NASPGHAN Physiology Lecture Series

GI Physiology Module: Absorption of Water and Ions

Jason Soden, MD

Reviewers:
George Fuchs MD: UAMS College of Medicine / Arkansas Children's Hospital
Wayne Lencer MD: Harvard Medical School / Boston Children's Hospital

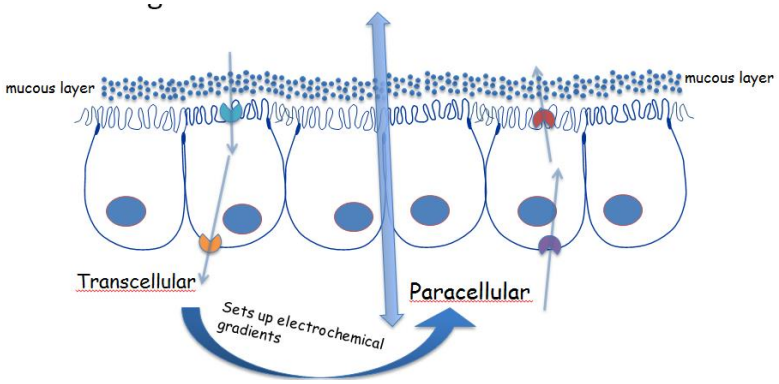
Series Editors: Daniel Kamin, MD and Christine Waasdorp Hurtado, MD

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

I. Background: Fluid and Electrolyte Balance in the GI Tract
   a. Regulation of fluid transport in gut is critical for normal intestinal function
   b. Water follows the osmotic gradient set by electrolyte transit
   c. The regulation of electrolyte balance is therefore a key principal to understanding intestinal fluid balance in health and disease
      i. In healthy state, only 100mL of fluid exits the gut (via stool) per day

II. Intestinal Epithelial cells function as gatekeepers for fluid and ion transit
   a. Tight junctions: restrict passive flow of solutes.
   b. Paracellular transport of water and electrolytes across tight junctions can occur but most follow electrochemical gradient
   c. Transcellular transport proteins: allow transport of molecules and waters across epithelial barrier, often via active transport against electrochemical gradient
      i. Subject to transcriptional and posttranscriptional regulation
      ii. Mechanistic examples:
         1. Primary Active Transport: Na-ATPase
         2. Secondary Active Transport: Na-GLUC cotransporter
         3. Facilitated Diffusion: Glut-5 (fructose transporter)



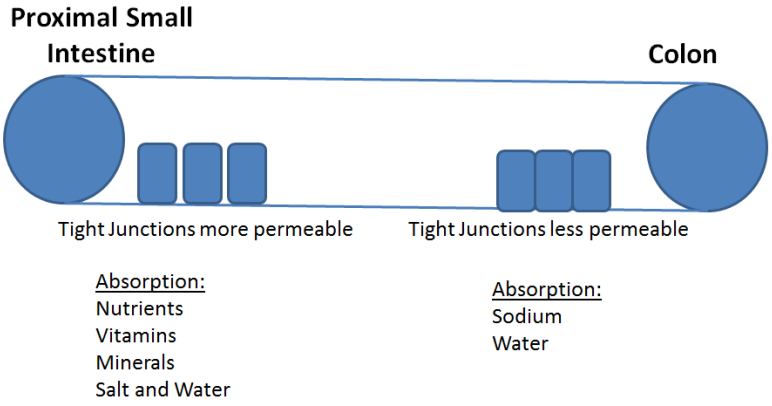
III. Anatomic Considerations

a. Based on villi (absorptive) and crypts (secretory), simultaneous absorption and secretions occurs at all levels of the intestine

i. Absorption primarily depends on molecular cotransport with sodium

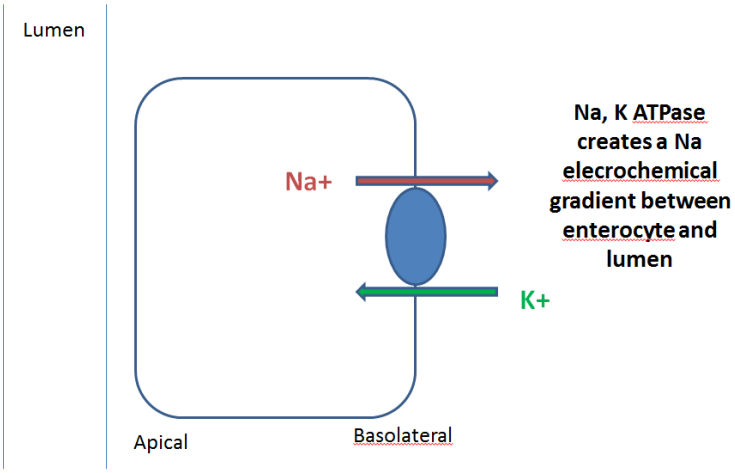
ii. Secretion primarily follows chloride and bicarbonate

b. Locational specialization occurs within the gut



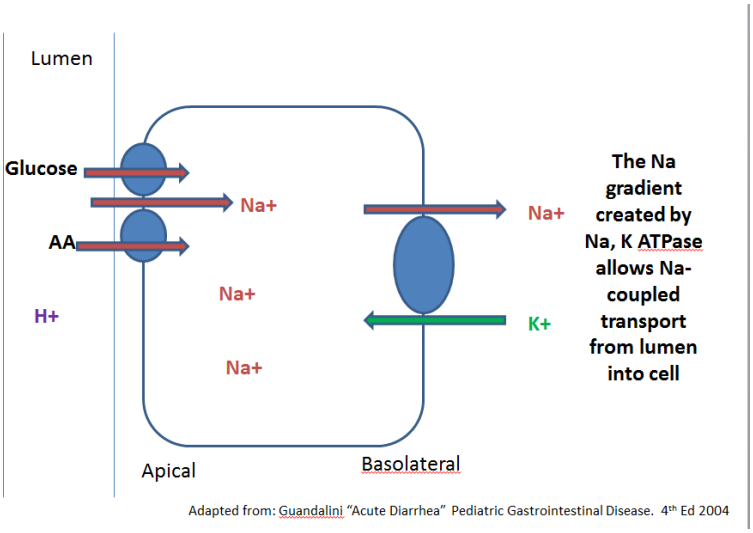
IV. Key examples of Cellular Transport Proteins

a. Na, K ATPase



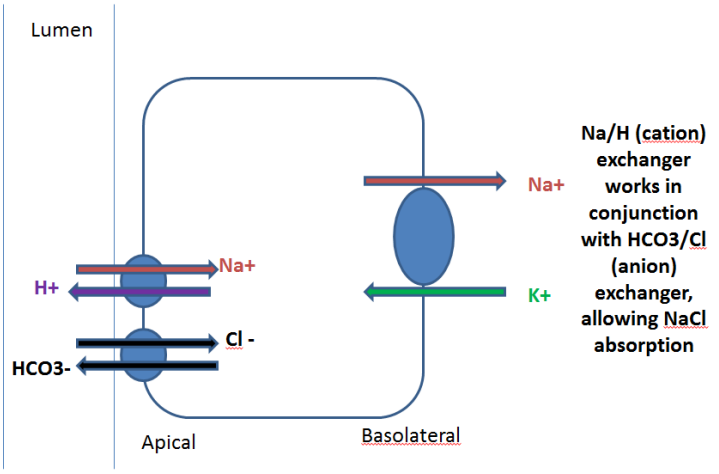
Adapted from: Guandalini "Acute Diarrhea" Pediatric Gastrointestinal Disease. 4th Ed 2004

b. Na-coupled Transport (eg: Sodium-Glucose cotransporter)



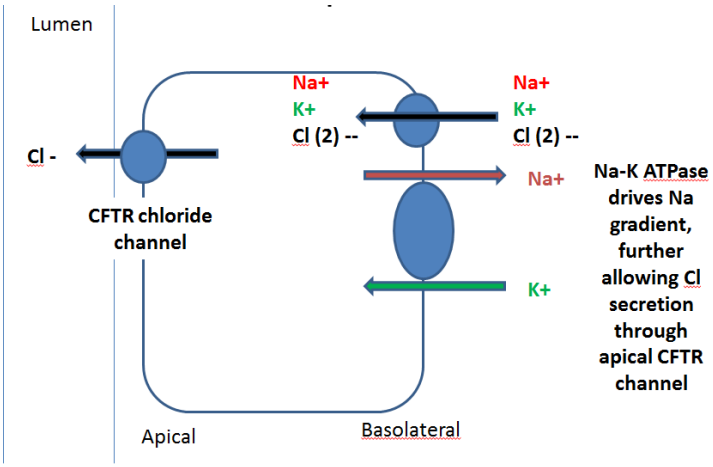
Adapted from: Guandalini "Acute Diarrhea" Pediatric Gastrointestinal Disease. 4th Ed 2004

c. NaCl Co-transport

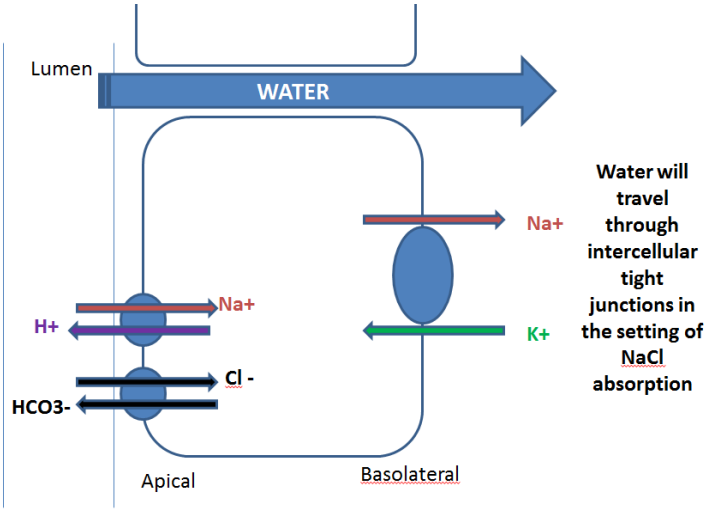


Adapted from: Guandalini "Acute Diarrhea" Pediatric Gastrointestinal Disease. 4th Ed 2004

d. Chloride secretion



e. Ultimately, water follows the NaCl gradient



Adapted from: Guandalini "Acute Diarrhea" Pediatric Gastrointestinal Disease. 4th Ed 2004

V. Absorption and Secretion in Health versus Diarrheal States

a. In healthy state, absorption (villus) > secretion (crypts)

b. In diarrheal state, chloride secretion (crypt) may be higher than villous NaCl absorption

   i. The pathophysiology of individual diarrheal disease is dependent on how the process affects ion absorption or secretion

c. Basic clinical mechanisms:

   i. Osmotic diarrhea: Malabsorption of solute (eg, carbohydrate / lactose) from small intestine drives fluid losses in colon

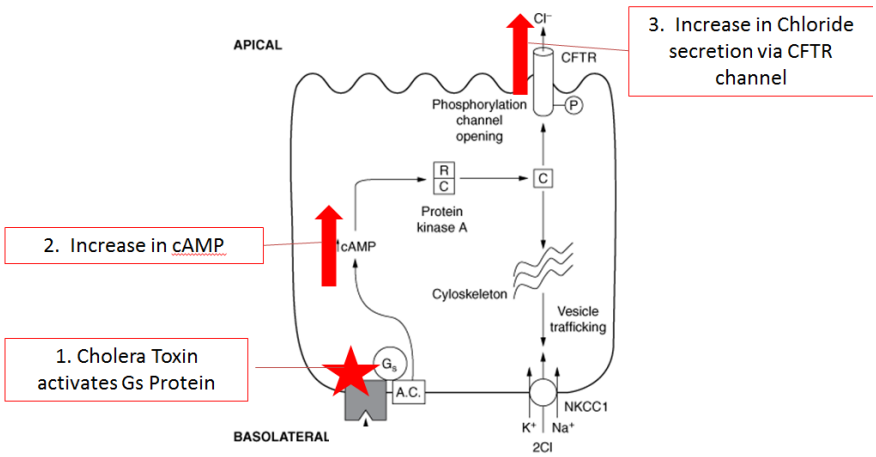
   ii. Secretory Diarrhea: Electrolyte secretion (eg, chloride secretion from crypts) drives small intestinal fluid losses

d. Repetitive molecular pathways exist in various infectious diarrheal states

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 cytoskeletan	Clostridium species	

Adapted from: Fasano: "Bacterial Infections" Pediatric Gastrointestinal Disease. 4th Ed 2004

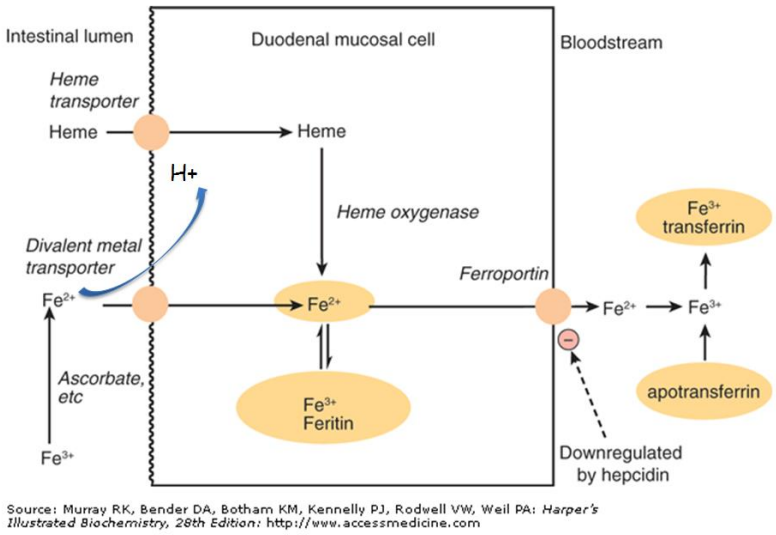
i. Example: Cholera



Adapted from: Barrett KE: Gastrointestinal Physiology. www.accessmedicine.com

VI. Mineral and Vitamin Absorption

a. Iron
   i. Ferrous iron is absorbed in proximal small intestine
   ii. Ferrous iron is converted to ferric iron, which is coupled with transferrin for transport
   iii. The liver plays a major role in regulation of iron transport



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

b. Calcium
   i. Absorbed in duodenum
   ii. Regulated by 1,25 hydroxy vitamin D, which regulates the apical, intracellular, and basolateral transport mechanisms

c. Magnesium
   i. Absorbed throughout GI tract, and regulation of absorption is dependent on dietary intake

d. Water Soluble Vitamins
   i. B vitamins and vitamin C are easily taken up by cells, and are generally not stored in tissue
   ii. Vitamin B12:
      1. Requires intrinsic factor for absorption
      2. Partially stored in liver

e. Fat Soluble Vitamins
   i. Digestion, absorption, and transport follows dietary fat
   ii. Stored in hepatocytes and adipocytes

f. Vitamin and mineral excess and deficiency states

Micronutrient	Pathophysiology	syndrome	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