Normal functions of the stomach

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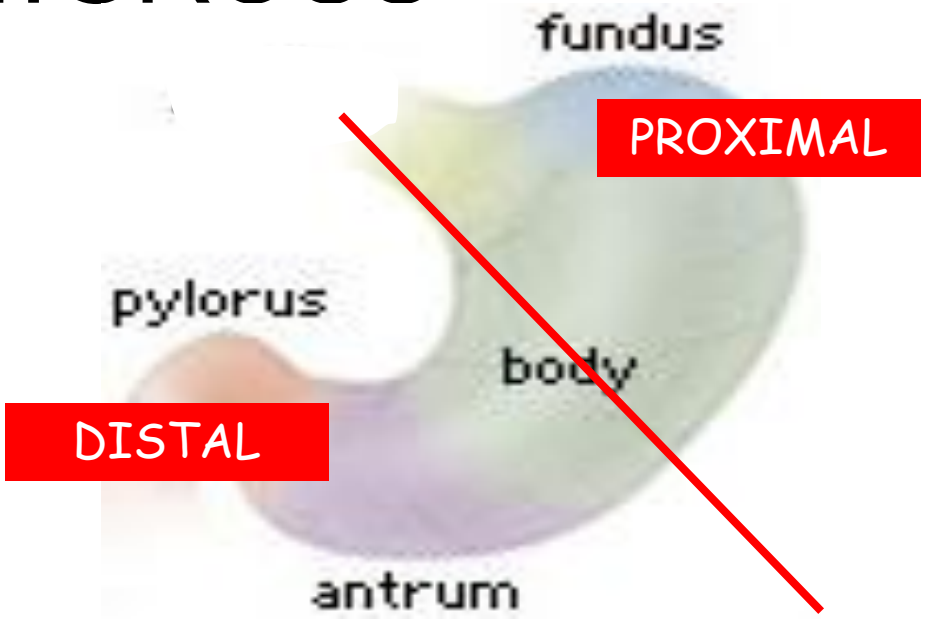
2018

Functional anatomy of the stomach…GROSS

- Anatomically 4 parts:
  - fundus
  - corpus
  - antrum
  - pylorus



- Functionally divided in to two parts
  - Proximal stomach – upper 2/3 of the body
    - Has storage function
  - Distal stomach – lower 1/3 of the body and antrum
    - Mechanical and chemical digestion, and propulsion

Function of the stomach

1. **Motor function**
   - stores food
   - secretes and mixes food with acid, mucous and pepsin
   - participates in digestion (mechanical & chemical)
   - releases food at a controlled, steady rate into the duodenum

2. **Secretory function**
   - pepsinogen: digestion
   - acid: digestion & protective function
   - intrinsic factor: vitamin B12 absorption
   - gastrin: endocrine function

3. **Protective function**

Normal functions of the stomach I

Secretory functions of the stomach

Lecture objectives

The student should be able to

1. describe the different types of secretions of the stomach and their functions

2. describe the process of HCl secretion in stomach and factors regulating it

3. List the consequences of altered HCl secretion

4. Outline methods of modifying HCl secretion & their clinical relevance

Gastric secretions ‘gastric juice’

About 2.5 L / day

- Oxyntic glands
  - Proximal stoamch – fundus and proximal 80% of the body
  - Secrete HCl, pepsinogen, intrinsic factor and mucous
- Pyloric glands
  - Distal stomach – antrum and distal 20% of the body
  - Secrete gastrin and mucous
- Mucous secreting cells

- At low rates of secretion (inter-digestive period)
  - Stomach secretes a small amount of gastric juice
  - Mainly mucous, little pepsin, NaCl with small amount of H^+ and K^+

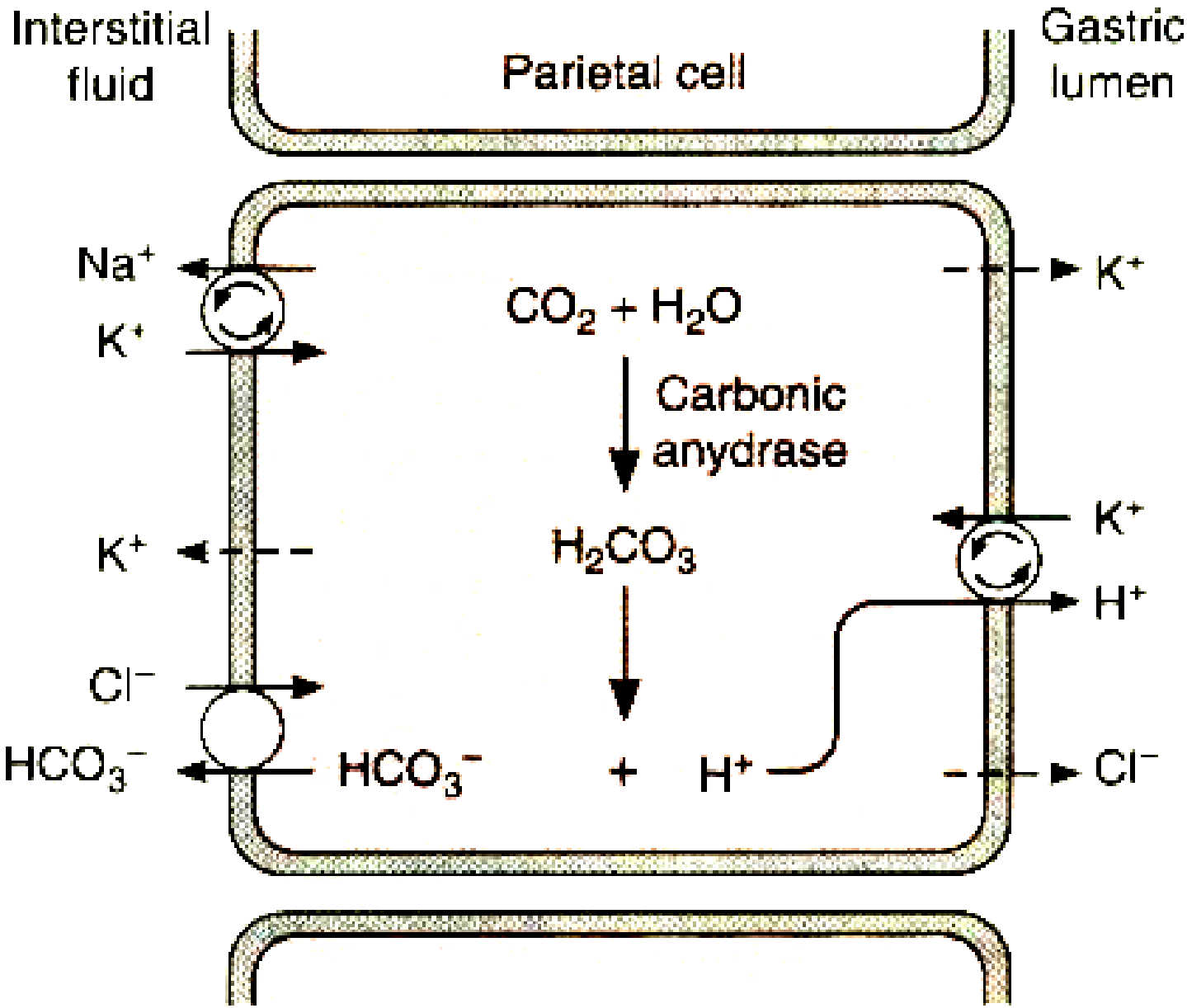
- During a meal, H^+ increases and Na^+ decreases by an equal amount

- Emotional stimuli stimulate secretion of gastric juice rich in pepsinogen and acid - Contribute to development of peptic ulcers

HCl

- Secreted by parietal cells
- Function
  - Kills pathogens
  - Activates pepsinogen; starts protein digestion
  - Stimulates flow of bile
- pH of gastric juice is very low; ≈1-2
- Low pH is created by <u>active</u> secretion of H^+ into gastric lumen
- <u>Primary active transport</u> by H^+-K^+ -ATPase (proton pump) located in luminal membrane of parietal cells

HCl formation and secretion in the parietal cell

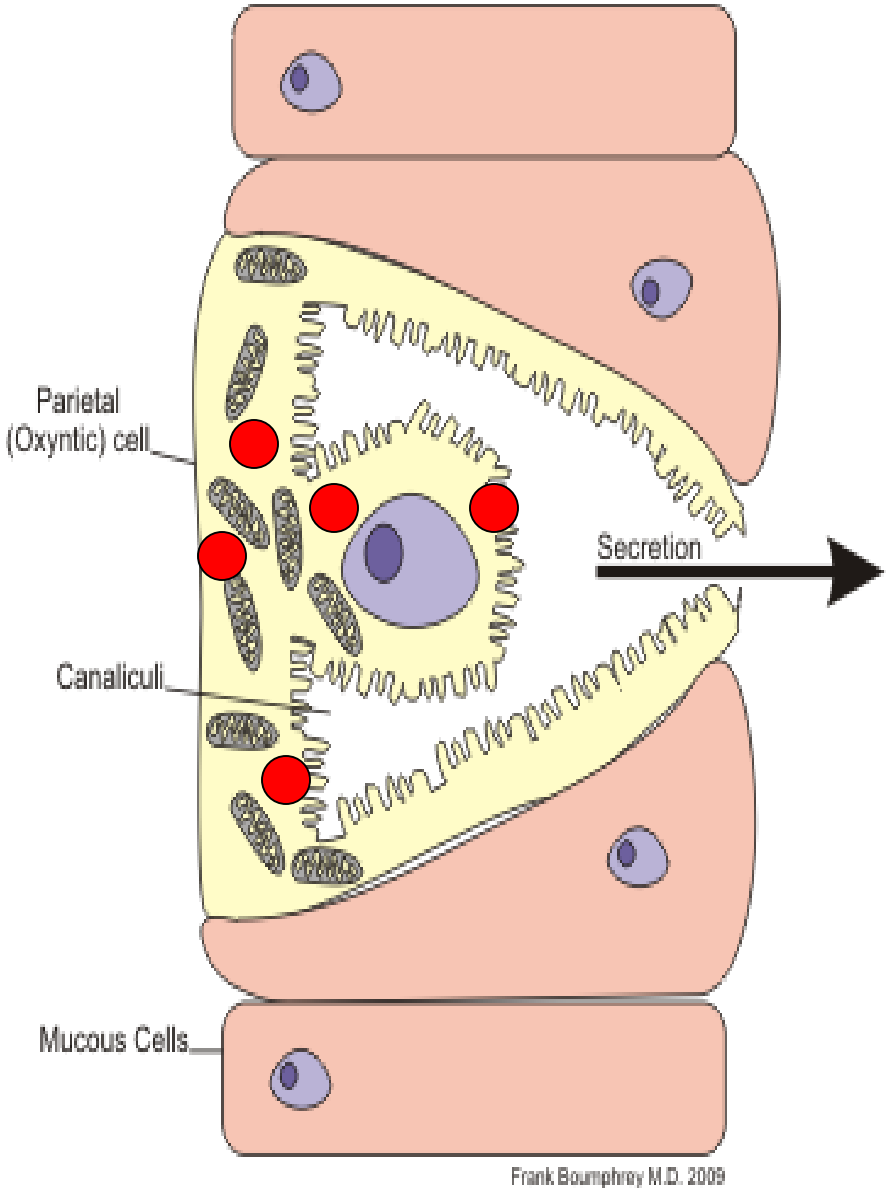


HCl secretion in parietal cells contd....

- H^+ comes from hydration of CO_2 (catalyzed by carbonic anhydrase)
- Exchanged for K^+ against a concentration gradient
- HCO_3^- formed is exchanged for Cl^- in basolateral membrane
- Secretion of H^+ is balanced by secretion of equal amount of HCO_3^- into blood
- Increased pH of venous blood leaving stomach after a meal = ‘alkaline tide’

HCl secretion in parietal cells

- At rest, tubulovesicular structures with H^+-K^+ ATPase molecules remain inside cells
- When parietal cells are stimulated, these move to apical membrane and fuse with it
- Inserting H^+-K^+ ATPase molecules into the membrane
- Exchanges H^+ for K^+

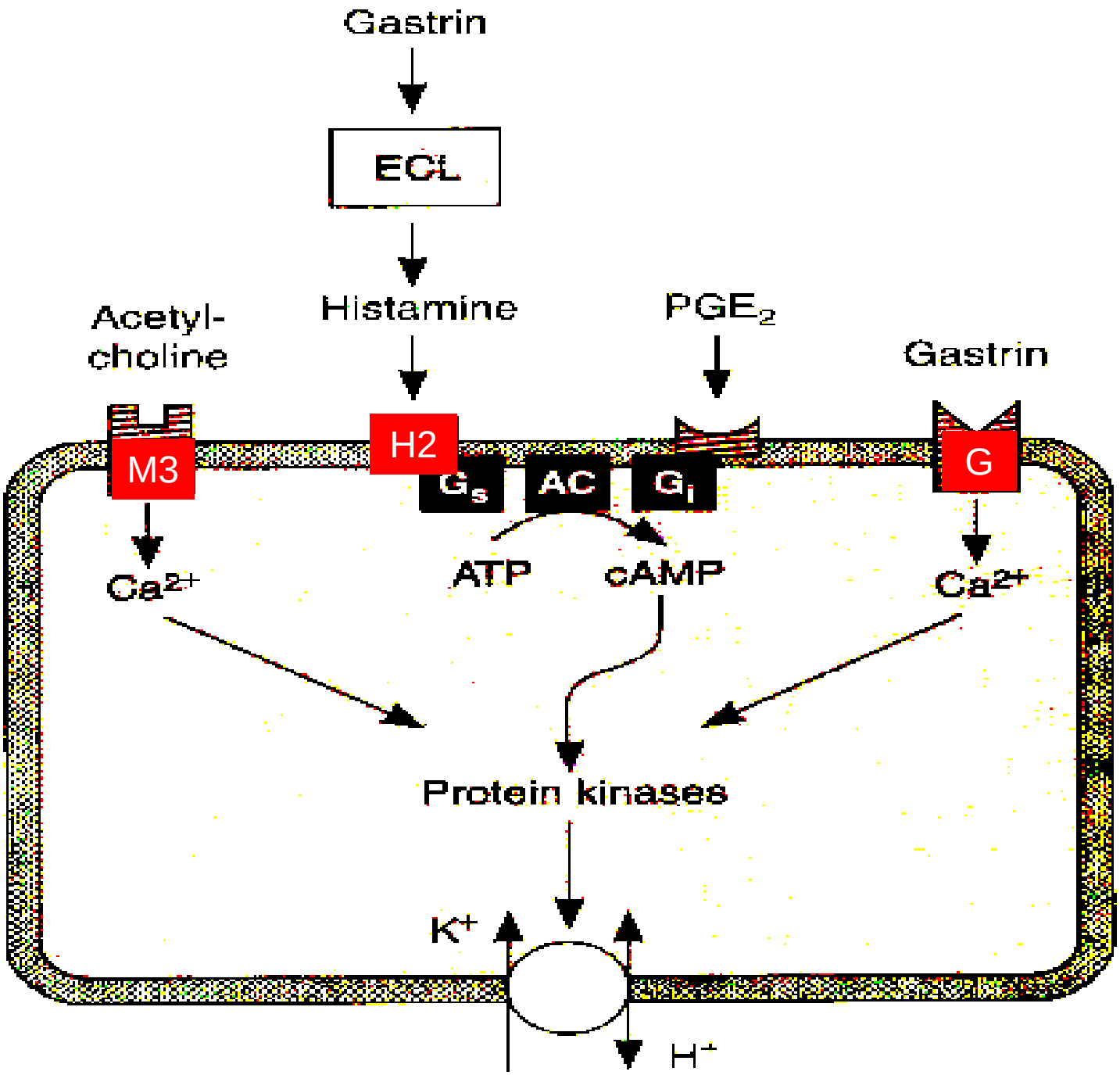


Factors regulating HCl secretion in the stomach

- Acetyl choline (M3 receptors)
- Histamine (H2 receptors)
- Gastrin (stimulate histamine secretion by ECL cells)

- Secretory response to a combination of 2 or more of above is greater than of one alone.

- Each factor augments response to another factor ‘POTENTIATION’


Gastrin
ECL
Histamine
Acetyl-
choline
PGE2
Gastrin
M3
H2
Gs
AC
Gi
G
ATP
cAMP
Ca2+
Ca2+
Protein kinases
K+
H+

Physiologic regulation of gastric secretion

- Cephalic phase (20%) – Mainly stimulatory
- Gastric phase (70%) – Mainly stimulatory
- Intestinal phase – Mainly inhibitory

- Considerable overlap between phases

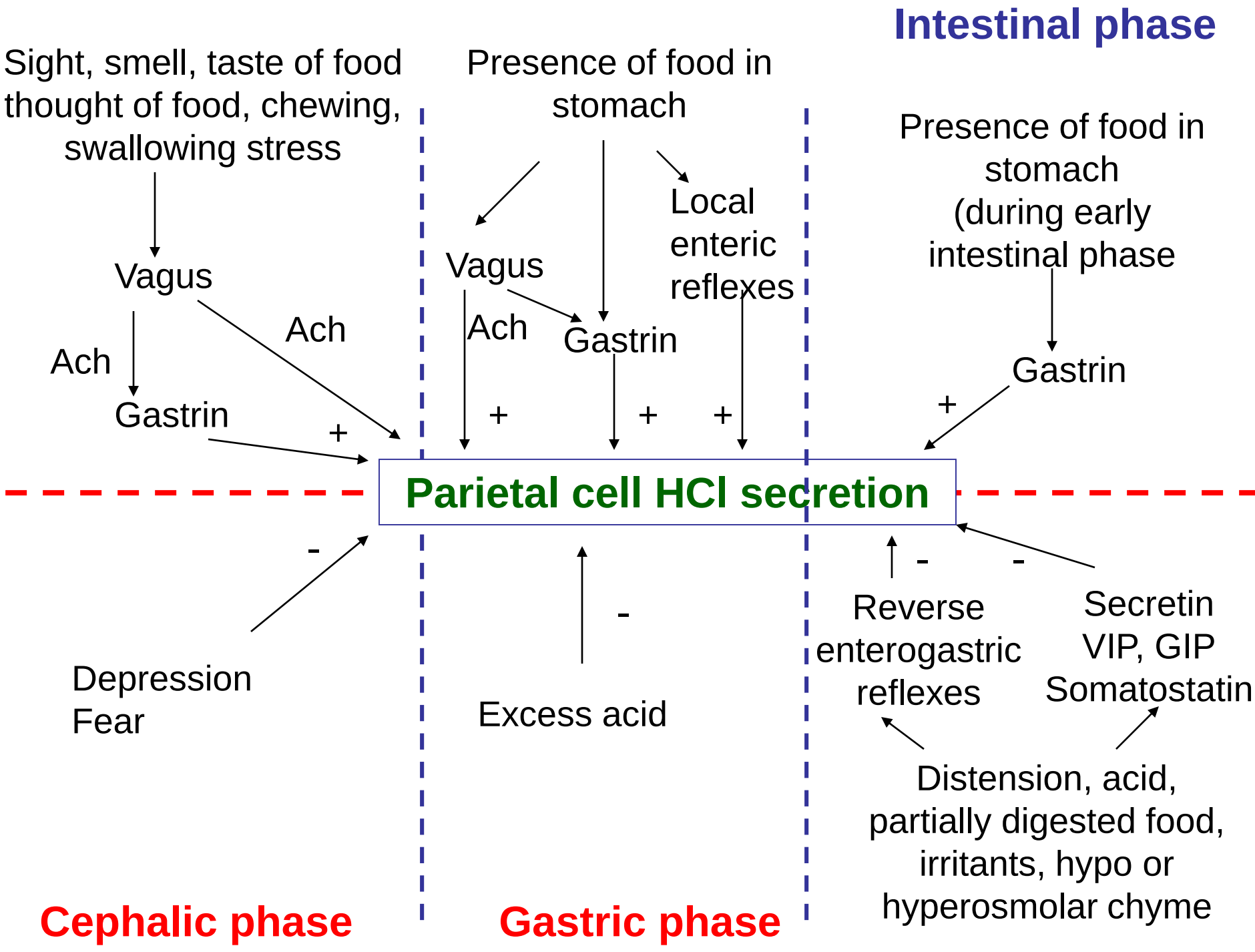
- In each phase, acid secretion is increased by either

  – long vago-vagal reflexes (cerebral cortex and appetite centers →dorsal motor nuclei of vagi → vagi → stomach)

  – local nervous secretory reflexes/ short reflexes

  – gastrin release

- Or combination of above factors


Intestinal phase
Sight, smell, taste of food
thought of food, chewing,
swallowing stress
Presence of food in
stomach
Presence of food in
stomach
(during early
intestinal phase
Vagus
Ach
Gastrin
+
Vagus
Ach
Gastrin
Local
enteric
reflexes
+
+
+
Gastrin
+
Parietal cell HCl secretion
-
Depression
Fear
-
Excess acid
-
-
Reverse
enterogastric
reflexes
Secretin
VIP, GIP
Somatostatin
Distension, acid,
partially digested food,
irritants, hypo or
hyperosmolar chyme
Cephalic phase
Gastric phase

https://www.youtube.com/watch?v=p-X1lB_s2gc

Pepsinogen secretion

- Inactive precursor of pepsin
- Contained in zymogen granules of chief cells

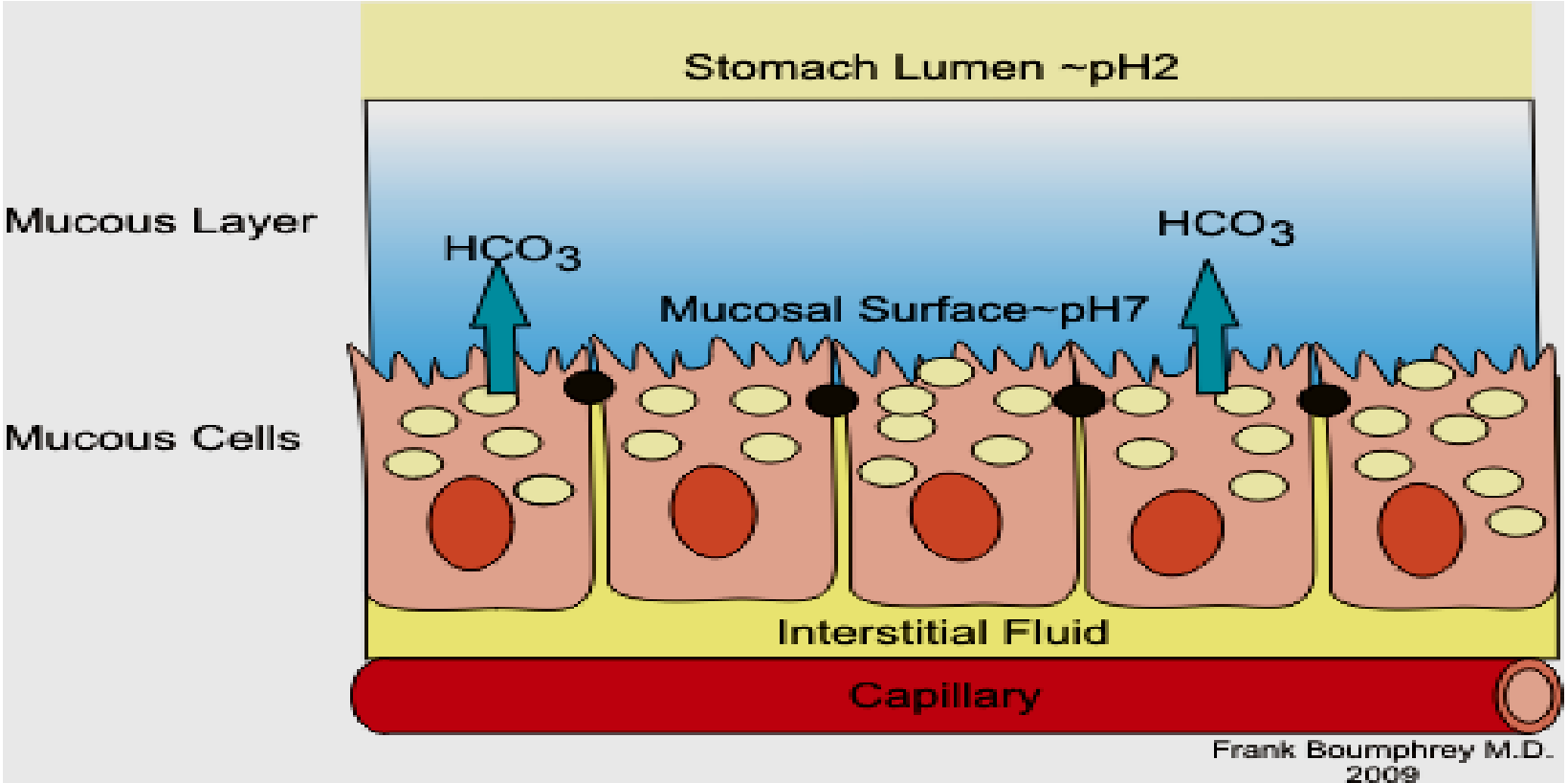
- Secretion stimulated by Ach from vagus nerve or from ENS

- HCl
  - promotes pepsinogen secretion
  - activates pepsinogen to pepsin

- Pepsin is a proteolytic enzyme
- Acts around pH 1.8-3.5, inactive at alkaline pH

Mucous secretion

- Made of mucins which are glycoprotein substances
- Form a gel coating mucosa
- Traps HCO_3^- : creates alkaline environment
- Protects underlying mucosa



Intrinsic Factor secretion

- Binds vitamin B_{12}
- This binding is essential for vitamin B_{12} absorption from intestines
- Secreted by parietal cells

- Destruction of parietal cell leads to
  - Achlorohydria - READ
  - Pernicious anaemia – READ

READ - Effects of gastrectomy

Resistance of gastric mucosa to auto digestion

- Depends on : integrity of mucosal barrier
  - adequate blood flow
  - mucous and HCO_3^- production
  - trefoil peptides
  - cellular renewal
  - chemicals – prostaglandins: decrease acid secretion

- Refer role of NSAIDs in gastritis/ ulcers

Disorders

Gastritis

- Causes :
  - *Helicobacter Pylori*
  - Long term aspirin and alcohol use
- Mucosal damage and atrophy and ulcers
- Mucosal atrophy – achlorohydria – pernicious anaemia

Gastric & duodenal ulcers (peptic ulcers)

- Causes :
  - Breakdown of mucosal barrier
  - Reduced neutralization of acid
  - Increased acid secretion

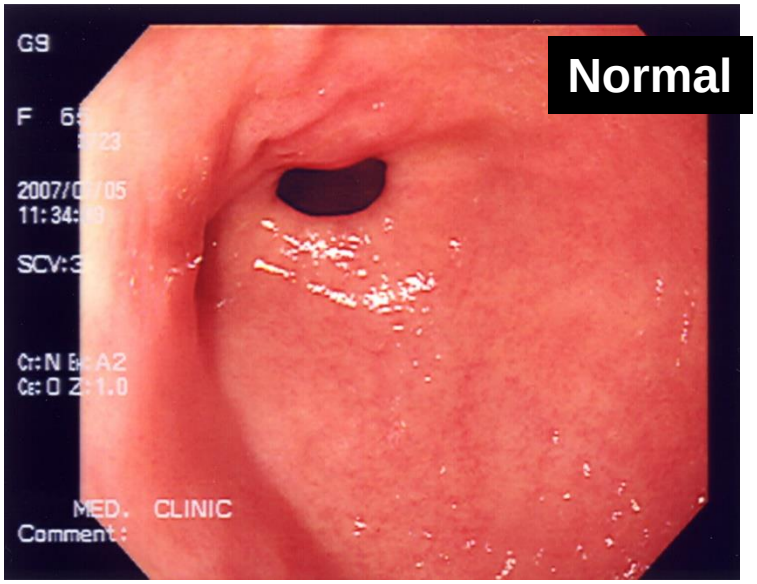
- Gastric ulcers – reduced defense mechanism
- Duodenal ulcers – increased gastric acid

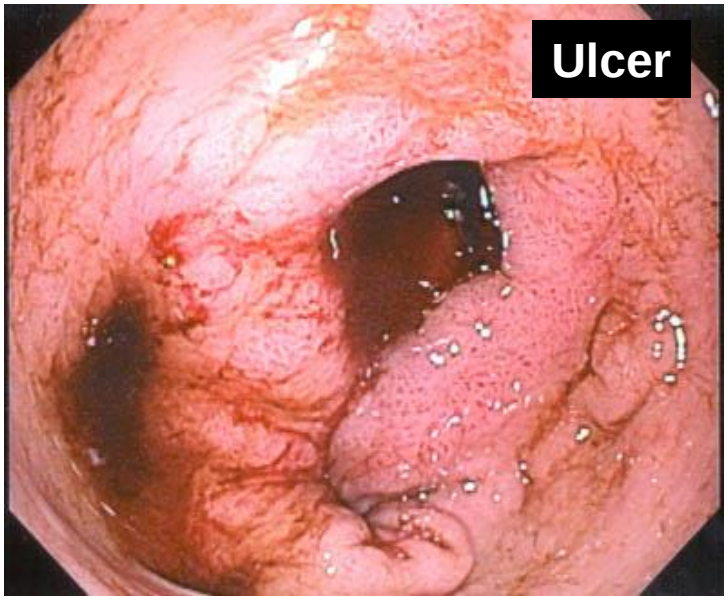
- Role of *H. Pylori*
- Aspirin & other NSAIDs - READ

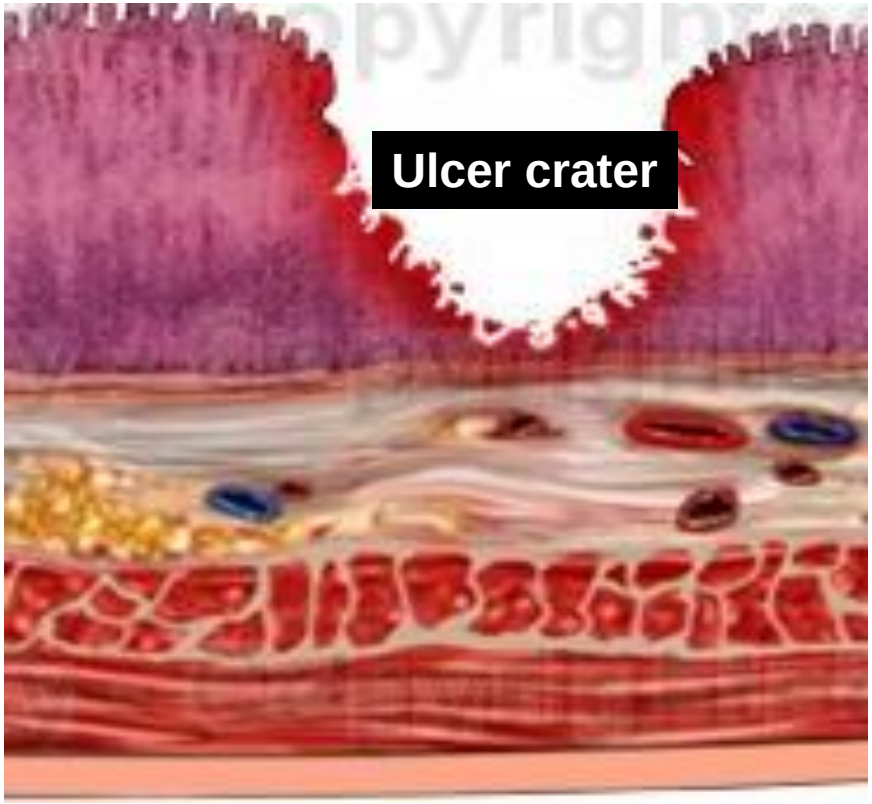
Gastrinoma

- Tumor leading to prolonged secretion of acid

Gastric mucosal inflammation & ulceration







Methods of modifying HCl secretion & their clinical relevance

- Acid suppression – long term
  - H_2 receptor blockers
  - Proton-pump inhibitors
  - Antacids
- H pylori eradication
  - Antibiotics
- Surgery
  - Gastrectomy
  - Vagotomy

H2 receptor blockers

Proton pump inhibitors