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UNIVERSITY OF LIVERPOOL

Year 1 MBChB –
Gastrointestinal system

Gut fluid balance - Intestinal secretion and absorption

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Learning Outcomes:

- LO1 - Describe the secretion and absorption of water along the GI tract
- LO2 - Define the role of the small and large bowel in maintaining fluid balance
- LO3 - Describe factors which influence absorption and secretion in the intestine to maintain overall daily gut fluid balance
- LO4 - Describe and explain the cellular mechanisms of intestinal absorption and secretion of water and electrolytes
- LO5 - Define the different mechanisms leading to malabsorption of water and electrolytes resulting in diarrhoea (excessive loss of water in the faeces)
- LO6 - Be able to understand why ingestion of glucose-electrolyte solution (Oral rehydration therapy) has proven to be effective at reducing fluid loss in patients with excessive diarrhoea (e.g. Cholera)

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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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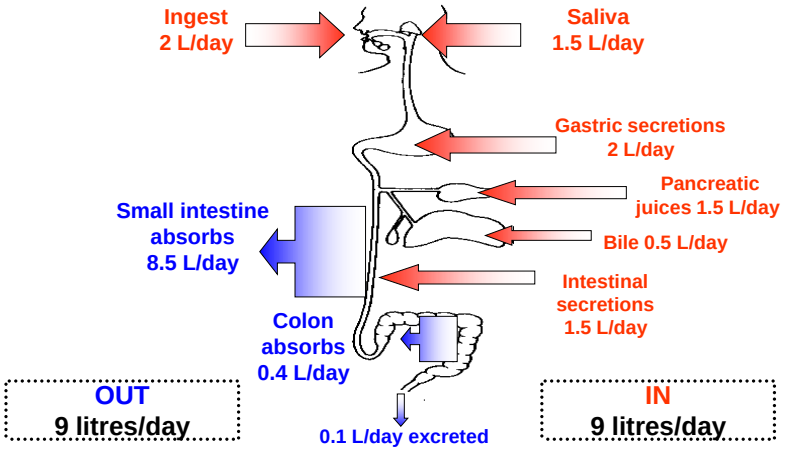
Overall daily gut fluid balance



OUT
9 litres/day

IN
9 litres/day

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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

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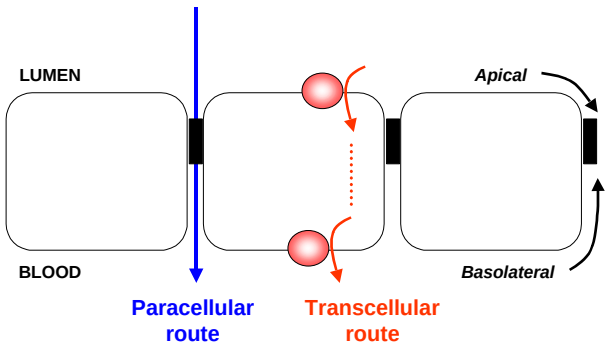
Membrane domains and transport routes



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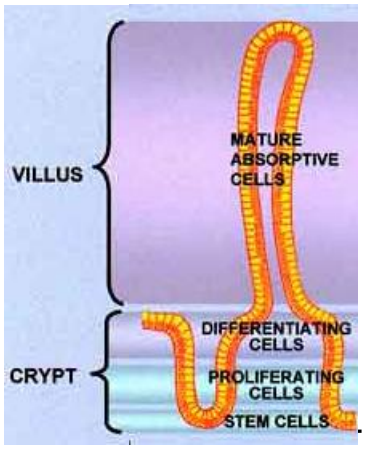
Absorption in the villus: secretion the crypt

net absorption

net secretion



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Factors affecting absorption and secretion

Number and state of enterocytes

Blood & lymph flows

Nutrient intake

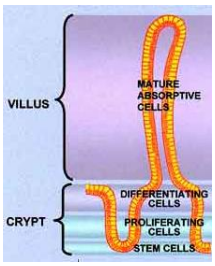
Gastric motility

Intestinal motility

Hormonal

Paracrine

Neural



Absorption

Secretion

Excretion

Luminal factors
Irritants,
Bacterial toxins,
Bile

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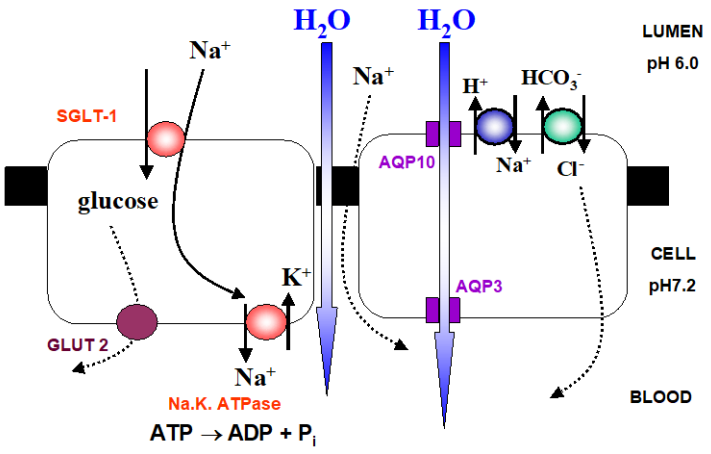
Na^+-coupled nutrient absorption

.....energy-dependent transport



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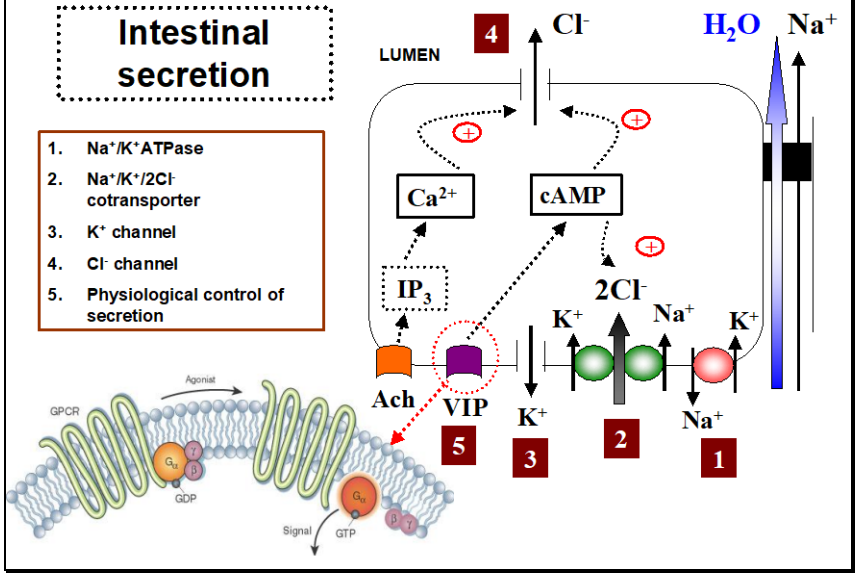
Intestinal secretion

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



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Diarrhoeal disease

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

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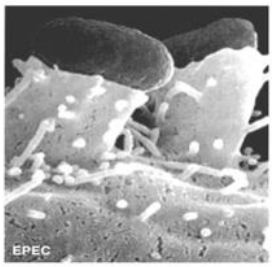
TRAVELLERS DIARRHOEA

BACTERIA	VIRUSES	PARASITES
Vibrio cholerae (F/W) Campylobacter jejuni (F/W) Clostridium difficile (F) Clostridium botulinum (F) Yersinia sp. (F) Shigella sp. (F) Salmonella sp. (F) E. coli (F)	Norwalk (F/W) Hepatitis A (F) Rotavirus (W)	Entamoeba histolytica (F/W) Giardia intestinalis (W) Cryptosporidium sp. (W)

F = food borne,
W = water borne



E.coli

Salmonella sp.

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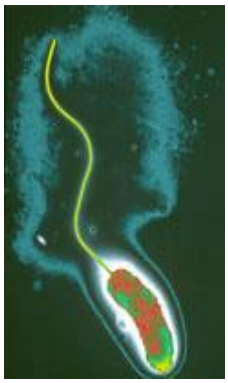
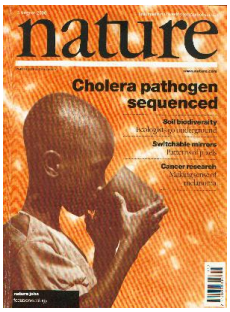
Cholera and cholera toxin

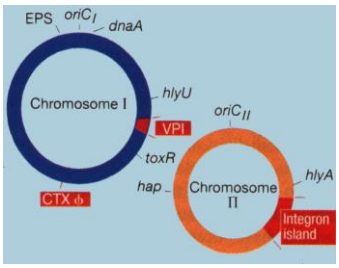


Vibrio cholerae-
a comma shaped bacterium

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

John F. Heidelberg et al., 3 August 2000 Nature **406**, 477-482





(I) 2.96 Megabases (II) 1.07 Mb

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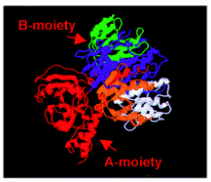
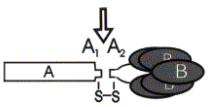
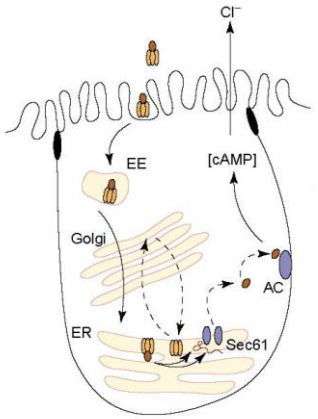
Cholera toxin and transport into intestinal cells

B Cholera







Sandvig & van Deurs. FEBS Lett. 2002: 529; 49-53

Lencer & Tsai. TIBS: 2003; 28; 639-45

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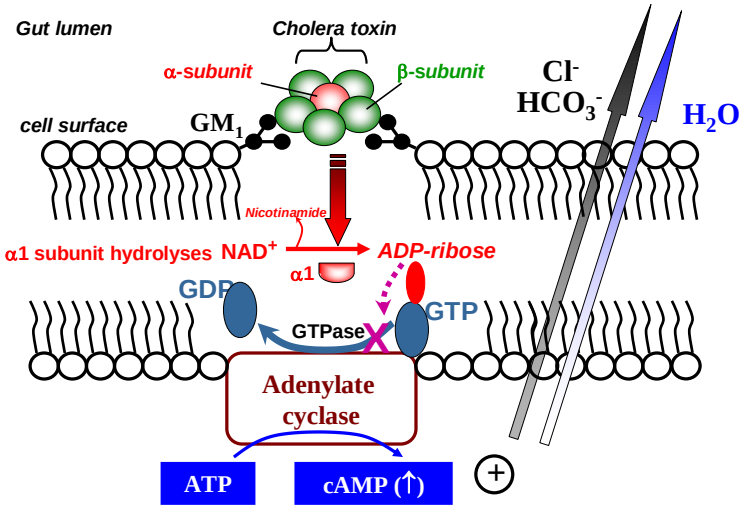
Cholera toxin-induced intestinal secretion



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Vibrio cholerae colonizing human epithelial cells

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.

Rice water stool

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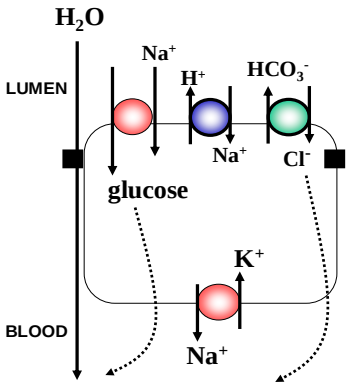
Oral rehydration therapy *



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