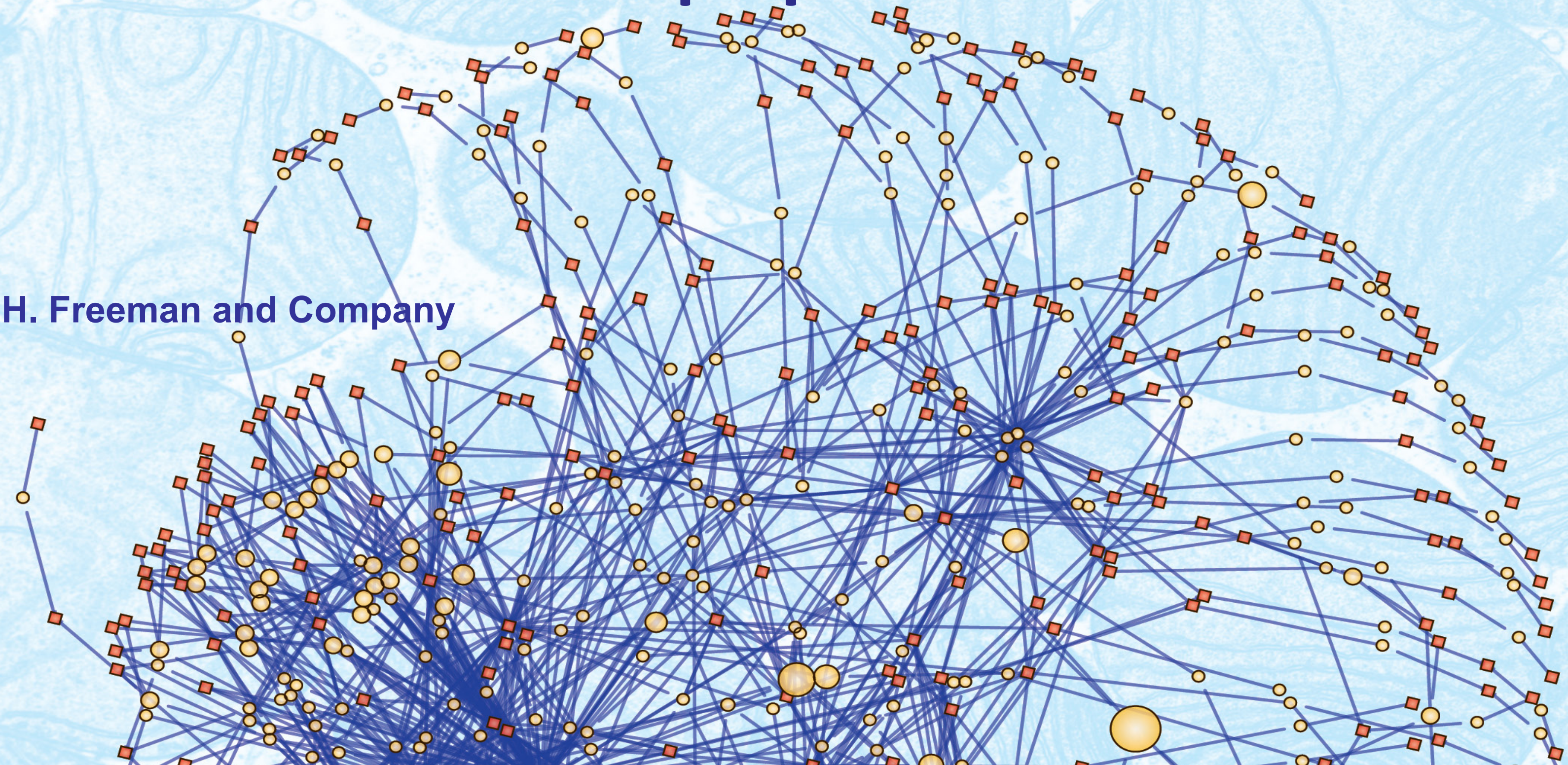
Lehninger

SIXTH EDITION

Principles of Biochemistry

David L. Nelson | Michael M. Cox

10| Lipids



Lipids: Structurally Diverse Class

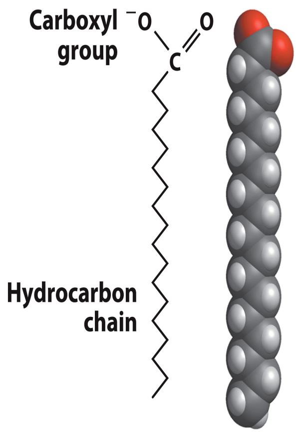


Figure 10-2a
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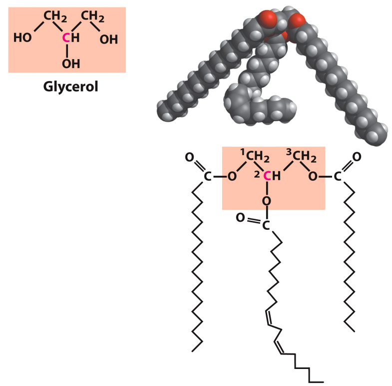

1-Stearoyl, 2-linoleoyl, 3-palmitoyl glycerol, a mixed triacylglycerol

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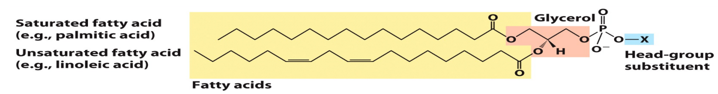

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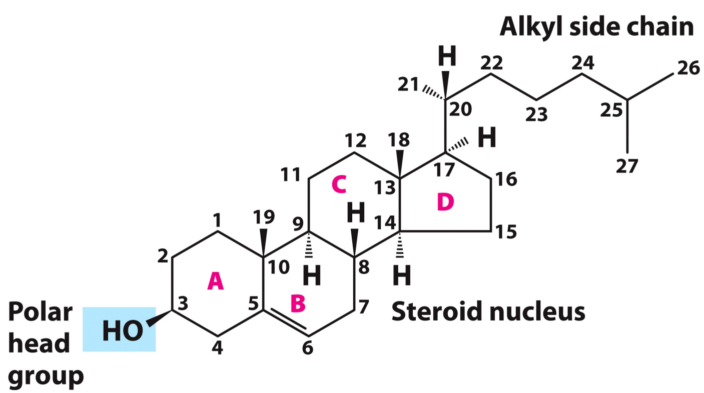

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(d)
Ubiquinone: a mitochondrial electron carrier (coenzyme Q)
(*n* = 4 to 8)

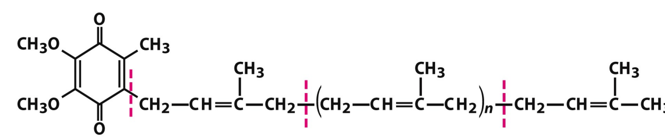

Figure 10-22d
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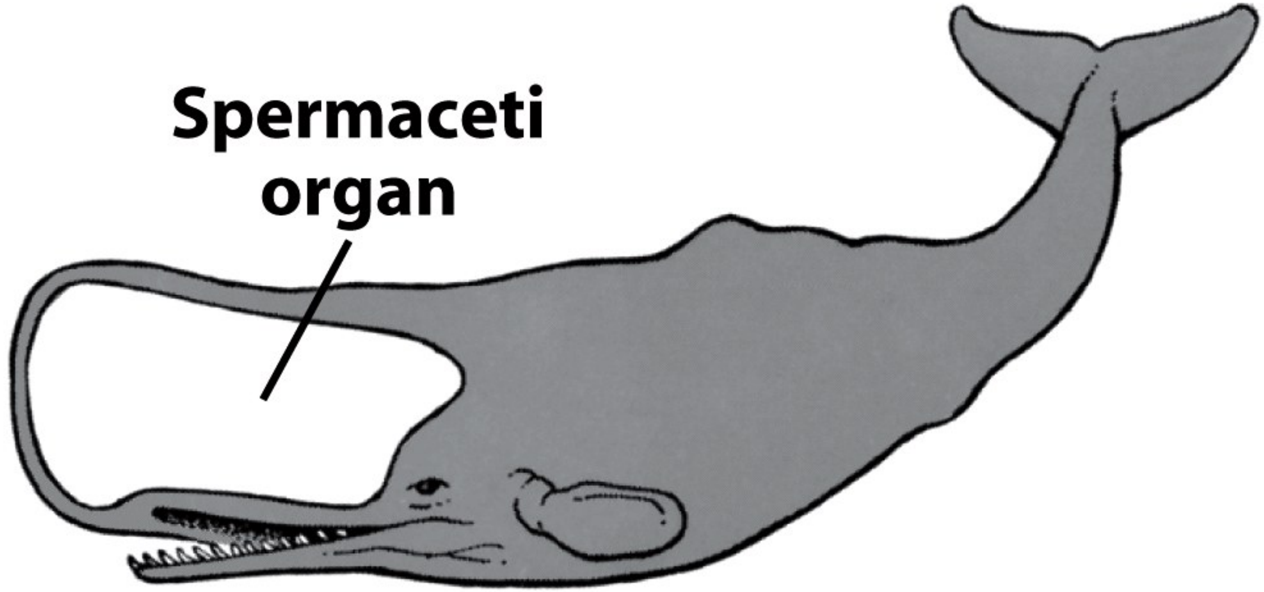
Organic molecules that are characterized by low solubility in water, that is, are relatively hydrophobic.

Biological Functions of Lipids

- Storage of energy
  - Reduced compounds: lots of available energy
  - Hydrophobic nature: good packing
- Insulation from environment
  - Low thermal conductivity
  - High heat capacity (can "absorb" heat)
  - Mechanical protection (can absorb shocks)
- Water repellant
  - Hydrophobic nature: keeps surface of the organism dry
    - Prevents excessive wetting (birds)
    - Prevents loss of water via evaporation
- Buoyancy control and acoustics in marine mammals
  - Increased density while diving deep helps sinking (just a hypothesis)
  - Spermaceti organ may focus sound energy: sound stun gun?



Box 10-1
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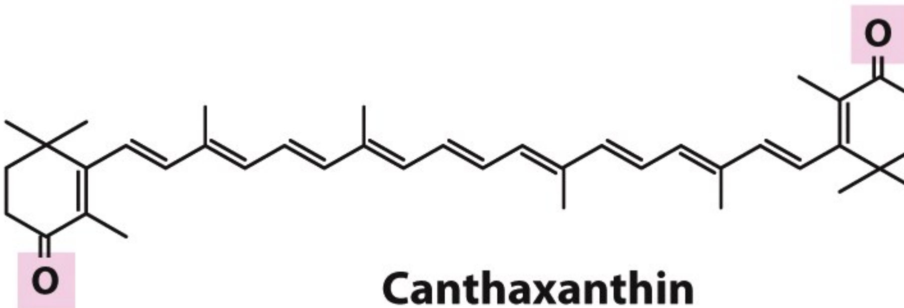
- Feeds on squid (in very deep water >1,000m deep)
- Rests quietly waiting (without constant swimming effort)
- In order to do so, its density must be equal to the surrounding water → changes in buoyancy
- Deep sea water is colder than the surface, spermaceti oil freezes (becomes denser) → matching the density of water
- When the whale returns to the surface, the oil warms up and melts decreasing the density to match surface water density

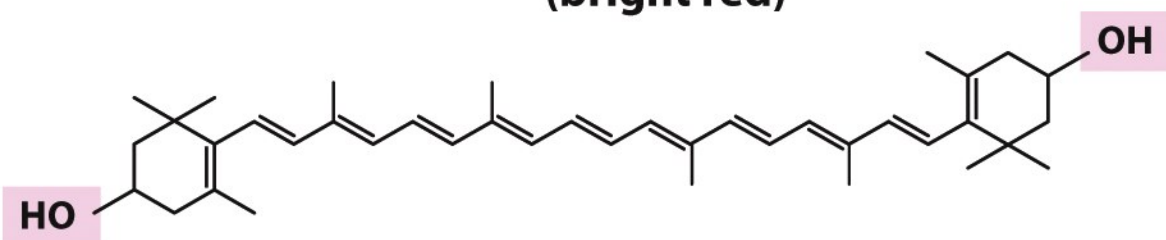
More Functions

- Membrane structure
  - Main structure of cell membranes
- Cofactors for enzymes
  - Vitamin K: blood clot formation
  - Coenzyme Q: ATP synthesis in mitochondria
- Signaling molecules
  - Paracrine hormones (act locally)
  - Steroid hormones (act body-wide)
  - Growth factors
  - Vitamins A and D (hormone precursors)
- Pigments
  - Color of tomatoes, carrots, pumpkins, some birds
- Antioxidants
  - Vitamin E

Lipids can provide pigment



Canthaxanthin
(bright red)



Zeaxanthin
(bright yellow)

✓ Minor differences in the chemistry of these compounds produce pigments of strikingly different colors

✓ Birds obtain the pigments that color their feathers red or yellow by eating plant materials that contain carotenoid pigments (e.g., canthaxanthin and zeaxanthin)

✓ The differences in pigmentation between male and female birds are the result of differences in intestinal uptake and processing of carotenoids.

Classification of Lipids

- Based on the structure and function
  - Lipids that do not contain fatty acids: cholesterol, terpenes, …
  - Lipids that contain fatty acids (complex lipids)
    - can be further separated into:
      - storage lipids and membrane lipids

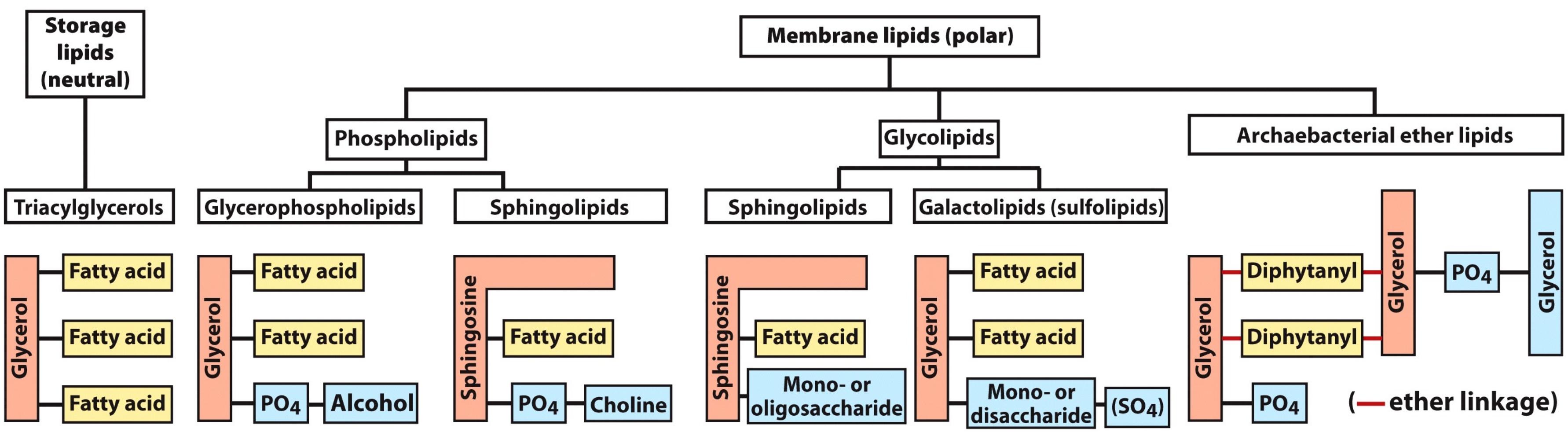


Figure 10-7
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10.1 Storage Lipids

- Derivatives of fatty acids
- Fatty acids are hydrocarbon derivatives
- Low oxidation state (highly reduced)
- Cellular oxidation is highly exergonic

Fatty Acids

- Carboxylic acids with hydrocarbon chains containing between 4 to 36 carbons
- Almost all natural fatty acids have an even number of carbons
- Most natural fatty acids are unbranched
- Saturated: no double bonds between carbons in the chain
- Monounsaturated: one double bond between carbons in the alkyl chain
- Polyunsaturated: more than one double bond in the alkyl chain

Fatty Acid Nomenclature

TABLE 10–1 Some Naturally Occurring Fatty Acids: Structure, Properties, and Nomenclature

Carbon skeleton	Structure*	Systematic name[†]	Common name (derivation)	Melting point (°C)	Solubility at 30 °C (mg/g solvent)	
					Water	Benzene
12:0	$CH_3(CH_2)_{10}COOH$	*n*-Dodecanoic acid	Lauric acid (Latin *laurus*, "laurel plant")	44.2	0.063	2,600
14:0	$CH_3(CH_2)_{12}COOH$	*n*-Tetradecanoic acid	Myristic acid (Latin *Myristica*, nutmeg genus)	53.9	0.024	874
16:0	$CH_3(CH_2)_{14}COOH$	*n*-Hexadecanoic acid	Palmitic acid (Latin *palma*, "palm tree")	63.1	0.0083	348
18:0	$CH_3(CH_2)_{16}COOH$	*n*-Octadecanoic acid	Stearic acid (Greek *stear*, "hard fat")	69.6	0.0034	124
20:0	$CH_3(CH_2)_{18}COOH$	*n*-Eicosanoic acid	Arachidic acid (Latin *Arachis*, legume genus)	76.5		
24:0	$CH_3(CH_2)_{22}COOH$	*n*-Tetracosanoic acid	Lignoceric acid (Latin *lignum*, "wood" + *cera*, "wax")	86.0		
16:1(Δ^9)	$CH_3(CH_2)_5CH{=}CH(CH_2)_7COOH$	*cis*-9-Hexadecenoic acid	Palmitoleic acid	1 to –0.5		
18:1(Δ^9)	$CH_3(CH_2)_7CH{=}CH(CH_2)_7COOH$	*cis*-9-Octadecenoic acid	Oleic acid (Latin *oleum*, "oil")	13.4		
18:2($\Delta^{9,12}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-9,12-Octadecadienoic acid	Linoleic acid (Greek *linon*, "flax")	1–5		
18:3($\Delta^{9,12,15}$)	$CH_3CH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_7COOH$	*cis*-,*cis*-,*cis*-9,12,15-Octadecatrienoic acid	α-Linolenic acid	–11		
20:4($\Delta^{5,8,11,14}$)	$CH_3(CH_2)_4CH{=}CHCH_2CH{=}CHCH_2CH{=}CHCH_2CH{=}CH(CH_2)_3COOH$	*cis*-,*cis*-,*cis*-,*cis*-5,8,11,14-Icosatetraenoic acid	Arachidonic acid	–49.5		

*All acids are shown in their nonionized form. At pH 7, all free fatty acids have an ionized carboxylate. Note that numbering of carbon atoms begins at the carboxyl carbon.

[†]The prefix *n*- indicates the "normal" unbranched structure. For instance, "dodecanoic" simply indicates 12 carbon atoms, which could be arranged in a variety of branched forms; "*n*-dodecanoic" specifies the linear, unbranched form. For unsaturated fatty acids, the configuration of each double bond is indicated; in biological fatty acids the configuration is almost always cis.

Table 10-1
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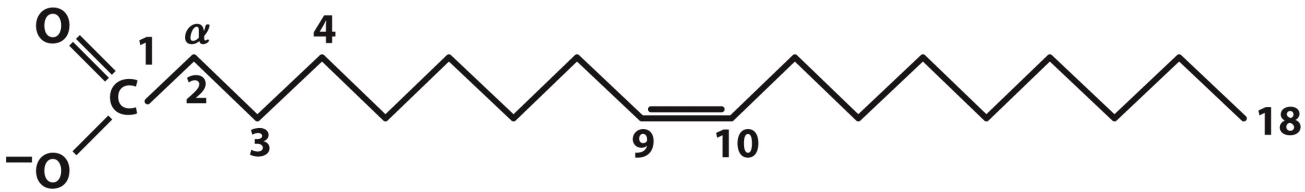
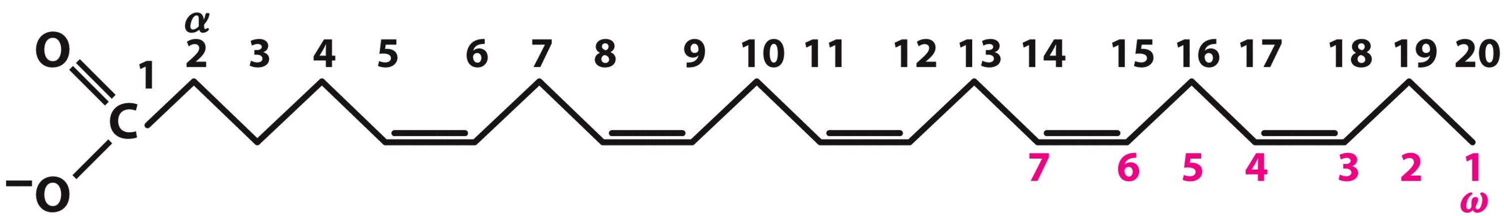
Fatty Acid Nomenclature



(a) 18:1(Δ^9) *cis*-9-Octadecenoic acid



(b) 20:5($\Delta^{5,8,11,14,17}$) Eicosapentaenoic acid (EPA), an omega-3 fatty acid

(a)**Standard nomenclature** – # 1 to the carboxyl carbon (C-1), and α to the carbon next to it. The position of any double bond(s) is indicated by Δ followed by a superscript number indicating the lower-numbered carbon in the double bond.

(b)**Polyunsaturated fatty acids (PUFAs) nomenclature** – # 1 to the methyl carbon at the other end of the chain (also designated ω; the last letter in the Greek alphabet). The positions of the double bonds are indicated relative to the ω carbon.

Omega-3 PUFA

- Omega-3 fatty acids are essential nutrients
  - Humans need them but cannot synthesize one
  - No synthetic pathway in humans to make the ω-3 PUFA α-linolenic acid; 18:3($\Delta^{9,12,15}$) ALA
- Must be obtained in the diet
  - Including ALA, DHA, and EPA
    - Although DHA and EPA can be synthesized from ALA
- Imbalance in ω-6 and ω-3 leads to an increased risk of cardiovascular disease

Solubility and Melting Point of Fatty Acids

- Solubility
  - decreases as the chain length increases

- Melting Point
  - decreases as the chain length decreases
  - decreases as the number of double bonds increases

  At room temperature, saturated fatty acids (from 12:0 to 24:0) have a waxy consistency, whereas unsaturated fatty acids of the same lengths are oily liquids

Conformation of Fatty Acids

- The saturated chain tends to adopt extended conformations
- The double bonds in natural unsaturated fatty acids are commonly in cis configuration, which kinks the chain

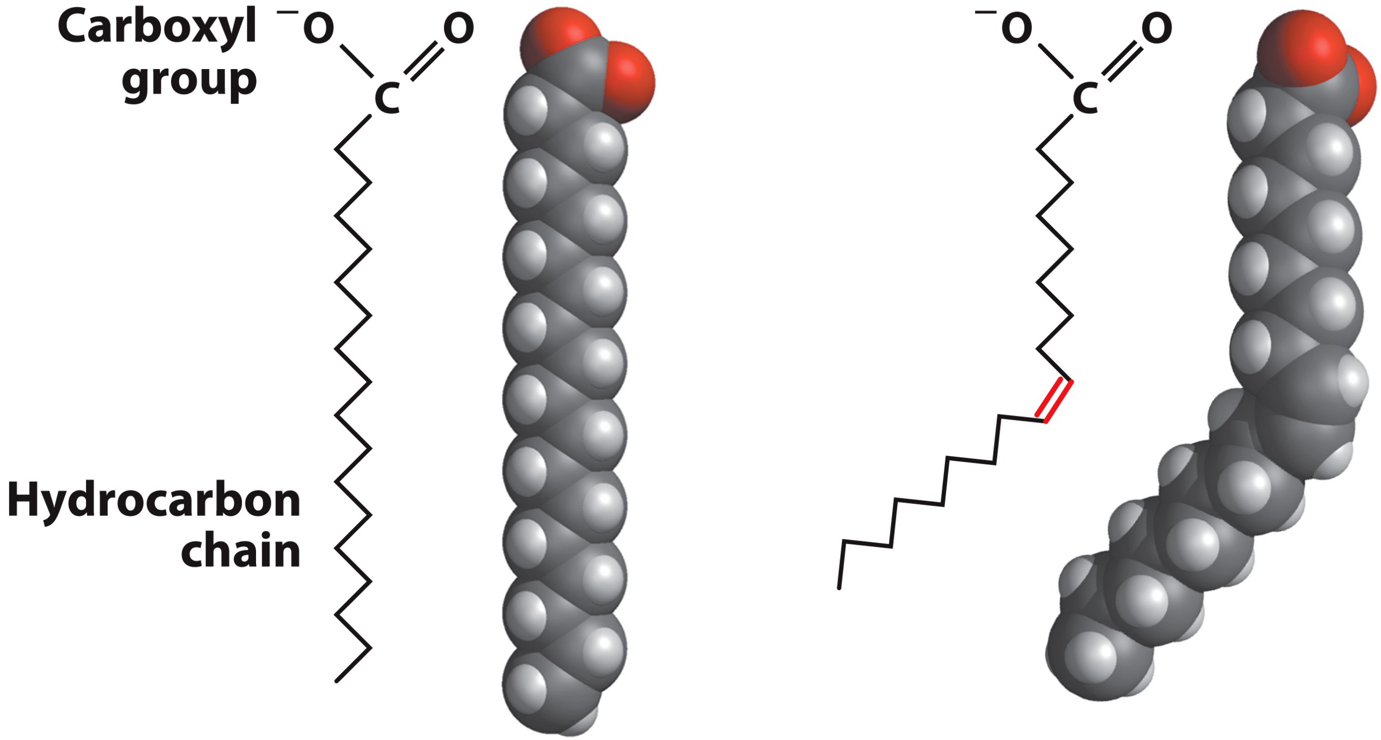


Figure 10-2ab
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Melting Point and Double Bonds

- Saturated fatty acids pack in a fairly orderly way
  - extensive favorable interactions
- Unsaturated cis fatty acid pack less orderly due to the kink
  - less-extensive favorable interactions
- It takes less thermal energy to disrupt disordered packing of unsaturated fatty acids:
  - unsaturated cis fatty acids have a lower melting point

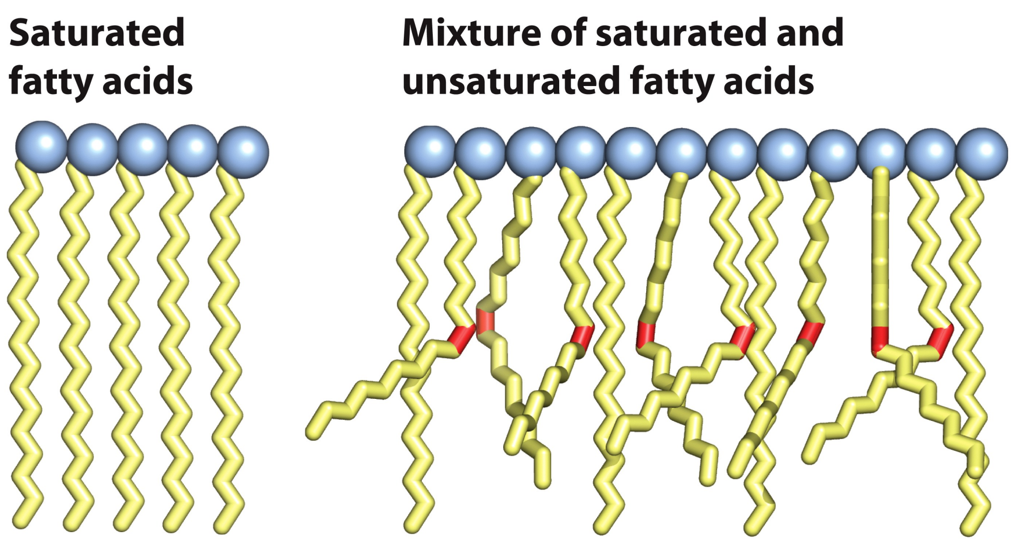

Figure 10-2cd
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Trans Fatty Acids

- Trans fatty acids form by partial dehydrogenation of unsaturated fatty acids
  - Done to increase shelf life or stability at high temperature of oils used in cooking (especially deep frying)
- A trans double bond allows a given fatty acid to adopt an extended conformation
- Trans fatty acids can pack more regularly and show higher melting points than cis forms
- Consuming trans fats increases risk of cardiovascular disease
  - Avoid deep-frying partially hydrogenated vegetable oils
  - Current trend: reduce trans fats in foods (Wendy's, KFC)

TABLE 10–2 Trans Fatty Acids in Some Typical Fast Foods and Snacks

	Trans fatty acid content	
	In a typical serving (g)	**As % of total fatty acids**
French fries	4.7–6.1	28–36
Breaded fish burger	5.6	28
Breaded chicken nuggets	5.0	25
Pizza	1.1	9
Corn tortilla chips	1.6	22
Doughnut	2.7	25
Muffin	0.7	14
Chocolate bar	0.2	2

Source: Adapted from Table 1 in Mozaffarian, D., Katan, M.B., Ascherio, P.H., Stampfer, M.J., & Willet, W.C. (2006). Trans fatty acids and cardiovascular disease. *N. Engl. J. Med.* **354**, 1604–1605.

Note: All data for foods prepared with partially hydrogenated vegetable oil in the United States in 2002.

Table 10-2
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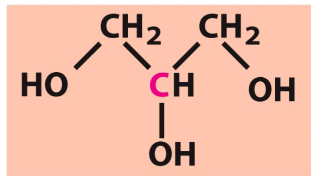
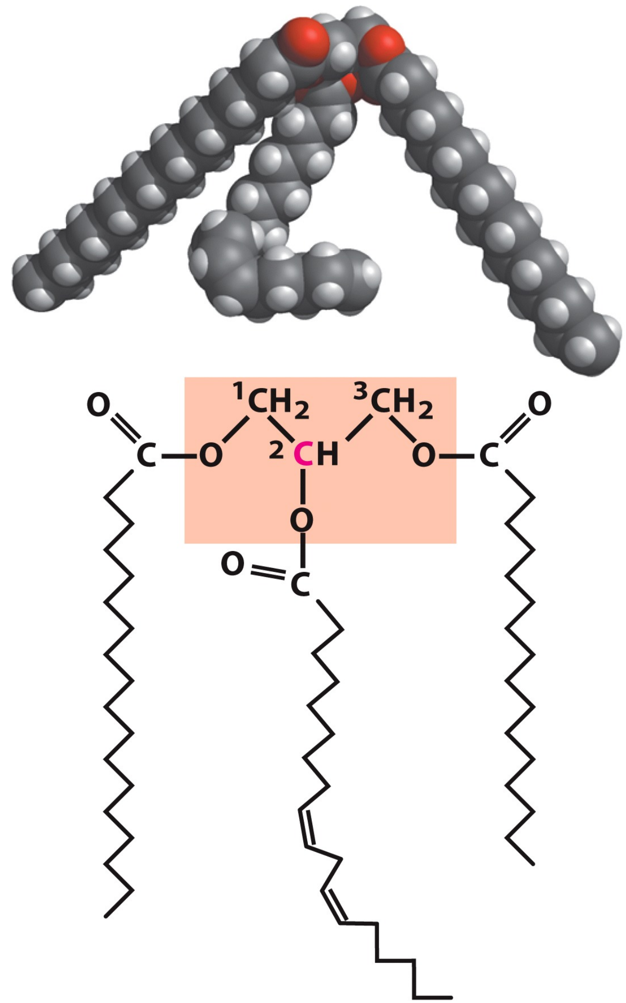
Triacylglycerols (Nonpolar)

- Majority of fatty acids in biological systems are found in the form of triacylglycerols
- Solid ones are called fats
- Liquid ones are called oils
- The primary storage form of lipids (body fat)
- Less soluble in water than fatty acids due to the lack of charged carboxylate group
- Less dense than water: fats and oils float

Triacylglycerols



Glycerol



1-Stearoyl, 2-linoleoyl, 3-palmitoyl glycerol,
a mixed triacylglycerol

Figure 10-3
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Fats Provide Efficient Fuel Storage

- The advantage of fats over polysaccharides:
  - Fatty acids carry more energy per carbon because they are more reduced
  - Fatty acids carry less water per gram because they are nonpolar

- Glucose and glycogen are for short-term energy needs, quick delivery
- Fats are for long-term (months) energy needs, good storage, slow delivery

Fats Provide Efficient Fuel Storage

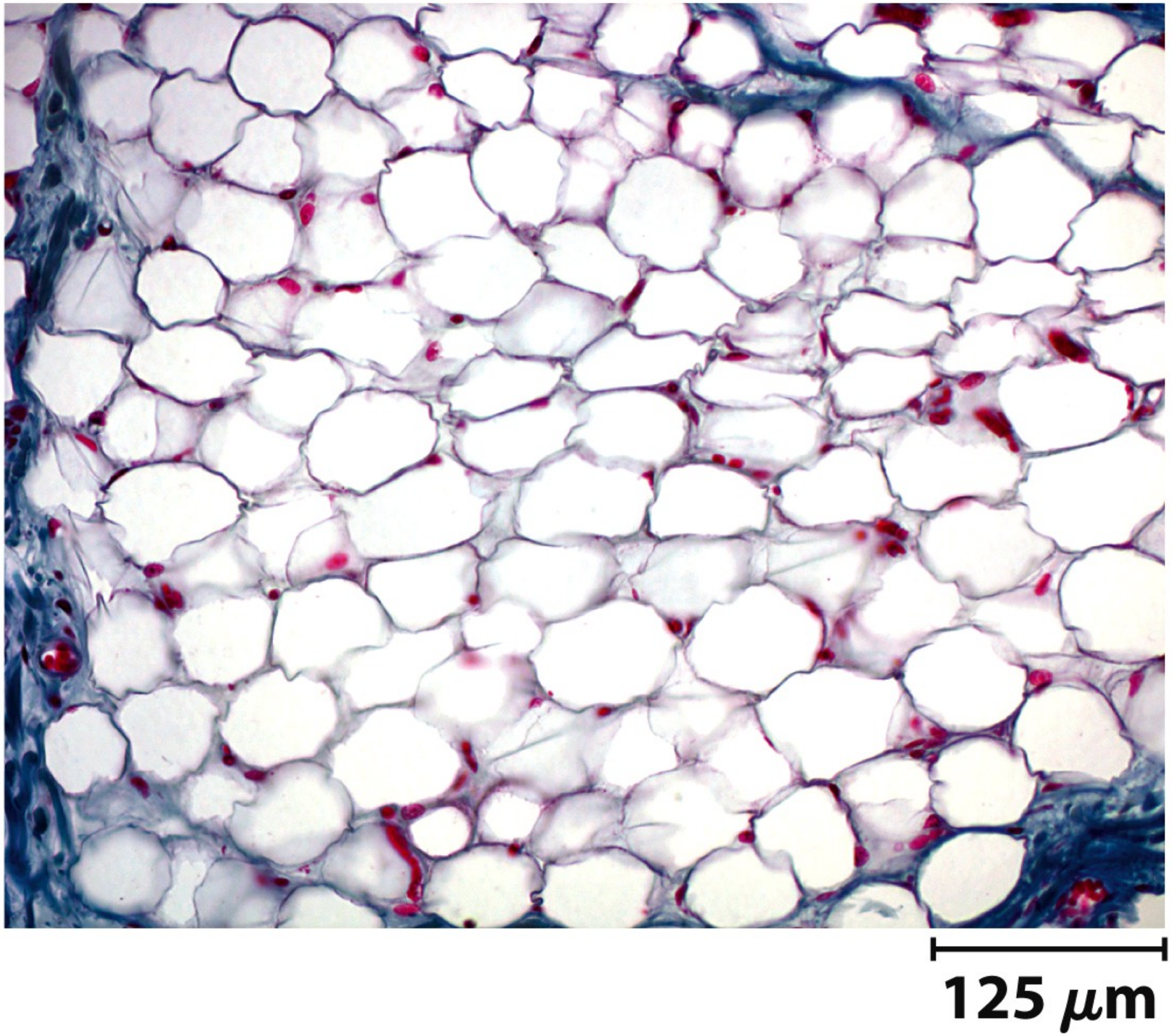

Figure 10-4a
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Waxes

- Waxes are esters of long-chain saturated and unsaturated fatty acids with long-chain alcohols
- Insoluble and have high melting points ~ 60 – 100 ^{o}C
- Variety of functions:
  - Storage of metabolic fuel in plankton
  - Protection and pliability for hair and skin in vertebrates
  - Waterproofing of feathers in birds
  - Protection from evaporation in tropical plants and ivy
  - Used by people in lotions, ointments, and polishes

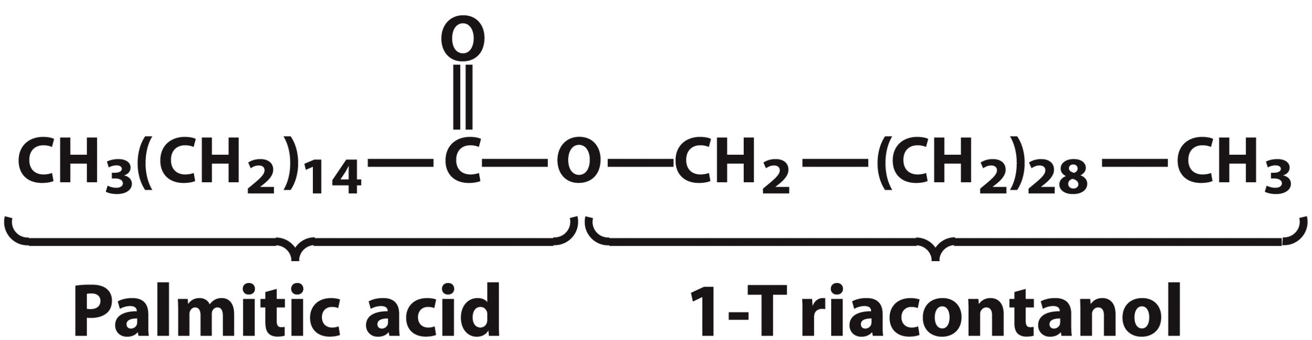

Figure 10-6a
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Wax: The Material of the Honeycomb

Beeswax is a mixture of a large number of lipids, including esters of triacontanol, and a long-chain alkane hentiacontane

Figure 10-6b
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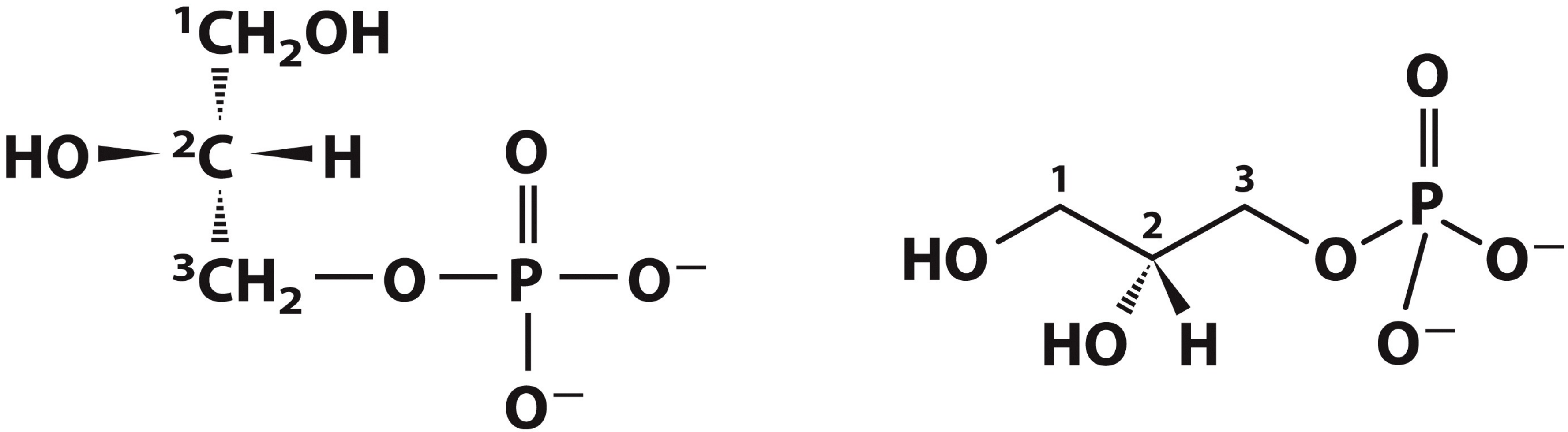
Structural Lipids in Membranes (Polar)

- Contain polar head groups and nonpolar tails (usually attached fatty acids)
- Diversification can come from:
  - modifying a different backbone
  - changing the fatty acids
  - modifying the head groups
- The properties of head groups determine the surface properties of membranes
- Different organisms have different membrane lipid head group compositions
- Different tissues have different membrane lipid head group compositions

Glycerophospholipids

- Primary constituents of cell membranes
- Two fatty acids form ester linkages with the first and second hydroxyl groups of L-glycerol-3-phosphate
- Head group is charged at physiological pH



L-Glycerol 3-phosphate (*sn*-glycerol 3-phosphate)

Figure 10-8
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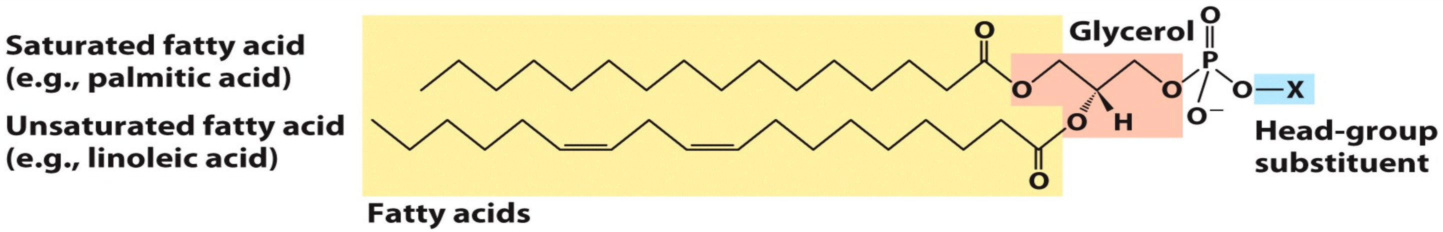
Glycerol itself is not chiral.
However, glycerol is ***prochiral*** *– it can be converted to a chiral compound by adding a substituent such as phosphate to either of the* $-CH_2OH$ *groups.*

General Structure of Glycerophospholipids

- Unsaturated fatty acids are commonly found connected to C2
- The highly polar phosphate group may be further esterified by an alcohol; such substituent groups are called the head groups



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Examples of Glycerophospholipids

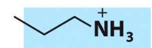
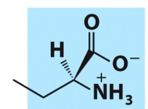
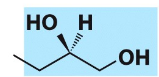
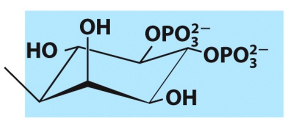
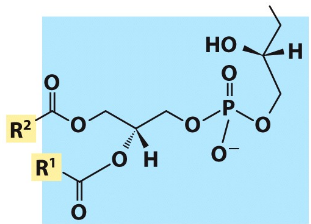
Name of glycerophospholipid	Name of X—O	Formula of X	Net charge (at pH 7)
Phosphatidic acid	—	—H	−2
Phosphatidylethanolamine	**Ethanolamine**		0
Phosphatidylcholine	**Choline**		0
Phosphatidylserine	**Serine**		−1
Phosphatidylglycerol	**Glycerol**		−1
Phosphatidylinositol 4,5-bisphosphate	***myo*-Inositol 4,5-bisphosphate**		−4*
Cardiolipin	**Phosphatidyl-glycerol**		−2

Figure 10-9
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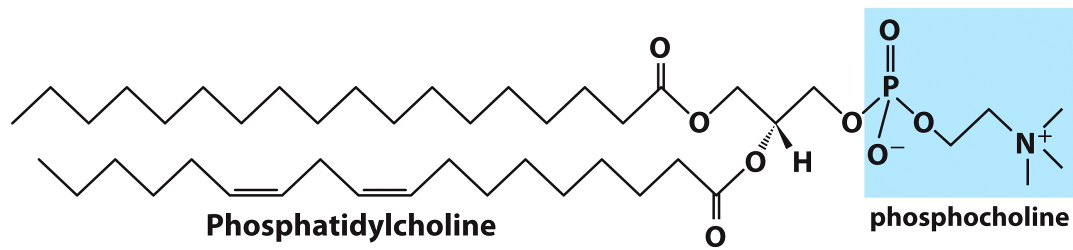
Phosphatidylcholine

- Phosphatidylcholine is the major component of most eukaryotic cell membranes
- Many prokaryotes, including *E. coli,* cannot synthesize this lipid; their membranes do not contain phosphatidylcholine



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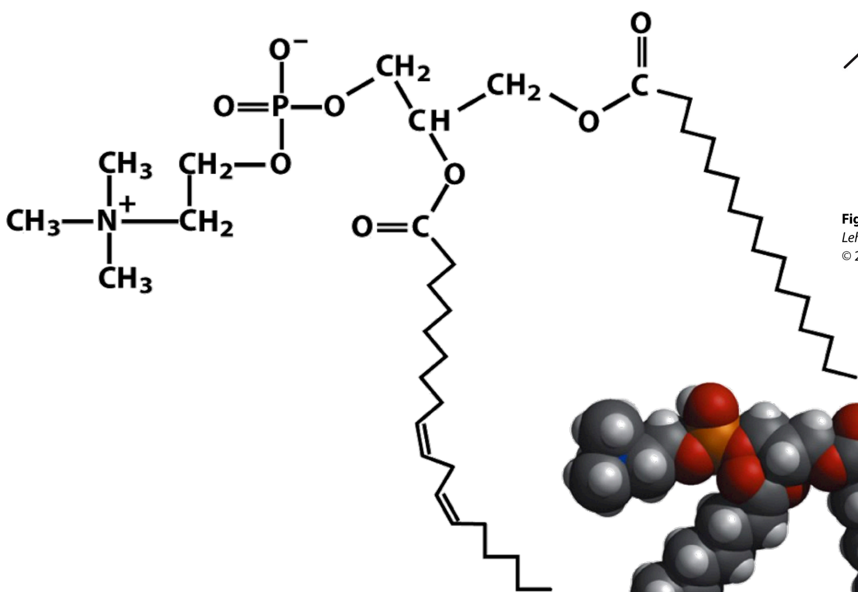

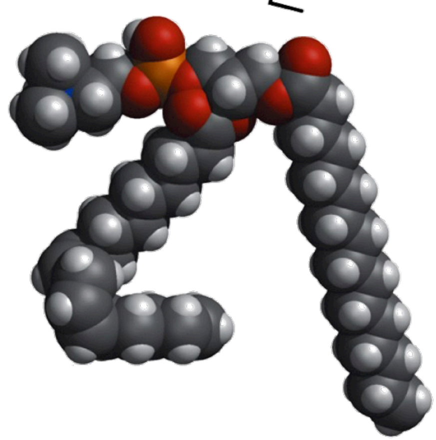

Phosphatidylcholine

Ether Lipids: Plasmalogen

- Vinyl ether analog of phosphatidylethanolamine
- Common in vertebrate heart tissue
- Also found in some protozoa and anaerobic bacteria
- Function is not well understood
  - Resistant to cleavage by common lipases but cleaved by few specific lipases
  - Increase membrane rigidity?
  - Sources of signaling lipids?
  - May be antioxidants?

Ether Lipids: Plasmalogen

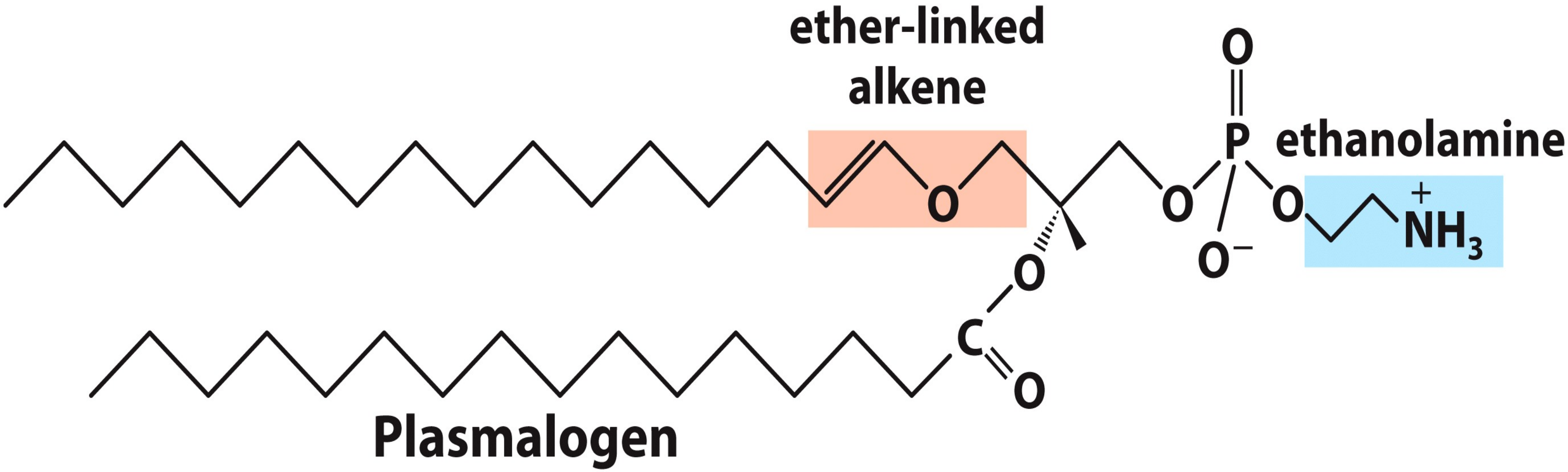

Figure 10-10
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Ether Lipids: Platelets-Activating Factor

- Aliphatic ether analog of phosphatidylcholine
- Acetic acid has esterified position C2
- First signaling lipid to be identified
- Stimulates aggregation of blood platelets
- Plays role in mediation of inflammation

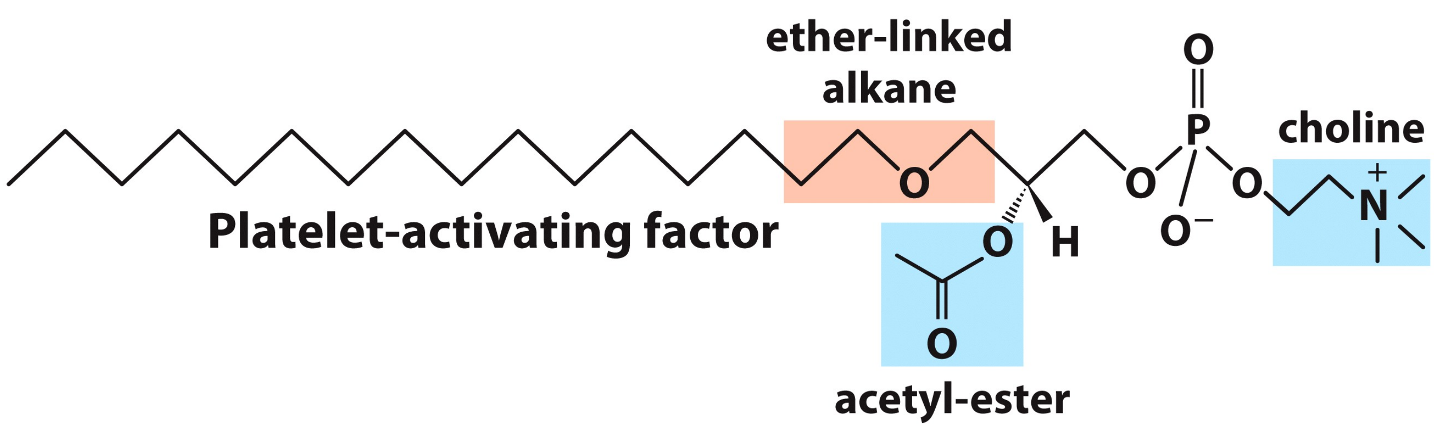

Figure 10-10
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Sphingolipids

- The backbone of sphingolipids is NOT glycerol
- The backbone of sphingolipids is a long-chain amino alcohol sphingosine
- A fatty acid is joined to sphingosine via an amide linkage rather than an ester linkage as usually seen in lipids
- A polar head group is connected to sphingosine by a glycosidic or phosphodiester linkage
- The sugar-containing glycosphingolipids are found largely in the outer face of plasma membranes

Sphingolipids

Ceramide is the parent compound for this group (structurally similar to diacylglycerol).

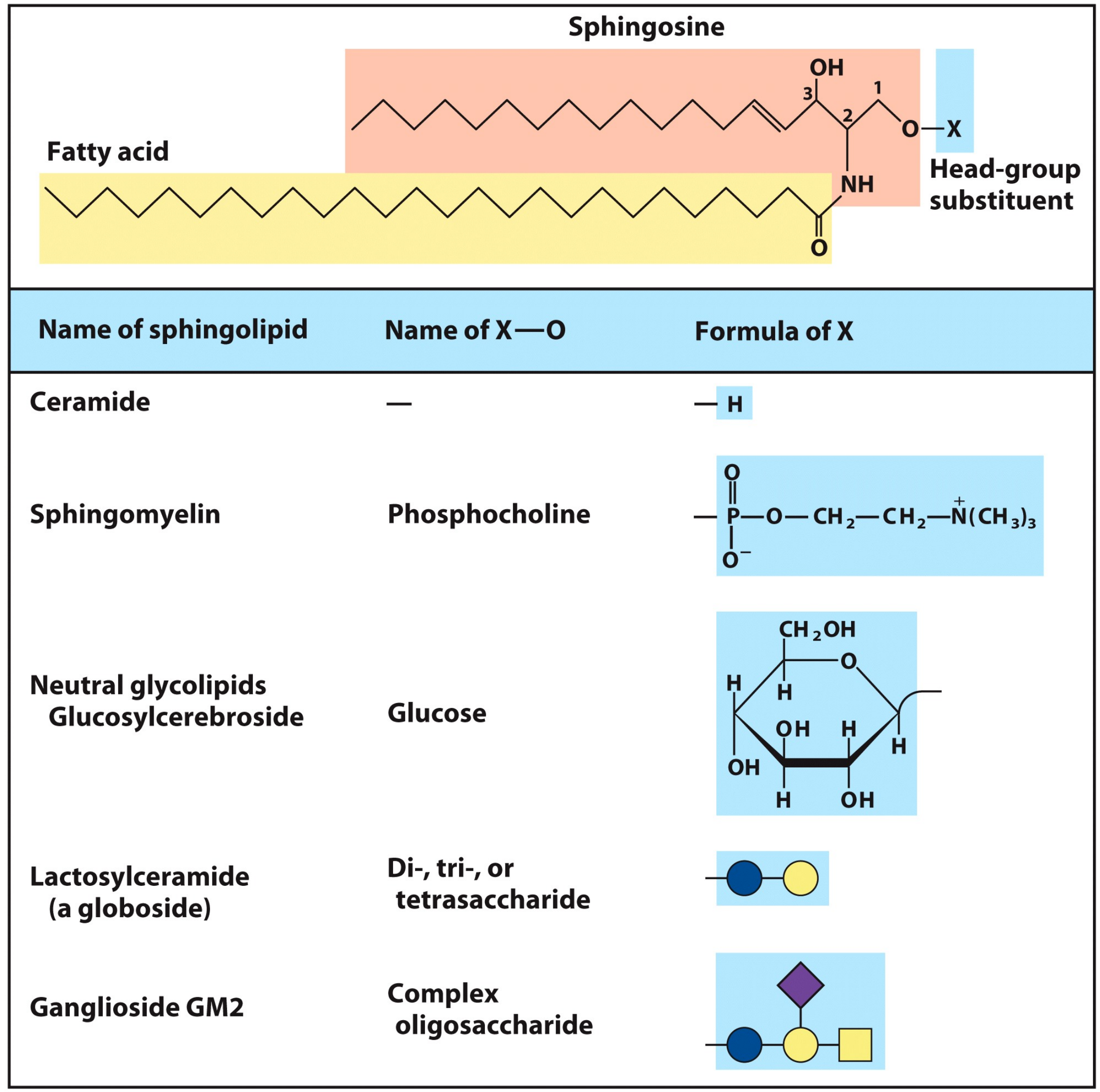

Figure 10-13
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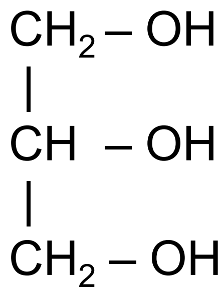
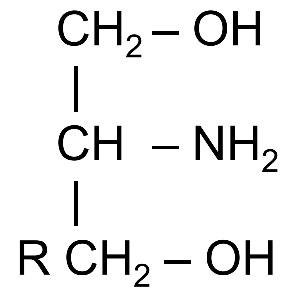
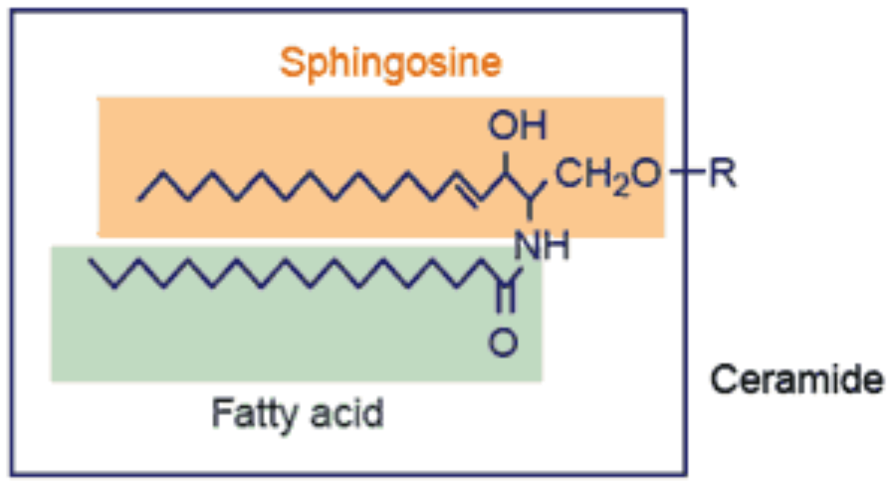


glycerol



sphingosine



Substituent (R)	Sphingolipid
H	Ceramide
Phosphocholine	Sphingomyelin
Sugar(s)	Glycosphingolipid

1. ***J. Stiban*, *D. Fistere and M. Colombini (2006)*** Dihydroceramide hinders **ceramide** channel formation: Implications on apoptosis. *Apoptosis. 11(5): 773-780.*

2. ***J. Stiban****, L. Caputo and M. Colombini (2008)* **Ceramide** synthesis in the endoplasmic reticulum can permeabilize mitochondria to proapoptotic proteins. *J. Lipid Res. 49(3): 625-634.*

3. ***J. Stiban****, L.C. Silva and A.H. Futerman (2008)* **Ceramide**-containing membranes: the interface between biophysics and biology. *Trends Glycosci. Glycotech. 20(116):* 297–313.

4. ***J. Stiban*, *R. Tidhar and A.H. Futerman (2009)*** ***Ceramide*** Synthases: Roles in Cell Physiology and Signaling, *In: 'Sphingolipids as Signaling and Regulatory Molecules' Landes Bioscience*

5. *Y. Pewzner-Jung Y, H. Park, E.L. Laviad, L.C. Silva, S. Lahiri,* ***J. Stiban****, et. al.* A critical role for **ceramide** synthase 2 in liver homeostasis: I. alterations in lipid metabolic pathways.(2010) *J. Biol. Chem. 285(14): 10902-10910.*

6. *S. Samanta,* ***J. Stiban*****,** *T.K. Maugel and M. Colombini (2011)* Visualization of **ceramide** channels by transmission electron microscopy. *Biochim. Biophys. Acta - Biomembranes 1808(4):1196-1201.*

7. ***J. Stiban*** *and M. Perera* (2015) Very long chain **ceramides** interfere with C16-ceramide channel formation: A plausible mechanism for regulating the initiation of intrinsic apoptosis. *Biochim. Biophys. Acta 1848(2): 561-567.*

8. *M. Abou-Ghali and* ***J. Stiban*** (2015) Regulation of **ceramide** channel formation and disassembly: Insights on the initiation of apoptosis. *Saudi J. Biol. Sci.* 22(6): 760-772

Sphingomyelin

- Ceramide (sphingosine + amide-linked fatty acid) + phosphocholine attached to the alcohol
- Sphingomyelin is abundant in myelin sheath that surrounds some nerve cells in animals

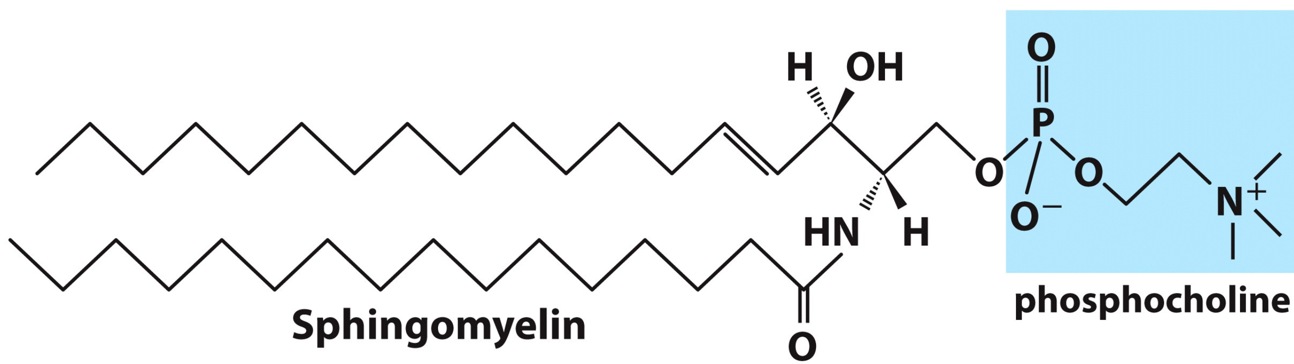


Figure 10-14
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Sphingomyelin is structurally similar to phosphatidylcholine

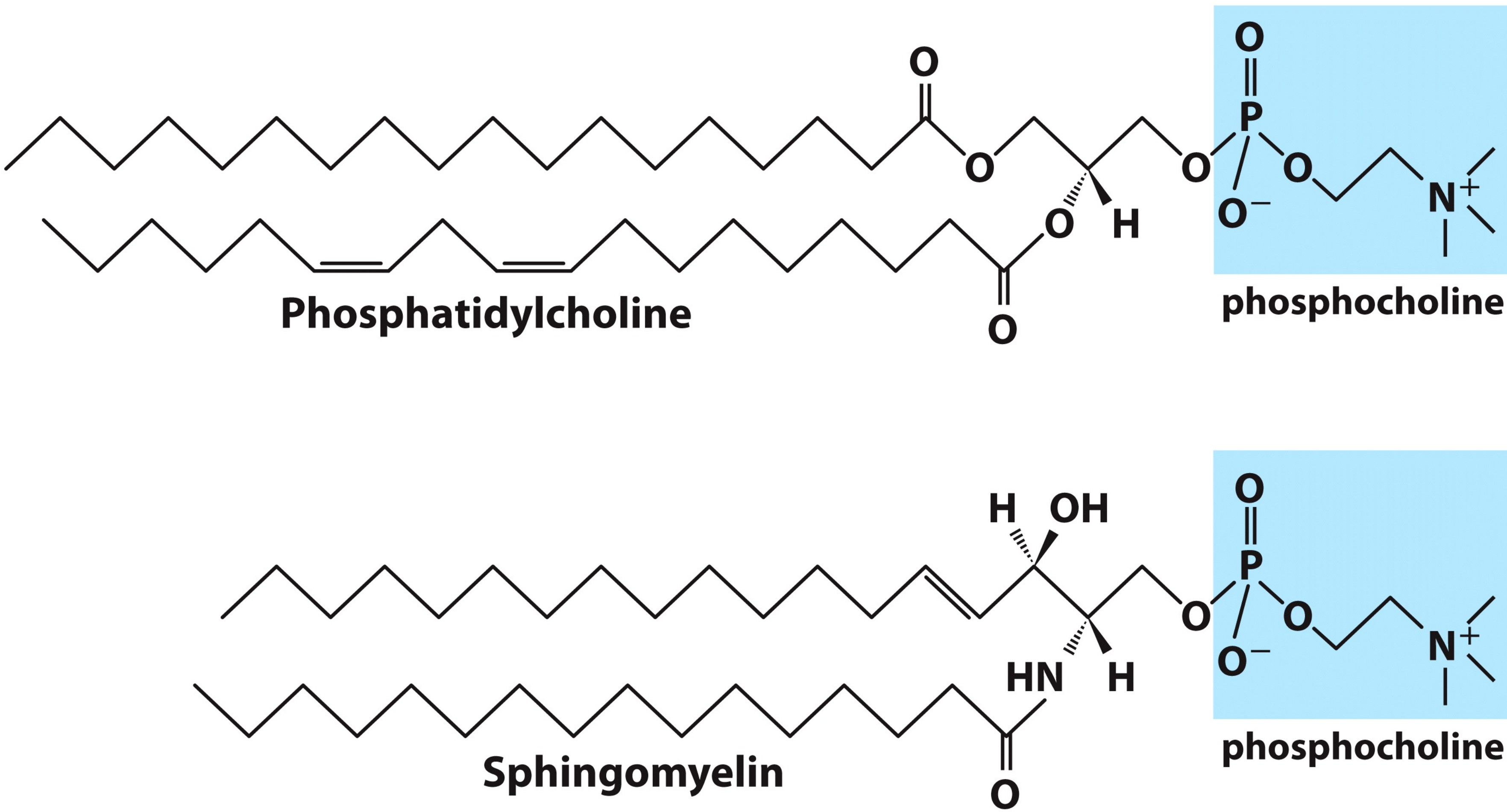

Figure 10-14
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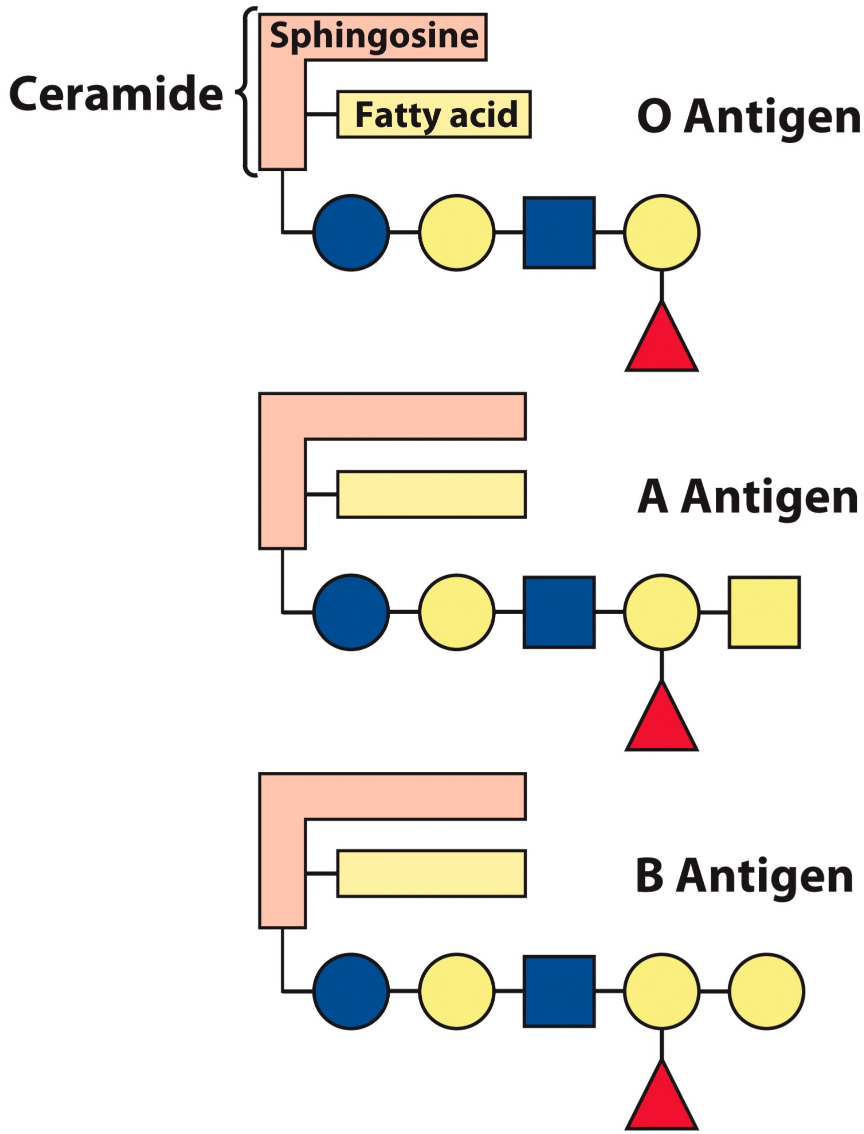
Glycosphingolipids and Blood Groups

- The blood groups are determined in part by the type of sugars located on the head groups in glycosphingolipids.
- The structure of sugar is determined by an expression of specific glycosyltransferases
  - Individuals with no active glycosyltransferase will have the **O antigen**
  - Individuals with a glycosyltransferase that transfers an N-acetylgalactosamine group have **A blood group**
  - Individuals with a glycosyltransferase that transfers a galactose group have **B blood group**

Glycosphingolipids determine blood groups



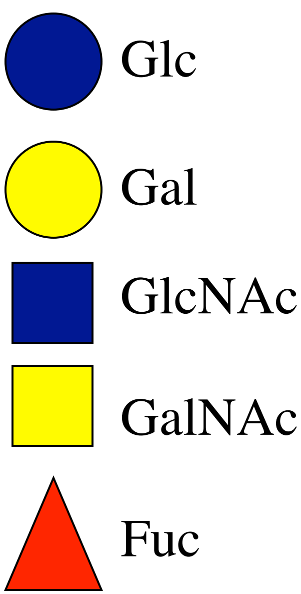


Figure 10-15
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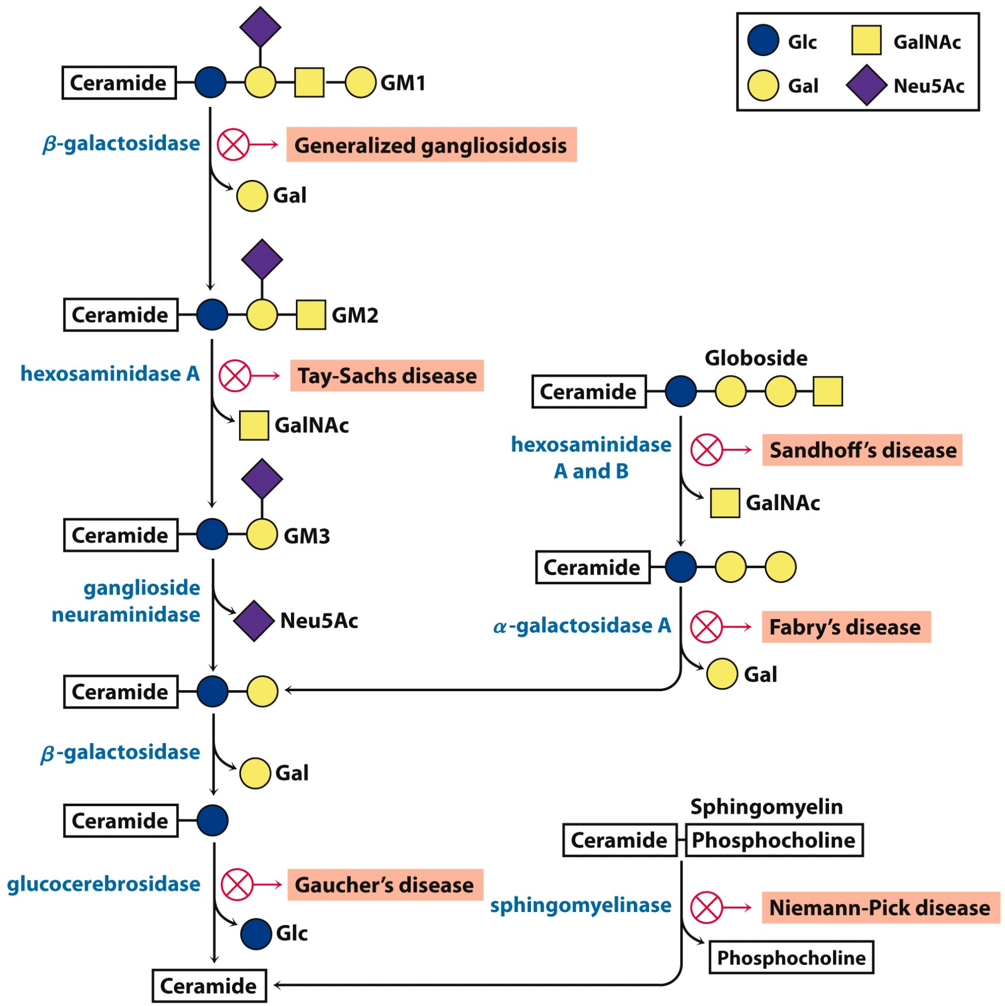
Defects in the turnover of membrane lipids lead to a number of diseases



Box 10-1 figure 1
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Sterols and Cholesterol

- Sterol
  - Steroid nucleus: four fused rings
  - Hydroxyl group (polar head) in the A-ring
  - Various nonpolar side chains
- The steroid nucleus is almost planar

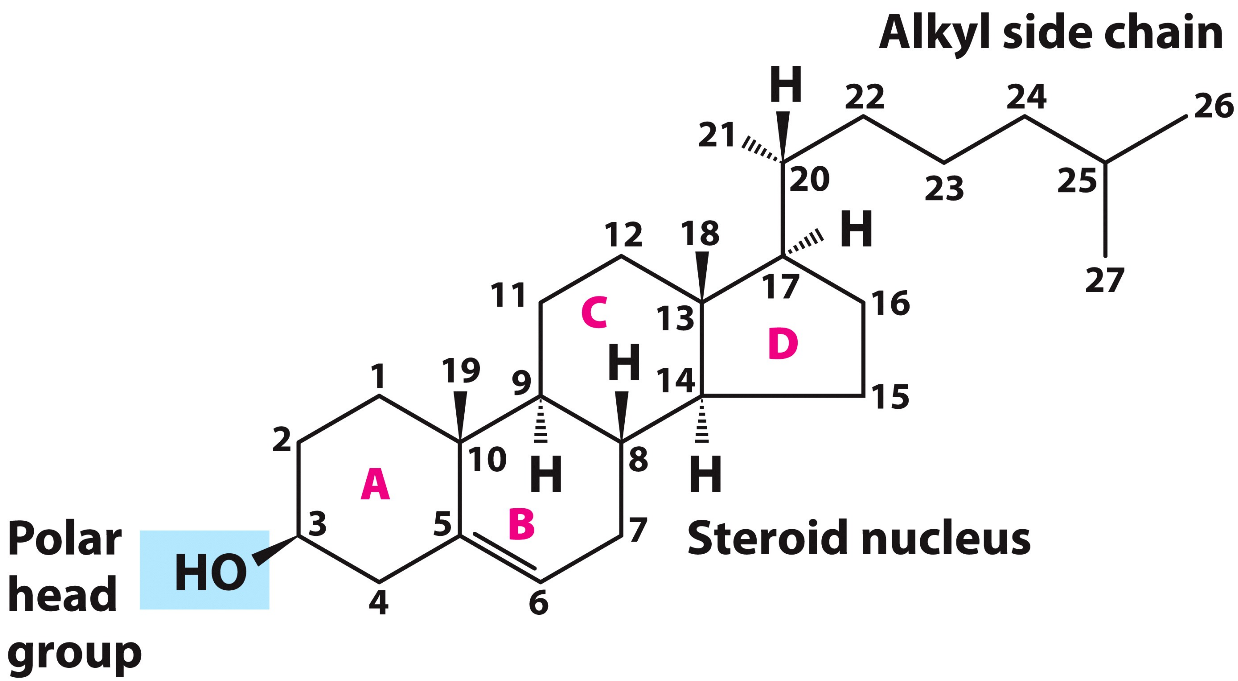

Figure 10-17
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Physiological Role of Sterols

- Cholesterol and related sterols are present in the membranes of most eukaryotic cells
  - Modulate fluidity and permeability
  - Thicken the plasma membrane
  - Most bacteria lack sterols
- Mammals obtain cholesterol from food or synthesize it *de novo* in the liver
- Cholesterol, bound to proteins, is transported to tissues via blood vessels
  - Cholesterol in low-density lipoproteins tends to deposit and clog arteries
- Many hormones are derivatives of sterols

Membrane microdomains (rafts)

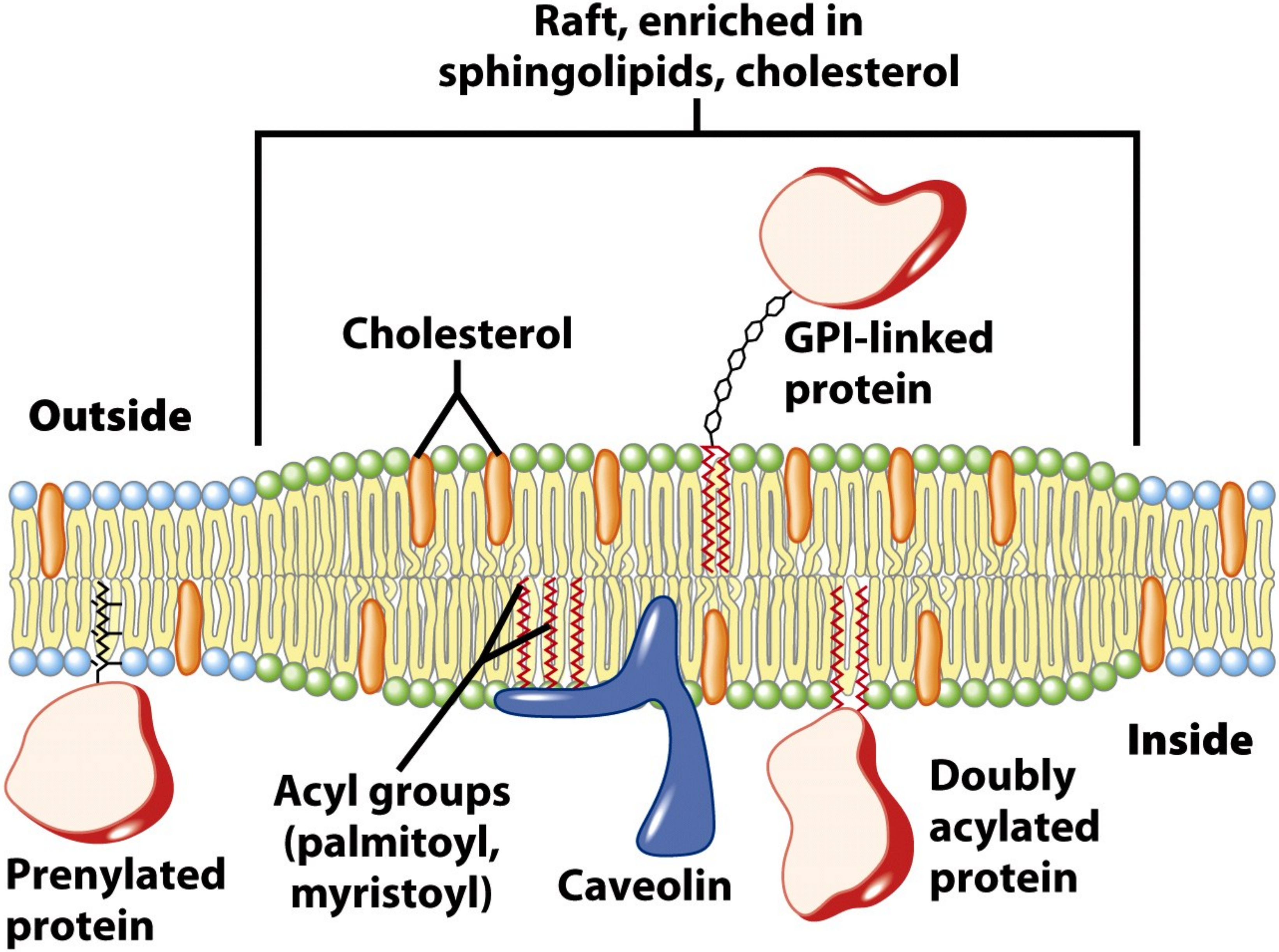

Figure 11-20a
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Synthesis of cholesteryl esters

Esterification converts cholesterol to an even more hydrophobic form for storage and transport.

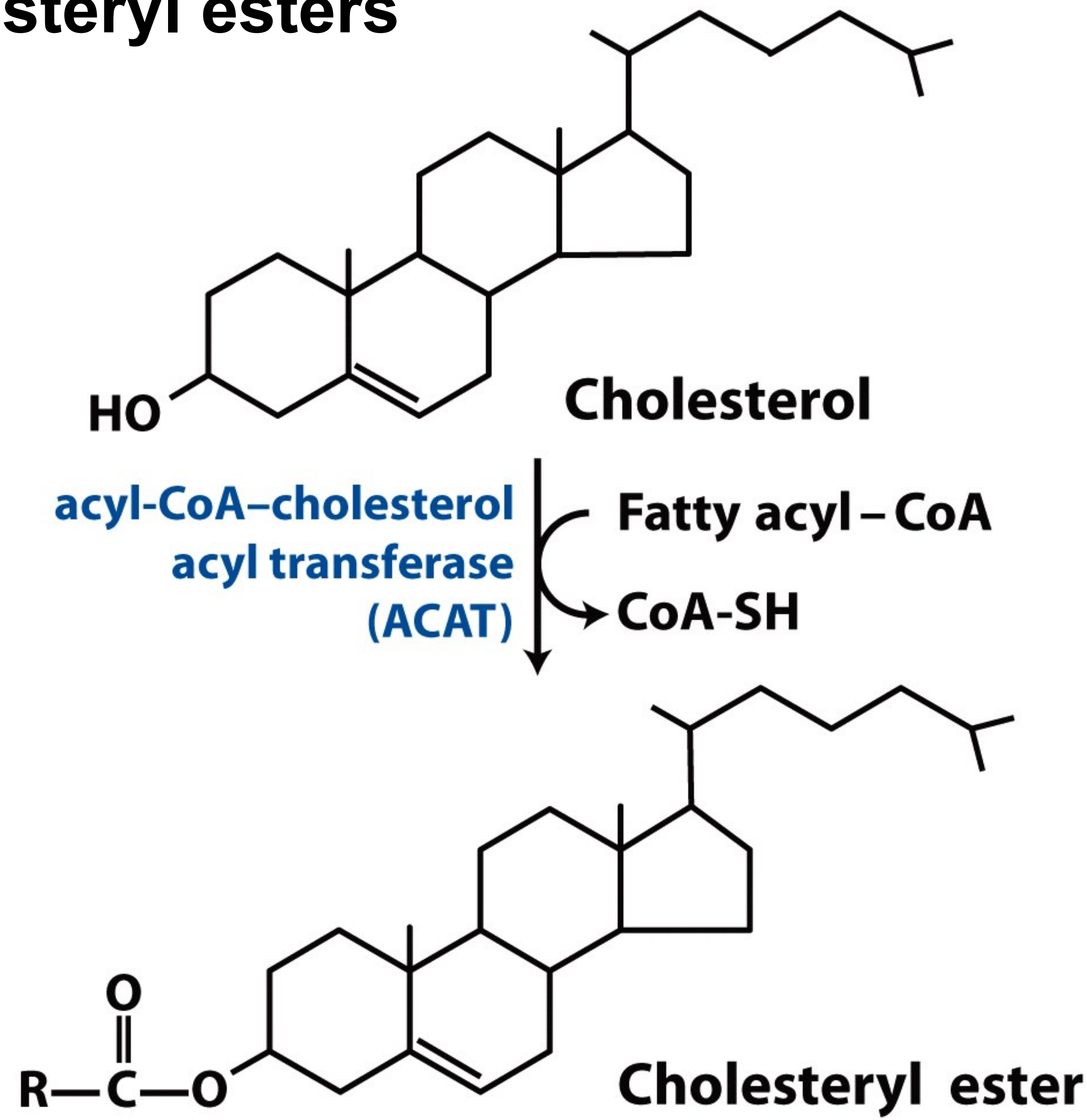

Figure 21-38
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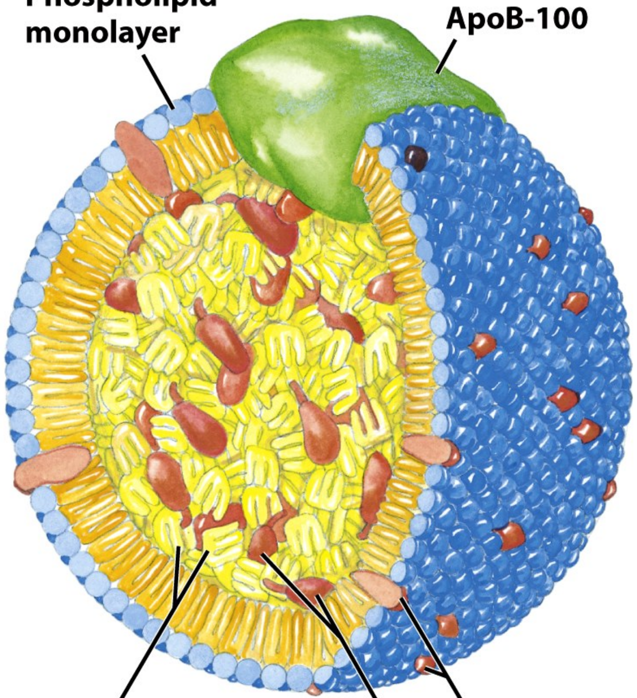
Figure 21-40b
Lehninger Principles of Biochemistry, Fifth Edition

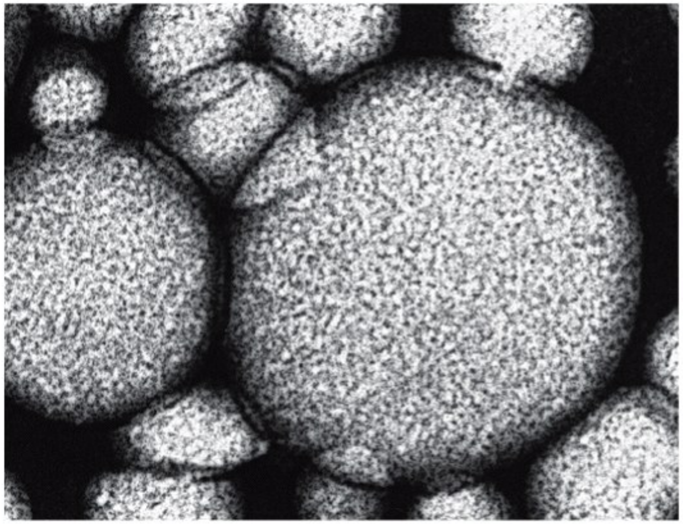
TABLE 21–1 Major Classes of Human Plasma Lipoproteins: Some Properties

Lipoprotein	Density (g/mL)	Composition (wt %) Protein	Phospholipids	Free cholesterol	Cholesteryl esters	Triacylglycerols
Chylomicrons	<1.006	2	9	1	3	85
VLDL	0.95–1.006	10	18	7	12	50
LDL	1.006–1.063	23	20	8	37	10
HDL	1.063–1.210	55	24	2	15	4

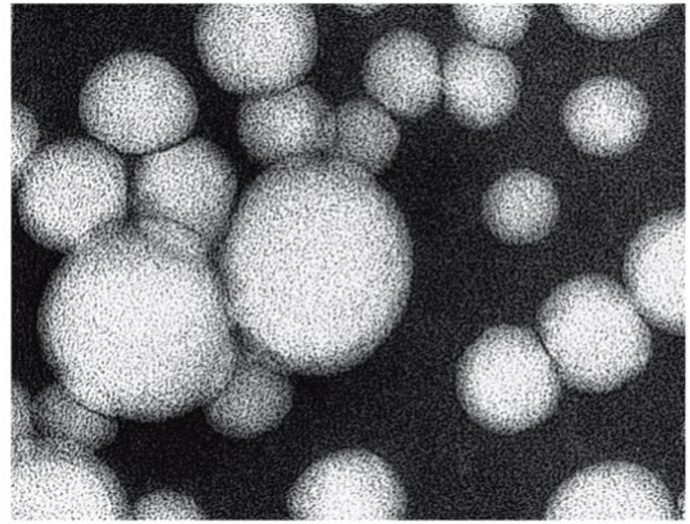


- Structure of an LDL molecule
- Apolipoprotein B-100 (apoB-100) is one of the largest single polypeptide chains known (4,636 aa; M_r 513,000)

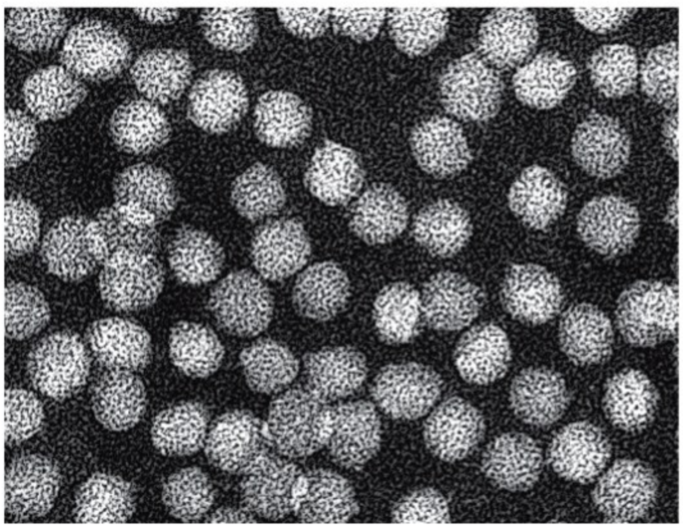
- One particle of LDL contains a core with about **1,500 molecules of cholesteryl esters**, surrounded by a shell composed of about 500 more molecules of cholesterol, 800 molecules of phospholipids, and one molecule of apoB-100



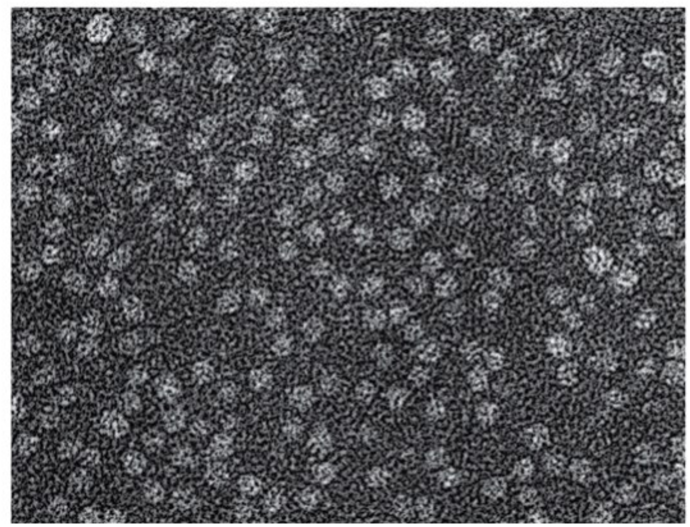
Chylomicrons (×60,000)



VLDL (×180,000)



LDL (×180,000)



HDL (×180,000)

Figure 21-39b
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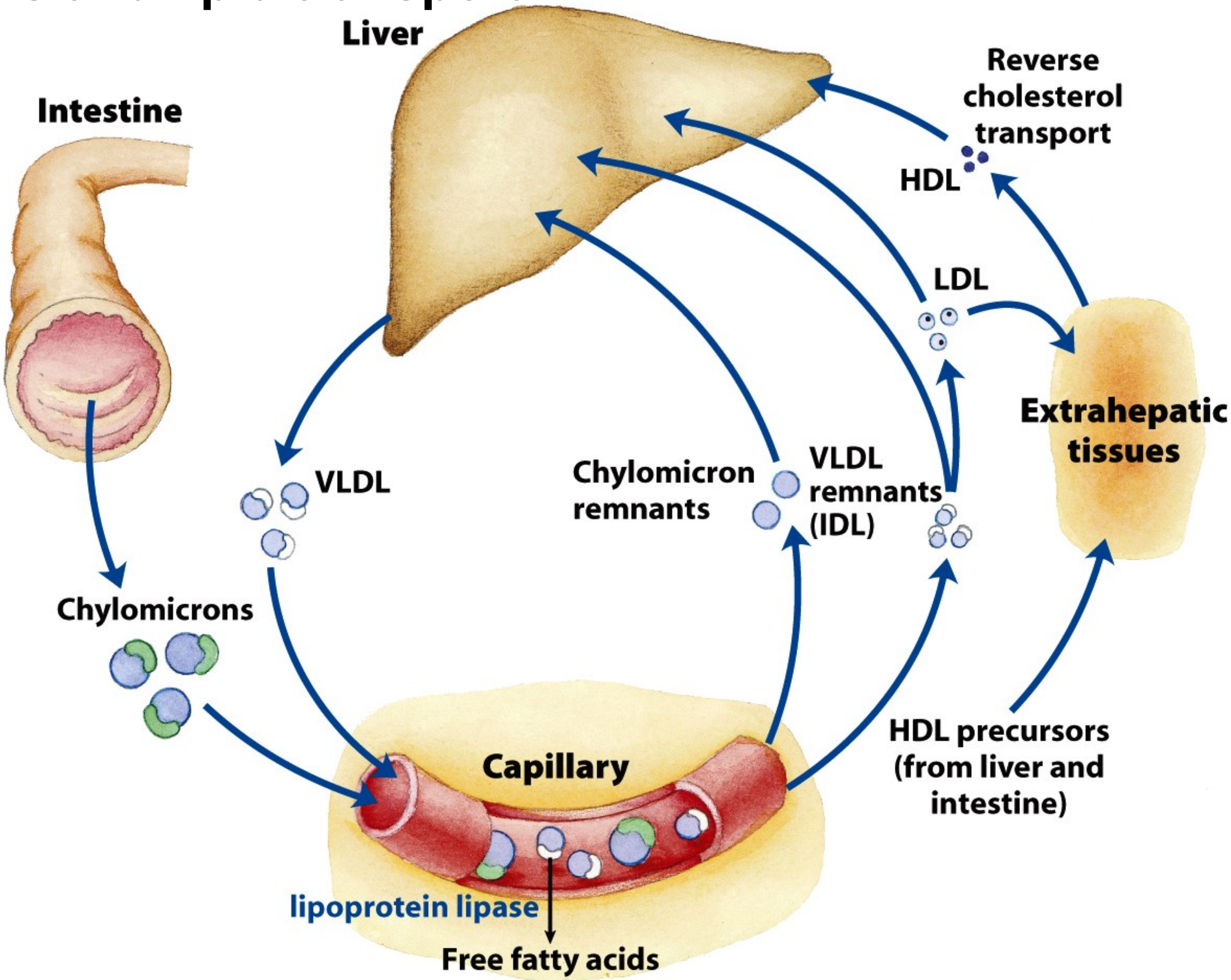
Lipoproteins and lipid transport



Mammary, muscle, or adipose tissue

Figure 21-40a
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- Dietary lipids are packaged into **chylomicrons**
- Much of their triacylglycerol content is released by lipoprotein lipase to adipose and muscle tissues during transport through capillaries
- Remaining chylomicrons (containing largely protein and cholesterol) are taken up by the liver
- Endogenous lipids and cholesterol from the liver are delivered to adipose and muscle tissue by **VLDL**
- Extraction of lipid from VLDL (along with loss of some apolipoproteins) gradually converts some of it to **LDL**, which delivers cholesterol to extrahepatic tissues or returns to the liver
- The liver takes up LDL, VLDL remnants, and chylomicron remnants by **receptor mediated endocytosis**
- Excess cholesterol in extrahepatic tissues is transported back to the liver as **HDL**
- In the liver, some cholesterol is converted to **bile salts**

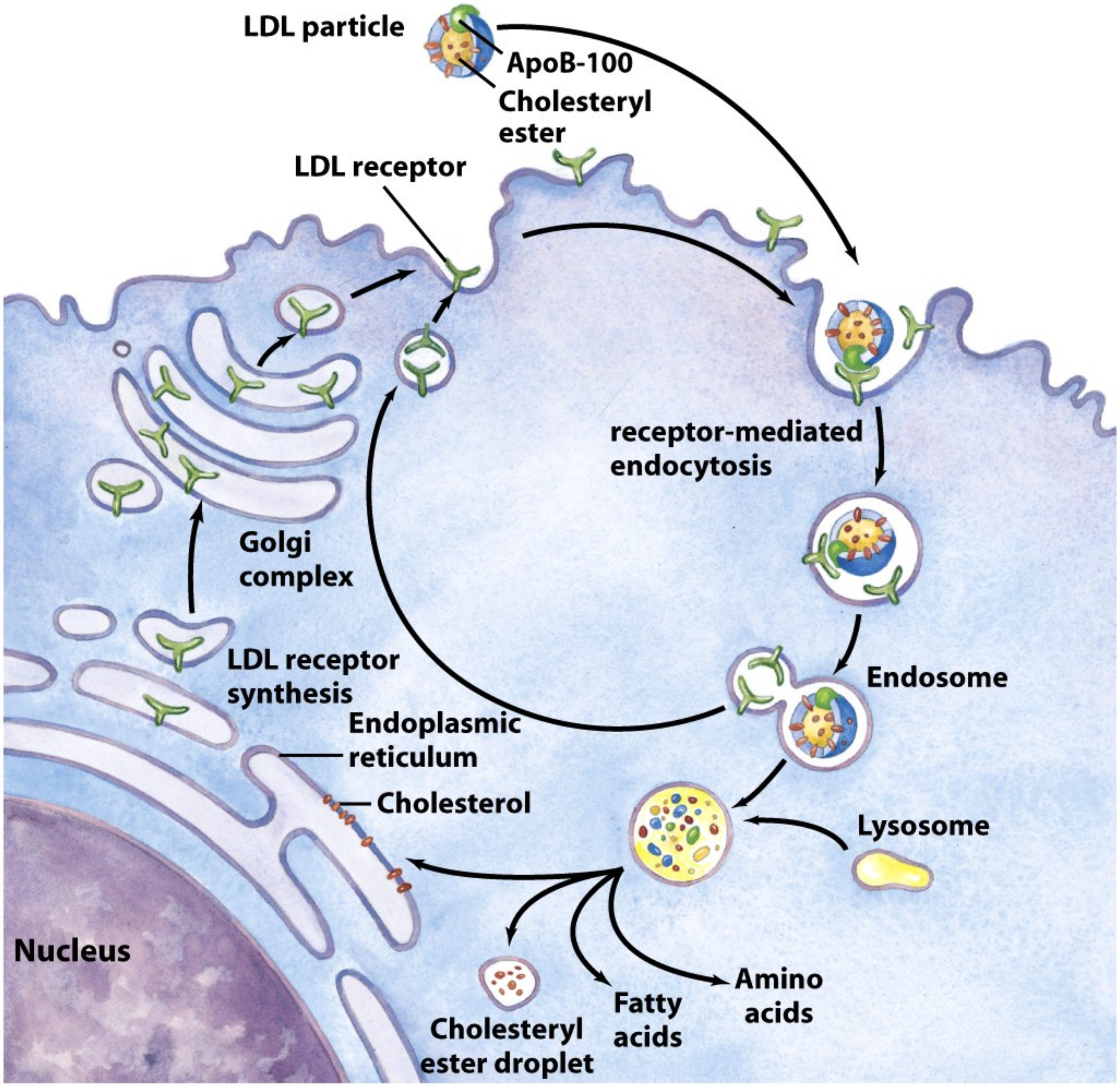

Figure 21-42
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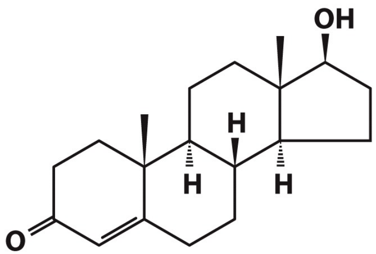
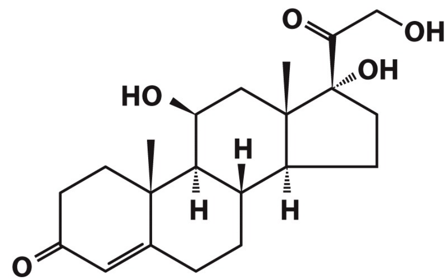
Steroid Hormones

- Steroids are oxidized derivatives of sterols
- Steroids have the sterol nucleus, but lack the alkyl chain found in cholesterol
- More polar than cholesterol
- Steroid hormones are synthesized from cholesterol in gonads and adrenal glands
- They are carried through the body in the bloodstream, usually attached to carrier proteins
- Many of the steroid hormones are male and female sex hormones

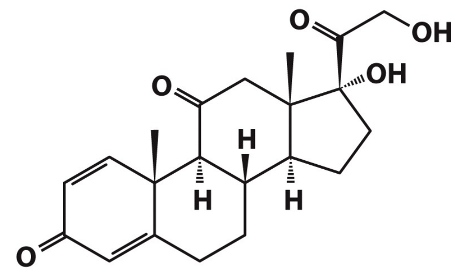
Steroid Hormones



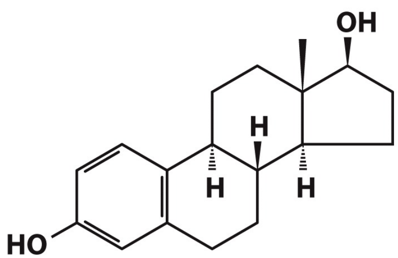
Testosterone



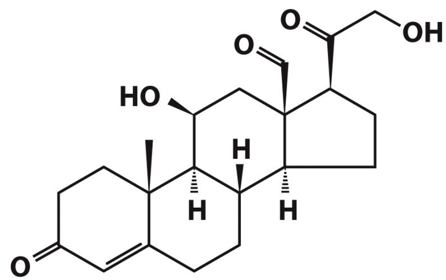
Cortisol



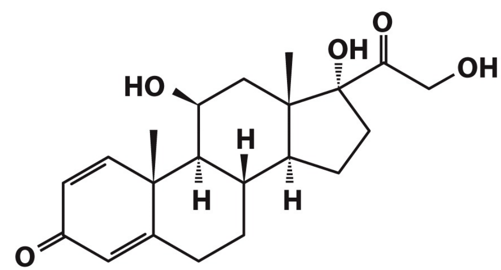
Prednisone



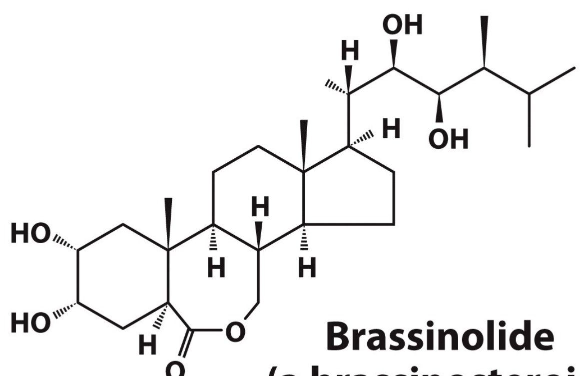
β-Estradiol



Aldosterone



Prednisolone



Brassinolide (a brassinosteroid)

Figure 10-19
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Biologically Active Lipids

- Are present in much smaller amounts than storage or structural lipids
- Play vital roles as signaling molecules between nearby cells
- Lipid soluble vitamins (A, D, E, and K)

Signaling Lipids

- Paracrine lipid hormones are present in small amounts but play vital roles as signaling molecules between nearby cells
- Enzymatic oxidation of arachidonic acid yields
  - prostaglandins,
  - thromboxanes,
  - leukotrienes
- Arachidonic acid: $20{:}4(\Delta^{5,8,11,14})$

Arachidonic Acid Derivatives as Signaling Lipids

- Variety of functions:
  - Inflammation and fever, increase in body temperature (prostaglandins)
  - Formation of blood clots (thromboxanes)
  - Smooth muscle contraction in lungs; overproduction causes asthmatic attacks (leukotrienes)
  - Smooth muscle contraction in uterus during labor and menstruation (prostaglandins)

Nonsteroidal antiinflammatory drugs (NSAIDs) such as **aspirin** and **ibuprofen** block the formation of prostaglandins and thromboxanes from arachidonate by inhibiting the enzyme cyclooxygenase (prostaglandin H2 synthase).

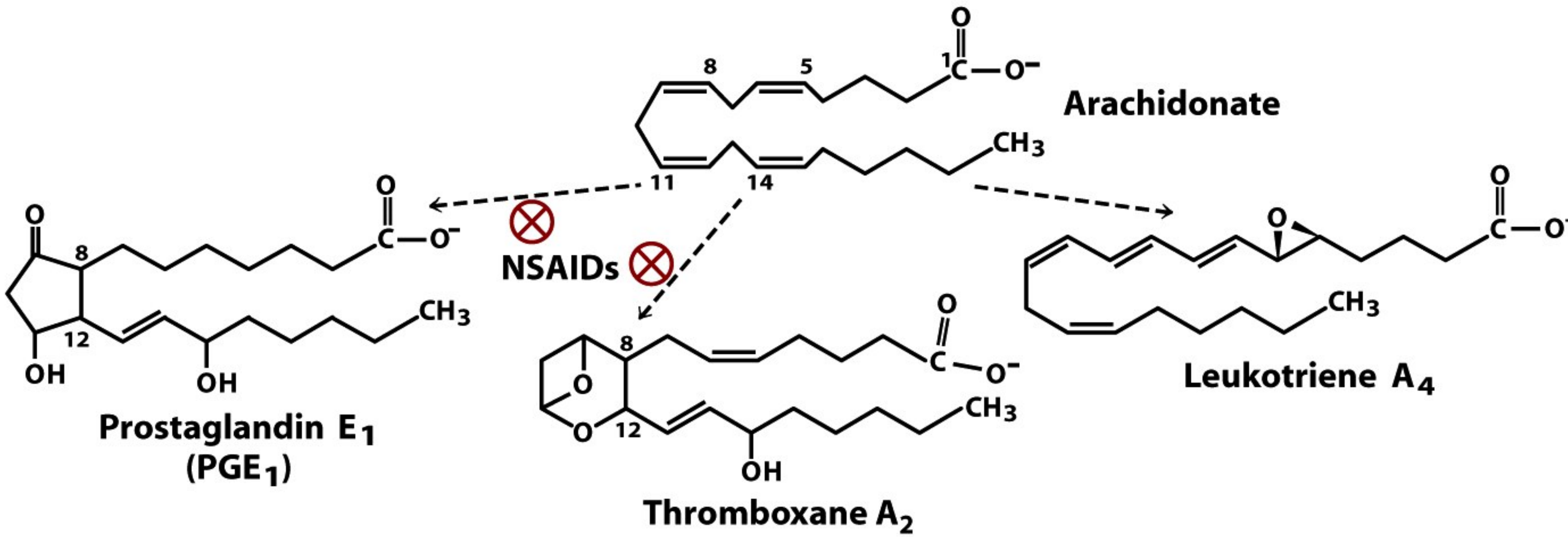

Figure 10-18
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Vitamin D regulates calcium uptake

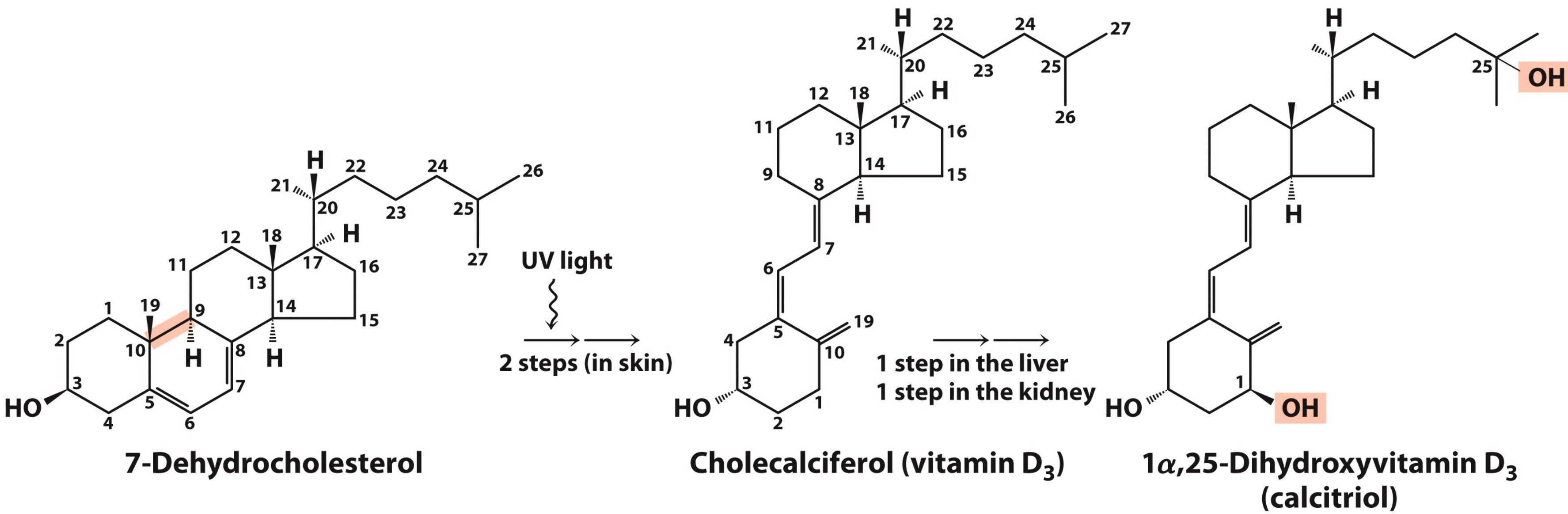

Figure 10-20a
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Vitamin A (Retinol)

- Involved in visual pigment
- Precursor for other hormones involved in signaling

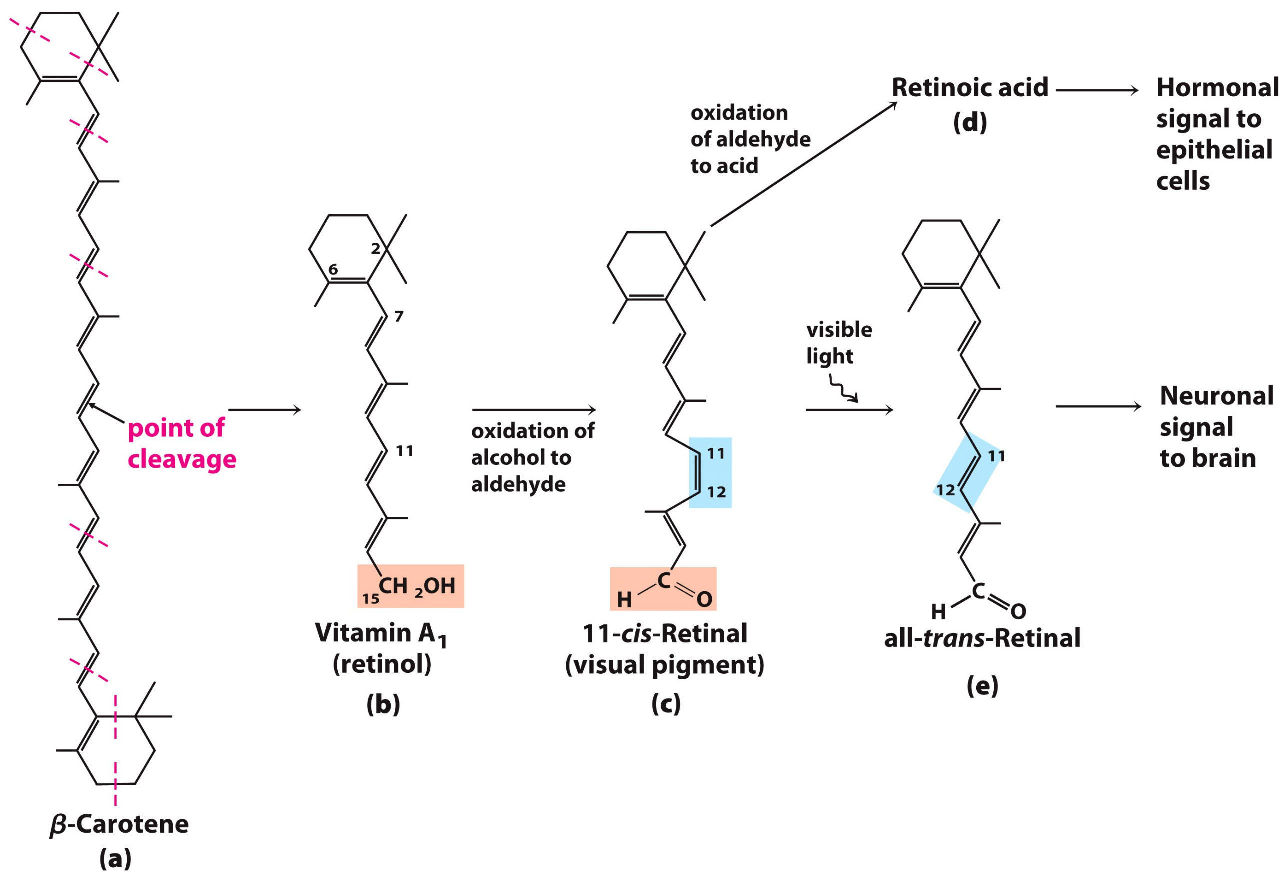

Figure 10-21
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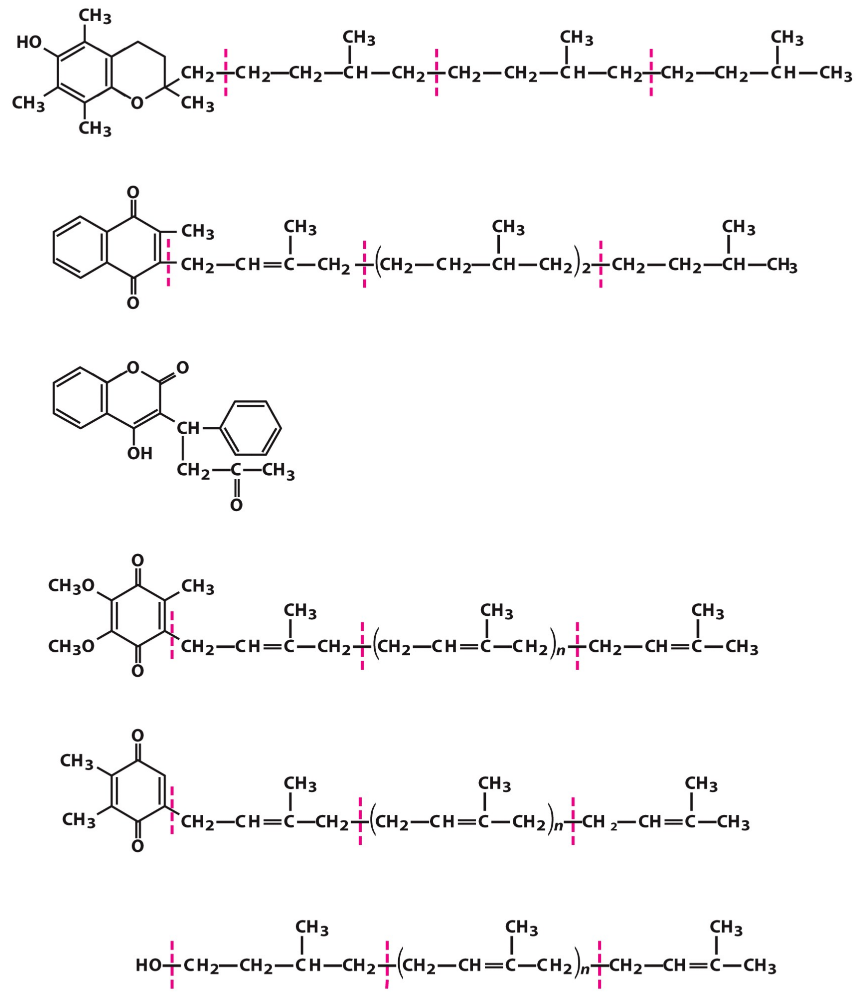
Vitamin E, K, and other lipid quinones are antioxidants



(a) **Vitamin E: an antioxidant**

(b) **Vitamin K_1: a blood-clotting cofactor (phylloquinone)**

(c) **Warfarin: a blood anticoagulant**

(d) **Ubiquinone: a mitochondrial electron carrier (coenzyme Q) (*n* = 4 to 8)**

(e) **Plastoquinone: a chloroplast electron carrier (*n* = 4 to 8)**

(f) **Dolichol: a sugar carrier (*n* = 9 to 22)**

Figure 10-22
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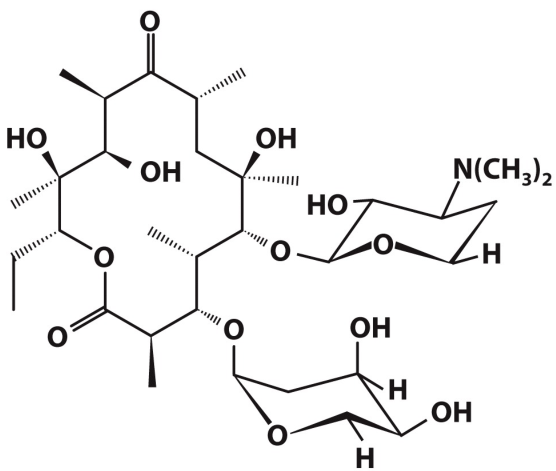
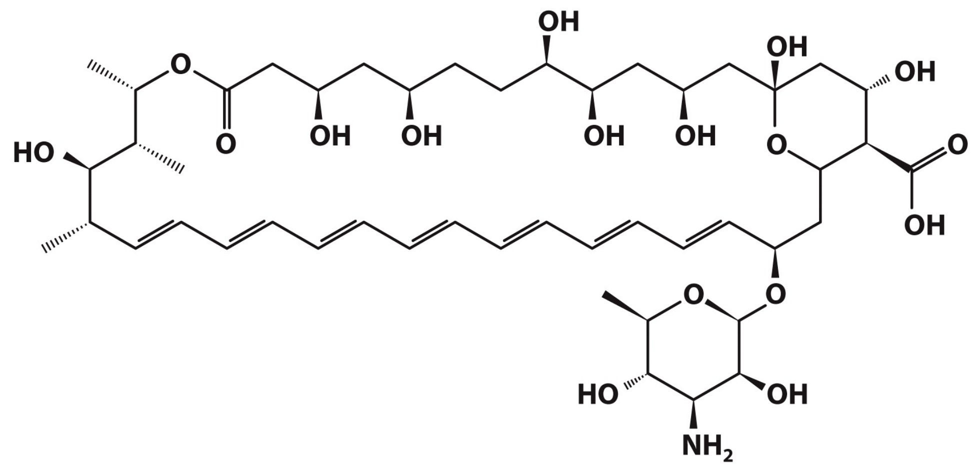
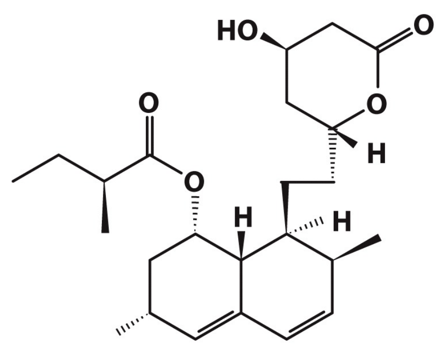
Polyketides are biologically active lipids with medicinal uses



Erythromycin (antibiotic)



Amphotericin B (antifungal)



Lovastatin (statin)

Figure 10-24
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