**OBJECTIVES**

- After this session, the attendee will have a better understanding of:
  - The link connecting H. pylori & Gastric Cancer
  - Screening for H. Pylori
  - Treatment/Eradication of H. pylori

**GASTRIC CANCER HISTORY**

- One of our oldest foes
  - 3000 BC hieroglyphics
  - Cancer incidence Italy (1760 – 1839)
    - Most common and lethal cancer
  - Leading worldwide cause of cancer deaths until 1980
    - Surpassed by lung cancer
AGE STANDARDIZED MORTALITY RATES: DECREASING GASTRIC CANCER DEATHS

HELICOBACTER PYLORI FACTS

• Gram negative, flagellated, spiral-shaped bacterium
• Curved, non-sporulating
• Originally thought to be Campylobacter sp.
• In 1983, BJ Marshall and JR Warren discovered this slow growing bacterium in stomachs of patients with chronic gastritis
  • Suggested its causal role in gastroduodenal ulcers
  • A 20th century GI milestone

ULCER TALES

• Disbelief in infectious agent inducing gastric ulcers
• Barry Marshall
• Koch’s postulate
• Self experimentation in 1984
• Nobel Prize in Medicine 2005
• Now, H pylori linked with:
  • Gastric adenocarcinoma
  • Intestinal & Diffuse types
  • Lymphomas
  • ? Pancreatic, Hepatobiliary and Colorectal cancer

H PYLORI INFECTION AND THE DEVELOPMENT OF GASTRIC CANCER

• Uemura et al., NEJM 2001, 345(11): 784
• First long term, prospective study
• Japan, 1990 to 1993
• 1526 consecutive patients with NUD, GU, DU or gastric hyperplastic polyps
  • 1246 Hp +ve, 280 Hp -ve
• Endoscopy with biopsy - histology and RUT, serology
**RESULTS**

**DISTRIBUTION OF GASTRIC CANCER & H. PYLORI**

- Age adjusted gastric CA incidence
- H. pylori prevalence

**IARC ESTIMATES HP INDUCED GASTRIC CANCER:**
- Developed countries 36%
- Developing countries 47%

**HOW DOES H PYLORI CAUSE GASTRIC CANCER?**

- **Host Immune Response**
  - Cytokine polymorphisms (IL-1 Beta)
  - Neutrophil activation (CD11a/b with ICAM-1)

- **Epithelial Response**
  - Apoptotic pathways
  - Cell signalling events

- **Environmental Factors**
  - Diet (salt, low antioxidants)
  - Hypochlorhydria and lack of ascorbic acid
  - HbA1c
  - Obesity

**SCREENING FOR HELICOBACTER PYLORI**
HOW DO WE TEST FOR HP?

○ Invasive
  • Endoscopic biopsy and histological exam
  • Rapid urease test
  • Culture
  • Non-invasive
    • Serology (ELISA)
    • UBT
    • Stool Antigen test

HP TESTS - INVASIVE

○ Biopsy
  • Antrum ± Gastric body
  • H&E
  • Warthin-Starry silver stain
  • SEN: 95%, SPEC: 99%

○ Rapid Urease
  • Urea + pH indicator in well – change with urease
  • SEN: 85-95%, SPEC: 95-100%

HP TESTS – NON-INVASIVE

○ Serology - IgG ELISA
  • SEN: 85-90%, SPEC: 80-85%
  • PPV: low in NA
  • Can stay positive after eradication

○ Stool Ag – SEN/SPEC: 90-94%

○ Urea Breath Test (UBT)
  • $^{14}$C or $^{13}$C – labelled urea
  • SEN: 90-96%, SPEC: 90-98%

FALSE NEGATIVE BREATH TESTS

○ Ongoing treatment with PPI, H2RAs and bismuth
○ False negatives seen
○ Inhibits H. pylori activity
○ Therefore, stop PPI, H2RAs and/or bismuth at least 1 week prior to breath tests, 14 days preferable
WHO SHOULD WE TEST/SCREEN?

○ PUD
  • Active or prior history
  • No empiric therapy!
○ MALT lymphoma
○ ? Family history of gastric cancer
○ Uninvestigated dyspepsia < age 55
○ Family History: Gastric cancer from endemic areas
○ You are willing (and able) to treat a +ve result

GASTRIC CANCER SCREENING

• Organized programs: Japan, Korea
  • Japan: Age 50 (Barium swallow annually, or EGD 2-3 yrs
  • Korea: EGD 40-75 Q2 yrs
• No organized programs in Western countries

• High Risk groups:
  • Gastric adenomas
  • Pernicious anemia
  • Gastric Intestinal Metaplasia
  • Genetic syndrome (FAP, Lynch, Peutz-Jeghers, Juvenile polyposis)

TREATMENT/ERADICATION OF HELICOBACTER PYLORI

THERAPY

• Goal is to fully eradicate H. pylori
• Increasing antibiotic resistance

- **Metronidazole**: 25-30%
- **Clarithromycin**: 15-20%
- **Levofoxacin**: 15-25%
MANY POTENTIAL REGIMENS

- Triple therapy?
- Sequential therapy
- Quadruple therapy
- CLAMET therapy

Changes since 2015 Helicobacter Canadian Consensus Conference

TRIPLE THERAPY

- Only give in areas where clarithromycin resistance is <15%
- At present, in Canada, clarithromycin resistance may be as high as 20%
- HP-PAC
  1. PPI BID
  2. Amoxicillin 1g PO BID
  3. Clarithromycin 50mg PO BID
- Give for 10-14 days
  - The old standard - now not recommended as first line therapy

SEQUENTIAL THERAPY

- PPI BID for 10-14 days
  - Days 1-5 (7)
    - Amoxicillin 1g PO BID
  - Days 6-10 (14)
    - Clarithromycin 500mg PO BID
    - Metronidazole 50mg PO BID

CLAMET THERAPY

- The new first line therapy

PPI BID
AMOXICILLIN 1G BID
CLARITHROMYCIN 500MG BID
METRONIDAZOLE 500MG BID

14 DAYS
BISMUTH BASED QUADRUPLE THERAPY

- The new first line therapy

PPI BID
BISMUTH SUBSALICYLATE 525MG (2 TABS) QID
TETRACYCLINE 500MG QID
METRONIDAZOLE 500MG QID

14 DAYS

TREATMENT PEARLS

- Compliance is paramount
  - noncompliance leads to resistance
- Patient education - spend a little more time....
  - tell patients to plan so they can finish
- Use blister packs

WHO TO CONFIRM ERADICATION?

- Persistent symptoms
- PUD
- MALT
- Resection for early gastric cancer

SUMMARY

- In this session, we have reviewed:
- The link between H pylori and Gastric cancer
  - 36-47% of all cases worldwide
- How and who to screen for H pylori infection
  - UBT or biopsy
- How to eradicate H pylori
  - CLAMET or Bismuth quadruple therapy