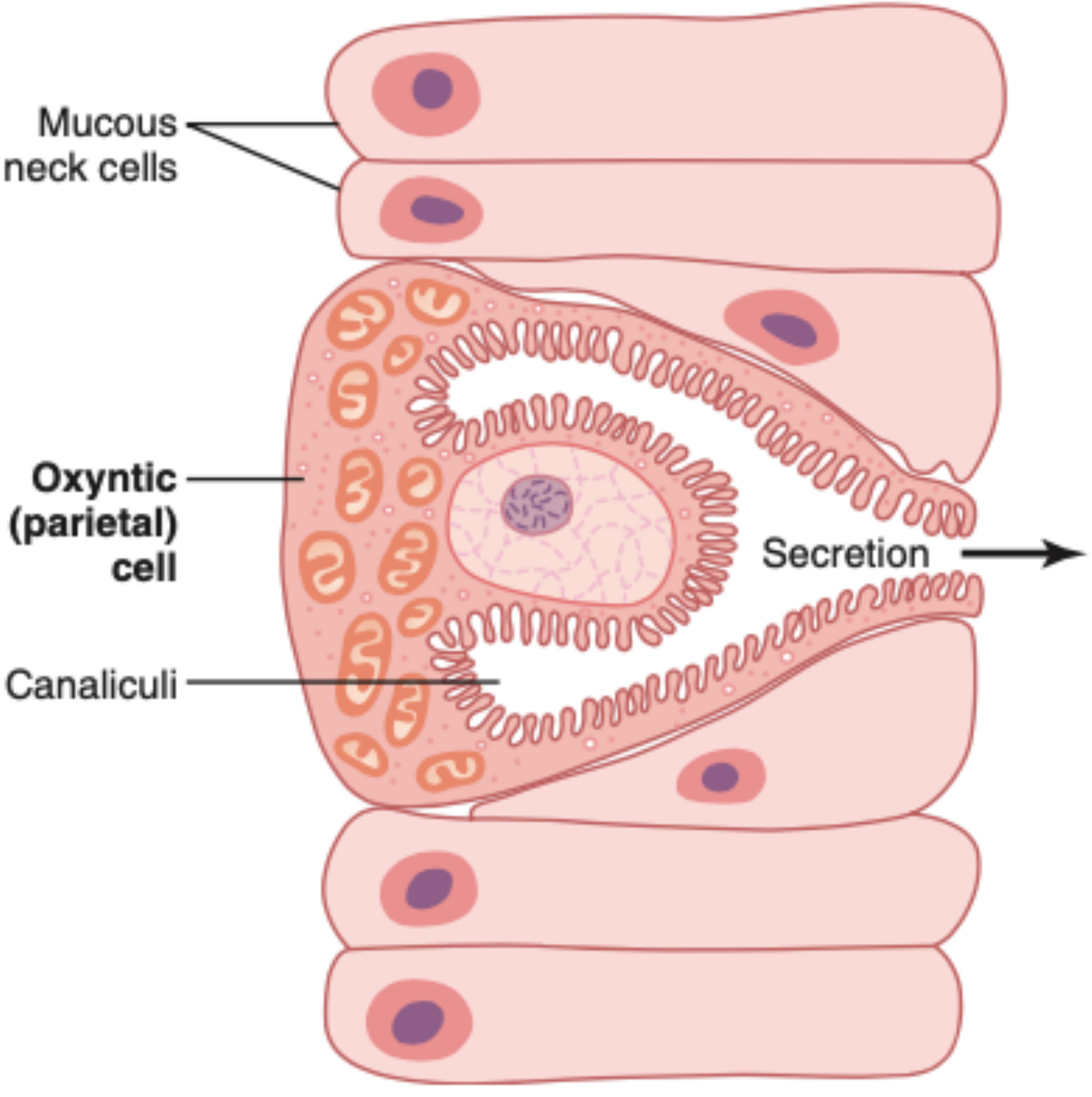
Name two anemias seen in patients with gastrectomy.

- *1) Pernicious anemia :-*
    - due to intrinsic factor deficiency.
- *2) Iron deficiency anemia :-*
    - Dietary iron - ferric form (Fe3+).
    - Iron absorbable - ferrous form (Fe2+).
    - Conversion requires gastric acid.

Gastric HCl secretion


Mucous neck cells
Oxyntic (parietal) cell
Canaliculi
Secretion

MECHANISM of ACID SECRETION

- DAVENPORT & FISHER.
- 2 step process :
  - Secretion of H+.
  - Secretion of Cl-.

- *APICAL membrane :*
  - Proton pump (H+ K+ ATP ase).
  - Chloride channels.
  - Leaky K+ channels.
- *BASOLATERAL membrane :*
  - Cl- /HCO3- exchanger.
  - Na+ K+ ATPase.
  - Leaky K+ channels.

MECHANISM of ACID SECRETION

1. **CO_2** (tissue metabolism) + **H_2O** —> **H_2CO_3** (Carbonic Anhydrase).

2. **H_2CO_3 —> H^+ + HCO_3^-.**

3. At apical membrane; *<u>H+ secreted into lumen in exchange for K+</u>* by proton pump (H+ K+ ATPase : primary active transport).

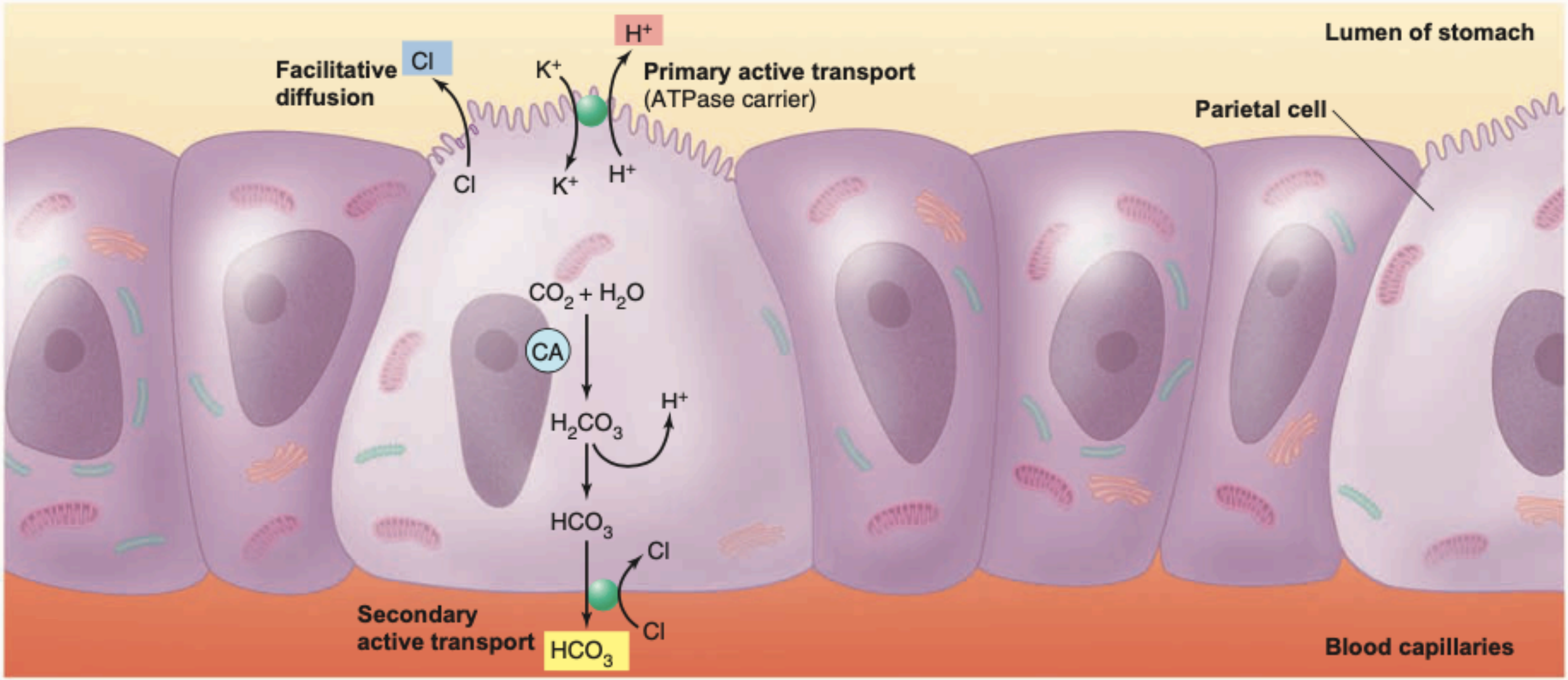
4. *<u>K+ moves out of the cell</u>* by leaky channels on apical & basolateral membrane.

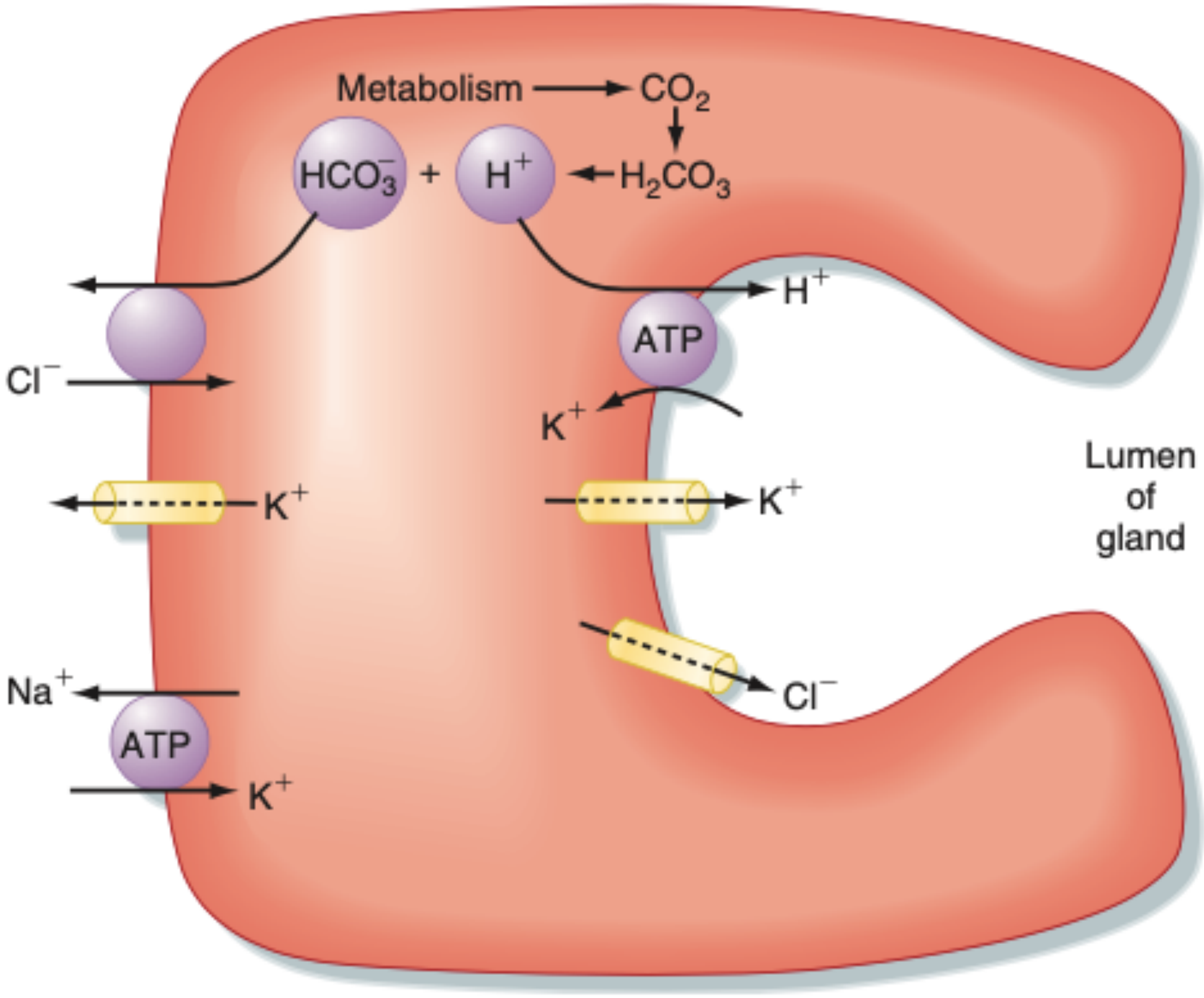
5. At basolateral membrane; *HCO3- released into blood in exchange for Cl-* via a Cl- HCO3- exchanger.

6. **Na+ K+ ATPase** exchanges **3Na+** out in exchange for **2 K+** ions.

7. *Cl- passively moves out* into the canaliculi down its electrochemical gradient.

8. In the canalicular lumen, ***H+ & Cl- combines to form HCl*** which is then secreted into gastric lumen.


Lumen of stomach
Facilitative diffusion
Cl
Cl
K+
K+
H+
H+
Primary active transport
(ATPase carrier)
Parietal cell
CO2 + H2O
CA
H2CO3
H+
HCO3
Cl
Cl
Secondary active transport
HCO3
Blood capillaries


Metabolism
CO_2
HCO_3^-
+
H^+
H_2CO_3
H^+
ATP
Cl^-
K^+
K^+
K^+
Lumen of gland
Cl^-
Na^+
ATP
K^+

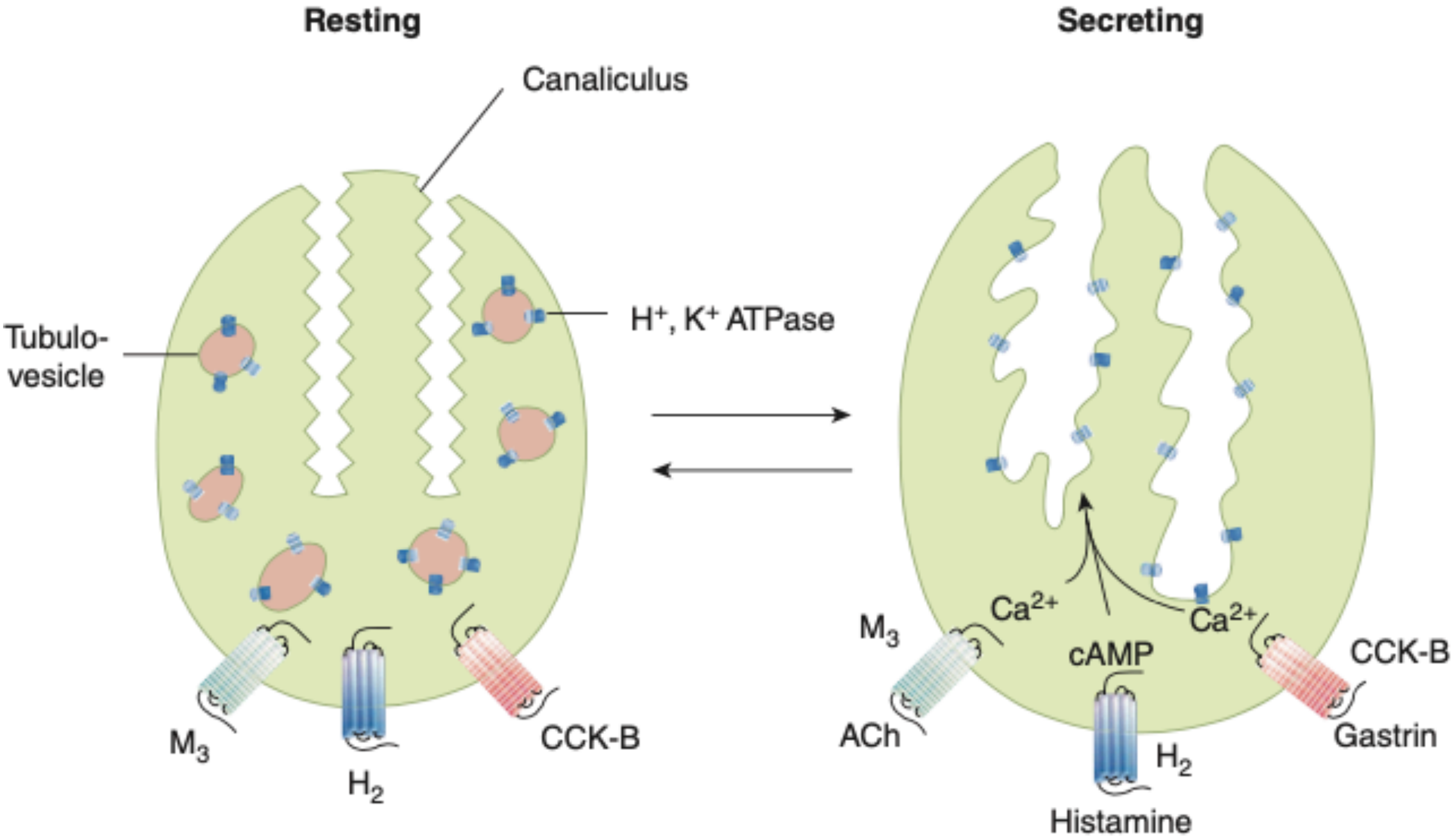
For every H+ ion secreted into gastric lumen; one HCO3- is absorbed into blood : ***POSTPRANDIAL ALKALINE TIDE.***

(Blood & urine).

REGULATION of ACID SECRETION

- **STIMULATORS**
  - *Parasympathetic stimulation*
  - *Histamine*
  - *Gastrin*
  - Hypoglycaemia
  - Caffeine, alcohol, Stress, NSAIDs

- **INHIBITORS**
  - Somatostatin
  - Low pH in stomach
  - Secretin, Cholecystokinin
  - Prostaglandins.
  - Sympathetic stimulation
  - Hyperglycaemia.


Resting
Secreting
Canaliculus
Tubulo-
vesicle
H+, K+ ATPase
M3
H2
CCK-B
Ca2+
Ca2+
M3
cAMP
CCK-B
ACh
H2
Gastrin
Histamine

STIMULATION OF HCl SECRETION

- **1) ACETYLCHOLINE :**
    - Secreted by Cholinergic nerve endings.
    - Direct action : Binds to M3 muscarinic receptors on parietal cells.
    - Opens a Ca2+ channels :- increase intracellular Ca2+ :- stimulate acid secretion.
    - Indirect action : stimulating ECL cells to secrete histamine.
    - *Blocked by ATROPINE*.

- **2) HISTAMINE :-**
  - Released by ECL cells.
  - Paracrine action on nearby parietal cells.
  - Binds to H2 receptors.
  - Activate adenylyl cyclase : increase cAMP levels :- increases acid production in parietal cells.
  - *Blocked by H2 receptor blockers : RANITIDINE, CIMETIDINE.*

- **3) GASTRIN :-**
  - Secreted by G cells in antrum.
  - Endocrine action : reaches by blood.
  - Binds to CCK-B receptors on parietal cells.
  - Increases acid secretion by Ca2+ pathway.
  - Also stimulates Histamine release.

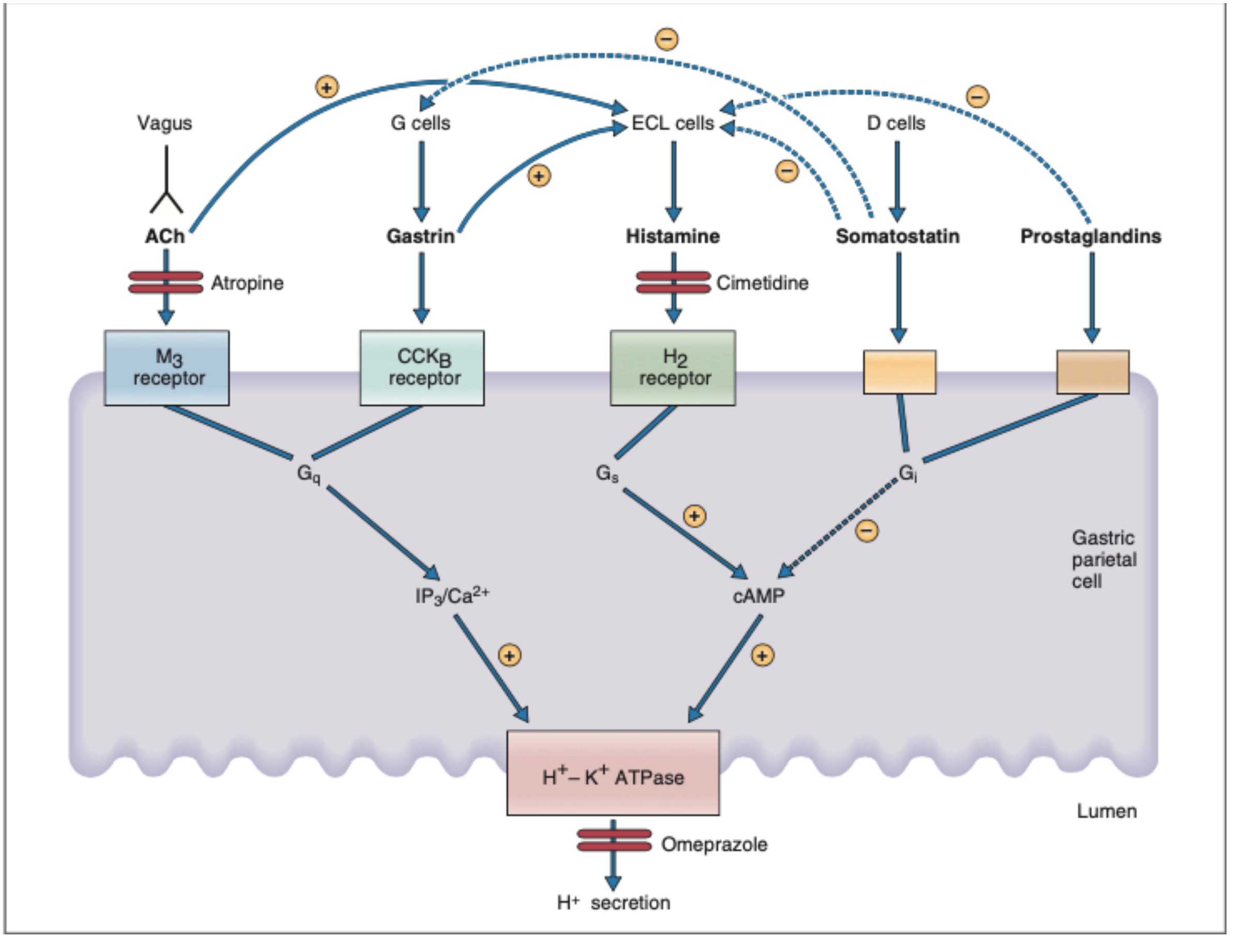
- 3 agents : Acetylcholine, Histamine, Gastrin.
  - Potentiate each other's action : **SYNERGISM**.
  - *Physiological significance :*
    - high rate of change of gastric secretion achieved by even a small rise in stimuli release.
- *Therapeutic significance :*
    - Secretion markedly inhibited by blocking action of only one of triggers (most commonly *Histamine :- H2 antagonists).*

- *VAGUS (parasympathetic stimulation)* : most potent stimulator of HCl secretion.
    - Acts directly on M3 receptors via Acetylcholine.
    - Release of gastrin by G cells via GRP.
    - Release of Histamine by stimulating ECL cells.

- ATROPINE
  - Will not block acid secretion completely?
  - Dual action of vagal stimulation.
  - Muscarinic blocker alone.

INHIBITION OF HCl SECRETION

- SOMATOSTATIN :-
  - Secreted by D cells.
  - Inhibit Histamine secretion & acid secretion by Gi pathway.
- PROSTAGLANDINS E & I :-
  - Lowers cAMP concentration & inhibits acid secretion.


Vagus
G cells
ECL cells
D cells
ACh
Gastrin
Histamine
Somatostatin
Prostaglandins
Atropine
Cimetidine
M3 receptor
CCKB receptor
H2 receptor
Gq
Gs
Gi
IP3/Ca2+
cAMP
Gastric parietal cell
H+– K+ ATPase
Lumen
Omeprazole
H+ secretion

PHASES of GASTRIC ACID SECERTION

- Interdigestive phase or basal secretion.
- Cephalic phase
- Gastric phase
- Intestinal phase.

INTERDIGESTIVE/ BASAL SECRETION

- No stimulation from brain or GI tract.
- Basal rate of secretion between meals.
- Secretion : almost entirely mucus, little pepsin & almost no acid.
- Raised in *abnormal conditions : emotional stimuli, Duodenal ulcer.*

CEPHALIC PHASE

- Sight, smell, taste or even thought of food.
- Occurs even before food enters stomach.
- 30% of total gastric acid secretion in response to a meal.
- Conditioned & unconditioned reflexes.
- Mediated by Vagus.
- Pathway :
    - Cortex & appetite centers of Amygdala & Hypothalamus —> VAGUS (Acetylcholine & Gastrin).

- **SHAM FEEDING :**
  - Experimental evidence for cephalic phase of secretion.
  - Experimental animal : dog.
  - Esophagus is exposed in neck & divided with two ends exposed to exterior.
  - When dog eats, food comes out of esophagus in neck.
  - Cannula inserted in stomach : collect gastric juice.

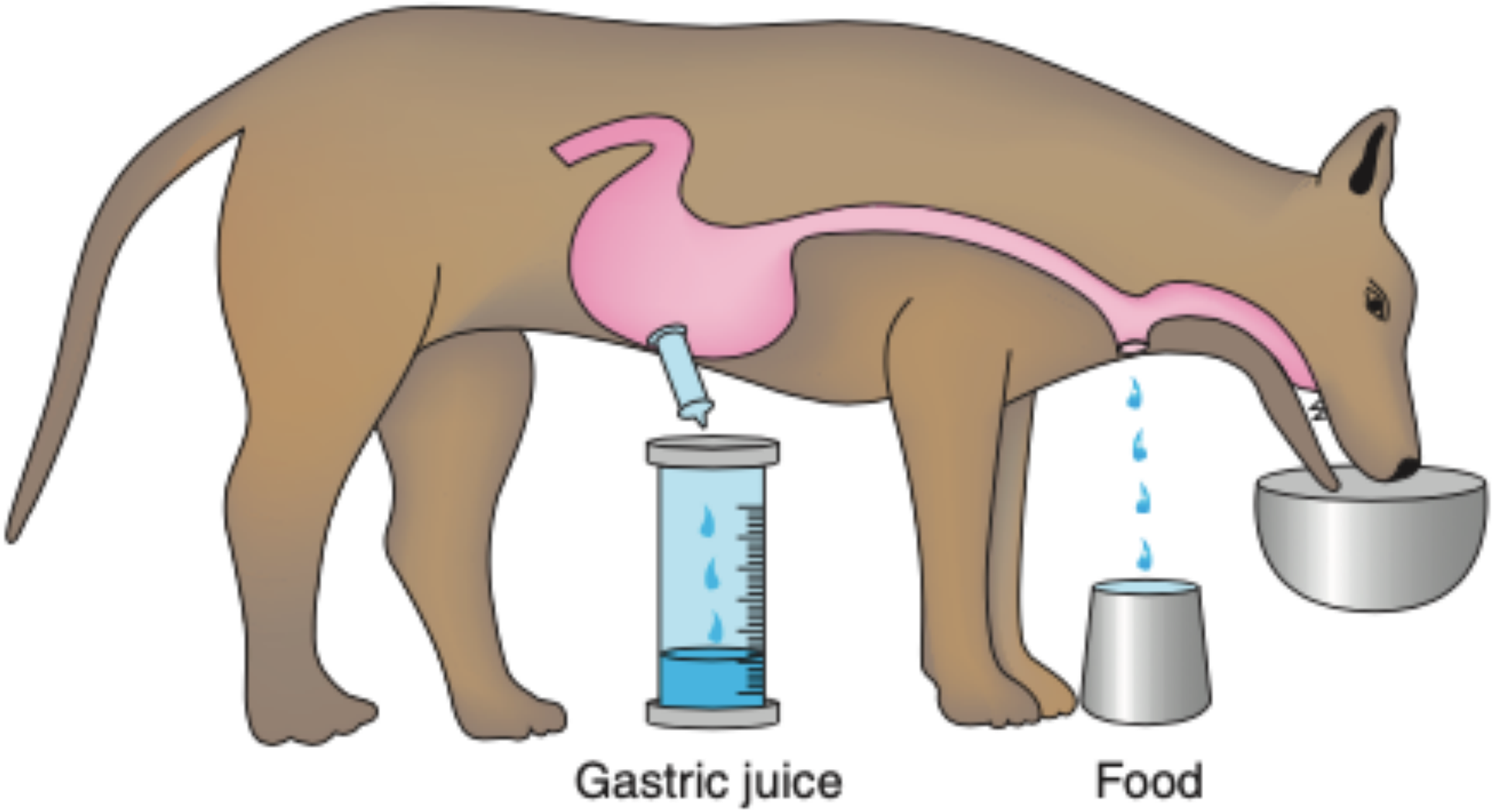


Fig. 7.3-10 Sham feeding experiment to demonstrate initiation of cephalic phase of gastric secretion.

- *Observation* :
    - when dog eats, gastric secretion increases even if food doesn’t reach stomach.
        - Secretion stops in case of ***total vagotomy***.
- *Inference* :
    - cephalic phase of gastric secretion exists.
    - mediated by vagus.

GASTRIC PHASE

- 70% of secretion.
- Starts when food enters stomach.
- Distension of stomach : detected by stretch receptors —> vagus.
- Mediated by

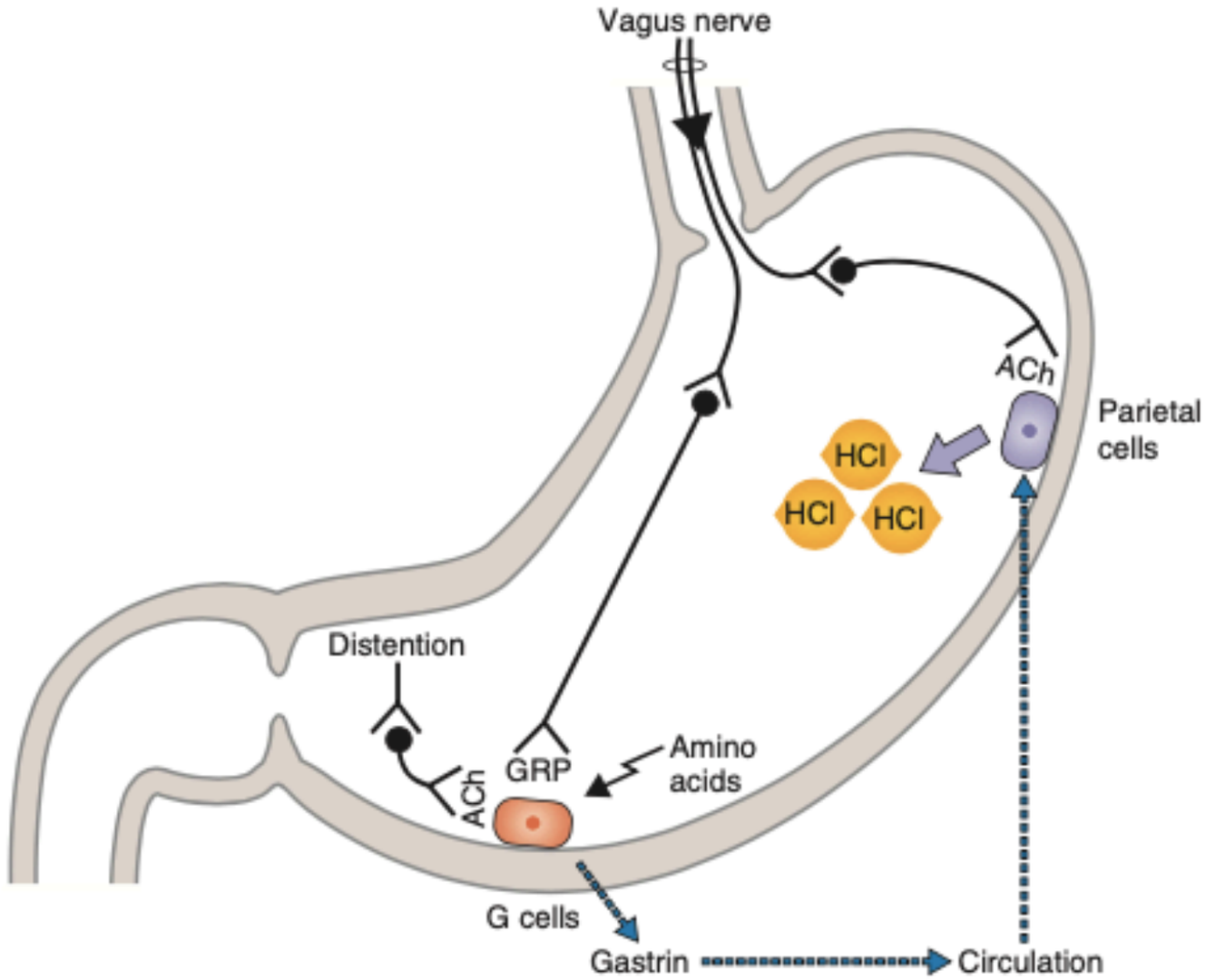
1. Long Vago-vagal reflexes.
2. Local enteric reflexes.
3. Gastrin - Histamine mechanism.

INTESTINAL PHASE

- 10% of secretion.
- Partially digested acidic chyme reached intestine.
- Mediated by *GASTRIN* (intestinal G cells).

- Net effect of intestinal phase : INHIBITION of gastric secretion.
- Acidic chyme in duodenum :
    - Enterogastric reflex & Secretin (S cells).
- Fatty food content :
    - CCK, GIP, VIP, Glucagon.
- Purpose : slow passage of chyme from stomach into an already filled intestinal lumen.

REGULATION OF HCl SECRETION



Phase	% of HCl Secretion	Stimuli	Mechanisms
Cephalic	30%	Smell, taste, conditioning	Vagus → parietal cell Vagus → gastrin → parietal cell
Gastric	60%	Distention	Vagus → parietal cell Vagus → gastrin → parietal cell
		Distention of antrum	Local reflex → gastrin → parietal cell
		Amino acids, small peptides	Gastrin → parietal cell

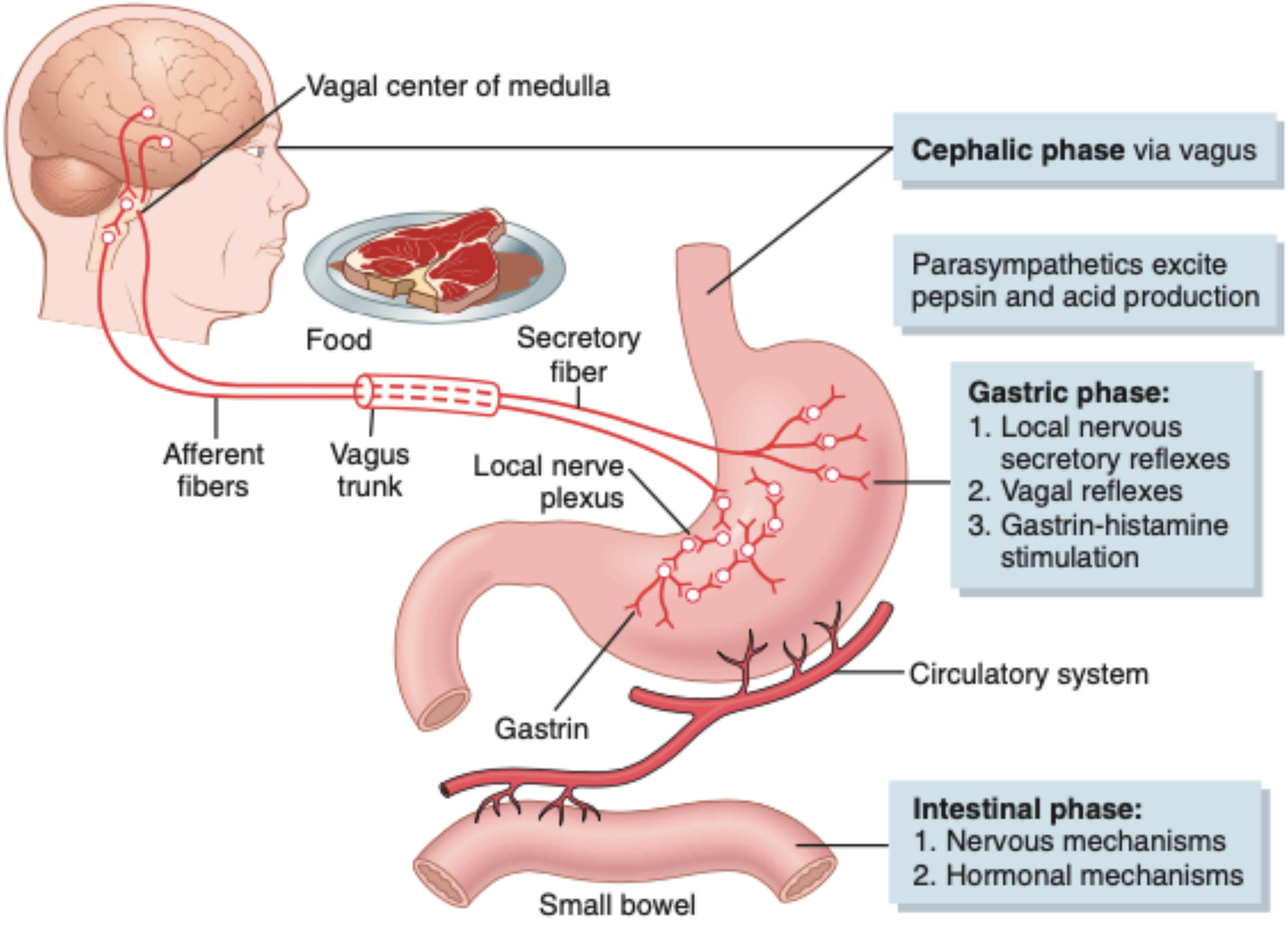


Figure 65-7. Phases of gastric secretion and their regulation.