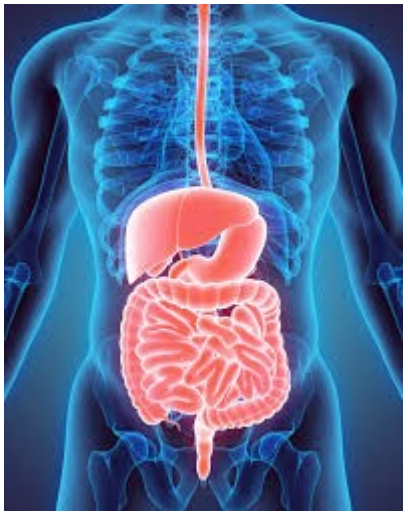
PATHOPHYSIOLOGY OF GASTROINTESTINAL SYSTEM



Course Name: Pathophysiology

Course Code: 0520300

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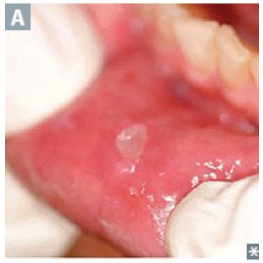
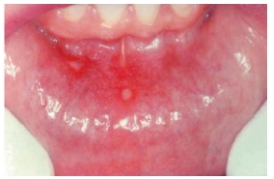
A-ORAL INFLAMMATORY LESIONS

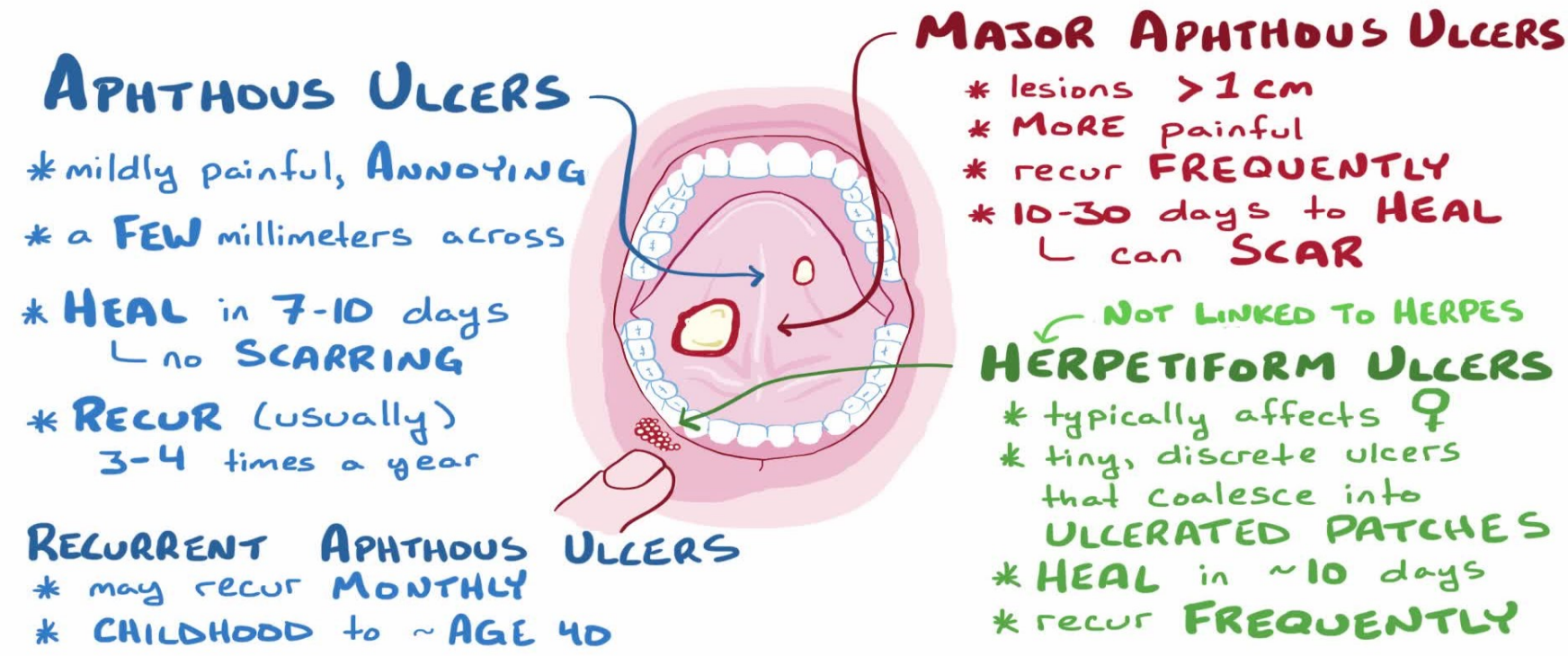
1- Aphthous Ulcers (Canker Sores)





- These common superficial mucosal ulcerations affect up to 40% of the population.
- They are more frequent in the first 2 decades of life, extremely painful, and often recur.
- Symptoms may include sensations such as **burning, itching, or stinging**.
- Although the cause of aphthous ulcers is unknown, they tend to be familial and may be associated with celiac disease, inflammatory bowel disease, Behçet disease and HIV/AIDS.
- Ulcers can be solitary or multiple; typically, they are shallow, with a hyperemic base covered by a thin exudate and rimmed by a narrow zone of erythema. In most cases they resolve spontaneously in 7 to 10 days but can recur.

Types of Aphthous ulcers



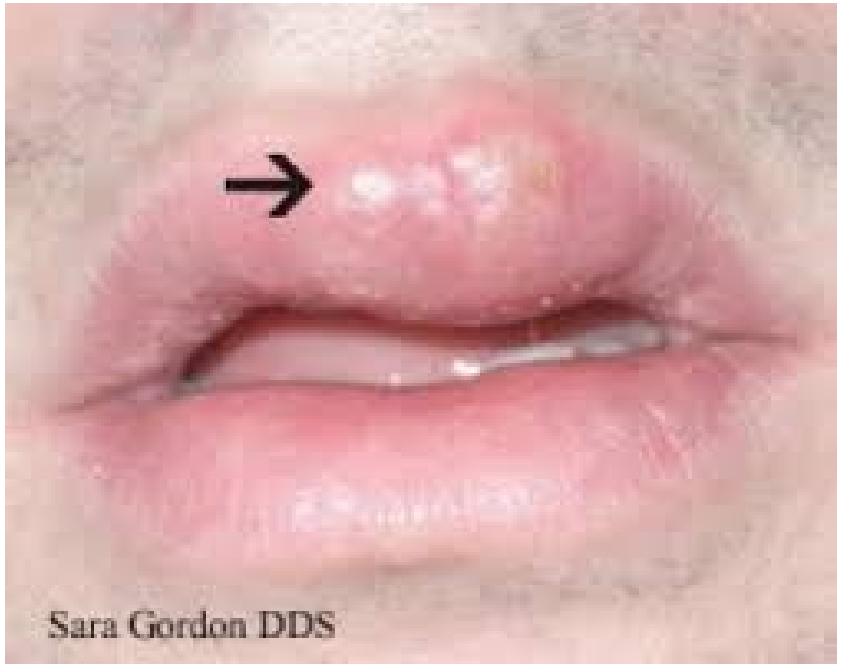
wikimedia.org/wiki/File:Aphthous_Ulcers.webm

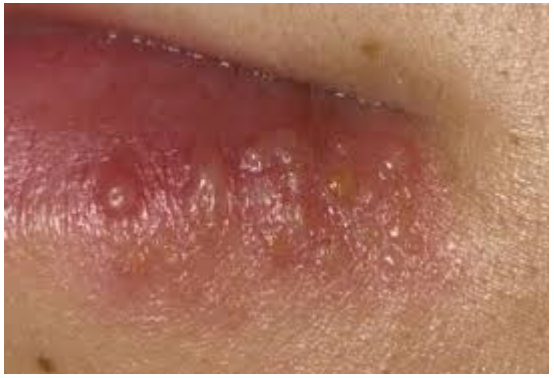
A- ORAL INFLAMMATORY LESIONS

2-Herpes Simplex Virus Infections

- Herpes simplex virus 1 and 2 (HSV-1 and HSV-2), causes a self-limited infection.
- Both HSV-1 (which produces most cold sores) and HSV-2 (which produces most genital herpes) are contagious and incurable.
- HSV is passed from person to person by saliva (either directly, or by drinking from the same glass or cup) or by skin contact.
- Symptoms of herpes simplex virus infection include watery blisters in the skin or mucous membranes of the mouth, lips, nose or genitals.
- Most adults harbor latent HSV-1, and the virus can be reactivated, resulting in a so-called “cold sore” or recurrent herpetic stomatitis.
- Factors associated with HSV reactivation include trauma, allergies, exposure to ultraviolet light and extremes of temperature, upper-respiratory tract infections, pregnancy, menstruation, and immunosuppression.
- Although lesions typically resolve within 7 to 10 days, they can persist in immunocompromised patients, who may require systemic anti-viral therapy.

2-Herpes Simplex Virus Infections





A- ORAL INFLAMMATORY LESIONS

3- Oral Candidiasis (Thrush)

- **Candidiasis is the most common fungal infection of the oral cavity.** *Candida albicans* is a normal component of the oral flora and only produces disease under unusual circumstances.

Predisposing factors include the following:

- Immunosuppression
- The specific strain of *C. albicans*
- The composition of the oral microbial flora (microbiota)

- ✓ Broad-spectrum antibiotics that alter the normal microbiota can promote oral candidiasis.
- ✓ The three major clinical forms of oral candidiasis are pseudomembranous, erythematous, and hyperplastic.
- ✓ The pseudomembranous form is most common and is known as *thrush.* This condition is characterized by a superficial, curdlike, gray to white inflammatory membrane composed of matted organisms enmeshed in a fibrinosuppurative exudate that can be readily scraped off to reveal an underlying erythematous base.

B- REFLUX ESOPHAGITIS

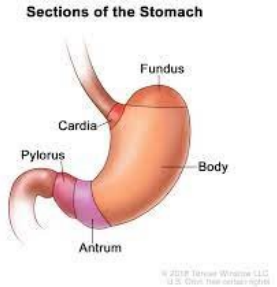
- **Reflux of gastric contents into the lower esophagus is the most frequent cause of esophagitis.**
- The associated clinical condition is termed *gastroesophageal reflux disease (GERD).*
- High lower esophageal sphincter (LES) tone protects against reflux of acidic gastric contents, which are under positive pressure.
- Gastroesophageal reflux is a condition caused by the **backflow of stomach contents into the esophagus.**
- Conditions that decrease lower esophageal sphincter (LES) tone or increase abdominal pressure contribute to GERD and include alcohol and tobacco use, obesity, central nervous system depressants, pregnancy, hiatal hernia, delayed gastric emptying, and increased gastric volume. In many cases, no definitive cause is identified.
- **Signs and Symptoms:** Transient decreases in LES tone. Commonly presents as heartburn, regurgitation, dysphagia. May also present as chronic cough, hoarseness (laryngopharyngeal reflux). Associated with asthma.
- Complications include erosive esophagitis, strictures, and Barrett esophagus (metaplasia).

C- STOMACH DISEASES

1- Acute and chronic gastritis

- Gastritis is a mucosal inflammatory process. When inflammatory cells are absent or rare, the term *gastropathy* can be applied.
- The spectrum of acute gastritis ranges from asymptomatic disease to mild epigastric pain, nausea, and vomiting.
- Causative factors include any agent or disease that interferes with gastric mucosal protection.
- Acute gastritis can progress to gastric ulceration.
- The most common cause of chronic gastritis is *H. pylori* infection; most remaining cases are caused by NSAIDs, alcohol, or *autoimmune gastritis.*
- *H. pylori* gastritis typically affects the antrum and is associated with increased gastric acid production.
- *H. pylori* gastritis induces mucosa-associated lymphoid tissue (MALT) that can give rise to B-cell lymphomas (MALTomas).
- *Autoimmune gastritis* causes atrophy of the gastric body oxyntic glands, which results in decreased gastric acid production, antral G-cell hyperplasia, achlorhydria, and vitamin B12 deficiency. Anti–parietal cell and anti–intrinsic factor antibodies are typically present.

C- STOMACH DISEASES
2- **Helicobacter pylori Gastritis**



- These spiral-shaped or curved bacilli are present in gastric biopsy specimens from almost all patients with duodenal ulcers and a majority of those with gastric ulcers or chronic gastritis.
- Acute *H. pylori* infection is subclinical in most cases; rather, it is the chronic gastritis that ultimately brings the afflicted person to medical attention.
- *H. pylori* infection most often presents as an *antral gastritis with increased acid production.*
- The increased acid production may give rise to peptic ulcer disease of the duodenum or stomach.
- While in most cases *H. pylori* gastritis is limited to the antrum, in some individuals it progresses to involve the gastric body and fundus, resulting in reduced parietal cell mass and acid secretion.

C- STOMACH DISEASES

Helicobacter pylori Gastritis

Four features are linked to *H. pylori* virulence:

1-Flagella, which allow the bacteria to be motile in viscous mucus

2- *Urease,* which generates ammonia from endogenous urea, thereby elevating local gastric pH around the organisms and protecting the bacteria from the acidic pH of the stomach

3- *Adhesins,* which enhance bacterial adherence to surface foveolar cells (surface mucus cells)

4- *Toxins,* such as that encoded by cytotoxin-associated gene A *(CagA),* that may be involved in ulcer or cancer development.

→ These factors allow *H. pylori* to create an imbalance between gastroduodenal mucosal defenses and damaging forces that overcome those defenses.

C- STOMACH DISEASES

3- Peptic ulcer diseases

	Gastric ulcer	Duodenal ulcer
PAIN	Can be greater with meals—weight loss	Decreases with meals—weight gain
H PYLORI INFECTION	~ 70%	~ 90%
MECHANISM	↓ mucosal protection against gastric acid	↓ mucosal protection or ↑ gastric acid secretion
OTHER CAUSES	NSAIDs	Zollinger-Ellison syndrome
RISK OF CARCINOMA	↑	Generally benign
	Biopsy margins to rule out malignancy	Not routinely biopsied

D- DISORDERS OF THE INTESTINES AND COLON

1- Irritable Bowel Syndrome (IBS)

Recurrent abdominal pain associated with ≥ 2 of the following:

→ Related to defecation

→ Change in stool frequency

→ Change in form (consistency) of stool

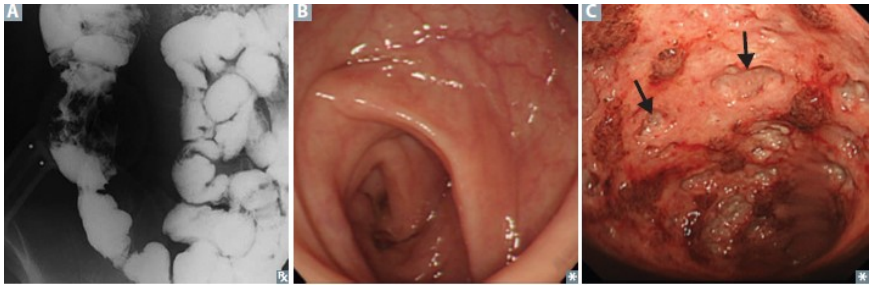
- No structural abnormalities. Most common in middle-aged females. Chronic symptoms may be diarrhea-predominant, constipation-predominant, or mixed.
- Left lower quadrant abdominal pain is often brought on or made worse by eating. Passage of stool or flatus may provide some relief.
- Pathophysiology is multifaceted.
- May be associated with fibromyalgia and mood disorders (anxiety, depression).
- First-line treatment is lifestyle modification and dietary changes.

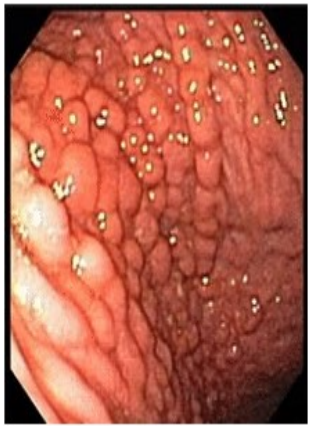
D- DISORDERS OF THE INTESTINES AND COLON

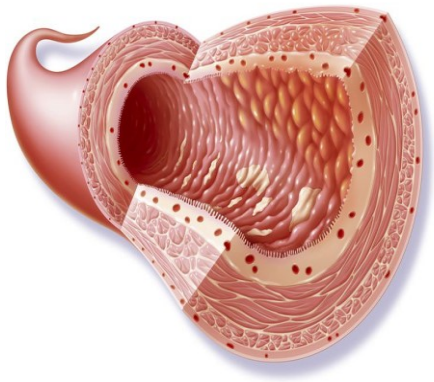
2- Inflammatory Bowel Disease (IBD)

- The term inflammatory bowel disease includes the conditions: Crohn's disease and ulcerative colitis
- Both of these diseases are characterized by chronic inflammation of various regions of the G.I. tract
- The pathogenesis of IBD involves genetic susceptibility, failure of immune regulation, and triggering by microbial flora.
- Chron's diseases: The inflammatory lesions are present with a "skip" pattern that intersperses areas of inflammation with normal looking, non-inflamed tissue.
- Ulcerative colitis: pattern of inflammation is continuous throughout the affected areas.

	Crohn disease	Ulcerative colitis
LOCATION	Any portion of the GI tract, usually the terminal ileum and colon. Skip lesions, rectal sparing.	Colitis = colon inflammation. Continuous colonic lesions, always with rectal involvement.
GROSS MORPHOLOGY	Transmural inflammation → fistulas. Cobblestone mucosa, creeping fat, bowel wall thickening ("string sign" on small bowel follow-through A), linear ulcers, fissures.	Mucosal and submucosal inflammation only. Friable mucosa with superficial and/or deep ulcerations (compare normal B with diseased C). Loss of haustra → "lead pipe" appearance on imaging.
MICROSCOPIC MORPHOLOGY	Noncaseating granulomas, lymphoid aggregates.	Crypt abscesses/ulcers, bleeding, no granulomas.
COMPLICATIONS	Malabsorption/malnutrition, colorectal cancer (↑ risk with pancolitis).	
	Fistulas (eg, enterovesical fistulae, which can cause recurrent UTI and pneumaturia), phlegmon/abscess, strictures (causing obstruction), perianal disease.	Fulminant colitis, toxic megacolon, perforation.
INTESTINAL MANIFESTATION	Diarrhea that may or may not be bloody.	Bloody diarrhea (usually painful).
EXTRAINTESTINAL MANIFESTATIONS	Rash (pyoderma gangrenosum, erythema nodosum), eye inflammation (episcleritis, uveitis), oral ulcerations (aphthous stomatitis), arthritis (peripheral, spondylitis).	
	Kidney stones (usually calcium oxalate), gallstones. May be ⊕ for anti-*Saccharomyces cerevisiae* antibodies (ASCA).	1° sclerosing cholangitis. Associated with MPO-ANCA/p-ANCA. Myeloperoxidase Perinuclear anti-neutrophil cytoplasmic antibodies
TREATMENT	Glucocorticoids, azathioprine, antibiotics (eg, ciprofloxacin, metronidazole), biologics (eg, infliximab, adalimumab).	5-aminosalicylic acid preparations (eg, mesalamine), 6-mercaptopurine, infliximab, colectomy.
DISEASE ACTIVITY	Fecal calprotectin used to monitor activity and distinguish from noninflammatory diseases (irritable bowel).	







Crohn's disease –> **cobblestone" appearance** to the mucosa