

GI Physiology Module: Absorption of Water and Ions

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Physiology Education Series

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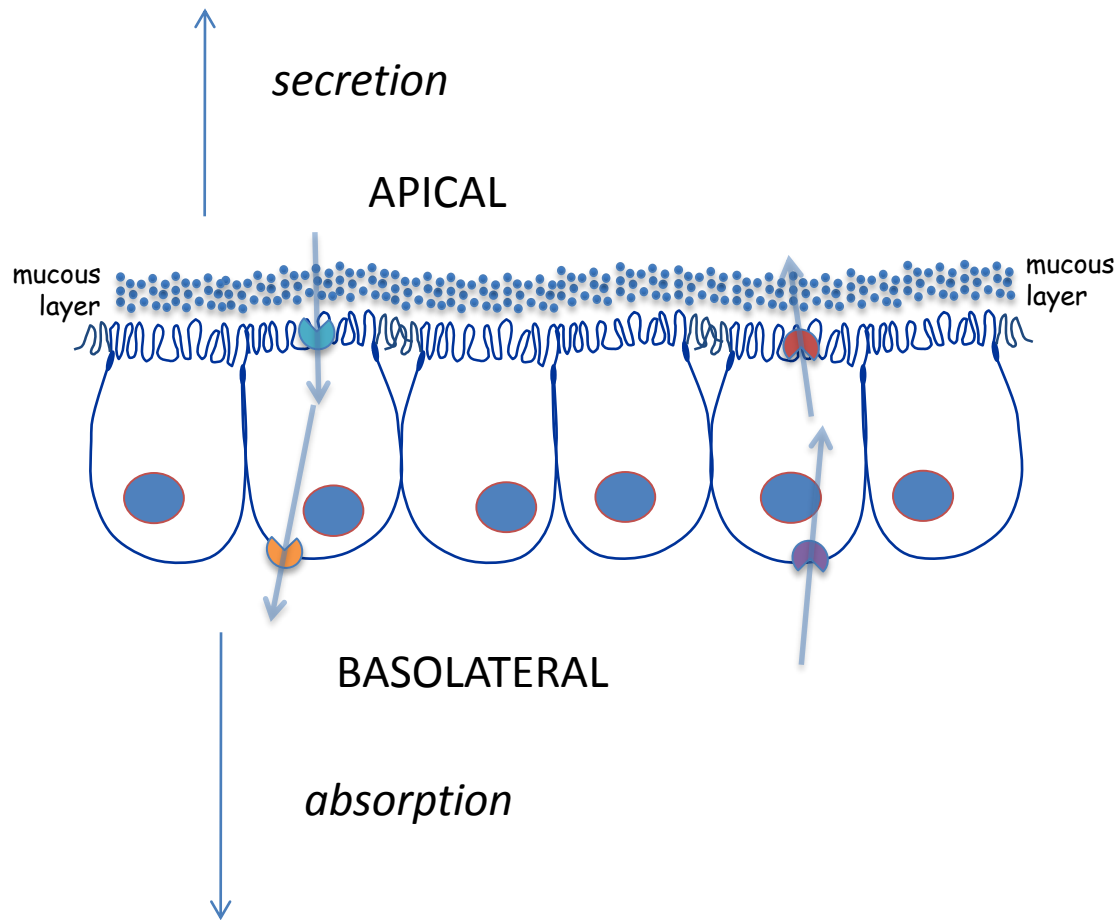
Objectives

1. Understand the mechanisms of intestinal transport of ions
2. Know the location of transport and secretion of ions
3. Understand the absorption of vitamins and minerals
4. Understand the phenomenon of changes in nutrient absorption with luminal nutrient concentration
5. Mechanisms of diarrhea
6. Identify signs and symptoms of excess vitamin and mineral absorption and signs and symptoms of deficiency

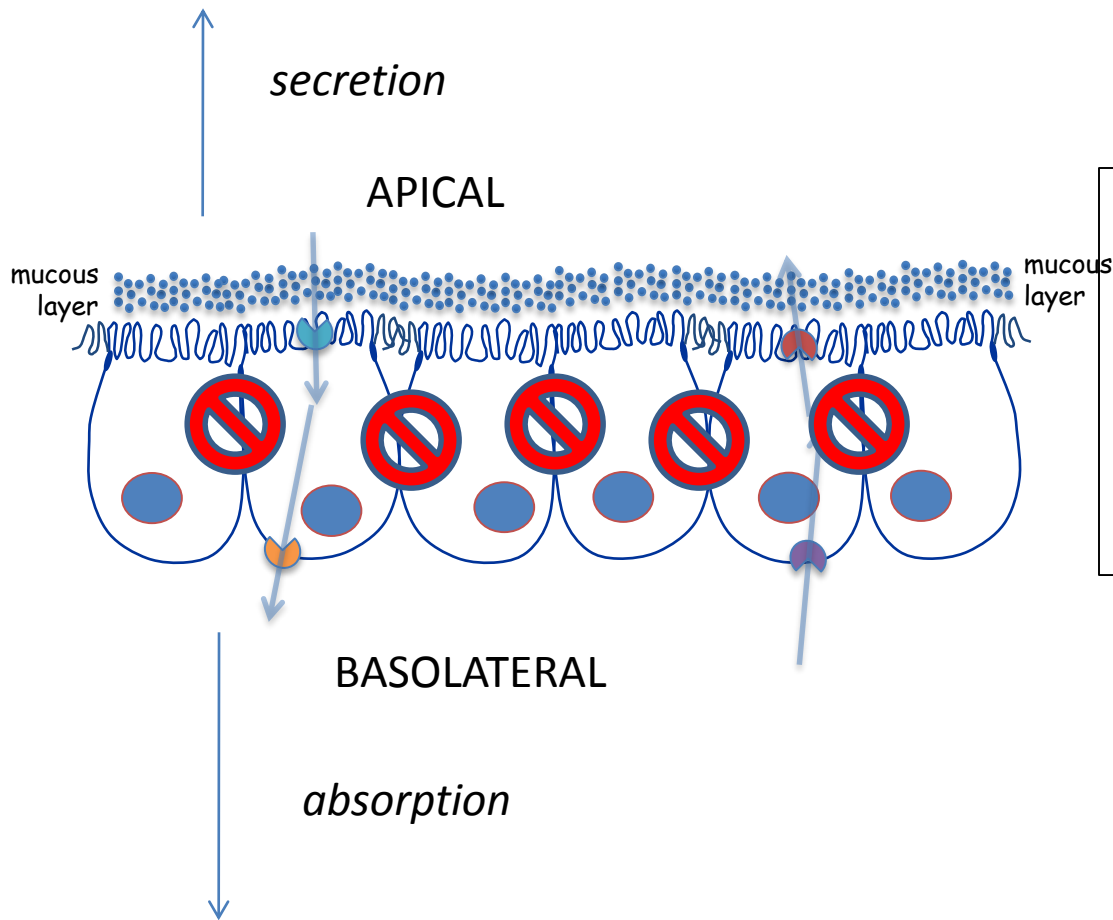
Key Concepts: GI Fluid and Electrolyte Balance

- Regulation of fluid transport in the gut is critical for normal intestinal function
- Large amounts of fluid are secreted into and absorbed from the gut daily
- Because water follows an osmotic gradient, the understanding of electrolyte transit is key to understanding intestinal fluid balance in health and disease

Intestinal Epithelial Cells as Gatekeepers for Ion and Fluid Movement

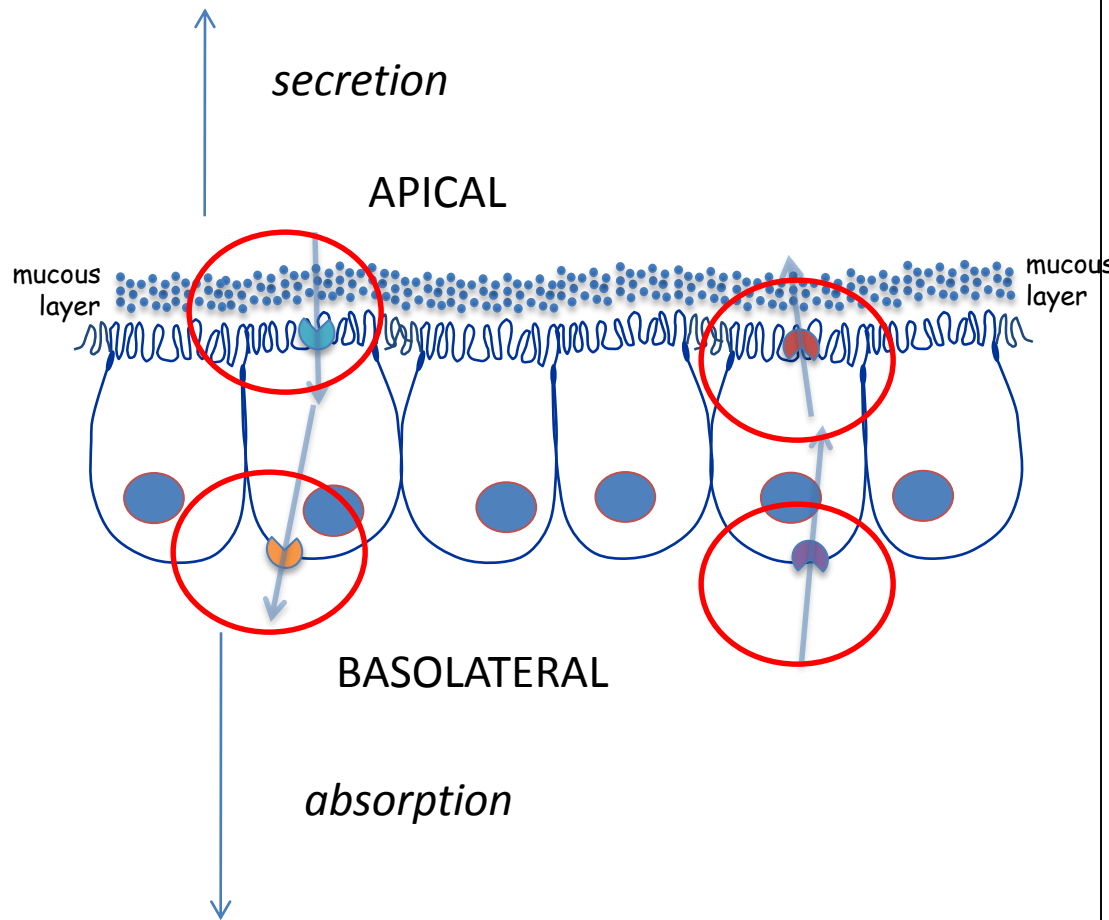


Tight Junctions



Intracellular TIGHT JUNCTIONS restrict passive flow of solutes after secretion or absorption

Transepithelial Transport: Transcellular

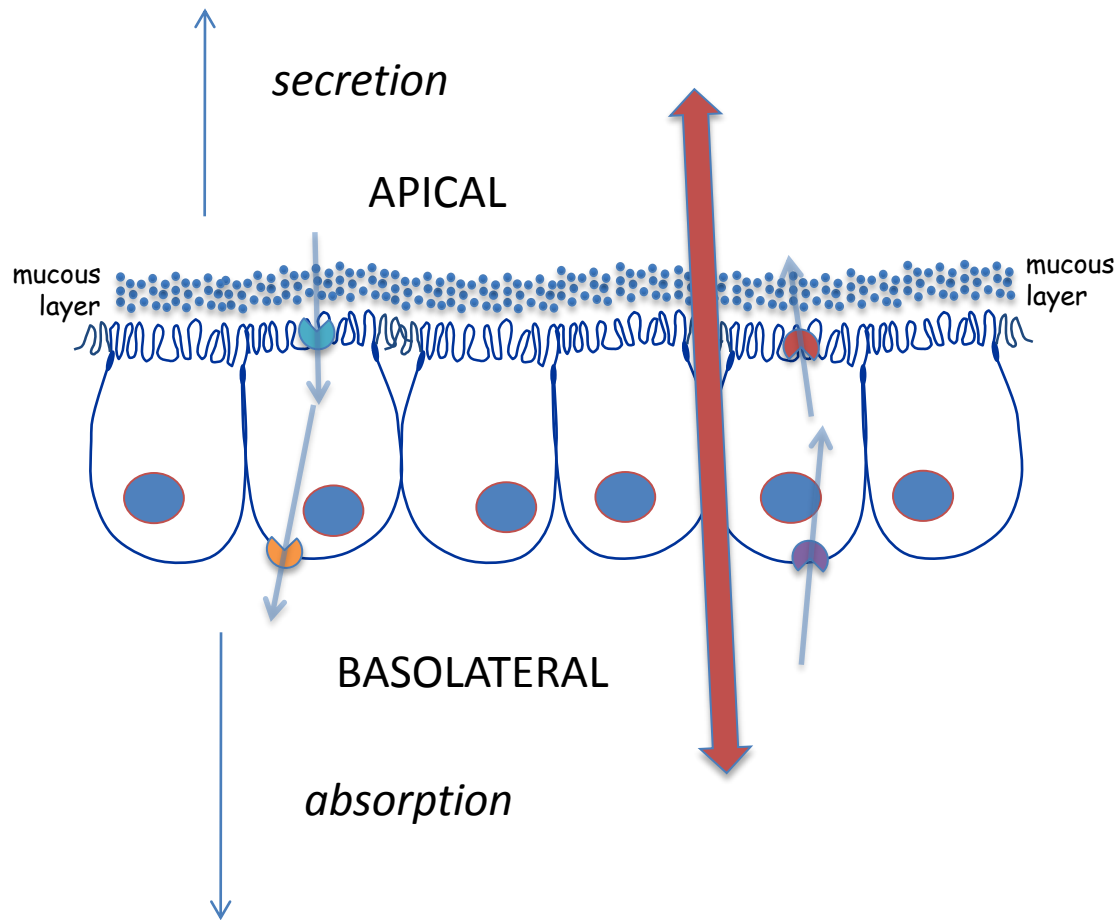


- Employs membrane transporters to move molecules and water through cells
- May work against electrochemical gradient
 - Requires energy/ATP
- Subject to transcriptional and posttranscriptional regulation

Mechanisms of Transcellular Transport

	Mechanism	Example
Primary Active Transport	Utilizes energy (ATP) to drive ion against electrochemical gradient	Na-ATPase
Secondary Active Transport	Co-Transport of molecules with (ATP-driven) ion transport	Na-GLUC cotransporter
Facilitated Diffusion	Specific transporters facilitate passive transport across epithelial layer	Glut-5 (fructose)

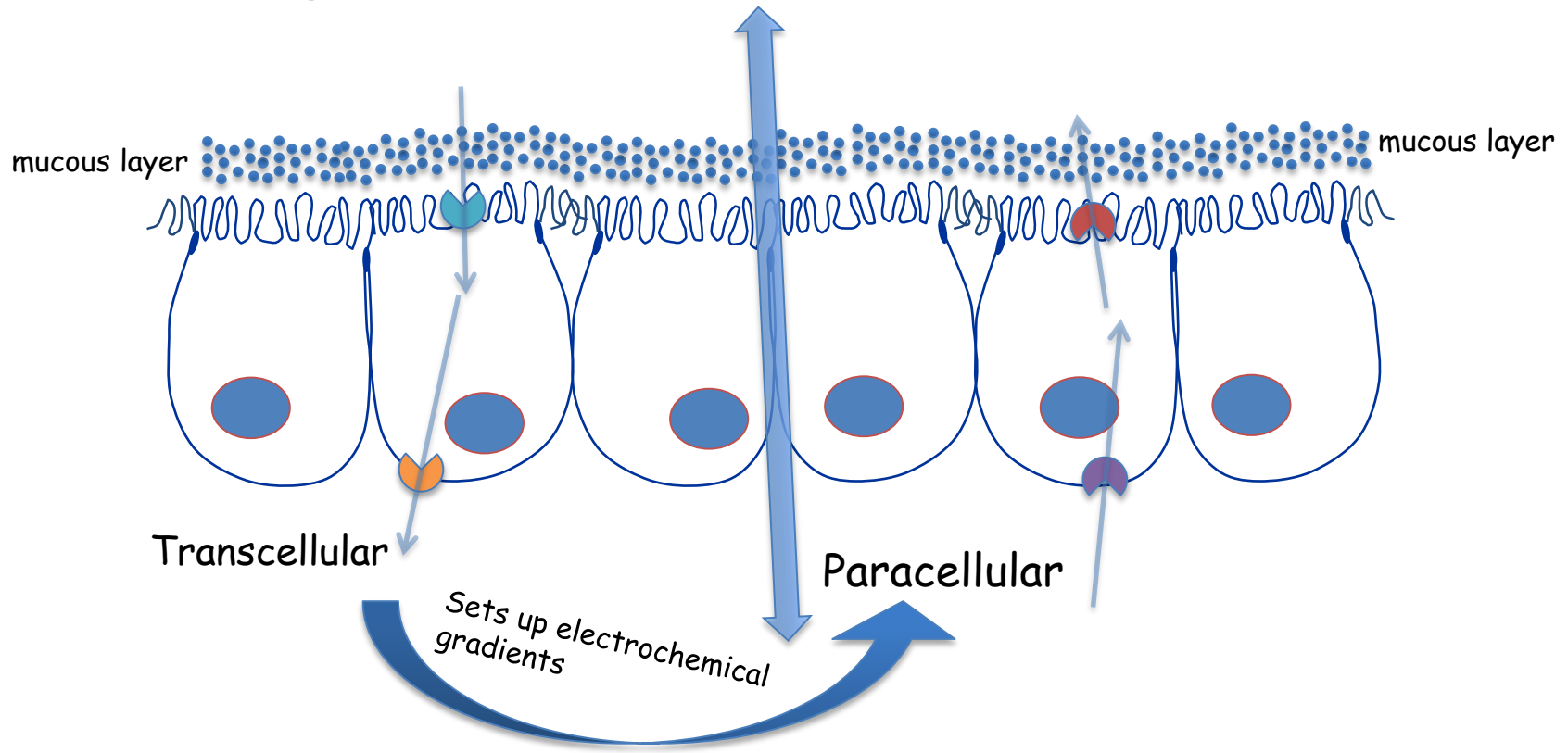
Transepithelial Transport: Paracellular



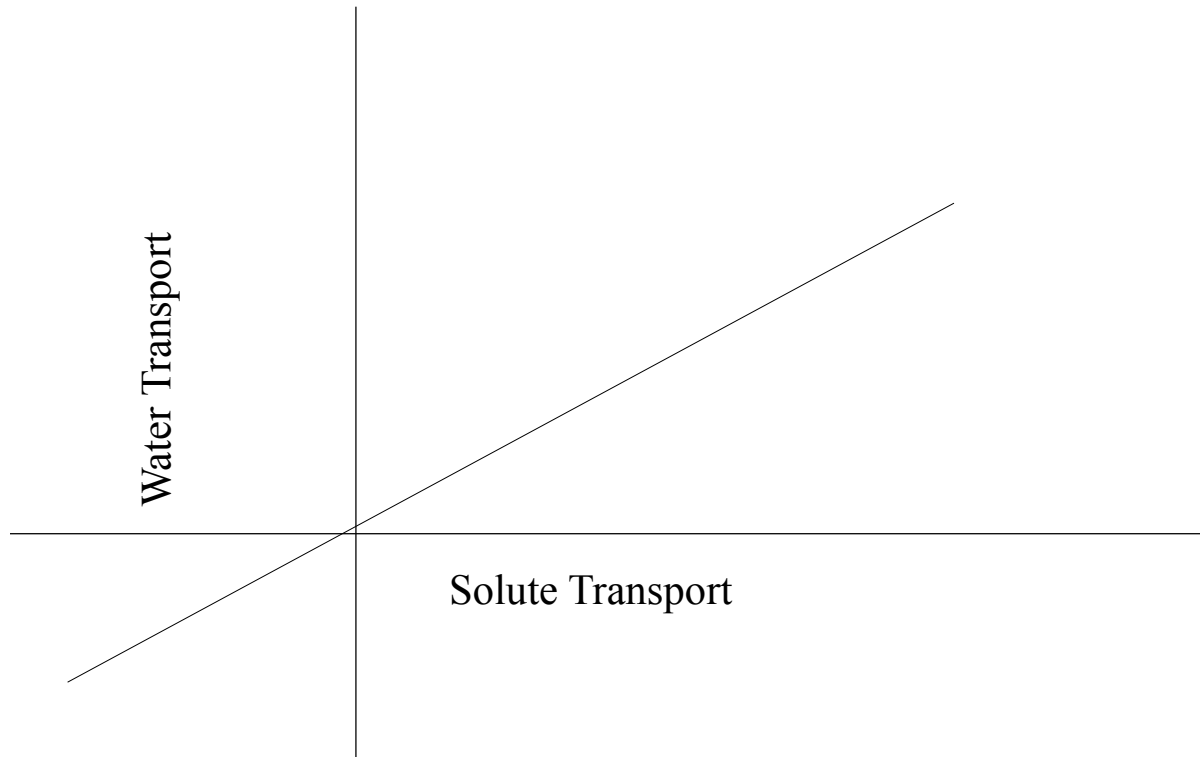
- Movement of solutes and water through tight junctions
- Dictated primarily by electrochemical gradient

Transepithelial Transport: Summary

MEMBRANE TRANSPORT PROTEINS drive
TRANSCELLULAR transport of ions, which
sets up ELECTROCHEMICAL GRADIENT to
allow PARACELLULAR transport of fluid
through TIGHT JUNCTIONS

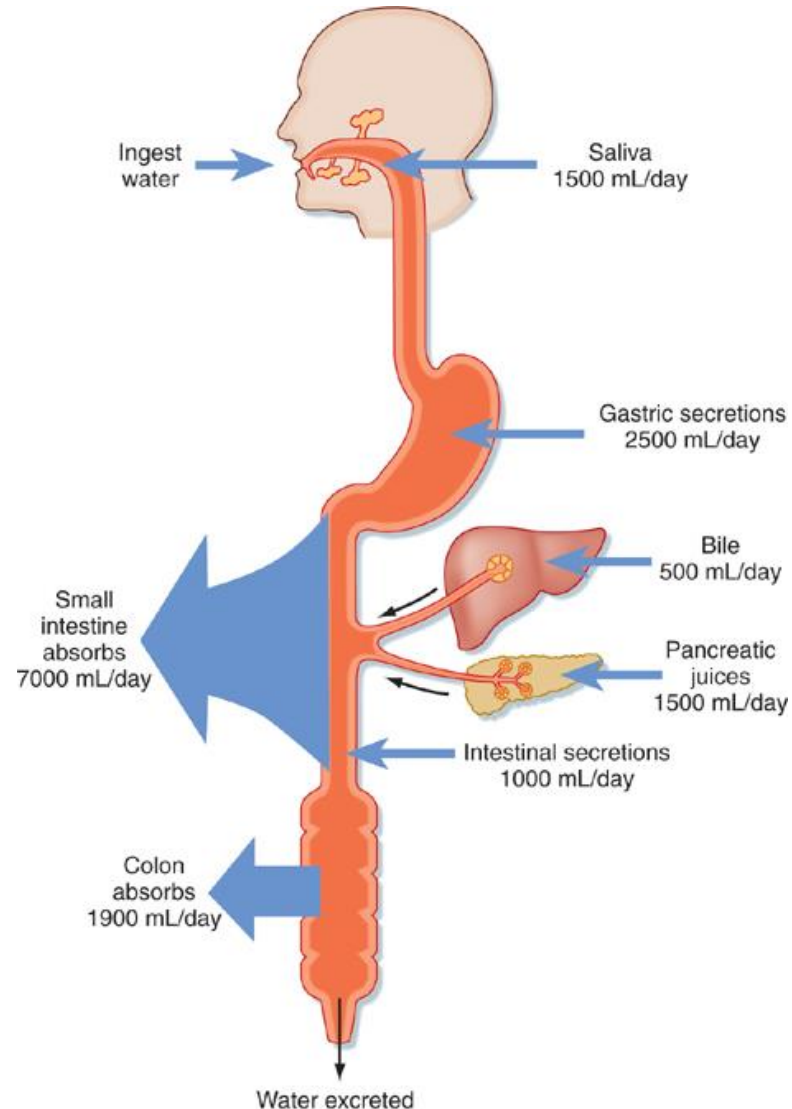


Overview of fluid movement in the GI tract



Overview of fluid movement in the GI tract

NET Fluid
entering
bowel: 8.5 L
/ day



Koeppen and Stanton: Berne & Levy Physiology, 6th Edition.
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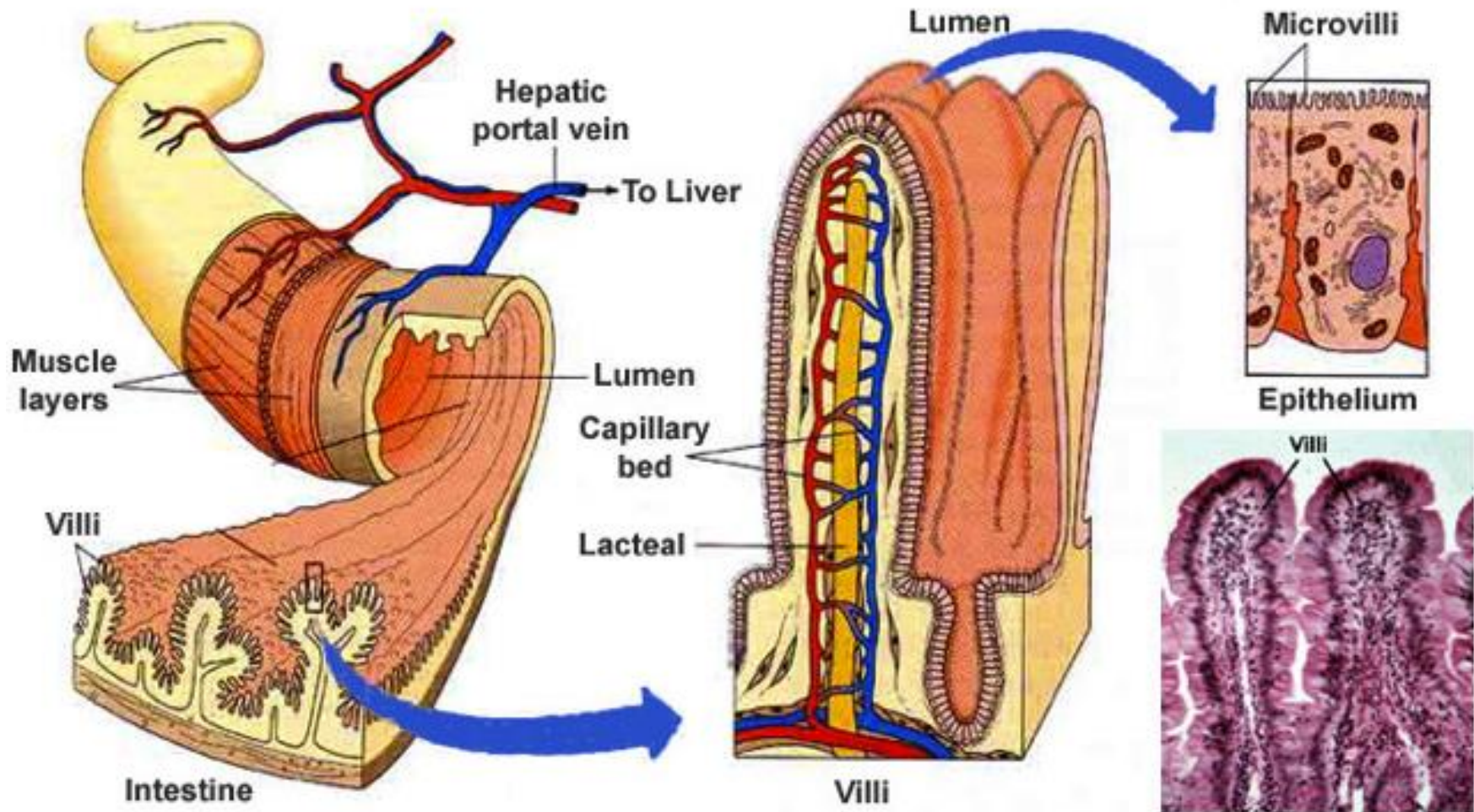
NET Fluid
reabsorbed
by bowel:
8.4 L / day

NET Fluid
loss via
stool: 100
mL / day

Anatomic Considerations

- Based on the functional structure of the villi and crypts, simultaneous secretion and absorption occur at all levels of the intestine
- Based on surface amplification of the intestine, surface area (and function) increase by 600 FOLD
- The small intestine and colon have separate functions, primarily related to expression and localization of epithelial transport systems

Gut Surface Area Amplification



Location – Based Specialization within the Gut

Proximal Small Intestine

Colon



Tight Junctions more permeable

Tight Junctions less permeable

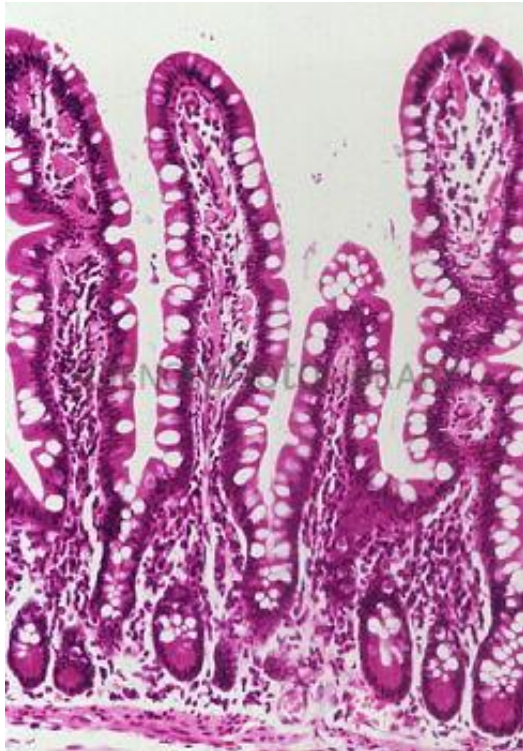
Absorption:

Nutrients
Vitamins
Minerals
Salt and Water

Absorption:

Sodium
Water

Simultaneous secretion and absorption occur in any segment of the intestine



Villi = Absorption

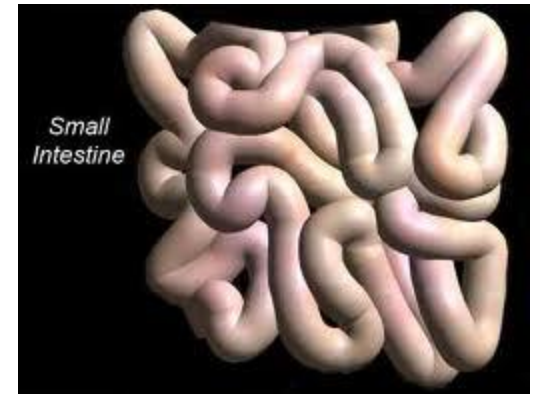
- Fluid absorption primarily depends on sodium transport
- Na may be Coupled with chloride, nutrients, bile acids, and other solutes

Crypt = Secretion

- Primarily follows Chloride and bicarbonate

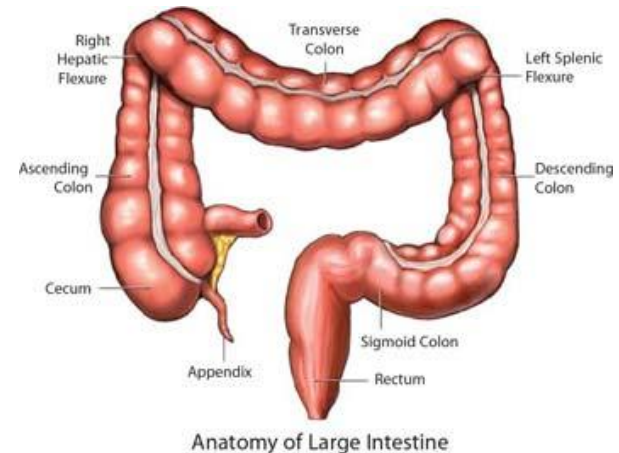
Small Intestinal Ion Transport Mechanisms

- Ion transport:
 - Bicarbonate secretion
 - Electroneutral NaCl absorption
 - Chloride Secretion
- Nutrient, mineral, other:
 - Sodium-coupled nutrient absorption
 - Proton-coupled nutrient absorption
 - Sodium-coupled bile acid absorption
 - Calcium absorption
 - Iron absorption



Colonic ion transport mechanisms

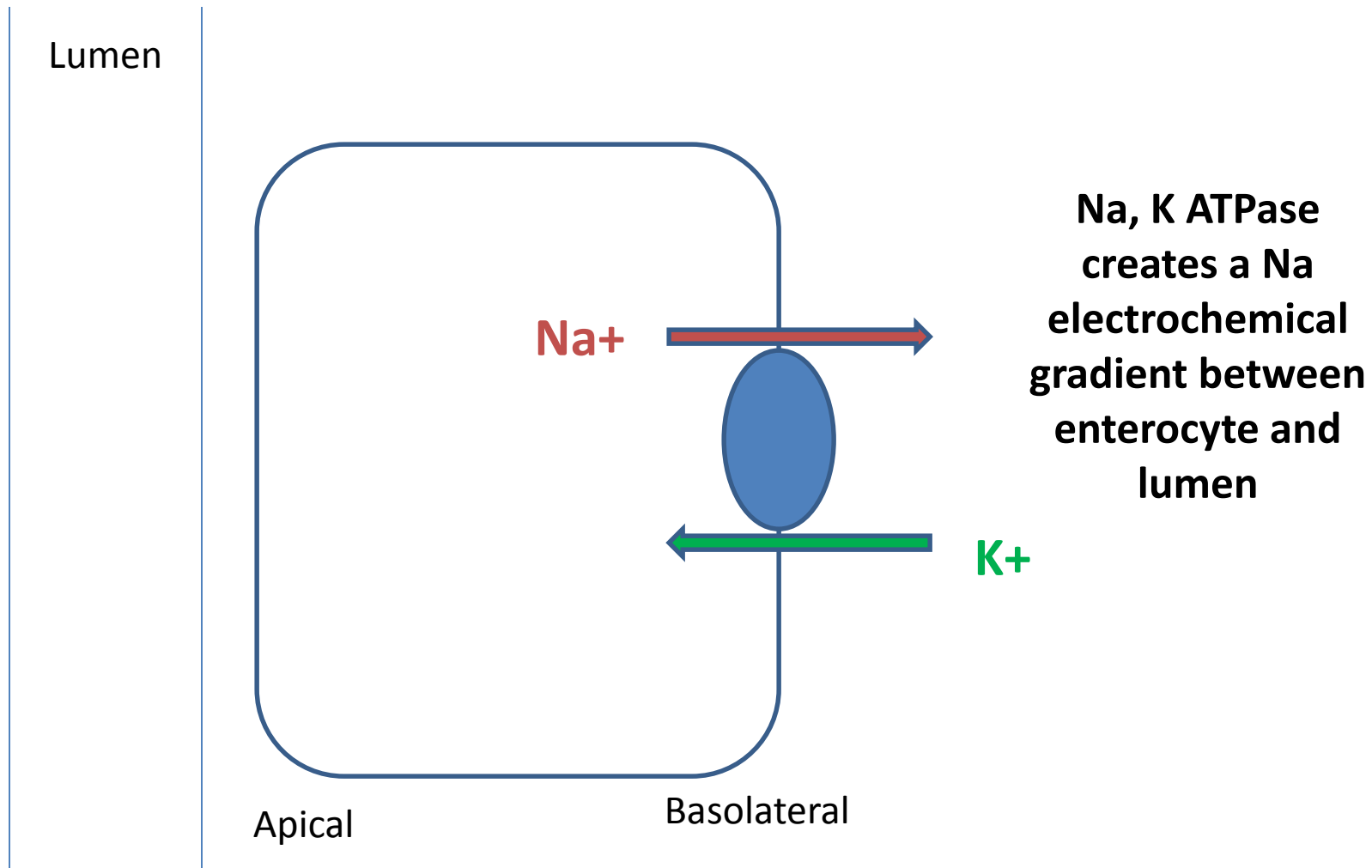
- Sodium Absorption:
 - Electrogenic sodium absorption
 - Electroneutral NaCl Absorption
- Potassium secretion and absorption
- Chloride secretion
- Short Chain fatty acid (SCFA) absorption



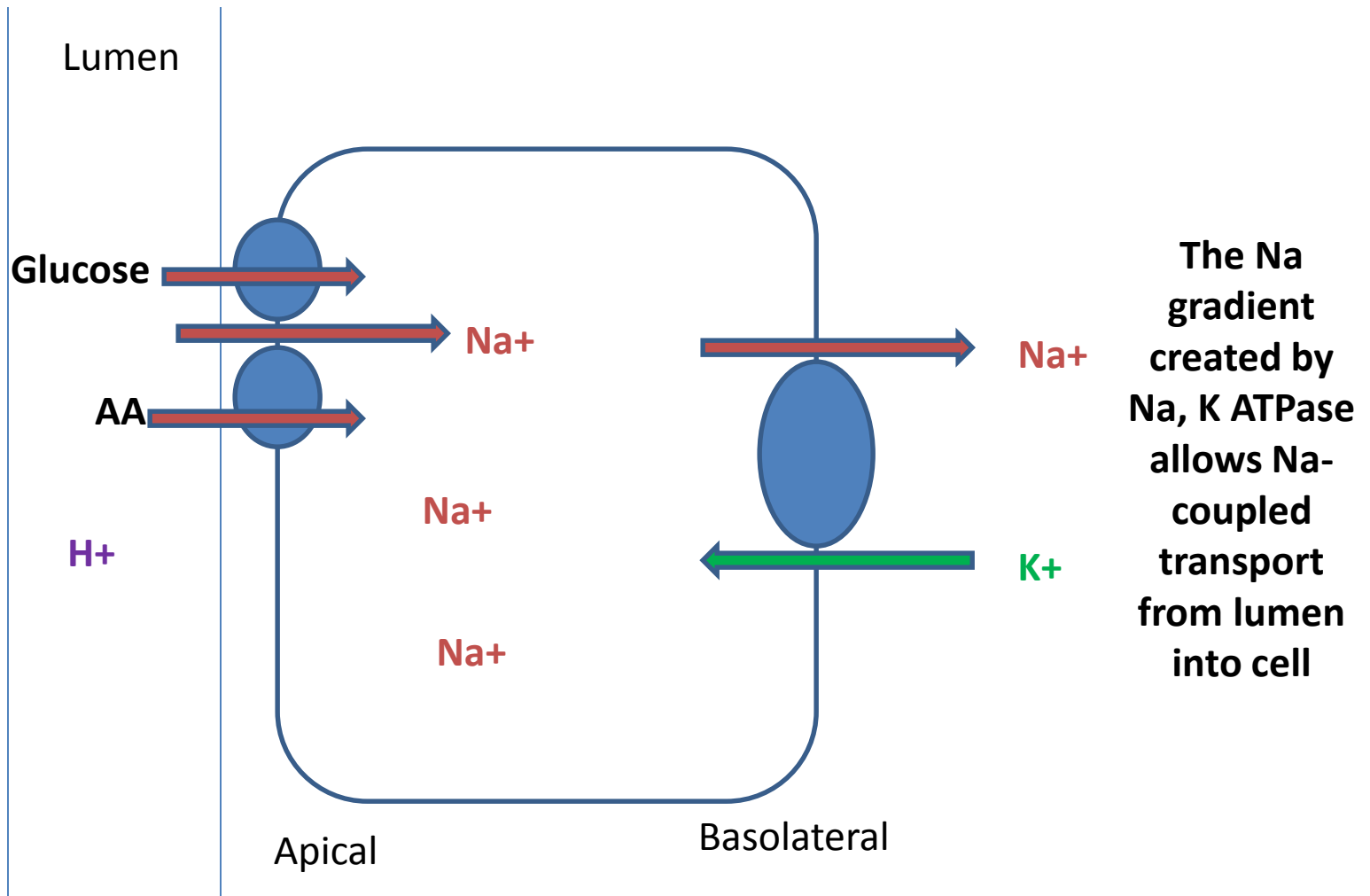
Cellular Basis of Transport

- Summarize key examples of transport proteins
- Examples:
 - Sodium
 - Chloride
 - bicarbonate
- Describe mechanisms of diarrhea

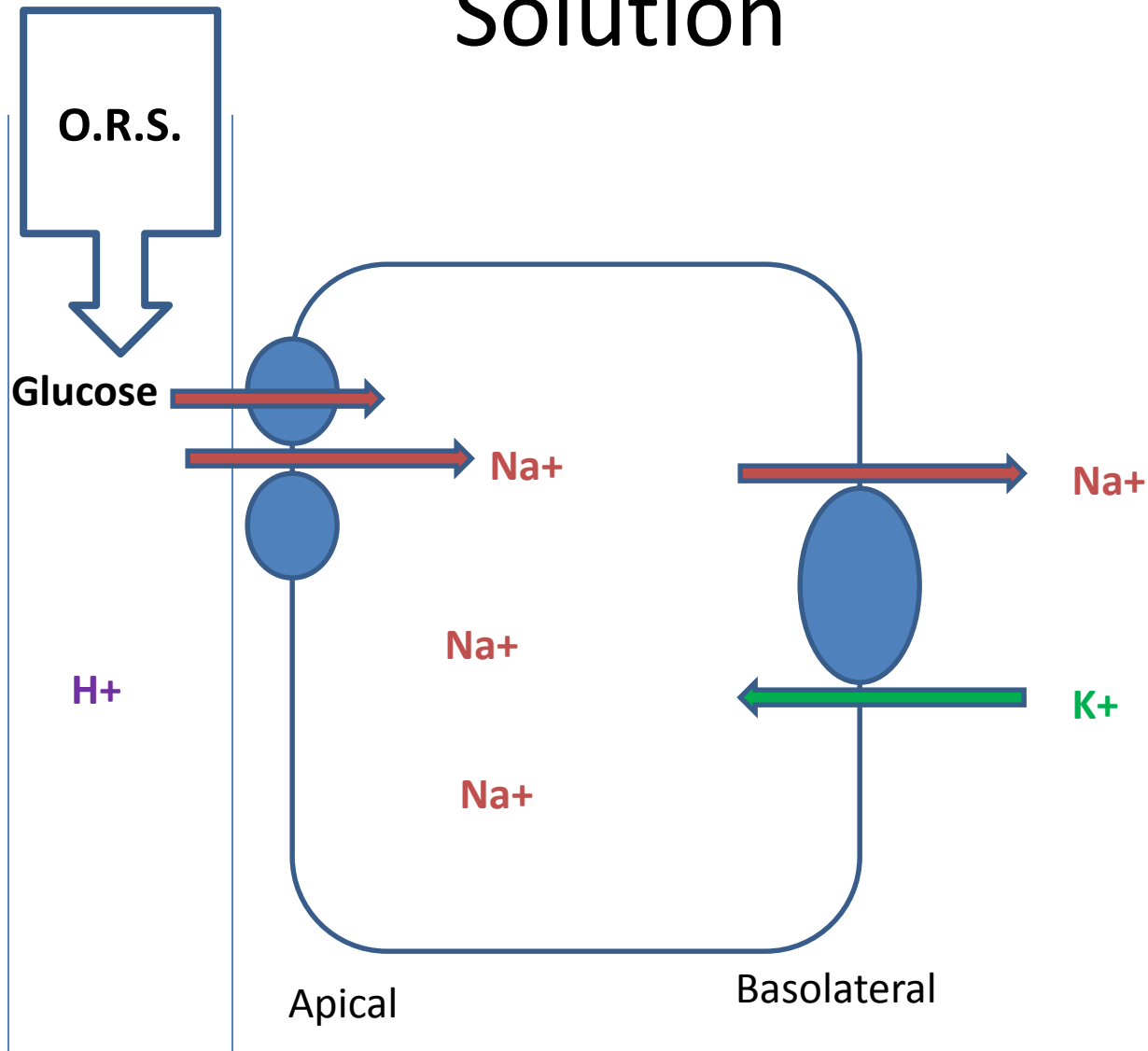
Concept 1: Na, K ATPase



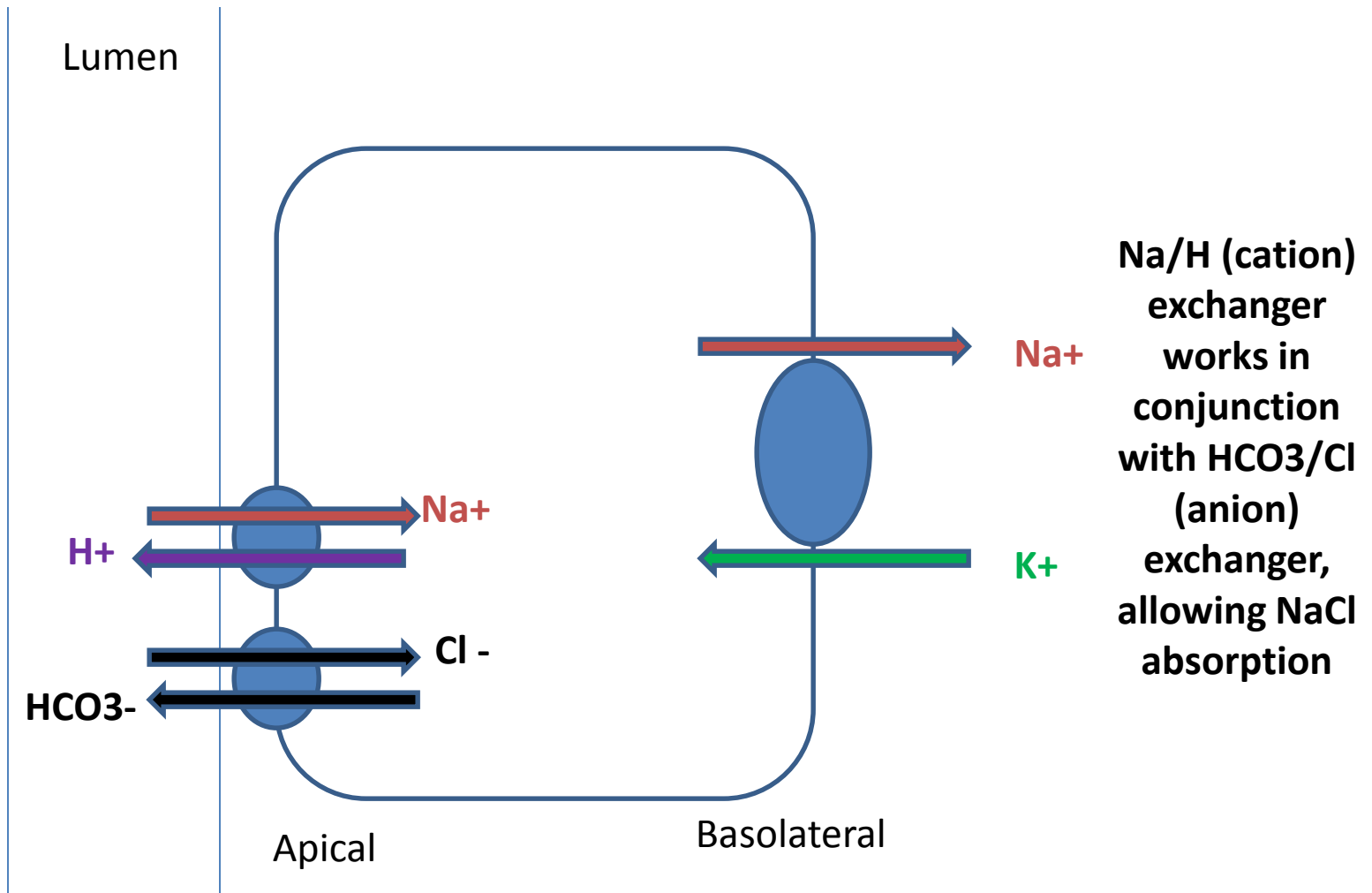
Concept 2: Na Coupled Transport



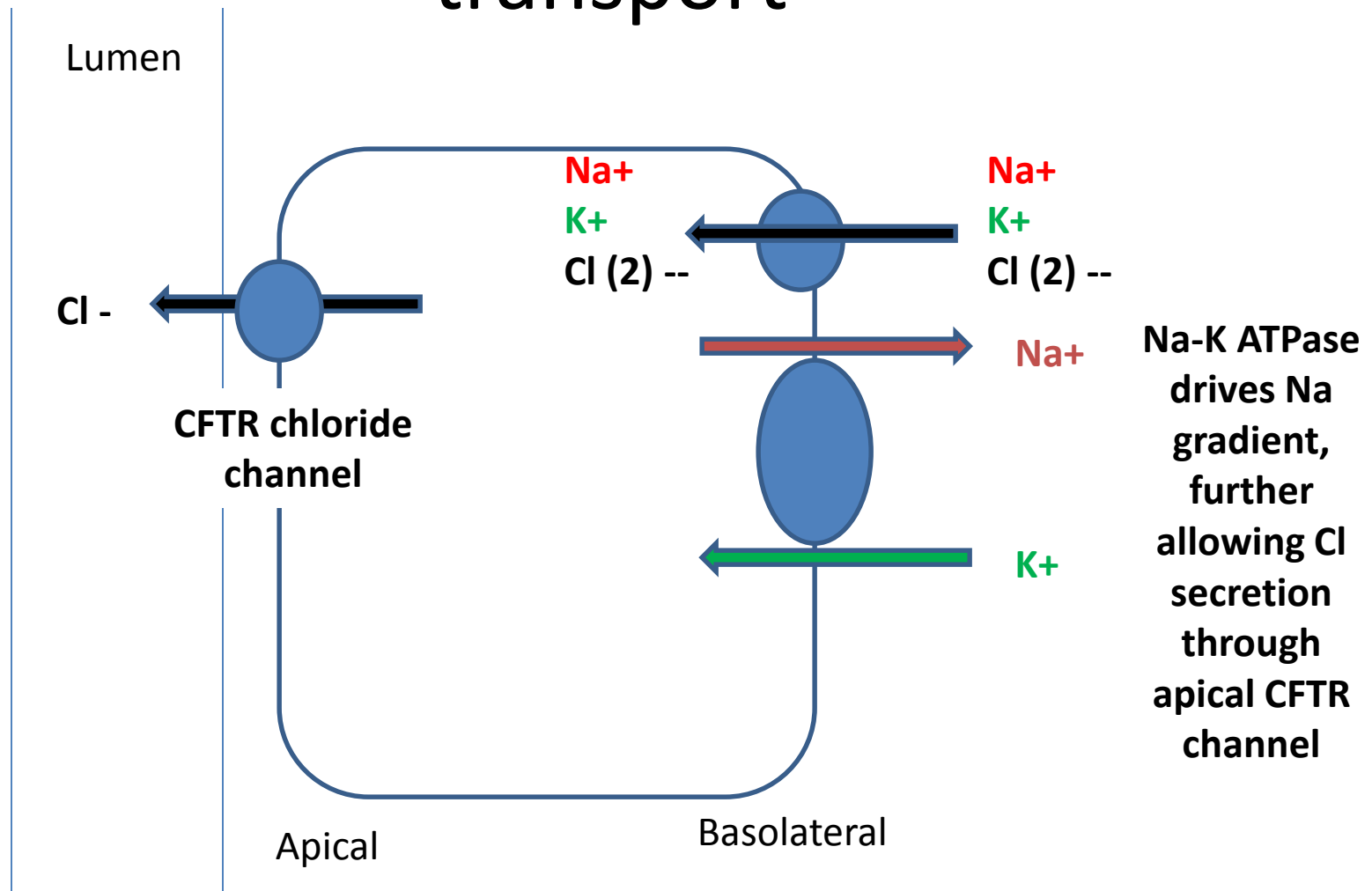
Clinical Application: Oral Rehydration Solution



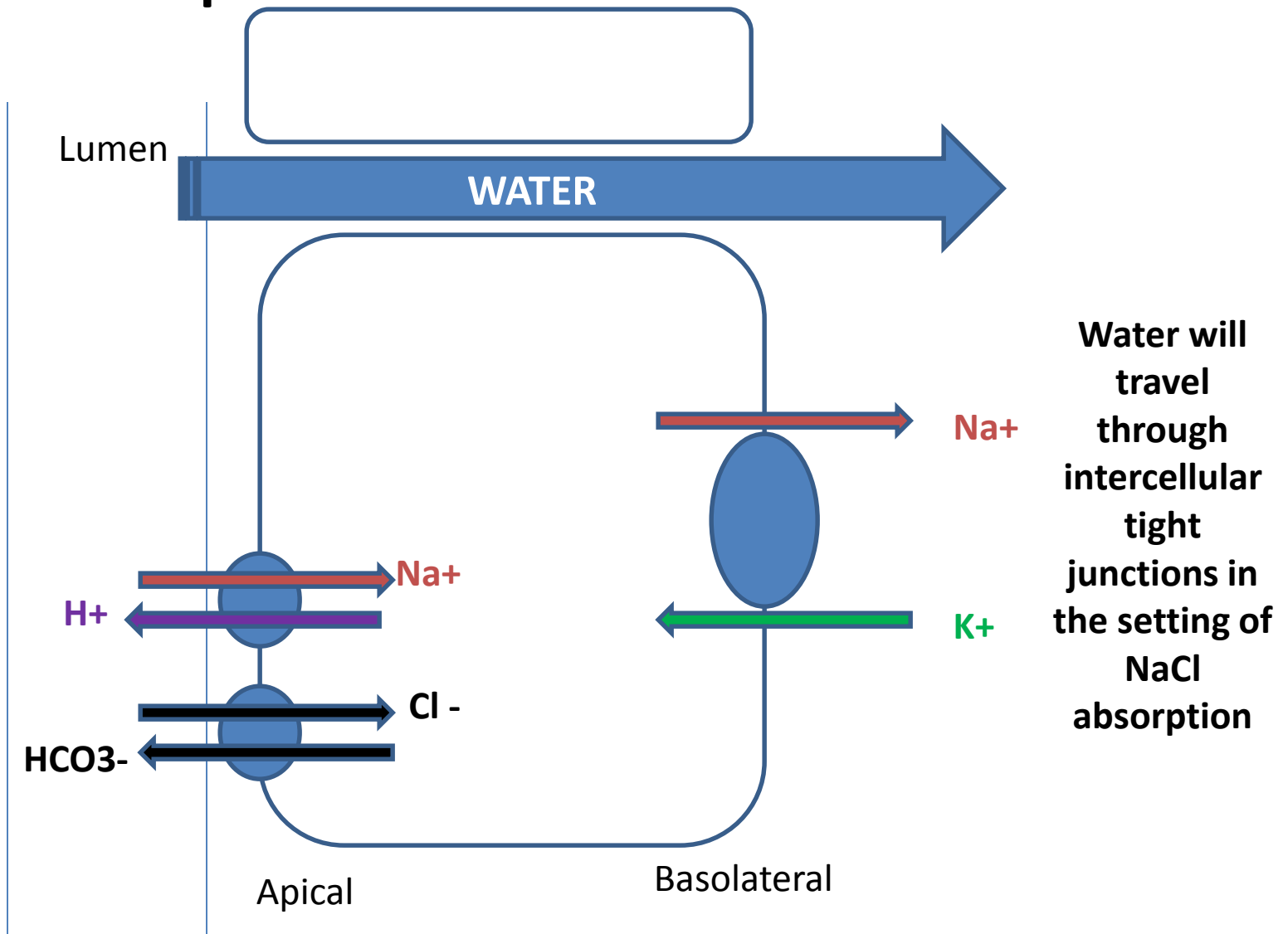
Concept 3: NaCl Co-transport is mediated by TWO transport proteins



Concept 4: Chloride secretion occurs in conjunction with basolateral Na, K, Cl transport

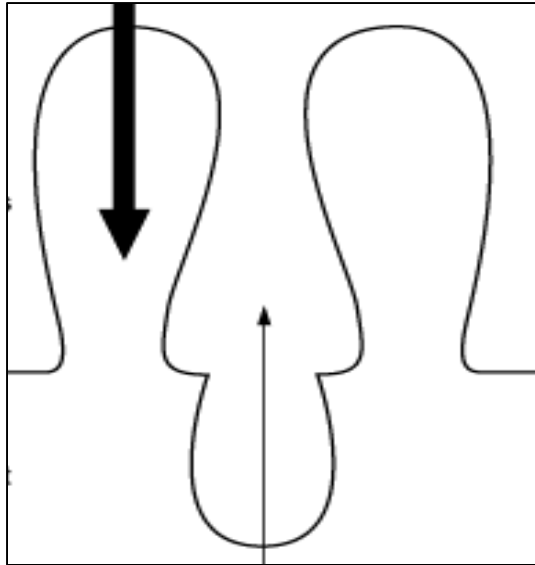


Concept 5: Water follows NaCl



Absorption and Secretion in Health versus Diarrheal States

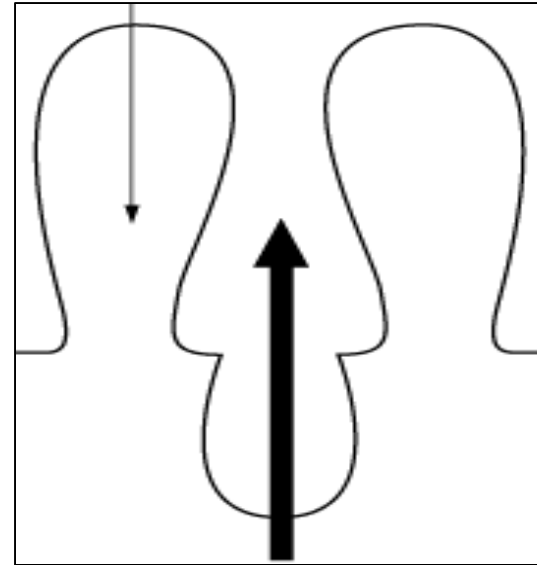
**NaCl,
Nutrient
absorption**



Chloride
secretion

Healthy

NaCl absorption



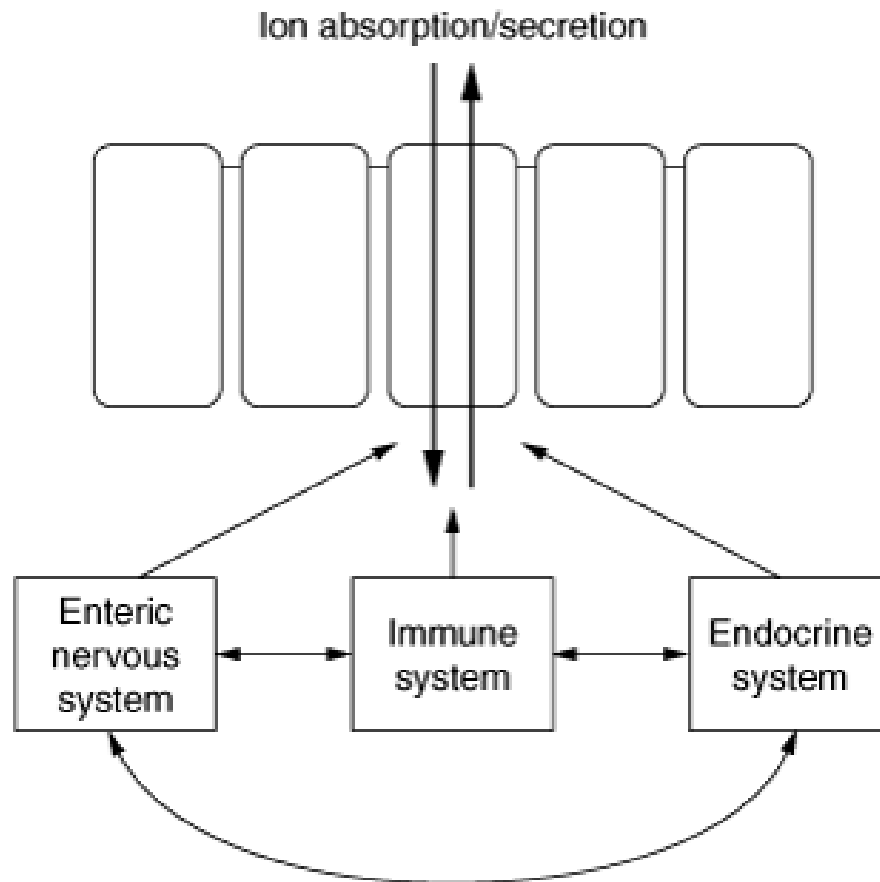
Chloride Secretion

Diarrhea

Adapted from: Barrett KE: Gastrointestinal Physiology.

www.accessmedicine.com

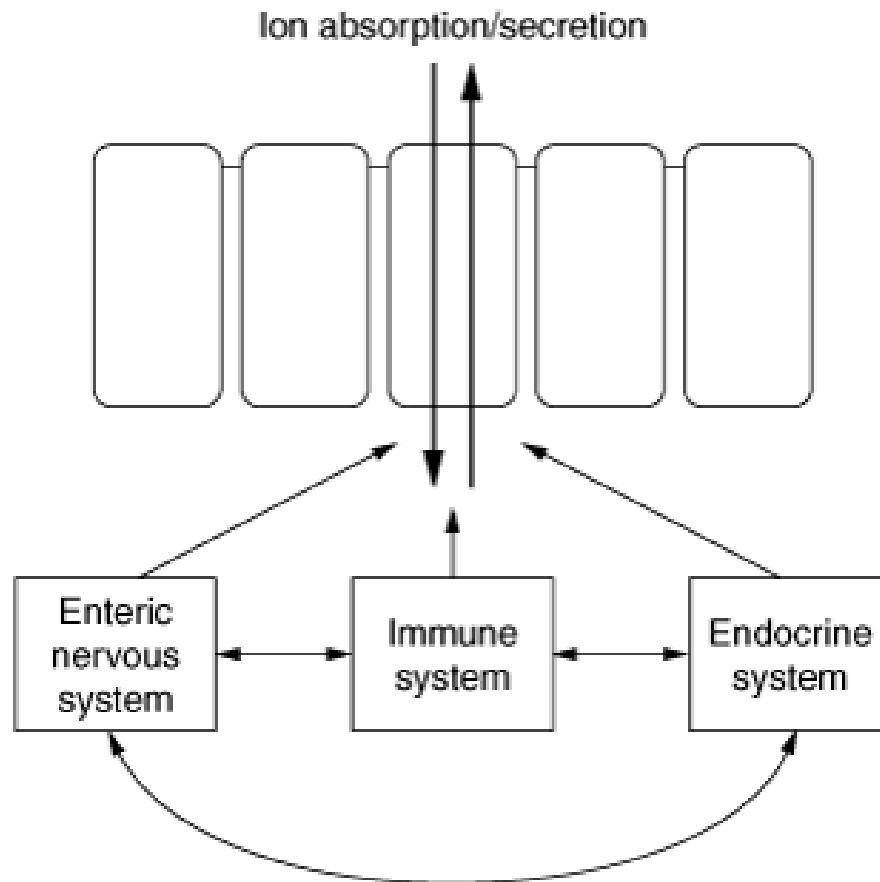
Multiple Systems Interact in Regulation of Ion Transport and Secretion



Source: Barrett KE: *Gastrointestinal Physiology*;
<http://www.accessmedicine.com>

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Multiple Systems Interact in Regulation of Ion Transport and Secretion

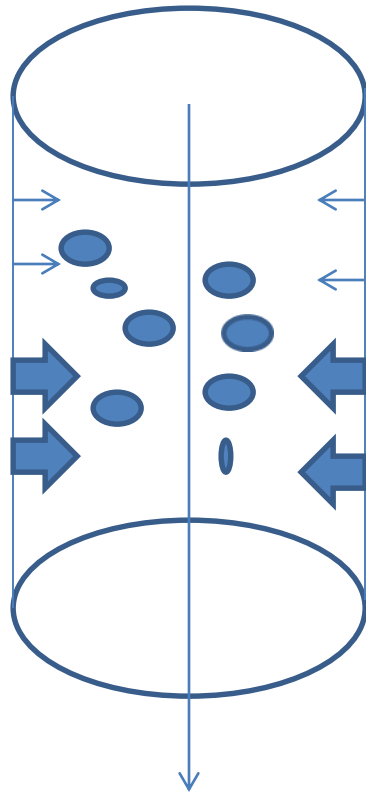


- Key to Pathophysiology: Infection, inflammation, gut hormones, and ENS chemical mediators all regulate transport mechanisms
- Repetitive or redundant pathways, including cAMP, cGMP, and Calcium activation

Source: Barrett KE: *Gastrointestinal Physiology*;
<http://www.accessmedicine.com>

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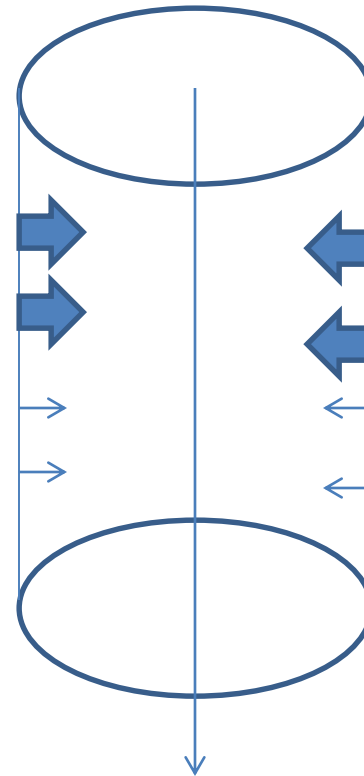
Mechanisms of Diarrhea: Osmotic versus Secretory



Osmotic Diarrhea:
Solute-driven water losses
more prominent in the colon

Small Intestine

Colon

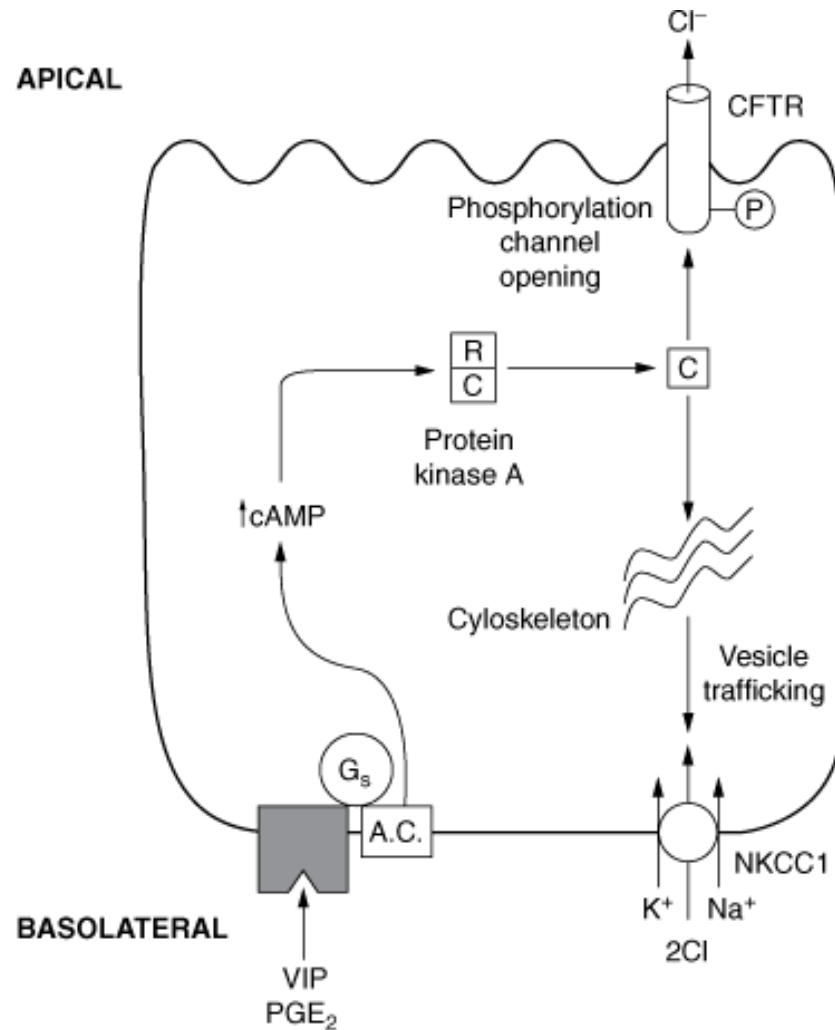


Secretory Diarrhea:
Crypt secretion leads to more prominent small
intestinal losses

Mechanisms of Bacterial Pathogens

Signal/pathway	Examples	Mechanism
cAMP	Cholera toxin Heat labile E Coli (ETEC)	Blocks NaCl absorption Stimulates anion secretion
cGMP	Heat stable E Coli (EAEC) Klebsiella	Blocks NaCl absorption Stimulate anion secretion
Ca++ / protein kinase C	C Difficile enterotoxin	
Pore forming toxin	Staph Aureus α -toxin C. perfringes	Pore formation along brush border membrane
Toxin blocking protein synthesis	EHEC Shiga toxin Shigella Shiga toxin	A1 subunit of toxin binds ribosome and interrupts protein synthesis
Toxin inducing protein synthesis	Staph toxin A EAggEC toxin	Upregulate proinflammatory cytokines
Toxin affecting cytoskeleton	Clostridium species	

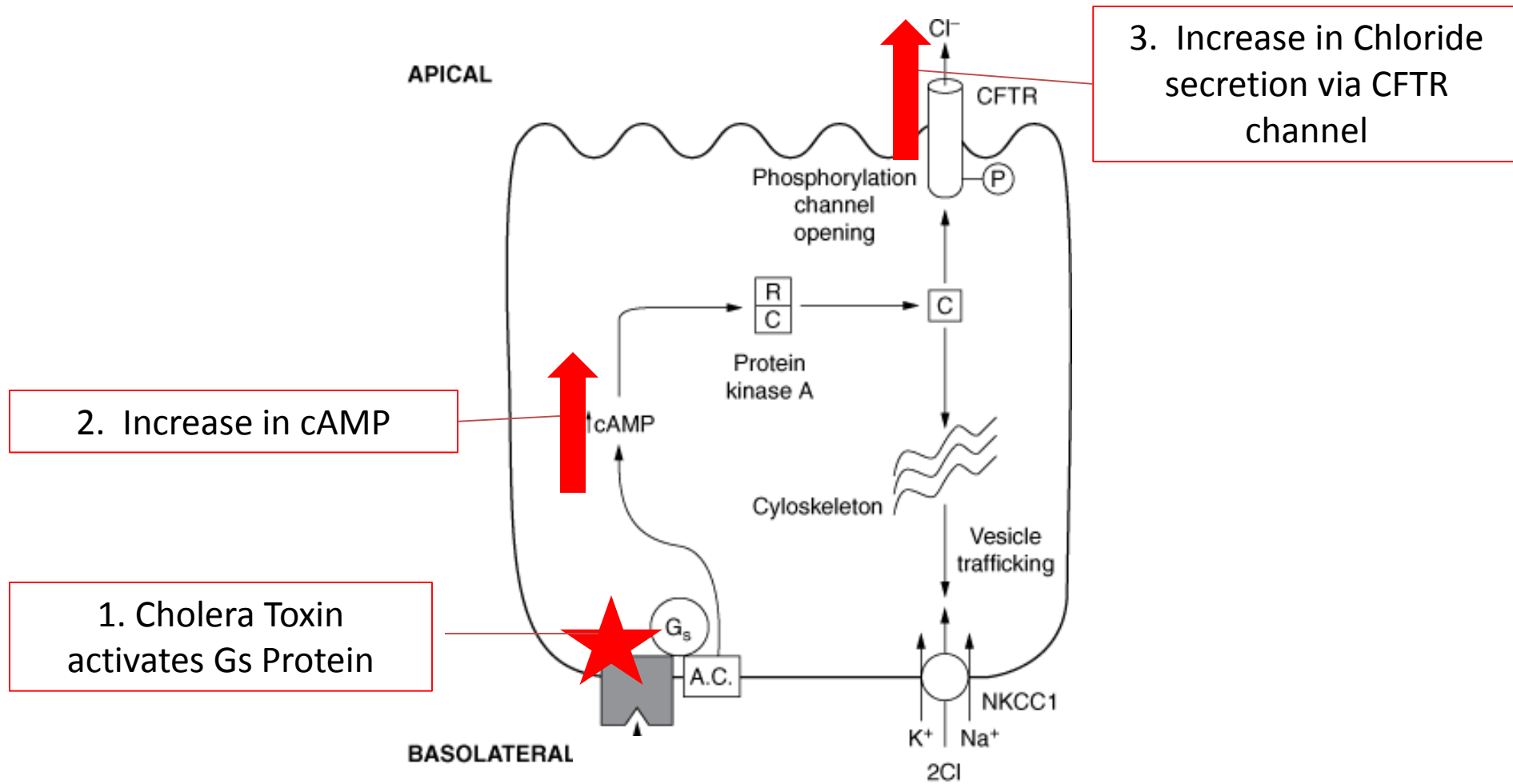
cAMP and Chloride secretion



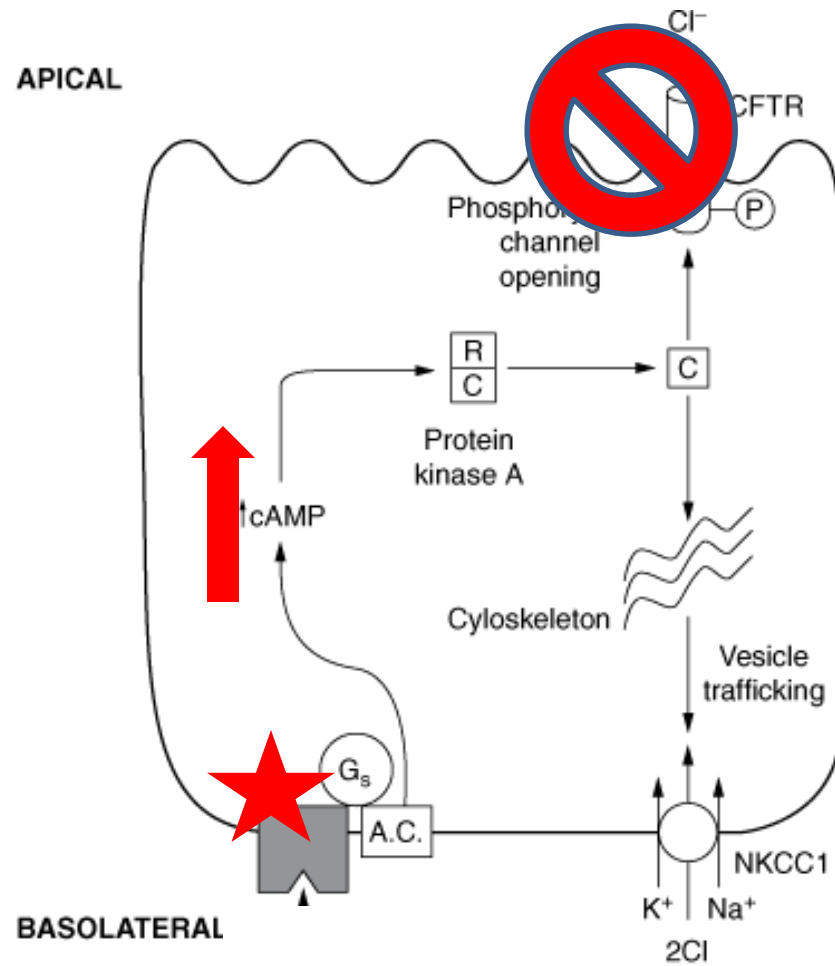
Adapted from: Barrett KE: Gastrointestinal Physiology.

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Pathogenesis of Cholera



CFTR mutation and cholera



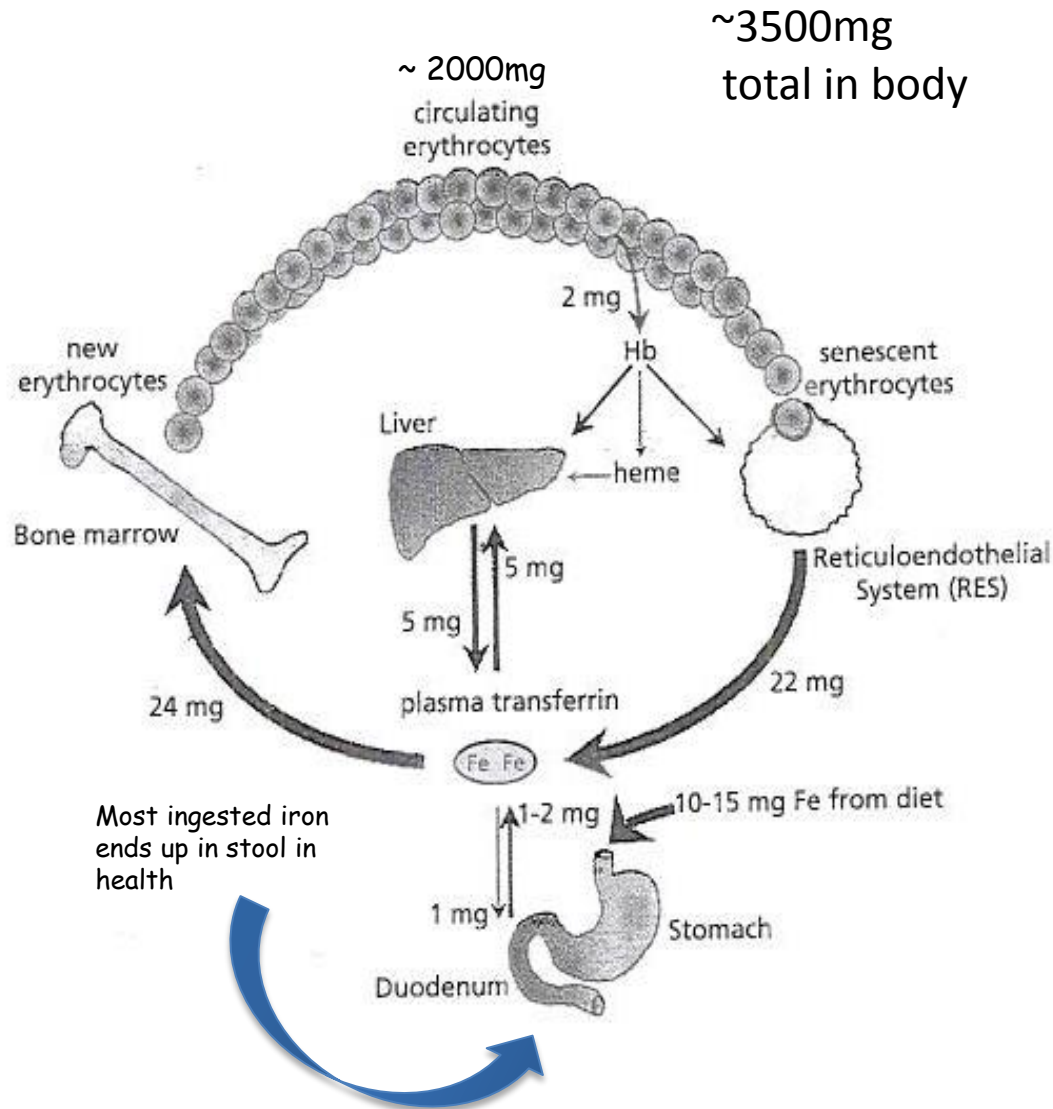
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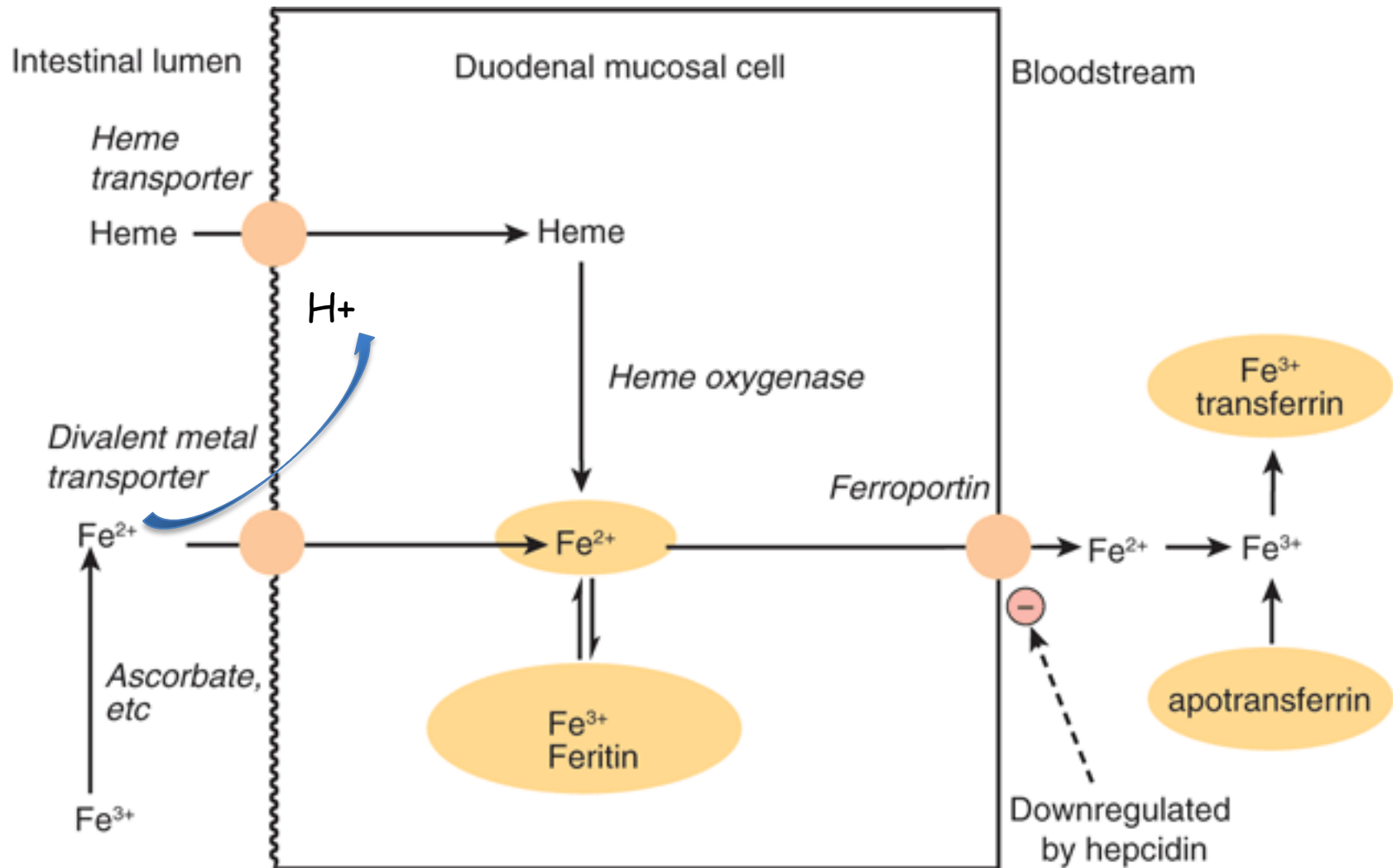
Minerals and Vitamins

- Iron
- Calcium
- Magnesium
- Water Soluble Vitamins
- Fat Soluble Vitamins

Iron Metabolism and Balance



Iron Absorption



Source: Murray RK, Bender DA, Botham KM, Kennelly PJ, Rodwell VW, Weil PA: *Harper's Illustrated Biochemistry*, 28th Edition: <http://www.accessmedicine.com>

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Calcium and Magnesium Absorption

- Calcium
 - Absorbed primarily in duodenum
 - 1,25 OH Vit D regulates:
 - Enterocyte apical Ca Channel
 - Intracellular protein calbindin (shepards to export pump)
 - Basolateral Ca-ATPase
 - Vit D independent transport follows concentration gradient
- Magnesium
 - Absorbed throughout GI tract
 - Regulation of Mg absorption is dependent on dietary intake
 - Mg Channel upregulated in low Mg states to promote absorption

Water Soluble Vitamins

- Vitamin C
- B vitamins
 - Thiamine
 - Riboflavin
 - Niacin
 - B6
 - Folate
 - B12
 - Biotin
 - Pantothenic acid
- Water soluble
- Taken up easily by cells (B12 requires IF)
- In general, water soluble vitamins are not stored in tissue
 - Exclusions: B12 (liver storage)

Fat Soluble Vitamins

- A
- D
- E
- K
- Digested, absorbed, and transported with dietary fat
- Stored in liver, fat cells

Micronutrient	Pathophysiology	Clinical deficiency syndrome	Clinical overload syndrome	Laboratory evaluation
Minerals and trace elements				
Calcium	Fat malabsorption	Paresthesias, tetany, bone demineralization	*GI, GU, bone complaints	Serum Ca, PTH, DEXA scan
Magnesium	Fat malabsorption and high GI fluid losses	Weakness, cardiac, CNS	*Weakness, cardiac	Serum Mg
Zinc	GI fluid losses	Poor growth, skin, hair, diarrhea	*Vomiting, headache, diarrhea, Cu deficiency	Serum Zn, low alkaline phosphatase
Copper	Overload more common in cholestasis	*Hemolytic anemia, neutropenia	Hepatic overload, neuropsychiatric	Serum Cu
Manganese	Overload more common in cholestasis	*Poor growth, ataxia, skeletal	Neurotoxicity	Serum Mn
Iron	Absorbed proximally; not routinely in TPN	Microcytic anemia, irritability	Hepatotoxicity, GI bleeding, vomiting	Ferritin, TIBC, Iron Binding Cap, Hgb, HCT, peripheral smear
Selenium	Absorbed throughout small bowel	Myopathy, cardiomyopathy	*Thyroid enlargement	Serum selenium
Fat-soluble vitamins				
A	Fat malabsorption, cholestasis	Xerophthalmia, blindness	Increased ICP, hepatitis, vomiting	Vitamin A: retinol binding protein ratio
D	Fat malabsorption, cholestasis	Hypocalcemia, hypophosphatemia, rickets	Emesis, renal impairment	25-OH vitamin D
E	Fat malabsorption, cholestasis	Myopathy, neuropathy, ataxia, hemolytic anemia	coagulopathy	Vitamin E: total serum lipid ratio
K	Fat malabsorption, cholestasis	Bleeding	Hemolytic anemia	Prothrombin time, PIVKA assay
Water-soluble vitamins				
B12	Gastric or ileal resection	Megaloblastic anemia, CNS including ataxia	None known	Serum B12, methylmalonic acid, homocysteine
Folate	Absorbed proximally	Anemia, thrombocytopenia, stomatitis, glossosis	None known	Serum Folate

Summary

- Electrolyte absorption and secretion is tightly regulated, and forms the basis of fluid and solute transport and balance in both healthy and diarrheal states
- Individual mechanisms exist for mineral and vitamin absorption and transport

Please send any questions or comments to

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- Daniel.Kamin@childrens.harvard.edu