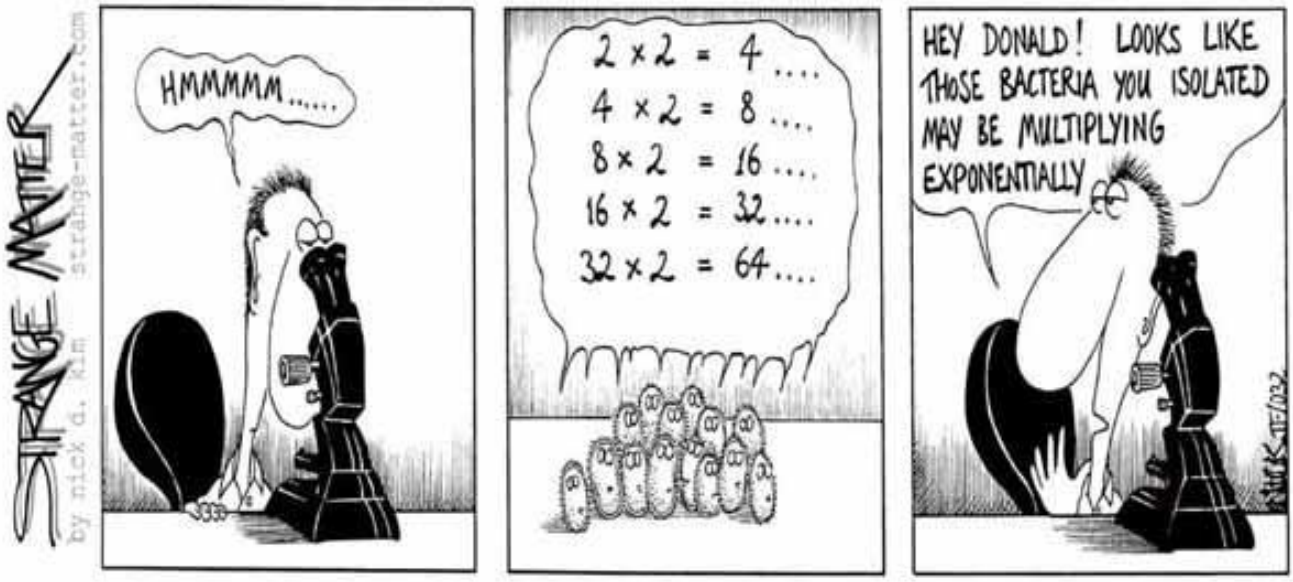
Micro Team 429©

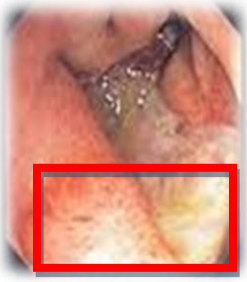
Present :

Role of H.pylori in Peptic Ulcer and drugs used in Treatment

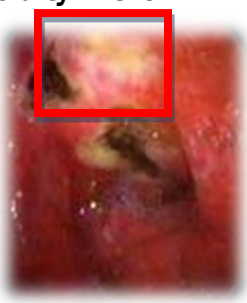


NOTES :
ABAN BAHABRI
ABDULMAJEED AL-SADHAN
REVISED BY :
ISMAIL RASLAN
DONE BY :
ABDULMAJEED AL-SADHAN

Peptic ulcer :



- Is an ulcer define as mucosal erosions(≥ 0.5cm) associated with the over usage of NSAIDs. (e.g : Aspirin)
- Peptic ulcer is created in an acidic area (very painful). The acidity in the stomach is (1.5-2)
- 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 :

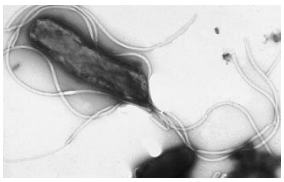
- Abdominal pain, epigastric with severity relating to mealtime (3 hours after meal with gastric ulcer).
- Bloating and abdominal fullness.
- Nausea and vomiting.
- Loss of appetite and weight loss.
- Haematemesis (vomiting of blood) due to gastric or esophagus damage.
- Melena (foul-smelling dark brown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

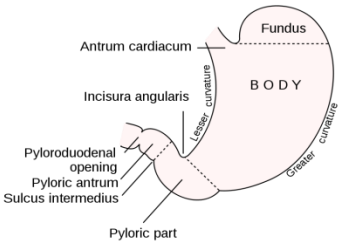
If we don't treat the peptic ulcer well , it may lead to perforation

Old-management :

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

Now we use the Gastrectomy only 4 cancer





Helicobacter pylori :

- 1982 in Perth (Australia),Warren and Marshal.
- Only effect the humans
- Usually effect the antrum + pyloric
- 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.
    - Helicobacter pylori look like the Campylobacter.pylori only in the shape
    - Campylobacter.pylori : (bacteria that cause diarrhea after eat chicken)
- 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.

Laboratory characteristics :

- **Morphology and staining :**

small, Gram-negative, spiral rods, motile by polar flagella (4-6) . (Flagella help in movement and to go inside the mucosa)

- **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. (slow growing)

- **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.

(H.pylori the only bacteria that's can survive in the Acidity of the stomach (1.5-2) , because of it is srongly urease – positive that's convert the urea to ammonia to change the PH to be Alkaline . also it is covered the bacteria inside the mucosa)

Diagnosis :

Checking for dyspeptic patients for H pylori.

Non-invasive methods (FIRST)	Invasive methods (most reliable) (only if the non-invasive was +ve)
Blood antibody test (IgG, IgM or IgA).	• Endoscopy followed by Histological examination.
Stool antigen test.	• Endoscopy followed by culturing the bacteria.
Carbon urea breath test (C^{14} or C^{13}). The patient drink the c14 then it is give ammonia	

Genome : (Not important)

- 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 pathogenesity island (PAI).

Pathophysiology : very important

- To colonize the stomach, H pylori must survive acidity.
- Using flagella, H pylori moves through stomach lumen and drill into the mucoid 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 neutalizes gastric acid. (as we said it b4)
- Ammonia is toxic to epithelial cells along with proteases, vacA protein and phospholipases produced by H pylori and could damage epithelial cells.
- 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: (not official)
  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 (south America) 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.
- 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 (outside the body) H.pylori is sensitive to amoxycillin, tetracycline, metronidazole, macrolides (clarithromycin).
- However, in vivo(inside the body) 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 :

(Proton pump + two kinds of Antibiotics)

1- One-week combination of Omeprazole, Clarithromycin and Tinidazole the rate of eradication was 95%-100%.
2- 10 days' combination of Ranitidine Bismuth citrate, Amoxycillin and Clarithromycin with eradication rate of no more than 75%.
3- 10 days combination of Ranitidine Bismuth citrate, Clarithromycin and metronidazole with an eradication rate of 90%.
4- One-week combination of Omeprazole, Amoxycillin and metronidazole the rate of eradication was 96%-(very cost effective).

Quadruple Therapies :

- 7days regimen of combination of Amoxycillin , metronidazole, Ranitidine Bismuth Citrate and proton pump inhibitor (Omeprazole) 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.

  - So , why the Triple therapies better than the Quadruple therapies ?!

THE END , BEST WISHES