

# Digestive system

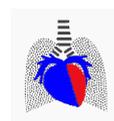
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<http://vh.cuni.cz>

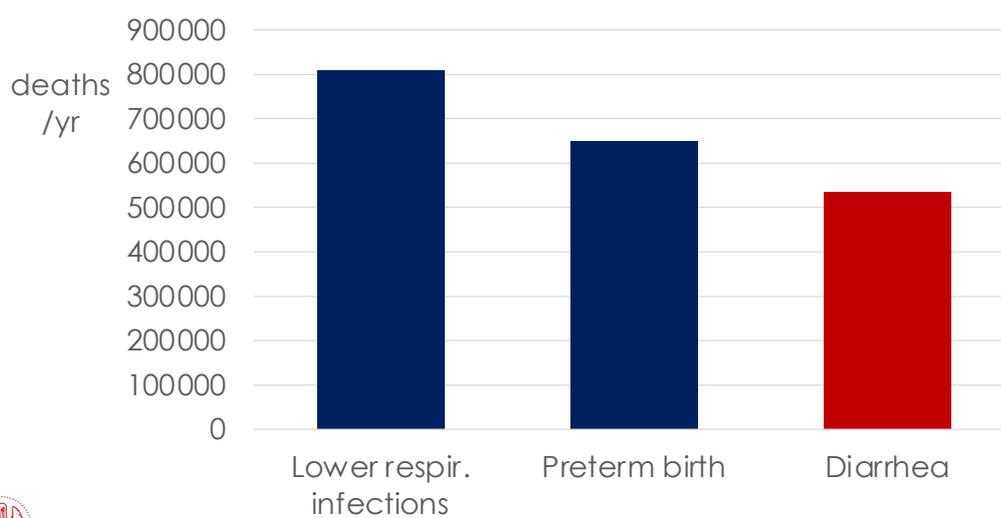


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## Causes of death: children $\leq 5$ yr



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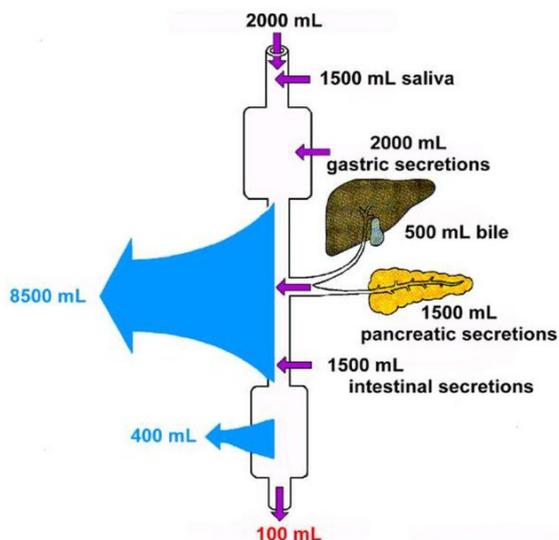
## Integrated response to meal: phases

- cephalic & oral
- esophageal
- gastric
- small intestinal
- colonic



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## Secretion



- H<sub>2</sub>O
  - enzymes work in solution
- ions
  - movement of H<sub>2</sub>O
  - sometimes also of nutrients
- proteins
  - enzymes, mucin
- signaling molecules



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## Cephalic phase

### ■ stimuli:

- cognitive
  - anticipation, thinking, talking,...
- olfactory
- visual
- auditory



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## Oral phase

### ■ stimuli:

- mechanical in mouth
- taste



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## Cephalic & oral phase

- parasympathetic activation:
  - ↑ saliva secretion
  - relaxation of the upper part of the stomach
  - ↑ gastric HCl secretion
  - ↑ pancreatic enzymes secretion
  - gallbladder contraction, sphincter of Oddi relaxation
  - ↑ motility of the small intestine



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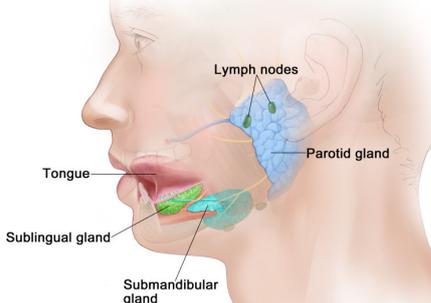
## Mouth

- mastication
- saliva
  - lubrication (mucus)
  - solubilization for taste
  - amylase (starch)
  - antibacterial
- lingual lipase
- minimal absorption (alcohol, some drugs)



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## Salivary glands



	serous	mixed	mucous
parotid			
sublingual			
submandibular			
small in mouth			

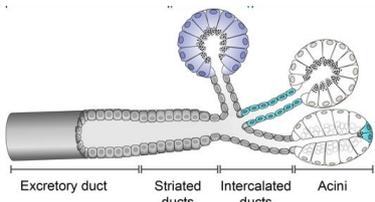
~10%



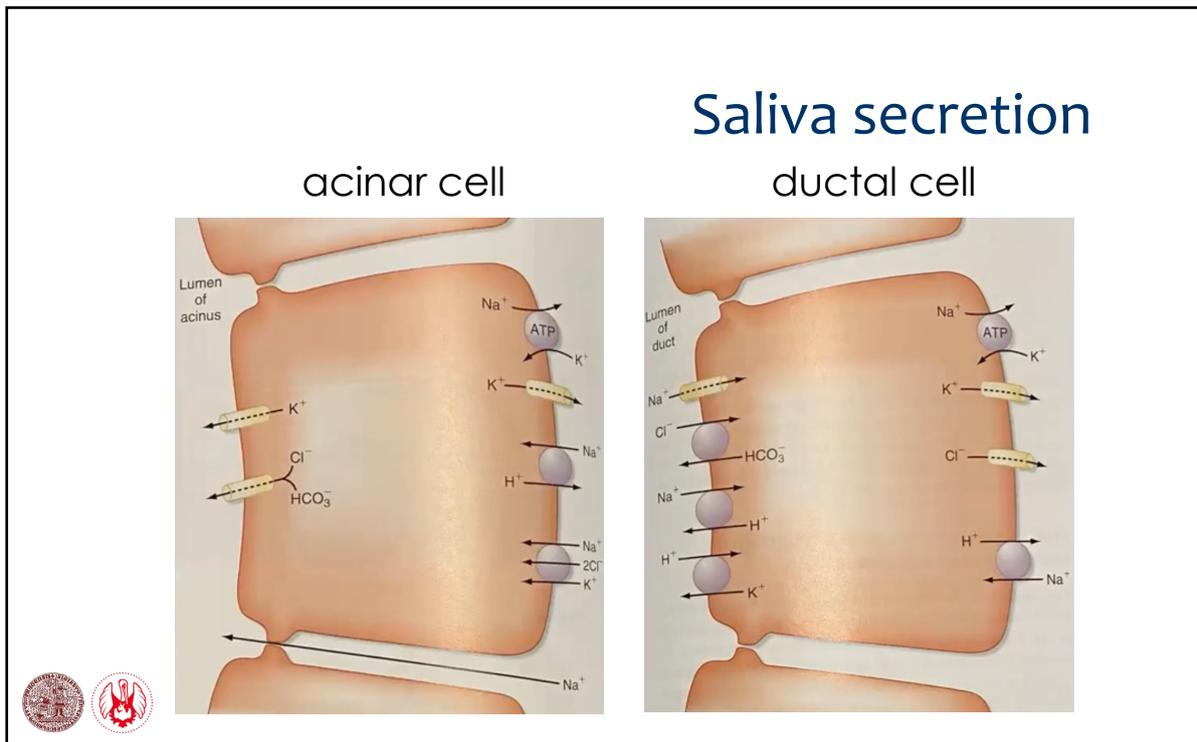
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## Saliva

- large flow rate relative to size
- hypotonic, alkaline ( $\text{pH} \leq 8$ ), high  $\text{K}^+$  (useful in stomach)
  - primary secretion isotonic (driven by apical  $\text{Cl}^-$  channels  $\rightarrow$  osmotic & el. gradient  $\rightarrow$   $\text{Na}^+$  &  $\text{H}_2\text{O}$  follow paracellularly)
  - duct cells reabsorb  $\text{Na}^+$  &  $\text{Cl}^-$  & secrete  $\text{K}^+$  &  $\text{HCO}_3^-$  (**CFTR**)
- amylase, lipase, mucin (glycoproteins), lysozyme (antibacterial)
- growth factors - GIT lining maintenance (survive low pH)




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## Regulation of salivation

### ■ parasympathicus:

- cephalic & oral phase, during and after meals
- $\uparrow$  secretion of amylase & mucin
- $\uparrow$  transport in ducts

→ more saliva

### ■ sympathetic

- $\uparrow$  protein secretion

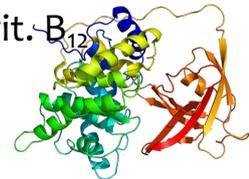
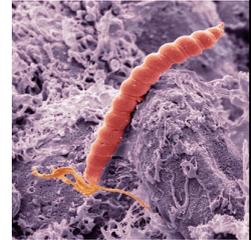
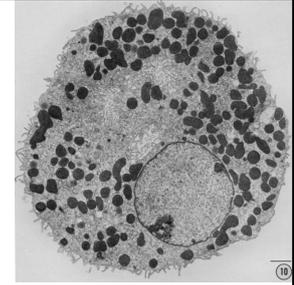
→ *sticky mouth*



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## Response to meal: Gastric phase

- stomach = strange organ
  - full of strong acid (pH 5 to 1)
    - $\uparrow\uparrow$  energy demand ( $10^6$  gradient: pH  $\sim$ 7 vs. 1)
    - need to protect itself
  - just to activate pepsin? (+denaturing)
    - 20% of protein digestion, not essential
  - protection against microbes from food
    - (not all do mind)
  - intrinsic factor – glycoprotein necessary for vit. B<sub>12</sub> (cobalamin) absorption in ileum, needs  $\downarrow$  pH
  - grinding, storage

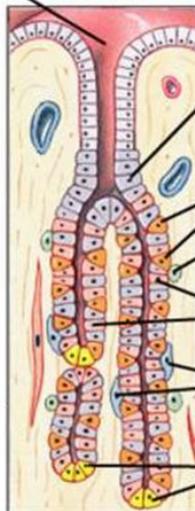


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## Gastric juice

Source	Substance Secreted	Function
Mucous neck cell	Mucus	Physical barrier between lumen and epithelium
	Bicarbonate	Buffers gastric acid to prevent damage to epithelium
Parietal cells	Gastric acid (HCl)	Activates pepsin; kills bacteria
	Intrinsic factor	Complexes with vitamin B <sub>12</sub> to permit absorption
Enterochromaffin-like cell	Histamine	Stimulates gastric acid secretion
Chief cells	Pepsin(ogen)	Digests proteins
	Gastric lipase	Digests fats
D cells	Somatostatin	Inhibits gastric acid secretion
G cells	Gastrin	Stimulates gastric acid secretion

Opening of gastric gland



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## Pepsins

- group of proteases
- activation by small N-terminal fragment cleavage
  - only at  $\text{pH} < 5$ , slow at  $\text{pH} 3-5$ , very fast at  $\text{pH} < 3$
  - autoactivation
- activity also pH dependent
  - pH optimum = 1.8-3.5  
(reversible inactivation at  $\text{pH} > 3.5$ )
  - irreversible inactivation at  $\text{pH} > 7.2$

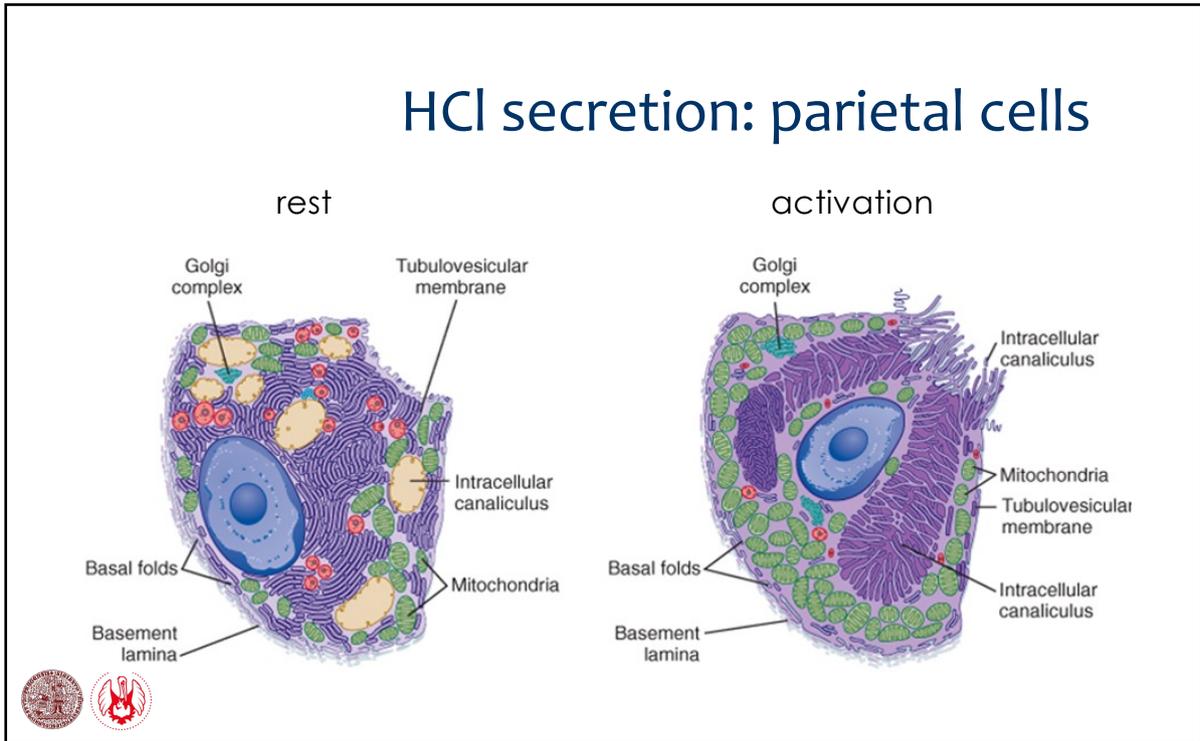


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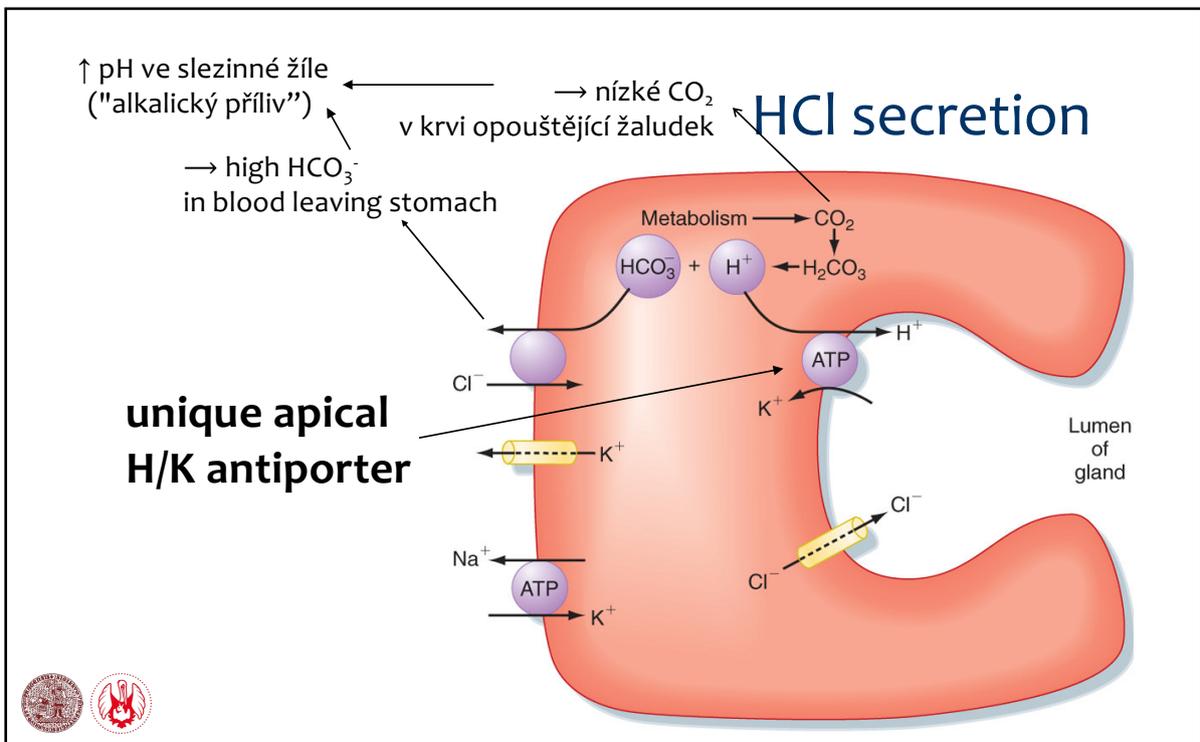


HCl secretion:  
parietal cells

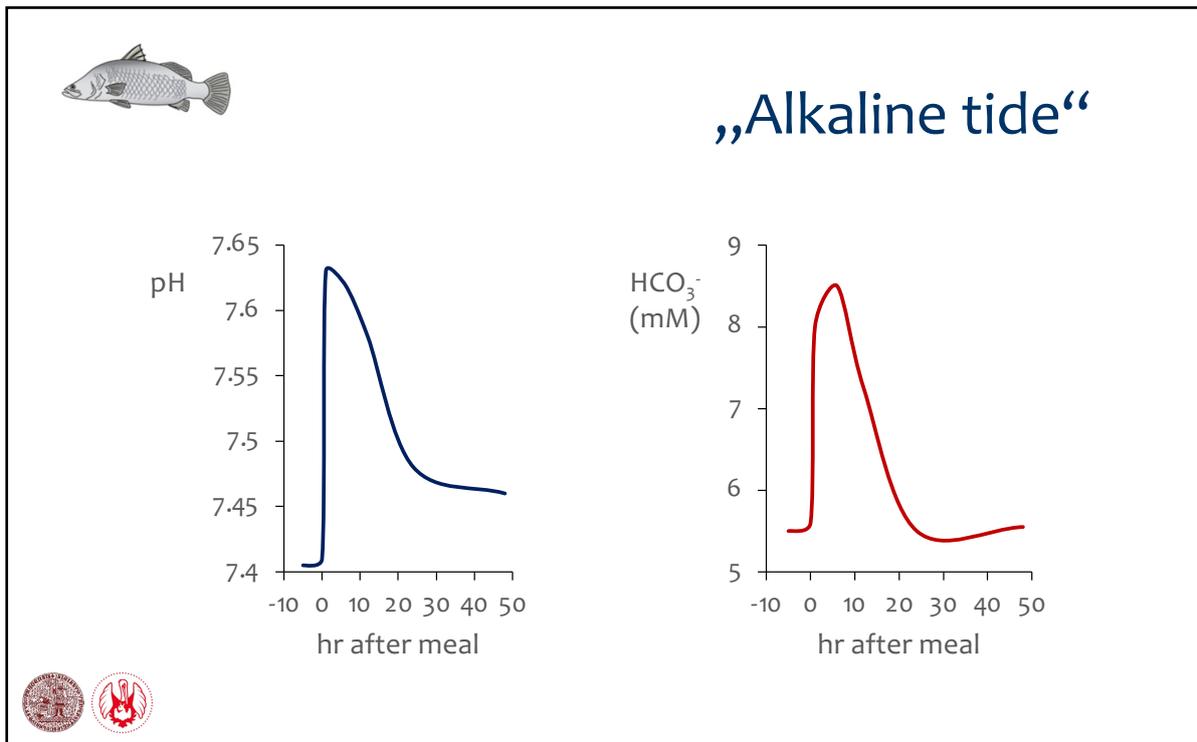
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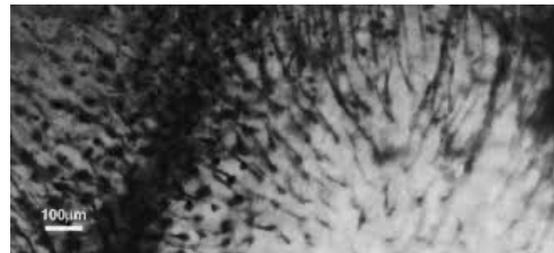
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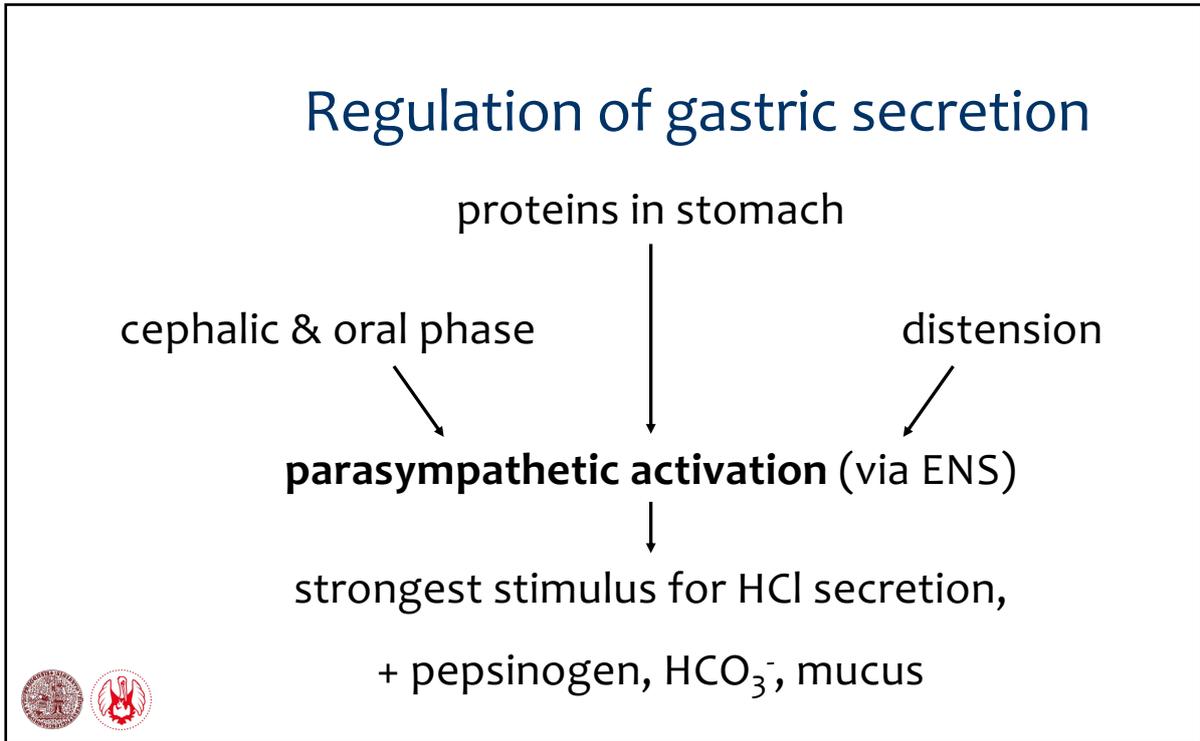
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## Protection of mucosa from acid

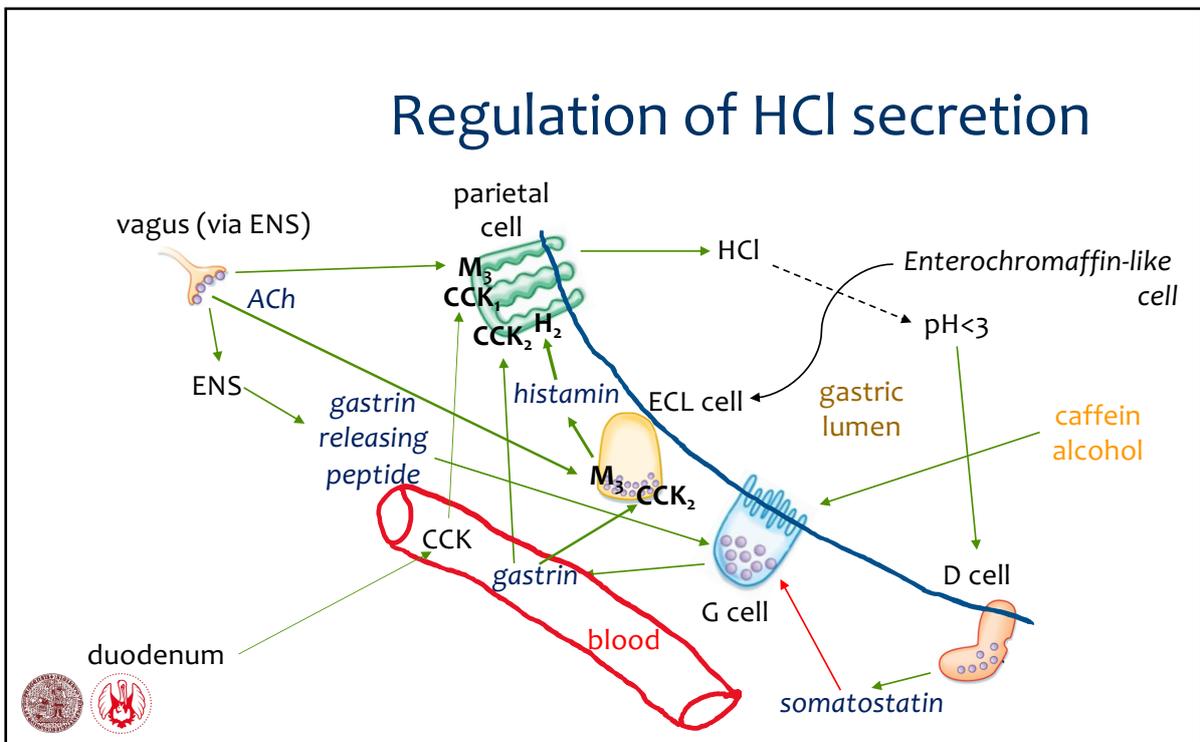
- continuously renewed mucus layer (~0.2 mm) from the glands mouth & from surface epithelium
  - large glycoproteins – sugars shield the proteineous part
- HCO<sub>3</sub><sup>-</sup> secretion underneath mucus (& into it)
- viscous fingering - HCl "shoots out " from the mouth of the glands only through a narrow channel
- protection of glands???



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## Regulation of pepsinogen secretion (chief cells)

- less complex than HCl regulation
- stimulation: ACh (M1 & M3 receptors) from the vagus & ENS (cephalic, oral & gastric phase, vagal-vagal reflex from gastric distension) > CCK >> gastrin, gastrin releasing peptide (GRP), secretin, VIP, histamine
- inhibition: somatostatin



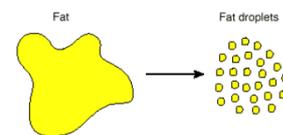
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## Other digestion in stomach

- saccharides
  - remnants of amylase activity, negligible

- lipids

- emulsification (mixing movements)
- gastric lipase: ~10% of all lipid hydrolysis, not essential



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## Small intestinal phase (overlap with gastric phase)

- mechanical & chemical stimuli  
(many receptors in duodenum)
- interruption of MMC
- ↑ pancreatic secretion + gut secretion  
(mainly Brunner's glandulae of duodenum, also  
Lieberkühn's crypts of ileum: mucus +  $\text{HCO}_3^-$ )
- gallbladder contraction, sphincter of Oddi relaxation
- regulation of gastric emptying
- ↓ gastric HCl secretion



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## Small intestine

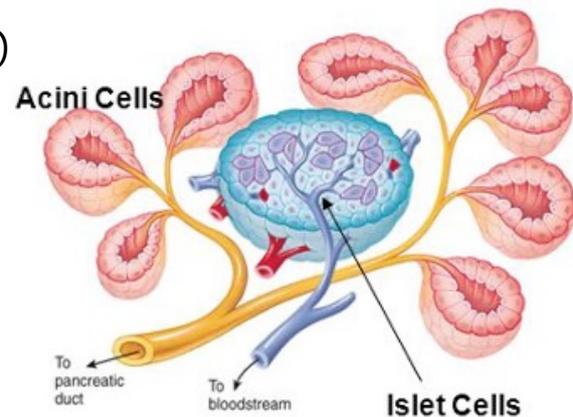
- large internal surface area (~200 m<sup>2</sup>)
  - length (5-7 m)
  - villi + crypts
  - microvilli
- pH ~7 - 7.8  
( $\text{HCO}_3^-$  mainly from pancreas,  
also duodenal glands)



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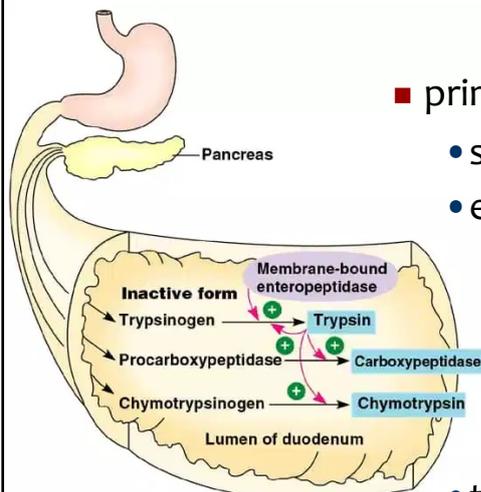
## Pancreas - essential for all digestion

- similar to salivary glands
  - acini – enzymes
  - ducts –  $\text{HCO}_3^-$  ( $\leq 140$  mM)
- exocrine & endocrine functions completely separate
  - endocrine much older
- ~1.5 l/d



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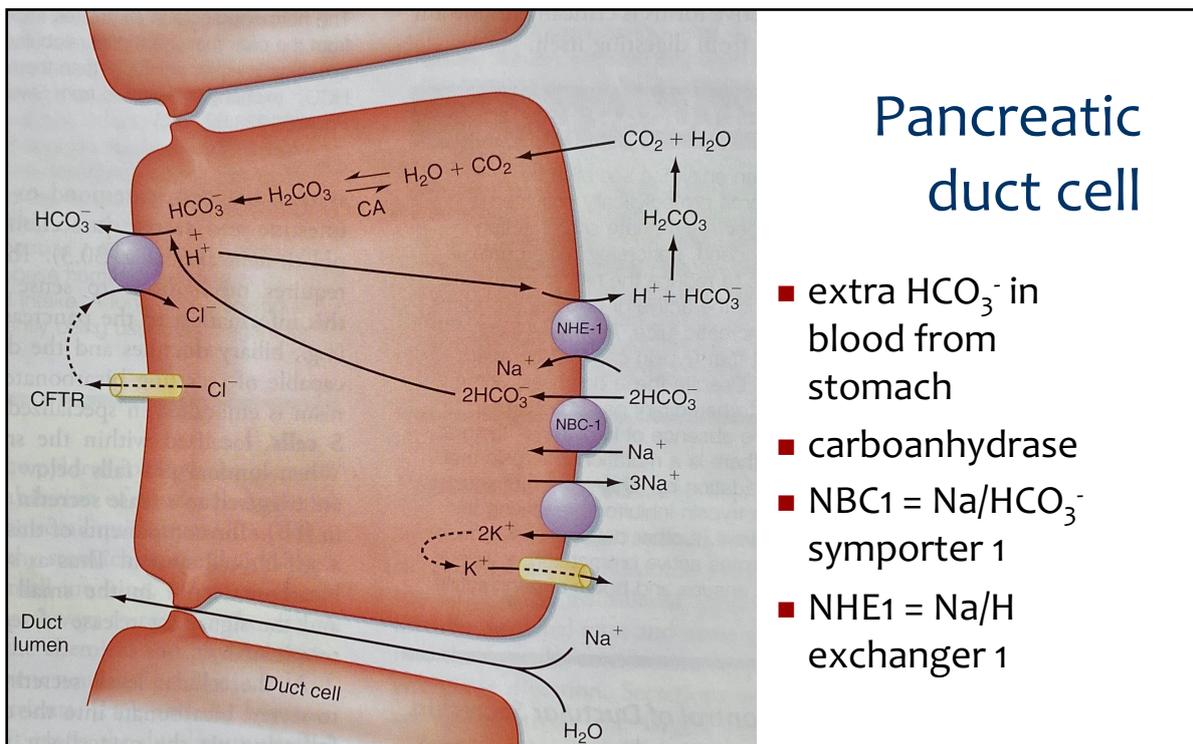
## Pancreatic secretion



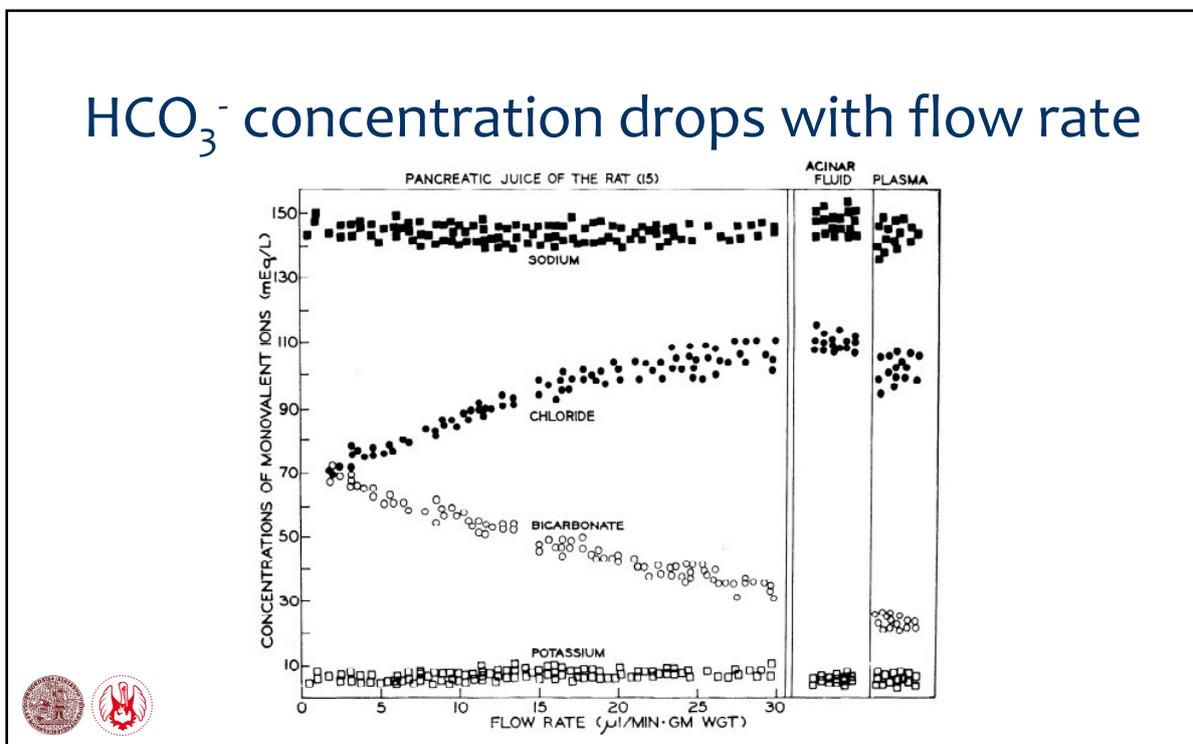
- primary:
  - similar ions as in plasma
  - enzymes (all inactive):
    - trypsin, chymotrypsin, proelastase, procarboxypeptidase A & B
    - amylase
    - lipase
    - (deoxy)ribonuclease
  - trypsin inhibitors (trypsin activates all)
- ducts:  $\text{H}_2\text{O}$ ,  $\text{HCO}_3^-$  (exchange for  $\text{Cl}^-$ : CFTR)



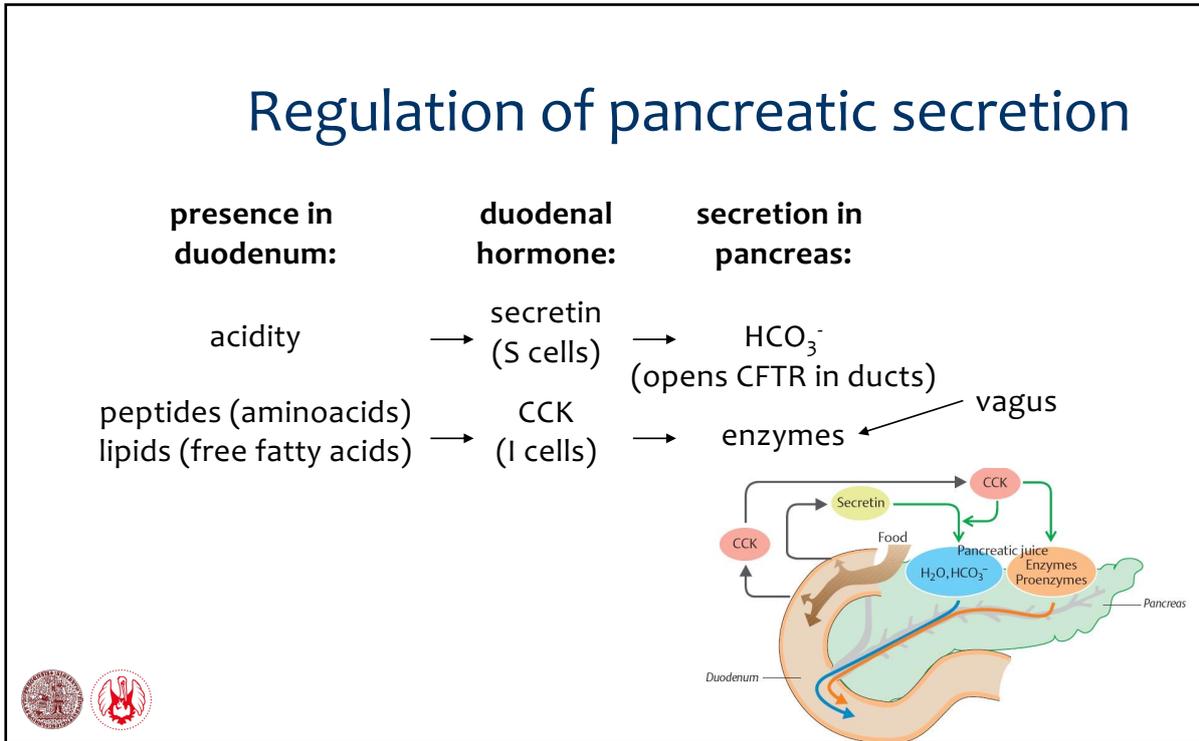
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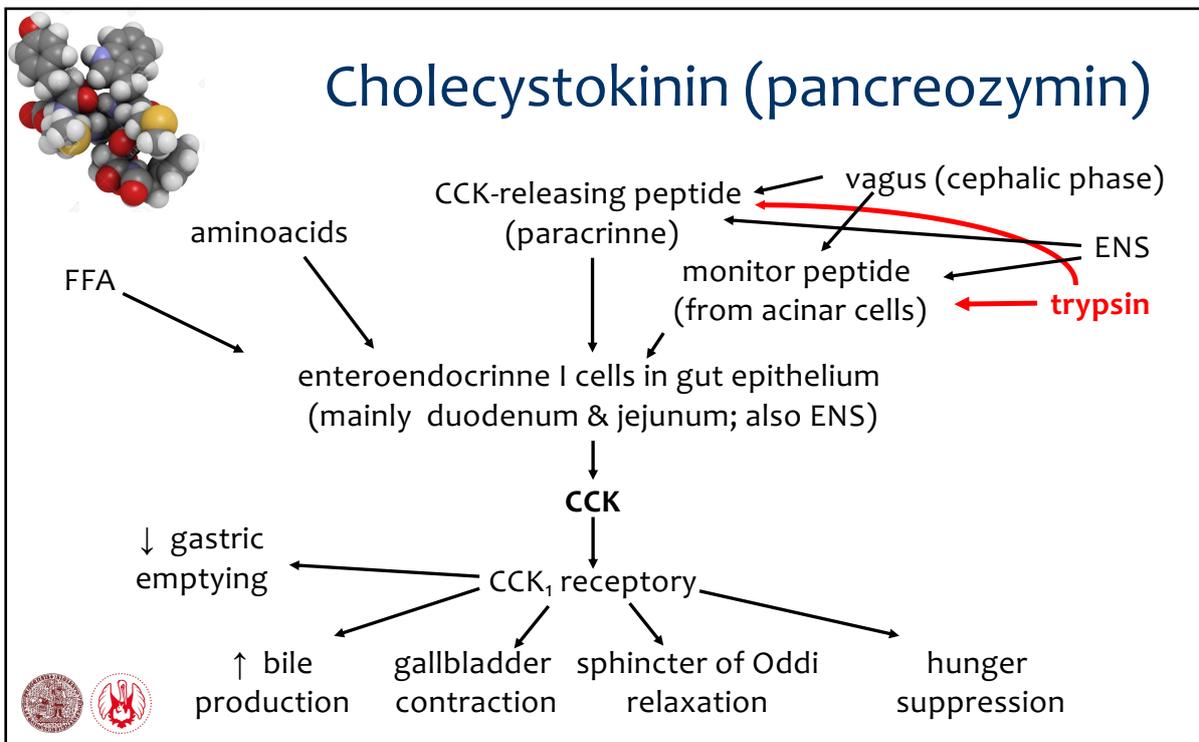
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## Bile (gall)

- produced in liver (~500 ml/d)
- pH ~ 7-8, ~600 mOsm/l
- elimination of cholesterol & bilirubin
- important for normal intestinal microflora
- lipid emulsification = ↑ surface

**Fat Globule**      **Bile Salt**      **Emulsified Droplets**

Hydrophobic Side      Hydrophilic Side

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## Bile acids (steroid)

synthesis in the liver (cholesterol oxidation by cytochrome P450)

- conjugated (in liver) with taurine or glycine  
→ soluble bile salts
- deconjugated by bacteria  
spares aa from defecation of bile acids

cholic acid      CDCA

chenodeoxycholic acid      LCA

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## Enterohepatic circulation of bile acids

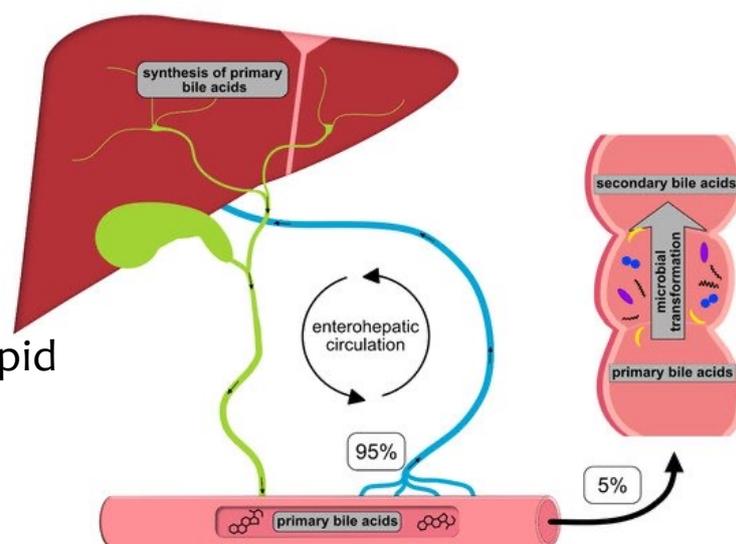
- 95% bile. salts recycled from the end of the ileum (fat absorption complete)
  - apical Na bile acid co-transporter (ASBT) + basolateral organic solute transporter (OST)  $\alpha+\beta$
  - Intestine: passive absorption after deconjugation by bacteria
  - Uptaken up by cholangiocytes in liver capillaries (150 ml bile/d; hepatocytes 450)
- minimal overflow into the colon and arterial blood



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## Enterohepatic circulation of bile acids

- 3-4x/d
- dysfunction → diarrhoea
- recycling of lipid xenobiotics (↑ damage)



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## Small intestine enzymes

dipeptides  $\xrightarrow{\text{dipeptidases}}$  amino acids

maltose  $\xrightarrow{\text{maltase}}$  glucose + glucose

lactose  $\xrightarrow{\text{lactase}}$  glucose + galactose

sucrose  $\xrightarrow{\text{sucrase}}$  glucose + fructose

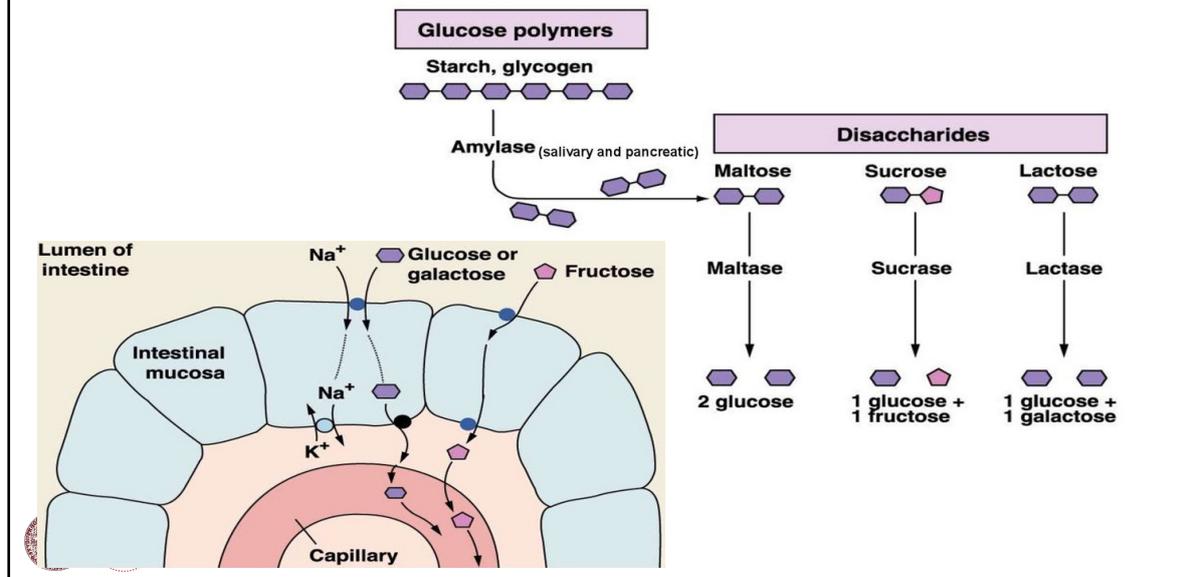
di- & monoglycerides  $\xrightarrow{\text{lipases}}$  fatty acids + glycerol

nucleotides  $\xrightarrow{\text{nucleotidases}}$  nucleosides  $\xrightarrow{\text{nucleosidases}}$  sugars + bases

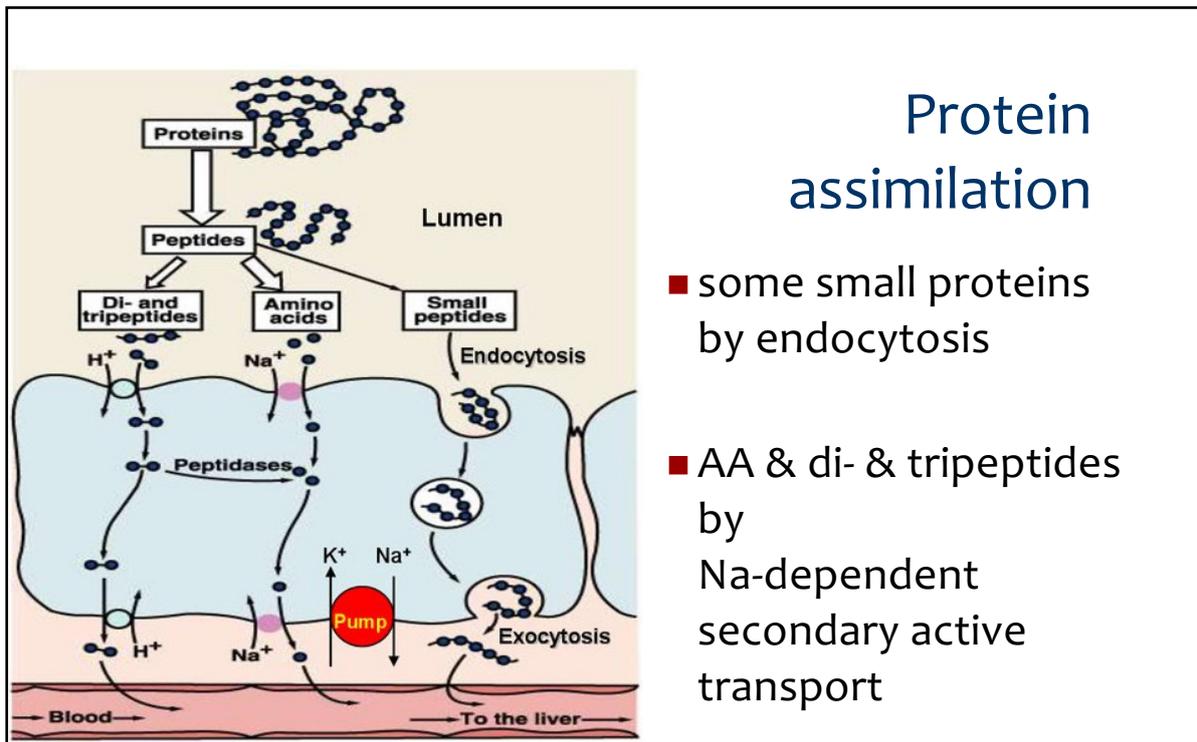


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## Carbohydrate assimilation



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## Absorption of lipids

- fats mainly in the form of triglycerides
- triglycerides broken down into glycerol + fatty acids
- free fatty acids absorbed by diffusion and protein carriers (poorly defined)



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## Large intestine

- $\text{HCO}_3^-$  - neutralization of acids formed by the intestinal flora
- mucus - protection, lubrication
- absorption of vitamins B & K made by bacteria in colon



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## Satiety

- distension inhibits intake
  - ↓ stomach size (bariatric surgery) → ↓ meal size
- cholecystokinin = satiety hormone
  - ↑ by nutrients
  - inhibits food intake (CCK receptors v CNS)
- glucagon-like peptide 1 (GLP-1)
- peptide YY (PYY)



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