



THE GASTROINTESTINAL SYSTEM

Clinical Foundations



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Part I: Disorders of the Esophagus

Chapter 1: Gastroesophageal Reflux Disease and Barrett's Esophagus

Overview

Gastroesophageal reflux disease (GERD) results from the retrograde flow of gastric contents into the esophagus due to a dysfunctional lower esophageal sphincter (LES), a hiatal hernia, delayed gastric emptying, or transient LES relaxations that occur more frequently than normal. It is one of the most common gastrointestinal complaints seen in both primary care and specialist practice.

Clinical Features

Patients typically report retrosternal burning (heartburn) that worsens after meals, when lying supine, or with bending forward, and is often relieved by antacids. Regurgitation, a sour taste in the mouth, and chronic cough or hoarseness from extra-esophageal reflux are also common. Alarm features such as dysphagia, odynophagia, weight loss, or gastrointestinal bleeding warrant prompt endoscopic evaluation.

Barrett's Esophagus

Chronic reflux exposes the distal esophageal mucosa to repeated acid injury, and in a subset of patients the normal stratified squamous epithelium undergoes metaplastic transformation into columnar epithelium with goblet cells - a condition known as Barrett's esophagus. Endoscopically this appears as salmon-colored mucosa extending proximally from the gastroesophageal junction, in contrast to the pale, glossy squamous mucosa. Barrett's esophagus is the single most important risk factor for esophageal adenocarcinoma, and any suspicious mucosa identified at endoscopy must be biopsied to confirm intestinal metaplasia and assess for dysplasia.

Diagnosis and Management

Uncomplicated GERD is usually a clinical diagnosis, managed initially with lifestyle modification (weight loss, elevating the head of the bed, avoiding late meals) and acid suppression with proton pump inhibitors. Endoscopy is reserved for patients with alarm symptoms, long-standing symptoms, or those being screened for Barrett's esophagus. Once Barrett's esophagus is confirmed, patients enter a surveillance program with periodic endoscopy and biopsy, with the interval determined by the presence and grade of dysplasia.

Quick Reference

Key Fact	Detail
Trigger endoscopy for	Any ALARM feature present
Endoscopic finding	Salmon-colored mucosa, distal esophagus
Confirms diagnosis	Biopsy showing intestinal metaplasia
First-line treatment	Proton pump inhibitor + lifestyle change

MNEMONIC: ALARM

A - Anemia (iron deficiency)

L - Loss of weight (unintentional)

A - Anorexia

R - Recent onset, progressive symptoms

M - Melena / hematemesis / mass

Chapter 2: Achalasia

Overview

Achalasia is a primary esophageal motility disorder caused by the degeneration of inhibitory neurons in the myenteric (Auerbach's) plexus of the esophageal wall. Loss of these neurons impairs relaxation of the lower esophageal sphincter and abolishes normal peristalsis in the esophageal body.

Clinical Features

Patients present with progressive dysphagia to both solids and liquids from the outset - a pattern that helps distinguish achalasia from mechanical obstruction, where solid food dysphagia typically precedes liquid dysphagia. Regurgitation of undigested food, nocturnal aspiration, chest discomfort, and weight loss are common accompanying features.

Diagnosis

Esophageal manometry is the gold standard and demonstrates elevated lower esophageal sphincter pressure that fails to relax appropriately with swallowing, along with absent peristalsis. Barium esophagram classically shows a dilated esophageal body tapering to a smooth, symmetric narrowing at the gastroesophageal junction, described as a 'bird's beak' appearance. Endoscopy is important to exclude pseudoachalasia caused by a malignant lesion at the gastroesophageal junction.

Management

Treatment aims to reduce LES pressure and relieve outflow obstruction. Options include pneumatic balloon dilation, surgical (Heller) myotomy often combined with a partial fundoplication to limit post-procedural reflux, and increasingly, peroral endoscopic myotomy (POEM). Botulinum toxin injection and pharmacologic agents such as calcium channel blockers or nitrates offer temporary relief and are generally reserved for patients who are poor candidates for definitive therapy.

Quick Reference

Key Fact	Detail
Gold-standard test	Esophageal manometry
Key exclusion	Pseudoachalasia from GEJ malignancy
Definitive options	Heller myotomy, POEM, pneumatic dilation
Temporizing option	Botulinum toxin injection

MNEMONIC: **BIRDS**

B - Bird's-beak tapering on barium swallow
 I - Incomplete LES relaxation
 R - Regurgitation of undigested food
 D - Dysphagia to solids AND liquids
 S - Swallowing peristalsis is absent

Chapter 3: Diffuse Esophageal Spasm

Overview

Diffuse esophageal spasm is a motility disorder characterized by simultaneous, uncoordinated, high-amplitude contractions of the esophageal body, in contrast to the organized, sequential peristaltic wave seen in normal swallowing.

Clinical Features

Patients often present with intermittent chest pain that can closely mimic angina, sometimes precipitated by hot or cold liquids, along with intermittent dysphagia to solids and liquids. Because the presentation overlaps with cardiac chest pain, cardiac causes must be excluded first.

Diagnosis

Esophageal manometry shows simultaneous contractions in a significant proportion of swallows, with normal relaxation of the LES distinguishing this condition from achalasia. Barium esophagram may show a corkscrew or 'rosary bead' appearance of the esophagus due to the uncoordinated contractions.

Management

First-line therapy focuses on smooth muscle relaxation with calcium channel blockers or nitrates, along with treatment of any underlying anxiety or reflux disease that may be contributing. Refractory cases are sometimes managed with botulinum toxin injection or, rarely, surgical myotomy.

Quick Reference

Key Fact	Detail
Manometry finding	Simultaneous high-amplitude contractions
Barium finding	Corkscrew esophagus
First step	Exclude cardiac chest pain
Treatment	Calcium channel blockers or nitrates

MNEMONIC: CORK

- C - Chest pain mimicking angina
- O - Odd, uncoordinated simultaneous contractions
- R - Relaxation of LES is normal
- K - Kicked off by hot or cold liquids

Chapter 4: Boerhaave Syndrome

Overview

Boerhaave syndrome refers to spontaneous, full-thickness rupture of the esophagus, most often occurring at the left posterolateral wall of the distal esophagus just above the gastroesophageal junction. It typically follows a sudden rise in intraesophageal pressure against a closed glottis, classically triggered by forceful vomiting or retching, often in the setting of heavy alcohol use or a large meal.

Clinical Features

The classic presentation is severe, tearing retrosternal or epigastric chest pain immediately following an episode of forceful vomiting. Subcutaneous emphysema, palpable as crepitus over the chest wall or neck, results from air tracking from the mediastinum. Patients may rapidly develop signs of mediastinitis and septic shock, including tachycardia, hypotension, and fever, making this a true surgical emergency.

Diagnosis

A water-soluble contrast esophagram (such as Gastrografin) is the investigation of choice to confirm perforation and localize the leak, as barium can worsen mediastinal inflammation if it extravasates. Upper endoscopy is generally avoided initially, as insufflation of air can extend the perforation. Chest imaging often shows pneumomediastinum, pleural effusion, or a widened mediastinum.

Management

Boerhaave syndrome carries a high mortality if untreated, and management requires urgent surgical consultation for repair or drainage, alongside broad-spectrum antibiotics, fluid resuscitation, and nil by mouth status. Outcomes are strongly time-dependent, underscoring the importance of early recognition.

Quick Reference

Key Fact	Detail
Best initial test	Water-soluble contrast esophagram
Avoid initially	Upper endoscopy (may extend tear)
Classic sign	Crepitus over chest wall / neck
Management	Urgent surgical repair + antibiotics

MNEMONIC: TEARS

T - Tearing chest/back pain
 E - Emesis (forceful) precedes rupture
 A - Air in mediastinum / subcutaneous emphysema
 R - Rupture is full-thickness
 S - Surgical emergency

Chapter 5: Mallory-Weiss Tear

Overview

A Mallory-Weiss tear is a longitudinal mucosal (and submucosal) laceration at the gastroesophageal junction, most commonly on the gastric side, caused by a sudden increase in intra-abdominal and intragastric pressure - classically from forceful retching or vomiting after a bout of heavy alcohol consumption. Unlike Boerhaave syndrome, the tear does not extend through the full thickness of the esophageal wall.

Clinical Features

The typical history is one of repeated retching or vomiting followed by hematemesis, often bright red. Most patients are hemodynamically stable, and the bleeding is frequently self-limited.

Diagnosis and Management

Upper endoscopy both confirms the diagnosis and allows for therapeutic intervention if active bleeding is identified, using techniques such as injection therapy, thermal coagulation, or clipping. Most tears heal spontaneously within a few days, and supportive care with acid suppression is often sufficient when bleeding has stopped.

Quick Reference

Key Fact	Detail
Distinguishing feature	Mucosal tear only (vs. Boerhaave)
Diagnosis	Upper endoscopy
Most cases	Resolve spontaneously
Endoscopic therapy if active	Clipping, injection, or thermal

MNEMONIC: **RETCH**

- R - Retching precedes bleeding
- E - Ethanol (alcohol) is a common trigger
- T - Tear is mucosal only, not full-thickness
- C - Cardia / GE junction is the site
- H - Hematemesis, usually self-limited

Part II: Gastric and Duodenal Disorders

Chapter 6: Peptic Ulcer Disease

Overview

Peptic ulcer disease (PUD) refers to mucosal defects extending through the muscularis mucosae of the stomach or duodenum, arising from an imbalance between mucosal protective factors and injurious factors such as acid and pepsin. The two dominant causes worldwide are *Helicobacter pylori* infection and nonsteroidal anti-inflammatory drug (NSAID) use.

Clinical Features

Duodenal ulcers classically cause epigastric pain that is relieved by food and recurs two to three hours after eating, often waking the patient at night, reflecting the pain-relieving buffering effect of a meal followed by a rebound in acid secretion. Gastric ulcers, by contrast, may cause pain that worsens with eating. Alarm features - weight loss, bleeding, early satiety, or anemia - should prompt endoscopic evaluation to exclude malignancy, particularly with gastric ulcers.

Diagnosis

Upper endoscopy allows direct visualization and biopsy, particularly important for gastric ulcers given the risk of malignancy. *H. pylori* status can be assessed via urea breath testing, stool antigen testing, or biopsy-based methods (rapid urease test, histology) at the time of endoscopy.

Management

H. pylori-positive ulcers are treated with eradication therapy alongside acid suppression, while NSAID-associated ulcers are managed by discontinuing the offending agent and starting a proton pump inhibitor. Complications to watch for include bleeding, perforation, and gastric outlet obstruction.

Quick Reference

Key Fact	Detail
Most common cause	<i>H. pylori</i> infection
Other major cause	NSAID use
Endoscopic finding	Clean-based duodenal ulcer
First-line eradication	PPI + amoxicillin + clarithromycin

MNEMONIC: NIGHT

N - Nocturnal pain (wakes the patient)
 I - Improves with food
 G - Gnawing epigastric quality
 H - *H. pylori* is the leading cause
 T - Treat with eradication therapy

Chapter 7: Zollinger-Ellison Syndrome

Overview

Zollinger-Ellison syndrome results from a gastrin-secreting neuroendocrine tumor (gastrinoma), most often located in the duodenum or pancreas, which drives excessive gastric acid secretion. A substantial proportion of cases occur as part of multiple endocrine neoplasia type 1 (MEN1).

Clinical Features

Patients present with severe, often multiple, and treatment-refractory peptic ulcers, sometimes in atypical locations such as the distal duodenum or jejunum. Chronic diarrhea, resulting from acid inactivation of pancreatic enzymes and direct mucosal injury, is another characteristic feature.

Diagnosis

The initial step is measurement of fasting serum gastrin, ideally with the patient off proton pump inhibitors, as PPIs can cause a secondary rise in gastrin. Markedly elevated gastrin in the setting of low gastric pH is suggestive. Because PPI-induced hypergastrinemia can confound results, a secretin stimulation test is used to confirm the diagnosis: in gastrinoma, secretin administration paradoxically increases gastrin levels, whereas normal physiology would suppress it. Cross-sectional and somatostatin receptor imaging help localize the tumor once biochemically confirmed.

Management

High-dose proton pump inhibitors control acid hypersecretion, while surgical resection is pursued for localized disease. All patients should be evaluated for MEN1, given the implications for screening of other endocrine tumors.

Quick Reference

Key Fact	Detail
Screening test	Fasting serum gastrin
Confirmatory test	Secretin stimulation test
Paradoxical response	Gastrin rises after secretin
Associated syndrome	MEN1

MNEMONIC: SECRET

S - Secretin test confirms diagnosis
 E - Elevated fasting gastrin
 C - Chronic diarrhea
 R - Refractory, multiple ulcers
 E - Ectopic/atypical ulcer sites
 T - Tumor = gastrinoma (check for MEN1)

Chapter 8: Helicobacter pylori Infection and Treatment

Overview

Helicobacter pylori is a spiral, urease-producing, gram-negative bacterium that colonizes the gastric mucosa and is the leading infectious cause of peptic ulcer disease worldwide. Chronic infection is also linked to gastric adenocarcinoma and MALT lymphoma.

Diagnosis

Non-invasive testing includes the urea breath test and stool antigen test, both of which require discontinuation of proton pump inhibitors and antibiotics for an appropriate washout period beforehand to avoid false negatives. Endoscopic biopsy allows histologic identification and rapid urease testing.

Treatment

First-line therapy in regions without significant clarithromycin resistance is triple therapy: a proton pump inhibitor combined with amoxicillin and clarithromycin for 10 to 14 days. In areas of higher resistance, or with prior macrolide exposure, bismuth-based quadruple therapy (PPI, bismuth subsalicylate, metronidazole, and tetracycline) is preferred. Confirmation of eradication with a urea breath test or stool antigen test is recommended in patients with a complicated ulcer or persistent symptoms.

Quick Reference

Key Fact	Detail
First-line regimen	PPI + amoxicillin + clarithromycin
If macrolide resistance	Bismuth quadruple therapy
Confirm cure with	Urea breath test or stool antigen
Testing requires	PPI/antibiotic washout beforehand

MNEMONIC: **TRIPLE**

T - Treat for 10-14 days

R - Regimen = PPI-based

I - Includes amoxicillin

P - Plus clarithromycin

L - Look for resistance/prior macrolide use

E - Eradication confirmed by breath/stool test

Part III: Disorders of the Pancreas

Chapter 9: Acute Pancreatitis

Overview and Etiology

Acute pancreatitis is an inflammatory process resulting from premature activation of pancreatic digestive enzymes within the gland itself, leading to autodigestion and a local and sometimes systemic inflammatory response. Gallstones and alcohol use together account for the large majority of cases, with gallstones being the single most common overall cause, followed closely by alcohol. Other causes include hypertriglyceridemia, post-ERCP injury, certain medications, and, less commonly, hypercalcemia or structural anomalies.

Clinical Features

The hallmark presentation is severe, constant epigastric pain that often radiates to the back, frequently accompanied by nausea and vomiting. Physical examination may reveal epigastric tenderness, and in severe hemorrhagic cases, Cullen's sign (periumbilical ecchymosis) or Grey Turner's sign (flank ecchymosis) may be present.

Diagnosis

Diagnosis requires at least two of three criteria: characteristic abdominal pain, serum lipase or amylase elevated at least three times the upper limit of normal, and characteristic findings on cross-sectional imaging. Lipase is generally preferred over amylase due to its greater specificity and longer half-life.

Severity Assessment and Management

Several scoring systems, including Ranson's criteria and the BISAP score, help stratify severity. A hematocrit that fails to fall - or that drops significantly - within the first 48 hours despite adequate fluid resuscitation is an important early marker of a more severe course, reflecting ongoing third-spacing of fluid and hemoconcentration. Management is largely supportive: aggressive intravenous fluid resuscitation, analgesia, and early enteral feeding as tolerated. Antibiotics are reserved for confirmed infected necrosis rather than used prophylactically. Underlying gallstones warrant cholecystectomy, typically during the same admission for mild cases.

Quick Reference

Key Fact	Detail
Most common cause	Gallstones
Preferred enzyme test	Lipase (more specific than amylase)
Diagnosis needs	2 of 3: pain, enzymes, imaging
Key 48-hour marker	Hematocrit drop >10% despite fluids (HELPS)
Antibiotics indicated for	Confirmed infected necrosis only

MNEMONIC: GETSMASHED

G - Gallstones
E - Ethanol
T - Trauma
S - Steroids
M - Mumps
A - Autoimmune
S - Scorpion sting
H - Hyperlipidemia/Hypercalcemia
E - ERCP
D - Drugs

Chapter 10: Chronic Pancreatitis

Overview

Chronic pancreatitis represents irreversible fibrosis and progressive destruction of pancreatic parenchyma, most commonly resulting from long-standing heavy alcohol use, though it may also follow recurrent acute pancreatitis, genetic conditions such as cystic fibrosis, or autoimmune disease.

Clinical Features

Patients experience recurrent or chronic dull epigastric pain, often radiating to the back. As exocrine function declines, malabsorption develops, manifesting as steatorrhea - greasy, foul-smelling, difficult-to-flush stools - along with weight loss. Loss of endocrine function eventually leads to diabetes mellitus.

Diagnosis

Cross-sectional imaging, particularly CT, often reveals pancreatic calcifications, ductal dilation, and glandular atrophy - findings that are highly suggestive once present, though early disease may require more sensitive tests such as MRCP or endoscopic ultrasound.

Management

Pain control, alcohol cessation, and pancreatic enzyme replacement therapy for exocrine insufficiency form the mainstay of management. Because fat malabsorption accompanies exocrine insufficiency, patients are also at risk of fat-soluble vitamin (A, D, E, and K) deficiency and should be monitored and supplemented accordingly. Diabetes arising from endocrine insufficiency is managed as in other forms of diabetes.

Quick Reference

Key Fact	Detail
Imaging hallmark	Pancreatic calcifications on CT
Malabsorbed vitamins	A, D, E, K (fat-soluble)
Management	Enzyme replacement + alcohol cessation
Endocrine complication	Diabetes mellitus

MNEMONIC: **CALCIFY**

C - Chronic alcohol use, usual cause
 A - Aching pain radiates to back
 L - Loss of exocrine function -> steatorrhea
 C - Calcifications seen on CT
 I - Insulin loss -> diabetes
 F - Fat-soluble vitamin deficiency (A,D,E,K)
 Y - Years of injury needed to develop

Part IV: Disorders of the Gallbladder and Biliary Tree

Chapter 11: Cholelithiasis and Acute Cholecystitis

Gallstone Formation and Risk Factors

Gallstones form when bile becomes supersaturated with cholesterol or bilirubin, or when gallbladder motility is impaired, allowing crystals to nucleate and grow. Classic risk factors are often summarized by the mnemonic 'female, fat, forty, and fertile,' reflecting the increased risk associated with female sex, obesity, age around forty, and multiparity, though gallstones can occur outside these groups as well.

Biliary Colic

Many gallstones are asymptomatic. When symptomatic, they typically cause biliary colic: episodic right upper quadrant or epigastric pain, often triggered by fatty meals, that builds over minutes and resolves within a few hours as the stone transiently obstructs and then disimpacts from the cystic duct.

Acute Cholecystitis

When a stone persistently obstructs the cystic duct, gallbladder inflammation ensues, producing acute cholecystitis. Unlike biliary colic, the pain is constant, often accompanied by fever, nausea, and vomiting. Murphy's sign - inspiratory arrest during palpation of the right upper quadrant - is a classic finding. Right upper quadrant ultrasound is the first-line imaging study, typically showing gallstones, gallbladder wall thickening, and pericholecystic fluid.

Management

Acute cholecystitis is managed with intravenous fluids, analgesia, antibiotics, and early laparoscopic cholecystectomy, generally within 72 hours of symptom onset when feasible. Patients who are poor surgical candidates may be managed initially with percutaneous cholecystostomy.

Quick Reference

Key Fact	Detail
Classic risk profile	Female, Fat, Forty, Fertile
Biliary colic duration	Minutes to a few hours, self-resolving
Cholecystitis sign	Murphy's sign (inspiratory arrest)
Imaging of choice	RUQ ultrasound
Definitive treatment	Laparoscopic cholecystectomy

MNEMONIC: FEMALE / STONE

FEMALE (risk factors) - Forty, Estrogen/OCP, Multiparity, Adiposity, Lipid drugs/rapid weight loss, Ethnicity
 STONE (cholecystitis) - Sonography first, Tenderness RUQ, Onset constant pain, Nausea/vomiting/fever, Elevated WBC

Chapter 12: Choledocholithiasis and Ascending Cholangitis

Choledocholithiasis

Choledocholithiasis refers to the presence of a gallstone within the common bile duct, which can obstruct bile flow and lead to jaundice, elevated liver enzymes in a cholestatic pattern, and biliary dilation on imaging.

Ascending Cholangitis

When an obstructed and stagnant biliary system becomes secondarily infected, ascending cholangitis develops - a potentially life-threatening condition requiring prompt recognition. The classic Charcot's triad consists of fever, jaundice, and right upper quadrant pain; when altered mental status and hypotension are also present, this constitutes Reynolds' pentad, signaling more severe, suppurative disease.

Management

Initial management includes intravenous fluids and broad-spectrum antibiotics. However, antibiotics alone are insufficient to relieve the underlying obstruction, and patients who do not rapidly improve - or who present with severe disease - require urgent biliary decompression, most commonly via endoscopic retrograde cholangiopancreatography (ERCP), with percutaneous or surgical drainage as alternatives when ERCP is not feasible.

Quick Reference

Key Fact	Detail
Charcot's triad	Fever + jaundice + RUQ pain
Reynolds' pentad adds	Confusion + hypotension
First-line treatment	IV fluids + antibiotics
If no improvement	Urgent ERCP for decompression

MNEMONIC: CHARM / URGENT

CHARM - Charcot's triad, Hepatic duct obstruction, Ascending infection, RUQ tenderness, Markedly elevated bilirubin/ALP

URGENT - Ultrasound/labs first, RUQ pain, Give fluids+antibiotics, ERCP if no response, Nonresponders decompressed, Treat sepsis

Chapter 13: Primary Sclerosing Cholangitis and Primary Biliary Cholangitis

Primary Sclerosing Cholangitis

Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease characterized by progressive inflammation and fibrosis of both intrahepatic and extrahepatic bile ducts, leading to multifocal strictures. It has a strong association with inflammatory bowel disease, particularly ulcerative colitis, and is more common in men. Cholangiography (usually MRCP) reveals a characteristic 'beaded' appearance of alternating strictures and dilations. PSC carries a significantly elevated risk of cholangiocarcinoma, and patients require ongoing surveillance.

Primary Biliary Cholangitis

Primary biliary cholangitis (PBC), by contrast, is an autoimmune condition predominantly affecting middle-aged women, involving progressive destruction of small intrahepatic bile ducts. Fatigue and pruritus, often worse at night, are prominent early symptoms, and laboratory testing typically shows a markedly elevated alkaline phosphatase with a positive antimitochondrial antibody, which is highly specific for the diagnosis.

Management

Ursodeoxycholic acid is the mainstay of therapy for PBC, slowing disease progression in many patients, with newer agents available for those with an inadequate response. Management of PSC is more limited, focused on surveillance for cholangiocarcinoma and colorectal cancer (given the IBD association), symptomatic treatment of pruritus, and consideration of liver transplantation in advanced disease.

Quick Reference

Key Fact	Detail
PSC imaging finding	Beaded intra/extrahepatic ducts
PSC feared complication	Cholangiocarcinoma
PBC diagnostic antibody	Antimitochondrial antibody (AMA)
PBC first-line treatment	Ursodeoxycholic acid

MNEMONIC: BEADS / ITCH

BEADS (PSC) - Bile duct beading on MRCP, Elevated ALP, Association with UC, Duct strictures, Surveillance for cholangiocarcinoma

ITCH (PBC) - Itching worse at night, Transaminases mildly up, Cholestatic ALP rise, Hallmark AMA positive

Part V: Hepatology

Chapter 14: Viral Hepatitis B: Interpreting Serology

Overview

Hepatitis B virus (HBV) infection is diagnosed and staged largely through interpretation of a panel of serologic markers, which together indicate whether a patient has acute infection, chronic infection, resolved infection, or vaccine-induced immunity.

Key Markers

Hepatitis B surface antigen (HBsAg) indicates active infection, whether acute or chronic, and its persistence beyond six months defines chronic infection. Hepatitis B surface antibody (anti-HBs) indicates immunity, either from natural resolution of infection or from vaccination. Hepatitis B core antibody (anti-HBc) indicates past or present infection with the virus itself and is notably absent after vaccination, since the vaccine contains only surface antigen. The IgM subtype of anti-HBc is a marker of recent (acute) infection, while IgG anti-HBc persists long-term. Hepatitis B e antigen (HBeAg) reflects active viral replication and higher infectivity.

Common Patterns

A patient who is HBsAg-negative, anti-HBs-positive, and anti-HBc-negative has vaccine-induced immunity, having never been infected with the actual virus. A patient who is HBsAg-positive, IgM anti-HBc-positive, and HBeAg-positive has acute infection with high infectivity. Chronic infection is characterized by persistent HBsAg positivity beyond six months, typically with IgG (rather than IgM) anti-HBc. Recognizing these patterns allows clinicians to distinguish immunity from infection, and acute from chronic disease, without ambiguity.

Quick Reference

Key Fact	Detail
HBsAg+, IgM anti-HBc+, HBeAg+	Acute, highly infectious
HBsAg-, anti-HBs+, anti-HBc-	Vaccine immunity
HBsAg+ beyond 6 months	Chronic infection
Anti-HBc positive	True past or current infection (not vaccine)

MNEMONIC: SHIELD

S - Surface antigen (HBsAg) = active infection
 H - High infectivity if HBeAg positive
 I - IgM anti-core = acute infection
 E - Envelope antigen marks replication
 L - Lasting >6 months = chronic
 D - Development of anti-HBs = immunity

Chapter 15: Hereditary Hemochromatosis

Overview

Hereditary hemochromatosis is an autosomal recessive disorder, most commonly resulting from mutations in the HFE gene, that leads to inappropriately increased intestinal iron absorption and progressive iron deposition in multiple organs.

Clinical Features

Because iron accumulates gradually, symptoms typically emerge in mid-adulthood and include fatigue, bronze-toned skin pigmentation from cutaneous iron and melanin deposition, new-onset diabetes mellitus ('bronze diabetes') from pancreatic islet cell damage, arthropathy particularly affecting the second and third metacarpophalangeal joints, and restrictive or dilated cardiomyopathy.

Diagnosis and Management

Elevated ferritin and transferrin saturation are the initial screening tests, with genetic testing for HFE mutations used for confirmation. Liver biopsy may be used to assess the degree of fibrosis in selected cases. Management centers on therapeutic phlebotomy to reduce total body iron stores, which can prevent or reverse many complications if initiated before irreversible organ damage occurs.

Quick Reference

Key Fact	Detail
Genetic defect	HFE gene mutation
Screening labs	Ferritin, transferrin saturation
Confirmatory test	Genetic testing
Treatment	Therapeutic phlebotomy

MNEMONIC: **BRONZE**

B - Bronze skin pigmentation
 R - Restrictive cardiomyopathy
 O - Occurs from HFE gene mutation
 N - New-onset diabetes ('bronze diabetes')
 Z - Zealous iron absorption
 E - Elevated ferritin & transferrin saturation

Chapter 16: Wilson Disease

Overview

Wilson disease is an autosomal recessive disorder of copper metabolism caused by mutations in the ATP7B gene, which encodes a copper-transporting ATPase required for biliary copper excretion. Impaired excretion leads to progressive copper accumulation, particularly in the liver, brain, and cornea.

Clinical Features

The disease typically presents in children, adolescents, or young adults, with a combination of hepatic and neuropsychiatric manifestations. Hepatic involvement ranges from asymptomatic transaminase elevation to acute liver failure or cirrhosis. Neurologic and psychiatric features include tremor, dysarthria, dystonia, and personality or behavioral changes. Kayser-Fleischer rings - golden-brown deposits of copper at the periphery of the cornea, best seen on slit-lamp examination - are a hallmark finding, particularly in patients with neurologic disease.

Diagnosis and Management

Serum ceruloplasmin is typically low, while 24-hour urinary copper excretion is elevated, reflecting increased free (non-ceruloplasmin-bound) copper. Treatment relies on copper chelation with agents such as penicillamine or trientine, along with zinc to reduce intestinal copper absorption, and dietary avoidance of copper-rich foods. Liver transplantation may be required in fulminant hepatic failure or advanced cirrhosis.

Quick Reference

Key Fact	Detail
Gene involved	ATP7B
Classic eye finding	Kayser-Fleischer rings
Key labs	Low ceruloplasmin, high urinary copper
Treatment	Chelation (penicillamine/trientine) + zinc

MNEMONIC: COPPER

C - Ceruloplasmin is low
 O - Ocular Kayser-Fleischer rings
 P - Psychiatric / personality changes
 P - Penicillamine (or trientine) treatment
 E - Elevated urinary copper excretion
 R - Recessive inheritance (ATP7B gene)

Chapter 17: Alpha-1 Antitrypsin Deficiency

Overview

Alpha-1 antitrypsin deficiency is an autosomal codominant disorder resulting from mutations in the SERPINA1 gene, leading to production of a misfolded alpha-1 antitrypsin protein. Rather than being secreted normally, the abnormal protein polymerizes and accumulates within hepatocytes.

Clinical Features

The deficiency of circulating alpha-1 antitrypsin leaves the lungs unprotected against neutrophil elastase, resulting in early-onset, predominantly panacinar emphysema, especially in the lower lung zones, and often occurring in nonsmokers at a younger age than typical COPD. Separately, the intrahepatic accumulation of misfolded protein causes direct hepatocyte injury, which can progress to cirrhosis and hepatocellular carcinoma.

Diagnosis and Management

Liver biopsy classically shows PAS-positive, diastase-resistant globules within hepatocytes, representing the accumulated misfolded protein. Diagnosis is confirmed with serum alpha-1 antitrypsin levels and phenotyping or genotyping. Management is largely supportive: smoking cessation is critical to slow pulmonary decline, augmentation therapy with pooled human alpha-1 antitrypsin can benefit those with emphysema, and liver transplantation may be required for advanced liver disease, which also corrects the underlying metabolic defect.

Quick Reference

Key Fact	Detail
Gene involved	SERPINA1
Lung finding	Panacinar emphysema, lower lobes
Liver biopsy finding	PAS-positive, diastase-resistant globules
Critical intervention	Smoking cessation

MNEMONIC: PANIC

P - PAS-positive globules in hepatocytes
 A - Antitrypsin protein misfolds
 N - Nonsmoker, young-onset emphysema
 I - Increased cirrhosis / HCC risk
 C - Codominant inheritance (SERPINA1)

Chapter 18: Complications of Cirrhosis and Portal Hypertension

Portal Hypertension and Varices

As cirrhosis progresses, increased resistance to portal blood flow leads to portal hypertension, promoting the development of portosystemic collateral vessels, including esophageal and gastric varices. Because a first variceal bleed carries substantial mortality, patients with medium or large varices identified on screening endoscopy are typically started on a non-selective beta-blocker, such as propranolol or nadolol, as primary prophylaxis to reduce portal pressure and bleeding risk.

Acute Variceal Hemorrhage

Active variceal bleeding is a medical emergency. Alongside resuscitation and urgent endoscopy for band ligation or sclerotherapy, vasoactive medication - most commonly octreotide - is started immediately to reduce splanchnic blood flow and portal pressure. Prophylactic antibiotics are also given, as bacterial infection is common and worsens outcomes in this setting.

Hepatic Encephalopathy

Hepatic encephalopathy arises from the accumulation of neurotoxic substances, particularly ammonia, that are normally cleared by the liver. Clinical features range from subtle cognitive slowing to overt confusion, with asterixis (a flapping tremor on wrist extension) a classic examination finding. Lactulose is first-line therapy, acting as an osmotic laxative that also traps ammonia in the gut lumen as ammonium ion, while rifaximin is typically added for recurrent or refractory episodes to reduce ammonia-producing gut flora.

Spontaneous Bacterial Peritonitis

Spontaneous bacterial peritonitis (SBP) is an infection of ascitic fluid without an identifiable intra-abdominal source, occurring due to translocation of gut bacteria across a compromised intestinal barrier. Diagnosis is made by paracentesis, with an ascitic fluid polymorphonuclear (PMN) cell count greater than 250 cells/mm³ considered diagnostic, prompting empiric antibiotic therapy even before culture results return.

Quick Reference

Key Fact	Detail
Primary variceal prophylaxis	Non-selective beta-blocker
Active variceal bleed drug	Octreotide
Hepatic encephalopathy first-line	Lactulose
SBP diagnostic threshold	Ascitic PMN > 250 cells/mm ³

MNEMONIC: **BETA / BLEED / FLAP / GUARD**

BETA - Beta-blocker prevents first variceal bleed

BLEED - Band ligation, octreotide, resuscitation, antibiotics

FLAP - Flapping tremor, Lactulose first-line, Ammonia driven, Precipitant sought

GUARD - ANC >250 diagnostic, Urgent empiric antibiotics for SBP

Chapter 19: Budd-Chiari Syndrome

Overview

Budd-Chiari syndrome results from obstruction of hepatic venous outflow, most commonly due to thrombosis of the hepatic veins or, less often, the inferior vena cava. It is strongly associated with underlying hypercoagulable states, including myeloproliferative disorders such as polycythemia vera, as well as pregnancy, oral contraceptive use, and malignancy.

Clinical Features

The classic triad is abdominal pain, ascites, and tender hepatomegaly, typically developing subacutely, though presentations range from asymptomatic to fulminant liver failure depending on the speed and extent of venous occlusion.

Diagnosis and Management

Doppler ultrasound is the initial imaging investigation of choice, demonstrating absent or reversed flow in the hepatic veins. Management includes anticoagulation, treatment of the underlying hypercoagulable disorder, and, in more advanced cases, interventions to relieve venous obstruction such as angioplasty, transjugular intrahepatic portosystemic shunt (TIPS), or liver transplantation.

Quick Reference

Key Fact	Detail
Most common association	Hypercoagulable state
Classic triad	Abdominal pain, ascites, tender hepatomegaly
First-line imaging	Doppler ultrasound
Management	Anticoagulation +/- TIPS or transplant

MNEMONIC: CLOT

C - Congested liver (hepatomegaly)

L - Liver vein thrombosis

O - Options: anticoagulation, TIPS, transplant

T - Triad: pain, ascites, hepatomegaly

Part VI: Inflammatory, Infectious, and Malabsorptive Disorders of the Bowel

Chapter 20: Ulcerative Colitis and Crohn's Disease

Overview

Ulcerative colitis and Crohn's disease are the two principal forms of inflammatory bowel disease (IBD), both thought to arise from a dysregulated immune response to gut microbiota in genetically susceptible individuals, though they differ substantially in distribution and behavior.

Ulcerative Colitis

Ulcerative colitis involves continuous mucosal inflammation that begins in the rectum and extends proximally to a variable extent, without skip lesions, and is confined to the colon. Patients typically present with bloody diarrhea, tenesmus, and abdominal pain. Colonoscopy shows friable, erythematous mucosa with loss of the normal vascular pattern, and pseudopolyps in more chronic disease. Perinuclear antineutrophil cytoplasmic antibody (p-ANCA) is more commonly positive in ulcerative colitis than in Crohn's disease.

Crohn's Disease

Crohn's disease can affect any part of the gastrointestinal tract from mouth to anus, most often the terminal ileum and colon, with characteristic skip lesions - segments of diseased bowel separated by normal mucosa - and transmural inflammation. This transmural involvement predisposes to complications not typically seen in ulcerative colitis, including fistulas, abscesses, and strictures. Colonoscopy may reveal a cobblestone appearance, and biopsy often shows non-caseating granulomas. Anti-Saccharomyces cerevisiae antibody (ASCA) is more commonly positive in Crohn's disease.

Extraintestinal Associations and Management

Both conditions are associated with extraintestinal manifestations, including arthritis, uveitis, and skin changes such as erythema nodosum and pyoderma gangrenosum. Primary sclerosing cholangitis is much more strongly linked to ulcerative colitis than to Crohn's disease. Management for both conditions is tiered, ranging from 5-aminosalicylates and corticosteroids for induction, to immunomodulators and biologic agents (such as anti-TNF therapies) for maintenance and more severe disease, with surgery reserved for complications or medically refractory disease - noting that surgery can be curative in ulcerative colitis (via colectomy) but is not curative in Crohn's disease, given its potential to recur anywhere along the GI tract.

Quick Reference

Key Fact	Detail
UC antibody	p-ANCA
Crohn's antibody	ASCA
Transmural disease	Crohn's disease
Stronger PSC association	Ulcerative colitis

MNEMONIC: CLOSE / SKIP

CLOSE (UC) - Continuous, Limited to colon, Only starts at rectum, Smoking protective, Extends proximally
SKIP (Crohn's) - Skip lesions, Kissing cobblestones, Involves any GI segment, Perianal/penetrating disease

Chapter 21: Celiac Disease

Overview

Celiac disease is an immune-mediated enteropathy triggered by dietary gluten in genetically susceptible individuals, leading to inflammation and villous atrophy of the small intestinal mucosa, predominantly affecting the duodenum and proximal jejunum.

Clinical Features

Presentations range from classic malabsorptive symptoms - chronic diarrhea, bloating, weight loss, and iron-deficiency anemia - to more subtle or extraintestinal manifestations, including dermatitis herpetiformis, an intensely pruritic, blistering rash typically on extensor surfaces such as the elbows and knees, which reflects IgA deposition in the skin.

Diagnosis and Management

Anti-tissue transglutaminase IgA antibody is the preferred initial serologic test, given its high sensitivity and specificity, with confirmation by duodenal biopsy showing villous atrophy, crypt hyperplasia, and intraepithelial lymphocytosis. Total IgA should be checked alongside serology, as IgA deficiency (more common in celiac disease) can cause false-negative results. Management is strict lifelong avoidance of dietary gluten, which typically leads to symptomatic and histologic improvement.

Quick Reference

Key Fact	Detail
First-line test	Anti-tissue transglutaminase IgA
Confirmatory test	Duodenal biopsy
Check alongside serology	Total IgA level
Treatment	Strict gluten-free diet

MNEMONIC: **VILLI**

- V - Villous atrophy on biopsy
- I - IgA tTG antibody is the screening test
- L - Lifelong gluten-free diet is treatment
- L - Linked to dermatitis herpetiformis
- I - Iron-deficiency anemia is common

Chapter 22: Whipple Disease

Overview

Whipple disease is a rare, chronic systemic infection caused by the bacterium *Tropheryma whipplei*, which infiltrates the small intestinal lamina propria and can disseminate to affect joints, the central nervous system, and other organs.

Clinical Features

The classic presentation includes migratory arthralgia, chronic diarrhea with malabsorption and weight loss, and neurologic or cognitive symptoms in more advanced disease, reflecting the systemic nature of the infection.

Diagnosis and Management

Small bowel biopsy showing periodic acid-Schiff (PAS)-positive foamy macrophages infiltrating the lamina propria is diagnostic. Treatment requires prolonged antibiotic therapy, often beginning with an agent capable of crossing the blood-brain barrier (such as ceftriaxone) followed by an extended course of oral antibiotics, given the risk of relapse, particularly with central nervous system involvement.

Quick Reference

Key Fact	Detail
Causative organism	<i>Tropheryma whipplei</i>
Diagnostic biopsy finding	PAS-positive macrophages
Classic triad	Arthralgia, diarrhea, weight loss
Treatment	Prolonged antibiotics, CNS-penetrating initially

MNEMONIC: PASTA

P - PAS-positive foamy macrophages

A - Arthralgia, migratory

S - Systemic (CNS) involvement possible

T - *Tropheryma whipplei* is the organism

A - Antibiotics for a prolonged course

Chapter 23: Clostridioides difficile Colitis

Overview

Clostridioides difficile is a spore-forming, toxin-producing bacterium that causes colitis when normal colonic flora is disrupted, most often by antibiotic use, allowing *C. difficile* to proliferate and produce toxins that damage the colonic mucosa.

Clinical Features

Patients typically develop watery diarrhea, abdominal cramping, and fever, usually within days to weeks of antibiotic exposure. In severe cases, colonoscopy reveals characteristic yellow-white pseudomembranes adherent to the colonic mucosa, and fulminant disease can progress to toxic megacolon.

Diagnosis and Management

Diagnosis relies on stool testing for *C. difficile* toxin or toxigenic strains, typically using a combination of nucleic acid amplification testing and toxin enzyme immunoassay. First-line treatment has shifted away from metronidazole toward oral vancomycin or fidaxomicin, both of which achieve higher concentrations within the colonic lumen. Recurrent disease may warrant fecal microbiota transplantation.

Quick Reference

Key Fact	Detail
Usual trigger	Recent antibiotic use
Diagnostic test	Stool toxin / NAAT testing
First-line treatment	Oral vancomycin or fidaxomicin
Recurrent disease option	Fecal microbiota transplantation

MNEMONIC: TOXIC

T - Toxin-mediated diarrhea
 O - Oral vancomycin/fidaxomicin first-line
 X - eXposure to antibiotics is the trigger
 I - Infection control / isolation needed
 C - Colonoscopy may show pseudomembranes

Chapter 24: Ischemic Colitis

Overview

Ischemic colitis results from reduced blood flow to the colon, most commonly in the setting of a hypotensive episode, atherosclerotic disease, or a low-flow state, disproportionately affecting so-called 'watershed' regions where overlapping arterial supply is least robust - particularly the splenic flexure (supplied at the border of the superior and inferior mesenteric artery territories) and the rectosigmoid junction.

Clinical Features

Patients, often elderly and with vascular risk factors, present with crampy abdominal pain, typically left-sided, followed by bloody diarrhea.

Diagnosis and Management

Colonoscopy is the primary diagnostic tool, showing mucosal edema, hemorrhage, and ulceration corresponding to the affected watershed territory. Most cases are managed supportively with bowel rest, intravenous fluids, and correction of the underlying hemodynamic cause, while more severe cases with evidence of transmural infarction or perforation require surgical resection.

Quick Reference

Key Fact	Detail
Most vulnerable region	Splenic flexure
Typical trigger	Hypotensive episode
Diagnosis	Colonoscopy
Severe disease requires	Surgical resection

MNEMONIC: FLOW

F - Flexure (splenic) most vulnerable
 L - Low-flow state is the usual trigger
 O - Older patients typically affected
 W - Watershed area ischemia

Chapter 25: Diverticulitis

Overview

Diverticulosis refers to the presence of outpouchings (diverticula) of colonic mucosa through weak points in the muscular wall, most commonly in the sigmoid colon, and becomes more prevalent with age, particularly in the setting of a low-fiber diet. Diverticulitis occurs when a diverticulum becomes obstructed and inflamed, sometimes progressing to micro- or macro-perforation.

Clinical Features

The typical presentation is left lower quadrant pain, low-grade fever, and leukocytosis, sometimes with a palpable mass or localized peritoneal signs if a walled-off abscess has formed.

Diagnosis and Management

CT of the abdomen and pelvis with contrast is the imaging modality of choice, both confirming the diagnosis and identifying complications such as abscess, fistula, or free perforation; colonoscopy is deferred in the acute setting due to perforation risk, but is typically performed some weeks later to exclude malignancy. Uncomplicated diverticulitis is often managed with oral antibiotics and dietary modification on an outpatient basis, while complicated disease (abscess, perforation, or obstruction) may require intravenous antibiotics, percutaneous drainage, or surgery.

Quick Reference

Key Fact	Detail
Imaging of choice	CT abdomen/pelvis with contrast
Avoid acutely	Colonoscopy (perforation risk)
Uncomplicated management	Oral antibiotics, outpatient
Complicated disease	Drainage or surgery

MNEMONIC: **LEFT**

L - LLQ pain, classic location

E - Elevated WBC

F - Fever, usually low-grade

T - CT scan is the imaging test of choice

Chapter 26: Acute Appendicitis

Overview

Acute appendicitis results from obstruction of the appendiceal lumen, most often by a fecalith, lymphoid hyperplasia, or, less commonly, a tumor, leading to increased intraluminal pressure, bacterial overgrowth, and inflammation that can progress to ischemia and perforation if untreated.

Clinical Features

The classic history is periumbilical pain (reflecting visceral referred pain) that migrates to the right lower quadrant as the inflamed appendix irritates the adjacent parietal peritoneum, accompanied by anorexia, nausea, and low-grade fever. Examination often reveals tenderness at McBurney's point, along with signs such as rebound tenderness, guarding, and pain with psoas or obturator stretch.

Diagnosis and Management

CT of the abdomen and pelvis is the standard imaging study in non-pregnant adults, given its high sensitivity and specificity, while ultrasound is often preferred as the initial test in children and pregnant women to avoid radiation exposure. Management is prompt appendectomy, typically performed laparoscopically, with antibiotics given perioperatively; in selected cases of uncomplicated appendicitis, antibiotic-only management is an alternative to surgery, though with a meaningful risk of recurrence.

Quick Reference

Key Fact	Detail
Classic pain pattern	Periumbilical -> RLQ migration
Imaging in adults	CT abdomen/pelvis
Imaging children/pregnancy in	Ultrasound preferred
Treatment	Appendectomy

MNEMONIC: **MIGRATE**

M - McBurney's point tenderness
 I - Inflammation from luminal obstruction
 G - Guarding / rebound tenderness
 R - Radiology (CT) confirms diagnosis
 A - Anorexia, nausea common
 T - Transition of pain (periumbilical to RLQ)
 E - Emergent appendectomy

Part VII: Gastrointestinal Oncology

Chapter 27: Hereditary Colorectal Cancer Syndromes

Familial Adenomatous Polyposis

Familial adenomatous polyposis (FAP) is an autosomal dominant condition caused by germline mutations in the APC tumor suppressor gene, resulting in the development of hundreds to thousands of adenomatous colonic polyps, typically beginning in adolescence. Left untreated, progression to colorectal cancer is essentially inevitable, usually by the third or fourth decade of life. Because of this near-certain malignant potential, prophylactic colectomy is recommended once polyps are identified, rather than relying on ongoing surveillance colonoscopy alone.

Lynch Syndrome

Lynch syndrome (hereditary nonpolyposis colorectal cancer) is caused by germline mutations in DNA mismatch repair genes, leading to microsatellite instability and a markedly increased lifetime risk of colorectal cancer - typically right-sided and occurring at a younger age than sporadic cancers - as well as endometrial, ovarian, and other extracolonic cancers. Because of this early and elevated risk, affected individuals and at-risk family members begin colonoscopy screening much earlier than the general population, often in their twenties, with more frequent surveillance intervals thereafter.

Clinical Approach

In both conditions, genetic counseling and testing of at-risk relatives are essential once an index case is identified, allowing earlier initiation of appropriate surveillance or prophylactic intervention before cancer develops.

Quick Reference

Key Fact	Detail
FAP gene	APC
FAP management	Prophylactic colectomy
Lynch gene defect	DNA mismatch repair genes
Lynch extracolonic cancer	Endometrial cancer

MNEMONIC: POLYPS / EARLY

POLYPS (FAP) - Prophylactic colectomy, Onset in adolescence, Loss of APC gene, Youth screening, Progresses to cancer inevitably, Surveillance alone insufficient

EARLY (Lynch) - Endometrial cancer risk, Autosomal dominant, Right-sided colon cancer, Lynch = mismatch repair genes, Younger screening age

Chapter 28: Carcinoid Tumors and Carcinoid Syndrome

Overview

Carcinoid tumors are neuroendocrine neoplasms that most commonly arise in the gastrointestinal tract, particularly the small bowel and appendix, and are capable of secreting vasoactive substances, most notably serotonin.

Carcinoid Syndrome

When a carcinoid tumor is confined to the gut, secreted serotonin is largely metabolized during first-pass hepatic metabolism before reaching the systemic circulation, so patients typically remain asymptomatic from a hormonal standpoint. Carcinoid syndrome - characterized by episodic flushing, watery diarrhea, wheezing, and eventually right-sided cardiac valvular disease (tricuspid regurgitation and pulmonic stenosis) from serotonin-induced fibrosis - therefore usually only becomes apparent once liver metastases develop, allowing serotonin to bypass hepatic degradation and reach the systemic circulation directly.

Diagnosis and Management

Elevated urinary 5-hydroxyindoleacetic acid (5-HIAA), a serotonin metabolite, supports the diagnosis, alongside imaging to localize the primary tumor and assess for metastatic disease. Somatostatin analogs, such as octreotide, are the mainstay of symptomatic management, in addition to surgical resection of the primary tumor and, where feasible, metastatic disease.

Quick Reference

Key Fact	Detail
Diagnostic urine test	5-HIAA
Why symptoms need liver mets	Bypasses hepatic first-pass metabolism
Cardiac finding	Tricuspid regurgitation, pulmonic stenosis
Symptom control	Somatostatin analog (octreotide)

MNEMONIC: **FLUSH**

F - Flushing episodes
 L - Liver metastases required for systemic symptoms
 U - Urinary 5-HIAA elevated
 S - Serotonin-secreting tumor
 H - Heart valve fibrosis (tricuspid regurgitation)

Part VIII: Gastrointestinal Pharmacology

Chapter 29: Acid-Suppressive and Motility Agents

Proton Pump Inhibitors

Proton pump inhibitors (PPIs), such as omeprazole, work by irreversibly inhibiting the H⁺/K⁺ ATPase (the proton pump) on the luminal surface of gastric parietal cells, the final common pathway of acid secretion regardless of the stimulating pathway. Because inhibition is irreversible, acid suppression persists until new pump molecules are synthesized, providing durable acid suppression with once- or twice-daily dosing. PPIs are first-line therapy for GERD, peptic ulcer disease, and *H. pylori* eradication regimens, and are used for stress ulcer prophylaxis in critically ill patients.

H₂ Receptor Antagonists

Histamine H₂ receptor antagonists, such as famotidine, competitively and reversibly block histamine-mediated stimulation of acid secretion. They are generally less potent than PPIs but act more quickly, making them useful for on-demand symptom relief or in patients unable to tolerate PPIs.

Other Agents

Antacids provide rapid but short-lived symptomatic relief by directly neutralizing existing gastric acid. Sucralfate forms a protective barrier over ulcerated mucosa. Prokinetic agents, such as metoclopramide, enhance gastric emptying and are used in conditions such as gastroparesis, while antiemetics spanning several drug classes (serotonin antagonists, dopamine antagonists, antihistamines) are selected based on the underlying cause of nausea and the desired side-effect profile.

Quick Reference

Key Fact	Detail
PPI mechanism	Irreversible H ⁺ /K ⁺ ATPase inhibition
H₂ blocker mechanism	Reversible histamine H ₂ receptor block
Fastest relief	Antacids (short-acting)
Mucosal protectant	Sucralfate

MNEMONIC: PUMP

- P - Proton pump is irreversibly blocked
- U - Used for GERD, PUD, *H. pylori* regimens
- M - Morning dosing, before meals
- P - Prolonged acid suppression (new pumps must be made)

