**Key concepts in Digestion...**

*‘Travellers Health’ module*

**Gut secretion and absorption**

...physiology and pathology...

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**Gut secretion and absorption**

Fluid and electrolyte transport are important functions of the gastrointestinal tract (even in the absence of food)

Epithelial cells may...

- **secrete water and electrolytes**
  i.e. transport from blood to gut lumen

- **absorb water and electrolytes**
  i.e. transport from gut lumen to blood

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**Overall daily gut fluid balance**

<table>
<thead>
<tr>
<th>Ingest</th>
<th>Saliva</th>
<th>Small intestine absorbs</th>
<th>Gastric secretions</th>
<th>Pancreatic juices</th>
<th>Bile</th>
<th>Intestinal secretions</th>
<th>Colon absorbs</th>
<th>OUT 9 litres/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 L/day</td>
<td>1.5 L/day</td>
<td>8.5 L/day</td>
<td>2 L/day</td>
<td>1.5 L/day</td>
<td>0.5 L/day</td>
<td>1.5 L/day</td>
<td>0.4 L/day</td>
<td></td>
</tr>
</tbody>
</table>
Movement of water and solutes

- Water moves down osmotic gradients
- Electrolytes move down electrochemical gradients
- To move solutes against their concentration gradients requires energy
- Energy is supplied by sodium gradients (generated by the sodium pump) and by proton gradients

Membrane domains and transport routes

Absorption in the villus: secretion the crypt

net absorption

net secretion
Factors affecting absorption and secretion

- Nutrient intake
- Gastric motility
- Intestinal motility
- Blood & lymph flows
- Number and state of enterocytes
- Hormonal factors
- Paracrine factors
- Neural factors

Absorption

Secretion

Excretion

Luminal factors: Irritants, Bacterial toxins, Bile

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Na⁺-coupled nutrient absorption

......energy-dependent transport

Na⁺,K⁺ ATPase

ATP → ADP + Pᵢ

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Intestinal secretion

1. Na⁺/K⁺ ATPase
2. Na⁺/K⁺/2Cl⁻ cotransporter
3. K⁺ channel
4. Cl⁻ channel
5. Physiological control of secretion

Ach, VIP
**Diarrhoeal disease**

<table>
<thead>
<tr>
<th>TYPE OF DIARRHOEA</th>
<th>MECHANISM</th>
<th>CAUSES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypermotility</td>
<td>Transport too fast for absorption</td>
<td>High fibre diet Diabetes - adrenergic neuropathy</td>
</tr>
<tr>
<td>Osmotic</td>
<td>Non-solute absorption (enzyme deficiency/villous atrophy)</td>
<td>Lactase deficiency Coeliac (sprue) disease</td>
</tr>
<tr>
<td>Defective transport</td>
<td>Na⁺ or Cl⁻ transporters absent</td>
<td>Sodium/chloride diarrhoea (rare congenital defects)</td>
</tr>
<tr>
<td>Secretory</td>
<td>Inflammatory Blood hormones Tumours Enterotoxins Viruses/Parasites</td>
<td>Pancreas- VIP secreting Thyroid - calcitonin secreting V. cholerae, E.coli etc Rotavirus/Giardia sp. etc.</td>
</tr>
</tbody>
</table>

**TRAVELLERS DIARRHOEA**

<table>
<thead>
<tr>
<th>BACTERIA</th>
<th>VIRUSES</th>
<th>PARASITES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vibrio cholerae (F)</td>
<td>Norwalk (F/W)</td>
<td>Entamoeba histolytica (F/W)</td>
</tr>
<tr>
<td>Campylobacter jejuni (W)</td>
<td>Hepatitis A (F)</td>
<td>Giardia intestinales (W)</td>
</tr>
<tr>
<td>Clostridium difficile (F)</td>
<td>Rotavirus (W)</td>
<td>Cryptosporidium sp. (W)</td>
</tr>
<tr>
<td>Clostridium botulinum (F)</td>
<td></td>
<td>Yersinia sp. (F)</td>
</tr>
<tr>
<td>Shigella sp. (F)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Salmonella sp. (F)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E.coli (F)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

F = food bourne, W = water bourne

**Cholera and cholera toxin**

DNA sequence of both chromosomes of the cholera pathogen *Vibrio cholerae*

John F. Heidelberg et al., 3 August 2000 Nature 406, 477-482
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**Cholera toxin and transport into intestinal cells**

*Sandvig & van Deurs, FEBS Lett. 2002: 529; 49-53*  
*Lencer & Tsai, TIBS: 2003; 28; 639-45*

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**Cholera toxin-induced intestinal secretion**

*GTPase*  
*Adenylate cyclase*  
*β-subunit*  
*α-subunit*  
*NAD*  
*H₂O*  
*Cl⁻*  
*HCO₃⁻*  
*ATP*  
*cAMP (↑)*  
*GDP*  
*GTP*  
*X*  
*ADP-ribose*  
*cell surface*  
*Gut lumen*  
*Cholera toxin*  
*α₁ subunit hydrolyses Nicotinamide*  
*GM₁*  
*α₁ subunit*  
*GTPase*  
*GTP*  
*ADP-ribose*  
*Adenylate cyclase*  
*µاخت_ام_نا*  
*

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**Vibrio cholerae colonizing human epithelial cells**

~2h, speeded up x300.

As more bacteria adhere to the host cell surface and secrete cholera toxin, the host cells begin to pump out water and salt due to constitutive activation of adenylate cyclase. In the intestine, the water is pumped into the intestinal lumen, resulting in watery diarrhoea.

*Julie Theriot & Claudette Gardel*

*http://cmgm.stanford.edu/theriot/movies.html*
Oral rehydration therapy *

* water, electrolytes and glucose: efficient use of available transporters