PEPTIC ULCER DISEASE

DR SHIMOLI CONRAD A.

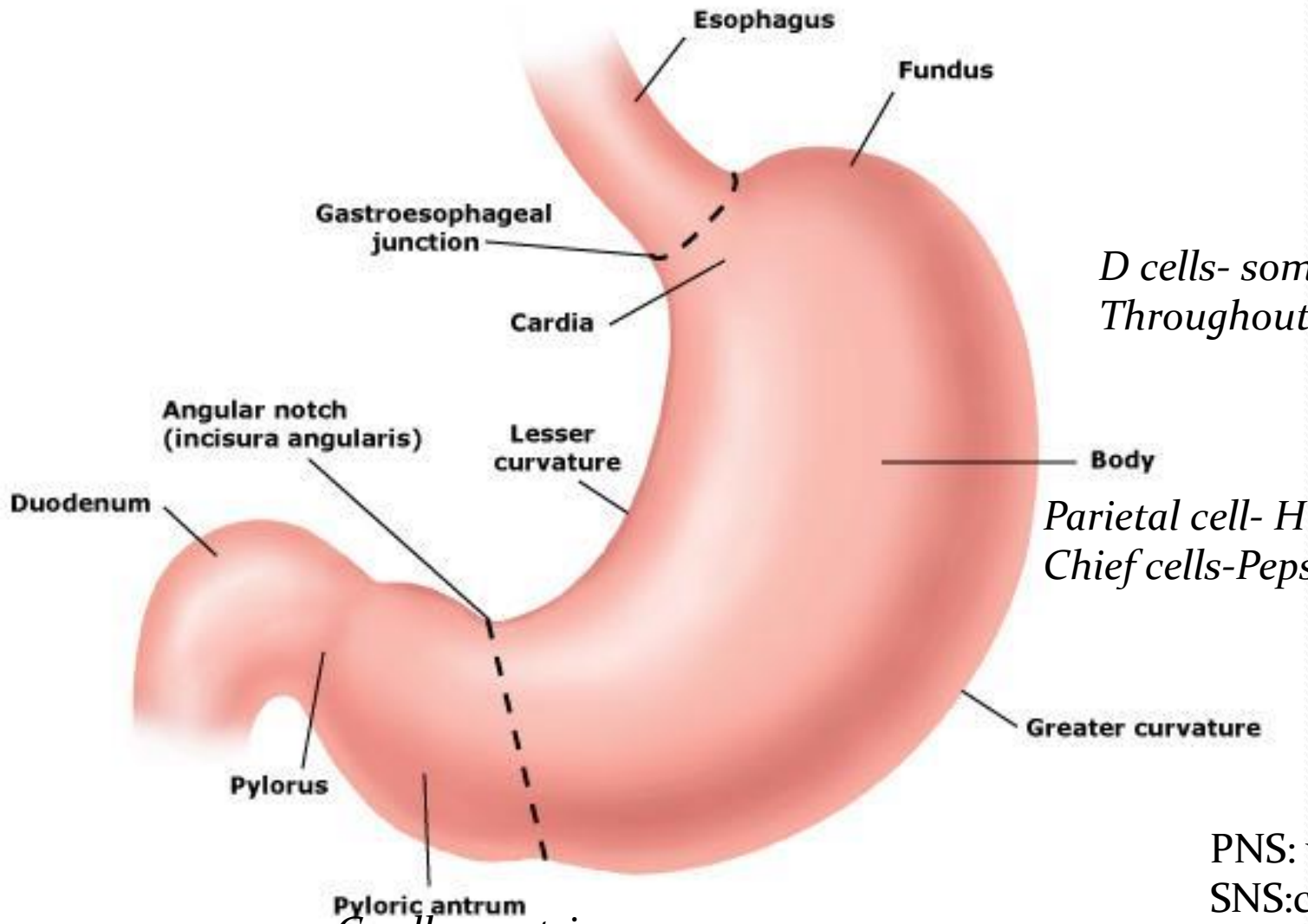
OBJECTIVES

1. Definitions
2. Normal gastric physiology
3. Epidemiology
4. Etiology of PUD
5. Pathogenesis of PUD
6. Investigations
7. Management
8. Non ulcer dyspepsia

INTRODUCTION

- Peptic ulcers are defects in the gastric or duodenal mucosa that extend through the muscularis mucosa

NORMAL GASTRIC PHYSIOLOGY



D cells- somatostatin
Throughout the stomach

Parietal cell- HCL & IF
Chief cells-Pepsinogen

PNS: vagus
SNS:celiac plexus

G cells- gastrin

Gastroduodenal mucosal defense

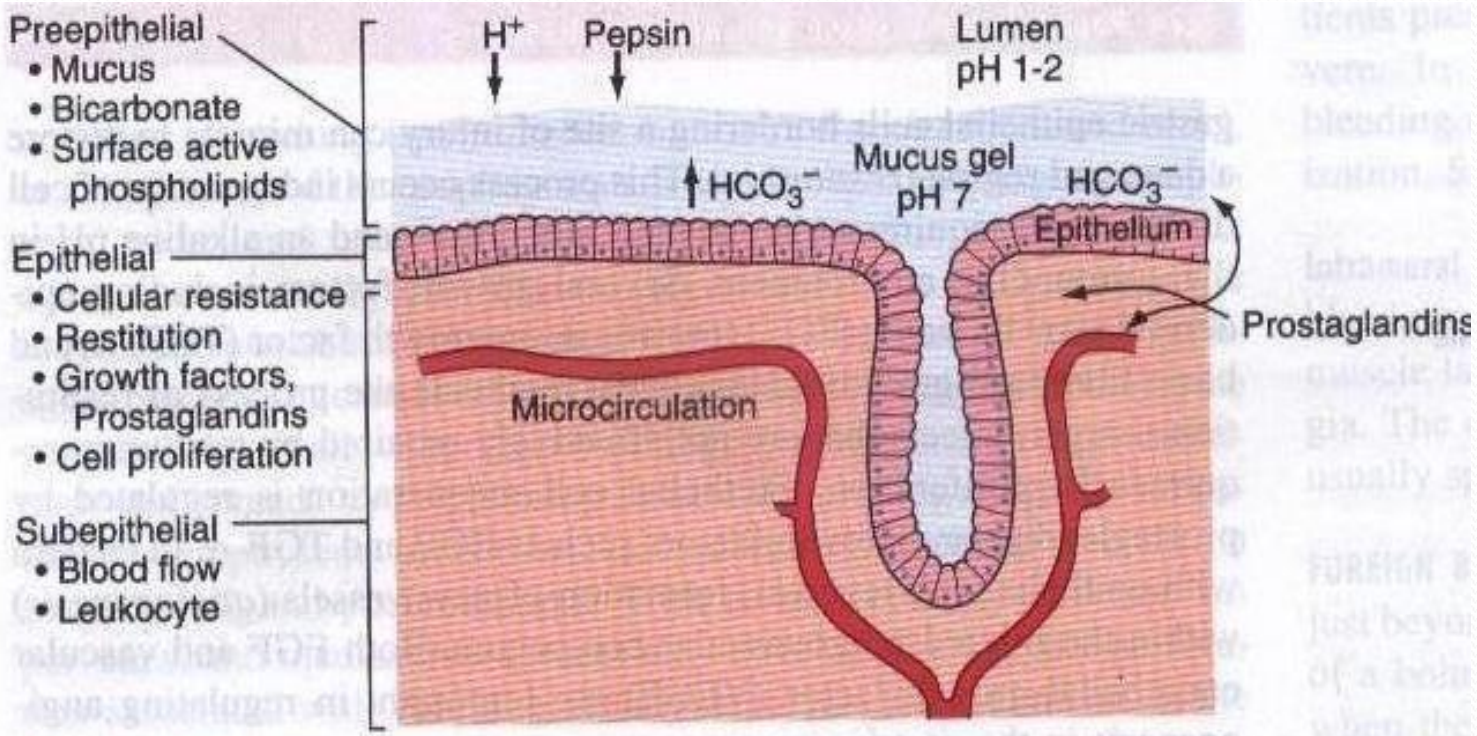


FIGURE 274-3 Components involved in providing gastroduodenal mucosal defense and repair.

Role of prostaglandins in gastric defense & repair

- regulate release of mucosal bicarbonate & mucus
- Inhibit parietal cell secretion
- Maintain mucosal blood flow
- Epithelial cell restitution

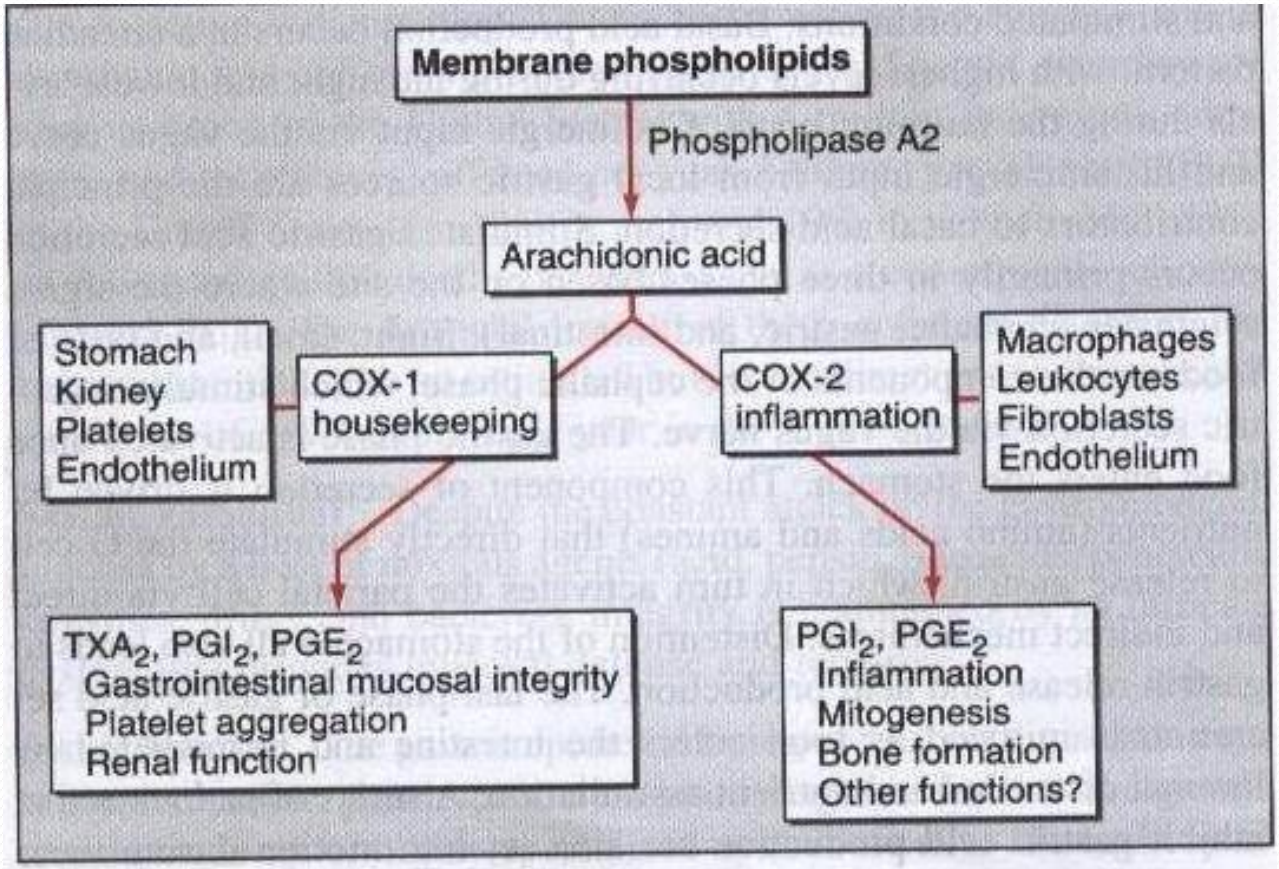


FIGURE 274-4 Schematic representation of the steps involved in synthesis of prostaglandin E_2 (PGE_2) and prostacyclin (PGI_2). Characteristics and distribution of the cyclooxgenase (COX) enzymes 1 and 2 are also shown. TXA_2, thromboxane A_2.

EPIDEMIOLOGY

- DU > GU
- DU occur in 6-15% of the western pop
- GU occur later than DU with peak incidence 6th decade

- Eradication of H.pyroli has reduced recurrence rates

EPIDEMIOLOGY

- In the developing world 80% of the pop may be infected with H.PYLORI by the age of 20yrs cf to western world where it is 20-50%
- Two factors that lead to higher colonization states are:
  - Poor social-economic status
  - Less education

EPIDEMIOLOGY

- Transmission of H.pyroli occurs from person to person through:
  - Oral-oral route
  - Fecal-oral route

Etiology of PUD

- **Most common etiologic factors**

1. *H pylori* infection
2. Nonsteroidal anti-inflammatory drugs (NSAID) use

Other causes of PUD

- Severe physiologic stress
  - Burns
  - CNS trauma
  - Surgery
  - Severe medical illness

Other causes of PUD

- Hypersecretory states (uncommon)
  - Gastrinoma (Zollinger-Ellison syndrome) or multiple endocrine neoplasia (MEN-I)
  - Antral G cell hyperplasia
  - Systemic mastocytosis
  - Basophilic leukemias
- Others include:
  - Alcohol
  - Bile reflux

Diseases associated with an ↑ risk of PUD

- Include cirrhosis, chronic obstructive pulmonary disease, renal failure, and organ transplantation.
- Additional rare, miscellaneous causes include radiation-induced or chemotherapy-induced ulcers, vascular insufficiency (crack cocaine), and duodenal obstruction.

PATHOGENESIS & PATHOPHYSIOLOGY

- Occurrence of an ulcer is due to an imbalance btn aggressive and defensive mechanisms
- Aggressive factors include:
  - **H.pylori, NSAIDS, alcohol, bile salts, acid pepsin**
- Defensive mechanisms include:
  - Tight intercellular junctions, mucus, mucosal blood flow, cellular restitution, epithelial renewal

H. PYLORI

- H. pylori: a G-ve rod, s shaped with multiple flagella.

Transmission

- The most common route of HP infection is either oral-to-oral (stomach contents are transmitted from mouth to mouth) or fecal-to-oral (from stool to mouth) contact.
- Parents and siblings seem to play a primary role in transmission.

- **Gender-** No gender predilection is known; however, females have a higher incidence of reinfection (5-8%) than males.
- **Race:** The prevalence rate is approximately 20% in white persons, 54% in African American persons,60% in Hispanic persons. In developing world 80% popn infected by age 20.
- **Age:** infection is acquired most frequently during childhood. Children and females have a higher incidence of reinfection (5-8%) than adult males.

- A strong association has been reported between HP infection &:
  - Gastritis
  - PUD
  - Gastric MALT lymphoma
  - Gastric ca : adenocarcinoma of the body & antrum of the stomach.

PATHOPHYSIOLOGY

- The end result of H.pylori infection is determined by interplay between bacterial and host factors.

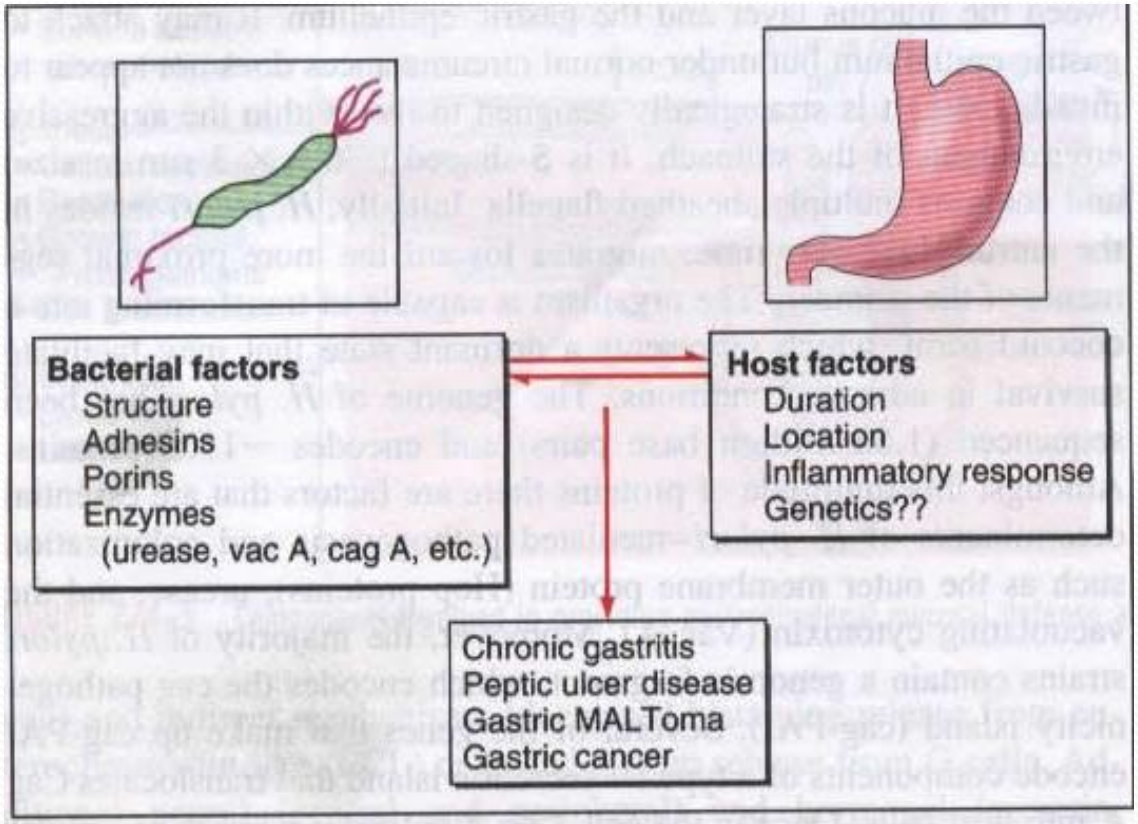


FIGURE 274-6 Outline of the bacterial and host factors important in determining *H. pylori*–induced gastrointestinal disease. MALT, mucosal-associated lymphoid tissue.

PATHOPHYSIOLOGY

- BACTERIAL FACTORS:
- H.pyroli is able to have gastric residence by producing urease which generates ammonia by catalyzing urea. The ammonia generated alkalinize surrounding PH & damage epithelial cells
- Virulence factors:
  - Different strains produce different virulence factors
  - The bacterial genome encodes the virulence factors Cag A and pic B: stimulate production of cytokines & chemotactic factors
  - VAC A gene encodes for Vac A: vacuolating cytotoxin

PATHOPHYSIOLOGY

- *Surface factors* that are chemotactic for neutrophils and monocytes which in turn contribute to epithelial cell injury
- *Proteases and phospholipases* that breakdown the glycoprotein lipid of the mucus gel hence reducing the efficacy of this first line of defense
- *Adhesins* that facilitate attachment of the bacteria to epithelial cells
- *H.pylori LPS* has low immunologic activity thus leading to a smoldering inflammation
- HP induce apoptosis of epithelial cells & T cells: upregulated FasL & caspases induce apoptosis.

PATHOPHYSIOLOGY

HOST FACTORS:

1. Host response includes recruitment of neutrophils, lympocytes(T and B),macrophages and plasma cells
2. The pathogen leads to local injury by binding to class II MHC molecules expressed on gastric epithelial cells leading to apoptosis
3. Bacterial strains that encode cag-PAI can introduce cagA into the host cells leading to cytokine production and further cell injury.

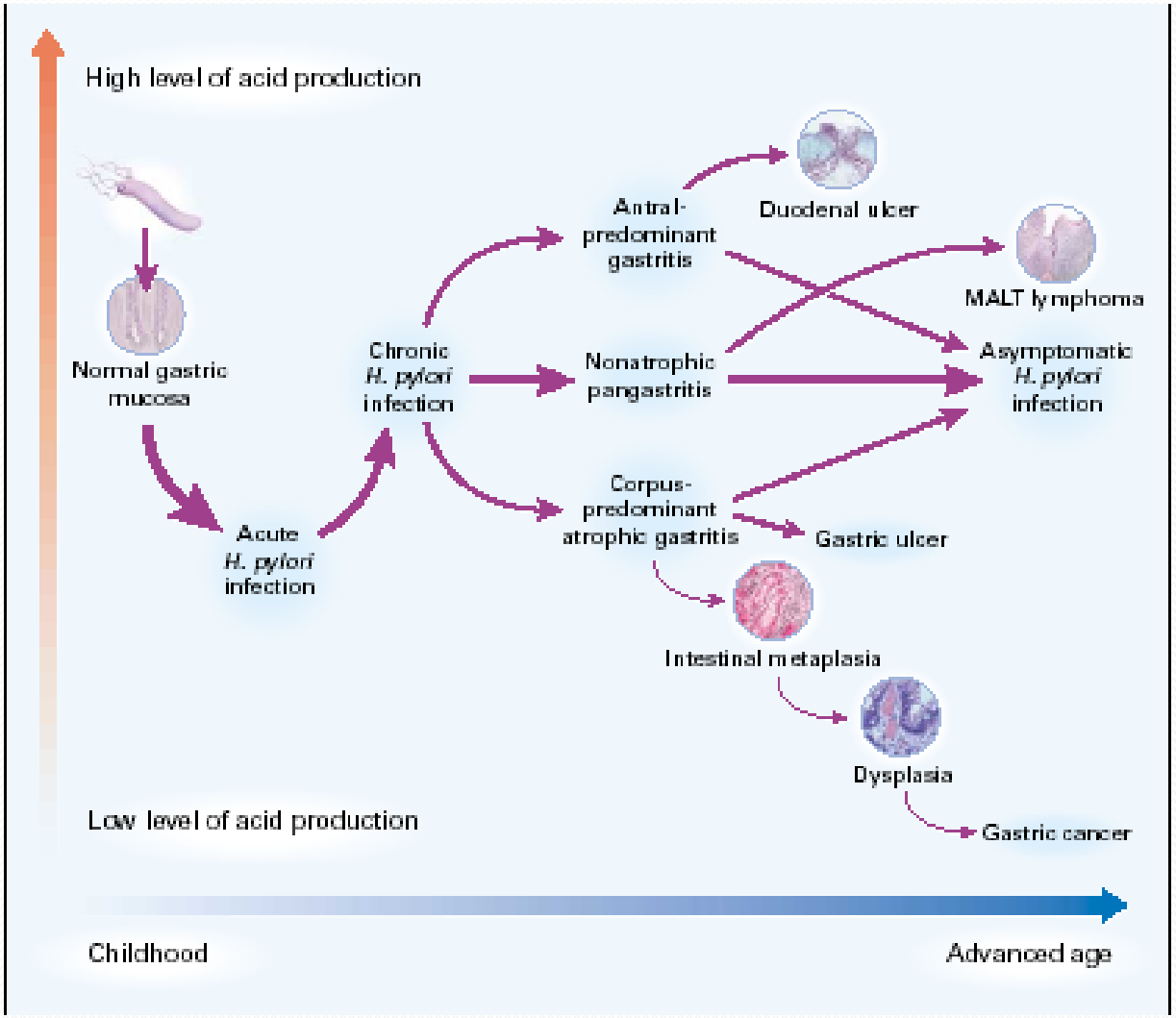
   -the cytokines include IL-1 alpha and beta, IL-2,IL-6 and IL-8,TNF alpha and interferon gamma

4. Activated neutrophils- reactive oxygen & nitrogen species cause epithelial damage & apoptosis.

Pathophysiology

- HP can produce and release several bioactive factors that may directly affect the stomach's parietal cells, which produce HCL, and enterochromaffinlike (ECL) cells (i.e., G cells and D cells), which produce gastrin and somatostatin, respectively.
- Evidence suggests that HP inhibits D cells and stimulates G cells.

Natural history of H. pylori infection



PATHOLOGY

- DUs most often occur in the first portion of the duodenum 95% the time with 90% located within the pylorus
- Usually 1 cm in diameter but occasionally get to 3-6cm called giant ulcers
- Ulcers are sharply demarcated with depth at times reaching the musclaris propria
- The base of the ulcer often consists of an area of eosinophilic necrosis with surrounding fibrosis
- Malignant duodenal ulcers are extremely rare

PATHOLOGY

- Gastric ulcers can represent a malignancy
- Benign GUs are located distal to the junction btn antrum and the acid secretory mucosa
- The antral mucosa extends about 2/3 of the distance of the lesser curve and 1/3 up the way of the greater curve
- Benign Gus are rare at the gastric fundus and histologically similar to DUs
- Benign Gus ass. with H.pylori are associated with antral gastritis
- NSAID related Gus are not accompanied by chronic active gastritis

NSAIDS INDUCED PUD

- The spectrum of NSAIDS induced disease ranges from nausea and dyspepsia to serious GIT complications such as frank peptic ulceration complicated by bleeding and or perforation

- Even 75mg of Aspirin can lead to serious GIT ulceration and hence no dose of NSAIDS is completely safe

- Established risk factors include:
  - Advanced age
  - Concurrent of anticoagulants
  - History of ulcer
  - Serious multisystemic disease
  - Concomitant use of glucocorticoids
  - High doses of NSAIDS
  - Multiple NSAIDS

PATHOPHYSIOLOGY OF NSAIDS

- Prostaglandins play an important role in mucosal integrity and repair
- NSAIDS inhibit COX thus decrease PGs
  - Incr HCL, decr mucus secr, decr bicarb, decr epithelial cell prolife.
- Direct toxicity: 'ion trapping'

  NSAIDS are weak acids that remain in a nonionized lipophillic can lead to cell injury once trapped intracellularly in the ionized form.

HISTORY

- The typical pain pattern of DU occurs 90mins to 3h after a meal and is frequently relieved by antacids or food
- Pain that awakes the patient from sleep at 3am is typical of DU
- In pain associated with GU discomfort may actually be ppt by food.
- Dyspepsia that becomes constant, is no longer relieved by antiacids or radiates to the back may indicate a penetrating ulcer

- NSAID-induced gastritis or ulcers are usually silent.
- Sudden onset of symptoms may indicate perforation.
- Gastritis may present as bleeding, which is more likely in elderly patients.
- Symptoms consistent with anemia (e.g., fatigue, dyspnea) may manifest.

Clinical picture

- Epigastric pain (the most common symptom)
- Gnawing or burning sensation
  Occurs 2-3 hours after meals
  Relieved by food or antacids
- Patient awakens with pain at night.
- May radiate to the back (consider penetration)
- Nausea
  Vomiting, which might be related to partial or complete gastric outlet obstruction

Clinical picture

- Dyspepsia, including belching, bloating, distention, and fatty food intolerance

- Heartburn
- Chest discomfort

- Anorexia, weight loss
- Hematemesis or melena resulting from gastrointestinal bleeding
- Dyspeptic symptoms that might suggest PUD are not specific because only 20-25% of pts with symptoms suggestive of peptic ulceration are found on investigation to have a peptic ulcer.

DIAGNOSIS: NON ENDOSCOPIC TESTS

1. HP fecal antigen test (FAT)
   - This is a novel rapid test based on monoclonal antibody immunochromatography of stool samples. It has been reported to be very specific (98%) and sensitive (94%).
   - Indicate active infection & useful after Rx
2. Carbon 13 urea breath test (UBT)
   - The carbon 13 urea breath test is based on the detection of the products created when urea is split by the organism.
   - Sensitivity & specificity: 95%
   - Active infection & useful after Rx

3. The serology test: antibody testing

- Has a high (>90%) specificity and sensitivity.
- IgG antibodies against HP by the means of ELISA, LAT in serum, whole blood or urine.
-Present 21 days after infection & remain present long after eradication.
- thus only useful before not after Rx.
-It is useful for detecting a newly infected patient

NB:*Testing to prove H. pylori eradication appears to be most accurate if performed at least 4 wk after the completion of antibiotic therapy: FAT &UBT*

Upper GI endoscopy

- Preferred diagnostic test in the evaluation of patients with suspected PUD
- Highly sensitive for the diagnosis of gastric and duodenal ulcers
- Allows for biopsies and cytologic brushings in the setting of a gastric ulcer to differentiate a benign ulcer from a malignant lesion
- Allows for detection of *H pylori* infection with antral biopsies
- Tests

1. Histology: sensitivity & specificity > 95%
2. Rapid urease testing : sen >90% specificity >95 %
3. Culture : high specificity. Antibiotic sensitivity
4. PCR: high sensitivity. Antibiotic sensitivity

Management

Table 1. Indications for Diagnosis and Treatment of *H. pylori* (ACG)

Established

- Active peptic ulcer disease (gastric or duodenal ulcer)
- Confirmed history of peptic ulcer disease (not previously treated for *H. pylori)*
- Gastric MALT lymphoma (low grade)
- After endoscopic resection of early gastric cancer
- Uninvestigated dyspepsia (depending upon *H. pylori* prevalence)

Treatment

- A number of Rx options exist for pts presenting with symptoms suggestive of PUD or ulcer like dyspepsia: including empiric antisecretory therapy,
- empiric triple therapy for *H P*
- .

- **Perform endoscopy early in pts older than 45-50 years and in pts with associated so-called alarm symptoms, such as dysphagia, recurrent vomiting, weight loss, or bleeding.**

Treatment

- *Proton pump inhibitors* -- Bind to proton pump of parietal cell, inhibiting secretion of hydrogen ions into gastric lumen.
- Relieve pain and heal peptic ulcers more rapidly than H2 antagonists.

PPI-based triple therapies consist of a 14-day Rx of the following:

- Omeprazole: 20 mg PO bid or
- Lansoprazole 30 mg PO bid or
- Rabeprazole 20 mg PO bid or
- Esomeprazole 40 mg PO qd

Plus:

- Clarithromycin 500 mg PO bid and
- Amoxicillin 1 g PO bid

The alternative combination therapy consists

- Omeprazole: 20 mg PO bid or
- Lansoprazole 30 mg PO bid or
- Rabeprazole 20 mg PO bid or
- Esomeprazole 40 mg PO qd
- **Plus:**
- **Clarithromycin: 500 mg PO bid and**
- **Metronidazole (Flagyl): 400 mg PO bid**

- NB: Eradication 70-85% due to incr clarithromycin resistance.

Quadruple therapies for *H P* Is are reserved for pts failed a course of Rx & are RX for 14 days

- PPI PO bid and
- Bismuth 525 mg PO qid and
- Metronidazole 500 mg PO qid and
- Tetracycline 500 mg PO qid

- NB: Eradication 75-90 %

Alternative to quadruple therapy

- PPI PO bd
- Levofloxacin
- Amoxil 1g PO bd
- 10 days
- More effective & better tolerated than bismuth quadruple Rx.

Surgical care

- Potential indications for SX refractory disease. Complications of PUD include the following:
- Refractory, symptomatic PUD, though rare with the cure of *H P Ix*
- Perforation usually is managed emergently with surgical repair. However, this is not mandatory for all pts.
- Obstruction can complicate PUD, particularly if PUD is refractory to aggressive antisecretory therapy, *H pylori* eradication, or avoidance of NSAIDs.
- Penetration, particularly if not walled off or if a gastrocolic fistula develops, is a potential complication of PUD.

- Bleeding, particularly in pts with massive hemorrhage & hemodynamic instability, recurrent bleeding on medical therapy, and failure of therapeutic endoscopy to control bleeding.

Prognosis

- Excellent even in patients with MALTomas
- Gastric adenocarcinoma worst prognosis
- Rate of reinfection very low 1-2%
- Children & females higher 5-8%

THANKYOU