Absorption and Malabsorption

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#### The intestine has a very large surface area for absorption

<table>
<thead>
<tr>
<th>Type of Surface</th>
<th>Amplification Factor</th>
<th>Surface Area (cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucosal cylinder</td>
<td>1</td>
<td>3,300</td>
</tr>
<tr>
<td>Fold of Kerkring</td>
<td>3</td>
<td>10,000</td>
</tr>
<tr>
<td>Villi</td>
<td>10</td>
<td>100,000</td>
</tr>
<tr>
<td>Microvilli</td>
<td>20</td>
<td>2,000,000</td>
</tr>
</tbody>
</table>

Total surface area = 200 m²  
Double Tennis Court = 175 m²

#### Digestion of Carbohydrate Occurs in the Intestinal Lumen and at the Brush Border

- **Lumen**: Starch is broken down by salivary and pancreatic amylase.
- **Brush border**: Sucrase and lactase break down sucrose and lactose, respectively.
- **Glucoamylase**: Breaks down oligomers to glucose.

Diagram showing the processes and enzymes involved in the breakdown of carbohydrates in the intestinal lumen.
Cell Model

Na+/K+ ATPase on basal-lateral membrane pumps out 3 Na+ and pumps in 2 K+ maintaining an electrochemical Na+ gradient

SGLT1 – Sodium/Glucose co-transporter on apical membrane makes use of this gradient
MEAL GLUCOSE IS COMPLETELY ABSORBED ALONG THE HUMAN SMALL INTESTINE

500 ml meal, 50g glucose

Duodenum       Jejunum       Ileum

glucose absorbed (%)

50 100 150 200 250 300
distance from teeth (cm)

MEAL LACTOSE ABSORPTION IS VARIABLE BETWEEN INDIVIDUALS DUE TO GENETIC DIFFERENCES IN LACTASE ACTIVITY

500 ml meal, 50g lactose

Duodenum       Jejunum       Ileum

glucose absorbed (%)

50 100 150 200 250 300
distance from teeth (cm)
In patients with lactase deficiency, net fluid accumulation persists in jejunum and ileum.

[Diagram showing net fluid movement and lactase deficiency in different regions of the gut.]
Breath H₂ excretion increases after lactose load in lactase deficiency

<table>
<thead>
<tr>
<th>Time (hr)</th>
<th>Lactase deficiency after lactose load</th>
<th>Normal after lactose load</th>
<th>Normal and lactase deficiency after glucose load</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Δ H₂ excretion (ml/min)

THERE ARE THREE SITES OF PROTEIN DIGESTION

1. pepsins, pancreatic proteases
2. Brush Border Peptidases
3. Cytoplasmic peptidases

- Proteins:
  - Oligopeptides and amino acids
  - Amino acids + dipeptides and tripeptides
- Lumen:
  - Amino acids
  - Dipeptides and tripeptides

- Brush Border Peptidases:
  - Amino acids
  - Dipeptides and tripeptides
REMOVAL OF DIETARY PROTEIN BY DIGESTION AND ABSORPTION OCCURS THROUGHOUT THE SMALL INTESTINE

500 ml meal, 25 g protein

- protein digestion is slow in onset and incomplete

AMINO ACIDS, DIPEPTIDES AND TRIPEPTIDES ARE ABSORBED BY SPECIFIC TRANSPORTERS

- There are at least five apical transporters for aa's - each one transports a specific group of aa.
What is a Micelle?

- An organized aggregate of molecules containing polar (or ionic) heads and non-polar tails
  - Non-polar tails point inwards and polar heads point outwards, interacting with water molecules.

A Mixed Micelle is composed of polar and non-polar lipids

**Composition of a Mixed Micelle**

- Polar
  - bile acids
  - fatty acids
  - monoglyceride
  - lecithin
  - cholesterol
  - fat soluble vitamins

- Non-Polar

- Bile acids and polar lipids are located at the outer surface of a micelle while non-polar lipids are located in the center.
ABSORPTION OF LIPOLYTIC PRODUCTS OCCURS THROUGHOUT THE SMALL INTESTINE

500 ml meal, 30 g triglyceride

- Duodenum
- Jejunum
- Ileum

95% absorption of triglyceride
CHRONIC PANCREATITIS

Relationship Between Lipase Output and Steatorrhea

<table>
<thead>
<tr>
<th>Lipase Output (% of normal)</th>
<th>Fecal Fat, g/24 hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>50</td>
<td>50</td>
</tr>
<tr>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>Normal</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Bile acid-induced diarrhea results from ileal dysfunction

Ileum is the only site of active bile acid absorption
Limited Ileal Resection
(<100cm)

- Increased Bile Salt production by liver able to compensate for losses
- Fat absorption not compromised
- Increased bile salt delivery to colon produces secretory diarrhea, responds to cholestyramine
- Antimotility drugs may counter rapid transit
- B12 absorption may be compromised

Long-term Management

Limited Ileal Resection
<100cm resected

Standard
- Regular diet
- Multivitamin

As needed
- Cholestyramine
- Antimotility agent

Monitor
- Bone density
- Fat-soluble vitamins
- Vitamin B₁₂
- Urine oxalate
**Extensive ileal resection (>100cm)**

- Liver can’t compensate → Bile Acid pool reduced → Impaired micelle formation → Fatty Acids reach colon → Hydroxylation of FA by colonic bacteria → secretory diarrhea and steatorrhea.
- FA bind Ca$^{++}$ resulting in free oxylate, absorbed by colon → hyperoxyalurea → oxylate renal stones
- B12 supplement always necessary
- High Ca$^{++}$, low fat, low oxylate diet helpful
- Cholestyramine may worsen diarrhea

**Long-term Management**

**Ileal Resection**

- **Standard**
  - Diet: low fat, low oxalate
  - Vitamin B$_{12}$
  - Multivitamin and mineral
  - Calcium
  - Antimotility agent

- **As needed**
  - ? cholestyramine

- **Monitor**
  - Bone density
  - Fat-soluble vitamins
  - Urine oxalate
Length of Ileal Resection, Degree of Steatorrhea and Response to Cholestyramine

Fecal fat (g/day) vs. Length of Ileum removed (cm)

Steatorrhea
Colorrheic Diarrhea

Hydroxy fatty acids (OHFA) are produced from dietary lipids by enzymes of enteric bacteria

Oleic Acid (Dietary lipids do not contain OHFA)

CH₃ - (CH₂)₇ - CH = CH - (CH₂)₇ - COOH

Hydroxylation by Enteric Bacteria

OH

Hydroxy Stearic Acid

CH₃ - (CH₂)₇ - CH - CH₂ - (CH₂)₇ - COOH

Ricinoleic acid, the active ingredient of castor oil, is an OHFA
Several features help distinguish bile acid-induced from fatty acid-induced diarrhea

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Bile Acid</th>
<th>Fatty Acid</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Length of resection</td>
<td>small</td>
<td>large</td>
</tr>
<tr>
<td>2. Fecal BA output</td>
<td>↑</td>
<td>↑↑</td>
</tr>
<tr>
<td>3. Fecal BA loss compensated by hepatic BA synthesis</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>4. BA pool size</td>
<td>normal</td>
<td>↓</td>
</tr>
<tr>
<td>5. Duodenal [BA]</td>
<td>normal</td>
<td>↓</td>
</tr>
<tr>
<td>6. Steatorrhea</td>
<td>normal or mild</td>
<td>&gt;20 g/24 hrs</td>
</tr>
<tr>
<td>7. Responds to low fat diet</td>
<td>no</td>
<td>yes</td>
</tr>
<tr>
<td>8. Responds to cholestyramine</td>
<td>yes</td>
<td>no</td>
</tr>
</tbody>
</table>

Vitamin D Metabolism

- Sunlight exposure produces Vitamin D3
- Vitamin D3 is converted to 25 OH Vit. D in the liver
- 25 OH Vit. D is converted to 1,25 (OH)2 Vit. D in the kidneys
- 1,25 (OH)2 Vit. D promotes Calcium absorption
- Calcium and Vitamin D are essential for bone health
Treatment of Steatorrhea

- Ingest potent enzymes
- Protect enzymes
  reduce H+ (H-2 blocker) or
  ingest enteric-coated
- Decrease dietary fat

Chronic Pancreatitis

Long-Chain Triglyceride (LCT) and Medium-Chain Triglyceride (MCT) Absorption

LCT and MCT absorption process:
- Long-chain triglycerides
- Medium-chain triglycerides
- Lipase
- Bile salts
- Micelle
- LCFA
- Lymph
- ApoB

Portal blood

ACG
Enteric Hyperoxaluria
Dietary Cobalamin

“Everything that walks, swims, or flies contains Vitamin B12. Nothing that grows from the ground contains Vitamin B12.”

Decreased absorption in elderly.

Daily requirement from diet only 1mcg/d

Deficiency can be seen in strict vegans
Causes of B12 Deficiency

Inadequate Intake
- Vegans

Inadequate liberation from food
- Food Cobalamin Malabsorption

Lack of Intrinsic Factor
- Pernicious Anemia, Gastrectomy

Impaired proteolytic degradation of R-B12 complex
- Pancreatic Insufficiency, ZE Syndrome
Causes of B12 Deficiency

Infection (competition for luminal B12)
- Bacterial overgrowth
- strictures
- blind loop
- motility disorders
- Diphyllobothrium latum

Causes of B12 Deficiency

Absent or non-functioning Ileal mucosa
- Crohn’s Disease, Tropical Sprue,
- Lymphoma, TB, Ileal Resection

Abnormal translocation across enterocyte
- Juvinile PA, Transcobalamin II Deficiency,
- Imerslund-Grasbeck syndrome

Drugs
- Colchicine, Biguanide, Nitrous Oxide, PAS
### SCHILLING TEST AS A MEASUREMENT OF VIT B12 ABSORPTION

<table>
<thead>
<tr>
<th>Stage</th>
<th>Food-Cobalamin Malabsorption</th>
<th>Pernicious Anemia or Gastrectomy</th>
<th>Pancreatic Insufficiency</th>
<th>Bacterial Overgrowth</th>
<th>Ileal Resection or Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Vit B12</td>
<td>Normal</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>2) Vit B12 + Intrinsic Factor</td>
<td>Normal</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Decreased</td>
<td>Decreased</td>
</tr>
<tr>
<td>3) Vit B12 + Pancreatic Enzymes</td>
<td>Normal</td>
<td>Decreased</td>
<td>Decreased</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4) Abx followed by Vit B12</td>
<td>Normal</td>
<td></td>
<td></td>
<td>Decreased</td>
<td></td>
</tr>
</tbody>
</table>

### Vitamin and Mineral Deficiencies

**Manifestations**

<table>
<thead>
<tr>
<th>Vitamin B₁₂ / Folate</th>
<th>anemia, glossitis, cheilitis, angular stomatitis, diarrhea*, paresthesias*, ataxia*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron</td>
<td>*Vitamin B₁₂ only</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>osteoporosis, osteomalacia, paresthesias, tetany</td>
</tr>
<tr>
<td>Calcium / magnesium</td>
<td></td>
</tr>
<tr>
<td>Zinc</td>
<td>anorexia, diarrhea, rash, alopecia</td>
</tr>
<tr>
<td>Vitamin A</td>
<td>night blindness, dry eyes, hyperkeratosis, diarrhea</td>
</tr>
<tr>
<td>Vitamin K</td>
<td>ecchymoses, bleeding</td>
</tr>
<tr>
<td>Vitamin E</td>
<td>paresthesias, ataxia, retinopathy</td>
</tr>
</tbody>
</table>
It’s 9:55. I’m so outta here!

Good Luck on Final, Boards, and Wards.