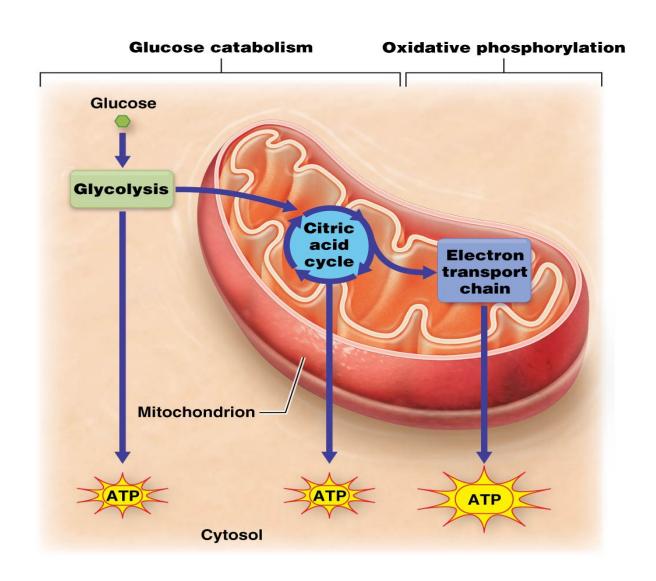
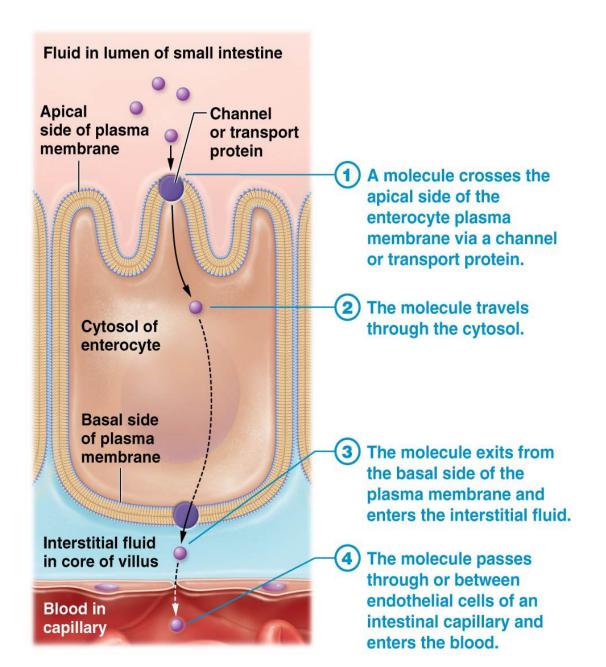
## Metabolism (C26)



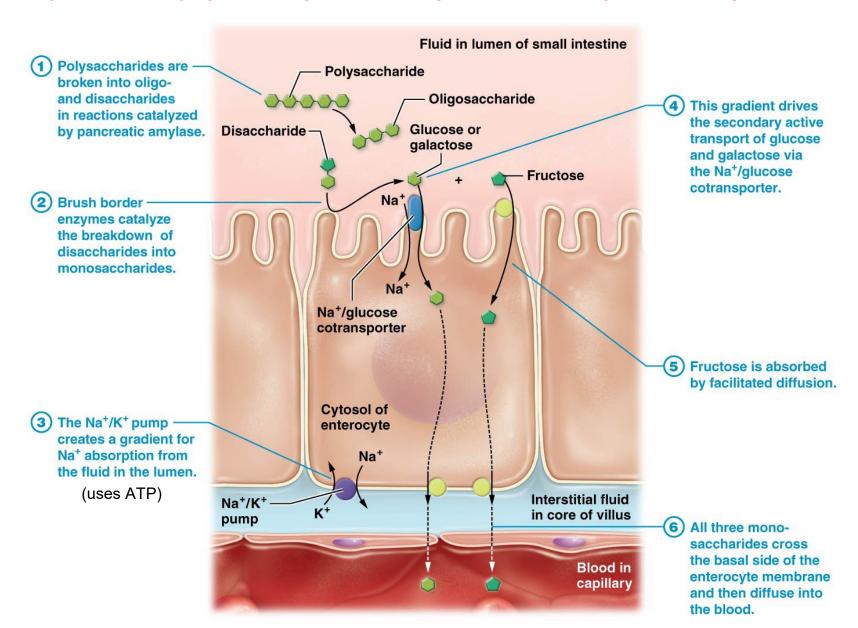
Path taken by hydrophilic molecules absorbed into blood through an enterocyte.



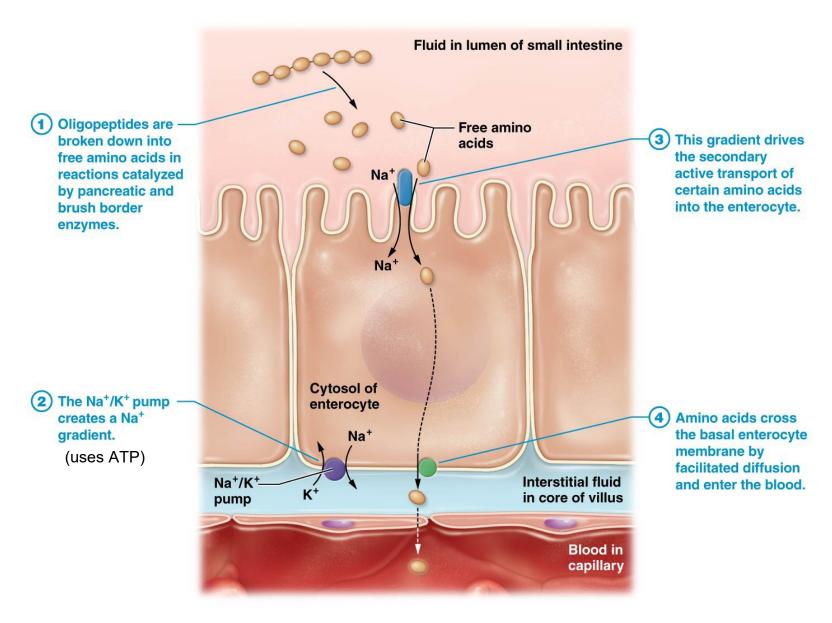
#### Carbohydrate (hydrophilic molecule) digestion and absorption in the small intestine



Can you find the symports, antiports, and uniports? Active vs passive transporters?

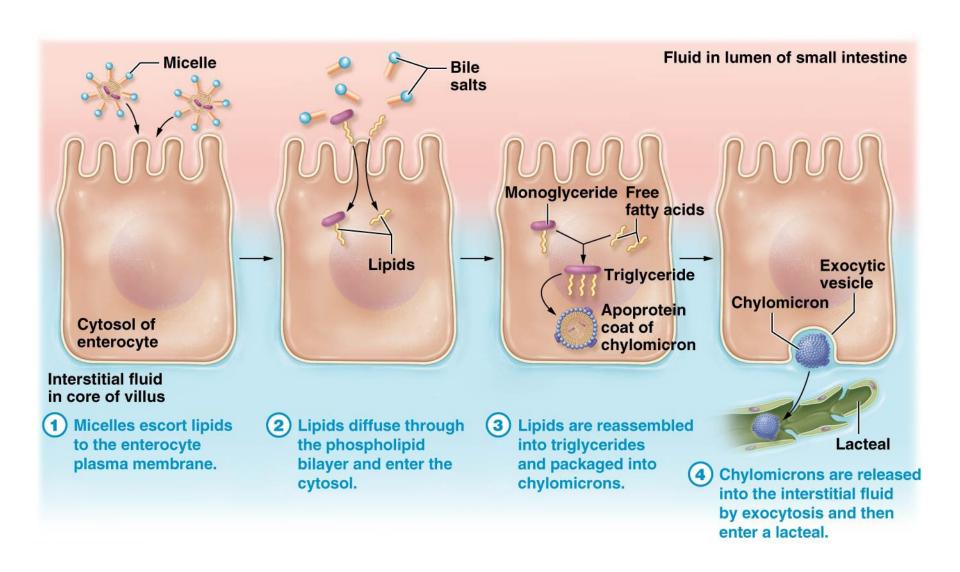


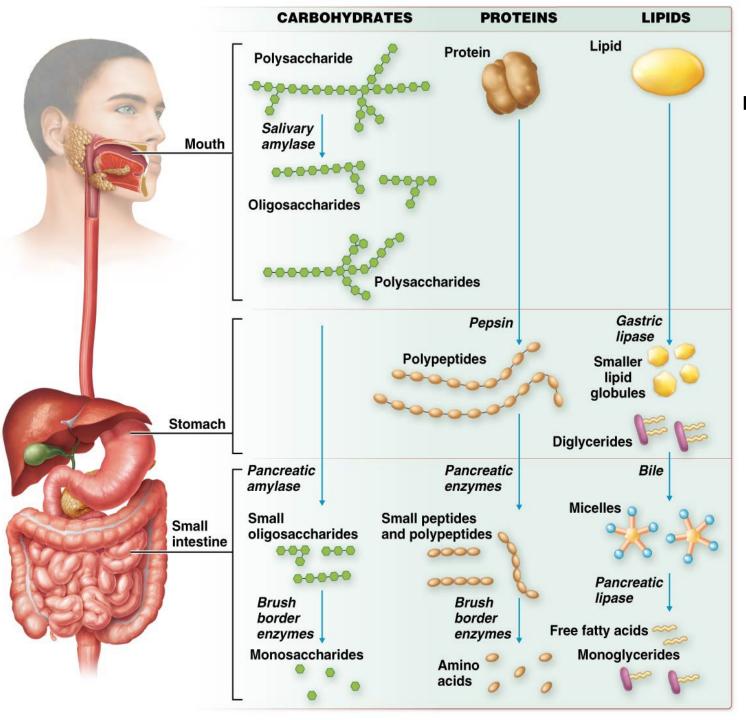
#### Amino acid digestion and absorption in the small intestine.



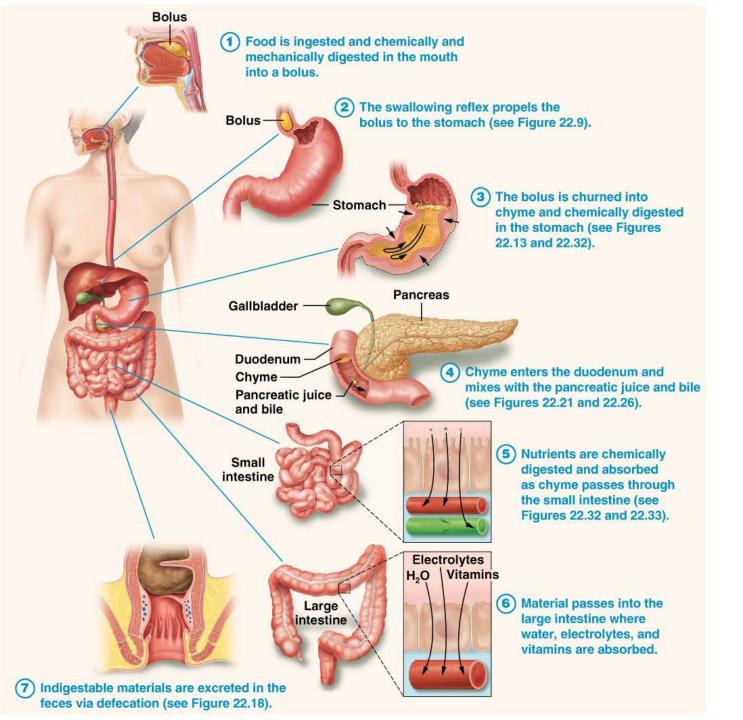
What is secondary active transport?

#### Lipid (hydrophobic molecule) digestion and absorption in the small intestine



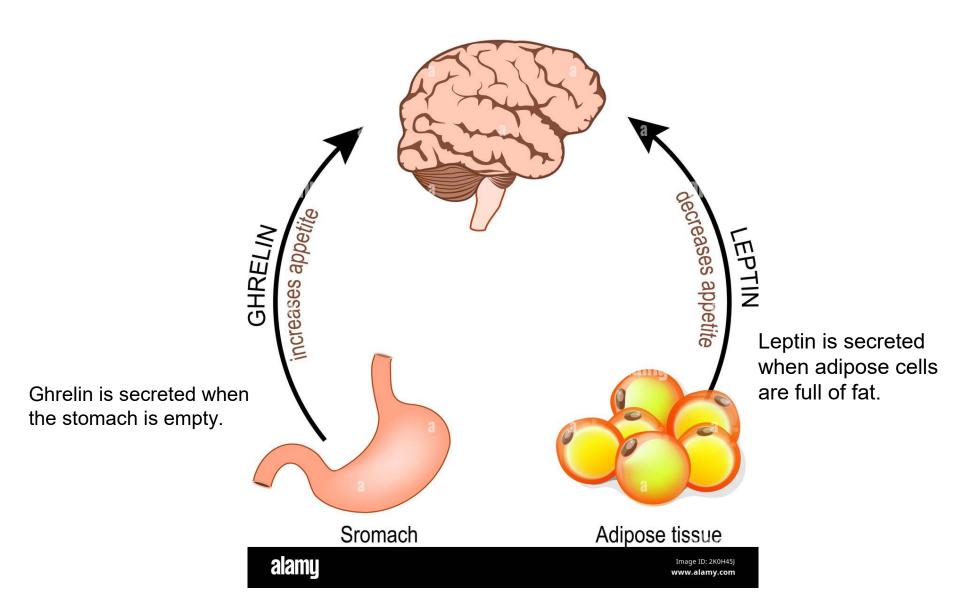


Summary of the digestion of carbohydrates, proteins, and lipids.



# The Big Picture of Digestion.

# Leptin & Ghrelin

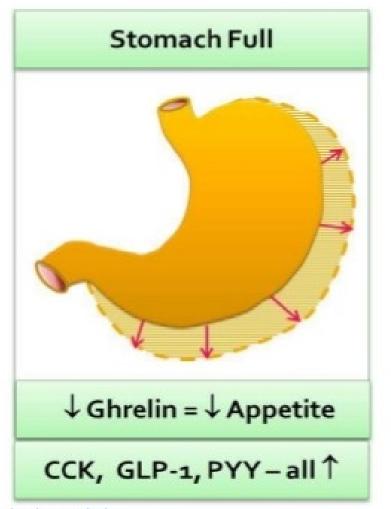


COX – Cholecystokinin GLP1 – Glucagon-like peptide 1 PYY – Peptide YY

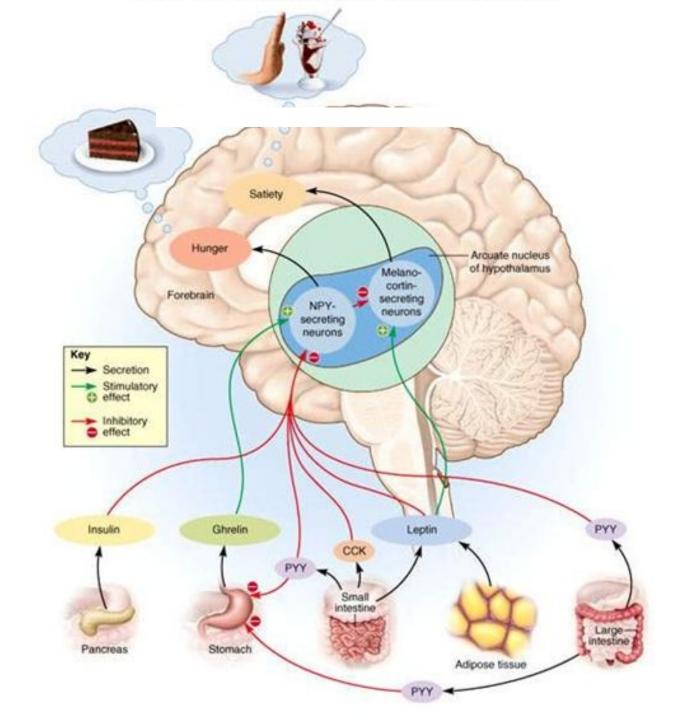
Primarily regulated by feeding

(Crespo *et al.,* 2014)





http://www.nutridesk.com.au/stomach-intestine-ghrelin-cck-glp-1-gut-hormones.phtml



# **Carbohydrate Digestion**



- Starch the most digestible carbohydrate
  - starch is first digested to:
    - oligosaccharides up to eight glucose residues long
    - then into the disaccharide maltose
    - finally to glucose which is absorbed by the small intestine
  - process begins in the mouth
    - salivary amylase hydrolyzes starch into oligosaccharides
    - amylase works best at pH of 6.8 7.0 of oral cavity
    - amylase quickly denatured on contact with stomach acid and digested by pepsin
- Cellulose indigestible glucose polymer!
- What is glycogen?
- Do we have enzymes to digest glycogen?

# **Carbohydrate Digestion**



- salivary amylase stops working in stomach at pH less than 4.5
  - 50% of dietary starch digested before it reaches small intestine
- when reaching the small intestine, pancreatic amylase converts starch to oligosaccharides and maltose within 10 minutes
- oligosaccharides and maltose contact brush border enzymes (dextrinase, glucoamylase, maltase, sucrase, and lactase) /// these act to turn oligosaccharides, maltose, sucrose, lactose, and fructose into glucose
- lactose becomes indigestible after age 4 in many humans due to decline in lactase production (lactose intolerance)

# **Carbohydrate Absorption**



- plasma membrane of the absorptive cells has transport proteins that absorb monosaccharides as soon as the brush border enzymes creates monosaccharides
- 80% of absorbed sugar is the monosaccaride glucose
  - Moved from small intestine's lumen across apical enterocyte by sodium-glucose transport proteins (SGLT) and secondary active transport of the sodium-potasium ATP pump in the basal membrane
  - then glucose is transported out the base of absorptive cell into ECF by facilitated diffusion
  - sugar entering ECF increases its osmolarity /// draws water by osmotic drag from the lumen of the intestine, through now leaky tight junctions between epithelial cells
  - water carries additional glucose and other nutrients with it by solvent drag through leaky junctions
  - See next slide

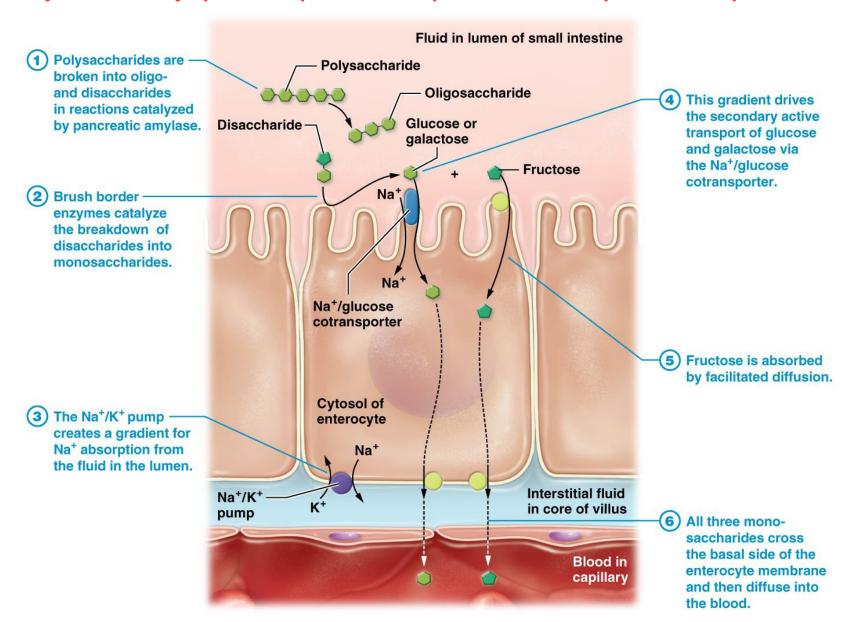
# **Carbohydrate Absorption**

- sodium-glucose transport proteins (SGLT) (also transports galactose)
- The SGLT-1 was the first transporterstudied. This protein is encoded by SLC5A1 gene (Turk et al., 1994). The SGLT1 protein controls the import of glucose in enterocytes and epithelial cells in the small intestine and proximal convoluted tubules in nephrons, respectively.
- fructose is absorbed by facilitated diffusion
- some glucose and galactose may also be transported out of the base of the cell by facilitated diffusion
- absorbed by blood capillaries in the villus
- hepatic portal system delivers these sugars to the liver

#### Carbohydrate digestion and absorption in the small intestine.



#### Can you find the symports, antiports, and uniports? Active VS passive transporters?



## Lactose Intolerance

- At birth, all mammals (including humans) have the enzyme lactase to digest lactose (sugar in milk)
- Many will lose lactase as they age. At around age four the transcription factor to make lactase is inhibited. Now unable to digest lactose.
- If lactose passes undigested into large intestine
  - increases osmolarity of intestinal contents
  - causes water retention in the colon and diarrhea
  - gas production by bacterial fermentation of the lactose
- Lactose intolerance occurs in many populations //
  - 15% American whites
  - 90% of American blacks
  - 70% of Mediterranean's
  - nearly all of Asian descent
- Lactose intolerant people may consume dairy products like yogurt and cheese because bacteria in manufacturing process break down lactose

# **Proteins**



- <u>amino acids</u> absorbed by the small intestine come from three sources:
  - dietary proteins
  - digestive enzymes digested by each other
  - epithelial cells sloughed off mucosa and digested by enzymes
- endogenous amino acids from last two sources total about 30g/day
- exogenous amino acids from our diet total about 44 to 60 g/day
- proteases (peptidases)
  - enzymes that digest proteins
  - begin their work in the stomach in optimum pH of 1.5 to 3.5
  - pepsin hydrolyzes any peptide bond between tyrosine and phenylalanine
    - pepsin digests 10-15% of dietary protein into shorter peptides and some free amino acids

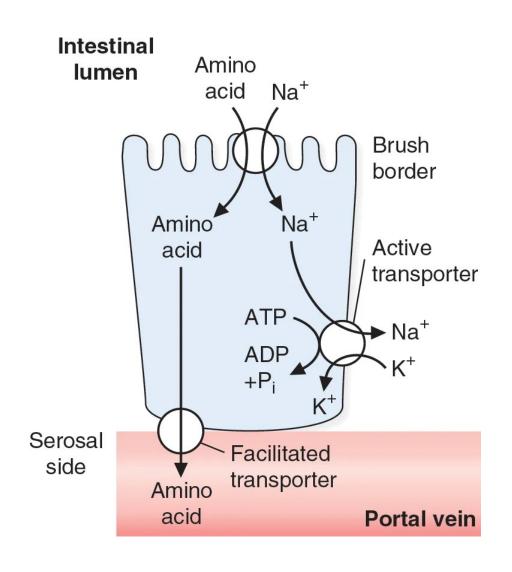
# **Proteins**

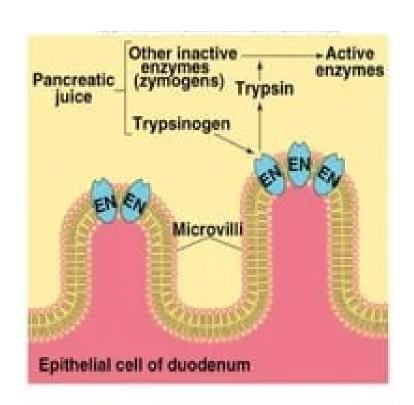


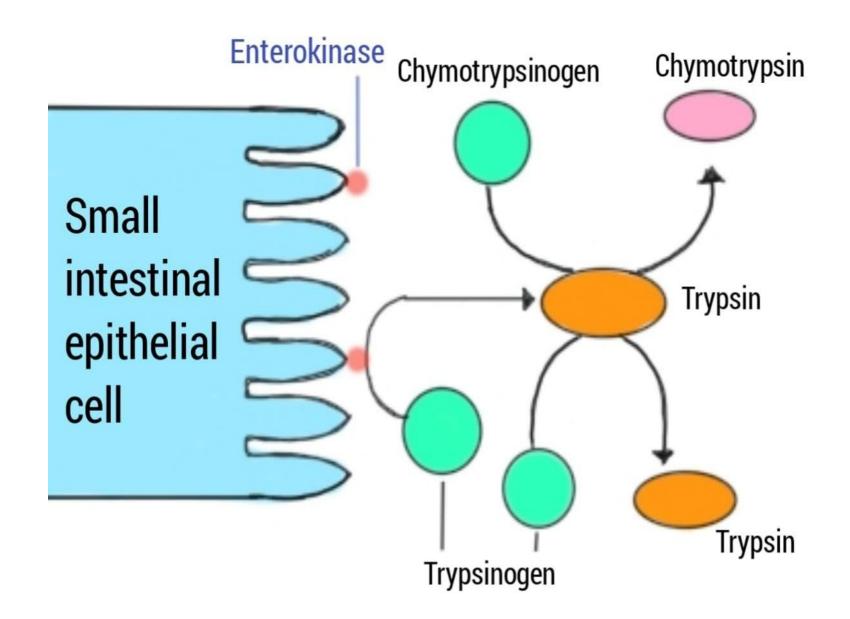
- Protein digestion started in stomach continue in the small intestine
  - Gastric pepsin inactivated when it passes into the duodenum and mixes with the alkaline pancreatic juice (pH 8)
  - pancreatic enzymes trypsin and chymotrypsin take over the process
  - hydrolyzing polypeptides into even shorter oligopeptides
  - oligopeptides taken apart one amino acid at a time by three more enzymes
    - carboxypeptidase removes amino acids from –COOH end of the chain
    - aminopeptidase removes them from the –NH<sub>2</sub> end
    - dipeptidase split dipeptides in the middle and release two free amino acids
  - carboxypeptidase is a pancreatic secretion
  - aminopeptidase and dipeptidase are brush border enzymes

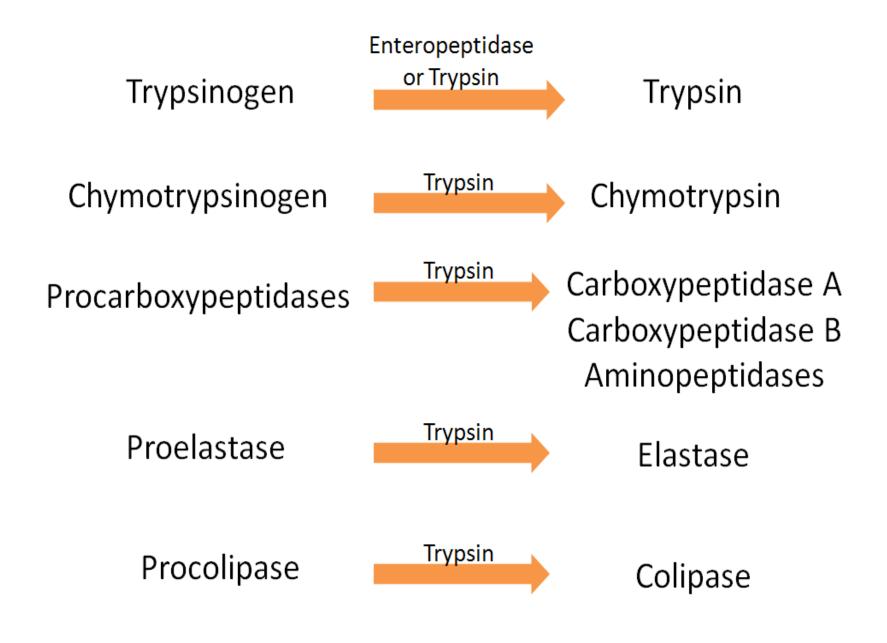
### **Protein Digestion and Absorption**

Pancreatic enzymes take over protein digestion in small intestine by hydrolyzing polypeptides into shorter oligopeptides









#### Small intestine

Actions of pancreatic enzymes

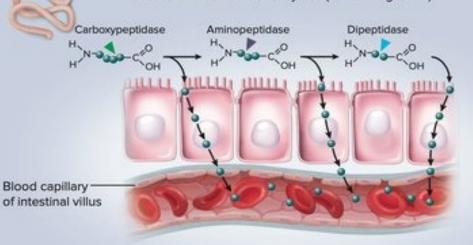


Trypsin (▲) and chymotrypsin (▲) hydrolyze other peptide bonds, breaking polypeptides down into smaller oligopeptides.

OH Carboxypeptidase ( ) removes one amino acid at a time from the carboxyl (—COOH) end of an oligopeptide.

#### Small intestine

Actions of brush border enzymes (contact digestion)



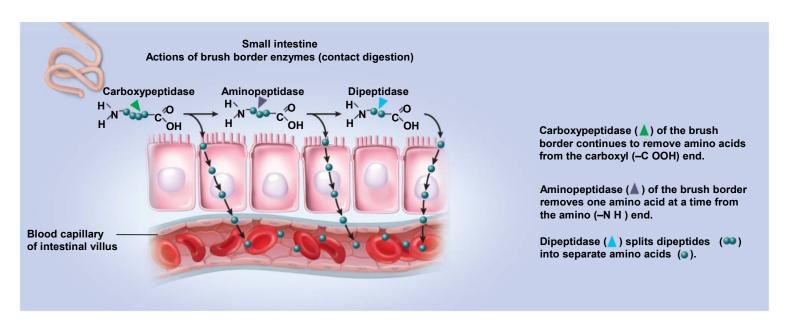
Carboxypeptidase ( ) of the brush border continues to remove amino acids from the carboxyl (—COOH) end.

Aminopeptidase ( ) of the brush border removes one amino acid at a time from the amino (—NH<sub>2</sub>) end.

Dipeptidase ( ) splits dipeptides ( ) into separate amino acids ( ).



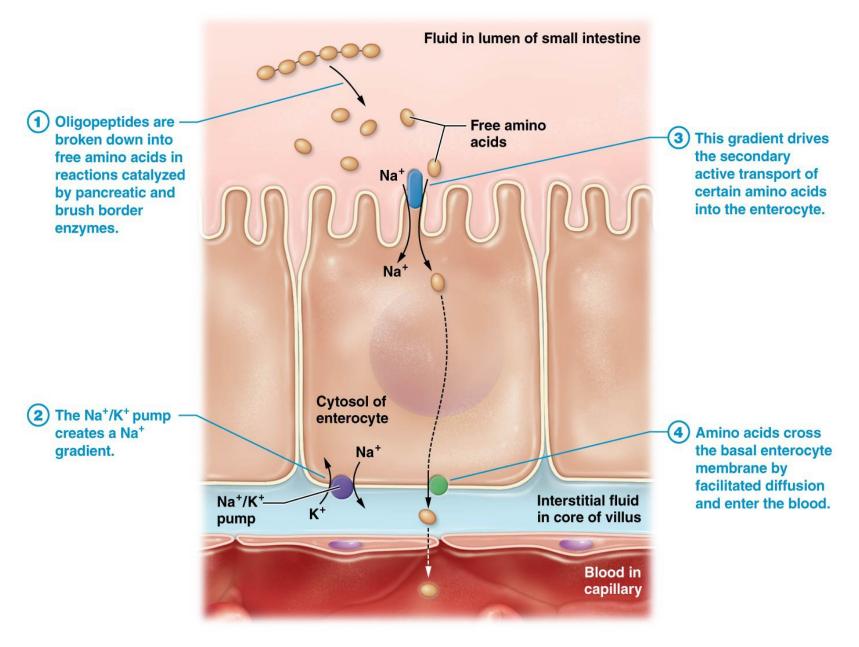
# **Protein Digestion and Absorption**



- brush border enzymes finish task, producing free amino acids that are absorbed into intestinal epithelial cells
  - sodium-dependent amino acid cotransporters move amino acids into epithelial cells
  - facilitated diffusion moves amino acids into blood stream
- infants absorb proteins by pinocytosis (maternal IgA) and release into the blood by exocytosis

#### Amino acid digestion and absorption in the small intestine.





What is secondary active transport?

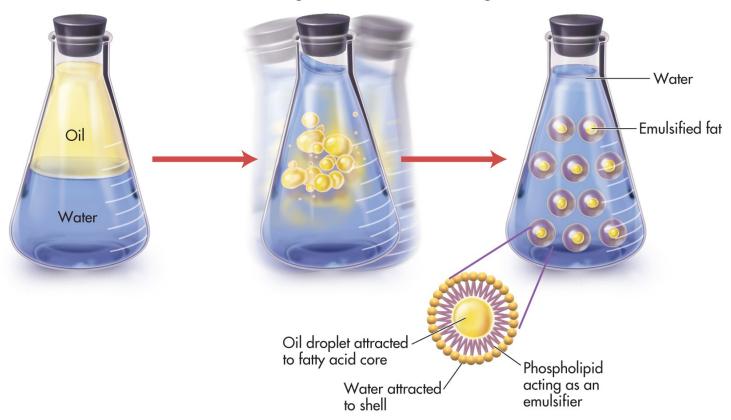
# Lipids



- Hydrophobic quality of lipids makes their digestion and absorption more complicated that carbohydrates and proteins
- Lipases fat digesting enzymes
  - lingual lipase secreted by the intrinsic salivary glands of the tongue /// generally thought to be inactive in mouth, but activated by stomach acids // acidic enzyme
  - stomach's chief cells also produces gastric lipase // 10-15% of lipids digested before reaches duodenum // acidic enzyme // more important for neonates
  - pancreatic lipase in the small intestine digest most of the fats in food
  - fat enters duodenum as large globules exposed to lipase only at their surface
  - globules broken up into smaller emulsification droplets by certain components of bile // lecithin and bile acids

# Lipids

#### **Emulsifiers and Agitation in Salad Dressing**





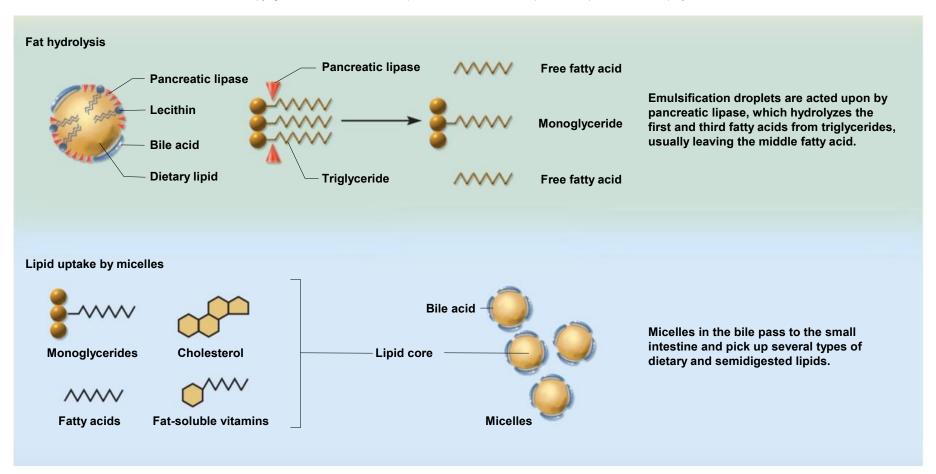
# Lipids

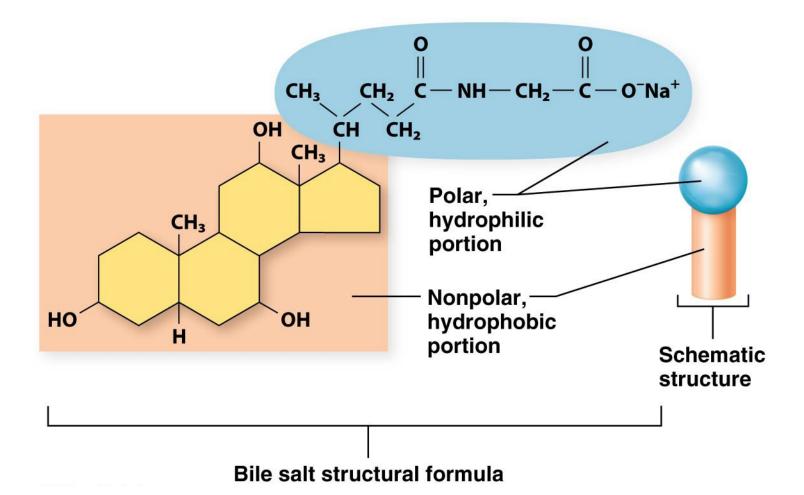
- agitation by segmentation breaks up the fats into droplets as small as 1 µm in diameter
- the coating of lecithin and bile acids keep it broken up
- exposing far more of its surface to enzymatic action
- there is enough pancreatic lipase in the small intestine after a meal to digest the average daily fat intake in as little as 1 to 2 minutes
- lipase acts on triglycerides
  - removes the first and third fatty acids from glycerol backbone
  - leaves the middle one
  - the product of lipase action are two free fatty acids (FFAs) and a monoglyceride



# **Fat Hydrolysis and Micelles**

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### Micelles Role in Lipid Digestion and Absorption

- absorption of free fatty acids, monoglycerides, and other lipids depends on minute droplets in the bile called micelles
  - Micelles are formed in in the liver as well as in the duodenum
  - consist of 20 to 40 bile acid molecules aggregated with their hydrophilic side groups facing outward and their hydrophobic steroid rings facing inward
  - bile phospholipids and cholesterol diffuse into the center of the micelle to form its core

## Micelles Role in Lipid Digestion and Absorption

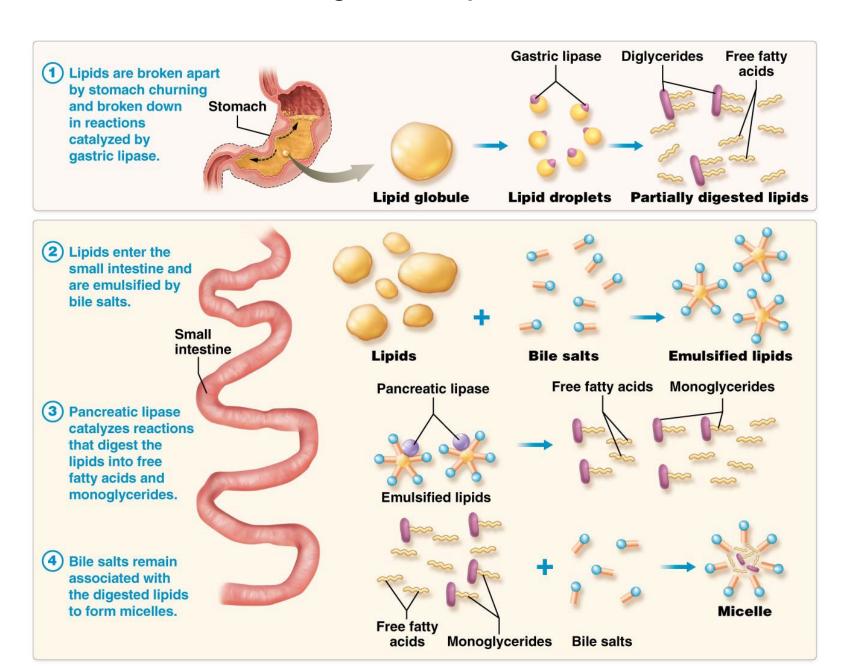
micelles pass down the bile duct into the duodenum /// where they absorb fat soluble vitamins, more cholesterol, and the FFAs and monoglycerides produced by fat digestion

they transport lipids to the surface of the intestinal absorptive cells

lipids leave the micelles and diffuse through the plasma membrane into the cells

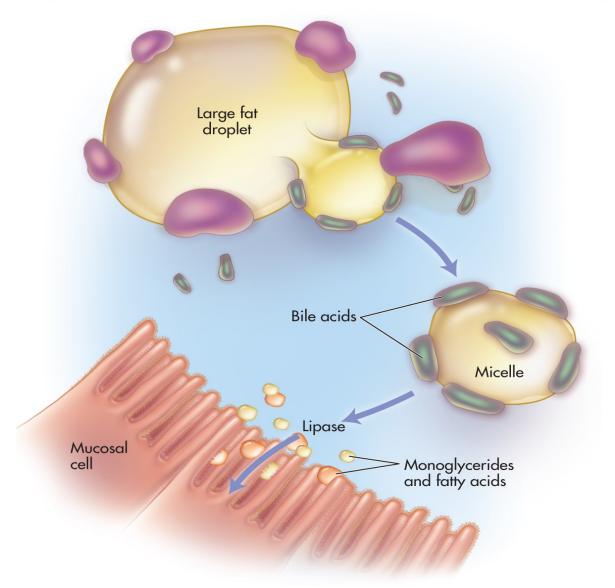
micelles are reused (enterohepatic circulation) /// Reabsorbed in ileum / go back to liver via hepatic portal circulation / returned to bile / secreted back into duodenum

#### Digestion of lipids.



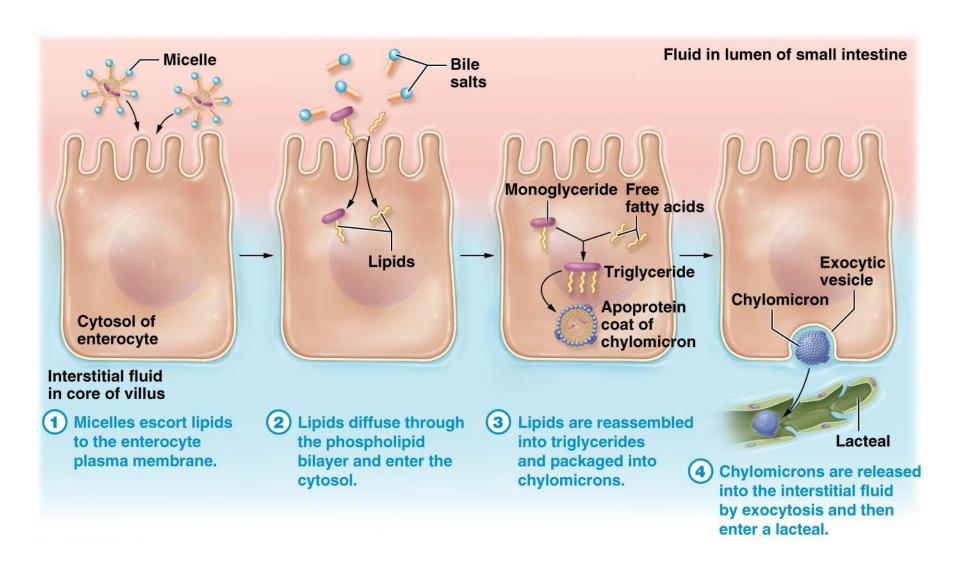
# Fat Digestion and Absorption

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#### Lipid absorption in the small intestine.

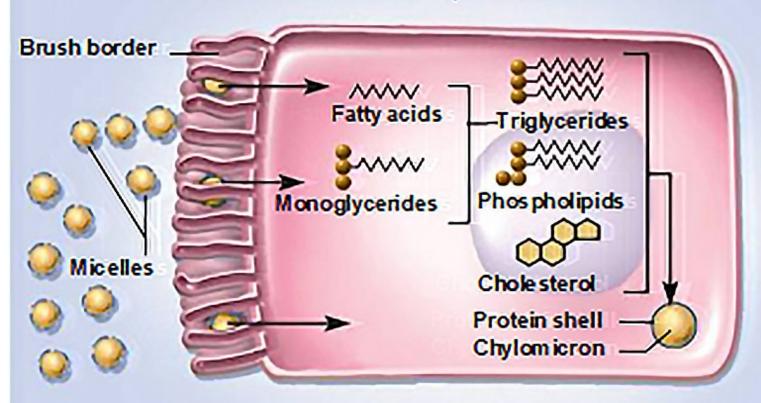




## **Lipid Absorption**

#### Chylomicron formation

#### A bsorptive cell



Intestinal cells absorb lipids from micelles, resynthesize triglycerides, and package triglycerides, cholesterol, and phospholipids into 85protein-coated chylomicrons.

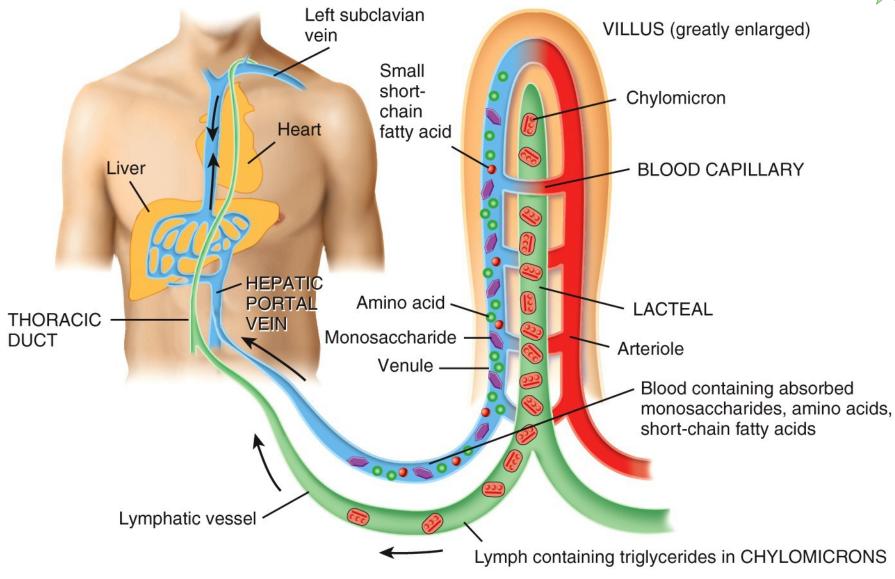
## **Lipid Absorption**



#### Within the jejunum absorptive cells

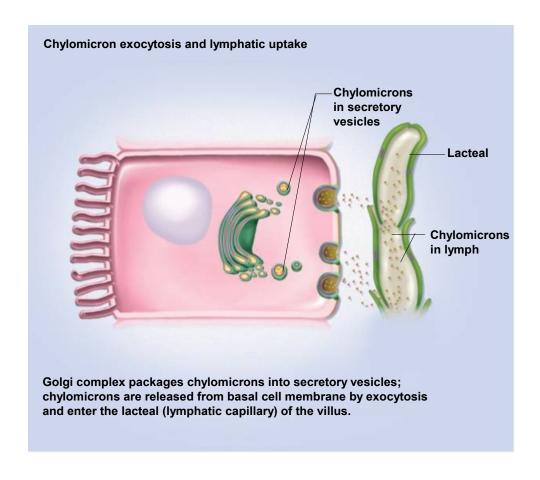
- free fatty acids and monoglycerides are transported to the smooth ER
- resynthesized into triglycerides
- golgi complex coats these with phospholipids and protein to form chylomicrons
- Chylomicrons loaded with fat soluble molecules including trigycerides, lecithin, fat soluble vitamins, etc.
  - packaged into secretory vesicles that migrate to basal surface of cell ///
    release their contents into the core of the villus (lamina propria) ///
    taken up
    by more porous lacteal into the lymph /// white, fatty intestinal lymph
    (chyle) flows into larger and larger lymphatic vessels until they reenter the
    bloodstream





(b) Movement of absorbed nutrients into blood and lymph

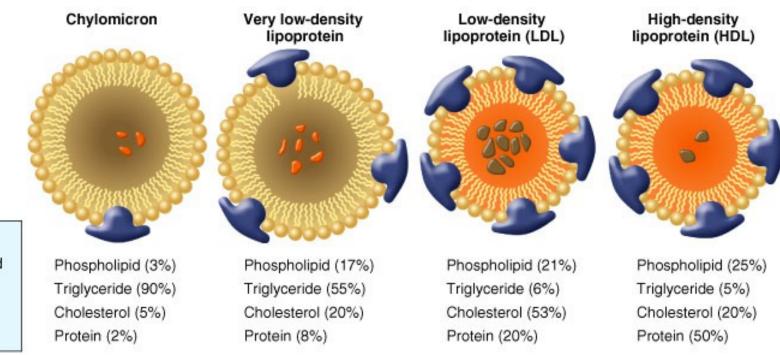
### **Chylomicrons and the Lymphatics**



Chylomicrons are released into the lymphatic system in the lacteals of the villi. They enter the bloodstream when lymphatic fluid enters the subclavian vein via the thoracic duct.

# **Serum Lipoproteins**

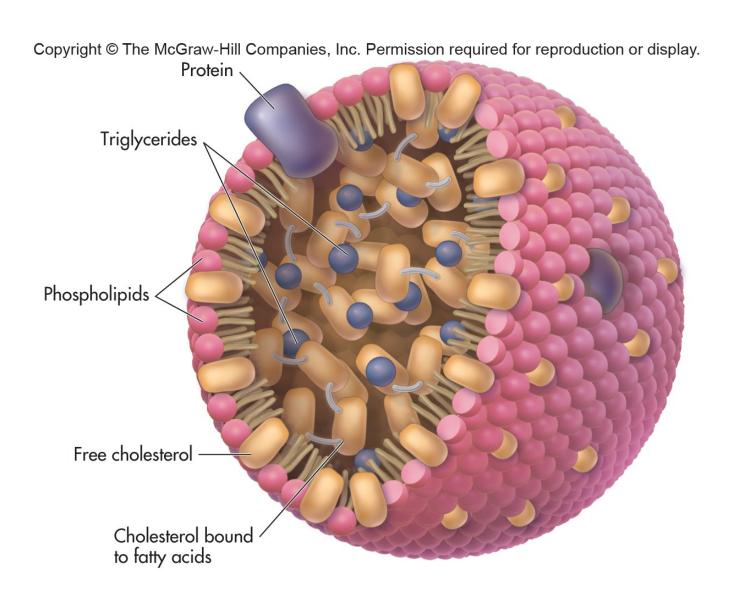




Phospholipid
Triglyceride
Cholesterol
Protein

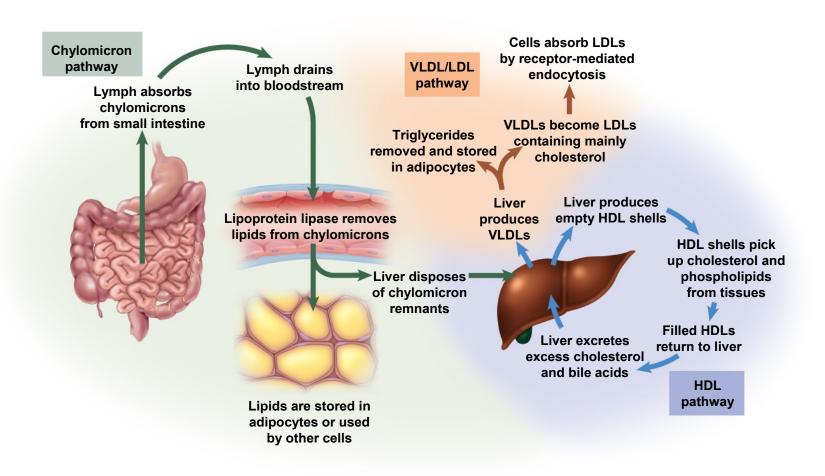
(a) Lipoprotein types

## Composition and Roles of Lipoproteins

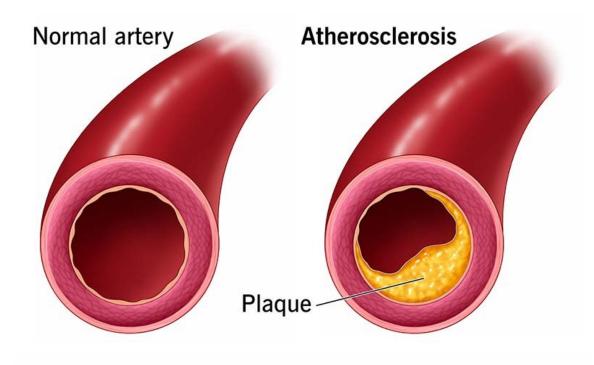


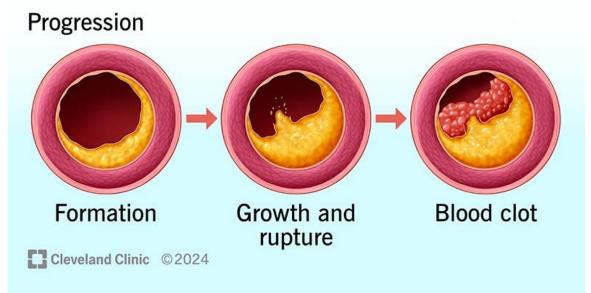


### **Lipoprotein Processing Pathways**

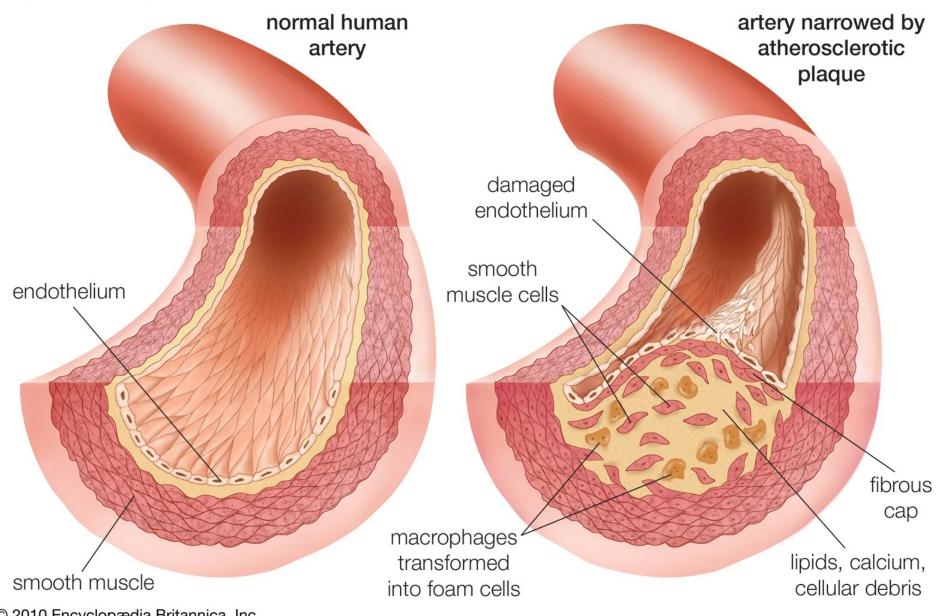


### **Atherosclerosis**

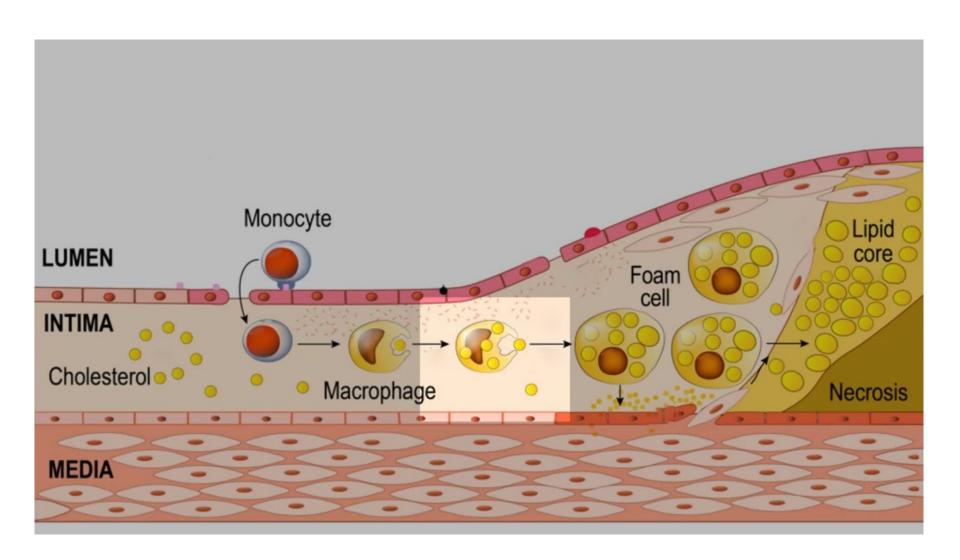


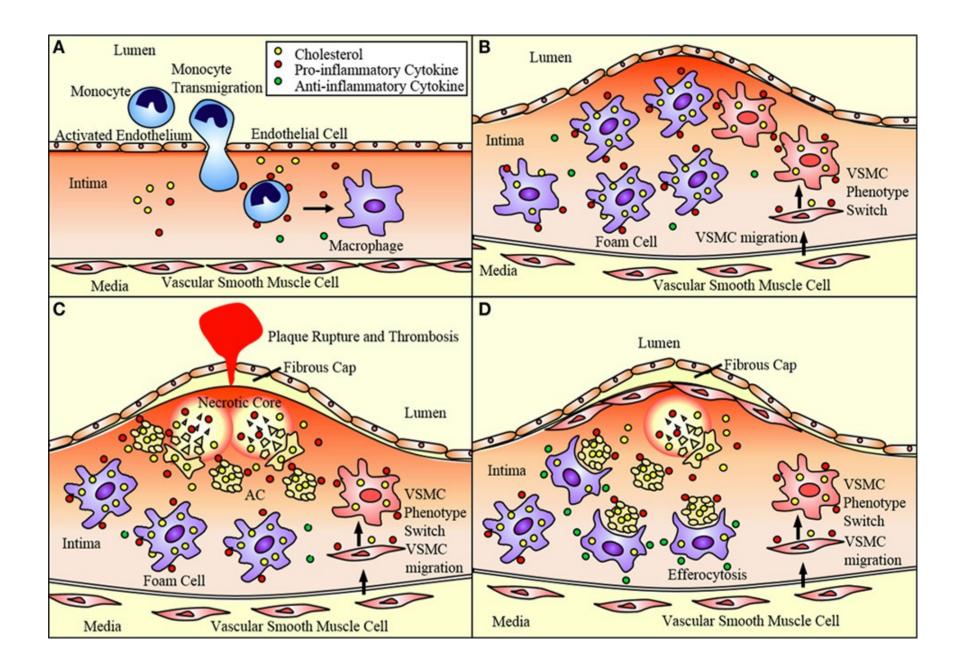


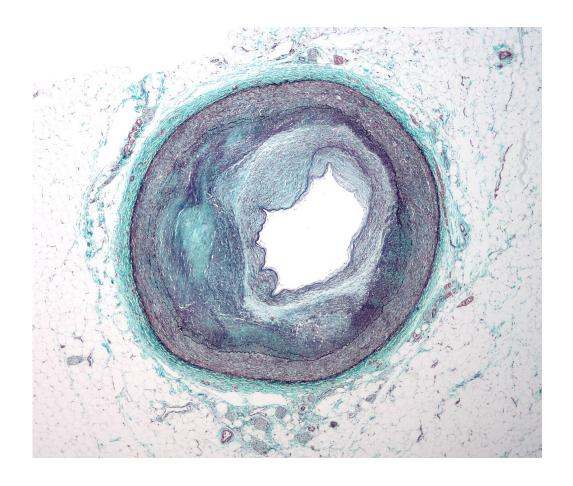
#### **Atherosclerosis**



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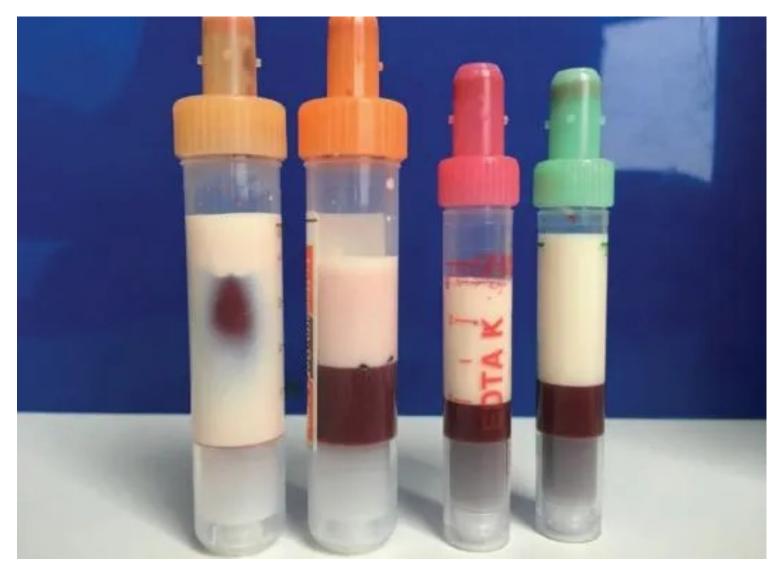






What's the difference between arteriosclerosis and atherosclerosis?

Atherosclerosis happens when your arteries become narrow due to a buildup of plaque. It's caused by inflammation in the arteries. Atherosclerosis progresses to arteriosclerosis, a condition in which your arteries become stiff. Arteriosclerosis is caused by elastin fibers in your arteries losing elasticity and calcium-phosphate salt moving into the soft plaque to make it hard.Oct 5, 2022



A man in Germany had extraordinarily high levels of triglycerides, a type of fat, in his blood. Above, samples of the man's blood about two hours after they were drawn. The white is the fat.



## **Vitamins**



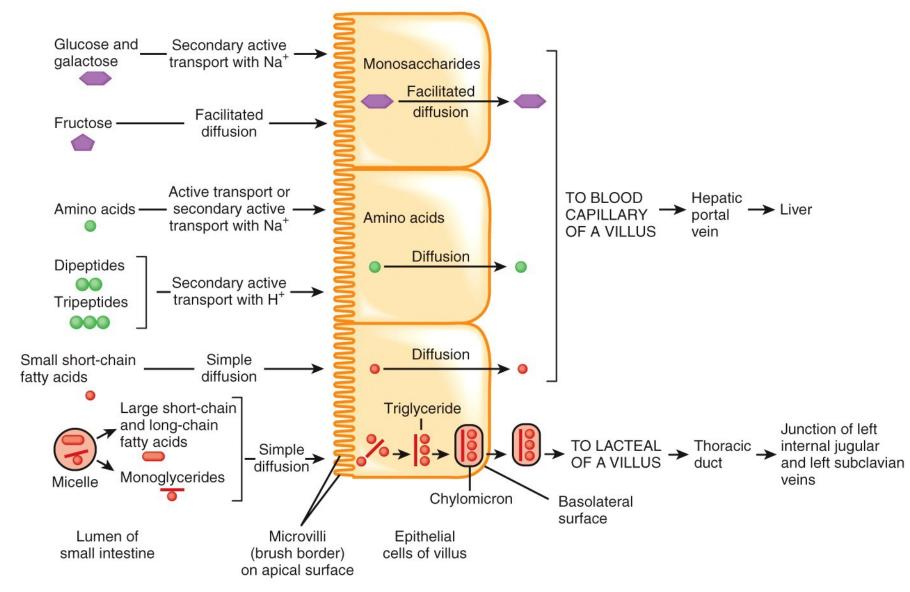
Vitamins are essential nutrients (must come from diet // we can not make them)

absorbed unchanged

fat-soluble vitamins - A, D, E and K absorbed with other lipids // if they are ingested without fat-containing food, they are not absorbed at all, but are passed in the feces and wasted // Why do we put fatty dressing on our salads?

water-soluble vitamins, like B and C vitamins are absorbed by simple Diffusion /// B<sub>12</sub> requires gastric intrinsic factor to be absorbed into body

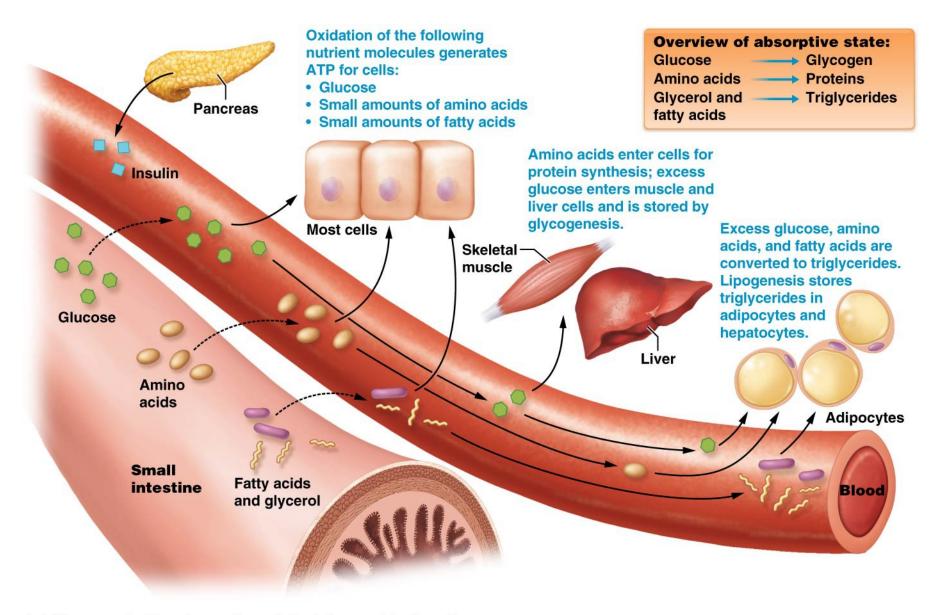




(a) Mechanisms for movement of nutrients through absorptive epithelial cells of villi

#### **The Absorptive State**

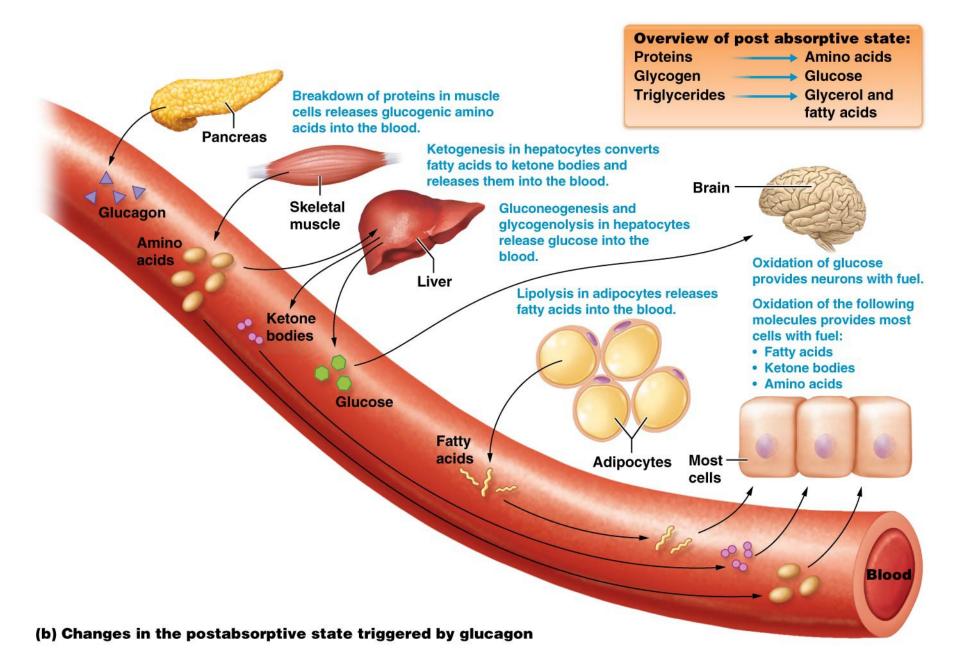




(a) Changes in the absorptive state triggered by insulin.

#### The Post Absorptive State







### Hormonal Regulation of Digestion (1 of 3)

Gastrin // hormone // produced by G cells of gastric pit

Stimulate gastric secretions

Stimulate lower esophageal sphincter to contract // prevents "heart burn"

Relax pyloric sphincter // allows small amount of chyme to enter duodenum and

By relaxing pyloric sphincter and allowing only small volumes of chyme to enters duodenum it then gives time to process chyme



### Hormonal Regulation of Digestion (2 of 3)

- Chyme leaving stomach stimulates duodeum's enteroendocrine cells to release secretin and cholecystokinin
  - These hormones stimulate different types of secretions from the pancreas and gall bladder
  - CCK suppress gastric secretion and interacts with hypothalamus to stimulate satiety // stimulate pancreas to produce and release more hormones // stimulate gall bladder to release bile
  - Another type of enteroendocrine cells secrete glucose-dependent insulinotropic peptide (GIP) /// this was called gastrin-inhibiting peptide
    - » stimulates insulin secretion in preparation for processing nutrients about to be absorbed by the small intestine // reduces gastric contractions

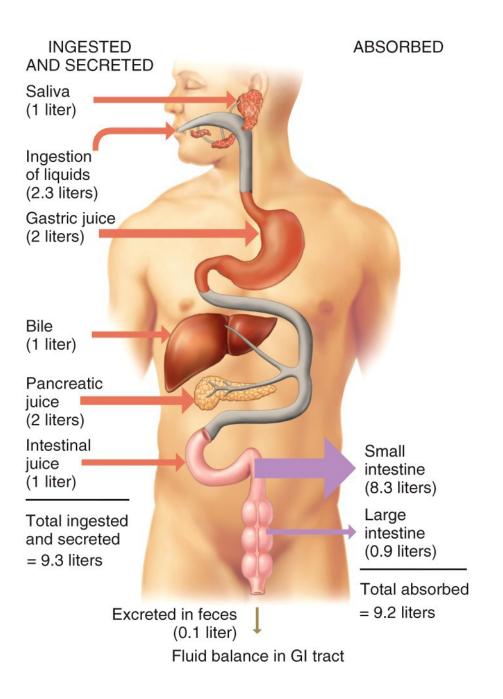


## Hormonal Regulation of Digestion (2 of 2)

- cholecystokinin (CCK) secreted by mucosa of duodenum in response to arrival of fats in small intestine
  - stimulate pancreatic acini to secrete enzymes
  - strongly stimulates gall bladder
  - induces contractions of the gallbladder and relaxation of hepatopancreatic sphincter causing discharge of bile into the duodenum
- secretin released from duodenum in response to acidic chyme arriving from the stomach
  - stimulates ducts in both liver and pancreas to secrete more sodium bicarbonate
  - raising pH to level pancreatic and intestinal digestive enzymes require

### **Small Intestine VS Large Intestine**

- Small intestine functions:
  - Digestion (mechanical and chemical)
  - Absorption of nutrients across mucosa /// active and passive
  - 99.9 percent of nutrients absorbed in small intestine
- Large intestine functions:
  - Eliminate food residue
  - Compaction
  - Recover water

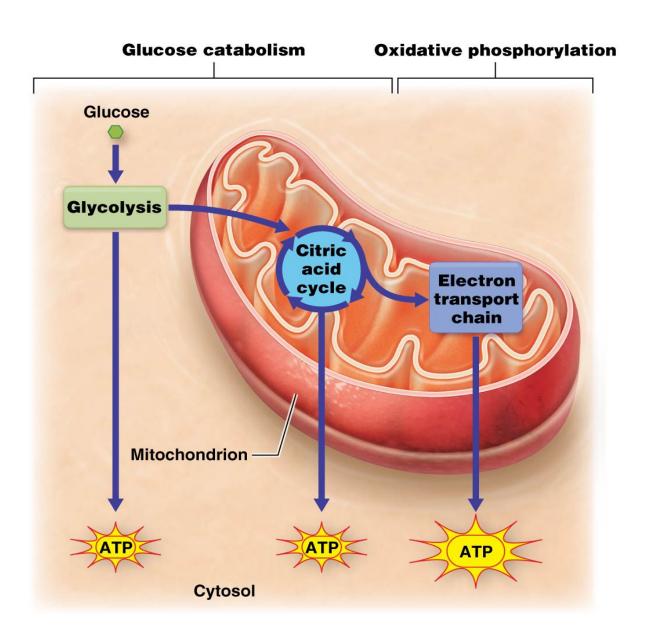


## Review of Metabolism

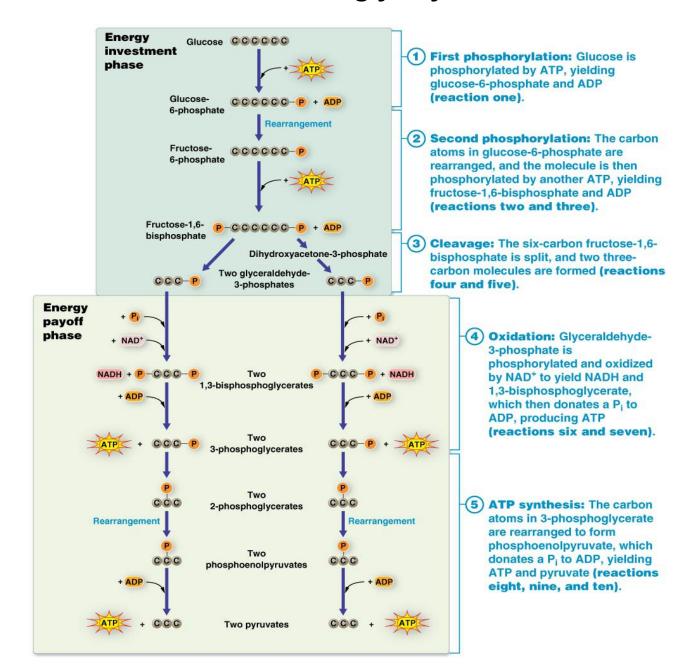
- > Gycolysis
- > Kreb's Cycle
- > Electron Transport Chain
- > Anabolism VS Catabolism

Overview of glucose catabolism and oxidative phosphorylation.

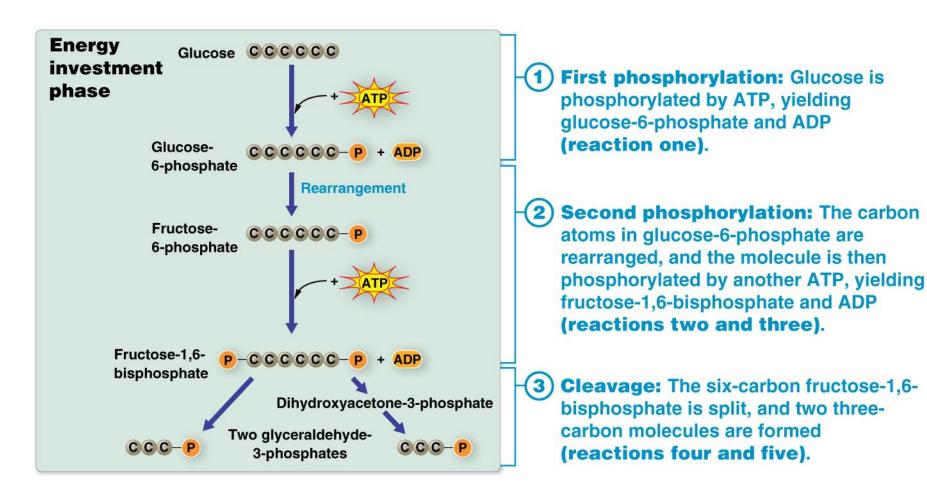




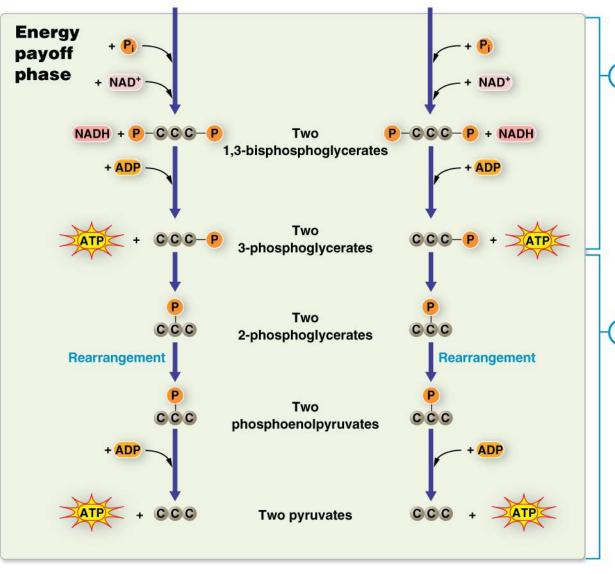
#### The reactions of glycolysis.



#### The reactions of glycolysis.



#### The reactions of glycolysis.

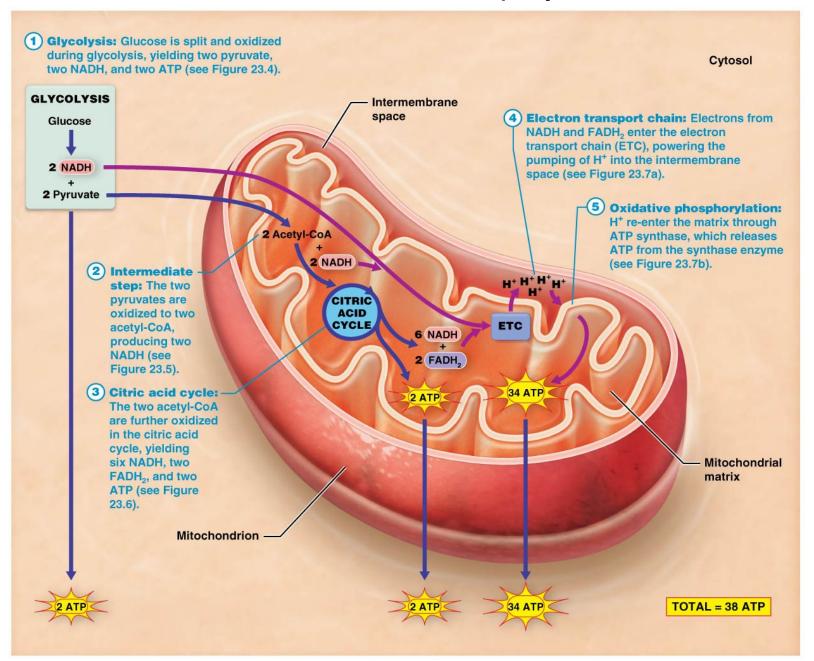


4 Oxidation: Glyceraldehyde-3-phosphate is phosphorylated and oxidized by NAD<sup>+</sup> to yield NADH and 1,3-bisphosphoglycerate, which then donates a P<sub>i</sub> to ADP, producing ATP (reactions six and seven).

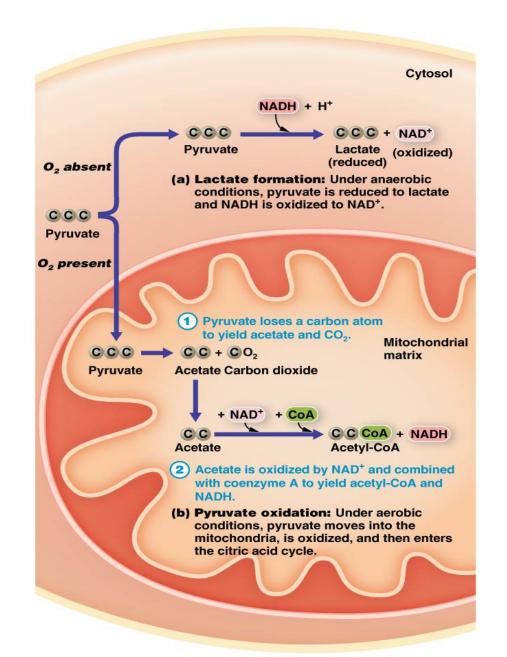
5 ATP synthesis: The carbon atoms in 3-phosphoglycerate are rearranged to form phosphoenolpyruvate, which donates a P<sub>i</sub> to ADP, yielding ATP and pyruvate (reactions eight, nine, and ten).

## The Big Picture of Glucose Catabolism and Oxidative Phosphorylation

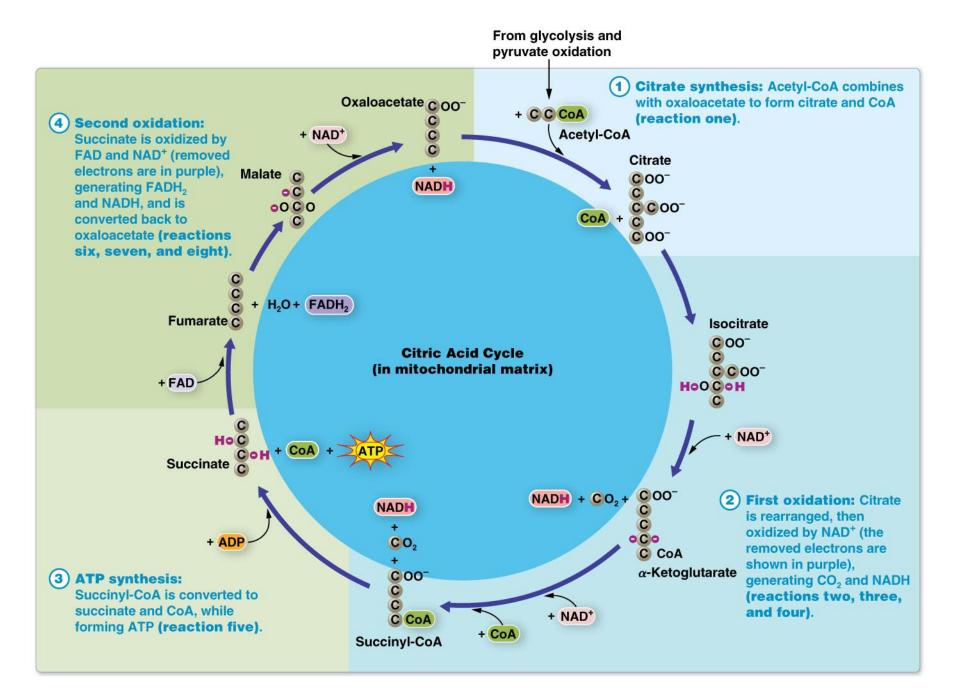




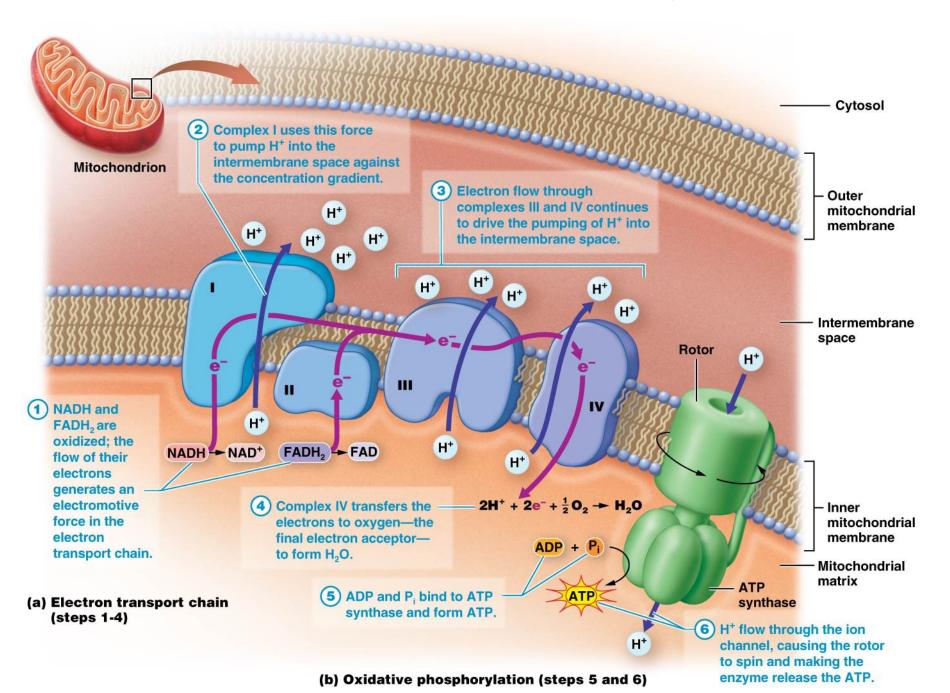
### Intermediate step: the fate of pyruvate after glycolysis.



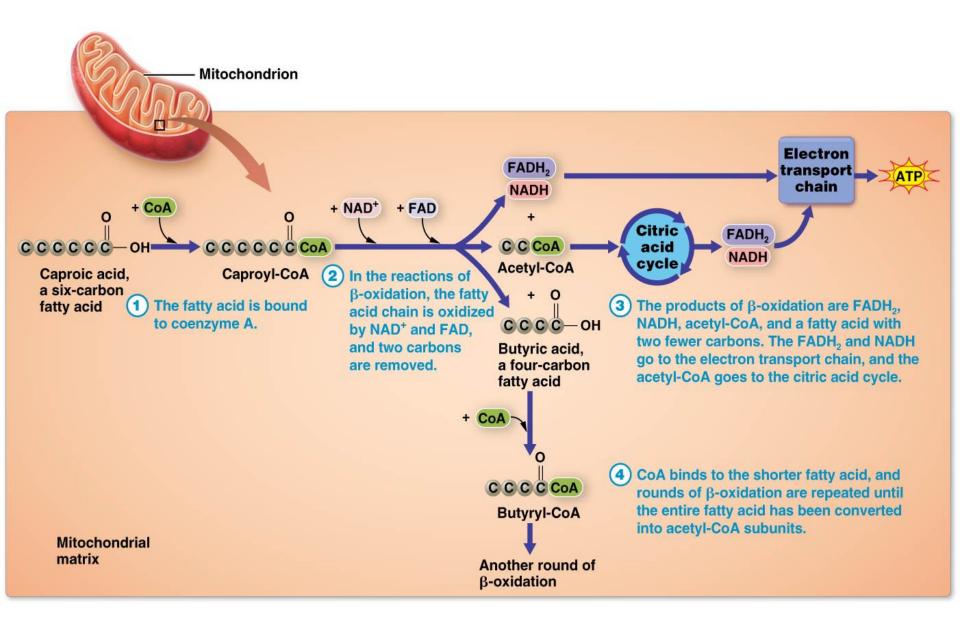
#### The citric acid cycle.



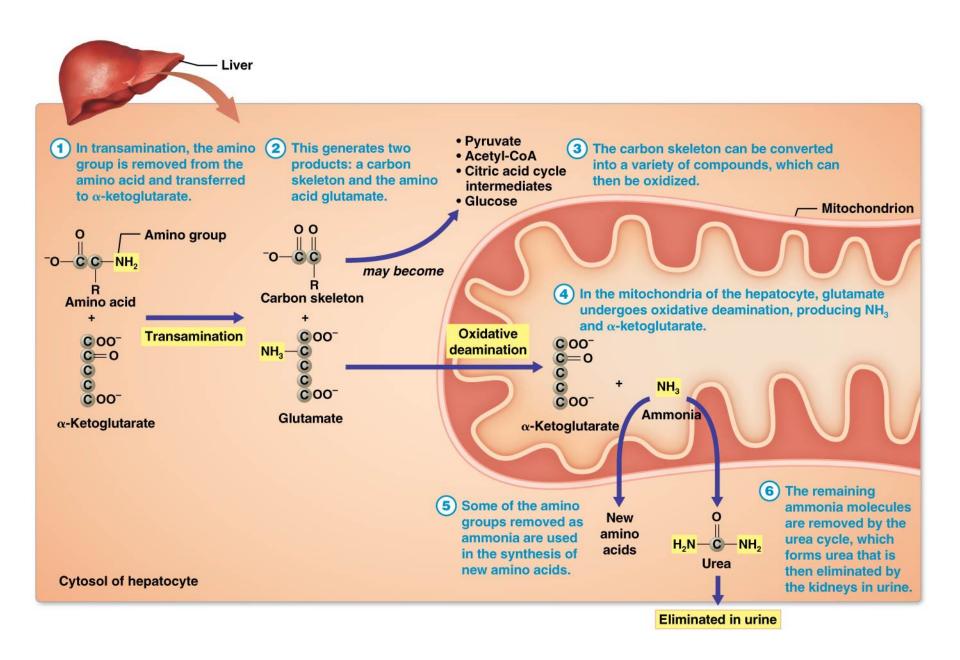
#### The electron transport chain and oxidative phosphorylation.



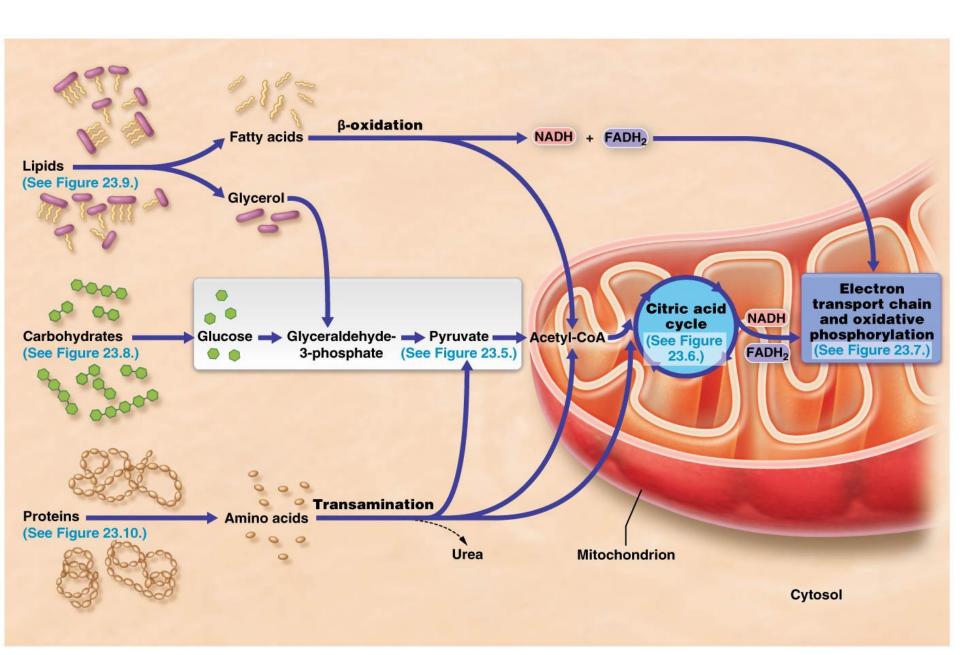
### Fatty acid catabolism and β-oxidation.



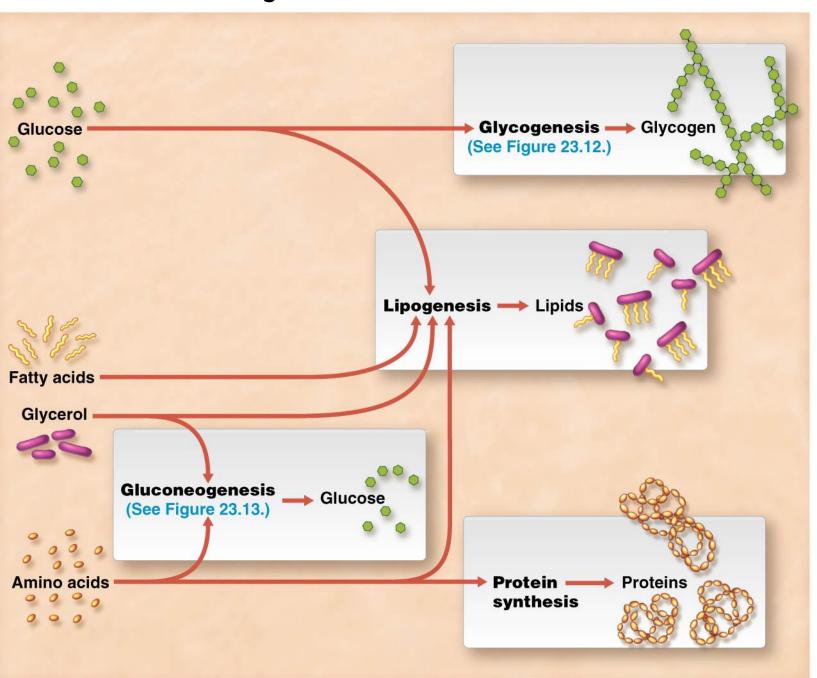
#### Amino acid catabolism.



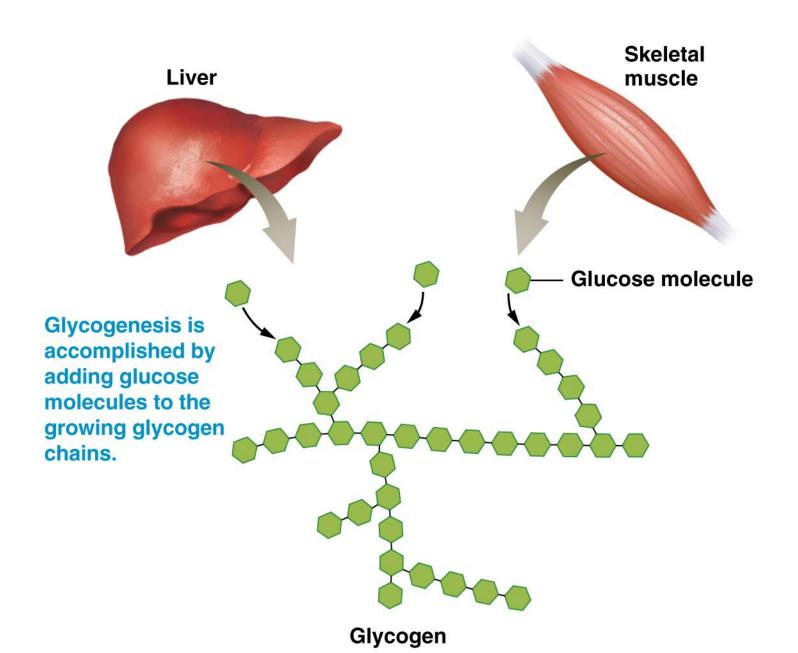
### The Big Picture of Nutrient Catabolism



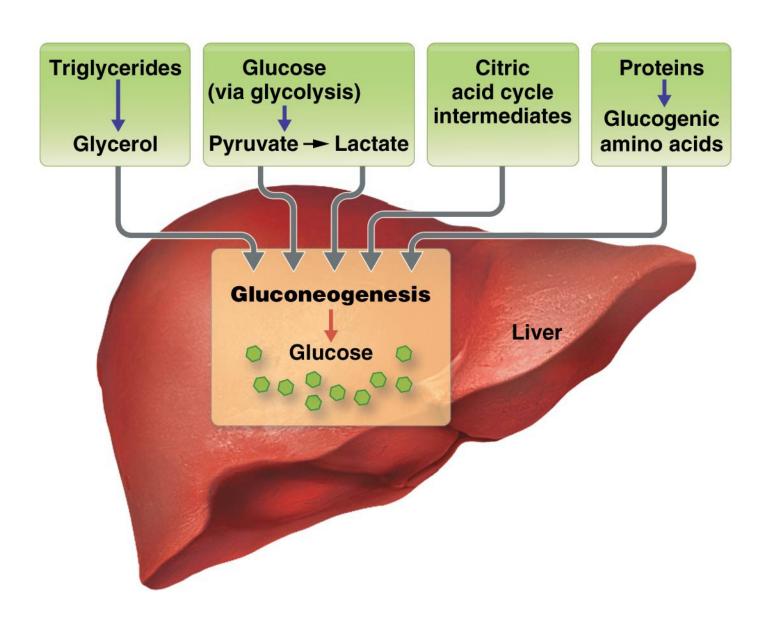
#### **The Big Picture of Nutrient Anabolism**



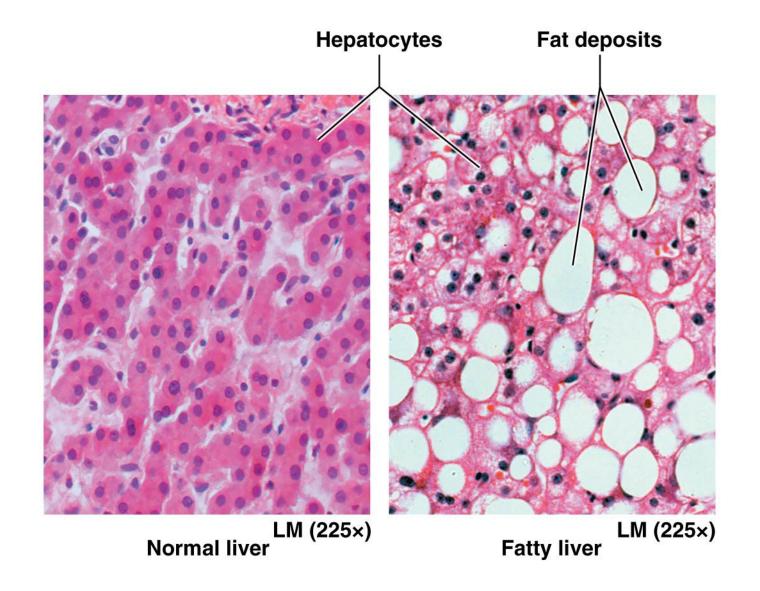
### Glycogenesis.



## Gluconeogenesis.



## **Too Much Lipogenisis in Hepatocytes**

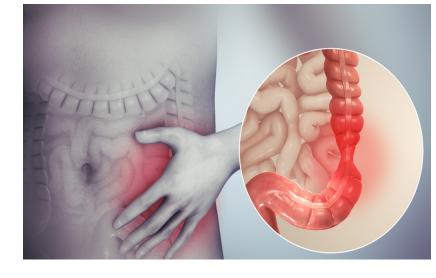


# **GI Tract Diseases**

- > Irritable Bowel Syndrome
- > Crohn Disease
- > Ulceratis Colitis
- > Celiac Disease

### Irritable Bowel Syndrome

Irritable bowel syndrome (IBS) is a common disorder that affects the large intestine. Signs and symptoms include cramping, abdominal pain, bloating, gas, and diarrhea or constipation, or both. IBS is a chronic condition that you'll need to manage long term.



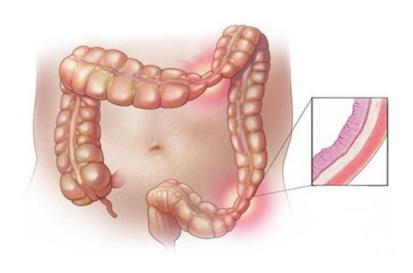
Only a small number of people with IBS have severe signs and symptoms. Some people can control their symptoms by managing diet, lifestyle and stress. More-severe symptoms can be treated with medication and counseling.

IBS doesn't cause changes in bowel tissue or increase your risk of colon-rectal cancer.

Symptoms - The signs and symptoms of IBS vary. The most common include: abdominal pain, cramping or bloating that is typically relieved or partially relieved by passing a bowel movement /// Excess gas /// Diarrhea or constipation — sometimes alternating bouts of diarrhea and constipation // Mucus in the stool

Most people with IBS experience times when the signs and symptoms are worse and times when they improve or even disappear completely.

# WHAT ARE THE SYMPTOMS OF IRRITABLE BOWEL SYNDROME?



BACK PAIN

✓ URINARY INCONTINENCE

PAIN DURING SEXUAL INTERCOURSE

STOMACH CRAMPS

ABDOMINAL PAIN

DIARRHEA

CONSTIPATION

**BLOATING** 

FLATULENCE

INCONTINENCE

STOOLS THAT CONTAIN MUCUS

LETHARGY AND DROWSINESS

**Crohn's Disease** is a chronic, inflammatory disease of the gastrointestinal tract. It is an autoimmune disorder, meaning your body's immune system mistakenly attacks healthy tissue in your body.

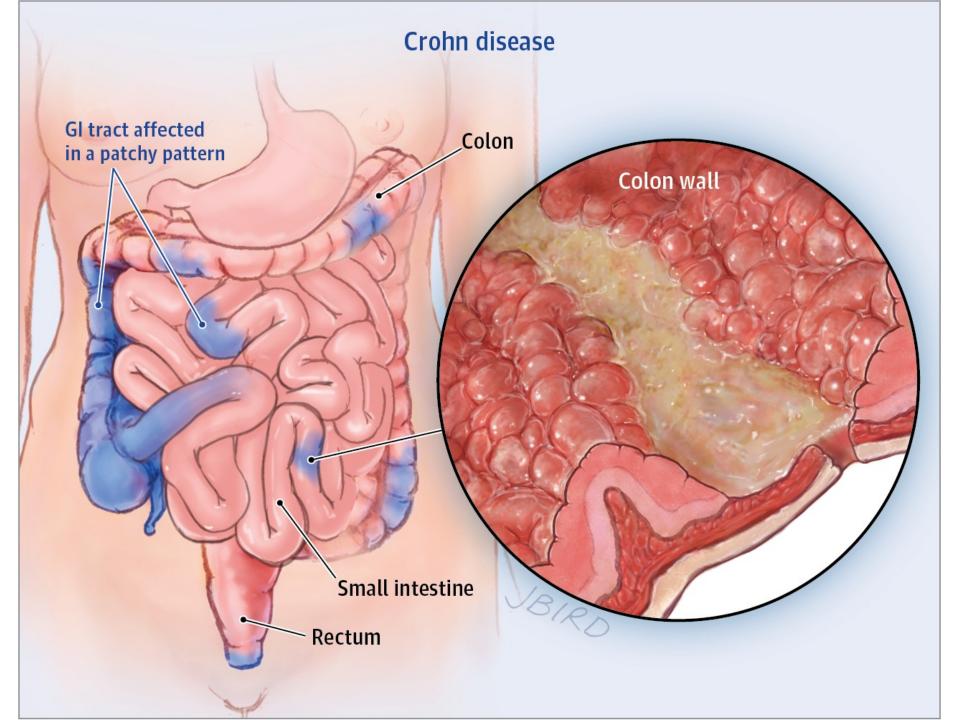
Crohn's disease is chronic (ongoing), and may appear and disappear at various times. Initially, it may affect only a small part of your gastrointestinal tract, but the disease has the potential to progress extensively.

Who Gets Crohn's Disease? When?

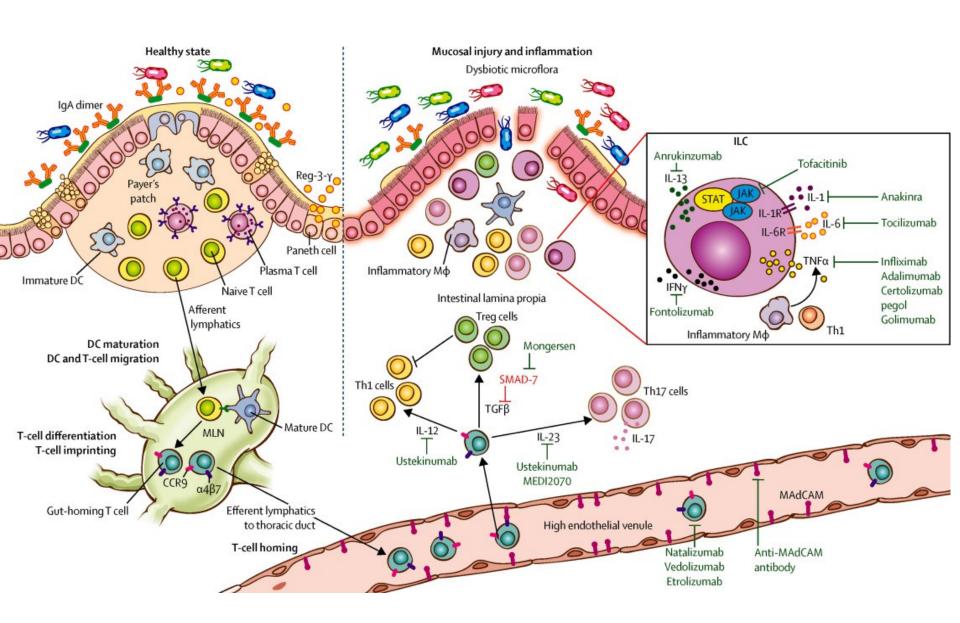
Crohn's disease appears early in life; approximately one-sixth of patients have symptoms before 15 years of age. Although the cause is unknown, doctors suspect a genetic influence, since many members of the same family may be affected. Crohn's disease affects the Jewish population more than the general population.

Crohn's disease often begins in a person's teens or twenties, though some patients experience symptoms even earlier. Most common symptoms include (see next slide)

#### Crohn's disease Eye inflammation Stomatitis Mount Ulcer Skin Liver and **Ulcers** bile duct and sores Inflammation Stomach Vomiting Intestinal Diarrhea Abdominal pain Fever Cramping Weight loss Ulcers in Decreased appetite digestive tract Joint Rectal Pain and bleeding swelling ©Designua / Shutterstock.com



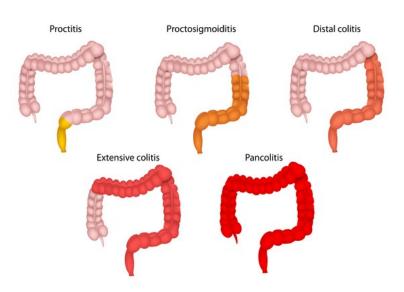
#### **Crohn Disease**



**Ulcerative Colitis** (UC) is a disease that affects your large intestine, or colon. It causes irritation and swelling called inflammation. ... UC is a type of inflammatory bowel disease, but it's different from other diseases with similar symptoms, like Crohn's disease or irritable bowel syndrome.

Ulcerative colitis is usually only in the innermost lining of the large intestine (colon) and rectum. Forms range from mild to severe. Having ulcerative colitis puts a patient at increased risk of developing colon cancer. Symptoms include rectal bleeding, bloody diarrhea, abdominal cramps, and pain.

#### TYPES OF ULCERATIVE COLITIS



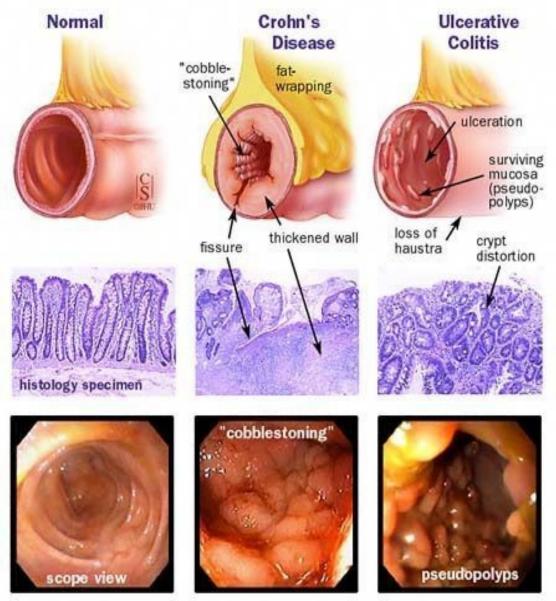
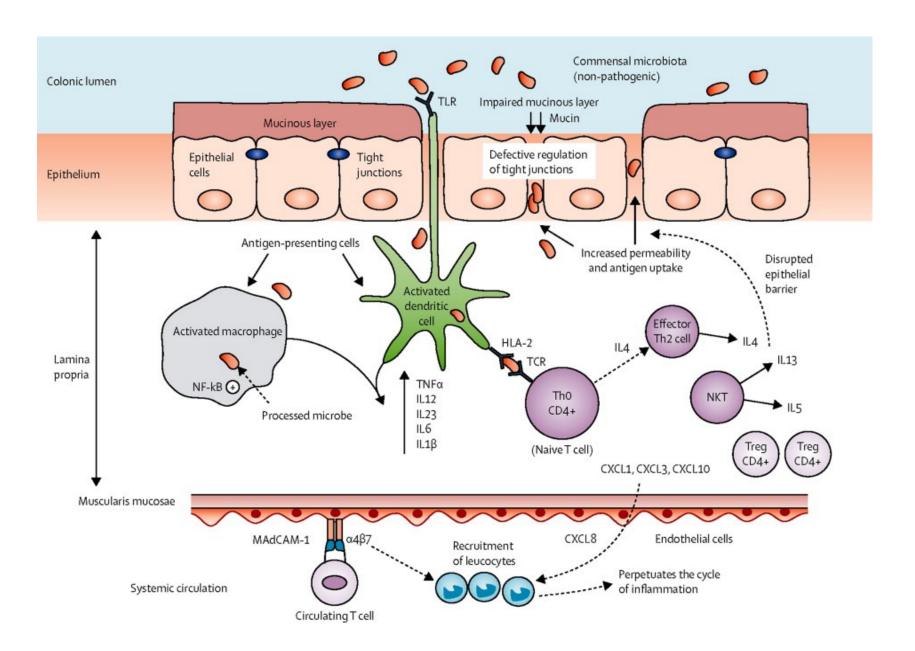


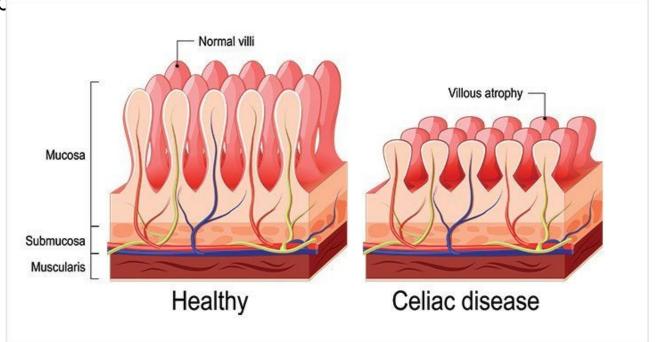
Figure 4. Gross (top), histological (center), and endoscopic (bottom) appearance of normal colon, Crohn's disease, and ulcerative colitis.

## **Ulcerative Colitis Pathophysiology**

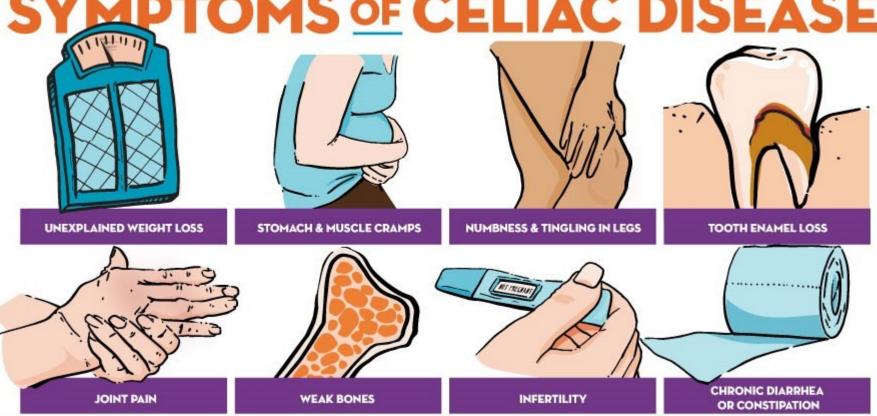


### Celiac Disease

Celiac disease is caused by a hypersensitivity that causes an immune disease condition. The immune response causes damage to their small intestine. People with celiac disease are hypersensitive to gluten. To control the disease you need to eliminate gluten from their diet. Gluten is a protein found in wheat, rye, and barley. Loss of microvilli inhibit nutrient absorp.

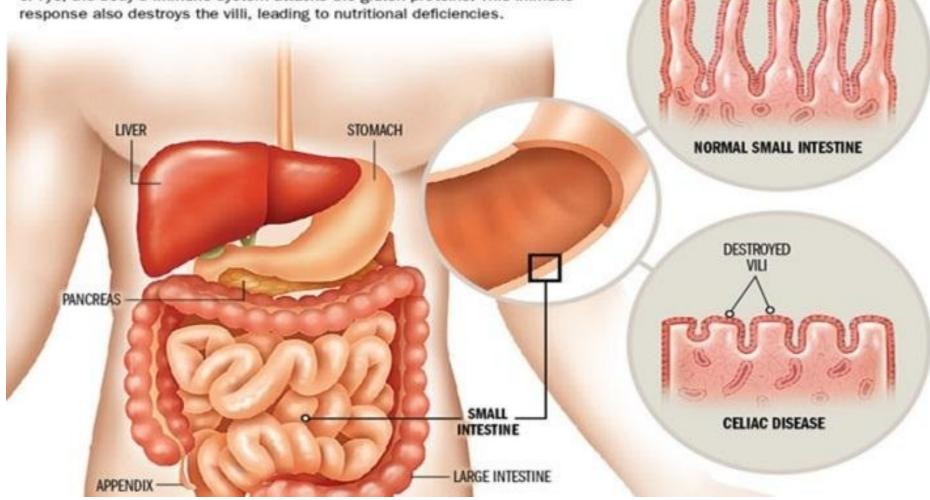




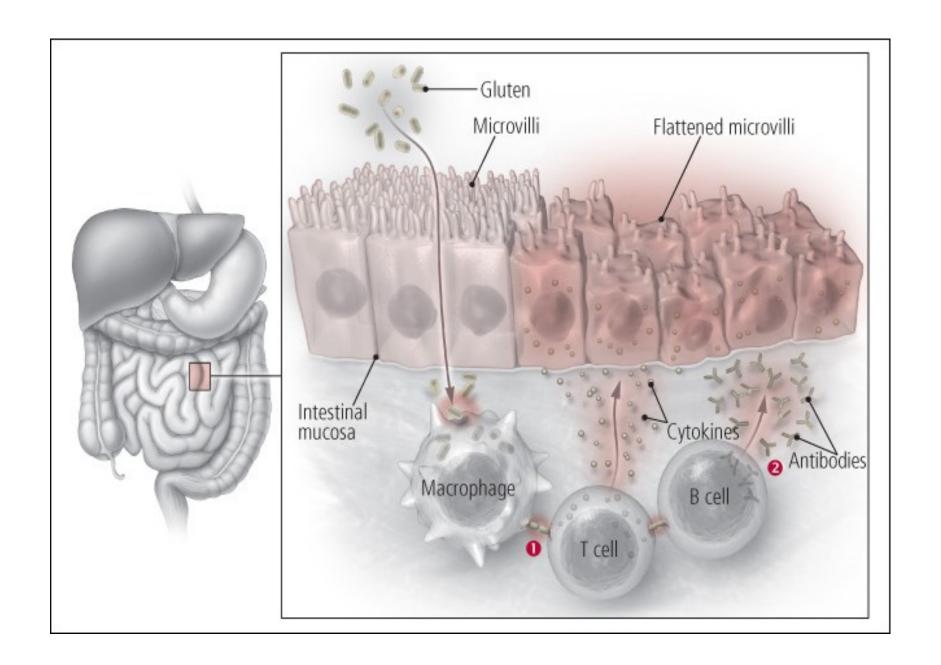


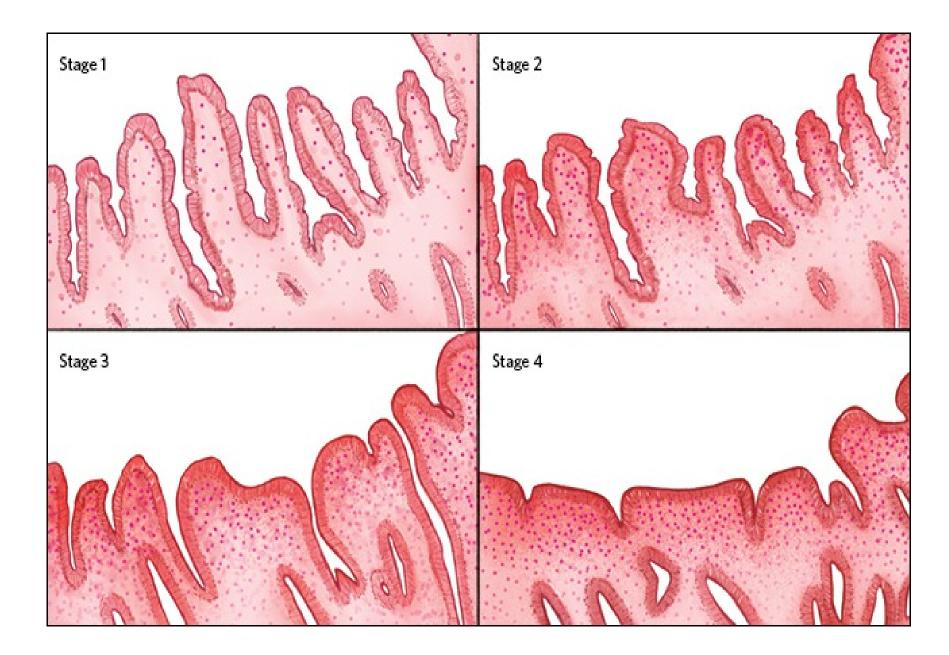
## Damage from celiac disease

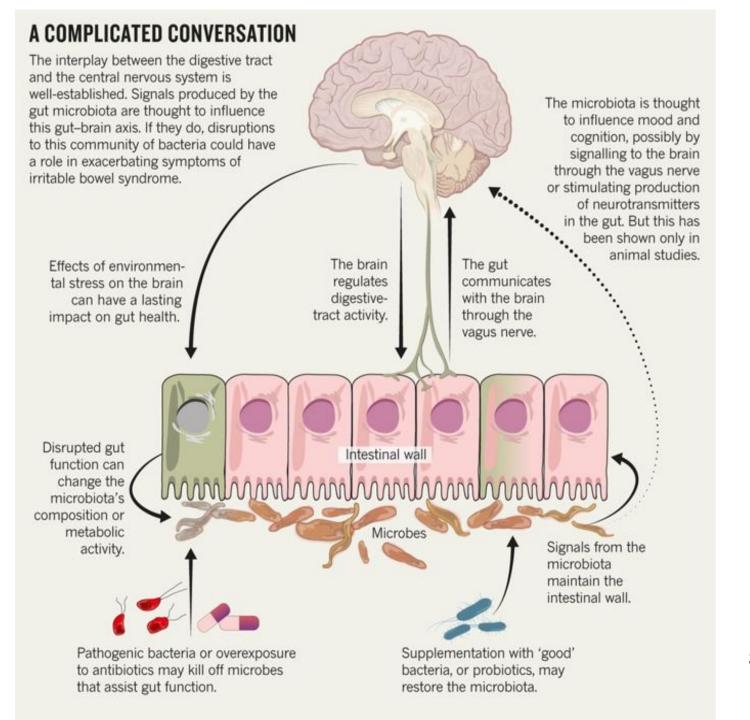
In a healthy small intestine, tiny hairlike projections called villi absorb nutrients from food. When people with celiac disease eat foods containing wheat, barley, or rye, the body's immune system attacks the gluten proteins. This immune response also destroys the villi, leading to nutritional deficiencies.



VILI







See home page link Openbiome.

#### The Big Picture of Digestion.



