I. Anatomy
A. Intraperitoneal organ arising from embryonic foregut
B. Divided into regions as shown in Figure 1 below
C. Blood supply of the stomach is via branches of the celiac trunk
   1. Lesser curvature supplied by the right and the left gastric arteries
   2. Cardia supplied by the left gastric artery
   3. Greater curvature supplied by right gastroepiploic artery inferiorly and the left gastroepiploic artery superiorly
   4. Fundus supplied by the short gastric artery
D. Innervation by vagal and sympathetic nerves
   1. Myenteric plexus (Auerbach's plexus) between outer longitudinal and middle circular layers
   2. Submucus plexus (Meissner's plexus) between circular muscular layer and the mucosa
   3. Myenteric plexus and submucus plexus constitute the enteric nervous system

II. Physiology
A. Stomach layers: mucosa, submucosa, muscularis, and serosa
B. Gastric cell type and cell functions (see Table 1)

<table>
<thead>
<tr>
<th>Table 1. Gastric Cells and Their Specific Functions</th>
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</thead>
<tbody>
<tr>
<td>Parietal (oxyntic) cells</td>
</tr>
<tr>
<td>Chief (zymogen) cells</td>
</tr>
<tr>
<td>Mucous cells</td>
</tr>
</tbody>
</table>

C. Gastric endocrine cells secrete hormones
   1. G cells—gastrin
   2. Enterochromaffin-like (ECL) cells—histamine
   3. Enterochromaffin cells—atrial natriuretic peptide and melatonin
   4. Gastric D cells—somatostatin
D. All of the above-mentioned gastric cells are present in the fundus, cardia, and antrum, except chief cells, which are, only in the fundus
E. The fundus acts a reservoir for food. The body is a mixing chamber. The muscular antrum releases small volumes intermittently into the duodenum
F. Total gastric volume ranges from 30 mL in newborns to 2 L in adults

III. Development
A. Originates from the primitive foregut
B. By the end of the 4th week, the stomach is recognized as a fusiform dilation
C. Enlarges ventrodorsally, with faster dorsal growth creating greater curvature
D. Stomach rotates 90° clockwise on longitudinal axis
E. The primitive gut is lined by endoderm that is mainly columnar or cuboidal epithelium. Foveolar cells produce protective mucus and line the primitive gastric crypts
F. Foveolar epithelium eventually covers the surface of the stomach and the upper two-thirds of the gastric pits
G. Primitive epithelium is encircled by the splanchnic mesoderm
H. Mesoderm differentiates into smooth muscle layers
IV. Normal Histology of gastric pits/glands

A. Organized by region
   1. Apical region is at the mucosal surface of the stomach also called the isthmus, or neck region of the pit. Extends a short distance down the length of the gastric pit.
   2. Body refers to tubular area between neck and base of pit
   3. Base

B. Cell types in gastric glands
   1. Mucous cells - generated in base of pit and migrate up the pit as they mature
   3. Chief cells – stain blue with H and E. Secret pepsinogen, other zymogens and intrinsic factor
   4. G cells – secrete gastrin in response to antral distension to promote acid secretion from parietal cells

C. Cellular make up of gastric pits by region
   1. Cardia – shallow pits shallow containing mainly mucous cells. Very few parietal or chief cells present
   2. Fundus – deep, branched pits contain mucous cells at the apex; parietal/oxyntic cells in the expanded body of the gland; and chief cells and neuroendocrine cells at the base. Chief cells are found only in the fundus.
   3. Antrum – deep pits containing mucous, parietal, and neuroendocrine (antral G cells and D cells).

Recommended Reading


2B. Congenital Anomalies of the Stomach

Katherine McGoogan, MD
Christopher Jolley, MD

II. Congenital Gastric Outlet Obstruction
A. Pyloric atresia
   1. Associated with:
      a. Junctional epidermolysis bullosa
      b. Down syndrome
      c. Autosomal-recessive familial form
   2. Presentation at birth
      a. History of polyhydramnios
      b. Nonbilious emesis
      c. Feeding difficulties
      d. Abdominal distention
      e. Stomach rupture within the first 12 hours of life can occur
   3. Incidence is 3:100,000
B. Antral webs
   1. Presentation depends on degree of obstruction
   2. Can appear as a thin septum near the pylorus
C. Diagnosis of gastric outlet obstruction
   1. Large dilated stomach on abdominal films or in-utero ultrasound
   2. Upper GI series can show a pyloric dimple sign in pyloric atresia: a shallow cavity at the proximal point of the atresia
   3. Upper endoscopy can identify antral webs
D. Treatment of gastric outlet obstruction
   1. Correction of dehydration
   2. Correction of hypochloremic alkalosis
   3. Nasogastric decompression
   4. Surgical or endoscopic repair

II. Gastric Duplication
A. Usually occurs within the wall of the stomach along the greater curvature
B. Often does not communicate with the stomach lumen
C. Male:female ratio is 1:2
D. Composition
   1. Alimentary epithelium
   2. Submucosa
   3. Smooth muscle coat
E. Presentation
   1. Palpable cyst
   2. Symptoms of gastric outlet obstruction (65%)
   3. Bleeding if ectopic gastric tissue present (30%)
   4. Volvulus
   5. Perforation
   6. Weight loss with failure to thrive
   7. Pancreatitis if coexisting pancreatic duplication
F. Diagnosis
   1. Upper GI series may show extrinsic defect on the lesser curve of the stomach
   2. CT or ultrasound may outline the cystic structure
G. Treatment
   1. Excision at time of discovery
   2. Partial gastrectomy
III. Gastric Volvulus
   A. Has acute and chronic forms
   B. More frequently found in adults
   C. Presentation triad
      1. Sudden, severe epigastric pain
      2. Intractable emesis and retching
      3. Inability to pass a tube into the stomach
   D. Often associated with other defects
      1. Intestinal malrotation
      2. Diaphragmatic defect
      3. Asplenia
   E. Imaging modalities
      1. Upper gastrointestinal series
      2. Computed tomography
   F. Treatment is emergent surgery

IV. Congenital Microgastria
   A. Very rare anomaly
   B. Small, incompletely rotated stomach
   C. Associated with malrotation, situs inversus, and skeletal anomalies
   D. Presentation
      1. Postprandial vomiting
      2. Malnutrition
      3. Rapid gastric emptying → diarrhea
      4. Dumping syndrome
      5. Dilated esophagus
   E. Diagnosis by upper gastrointestinal contrast study
   F. Treatment
      1. Conservative management with frequent small feedings in less severe cases
      2. Surgical attachment of a jejunal pouch to enlarge the reservoir
      3. Nasojejunal or jejunostomy continuous feedings
      4. Treatment for gastroesophageal reflux
      5. Prokinetic agents to assist with gastric emptying

V. Pyloric Stenosis (see Pyloric Stenosis chapter)

Recommended Reading


Hypertrophic pyloric stenosis is the most common surgical disorder of the stomach in infants. The incidence is variable, but appears to be increasing.

I. Presenting Signs and Symptoms
   A. Nonbilious vomiting is the initial sign; emesis may contain streaks of bright red blood or coffee grounds. Vomiting may be projectile
   B. Dehydration, weight loss, and FTT
   C. Onset as early as 7 days or as late as 5 months
   D. M:F ratio 5:1
   E. Vomiting produces hypercarbia, hypochloremia, and alkalosis

II. Differential Diagnosis
   A. Antral web
   B. Annular pancreas
   C. Duodenal stenosis
   D. Pyloric channel ulcer
   E. Gastritis
   F. Allergic gastroenteropathy
   G. Pylorospasm
   H. Gastroesophageal reflux

III. Physical Examination and Imaging
   A. Pyloric mass found in mid-right epigastric area deep in the abdomen in 80% of patients
   B. Imaging is indicated if emesis is bilious or if no pyloric mass is found
   C. Upper GI series and pyloric ultrasonography reveal elongated pyloric channel
   D. Upper GI also reveals semilunar indentations on antrum from hypertrophied muscle and “double track” pyloric channel
   E. Ultrasonography reveals pyloric length ≥16 mm or pyloric muscle thickness ≥4 mm

IV. Treatment
   A. Correction of dehydration and hypochloremic alkalosis is essential to prevent postoperative complications, especially apnea
   B. Ramstedt pyloromyotomy is curative
   C. Post-operative vomiting occurs in 50% of cases due to local edema, delayed gastric emptying, and GER
   D. Normal pyloric thickness on ultrasound is seen by 6 weeks postoperative, but some abnormalities of the gastric outlet may persist on barium studies

Recommended Reading:

Infantile colic refers to prolonged episodes of crying in otherwise healthy infants, which is not relieved by routine comfort measures. Colic affects 700,000 infants each year in the US. The underlying etiology has not been identified.

I. Identification of Infantile Colic
   A. Rule of 3’s
      1. Periods of crying lasting for 3 hours or more per day
      2. Periods of crying occurring 3 or more days per week for >3 weeks
      3. Problem usually resolves by 3 months of age
   B. Episodes common in late afternoon/evening
   C. Prevalence 9%–26% of all infants
   D. Often interpreted as a disturbance of the GI tract because of infant grimacing, drawing up of legs, and excessive flatulence

II. Proposed Etiologies
   A. Excessive GI gas production from colonic fermentation of malabsorbed dietary carbohydrate
      1. Trial of simethicone in colic shows no efficacy
      2. Breath hydrogen tests do not support this proposed etiology
      3. Excessive rectal gas is likely secondary to excessive crying and aerophagia.
   B. Mode of feeding
      1. Prevalence, pattern, and amount of crying associated with colic are similar in breast- and bottle-fed babies
   C. Protein Allergy/Intolerance
      1. Some data indicates that a switch to hydrolyzed formula improves crying behavior
      2. Consider short trial of hydrolyzed formula in infants already being fed infant formula, especially in those with blood in the stool
   D. Abnormal Motility
      1. No data to support this proposed mechanism
   E. GERD
      1. Study of 24 infants with colic ≤3 months showed only 1 infant with GER
      2. Controlled study of acid blockers in colic showed no difference from placebo
      3. Consider limited empiric trial of antireflux medication in infants with colic accompanied by emesis
   F. Gut hormones
      1. Motilin—basal levels elevated in colicky babies independent of their diet
      2. Motilin levels higher in infants who later develop colic
   G. Non-GI Pathology
      1. Dutch study showed two-fold increased prevalence of colic in infants of smoking mothers
      2. Canadian study showed increased colic in infants of mothers with high maternal anxiety, maternal alcohol consumption at 6 weeks, and shift work during pregnancy
      3. Lower risk of colic in infants of mothers with stable partnership, full-time employment
III. Warning Signs in a Colicky Infant that Require Investigation for Underlying Organic Disease
   A. Forceful or bilious vomiting
   B. GI bleeding: hematemesis, hematochezia
   C. Failure to thrive
   D. Diarrhea
   E. Constipation
   F. Fever
   G. Lethargy
   H. Hepatosplenomegaly
   I. Bulging fontanelle
   J. Micro/macrocephaly
   K. Seizures
   L. Abdominal tenderness, distention

IV. Complications of Colic
   A. Early discontinuation of breast feeding, frequent formula changes, maternal distress and irritability, suboptimal father-infant interactions, increased risk for abuse
   B. Later in life, some studies have identified more impulsive cognitive style, hyperactivity, academic difficulties

Recommended Reading


2E. Gastritis
Sharmila Zawahir, MD
Samra Blanchard, MD

I. Infections
A. *H pylori*
   1. Most common cause of gastritis worldwide
   2. Acute infection produces neutrophilic response, followed by chronic infection with lymphocyte and plasma cell infiltrates (see chapter on *H pylori*)
B. Other bacteria
   1. *H heilmannii:* from cats, causes chronic active gastritis, associated with gastric carcinoma and MALT lymphoma
   2. *M tuberculosis:* rare cause of granulomatous gastritis, with gastric ulcers and mucosal hypertrophy on endoscopy
   3. *Bacillus cereus:* acute necrotizing gastritis
C. Viral
   1. Cytomegalovirus
      a. More common in immunosuppressed patients; but possible in immunocompetent
         1) Usually associated with Ménétrier’s disease (see below)
         2) Hyperplastic gastric folds, protein-losing enteropathy, and hypoalbuminemia
      b. Infection in gastric fundus and body \(\rightarrow\) wall thickening, ulceration, hemorrhage, and perforation
      c. Histology: acute and chronic inflammation, intranuclear cytoplasmic inclusions in endothelial and epithelial cells; cytomegalic cells
      d. Deeper inflammation of mucosa compared to HSV
      e. Diagnosis by viral culture of mucosal biopsies, immunohistochemical detection of CMV early antigen
      f. Management: spontaneous recovery in 1–2 months, or ganciclovir
   2. Other uncommon causes: hepatitis C virus, EBV, HHV-7, measles, varicella, influenza, HSV
D. Parasitic
   1. Cryptosporidiosis: rare cause of PUD and erosive gastritis
   2. Fish parasites *Anisakia simplex* (found in sushi and sashimi in Japan), and *Eustrongylides wenrichi* (fresh water fish) both cause eosinophilic gastritis in humans
   3. *Giardia lamblia* can infect stomach and cause reactive gastritis, chronic atrophic gastritis, or chronic active gastritis
E. Fungal (most common in immune compromised patients in association with systemic fungal infection)
   1. *Candida albicans* is the most common fungal organism causing gastritis
   2. Aspergillus can cause focal invasive gastritis. Risk factors are neutropenia, mucositis and glucocorticoid use

II. Reactive Gastropathy
A. Reactive changes in gastric mucosa caused by ischemia, chemical agents, or trauma
B. Endoscopic: antral erythema, erosions, and ulcerations
C. Histology: foveolar hyperplasia, mucosal edema, paucity of inflammatory cells
D. Stress gastropathy
   1. Occurs in setting of physiologic stress with secondary hypoperfusion
   2. Risk factors: gastric hypersecretion, mechanical ventilation, steroids, coagulopathy, sepsis
   3. Physiologic stress: shock, hypoxemia, burns, major surgery, multiple organ system failure, or head injury
   4. Erosions are multiple, superficial, and typically asymptomatic
   5. Risk of perforation is low, except in newborns with reactive gastropathy
   6. Can present with upper GI bleeding
   7. Initially involves fundus and proximal body, followed by antrum
   8. Within 24 hours of stress event
E. Neonatal gastropathy
   1. Typically seen in sick infants in NICU setting
   2. Infants on prostaglandin E to maintain patency of PDA
   3. Focal foveolar hyperplasia
   4. Antral mucosal thickening may cause gastric outlet obstruction
   5. Indomethacin, dexamethasone
   6. Other possible causes include: traumatic suctioning of upper GI tract, fetal distress, hypergastrinemia with maternal stress or antacid use, hyperpepsinogenemia, cow milk allergy

F. Medications causing gastritis
   1. NSAIDs
      a. Topical effect: antral erosions and acute hemorrhage within 15–30 minutes of ingestion
      b. Systemic effect: inhibition of COX-2–mediated production of prostaglandins
         1) Prostaglandins promote gastric mucosal blood flow and secretion of mucous and bicarbonate
         2) Lack of prostaglandins compromises mucosal integrity and protective barrier
         3) Increased platelet-activating factor induces platelet dysfunction
      c. Young children: ulceration at antrum and incisura
      d. Older children/adults: reactive gastropathy with epithelial hyperplasia, mucin depletion, enlarged nuclei, smooth muscle hyperplasia, vascular ectasia, and edema
      e. Factors increasing complications from NSAIDs: concomitant use of aspirin or second NSAID, high drug dose, age >65 years, anticoagulant use, H pylori infection
      f. Prevention of NSAID gastropathy by concomitant use of PPI or misoprostol (cytoprotectant)
      g. H2 receptor antagonists are not effective for prevention of gastropathy
   2. Other medications causing gastropathy
      a. Valproic acid, dexamethasone, chemotherapy, KCl, iron, long-term fluoride ingestion
   3. Alcohol gastropathy
      a. Subepithelial hemorrhages with minimal inflammation
      b. Gastropathy is more severe when combined with NSAID or aspirin

G. Traumatic gastropathy
   1. Subepithelial hemorrhages in fundus and proximal body due to forceful retching/vomiting
   2. Ulcerations on gastric wall next to or opposite a PEG or standard gastrostomy tube
   3. Mallory-Weiss tears immediately above and below the GE junction
   4. Linear erosions in herniated gastric mucosa of large hiatal hernias
   5. Long-term nasogastric tube use
   6. Gastric prolapse through gastrostomy tract

H. Exercise-induced gastropathy or gastritis
   1. Long distance runners may experience altered blood circulation and motility during and just after running
   2. Symptoms, usually post-exercise: abdominal cramps or epigastric pain, nausea, GER, vomiting
   3. Anemia from chronic blood loss
   4. Endoscopy: erosive and nonerosive gastropathy in all parts of the stomach

I. Radiation gastropathy
   1. Exact tolerance level of stomach to radiation dose is not known
   2. Erosions and ulcerations may progress to bleeding, perforation, fibrosis, and gastric outlet obstruction
   3. Acid suppression does not prevent radiation injury
J. Corrosive gastropathy
1. Severity depends on concentration, duration of exposure, volume, and amount of food in stomach at time
2. Acid ingestion primarily causes gastric injury
3. Gastric injury also possible with large volume alkali ingestion
4. Acid pools in antrum because of acid-induced pylorospasm
5. Endoscopy: friability, erythema, ulcers, hemorrhage, necrosis
6. Healing may lead to antral and pyloric strictures
7. Common agents: oral iron, zinc-containing foreign bodies and fluids, lithium or mercuric oxide button batteries, pine oil cleaner, hydrogen peroxide, potassium permanganate

K. Duodenogastric reflux (bile gastropathy)
1. Reflux of duodenal contents into the stomach occurs normally for about 5% of a 24-hour period in adults
2. May produce gastric mucosal inflammation, intestinal metaplasia, gastric carcinoma
3. Symptoms: bilious emesis, oral bile reflux, nonspecific reflux symptoms
4. Endoscopy shows erosions and erythema. Bile in the stomach is not proof of pathologic bile gastropathy
5. Histology: reactive gastropathy
6. Management
   a. PPI may be effective
   b. Prokinetics not thoroughly evaluated
   c. Limited evidence for bile acid–binding agents
   d. If refractory to medical therapy: Roux-en-Y duodenojejunostomy

III. Granulomatous Gastritis
A. Noninfectious
   1. Inflammatory bowel disease (IBD)
      a. Focal gastritis associated with Crohn disease is the most common cause of granulomatous gastritis
   2. Chronic granulomatous disease (CGD)
      a. Inherited immune disorder, more often in boys
      b. Upper GI symptoms with severe gastroenteritis, oral aphthous ulceration
      c. Chronic active focal gastritis in antrum with granulomas or multinuclear giant cells
      d. Diagnostic finding at endoscopy: lipochrome-pigmented histiocytes
   3. Other causes of noninfectious granulomatous gastritis: sarcoidosis, lymphoma, Wegener granulomatosis
B. Infectious: TB, syphilis, histoplasmosis, parasites, foreign body granulomas

IV. Eosinophilic Gastritis
A. Diagnosis based on typical symptoms of gastritis (vomiting, abdominal pain, blood loss, gastric outlet obstruction), eosinophilic gastric infiltrate, and exclusion of other causes of eosinophilic infiltrate
B. Most often occurs as part of eosinophilic gastroenteritis
C. Other causes of mucosal eosinophilia: Crohn disease, scleroderma, parasitic infection
D. Eosinophilic infiltrate may be in mucosal, muscular, or serosal layers
E. Specific allergen sometimes identified: cow milk/soy protein, egg, wheat
F. Endoscopic findings: friability, erythema, erosions, swollen folds, pseudopolyps (antral)
G. Peripheral eosinophilia present in 50% of adults
H. Treatment: hypoallergenic diets, steroids, antiallergic medications

V. Lymphocytic Gastritis
A. Etiology
   1. Celiac disease
   2. Ménétrier disease
   3. CMV
   4. Chronic varioliform gastritis
   5. Crohn disease
   6. Idiopathic
VI. Hyperplastic
   A. Ménétrier disease
      1. Typical age of presentation in childhood is 4 years; however, can be seen in neonates
      2. Usually benign and self-limited in children
      3. In adults, this may be a premalignant condition
      4. Associated with CMV infection
      5. Giant gastric folds, increased mucus secretion, decreased acid secretion, protein-losing gastropathy
      6. Differential for giant gastric folds:
         a. Lymphoma
         b. *H pylori*, CMV, anisakiasis
         c. Granulomatous gastridites
         d. Plasmocytoma
         e. SLE
      7. Endoscopy: giant rugal folds, erythema
      8. Histology: elongated, tortuous foveolae; decreased parietal and chief cell glands, cystic dilations, edematous lamina propria with increased eosinophils and lymphocytes
      9. Raised CMV IgM, positive CMV PCR, positive tissue culture
   B. PPI Gastropathy
      1. Long-term or high-dose PPI use causes parietal cell hyperplasia
      2. Occurs within 10–48 months of starting PPI
      3. No dysplasia
      4. Histology:
         a. Sessile—hyperplastic, glandular dilation, foveolar hyperplasia, mild inflammation
         b. Pedunculated—fundic gland polyp with cystic glandular dilation
      5. Typically resolves with cessation of therapy

VII. Portal Hypertensive Gastropathy
   A. Occurs in both cirrhotic and noncirrhotic portal hypertension, but more common in cirrhotic
   B. Unrelated to severity of liver disease, size of esophageal varices, or hypersplenism
   C. Endoscopic diagnosis
      1. Mild: 2–5 mm erythematous patches in a mosaic pattern
      2. Severe: cherry-red spots, confluent hemorrhagic appearance
   D. Histology:
      1. Ectasia of mucosal capillaries and venules, submucosal venous dilation, no significant inflammatory infiltrate
      2. Diagnosis is visual; biopsies are not necessary and may promote bleeding
   E. Therapy
      1. Nonselective beta blockers (propranalol, nadolol) reduce portal venous pressure and may improve blood loss
      2. Somatostatin analogues are used to control acute bleeding

VIII. Celiac Gastritis
   A. Intraepithelial lymphocytic infiltrate in antrum, without gross endoscopic findings
   B. Histology normalizes on gluten-free diet

IX. Graft vs Host Disease
   A. Acute GVHD: 21–100 days after transplant
      1. Anorexia, nausea, vomiting, upper abdominal pain
      2. Variable endoscopic findings in stomach
      3. Histology
         a. Early: crypt cell apoptosis and drop-out
         b. Advanced: gastric ulceration, edema, fibrosis, perforation
   B. Chronic GVHD rarely involves stomach

X. Uremic Gastropathy
   A. Acute renal failure or associated physiologic stresses may cause gastritis
   B. GI bleed associated with ulcers/erosions
   C. Gastric pH may increase in chronic renal failure due to increased urea in all tissues
XI. Autoimmune Gastritis:

A. Henoch-Schönlein purpura
   1. Immune complex–mediated vasculitis of small- and medium-sized vessels, which peaks in 4–6 year olds
   2. Involves skin, GI tract, kidneys and joints
   3. Colicky abdominal pain, nausea, vomiting, GI bleed
   4. Less common findings: intramural hematoma, intussusception, bowel infarction, bowel perforation, pancreatitis, appendicitis, cholecystitis
   5. Upper endoscopy is usually not required for diagnosis; however, may show hemorrhagic, edematous mucosa with erosions in stomach, duodenum, and jejunum
   6. Histology: leukocytoclastic vasculitis is often missed in shallow endoscopic biopsies

B. Pernicious Anemia
   1. Achlorhydria, intrinsic factor deficiency, and B₁₂ deficiency
   2. Upper endoscopy shows absent or thin rugae
   3. Histology shows atrophic fundic gland gastritis, absence of parietal cells
   4. Complication: gastric adenocarcinoma

C. Autoimmune thyroiditis and goitrous juvenile hypothyroidism associated with gastritis and mucosal atrophy

D. Vitiligo associated with autoimmune atrophic gastritis

E. SLE associated with hypertrophic gastropathy

F. Connective tissue disorders may have associated mast cell or eosinophilic gastritis

XII. Collagenous Gastritis

A. Rare: presents with chronic iron deficiency anemia and epigastric pain

B. Endoscopic findings are nonspecific and nondiagnostic

C. Biopsies show subepithelial collagen fibrosis, with inflammatory infiltrate in the lamina propria

D. Some improvement with acid suppression and steroids

XIII. Cystinosis

A. Intralysosomal deposition of cystine causes damage to many organs

B. Cysteamine lowers intracellular cystine, but causes hypergastrinemia and gastric hypersecretion, even after a single dose

XIV. Hypersecretory States

A. Zollinger-Ellison syndrome (see chapter on Secretory Tumors)

B. Systemic mastocytosis
   1. Mast cell accumulation in skin, bone, bone marrow, liver, spleen, and GI tract
   2. Excess histamine and cytokines produce gastric hypersecretion
   3. Isolated cutaneous is the most common form (urticaria pigmentosa)
   4. Systemic form: normal serum gastrin levels
   5. Endoscopy: gastric and duodenal ulcerations and urticaria-like papules
   6. Anesthesia is risky
   7. Management is with H1 and H2 blockers and acid-suppressive therapy

C. Short bowel syndrome
   1. Gastric hypersecretion because of lack of negative feedback inhibiting gastrin secretion
   2. Hypersecretion may be transient, or persistent with PUD
   3. May worsen nutritional status by inactivating pancreatic lipase and deconjugating bile salts

D. Hyperparathyroidism
   1. Hypercalcemia causes increased gastric acid secretion
   2. Usually causes duodenal ulcer
Recommended Reading


**2F. Helicobacter Pylori**

*Helicobacter pylori (H pylori)* is a slow-growing, Gram-negative, curved or S-shaped rod. This pathogen is responsible for a wide spectrum of disease.

**I. Epidemiology**

A. Increased risk of infection: developing countries, lower socioeconomic status, crowded living conditions, and household contacts

B. Transmission
   1. Most commonly direct person-person contact
   2. Water is a possible source, particularly home cisterns and water barrels in which organisms may form biofilms

C. Acquired in early childhood
   1. Infection may clear spontaneously
   2. Life-long infection is common after the first infection
   3. Infants are rarely infected, even if the mother is infected

D. Prevalence is decreasing in the developed and developing world

E. Re-infection rates are low, but recrudescence (same strain within 12 months) is common
   1. Re-infection is more likely in children <10 years old
   2. Re-infection rates are higher in developing areas with poor water and sanitation, and high population density

F. Organism colonizes gastric tissue, including areas of gastric metaplasia and/or ectopy in the duodenum, esophagus, and other sites

G. Infection produces chronic gastritis, which may remain asymptomatic

**II. Host Factors**

A. Natural reservoir: humans

B. Most often transmitted by asymptomatic individuals

C. Infection produces local and systemic host response

D. Impact of host genotype:
   1. Polymorphism of inflammatory cytokine IL-1β associated with corpus gastritis, hypochlorhydria, gastric atrophy, and gastric adenocarcinoma; but decreased risk of duodenal ulcer
   2. In the absence of proinflammatory IL-1β polymorphism, infection produces antral gastritis or self-limited infection

E. Impact of host immune response
   1. Antral gastritis: associated with increased acid production and duodenal ulceration
   2. Corpus gastritis: associated with decreased acid production and gastric ulcerations, as well as adenocarcinoma
   3. Humoral immune response leads to tissue damage, but not eradication of infection
   4. *H pylori*-specific IgA and IgG seen early in infection

F. Acid homeostasis
   1. Acute infection associated with transient hypochlorhydria (several months), which may facilitate transmission
   2. Antral predominant infection
      a. Increased gastrin production causes:
         1) Increased acid production
         2) Increased parietal cell mass → increased acid delivery to duodenum, producing gastric metaplasia
3. Pan-gastritis/corpus predominant infection
   a. Decreased acid production from infection leads to decreased gastrin production, and therefore hypochlorhydria
   b. Gastric epithelial cell proliferation and progressive gland loss, leading to gastric atrophy
   c. Atrophy increases risk of gastric ulceration and gastric adenocarcinoma

III. Bacterial Factors
   A. *H pylori* genome mutates rapidly by DNA incorporation from different strains
   B. Ingestion of organism leads to colonization of gastric mucous layer
      1. Inhibitors: acidity, motility, initial host immune response
      2. Hydrolyzes urea locally, increasing the local pH and promoting survival
      3. Flagella promotes motility to remain in mucous layer; nonflagellated forms are not pathogenic
   C. Outer membrane proteins (OMPs)
      1. Bind to antigens on gastric epithelial cells, preventing mechanical clearance
      2. DupA (duodenal ulcer promoting cytotoxin): associated with duodenal ulcer disease
   D. Cytotoxin-associated gene (CagA)
      1. Fragment of DNA encoding for components of type 4 secretion system, which enable the organism to transport proteins into other cells
      2. CagA+ strain infection increases risk of peptic ulcer disease (PUD) and gastric cancer
   E. Vacuolating cytotoxin (VacA)
      1. Pore-forming protein in 50% of *H pylori* strains
      2. Associated with severe disease, as it helps protect organism from gastric acid

IV. Clinical Implications of Infection
   A. GI system
      1. Chronic gastritis
         a. Reversible with eradication
      2. Ulcer disease: duodenal/gastric
         a. Less common in children
         b. Antral predominant infection: increased risk of duodenal ulcer
         c. Corpus predominant infection: increased risk of gastric ulceration and gastric malignancy
         d. DU associated with increased acid output
         e. 90% of DU children have antral *H pylori* colonization
      3. GER/GERD: no evidence for correlation with *H pylori* infection
      4. Gastric carcinoma
         a. Linked to CagA+ strains
         b. Early childhood infection increases risk
         c. Associated with reduced acid output and corpus predominant gastritis
         d. Gastritis → atrophy → intestinal metaplasia → dysplasia
      5. MALT lymphoma
         a. Increased risk of this primary gastric malignancy
         b. Eradication of *H pylori* infection leads to regression and remission in 70%–80% of established MALT
   B. Extraintestinal
      1. Iron deficiency anemia:
         a. Multiple mechanisms: chronic blood loss from gastritis/erosions/ulcers; hypochlorhydria decreases iron bioavailability; vitamin C deficiency; sequestration of iron by antral *H pylori* organisms
      2. Short stature reported in some population studies: more pronounced in males
      3. ITP
      4. Chronic urticaria
   C. Proposed benefits of infection
      1. Stimulation of local and systemic immune system, which may help promote host defense to exogenous pathogens
      2. Protection from diarrheal diseases
V. Diagnosis:

A. Indications for *H pylori* testing

1. PUD diagnosed by endoscopy, family history of gastric cancer, documented MALT lymphoma, refractory iron deficiency anemia without other cause
2. Not indicated for recurrent abdominal pain or non-ulcer dyspepsia, asymptomatic children, or newly diagnosed GERD

B. Invasive

1. Endoscopy with biopsy
   a. Most reliable for diagnosis and identification of infection
   b. Nodularity in stomach more common in children than in adults
      1) Cobblestone appearance: 1–4 mm in diameter, uniform color and smooth
      2) Most frequently seen in antrum
   c. Histology
      a. Superficial infiltrate of plasma cells and lymphocytes
      b. Lymphoid follicles with germinal centers are very suggestive of infection
      c. Atrophy
         1) Very rare in Western children
         2) Loss of glandular tissue
      d. Stains for identifying *H pylori* in tissue
         1) Silver: Warthin-Starry, Dieterle, Steiner, Genta
         2) Modified Romanovsky
         3) Sayeed stains
      e. Site of biopsy:
         1) Mid-antrum is best for children; in adults, cardia is also a good site
         2) Chronic PPI use can shift antrum-predominant to corpus-predominant gastritis
   2. Culture
      a. Fastidious organism: requires microaerophilic environment and complex media
      b. High specificity, but sensitivity varies between labs
      c. Multiple biopsies increase yield
      d. Culture allows for antibiotic sensitivity testing
   3. Rapid urease test on gastric biopsy tissue
      a. Urea breakdown by bacteria causes color change of pH indicator
      b. Sensitivity increases with the size of the sample
      c. Sens/Spec: 89/98%

C. Noninvasive

1. Urea Breath Test
   a. Patient injects urea labeled with $^{13}$C isotope
   b. Safe in young infants, readily repeated
   c. Urea hydrolysis produces labeled $^{13}$CO$_2$ and appears in the breath in minutes
   d. Can be used for diagnosis as well as post-treatment assessment
   e. Sens/Spec: 88–95/95%–100%
   f. False negative produced by antisecretory therapy, antibiotics

2. Serological tests
   a. Early specific IgM, and later, persistent specific IgA and IgG
   b. Not consistently sensitive or specific enough for use as sole diagnostic marker of infection
   c. Specific IgG tests (most common) have better sensitivity than IgA tests, but cannot differentiate past vs active infection
      1) Sens/Spec: 90-100/76%–96%
   d. Antibodies may not be detectable early in infection
3. Stool antigen test
   a. Monoclonal antibody–based test has high sensitivity and specificity
      1) Sens/Spec: 95/97%
      2) Polyclonal-based test only 94/86%
   b. Reported correlation between severity of gastritis and positivity in stool
   c. False negative with PPI

VI. Treatment
A. Endpoint is eradication of infection
B. Conventional regimens
   1. Anti-secretory agent plus two or three antimicrobial agents for 10–14 days
      a. PPI + clarithromycin + amoxicillin or metronidazole x 10–14 days
      b. Addition of PPI increases eradication rates: inhibition of gastric acid may increase the effectiveness of acid-sensitive antibiotics (i.e., clarithromycin)
      c. Most common prescribed antibiotics: amoxicillin, metronidazole, clarithromycin, and tetracycline
   2. Bismuth: unknown mechanism; contraindicated due to association with encephalopathy and acute renal failure
C. Sequential regimens
   1. PPI + amoxicillin x 5 days, then 5 days of triple therapy (PPI + two antibiotics)
   2. Amoxicillin can decrease bacterial load and prevent clarithromycin resistance
D. Treatment failure
   1. Sources
      a. Patient noncompliance
      b. Antibiotic resistance
      c. Inadequate drug delivery
   2. Clarithromycin should not be used for treatment failure
   3. Some suggest bismuth-based quadruple therapy, or PPI + amoxicillin + tetracycline
   4. Tetracycline not recommended in children <12 years
   5. Antibiotic resistance
      a. Rates are increasing, and may have been present prior to therapy (primary)
      b. High resistance to metronidazole and clarithromycin reported
      c. Very low reported resistance for amoxicillin
E. Adjunctive therapy
   1. Probiotics to improve eradication: conflicting reports
F. Vaccination
   1. Would be cost-effective; trials are ongoing

Recommended Reading


2G. Ingestions and Trauma

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Significant injury can occur from ingestions, both foreign body and caustic, which are frequent during childhood. More significant injury may occur from trauma resulting in brain and organ damage. Abdominal injuries from trauma are the third leading cause of pediatric traumatic death.

I. Gastric Ingestions

A. Foreign objects: (see Esophageal Foreign Bodies)
   1. Often asymptomatic at time of presentation
   2. Evaluation: Always obtain an x-ray to assess position of suspected foreign object
      a. Radiolucent objects: wood, glass, plastic
      b. Assess for red flag symptoms: decreased appetite, food refusal, fever, nausea/vomiting, hematemesis, abdominal pain
   3. Lead intoxication
      a. Lead intoxication can occur with ingested toys secondary to gastric acid dissolution of lead
      b. Immediate removal recommended if lead is suspected

B. Sharp and elongated objects:
   1. Account for 15%–35% of perforations following foreign body ingestion (i.e., bones, toothpicks, razors, toy pieces, and long straight pins)
   2. Most can be managed conservatively (with weekly abdominal films to monitor passage)
   3. Increased risk of perforation if multiple objects were ingested
   4. Rule of thumb: objects >5 cm length (>3 cm in younger children) and >2 cm diameter are unlikely to pass the pylorus. Consider endoscopic removal of long or large objects while in stomach
   5. Majority of perforations (postesophagus) occur near duodenal loop or ileocecal valve

C. Coins: most frequently ingested foreign body in children in the United States and Europe
   1. Symptoms of gastric outlet obstruction or pain/peritonitis require immediate endoscopic removal
   2. Coins <2.5 cm diameter usually pass spontaneously
   3. If coin does not pass stomach after 4 weeks, endoscopic removal is likely needed
   4. Counsel parents to return to the emergency room if their child has red flag signs/symptoms

D. Gastric button batteries: (see Esophageal Foreign Bodies)

E. Bezoars: tightly packed collection of partially digested or undigested material. Often form in patients with delayed gastric emptying or motility
   1. Assess location with abdominal film or barium study
   2. Surgical removal may be necessary for large bezoars or antral bezoars
   3. Trichobezoars: hair bezoar; may give symptoms of gastric outlet obstruction or intestinal obstruction
   4. Phytobezoar: plant fibers - citrus, persimmon, cactus fruit, cloth fibers are common
   5. Lactobezoars: milk-based bezoar; often have symptoms of vomiting, feeding intolerance, and increased gastric residual volume. Withholding feedings for 2–3 days while giving IVF will often dissolve lactobezoars
   6. Phyto and trichobezoars can cause gastritis and iron deficiency anemia

F. Magnets—risk of abdominal trauma depends on quantity of magnets ingested:
   1. If single magnetic object was ingested and is already postpyloric, monitor with serial abdominal films. If in stomach, may consider removal
   2. Multiple magnetic objects can appear on x-ray as single object. Consider endoscopic removal if single magnet is seen in stomach
3. If multiple magnets are ingested, immediate intervention is necessary due to the high risk of magnetic attractive forces across adjacent bowel loops leading to intestinal perforation, bowel obstruction (possible volvulus), and fistula formation in small/large intestine.

4. If multiple magnets are in the stomach: urgent endoscopic removal.

5. If magnets are post-pyloric: obtain surgical consult for possible surgical removal.

G. Corrosive gastritis: (see Esophageal Caustic Injury)
   1. Most common from 12 months to 2 years of age. Less common than esophageal injury.
   2. May be caused by corrosion due to ingestion of strong acid (low pH) or alkaline (high pH) ingestion.
   3. Acid ingestions generally are more likely to cause stomach injury than alkali ingestions because of resistance of pharynx/esophageal squamous epithelium to coagulative necrosis. Alkaline ingestions are overall more common in incidence due to: (1) harsh taste of acids and (2) common presence of alkali in household products.

H. Severity:
   1. Dependent on concentration, amount, type of agent ingested, and length of time in the stomach. Ingestion can lead to damaged mucosa (friability/erythema), ulceration, gastrointestinal hemorrhage, necrosis, and perforation.
   2. In the long-term, corrosive ingestions carry increased risk of antral and pyloric stricture formation (~4–6 weeks), which can lead to gastric outlet obstruction.
   3. EGD is contraindicated if perforation is expected.

I. Acid ingestion:
   1. Leads to coagulative necrosis and eschar formation especially in the antrum.
   2. Strong acid in antrum due to prepyloric spasm.

J. Alkali ingestion:
   1. Lye-based (NaOH, KOH) drain cleaners, ammonia, and dishwashing soap.
   2. Causes mucosal liquefactive necrosis → deep penetration of mucosal layers.

K. Other agents:
   1. Oral iron, zinc-containing foreign bodies, pine oil cleaner, nonsteroidal anti-inflammatory agents (i.e., ibuprofen), oxidizing agents (hydrogen peroxide), and bleach (pH ~7).
   2. Bleach produces ulceration that does not result in strictureing.

L. Treatment for caustic ingestion:
   1. Antibiotics, anti-reflux therapy (avoid induced emesis and gastric lavage).
   2. May need to make NPO if deep burns and/or perforation suspected.
   3. Steroid therapy is controversial.

II. Abdominal Trauma
   A. Epidemiology:
      1. Serious abdominal injuries account for ~8% admissions to pediatric trauma centers. It is the third leading cause of pediatric traumatic death after head and thoracic injuries.
      2. Most common unrecognized fatal injury in trauma cases.
      3. 85% cases resultant of blunt trauma, such as:
         a. Lap belt injury: can lead to both small bowel injury from motor vehicle collision & traumatic diaphragmatic hernia.
         b. Bicycle injuries.
         c. Sports-related injuries.
         d. Child abuse.
      4. With blunt trauma, children are at higher risk of solid organ injury (spleen is the #1 solid organ injured; liver is #2, but liver injury is the most common cause of lethal hemorrhage).
         a. Solid organ injury is more common in children (vs adults) due to proportionally larger solid organs, less subcutaneous fat, and less protective abdominal musculature in children.
      5. Abdominal distension and vomiting are often late-onset findings.
   B. Examination: physical exam of abdomen, with rectal examination for blood.

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C. Diagnostic testing: only performed for intraabdominal injury in a stable patient; a rapid 
abdominal CT is first choice
   1. Other imaging options: Focused Abdominal Sonography for Trauma (FAST)
   2. Diagnostic peritoneal lavage
   3. Duodenal injury: rare, but often associated with a delayed diagnosis due to delayed 
symptoms
   4. Associated with symptoms of gastric outlet obstruction
   5. Hematomas often managed nonoperatively with decompression and bowel rest
   6. Perforation requires surgical repair

**Recommended Reading**


