Digestion and absorption in the GI tract

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Digestion of various foods

• 3 main group of nutrients:
  – Carbohydrates (CHO)
  – Proteins
  – lipids

• Hydrolysis: basic process of digestion
Basic principal of GI absorption

- Anatomical basis of absorption
- Absorptive surface of the small intestinal mucosa-villi
- Basic mechanism of absorption:
  - Active transport, Diffusion, Facilitated transport, Solvent drag
Intestine as cylinder

- Structure: Intestine as cylinder
- Relative surface increase (cylinder = 1): 1
- Surface area (m²): 0.33

Circular folds

- Structure: Circular folds
- Relative surface increase (cylinder = 1): 3
- Surface area (m²): 1

Villi

- Structure: Villi
- Relative surface increase (cylinder = 1): 30
- Surface area (m²): 10

Microvilli

- Structure: Microvilli
- Relative surface increase (cylinder = 1): 600
- Surface area (m²): 200
Digestion of carbohydrate

• Dietary source of CHO
  – Polysaccharides:
    • Starch: amylopectin, amylose (plant source)
    • Glycogen (animal source)
  – Disaccharides: sucrose, lactose,
  – Monosaccharides: glucose
Digestion of carbohydrate

- Digestion of CHO in the mouth and duodenum:
  - Salivary $\alpha$-amylase (ptyalin)
  - Pancreatic $\alpha$-amylase
- : maltose, maltotriose, dextrines

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Digestion of CHO in the small intestine

Digestion of disaccharides & small glucose polymers by brush border enzymes

- Lactase, Sucrase, α-dextrinase(isomaltase), maltase*

Glucose, fructose, galactose

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# Table 27.6: The Digestion of Disaccharides and Oligosaccharides by Brush Border Enzymes

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Substrate</th>
<th>Site of Action</th>
<th>Products</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sucrase</td>
<td>Sucrose</td>
<td>α-1,2-glycosidic linkage</td>
<td>Glucose and fructose</td>
</tr>
<tr>
<td>Lactase</td>
<td>Lactose</td>
<td>β-1,4-glycosidic linkage</td>
<td>Glucose and galactose</td>
</tr>
<tr>
<td>Isomaltase</td>
<td>α-Limit dextrins</td>
<td>α-1,6-glycosidic linkage</td>
<td>Glucose, maltose, and oligosaccharides</td>
</tr>
<tr>
<td>Maltase</td>
<td>Maltose, maltotriose</td>
<td>α-1,4-glycosidic linkage</td>
<td>Glucose</td>
</tr>
</tbody>
</table>
Absorption of carbohydrates

- Duodenum and jejunum
  - At apical membrane
    - Glucose & galactose: Na/Glucose transporter (SGLT1)
    - Fructose: facilitated transport; glucose transporter (GLUT5)
  - At basolateral membrane
    - Facilitated transport (GLUT 2)

- Most ingested CHO is digested and absorbed within the first 20% of the SI.
  - 6-10% starch escape adsorption in SI (carbon source for colonic bacteria)
Absorption mechanisms for glucose, galactose, fructose.
The Lack of Some Digestive Enzymes Impairs Carbohydrate Absorption
The mechanism for osmotic diarrhea resulting from lactase deficiency

1. Lactase deficiency
   - Lactic acid production by bacteria
   - Accumulation of lactose in intestinal lumen
2. Increased luminal osmolality
3. Fluid accumulation in lumen
4. Luminal distension
5. Enhanced peristalsis
6. Watery diarrhea
Digestion of proteins

- Proteins sources
  - Proteins of diet (All of them absorbed)
  - Digestive secretion of GI
  - Exfoliate epithelial cells
    - Colonic bacteria
    - Colonic mucus protein
    - Protein in feces
• Digestion of proteins in the stomach
  – HCL and pepsin (~15%)
✓ Digestion of proteins by pancreatic enzyme (50%)

Trypsinogen

Enteropeptidase

Trypsin

**proenzyme**
  Trypsinogen
  Chymotrypsinogen
  Procarboxypeptidase
  Proelastase

**active enzyme**
  Trypsin
  Chymotrypsin
  Carboxypeptidase
  Elastase

**small peptide**
• Digestion of peptides by peptidase in the SI:
  – Entrocyte brush border enzymes (20 type): (peptide $\geq$ 4 or more aa)
    • Aminopeptidase
    • Dipeptidase
    • Tripeptidase
• Digestion continues in the cytosol of duodenal and jejunal epithelial cells: (di or tripeptides)
  
  Single amino acids
Absorption of proteins

Absorption of small peptide: (jejunum>ileum)
- Secondary active transport; with H^+
  - Role of luminal Na/H^+ exchanger
- Cleavage of small peptide in the enterocyte
- Absorption of single aa in BL membrane

Absorption of amino acids: (ileum > jejunum)
- By aa-transporter (Na-dependent/independent)
- By diffusion

Absorption of intact proteins and large peptides???
Protein digestion and absorption

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Defect in amino acids absorption

- Hartnup's disease: defective renal & intestinal transport of neutral aa
- Cystinuria: defective renal & intestinal transport of basic aa

Non of them results in protein malnutrition (why?)
Digestion of fats

- Fats of diet:
- TG, sterols, phospholipids, vitamins
  - Chemical formula of some common lipids:

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Digestion of fats

- Lingual lipase
- Gastric lipase

15% of fat digestion occur in stomach

FFA reach duodenum….CCK release …… stimulate:

1. Flow of bile by contraction of GB and relaxation of Oddi sphincter
2. Secretion of pancreatic enzymes

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• Digestion of fat in the intestine
  – Emulsification of fat droplets by Bile salts & lecithin
  – **Emulsification**: Transformation of solid fat and oil mass into an emulsion of fine oil droplets in water…..increase in oil-water interface

• Digestion of triglycerides by pancreatic **lipase**
  – Activity of Pancreatic lipase is proportional to the surface area of oil phase
  – Role of **co-lipase**:• Prevent lipase inactivation by bile salts
    • Anchor lipase to fat droplet surface

 2 fatty acids+ 2-monoglyceride

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- Digestion of esters by pancreatic carboxyl ester hydrolase
  - free cholesterol + FFA

- Digestion of phospholipids by pancreatic Phospholipase A$_2$ (PLA$_2$)
  - lysophosphatidies+ FFA
Role of Bile Salts in accelerating fat digestion

Formation of micelles with products of fat digestion
Absorption of lipid digestion product

• Most of fat absorption in midjejunum
• The function of micelles in lipid absorption
  
  Diffuse among the microvilli.....saturate an unstirred layer with fat digestion products*

• Transport of lipids across brush border membrane; simple diffusion

Complete absence of:
– Bile acids.................absorption of 50% lipids
– Pancreatic lipase.......all lipids are poorly absorbed
Handling of lipids inside the intestinal entrocyte

→ Cytosolic lipid transport
→ Resynthesis of lipids in the SER
→ Chylomicron formation and transport
→ Entrance of chylomicron to lacteal
→ Direct absorption of fatty acids into the portal blood

– Absorption of bile acids in the terminal ileum

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Fat droplet

Bile salts
Phospholipids

Emulsion droplets

Bile salts
Pancreatic lipase

Micelles

Free molecules of fatty acids and monoglycerides

Lumen of intestinal tract

Diffusion
Fat malabsorption results in increased levels of fecal fat excretion.

**Steatorrhea:** presence of more than 7 g/day of FAs in the stool.

Potential causes of fat malabsorption:

- Fat emulsification is poor in patients who have had a *gastrectomy* and who experience rapid dumping of ingested food into the small intestine.
- Patients with *hypersecretion of gastric acid* (e.g., Zollinger-Ellison syndrome) may have an acidic duodenal environment that inhibits pancreatic lipase.
- *Biliary obstruction or cholecystectomy* (removal of the gallbladder) reduces the availability of bile.
- Patients with *pancreatic insufficiency* (e.g., cystic fibrosis) have inadequate pancreatic lipase secretion.
- *Abetalipoproteinemia* is a rare condition in which the assembly of triglyceride and apoproteins is defective.
Absorption in the small intestine

- Absorption of water: isosmotic absorption*
Fluid balance in GI

- Ingest: 2000 ml/day water
- Saliva: 1500 ml/day
- Gastric secretions: 2000 ml/day
- Bile: 500 ml/day
- Pancreatic juices: 1500 ml/day
- Intestinal secretions: 1500 ml/day
- Small intestine absorbs: 8500 ml/day
- Colon absorbs: 400 ml/day
- - 100 ml/day
Absorption of electrolytes

– Active transport of sodium:
  ✓ Na/glucose, Na/amino acid cotransporter in SI
  Ø Na-H exchanger in SI
  Ø Parallel Na-H and CL-HCO3 exchangers in ileum and proximal colon

• Aldosterone greatly enhances Na absorption
Na absorption by the jejunum, ileum.
Mechanisms of NaCl absorption & K secretion by the colon
Absorption of chloride
Transport of Na\(^+\), K\(^+\), Cl\(^-\), HCO_3\(^-\) in the small and large intestine

<table>
<thead>
<tr>
<th>segment</th>
<th>Na(^+),</th>
<th>K(^+),</th>
<th>Cl(^-)</th>
<th>HCO_3(^-)</th>
</tr>
</thead>
<tbody>
<tr>
<td>jejunum</td>
<td>Actively absorbed: ↑ by sugar, aa</td>
<td>Passively absorbed followed by water absorption</td>
<td>absorbed</td>
<td>absorbed</td>
</tr>
<tr>
<td>ileum</td>
<td>Actively absorbed</td>
<td>Passively absorbed</td>
<td>Absorbed: some in exchanged for HCO_3</td>
<td>Secreted: in exchange for Cl(^-)</td>
</tr>
<tr>
<td>colon</td>
<td>Actively absorbed</td>
<td>Net secretion occurs when [K(^+)] in lumen &lt;25 mM</td>
<td>Absorbed in exchanged for HCO_3</td>
<td>Secreted: in exchange for Cl(^-)</td>
</tr>
</tbody>
</table>
• Secretory diarrhea: Cholera
Absorption in the large intestine

- Absorption and secretion of electrolytes and water
- Maximum absorption capacity of the large intestine: 8 liter

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Physiological regulation of salt and water absorption

- **Endocrine control:**
  - Increase net absorption of salt and water
    - Aldosterone, Glucocorticoids, Opioids, Somatostatin

- **Neural regulation:**
  - Parasympathetic
    - Diminishes absorptive flux and enhance secretion
  - Sympathetic
    - Enhance net absorption
      - Diabetic diarrhea due to autonomic neuropathy

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**Diarrhea**

Diarrhea is defined as an increase in stool fluid volume of more than 200 mL within 24 hours. In general terms, diarrhea may result from the delivery of more fluid to the colon than the colon can absorb, or it may result if feces move too rapidly through the colon to allow the colon to adequately absorb fluid. The general causes of diarrhea are:

- Osmotic diarrhea occurs when there is an agent in the intestine that causes water to be retained in the lumen. The agent may be a malabsorbed nutrient or an exogenous agent such as saline laxatives.

- Rapid intestinal motility may cause diarrhea due to transit times that are too brief to complete fluid and electrolyte absorption.
Diarrhea cont.

- Secretary diarrhea occurs when there is excess endogenous fluid secretion by enterocytes and colonocytes. Bacterial food poisoning is a common cause of secretory diarrhea (e.g., traveler’s diarrhea caused by enterotoxigenic *E coli*). *Rare causes* of secretory diarrhea include hormone-secreting tumors that release secretagogues such as VIP or serotonin.

- Inflammation of the bowel may cause diarrhea as a result of increased fluid secretion and motility (e.g., inflammatory bowel disease).

*Diarrhea may cause excessive loss of K+ and HCO3 in feces, resulting in hypokalemia and metabolic acidosis.*

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Absorption of others ions

**Calcium:** actively absorbed by all segments

- Action of Vit D
  - Calbindin (CaBP)
  - $\text{Ca}^{2+} - \text{ATPase} / \text{Na}^+ - \text{Ca}^{2+}$ exchanger at basolateral membrane

**Iron:**
- Heme iron is taken up by facilitated transport
- Iron split from heme by hemeoxygenase

**Absorption of water soluble vitamins:**
- Facilitated transport (folic acid, Vit B2), diffusion (Vit B6), co-transport with $\text{Na}^+$ (Vit C)
- Cobalamin (Vit B12) binds to IF in the small intestine before endocytosis by enterocytes in the ileum
The intestinal absorption of vitamin B12

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Vitamin B12 assimilation

Stomach
- Vitamin B$_{12}$/haptocorrin complexes + Intrinsic factor

Small intestine
- (Pancreatic proteases digest haptocorrin)
- Vitamin B$_{12}$/intrinsic factor
- (Receptor-mediated absorption in ileum)

Blood
- Transcobalamin/vitamin B$_{12}$
With best wishes for you!

Dr. Z Akbari