Abdominal Pain & IBS
(The slides have been changed)

No.22

Editing file

Lecture outlines:

- ★ Sample questions for lecture topics
- ★ Anatomy and physiology of abdominal pain
- ★ Acute abdominal pain identification and examples
- ★ Chronic abdominal pain identification and examples
- ★ Peptic ulcer disease
- ★ IBS
- ★ Celiac Disease

Notes:

1. We took some notes from **AMBOSS** (written in **Blue**)
2. **The doctor said that his slides are enough :)**
3. We have put some slides from team 439 that are related to lecture. They are extra and not mentioned in our slides. You can either read it or skip it.

Color index

Original text
Females slides
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Doctor's notes [438]
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Text book
Important
Golden notes
Extra

Anatomy and Physiology of Abdominal Pain

◄ Factors Affecting Pain Perception in the Abdomen:

1. Nature of the stimulus (Is it stabbing, inflammatory, or distension?)
2. Type of neuroreceptor (that senses the pain)
3. Anatomy of the neural pathways from the site of injury to the CNS

Pain resulting from abdominal pathology is transduced in different ways by sensory afferent fibers that travel with the autonomic and somatic nervous systems

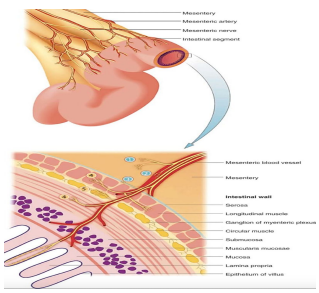
Crosstalk between the two systems can result in yet more variation in the perception of abdominal distress.

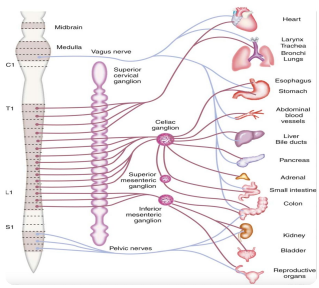
This unique neuroanatomy results in **three distinct types of pain**: visceral, somatic-parietal, and referred.

◄ Perception of Abdominal Pain Based on Pain Type:

1- **Visceral Pain:** vague in both onset and localization and perceived as a dull sensation in the **abdominal midline**. (**V**isceral = **V**ague)

- Visceral Peritoneum Lining the organs, nerve endings are mostly all **autonomic**.
- Gut organs are insensitive to stimuli such as burning and cutting but are sensitive to distension, contraction, twisting and stretching.
- Pain from unpaired structures is usually, but not always, felt in the midline.
- Visceral pain results from **stretch** and **distention** transduced by **mechanoreceptors** and, in more severe situations, the presence of inflammatory mediators detected by the silent nerve endings.
- Cutting and burning of abdominal viscera is not perceived as noxious e.g. polypectomy vs gaseous overdistention during colonoscopy (when you cut down or burn the viscera, the brain won't receive that as pain, however, when you distend it with gases for example, you'll feel the pain)





Abdominal Pain

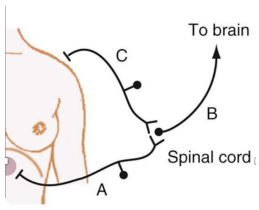
◀ Perception of Abdominal Pain Based on Pain Type:

2- Somatic-Parietal Pain: intense, sharp, and **well localized**.

- Somatic-parietal pain arising from **noxious stimulation of the parietal peritoneum**: more intense and precisely localized than the visceral pain.
- Example of this type of pain: **acute appendicitis**, in which early vague periumbilical visceral pain originating within the appendix is followed by localized somatic-parietal pain at McBurney's point that is produced by inflammatory involvement of the parietal peritoneum adjacent to the appendix. (Acute appendicitis is initially perceived as vague, visceral pain, later on it becomes a localized, somatic-parietal pain due to stimulation of the parietal peritoneum by inflammation)
- Somatic-parietal abdominal pain is usually aggravated by **movement** or **vibration**.

3- Referred Pain: perceived at a point **distant from the inciting pathology** and may be perceived to be outside the abdomen entirely.

- Referred pain is felt in areas **remote** from the diseased organ and results when visceral afferent neurons and somatic afferent neurons from a different anatomic region **converge** on second-order neurons in the spinal cord at the same spinal segment.
- E.g. Kehr's and Murphy's signs
- Pain perceived at a site distant from the source of stimulus why? The theory is based on the embryological origin of the organs & interconnected nerves.
- Gallbladder pain, for example, may be referred to the back or shoulder tip.
- Right Shoulder Pain —> With Cholecystitis and Perforated PUD
- Left Shoulder Pain —> With Diaphragmatic irritation due to splenic rupture
- Left-Sided Chest and Arm Pain —> MI



The acute abdomen is a consequence of one or more pathological processes:

Inflammation

Pain develops **gradually**, usually over several hours.

Perforation

Pain starts **abruptly**; it is severe and leads to **generalised peritonitis.**

Obstruction

Pain is **colicky**, **with spasms** that cause the patient to **writhe around** and double up.

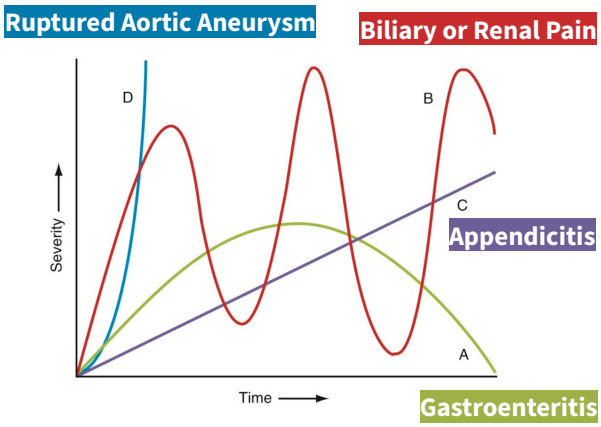
Approach to Abdominal Pain

History Taking:

Most important thing in approaching abdominal pain is a **GOOD history taking**.

◀ Chronology:

The chronological arrangement of different types of pain:



A. Gastroenteritis
B. Biliary or renal pain
C. Appendicitis
D. Ruptured aortic aneurysm/perforated viscus

◀ Intensity and Character of Pain:

Acute abdominal pain presentations based on Severity:

1. **Prostrating and Physically Incapacitating:** severe life-threatening disease e.g. perforated viscus, ruptured aneurysm, or severe acute pancreatitis.

2. **Gradual onset, colicky and intermittent** accompanied with **nausea** and **vomiting** e.g. **obstruction of a hollow viscus** e.g. SBO (small bowel obstruction), renal colic, or biliary pain, present with gradual onset of cramping pain that follows a sinusoidal pattern of intense pain alternating with a period of relief.

3. Gradually increasing discomfort, vague and poorly localized, **becoming more localized as the pain intensifies**, e.g., inflammation, as with **acute appendicitis** or **diverticulitis**.

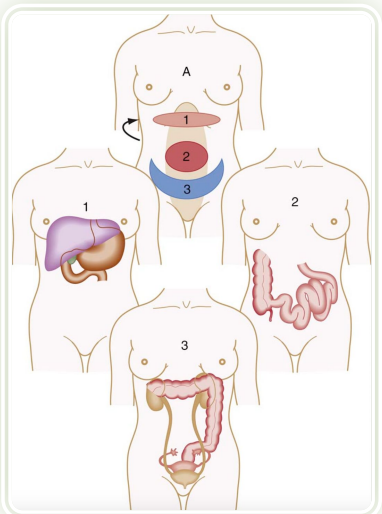
◀ Location:

You want to know where the pain is,

Epigastric Pain: think about proximal GI tract like distal esophagus, duodenum, stomach, liver, biliary system, and pancreas.

Mid Abdomen: small intestines (jejunum), right colon.

Hypogastric: remainder of colon, genitourinary tract.



Approach to Abdominal Pain

◄ Aggravating and Alleviating Factors:

- The relationship of pain to **positional changes**, **meals**, **bowel movements**, and **stress** may yield important diagnostic clues.
- Patients with **peritonitis** lie **motionless**, whereas those with **renal colic** may **writhe** in an attempt to find a comfortable position.
- Certain foods exacerbate pain. A classic example is the relationship between the intake of **fatty foods** and **development of biliary pain and pancreatic pain**.
- Pain associated with **duodenal ulcer** is often **alleviated by meals**. By contrast, patients with **gastric ulcer** or chronic **mesenteric ischemia** may report **exacerbation of pain with eating**.

◄ Associated Symptoms:

- Constitutional symptoms (e.g., fever, chills, night sweats, weight loss, myalgias, arthralgias)
- Digestive function (e.g., anorexia, nausea, vomiting, flatulence, diarrhea, constipation), and jaundice.
- Dysuria, changes in menstruation, and pregnancy should be solicited from the patient.
- **Clear vomitus suggests gastric outlet obstruction**, whereas **feculent vomitus suggests more distal small bowel or colonic obstruction**. (feculent=vomiting feces)

◄ Past Medical History (PMHx):

- Previous experience with similar symptoms suggests a recurrent problem. Patients with a history of partial SBO, renal calculi, or pelvic inflammatory disease **are likely to have recurrences**.
- A patient whose presentation suggests intestinal obstruction, and who has no prior surgical history, **deserves special attention because of the likelihood of surgical pathology such as a hernia or neoplasm**.
- Patients with a systemic illness, such as scleroderma, SLE, nephrotic syndrome, porphyria, familial Mediterranean fever (FMF) or sickle cell disease, often have abdominal pain **as a manifestation of the underlying disorder**.

Abdominal Pain

◀ Approach to Abdominal Pain:

How to approach Abdominal Pain?

By Physical Examination.

◀ Steps to Abdominal Physical Examination (Px):

1. Inspection
2. Auscultation (in GIT examination, auscultation always comes after inspection because we don't want to stimulate the viscera with palpation before we auscultate)
3. Palpation (superficial and deep palpation)
4. Percussion (for splenomegaly, ascites, etc.)

◀ Laboratory Workup (W/U)

You want to be **specific** with the labs that you order, because if you request too much labs you might get troubled with results that are not important to you and you might raise unneeded anxiety for the patient.

1. Hx + Px are **insufficient** for sole and firm diagnosis of acute abdominal pain presentation.
2. Basic labs to be ordered **CBC** with diff, **CMP** (Comprehensive Metabolic Panel) looking at **BUN**, **Cr**, and **glucose** levels is useful.
3. Urine or serum pregnancy testing must be performed in all women of reproductive age
4. **Liver panel**, **amylase**, and **lipase** for **epigastric pain**.

◀ Image Studies:

- CT scan (quick and shows you a lot)
- FAST (focused assessment with sonography in trauma) (Bedside, usually done in the ER, looking for possible free fluids that would indicate perforated viscus)
- US of the RUQ (in biliary colic)
- MRI (expensive, not used in claustrophobia, indicated **in patients who are pregnant/at risk of radiation to detect appendicitis**)
- HIDA scan (^{99m}Tc-labeled hydroxyl iminodiacetic acid) (to evaluate the gallbladder)

Acute Abdominal Pain

◄ Background:

- Definition: **Pain of less than 1 week in duration**.
- Medical attention sought within the **first 24 to 48 hours**.
- Frequent complaint prompting emergency department presentation.
- ~ **40%** of ER presentation for abdominal pain have **nonspecific findings**.
- 60% of causes are surgical disorders that warrant further evaluation and intervention.
- In a small number, life-threatening pathologies are present.

Causes of acute abdominal pain (presented in an Emergency Department):

Cause	The Percentage (%)
Nonspecific Abdominal Pain	**35**
Appendicitis	17
Bowel obstruction	15
Urologic disease	6
Biliary disease	5
Diverticular disease	4
Pancreatitis	2
Medical illness	1
Other	15

An area for your notes

Acute Abdominal Pain Presentations

Comparison of common causes of acute abdominal pain						
Cause	**Onset**	**Location**	**Character**	**Descriptor**	**Radiation**	**Intensity**
Appendicitis	Gradual	Periumbilical area early; RLQ late	Diffuse early; **localized later**	Aching	None	++
Cholecystitis	**Acute**	Mid-epigastrium, RUQ, right scapula	Localized	Constricting	**Scapula**	++
Pancreatitis	Acute	Epigastrium, T10-L2 area of the back	Localized	Boring	**Midback**	++ to +++
Diverticulitis	Gradual	**LLQ**	**Localized**	Aching	None	++ to +++
Perforated peptic ulcer	**Sudden**	Epigastrium	Localized early, **diffuse later**	Burning	None	+++
SBO	Gradual	Periumbilical area	Diffuse	Cramping	None	++
Mesenteric ischemia, infarction	Sudden	Periumbilical area	Diffuse	Agonizing	None	+++
Ruptured abdominal aortic aneurysm	**Sudden**	Abdomen, back, flank	Diffuse	**Tearing**	None	+++
Gastroenteritis	Gradual	Periumbilical area	Diffuse	Spasmodic	None	+ to ++
Pelvic inflammatory disease	Gradual	Either LQ, pelvis	Localized	Aching	**Upper thigh**	++
Ruptured ectopic pregnancy	Sudden	Either IQ, pelvis	Localized	Sharp	None	++

+, mild; ++, moderate; ++, severe; LQ, lower quadrant.

Acute Appendicitis

◀ Definition

Acute appendicitis is the acute inflammation of the appendix, typically due to an **obstruction** of the appendiceal lumen. It is the **most common cause of acute abdomen requiring emergency surgical intervention in both children and adults.** The characteristic features of acute appendicitis are **periumbilical abdominal pain that migrates to the right lower quadrant (RLQ), anorexia, nausea, fever, and RLQ tenderness.**

Uncomplicated Appendicitis: appendicitis with no evidence of an **appendiceal fecalith**, an **appendiceal tumor, or complications.**

Complicated Appendicitis: appendicitis associated with **perforation, gangrene, abscess,** an inflammatory mass, an appendiceal fecalith, or an appendiceal tumor.

◀ Etiology:

Caused by **obstruction of the appendiceal lumen** due to:

- **Impaction (obstruction) of the appendiceal orifice by a fecula (small stool ball).** (most common cause), **Appendiceal fecalith:** (concretion of feces that develops in the appendix that can obstruct the appendiceal lumen) and **fecal stasis** (35% of cases): **most common cause in adults**.
- **Lymphoid tissue hyperplasia:** (60% of cases): most common cause in **children and young adults**.
- **Neoplasm** (uncommon): more likely in patients > **50** years of age
- **Parasitic infestation** (uncommon)

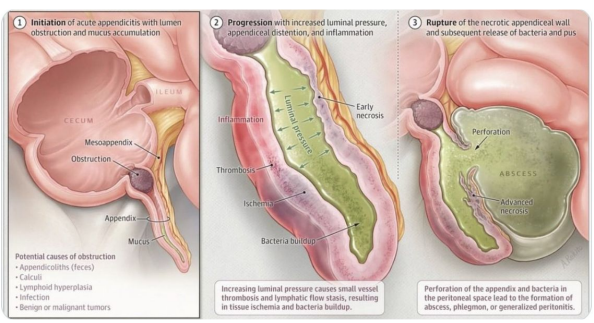
◀ Clinical presentation

- **Prodromal symptoms** of **anorexia, nausea, and vague periumbilical pain.**
- **6 to 8 hours** later, **pain migration to RLQ** + peritoneal signs develop. (pain becomes more localized)
- Usually happens in the younger population.

lifetime risk of appendicitis is 8.6% for males and 6.7% for females in Western countries and 17% in males and 13.5% in Asia.

◀ Imaging studies:

- US (**Start with US**, the downside of US is that it is operator dependant)
- CT (first initial along with US)
- MRI (**In pregnancy when US is inconclusive**)



Acute Appendicitis cont.

◀ Clinical presentation

Migrating abdominal pain: most common and specific symptom

- **Initial diffuse periumbilical pain:** caused by the irritation of the visceral peritoneum (pain is referred to T8–T10 dermatomes)
- Localizes to the RLQ within 12–24 hours: caused by the irritation of the parietal peritoneum

Associated nonspecific symptoms:

- Nausea
- Anorexia
- Vomiting
- Low-grade fever
- Diarrhea

Clinical signs of appendicitis:

- **McBurney point tenderness** (RLQ tenderness) (Tenderness at the junction of the lateral third and medial two-thirds of a line drawn from the right anterior superior iliac spine to the umbilicus)
- **RLQ** guarding and/or rigidity
- **Rebound** tenderness (Blumberg sign), especially in the RLQ
- **Rovsing** sign: RLQ pain elicited on deep palpation of the LLQ
- **Psoas** sign:

  1- can be performed in two different ways Can be elicited on flexing the right hip with stretched leg against resistance

  2- RLQ pain may be elicited on passive extension of the right hip when the patient is positioned on their left side.

- **Obturator sign:** RLQ pain on passive internal rotation of the right hip with the hip and knee flexed

The location of the pain may be variable as the appendix's location varies, especially in **pregnant women.**

◀ Diagnostics:

Acute appendicitis is usually a clinical diagnosis supported by laboratory findings (e.g., **leukocytosis with left shift**). Confirmatory **imaging** is recommended if the diagnosis is uncertain.

Acute Appendicitis cont.

◀ Diagnostics cont.:

Laboratory studies:

- CBC: **mild leukocytosis with left shift**
- CRP: elevated (> 10 mg/L)
- BMP: ↑ creatinine, electrolyte abnormalities may be present in patients with severe vomiting and diarrhea
- Urinalysis: typically normal in appendicitis; possible findings of mild pyuria and/or hematuria

Tests to evaluate differential diagnoses:

- Urine/serum β-hCG test: perform in all women of reproductive age to rule out pregnancy (including ectopic pregnancy)

Imaging:

Options for first-line imaging in nonpregnant adults:

- CT abdomen
- Ultrasound abdomen

First-line imaging for pregnant adults and children:

- **Ultrasound abdomen**

Abdominal ultrasound (Supportive findings):

- Distended appendix (diameter > 6 mm)
- Noncompressible, aperistaltic, distended appendix
- **Target sign:** concentric rings of hypo- and hyperechogenicity in the axial/transverse section of the appendix

While abdominal ultrasound can confirm the diagnosis of acute appendicitis, normal ultrasound findings do not reliably rule out appendicitis.

CT abdomen with IV contrast:

- **CT abdomen is the most accurate initial imaging modality for appendicitis.**

Supportive findings:

- Distended appendix (diameter > 6 mm)
- Edematous appendix with periappendiceal fat stranding

Acute Appendicitis cont.

◀ The Alvarado Score for Predicting Acute Appendicitis:

Feature	Points
Migration of pain	1
Anorexia	1
Nausea	1
Tenderness in RLQ	**2**
Rebound tenderness	1
Elevated temperature	1
Leukocytosis	**2**
Left WBC shift	1
Sum	10

Interpretation:

- A score of **5 to 6** is **suggestive** of appendicitis
- A score of **7 to 8** indicates **probable** appendicitis
- A score of **9 to 10** indicates that appendicitis is **likely**.
- Patients with scores **greater than or equal to 5** should be evaluated by a surgeon or undergo an imaging study to look for appendicitis.

◀ Acute appendicitis in children:

- In children, **mesenteric adenitis (or lymphadenitis)** is frequently **mistaken** for acute appendicitis but is often preceded by **a sore throat and is self-limited**

- Mesenteric adenitis may also be caused by **Yersinia enterocolitica -> acute appendicitis mimicker**

Acute Appendicitis cont.

◀ Treatment:

Supportive care:

- **Bowel rest (NPO)**
- Intravenous fluids

Empiric antibiotic therapy for acute appendicitis

- **Indication:** all patients with acute appendicitis
- **Required coverage:** against gram-negative and anaerobic organisms

Preoperative antibiotics for uncomplicated appendicitis:

- **Cefoxitin**
- **Cefazolin ; PLUS metronidazole**

Nonoperative management for appendicitis:

- Duration for early **uncomplicated appendicitis** (not yet standardized): Consider initial parenteral antibiotics for at least **2–3 days then switch to oral antibiotics for 7 days.**
- Duration for **complicated appendicitis** (appendiceal mass or appendiceal abscess): **3–5 days**

Operative management:

Appendectomy:

- Appendectomy within **24 hours of diagnosis** is the current standard of care for acute **uncomplicated** appendicitis.
- Relative contraindications: **Appendiceal mass and Appendicular abscess**

◀ Complications of acute appendicitis:

1- Appendiceal abscess: a localized collection of pus and necrotic tissue that forms around an inflamed appendix, which typically follows an untreated perforated appendix

- Clinical features: manifests as a tender mass in the RLQ in an acutely ill patient (i.e., high-grade fever, possible paralytic ileus, leukocytosis, signs of sepsis)

2- Perforated appendix

Acute Biliary Disease

Introduction

- Spectrum between biliary pain ("biliary colic") and acute cholecystitis.
- Biliary pain is a syndrome of **RUQ or epigastric pain,** usually **postprandial**, caused by **transient obstruction** of the cystic duct by a gallstone; it is self-limited, generally lasting **less than 6 hours**.
- Acute cholecystitis is, in most cases, caused by **persistent obstruction** of the cystic duct by a gallstone. Compare this to acalculous cholecystitis (which usually occurs in very sick ICU patients).

◄ Acute Cholecystitis:

- Acute cholecystitis refers to the acute inflammation of the gallbladder, which is typically due to **cystic duct obstruction by a gallstone** (acute calculous cholecystitis).
- Prevalence: most common complication of **cholelithiasis**

Etiology: Acute calculous cholecystitis: most common form

Cause: obstructing cholelithiasis

Pathophysiology:

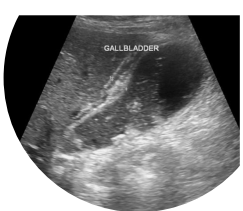
- Cholelithiasis → passage of gallstones into the cystic duct → cystic duct obstruction → distention and inflammation of the gallbladder
- Secondary bacterial infection may also be present (E. coli, Klebsiella, Enterobacter, Enterococcus spp. most common) but is not necessary for the development of cholecystitis.

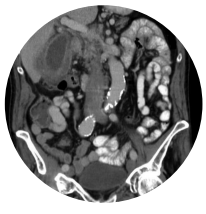
◄ Clinical Presentation of Acute Cholecystitis:

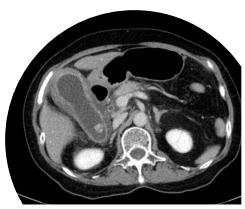
- The pain usually is a dull ache that is **localized to the RUQ** or **epigastrium** with **radiation around the back to the right scapula.** Nausea, vomiting, and low-grade fever are common.
- On examination, RUQ tenderness, guarding, and **Murphy sign** (inspiratory arrest on palpation of the RUQ) are typical. (You press on the RUQ and ask the patient to take a deep breath, if they stop suddenly, this indicates a positive murphy sign)
- The WBC count is usually mildly elevated but may be normal.
- Mild elevations in serum total bilirubin and alkaline phosphatase levels are common. (especially in cases of choledicolithiasis)

◄ Imaging Findings:

- US is the preferred initial
- CT Scan







Acute Cholecystitis

◀ Clinical features of Acute Cholecystitis:

1- Right upper quadrant pain

- Typically more severe and prolonged (> 6 hours) than in biliary colic
- Postprandial
- Radiation to the right scapula (due to referred pain from phrenic nerve irritation)

2- Positive Murphy sign: sudden pausing during inspiration upon deep palpation of the RUQ due to pain

- Murphy sign may be falsely negative in patients > 60 years.

3- Guarding

4- Fever, malaise, anorexia

5- Nausea and vomiting

Note: Acute cholecystitis should always be suspected in a patient with a history of gallstones who presents with RUQ pain, fever, and leukocytosis

Tokyo Criteria for the Diagnosis of Acute Cholecystitis

A	**Local signs of inflammation**
	1. Murphy sign 2. RUQ mass, tenderness, or pain
B	**Systemic signs of inflammation**
	1. Fever 2. Elevated C-reactive protein 3. Elevated WBC count
C	**Imaging findings characteristic of cholecystitis**
Definite Diagnosis: One item in A and one item in B or C, when acute cholecystitis is suspected clinically	

Acute Cholangitis

◀ Introduction:

Acute cholangitis (ascending cholangitis) refers to a bacterial infection of the biliary tract, typically secondary to biliary obstruction and stasis (e.g., due to choledocholithiasis, biliary stricture).

◀ Pathophysiology:

Biliary tract obstruction → bile stasis with increased intraductal pressure → bacterial translocation into the bile ducts → bacterial infection ascends the biliary tract (even into the hepatic ducts)

Causes:

- Choledocholithiasis (most common)
- Malignant obstruction (e.g., due to cholangiocarcinoma, pancreatic cancer, etc)
- Acute pancreatitis

Biliary strictures:

- Congenital, Infectious (e.g., HIV), Inflammatory e.g., primary sclerosing cholangitis and IgG4-related sclerosing cholangitis) Iatrogenic (e.g., ERCP, stent placement)

Contamination of bile with intestinal contents:

- Manipulation of the biliary tract (e.g., papillotomy, stent placement, **ERCP**, liver transplantation)

◀ Clinical features:

Mainly in setting of **choledocholithiasis**

Charcot's triad:

- Intermittent RUQ pain + jaundice + fever
- Charcot triad, which consists of RUQ pain, fever, and jaundice, is the classical clinical manifestation of acute cholangitis though not all patients manifest with the triad.

Reynold's pentad:

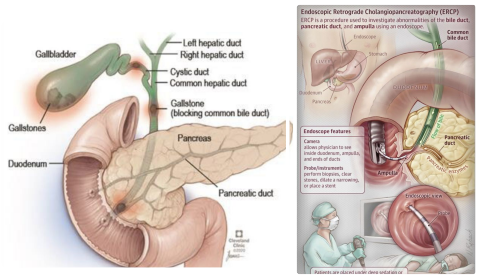
- Charcot's triad + **metabolic encephalopathy (mental status changes) and hemodynamic instability (hypotension).**

Features of sepsis, septic shock, and multi organ dysfunction may be present, depending on the severity of disease at presentation.

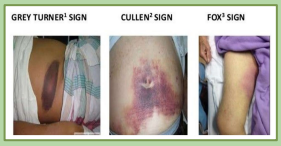
Acute Cholangitis

◀ Management:

Management: I**V antibiotics** and Endoscopic retrograde cholangiopancreatography (**ERCP**)



Acute Pancreatitis

Features 	• Acute pain in the epigastrium that is constant, unrelenting, **radiating to the back or left scapular region.** • **Fever, anorexia, nausea, and vomiting** are typical. • Patients are usually **tachycardic and tachypneic.** • In rare patients, flank or periumbilical ecchymoses **(Grey-Turner or Cullen sign, respectively)** develop in the setting of pancreatic necrosis with hemorrhage.
Etiology	Most Common Causes of Acute Pancreatitis: • Alcohol, Cholelithiasis, Common Bile Duct Stone, Hypercalcemia, Trauma, Infections, etc.
Physical examination	• Physical examination reveals an acutely ill patient in considerable distress. • Abdominal examination reveals **hypoactive bowel sounds** and marked **tenderness** to percussion and palpation in the **epigastrium**. Abdominal rigidity is a variable finding.
Laboratory studies	Depending on the cause and severity of pancreatitis, **serum electrolyte, calcium, and blood glucose levels and liver biochemical test and arterial blood gas** results may be abnormal. If Negative workup, this could indicate **microlithiasis**
Radiological studies	**US** is useful for identifying gallstones as a potential cause of pancreatitis. CT is reserved for patients with severe or complicated pancreatitis.

Acute Pancreatitis

◀ Acute pancreatitis diagnosis per revised ATLANTA Classification:

2 out of 3 for Diagnosis:

1. Abdominal pain consistent with the disease
2. A **threefold increase** in serum amylase or lipase levels (lipase is MORE specific)
3. Imaging findings consistent with acute pancreatitis

- Most cases of acute pancreatitis are mild and self-limited
- 20% local or systemic complications, including hypovolemia and shock, renal failure, liver failure, acute hypoxemic respiratory failure via ARDS, and hypocalcemia.

- Severity index scores for acute pancreatitis:
  APACHE II score, **Ranson's criteria**, and **BISAP** score.

BISAP score	
BUN	BUN >**25 mg/dL** (8.9 mmol/L) **(1 point)**
Impaired mental status	Abnormal mental status with a Glasgow coma score <15 **(1 point)**
SIRS	Evidence of SIRS (systemic inflammatory response syndrome) **(1 point)**
Age	Age >60 years old **(1 point)**
Pleural effusion	Imaging study reveals pleural effusion **(1 point)**
0-2 Points: Lower mortality (<2 percent)	
3-5 Points: Higher mortality (>15 percent)	

SIRS indicates one of the following:

1. Temperature above 38 (fever)
2. HR > 90 (tachycardia)
3. WBCs (leukocytosis)
4. Blood Pressure (hypotension)

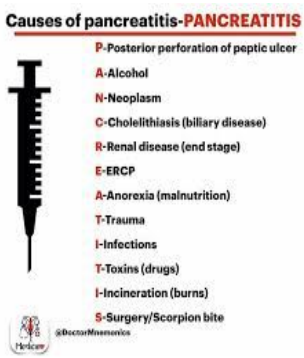
Acute Pancreatitis

Introduction

- There is inflammation of the pancreas resulting from prematurely activated pancreatic digestive enzymes that invoke pancreatic tissue autodigestion.
- Most patients with acute pancreatitis have mild to moderate disease but up to 25% have severe disease.
- There are two forms of acute pancreatitis, mild and severe:
  a. **Mild acute pancreatitis** is most common and responds well to supportive treatment.
  b. **Severe acute pancreatitis** (necrotizing pancreatitis) has significant morbidity and mortality.

◀ Causes

- **Gallstones (40%)**—The gallstone passes into the bile duct and blocks the ampulla of Vater. "ALWAYS consider gallstone pancreatitis and rule it out even in pt with hx of alcohol use"
- **Alcohol abuse (40%)**
- Post-ERCP[1] —Pancreatitis occurs in up to 10% of patients undergoing ERCP[2] .
- Viral infections (e.g., mumps, Coxsackievirus B)
- Drugs: Sulfonamides, thiazide **diuretics,NSAIDS,** furosemide, estrogens, HIV medications.
- Postoperative complications. (high mortality rate)
- Scorpion bites.
- Pancreas divisum[3].
- Pancreatic cancer.
- Hypertriglyceridemia, hypercalcemia.
- Uremia.
- Blunt abdominal trauma **(most common cause of pancreatitis in children)**



★ Clinical Features

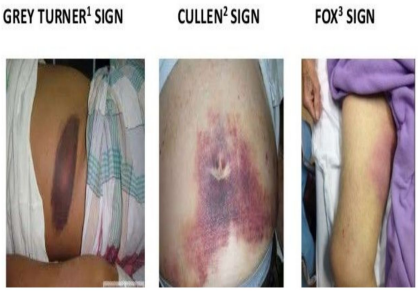
Symptoms:

1. Abrupt onset of severe abdominal pain, usually in the epigastric region.
- **May radiate to back** (50% of patients).
- Often steady, dull, tenderness and severe; worse when supine and after meals

2. Nausea and **vomiting**, anorexia

Signs:

1. Low-grade fever, tachycardia, hypotension, leukocytosis.
2. Epigastric tenderness, abdominal distention.
3. Decreased or absent bowel sounds indicate partial ileus.
4. The following signs are seen with hemorrhagic-pancreatitis as blood tracks along fascial planes:
   - ➢ **Grey Turner's sign** (flank ecchymoses)
   - ➢ **Cullen's sign** (periumbilical ecchymoses)
   - ➢ **Fox's sign** (ecchymosis of inguinal ligament)



Signs of severe Necrotizing Pancreatitis:
- Cullen sign: Blue discoloration around the umbilicus -> due to hemoperitoneum.
- Turner's sign: Bluish purple discoloration of flanks -> tissue catabolism of Hb

1- "**Endoscopic retrograde cholangiopancreatography**"
2- Presumably because of back pressure from injection of contrast material into the ductal system. Most people have asymptomatic increase in amylase, only 2-8% of pt will actually develop symptomatic pancreatitis.
3- Is a congenital anomaly in the anatomy of the ducts of the pancreas in which a single pancreatic duct is not formed, but rather remains as two distinct dorsal and ventral ducts.

Acute Pancreatitis

◀ Diagnosis

1 Laboratory studies:

- **Serum amylase** is the most common test **(Best initial test)**, but many conditions cause hyperamylasemia (nonspecific) and its absence does not rule out acute pancreatitis (nonsensitive). However, if levels are more than five times the upper limit of normal, there is a high specificity for acute pancreatitis.
- **Serum lipase**—**(more specific for pancreatitis than amylase).**
- LFTs. "To identify cause (gallstone pancreatitis)."
- Hyperglycemia, hypoxemia, and leukocytosis may also be present.
- Order the following for assessment of prognosis **(Ranson's criteria):** glucose, calcium, hematocrit, BUN, arterial blood gas (PaO2, base deficit), LDH, AST, WBC count

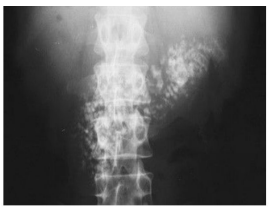
TABLE 3-3 Ranson's Criteria

Admission Criteria (GA LAW)	Initial 48 Hours Criteria (C HOBBS)	Mortality
Glucose >200 mg/dL	Calcium <8 mg/dL Decrease in Hematocrit >10%	<3 criteria—1%
Age >55 years	Pa_{O_2} <60 mm Hg	3–4 criteria—15%
LDH >350	BUN increase >8 mg/dL	5–6 criteria—40%
AST >250	Base deficit >4 mg/dL	>7 criteria—100%
WBC >16,000	Fluid sequestration >6 L	

2 Radiological studies:

1. Abdominal radiograph:

- Has a limited role in the diagnosis of acute pancreatitis.
- More helpful in **ruling out** other diagnoses, such as intestinal perforation (free air).
- The presence of calcifications can suggest chronic pancreatitis.
- if severe; "**sentinel loop**" or "**colon cutoff sign**" may be seen.



2. Abdominal ultrasound:

- Can help in **identifying cause** of pancreatitis (e.g., gallstones).
- Useful for following up pseudocysts or abscesses.

3. CT scan of the abdomen:

- **Most accurate test** for diagnosis of acute pancreatitis and for identifying complications of the disease."
- Indicated in patients with severe acute pancreatitis.

4. ERCP (indications):

- Severe gallstone pancreatitis with **biliary obstruction**.
- To identify uncommon causes of acute pancreatitis **if disease is recurrent**.

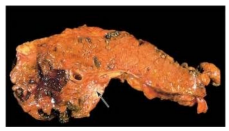
Acute pancreatitis

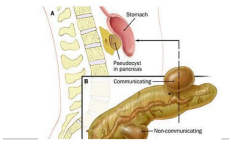
Complications

1. Pancreatic necrosis (may be sterile or infected):

- **Sterile pancreatic necrosis**—Half of all cases resolve spontaneously. Should be monitored closely in an ICU.
- **Infected pancreatic necrosis**—has high mortality rate (results in multiple organ failure in 50% of cases); surgical debridement and antibiotics indicated.

The only way to distinguish sterile from infected necrosis is via CT-guided percutaneous aspiration with Gram stain/culture of the aspirate.



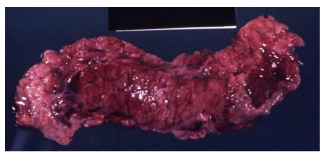


2. Pancreatic pseudocyst:

- Encapsulated fluid collection that appears 2 to 3 weeks after an acute attack— unlike a true cyst, it lacks an epithelial lining.
- Complications of untreated pseudocysts include rupture, infection, gastric outlet obstruction, fistula, hemorrhage into cyst, and pancreatic ascites.
- Diagnosis: CT scan is the study of choice.
- Treatment:
  - ➢ Cysts <5 cm: observation.
  - ➢ Cysts >5 cm: drain either percutaneously or surgically.

3. Hemorrhagic pancreatitis:

- Characterized by Cullen's sign, Grey Turner's sign, and Fox's sign.
- CT scan with IV contrast is the study of choice.



4. Adult respiratory distress syndrome —a life-threatening complication with high mortality rate.

5. Pancreatic ascites/pleural effusion. "The most common cause is inflammation of peritoneal surfaces."

6. Ascending cholangitis. "Due to gallstone in ampulla of Vater, leading to infection of biliary tract"

7. Pancreatic abscess (rare). "Develops over 4 to 6 weeks and is less life threatening than infected pancreatic necrosis."

Treatment

1. Patients with mild acute pancreatitis:

- Bowel rest (NPO).
- IV fluids. "Correct electrolyte abnormalities."
- Pain control.
- Nasogastric tube. "If severe nausea/vomiting or ileus present."

2. Patients with severe pancreatitis:

- Should be admitted to the ICU.
- Early enteral nutrition in the first 72 hours is recommended through a nasojejunal tube.
- If the severe acute pancreatitis has not resolved in a few days, supplemental parenteral nutrition should be started.
- If more than 30% of the pancreas is necrosed, prophylactic antibiotics (imipenem) should be considered to prevent infection. "Which has high morbidity and mortality"

Peptic Ulcer Disease (PUD)

Introduction

- The term PUD is used to include ulcerations and erosions in the **stomach and duodenum.**
- Lesions are called "peptic" because the **enzyme pepsin**, which is proteolytic at an acidic pH plays a major role in causing the mucosal breaks.
- Majority of peptic PUD is driven by **Helicobacter pylori (Hp)**.

◀ PUD Epidemiology:

- As many as 4 million people worldwide are affected by PUD.
- Hp infection acquired during childhood or adolescence became manifested as peptic diseases in later years.
- As Hp infection gradually declined in the population over time, the prevalence of infection also **gradually shifted from a younger toward older age groups**.
- The incidence of DU and GU has **declined** in parallel with the decline in the prevalence of Hp infection, likely a result of improved sanitary conditions and a safer food and water supply.

◀ PUD Etiology:

1. H. Pylori infection (most common cause)
2. NSAIDs
3. Zollinger Ellison Syndrome: a tumor that increases gastrin release

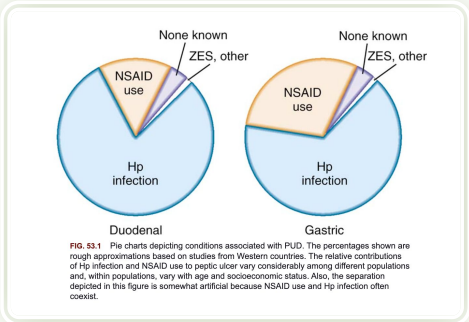


FIG. 53.1 Pie charts depicting conditions associated with PUD. The percentages shown are rough approximations based on studies from Western countries. The relative contributions of Hp infection and NSAID use to peptic ulcer vary considerably among different populations and, within populations, vary with age and socioeconomic status. Also, the separation depicted in this figure is somewhat artificial because NSAID use and Hp infection often coexist.

◀ PUD Clinical Presentation:

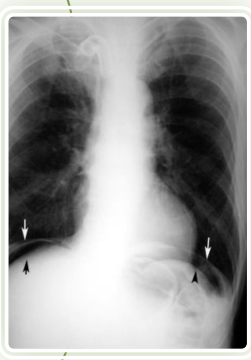
- PUD pain is mainly **epigastric pain**.
- Pain is typically associated with **hunger** [1], occurs at night, and is often relieved by food and antacids.
- Often patients complain of **dyspeptic symptoms such as nausea, bloated sensation, and fullness**.
- Chronic NSAID users, typically older adult patients, can present with ulcer **bleeding** or **perforation** without prior ulcer symptoms.

1. Keep in mind that gastric ulcers typically cause pain **after eating**, whereas duodenal ulcers tend to be **relieved by eating**.

Perforated Peptic Ulcer

Introduction

- 5% of patients with PUD present with perforation.
- Improved therapeutic modalities, including **PPIs**, **eradication of Hp**, and **endoscopic methods for control of hemorrhage**, have reduced the number of patients with PUD who require surgical intervention



Air under diaphragm: indicates a perforated viscus

◀ Perforated PUD Clinical Presentation:

- Patients with a perforated peptic ulcer typically present with the **sudden onset of severe diffuse abdominal pain**.
- These patients may be able to specify the precise moment of the onset of symptoms.
- In the usual case, the afflicted patient presents acutely with excruciating abdominal pain, often **without prodromal symptoms**.
- Abdominal examination **reveals peritonitis, with rebound tenderness, guarding, and abdominal muscular rigidity**.
- Distinguishing perforated ulcer from other causes of a perforated viscus (e.g., perforated colonic diverticulum, perforated appendicitis) **may not be possible.**

An area for your notes

Chronic abdominal pain

Background

- Abdominal pain occurring **for 6 months, either constantly or intermittently.**
- Evaluation begins with a detailed history and careful physical examination.

Examples of Etiologies for Chronic Abdominal Pain:

- The differential diagnosis is extensive and includes functional disorders (as IBS) and so-called organic disorder (as Celiac disease).

Irritable Bowel Syndrome (IBS)

◀ Background:

- IBS is a **functional bowel disorder**, characterized by **abdominal pain** and **disordered bowel habit**.
- The exact etiology remains **unknown**, and it is unlikely that there is one unifying explanation.
- The condition affects up to 10% of people and represents a considerable **financial burden** to health services.

◀ IBS Clinical Presentation:

- The pain in IBS may be either **aggravated** or **relieved** by **defecation**, and its onset is associated with an increase or decrease in stool **frequency** (the number of times you go to the toilet), or with **looser** or **harder stools** (change in form).

- The pain often is poorly localized, waxes and wanes, may be aggravated by eating, and can occur in any part of the abdomen, although it more typically is located in the **lower abdomen**.

- Exacerbation of pain by **life events or difficult life situations is common** (stress).

- Abdominal pain that is continuous or unrelated to defecation or that is induced by menstruation, urination, or physical activity is **unlikely to be explained by IBS**.

IBS Continued

◄ Criteria for IBS Diagnosis:

Manning Criteria	Kruis Criteria Patient's History
• Abdominal distention • **Abdominal pain eased after bowel movement** • Feeling of incomplete emptying • Looser stools at onset of abdominal pain • **More frequent bowel movements at onset of abdominal pain** • **Mucus per rectum**	• Abdominal pain • Flatulence • Irregularity of bowel movements • **Mixed diarrhea and constipation** • **Pellet-like stools or mucus** • **Symptoms for more than 2 yr**

Rome IV Criteria

Recurrent abdominal pain at least **1 day/week in the last 3 months** associated with **2 or more** of the following:

- **Related to defecation (Relieved by defecation).**
- **Associated with a change in frequency of stool**
- **Associated with a change in form (appearance) of stool**

◄ Alarming Symptoms (NOT IBS):

1. **Blood in stool (Rectal bleeding)**
2. **Weight Loss & Decreased Appetite**
3. **Nocturnal Symptoms: Nocturnal Diarrhea Pain worse at night**
4. **Extra-Intestinal Manifestations: Arthralgia, Jaundice, Elevated LFTs, Rash, Blurry Vision and Conjunctivitis.**
5. **Age >50 years; Male gender**
6. **Family history of colon cancer**
7. **Anemia**

Irritable bowel syndrome (IBS) cont..

IBS Management

- Guidelines for the management of IBS recommend that a positive diagnosis **should be made clinically**, without the need for recourse to investigations to exclude organic disease.
- However, available symptom-based diagnostic criteria perform only modestly, although this can be improved by incorporating other items from the clinical history and a limited panel of investigations.
- There is **no role for exhaustive investigation to confirm the diagnosis**, although **screening for celiac disease and bile acid diarrhea may be of value**, as these conditions can present with similar symptoms.
- Dietary changes, including a **low fermentable oligo-, di-, and mono-saccharides and polyols (FODMAP) diet or soluble fiber**, can improve symptoms in some people.

Management:

- Medical therapy with **antispasmodics**, **laxatives**, **secretagogues**, drugs acting on **opioid and 5-hydroxytryptamine receptors**, **antidepressants**, and **antibiotics**, and alternative approaches such as **psychological therapies and probiotics** have been demonstrated to be more effective than placebo in systematic reviews of randomized controlled trials.
- Despite the use of these interventions, the condition is likely to follow a chronic relapsing and remitting course, and **no therapy is proven to alter the natural history**.

i 21.65 Dietary management of irritable bowel syndrome

- Eat regularly and avoid missing meals
- Take time to eat
- Ensure adequate hydration and avoid carbonated and caffeinated drinks
- Reduce alcohol intake
- Reduce intake of 'resistant' starch and insoluble fibre
- Avoid foods with artificial sweeteners
- Consider a wheat-free diet
- Consider a lactose exclusion diet
- Consider a diet low in FODMAPs

(FODMAPs = fermentable oligo-, di- and monosaccharides, and polyols)

Celiac Disease

Background

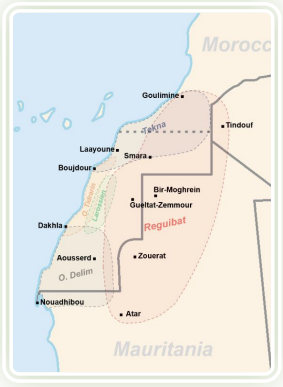
- Celiac disease is a chronic, immune-mediated enteropathy that is triggered by the ingestion of gluten in genetically susceptible individuals.
- The disease is characterized by **small intestinal villus atrophy** with concomitant **elevations in antibody levels against gliadin and tissue transglutaminase**.
- Commonly associated with autoimmune diseases **(like Hashimoto's and Type 1 DM)**

Clinical Presentation:

- Patients can present with a myriad of symptoms related to **malabsorption** (including **weight loss, diarrhea, and iron deficiency anemia**) and extra-intestinal symptoms including **metabolic bone disease**, **infertility**, and **neuropsychiatric disorders**. Celiac disease is treated with **complete avoidance of dietary gluten**.

◄ Epidemiology:

- The prevalence of both diagnosed and undiagnosed celiac disease has increased in recent decades.
- Involves wide geographic distribution and affects individuals from multiple and diverse ethnic and racial backgrounds.
- The overall prevalence of celiac disease in Europe has been estimated at 1%, with the highest reported prevalence of 2.4% in Finland.
- Factors such as **predominant HLA haplotype (HLA-DQ2 , HLA-DQ8)**, **timing of introduction of gluten into the diet**, differences in the **gliadin concentration of infant formulas**, and **interobserver variation in interpreting small intestinal biopsy findings** might explain differences in prevalence.
- Celiac disease is particularly prevalent in the **Punjab region** of northwest India, **where wheat rather than rice has, for many generations, been a staple of the diet**.
- The condition has been reported in blacks, Arabs, Hispanics, Israeli Jews, Sudanese of mixed Arab-black descent, and Cantonese and is particularly **high among the Saharawi population in northwest Africa**.



Celiac Disease

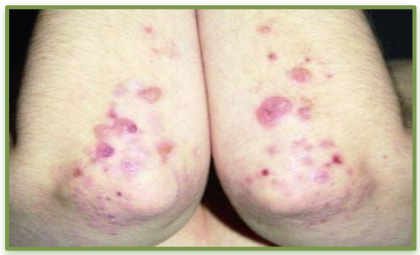
◄ Clinical Presentation:

In both children and adults, mild or asymptomatic cases are more common than the classic presentation of the disease.

Gastrointestinal Symptoms:

- Many adults present with GI symptoms including **diarrhea, steatorrhea, abdominal bloating, flatulence, and weight loss** similar to those seen in childhood celiac disease (failure to thrive, growth failure, delayed puberty, 2ndry hyperparathyroidism).
- Diarrhea often is **episodic**, **nocturnal**, **early morning**, and **postprandial diarrhea** are common.
- In certain instances, celiac disease might have non-specific presentation that **mimics small intestinal malabsorptive disorders**.

Extra-intestinal Symptoms:



- **Metabolic bone disease**
- **Infertility**
- **Neuropsychiatric disorders:** peripheral neuropathies, headache, ataxia, depression, irritability
- **Dermatologic associations:** dermatitis herpetiformis

Extraintestinal Manifestations of Celiac Disease

Manifestation	Probable Cause(s)
CUTANEOUS	
Ecchymoses and petechiae	Vitamin K deficiency; rarely, thrombocytopenia
Edema	Hypoproteinemia
Dermatitis herpetiformis	Epidermal (type 3) tTG autoimmunity
Follicular hyperkeratosis and dermatitis	Vitamin A malabsorption, vitamin B complex malabsorption
ENDOCRINOLOGIC	
Short stature, delayed puberty	Malnutrition, hypothalamic-pituitary dysfunction
Amenorrhea, infertility, impotence	Malnutrition, hypothalamic-pituitary dysfunction, immune dysfunction
Secondary hyperparathyroidism	Calcium and/or vitamin D malabsorption with hypocalcemia
HEMATOLOGIC	
Anemia	Iron, folate, or vitamin B_{12}, deficiency
Hemorrhage	Vitamin K deficiency; rarely, thrombocytopenia due to folate deficiency
Thrombocytosis, Howell-Jolly bodies	Hyposplenism
HEPATIC	
Elevated liver biochemical test levels **Autoimmune hepatitis**	Lymphocytic hepatitis Autoimmunity
MUSCULAR	
Atrophy	Malnutrition due to malabsorption
Weakness	Generalized muscle atrophy, hypokalemia
NEUROLOGIC	
Peripheral neuropathy	Deficiencies of vitamin B_{12} and thiamine; immune-based neurologic dysfunction
Ataxia	Cerebellar and posterior column damage
Demyelinating CNS lesions	Immune-based neurologic dysfunction
Seizures	Unknown
SKELETAL	
Osteopenia, osteomalacia, and osteoporosis	Malabsorption of calcium and vitamin D, secondary hyperparathyroidism, chronic inflammation
Osteoarthropathy	Unknown
Pathologic fractures	Osteopenia and osteoporosis

tTG, tissue transglutaminase.

Celiac Disease

◄ Celiac Disease Diagnosis:

- **Celiac serology tests** (initial testing) and **small intestinal biopsy via Esophagogastroduodenoscopy (EGD)** (confirmation) are the **most reliable** diagnostic tests for celiac disease.

- Most serological assay **specific** for diagnosis and monitoring of celiac disease is **IgA tTG assay** (initial test).

- HLA-based testing and/or a gluten challenge are options for patients **not consuming gluten**: (second-line testing after unclear initial evaluation).

Routine studies:

- **IgA tissue transglutaminase antibody (tTG IgA):**
  initial test, crucial part of celiac disease serology
  Widely available test with high specificity (≥ 96%)
  Risk of false negatives (e.g., in IgA deficiency, gluten-free diet)
- **Total IgA**
  Indicated for all patients because of the high prevalence of IgA deficiency in patients with celiac disease.

Endoscopy (EGD with small intestine biopsy):

- **Indications:** positive serology or high clinical suspicion despite negative serology (**confirmatory**)
- **Histological findings:** Intraepithelial lymphocytic infiltration, Crypt hyperplasia, Villous atrophy

◄ Management:

Treatment:

- **Following a gluten-free diet (GFD)** "Abstain from products containing wheat, rye, barley, or spelt".
- Recommend referral to a **nutritionist** to assist with GFD

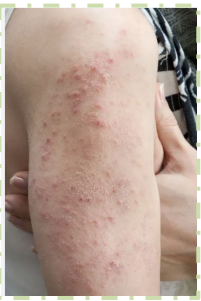
Refractory Celiac Disease:

- Refers to **persistent villus atrophy and malabsorption despite strict gluten avoidance.**
- In a subset of individuals who have a **clonal T-cell receptor rearrangement**, can be a **precursor to enteropathy associated T-cell lymphoma.**
- The condition manifests with one of three possible courses
  - Only partial improvement despite gluten-free diet
  - Initial improvement followed by relapse despite maintaining gluten-free diet
  - Nonresponsive celiac disease (no response to gluten-free diet)

Cases (DR's slides)

◄ Case study 1:

A 36-year-old female with history of **autoimmune thyroiditis** on 75 mcg of levothyroxine PO once daily presents to her endocrinologist for an urgent visit for **progressive fatigue**.
On further detailed history taking the patient complains of **new-onset non-bloody chronic diarrhea for the past 4 months** and **rash on her arms bilaterally** (see image). Patient denies recent traveling or sick contacts.
Work-up including serum TSH and free T4 is within normal limits. CBC is notable for new onset **microcytic anemia.** Iron panel with findings of decreased ferritin and serum iron; and increased total iron binding capacity (TIBC).



What is the answer?

A. Anti-tissue transglutaminase (anti-tTG) level
B. Diagnostic colonoscopy to rule out ulcerative colitis
C. Bone marrow biopsy to assess for myelodysplastic syndrome (MDS)
D. Stool culture and parasitology to rule out helminthic infections

◄ Case study 2:

A 22-year-old female medical student is seen by the student health clinic for **two-year history of abdominal pain and diarrhea** that has been recently progressive. The pain is described in the **mid abdomen and hypogastrium and is associated with diarrhea.** The abdominal pain and diarrhea is worse when the patient **sits for her final exams.** The patient denies melena, hematochezia, weight loss, rash, or arthralgia. Blood work including CBC, CMP and CRP is within normal limits.

The likely diagnosis of patient's presentation is:

A. Crohn's disease
B. Irritable bowel syndromes (IBS)
C. Celiac disease
D. Endometriosis

answers: Case study 1: A, Case study 2:B

◀ Case study 3:

A 53-year-old male with history of **CAD** on **aspirin** presents to his primary care provider's office with **epigastric pain for the past 2 months** that is made worse **with fasting.** The pain is associated with **early satiety and epigastric bloating without diarrhea or constipation.** Patient denies unintentional weight loss. The pain is described as **stabbing** and localized. Notable blood work is positive for iron deficiency anemia.

1-The likely diagnosis of patient's presentation is:

A. Acute pancreatitis
B. Mesenteric ischemia
C. Peptic ulcer disease
D. Irritable bowel syndrome

2-In the aforementioned clinical scenario, the best next step in management is:

A. Obtain an US abdomen
B. Order a CT scan of the abdomen and pelvis
C. Outpatient referral to cardiology for cardiac workup
D. Arrange for an upper endoscopy

answers: 1:C, 2:D

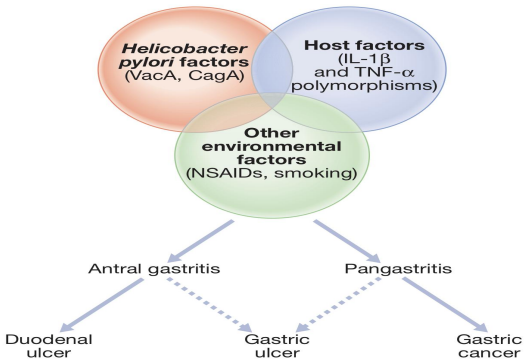
Peptic Ulcer Disease (PUD)

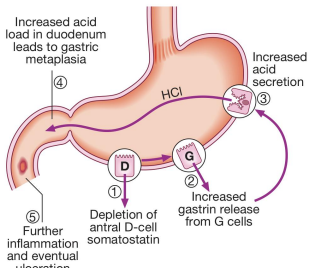
Definition

- The term 'peptic ulcer' refers to an ulcer in the lower oesophagus, **stomach** or **duodenum**, in the jejunum after surgical anastomosis to the stomach or, rarely, in the ileum adjacent to a Meckel's diverticulum.
- **What's the difference between an ulcer and erosion?**
  - Ulcers: Penetrate muscularis mucosae
  - Erosions: Don not penetrate muscularis mucosae
- Note: Gastric and duodenal ulcers coexist in 10% of patients and more than one peptic ulcer is found in 10–15% of patients.

◄ Etiology:

1) **Helicobacter pylori infection 80%[1] (most common)***
2) **NSAIDs (e.g. Aspirin):** inhibit prostaglandin production which is the major stimulant for mucus production that form the protective barrier, leads to impaired mucosal defenses.
3) **Zollinger–Ellison syndrome**
4) **Smoking (**Gastric more than duodenal)

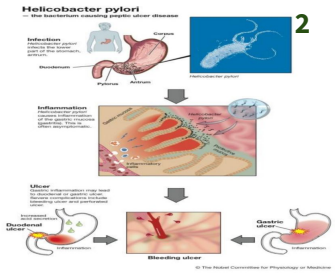


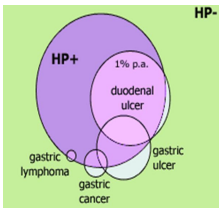


***The strongest evidence for the pathogenic role of H. pylori in peptic ulcer disease is the marked decrease in the recurrence rate of ulcers following the eradication of infection.**

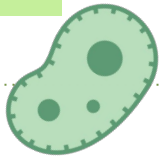
◄ Epidemiology & Transmission of H. pylori infection:

- **Socioeconomic status of the family is the main risk factor** as reflected by the level of sanitation and household hygiene. These infections are **probably acquired in childhood** by **person-to-person** contact (Fecal-oral route, Gastro-oral route or Oral-oral route)
- The vast **majority of colonised people remain healthy and asymptomatic**, and only a minority develop clinical disease.
- **95% of duodenal ulcer** patients and **85% of gastric ulcer** patients **are infected with H. pylori**. The remaining 15% of gastric ulcers are caused by NSAIDs.





◄ Microbiology of H. pylori:



❖ **Gram <u>negative spiral</u> organism with following characteristics:**
- Slow growing, **microaerophilic**
- Has multiple flagella at one end, which make it **highly motile**, allowing it to burrow and live beneath the mucus layer adherent to the epithelial surface.
- **Urease producing**

1) The most common human infection worldwide
2) Once H. pylori acquired it causes mucosal inflammation (Gastritis) that is often asymptomatic which leads to ulcer

Peptic Ulcer Disease (PUD) *cont'*

◄ Clinical presentation:

- Recurrent episodes of **epigastric pain** that is described as **dull**, sore, and gnawing. Although the most common cause of upper GI bleeding is PUD, the majority of those with ulcers do not bleed.
- **How to differentiate between gastric and duodenal ulcer?**
  - **Gastric ulcer:** pain is **G**reater after a meal, hence the weight loss.
  - **Duodenal ulcer:** pain **D**ecreases after a meal

EXTRA	Duodenal ulcer	Gastric ulcer
Pathogenesis	Caused by an increase in offensive factors (higher rates of basal and stimulated gastric acid secretion)	Caused by a decrease in defensive factors (gastric acid level is normal/low unless ulcer is pyloric or prepyloric)
H.pylori infection	90%	85%
Malignant potential	**Low** (malignancy is very rare)	**High** (5%-10% are malignant); therefore must **always be biopsied** and followed up to ensure healing.
Locations	Majority are 1-2 cm distal to pylorus (usually on posterior wall)	Type **I** (Most common): on **less**er curvature Type **II**: Gastric and duodenal ulcer **(Two)** Type **III**: **Pre**pyloric (within 2cm of pylorus) Type **IV**: Near esophagogastric junction **(Door)**
Age distribution	Occurs in younger patients (<40 y/o)	Occurs in older patients (>40 y/o)
Associated blood type	Type O	Type A
Risk factors	NSAIDs	Smoking
Other	- Eating usually relieves pain - Nocturnal pain is more common than in gastric	- Eating worsens pain - Complication rates are higher than those of duodenal ulcers. There is a higher recurrence rate with medical therapy alone

One is **Less**, **Two** has **Two**, **Three** is **pre**, **Four** is by the **door**

◄ Investigations:

1) Endoscopic biopsy is the **gold standard**
2) If **perforation** is suspected, perform upright **CXR** to evaluate air under the diaphragm or CT scan of the abdomen.
3) In **recurrent or refractory cases**, check serum **gastrin levels** to screen for Zollinger-Ellison syndrome.
4) Patients should be tested for H. pylori infection (discussed in next page)

Peptic Ulcer Disease (PUD) *cont'*

◀ Tests for H.pylori:

Non-invasive

1) **Serum antigen:** Detects IgG antibodies to H.pylori. Lacks specificity as it can't differentiate between active and treated disease. (Low diagnostic yield)
2) **Urea Breath Test (UBT):** H. pylori urease converts radiolabeled urea (C14 or C13) to CO2 and ammonia; this test detects CO2 formed from urea metabolism. Has high sensitivity and specificity. PPIs may cause false results.
3) **Stool antigen:** Detects H. pylori antigens in stool. Cost-effective initial test for H.pylori. Patients should be off PPIs for 2 weeks.

Both of **UBT** and **stool antigen** methods are good to measure the **effect of treatment**

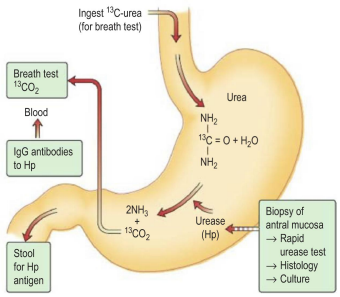


Figure 13.21 **Metabolism of urea by *Helicobacter pylori* (Hp).** The different tests available for the detection of *H. pylori* are shown.

Invasive (Endoscopic)

1) **Histology:** Specific but has a lot of false negatives (usually due to PPIs). H. pylori can be detected histologically on routine (Giemsa) stained sections of gastric mucosa obtained at endoscopy.
2) **Rapid urease test:** Cheap, quick, specific (>95%) with sensitivity of 85%. Can produce false negative if pt is on PPI. Gastric biopsies, usually antral unless additional material is needed to exclude proximal migration, are added to a substrate containing **urea and phenol red** . If H. pylori is **present**, the urease enzyme that the bacteria produce splits the urea to release ammonia, which raises the pH of the solution and causes a rapid colour change (**yellow to red**).
3) **Microbiological culture:** **GOLD standard,** This technique is typically used for patients with refractory H. pylori infection to identify the appropriate antibiotic regimen; routine culture is rare.
4) **PCR**

◀ Indications for H. Pylori eradication:

- **All** patients with proven ulcers who are **H. pylori-positive should be offered eradication** as primary therapy.
- **When is surgery indicated in PUD?**
  - In cases of emergency (**Perforation** or **Hemorrhage**)
  - Or elective (**Gastric flow obstruction**, **Persistent ulceration despite adequate medical therapy** or **Recurrent ulcer following gastric surgery**)

i 21.36 Indications for *Helicobacter pylori* eradication

Definite

- Peptic ulcer
- Extranodal marginal-zone lymphomas of MALT type
- Family history of gastric cancer
- Previous resection for gastric cancer
- *H. pylori*-positive dyspepsia
- Long-term NSAID or low-dose aspirin users
- Chronic (>1 year) PPI users
- Extragastric disorders:
  - Unexplained vitamin B_{12} deficiency*
  - Idiopathic thrombocytopenic purpura*
  - Iron deficiency anaemia* (see text)

Not indicated

- Gastro-oesophageal reflux disease
- Asymptomatic people without gastric cancer risk factors

*If *H. pylori*-positive on testing.
(MALT = mucosa-associated lymphoid tissue; NSAID = non-steroidal anti-inflammatory drug; PPI = proton pump inhibitor)

Management of PUD

◀ European Helicobacter Pylori study group guidelines

- **Triple therapy** with **omeprazole** (20 mg twice daily), **amoxicillin** (1 g twice daily), and **clarithromycin** (500 mg twice daily) **for 7 to 14 days.**
- A longer duration of treatment (14 versus 7 days) may be more effective in curing infection but this remains controversial. more than 14 days is not recommended

◀ Treatment regimens

Regimen[1]	comment
• (Triple therapy) **PPI**, **amoxicillin** 1 gm, **clarithromycin** 500 mg all twice daily for 7-14 days.	• 1st line treatment [2] regimen of choice (can substitute metronidazole 500 mg twice daily for amoxicillin but only in penicillin allergic patients) metronidazole has bad taste.
• (Quadruple therapy) **Bismuth** 525 mg, **metronidazole** 500 mg, **tetracycline** 500 mg all four times daily with **PPI** twice daily for 7-14 days. Please Make Tummy Better	• Can be used as 1st line treatment (7-14 days) but generally reserved for retreatment (14 days) Quadruple therapy can be used when there is resistance to clarithromycin
• PPI, amoxicillin 1 gm, metronidazole 500 mg all twice daily for 14 days	• 1st line treatment in macrolide allergic patients and retreatment if failed 1st line treatment of choice

Treatment Regimen	Duration (days)	Eradication Rate (%)
Omeprazole 20 mg BID + **Amoxicillin** 1 g BID + **Clarithromycin** 500 mg BID	14	80 - 86
Lansoprazole 30 mg BID + **Amoxicillin** 1 g BID + **Clarithromycin** 500 mg BID	10 - 14	86
Bismuth subsalicylate 525 mg QID + **Metronidazole** 250 mg QID + **Tetracycline** 500 mg + **PPI**	PPI for another 14 taken OD or BID)	80

OD = Once a day. | **BID** = twice a day. | **QID** = 4 times a day.

1- all of them are 1st line therapy. But it depends on the region.

2- According to Dr this is **NOT** the first line therapy in saudis because of high rates (>20%) of clarithromycin resistance!
It is the first line of treatment if there is no clarithromycin resistance.

SO Bottom line, what is the first line in our region? (Quadruple therapy) **Bismuth**, **metronidazole**, **tetracycline**, **PPI for 14 days**

◀ Clarithromycin-resistant bacteria

- Pooled data from 20 studies involving 1975 patients treated with standard triple therapy showed an eradication rate of 88% in clarithromycin-sensitive strains vs 18% in clarithromycin-resistant strains.
- **A 10-day sequential regimen**
  - **First 5 days: PPI** and **amoxicillin** 1 g, each given twice daily.
  - **second 5 days: PPI, clarithromycin 500 mg,** and **tinidazole** 500 mg, each given twice daily.
- Improved overall eradication rates compared with standard PPI triple therapy (89% vs. 77 %), but was particularly better for clarithromycin-resistant bacteria (**89%** vs. 29%).

◀ Concomitant therapy[1]

- Novel regimen which was proved successful in the presence of clarithromycin resistance. This is a **4-drug regimen** containing a **PPI** ,**clarithromycin** (500 mg, b.i.d.), **amoxicillin** (1 g, b.i.d.) and **metronidazole** (500 mg, b.i.d.) which are all given for the entire duration of therapy.

		Eradicated		
Analysis Population	N	N	Percent	95% CI for Percent Eradicated
Intention to Treat (ITT)	1463			
14-day Standard	488	401	82.2%	78.5%, 85.5%
5-day Concomitant	489	360	73.6%	69.5%, 77.5%
10-day Sequential	486	372	76.5%	72.5%, 80.2%

◀ Rescue therapy[2]:

Regimen	comment
• **PPI**, **levofloxacin** 250 to 500 mg, **amoxicillin** 1 gm all twice daily **for 14 days**	• "Rescue" therapy for those failing **two course** of above treatments
• **PPI**, **rifabutin** 150 mg, **amoxicillin** 1 gm all twice daily for 14 days	• Alternative "rescue" therapy
• Based on culture	• If all medications listed above didn't work then we do culture. Why usually we don't do culture? because it takes time, we usually do UBT, endoscopy and routine histopathology

- Poor compliance with medication, and patient demographics such as younger age, smoking, prior antibiotic use, and underlying condition (functional dyspepsia vs. peptic ulcer).
- Some patients don't continue their therapy course, why?
  - They think they are already cured (but actually it was PPI relief)
  - They want to stop because of therapy's side effects

1- first line along with quadruple therapy in Saudi Arabia (if both are choices in the exam, choose quadruple)

2- When some patients had resistance for sequential therapy, they came up with rescue therapy.

Peptic Ulcer Disease (PUD) *cont'*

◀ Complications of PUD:

	Clinical findings	Diagnostic studies	Management	Other
Perforation	**Acute, severe abdominal pain**, signs of peritonitis, hemodynamic instability	**Upright CXR (free air under diaphragm),** CT scan is the most sensitive for perforation (detects free abdominal air)	**Emergency surgery** to close perforation and perform definitive ulcer operation (such as highly selective vagotomy or truncal vagotomy/pyloroplasty)	Can progress to sepsis and death if untreated
Gastric outlet obstruction	**Nausea/vomiting** (poorly digested food), epigastric fullness/early satiety. weight loss	**Barium swallow and upper endoscopy**; saline load test (empty stomach with as nasogastric tube, add 750mL saline, aspirate after 30min - test is positive if aspirate >400mL	**Initially, nasogastric suction**; replace electrolyte/ volume deficits; supplement nutrition if obstruction is long standing. **Surgery is eventually necessary in 75% of patients**	Most common with duodenal ulcers and type III gastric ulcers
GI bleeding	Bleeding may be slow (leading to **anemic symptoms**) or can be rapid and severe (leading to shock)	Stool guaiac, **upper GI endoscopy** (diagnostic and therapeutic)	**Resuscitation**; diagnose site of bleed via endoscopy and treat; **perform surgery for acute bleeds** that require transfusion of 6U or more of blood	**PUD is the most common cause of upper GI bleeding**

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