Gastrointestinal System
Session 5
Gastric Disease

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Learning outcomes

- *1. Describe the prevalence and incidence of common disorders affecting the stomach*
- *2. Describe the presentation, investigation and outline the management of common Gastric disorders*
- *3. Describe the clinical features and natural history of ulcer disease*
- *4. Explain the importance of Helicobacter Pylori in causing chronic gastritis*
- *5. Outline the principles of modern ulcer treatment*
- *6. Outline the ways in which gastric acid secretion may be reduced by drugs*

References

- Gastrointestinal system – crash course. 4th Edition, Mosby [2008]

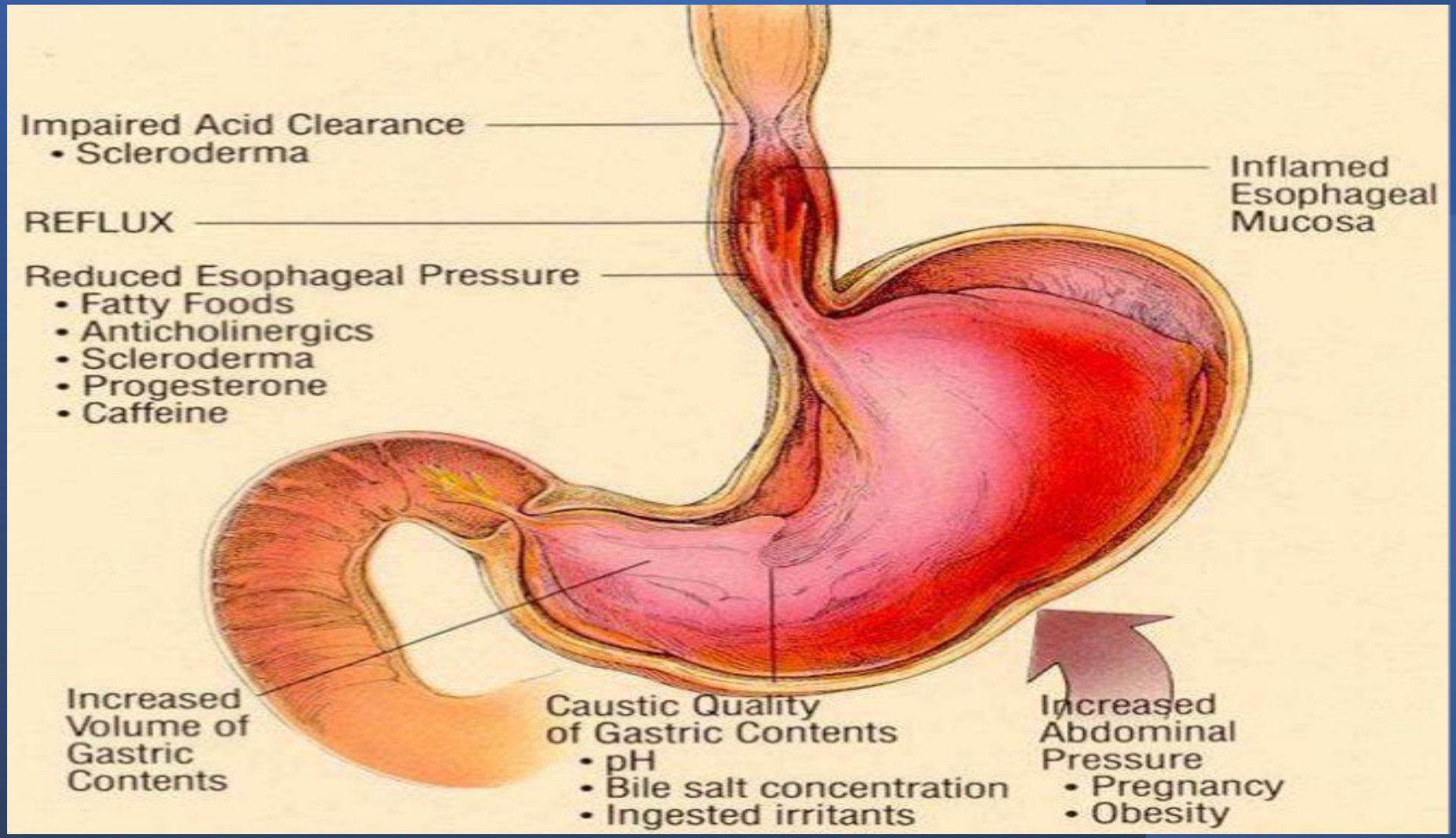
1. Describe the prevalence and incidence of common disorders affecting the stomach

- Gastrointestinal (GI) symptoms are widespread and carry heavy economic and social consequences.
- It is estimated that in the United States 11% of the population suffer from a chronic digestive disease, with a prevalence rate as high as 35% for those 65 years and over .
- Functional gastrointestinal disorders (FGIDs), represented by functional dyspepsia (FD) and irritable bowel syndrome (IBS), include variable combinations of chronic or acute gastrointestinal symptoms not explained by structural or biochemical abnormalities.
- Worldwide the prevalence rates in the general population of dyspepsia/FD and IBS according to Rome III diagnostic criteria are 5.3–20.4% and 1.1–29.2%, respectively.

2. Describe the presentation, investigation and outline the management of common Gastric disorders

- **Gastro-oesophageal reflux disease (GORD):**
- **anti-reflux mechanisms**:
- Lower oesophageal sphincter – which is usually closed and transiently relaxes as part of physiology of swallowing to allow bolus to move into stomach
- Oesophagus enters stomach in abdominal cavity
- Pressure in abdominal cavity is higher than that of thoracic
- Right crus of diaphragm acts as sling around the lower oesophagus

- **Clinical features of GORD occur when antireflux mechanisms fail and there is prolonged contact of gastric juices with lower oesophageal mucosa**.


Impaired Acid Clearance
• Scleroderma
REFLUX
Reduced Esophageal Pressure
• Fatty Foods
• Anticholinergics
• Scleroderma
• Progesterone
• Caffeine
Inflamed Esophageal Mucosa
Increased Volume of Gastric Contents
Caustic Quality of Gastric Contents
• pH
• Bile salt concentration
• Ingested irritants
Increased Abdominal Pressure
• Pregnancy
• Obesity

Clinical features

- **Dyspepsia (heartburn) is the medical term for indigestion, a symptom which includes epigastric pain, heartburn, distension, nausea or 'an acid feeling' occurring after eating or drinking.**
- **CAUSES**
- functional dyspepsia
- reflux disease
- ulcer disease
- gastric cancer
- biliary tract disease
- chronic pancreatitis, pancreatic cancers
- hepatic
- Diabetes mellitus.
- Antibiotics, iron and other medications.
- NSAIDs

Investigations and diagnosis

- **Usually clinical diagnosis made without investigation on symptoms alone, no need to investigate unless alarming symptoms (such as dysphagia) or hiatus hernia is suspected (which would be investigated by endoscopy)**

Management

- **Lifestyle**
- Lose weight.
- stop smoking.
- reduce alcohol consumption.
- reduce consumption of food groups known to aggravate the symptoms(e.g. chocolate, fatty foods, coffee) .
- eating smaller meals

Medications

- **Simple antacids** – e.g. calcium carbonate (neutralises acid)
- **Raft antacids–** e.g. Gaviscon liquid, taken after eating which creates protective raft that sits on top of stomach contents to prevent reflux
- **PPIs –** e.g. omeprazole – reduction in acid secretion by parietal cells
- **H2 antagonists** – e.g. ranitidine – blocks H2 receptors which reduced acid secretion

Complications

- **Continual contact of gastric juices with oesophageal mucosa can lead to metaplastic change → Barrett's oesophagus**

3. Describe the clinical features and natural history of ulcer disease

- **Peptic ulcer disease (PUD):**
- Peptic ulcer is break in superficial epithelial cells penetrating down into Muscularis mucosa of either stomach (GU) or duodenum (DU). Most DUs are found in duodenal cap and GU are most commonly seen in lesser curvature of stomach.
- Ulcer disease has become a disease predominantly affecting the older population, with the peak incidence occurring between 55 and 65 years of age.

pathogenesis

- Gastric hyperacidity is fundamental to the pathogenesis of PUD.
- The acidity that drives PUD may be caused by :
- *1. H. pylori* infection.
- 2. parietal cell hyperplasia.
- 3. excessive secretory responses, or impaired inhibition of stimulatory mechanisms such as gastrin release. For example, **Zollinger-Ellison syndrome,** characterized by multiple peptic ulcerations in the stomach, duodenum, and even jejunum.

- **Cofactors in peptic ulcerogenesis include**
- chronic NSAID use.
- cigarette smoking, which impairs mucosal blood flow and healing.
- high-dose corticosteroids, which suppress prostaglandin synthesis and impair healing.

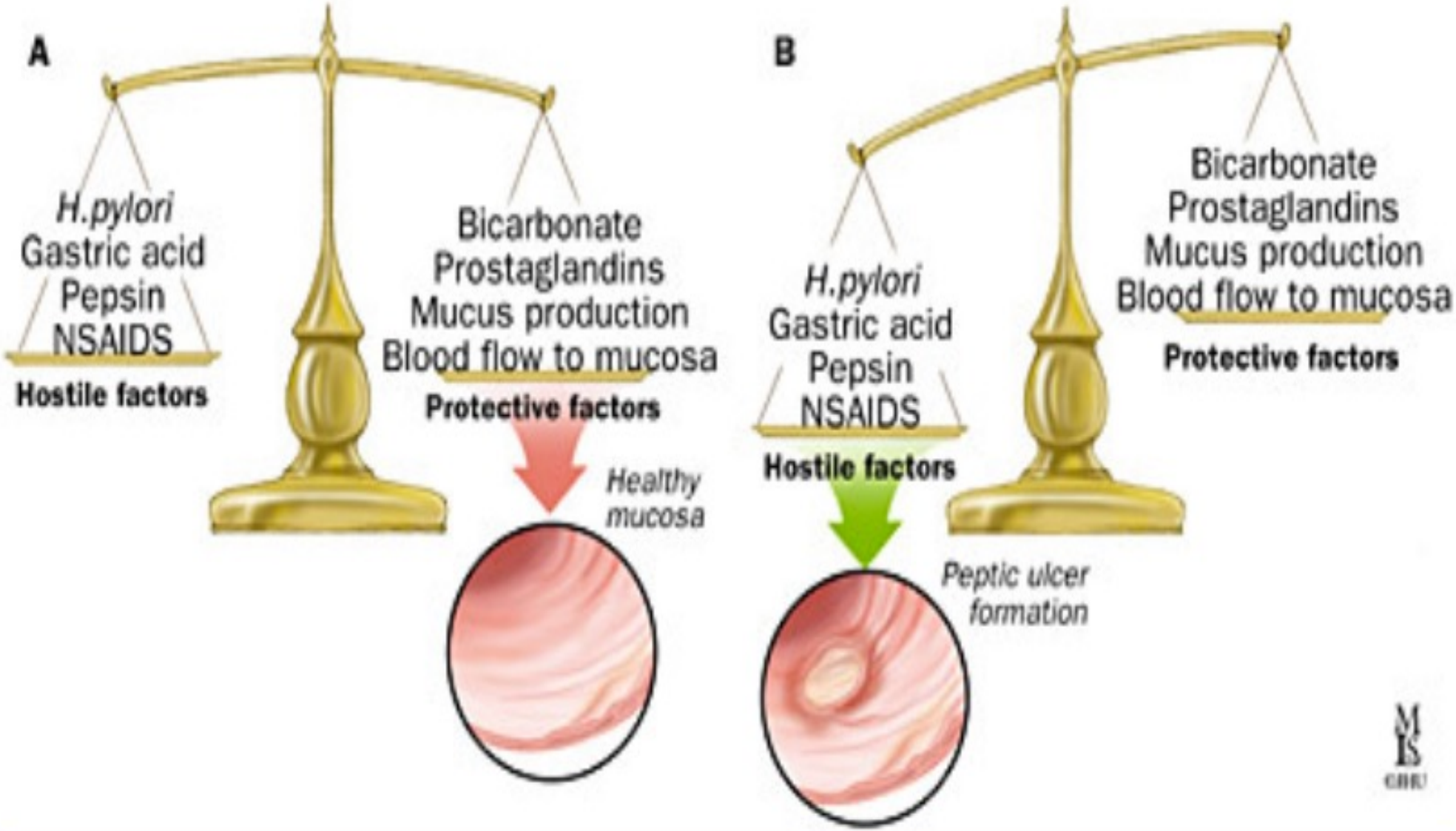
- Peptic ulcers are more frequent in persons with alcoholic cirrhosis, chronic obstructive pulmonary disease, chronic renal failure, and hyperparathyroidism ، In the latter two conditions, hypercalcemia stimulates gastrin production and therefore increases acid secretion.

- Finally, psychologic stress may increase gastric acid production and exacerbate PUD.

Injury to gastric and duodenal mucosa develops when deleterious effects of gastric acid overwhelm the defensive properties of the mucosa.

Inhibition of endogenous prostaglandin synthesis leads to a decrease in epithelial mucus, bicarbonate secretion, mucosal blood flow, epithelial proliferation, and mucosal resistance to injury.

Lower mucosal resistance increases the incidence of injury by endogenous factors such as acid, pepsin, and bile salts as well as exogenous factors such as NSAIDs, ethanol and other noxious agents


A
H.pylori
Gastric acid
Pepsin
NSAIDS
Hostile factors
Bicarbonate
Prostaglandins
Mucus production
Blood flow to mucosa
Protective factors
Healthy mucosa
B
H.pylori
Gastric acid
Pepsin
NSAIDS
Hostile factors
Bicarbonate
Prostaglandins
Mucus production
Blood flow to mucosa
Protective factors
Peptic ulcer formation

Epidemiology

- Duodenal Ulcers found in ~10% adult population and are 2-3 times more common than GUs.

- In developed countries increased prevalence of NSAID-associated GUs and decreasing prevalence of H pylori associated ulceration

Clinical features

- Recurrent, burning epigastric pain (pain is often worse at night and when hungry with Duodenal Ulcers and relieved when eating).
- Persistent, severe pain suggest penetration of ulcer into other organs
- Back pain suggest penetrating posterior ulcer.
- nausea, vomiting .
- With GUs can get weight loss and anorexia
- May be asymptomatic and present for first time with hematemesis when ulcer has perforated blood vessel(s)

Investigations

- Investigate *H pylori* infection

- In older patients (over 55y/o) or with other alarming symptoms → endoscopy to exclude cancer

Management

- The goal of therapy for peptic ulcer disease is to relieve symptoms, heal craters, prevent recurrences, and prevent complications.
- **Medical therapy** should include treatment with drugs, and attempt to accomplish the following:
- 1) reduce gastric acidity by mechanisms that inhibit or neutralize acid secretion.
- 2) coat ulcer craters to prevent acid and pepsin from penetrating to the ulcer base.
- 3) provide a prostaglandin analog.
- 4) remove environmental factors such as NSAIDs and smoking, and 5) reduce emotional stress (in a subset of patients).

Management cont.

- If due to H pylori infection → **Triple Therapy**
  - Proton Pump Inhibitor – Omeprazole
  - Antibiotics – Clarithromycin / Amoxicillin
  - H_2 Antagonist – Cimetidine
- If taking NSAIDs – stop or review – use alternatives (NSAIDs with lower risk of causing PUD), or use prophylactic PPI as well as NSAID

- Surgical therapy

Complications of PUD

- **Haemorrhage of blood vessel** which ulcer has eroded → presents with hematemesis and melena
- **Perforation of the ulcer** – more common in DUs than GUs – usually perforate into peritoneal cavity
- **Gastric outlet obstruction** → can be pre-pyloric, pyloric or duodenal. Occurs either because of active ulcer with oedema or due to healing of an ulcer with associated fibrosis (scarring). Gastric outlet obstruction normally presents as vomiting without pain.

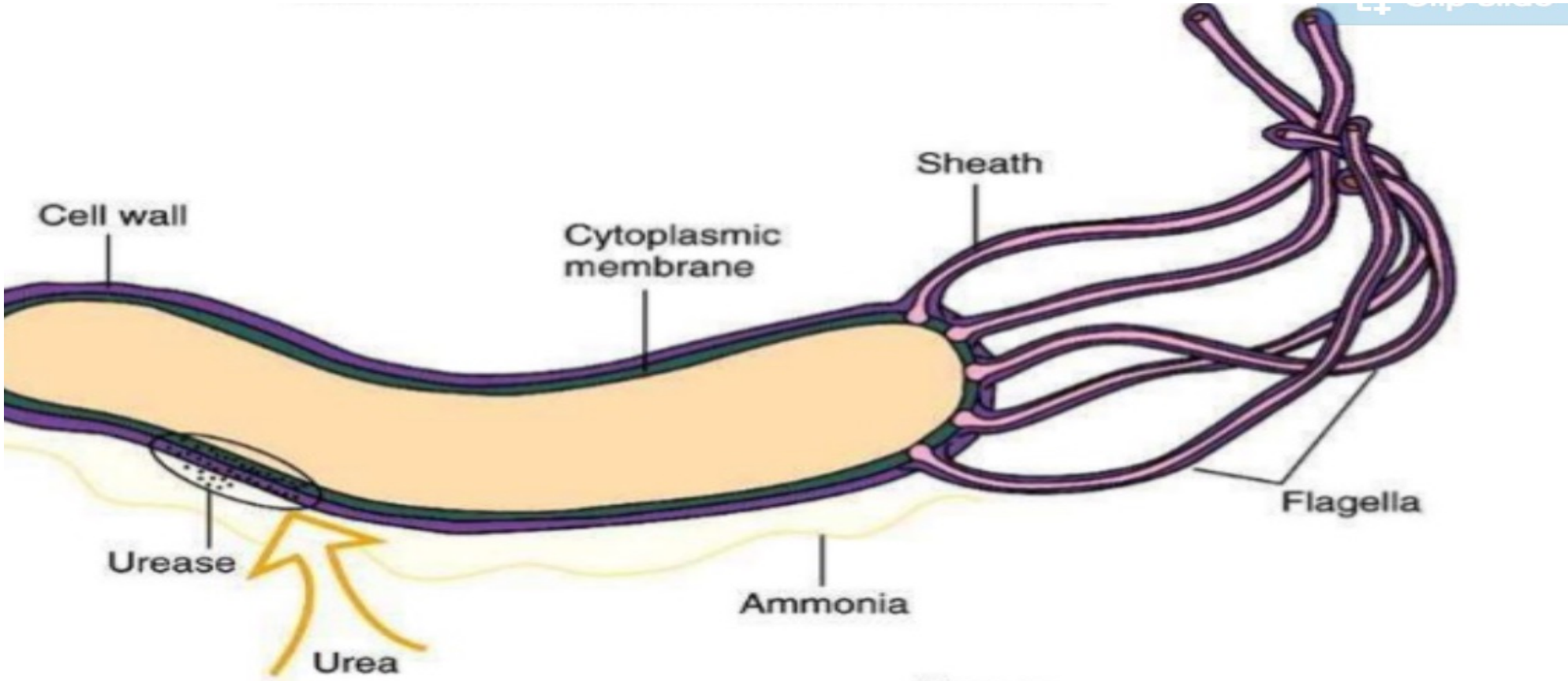
4. Explain the importance of Helicobacter Pylori in causing chronic gastritis

- ***Helicobacter pylori* infection** :

- *H pylori* is a **gram negative, aerobic, helical, urease producing bacterium** that resides in the stomach of infected individuals .

- Production of urease produces ammonia, which neutralises acidic environment, which allows bacterium to survive.

- It colonises gastric epithelium – in mucous layer or just beneath. Damage to epithelia occurs through enzymes released and through induction of apoptosis. Damage also occurs due to the inflammatory response to the infection (inflammatory cells and mediators)



$$CO(NH_2)_2 + H_2O \xrightarrow{\text{Urease}} CO_2 + 2NH_3$$

Urea — Ammonia

Diagnosis

- IgG detected in serum (relatively good sensitivity and specificity)

- ^{13}C-urea breath test (^{13}C-urea ingested – if H pylori present the urease produced will break down ^{13}C-urea to NH3 and CO2 – CO2 (where the carbon is ^{13}C) will be exhaled on breath and detected).

- Can also take gastric sample by endoscopy and detect by histology and culture . And Rapid urease test.

1. Patient drinks HN-*C-NH_2.

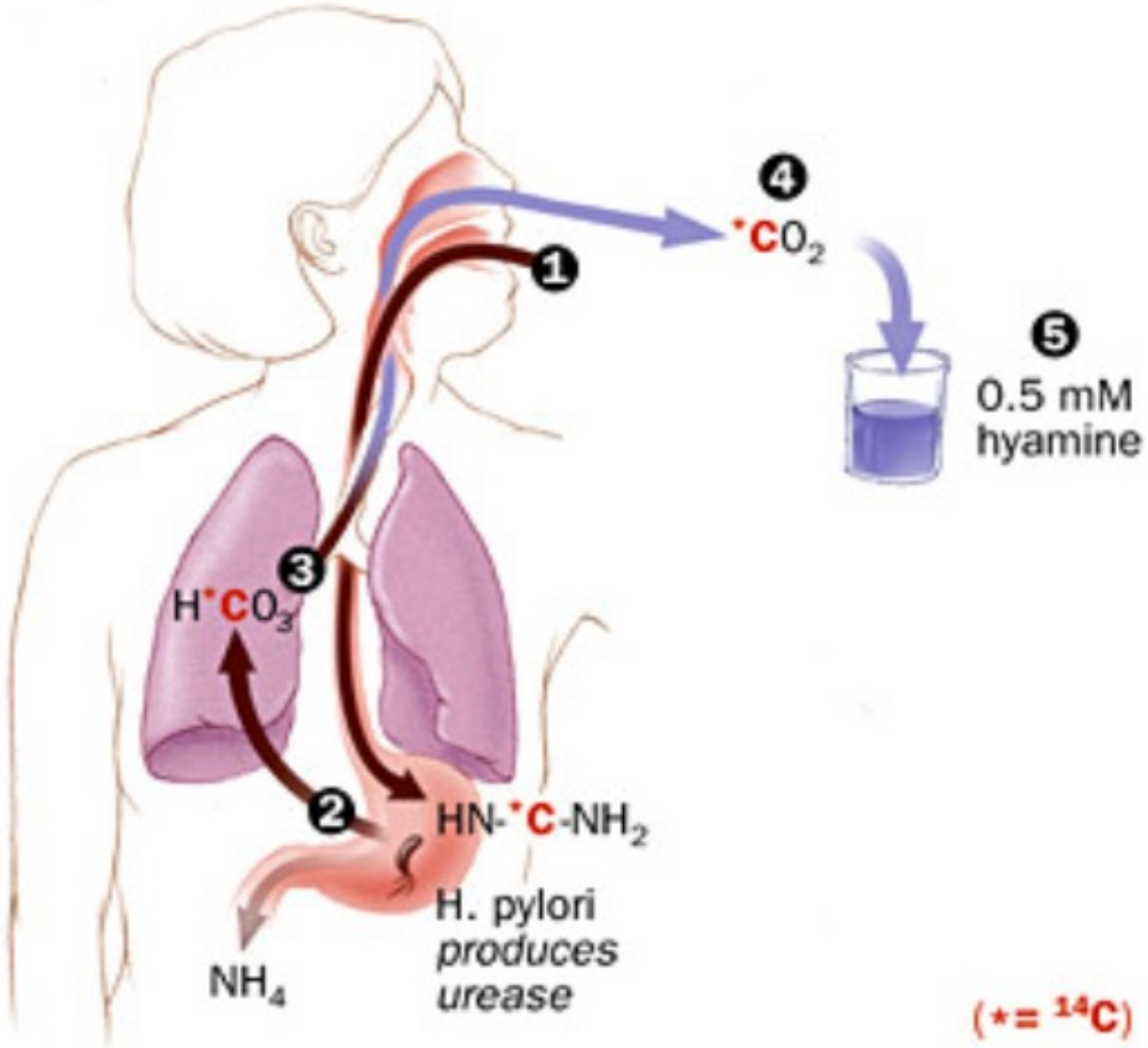
   In the stomach, HN-*C-NH_2 is broken down by urease into H*CO_3 and NH_4.

2. H*CO_3 travels to the lung and is...

3. ...expired...

4. ... as *CO_2 into...

5. ... a 0.5 mM hyamine solution, where a scintillation cocktail is added to test for *C.




SZYBKI TEST UREAZOWY
Do wykrywania Helicobacter pylori
- pozytywny
- negatywny
Wytwórca i dystrybutor:
INSTYTUT ŻYWNOŚCI I ŻYWIENIA
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tel./fax: +48 (22) 550 96 67
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Treatment

- Triple therapy.
    - **Proton Pump Inhibitor – Omeprazole**
    - **Two Antibiotics – Clarithromycin / Amoxicillin**
    - H_2 Antagonist (if severe)
- 7-14 day treatment –
- 14 days more effective but side-effects of treatment may put patients off finishing two week course

H pylori causing gastric disease:

- **Gastritis**
- Usual effect of infection, which is usually asymptomatic.
- Chronic gastritis causes **hypergastrinaemia** due to gastrin release from antral G cells → this increased acid production is usually asymptomatic but can lead to duodenal ulceration (which will eventually produce symptoms)

Peptic ulcer disease

- **Duodenal ulcers (DUs)** → prevalence of DU due to H pylori is falling due to decreased prevalence of H pylori infection.

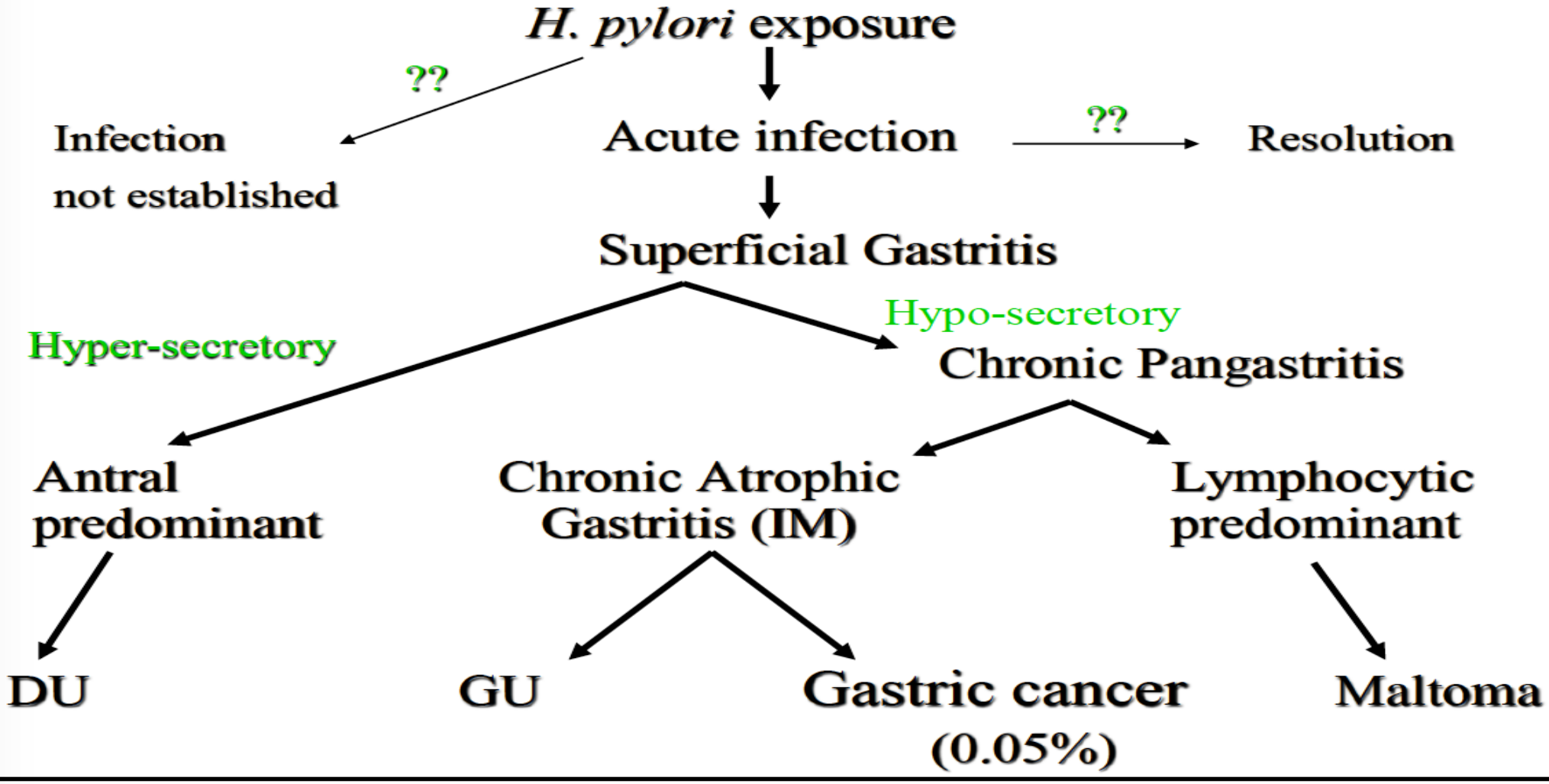
- If ulcers due to H pylori infection, eradication of infection relieves symptoms and decreases chances of recurrence.

- The precise mechanism of ulceration is unclear (only occurs in 15% of infected people) → factors implicated though are genetic predispositions, bacterial virulence, increased gastrin secretion and smoking

- **Gastric ulcers (GUs) → associated with gastritis affecting the body as well as antrum, which can cause parietal cell loss → reduction in acid production. Ulceration thought to occur due to reduction in gastric mucosal resistance due to cytokine production as a result of infection**

Gastric cancer

Pathways to Disease



5.Outline the principles of modern ulcer treatment

- If due to H pylori infection → **Triple Therapy**
  - **Proton Pump Inhibitor – Omeprazole**
  - **Two Antibiotics – Clarithromycin / Amoxicillin**
  - H_2 Antagonist (if severe)
- If taking NSAIDs – stop or review – use alternatives (NSAIDs with lower risk of causing PUD), or use prophylactic PPI as well as NSAID
- PPI – e.g. omeprazole

GI safety of non-selective NSAIDs

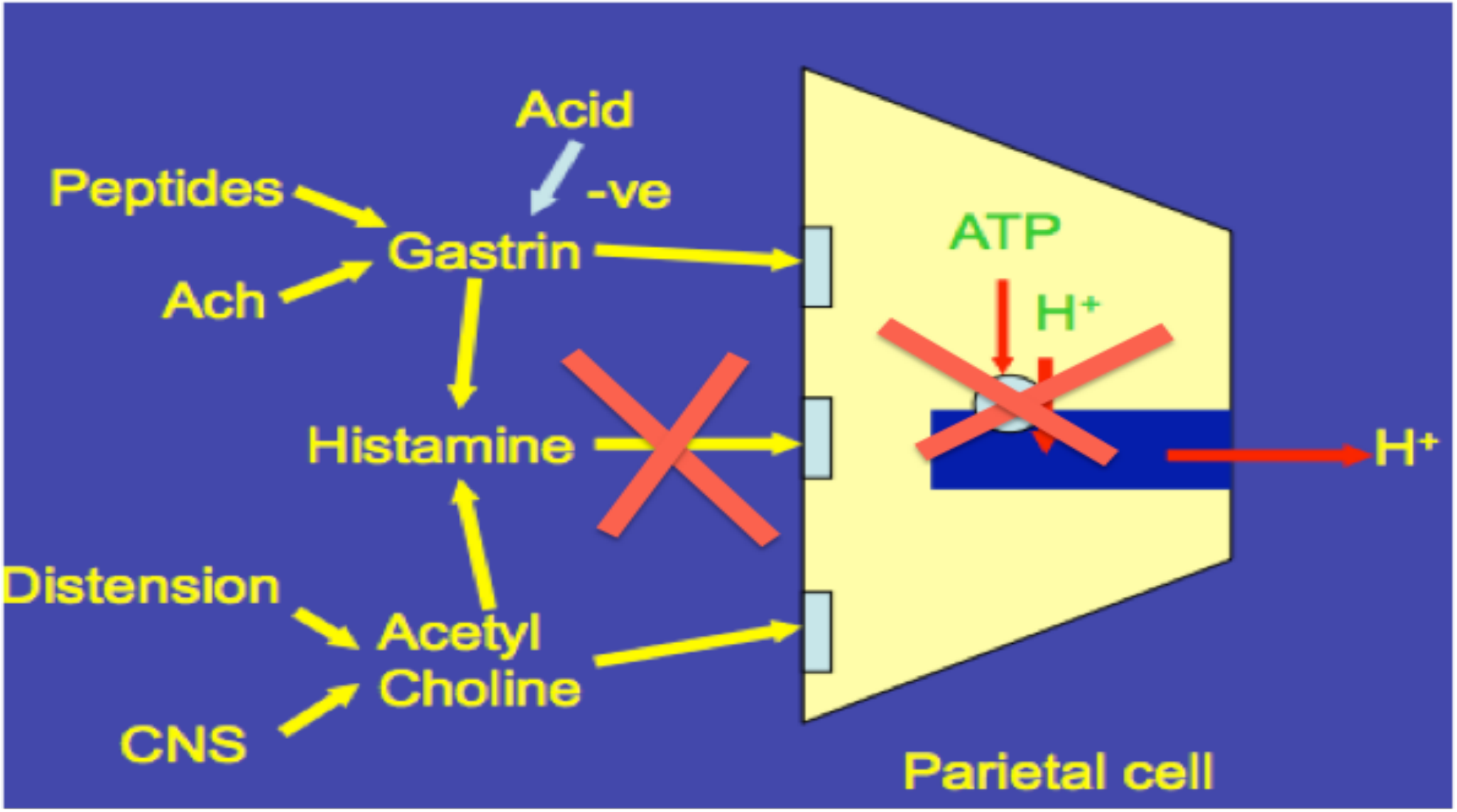
RR of different NSAIDs could differ by 10-fold

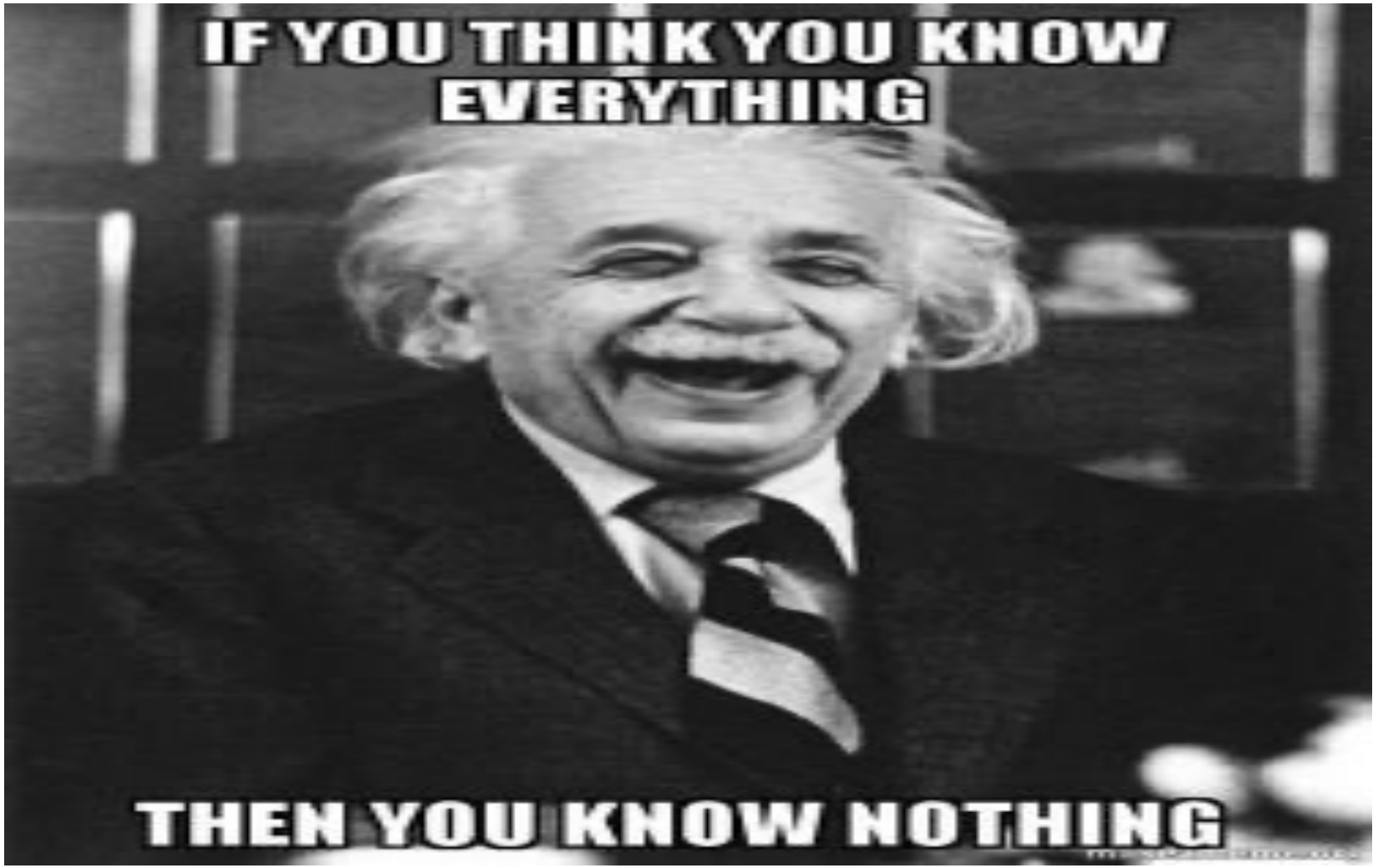
Lowest risk	Ibuprofen * Diclofenac	
Moderate risk	Indomethacin Naproxen Sulindac Aspirin	
Highest risk	Azapropazone Tolmetin Ketoprofen Piroxicam	Longer half-time

Br Med J 1996 ; 312 : 1563 – 1566.

6. *Outline the ways in which gastric acid secretion may be reduced by drugs*

- Acid secretion may be reduced by inhibition of:
- **Histamine at H_2 Receptors** antagonists reduce gastric acid production by blocking the H2 receptor on the parietal cell
  - **E.g. Cimetidine, ranitidine, famotidine and nizatidine.**
  - Removes the amplification of Gastrin/Ach signal
- **Proton Pump Inhibitors (PPIs)**
  - **E.g. Omeprazole, lansoprazole, pantoprazole, rabeprazole, and esomeprazole**
  - inactivates the parietal cell hydrogen-potassium ATPase located on the lumenal surface. ATPase acts as a proton pump and constitutes the final common pathway in the secretion of hydrogen ions. This class of medicines is now considered the gold standard in medical therapy of peptic ulcer disease


Acid
-ve
Peptides
Gastrin
Ach
ATP
H+
Histamine
H+
Distension
Acetyl
Choline
CNS
Parietal cell


IF YOU THINK YOU KNOW
EVERYTHING
THEN YOU KNOW NOTHING