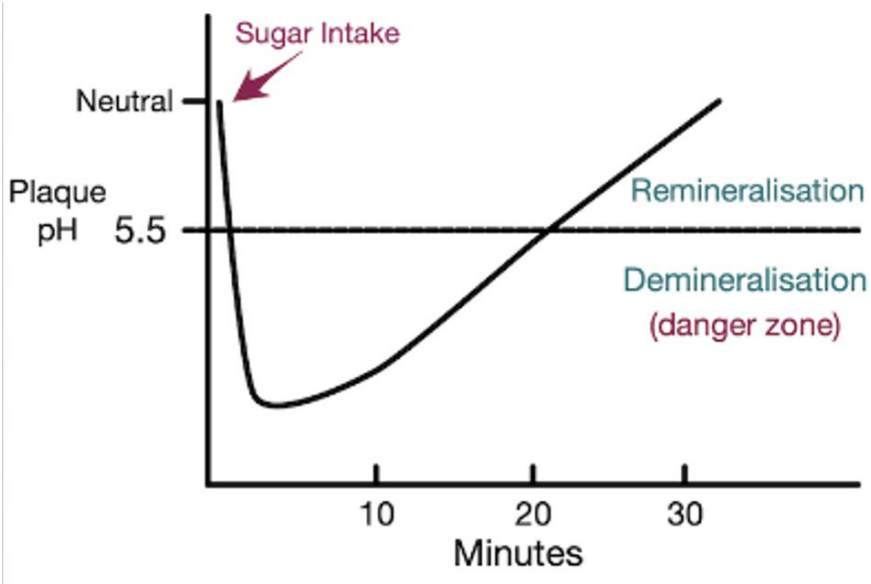
Saliva, ENS, Hormones

What are the functions of saliva?

- Tooth maintenance
- Lubrication
- Antifungal/antibacterial – IgA
- Digestive (amylase)

The Stephan Curve



On the Stephan curve, pH must be kept close to 7. Critical pH is 5.5, tooth demineralise when pH is lower than this. This can lead to tooth decay, gum disease, and increased plaque.
If there is low pH for a prolonged time, the lack of saliva can lead to rampant caries

Salivary glands

Innervation of salivary glands

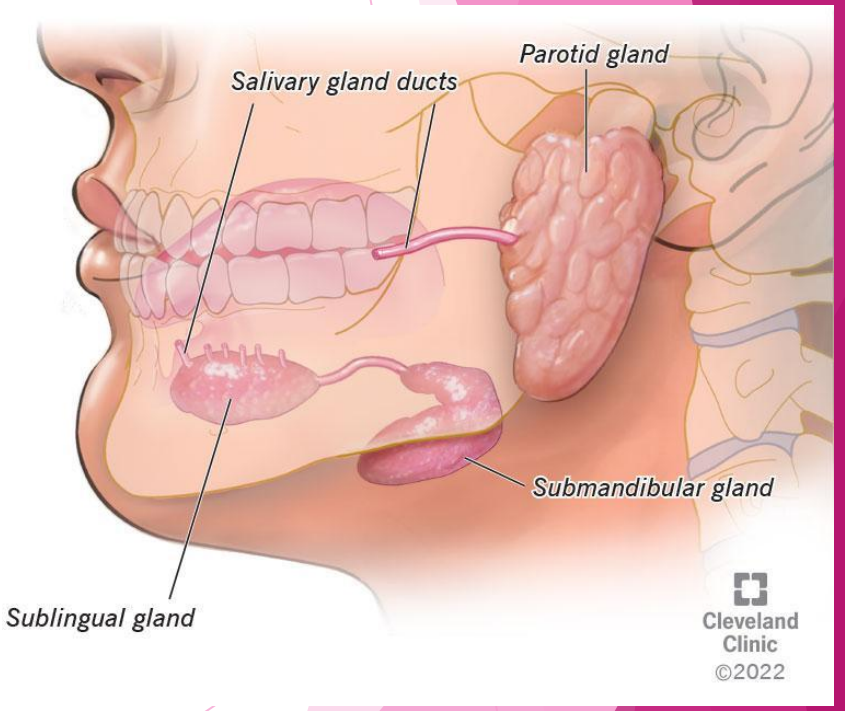
- Submandibular and sublingual glands: superior pons sends signal via facial nerve (CN VII)
- Parotid glands: inferior medulla sends signal via glossopharyngeal nerve (CN IX)

Salivary gland secretions

- Parotid produces serous saliva
- Sublingual produces mucous saliva
- Submandibular produces serous/mucous i.e. mixed saliva

Stimulation and inhibition of saliva production

- Stimulants: mastication, taste, smell, anticipation. These stimulate salivary nuclei in the superior pons and inferior medulla.
- Inhibition: fear and vomiting



Saliva

Constituents of saliva

- Glycoproteins – layers slide over each other; difficult to pull apart
- All salivary glands secrete both protein and fluid
- The constituent of saliva depends on the nature of protein secreted from the gland

Cells of salivary glands

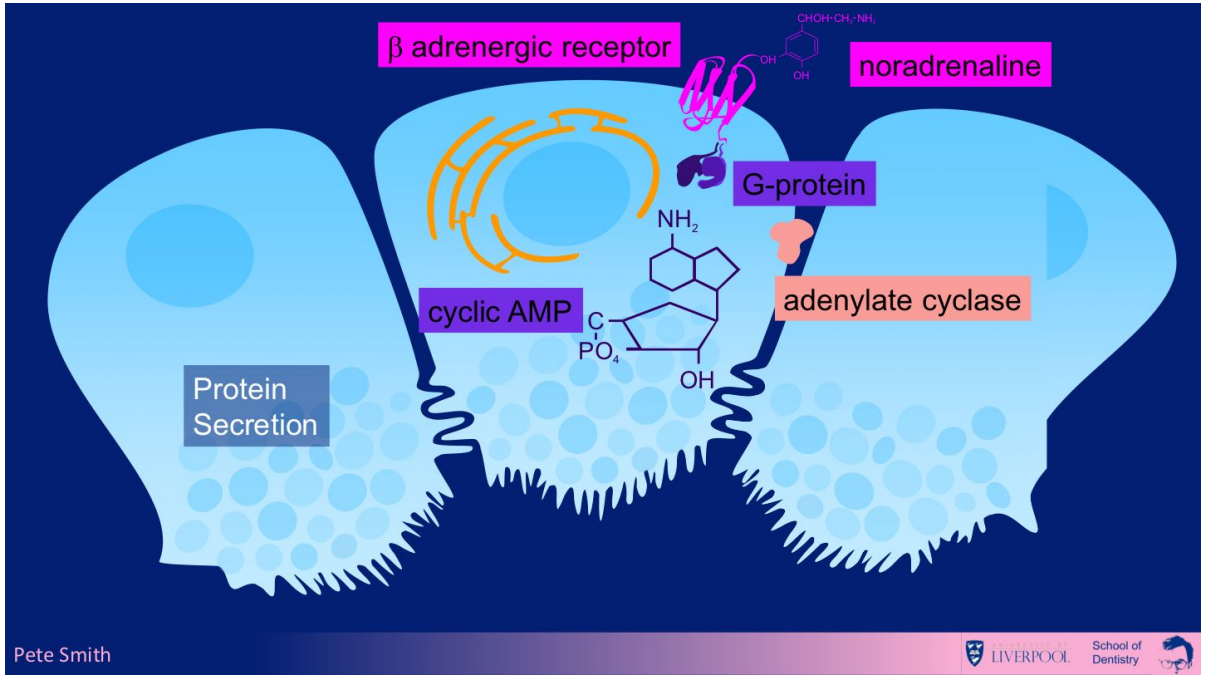
- Myoepithelial cells contract to increase speed of release
- Acinar cells can either be serous or mucous, but these produce saliva

Stimulus secretion coupling process

- Process whereby both protein and fluid are secreted simultaneously as to prevent protein from blocking the apical side of the acinar cells
- (The basal side of the cell is the side that faces the basement membrane i.e. the connective tissue layer the cell lives on. The apical side is the side that faces the opposite direction, usually towards the lumen (inside) of a tube.

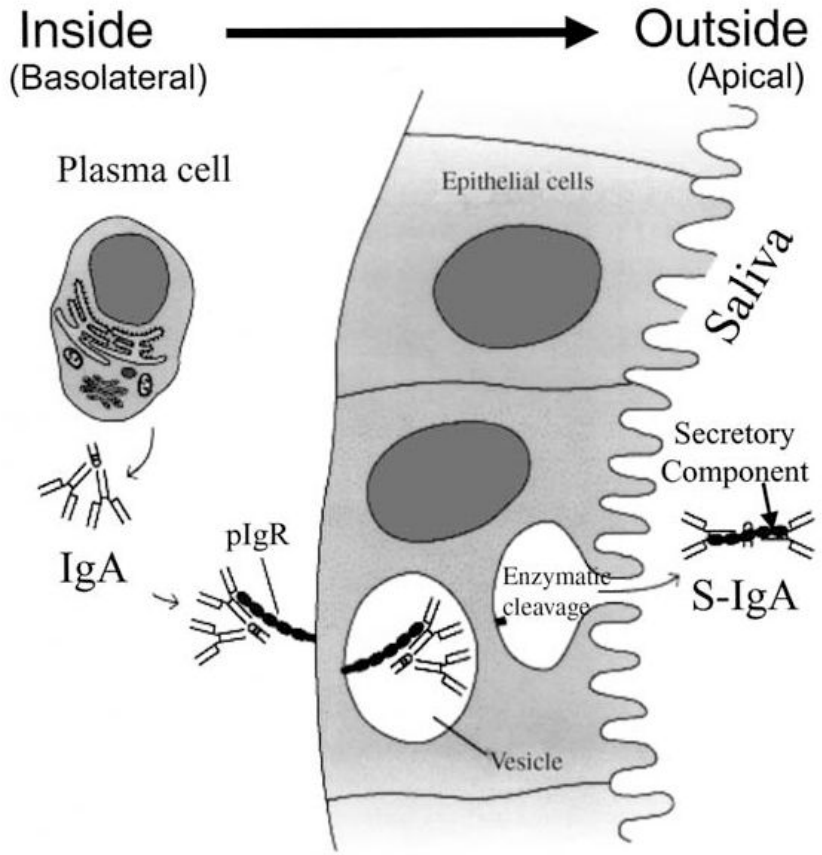
Protein secretion occur in saliva

- The sympathetic NS stimulates release of noradrenaline
- Noradrenaline binds to a beta-adrenergic receptor on the acinar cell which is coupled to a G protein (GS TYPE)
- G protein subunit activates adenylate cyclase
- Adenylate cyclase causes cAMP production
- cAMP stimulates transcription of proteins, formation of secretory vesicles and exocytosis



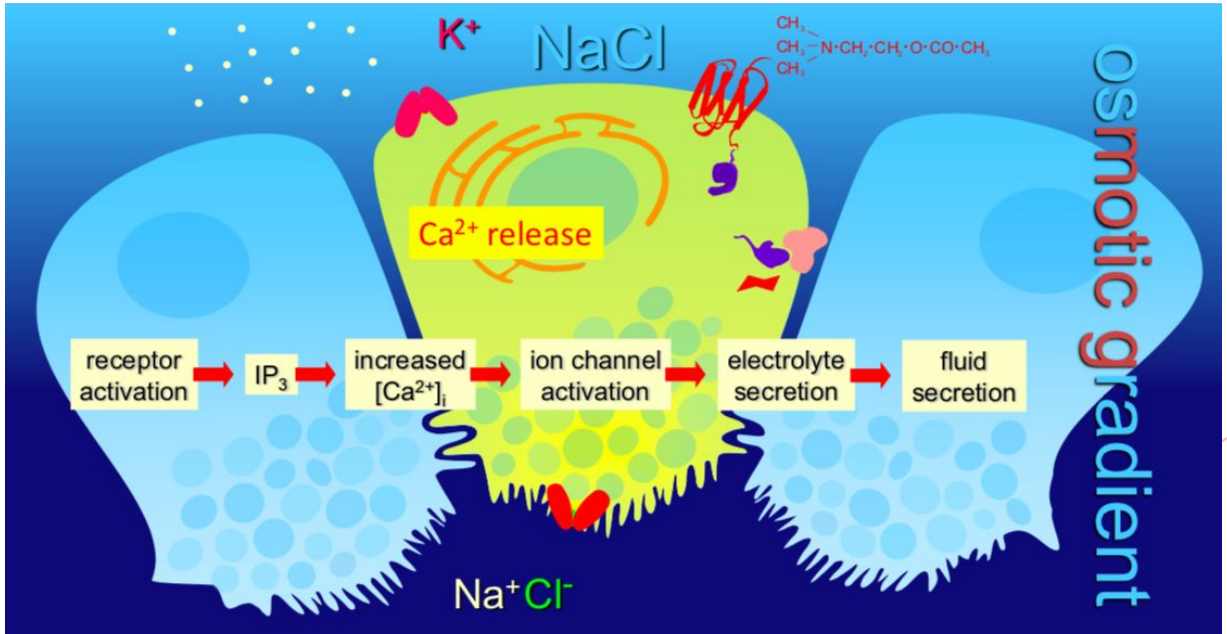
Acinar cells secrete IgA

- IgA binds to a polymeric immunoglobulin receptor (PIgR) on the basolateral membrane of acinar cell
- Endocytosis of receptor with the protein
- The IgA and its receptor are transported to the apical membrane where IgA is released into the gland



Fluid Secretion in saliva

- The parasympathetic NS stimulates release of acetylcholine
- Ach binds to a M3 muscarinic receptor bound to a G protein (GQ TYPE) which initiates activation of phospholipase C
- Phospholipase C causes production of IP3 which binds to IP3 receptors (on ER) and so stimulates release of Ca^{2+} on ER
- Ca^{2+} activates K^+ channels on the basolateral membrane to open and Cl^- channels on the apical (more -ve side) membrane to open causing a charge gradient
- This causes Na^+ to move across the paracellular junction (permeable to Na^+) causing an osmotic gradient moving water into the salivary gland

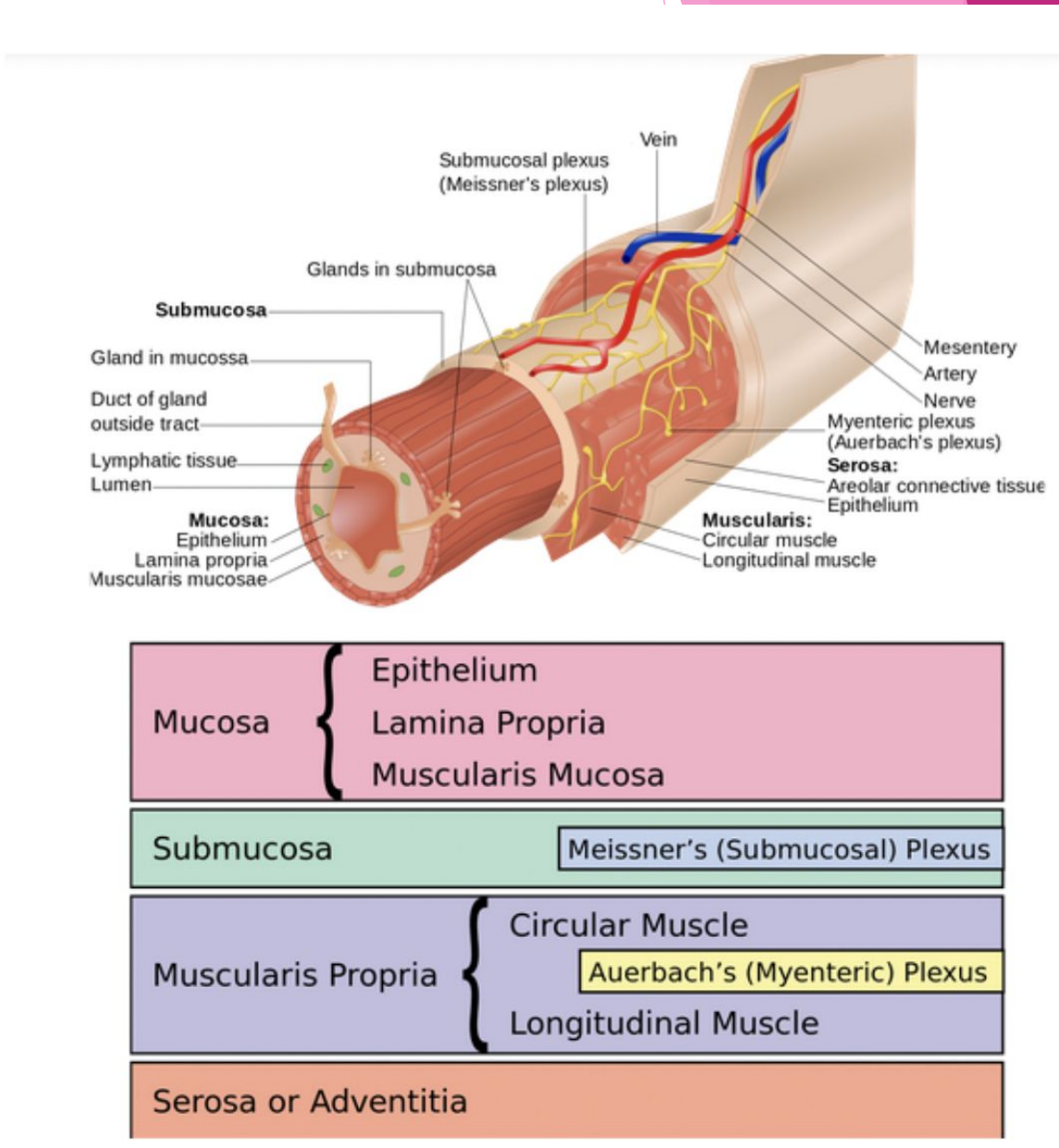


Layers of the GI tract

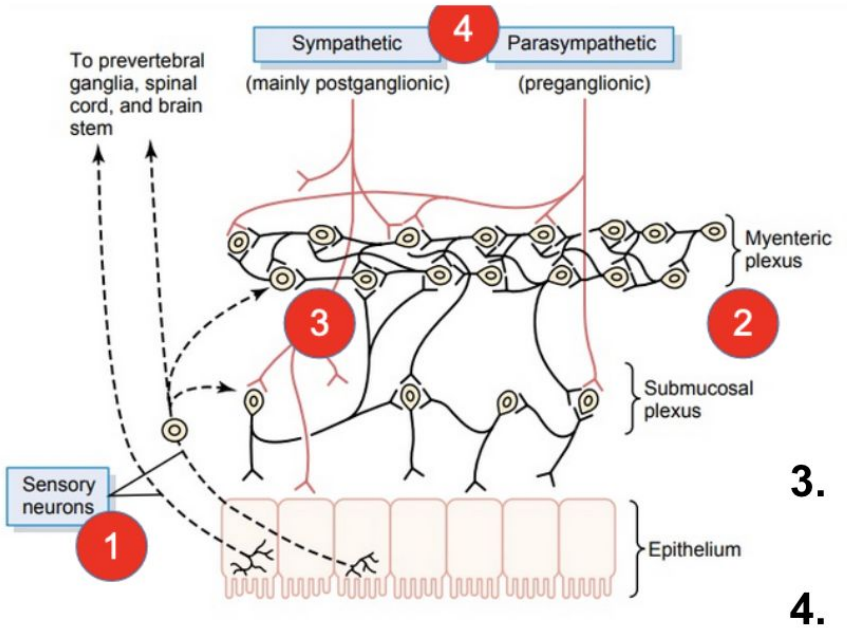
Layers of the GI Tract

From Deep to Superficial:

1. **Mucosa (in contact with food)**
   - I. Epithelium - Simple Columnar, Non-keratinzed Squamous
   - II. Lamina Propria
   - III. Muscularis Mucosae
2. **Submucosa**
   - **Contains the Submucosal (Meissner's) Plexus**
4. **Muscularis**
   - **I. Circular Muscle**
   - **II. The Myenteric (Auerbach's) Plexus**
   - **III. Longitudinal Muscle**
5. **Serosa (continuous with the peritoneum)**
   - I. Areolar Connective Tissue
   - **II. Visceral Peritoneum**



The Enteric Nervous System



1. **Food in the gut is detected** by chemoreceptors (chemicals in food) and baroreceptors (distention of the gut from the bolus). This triggers **sensory (afferent) neurons (Vagal / CN X Nerves)**

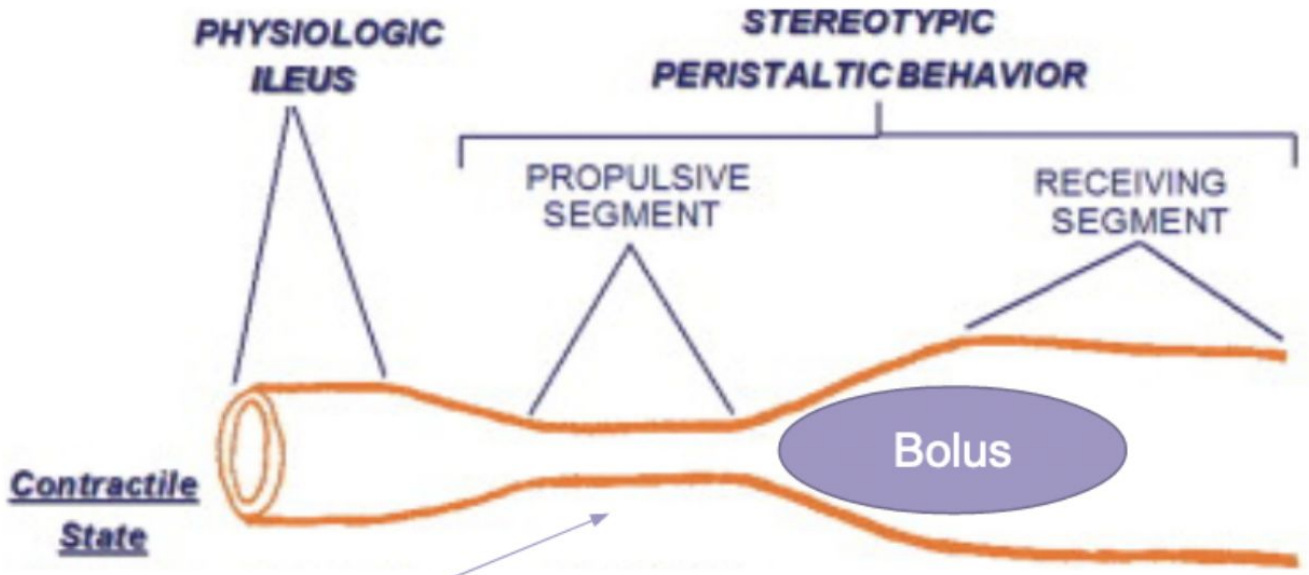
2. These sensory neurons can relay that information to the **Central Nervous System (CNS)** and to the **Enteric Nervous System (ENS)**

   The ENS is made up of 2 plexuses.
   - I. **Myenteric Plexus (Auerbach)** → Located in between the circular and longitudinal muscles. Cause **contractions** of the muscle wall, to help push the bolus along
   - II. **The Submucosal Plexus (Meissner)** → Located in the submucosa of the GI wall. This controls **secretion and absorption** within the gut.

3. **Inter-neurons connect the 2 ENS plexuses**. This way, they can **coordinate** their actions together

4. **The rate of action of the ENS is modulated by the CNS**. It achieves this by sending impulses from the brain, down to the gut **(efferent neurons)**
   - I. **Increasing Action → Parasympathetic NS** increases gastric motility + secretion ('rest and digest')
   - II. **Decreasing Action → Sympathetic NS** decreases gastric motility ('fight or flight')

Neurotransmitter of the ENS



Propulsive/Contracting Segment

- Circular muscle contracts
- Longitudinal muscle relaxes
- Neurons release noradrenaline

Receptive/Relaxing Segment

- Circular muscle relaxes
- Longitudinal muscle contracts
- **Neurons release acetylcholine (ACh) and Nitrous Oxide (NO)**

Gastric Muscles + Motility

From Deep to Superficial:

1. Mucosa (in contact with food) (with rugae/folds, to increase surface area)
   - Epithelium - Simple Columnar
   - Lamina Propria
   - Muscularis Mucosae
2. Submucosa
   - Contains the Submucosal (Meissner's) Plexus
3. Muscularis
   - Oblique Muscle
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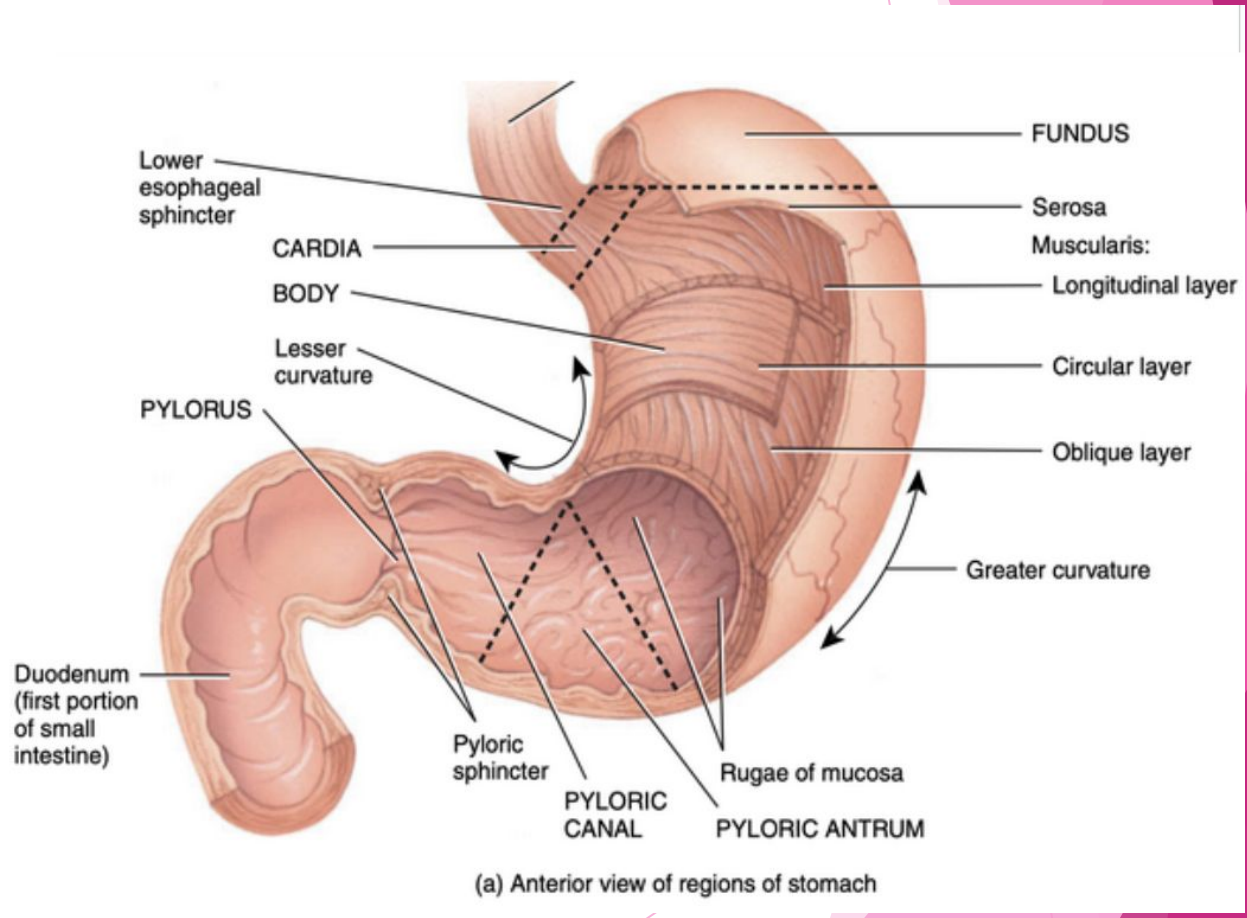


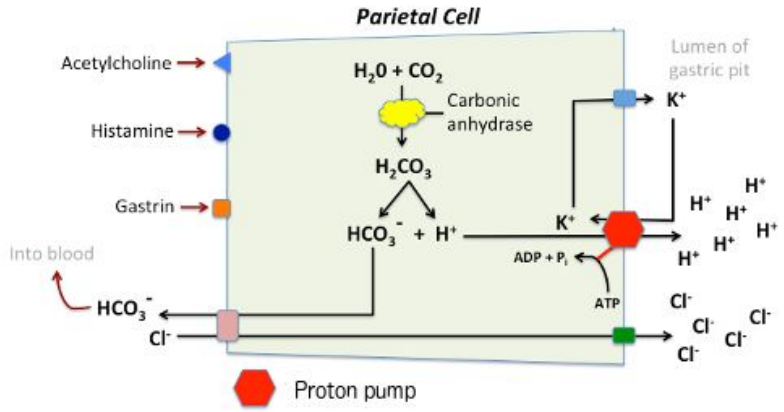
(a) Anterior view of regions of stomach

Gastric Cells and Secretions

Area of the Stomach	Major Cell Types Found	Secretions	Function of Secretion
Fundus	Mucous/Epithelial cells	Mucous, HCO_3^-	Provides a lubricated, higher pH microenvironment next to the gastric epithelial lining – **a protective mechanism** against the harsh contents of the stomach
		Gastric lipase	Lipid digestion
Corpus	Mucous/Epithelial cells	(See above)	(See above)
	Chief cells*	Pepsinogen	A **pro-peptide** which is then **activated by stomach acid** into the active enzyme pepsin – protein digestion
	Parietal cells	HCl	**Breaks down food** and kills bacteria **Converts pepsinogen to pepsin**
		Intrinsic factor	**Transportation and absorption of B_{12}** to the terminal ileum (Vitamin B_{12} is needed for erythropoiesis)
	Enterochromaffin-like (ECL)	Histamine	**Stimulates parietal cells** to release HCl
Antrum	Mucous/Epithelial cells	(See above)	(See above)
	Chief cells*	(See above)	(See above)
	G-Cells	Gastrin	Increases gastric motility Increases secretion of mucous **increases secretion of HCl directly by stimulating parietal cells, and indirectly by stimulating ECLs**
	D-Cells	Somatostatin	Acts locally to **decrease** gastric secretions, gastric motility and gastric hormones such as gastrin

*Chief cells are common to the corpus and the antrum

Gastric Acid Secretion



HCl Stimulation - 3 methods

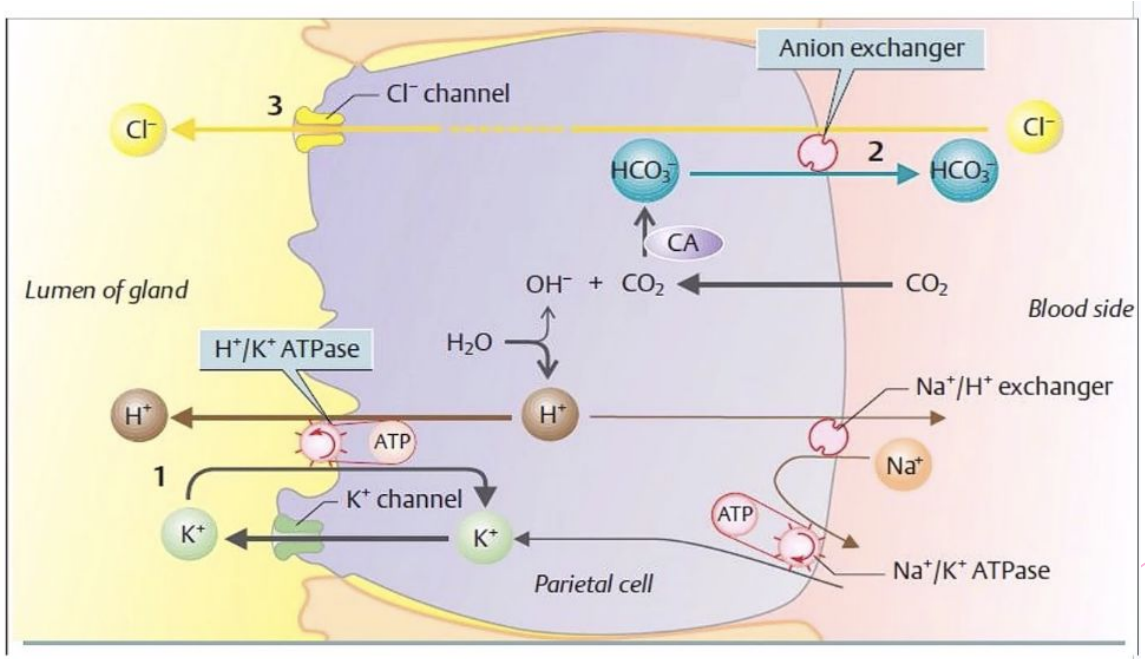
1. CN X (vagus nerve) releases acetylcholine - binds to M3 receptors. Also encourages the release of Histamine and gastrin
2. ECL cells release histamine - binds to H2 receptors
3. G-Cells release gastrin - CCK2 receptors. Also encourages the release of histamine

HCl Inhibition

- D-Cells release Somatostatin (binds to SST2 receptors)
- Note that somatostatin also inhibits histamine and gastrin

HCl Release

1. The reaction [CO2 + H2O ⇌ H2CO3 ⇌ H+ + HCO3-] is carried out by carbonic anhydrase.
    1. HCO3- -> transported out of the basolateral membrane of the cell***, into the blood, whilst Cl- is brought in (HCO3 -/Cl- antiporters)
    2. H+ -> transported out of the apical membrane of the cell, into the lumen, whilst K+ is brought in (H+/K+ ATPases)
2. Cl- (and K+) are transported out of the apical membrane, into the lumen
3. H+ and Cl- join inside the stomach to form HCl (i.e. HCl is not formed inside parietal cells). (Stomach pH 1.5-2.5)



Gastric Secretion Phases

Cephalic Phase

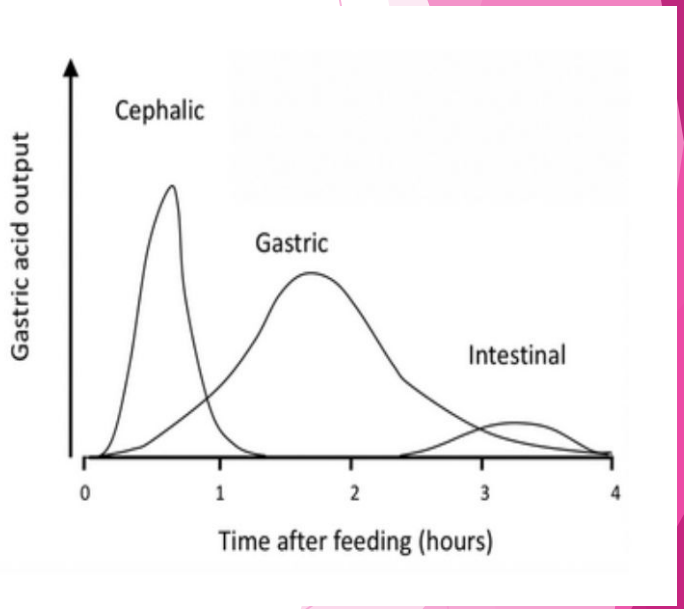
- Upon smelling/seeing/anticipating food, a large amount gastric acid (HCl + enzymes) will be released for a short amount of time

Gastric Phase

- 2 stimuli result in a large amount of gastric acid being released over a long period time
- Stomach receives bolus and distends (detected by afferent vagal fibres). This results in a decrease in gastric tone and receptive relaxation to help accommodate the food (carried out by efferent vagal fibres) (vago-vagal reflex)
- Stomach detects peptides and amino acids by chemoreceptors – peptides are buffers and they make the stomach more alkaline. The stomach releases more acid to compensate.

Intestinal Phase

- Duodenal cells can also detect stretch and the acidity of chyme – G-Cells in the duodenum can release gastrin which travels via the blood to the stomach to act on parietal cells



The Migrating Myoelectric Complex (MMC)

Gut is mobile even when there is no food in it, so in between meals, gut needs to be clean from residual contents, performed by MMC

4 phases

1. Quiescent – no activities going on
2. Initiates random contractions
3. Burst of contractions (max amplitude and duration)
4. Rapid decrease of contractions

Most waves happen in antrum (phase 3 – motilin, ghrelin, vagus nerve), rest is in duodenum (somatostatin, serotonin (5-HT), xenin)

Eating food disrupts this cycle

Cholecystokinin (CCK)

- Made in – duodenum (I cells)
- Secreted due to – fat and protein in duodenum
- Act on – acinar cells in pancreas, gallbladder, vagal afferent neurones
- Function – digestive enzymes release, GB contracts – bile release, inhibit food intake, induces satiety

Gastrin

- Made in- Stomach Antrum (G cells)
- Secreted due to- stomach distension, Ach release
- Act on- ECL- to activate parietal cells
- Function- histamine release, HCl release (increase acidity and gastric motility), pepsinogen-> pepsin

Histamine

- Made in stomach (ECL cells)
- Secreted due to- gastrin stimulation, Ach release
- Act on- parietal cells in stomach
- Function- HCl release

Somatostatin

- Made in – stomach pylorus duodenum, islets in pancreas (D cells)
- Secreted due to – food in stomach sympathetic stimuli
- Act on – parietal cells in stomach, ECL, G cells, gallbladder, small intestine, exocrine cells in pancreas
- Function – decrease HCL, histamine, gastrin, HCO3- release, GB contraction and bile release, stops GI blood flow and absorption

Secretin

- Made in duodenum (S cells)
- Secreted due to- low pH of chyme
- Act on- ductal cells in pancreas, parietal cells in stomach
- Function-HCO3- release, stops HCl release

Gastric inhibitory peptide (GIP)

- Made in: duodenum (K cells), jejunum (K cells)
- Secreted due to: fatty chyme
- Act on: B cells in pancreas
- Function: insulin secretion

Peptide YY

- Made in: ileum and colon (L cells)
- Secreted due to: after food ingestion
- Act on: intestines
- Function: increase water absorption, inhibits gastric motility, decrease gastric motility, increase efficiency of digestion and satiety

Glucagon like peptide (GLP)

- Made in: duodenum (L cells)
- Secreted due to: fat and protein in duodenum
- Act on: B cells in pancreas, vagal afferent neurones
- Function: insulin secretion, inhibits food intake, induces satiety

Vasoactive intestinal peptide (VIP)

- Made in: enteric neurones
- Act on: parietal cells in stomach, chief cells in stomach, pancreas, intestine
- Function: stops HCl release, pepsinogen release, increase secretion of H_2O in juice, inhibits absorption

Motilin

- Made in: duodenum/small intestine
- Secreted due to: fasting, neural stimuli
- Act on: duodenum
- Function: increase gastric motility, starts migrating motor complex

The myenteric (Auerbach's) plexus of the ENS is located in between which 2 layers of GI tract wall?

A. Mucosa + submucosa
B. Submucosa + muscularis mucosa
C. Submucosa + circular muscle
D. Circular muscle + longitudinal muscle
E. Longitudinal muscle + serosa

The following will result in increased gastric secretion

A. Increasing circulating secretin
B. Inhibitory vagal efferents
C. Acid in the stomach lumen
D. Pepsins and amino acids in the stomach lumen
E. Increased circulating somatostatin

Which of the following neurotransmitters is responsible for the relaxation of the gut lumen distal to the bolus during peristalsis?

A. Nitric oxide
B. Prostaglandin
C. Arachidonic acid
D. Noradrenaline
E. Somatostatin

Which cranial nerve senses distension in the gut lumen via baroreceptors, and sends signals to the CNS via afferent nerve fibres?

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B. Facial nerve
C. Glossopharyngeal
D. Vagus
E. Hypoglossal

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