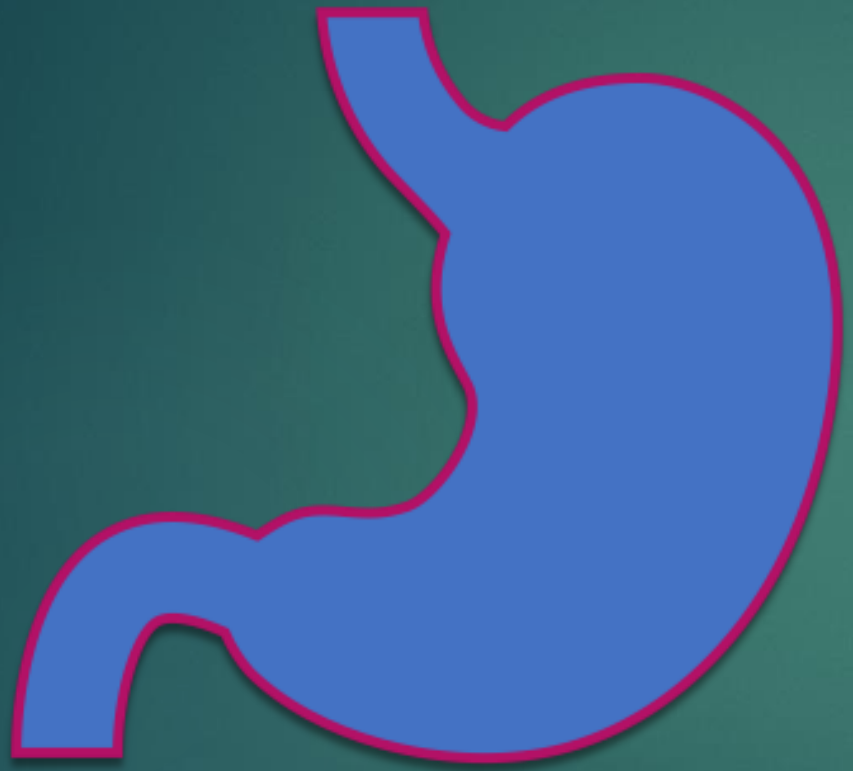


Gastrointestinal and metabolic physiology

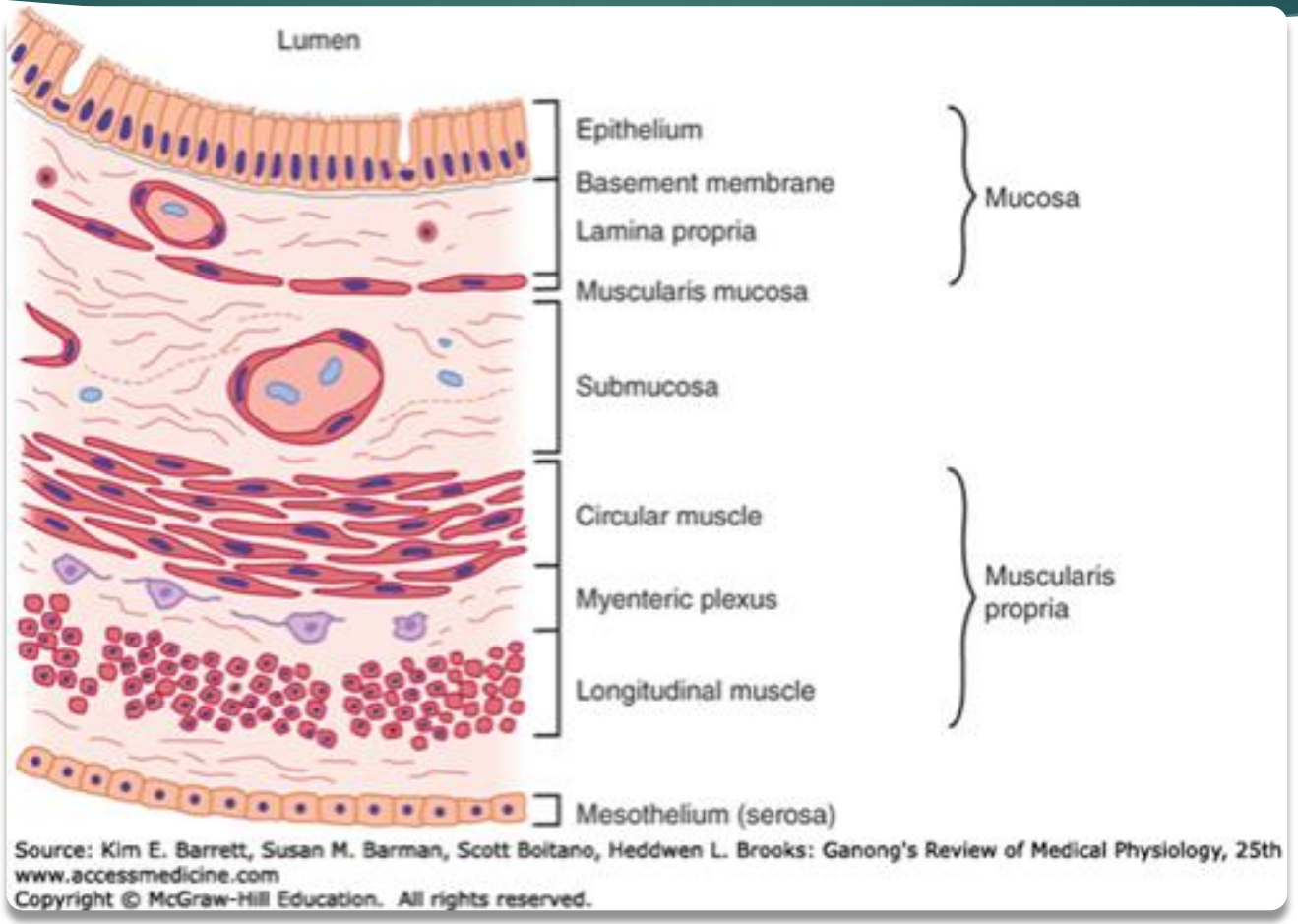
BELEN KORNFELD

EASTERN AND GREATER SOUTHERN SURGICAL SKILLS NETWORK SRMO

Overview

- Gastrointestinal structure and functions
- Gastrointestinal hormones
- Absorption & digestion
- Liver and biliary system functions
- Gastrointestinal motility
- Metabolism

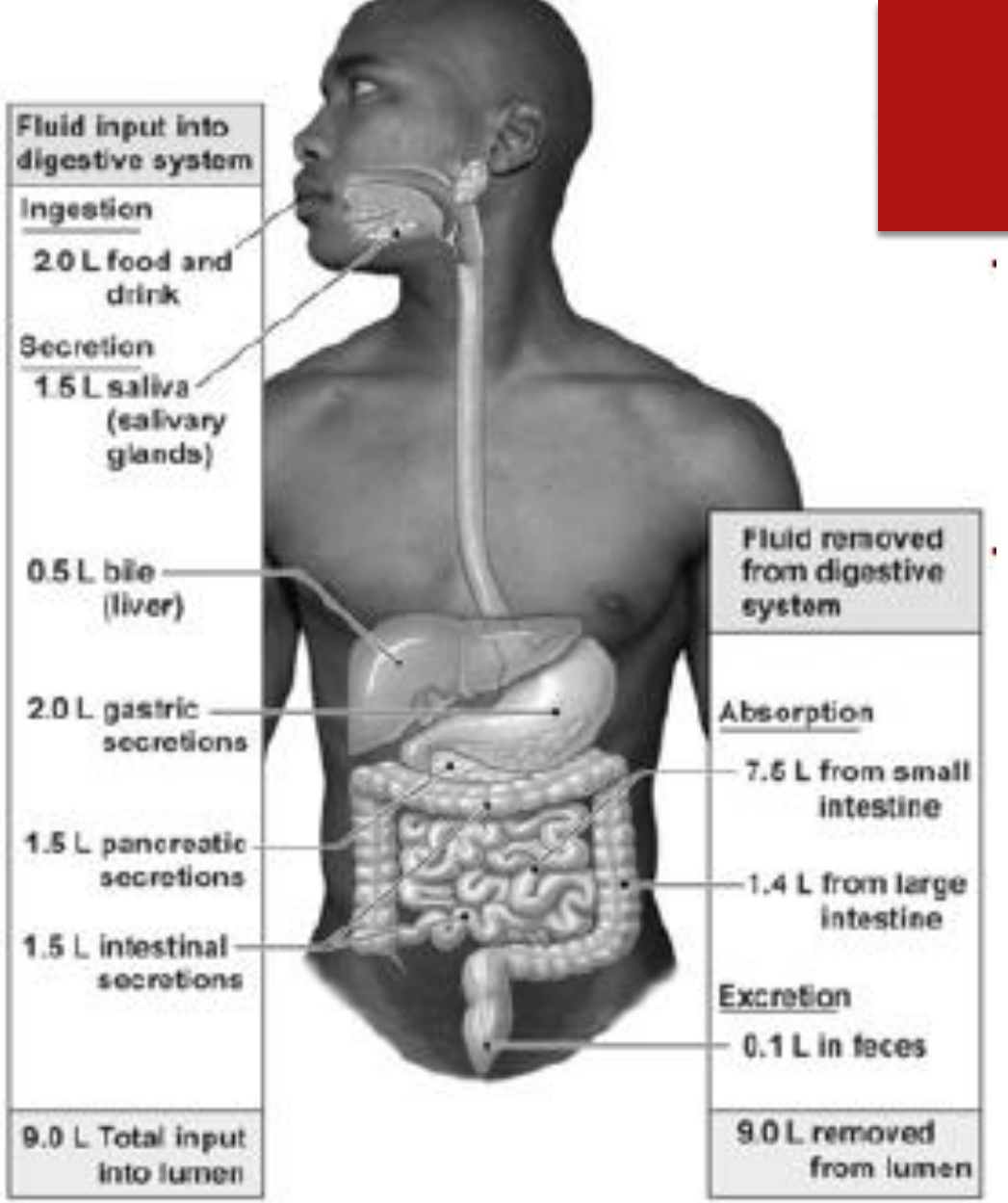
Gastrointestinal mucosa structure



Source: Kim E. Barrett, Susan M. Barman, Scott Boitano, Heddwen L. Brooks: Ganong's Review of Medical Physiology, 25th
www.accessmedicine.com

GIT Functions

- Primary function = absorb water and nutrients
  - Secretion
  - Digestion
  - Absorption
  - Motility
- Secondary function
  - Fluid/ electrolyte balance
  - Protection- immunological



GIT Secretions

- Salivary secretion
- Gastric secretion
- Pancreatic secretion
- Biliary secretion

Gastrointestinal functions – Salivary secretion

Parotid salivary gland

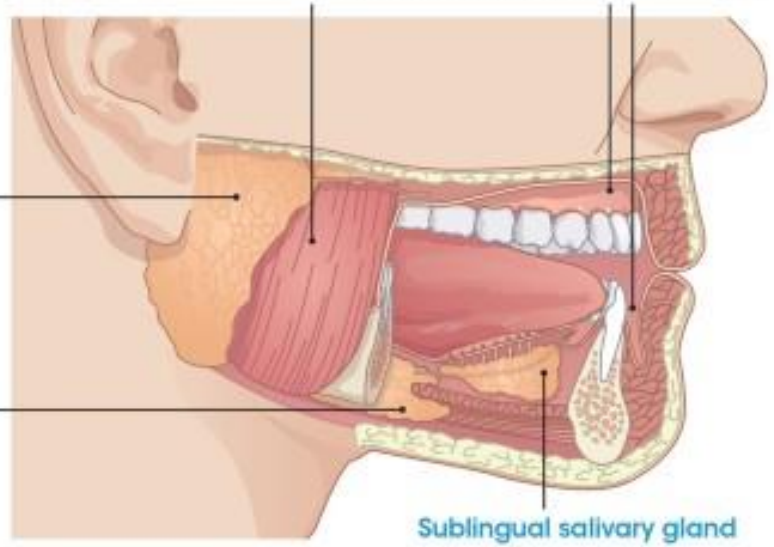
- Serous, watery secretions
- **High inorganic content (calcium, bicarbonate)**
- Responsible for 20% of unstimulated salivary flow

This proportion rises to 50-60% for stimulated salivary flow

Submandibular salivary gland

- Mixture of serous and mucous secretions
- Responsible for 65% of unstimulated salivary flow

Minor salivary glands in lips and oral mucosa (especially buccal) are collectively responsible for 8-10% of unstimulated salivary flow

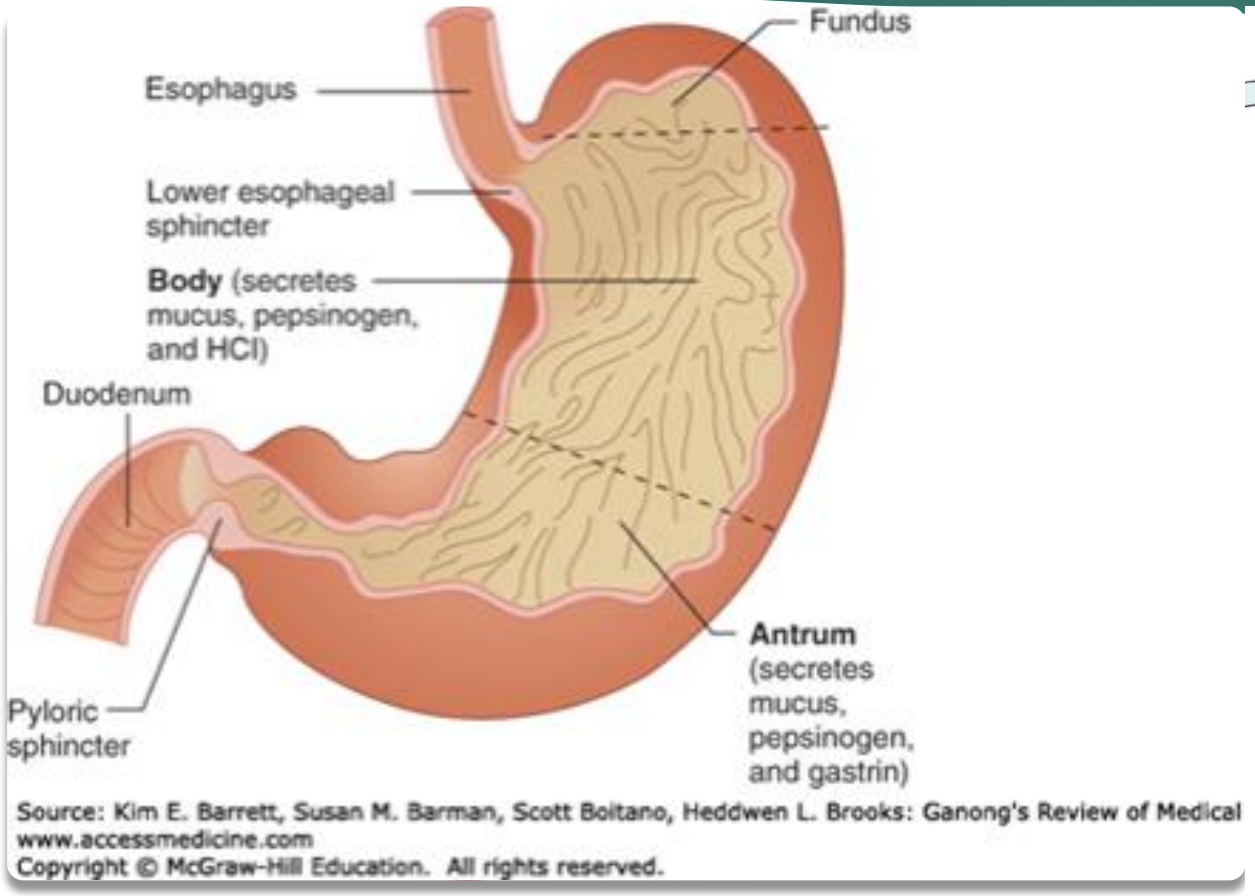


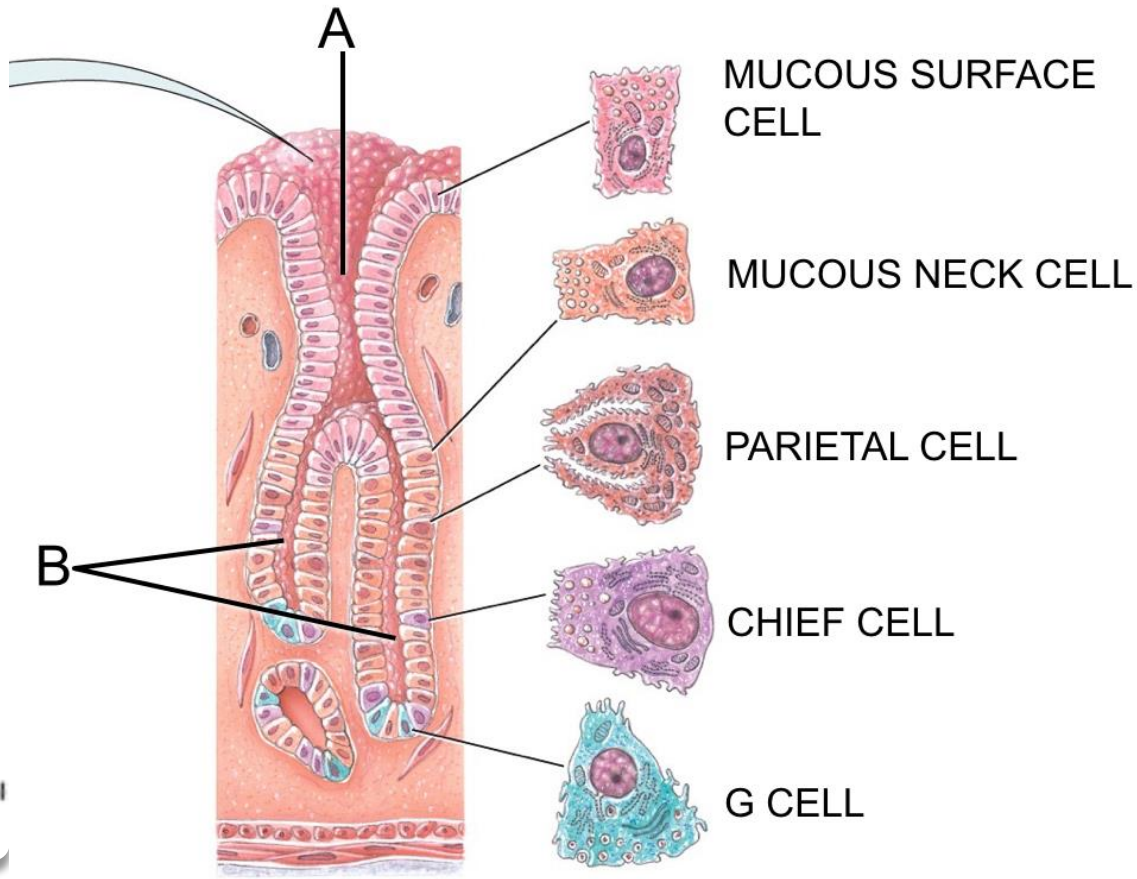
Sublingual salivary gland

- Mucous secretions (more viscous)
- Responsible for 5-7% of unstimulated salivary flow

- 1.5 L / day
- 3 paired salivary glands
  - Parotid
  - Submandibular
  - Sublingual
- Functions
  - Lubricate - mucin
  - Initiate digestion –amylase
  - Immunological function- IgA , lysozymes
  - Neutralise HCL – hypotonic. Oral pH 7

Gastrointestinal functions – Gastric acid secretion



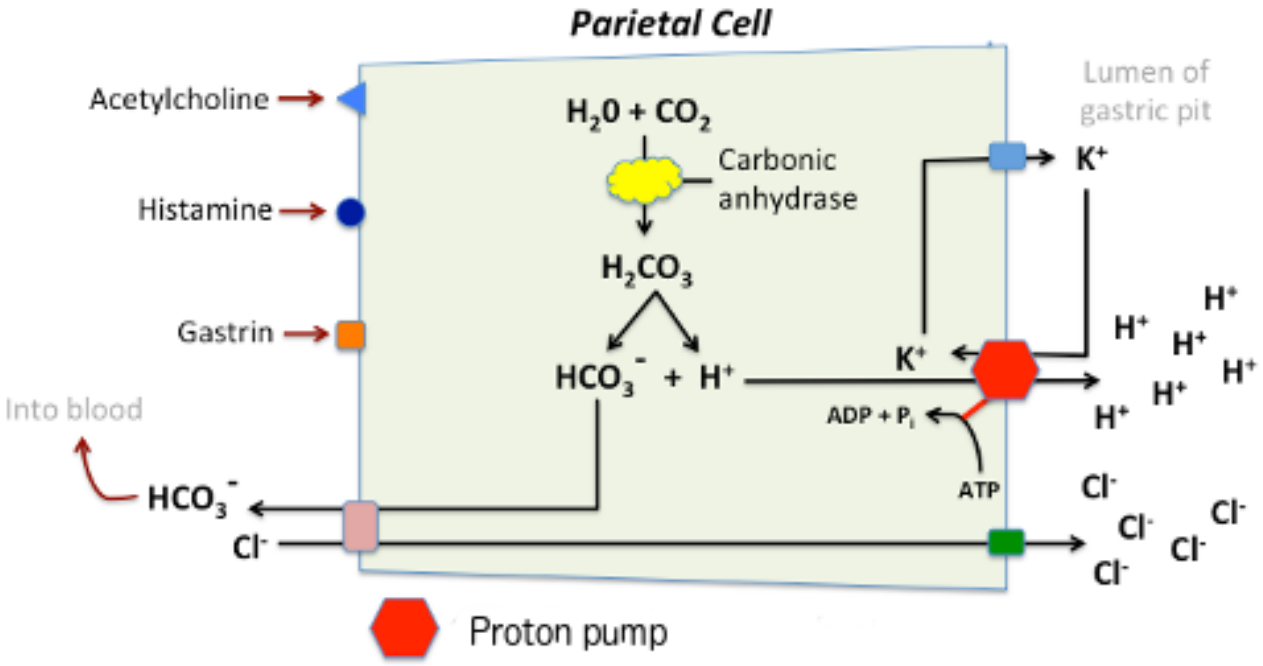


Question 1

S Removal of the part of the stomach nearest the pylorus would be expected to reduce gastric acid secretion Because
R the part of the stomach nearest the pylorus secretes most of the hydrochloric acid

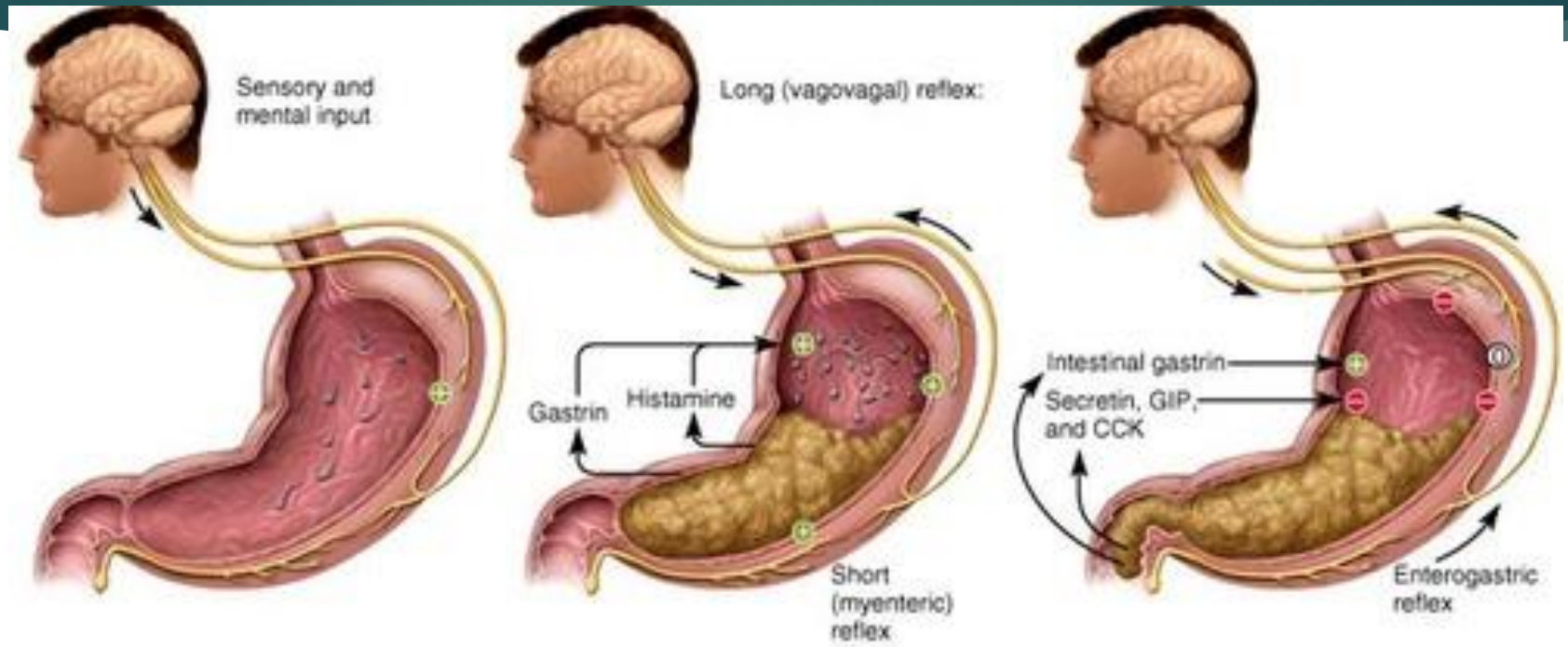
S is true, R is true and a valid explanation of S	A
S is true, R is true but not a valid explanation of S	B
S is true and R is false	C
S is false and R is true	D
Both S and R are false	E

Gastric Acid Secretion



- 2.5 L/ day
- Constituents:
  - Cations: Na, K, Mg, H + (pH 1)
  - Anions: Cl- , HPO4, SO4
  - Pepsin, lipase
  - Mucus
  - Intrinsic factor
- Increase sections
  - Agonists of Parietal cells - gastrin, histamine, ACH
- Decreased by:
  - PPI, hormones – CKK, somatostatin,

Phases of Digestion



Question 2

With respect to gastric secretion
1: vagal stimulation increases the secretion of acid and pepsin.
2: resection of large segments of small intestine is associated with hypersecretion of acid.
3: vagotomy abolishes acid production.
4: vagotomy abolishes gastric motility.

Pancreas function- Exocrine

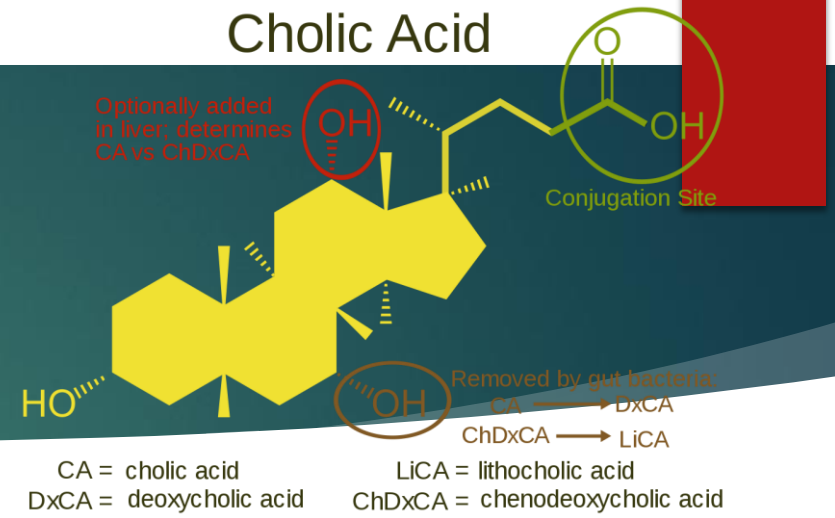
- Exocrine: Pancreatic juice; 1.5 L, pH8
- Contents: granules containing zymogens, high in HCO3 (alkaline), Cations, anions
- Enzymes: see table
- Cations: Na, K Ca, Mg.
  Anions: HCO3, CL, SO4, PO4
- Stimulated by :
  - ACH (via Phospholipase C – liver cells) → acinar cells → ↑ zymogen granules (low vol)
  - secretin - ↑ bicarb, poor enzymes → stimulares CCK
- CCK: ↑ enzymes , low vol

Trypsin (trypsinogen)	Enteropeptidase	Proteins and polypeptides	Cleave peptide bonds on carboxyl side of basic amino acids (arginine or lysine)
Chymotrypsins (chymotrypsinogens)	Trypsin	Proteins and polypeptides	Cleave peptide bonds on carboxyl side of aromatic amino acids
Elastase (proelastase)	Trypsin	Elastin, some other proteins	Cleaves bonds on carboxyl side of aliphatic amino acids
Carboxypeptidase A (procarboxypeptidase A)	Trypsin	Proteins and polypeptides	Cleave carboxyl terminal amino acids that have aromatic or branched aliphatic side chains
Carboxypeptidase B (procarboxypeptidase B)	Trypsin	Proteins and polypeptides	Cleave carboxyl terminal amino acids that have basic side chains
Colipase (procolipase)	Trypsin	Fat droplets	Binds pancreatic lipase to oil droplet in the presence of bile acids
Pancreatic lipase	…	Triglycerides	Monoglycerides and fatty acids
Cholesteryl ester hydrolase	…	Cholesteryl esters	Cholesterol
Pancreatic α-amylase	Cl^-	Starch	Same as salivary α-amylase
Ribonuclease	…	RNA	Nucleotides

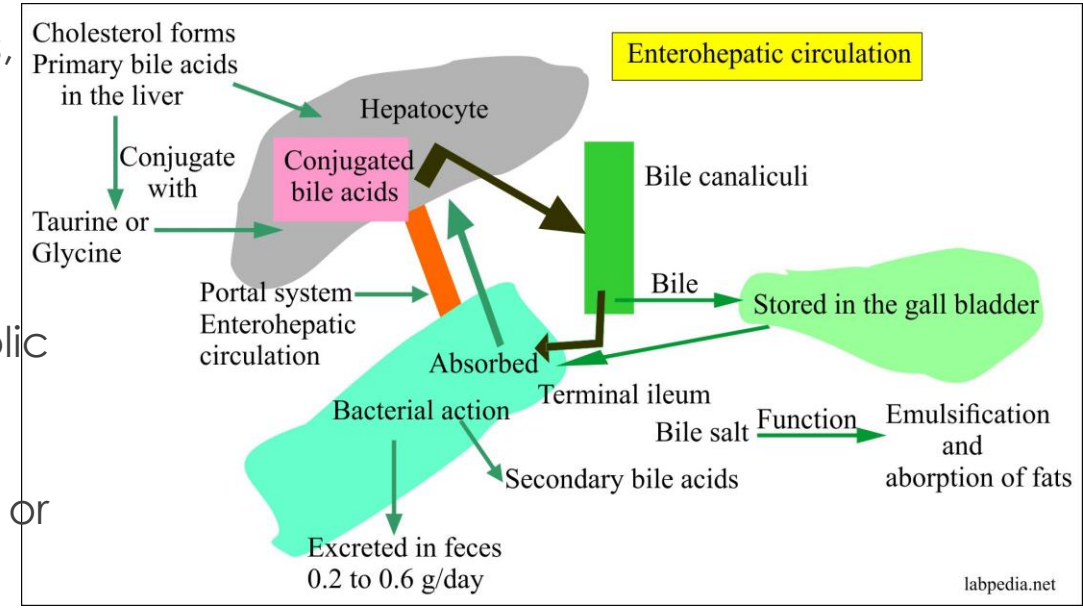
Question 3

The exocrine secretion of the pancreas contains
1: phospholipase A
2: ribonuclease and deoxyribonuclease which split nucleotides from nucleic acids
3: chloride at about 130 mmol/l concentration
4: prolipase from nucleic acids

Biliary Secretion



- 500 ml/ day, formed from cholesterol
- Bile constitutes : 97% water, 0.7% bile salts, 0.2% bile pigments, 0.06% cholesterol, 0.7% inorganic salts, 0.15% FAs, 0.2% phosphatidylcholine 0.1% Fat
- Bile pigments: bilirubin (yellow), biliverdin – reabsorbed
- Bile acids - 0.2-0.4g/d synthesis (total pool 3.5 g)
  - 4 main forms: 50% cholic acid liver), 30% chenodeoxycholic acid (liver) , 15% deoxycholic acid, lithocholic 5%
  - Conjugated in colon by gut bacteria : cholic acid → deoxycholic acid, chenodeoxycholic acid → lithocholic, or ursodeoxycholic acid
  - Action: ↓ surface tension, emulsification→ absorbed by BB TI
  - 90-95% absorbed from SI (terminal ileum) in conjugated form
  - 5-10% enter colon → converted to deoxycholic acid (absorbed) or litholithic acid (faeces)



Question 4

The bile acids are converted in the colon to
1: chenodeoxycholic acid
2: deoxycholic acid
3: cholic acid
4: taurocholic acid

Question 5

With respect to bile salts

1: they are absorbed largely from the ileum

2: the primary bile salts are cholate and chenodeoxycholate and are conjugated with glycine or taurine in the liver

3: they are synthesised from cholesterol and are concentrated in the gall bladder

4: about 90% of cholate and chenodeoxycholate which enter the small intestine are absorbed from the jejunum and recirculate to the liver

Gastrointestinal regulation

- Hormones/ paracrine
- Other peptides – peptide YY, Ghrelin, substance P, GRP, guanylin
- Enteric nervous system
  - ANS
    - Parasympathetic cholinergic activity → increases activity of intestinal SM
    - Sympathetic - noradrenaline activity → decreases, sphincters contract

Digestive hormones in the GI tract

HORMONE	LOCALIZATION	MAIN PHYSIOLOGIC ACTIONS
Gastrin	Gastric antrum, duodenum (G cells)	**-stimulate secretion of gastric acid and intrinsic factor from parietal cells** **-stimulate secretion of pepsinogen from chief cells** -promotes gastric and intestinal motility, mucosal growth
Cholecystokinin (CCK)	Duodenum, jejunum (I cells)	**-stimulate gallbladder contraction** **-stimulates release of pancreatic enzymes** **-relaxes sphincter of Oddi for release of bile and enzymes** -role in inducing satiety
Secretin	Duodenum, jejunum (S cells)	**-stimulate secretion of HCO_3 from pancreas** -inhibits gastrin and gastric acid secretion
Vasoactive intestinal peptide (VIP)	Enteric nerves	**-increases water and electrolyte secretion from pancreas and gut** -relaxes smooth muscles (via nitric oxide) of the gut
Gastric inhibitory polypeptide (GIP)	Duodenum, jejunum (K cells)	**-reduces gastric acid secretion** and intestinal motility **-stimulates insulin release**
Motilin	Throughout the gut (Mo cells and ECL cells)	**-increases small bowel motility (MMC during fasting) and gastric emptying**
Somatostatin	Stomach, small intestine, and pancreas (D cells)	**-inhibits secretion and action of many hormones, including all of the above**

GIT regulation cont.

- Other Peptides
  - Peptide YY - released from jejunum
    - inhibits gastric acid secretion, motility.
    - Stimulated by fat,
  - Ghrelin – stomach→ acts on pituitary R;s → GH
  - Substance P , GRP, guanylin

- Neural control
  - ANS
    – parasympathetic cholinergic activity → ↑ SM contraction. Vagal/Sacral preganglionic nerves
    - sympathetic NA activity → ↓ motility, sphincters contract. Postganglionic. Inhibits ACH by binding alpha-2 Rs
  - Bloods vessels: dual innervation
    - extrinsic: NA --> vasoconstriction
    - intrinsic: enteric nervous system : VIP, NO

Question 6

Which of the following results in an increase in the pH of duodenal contents?

A. gastrin-releasing peptide

B. secretin

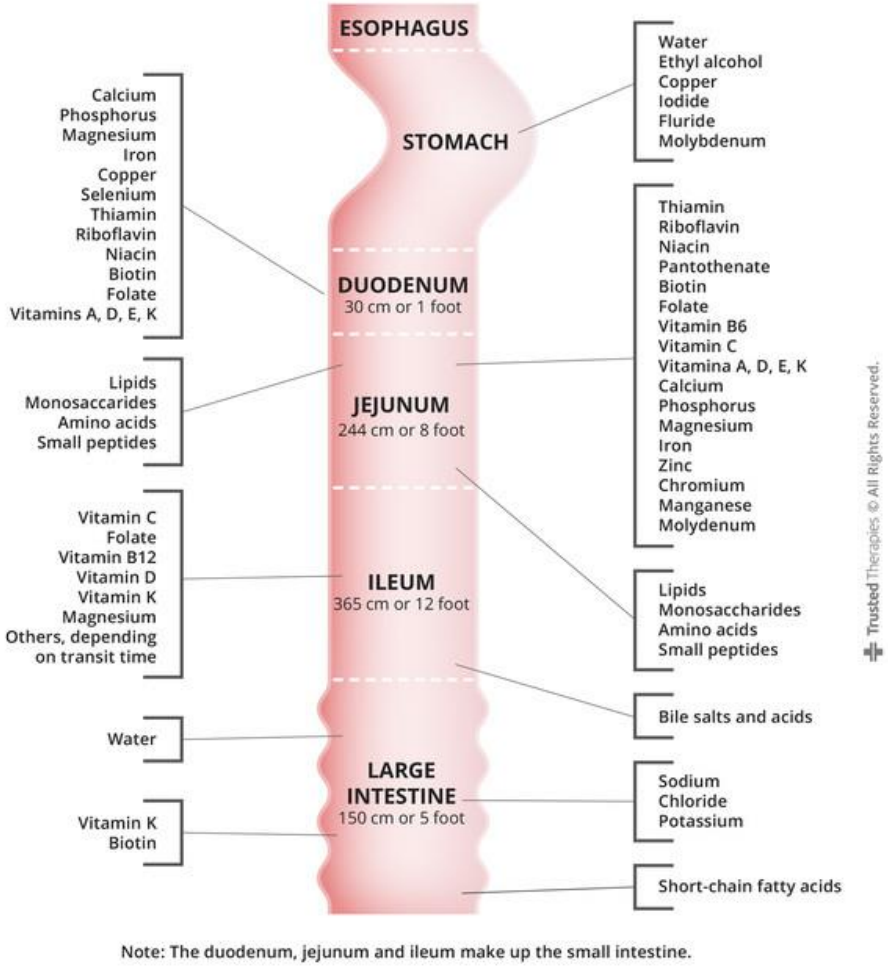
C. intrinsic factor

D. cholecystokinin

E. gastrin

Absorption

- CHO (whole SI) → broken down by alpha-alkylase – SI can absorb disaccharides (lactose, sucrose) & monosaccharides (glucose & fructose)
  - Enterokinase (duo- upper SI) : H+, polysaccharides
- AAs (whole SI)
- Water + fat sol vitamins * except B12* (upper & mid SI)
- Long chain FA, conversion to Tgl –(mostly upper SI)
- B12 (terminal ileum)
- Na (whole SI & LI)
- Other electrolytes: K, Ca, Cl, SO4 (upper SI)
- Fe (upper SI): 3-6% ingested absorbed, almost all in dup
  - Consumed in Ferric (Fe3+) → fe reductase BB enterocytes → Fe2 2+ → absorbed in dup →transported into rbc by DMT1 (stored as ferritin), remained transported out of rbc by basolateral ferroportin I→ Fe2+ converted to Fe3+ & bound to transferrin
  - 70% Hb, 3% myoglobin, rest is ferritin



Note: The duodenum, jejunum and ileum make up the small intestine.

Absorption

- Glucose: Enter cells with NA on SGLT symporter then GLUT 2 to enter interstitium,
- Fructose: enters cells via GLUT 5, then GLUT to interstitium
- Fat – 95%, duo
  - Lipase hydrolyse 1&3 bond triglycerides → 2-monoglycerides & FFAs
  - Colipase is activated by trypsin
  - Emulsified by bile salts &lecithin strongly → micelles → distal ileum
  - FA < 10-12 atoms can be water sol → enterocytes → blood → circulate FFA
  - Chylomicons → lymphatics (too large)
  - Long chain FAs – absorbed upper SI, ileum
- AAs: many transporters – rapid absorption in dup + jejunum, slow in ileum
  - 5 transporters - all cotransport with Na
  - 2 transporters - require Ca &Cl
  - 2 systems - independent of Na
- B12 – needs IF → terminal ileum
- Water sol: thiamine, riboflavin, niacin, peroxidase, pantothenates, biotin, ascorbic acid.
  ** require Na cotransport
- Ca – 30-80% absorbed
  - Requires vitamin D derivative
  - Inhibited by phosphates and oxalates (form insoluble salts with Ca)

Question 7

Resection of the ileum markedly reduces the absorption of

1: bile salts

2: vitamin B12

3: fat-soluble vitamins

4: ferrous iron

Gastrointestinal motility

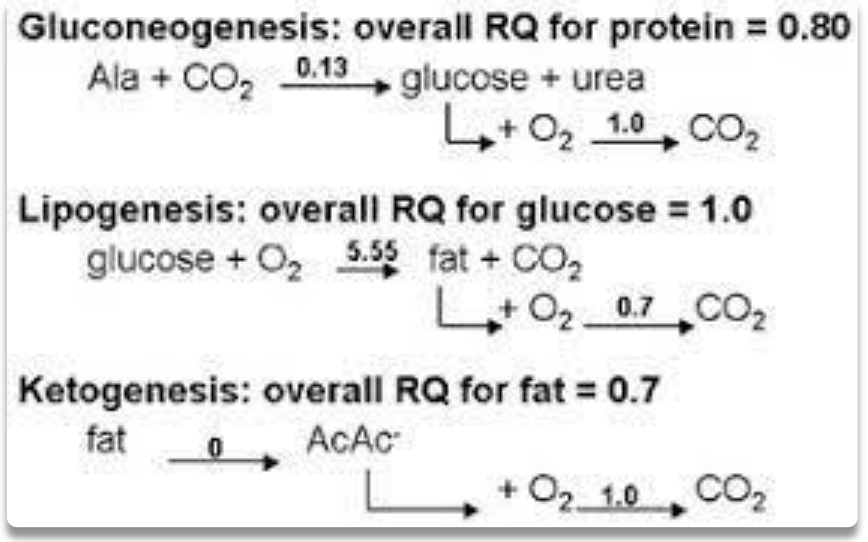
- Peristalsis
  - Reflex response initiated when gut wall stretched by intraluminal contents
  - Circular contraction, propels contents **2-25cm/sec**
  - Increased/ decreased by ANS, but occurs independently
- Segmentation
  - mixing of chyme to allow time for digestion & absorption
  - Promotes retrograde movement of chyme, persists as long as chyme remains in lumen, controlled by ENS
- Basic electrical rhythm (BER)
  - Spontaneous RMP **-65 to -45 mV**, initiated by interstitial cells of cajal (mesenchymal pacemaker cells) - located in outer circular SM layer
  - Rates: stomach = 4/min, duo= 12/min, ileum 8/min, colon 2/min, cecum 6/min
- MMC
  - Modified cycles of motility during fasting
  - Phase I – quiescent period
  - Phase II-irregular electrical and motor activity
  - Phase III- burst of regular activity
  - Initiated by motilin, 5cm/min at ~90 min intervals
  - Increase of gastric secretion, bile flow, pancreatic secretion

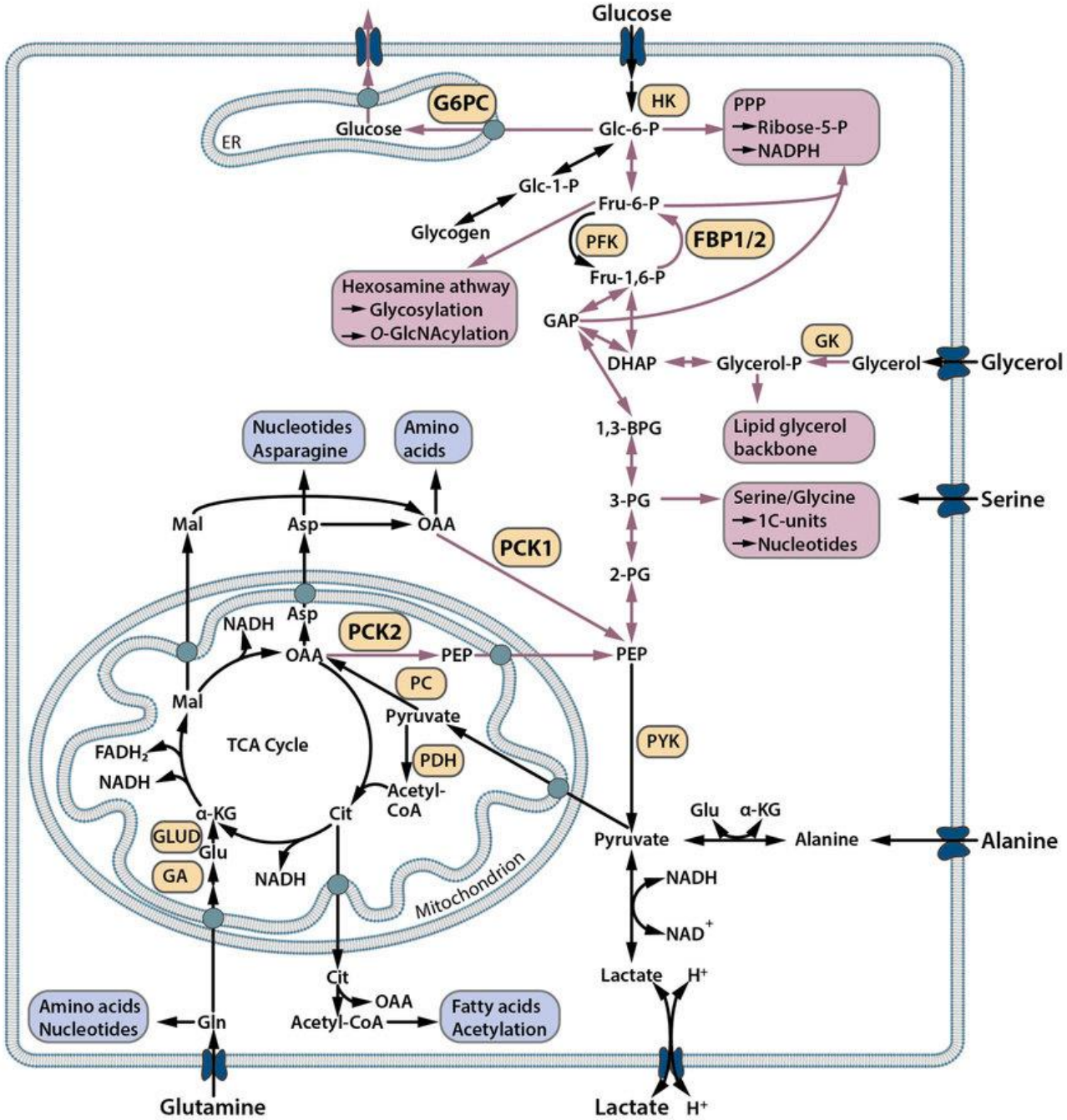
Question 8

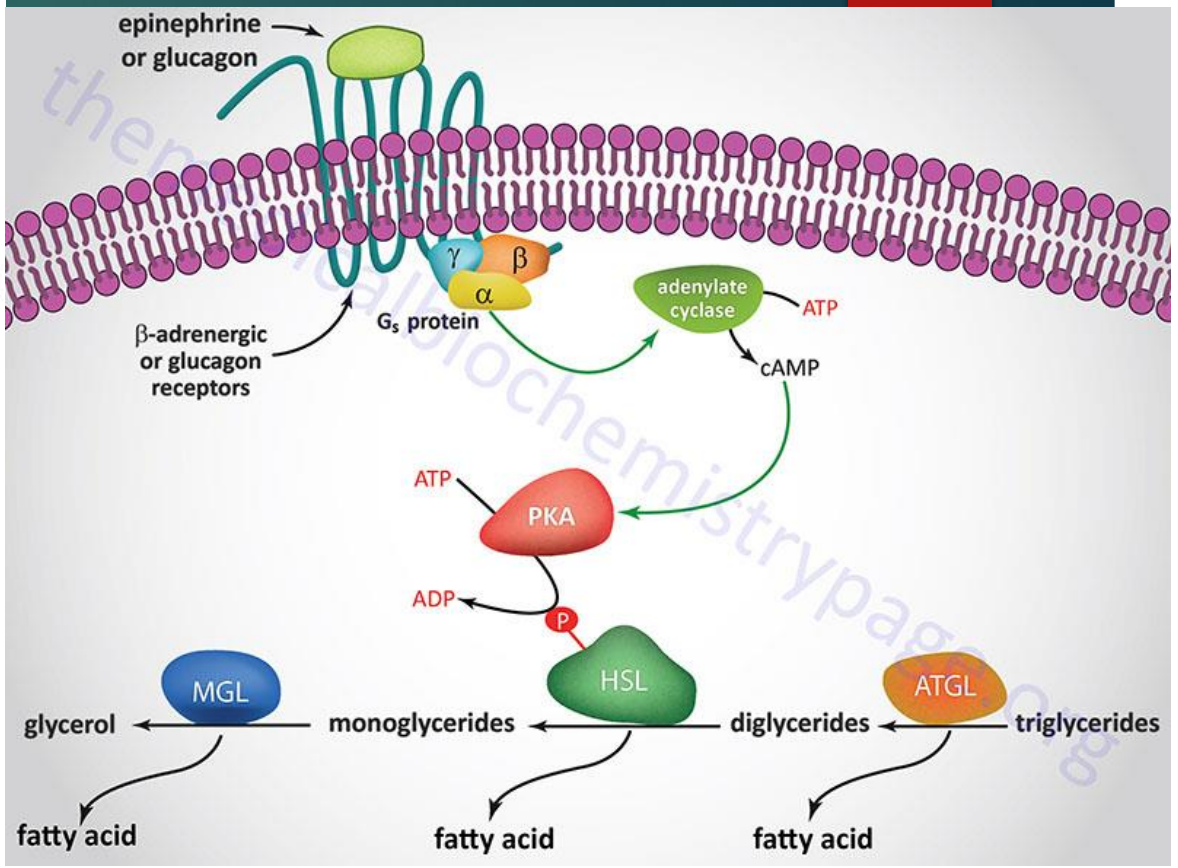
In the small intestine
1: the most significant single factor that increases the luminal surface area is the presence of villi
2: mucosal cells are formed from undifferentiated cells in the crypts of Lieberkuhn
3: peristalsis is the only type of movement demonstrated
4: the frequency of slow waves decreases from the jejunum to the ileum

Metabolism

- Respiratory quotient (RQ) – CO2 production compared to O2 consumed by cells
- CHO = 1.0, fat = 0.7, protein = 0.82
- SDA (specific dynamic action) : % energy of food used to burn itself:
  CHO = 6%, Fat =4%, protein = 30%
- Energy transfer: energy stored in phosphate bonds (ATP, phosphocreatine, co-enzyme A)




Glucose
G6PC
ER
Glucose
HK
Glc-6-P
PPP
Ribose-5-P
NADPH
Glc-1-P
Glycogen
Fru-6-P
PFK
FBP1/2
Fru-1,6-P
Hexosamine athway
Glycosylation
O-GlcNAcylation
GAP
GK
DHAP
Glycerol-P
Glycerol
Glycerol
Nucleotides
Asparagine
Amino acids
1,3-BPG
Lipid glycerol backbone
3-PG
Serine/Glycine
1C-units
Nucleotides
Serine
Mal
Asp
OAA
PCK1
2-PG
NADH
Asp
PCK2
OAA
PEP
PEP
PC
Mal
Pyruvate
TCA Cycle
PYK
FADH2
NADH
PDH
Acetyl-CoA
α-KG
Cit
Glu
α-KG
GLUD
Glu
Pyruvate
Alanine
Alanine
GA
NADH
Mitochondrion
NADH
NAD+
Cit
Lactate
H+
Amino acids
Nucleotides
Gln
OAA
Acetyl-CoA
Fatty acids
Acetylation
Glutamine
Lactate
H+


epinephrine
or glucagon
β-adrenergic
or glucagon
receptors
γ
β
α
Gs protein
adenylate
cyclase
ATP
cAMP
ATP
PKA
ADP
P
HSL
MGL
ATGL
glycerol
monoglycerides
diglycerides
triglycerides
fatty acid
fatty acid
fatty acid

Question 9

S.The respiratory quotient of the stomach during secretion of gastric juice is less than one BECAUSE R. the stomach takes up more CO_2 from the arterial blood than it puts into the venous blood

S is true, R is true and a valid explanation of S	A
S is true, R is true but not a valid explanation of S	B
S is true and R is false	C
S is false and R is true	D
Both S and R are false	E

Question 10

Endogenously-derived triglyceride circulating in the plasma is

1: transported primarily as very low density lipoprotein

2: increased by carbohydrate excess in the diet

3: removed from the circulation by both muscle and adipose tissue

4: increased when plasma cholesterol levels rise

Thank you ☺