# Pentose Phosphate Pathway

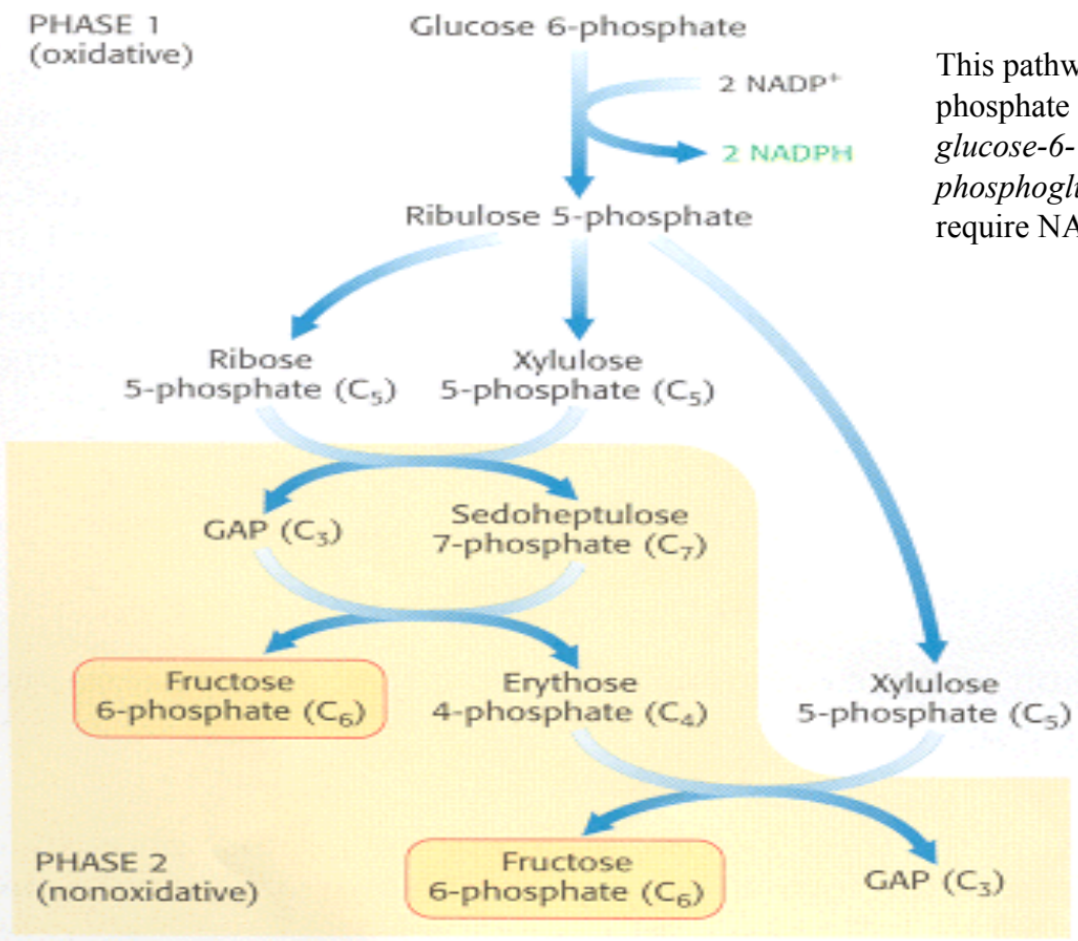
The production of five-carbon monosaccharides (pentoses) and nicotinamide adenine dinucleotide phosphate (NADPH)

- Glucose 6-phosphate □ glycolysis
- Has other catabolic fates□ oxidation to pentose phosphates in the pentose phosphate pathway
- Through the pentose phosphate pathway , glucose in the cytosol generates important intermediates not produced in other pathways

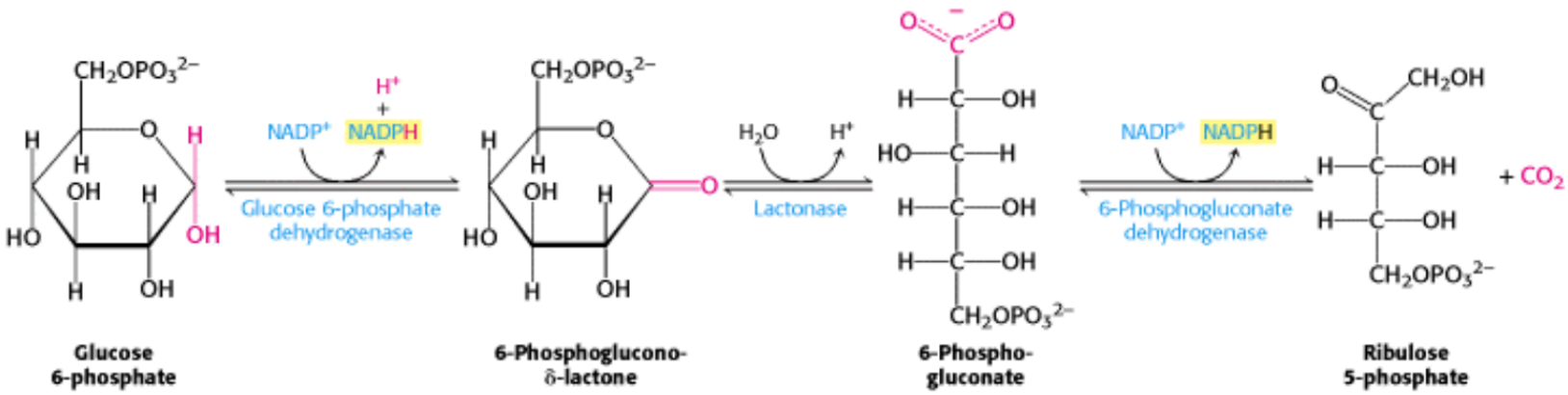
1. **Pentose phosphatases**
2. **NADPH Generation**

- Rapidly dividing cells, such as those of bone marrow, skin, and intestinal mucosa, use the pentoses to make
  - RNA, DNA
  - coenzymes as ATP, NADH, FADH2, and coenzyme A.
- Other cells will utilize NADPH, needed for reductive biosynthesis
- NADPH also used to combat the damaging effects of oxygen radicals ( Erythrocytes and cornea cells)- directly exposed to oxygen
- Tissues that carry out extensive fatty acid synthesis (liver, adipose, lactating mammary gland) or very active synthesis of cholesterol and steroid hormones (liver, adrenal gland, gonads)

- The pathway reactions that include the dehydrogenase reactions and therefore the formation of NADPH from NADP+ are called the oxidative reactions of the pathway.
- The pentose phosphate pathway also synthesizes three-, four-, five-, six-, and seven-carbon sugars.




This pathway begins by oxidizing glucose-6-phosphate in two consecutive reactions catalyzed by *glucose-6- phosphate dehydrogenase* and *6-phosphogluconate dehydrogenase*. Both reactions require NADP+ as cosubstrate




**The Rate of the Pentose Phosphate Pathway Is Controlled by the Level of NADP+** It is strongly inhibited by NADPH and fatty acid CoAs.

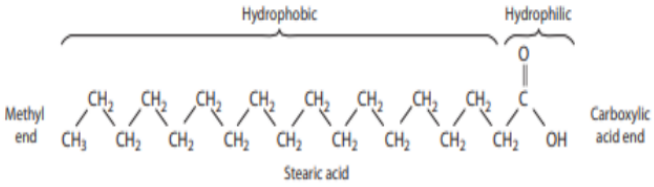
- The pathway's activity is low in skeletal muscle because of the limited demand for NADPH (fatty acid synthesis) in this tissue and also because of muscle's reliance on glucose and fatty acids for energy metabolism.

# LIPIDS

Chapter 5

- The property that sets lipids apart from other major nutrients is their solubility in organic solvents such as ether, chloroform, and acetone
- Many diverse molecules fit the criteria and are thus considered lipids
- The lipids discussed- limited to those most relevant to human nutrition
  - Fatty acids
  - Triacylglycerols, diacylglycerols, and monoacylglycerols
  - **Phospholipids**
  - **Sphingolipids**
  - Sterols (cholesterol, bile acids, and phytosterols).

- Fatty acids are composed of a hydrocarbon chain with a methyl group at one end and a carboxylic acid group at the other
- Polar, hydrophilic end and a nonpolar, hydrophobic end that is insoluble in water
- lengths of the hydrocarbon chains: 4-24 Carbons
- most common fatty acids in nature are 18 carbons.
- They are of vital importance as an energy
- Saturated (SFA)
  - Monounsaturated (MUFA)
  - Polyunsaturated (PUFA). Notre: may contain as many as 6 double bonds.



The *cis* isomer
□bending of the molecule into a U-like orientation
*Trans* □ linear shape
Naturally occurring unsaturated fatty acids are of the *cis* configuration

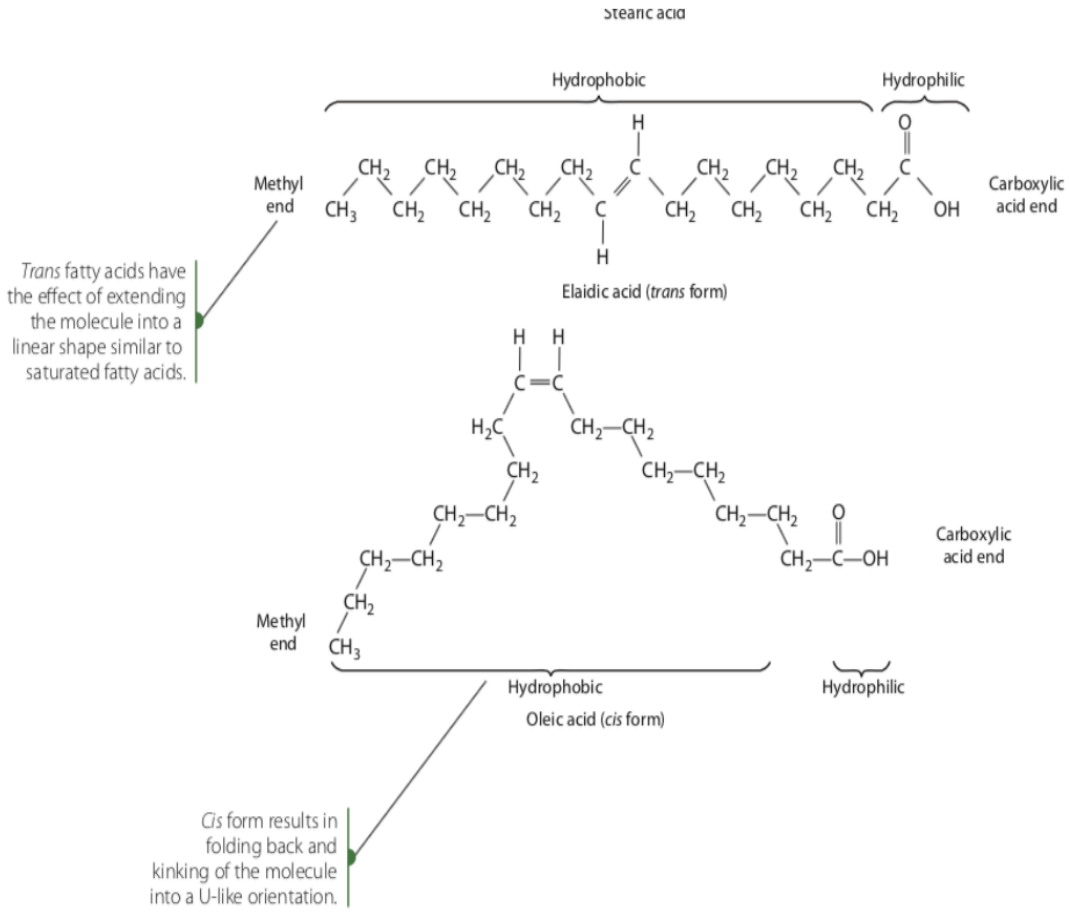
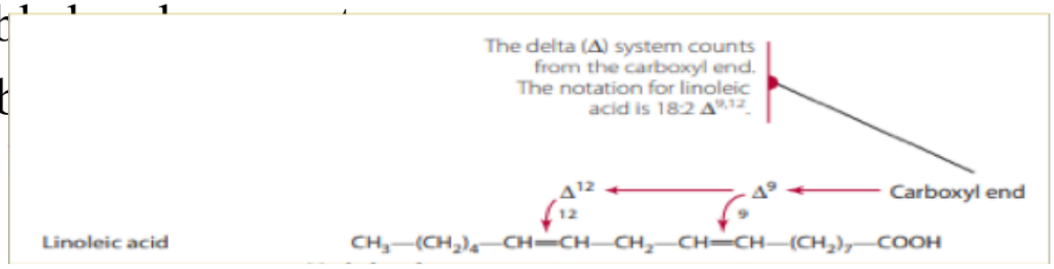



**Figure 5.1** Structures of selected fatty acids.

# Fatty Acid Nomenclature

- The delta (Δ) system of notation has been established to denote the chain length of the fatty acids and the number and position of any double bonds that may be present.
- For example, the notation 18:2 Δ9,12 describes linoleic acid.
- 18: number of carbon atoms
- 2: total number of doub
- 9,12: designate the carb bonds begin, counting fatty acid.



- A second commonly used system of notation locates the position of double bonds on carbon atoms counted from the methyl, or omega ($\omega$), end of the hydrocarbon chain.
- Linoleic acid: would 18:2 $\omega$-6. Substitution of the omega symbol with the letter n has been

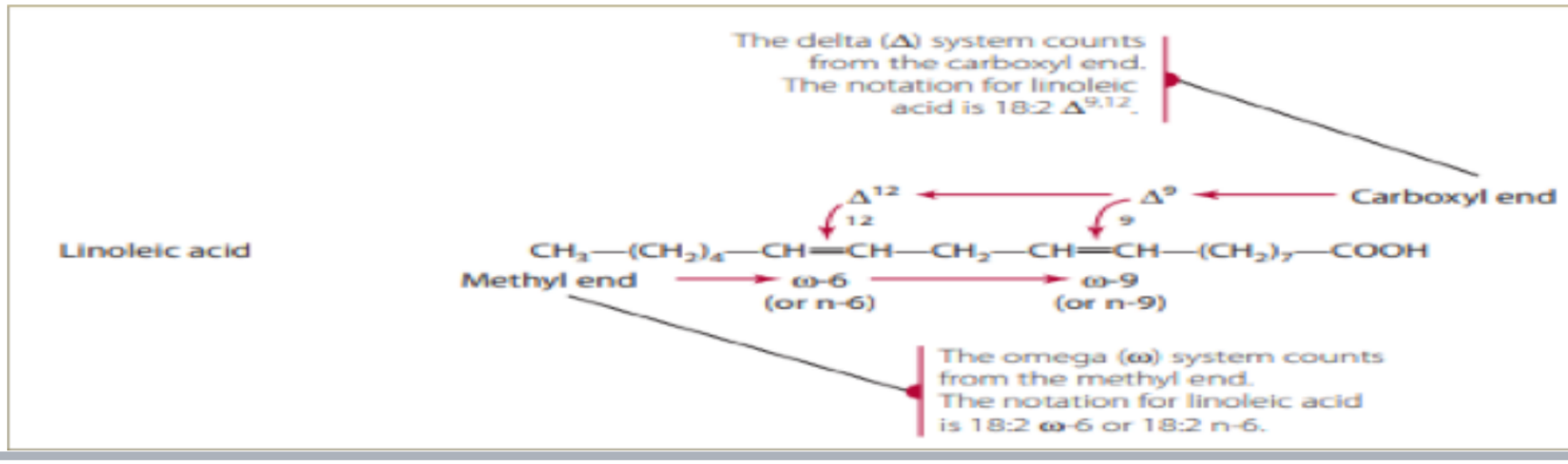



**Table 5.1** Some Naturally Occurring Fatty Acids

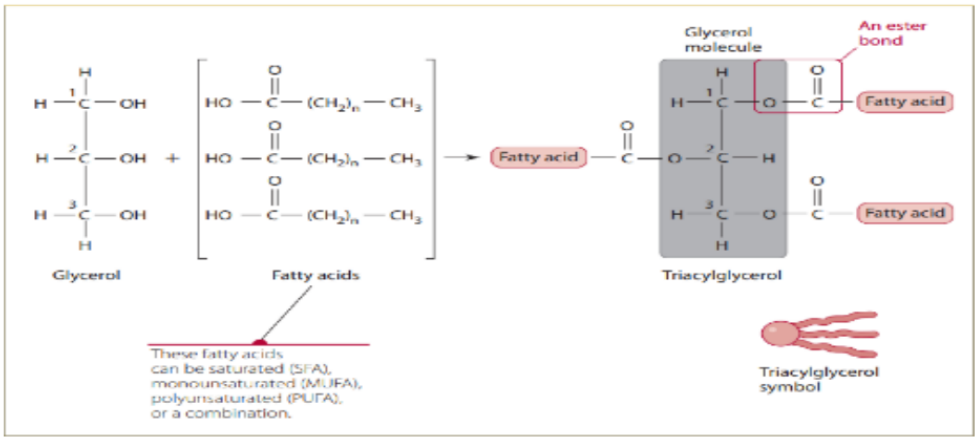
| Notation | Common Name | Formula | Source* |
|---|---|---|---|
| **Saturated Fatty Acids** | | | |
| 14:0 | Myristic acid | $CH_3-(CH_2)_{12}-COOH$ | Coconut and palm kernel oil, fish oils |
| 16:0 | Palmitic acid | $CH_3-(CH_2)_{14}-COOH$ | All animal and plant fats, notably palm oil |
| 18:0 | Stearic acid | $CH_3-(CH_2)_{16}-COOH$ | All animal and plant fats, notably cocoa butter |
| 20:0 | Arachidic acid | $CH_3-(CH_2)_{18}-COOH$ | Peanut oil, wild-caught salmon oil |
| 24:0 | Lignoceric acid | $CH_3-(CH_2)_{22}-COOH$ | Peanut oil |
| **Unsaturated Fatty Acids** | | | |
| 16:1 $\Delta^9$ (n-7) | Palmitoleic acid | $CH_3-(CH_2)_5-CH=CH-(CH_2)_7-COOH$ | Fish oils, poultry fat |
| 18:1 $\Delta^9$ (n-9) | Oleic acid | $CH_3-(CH_2)_7-CH=CH-(CH_2)_7-COOH$ | All animal and plant fats |
| 18:2 $\Delta^{9,12}$ (n-6) | Linoleic acid | $CH_3-(CH_2)_4-CH=CH-CH_2-CH=CH-(CH_2)_7-COOH$ | Most plant oils, poultry fat |
| 18:3 $\Delta^{9,12,15}$ (n-3) | α-Linolenic acid | $CH_3-(CH_2-CH=CH)_3-(CH_2)_7-COOH$ | Linseed (flax), soybean, and canola oils |
| 20:4 $\Delta^{5,8,11,14}$ (n-6) | Arachidonic acid | $CH_3-(CH_2-CH=CH)_5-(CH_2)_3-COOH$ | Fish oils |
| 20:5 $\Delta^{5,8,11,14,17}$ (n-3) | Eicosapentaenoic acid | $CH_3-(CH_2-CH=CH)_5-(CH_2)_3-COOH$ | Marine algae and fish that consume the algae |
| 22:6 $\Delta^{4,7,10,13,16,19}$ (n-3) | Docosahexaenoic acid | $CH_3-(CH_2-CH=CH)_6-(CH_2)_2-COOH$ | Marine algae and fish that consume the algae |

*Fats and oils in the food supply contain many types of fatty acids of varying proportions. The sources listed here indicate foods that are comparatively enriched in the specific fatty acid.

# Triacylglycerols (Triglycerides)

- Most adipose tissue is composed of triacylglycerols, which represent a highly concentrated form of stored energy
- Accounts for nearly 95% of dietary fat

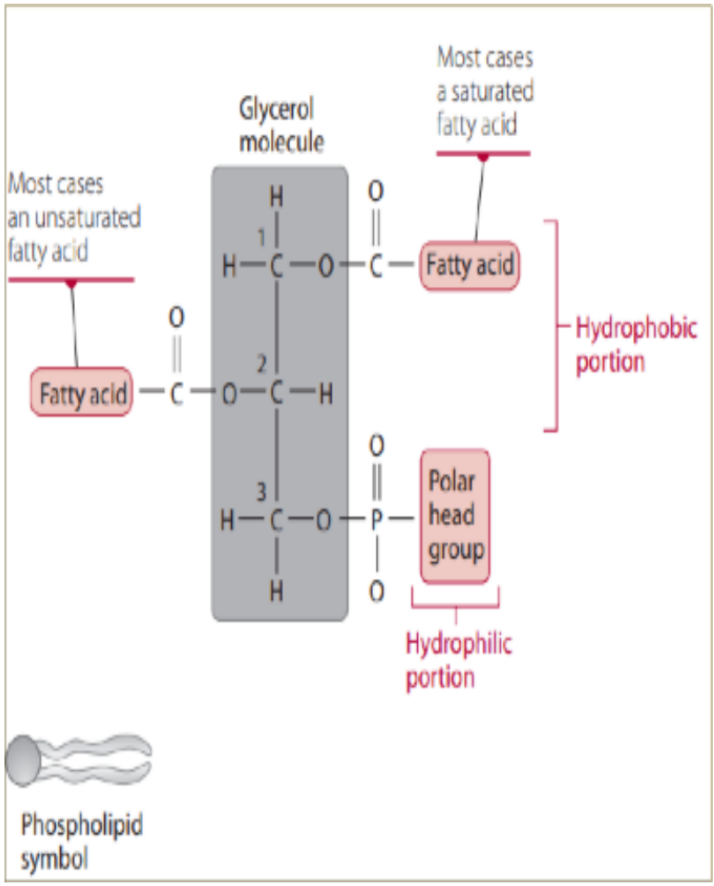
Acylglycerols
Diacylglycerol



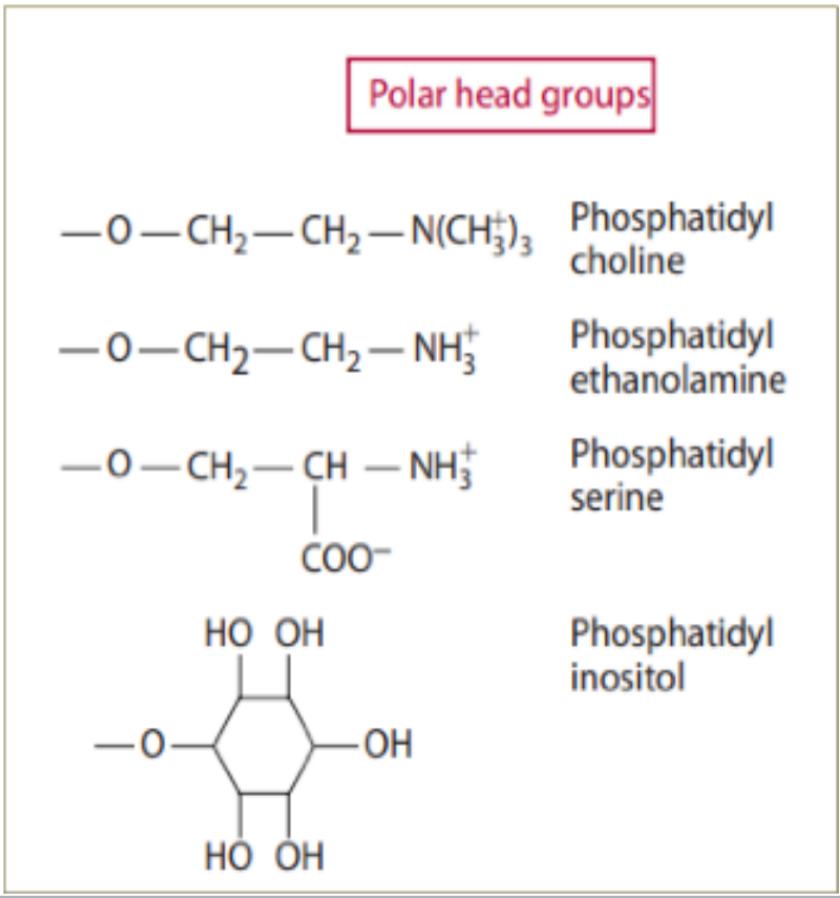

- Two unsaturated fatty acids cannot be synthesized in the body and must be acquired in the diet
- The two essential fatty acids are
- linoleic acid (18:2 n-6 or 18:2D9,12) ]
- alpha-linolenic acid (18:3 n-3 or 18:3D9,12,15)
- It is estimated that our human ancestors consumed foods that provided equal amounts of n-6 and n-3 fatty acids. Today, the intake of n-3 fatty acids is quite low and over- whelmed by n-6 fatty acids in the diet, with linoleic acid providing 80–90% of all PUFA
- wide- spread use of plant oils, such as soybean oil, in the production of manufactured food products and in foodservice frying oils, coupled with the relatively low intake of fish and other n-3 fatty acid sources in Western diets

# Phospholipids

- phosphate- containing lipids that form the structural basis of all cell membranes
- Glycerol forms the structural backbone of phospholipids. Fatty acids are esterified to the hydroxyl groups at the sn-1 and sn-2 positions of glycerol; a phosphate group is esterified at the sn-3 position and, in turn, a polar "head group" is esterified to the phosphate.




- Phospholipids are named according to the specific head group.
- Common head group molecules are choline, ethanolamine, serine, and inositol, each possessing an alcohol group through which esterification to the phosphate takes place
- Phosphatidylcholine: The most common in mammal tissue. Followed by Phosphatidylethanolamine.



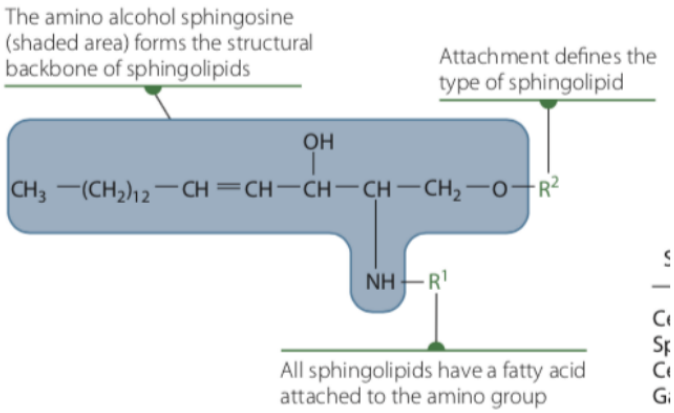
- Amphipathic nature: phospholipids form the foundational structure of lipid bilayers that comprise cell membranes that serve as a selective barrier for the passage of water-soluble and fat-soluble materials across the membrane
- Phospholipids also form a monolayer on the surface of bloodborne lipoprotein particles, thereby stabilizing the particles in the aqueous medium.
- Phospholipids are physiologically active compounds
- phosphatidylinositol plays a significant role in cell signaling

- Phosphatidylinositol in the plasma membrane can be doubly phosphorylated by ATP  phosphatidylinositol-4,5-bisphosphate (PIP2)
- Phosphorylated forms of phosphatidylinositol (PI) are called phosphoinositides and **play important roles in lipid signaling, cell signaling**
- The reversible phosphorylation and dephosphorylation reactions are catalyzed by phosphoinositide kinases and phosphatases in response to extracellular stimuli
- Phosphoinositides exert their physiological role by attracting regulatory proteins to the membrane
  - endocytosis, membrane fusion, and ion channels.

- Example: PIP2 and its role in insulin signaling pathways

# Sphingolipids

- found in the plasma membrane of all cells, although their concentration is highest in cells of the central nervous system
- Sphingolipids are built on the amino alcohol sphingosine (not glycerol) as the structural backbone




| Sphingolipid | $R^1$ | $R^2$ |
|---|---|---|
| Ceramide | Fatty acid | H |
| Sphingomyelin | Fatty acid | Phosphocholine |
| Cerebroside | Fatty acid | Galactose or glucose |
| Ganglioside | Fatty acid | Oligosaccharide |

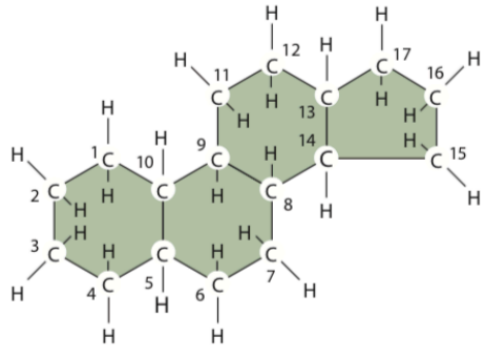
- Sphingomyelin: formed when phosphocholine is added to ceramide. Abundant in the myelin sheath of nerve tissues
- Cerebrosides: A single sugar molecule, either galactose (myelin sheath) or glucose (spleen and RBCs), attaches to the terminal hydroxyl group of ceramide.
- Gangliosides: have multiple sugar units. Located on the outer surface of membranes mainly in nerve tissue

# Sterols

- Characterized by having a four-ring steroid nucleus and at least one hydroxyl group, hence the name sterol (steroid alcohol).

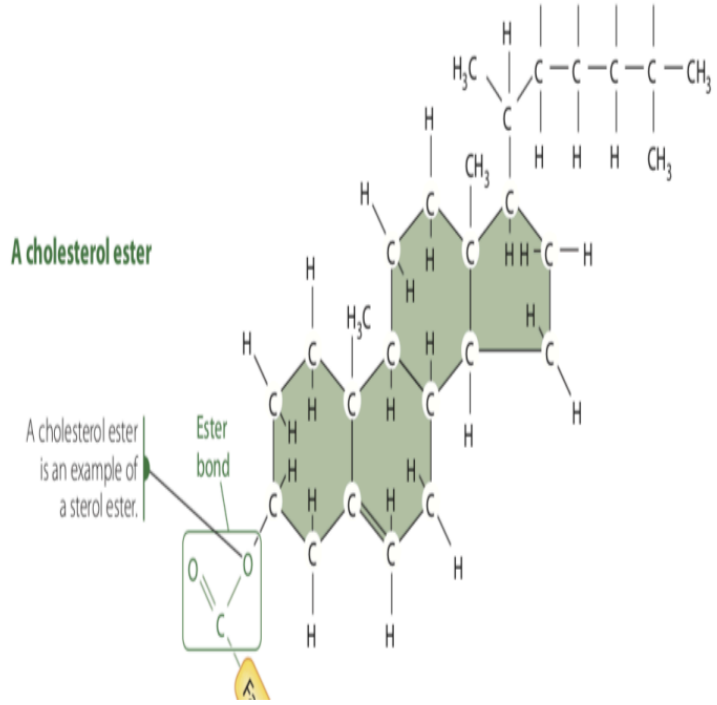
Three categories of sterols important to human nutrition

1. Cholesterol
2. Bile acids and salts
3. Phytosterols




# Cholesterol

- Most common sterol in humans
- Free form or the hydroxyl group at C-3 can be esterified with a fatty acid
- Amphipathic nature Important for membrane structure
- Cholesterol is an important constituent of plasma membranes. (nearly 25% of the lipids in plasma membranes of some nerve cells, but may be absent in intracellular membranes)



- Cells can regulate the amount of cholesterol in membranes by esterifying "excess" cholesterol with a fatty acid and storing the cholesterol esters in vesicles within the cytosol.
- When unesterified (free) cholesterol is needed, the cholesterol esters are hydrolyzed and free cholesterol is transported back to the membrane.
- Cholesterol serves as the precursor for many important steroids in the body, including the bile acids; steroid sex hormones such as estrogens, androgens, and progesterone; the adrenocortical hormones; and vitamin D

- **The major derivatives of cholesterol**

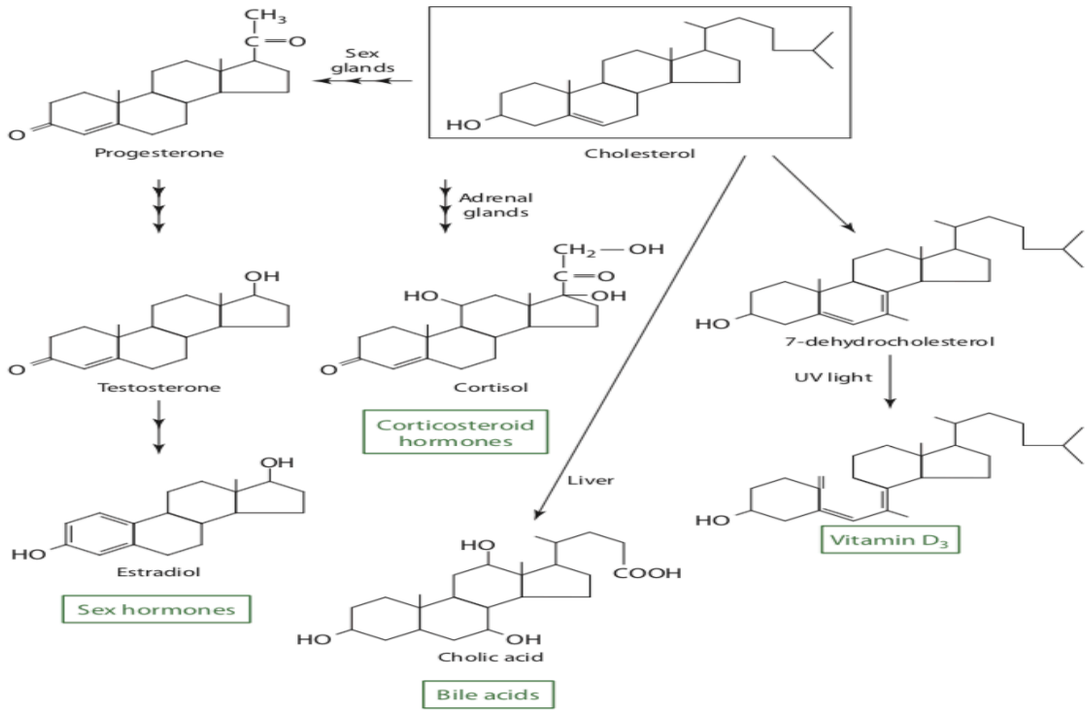



**Figure 5.10** The formation of physiologically important steroids from cholesterol. Only representative compounds from each category of steroid are shown.

- These steroids differ structurally from one another in the arrangement of double bonds in the ring system, the presence of carbonyl or hydroxyl groups, and the nature of the side chain at C-17. All of these structural modifications are mediated by enzymes that function as dehydrogenases, isomerases, hydroxylases, or desmolases. Desmolases remove or shorten the length of side chains on the steroid