anorectal junction (pectinate line, mucocutaneous junction, dentate line), where there are 8 to 12 anal crypts and 5 to 8 papillae. The canal is lined with anoderm, a continuation of the external skin. The anal canal and adjacent skin are innervated by somatic sensory nerves and are highly susceptible to painful stimuli. Venous drainage from the anal canal occurs through the caval system, but the anorectal junction can drain into both the portal and caval systems. Lymphatics from the anal canal pass to the internal iliac nodes, the posterior vaginal wall, and the inguinal nodes. The venous and lymphatic distributions determine how malignant disease and infection spread.

The rectum is a continuation of the sigmoid colon beginning at the level of the 3rd sacral vertebra and continuing to the anorectal junction. The rectal lining consists of red, glistening glandular mucosa, which has an autonomic nerve supply and is relatively insensitive to pain. Venous drainage occurs through the portal system. Lymphatic return from the rectum occurs along the superior hemorrhoidal vascular pedicle to the inferior mesenteric and aortic nodes.

The sphincteric ring encircling the anal canal is composed of the internal sphincter, the central portion of the levators, and components of the external sphincter. Anteriorly, it is more vulnerable to trauma, which can result in incontinence. The puborectalis forms a muscular sling around the rectum for support and assistance in defecation.

History: History should include the details of bleeding, pain, protrusion, discharge, swelling, abnormal sensations, bowel movements, incontinence, stool characteristics, use of cathartics and enemas, and abdominal and urinary symptoms. All patients should be asked about anal intercourse and other possible causes of trauma and infection.

Physical examination: Examination should be done gently and with good lighting. It consists of external inspection, perianal and intrarectal digital palpation, abdominal examination, and rectovaginal bidigital palpation. Anoscopy and rigid or flexible sigmoidoscopy to 15 to 60 cm above the anal verge are often included (see p. 98). Inspection, palpation, and anoscopy and sigmoidoscopy are best done with the patient in the left lateral (Sims') position or inverted on a tilt table. In cases of painful anal lesions, topical (lidocaine 5% ointment), regional, or even general anesthesia may be required. If it can be tolerated, a cleansing phosphate enema may facilitate sigmoidoscopy. Biopsies, smears, and cultures may be taken, and x-ray examination done if indicated.

Anal Fissure

(Fissure in Ano; Anal Ulcer)

An anal fissure is an acute longitudinal tear or a chronic ovoid ulcer in the squamous epithelium of the anal canal. It causes severe pain, sometimes with bleeding, particularly with defecation. Diagnosis is by inspection. Treatment is local hygiene, stool softeners, and sometimes botulinum toxin injection.

Anal fissures are believed to result from laceration by a hard or large stool, with secondary infection. Trauma (eg, anal intercourse) is a rare cause. The fissure may cause internal sphincter spasm, decreasing blood supply and perpetuating the fissure.

Symptoms and Signs

Anal fissures usually lie in the posterior midline but may occur in the anterior midline. Those off the midline may have specific etiologies, particularly Crohn's disease. An external skin tag (the sentinel pile) may be present at the lower end of the fissure, and an enlarged (hypertrophic) papilla may be present at

the upper end.

Infants may develop acute fissures, but chronic fissures are rare. Chronic fissures must be differentiated from cancer, primary lesions of syphilis, TB, and ulceration caused by Crohn's disease.

Fissures cause pain and bleeding. The pain typically occurs with or shortly after defecation, lasts for several hours, and subsides until the next bowel movement. Examination must be gentle but with adequate spreading of the buttocks to allow visualization.

Diagnosis

Diagnosis is made by inspection. Unless findings suggest a specific cause, further studies are not required.

Treatment

• Stool softeners

• Protective ointments, sitz baths

• Nitroglycerin ointment or botulinum toxin type A injection

Fissures often respond to conservative measures that minimize trauma during defecation (eg, stool softeners, psyllium, fiber). Healing is aided by use of protective zinc oxide ointments or bland suppositories (eg, glycerin) that lubricate the lower rectum and soften stool. Topical anesthetics (eg, benzocaine, lidocaine) and warm (not hot) sitz baths for 10 or 15 min after each bowel movement and prn give temporary relief.

Topical nitroglycerin 0.2% ointment, nifedipine cream 0.2% or 0.3%, arginine gel, and injections of botulinum toxin type A into the internal sphincter relax the anal sphincter and decrease maximum anal resting pressure, allowing healing. When conservative measures fail, surgery (internal anal sphincterotomy or controlled anal dilation) is needed to interfere with the cycle of internal anal sphincter spasm.

Anorectal Abscess

An anorectal abscess is a localized collection of pus in the perirectal spaces. Abscesses usually originate in an anal crypt. Symptoms are pain and swelling. Diagnosis is primarily by examination and CT or pelvic MRI for deeper abscesses. Treatment is surgical drainage.

An abscess may be located in various spaces surrounding the rectum and may be superficial or deep. A perianal abscess is superficial and points to the skin. An ischiorectal abscess is deeper, extending across the sphincter into the ischiorectal space below the levator ani; it may penetrate to the contralateral side, forming a "horseshoe" abscess. An abscess above the levator ani (ie, supralevator abscess) is quite deep and may extend to the peritoneum or abdominal organs; this abscess often results from diverticulitis or pelvic inflammatory disease. Crohn's disease (especially of the colon) sometimes causes anorectal abscess. A mixed infection usually occurs, with *Escherichia coli*, *Proteus vulgaris*, *Bacteroides*, streptococci, and staphylococci predominating.

Symptoms and Signs

Superficial abscesses can be very painful; perianal swelling, redness, and tenderness are characteristic. Deeper abscesses may be less painful but cause toxic symptoms (eg, fever, chills, malaise). There may be no perianal findings, but digital rectal examination may reveal a tender, fluctuant swelling of the rectal wall. High pelvirectal abscesses may cause lower abdominal pain and fever without rectal symptoms. Sometimes fever is the only symptom.

Diagnosis

• Clinical evaluation

• Rarely examination under anesthesia or CT

Patients who have a pointing cutaneous abscess, a normal digital rectal examination, and no signs of systemic illness do not require imaging. Those with any findings suggestive of a deeper abscess or Crohn's disease should have an examination under anesthesia at the time of drainage. Higher (supralevator) abscesses require CT to determine the intra-abdominal source of sepsis.

Treatment

• Incision and drainage

• Antibiotics for high-risk patients

Prompt incision and adequate drainage are required and should not wait until the abscess points. Many abscesses can be drained as an in-office procedure; deeper abscesses may require drainage in the operating room. Febrile, neutropenic, or diabetic patients or those with marked cellulitis should also receive antibiotics (eg, ciprofloxacin 500 mg IV q 12 h and metronidazole 500 mg IV q 8 h, ampicillin/sulbactam 1.5 g IV q 8 h). Antibiotics are not indicated for healthy patients with superficial abscesses. Anorectal fistulas may develop after drainage.

Anorectal Fistula

(Fistula in Ano)

An anorectal fistula is a tubelike tract with one opening in the anal canal and the other usually in the perianal skin. Symptoms are discharge and sometimes pain. Diagnosis is by examination and sigmoidoscopy. Treatment often requires surgery.

Fistulas arise spontaneously or occur secondary to drainage of a perirectal abscess. Predisposing causes include Crohn's disease and TB. Most fistulas originate in the anorectal crypts; others may result from diverticulitis, tumors, or trauma. Fistulas in infants are congenital and are more common among boys. Rectovaginal fistulas may be secondary to Crohn's disease, obstetric injuries, radiation therapy, or cancer.

Symptoms and Signs

A history of recurrent abscess followed by intermittent or constant discharge is usual. Discharge material is purulent, serosanguineous, or both. Pain may be present if there is infection. On inspection, one or more secondary openings can be seen. A cordlike tract can often be palpated. A probe inserted into the tract can determine the depth and direction and often the primary opening.

Diagnosis

• Clinical evaluation

• Sigmoidoscopy

Diagnosis is by examination. Sigmoidoscopy should follow to rule out Crohn's disease. Hidradenitis suppurativa, pilonidal sinus, dermal suppurative sinuses, and urethro-perineal fistulas must be differentiated from cryptogenic fistulas.

Treatment

• Various surgical procedures

• Medical treatment if caused by Crohn's disease

In the past, the only effective treatment was surgery, in which the primary opening and the entire tract are unroofed and converted into a "ditch." Partial division of the sphincters may be necessary. Some degree of incontinence may occur if a considerable portion of the sphincteric ring is divided. Alternatives to conventional surgery include advancement flaps, biologic plugs, and fibrin glue instillations into the fistulous tract.

If diarrhea or Crohn's disease is present, fistulotomy is inadvisable because of delayed wound healing. For patients with Crohn's disease, metronidazole, other appropriate antibiotics, and suppressive therapies can be given (see p. 171). Infliximab is very effective in closing fistulas caused by Crohn's disease.

Fecal Incontinence

Fecal incontinence is involuntary defecation.

Fecal incontinence can result from injuries or diseases of the spinal cord, congenital abnormalities, accidental injuries to the rectum and anus, procidentia, diabetes, severe dementia, fecal impaction, extensive inflammatory processes, tumors, obstetric injuries, and operations involving division or dilation of the anal sphincters.

Physical examination should evaluate gross sphincter function and perianal sensation and rule out fecal impaction. Anal sphincter ultrasonography, pelvic and perineal MRIs, pelvic floor electromyography, and anorectal manometry are also useful.

Treatment

• Program of stool regulation

• Perineal exercises, sometimes with biofeedback

• Sometimes a surgical procedure

Treatment includes a bowel management program to develop a predictable pattern of defecation. The program includes intake of adequate fluid and sufficient dietary bulk. Sitting on a toilet or using another customary defecatory stimulant (eg, coffee) encourages defecation. A suppository (eg, glycerin, bisacodyl) or a phosphate enema may also be used. If a regular defecatory pattern does not develop, a low-residue diet and oral loperamide may reduce the frequency of defecation.

Simple perineal exercises, in which the patient repeatedly contracts the sphincters, perineal muscles, and buttocks, may strengthen these structures and contribute to continence, particularly in mild cases. Biofeedback (to train the patient to use the sphincters maximally and to better appreciate physiologic stimuli) should be considered before recommending surgery in well-motivated patients who can understand and follow instructions and who have an anal sphincter capable of recognizing the cue of rectal distention. About 70% of such patients respond to biofeedback.

A defect in the sphincter can be sutured directly. When there is insufficient residual sphincter for repair, particularly in patients < 50 yr of age, a gracilis muscle can be transposed. Some centers attach a pacemaker to the gracilis muscle, as well as an artificial sphincter; these or other experimental procedures are available in only a few centers in the US, as research protocols. Alternatively, a Thiersch wire or other material can be used to encircle the anus. When all else fails, a colostomy can be considered.

Hemorrhoids

(Piles)

Hemorrhoids are dilated veins of the hemorrhoidal plexus in the lower rectum. Symptoms

include irritation and bleeding. Thrombosed hemorrhoids are painful. Diagnosis is by inspection or anoscopy. Treatment is symptomatic or with endoscopic banding, injection sclerotherapy, or sometimes surgery.

External hemorrhoids are located below the dentate line and are covered by squamous epithelium. Internal hemorrhoids are located above the dentate line and are lined by rectal mucosa. Hemorrhoids typically occur in the right anterior, right posterior, and left lateral zones. They occur in adults and children.

Symptoms and Signs

Hemorrhoids are often asymptomatic, or they may simply protrude. Pruritus ani is not commonly caused by hemorrhoids.

External hemorrhoids may become thrombosed, resulting in a painful, purplish swelling. Rarely, they ulcerate and cause minor bleeding. Cleansing the anal region may be difficult.

Internal hemorrhoids typically manifest with bleeding after defecation; blood is noted on toilet tissue and sometimes in the toilet bowl. Internal hemorrhoids may be uncomfortable but are not as painful as thrombosed external hemorrhoids. Internal hemorrhoids sometimes cause mucus discharge and a sensation of incomplete evacuation.

Strangulated hemorrhoids occur when protrusion and constriction occlude the blood supply. They cause pain that is occasionally followed by necrosis and ulceration.

Diagnosis

• Anoscopy

• Sometimes sigmoidoscopy or colonoscopy

Most painful hemorrhoids, thrombosed, ulcerated or not, are seen on inspection of the anus and rectum. Anoscopy is essential in evaluating painless or bleeding hemorrhoids. Rectal bleeding should be attributed to hemorrhoids only after more serious conditions are excluded (eg, by sigmoidoscopy or colonoscopy).

Treatment

• Stool softeners, sitz baths

• Rarely excision for thrombosed external hemorrhoids

• Injection sclerotherapy or rubber band ligation for internal hemorrhoids

Symptomatic treatment is usually all that is needed. It is accomplished with stool softeners (eg, docusate, psyllium), warm sitz baths (ie, sitting in a tub of tolerably hot water for 10 min) after each bowel movement and prn, anesthetic ointments containing lidocaine, or witch hazel (hamamelis) compresses (which soothe by an unknown mechanism). Pain caused by a thrombosed hemorrhoid can be treated with NSAIDs. Infrequently, simple excision of the hemorrhoid may relieve pain rapidly; after infiltration with 1% lidocaine, the thrombosed portion of the hemorrhoid is excised, and the defect is closed with an absorbable suture. Bleeding hemorrhoids can be treated by injection sclerotherapy with 5% phenol in vegetable oil. Bleeding should cease at least temporarily.

Rubber band ligation is used for larger, prolapsing internal hemorrhoids or those that do not respond to conservative management. With mixed internal and external hemorrhoids, only the internal component should be rubber band ligated. The internal hemorrhoid is grasped and withdrawn through a stretched 1/2-cm diameter band, which is released to ligate the hemorrhoid, resulting in its necrosis and sloughing. One hemorrhoid is ligated every 2 wk; 3 to 6 treatments may be required. Sometimes, multiple

hemorrhoids can be ligated at a single visit.

Infrared photocoagulation is useful for ablating small internal hemorrhoids, hemorrhoids that cannot be rubber band ligated because of pain sensitivity, or hemorrhoids that are not cured with rubber band ligation. Laser destruction, cryotherapy, and various types of electrodestruction are of unproven efficacy.

Surgical hemorrhoidectomy is required for patients who do not respond to other forms of therapy. Significant postoperative pain is common, as is urinary retention and constipation. Stapled hemorrhoidopexy is an alternative procedure for circumferential hemorrhoids, although its advantages and the indications have yet to be defined.

Levator Syndrome

Episodic rectal pain caused by spasm of the levator ani muscle.

Proctalgia fugax (fleeting pain in the rectum) and **coccydynia** (pain in the coccygeal region) are variants of levator syndrome. Rectal spasm causes pain, typically unrelated to defecation, usually lasting < 20 min. The pain may be brief and intense or a vague ache high in the rectum. It may occur spontaneously or with sitting and can waken the patient from sleep. The pain may feel as if it would be relieved by the passage of gas or a bowel movement. In severe cases, the pain can persist for many hours and recur frequently. The patient may have undergone various rectal operations for these symptoms, with no benefit.

Diagnosis

• Clinical evaluation

Physical examination can exclude other painful rectal conditions (eg, thrombosed hemorrhoids, fissures, abscesses). Physical examination is often normal, although tenderness or tightness of the levator muscle, usually on the left, may be present. Occasional cases are caused by low back or prostate disorders.

Treatment

• Analgesics, sitz baths

• Sometimes electrogalvanic stimulation

Treatment consists of explanations to the patient of the benign nature of the condition. An acute episode may be relieved by the passage of gas or a bowel movement, by a sitz bath, or by a mild analgesic. When the symptoms are more intense, physical therapy with electrogalvanic stimulation applied to the lower rectum is usually effective. Skeletal muscle relaxants or anal sphincter massage under local or regional anesthesia can be tried, but the benefit is unclear.

Pilonidal Disease

Pilonidal disease refers to an acute abscess or chronic draining sinus in the sacrococcygeal area.

Pilonidal disease usually occurs in young, hirsute, white males but can also occur in women. One or several midline or adjacent-to-the-midline pits or sinuses occur in the skin of the sacral region and may form a cavity, often containing hair. The lesion is usually asymptomatic; infected lesions are painful.

Treatment of an acute abscess is by incision and drainage. Usually, one or more chronic draining sinuses persist and must be extirpated by excision and primary closure or, preferably, by an open technique (eg, cystotomy, marsupialization). Antibiotics are generally not needed.

Proctitis

Proctitis is inflammation of the rectal mucosa, which may result from infection, inflammatory bowel disease, or radiation. Symptoms are rectal discomfort and bleeding. Diagnosis is by sigmoidoscopy, usually with cultures and biopsy. Treatment depends on etiology.

Proctitis may be a manifestation of sexually transmitted disease, certain enteric infections (eg, *Campylobacter*, *Shigella*, *Salmonella*), inflammatory bowel disease, or radiation treatments; it may be associated with prior antibiotic use. Sexually transmitted pathogens cause proctitis more commonly among homosexual men. Immunocompromised patients are at particular risk of infections with herpes simplex and cytomegalovirus.

Symptoms and Signs

Typically, patients report rectal bleeding or passage of mucus. Proctitis resulting from gonorrhea, herpes simplex, or cytomegalovirus may cause intense anorectal pain.

Diagnosis

• Proctoscopy or sigmoidoscopy

• Tests for syphilis and *Clostridium difficile*

Diagnosis requires proctoscopy or sigmoidoscopy, which may reveal an inflamed rectal mucosa. Small discrete ulcers and vesicles suggest herpes infection. Smears should be sent for culture of *Neisseria gonorrhoeae, Chlamydia* sp, enteric pathogens, and viral pathogens. Serologic tests for syphilis and stool tests for *C. difficile* toxin are done. Sometimes mucosal biopsy is needed. Colonoscopy may be valuable in some patients.

Treatment

• Various treatments depending on cause

Infective proctitis can be treated with antibiotics. Homosexual men with nonspecific proctitis may be treated empirically with ceftriaxone 125 mg IM once (or ciprofloxacin 500 mg po bid for 7 days), plus doxycycline 100 mg po bid for 7 days. Antibiotic-associated proctitis is treated with metronidazole (250 mg po qid) or vancomycin (125 mg po qid) for 7 to 10 days.

Radiation proctitis is usually effectively treated with topical formalin carefully applied to the affected mucosa. Alternative treatments include topical corticosteroids as foam (hydrocortisone 90 mg) or enemas (hydrocortisone 100 mg or methylprednisolone 40 mg) bid for 3 wk, or mesalamine (4 g) enema at bedtime for 3 to 6 wk. Mesalamine suppositories 500 mg once/day or bid, mesalamine 800 mg po tid, or sulfasalazine 500 to 1000 mg po qid for ≥ 3 wk alone or in combination with topical therapy may also be effective. Patients unresponsive to these forms of therapy may benefit from a course of systemic corticosteroids.

Pruritus Ani

Pruritus ani is anal and perianal itching.

The perianal skin tends to itch, which can result from numerous causes (see Table 21-1).

[**Table 21-1.** Causes of Pruritus Ani]

Occasionally, the irritation is misinterpreted by the patient as pain, so other causes of perianal pain (eg, abscess) should be ruled out.

Diagnosis is based on the appearance of the anal skin and relevant information from the history. The skin typically shows dullness and thickening, although the underlying pathology is often obscured by

excoriation caused by scratching and secondary infection. A scraping of local skin is taken to rule out a fungal infection, and a stool sample should be examined for ova and parasites. Visible lesions should be biopsied.

Foods suspected of causing pruritus ani should be eliminated from the diet. Clothing should be loose, and bed clothing light. After bowel movements, the patient should cleanse the anal area with absorbent cotton or plain soft tissue moistened with water. Liberal, frequent dusting with nonmedicated talcum powder or cornstarch helps combat moisture. Hydrocortisone acetate 1% ointment, applied sparingly qid, may relieve symptoms. Systemic causes and parasitic or fungal infections must be treated specifically.

Rectal Prolapse and Procidentia

Rectal prolapse is painless protrusion of the rectum through the anus. Procidentia is complete prolapse of the entire thickness of the rectum. Diagnosis is by inspection. Surgery is usually required in adults.

Transient, minor prolapse of just the rectal mucosa often occurs in otherwise normal infants. Mucosal prolapse in adults persists and may progressively worsen.

Procidentia is complete prolapse of the entire thickness of the rectum. The primary cause is unclear. Most patients are women > 60.

Symptoms and Signs

The most prominent symptom is protrusion. It may only occur while straining or while walking or standing. Rectal bleeding can occur, and incontinence is frequent. Pain is uncommon unless incarceration occurs.

Diagnosis

• Clinical evaluation

• Sigmoidoscopy, colonoscopy, or barium enema

To determine the full extent of the prolapse, the clinician should examine the patient while the patient is standing or squatting and straining. Rectal procidentia can be distinguished from hemorrhoids by the presence of circumferential mucosal folds. Anal sphincter tone is usually diminished. Sigmoidoscopy, colonoscopy, or barium enema x-rays of the colon must be done to search for other disease. Primary neurologic disorders (eg, spinal cord tumors) must be ruled out.

Treatment

• Elimination of causes of straining

• For infants and children: Sometimes strapping buttocks together

• For adults: Sometimes surgery

In infants and children, conservative treatment is most satisfactory. Causes of straining should be eliminated. Firmly strapping the buttocks together with tape between bowel movements usually facilitates spontaneous resolution of the prolapse. For simple mucosal prolapse in adults, the excess mucosa can be excised. For procidentia, an abdominal operation may be required. In patients who are very old or in poor health, a wire or synthetic plastic loop can encircle the sphincteric ring (Thiersch's procedure). Other perineal operations (eg, Delorme or Altemeier procedure) can be considered.

Chapter 22. Tumors of the GI Tract

Introduction

Various benign and malignant tumors can develop anywhere in the GI tract. Tumors of the mouth are discussed in Ch. 55.

Benign Esophageal Tumors

Although there are many types of benign esophageal tumors, most are of little consequence except for causing annoying swallowing symptoms (see p. 120) and rarely ulceration or bleeding. Leiomyoma, the most common, may be multiple but usually has an excellent prognosis.

Esophageal Cancer

The most common malignant tumor in the proximal two thirds of the esophagus is squamous cell carcinoma; adenocarcinoma is the most common in the distal one third. Symptoms are progressive dysphagia and weight loss. Diagnosis is by endoscopy, followed by CT and endoscopic ultrasound for staging. Treatment varies with stage and generally includes surgery with or without chemotherapy and radiation. Long-term survival is poor except for those with local disease.

Esophageal cancer accounts for an estimated 15,500 cases and 13,900 deaths in the US annually.

Squamous cell carcinoma: About 8000 cases occur annually in the US. It is more common in parts of Asia and in South Africa. In the US, it is 4 to 5 times more common among blacks than whites, and 2 to 3 times more common among men than women.

The primary risk factors are alcohol ingestion and tobacco use (in any form). Other factors include achalasia, human papillomavirus, lye ingestion (resulting in stricture), sclerotherapy, Plummer-Vinson syndrome, irradiation of the esophagus, and esophageal webs. Genetic causes are unclear, but 50% of patients with tylosis (hyperkeratosis palmaris et plantaris), an autosomal dominant disorder, have esophageal cancer by age 45, and 95% have it by age 55.

Adenocarcinoma: Adenocarcinoma occurs in the distal esophagus. Its incidence is increasing; it accounts for 50% of esophageal carcinoma in whites. It is 4 times more common among whites than blacks. Alcohol is not an important risk factor, but smoking is contributory. Adenocarcinoma of the distal esophagus is difficult to distinguish from adenocarcinoma of the gastric cardia invading the distal esophagus.

Most adenocarcinomas arise in Barrett's esophagus, which results from chronic gastroesophageal reflux disease and reflux esophagitis. In Barrett's esophagus, a metaplastic, columnar, glandular, intestine-like mucosa with brush border and goblet cells replaces the normal stratified squamous epithelium of the distal esophagus during the healing phase of acute esophagitis when healing takes place in the continued presence of stomach acid.

Other malignant tumors: Less common malignant tumors include spindle cell carcinoma (a poorly differentiated variant of squamous cell carcinoma), verrucous carcinoma (a well-differentiated variant of squamous cell carcinoma), pseudosarcoma, mucoepidermoid carcinoma, adenosquamous carcinoma, cylindroma (adenoid cystic carcinoma), primary oat cell carcinoma, choriocarcinoma, carcinoid tumor, sarcoma, and primary malignant melanoma.

Metastatic cancer constitutes 3% of esophageal cancer. Melanoma and breast cancer are most likely to metastasize to the esophagus; others include cancers of the head and neck, lung, stomach, liver, kidney, prostate, testis, and bone. These tumors usually seed the loose connective tissue stroma around the esophagus, whereas primary esophageal cancers begin in the mucosa or submucosa.

Symptoms and Signs

Early-stage esophageal cancer tends to be asymptomatic. When the lumen of the esophagus becomes constricted to < 14 mm, dysphagia commonly occurs. The patient first has difficulty swallowing solid food, then semisolid food, and finally liquid food and saliva; this steady progression suggests a growing malignant process rather than a spasm, benign ring, or peptic stricture. Chest pain may be present, usually radiating to the back.

Weight loss, even when the patient maintains a good appetite, is almost universal. Compression of the recurrent laryngeal nerve may lead to vocal cord paralysis and hoarseness. Compression of sympathetic nerves may lead to Horner's syndrome, and nerve compression elsewhere may cause spinal pain, hiccups, or paralysis of the diaphragm. Malignant pleural effusions or pulmonary metastasis may cause dyspnea. Intraluminal tumor involvement may cause odynophagia, vomiting, hematemesis, melena, iron deficiency anemia, aspiration, and cough. Fistulas between the esophagus and tracheobronchial tree may cause lung abscess and pneumonia. Other findings may include superior vena cava syndrome, malignant ascites, and bone pain.

Lymphatic spread to internal jugular, cervical, supraclavicular, mediastinal, and celiac nodes is common. The tumor usually metastasizes to lung and liver and occasionally to distant sites (eg, bone, heart, brain, adrenal glands, kidneys, peritoneum).

Diagnosis

• Endoscopy with biopsy

• Then CT and endoscopic ultrasound

There are no screening tests. Patients suspected of having esophageal cancer should have endoscopy with cytology and biopsy. Although barium x-ray may show an obstructive lesion, endoscopy is required for biopsy and tissue diagnosis.

Patients in whom esophageal cancer is identified require CT of the chest and abdomen to determine extent of tumor spread. If CT results are negative for metastasis, endoscopic ultrasound should be done to determine the depth of the tumor in the esophageal wall and regional lymph node involvement. Findings guide therapy and help determine prognosis.

Basic blood tests, including CBC, electrolytes, and liver function, should be done.

Prognosis

Prognosis depends greatly on stage, but overall is poor (5-yr survival: < 5%) because many patients present with advanced disease. Patients with cancer restricted to the mucosa have about an 80% survival rate, which drops to < 50% with submucosal involvement, 20% with extension to the muscularis propria, 7% with extension to adjacent structures, and < 3% with distant metastases.

Treatment

• Surgical resection, often combined with chemotherapy and radiation

Treatment decisions depend on tumor staging, size, location, and the patient's wishes (many choose to forgo aggressive treatment).

General principles: Patients with stage 0, I, or IIa disease (see Table 22-1) respond well to surgical resection; preoperative chemotherapy and radiation provide additional benefit. Those with stage IIb and III have poor survival with surgery alone; response and survival are enhanced by preoperative (neoadjuvant) use of radiation and chemotherapy to reduce tumor volume before surgery. Patients unable or unwilling to undergo surgery may receive some benefit from combined radiation and chemotherapy. Radiation or chemotherapy alone is of little benefit. Patients with stage IV disease require palliation and should not undergo surgery.

After treatment, patients are screened for recurrence by endoscopy and CT of the neck, chest, and abdomen at 6-mo intervals for 3 yr and annually thereafter.

Patients with Barrett's esophagus require intense long-term treatment for gastroesophageal reflux disease (see p. 125) and endoscopic surveillance for malignant transformation at 3- to 12-mo intervals depending on the degree of metaplasia.

Surgery: En bloc resection for cure requires removal of the entire tumor, proximal and distal margins of normal tissue, all potentially malignant lymph nodes, and a portion of the proximal stomach sufficient to contain the distal draining lymphatics. The procedure requires gastric pull-up with esophagogastric anastomosis, small-bowel interposition, or colonic interposition. Pyloroplasty is required to ensure proper gastric drainage because esophagectomy necessarily results in bilateral vagotomy. This extensive surgery may be poorly tolerated by patients > 75 yr, particularly those

[**Table 22-1.** Staging Esophageal Cancer*]

with underlying cardiac or pulmonary disease (ejection fraction < 40%, or forced expiratory volume in 1 sec [FEV_1] < 1.5 L/min). Overall, operative mortality is about 5%.

Complications of surgery include anastomotic leaks, fistulas, and strictures; bilious gastroesophageal reflux; and dumping syndrome. The burning chest pain of bile reflux after distal esophagectomy can be more annoying than the original symptom of dysphagia and may require subsequent Roux-en-Y jejunostomy for bile diversion. An interposed segment of small bowel or colon in the chest has a tenuous blood supply, and torsion, ischemia, or gangrene of the interposed bowel may result.

External beam radiation therapy: Radiation is usually used in combination with chemotherapy for patients who are poor candidates for curative surgery, including those with advanced disease. Radiation is contraindicated in patients with tracheoesophageal fistula because tumor shrinkage enlarges the fistula. Similarly, patients with vascular encasement by tumor may experience massive hemorrhage with tumor shrinkage. During the early stages of radiation therapy, edema may worsen esophageal obstruction, dysphagia, and odynophagia. This problem may require esophageal dilation or preradiation placement of a percutaneous gastrostomy feeding tube. Other adverse effects of radiation therapy include nausea, vomiting, anorexia, fatigue, esophagitis, excess esophageal mucus production, xerostomia, stricture, radiation pneumonitis, radiation pericarditis, myocarditis, and myelitis (spinal cord inflammation).

Chemotherapy: Tumors are poorly responsive to chemotherapy alone. Response rates (defined as ≥ 50% reduction in all measurable areas of tumor) vary from 10 to 40%, but responses generally are incomplete (minor shrinkage of tumor) and temporary. No drug is notably more effective than another.

Most commonly, cisplatin and 5-fluorouracil are used in combination. However, several other drugs, including mitomycin, doxorubicin, vindesine, bleomycin, and methotrexate, also are active against squamous cell carcinoma.

Palliation: Palliation is directed at reducing esophageal obstruction sufficiently to allow oral intake. Suffering caused by esophageal obstruction can be significant, with salivation and recurrent aspiration. Options include manual dilation procedures (bougienage), orally inserted stents, radiation therapy, laser photocoagulation, and photodynamic therapy. In some cases, cervical esophagostomy with feeding jejunostomy is required.

Relief provided by esophageal dilation rarely lasts more than a few days. Flexible metal mesh stents are more effective at maintaining esophageal patency. Some plastic-coated models can also be used to occlude tracheoesophageal fistulas, and some are available with a valve that prevents reflux when the stent must be placed near the lower esophageal sphincter.

Endoscopic laser therapy can palliate dysphagia by burning a central channel through the tumor and can be repeated if needed. Photodynamic therapy uses an injection of porfimer sodium, a hematoporphyrin

derivative that is taken up by tissues and acts as a photosensitizer. When activated by a laser beam directed on the tumor, this substance releases cytotoxic oxygen singlets that destroy tumor cells. Patients receiving this treatment must avoid sun exposure for 6 wk after treatment because the skin is also sensitized to light.

Supportive care: Nutritional support by enteral or parenteral supplementation enhances the tolerability and feasibility of all treatments. An endoscopically or surgically placed feeding tube provides a more distal route for feeding when the esophagus is obstructed.

Because nearly all cases of esophageal cancer are fatal, end-of-life care should always aim to control symptoms, especially pain and inability to swallow secretions (see also p. 3483). At some point, many patients need substantial doses of opioids. Patients should be advised to make end-of-life care decisions early in the course of disease and to record their wishes in an advance directive (see p. 3471).

Stomach Cancer

Etiology of stomach cancer is multifactorial, but *Helicobacter pylori* plays a significant role. Symptoms include early satiety, obstruction, and bleeding but tend to occur late in the disease. Diagnosis is by endoscopy, followed by CT and endoscopic ultrasound for staging. Treatment is mainly surgery; chemotherapy may provide a temporary response. Long-term survival is poor except for those with local disease.

Stomach cancer accounts for an estimated 21,000 cases and over 11,000 deaths in the US annually. Gastric adenocarcinoma accounts for 95% of malignant tumors of the stomach; less common are localized gastric lymphomas (see p. 1016) and leiomyosarcomas. Stomach cancer is the 2nd most common cancer worldwide, but the incidence varies widely; incidence is extremely high in Japan, China, Chile, and Iceland. In the US, incidence has declined in recent decades to the 7th most common cause of death from cancer. In the US, it is most common among blacks, Hispanics, and American Indians. Its incidence increases with age; > 75% of patients are > 50 yr.

Etiology

Helicobacter pylori infection is the cause of most stomach cancer. Autoimmune atrophic gastritis (see p. 133) and various genetic factors (see Gastrointestinal Stromal Tumors on p. 190) are also risk factors. Dietary factors are not proven causes.

Gastric polyps can be precursors of cancer. Inflammatory polyps may develop in patients taking NSAIDs, and fundic foveolar polyps are common among patients taking proton pump inhibitors. Adenomatous polyps, particularly multiple ones, although rare, are the most likely to develop cancer. Cancer is particularly likely if an adenomatous polyp is > 2 cm in diameter or has a villous histology. Because malignant transformation cannot be detected by inspection, all polyps seen at endoscopy should be removed. The incidence of stomach cancer is generally decreased in patients with duodenal ulcer.

Pathophysiology

Gastric adenocarcinomas can be classified by gross appearance:

- Protruding: The tumor is polypoid or fungating.
- Penetrating: The tumor is ulcerated.
- Superficial spreading: The tumor spreads along the mucosa or infiltrates superficially within the wall of the stomach.
- Linitis plastica: The tumor infiltrates the stomach wall with an associated fibrous reaction that causes a rigid "leather bottle" stomach.
- Miscellaneous: The tumor shows characteristics of ≥ 2 of the other types; this classification is the

largest.

Prognosis is better with protruding tumors than with spreading tumors because protruding tumors become symptomatic earlier.

Symptoms and Signs

Initial symptoms are nonspecific, often consisting of dyspepsia suggestive of peptic ulcer. Patients and physicians alike tend to dismiss symptoms or treat the patient for acid disease. Later, early satiety (fullness after ingesting a small amount of food) may occur if the cancer obstructs the pyloric region or if the stomach becomes nondistensible secondary to linitis plastica. Dysphagia may result if cancer in the cardiac region of the stomach obstructs the esophageal outlet. Loss of weight or strength, usually resulting from dietary restriction, is common. Massive hematemesis or melena is uncommon, but secondary anemia may follow occult blood loss. Occasionally, the first symptoms are caused by metastasis (eg, jaundice, ascites, fractures).

Physical findings may be unremarkable or limited to heme-positive stools. Late in the course, abnormalities include an epigastric mass; umbilical, left supraclavicular, or left axillary lymph nodes; hepatomegaly; and an ovarian or rectal mass. Pulmonary, CNS, and bone lesions may occur.

Diagnosis

• Endoscopy with biopsy

• Then CT and endoscopic ultrasound

Differential diagnosis commonly includes peptic ulcer and its complications.

Patients suspected of having stomach cancer should have endoscopy with multiple biopsies and brush cytology. Occasionally, a biopsy limited to the mucosa misses tumor tissue in the submucosa. X-rays, particularly double-contrast barium studies, may show lesions but rarely obviate the need for subsequent endoscopy.

Patients in whom cancer is identified require CT of the chest and abdomen to determine extent of tumor spread. If CT is negative for metastasis, endoscopic ultrasound should be done to determine the depth of the tumor and regional lymph node involvement. Findings guide therapy and help determine prognosis.

Basic blood tests, including CBC, electrolytes, and liver function tests, should be done to assess anemia, hydration, general condition, and possible liver metastases. Carcinoembryonic antigen (CEA) should be measured before and after surgery.

Screening: Screening with endoscopy is used in high-risk populations (eg, Japanese) but is not recommended in the US. Follow-up screening for recurrence in treated patients consists of endoscopy and CT of the chest, abdomen, and pelvis. If an elevated CEA dropped after surgery, follow-up should include CEA levels; a rise signifies recurrence.

Prognosis

Prognosis depends greatly on stage but overall is poor (5-yr survival: < 5 to 15%) because most patients present with advanced disease. If the tumor is limited to the mucosa or submucosa, 5-yr survival may be as high as 80%. For tumors involving local lymph nodes, survival is 20 to 40%. More widespread disease is almost always fatal within 1 yr. Gastric lymphomas have a better prognosis and are discussed in Ch. 118.

Treatment

• Surgical resection, sometimes combined with chemotherapy, radiation, or both

Treatment decisions depend on tumor staging and the patient's wishes (some may choose to forgo aggressive treatment—see p. 3471).

Curative surgery involves removal of most or all of the stomach and adjacent lymph nodes and is reasonable in patients with disease limited to the stomach and perhaps the regional lymph nodes (< 50% of patients). Adjuvant chemotherapy or combined chemotherapy and radiation therapy after surgery may be beneficial if the tumor is resectable.

Resection of locally advanced regional disease results in a 10-mo median survival (vs 3 to 4 mo without resection).

Metastasis or extensive nodal involvement precludes curative surgery, and at most, palliative procedures should be undertaken. However, the true extent of tumor spread often is not recognized until curative surgery is attempted. Palliative surgery typically consists of a gastroenterostomy to bypass a pyloric obstruction and should be done only if the patient's quality of life can be improved. In patients not undergoing surgery, combination chemotherapy regimens (5-fluorouracil, doxorubicin, mitomycin, cisplatin, or leucovorin in various combinations) may produce temporary response but little improvement in 5-yr survival. Radiation therapy is of limited benefit.

Gastrointestinal Stromal Tumors

Gastrointestinal stromal tumors are tumors of the GI tract derived from mesenchymal precursor cells in the gut wall. They result from mutations of a growth factor receptor gene, *CKIT*. Some are caused by previous radiation therapy to the abdomen for other tumors.

Tumors are slow growing, and malignant potential varies from minimal to significant. Most (60 to 70%) occur in the stomach, 20 to 25% in the small bowel, and a small number in the esophagus, colon, and rectum. Average age at presentation is 50 to 60.

Symptoms vary with location but include bleeding, dyspepsia, and obstruction. Diagnosis is usually by endoscopy, with biopsy and endoscopic ultrasound for staging. Treatment is surgical removal. The role of radiation and chemotherapy is unclear, but the tyrosine kinase inhibitor imatinib has been beneficial.

Small-Bowel Tumors

Small-bowel tumors account for 1 to 5% of GI tumors (over 5000 cases in the US annually).

Benign tumors include leiomyomas, lipomas, neurofibromas, and fibromas. All may cause abdominal distention, pain, bleeding, diarrhea, and, if obstruction develops, vomiting. Polyps are not as common as in the colon.

Adenocarcinoma, a malignant tumor, is uncommon. Usually it arises in the duodenum or proximal jejunum and causes minimal symptoms. In patients with Crohn's disease, the tumors tend to occur distally and in bypassed or inflamed loops of bowel; adenocarcinoma occurs more often in Crohn's disease of the small bowel than in Crohn's disease of the colon.

Primary malignant **lymphoma** (see p. 1016) arising in the ileum may cause a long, rigid segment. Small-bowel lymphomas arise often in long-standing untreated celiac sprue.

Carcinoid tumors (see p. 907) occur most often in the small bowel, particularly the ileum, and the appendix, and in these locations are often malignant. Multiple tumors occur in 50% of cases. Of those > 2 cm in diameter, 80% have metastasized locally or to the liver by the time of operation. About 30% of small-bowel carcinoids cause obstruction, pain, bleeding, or carcinoid syndrome. Treatment is surgical resection; repeat operations may be required.

Kaposi's sarcoma (see p. 753), first described as a disease of elderly Jewish and Italian men, occurs in an aggressive form in Africans, transplant recipients, and AIDS patients, who have GI tract involvement 40 to 60% of the time. Lesions may occur anywhere in the GI tract but usually in the stomach, small bowel,

or distal colon. GI lesions usually are asymptomatic, but bleeding, diarrhea, proteinlosing enteropathy, and intussusception may occur. A second primary intestinal cancer occurs in ≤ 20% of patients; most often it is lymphocytic leukemia, non-Hodgkin lymphoma, Hodgkin lymphoma, or adenocarcinoma of the GI tract. Treatment depends on the cell type and location and extent of the lesions.

Diagnosis

• Enteroclysis

• Sometimes push endoscopy or capsule video endoscopy

Enteroclysis (sometimes CT enteroclysis) is probably the most common study for mass lesions of the small bowel. Push endoscopy of the small bowel with an enteroscope may be used to visualize and biopsy tumors. Capsule video endoscopy can help identify small-bowel lesions, particularly bleeding sites; a swallowed capsule transmits 2 images/sec to an external recorder. The original capsule is not useful in the stomach or colon because it tumbles in these larger organs; a colon capsule camera with better optics and illumination is under development for use in these larger-diameter organs.

Treatment

• Surgical resection

Treatment is surgical resection. Electrocautery, thermal obliteration, or laser phototherapy at the time of enteroscopy or surgery may be an alternative to resection.

Polyps of the Colon and Rectum

An intestinal polyp is any mass of tissue that arises from the bowel wall and protrudes into the lumen. Most are asymptomatic except for minor bleeding, which is usually occult. The main concern is malignant transformation; most colon cancers arise in a previously benign adenomatous polyp. Diagnosis is by endoscopy. Treatment is endoscopic removal.

Polyps may be sessile or pedunculated and vary considerably in size. Incidence of polyps ranges from 7 to 50%; the higher figure includes very small polyps (usually hyperplastic polyps or adenomas) found at autopsy. Polyps, often multiple, occur most commonly in the rectum and sigmoid and decrease in frequency toward the cecum. Multiple polyps may represent familial adenomatous polyposis (see p. 192). About 25% of patients with cancer of the large bowel also have satellite adenomatous polyps.

Adenomatous (neoplastic) polyps are of greatest concern. Such lesions are classified histologically as tubular adenomas, tubulo-villous adenomas (villoglandular polyps), or villous adenomas. The likelihood of cancer in an adenomatous polyp at the time of discovery is related to size, histologic type, and degree of dysplasia; a 1.5-cm tubular adenoma has a 2% risk of containing a cancer vs a 35% risk in 3-cm villous adenomas. Serrated adenomas, a somewhat more aggressive type of adenoma, may develop from hyperplastic polyps.

Nonadenomatous (nonneoplastic) polyps include hyperplastic polyps, hamartomas, juvenile polyps, pseudopolyps, lipomas, leiomyomas, and other rarer tumors. Juvenile polyps occur in children, typically outgrow their blood supply, and autoamputate some time during or after puberty. Treatment is required only for uncontrollable bleeding or intussusception. Inflammatory polyps and pseudopolyps occur in chronic ulcerative colitis and in Crohn's disease of the colon. Multiple juvenile polyps (but not sporadic ones) convey an increased cancer risk. The specific number of polyps resulting in increased risk is not known.

Symptoms and Signs

Most polyps are asymptomatic. Rectal bleeding, usually occult and rarely massive, is the most frequent complaint. Cramps, abdominal pain, or obstruction may occur with a large lesion. Rectal polyps may be palpable by digital examination. Occasionally, a polyp on a long pedicle may prolapse through the anus.

Large villous adenomas may rarely cause watery diarrhea that may result in hypokalemia.

Diagnosis

• Colonoscopy

Diagnosis is usually made by colonoscopy. Barium enema, particularly double-contrast examination, is effective, but colonoscopy is preferred because polyps also may be removed during that procedure. Because rectal polyps are often multiple and may coexist with cancer, complete colonoscopy to the cecum is mandatory even if a distal lesion is found by flexible sigmoidoscopy.

Treatment

• Complete removal during colonoscopy

• Sometimes follow with surgical resection

• Follow-up surveillance colonoscopy

Polyps should be removed completely with a snare or electrosurgical biopsy forceps during total colonoscopy; complete excision is particularly important for large villous adenomas, which have a high potential for cancer. If colonoscopic removal is unsuccessful, laparotomy should be done.

Subsequent treatment depends on the histology of the polyp. If dysplastic epithelium does not invade the muscularis mucosa, the line of resection in the polyp's stalk is clear, and the lesion is well differentiated, endoscopic excision and close endoscopic follow-up should suffice. Patients with deeper invasion, an unclear resection line, or a poorly differentiated lesion should have segmental resection of the colon. Because invasion through the muscularis mucosa provides access to lymphatics and increases the potential for lymph node metastasis, such patients should have further evaluation (as in colon cancer —see p. 193).

The scheduling of follow-up examinations after polypectomy is controversial. Most authorities recommend total colonoscopy annually for 2 yr (or barium enema if total colonoscopy is impossible), with removal of newly discovered lesions. If 2 annual examinations are negative for new lesions, colonoscopy is recommended every 2 to 3 yr.

Prevention

Aspirin and COX-2 inhibitors may help prevent formation of new polyps in patients with polyps or colon cancer.

Familial Adenomatous Polyposis

Familial adenomatous polyposis (FAP) is a hereditary disorder causing numerous colonic polyps and resulting in colon carcinoma by age 40. Patients are usually asymptomatic but may have heme-positive stool. Diagnosis is by colonoscopy and genetic testing. Treatment is colectomy.

FAP is an autosomal dominant disease in which ≥ 100 adenomatous polyps carpet the colon and rectum. The disorder occurs in 1 in 8,000 to 14,000 people. Polyps are present in 50% of patients by age 15, and 95% by 35. Cancer develops before age 40 in nearly all untreated patients.

Patients also can develop various extracolonic manifestations (previously termed Gardner's syndrome), both benign and malignant. Benign manifestations include desmoid tumors, osteomas of the skull or mandible, sebaceous cysts, and adenomas in other parts of the GI tract. Patients are at increased risk of cancer in the duodenum (5 to 11%), pancreas (2%), thyroid (2%), brain (medulloblastoma in < 1%), and liver (hepatoblastoma in 0.7% of children < 5).

Symptoms and Signs

Many patients are asymptomatic, but rectal bleeding, typically occult, occurs.

Diagnosis

• Colonoscopy

• Genetic testing of patient and 1st-degree relatives

• Offspring screened for hepatoblastoma

Diagnosis is made by finding > 100 polyps on colonoscopy. Diagnosed patients should have genetic testing to identify the specific mutation, which should then be sought in 1st-degree relatives. If genetic testing is unavailable, relatives should be screened with annual sigmoidoscopy beginning at age 12, reducing frequency with each decade. If no polyps are evident by age 50, screening frequency is then the same as for average-risk patients.

Children of parents with FAP should be screened for hepatoblastoma from birth to age 5 yr with annual serum fetoprotein levels and possibly liver ultrasound.

Treatment

• Colectomy

• Endoscopic surveillance of remainder of GI tract

• Perhaps aspirin or coxibs

Colectomy should be done at the time of diagnosis. Total proctocolectomy, either with ileostomy or mucosal proctectomy and ileoanal pouch, eliminates the risk of cancer. If subtotal colectomy (removal of most of the colon, leaving the rectum) with ileorectal anastomosis is done, the rectal remnant must be inspected every 3 to 6 mo; new polyps must be excised or fulgurated. Aspirin or coxibs may inhibit new polyp formation. If new ones appear too rapidly or prolifically to remove, excision of the rectum and permanent ileostomy are needed.

After colectomy, patients should have upper endoscopy every 6 mo to 4 yr, depending on the number of polyps (if any) in the stomach and duodenum. Annual physical examination of the thyroid, and possibly ultrasound, also is recommended.

Peutz-Jeghers Syndrome

Peutz-Jeghers syndrome is an autosomal dominant disease with multiple hamartomatous polyps in the stomach, small bowel, and colon along with distinctive pigmented skin lesions.

Patients are at a significantly increased risk of GI and non-GI cancers; possibly the genetic defect involves a tumor suppressor gene. GI cancers include those of the pancreas, small intestine, and colon. Non-GI cancers include those of the breast, lung, uterus, and ovaries.

The skin lesions are melanotic macules of the skin and mucous membranes, especially of the perioral region, lips and gums, hands, and feet. All but the buccal lesions tend to fade by puberty. Polyps may bleed and often cause obstruction or intussusception.

Diagnosis is suggested by the clinical picture. Genetic testing is not routinely available but should be considered. First-degree relatives should be evaluated and have routine surveillance for cancers, but there is no firm consensus on specific tests and intervals.

Colonic polyps larger than 1 cm typically are removed.

Colorectal Cancer

Colorectal cancer (CRC) is extremely common. Symptoms include blood in the stool or change in bowel habits. Screening is with fecal occult blood testing. Diagnosis is by colonoscopy. Treatment is surgical resection and chemotherapy for nodal involvement.

CRC accounts for an estimated 153,000 cases and 52,000 deaths in the US annually. In Western countries, the colon and rectum account for more new cases of cancer per year than any anatomic site except the lung. Incidence begins to rise at age 40 and peaks at age 60 to 75. Overall, 70% of cases occur in the rectum and sigmoid, and 95% are adenocarcinomas. Colon cancer is more common among women; rectal cancer is more common among men. Synchronous cancers (more than one) occur in 5% of patients.

Etiology

CRC most often occurs as transformation within adenomatous polyps. Serrated adenomas are particularly aggressive in their malignant transformation. About 80% of cases are sporadic, and 20% have an inheritable component. Predisposing factors include chronic ulcerative colitis and granulomatous colitis; the risk of cancer increases with the duration of these disorders.

Populations with a high incidence of CRC eat low-fiber diets that are high in animal protein, fat, and refined carbohydrates. Carcinogens may be ingested in the diet but are more likely produced by bacterial action on dietary substances or biliary or intestinal secretions. The exact mechanism is unknown.

CRC spreads by direct extension through the bowel wall, hematogenous metastasis, regional lymph node metastasis, perineural spread, and intraluminal metastasis.

Symptoms and Signs

Colorectal adenocarcinoma grows slowly, and a long interval elapses before it is large enough to cause symptoms. Symptoms depend on lesion location, type, extent, and complications.

The right colon has a large caliber, a thin wall, and its contents are liquid; thus, obstruction is a late event. Bleeding is usually occult. Fatigue and weakness caused by severe anemia may be the only complaints. Tumors sometimes grow large enough to be palpable through the abdominal wall before other symptoms appear.

The left colon has a smaller lumen, the feces are semisolid, and cancer tends to encircle the bowel, causing alternating constipation and increased stool frequency or diarrhea. Partial obstruction with colicky abdominal pain or complete obstruction may be the initial manifestation. The stool may be streaked or mixed with blood. Some patients present with symptoms of perforation, usually walled off (focal pain and tenderness), or rarely with diffuse peritonitis.

In rectal cancer, the most common initial symptom is bleeding with defecation. Whenever

[
Table 22-2. Staging Colorectal Cancer*]

rectal bleeding occurs, even with obvious hemorrhoids or known diverticular disease, coexisting cancer must be ruled out. Tenesmus or a sensation of incomplete evacuation may be present. Pain is common with perirectal involvement.

Some patients first present with symptoms and signs of metastatic disease (eg, hepatomegaly, ascites, supraclavicular lymph node enlargement).

Diagnosis

• Colonoscopy

Screening tests: Early diagnosis depends on routine examination, particularly fecal occult blood (FOB) testing. Cancer detected by this method tends to be at an earlier stage and hence more curable. For average-risk patients, FOB testing should be done annually after age 50, with flexible sigmoidoscopy every 5 yr. Some authorities recommend colonoscopy every 10 yr instead of sigmoidoscopy. Colonoscopy every 3 yr may be even better. Screening of patients with high-risk conditions (eg, ulcerative colitis) is discussed under the specific condition.

CT colonography (virtual colonoscopy) generates 3D and 2D images of the colon using multidetector row CT and a combination of oral contrast and gas distention of the colon. Viewing the high-resolution 3D images somewhat simulates the appearance of optical endoscopy, hence the name. It has some promise as a screening test for people who are unable or unwilling to undergo endoscopic colonoscopy but is less sensitive and highly interpreter dependent. It avoids the need for sedation but still requires thorough bowel preparation, and the gas distention may be uncomfortable. Additionally, unlike with optical colonoscopy, lesions cannot be biopsied during the diagnostic procedure.

Video capsule endoscopy of the colon has many technical problems and is not currently acceptable as a screening test.

Diagnostic tests: Patients with positive FOB tests require colonoscopy, as do those with lesions seen on sigmoidoscopy or imaging study. All lesions should be completely removed for histologic examination. If a lesion is sessile or not removable at colonoscopy, surgical excision should be strongly considered.

Barium enema x-ray, particularly a double-contrast study, can detect many lesions but is somewhat less accurate than colonoscopy and is not preferred as follow up to a positive FOB test.

Once cancer is diagnosed, patients should have abdominal CT, chest x-ray, and routine laboratory tests to seek metastatic disease and anemia and to evaluate overall condition.

Elevated serum carcinoembryonic antigen (CEA) levels are present in 70% of patients with CRC, but this test is not specific and therefore is not recommended for screening. However, if CEA is high preoperatively and low after removal of a colon tumor, monitoring CEA may help to detect recurrence earlier. CA 199 and CA 125 are other tumor markers that may be similarly used.

Prognosis

Prognosis depends greatly on stage (see Table 22-2). The 10-yr survival rate for cancer limited to the mucosa approaches 90%; with extension through the bowel wall, 70 to 80%; with positive lymph nodes, 30 to 50%; and with metastatic disease, < 20%.

Treatment

• Surgical resection, sometimes combined with chemotherapy, radiation, or both

Surgery: Surgery for cure can be attempted in the 70% of patients presenting without metastatic disease. Attempt to cure consists of wide resection of the tumor and its regional lymphatic drainage with reanastomosis of bowel segments. If there is ≤ 5 cm of normal bowel present between the lesion and the anal verge, an abdominoperineal resection is done, with permanent colostomy.

Resection of a limited number (1 to 3) of liver metastases is recommended in select nondebilitated patients as a subsequent procedure. Criteria include those whose primary tumor has been resected, whose liver metastases are in one hepatic lobe, and who have no extrahepatic metastases. Only a small number of patients with liver metastases meet these criteria, but 5-yr postoperative survival is 25%.

Adjuvant therapy: Chemotherapy (typically 5-fluorouracil and leucovorin) improves survival by 10 to 30% in colon cancer patients with positive lymph nodes. Rectal cancer patients with 1 to 4 positive lymph nodes benefit from combined radiation and chemotherapy; when > 4 positive lymph nodes are found,

combined modalities are less effective. Preoperative radiation therapy and chemotherapy to improve the resectability rate of rectal cancer or decrease the incidence of lymph node metastasis are gaining favor.

Follow-up: Postoperatively, colonoscopy should be done annually for 5 yr and every 3 yr thereafter if no polyps or tumors are found. If preoperative colonoscopy was incomplete because of an obstructing cancer, a "completion" colonoscopy should be done 3 mo after surgery.

Additional screening for recurrence should include history, physical examination, and laboratory tests (eg, CBC, liver function tests) every 3 mo for 3 yr and then every 6 mo for 2 yr. Imaging studies (CT or MRI) are often recommended at 1-yr intervals but are of uncertain benefit for routine follow up in the absence of abnormalities on examination or blood tests.

Palliation: When curative surgery is not possible or the patient is an unacceptable surgical risk, limited palliative surgery (eg, to relieve obstruction or resect a perforated area) may be indicated; median survival is 7 mo. Some obstructing tumors can be debulked by endoscopic laser treatment or electrocoagulation or held open by stents. Chemotherapy may shrink tumors and prolong life for several months.

Newer drugs used singly or in drug combinations include capecitabine (a 5-fluorouracil precursor), irinotecan, and oxaliplatin. Monoclonal antibodies such as bevacizumab, cetuximab, and panitumumab are also being used with some effectiveness. No regimen is clearly more effective for prolonging life in patients with metastatic CRC, although some have been shown to delay disease progression. Chemotherapy for advanced colon cancer should be managed by an experienced chemotherapist who has access to investigational drugs.

When metastases are confined to the liver, ambulatory hepatic artery infusion with floxuridine or radioactive microspheres via an implantable sc pump or an external pump worn on the belt may offer more benefit than systemic chemotherapy; however, these therapies are of uncertain benefit. When metastases are also extrahepatic, intrahepatic arterial chemotherapy offers no advantage over systemic chemotherapy.

Anorectal Cancer

The most common anorectal cancer is adenocarcinoma. Squamous cell (nonkeratinizing squamous cell or basaloid) carcinoma of the anorectum accounts for 3 to 5% of distal large-bowel cancers. Basal cell carcinoma, Bowen's disease (intradermal carcinoma), extramammary Paget's disease, cloacogenic carcinoma, and malignant melanoma are less common. Other tumors include lymphoma and various sarcomas. Metastasis occurs along the lymphatics of the rectum and into the inguinal lymph nodes.

Risk factors include infection with human papillomavirus (HPV), chronic fistulas, irradiated anal skin, leukoplakia, lymphogranuloma venereum, and condyloma acuminatum. Gay men practicing receptive anal intercourse are at increased risk. Patients with HPV infection may manifest dysplasia in slightly abnormal or normal-appearing anal epithelium (anal intraepithelial neoplasia—histologically graded I, II, or III). These changes are more common among HIV-infected patients, particularly gay men. Higher grades may progress to invasive carcinoma. It is unclear whether early recognition and eradication improve long-term outcome; hence, screening recommendations are unclear.

Wide local excision is often satisfactory treatment of perianal carcinomas. Combination chemotherapy and radiation therapy result in a high rate of cure when used for anal squamous and cloacogenic tumors. Abdominoperineal resection is indicated when radiation and chemotherapy do not result in complete regression of tumor and there are no metastases outside of the radiation field.

Hereditary Nonpolyposis Colorectal Carcinoma

Hereditary nonpolyposis colorectal carcinoma (HNPCC) is an autosomal dominant disorder responsible for 3 to 5% of cases of colorectal cancer (CRC). Symptoms, initial diagnosis, and treatment are similar to other forms of CRC. HNPCC is suspected by history and is confirmed by genetic testing. Patients also require surveillance for other cancer, particularly endometrial and

ovarian cancer.

Patients with one of several known mutations have a 70 to 80% lifetime risk of developing CRC. Compared to sporadic forms of colon cancer, HNPCC occurs at a younger age (mid 40s), and the lesion is more likely to be proximal to the splenic flexure. The precursor lesion is usually a single colonic adenoma, unlike the multiple adenomas present in patients with familial adenomatous polyposis (FAP), the other main hereditary form of CRC.

However, similar to FAP, numerous extracolonic manifestations occur. Nonmalignant disorders include cafe-au-lait spots, sebaceous gland tumors, and keratoacanthomas. Common associated cancers include endometrial and ovarian tumors (39% risk of endometrial and 9% risk of ovarian by age 70). Patients also have an elevated risk of cancer of the ureter, renal pelvis, stomach, biliary tree, and small bowel.

Symptoms and Signs

Symptoms and signs are similar to other forms of CRC, and diagnosis and management of the tumor itself are the same. The specific diagnosis of HNPCC is confirmed by genetic testing. However, deciding who to test is difficult because (unlike FAP) there is no typical clinical appearance. Thus, suspicion of HNPCC requires a detailed family history, which should be obtained in all younger patients identified with CRC.

Diagnosis

• Clinical criteria followed by testing for microsatellite instability (MSI)

• Genetic testing for confirmation

To meet the Amsterdam II criteria for HNPCC, all three of the following historical elements must be present:

• Three or more relatives with CRC or an HNPCC-associated cancer

• CRC involving at least two generations

• At least one case of CRC before age 50

Patients meeting these criteria should have their tumor tissue tested for MSI, a DNA abnormality. If MSI is present, genetic testing for specific HNPCC mutations is indicated. Other authorities use additional criteria (eg, Bethesda criteria) to initiate MSI testing. If MSI testing is not available locally, the patient should be referred to an appropriate center.

Patients with confirmed HNPCC require ongoing screening for other cancers. For endometrial cancer, annual endometrial aspiration or transvaginal ultrasound is recommended. For ovarian cancer, options include annual transvaginal ultrasound and serum CA 125 levels. Prophylactic hysterectomy and oophorectomy are also options. Urinalysis may be used to screen for renal tumors.

First-degree relatives of patients with HNPCC should have colonoscopy every 1 to 2 yr beginning in their 20s, and annually after age 40. Female 1st-degree relatives should be tested annually for endometrial and ovarian cancer. More distant blood relatives should have genetic testing; if results are negative, they should have colonoscopy at the frequency for average-risk patients.

Treatment

• Surgical resection

The most common treatment is resection of the index lesion with frequent surveillance for another colon cancer and any associated tumors in other organs. Because most HNPCC tumors occur proximal to the splenic flexure, subtotal colectomy, leaving the rectosigmoid intact, has been suggested as an alternative.

In either case, close follow up is needed.

Pancreatic Cancer

Pancreatic cancer, primarily ductal adenocarcinoma, accounts for an estimated 37,000 cases and 33,000 deaths in the US annually. Symptoms include weight loss, abdominal pain, and jaundice. Diagnosis is by CT. Treatment is surgical resection and adjuvant chemotherapy and radiation therapy. Prognosis is poor because disease is often advanced at the time of diagnosis.

Most pancreatic cancers are exocrine tumors that develop from ductal and acinar cells. Pancreatic endocrine tumors are discussed below.

Adenocarcinomas of the exocrine pancreas arise from duct cells 9 times more often than from acinar cells; 80% occur in the head of the gland. Adenocarcinomas appear at the mean age of 55 yr and occur 1.5 to 2 times more often in men. Prominent risk factors include smoking, a history of chronic pancreatitis, and possibly long-standing diabetes mellitus (primarily in women). Heredity plays some role. Alcohol and caffeine consumption do not seem to be risk factors.

Symptoms and Signs

Symptoms occur late. By diagnosis, 90% of patients have locally advanced tumors that have involved retroperitoneal structures, spread to regional lymph nodes, or metastasized to the liver or lung.

Most patients have severe upper abdominal pain, which usually radiates to the back. The pain may be relieved by bending forward or assuming the fetal position. Weight loss is common. Adenocarcinomas of the head of the pancreas cause obstructive jaundice (often causing pruritus) in 80 to 90% of patients. Cancer in the body and tail may cause splenic vein obstruction, resulting in splenomegaly, gastric and esophageal varices, and GI hemorrhage. The cancer causes diabetes in 25 to 50% of patients, leading to symptoms of glucose intolerance (eg, polyuria and polydipsia).

Diagnosis

• CT or magnetic resonance cholangiopancreatography (MRCP)

• CA 19-9 antigen to follow (not for screening)

The preferred tests are an abdominal helical CT or MRCP. If CT or MRCP shows apparent unresectable or metastatic disease, a percutaneous needle aspiration of an accessible lesion might be considered to obtain a tissue diagnosis. If CT shows a potentially resectable tumor or no tumor, MRCP or endoscopic ultrasound may be used to stage disease or detect small tumors not visible with CT. Patients with obstructive jaundice may have ERCP as the first diagnostic procedure.

Routine laboratory tests should be done. Elevation of alkaline phosphatase and bilirubin indicate bile duct obstruction or liver metastases. Pancreas-associated antigen CA 19-9 may be used to monitor patients diagnosed with pancreatic carcinoma and to screen those at high risk. However, this test is not sensitive or specific enough to be used for population screening. Elevated levels should drop with successful treatment; subsequent increases indicate progression. Amylase and lipase levels are usually normal.

Prognosis

Prognosis varies with stage but overall is poor (5-yr survival: < 2%), because many patients have advanced disease at the time of diagnosis.

Treatment

• Whipple procedure

• Adjuvant chemotherapy and radiation therapy

• Symptom control

About 80 to 90% of cancers are considered surgically unresectable at time of diagnosis because of metastases or invasion of major blood vessels. Depending on location of the tumor, the procedure of choice is most commonly a Whipple procedure (pancreatoduodenectomy). Adjuvant therapy with 5-fluorouracil (5-FU) and external beam radiation therapy is typically given, resulting in about 40% 2-yr and 25% 5-yr survival. This combination is also used for patients with localized but unresectable tumors and results in median survival of about 1 yr. Newer drugs (eg, gemcitabine, irinotecan, paclitaxel, oxaliplatin, carboplatin) may be more effective than 5-FU-based chemotherapy, but no drug, singly or in combination, is clearly superior in prolonging survival. Patients with hepatic or distant metastases may be offered chemotherapy as part of an investigational program, but the outlook is dismal with or without such treatment and some patients may choose to forego it.

If an unresectable tumor is found at operation and gastroduodenal or bile duct obstruction is present or pending, a double gastric and biliary bypass operation is usually done to relieve obstruction. In patients with inoperable lesions and jaundice, endoscopic placement of a bile duct stent relieves jaundice. However, surgical bypass should be considered in patients with unresectable lesions if life expectancy is > 6 to 7 mo because of complications associated with stents.

Symptomatic treatment: Ultimately, most patients experience pain and die. Thus, symptomatic treatment is as important as controlling disease. Appropriate end-of-life care should be discussed (see also p. 3480).

Patients with moderate to severe pain should receive an oral opioid in doses adequate to provide relief. Concern about addiction should not be a barrier to effective pain control. For chronic pain, long-acting preparations (eg, transdermal fentanyl, oxycodone, oxymorphone) are usually best. Percutaneous or operative splanchnic (celiac) block effectively controls pain in most patients. In cases of intolerable pain, opioids given sc or by IV, epidural, or intrathecal infusion provides additional relief.

If palliative surgery or endoscopic placement of a biliary stent fails to relieve pruritus secondary to obstructive jaundice, the patient can be managed with cholestyramine (4 g po once/day to qid). Phenobarbital 30 to 60 mg po tid to qid may be helpful.

Exocrine pancreatic insufficiency is treated with tablets of porcine pancreatic enzymes (pancrelipase). The patient should take enough to supply 16,000 to 20,000 lipase units before each meal or snack. If a meal is prolonged (as in a restaurant), some of the tablets should be taken during the meal. Optimal intraluminal pH for the enzymes is 8; thus, some clinicians give a proton pump inhibitor or H_2 blocker 2 times/day. Diabetes mellitus should be closely monitored and controlled.

Cystadenocarcinoma

Cystadenocarcinoma is a rare adenomatous pancreatic cancer that arises as a malignant degeneration of a mucous cystadenoma and manifests as upper abdominal pain and a palpable abdominal mass. Diagnosis is made by abdominal CT or MRI, which typically shows a cystic mass containing debris; the mass may be misinterpreted as necrotic adenocarcinoma or pancreatic pseudocyst. Unlike ductal adenocarcinoma, cystadenocarcinoma has a relatively good prognosis. Only 20% of patients have metastasis at the time of operation; complete excision of the tumor by distal or total pancreatectomy or by a Whipple procedure results in a 65% 5-yr survival.

Intraductal Papillary-Mucinous Tumor

Intraductal papillary-mucinous tumor (IPMT) is a rare cancer resulting in mucus hypersecretion and ductal obstruction. Histology may be benign, borderline, or malignant. Most (80%) occur in women and in the tail of the pancreas (66%).

Symptoms consist of pain and recurrent bouts of pancreatitis. Diagnosis is made by CT, sometimes along with endoscopic ultrasonography, magnetic resonance cholangiopancreatography, or ERCP. Benign and

malignant disease cannot be differentiated without surgical removal, which is the treatment of choice. With surgery, 5-yr survival is > 95% for benign or borderline cases, but 50 to 75% for malignant tumors.

Pancreatic Endocrine Tumors

Pancreatic endocrine tumors arise from islet and gastrin-producing cells and often produce many hormones. They have 2 general manifestations. Nonfunctioning tumors may cause obstructive symptoms of the biliary tract or duodenum, bleeding into the GI tract, or abdominal masses. Functioning tumors hypersecrete a particular hormone, causing various syndromes (see Table 22-3). These clinical syndromes can also occur in multiple endocrine neoplasia, in which tumors or hyperplasia affects two or more endocrine glands, usually the parathyroid, pituitary, thyroid, or adrenals (see p. 909).

Treatment for functioning and nonfunctioning tumors is surgical resection. If metastases preclude curative surgery, various antihormone treatments may be tried for functioning tumors. Because of tumor rarity, chemotherapy trials have not identified definitive treatment. However, streptozotocin has selective activity against pancreatic islet cells and is commonly used, either alone or in combination with 5-fluorouracil or doxorubicin. Some centers use chlorozotocin and interferon.

Insulinoma

An insulinoma is a rare pancreatic β-cell tumor that hypersecretes insulin. The main symptom is fasting hypoglycemia. Diagnosis is by a 48- or 72-h fast with measurement of glucose and insulin levels, followed by endoscopic ultrasound. Treatment is surgery when possible. Drugs that block insulin secretion (eg, diazoxide, octreotide, Ca channel blockers, β-blockers, phenytoin) are used for patients not responding to surgery.

Of all insulinomas, 80% are single and may be curatively resected if identified. Only 10% of insulinomas are malignant. Insulinoma occurs in 1/250,000 at a median age of 50 yr, except in multiple endocrine neoplasia (MEN) type I (about 10% of insulinomas), when it occurs in the 20s. Insulinomas associated with MEN type I are more likely to be multiple.

Surreptitious administration of exogenous insulin can cause episodic hypoglycemia mimicking insulinoma.

Symptoms and Signs

Hypoglycemia secondary to an insulinoma occurs during fasting. Symptoms are insidious and may mimic various psychiatric and

[**Table 22-3.** Pancreatic Endocrine Tumors]

neurologic disorders. CNS disturbances include headache, confusion, visual disturbances, motor weakness, palsy, ataxia, marked personality changes, and possible progression to loss of consciousness, seizures, and coma. Symptoms of sympathetic stimulation (faintness, weakness, tremulousness, palpitation, sweating, hunger, nervousness) are often present.

Diagnosis

• Insulin level

• Sometimes C-peptide or proinsulin levels

• Endoscopic ultrasound

Plasma glucose should be measured during symptoms. If hypoglycemia is present (glucose < 40 mg/dL [2.78 mmol/L]), an insulin level should be measured on a simultaneous sample. Hyperinsulinemia of > 6 μU/mL (42 pmol/L) suggests an insulin-mediated cause, as does a serum insulin to plasma glucose ratio > 0.3 (μU/mL)/(mg/dL).

Insulin is secreted as proinsulin, consisting of an α chain and β chain connected by a C peptide. Because pharmaceutical insulin consists only of the β chain, surreptitious insulin administration can be detected by measuring C-peptide and proinsulin levels. In patients with insulinoma, C peptide is ≥ 0.2 nmol/L and proinsulin is ≥ 5 pmol/L. These levels are normal or low in patients with surreptitious insulin administration.

Because many patients have no symptoms (and hence no hypoglycemia) at the time of evaluation, diagnosis requires admission to the hospital for a 48- or 72-h fast. Nearly all (98%) with insulinoma develop symptoms within 48 h of fasting; 70 to 80% within 24 h. Hypoglycemia as the cause of the symptoms is established by Whipple's triad: (1) Symptoms occur during the fast; (2) symptoms occur in the presence of hypoglycemia; and (3) ingestion of carbohydrates relieves the symptoms. Hormone levels are obtained as described above when the patient is having symptoms.

If Whipple's triad is not observed after prolonged fasting and the plasma glucose after an overnight fast is > 50 mg/dL (> 2.78 mmol/L), a C-peptide suppression test can be done. During insulin infusion (0.1 U/kg/h), patients with insulinoma fail to suppress C peptide to normal levels (≤ 1.2 ng/mL [≤ 0.40 nmol/L]).

Endoscopic ultrasonography has > 90% sensitivity and helps localize the tumor. PET also may be used. CT has not proved useful, and arteriography or selective portal and splenic vein catheterization is generally unnecessary.

Treatment

• Surgical resection

• Diazoxide or sometimes octreotide for hypoglycemia

Overall surgical cure rates approach 90%. A small, single insulinoma at or near the surface of the pancreas can usually be enucleated surgically. If a single large or deep adenoma is within the pancreatic body or tail, if there are multiple lesions of the body or tail (or both), or if no insulinoma is found (an unusual circumstance), a distal, subtotal pancreatectomy is done. In < 1% of cases, the insulinoma is ectopically located in peripancreatic sites of the duodenal wall or periduodenal area and can be found only by diligent search during surgery. Pancreatoduodenectomy (Whipple procedure) is done for resectable malignant insulinomas of the proximal pancreas. Total pancreatectomy is done if a previous subtotal pancreatectomy proves inadequate.

If hypoglycemia continues, diazoxide starting at 1.5 mg/kg po bid with a natriuretic can be used. Doses can be increased up to 4 mg/kg. A somatostatin analog, octreotide (100 to 500 µg sc bid to tid), is variably effective and should be considered for patients with continuing hypoglycemia refractory to diazoxide. Patients who respond may be converted to a long-acting octreotide formulation given as 20 to 30 mg IM once/mo. Patients using octreotide may also need to take supplemental pancreatic enzymes because octreotide suppresses pancreatic enzyme secretion. Other drugs that have modest and variable effect on insulin secretion include verapamil, diltiazem, and phenytoin.

If symptoms are not controlled, chemotherapy may be tried, but response is limited. Streptozotocin has a 30 to 40% response rate, and when combined with 5-fluorouracil, a 60% response rate lasting up to 2 yr. Other agents include doxorubicin, chlorozotocin, and interferon.

Zollinger-Ellison Syndrome

(Z-E Syndrome; Gastrinoma)

Zollinger-Ellison syndrome is caused by a gastrin-producing tumor usually located in the pancreas or the duodenal wall. Gastric acid hypersecretion and peptic ulceration result. Diagnosis is by measuring serum gastrin levels. Treatment is proton pump inhibitors and surgical removal.

Gastrinomas occur in the pancreas or duodenal wall 80 to 90% of the time. The remainder occur in the splenic hilum, mesentery, stomach, lymph node, or ovary. About 50% of patients have multiple tumors. Gastrinomas usually are small (< 1 cm in diameter) and grow slowly. About 50% are malignant. About 40 to 60% of patients with gastrinoma have multiple endocrine neoplasia (see p. 909).

Symptoms and Signs

Zollinger-Ellison syndrome typically manifests as aggressive peptic ulcer disease, with ulcers occurring in atypical locations (up to 25% are located distal to the duodenal bulb). However, as many as 25% do not have an ulcer at diagnosis. Typical ulcer symptoms and complications (eg, perforation, bleeding, obstruction) can occur. Diarrhea is the initial symptom in 25 to 40% of patients.

Diagnosis

• Serum gastrin level

• CT, scintigraphy, or PET to localize

The syndrome is suspected by history, particularly when symptoms are refractory to standard acid suppressant therapy.

The most reliable test is serum gastrin. All patients have levels > 150 pg/mL; markedly elevated levels of > 1000 pg/mL in a patient with compatible clinical features and gastric acid hypersecretion of > 15 mEq/h establish the diagnosis. However, moderate hypergastrinemia can occur with hypochlorhydric states (eg, pernicious anemia, chronic gastritis, use of proton pump inhibitors), in renal insufficiency with decreased clearance of gastrins, in massive intestinal resection, and in pheochromocytoma.

A secretin provocative test may be useful in patients with gastrin levels < 1000 pg/mL. An IV bolus of secretin 2 µg/kg is given with serial measurements of serum gastrin (10 and 1 min before, and 2, 5, 10, 15, 20, and 30 min after injection). The characteristic response in gastrinoma is an increase in gastrin levels, the opposite of what occurs in those with antral G-cell hyperplasia or typical peptic ulcer disease. Patients also should be evaluated for *Helicobacter pylori* infection, which commonly results in peptic ulceration and moderate excess gastrin secretion.

Once the diagnosis has been established, the tumor or tumors must be localized. The first test is abdominal CT or somatostatin receptor scintigraphy, which may identify the primary tumor and metastatic disease. PET or selective arteriography with magnification and subtraction is also helpful. If no signs of metastases are present and the primary is uncertain, endoscopic ultrasonography should be done. Selective arterial secretin injection is an alternative.

Prognosis

Five- and 10-yr survival is > 90% when an isolated tumor is removed surgically vs 43% at 5 yr and 25% at 10 yr with incomplete removal.

Treatment

• Acid suppression

• Surgical resection for localized disease

• Chemotherapy for metastatic disease

Acid suppression: Proton pump inhibitors are the drugs of choice: omeprazole or esomeprazole 40 mg po bid. The dose may be decreased gradually once symptoms resolve and acid output declines. A maintenance dose is needed; patients need to take these drugs indefinitely unless they undergo surgery.

Octreotide injections, 100 to 500 µg sc bid to tid, may also decrease gastric acid production and may be

palliative in patients not responding well to proton pump inhibitors. A long-acting form of octreotide can be used 20 to 30 mg IM once/mo.

Surgery: Surgical removal should be attempted in patients without apparent metastases. At surgery, duodenotomy and intraoperative endoscopic transillumination or ultrasound help localize tumors. Surgical cure is possible in 20% of patients if the gastrinoma is not part of a multiple endocrine neoplasia syndrome.

Chemotherapy: In patients with metastatic disease, streptozocin in combination with 5-fluorouracil or doxorubicin is the preferred chemotherapy for islet cell tumors. It may reduce tumor mass (in 50 to 60%) and serum gastrin levels and is a useful adjunct to omeprazole. Patients with metastatic disease are not cured by chemotherapy.

Vipoma

A vipoma is a non-β pancreatic islet cell tumor secreting vasoactive intestinal peptide (VIP), resulting in a syndrome of watery diarrhea, hypokalemia, and achlorhydria (WDHA syndrome). Diagnosis is by serum VIP levels. Tumor is localized with CT and endoscopic ultrasound. Treatment is surgical resection.

Of these tumors, 50 to 75% are malignant, and some may be quite large (7 cm) at diagnosis. In about 6%, vipoma occurs as part of multiple endocrine neoplasia (see p. 909).

Symptoms and Signs

The major symptoms are prolonged massive watery diarrhea (fasting stool volume > 750 to 1000 mL/day and nonfasting volumes of > 3000 mL/day) and symptoms of hypokalemia, acidosis, and dehydration. In half, diarrhea is constant; in the rest, diarrhea severity varies over time. About 33% have diarrhea < 1 yr before diagnosis, but 25% have diarrhea ≥ 5 yr before diagnosis. Lethargy, muscular weakness, nausea, vomiting, and crampy abdominal pain occur frequently. Flushing similar to the carcinoid syndrome occurs in 20% of patients during attacks of diarrhea.

Diagnosis

• Confirmation of secretory diarrhea

• Serum VIP levels

• Endoscopic ultrasonography, PET, or scintigraphy can localize

Diagnosis requires demonstration of secretory diarrhea (stool osmolality is close to plasma osmolality, and twice the sum of Na and K concentration in the stool accounts for all measured stool osmolality). Other causes of secretory diarrhea and, in particular, laxative abuse must be excluded (see p. 88). In such patients, serum VIP levels should be measured (ideally during a bout of diarrhea). Markedly elevated levels establish the diagnosis, but mild elevations may occur with short bowel syndrome and inflammatory diseases. Patients with elevated VIP levels should have tumor localization studies, such as endoscopic ultrasonography, PET, and octreotide scintigraphy or arteriography to localize metastases.

Electrolytes and CBC should be measured. Hyperglycemia and impaired glucose tolerance occur in ≤ 50% of patients. Hypercalcemia occurs in 50% of patients.

Treatment

• Fluid and electrolyte replacement

• Octreotide

• Surgical resection for localized disease

Initially, fluids and electrolytes must be replaced. Bicarbonate must be given to replace fecal loss and avoid acidosis. Because fecal losses of water and electrolytes increase as rehydration is achieved, continual IV replacement may become difficult.

Octreotide usually controls diarrhea, but large doses may be needed. Responders may benefit from a long-acting octreotide formulation given 20 to 30 mg IM once/mo. Patients using octreotide may also need to take supplemental pancreatic enzymes because octreotide suppresses pancreatic enzyme secretion.

Tumor resection is curative in 50% of patients with a localized tumor. In those with metastatic tumor, resection of all visible tumor may provide temporary relief of symptoms. The combination of streptozocin and doxorubicin may reduce diarrhea and tumor mass if objective response occurs (in 50 to 60%). Chemotherapy is not curative.

Glucagonoma

A glucagonoma is a pancreatic α-cell tumor that secretes glucagon, causing hyperglycemia and a characteristic skin rash. Diagnosis is by elevated glucagon levels and imaging studies. Tumor is localized with CT and endoscopic ultrasound. Treatment is surgical resection.

Glucagonomas are very rare but similar to other islet cell tumors in that the primary and metastatic lesions are slow-growing: 15-yr survival is common. Eighty percent of glucagonomas are malignant. The average age at symptom onset is 50 yr; 80% of patients are women. A few patients have multiple endocrine neoplasia type I.

Symptoms and Signs

Because glucagonomas produce glucagon, the symptoms are the same as those of diabetes. Frequently, weight loss, normochromic anemia, hypoaminoacidemia, and hypolipidemia are present, but the most distinctive clinical feature is a chronic eruption involving the extremities, often associated with a smooth, shiny, vermilion tongue and cheilitis. The exfoliating, brownish red, erythematous lesion with superficial necrolysis is termed necrolytic migratory erythema.

Diagnosis

• Serum glucagon level

• CT and endoscopic ultrasonography to localize

Most patients with glucagonoma have glucagon levels > 1000 pg/mL (normal < 200). However, moderate elevations occur in renal insufficiency, acute pancreatitis, severe stress, and fasting. Correlation with symptoms is required. Patients should have abdominal CT followed by endoscopic ultrasonography; MRI or PET may be used if CT is unrevealing.

Treatment

• Surgical resection for localized disease

• Chemotherapy for metastatic disease

• Octreotide to suppress glucagon production

Resection of the tumor alleviates all symptoms. Unresectable, metastatic, or recurrent tumors are treated with combination streptozocin and doxorubicin, which may decrease levels of circulating immunoreactive glucagon, lessen symptoms, and improve response rates (50%) but are unlikely to improve survival. Octreotide injections partially suppress glucagon production and relieve the erythema, but glucose tolerance may also decrease because octreotide decreases insulin secretion. Octreotide may quickly reverse anorexia and weight loss caused by the catabolic effect of glucagon excess. Patients who

respond may be converted to a long-acting octreotide formulation given 20 to 30 mg IM once/mo. Patients using octreotide may also need to take supplemental pancreatic enzymes because octreotide suppresses pancreatic enzyme secretion.

Locally applied, oral, or parenteral zinc may cause the erythema to disappear, but resolution may occur after simple hydration or IV administration of amino or fatty acids, suggesting that the erythema is not solely caused by zinc deficiency.