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Small Intestine

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1. States the function of the small intestine.
    a. Digestion
    b. Absorption
    c. Secretion
    d. Motility
2. States four sources of digestive enzymes that contribute to the digestion of organic nutrients prior to their absorption.
    a. Saliva
    b. Pancreas
    c. Stomach
    d. Bacteria
3. Describes the role of the microvilli, the unstirred layer, and tight junctions in determining the rate at which a given nutrient is absorbed.
    a. Microvilli --> increase surface area for fast and efficient absorption
    b. Unstirred layer --> provides space for nutrients to diffuse through w/o being mixed w/ other material; monomeric FA equilibrate w/ micelles
    c. Tight junctions --> ensures selectivity of absorption
4. States the forms of the carbohydrates entering the duodenum from the stomach.
    a. Carbohydrates are mostly undigested, only salivary amylase before entering small intestine
    b. Enzymes for digestion are mainly in the lumen of the small intestine
5. Describes the role of the pancreas in carbohydrate digestion.
    a. Pancreatic amylase
    b. Other digestive enzymes
6. Identifies and describes the role of the brush-border enzymes involved in carbohydrate digestion.
    a. Enzymes produced in the ER are transported via vesicular transport to brush border
    b. Pancreatic proteases cleave protein into sucrase and isomaltase parts
    c. Other enzymes are maltase, lactase
    d. Break polysaccharides down to monosaccharides
7. Describes the pathways by which glucose, galactose and fructose cross the apical and basolateral membranes of enterocytes.
    a. Glucose/Galactose cross apical membrane via sodium/glucose transporter 1 (SGLT1)
        i. Na+/K+ ATPase exports sodium out to blood on basolateral side
        ii. Glucose/galactose stimulate Na+ absorption across epithelium
        iii. SGLT1 mutations can result in glucose-galactose malabsorption
    b. Fructose crosses apical membrane via GLUT5
    c. Glucose/Fructose out via GLUT 2
8. States the defect causing lactose intolerance.
    a. Lactase is deficient (brush-border enzyme)
    b. Lactose accumulates in bowel lumen
    c. Lactic acid production by bacteria --> gas
    d. Increased luminal osmolality
    e. Net water accumulation in lumen
    f. Luminal distension/Watery diarrhea
9. Describes the state of the proteins entering the duodenum from the stomach.
    a. Gastric/pancreatic proteases break down protein to polypeptides
    b. Fairly effective but brush border can break peptides down to tri/dipeptides, AA
10. Describes the role of the pancreas in protein digestion.
    a. Trypsinogen produced in pancreas activated by enterokinase on brush border
    b. Trypsin cleaves other pancreatic enzymes (chymotrypsinogen, proelastase, procarboxypeptidases

etc.)

11. Identifies and describes the role of the brush-border enzymes involved in protein digestion.
    a. 20 different peptidases
        i. Some for distinct substrates
        ii. Some for regions of peptides
            1) Trypsin cleaves to leave a basic carboxy terminal
            2) Chymotrypsin cleaves to give an aromatic carboxy terminal
            3) Elastase gives an aliphatic carboxy terminal
    b. Peptidases are anchored into brush border
    c. Some AA transporters are Na+ dependent; specific transporters for neutral, cationic, anionic AA
    d. Intestinal basolateral membrane has transporters similar to those of all cells
12. Describes the mechanism by which amino acids, di- and tripeptides are absorbed.
    a. Di/tripeptides absorbed by PepT1 in the brush border membrane
        i. Electrogenic proton/peptide cotransporter
        ii. Intracellular peptidases break up di/tripeptides
        iii. Beta-lactam antibiotics and ACE-inhibitors taken up this way
    b. Amino acids have specific transporters for neutral, cationic, anionic AA
        i. Separate transporter for proline in gut and renal tubule

    Defects in absorption
    a. Cystinuria - autosomal recessive; increased excretion of cationic AA and cysteine; renal stones enriched in cysteine
    b. Hatrnup disease - autosomal recessive; impaired absorption of neutral AA; major symptom is pellagra because niacin is synthesized from Trp
    c. Don't show symptoms of protein malnutrition b/c absorbing di/tripeptides
13. Describes the forms of the lipids entering the small intestine from the stomach.
    a. Physical breakdown and emulsification to small lipid particles
        i. Emulsification by proteins and phospholipids
    b. Gastric lipase breaks triglycerides down to diglyceride and free FA
    c. Can produce adequate lipolysis in some CF patients
14. Describes the role of the pancreas in lipid digestion.
    a. Pancreatic lipase
        i. Specific for 1 and 3 position FA
    b. Cholesterol esterase
        i. Cleaves FA from cholesterol
        ii. Position 2 FA
    c. Phospholipase A2
        i. Cleaves lecithin to lysolecithin (emulsifier)
    d. pH opitmum btwn 6 and 7 for all lipases; depend on neutralization of gastric acid
15. Describes the products of fat digestion by pancreatic lipase.
    a. 2-Monoglycerol
    b. 2 Free Fatty Acids
16. Describes the role of colipase.
    a. Anchors lipase to fat droplet
17. Describes the role of micelles in lipid absorption.
    a. Monoglycerides and long chain fatty acids enter cells after being incorporated into micelles
    b. Micelles can solubilize monoglycerides and long chain FA
    c. Uptake was thought to be by diffusion, but evidence indicates a brush border FA transport protein
    d. Absorbed FFA bound by FABP; as digestion proceeds more monomers shift out of micelles
    e. Bile salts are absorbed in terminal ileum
18. Describes the role of the endoplasmic reticulum in processing lipids absorbed across the apical membrane of enterocytes.
    a. Resynthesizes triglycerides
        i. 2MG + FFA --> TG
        ii. LysoPL + FFA --> PL

iii. Chol + FFA --> CholE
b. Packages them into chylomicrons released by exocytosis

19. Describes the composition and formation of chylomicrons.
    a. Triglycerides and phospholipids arrange around cholesterol molecules to form lipoproteins
    b. Apolipoproteins surround and coat the chylomicron
20. Describes the release of chylomicrons across the basolateral membrane of enterocytes.
    a. Exocytosis
    b. Diffusion into lacteals
21. Describes the role of lacteals in fat absorption.
    a. Absorb large chylomicrons
22. Defines steatorrhea.
    a. More than 5g/day of fat in fecal matter

- Cholesterol Absorption
    a. About 1200-1700mg/day enter intestines (300-500 from diet, rest from bile)
    b. Cholesterol esterase hydrolyzes dietary cholesterol esters
    c. About 50% of luminal cholesterol is absorbed
    d. ABC transporters pump plant sterols back into lumen
        i. Mutations in ABC 5/8 underlie sitosterolemia
        ii. Ezetimibe blocks permease mechanism (entry into enterocyte)
    e. Cholesterol moves to ER and is esterified by acyl coenzyme A:cholesterol acyltransferase (ACAT) and incorporated into chylomicrons
    f. After release of triglycerides in periphery, chylomicron remnants taken up by liver and cholesterol is secreted into bile or back into plasma as VLDLs and LDLs
- Calcium Absorption
    a. Characteristics
        i. Dietary intake about 1000 mg/day w/ net absorption of about 100 mg/day
        ii. Absorption mostly in duodenum and involves energy dependent, transcellular pathway (some is paracellular)
        iii. Regulated by 1,25-OH Vit D (1,25(OH)2 cholecalciferol)
    b. Mechanism
        i. Ca2+ enters via mediated diffusion through CaT1
        ii. Binds to calbindin in enterocyte
        iii. Exits across basolateral membrane via Ca2+-ATPase (PMCA1)
    c. Synthesis and Action of Vit D
        i. Formed by sun interacting w/ 7-dehydrocholesterol
        ii. Liver is first hydroxylation --> 25-OH-D3
        iii. Kidney is second hydroxylation --> 1,25-OH-D3 (PTH upregulates rxn)
        iv. Enters enterocyte to cause transcription of CaBP, CaT1, Ca2+ ATPase

23. Describes the absorption of fat-soluble vitamins.
24. Describes the absorption of water-soluble vitamins.
25. Describes the role of intrinsic factor in the absorption of vitamin B12.
    a. Talked about in stomach
26. Describes the changes in osmolarity that occur in chyme as it passes from the stomach to the duodenum and gives explanation for these changes.
    a. Leaky tight junctions permit large one-way water with equilibration occurring within a few minutes of entering duodenum
    b. Bicarbonate rich fluid also secreted by Brunner's glands to neutralize chyme
    c. Maximal absorptive capacity of 15 l/day
27. Describes the pathways by which sodium ions are absorbed in the small intestine.
    a. Ionic Pathway: Na+-H+, Cl--HCO3- countertransport; most important in humans
    b. NaCl cotransport
    c. Na+-Organic Solute cotransport
        i. D-hexoses
        ii. L-amino acids

iii. Water soluble vitamins
iv. Bile salts in ileum

28. Describes the relation between sodium absorption and water absorption.
    a. Local hypertonicity in lateral regions between cells results in water diffusing through aquaporins
    b. Secretion is local and in response to reflex stimulation prompted by distension or presence of solid material
    c. Absorption typically at villus cells, secretion in crypt cells
    d. Secretion involves uptake of Na+ and Cl- and release of Cl- across apical membrane via CFTR (cAMP activated)
    e. Secretion inducers
        i. Bacterial endotoxins (cholera)
            1) Cholera toxin activates adenylyl cyclase --> cAMP --> CFTR activation --> secretion --> watery diarrhea
            2) Can be treated w/ sugar/salt water drink to have villus cells absorb water while crypt cells are secreting (takes advantage of separate absorption/secretion cells)
        ii. Some unsat fatty acids (castor oil)
        iii. Bile acids
        iv. Anthrquinone cathartics (senna, cascara)
        v. Certain hormones (VIP)