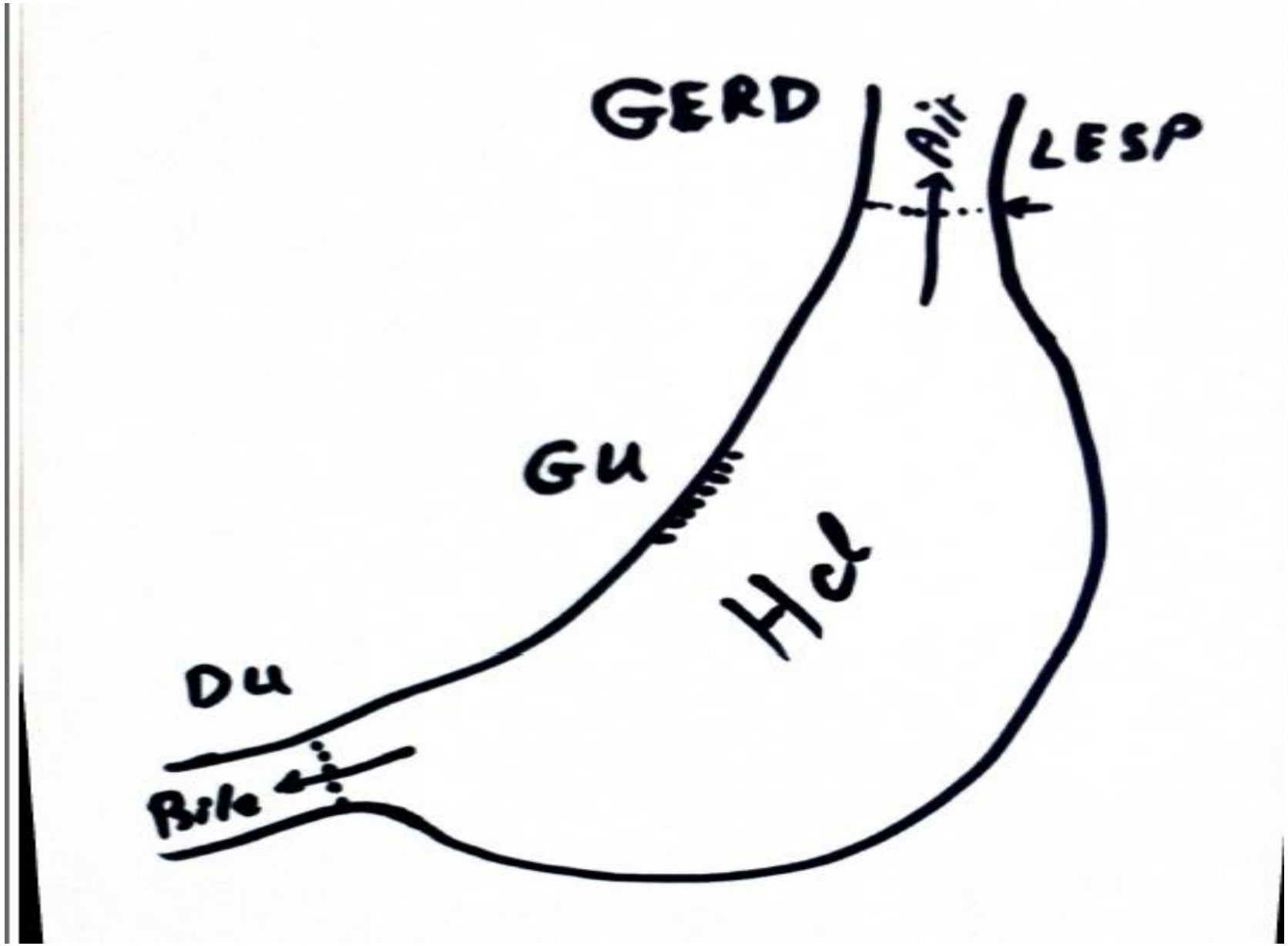
Acid-related disorders

Lecture 1

Prof. Ahmed Shaaban

Professor of pharmacology &

Senior consultant of endocrinology


GERD
Air
LESP
GU
Hcl
DU
Bile

Acid - related GIT diseases

They are very common clinically occurring in 35 % of adult people.

A) Peptic ulcer (PU):

Life time prevalence is 15% in men &10% in women.

1. Duodenal ulcer (DU):

The most common type. ↑Hcl caused by chronic H pylori infection.

2. Gastric ulcer (GU):

There is normal or low Hcl. Usually caused by chronic NSAIDs therapy reducing PG → diminished defensive mechanisms.

Also **acute gastritis** and **gastric erosion**. e.g. NSAIDs gastritis.

In the past 40 years the incidence of DU has been declining due to widespread use of antimicrobials while that of GU is increasing due to the extensive use of NSAIDs.

3. Stress ulcer:

By severe medical or surgical stress.

4. Zollinger - Ellison syndrome: Multiple extensive ulcers.

B)Gastroesophageal reflux disease (GERD):

↓LESP (lower esophageal sphincter pressure)

LESP is usually normal but reflux occurs during transient relaxation of LES by gastric distension.

Life time prevalence is 20%. In adults & children. Accordingly, it is more common than PU.

In addition, reflux symptoms occur in 50% of people.

Acid - related GIT diseases are due to imbalance between defensive and aggressive mechanisms.

Defensive mechanisms

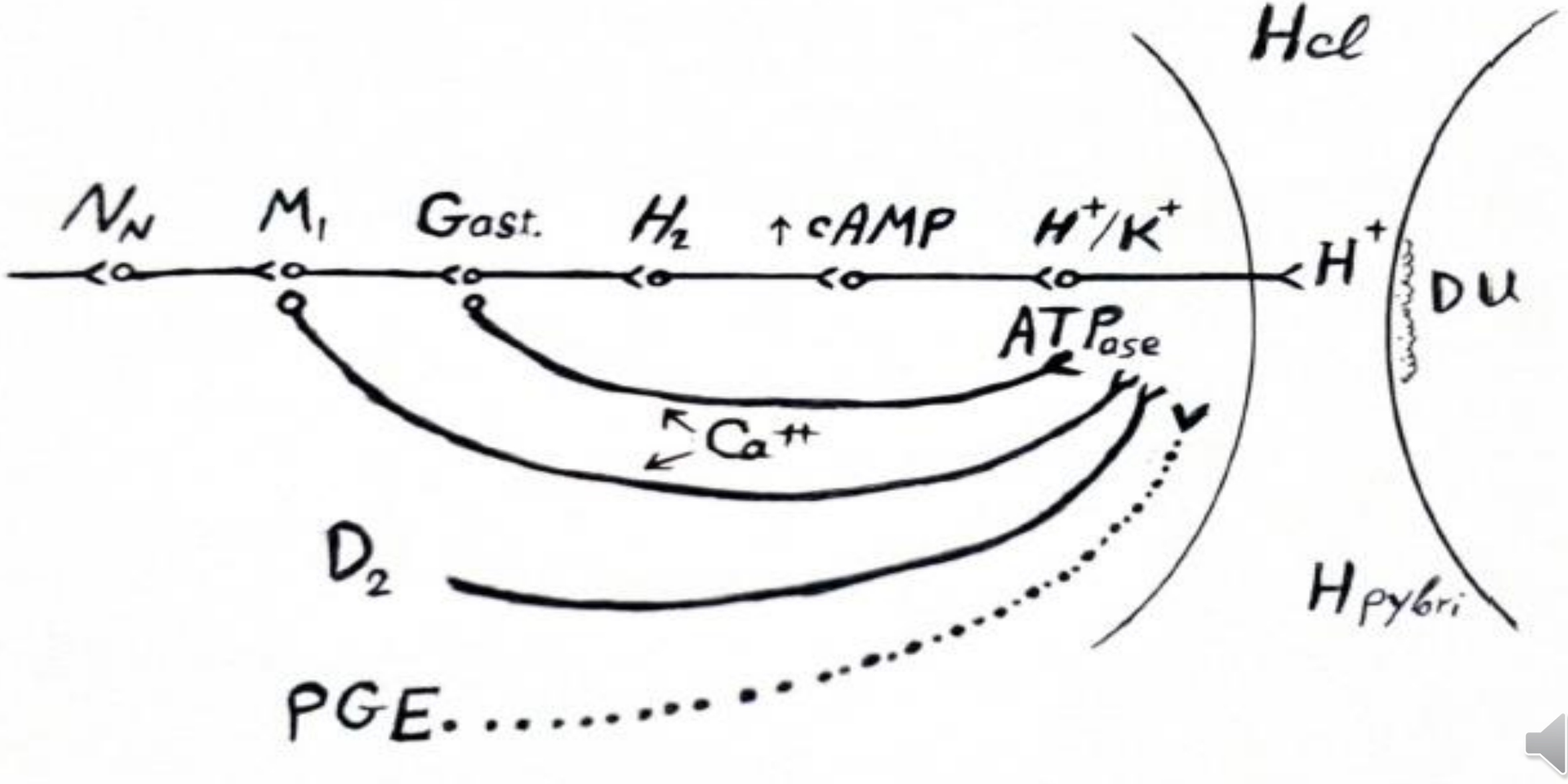
1. Mucus.
2. Na HCO3.
3. Integrity of gastric mucosa: tight junctions between cells prevent back diffusion of Hcl.
4. PG: decreases with age, with increased incidence of PU.

Aggressive mechanisms

A) Endogenous: 1. Hcl. 2. Pepsin. 3. Bile.

B) Exogenous:

1. Smoking: by ↑ Hcl, VC → ischemia & ↓ NaHCO3 by pancreas.
2. Stress.
3. **Drug – induced PU: drugs increasing Hcl.**


Hcl
N_N
M_1
Gast.
H_2
↑cAMP
H^+/K^+
H^+
DU
ATPase
Ca^{++}
D_2
H_{pylori}
PGE

Mechanism of Hcl secretion

H2 receptor stimulation →↑cAMP→ activation of protein kinase → stimulation of H+/K+ ATPase (proton pump) → H+ formation.

H+ pump occurs in apical canalicular membrane of parietal cell.

Activation of muscarinic (M1) & gastrin receptors increases permeability to Ca ++ leading to activation of proton pump. Their action is also mediated via H2 receptors. All these receptors are present in basolateral membrane of parietal cell.

Central dopamine receptors mediate increase Hcl secretion.

Prostaglandins (PGE), in contrast to other receptors, ↓Hcl secretion.

Drugs increasing Hcl secretion (Iatrogenic PU)

1. NSAIDs : by ↓PG.
2. Corticosteroids : by ↓PG.
3. Nicotine (smoker's ulcer): by stimulation of nicotinic receptors.
4. Cholinomimetics : by muscarinic M3 receptor stimulation.
5. Alpha methyl dopa: by parasympathetic predominance.
6. Gastrin: by stimulation of gastrin receptors.
7. Histamine: by stimulation of H2 receptors.
8. Antacids : may increase Hcl (rebound).
9. Calcium: increases gastrin.
10. Caffeine: by increase cAMP.
11. Dopamine agonists as L-dopa & bromocriptine.
12. Alcohol.

PEPTIC ULCER

Aetiology

Age: DU : 30 - 55 year. Men > women.

GU : 55 - 70 years (age of use of NSAIDs & ↓PGs). Women > men.

Genetic predisposition.

Blood group O.

Type A persons (people with stressful character).

Absence of breakfast.

Infrequent meals.

DU: fasting or nocturnal, relieved by food.

GU: increased by food.

Sleep disturbances:

↓sleep duration → ↓defense mechanism &↑Hcl.

Aggressive factors & drugs: mentioned before, very important

Patients individual tolerance:

a. Caffeine in coffee, tea, colas, chocolates, decaffenated coffee &tea.

b. Spicy food.

c. Citrus fruits.

The cause of DU is infection by H pylori, in almost all patients. H pylori infection is acquired in childhood with person to person transmission. There is high luminal Hcl.

The main cause of GU is NSAIDs: 25% of patients given NSAIDs have symptoms and 50% have endoscopic evidence of gastritis. 15% present with complications.

The ulcer is caused by defensive mechanism due to ↓PG. There is normal or low luminal Hcl, but this can cause ulcer in the gastric mucosa with diminished defensive mechanism. Accordingly, acid - suppressives are used, but are less effective than in DU. Also recurrence rates are higher.

Diagnosis

1. Epigastric pain and point tenderness, rhythmicity (relation to meals, nocturnal) & periodicity (symptoms for weeks or months).

- DU: fasting or nocturnal, relieved by food.
- GU: increased by food.

2. For H pylori: urea breath test or fecal antigen test. Stop antimicrobials 4 weeks, PPIs 2 weeks and H2 antagonists 24 hours before.

3. Endoscopy with biopsy for H pylori and to exclude malignancy.

Cancer in GU is > DU.

Treatment of peptic ulcer

A) Avoid aggressive factors and aetiology: mention them.

B) Diet:

Decrease manifestations and avoid flare by:

1. Small frequent meals & milk.

2. High fibers (mainly soluble) in fresh organic fruits & vegetables, legumes, Mechanism: antioxidant, antiinflammatory, cytoprotective and antimicrobial.

3. Bland diet only in severe acute cases.

4. ↑flavonoids in colored fresh organic fruits & vegetables, …

5. ↑vitamin A

6. Probiotics: anti-H pylori.

C. Drug therapy:

a. Acid - suppressive therapy

1. Proton pump inhibitors (PPIs).
2. H2 antagonists.
3. Anticholinergic drugs.
4. Sulpride.

b. Mucosal protectives (cytoprotectives)

1. Sucralfate.
2. PG analogues (e.g. misoprostol).

c. H pylori therapy

d. Antacids

Curative therapy : acid – suppressives & cytoprotectives.
Radical therapy : H pylori therapy.
Symptomatic therapy: antacids.