Lipids of Physiological Significance

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Objectives

- By the end of this lecture the first year students will be able to:
- Define and classify lipids
- Understand the physiological importance of lipids
- List the examples of simple and complex lipids
- Correlate implications of lipids in clinical conditions

Overview

- What are lipids?
- Classification of lipids
- Functions of lipids
- Simple lipids: Fatty acids, triacylglycerols, steroids
- Complex lipids: Phospholipids, sphingolipids, glycolipids
- Plasma lipid transport: types and functions of lipoproteins

What are lipids?

- A heterogeneous group of hydrophobic (water-insoluble) organic molecules that are soluble only in organic solvents
- Body lipids are compartmentalized (packed) in cell membranes, tissue and plasma

Functions of Lipids

- Lipids are essential components of biological membranes
- Lipids with hydrocarbon chains serve as major energy stores
- Cell signaling involves lipid molecules
  - e.g. Inositol tri-phosphate
- Fat-soluble vitamins, steroid hormones and prostaglandins are formed of lipids

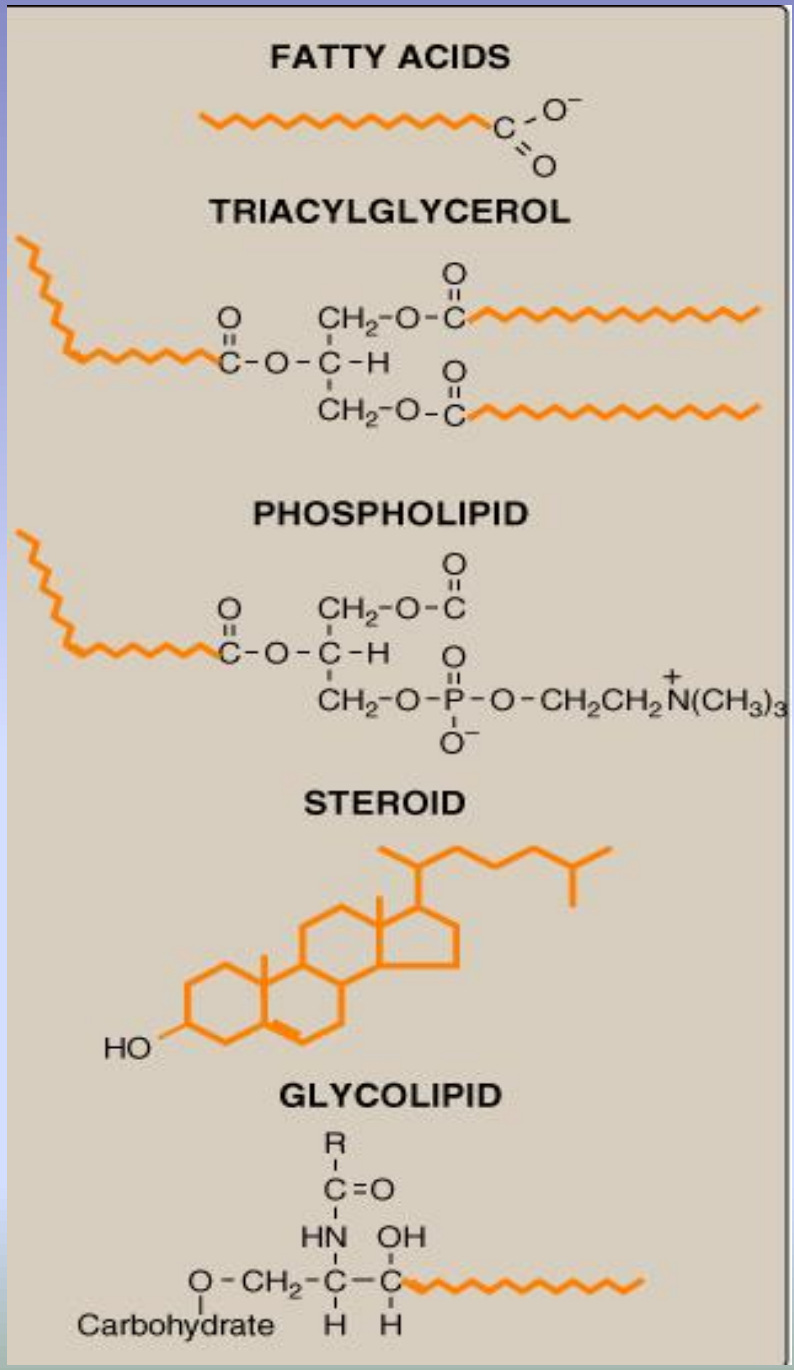
Lipids and disease

Diseases that are strongly associated with abnormality in lipid metabolism:

- Atherosclerosis
- Coronary artery disease
- Obesity
- Metabolic syndrome
- Hypertension

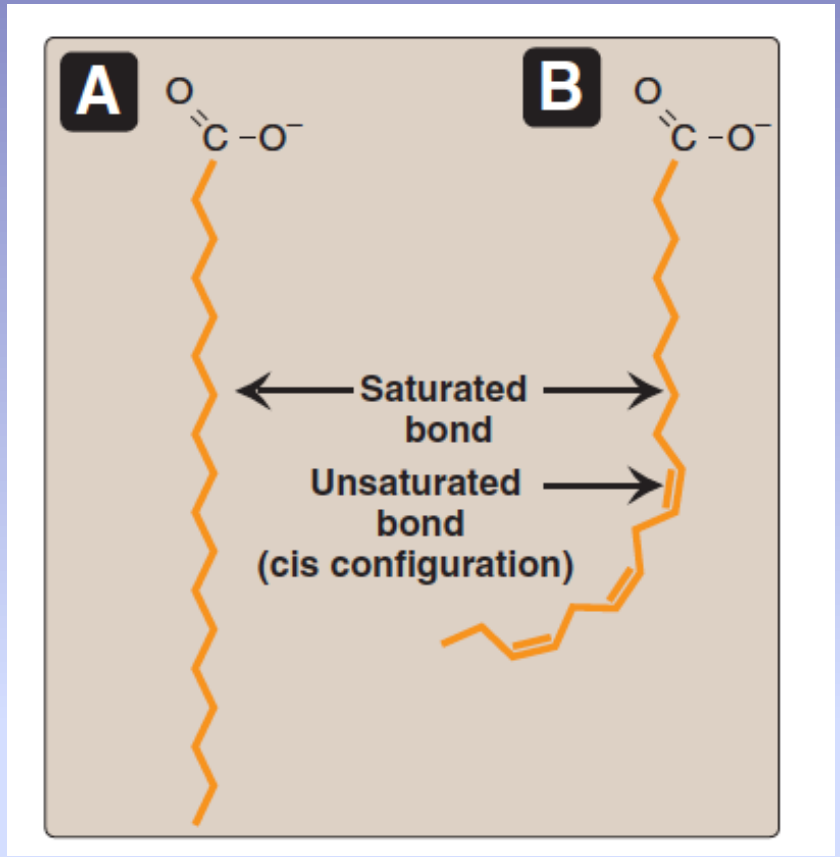
Classification of Lipids

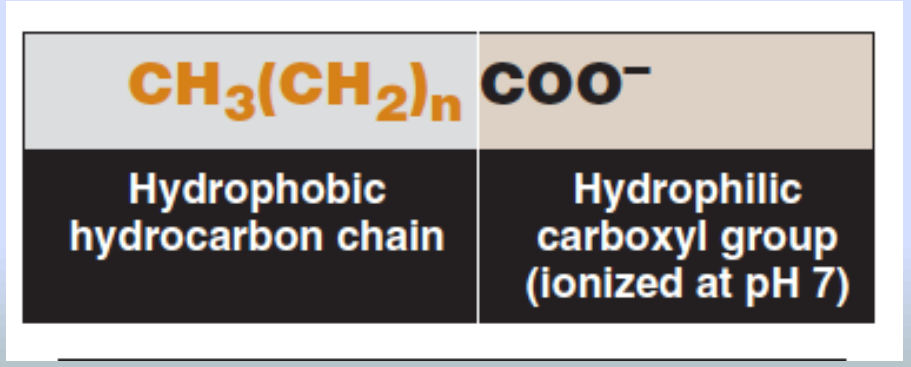
- Simple lipids:
  - Fatty acids
  - Triacylglycerols
  - Steroids (cholesterol)
- Complex lipids
  - Phospholipids
  - Sphingolipids
  - Glycolipids



Fatty Acids (FAs)

- FAs are carboxylic acids with long-chain hydrocarbon side groups
- They are amphipathic in nature (both hydrophilic and hydrophobic)
  - The carboxylic group (COOH) is hydrophilic
  - The hydrocarbon chain is hydrophobic





Fatty Acids (FAs)

- FAs are highly insoluble in water
- Must be transported in plasma with proteins
- Majority of plasma FAs are esters of:
  - Triacylglycerol
  - Cholesterol
  - Phospholipids

Chain length

- In mammals it varies from C_{16}–C_{18}
- Examples: palmitic, oleic, linoleic, stearic acids

Fatty Acids (FA)

Degree of saturation

- FAs may contain:
  - No double bonds (Saturated / *trans* form)
  - One or more double bonds (Mono or Polyunsaturated / *cis* form)

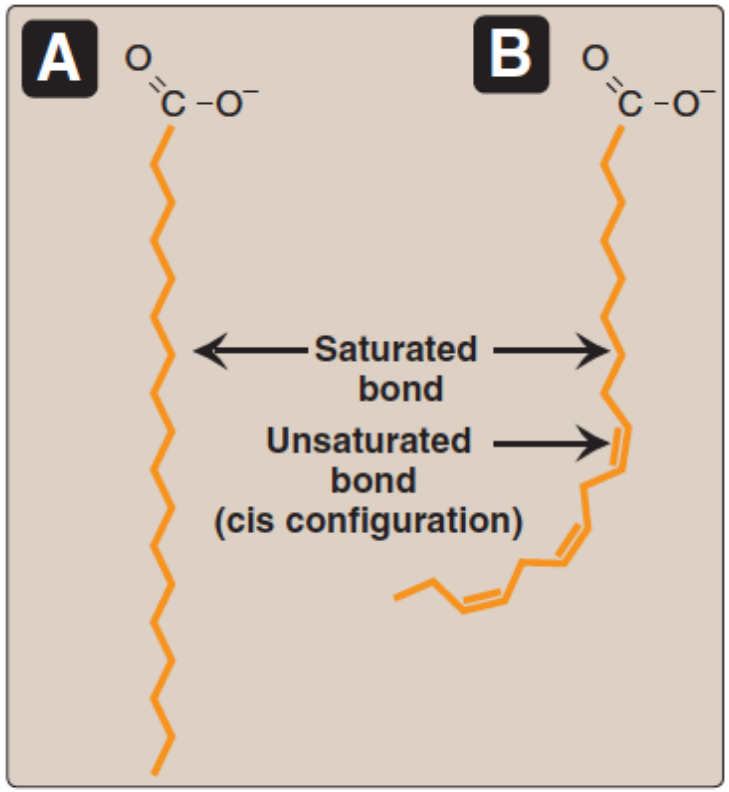


Figure 16.3
A saturated (A) and an unsaturated (B) fatty acid. Orange denotes hydrophobic portions of the molecules. [Note: Cis double bonds cause a fatty acid to "kink."]

Saturated FAs	Unsaturated FAs
12:0 Lauric acid	18:1 Oleic acid
16:0 Palmitic acid	18:2 Linoleic acid
18:0 Stearic acid	20:4 Arachidonic acid

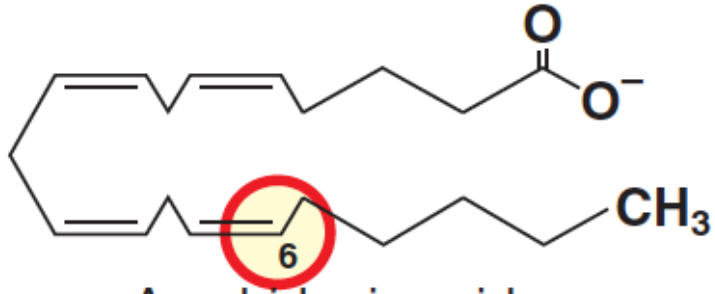
Essential Fatty Acids (FA)

- Linoleic acid (precursor of arachidonic acid)
- α-Linolenic acid
- Body cannot synthesize
- Must be supplied in the diet
- Deficiency can cause dermatitis, membrane function loss
- Arachidonic acid is essential when linoleic acid is deficient in the diet

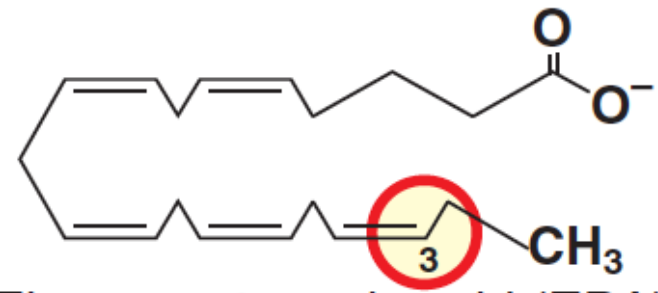
ω-3 and ω-6 fatty acids

ω = Omega

- Long-chain polyunsaturated FAs with first double bond starting with 3rd carbon from the methyl end
- They reduce serum triglycerides, blood pressure and risk for heart disease
- Major source: Fish
- Examples: α-linolenic acid, EPA (eicosapentaenoic acid), DHA (Docosahexaenoic acid)



Arachidonic acid
(20:4, ω-6)
found in seed oils



Eicosapentaenoic acid (EPA)
(20:5, ω-3)
found in fish oils

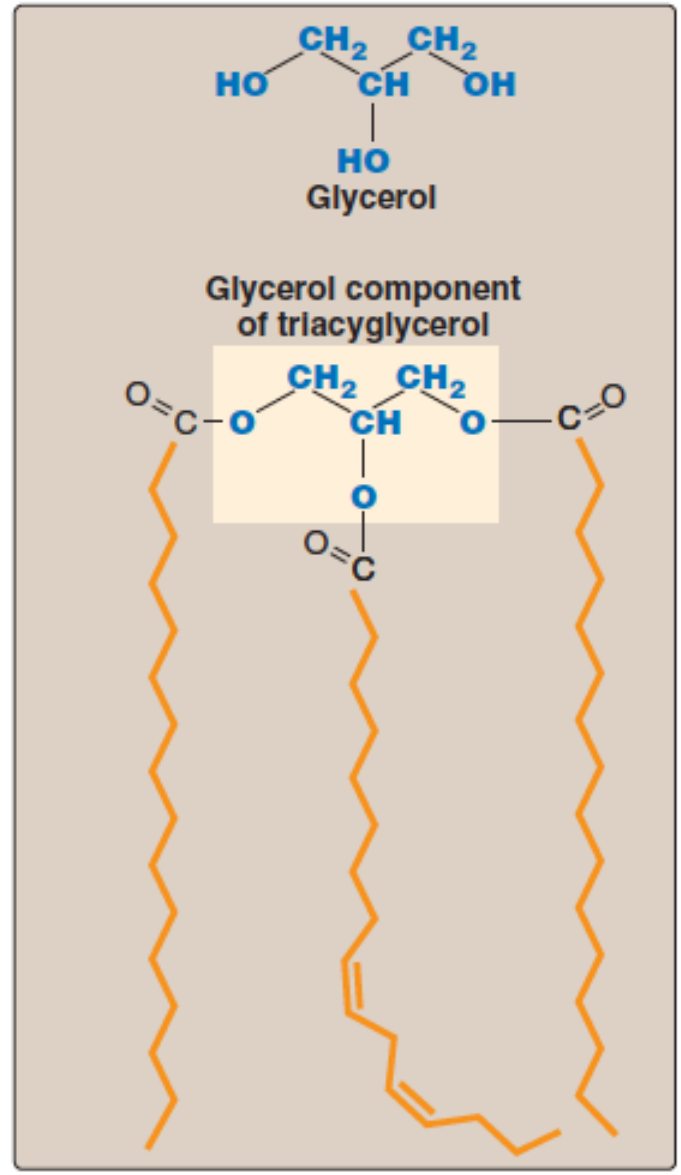
ω-3 and ω-6 fatty acids

ω-3 and ω-6 fatty acids

- Long-chain polyunsaturated FAs with first double bond starting with 6^{th} carbon from the methyl end
- They reduce serum cholesterol
- Major source: Vegetable oils, nuts
- Examples:
  - Linoleic acid 18:2

Triacylglycerols (TGs)

- TGs are tri-esters of fatty acids also called fats
- Three fatty acids are bonded to a glycerol molecule
- Constitutes majority of dietary lipids
- Stored in adipocytes (fat cells) as energy reservoir
- Not a component of cell membranes
- Subcutaneous layer of fats provides thermal insulation



Structure of a triacylglycerol

Steroids

- Derivatives of cyclopentanoperhydrophenanthrene ring
- Consists of four fused rings called steroid nucleus with an 8-carbon chain
- Steroids with a hydroxyl group are called sterols
- Cholesterol is a major sterol in humans and animals
- Cholesterol in plasma is bound to fatty acids called cholesteryl esters

Functions of cholesterol

- Component of cell membranes
- Precursor for:
  - Bile acids / Bile salts
  - Vitamin D
  - Steroid hormones (Aldosterone, cortisol, testosterone, estrogen, progesterone)
- High levels of plasma cholesterol is strongly associated with coronary artery disease and atherosclerosis

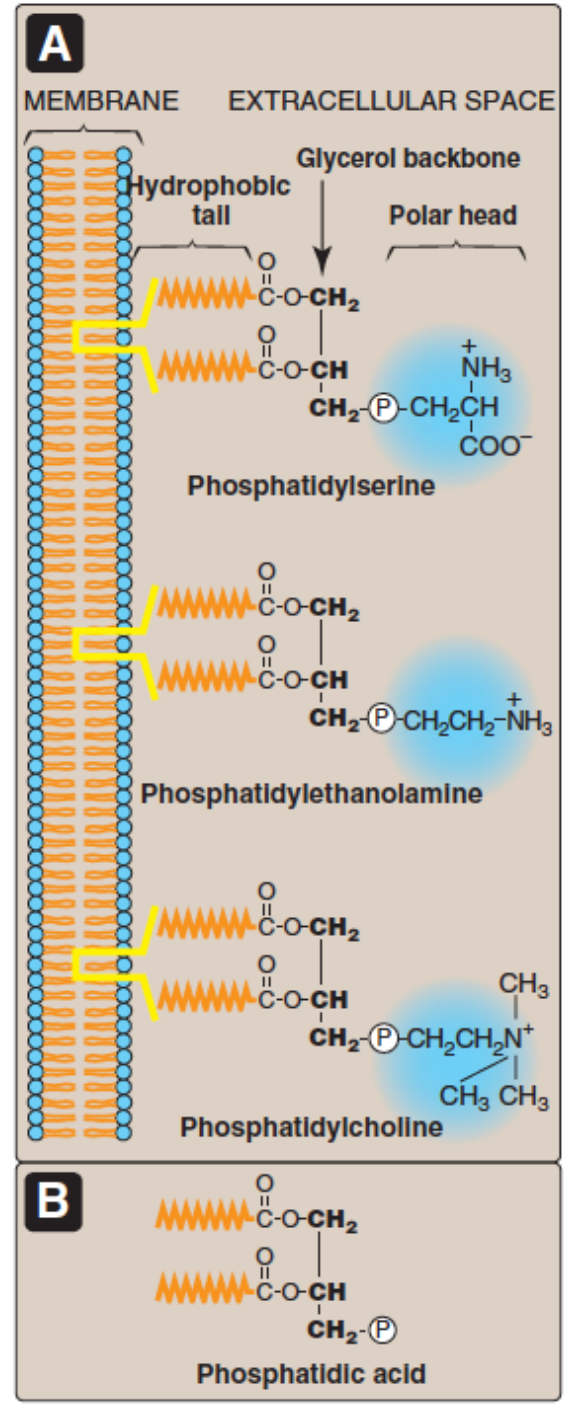
Phospholipids

- Two classes of phospholipids:
  - Glycerophospholipids (contain glycerol backbone)
  - Sphingophospholipids (contain sphingosine)

Glycerophospholipids

- Glycerol-3-PO_4 is bonded to two fatty acid chains
- The PO_4 group is linked to a hydrophilic group
- Amphiphilic in nature
  - Hydrophobic tail
  - Hydrophilic phosphoryl heads

Glycero-phospholipids



Phospholipids

- Major components of biological membranes
- Examples: phosphatidic acid, phosphatidyl – choline and serine

Sphinogophospholipids

- Long-chain fatty acids attached to sphingosine
- Example: Sphingomyelin
- An important component of myelin that protects and insulates nerve fibers

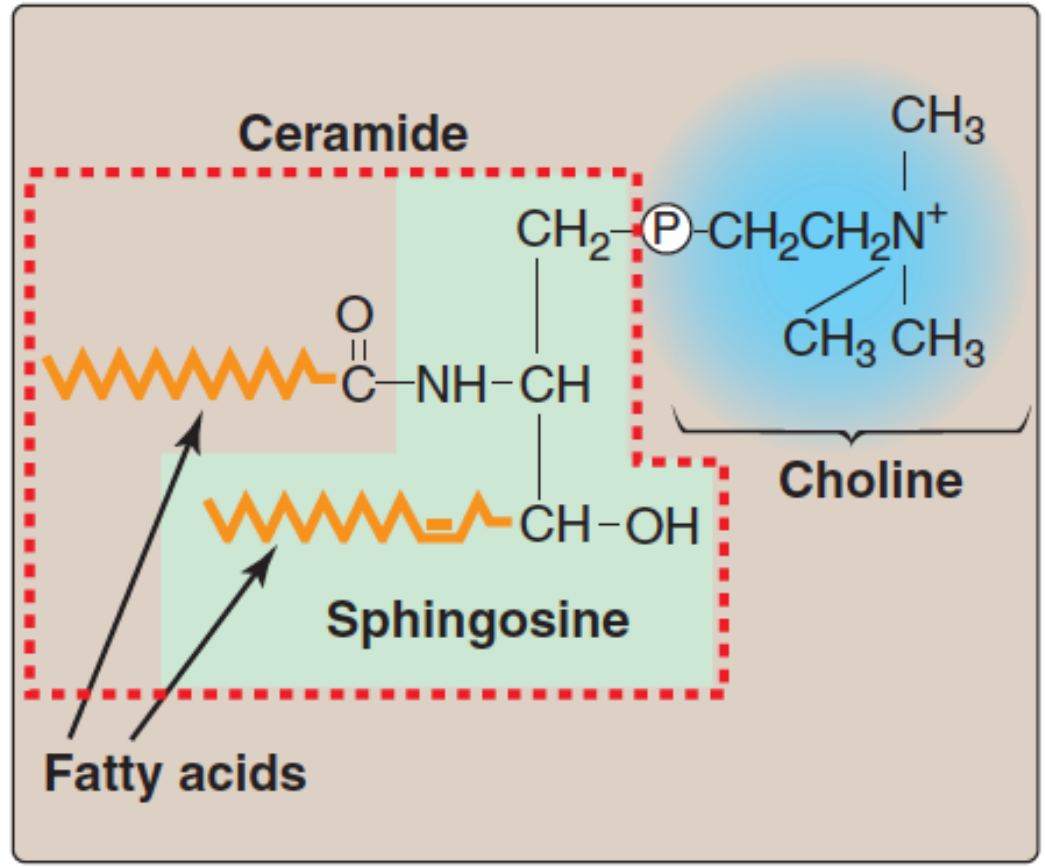


Figure 17.4
Structure of sphingomyelin, showing sphingosine (in green box) and ceramide components (in dashed box).

Glycolipids

- Contain both carbohydrate and lipid components
- Derivatives of ceramide
- A long chain fatty acid is attached to sphingosine
- Also called glycoshpingolipids
- Examples: Ganglioside, glactocerebroside
- Act as: Blood group antigens, cell surface receptors for bacteria/viruses

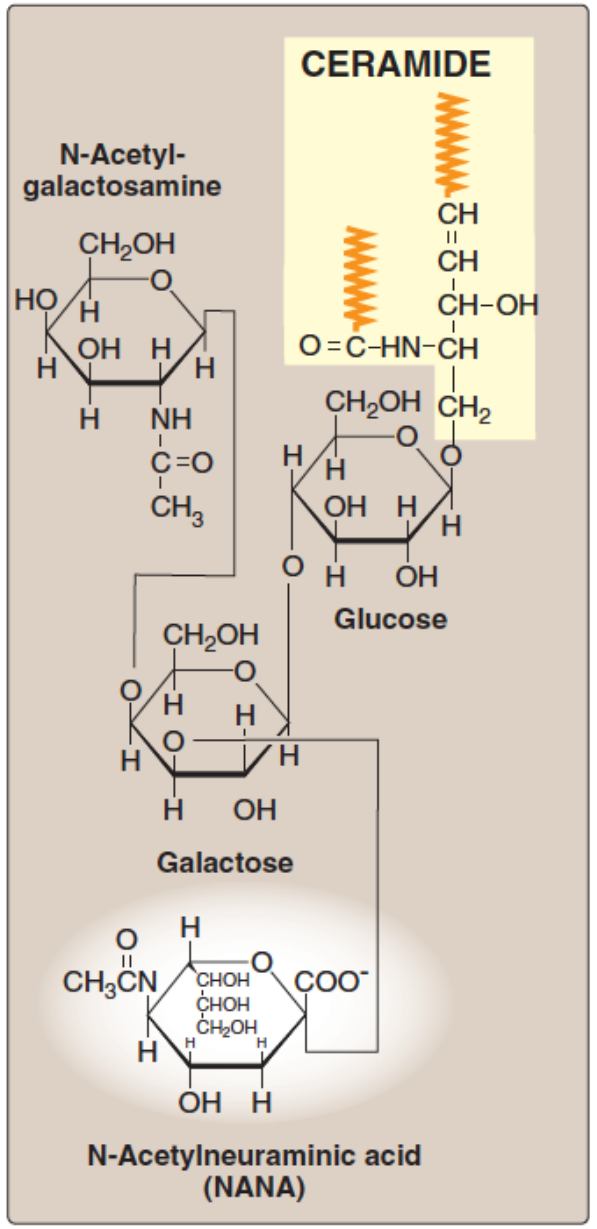


Figure 17.15
Structure of the ganglioside G_{M2}.

Transport of plasma lipids

- Plasma lipids are transported as lipoprotein particles (lipids + protein)
- Protein part: Apoproteins or apolipoproteins
  - Examples: Apolipoproteins A, B, C
  - Functions: lipid transport, enzymatic functions, ligands for receptors
- Lipid part: Contains lipids of various types

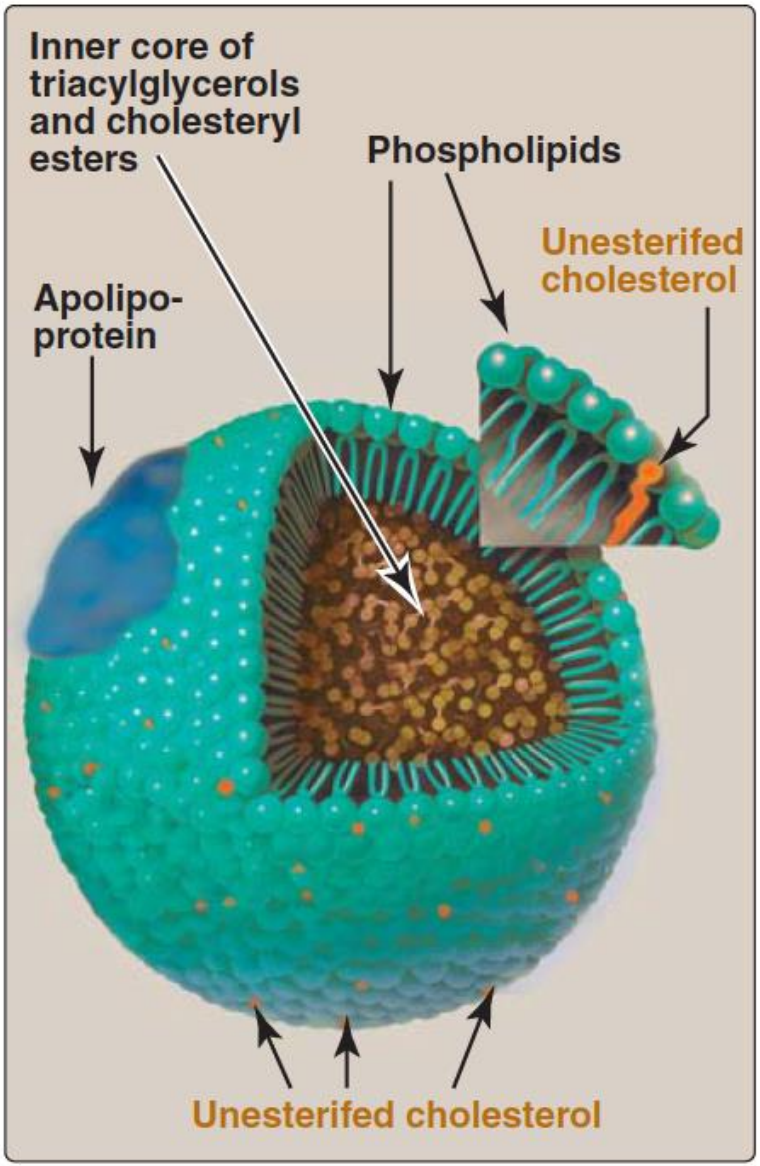
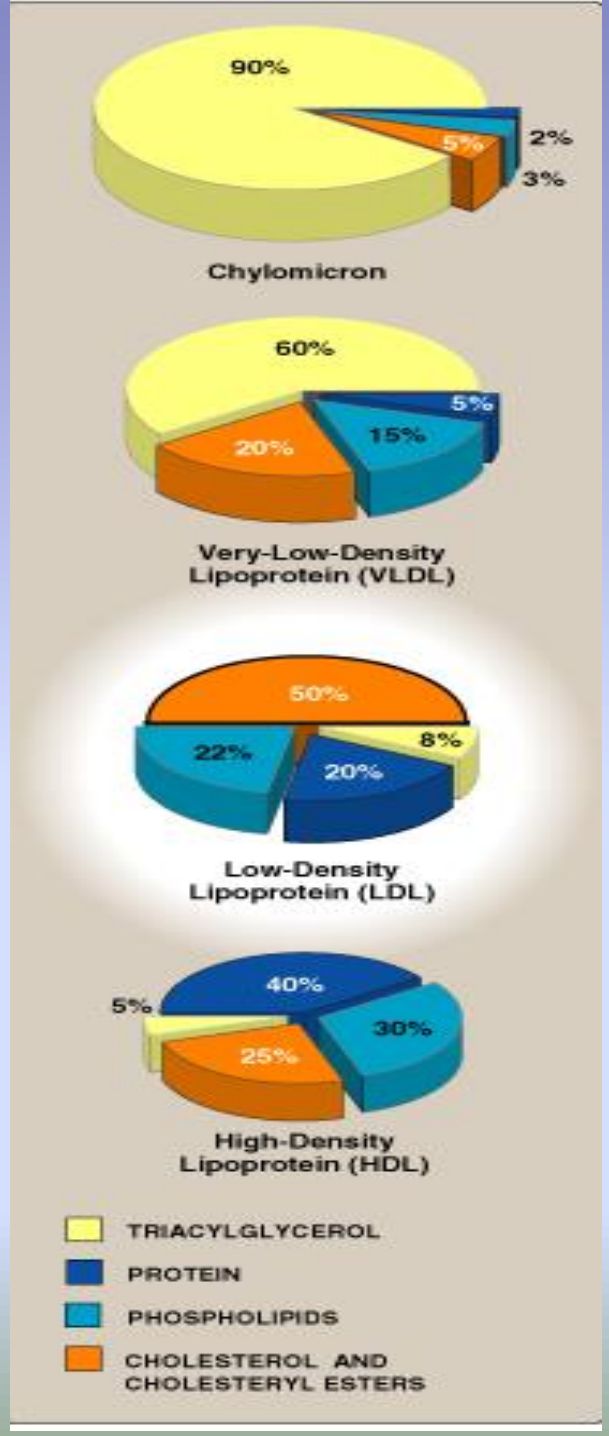


Figure 18.14
Structure of a typical lipoprotein particle.

Types and functions of lipoproteins

Lipoprotein	Transports
Chylomicrons	Dietary TGs
Very low density lipoprotein (VLDL)	Endogenous TGs
Low density lipoprotein (LDL)	Free cholesterol
High density lipoprotein (HDL)	Cholesteryl esters



Take home message

- Lipids are a group of hydrophobic molecules
- Perform essential physiological functions in the body
- Simple lipids include: fatty acids, TGs and steroids
- Complex lipids include: phospholipids, sphingolipids and glycolipids
- A number of diseases are associated with abnormal lipid metabolism

References

- Lippincott's Illustrated Reviews, Biochemistry, 6th edition, Denise R. Ferrier, Lippincott Williams & Wilkins, USA.
- Chapter 16: pages 181-182, 195-198
- Chapter 17, page 201-202, 205-206
- Chapter 18, page: 219-220, 226-232