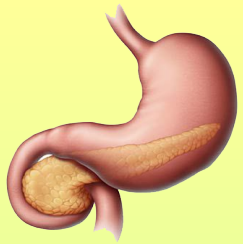
Pathophysiology of gastro-intestinal tract

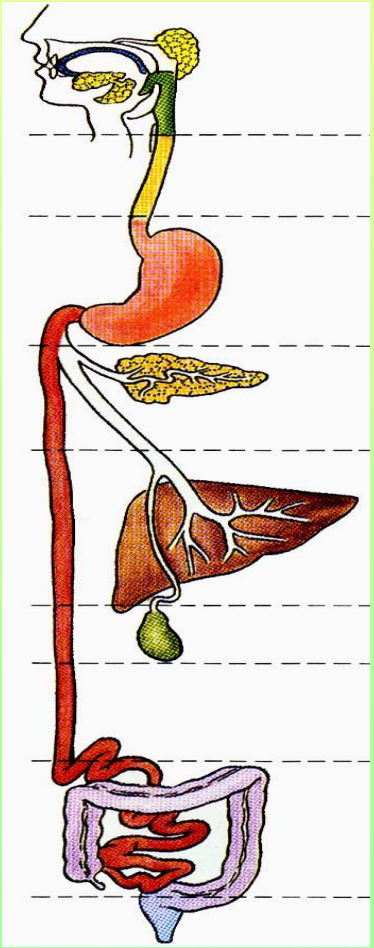


Gastro-intestinal tract

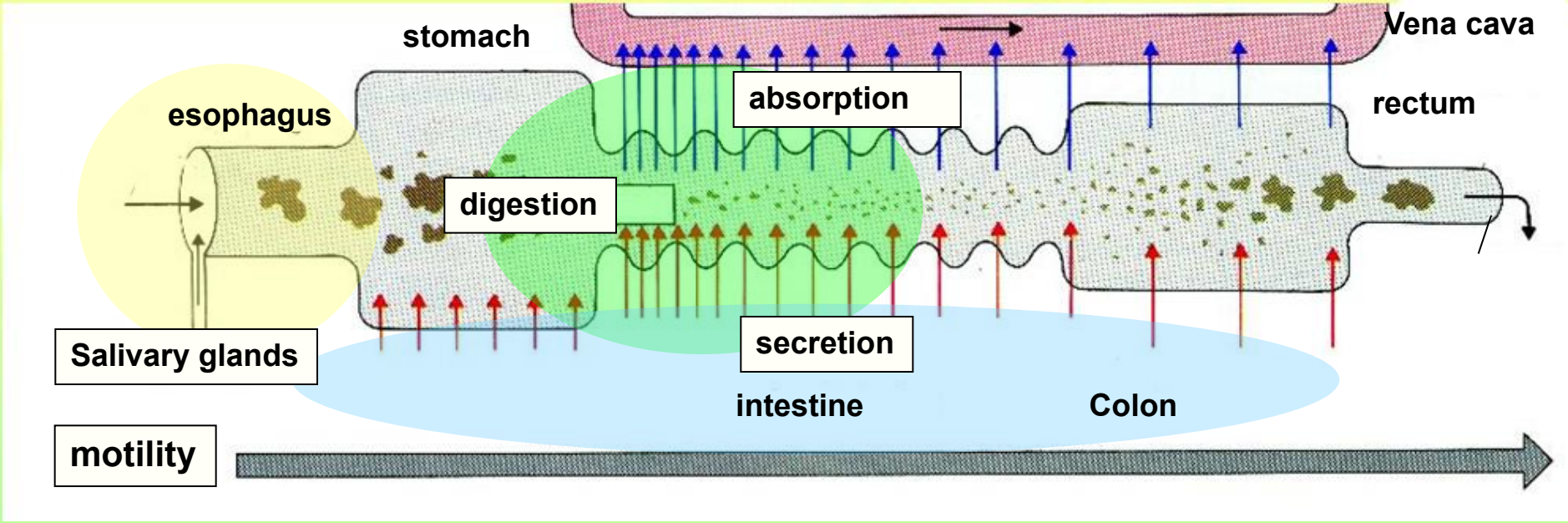
Кафедра

- Organs of oral cavity
- Esophagus
- Stomach
- Small and large intestine
- Secretory function of salivary glands, liver, pancreas

Neurohormonal regulation



Major processes in GIT

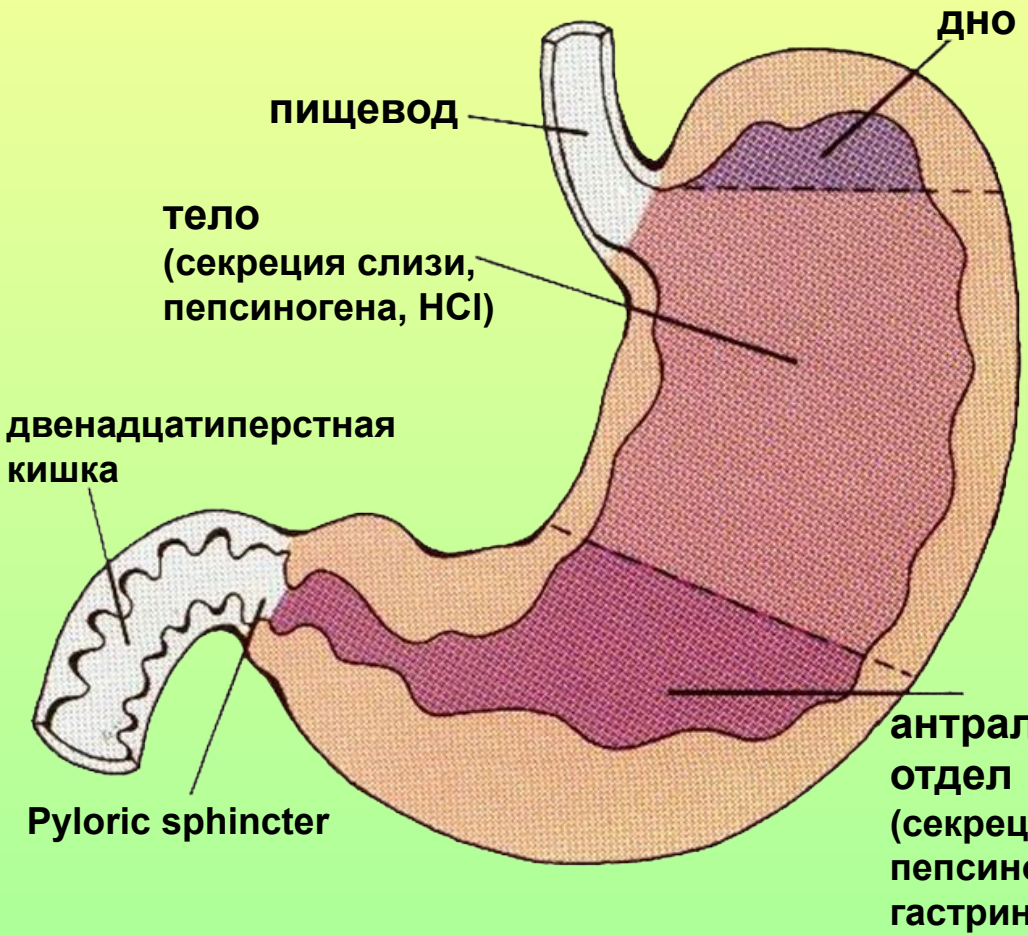


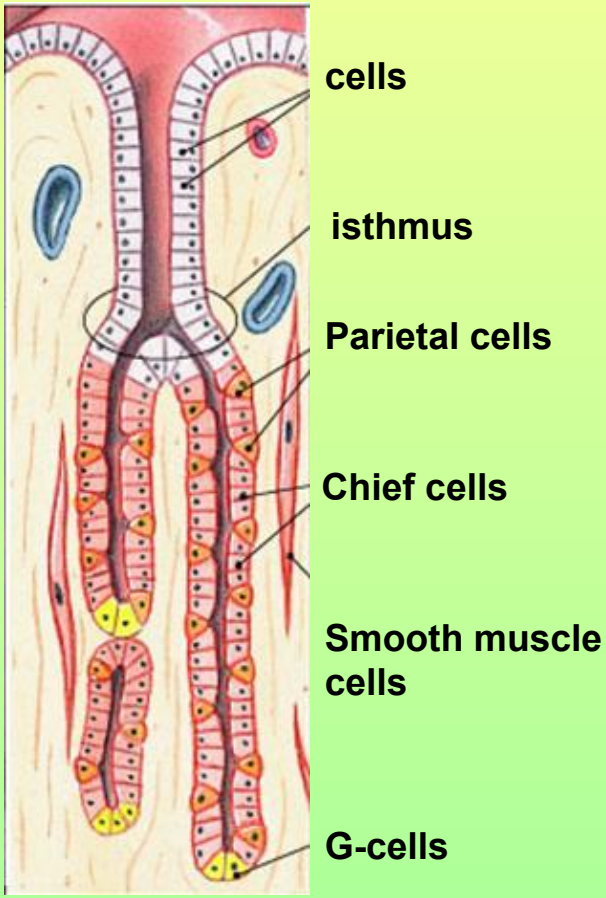
nutrition

digestion, absorption

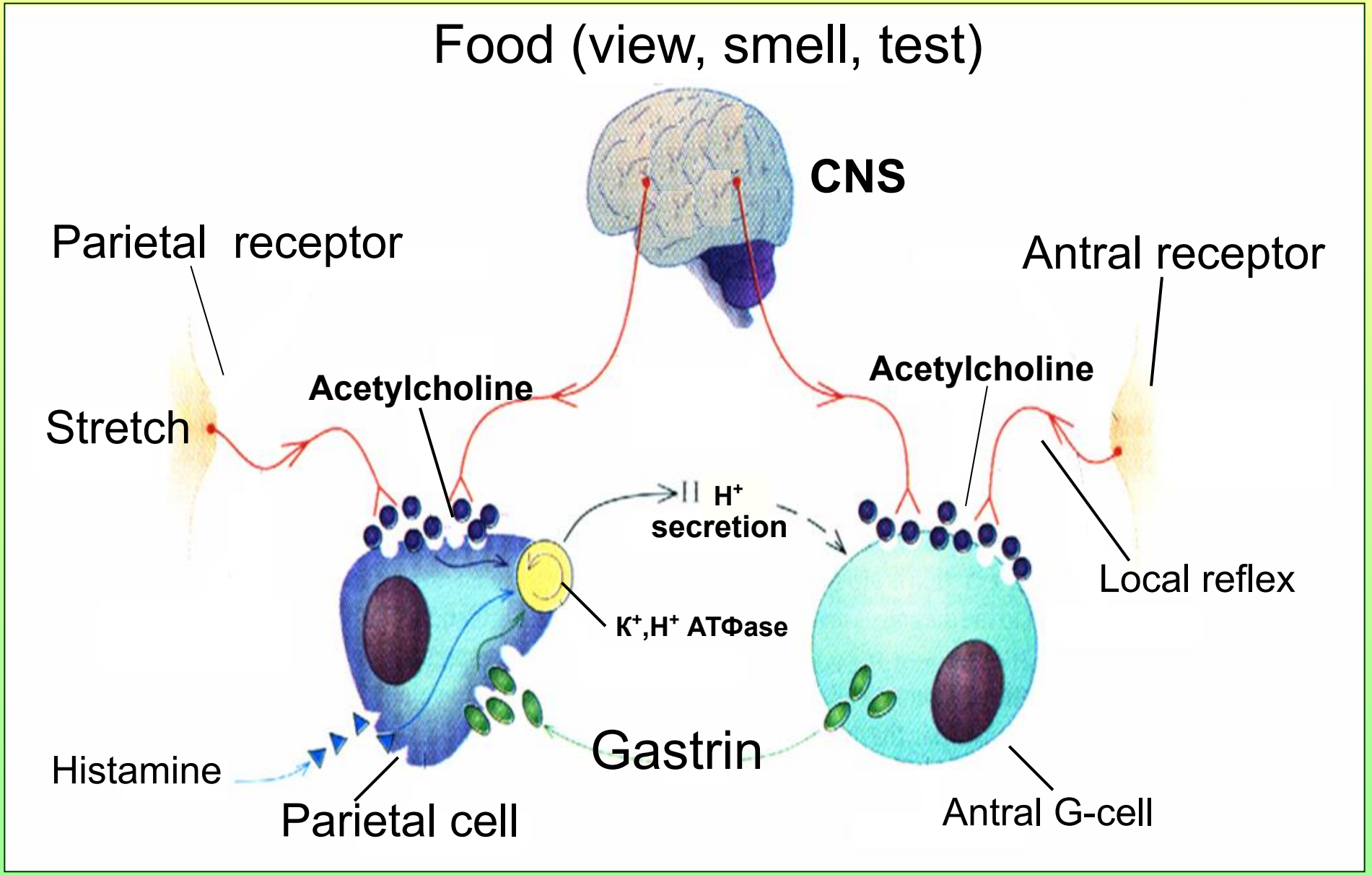
movement

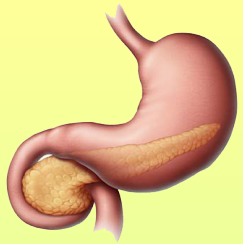
Physiology of the stomach





Regulation of gastric secretion





Mechanisms of gastric hypersecretion

- Stimulation:

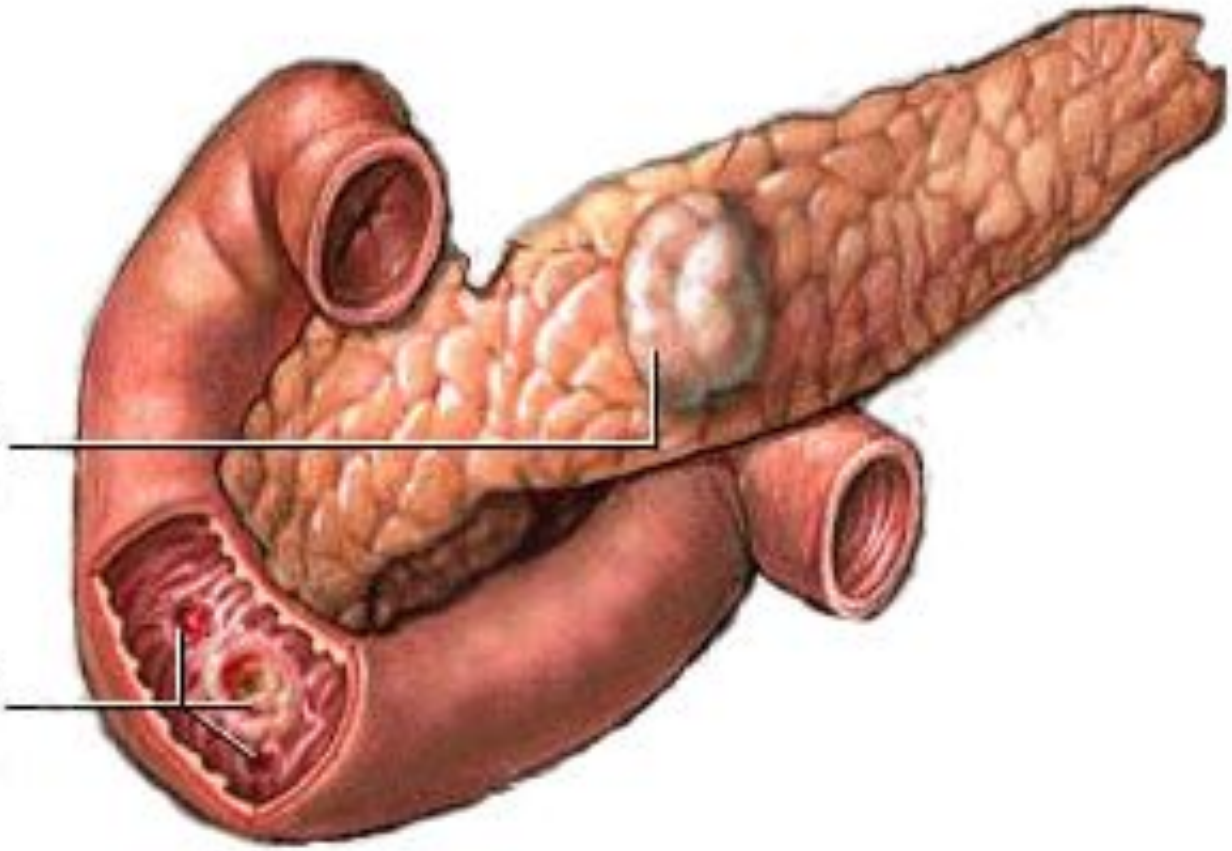
  neurogenic (vagotonia),

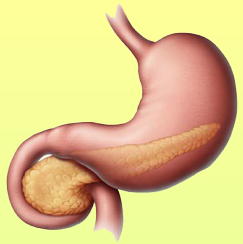
  hormonal (gastrin, histamine, ↑Ca^{2+} in hyperparathyroidism…)
- Failure of inhibitory mechanisms (antral, duodenal)
- Hyperplasia of the gastric glands

Gastrinoma (Zollinger-Ellison syndrome)

- Marked gastric hypersecretion
- Diarrhea
- Abdominal pain
- Peptic ulcer(s) of upper GI tract
- Gastro-esophageal reflux
- Gastrin-secreting tumor of the duodenum (75%), pancreas (24%), stomach, liver, ovary (1%).

Zollinger Ellison Syndrome

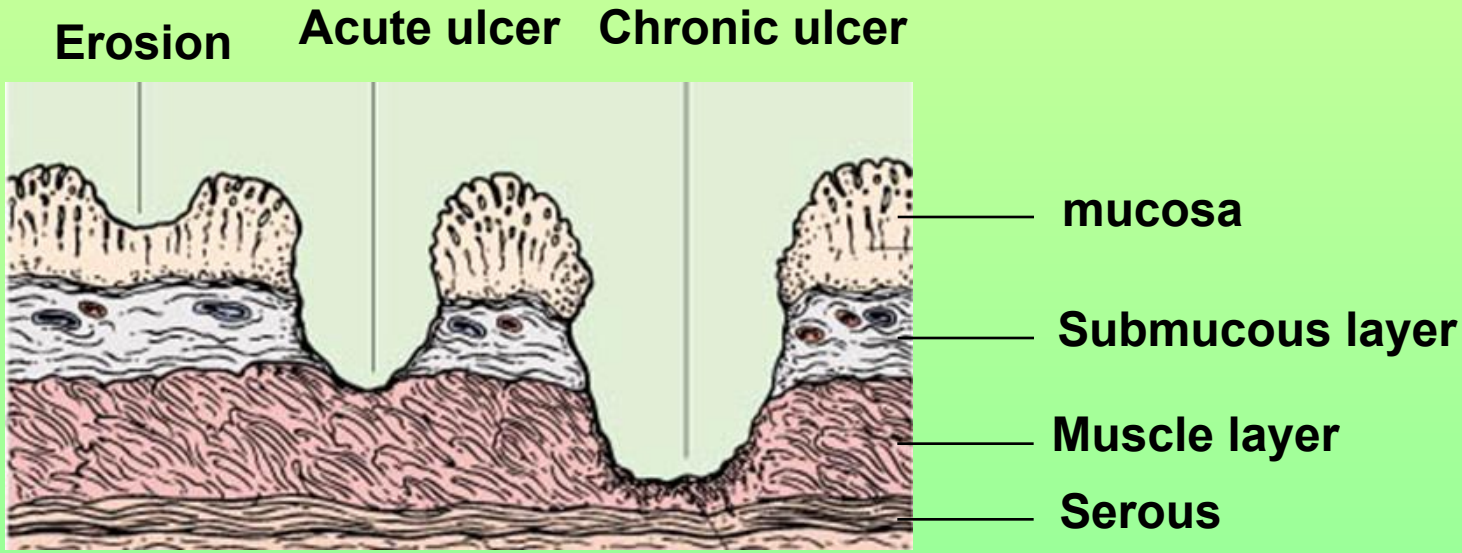




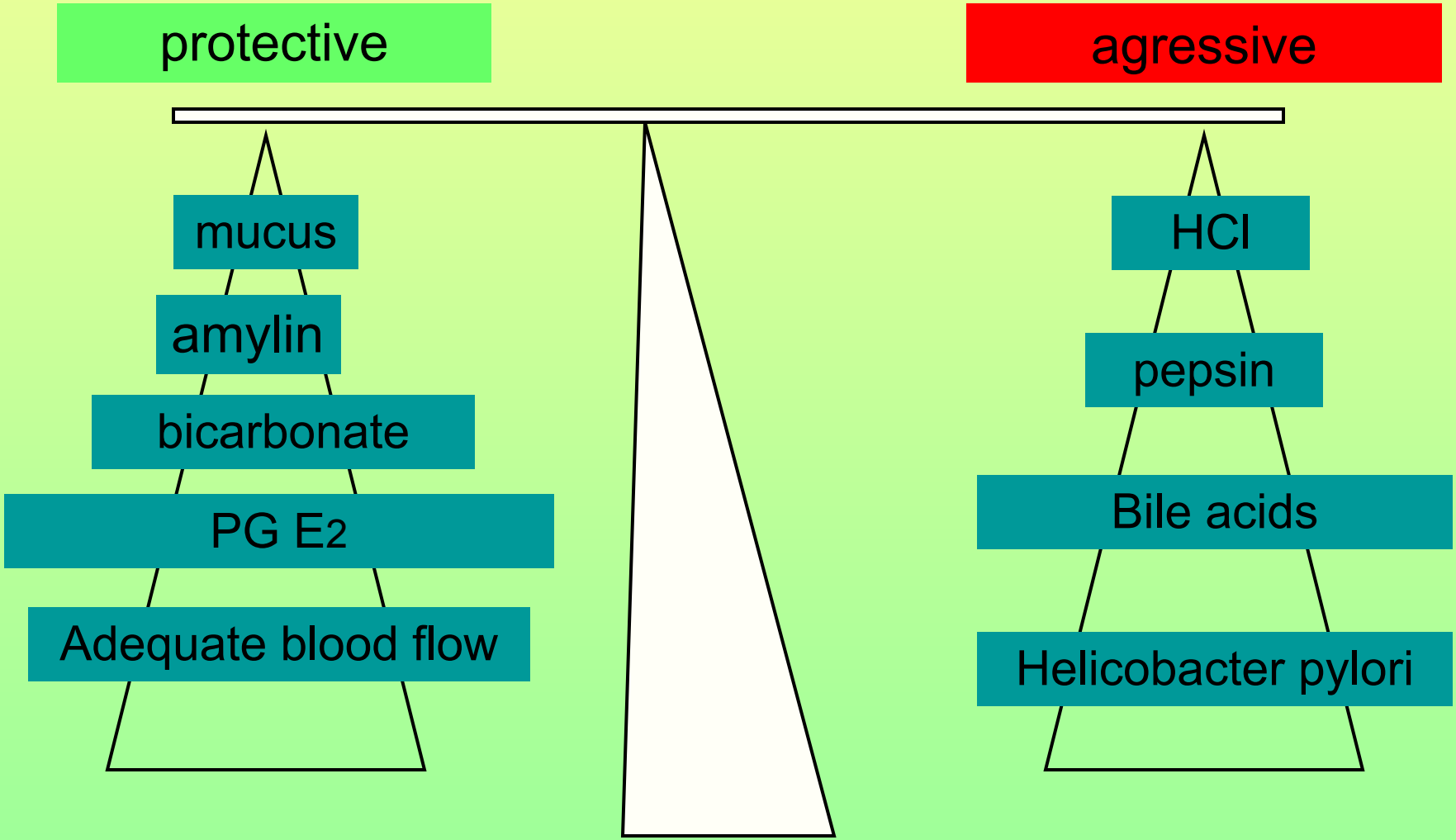
Pathogenic consequences of gastric hypersecretion

- Disorders of gastric motility (hypercontraction)
- Disorders of digestion
- Hyperkinesia
- Disorders of water-electrolyte and acid-base balance

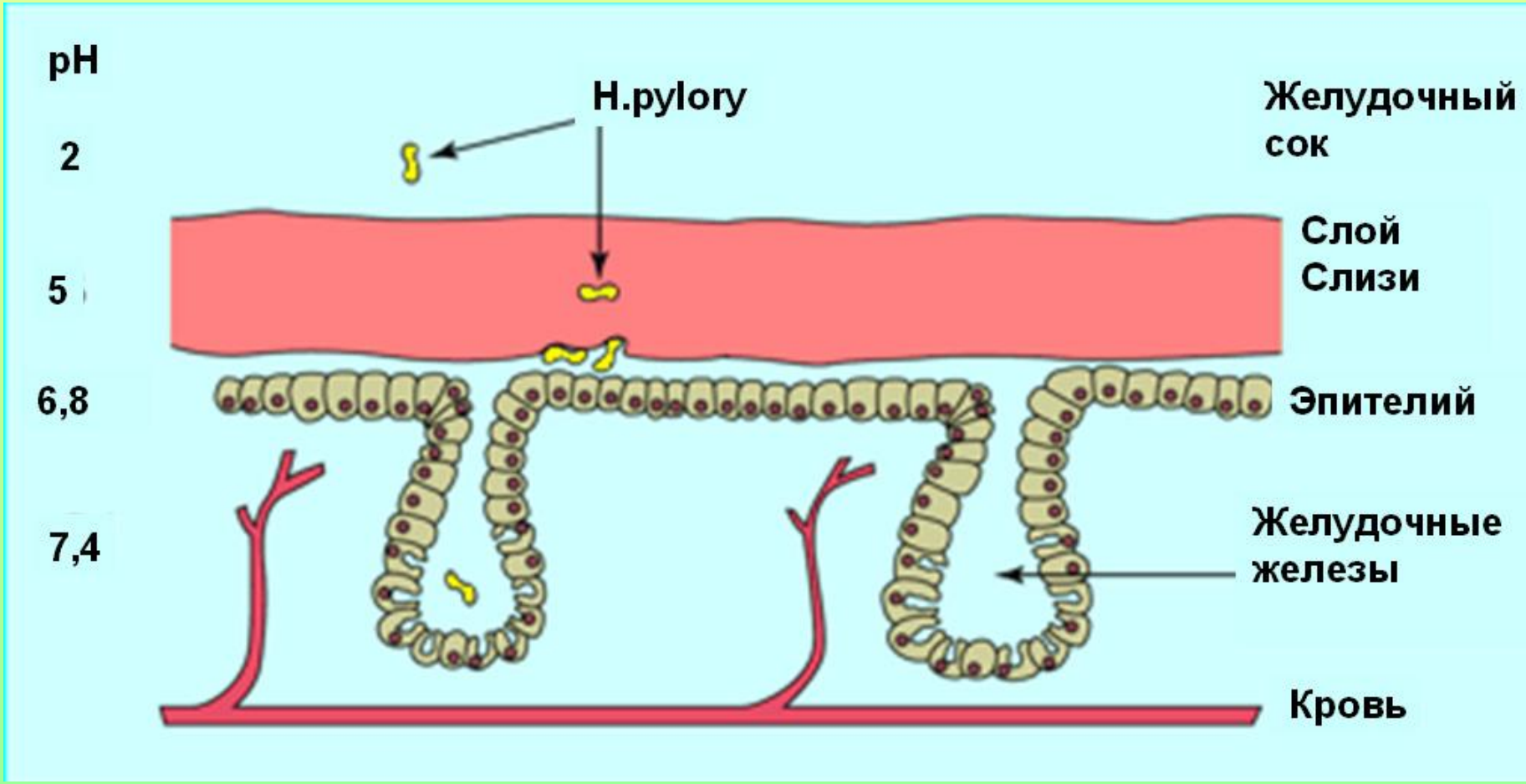
Development of acid-dependent diseases



Aggressive and protective factors of gastric juice



Helicobacter pylori

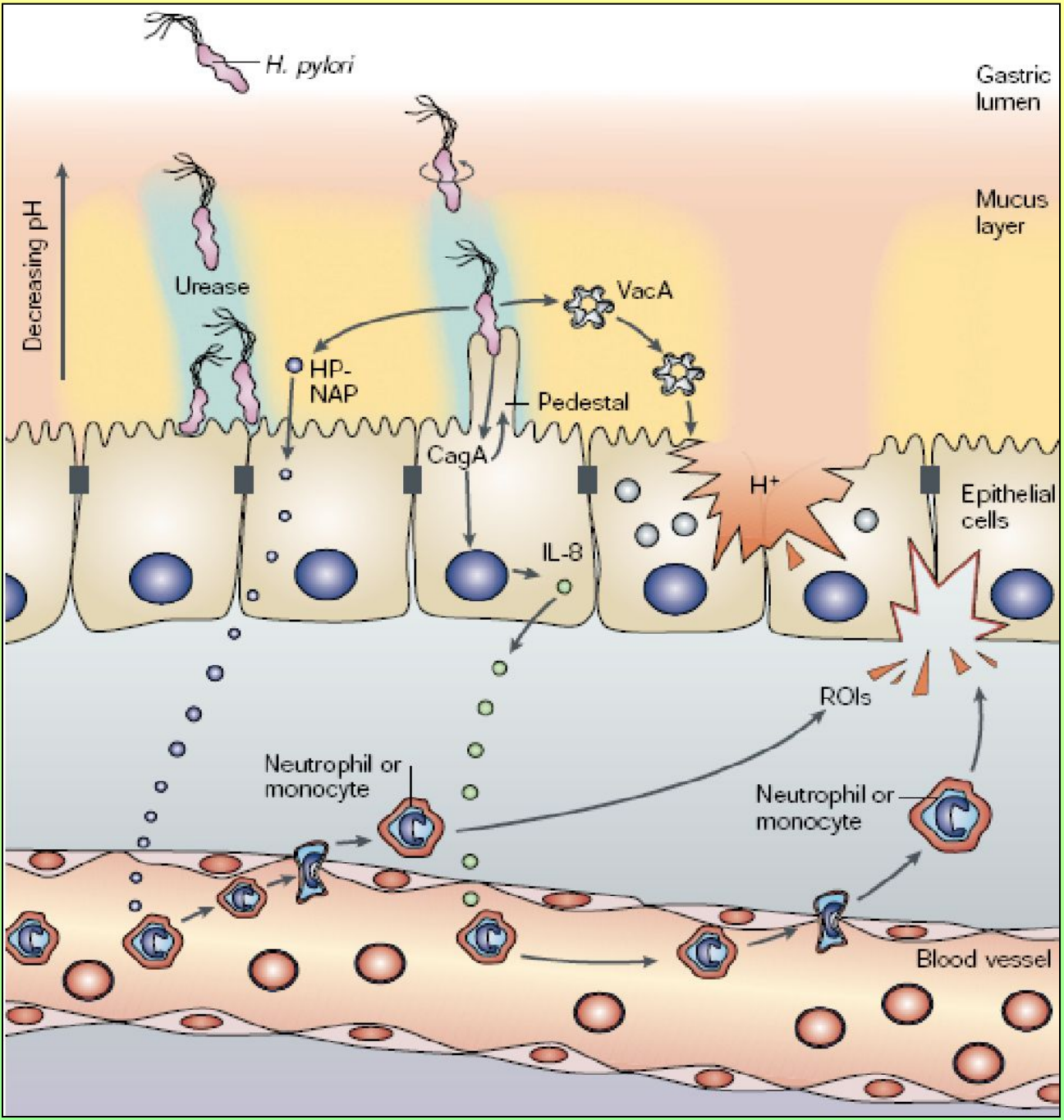


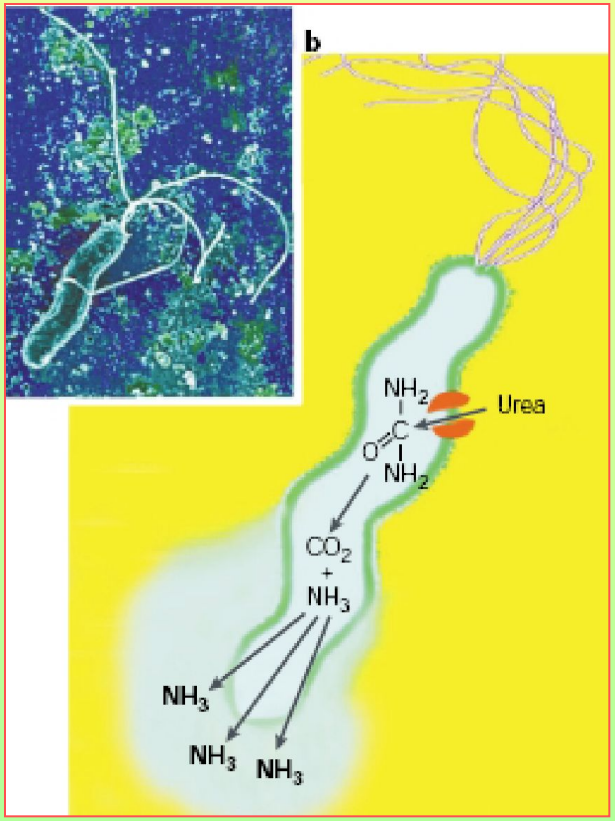
The role of Helicobacter pylori

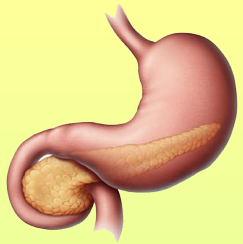
Helicobacter pylori

- **urease** → **urea** → **ammonia** → **Increase of pH in antrum** → **Gastrin production** → **Hyperproduction of HCl**
- **Increase of IFNγ , TNFα** → **apoptosis, slowing of regeneration and reparation**
- **Cytiotoxic effect**
- **cytotoxines (Vac A, Cag A…)** → **Injury of epithelium Infiltration with neutrophils**

Antral gastritis B, ulcer
Risk of cancer

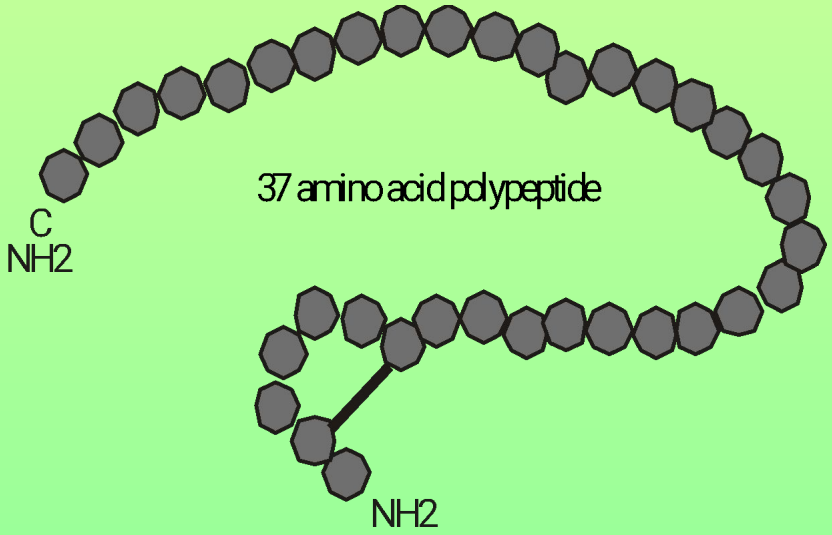

H. pylori
Gastric lumen
Mucus layer
Decreasing pH
Urease
VacA
HP-NAP
Pedestal
CagA
H+
Epithelial cells
IL-8
ROIs
Neutrophil or monocyte
Neutrophil or monocyte
Blood vessel

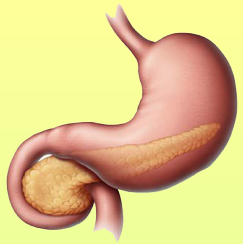

b
Urea
NH2
C
O
NH2
CO2
+
NH3
NH3
NH3
NH3



Ulceroprotective effect of amylin

- Inhibition of gastric secretion
- Stimulation of production of mucus
- Acceleration of healing of mucosa





Pathogenesis of gastro-esophageal reflux disease (GERD)

Motor dysfunction of the lower esophageal sphincter

Decreased mucosal resistance → **Gastro-esophageal reflux** ← Increase in intragastric pressure

Saliva → Decreased esophageal clearance

Gravity

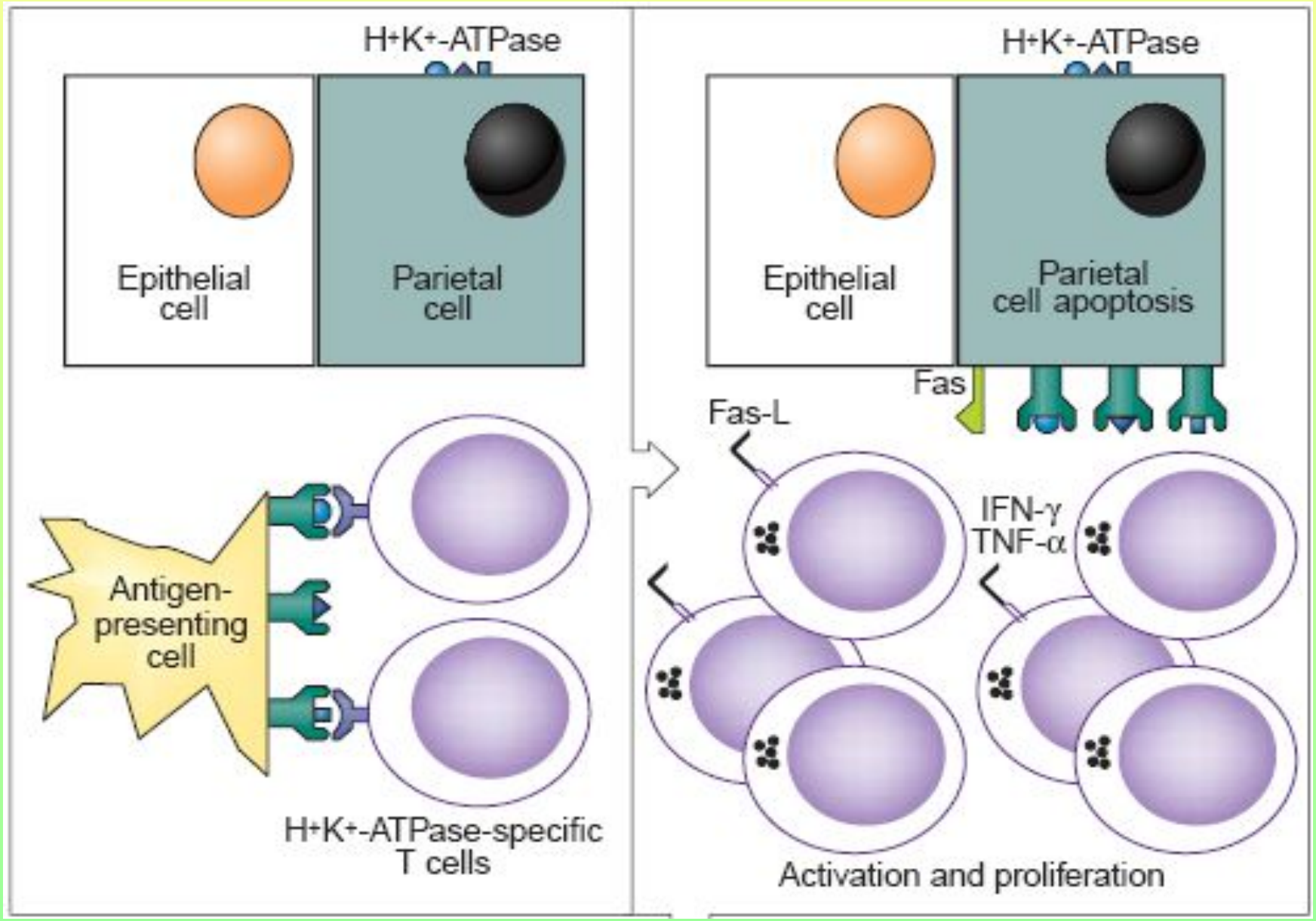
Esophageal peristaltics

Renewal of the epithelium

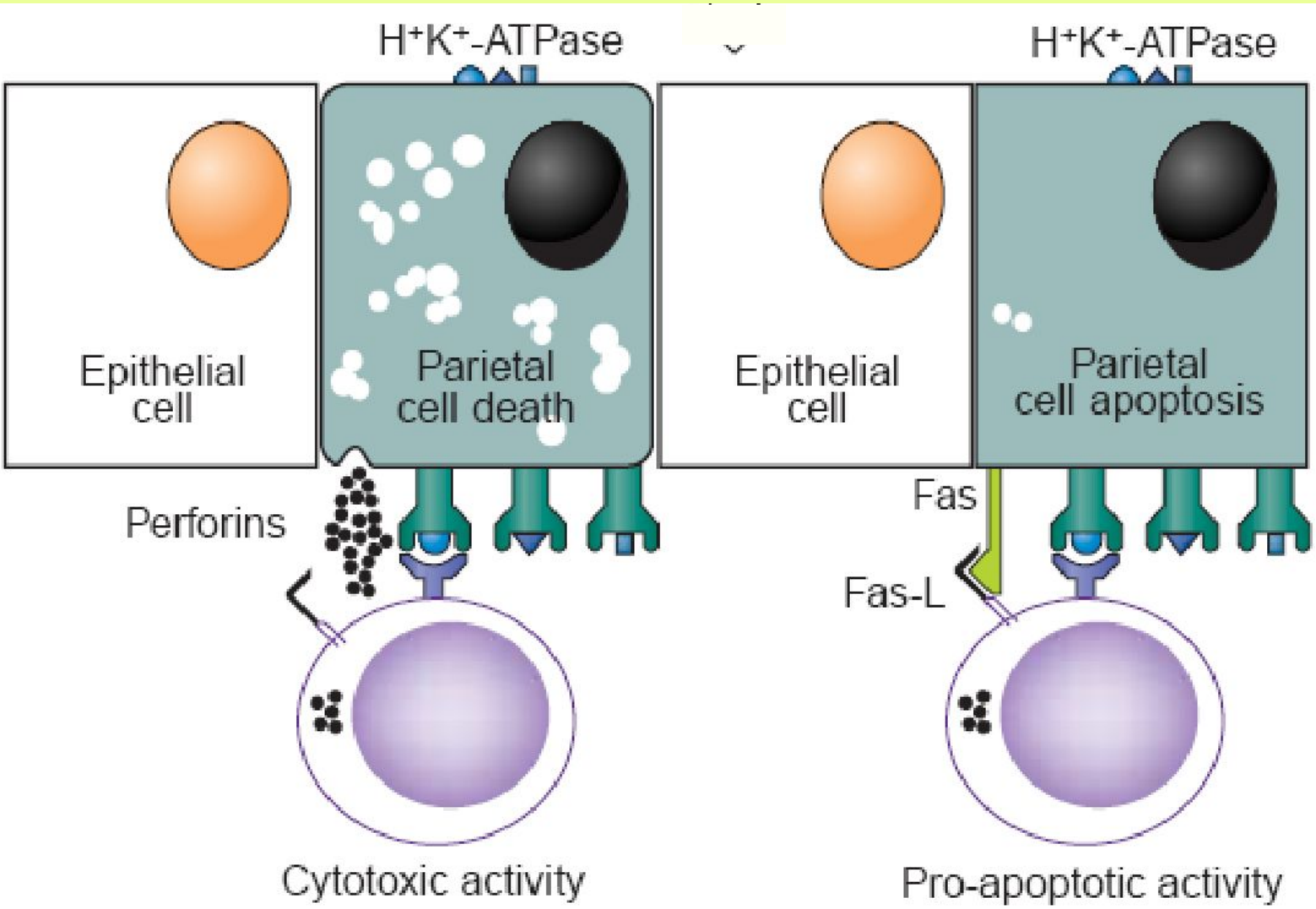
Mechanisms of gastric hyposecretion

- Disorders of regulation (neurogenic, hormonal)
- Atrophy of mucosa (autoimmune gastritis)
- Resection of the stomach

Induction of autoimunity against parietal cells



Mechanisms of immune-mediated parietal cell death leading to gastric atrophy



Complications of gastric hyposecretion

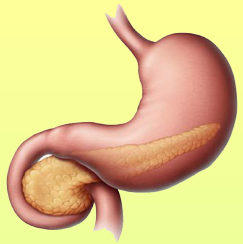
- Disorders of protein digestion
- Hypokinesia
- Disorders in barrier function
- Disorders of iron and vitamin B_{12} absorption
- Disorders of intestinal secretion and digestion

Increased gastric motility (gastric hyperkinesia)

- Neurogenic
- Increased production of HCl, gastrin, motilin …
- Hypercalcemia
- Pylorostenosis

Complications:

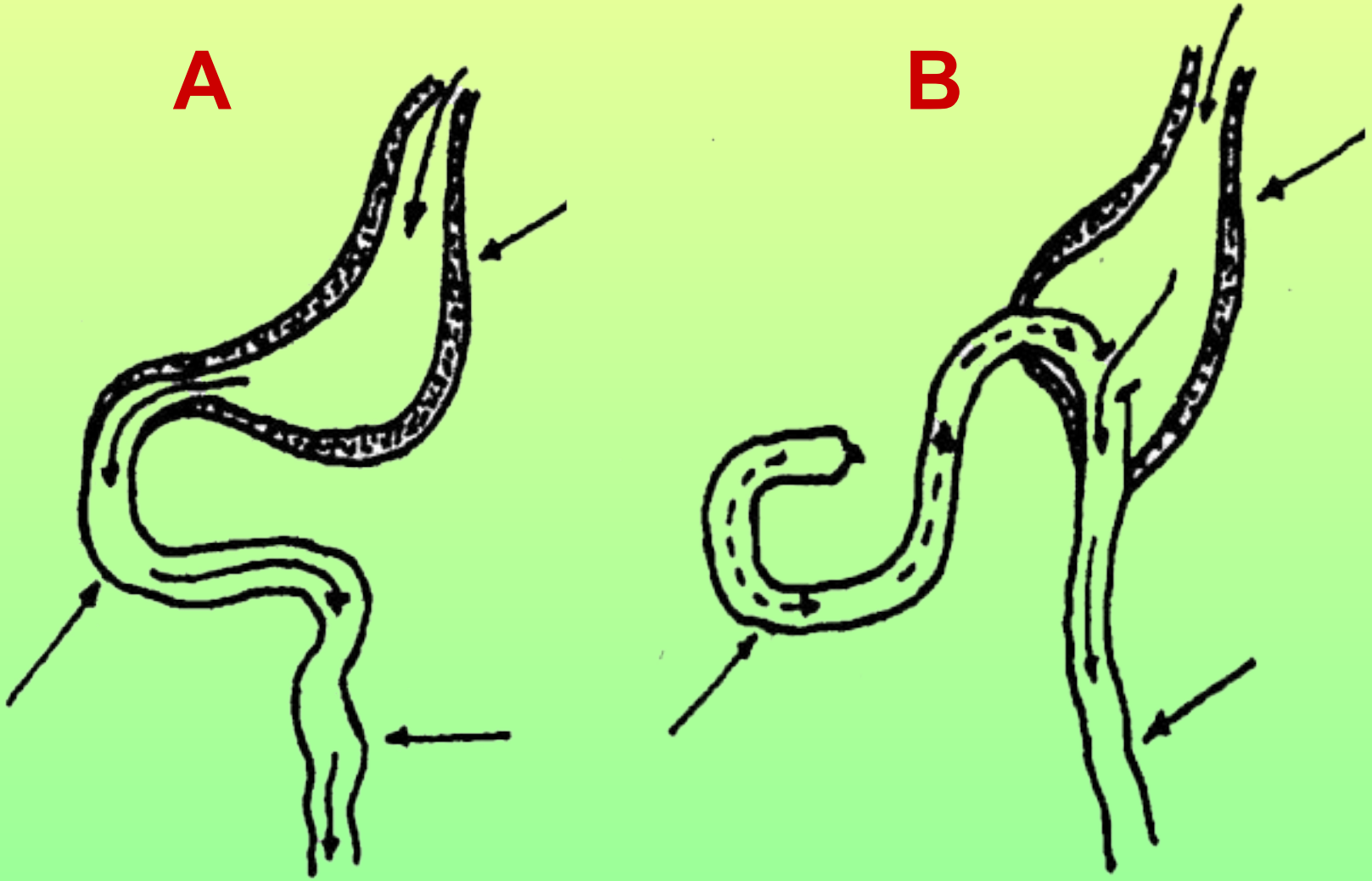
- Decrease volume adaptation
- Increase in intragastric pressure
- Increased tone of the stomach
- Dyspepsia



Decrease of gastric motility

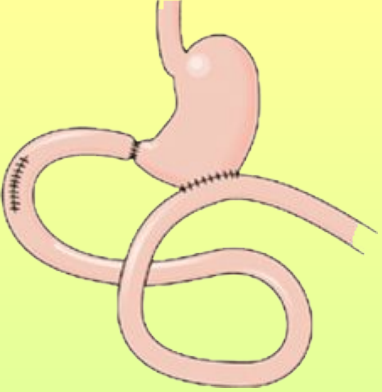
- Neurogenic
  - reflex gastroparesis
  - authonomic neuropathy (diabetes, alcoholism)
  - vagotomia
- Humoral
  - hyposecretion of HCL
  - increased production of HCl, GIP, amylin…
- Disorders of smooth muscle cell metabolism
  - anorexia
  - chronic intoxication
  - hypokalemia
  - ischemia

The passage of chyme through GI tract in normal conditions (A) and after resection of stomach (B)



The consequences of stomach resection

- Disorders in reservoir function of the stomach
- Decreased number of secretory cells (achlorhydria)
- Vitamin B_{12} deficiency → anemia
- Disturbance of fractional influx of chyme into the duodenum
- Disturbances in the regulation of secretory function of pancreas and liver
- Accelerated passage of chyme through the small intestine



Mechanisms of jejunal (postgastrectomy, dumping) syndrome

Кафедра

- **Early (~75%)**

  Dumping of the hyperosmolar chyme into the intestine

  - **Influx of water into the lumen**
  - **Stimulation of intestinal peristaltics**
  - **Stimulation of BAS formation (5-HT, VIP, kinins etc.)**

- **Late (~25%)**

  Absorption of high amount of carbohydrates into the blood

  - **Hyperglycemia ⇒ insulin release ⇒ hypoglycemia ⇒ activation of sympathetic nervous system ⇒ tachycardia, perspiration**