

# Midblock Pathology Summary

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**Source:**

**Males doctor slides and notes.**

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# GERD



## Gastroesophageal reflux disease (GERD):

Symptoms OR mucosal damage produced by the abnormal reflux of gastric contents into the esophagus.

### Physiologic GERD:

- Postprandial
- Short lived
- Asymptomatic
- No nocturnal symptoms

### Pathologic GERD:

- Symptoms
- Mucosal injury
- Nocturnal symptoms

## Pathophysiology:

- Abnormal lower esophageal sphincter: **Hiatal hernia**, frequent relaxation, hypotensive LES, food (alcohol) and medications.
- Increase abdominal pressure: Obesity, pregnancy and increased gastric volume.

## Clinical manifestations:

- Typical symptoms: Retrosternal heartburn and Regurgitation.
- Atypical symptoms: Coughing, chest pain, and wheezing.

## Diagnosis:

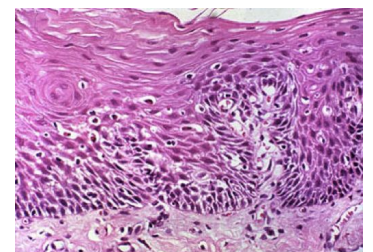
- Classic symptoms → clinically.
- Endoscopy → alarm sign and symptoms and failed medication trial.

## Complications:

Erosive esophagitis	Esophageal stricture	Barrett's Esophagus
40-60% of GERD symptoms	Narrowing due to healing of erosive esophagitis	<ul style="list-style-type: none"><li>- <b>Intestinal metaplasia</b> → abnormal columnar cells with goblet cells replace squamous cells.</li><li>- Can progress to <b>dysplasia and adenocarcinoma</b>.</li></ul>

## Pathological features of reflux esophagitis:

- Eosinophils and neutrophils.
- Elongation of lamina propria papillae.
- Basal zone hyperplasia.



# Ulcers



## Acute peptic ulcer

### Pathophysiology

- **Acute gastritis: NSAIDs or Alcohol**
- **Complication of severe stress:**
  - Severe burns (curlings)
  - Major trauma (cushing's ulcer)
  - CVA (cushing's ulcer)
- **Hyperacidity** zolinger-elison syndrome

**Morphology:** small and multiple

## Chronic peptic ulcer

- Mostly occurs in first part of duodenum or stomach 4:1 ratio.
- Esophagus → due to GERD.

	Gastric Ulcer	Duodenal ulcer
<b>Pathogenesis</b>	Disruption of DEFENSE 1- Mucus-HCO <sub>3</sub> <sup>-</sup> - by: <b>Bile reflux</b> 2- surface epithelial - by: <b>NSAIDS</b> (PG) or <b>H.pylori</b> (cytotoxins)	- <b>H. Pylori infect stomach</b> <ul style="list-style-type: none"> <li>• <b>Increase acid secretion.</b></li> <li>• Secretion reaches duodenum and cause metaplasia.</li> <li>• H. Pylori colonies metaplastic foci.</li> </ul>
<b>Location</b>	Antrum	First portion of duodenum
<b>FOOD</b>	Aggravate	Relieve
<b>Time of pain</b>	Shortly after food	2-3 hours after food
<b>vomiting</b>	Vomiting may occur	No vomiting
<b>Awaken at night</b>	No	Yes

### Symptoms

- Iron deficiency anemia due to bleeding.
- Gnawing or burning sensation.
- Frank hemorrhage.

### Morphology

- Ulcer is round to oval & **Punched out margin** (unlike cancer is heaped up)
- **Microscopy:**
  - Necrotic tissue.
  - Polymorph exudate.
  - Fibrous tissue.

# Diarrhea

- 3 or more loose or liquid stools per day
- Abnormally high fluid content of stool (>200-300 g/day)
- Normal osmolality is equal to serum 290 mosm/kg
- Major osmotes are Na<sup>+</sup>, K<sup>+</sup>, Cl<sup>-</sup>, and HCO<sub>3</sub><sup>-</sup>

## Classifications (Duration):

- Acute → 2 weeks
- Persistent → 2-4 weeks
- Chronic → 4 weeks in duration

	Secretory	Osmotic	Exudative	Motility-related
Osmotic gap	Normal <100 mosm/kg	High >125		
Fasting effect	No response	Fasting helps	Persists on fasting	
Stool	High stool output	Not massive	Blood and pus in stool	
Causes	<b>Increased secretion</b> due to: - <b>Bacterial toxin</b> (E. coli, cholera) - Zollinger elison tumors	<b>Poorly absorbed substance</b> that exert osmotic effect. 1- <b>Malabsorption</b> 2- laxatives	<b>Outpouring of blood</b> or mucus from inflamed or ulcerated mucosa. 1- inflammatory bowel disease 2- invasive infection 3- colon cancer	<b>Rapid movement</b> of food through intestine - <b>IBS</b> - Diabetic diarrhea - Hyperthyroid diarrhea

## Aetiology

Acute	Chronic
- <b>Infections:</b> viral gastroenteritis (rotavirus) - Food poisoning - Drugs - <b>Antibiotic-Associated Diarrhea:</b> Clostridium difficile	- <b>Infection:</b> Giardia lamblia, AIDS → cause other infections that cause diarrhea (Aids have low immunity) - Post-infectious why? Malabsorption lactose intolerance - Malabsorption - IBD - Endocrine disease - Colon cancer - IBS

## Complications

- 1- Dehydration
- 2- Electrolyte imbalance
- 3- Metabolic acidosis
- 4- Malnutrition

## Evaluation

<u>Acute</u>		<u>Chronic</u>	
Fecal leukocytes		Stool analysis ova, parasites	
Non present	Present	+ve	-ve
<b>Non-Inflammatory diarrhea</b> Suggests a small bowel source or colon but <b>without</b> mucosal injury.	<b>Inflammatory diarrhea</b> Suggests <b>colonic mucosa damage</b> caused by invasion: <ul style="list-style-type: none"> <li>• Shigellosis, Salmonellosis, Campylobacter or Yersinia infection, amebiasis).</li> <li>• Toxin (C difficile, E coli).</li> <li>• <b>Inflammatory bowel diseases.</b></li> </ul>	Infection	-ve Stool fat test (normal <20%) -ve Secretory, Non infectious and Inflammatory diarrhea
			+ve Malabsorption

# Malabsorption

## Pathophysiology

Malabsorption= inadequate digestion **Or** small intestine abnormalities.

Inadequate Digestion			Small Intestine abnormalities		
<b>Stomach</b> - postgastrectomy	<b>Pancreases</b> - Deficiency of pancreatic lipase - chronic pancreatitis - Cystic fibrosis - Pancreatic resection	<b>Bile</b> - Obstructive jaundice - Terminal ileal resection	<b>Mucosa</b> - Celiac disease - Tropical sprue - Whipple disease - Giardiasis	<b>Inadequate small intestine</b> - Intestinal resection - Crohn's disease	<b>Lymphatic obstruction</b> - Intestinal lymphangiectasia - Malignant Lymphoma

## Clinical Features

- **STEATORRHEA:** fat in stool. Soft yellowish, greasy stool.
- Growth retardation.
- Weight loss with similar diet.

Other features depend on deficient nutrient:

- **Protein** → muscle wasting, edema.
- **B12, folate, iron** → Anemia, fatigue.
- **Vit. D, calcium** → muscle cramp, osteomalacia, osteoporosis.
- **Vit K** → bleeding tendencies.

## Diagnosis

- Fecal fat study
- Blood test
- Stool study
- Endoscopy, biopsy

Celiac Disease	Lactose intolerance
<ul style="list-style-type: none"> <li>● Immune reaction to <b>gliadin fraction of gluten protein</b> (protein found in wheat)</li> <li>● Usually diagnosed in childhood -mid adult</li> <li>● Patients have raised antibody to gluten</li> <li>● <b>Class II HLA (DQ2 or DQ8)</b>, and to a lesser extent DQ8 (haplotype DR-4)</li> <li>● GI symptoms, depending on age (Childhood: Inadequate rate of weight gain, Young adult: Anemia)</li> </ul>	Lactose → Lactase (at brush border of enterocytes) → glucose + galactose <ul style="list-style-type: none"> <li>● Lactose intolerance: low or absent enzyme lactase.</li> <li>● Types:                             <ul style="list-style-type: none"> <li>○ Congenital: rare.</li> <li>○ Genetically programmed progressive loss.</li> <li>○ Transient: due to mucosal injury, infection, allergy. (viral gastroenteritis)</li> </ul> </li> </ul>

## Histology

- Fattened mucosa with villous atrophy
- Crypt hyperplasia
- Lymphocytosis



## Clinical features

- bloating
- Abdominal discomfort
- Flatulence

## Diagnosis

- Stool → increase fat
- Serology ( Anti-TTG-IgA)
- Biopsy; villous atrophy
- Improve symptoms on gluten withdrawal (wheat, barley, rye)

## Diagnostic method

- Improve symptoms on lactose free diet.
- H2 breath test after administer of oral dose of lactose.

## Complications

- Osteopenia, osteoporosis
- Infertility in women
- Short stature, anemia, malignancies, (Intestinal T-cell lymphoma)  
 - 10-15% of developing GI lymphoma

# Inflammatory bowel disease

	Crohn's Disease	Ulcerative COLITIS
Etiology	—	<ul style="list-style-type: none"> <li>Unknown</li> <li>Antibodies cross-react, Intestinal epithelium and some types of E. coli</li> </ul>
Location	<ul style="list-style-type: none"> <li><b>Mostly ileum</b> (could be anywhere)</li> <li>commonly perianal lesions (abscess, fistula, skin tags)</li> </ul>	<ul style="list-style-type: none"> <li><b>Rectum and colon</b></li> <li>Usually start in rectum and progress to colon (<b>without</b> skip) chronic (remission and relapse)</li> <li><b>ileum never involved</b></li> </ul>
Clinical features	<p>Mostly young adults</p> <ul style="list-style-type: none"> <li><b>Acute:</b> fever, diarrhea, right lower quadrant pain (appendicitis like)</li> <li><b>Chronic:</b> remission and relapse</li> </ul>	<p>Chronic (remission and relapse)</p> <p>In relapse:</p> <ul style="list-style-type: none"> <li>Fever &amp; leukocytosis</li> <li>Abdominal pain &amp; bloody diarrhea</li> <li>Mucous in stool</li> </ul>
Gross	<ul style="list-style-type: none"> <li>Segmental involvement (<b>Skip areas</b>)</li> <li>Marked fibrosis → narrow lumen</li> <li><b>Fissure</b> (ulcers look like knife stabs)</li> <li><b>Fistula</b></li> <li>Cobblestone effect (ulcer+edematous mucosa)</li> <li>Creeping fat</li> </ul>	<ul style="list-style-type: none"> <li>Mainly involves mucosa</li> <li>Diffuse hyperemia (a-lot of blood in vessels)</li> <li>Superficial ulcerations</li> <li>Regenerated mucosa show inflammatory pseudopolyps</li> </ul>
Microscopic	<ul style="list-style-type: none"> <li>Transmural</li> <li>Distortion of crypts</li> <li>Epithelioid granuloma</li> </ul>	<ul style="list-style-type: none"> <li>Restricted to mucosa</li> <li><b>Active phase:</b> crypt abscess (neutrophils)</li> <li><b>Chronic phase:</b> crypt atrophy</li> </ul>
Complications	<p>1- intestinal obstruction due to fibrosis</p> <p>2- Fistula</p> <ul style="list-style-type: none"> <li>ileum with colon</li> <li>Enterovesical (SI with bladder)</li> <li>Enterovaginal (fecal-vaginal discharge)</li> </ul> <p>3- Extraintestinal: Arthritis &amp; uveitis</p> <p>4- Slight risk of carcinoma (less than UC)</p>	<p><b>Acute phase:</b></p> <ul style="list-style-type: none"> <li>Bleeding</li> <li><b>Toxic megacolon</b> (dilation + obstruction)</li> </ul> <p><b>Chronic UC:</b> increased risk for Carcinoma, High-grade dysplasia increased risk of carcinoma<sup>1</sup></p> <p><b>Extraintestinal:</b> (more common in UC than Crohn's)</p> <ul style="list-style-type: none"> <li>Arthritis</li> <li>Uveitis</li> <li>Skin lesion (Pyoderma gangrenosum)</li> <li><b>Sclerosing pericholangitis:</b> fibrosis around bile duct → obstructive jaundice</li> </ul>

1- Indication for colectomy

# Polyps and tumors

Non-neoplastic polyps				
Hyperplastic	Hamartomatous (resemble origin)		Inflammatory polyps	Lymphoid polyps
	Juvenile	Peutz-Jehgers		
<ul style="list-style-type: none"> <li>- Sawtooth surface</li> <li>- Star shaped crypt</li> <li>- Well-formed glands</li> <li>- Differentiated goblet cells</li> <li>- &gt;50% rectosigmoid</li> </ul>	<ul style="list-style-type: none"> <li>- malformed gland and lamina propria</li> <li>- In adult called <b>retention polyps</b></li> </ul>	<ul style="list-style-type: none"> <li>- rare, autosomal dominant</li> <li>- Pigment around lip, oral mucosa, genitalia</li> <li>- ↑ risk of carcinoma of pancreas, breast lung, ovary &amp; uterus</li> </ul>	<ul style="list-style-type: none"> <li>- Longstanding IBD</li> <li>- Ulcerative colitis</li> <li>- Exuberant reparative response</li> <li>- pseudopolyps</li> </ul>	<ul style="list-style-type: none"> <li>- Peyer's patch</li> </ul>

## Adenoma (neoplastic polyp)

- Mainly in large bowel
- Epithelial proliferation and dysplasia
- Types:
  - **Tubular:** <25% villous polyps
    - Most common (75%)
  - **Villous:** >50% villous polyps
    - Least common, most dangerous
    - Rectal bleeding or anemia
  - **Tubulovillous:** 25%-50% villous

## Gene alteration in carcinoma pathway

- **APC loss:** hyperproliferation of normal epithelium
- **K-ras mutation:** early adenoma to intermediate adenoma
- **p53:** leads to cancer

## Familial Polyposis Syndrome (FPC)

- Defect of APC gene (tumor suppressor)
- On long arm of chromosome 5 (5q21)
- Many neoplastic polyps (500-2500)
- 100% colorectal cancer by midlife

## Chance of carcinoma in neoplastic polyps is related to:

- **Size** of polyps
- Proportion of **villous** structure
- Presence of **dysplasia**

## Gardener's Syndrome

- Polyposis coli
- **Osteomas**
- Epidermal cyst
- fibromatosis

## Turcot syndrome

- Polyposis coli
- **gliomas**
- fibromatosis

## Adenocarcinoma (large intestine)

- 98% of all colon cancer
- Predisposing factors:
  - IBD, adenomas, polyposis coli
  - High fat, low fiber diet

## Pathogenesis (2 pathways)

- Stepwise accumulation of mutations in tumor suppressor genes and oncogenes
- Mutation in DNA mismatch repair genes (MSH2, MSH6, mlh1, PMS2) →(HNPCC)

## Morphology

- **Left-sided:** encircling, early symptoms, bleeding.
- **Right-sided:** polypoid, fungating, iron deficiency anemia.
- If closer to anus: PR bleeding, feeling of incomplete defecation.

## Tumor markers

- **CEA & CA19-9;** to assess **recurrence**
- Found also in non-neoplastic conditions

## Malignant small intestine neoplasms

### Carcinoid Tumors

- Neoplasms of endocrine cells
- Carcinoid syndrome: (serotonin)
  - Flushing, asthma-like wheezing, right sided HF

### Lymphoma

- Low-grade MALT lymphoma
- High-grade non hodgkin's B-cell lymphoma
- Burkitt's lymphoma in ileocecal region