

ROLE OF *H.PYLORI* IN PEPTIC ULCER AND DRUGS USED IN TREATMENT

Dr. Fawzia Alotaibi

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PEPTIC ULCER


- ▶ **Peptic ulcer disease (PUD):**
- ▶ Is an ulcer define as mucosal erosions ($\geq 0.5\text{cm}$).
- ▶ Peptic ulcer is created in an acidic area (very painful).
- ▶ More Peptic ulcers are arise in duodenum than stomach.
- ▶ 4% of stomach ulcer can turn to be malignant tumor.
- ▶ Duodenal ulcers are generally benign.
- ▶ Multiple biopsies are needed to exclude cancer.




SIGNS AND SYMPTOMS

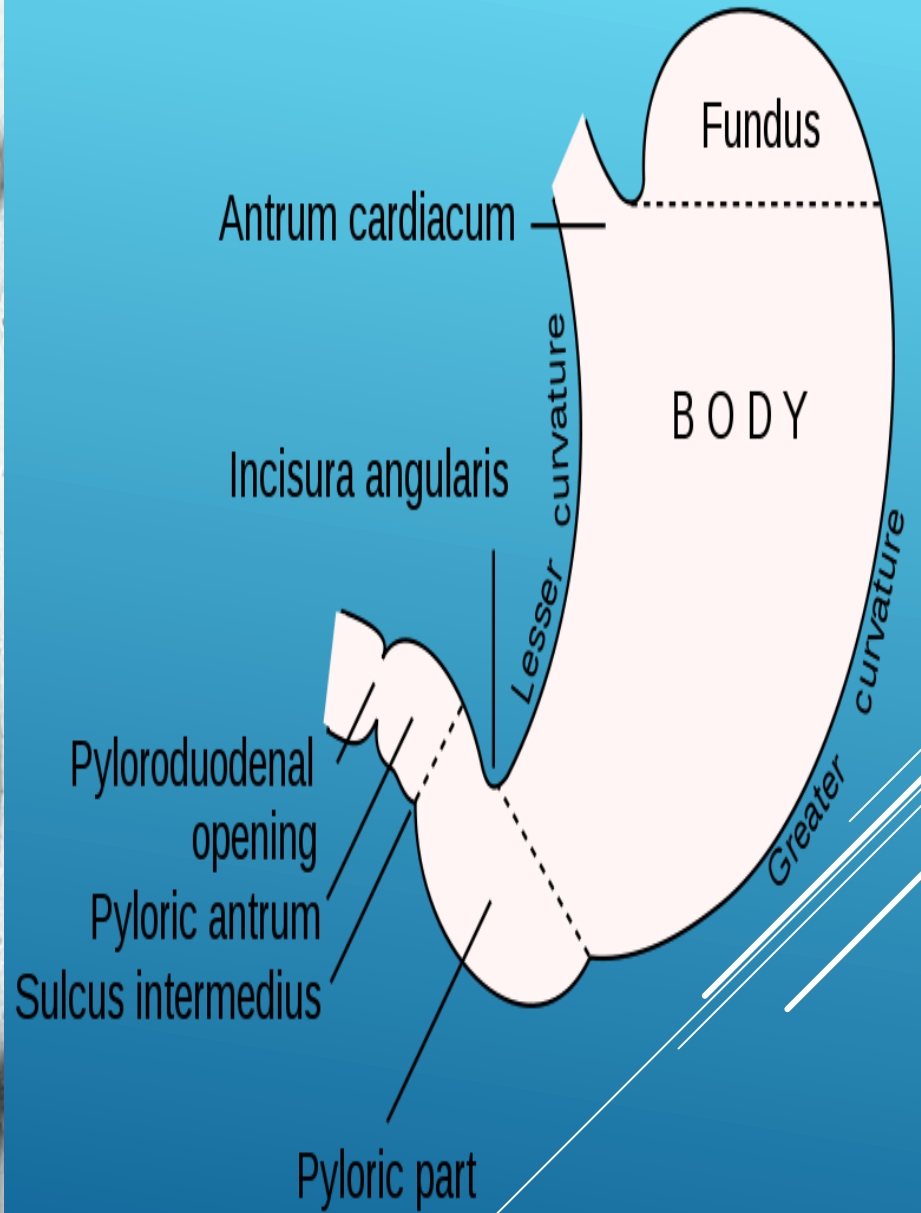
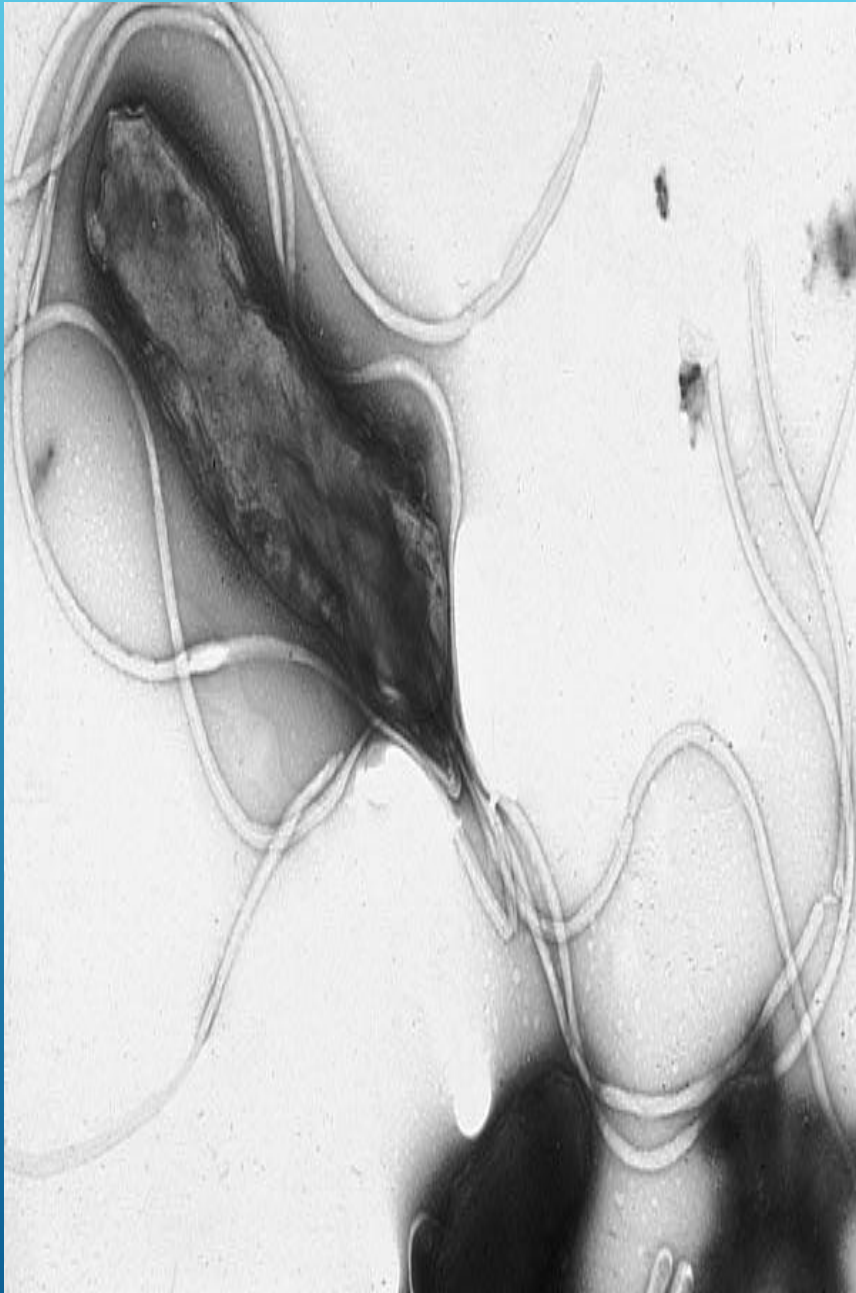
- ▶ Abdominal pain, epigastric with severity relating to mealtime (3 hours after meal with gastric ulcer).
- ▶ Bloating and abdominal fullness.
- ▶ Nausea and vomiting.
- ▶ Loss of appetite and weight loss.
- ▶ Haematemesis (vomiting of blood) due to gastric or esophagus damage.
- ▶ Melena (foul-smelling faeces due to oxidized hemoglobin iron).
- ▶ Rarely, Gastric or duodenal perforation leading to acute peritonitis (extremely painful-require urgent surgery).


OLD-MANAGEMENT

- ▶ Until recently every surgeon faced with a perforated peptic ulcer had to open the abdomen, sewing up the hole, and avoiding inflammation with cleansing abdomen cavity.
 - ▶ Peptic ulcer was a dangerous disease associated with high morbidity and mortality.
 - ▶ Gastrectomy (where part of the stomach or all is resected), is no longer used for peptic ulcer management.
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HELICOBACTER PYLORI

- 1982 in Perth (Australia), Warren and Marshal.
 - Helicobacter pylori (formerly known as Campylobacter.pylori or C.pyloridis) is found closely associated with gastric mucosa and causes chronic active gastritis, gastric and duodenal ulcer (Peptic ulcer) and could develop adenocarcinoma.
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- ▶ *H.pylori* plays a role in gastric and duodenal ulceration and probably also gastric cancer. Over 80% of individuals infected with the bacterium are asymptomatic.
 - ▶ More than 50% of the world's population harbour *H. pylori* in their upper gastrointestinal tract. Infection is more prevalent in developing countries.
 - ▶ The route of transmission is unknown, although it is known individuals typically become infected in childhood.
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LABORATORY CHARACTERISTICS

- **Morphology and staining** small, Gram-negative, spiral rods, motile by polar flagella.
 - **Culture:** on blood or chocolate agar in a moist microaerophilic atmosphere. For isolation from clinical specimens, use campylobacter selective medium. Small colonies grow after 3-7 days at 37°C.
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LABORATORY CHARACTERISTICS

- ▶ **Biochemical reactions:** catalase-positive; oxidase-positive;
strongly urease-positive.
 - ▶ **Typing:** a variety of nucleic acid methods have been developed, but there is no agreed typing scheme.
 - ▶ **Serology:** IgG and IgM to Cytotoxic Associated Gene A (CagA) and (VacA) for virulence strains.
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- A decorative graphic consisting of several parallel white lines of varying lengths, slanted diagonally from the bottom right towards the top right, set against a blue gradient background.

DIAGNOSIS

- ▶ test dyspeptic patients for *H pylori*.
- ▶ **Non-invasive methods:**
 - ▶ Blood antibody test (IgG, IgM or IgA).
 - ▶ Stool antigen test.
 - ▶ Carbon urea breath test (**C¹⁴** or **C¹³**).
- ▶ **Invasive methods (most reliable):**
 - ▶ Endoscopy followed by Histological examination.
 - ▶ Endoscopy followed by culturing the bacteria.

GENOME

- ▶ *H pylori* consist of large diversity of strains with 1.550 genes.
- ▶ Study of *H pylori* is centered on trying to understand the pathogenesis of genome database.
- ▶ *H pylori* contain 40kb-long Cag pathogenicity island (PAI) with over 40 pathogenetic genes.
- ▶ The **cagA gene** codes for the major *H pylori* virulence proteins.
- ▶ Asymptomatic patients carry *H pylori* strains lacking the Cag pathogenesis island (PAI).

PATHOPHYSIOLOGY

- ▶ To colonize the stomach, *H pylori* must survive acidity.
- ▶ Using flagella, *H pylori* moves through stomach lumen and drill into the mucoïd lining of stomach.
- ▶ Produces adhesions that binds to the epithelial cells.
- ▶ Produces large amounts of urease enzyme that break down urea into CO₂ + ammonia.
- ▶ This in-turn neutralizes gastric acid.
- ▶ Ammonia is toxic to epithelial cells along with proteases, vacA protein and phospholipases produced by *H pylori* and could damage epithelial cells.

PATHOPHYSIOLOGY- CONT

- ▶ Colonization of stomach or duodenum results in chronic gastritis (inflammation of stomach lining).
- ▶ Inflammation stimulate more production of gastric acid.
- ▶ This leads to gastric and duodenal ulcers, atrophy and later cancer.
- ▶ CagA protein was found to contribute to peptic ulcer.
- ▶ Free radical production in the gastric lining due to *H pylori* increases host cell mutation.
- ▶ *H pylori* induces the production of **TNF- α** and **Interleukin 6** that leads to host cells mutation.

PREVENTION

- ▶ **Eradication of infection will improve symptoms:**
- ▶ Such as (dyspepsia, gastritis, peptic ulcer and cancer).
- ▶ **Vaccination:**
- ▶ Promising results with studying adjuvant, antigens.
- ▶ Determining route of immunization (oral or intramuscular).
- ▶ **Dietary methods:** (eating broccoli, cabbage, honey, and drinking green tea).
- ▶ **Proper sanitation and clean sources of drinking water).**

EPIDEMIOLOGY

- ▶ Around **50%** of world's population harbor *H pylori*.
- ▶ **Third world** has more rate of infection.
- ▶ Infections are usually **acquired at childhood**.
- ▶ **Poor sanitary** conditions contribute to **high** rates.
- ▶ In USA high prevalence among **African-American** and **Hispanic** population-Due to **socioeconomic** status.
- ▶ **Higher hygiene** standards and widespread use of **antibiotics** behind lower rate of infection in the west.
- ▶ Overall frequency of *H pylori* infection is **declining**.
- ▶ Recently, antibiotics (metronidazole, clarithromycin) are becoming **resistance** to *H pylori*.


EPIDEMIOLOGY-CONT

- ▶ **Contagious** with an unknown route of transmission .
- ▶ **Person to person** (oral to oral or fecal-oral) route.
- ▶ **Transmission** occur mainly within families or community.
- ▶ **Fecal-oral** route of infection occur by ingestion contaminated food or water due poor hygiene.
- ▶ Using same spoons, forks and tooth brushes and kissing children mouth to mouth increases **oral-oral** route of infection.

ANTIBIOTIC SENSITIVITY

- ▶ **In vitro** *H.pylori* is sensitive to amoxicillin, tetracycline, metronidazole, macrolides (clarithromycin).
- ▶ However, **in vivo** their efficacy is often poor due to the low pH of the stomach, their failure to penetrate the gastric mucus and the low concentration of antibiotic obtained in the mucosa of the stomach.
- ▶ Recently , Metronidazole in developing countries is becoming resistance (80-90%).

TRIPLE THERAPIES

- ▶ One-week combination of Omeprazole, Clarithromycin and Tinidazole the rate of eradication was 95%-100%.
 - ▶ 10 days' combination of Ranitidine Bismuth citrate, Amoxicillin and Clarithromycin with eradication rate of no more than 75%.
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- ▶ 10 days combination of Ranitidine Bismuth citrate, Clarithromycin and metronidazole with an eradication rate of 90%.
- ▶ One-week combination of Omeprazole, Amoxicillin and metronidazole the rate of eradication was 96%-(very cost effective).

QUADRUPLE THERAPIES

- ▶ 7days regimen of combination of Omeprazole, Amoxicillin , metronidazole and proton pump inhibitor (PPI) have shown to increase the eradication rate up to 98%. Unfortunately it was followed by **side effects** such as **vaginal candidiasis** in 10% of women and **Pseudomembranous colitis** in 11% of patients.
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