Digestion and absorption
Physiological and pathophysiological

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Digestion, absorption and uptake
Not the same for all nutrients

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Anatomical physiology

- Proximal small bowel – most digestion and metabolism - with pancreato-biliary secretions
- Distal small bowel - important for bile acids, vitamin B12, and fluid and electrolytes
- Colon - important for fluid and electrolytes and short chain fatty acids from bacterial fermentation

Digestion

Three phases of digestion

- intraluminal
- brush border membrane / mucosal
- incorporation

Intraluminal digestion

- Commences in the mouth (amylase, lipase)
- Continues in stomach (acid and peptidases)
- Addition of bile and pancreatic secretions
- Completed in intestine (all nutrients)

- Role of gastric mill and sorting of foods

Gastric mill, sorting and emptying

Nutrient group-specific

1. Clear fluids
2. Simple carbohydrates
3. Protein and complex carbohydrates
4. Lipids

Occurs over seconds to hours
Relevance to pre-operative starving

Process of digestion and absorption also dependent on normal motility

1. Mixing of nutrients and enzymes (etc)
2. Transport along intestine
3. Control of speed of transit

Neurohumoral control crucial

Hormonal control - of pH

Gastric acid

- Increased by gastrin from G cells in antrum, duodenum & jejunum in response to food
- Gastrin inhibited by secretin

Pancreatic bicarbonate

- Increased by secretin from duodenal S cells in response to presence of acid

pH not neutral until distal small bowel

Hormones and digestion - example

CCK = pancreozymin

- chemically similar to gastrin; many subtypes
- stimulated by food in lumen
- causes release of bile and pancreatic fluid
- inhibited by somatostatin and luminal trypsin

3 phases of digestion/absorption

1: Enzymes – lingual and gastric but mainly pancreas & small bowel - in the lumen

- proteases to polypeptides
- amylases to smaller polysaccharides
- lipases to fat “globules”

2: Enzymes - brush border - acting locally

- proteases to oligopeptides (and amino acids)
- amylases to monosaccharides (sugar specific)

3 phases of digestion/absorption

3: Absorption / incorporation

- amino acids and monosaccharides
- to portal vein
- lipids
- micelles to chylomicrons to lymphatics
- MCT to portal vein

Carbohydrate digestion – phases 1 & 2

1: Amylases in lumen

to smaller polysaccharides

2: Enzymes - brush border - acting locally

sucrase	hydrolyses α1-4 bonds of oligosaccharides and sucrose
isomaltase	acts on α1-6 bonds of α-limit dextrins
maltase	acts on α1-4 bonds of oligosaccharides, maltose and maltotriose
lactase	hydrolyses lactose (only 25% adults)
trehalase	mushroom eaters' trehalose only

Protein digestion – phases 1 & 2

1: Lumen

- Protein breakdown by hydrolysis of α-peptide bonds
- Pepsinogens activated by low gastric pH to pepsins
- Inactivated in duodenum
- Pancreatic proteases take over
- Trypsinogen activated to trypsins
- Trypsins also activate elastase, carboxypeptidase, etc

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2: Brush border

- oligopeptides → ~ equal thirds:
- amino acids, dipeptides and tripeptides

Carbohydrate absorption

3: Absorption / incorporation – active and passive

Glucose, galactose and fructose
Have specific pathways

Glucose absorption active and passive

Glucose absorption is concentration dependent
Passive if high luminal load
Active if lower concentrations
SGLT1 sodium-dependent glucose transporter (1 glucose + 2 Na^+)
Sodium gradient requires the energy-using Na^+K^+ATPase
Glucose absorption approaches 100%

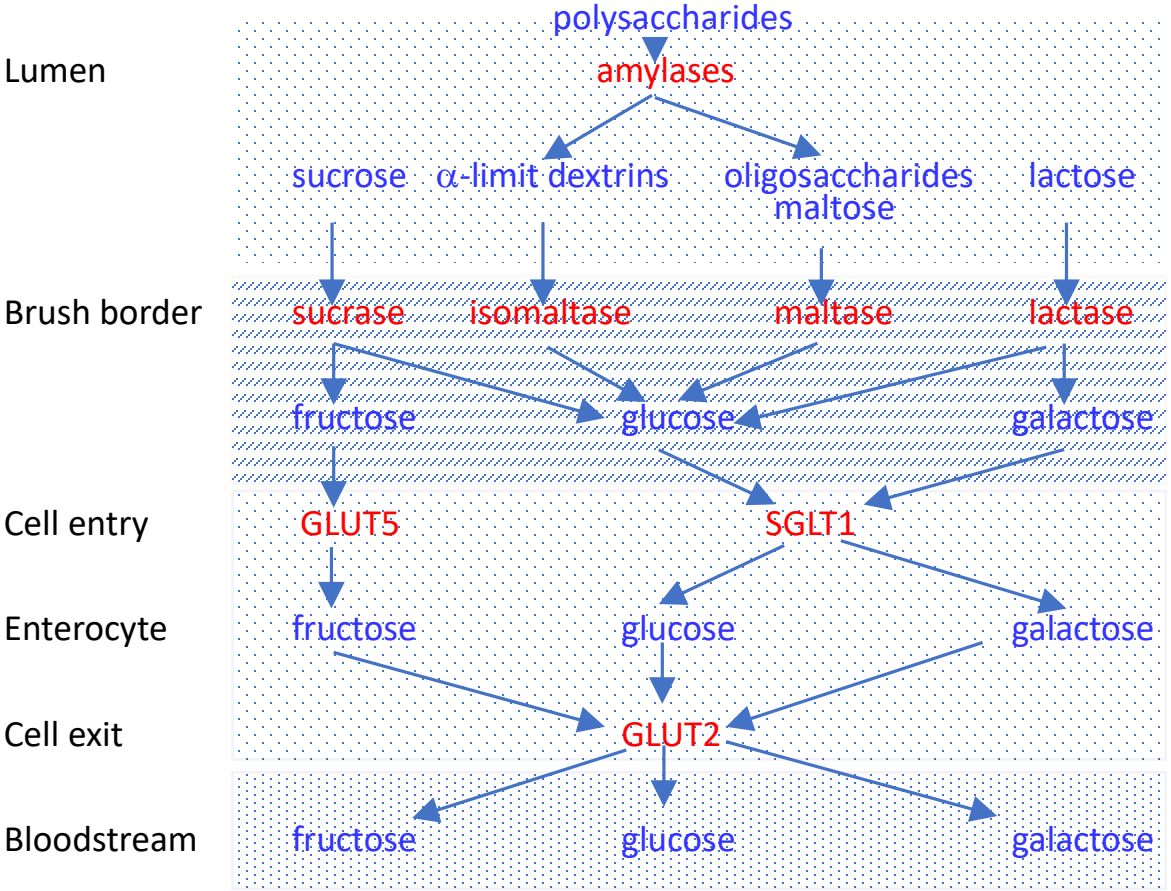
Glucose absorption

Glucose is internalised into the enterocyte
Then follows concentration gradient from apical zone
Leaves to bloodstream via basolateral GLUT2 carriers
Thus to portal vein

Galactose and fructose absorption

Galactose handled like glucose (less efficiently)
Fructose has GLUT5 instead of SGLT1 and its absorption is Na^+ independent but otherwise similar

Carbohydrates



“Protein” absorption

3: Absorption / incorporation – active and passive

Amino acids, dipeptides and tripeptides absorbed mainly via electrochemical gradients

Usually sodium-linked but no special transporters

Di- and tripeptides follow hydrogen ion gradient generated by Na^+/H^+ exchangers

Entry into cell more efficient for peptides than amino acids

“Protein” absorption

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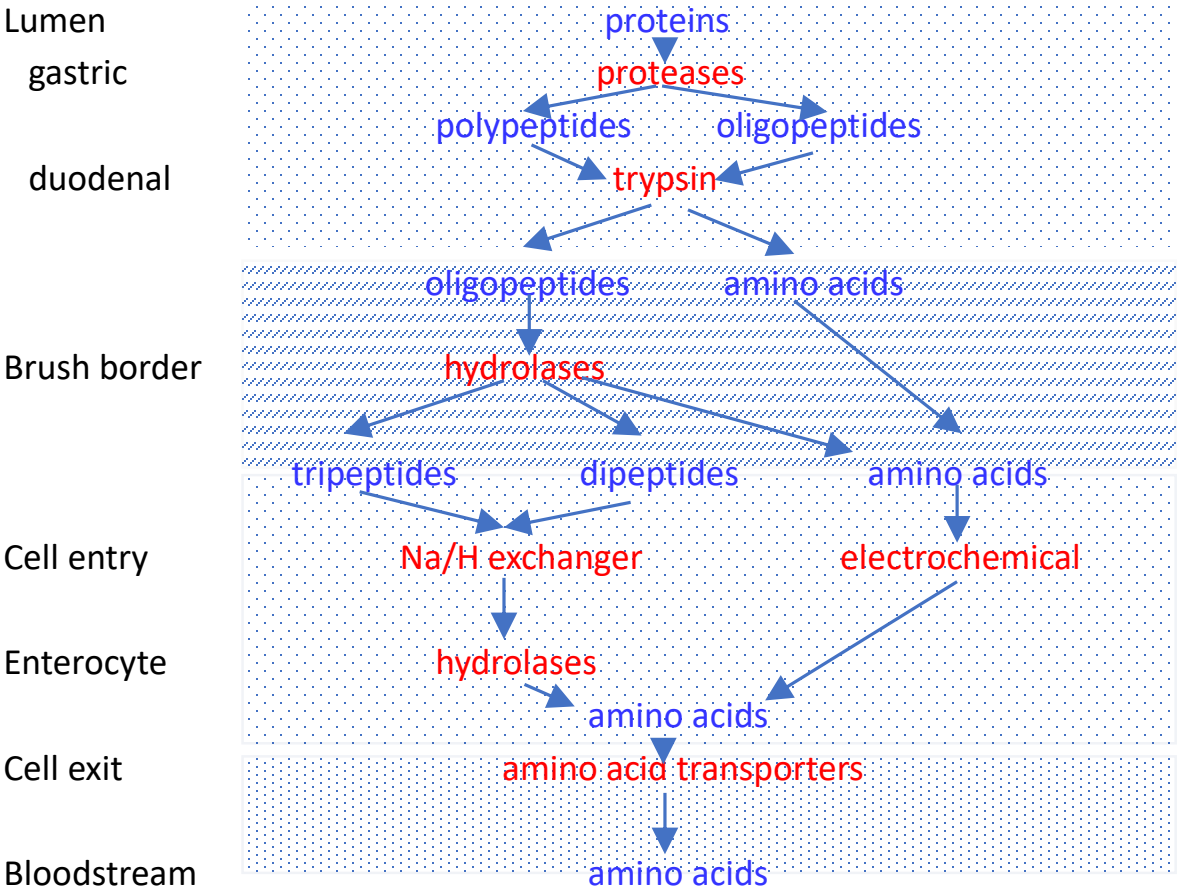
Within the cell more hydrolases - only amino acids reach blood stream - via amino acid transport proteins

Proteins


Lumen
gastric
duodenal
Brush border
Cell entry
Enterocyte
Cell exit
Bloodstream
proteins
proteases
polypeptides
oligopeptides
trypsin
oligopeptides
amino acids
hydrolases
tripeptides
dipeptides
amino acids
Na/H exchanger
electrochemical
hydrolases
amino acids
amino acid transporters
amino acids

Lipid digestion/absorption

1a: Luminal lipases
Formation of fat globules
1b: Luminal actions of bile salts
Formation of fat emulsion (1μm droplets)
1c: Luminal lipases (+ HCO_3^- and co-lipase)
Monoglycerides and fatty acids
1d: Micelle creation (2nm discs)
2: Luminal release of lipid products
into (very) proximal small intestine

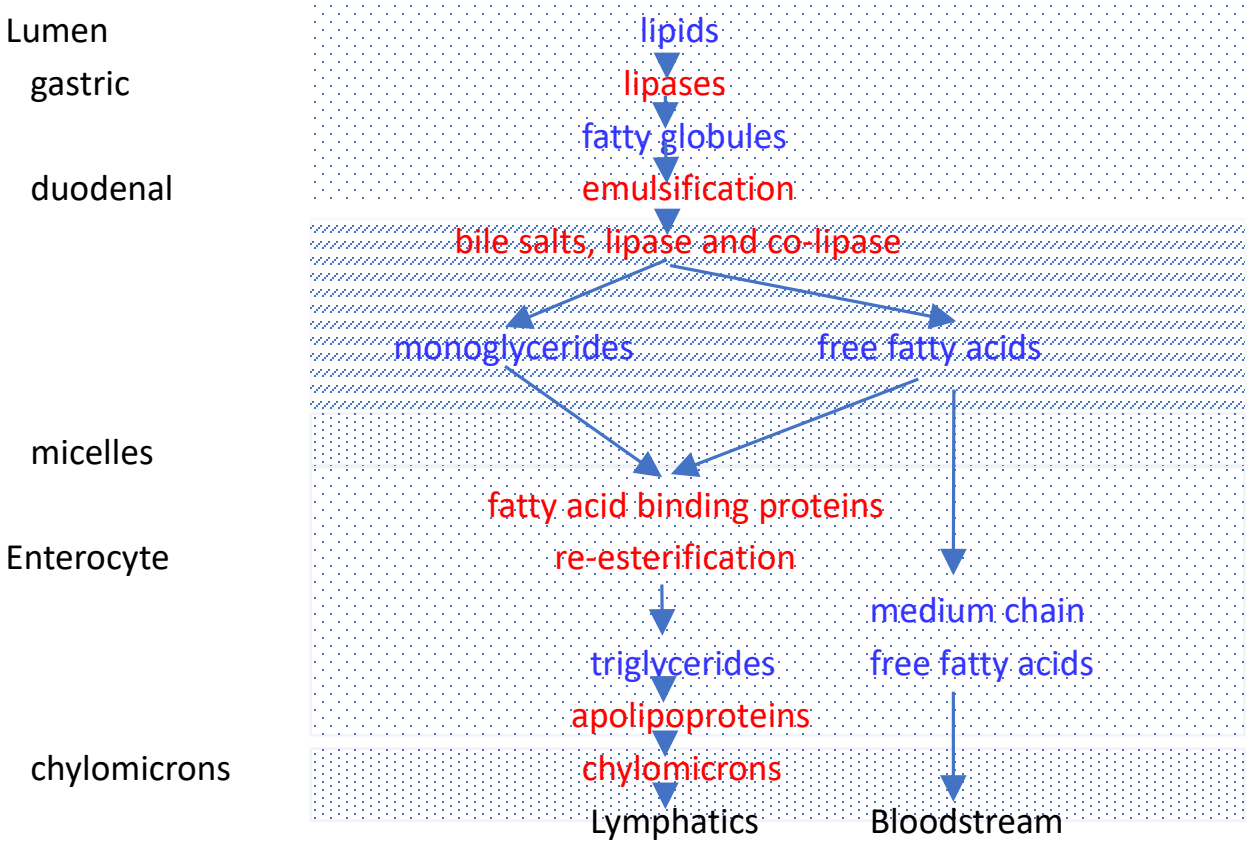
Lipid absorption

- Micelles release their contents directly into duodenal and jejunal cells
- Bile salt portions remain in lumen and are reabsorbed in distal ileum
- Medium chain fatty acids (water soluble) absorbed directly from lumen using energy dependent carrier system

Intracellular lipids

- Medium chain fatty acids are sufficiently soluble to pass into portal circulation
- Most free fatty acids link to fatty acid binding proteins
- New triglycerides formed in endoplasmic reticulum
- These new TGs are bound to apolipoproteins
- Chylomicrons are formed
- Via Golgi apparatus to exocytosis to lymphatics

Lipids


Lumen
gastric
duodenal
micelles
Enterocyte
chylomicrons
lipids
lipases
fatty globules
emulsification
bile salts, lipase and co-lipase
monoglycerides
free fatty acids
fatty acid binding proteins
re-esterification
triglycerides
apolipoproteins
chylomicrons
medium chain
free fatty acids
Lymphatics
Bloodstream

Importance of distal ileum

- Most parts of the intestine can compensate for disease or resection elsewhere
- But only distal ileal cells absorb vitamin B12 and bile salts

- Important in post-operative management
- Important in certain diseases (Crohn's/radiation damage)
- Adaptation of other parts of the GI tract does not permit absorption of vitamin B12 or bile salts

Micronutrient assimilation

- Digestion needed to liberate some micronutrients from food macromolecules
- Rarely clinically limited
- Binding to foods may be important eg phytate and zinc


vitamins

Fat soluble vitamins

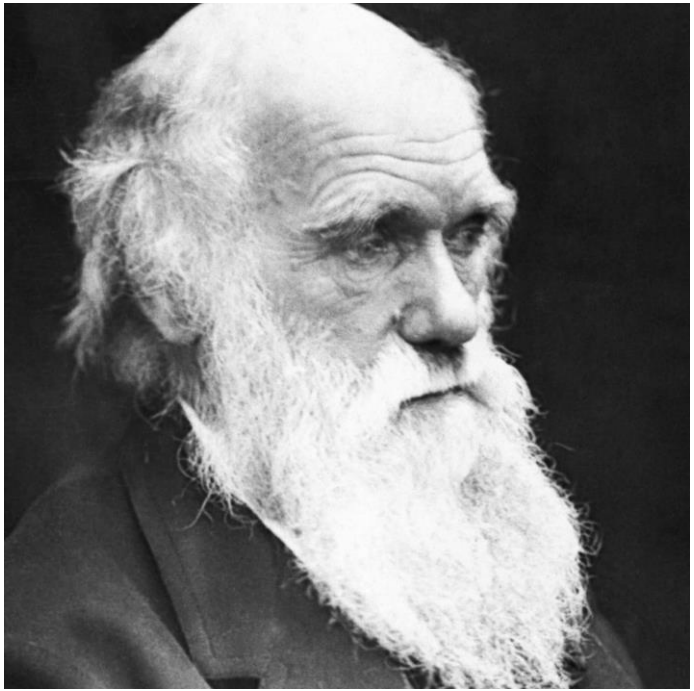
- Absorption in line with lipid absorption in general
- Entry to intestinal cells in general micelles
- Exit from cells by passive diffusion
- Active transport system exists for vitamin K in some circumstances

Water soluble vitamins

- Generally require release from associated dietary macromolecules
- Non-specific and forms part of digestive breakdown of proteins
- Free vitamins absorbed by enterocytes mainly via simple diffusion on concentration gradients

Complexity of vitamin B12

- Salivary R-protein strongly binds free vitamin B12
- Gastric parietal cells produce intrinsic factor
- Duodenal proteases release B12 from R-protein
- B12 binds instead to intrinsic factor
- IF–B12 complex recognised by distal ileal brush-border receptors
- Internalisation by endocytosis
- Free B12 leaves from cell base into circulation
- B12 bound to trans-cobalamin II for transport



Vitamin B12. Did he get it wrong ?

Trace elements - iron

- About 10% of 10-20mg dietary iron is absorbed
- More if iron deficient
- Haem iron from animal products readily absorbed via the brush border membrane as intact iron porphyrin
- Non-haem (vegetable) iron only absorbed in Fe^{2+} form
- Fe^{3+} must be reduced to Fe^{2+} by dietary ascorbate and iron reductases in the brush-border
- Fe^{2+} then to enterocytes via DMT1 (divalent metal ion transporter 1) - efficiency about 50% of haem iron

Trace elements -zinc

- Most dietary zinc is tightly sequestered in macromolecules
- Only after these are digested is zinc absorbed - largely by passive diffusion
- Easily compromised by phytate or high fibre diet
- Some competition for absorption by iron and copper

Trace elements - selenium

- Most dietary selenium is as plant selenoproteins
- Available only after effective protein digestion
- Then readily absorbed in the small intestine
- Passive and active pathways
- Deficiency seen when protein degradation impaired - especially where soil levels are low

Trace elements - other

- Non-specific release from dietary macromolecules
- Passive small intestinal absorption
- Percentage of dietary content absorbed is often low
- But rarely see clinical problems


SCRAP
METAL

Digestion, absorption and uptake
Not the same for all nutrients

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