Peptic Ulcer

By

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Def:

Loss of continuity of the epithelial lining of the gastroduodenal mucosa deep down to muscularis propria.

Sites

In that order

1. Duodenum → the commonest site.
2. Stomach.
3. Jejunum in
   1. Stomal ulcer.
   2. In zollinger- Ellison’s syndrome.
4. Oesophagus.
5. Meckel’s diverticulum.
Pathogenesis:

Disturbed gastroduodenal mucosal defense resulting from excess autopeptic power of the gastric juice over the defensive power of the GIT mucosa.

Type:

1. Acute peptic ulcer.
2. Chronic peptic ulcer.
<table>
<thead>
<tr>
<th></th>
<th><strong>G.U.</strong></th>
<th><strong>D.U.</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Incidence</strong></td>
<td>&lt; 1%</td>
<td>11 times more common</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>Older (boys)</td>
<td>Younger (25 - 45 ys)</td>
</tr>
<tr>
<td><strong>Sex</strong></td>
<td>♂ = ♀</td>
<td>♂ +++</td>
</tr>
<tr>
<td><strong>Acidity</strong></td>
<td>Normo or hypoacidity</td>
<td>hyperacidity</td>
</tr>
<tr>
<td><strong>Motility</strong></td>
<td>Delyed gastric emptying</td>
<td>hypermotility</td>
</tr>
<tr>
<td><strong>Samity history</strong></td>
<td>- ve</td>
<td>+++</td>
</tr>
<tr>
<td><strong>Blood group</strong></td>
<td>- ve</td>
<td>group O</td>
</tr>
</tbody>
</table>
Both:

- Develop in the mucosa exposed to the gastric juice.
- Same – behavior, histopathology, complications. except malignancy nay occur on top of G.U.
- Respond to rest, antacids.
- Excacerbation with stress.

Epidemiology:

- 5-10% of all indiiduals develop peptic ulcer in their life time.
- G.U. → peak occurrence 40-70 ys.
- D.U. → peak occurrence 25-45 ys.
- ♂ > ♀ → in D.U. but equal sex ratio in G.U.
Clinical picture:

1. Classic presentation →
   - pain
   - dyspepsia

2. Complicated →
   - Bleeding
   - Perforation
   - stenosis
     - gastric outlet obstruction
     - hourglass stomach
   - malignancy
     - 1-5% in G.U.
     - never in D.U.
Investigations:

- Radiography: → miss > 20% of D.U.
- Endoscopy → is the investigation of choice
  - Advantage →
    - More accurate
    - Direct biopsy for histopathological
    - Safe in co-operative patient.
    - Preferable in patient
      - Bleeding.
      - Dyspepsia.

- Malignancy is suspected if:
  - Large ulcer size
  - Outside the ulcer-beating ared
  - Nodular base.
**Common forms of peptic ulcer**

1. Helicobacter pylori-associated
2. NSAID-associated
3. Stress ulcer

**Uncommon specific forms of peptic ulcer**

1. Acid hypersecretion  
   a. Gastrinoma: inherited-MEN I, sporadic  
   b. Increased mast cells/basophils  
      Mastocytosis: inherited and sporadic  
      Basophilic leukemias  
   c. Antral G cell hyperfunction/hyperplasia

2. Other infections  
   a. Viral infection: herpes simplex virus type I, CMV  
   b. ? Other infections

3. Duodenal obstruction/disruption (congenital bands, annular pancreas)

4. Vascular insufficiency: Crack cocaine-associated perforations

5. Radiation-induced

6. Chemotherapy-induced (hepatic artery infusions)

7. ? Rare genetic subtypes  
   a. ? Amyloidosis type III (Van Allen-Iowa)  
   b. ? Tremor-nystagmus-ulcer syndrome of Neuhauser
■ **III of peptic ulcer**
  - Identify the cause → tailor therapy accordingly.
  - To reduce the aggressive factors.
  - Aiming at:
    1. Rapid reduction or resolution of symptoms.
    2. Acceleration of ulcer healing.
    3. ↓ the frequency of complication.
    4. To prevent recurrence.

■ **Lines of III**
  - Stop smoking.
  - Diet
    - Regular meals to buffer the intragastric acidity
    - Avoid irritants →
    - Home remedies.
Medical III:

1. Antacids:
   - Def: are weak bases reacting with gastric HcL to from salt & H₂O → buffering action
   - Action → to reduce – the gastric pH > 4

   - Indications
     1. Symptomatic ttt of hyperacidity
     2. GERD.
     3. High dose con be used in ttt of Du → ? Compliance

   - Adverse effects.
   - Dose – response relationship of the antacid is depending on the gastric secretory capacity
- Adverse effects
- Drug interaction
- Indications →
  - Syptomatie III of hyperacudty
  - GERD
  - High dose can be used in III of DU → ?
  Complication

2. **Mucosal cytoprotective agents.**

- carbenoxaloxone:
  - Is a synthetic derivative of glycyrrhizinic acid → liquorices constituent.
  - Action promotes healing of peptic ulcer sp. G.U.
- **Mechanism.**
  - ↑ mucosal – resistance →
    - ↑ Secretion ↑ viscosity of mucus
    - Alter its composition
    - ↓ back diffusion of H⁺ into mucosa
    - Slows down gastric epith. turnover
  - Affects pG metabolism
  - Reduces: pepsin chomotryptic activity

- **Indications:**
  - Biogastrone → ttt of G.U.
  - Duogastrone sustained release cap → ttt of D.U.
  - Pyrogathone → ttt of GERD.
- **S.E:**
  - Mineralocorticoid action.
  - More marked in hepatic, renal, cardiac & elderly patients.

- **Deglycyrrhizined liquorice → caved –S**
  - Less mineralocorticoid action.
  - Less ulcer healing efficacy.
**Sucralfate:**

- Aluminum sucrose sulphate → sulfated disaccharide.
- Used for ttt of P.U.D.
- Mechanism of action.
  - Polymerization & selective binding to the necrotic ulcer tissue → acts as a barrier to acid, pepsin, bile salts also, inhibits the pepsin activity.
  - Requires an acidic PH to be activated.
  - **S.E:** constipation.
  - **Dose:** 1gm 4 times on empty stomach “before meals”.
Colloidal- Bismuth compounds.

- T.B.D → Denol.
- Pepto-Bismol → bismuth subsalsylate.

Mechanisms.

- Acts locally in the presence of acidic medium by combing with the mucus, exudates in the ulcer crater providing a protective coat.
- May stimulate mucus production.
- Eradicate gastric H.P.

S.E:

- Black stool.
- Teeth discoloration.
- Unpleasant ammonical small
- In CRF → Enacephalopathy.

Dose: 120mg tab 1x4 before meals.
P.G analogues:
- Misoprisol
- Inoprostil

Action:
- Mild inhibitory effect on gastric HCL secretion.
- Mucosal cytoprotection against NSAID included injury.
  - ↑ mucus production
  - ↑ bicarb. secretion.
  - Maintain the gastric mucosal blood flow
  - Stimulates cell reneural & regeneration.
- Misoprostol
- E.g (Cytotic 20 ug tab t.d.s)
- S.E: diarrhea & ↑ uterine contractions.
- CI → pregnancy.
Gastric anti secretary drugs include:

- **H$_2$ receptor antagonists as:**
  - Cimitidine → Tagamet
  - Ranitidine → Zantac.
  - Famotidine → Pepcid.
  - Nizatidine → Axid.

- **Indication:**
  - DU – Bengin G.U.
  - Z.E. Syndrome.
  - Hyperscretory conditions → as systemic mastocytosis-MEN$_1$
**Mechanism:**

- Competitive inhibition of the histamine action at the H\textsubscript{2} receptors of the parietal cells.

**Side effects:**

- GIT
- CNS
- Endocrinal

**Drug interactions → inhibition of the cytochrome P450 enzyme system.**

**Rantidine:**

- More potent 5-10 times.
- More selective H\textsubscript{2} – receptor antagonst.
- Slightly longer duration of action.
- Less side effects.
**Famotidine:**
- 8-10 times more potent as Rantidine.
- Not inhibit cyt. P450.

**Nizaitidine → Similar to Famotidine.**

**For refractory cases:**
- Shift to other H₂ receptor blocker or PPI.
- need > 4wks +++.

**Proton pump inhibitors (PPI) as:**
- Omeprozole.
- Lanzoprazole
- Pantoprazole
- Esomeprozole (Nexium)
Produce dose related long lasting inhibition of basal & ↑ed gastric acid secretion.

Acts as a specific irreversible inhibition of the partial cell H⁺/K⁺ Atpase enz. after being activated by the strong acid environment of the secretory canalliculus of the parietal cell → single dose → inhibit 100% gastric acid secretion.
**Side effects:**

- Hypochlorhydria, 2ry hypergastrinaemia.
- Prolonged administration
  - Gastric carcinoid syndrome.
  - Bacterial colonization.
- Interfere with the oxidation of some drugs.

**Octreotides & their analogues:**

- Long acting somatostatin analogue.
- Significantly inhibit the secretion of the gastric & pancreatic hormones.

**Indications**

- ZES → ↓ tumor growth
- ↓ size of the metastasis.
- **Anti-cholinergic drugs:**
  - Used only as adjuvants to H₂ blocker specially in patients refractory to ttt or with nocturnal pain.
  - Limited use by their adverse effects.
  - **Ex:**
    - Antrenyl 5mg t.d.s.
    - Merbenyl 7.5mg t.d.s.

- **Selective antimuscarinic drugs:**
  - Action: selection → blockers of the peripheral M, muscarinic receptors near the gastric parietal cells
  - Selective inhibition of the gastric acid secretion.
  - Poorly penetrate BBB → minimal SE.

- **Containdications to antichotinergic drugs.**
- **Eradication of Helico-bacter pylori.**
# Antimicrobial Therapies for Treatment of H. Pylori Infection

<table>
<thead>
<tr>
<th>Therapy</th>
<th>Hp Drug 1</th>
<th>Hp Drug 2</th>
<th>Hp Drug 3</th>
<th>Notes</th>
<th>Success</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triple</td>
<td>Tetracycline HCl 500 mg q.i.d.</td>
<td>Metronidazole 250 mg t.i.d.</td>
<td>Bismuth subsalicylate 2 tablets q.i.d.</td>
<td>With meals for 14 days plus an antisecretory drug</td>
<td>&gt; 90%</td>
</tr>
<tr>
<td>Triple</td>
<td>Tetracycline HC1 500 mg q.i.d.</td>
<td>Clarithromycin 500 mg t.i.d.</td>
<td>Bismuth subsalicylate 2 tablets q.i.d.</td>
<td>With meals for 14 days plus an antisecretory drug</td>
<td>&gt; 90%</td>
</tr>
<tr>
<td>Triple</td>
<td>Amoxicillin 500 mg q.i.d.</td>
<td>Clarithromycin 500 mg t.i.d.</td>
<td>Bismuth subsalicylate 2 tablets q.i.d.</td>
<td>With meals for 14 days plus an antisecretory drug</td>
<td>&gt; 90%</td>
</tr>
<tr>
<td>Triple</td>
<td>Amoxicillin 500 mg q.i.d.</td>
<td>Metronidazole 250 t.i.d.</td>
<td>Bismuth subsalicylate 2 tablets q.i.d.</td>
<td>With meals for 14 days plus Drug an antisecretory</td>
<td>&gt; 80%</td>
</tr>
<tr>
<td>Triple</td>
<td>Clarithromycin 250 mg b.i.d.</td>
<td>Metronidazole 500 mg b.i.d.</td>
<td>Omeprazole 20 mg. b.i.d.</td>
<td>For 7 to 14 days</td>
<td>&gt; ~%</td>
</tr>
<tr>
<td>Dual</td>
<td>Amoxicillin 750 mg t.i.d</td>
<td>Clarithromycin 500 mg t.i.d</td>
<td></td>
<td>With meals for 14 days plus an antisecretory drug</td>
<td>&gt; 90%</td>
</tr>
<tr>
<td>Dual</td>
<td>Amoxicillin 750 mg t.i.d</td>
<td>Metronidazole 500 mg t.i.d</td>
<td></td>
<td>With meals for 14 days plus an antisecretory drug</td>
<td>&gt; 85%</td>
</tr>
<tr>
<td>Dual</td>
<td>Clarithromycin 500 mg t.i.d</td>
<td>Omeprazole 40 mg q.A.M.</td>
<td></td>
<td>With meals for 14 days</td>
<td>70-80%</td>
</tr>
<tr>
<td>Dual</td>
<td>Amoxicillin 1 gram b.i.d.</td>
<td>Omeprazole 20 mg b.i.d.</td>
<td></td>
<td>With meals for 14 days</td>
<td>35-60%</td>
</tr>
</tbody>
</table>
Nutritional supplement

- α – Leinoleic acid
- Flaxseed oil
- Vitamin A – E – C
- Omega-3 fatty acid
- High fiber content
- Probiotics
- Homeopathies.

- **Surgical +++:**
  - **Indications:**
    - Intractable ulcers, recurrent, jejunal ulcer.
    - Complicated ulcers:
      - Malignant ulcer.
      - Perforated ulcer.
      - Gastric outlet obstruction.
Alternative medicine:

- Acupuncture
- Chiropractic → spinal manipulative therapy.
- Relaxation techniques & psychotherapy.
- Yoga
- Herbal remedies.
  - Cat claw
  - Evening primrose
  - Liquorice
  - Tumerice
  - Peppermint
  - Aloe-vera
Truncal vagotomy and pyloroplasty

Operative mortality < 1%

Denervate 6-8 cm of esophagus

Operative mortality < 0.3%

Highly selective vagotomy without pyloroplasty
- Proximal gastric vagotomy
- Parietal cell vagotomy

Vagotomy and antrectomy with Billroth II anastomosis

Operative mortality 2%

Vagotomy and antrectomy with Billroth II anastomosis
## SURGICAL OPTIONS FOR PEPTIC ULCER

<table>
<thead>
<tr>
<th>Type</th>
<th>Location</th>
<th>Incidence</th>
<th>Treatment of Choice</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Body (lesser curve)</td>
<td>55-60%</td>
<td>Antrectomy (Billroth I)</td>
<td>Ulcer resected with specimen. Mortality/recurrence rate of 2%</td>
</tr>
<tr>
<td>II</td>
<td>In association with duodenal ulcer</td>
<td>20-25%</td>
<td>Vagotomy and antrectomy</td>
<td>Acid reduction and ulcer excision accomplished</td>
</tr>
<tr>
<td>III</td>
<td>Prepyloric</td>
<td>20%</td>
<td>Vagotomy and antrectomy</td>
<td>Behaves like duodenal ulcer</td>
</tr>
<tr>
<td>IV</td>
<td>High-lying near gastro esophageal junction</td>
<td>&lt;5%</td>
<td>Resection and esophago-gastrojejunostomy (Csendes)</td>
<td>More common in South America</td>
</tr>
</tbody>
</table>
D.U

HP eradication & PPI therapy

Cure

Persistence or recurrence

Hp eradication & PPI therapy

- Multiple failures
- severe symptoms
Exclude ZES

Elective H.S.V
G.U

Endoscopy & biopsy

Malignant
- Surgery

Benign
- HP eradication & PPI therapy
- Repeat endoscopy & biopsy
  - Cure
  - Persistent ulcer
    - Malignant
      - Surgery
    - Benign
Benign

HP eradication & PPI therapy

Repeat endoscopy & biopsy

Cure

Persistent ulcer

Malignant

Surgery

Benign

Repeat therapy

Cure

Not cure

Surgery
Recurrent ulcer symptoms

Endoscopy & biopsy

Hp. Eradication PPI therapy
exclude ZES

ZES +ve

PPI therapy +
Tumor localization
studies

ZES -ve

Ulcer heales

Follow up

Ulcer persists

Repeat therapy
(6-8wks)

Ulcer heales

Re-evaluate ZES
Test completeness of vagotomy

Surgery

Ulcer persists

Thank You