GASTRITIS AND PEPTIC ULCER DISEASES

Akos Ilias

SEMMELWEIS EGYETEM
Általános Orvostudományi Kar
Semmelweis Egyetem I. sz. Belgyógyászati Klinika
http://bel1.semmelweis.hu

Definition

- Inflammation associated with mucosal injury
- A histological term that needs biopsy to be confirmed
- Usually due to infectious agents (H pylori) , autoimmune & hypersensitivity reactions.
- Endoscopic mucosal changes of gastritis, 27% had a normal endoscopic biopsy specimen & 63 % had histological evidence of gastritis.
- Gastropathy: Epithelial cell damage without infalmmation

Classification

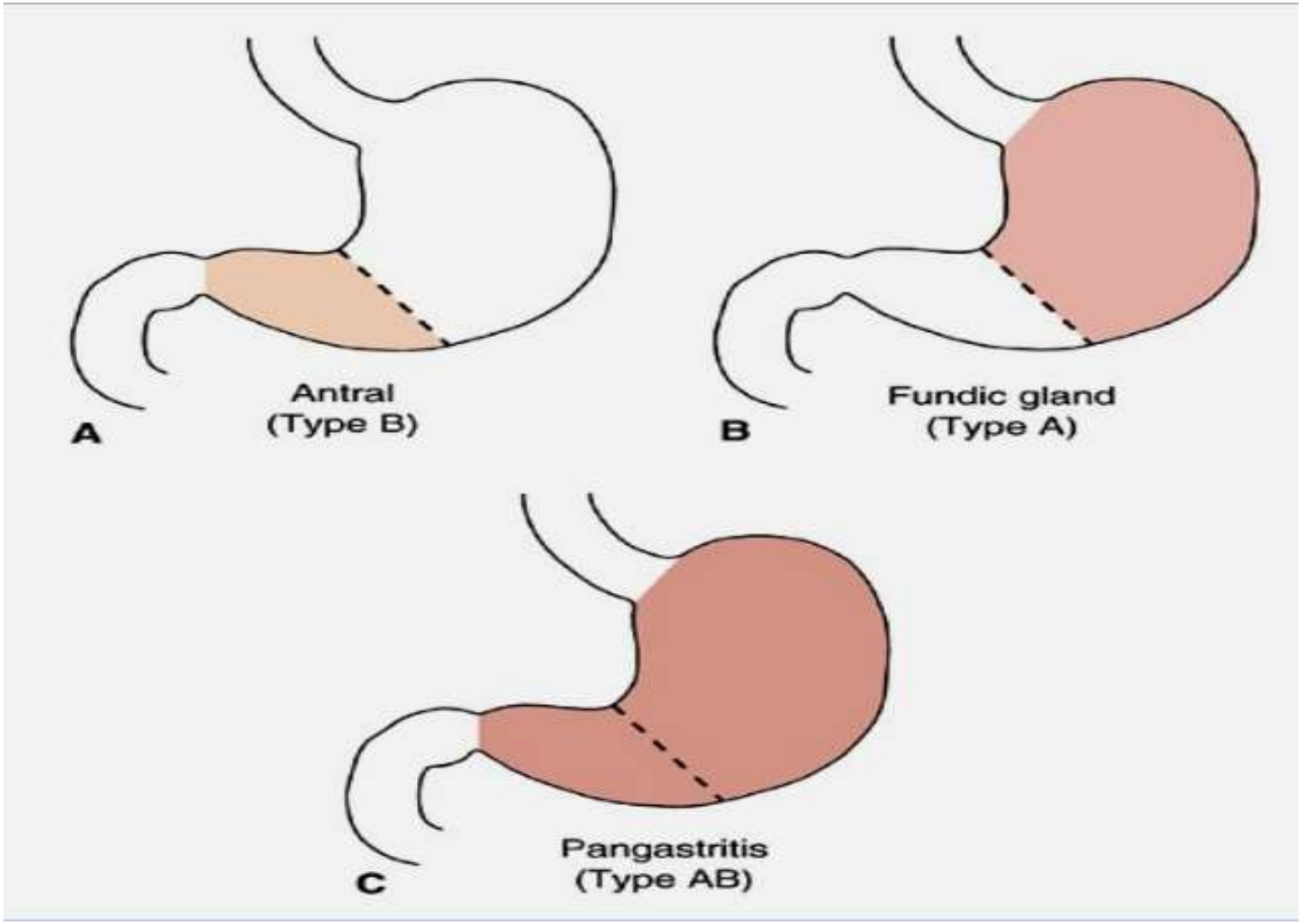
- Acute: short term inflammation with neurophilic infiltrate

- Infectious, stress, postoperativ, drugs

- Chronic:long standing with mononuclear cell infiltrate especially lymphocyte/maccrophages

- Type A - Autoimmun atrophic gastrtis 5 %
- Type B - Chronic active gatritis 80%
- Type C - Chemical 15 %

Localisation



Peptic Ulcer

- Ulcers are defined as a breach in the mucosa of the alimentary tract, which extends through the muscularis mucosa into the submucosa or deeper.

- An erosion differs from an ulcer in being partial thickness mucosal defect.

- Peptic ulcers usually chronic, often solitary lesions that occur in any portion of gastrointestinal tract exposed to the aggressive action of acid-peptic juices

Acid secretion

There are three primary pathways that stimulate gastric acid secretion

- 1) The neurocrine pathway which delivers transmitters such as acetylcholine post-ganglionic nerves on the stomach wall
- 2) The endocrine pathway which releases hormones such as gastrin
- 3) The paracrine pathway which releases histamine

Once pH is <3.5, pepsinogen is converted to the active proteolytic enzyme pepsin

Pathology

- Peptic ulcers are produced by an imbalance between the gastro-duodenal mucosal defense mechanisms and damaging forces of gastric acid and pepsin, combined with superimposed injury from environmental or immunologic agents

Pathology

- Imbalance between aggressive & protective factors

Aggressive factors
Gastric acid
Proteolytic enzyme

Protective factors
Mucosal layer
Bicarbonate secretion
Prostaglandins

- *H. pylori*

* Acid Secretion
* Pepsinogen Secretion
* NSAIDS
* Cigarette smoking
* Corticosteroid use

Mucus Production
* Bicarbonate Production
* Mucosal blood flow - more important in the development of stress ulcer
* High epithelial cell turnover
* Prostaglandins (PGE2) - stimulate mucus and bicarbonate production, and blood flow

Ethyology

- Duodenal: 90% H. pylori, 9 % NSAID, 1% other
- Gastric: 60 % H.pylori, 30 % NSAID, 10% other

Other:

- Zollinger-Elison Syndrom
- Hiatus hernia
- Stres
- Ischemia
- Crohn disease

Other mechanism

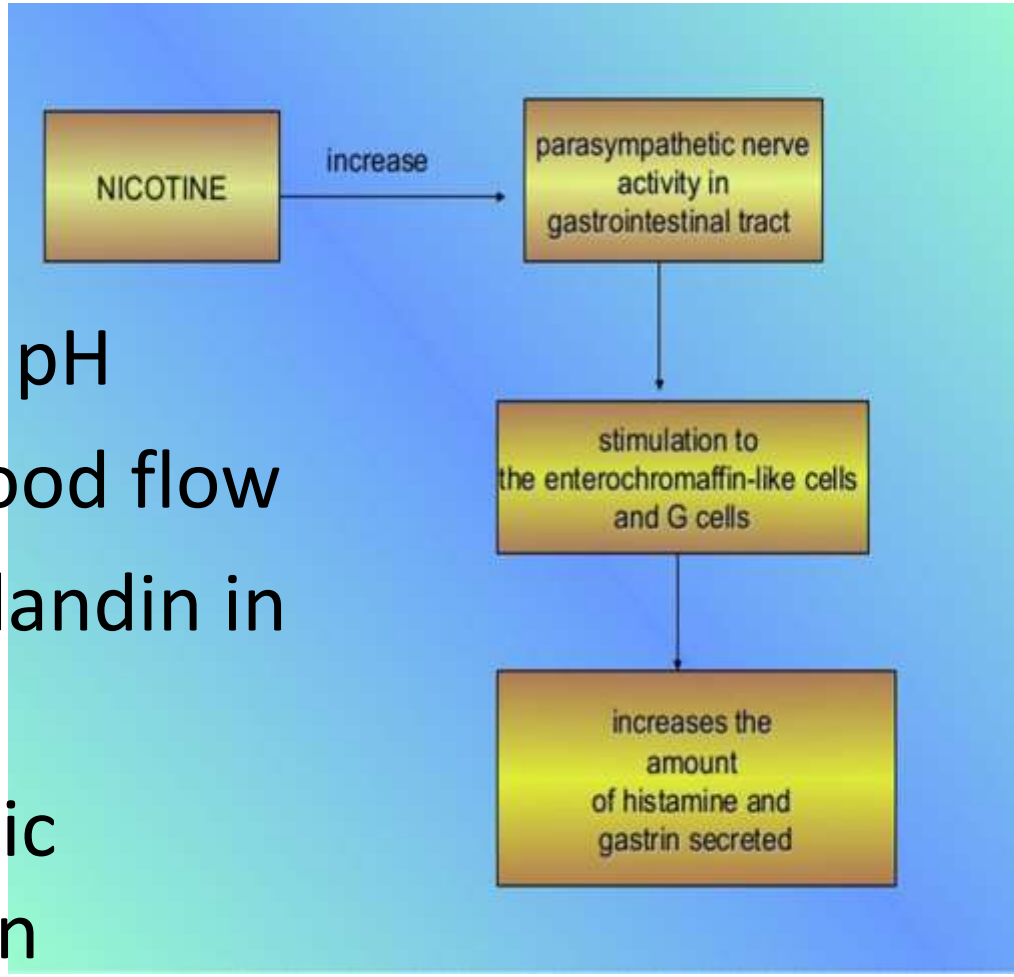
- Peptic ulcer caused due to high gastrin level and excess acid production. Gastrinoma may cause multiple peptic ulceration as in Zollinger Ellison syndrome. There is increased parietal cell mass
- Chronic use of NSAIDs (aspirin) causes suppression of mucosal prostaglandin and direct irritative topical effect

Stress ulcer pathophysiology

- Hypersecretion of acid –head trauma.
- Defects in gastric glycoprotein mucus –In critically ill patients, increased refluxed bile salts or uremic toxins can denude the glycoprotein mucous barrier
- Ischemia– Shock, sepsis, trauma can lead to impaired– perfusion of the gut

Smoking

- Increased rate of gastric emptying
- Decreased duodenal pH
- Reduced mucosal blood flow
- Inhibition of prostaglandin in mucosa
- Diminished pancreatic bicarbonate secretion



Stress ulcer risk factors

2 major risk factors for clinically significant bleeding due to stress ulcers are: Mechanical ventilation for > 48 hours & coagulopathy

- Shock
- Sepsis
- Hepatic failure
- Renal failure
- Multiple trauma
- Burns >35% total body surface area
- Organ transplant recipients
- Head or spinal trauma
- H/O peptic ulcer disease or upper GI bleeding

Symptoms

- Asymptomatic
- Epigastric pain (GU – eating provokes)
- Nausea
- Oral flatulence, bloating, distension and intolerance of fatty food
- Heartburn
- Pain radiating to the back

Hystory

- H. PYLORI
- Non Steroidal Anti-inflammatory Drugs/Aspirin
- Steroid therapy
- Smoking
- Excess alcohol intake
- Stool color/FOBT

Diagnostic Test and Procedures

a) Routine

- Routine lab tests are not useful in establishing the diagnosis of uncomplicated PUD
- Hct, HgB, and stool hemoccult are useful to detect bleeding

b) H.pylori test

- Histology
- Culture
- Biopsy/gram stain
- Biopsy/CLO test
- Urea breath test
- Serology

Sites of peptic ulcer

- Duodenum: First portion (Bulb). Anterior wall is more often affected.
- Stomach: Usually antrum. Lesser curvature (common) Anterior and posterior wall and greater curvature (less common).
- In the margins of a gastroenterostomy (stomal ulcer), in the anastomosis
- In the duodenum, stomach or jejunum of patients with Zollinger-Ellison syndrome.
- Within or adjacent to a Meckel's diverticulum that contains ectopic gastric mucosa

Size, penetration

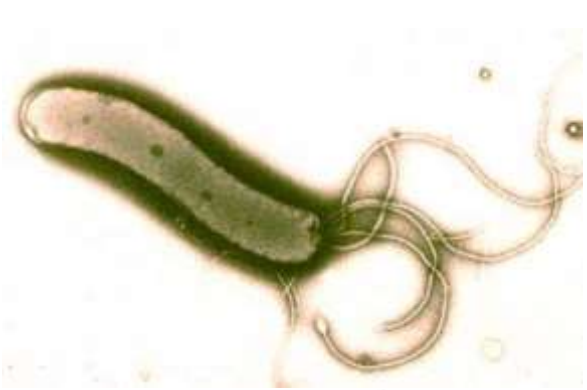
Shape: Round, oval or linear.

Size: Usually less than 2cm in diameter.

- Lesions less than 0.3 cm are likely to be shallow erosions.
- Giant ulcers are usually greater than 3cm in diameter.
- May also reach up to 10cm (particularly on lesser curvature),mortality rate is higher in these patients.
- Size does not differentiate benign from malignant ulcer.
- Some carcinomatous ulcers are less than 4cm and 10% of benign ulcers are more than 4cm

Depth of penetration :

- Superficial ulcer penetrate the mucosa into the muscularis mucosae.
- Deeply excavated ulcers having their bases on the muscularis propria.



Nobel prize 2005

The Lancet · Saturday 16 June 1984

UNIDENTIFIED CURVED BACILLI IN THE STOMACH OF PATIENTS WITH GASTRITIS AND PEPTIC ULCERATION*

BARRY J. MARSHALL J. ROBIN WARREN

Departments of Gastroenterology and Pathology, Royal Perth Hospital, Perth, Western Australia

Summary Biopsy specimens were taken from intact areas of antral mucosa in 100 consecutive consenting patients presenting for gastroscopy. Spiral or curved bacilli were demonstrated in specimens from 58 patients. Bacilli cultured from 11 of these biopsies were gram-negative, flagellate, and microaerophilic and appeared to be a

Patients and Methods

Patients

All patients referred for gastroscopy on clinical grounds were eligible for the study which continued until there were 100 participants who gave informed consent and in whom biopsy was considered to be safe. The study was approved by our hospital's human rights committee.

Questionnaire

Where possible patients completed a clinical questionnaire designed to detect a source of infection or show any relationship with "known" causes of gastritis or *Campylobacter* infection, rather than give a detailed account of each patient's history. The emphasis was on animal contact, travel, diet, dental hygiene, and drugs, rather

H. pylori

- The description of H.pylori was a major breakthrough in Gastroenterology.
- Initial work on H.pylori and peptic ulcer disease was refuted because the results were outside the current paradigm
- The recognition of H.pylori as a major pathogen changed the common beliefs about peptic ulcer disease.
- Peptic ulcer disease is a “simple” infectious disease.
- Schwarz’s dictum: NO ACID → NO ULCER
- has become: NO H.pylori (or NSAID) → NO ULCER.

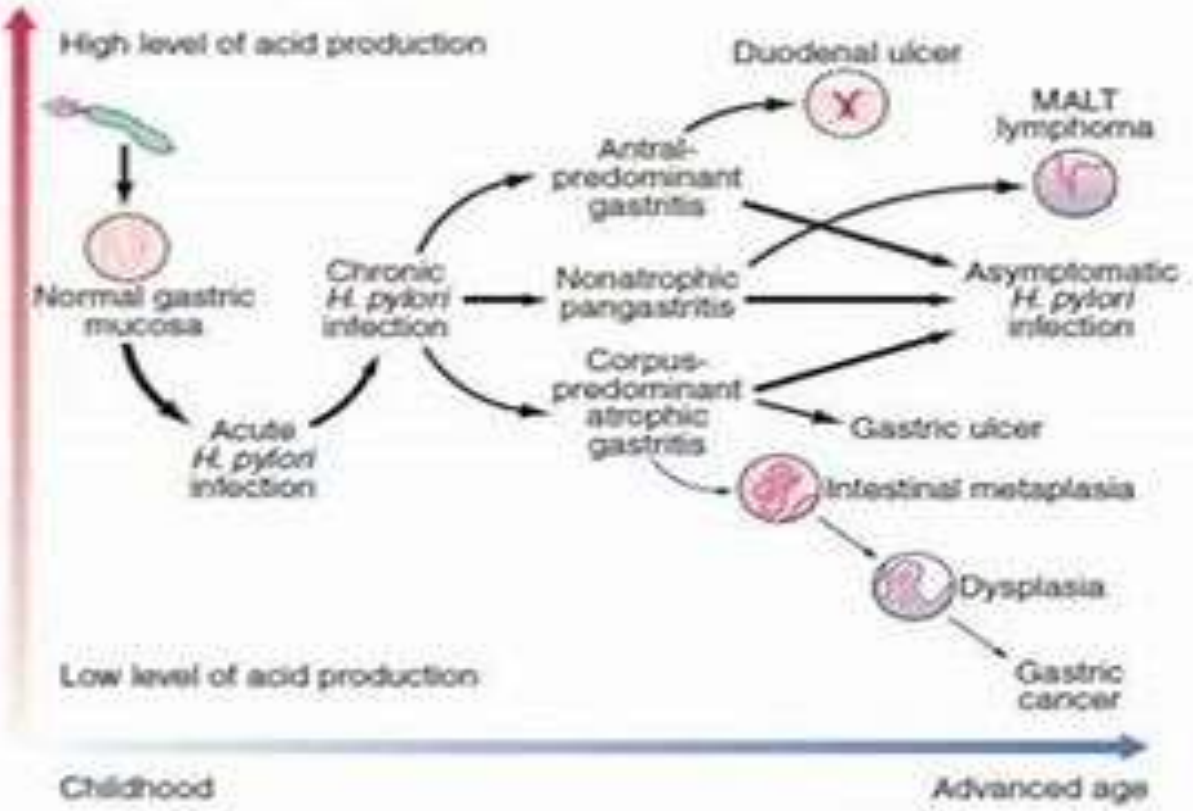
H. Pylori epidemiologie

- Estimated 50-60% of the world population is infected
- Person to Person Transmission
  - fecal-oral, oral-oral, gastro-oral
- Increased risk of infection
  - younger age
  - underdeveloped countries
  - lower socioeconomic status

H Pylori

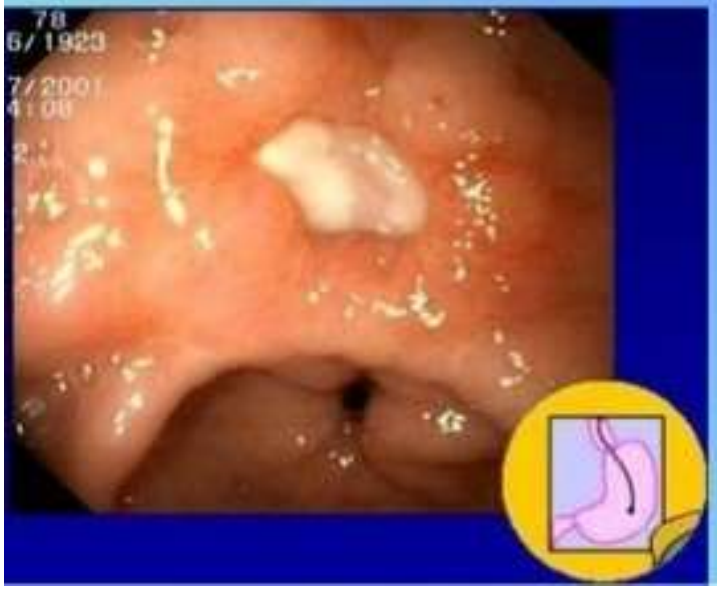
- A spiral shaped, microaerophilic, gram negative bacterium
- urease forms ammonia & bicarbonate that neutralize gastric acid& form a protective cloud around the organism
- Urease appears to be vital for its survival & colonization
- Spiral shape, flagella facilitate its passage through the mucus
- Helicobacter pylori is the most common chronic bacterial infection in humans
- The frequency of H.P for any age in any locality reflects rate of bacterial acquisition during childhood years &affected by: Density of housing. Overcrowding, Number of siblings, Sharing a bed. Lack of running water..

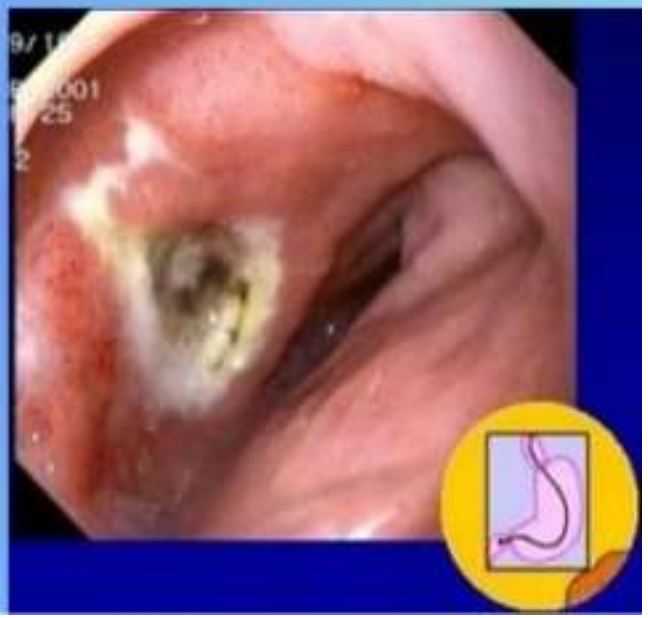
Natural history of H. pylori infection

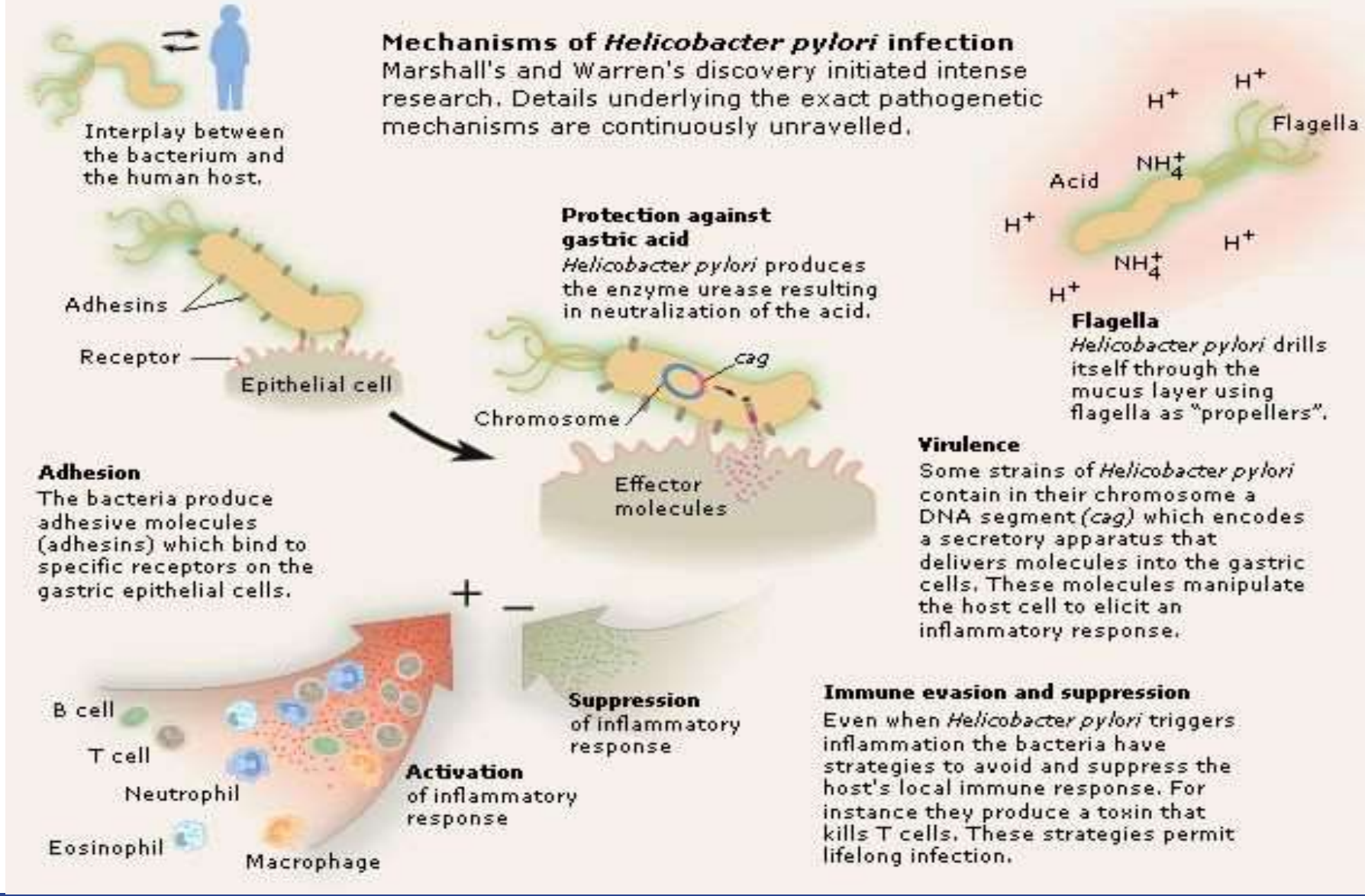


Longo DL et al. Harrison's gastroenterology & hepatology. McGraw-Hill, New York, USA, 2010.

- The bacterium persists in the stomach for decades in most people. Most individuals infected by *H. pylori* will never experience clinical symptoms despite having chronic gastritis. Approximately 10-20% of those colonized by *H. pylori* will ultimately develop gastric and duodenal ulcers. *H. pylori* infection is also associated with a 1-2% lifetime risk of stomach cancer and a less than 1% risk of gastric MALT lymphoma






Mechanisms of Helicobacter pylori infection
Marshall's and Warren's discovery initiated intense research. Details underlying the exact pathogenetic mechanisms are continuously unravelled.
Interplay between the bacterium and the human host.
Adhesins
Receptor
Epithelial cell
Adhesion
The bacteria produce adhesive molecules (adhesins) which bind to specific receptors on the gastric epithelial cells.
Protection against gastric acid
Helicobacter pylori produces the enzyme urease resulting in neutralization of the acid.
cag
Chromosome
Effector molecules
H+
NH4+
Acid
Flagella
Flagella
Helicobacter pylori drills itself through the mucus layer using flagella as "propellers".
Virulence
Some strains of Helicobacter pylori contain in their chromosome a DNA segment (cag) which encodes a secretory apparatus that delivers molecules into the gastric cells. These molecules manipulate the host cell to elicit an inflammatory response.
+
−
B cell
T cell
Neutrophil
Eosinophil
Macrophage
Activation of inflammatory response
Suppression of inflammatory response
Immune evasion and suppression
Even when Helicobacter pylori triggers inflammation the bacteria have strategies to avoid and suppress the host's local immune response. For instance they produce a toxin that kills T cells. These strategies permit lifelong infection.

Pathogenesis by H. pylori

- Damage of the protective mucosal layer. The epithelial cells are exposed to the damaging effect of acid-peptic digestion.
- Inflammation of the gastric mucosa.
- Chronically inflamed mucosa more susceptible to acid- peptic injury and prone to peptic ulceration.
- Ulcers occur at sites of chronic inflammation .
- - Antrum
- - Junction of antral and body- fundic mucosa (division between the inflamed antral mucosa and normal acid secreting mucosa).
- Pangastritis - When there is extensive gastritis, the ulcers are more proximally situated. In elderly patients gastric ulcers are more proximally situated as there is proximal migration of the antral-body mucosal junction.

H. pylori

- Annual rate of reinfection: 1%
- Annual rate of spontan eradikacion: 1%
- H.pylori associated antral gastritis induces increased acid secretion.
- H.pylori associated corpus gastritis induces reduced or even absent acid secretion.
- Pangastritis induces no overall change in acid production

H. Pylori tests

Determination of presence of H. pylori

- Serology : antibodies in blood, serum
- antigen in stool
- functional tests of the bacterium's urease enzyme with a carbon-labeled urea breath test (13C-UBT)
- Endscopy with biopsy and rapid urease test or culture or HE staining

Eradication

Certain indications for H.pylori eradication therapy:

- Peptic ulcer disease
- Mucosa-associated tissue lymphoma
- Atrophic gastritis
- Post-gastric cancer resection
- Patients who are first degree relatives of gastric cancer patients
- Patients' wishes

Debatable indications for H.pylori eradication therapy:

- Non-ulcer dyspepsia / functional dyspepsia
- Gastro-oesophageal reflux disease

Prevention of gastric cancer.

H. Pylori eradication

- Triple therapy 7-10-14 day, twice-daily

Use a PPI, amoxicillin, clarithromycin,

N.B. Metronidazole is substituted to amoxicillin for patients allergic to penicillin.

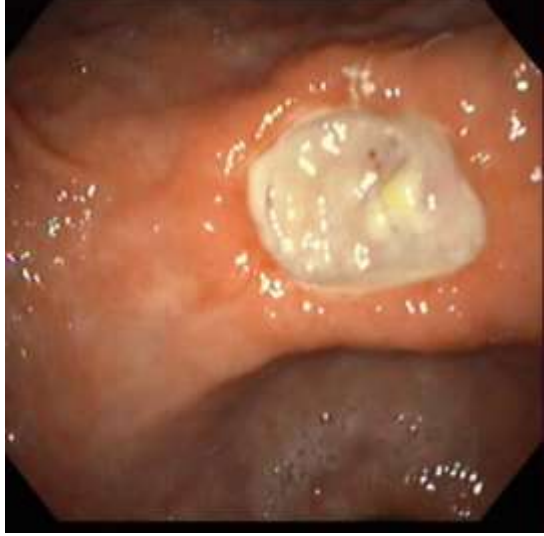
- Quadruple therapy 14 days (Bismuth-based regimen) consisting of: 1. Proton pump inhibitors (PPIs) 2. Bismuth subcitrate 3. Metronidazole 4. Tetracycline

•If a second course of HP therapy is required, the regimen should contain different antibiotics.

Endoscopy

- The endoscopic appearance of an ulcer may provide the most helpful prognostic information.
- The ulcer may have a clean base or have one of several stigmata of hemorrhage:
- a flat pigmented spot (red, purple, brown, or black),
- an adherent clot,
- a visible vessel (a smooth-surfaced protuberance or plug in the base of the ulcer),
- active bleeding (either oozing or spurting).
- The size of an ulcer is also a prognostic indicator.
- Patients with ulcers larger than 1 or 2 cm in diameter have increased rates of rebleeding and death, even after endoscopic hemostatic therapy.
- Large ulcers are more frequently found to have stigmata of recent hemorrhage than are small ulcers.

Endoscopy, biopsy



- Biopsy is necessary to distinguish between benign and malignant **gastric ulcers**.
  Biopsy should be taken from the ulcer edge.

- Several biopsies may be taken to exclude cancer.

- Repeat endoscopy(folow up) may be necessary if biopsies are negative and there is high index of suspicion.

Therapy

- MEDICAL TREATMENT
- a) ~~Antisceretory/Anti-acid Agents~~
- 1~~) H2-blockers~~
- 2**) Proton-pump inhibitors**
- 3~~) Antacids~~
- b) Cytoprotectives
- 1) Misoprostil
- 2) Sucralfate
- c) **H. pylori Agents**

Peptic ulcer diferential diagnosis

- Neoplasm of the stomach
- Pancreatitis
- Pancreatic cancer
- Diverticulitis
- Nonulcer dyspepsia (also called functional dyspepsia)
- Cholecystitis
- Gastritis
- GERD
- MI—not to be missed if having chest pain

Management / food

- Patients with endoscopic features indicating a low risk of further bleeding or death can therefore begin eating soon after the procedure.

- Patients with endoscopic findings suggesting a higher risk should receive nothing by mouth or only clear liquids for the first one or two days of hospitalization so that food in the stomach will not interfere with an urgent endoscopic or surgical procedure, which may be necessary if rebleeding ensues.

Complications

- Perforation & Penetration—into pancreas, liver and retroperitoneal space
- Peritonitis
- Bowel obstruction, Gastric outflow obstruction, & Pyloric stenosis
- Bleeding--occurs in 25% to 33% of all cases Gastric CA
- A recent meta-analysis found that an age over 60 years and use of NSAIDs for less than one month were associated with higher risks of complications.

Bleeding

- PU is the most common cause of acute hemorrhage in the UGI tract - 50% of cases.
- Although hospitalization and surgery for uncomplicated PU has decreased over the past 30 years,
- The number of hospital admissions for hemorrhage associated with PU has remained relatively unchanged.

Bleeding

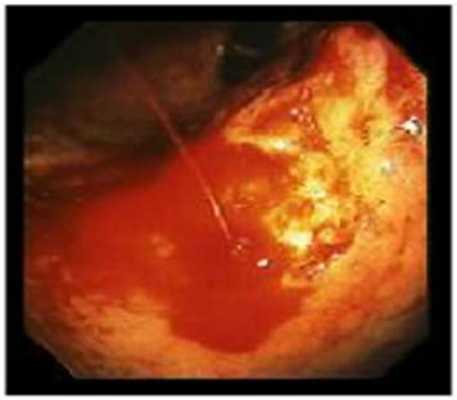
- Bleeding from ulcers ceases spontaneously in at least 80% of patients
- However, a subgroup of patients with bleeding ulcers does not fare as well.
- Overall mortality rate has remained around 6% for the past 30 years.
- The prevalence of Helicobacter pylori in patients with bleeding ulcers may be 15 to 20 percent lower than in patients with nonbleeding ulcers.

Forrest Classification

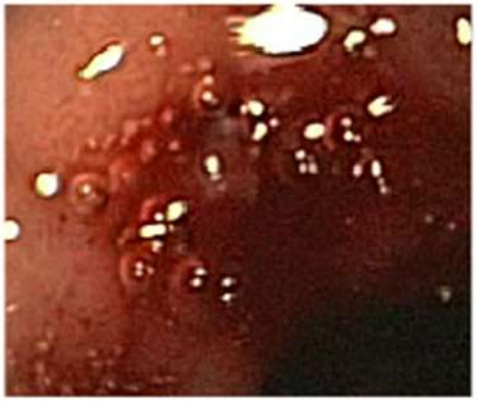
Forrest score	*Endoscopic appearance*	*Risk of rebleeding*[a]
Ia	Ulcer with active pulsating bleeding	55%
Ib	Ulcer with active nonpulsating bleeding	
IIa	Ulcer with a visible nonbleeding vessel	43%
IIb	Ulcer with an adherent clot	22%
IIc	Ulcer with hematin on ulcer base	10%
III	Ulcer with a clean base without signs of recent bleeding	5%

[a]Risk of rebleeding if endoscopic therapy is not performed.

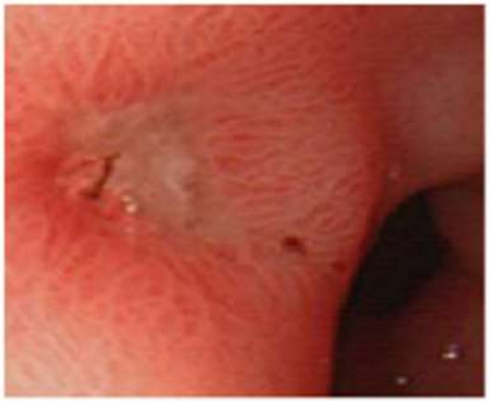
Source: Adapted from Laine, L.; Peterson, W. L. Bleeding Peptic Ulcer. *N. Engl. J. Med.* **1994**, *331*, 717–727.



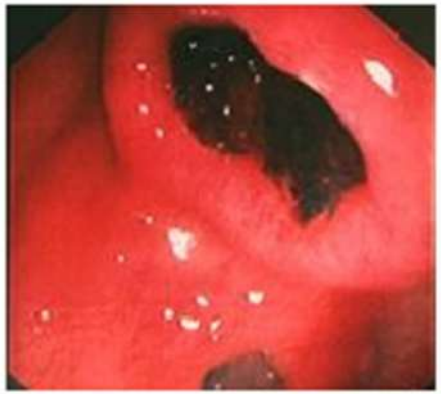
Forrest Ia
Arterial spurting



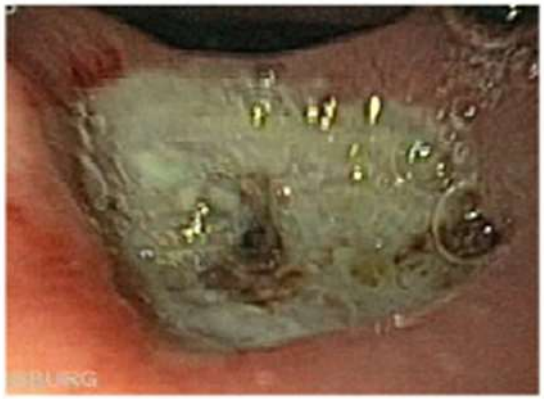
Forrest Ib
Oozing from ulcer base



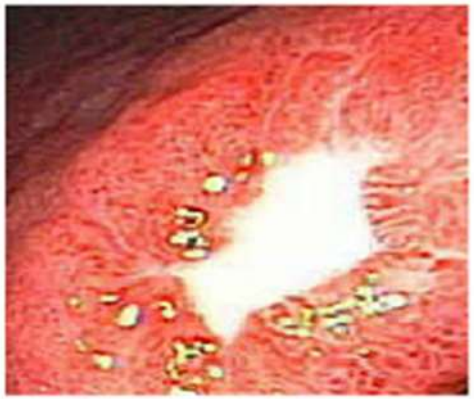
Forrest IIa
Visible vessel



Forrest IIb
Adherent clot



Forrest IIc
Black spots



Forrest III
Clean ulcer base

Surgery

- People who do not respond to medication, or who develop complications:

  Vagotomy - cutting the vagus nerve to interrupt messages sent from the brain to the stomach to reducing acid secretion.

  Pyloroplasty - the opening into the duodenum and small intestine (pylorus) are enlarged, enabling contents to pass more freely from the stomach. May be performed along with a vagotomy

Surgery

- There are 2 types of operations
  1. Gastrectomy: which could be total or partial, partial procedures where used using Billroth 1 or Billroth 2 techniques.
  2. Vagotomy: division of the vagus nerve which stimulate acid secretion, this could be (a) truncal (b) Selective (c) highly selective.

  Long term complications of surgery:

* Recurrent ulcer.
* Dumping effect.
* Diarrhea.
* Blind loop syndrome.
* Nutritional complications (iron-deficiency anemia, megaloblastic anemia, osteomalacia

Prevention

- Consider prophylactic therapy for the following patients:
  - Pts with NSAID-induced ulcers who require daily NSAID therapy
  - Pts older than 60 years
  - Pts with a history of PUD or a complication such as GI bleeding
  - Pts taking steroids or anticoagulants or patients with significant comorbid medical illnesses
- Prophylactic regimens that have been shown to dramatically reduce the risk of NSAID-induced gastric and duodenal ulcers include the use of a prostaglandin analogue or a proton pump inhibitor.
  - Misoprostol (Cytotec) 100-200 mcg PO 4 times per day
  - Omeprazole (Prilosec) 20-40 mg PO every day
  - Lansoprazole (Prevacid) 15-30 mg PO every day

Lifestyl

- Discontinue NSAIDs and use Acetaminophen for pain control if possible.
- Acid suppression--Antacids
- Smoking cessation
- No dietary restrictions unless certain foods are associated with problems.
- Alcohol in moderation
  - Men under 65: 2 drinks/day
  - Men over 65 and all women: 1 drink/day
- Stress reduction