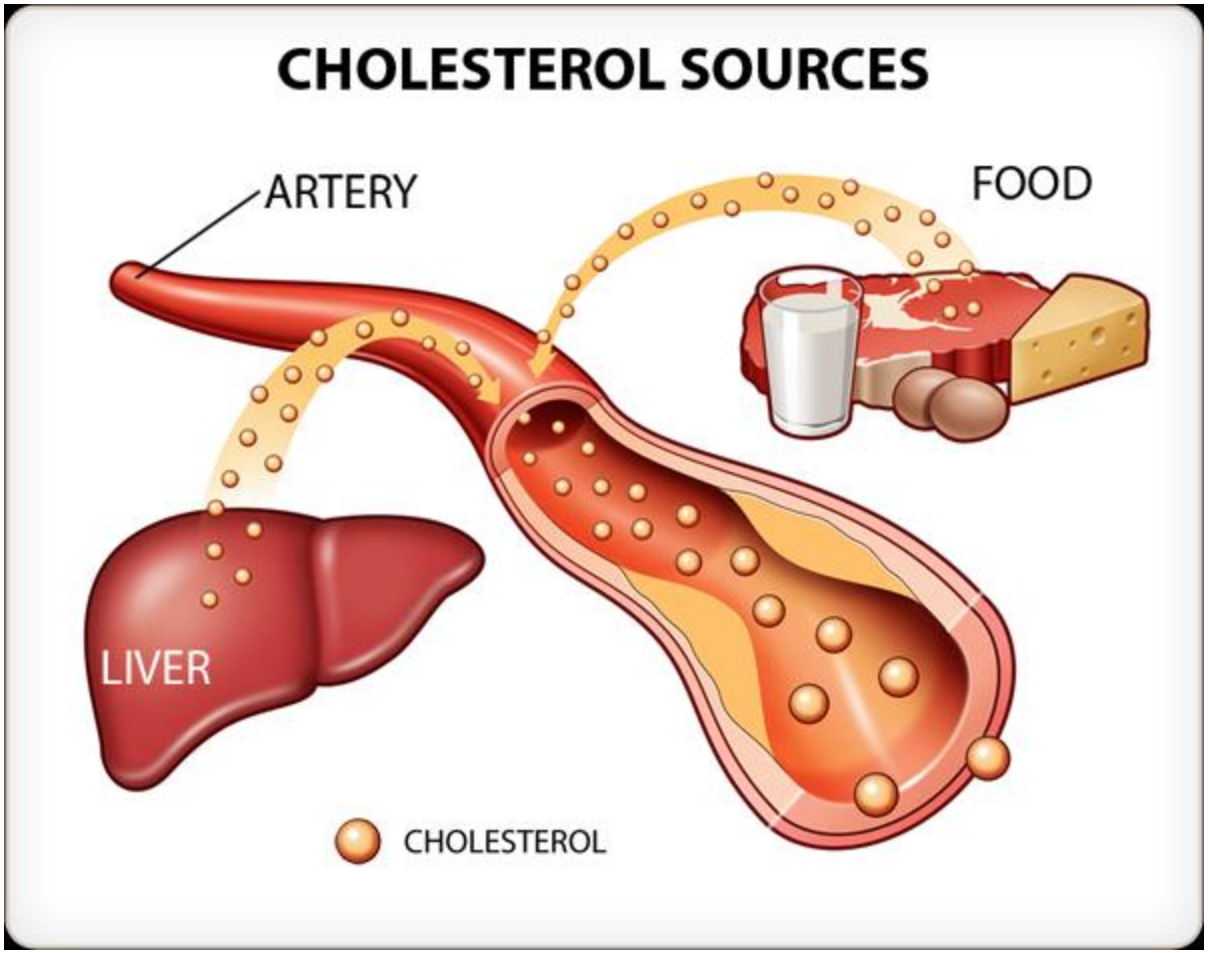
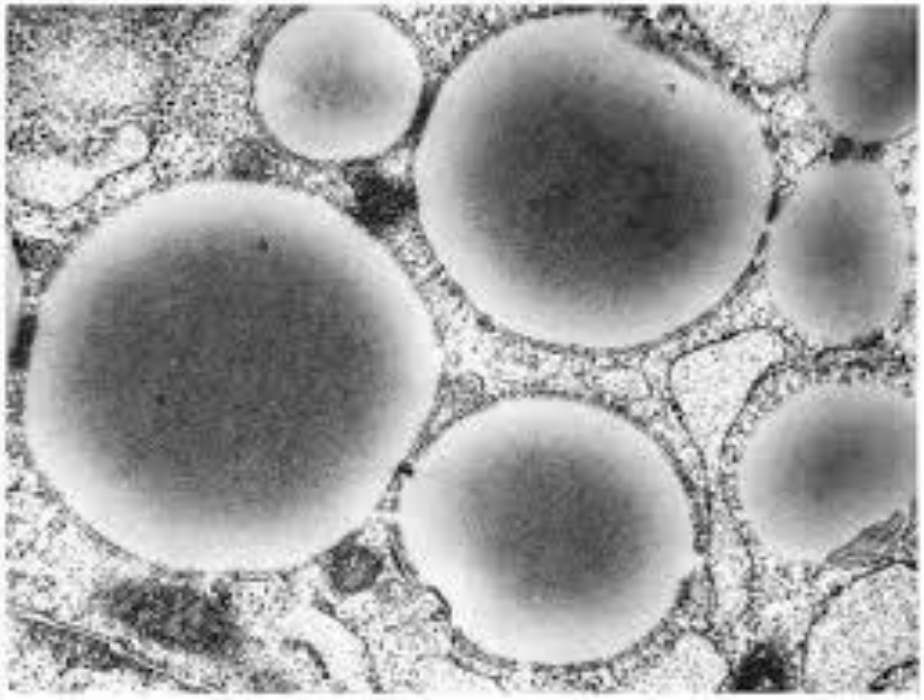
Lipids



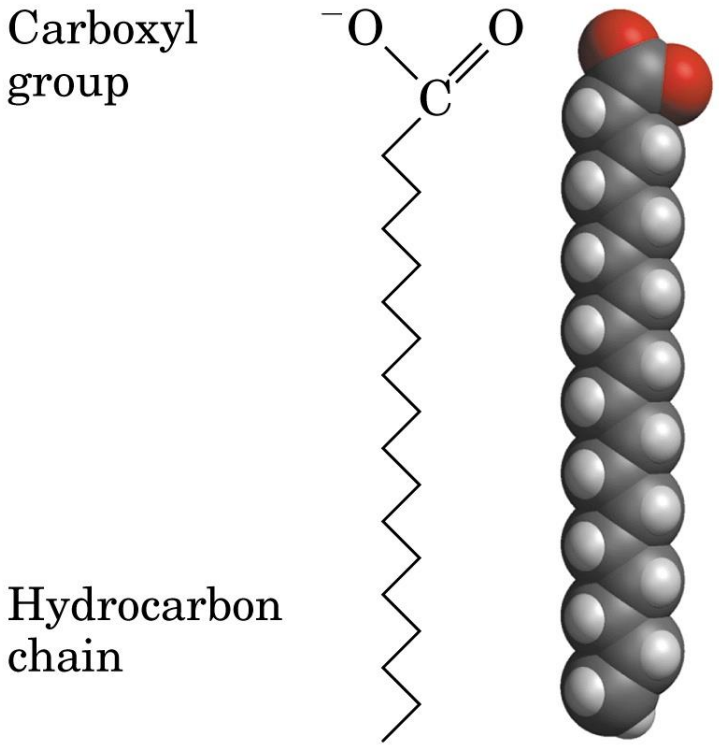
Biological functions of lipids

- The principle stored form of **energy**.
- The major **structural** elements of biological membranes.
- Enzyme cofactors
- Electron carriers
- Light-absorbing pigment
- Hydrophobic anchors
- Emulsifying agents
- Hormones
- Intracellular messengers



1. Storage lipids

- **Fats** & **oils** are used as stored forms of energy which are derivatives of **fatty acids**.
- **Fatty acids**: carboxylic acids with long hydrocarbon chains ranging from 4-36 C long.

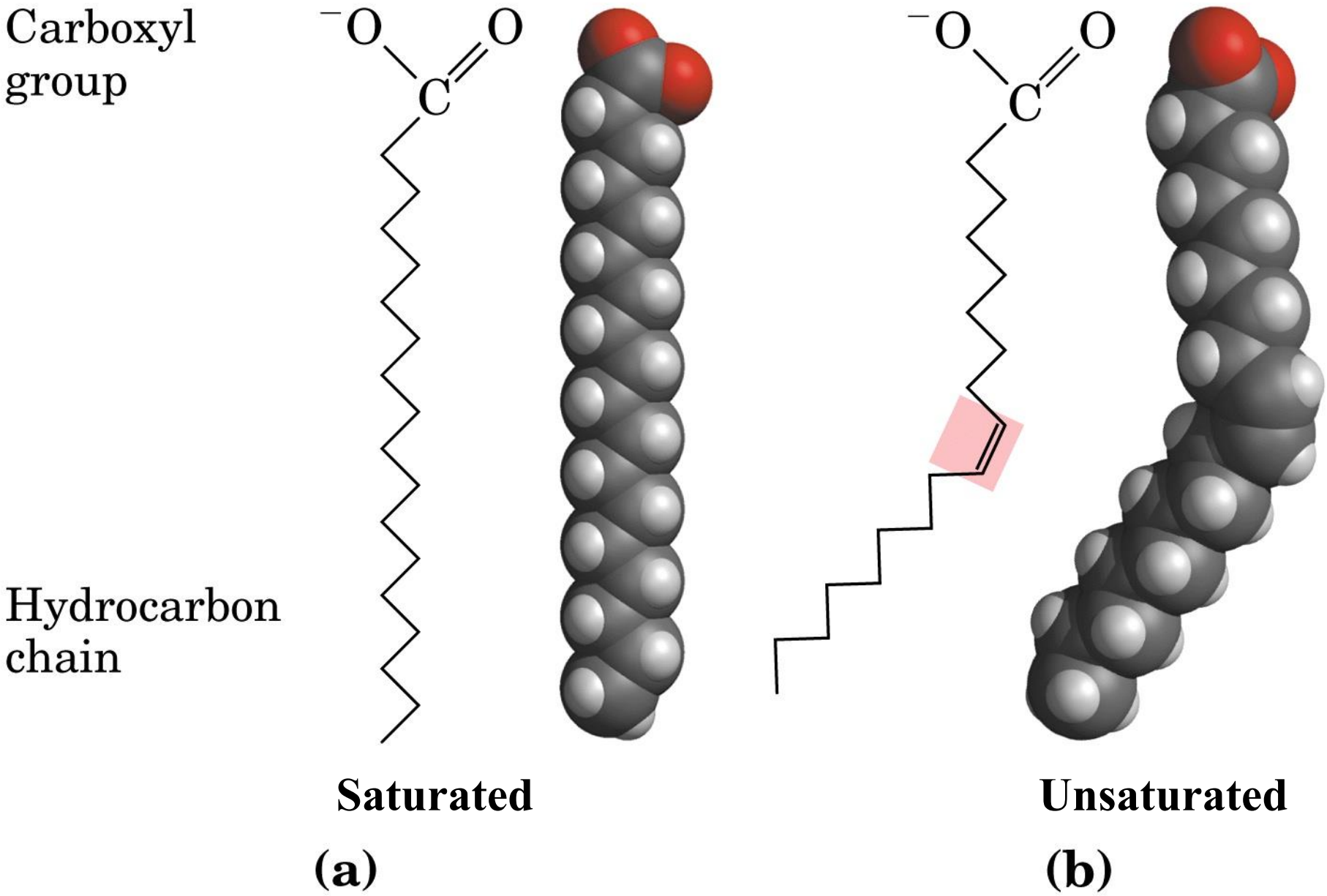


Storage lipids

- Two types of Fatty acid containing compounds:
  Triglycerides and waxes.
- Hydrocarbon chain:

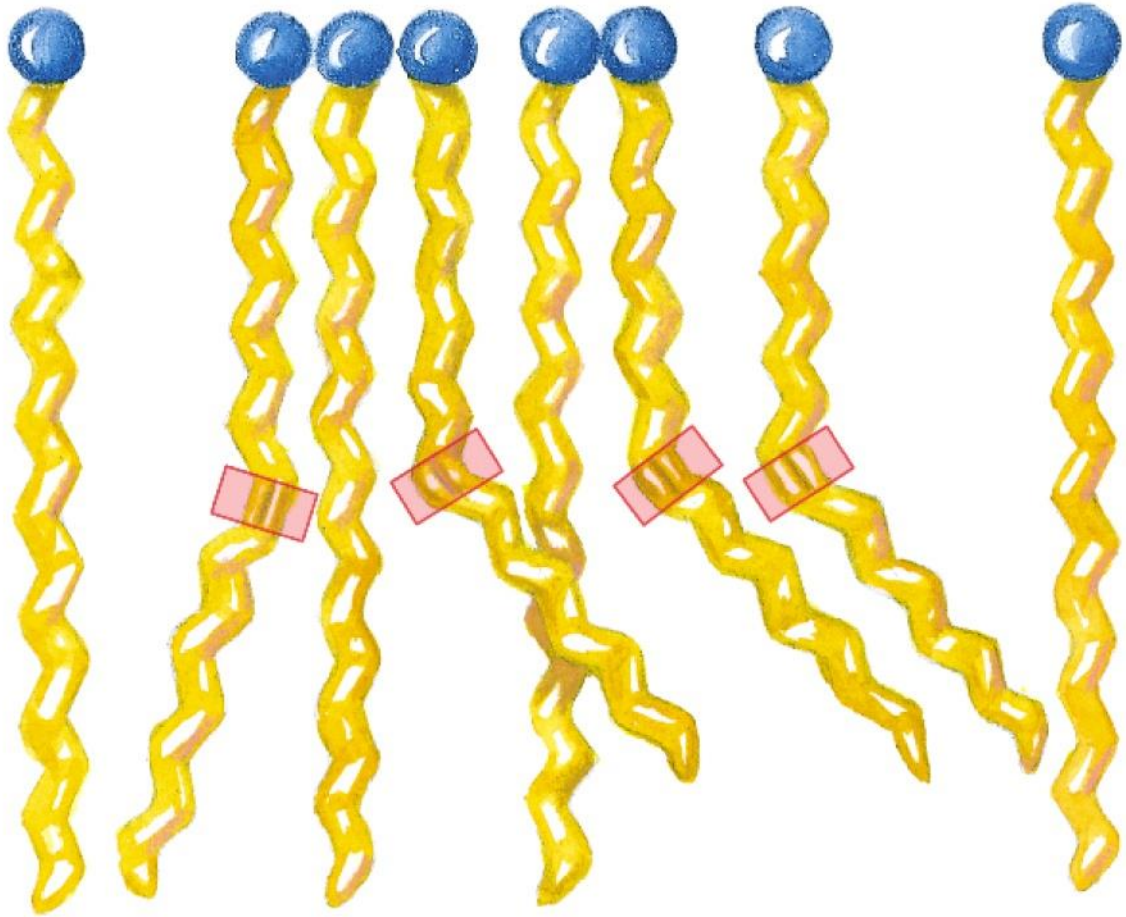
1. Saturated: contain no double bonds (wax)
2. Unsaturated: contain 1 or more double bonds (oil)
3. Unbranched
4. Branched

Wax


Carboxyl group
Hydrocarbon chain
Saturated
(a)
Unsaturated
(b)

Saturated
fatty acids

(c)



Mixture of saturated and
unsaturated fatty acids

(d)

Carbon skeleton	Structure*	Systematic name†	Common name (derivation)	Melting point (°C)	Solubility (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	−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")	−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		

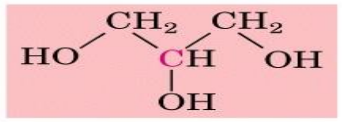
*All acids are shown in their nonionized form. At pH 7, all free fatty acids have an ionized carboxylate. Note that numbering of carbon atoms begins at the carboxyl carbon.

†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.

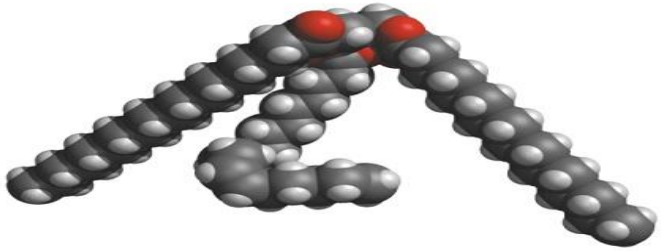
- **Triglycerides:**

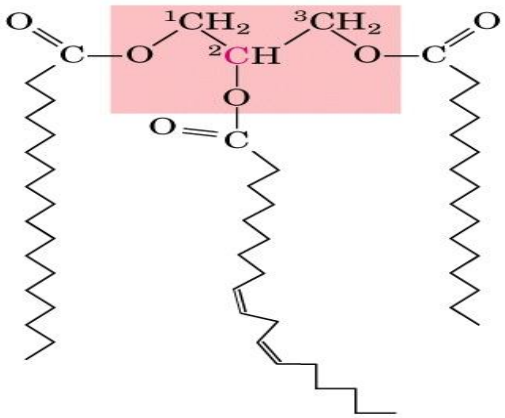
➢ Are composed of 3 fatty acids each in ester linkage with a single glycerol.

➢ Are **nonpolar**.



Glycerol



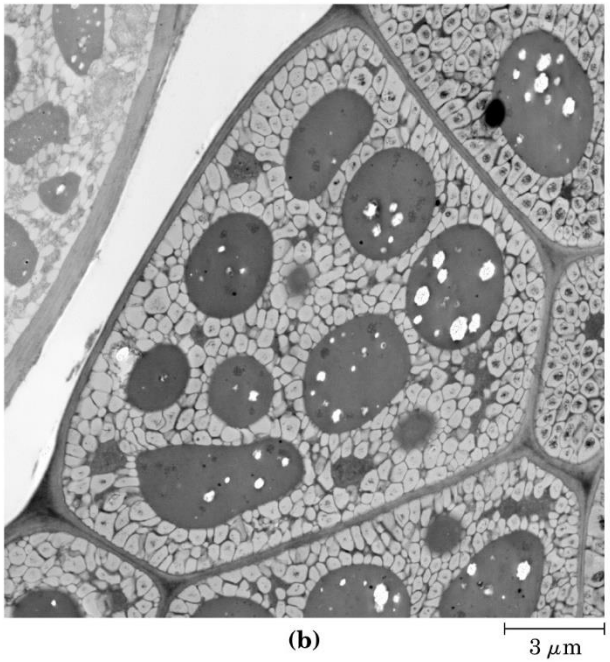


1-Stearoyl, 2-linoleoyl, 3-palmitoyl glycerol,
a mixed triacylglycerol

- **<u>Triglycerides</u>:**

➢ stored in **adipocytes**

➢ Adipocytes contain **lipases**



Adipocytes

Advantages to using triglycerides as stored fuel rather than polysaccharides

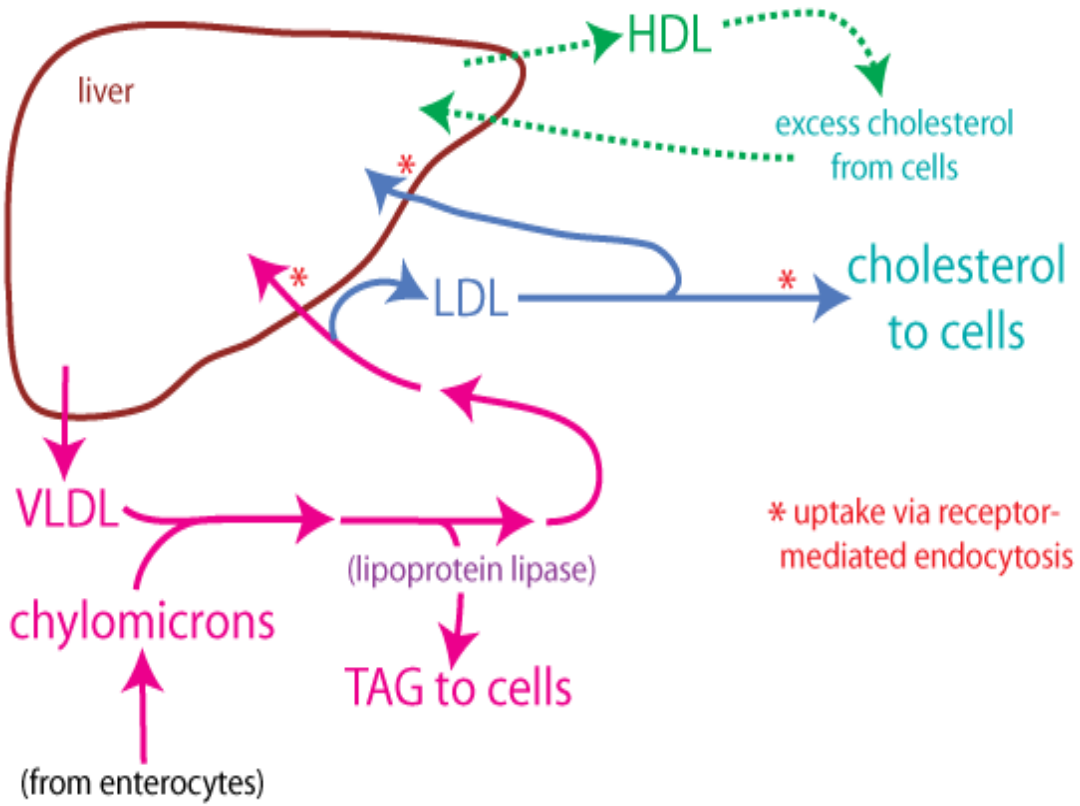
1. energy
2. water of hydration

	kcal/g dry weight	Water g/g dry weight
Carbohydrates	4	2-3
Triacylglycerol	9	0
Protein	4	2-3

Free Fatty Acids vs. Triglycerides In Blood

- Free fatty acids
- Carboxylic acid derivatives

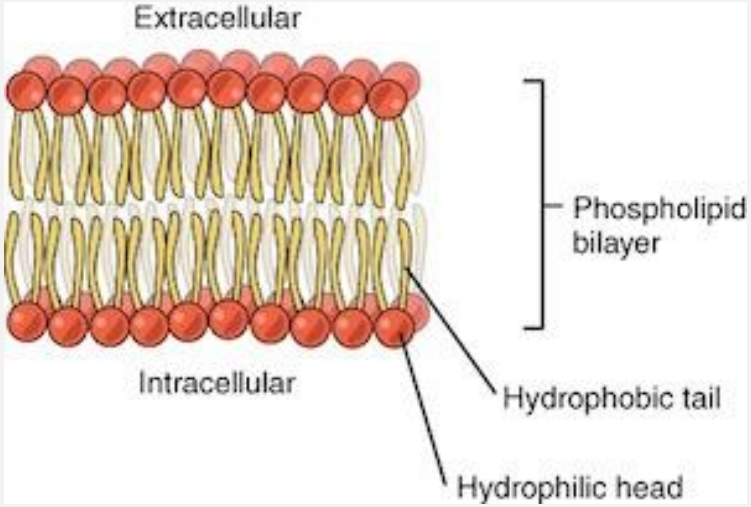
Summary of formation and fate of lipoproteins

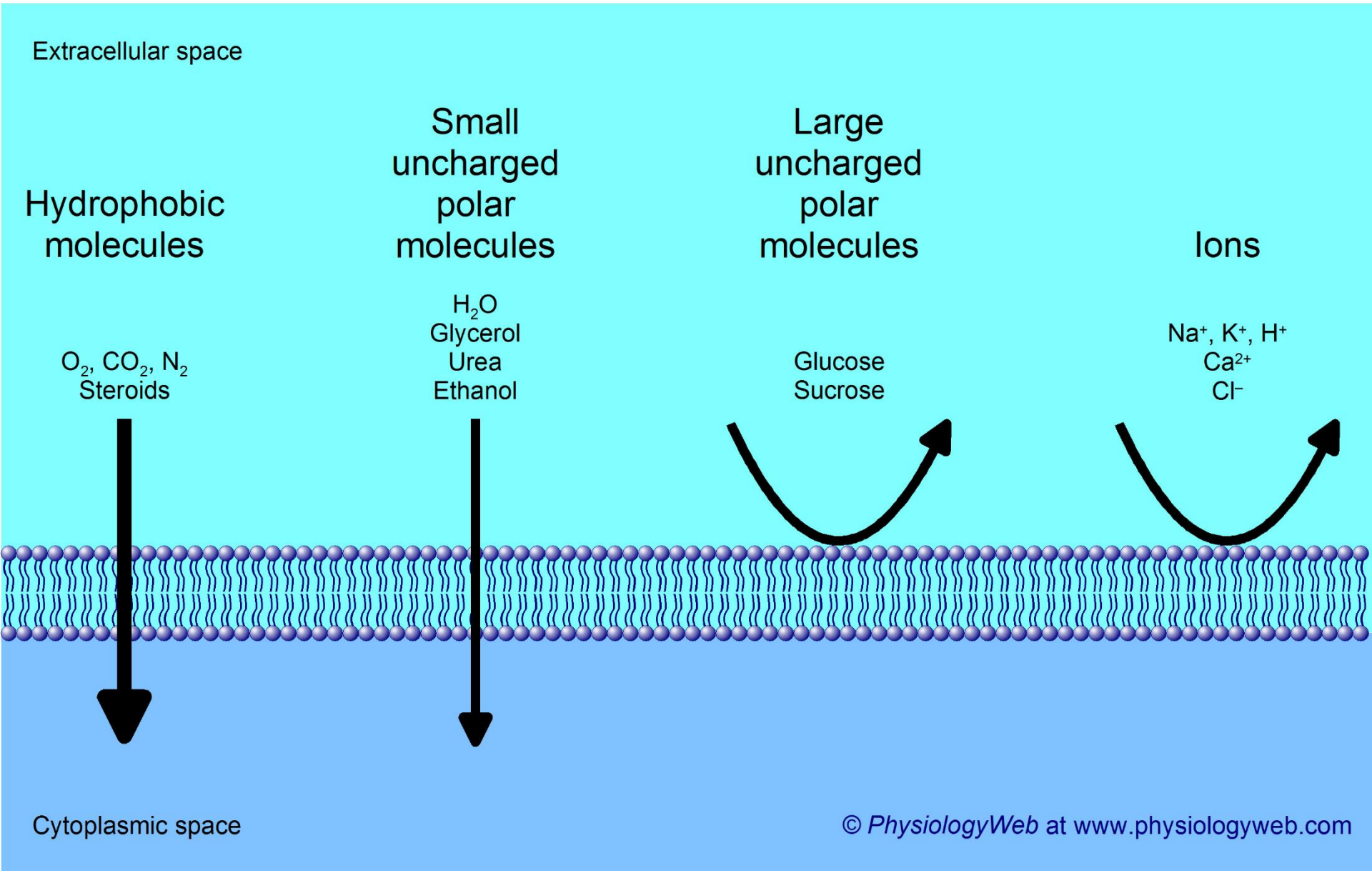


- Chylomicrons is a transporter of dietary lipids whereas VLDL is a transporter of endogenous lipids(mainly TGs).
- LDL transports cholesterol to peripheral cells while HDL transports cholesterol from peripheral cells back to liver.

2. Structural lipids in membrane

- Cell membrane is composed of **lipid bilayer**, which act as a barrier to the passage of polar molecules & ions.





2. Structural lipids in membrane

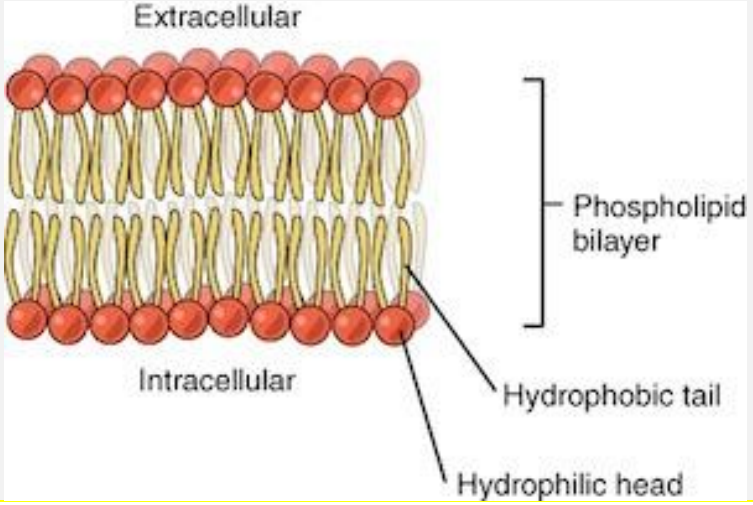
- Membrane lipids are **amphipathic**:
- **lipid packaging** into bilayers

  hydrophobic interactions with each other

  hydrophilic interactions with water.

- **<u>Types of membrane lipids</u>**:

1. Glycerophospholipids
2. Sphingolipids
3. sterols



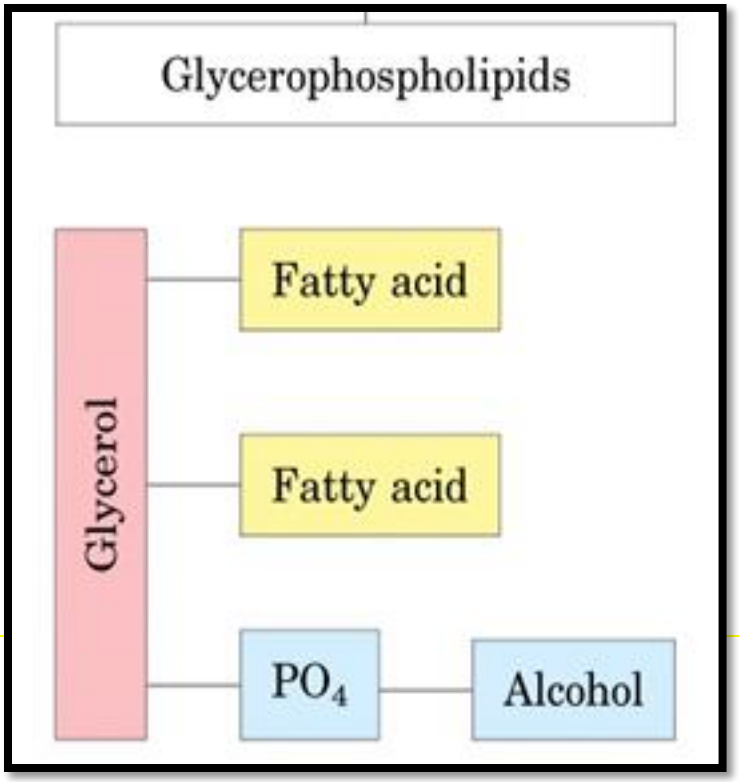
Structural lipids in membrane

- **Glycerophospholipids**:

  glycerol backbone to which are attached 2 fatty acids and a polar alcohol.

- **Sphingolipids**:

- **Sterols**:



Structural lipids in membrane

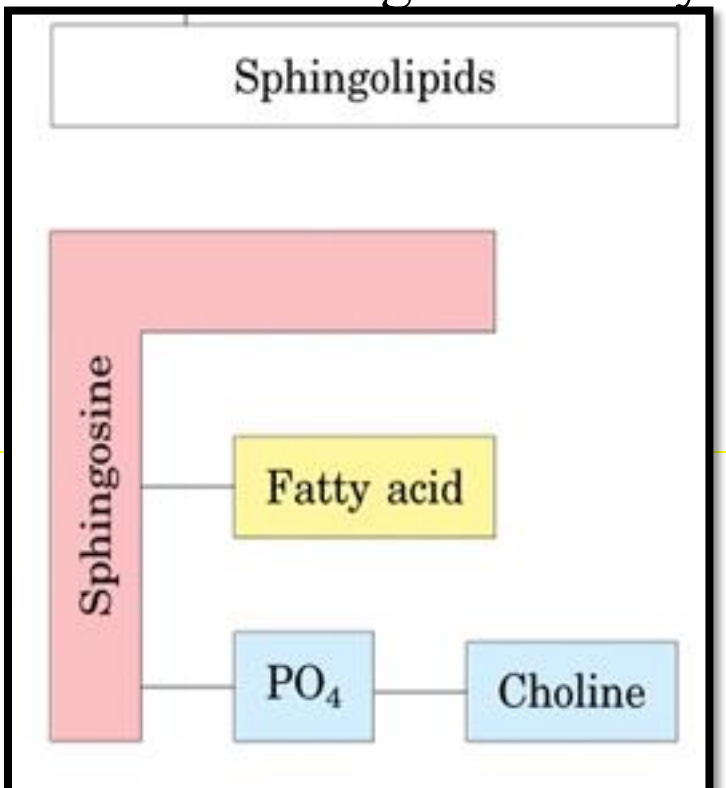
- **Glycerophospholipids**:

  glycerol backbone to which are attached 2 fatty acids and a polar alcohol.

- **Sphingolipids**:

  sphingosine backbone to which are attached a long-chain fatty acid & a polar alcohol.

- **Sterols**:



Structural lipids in membrane

- **Glycerophospholipids**:

  glycerol backbone to which are attached 2 fatty acids and a polar alcohol.

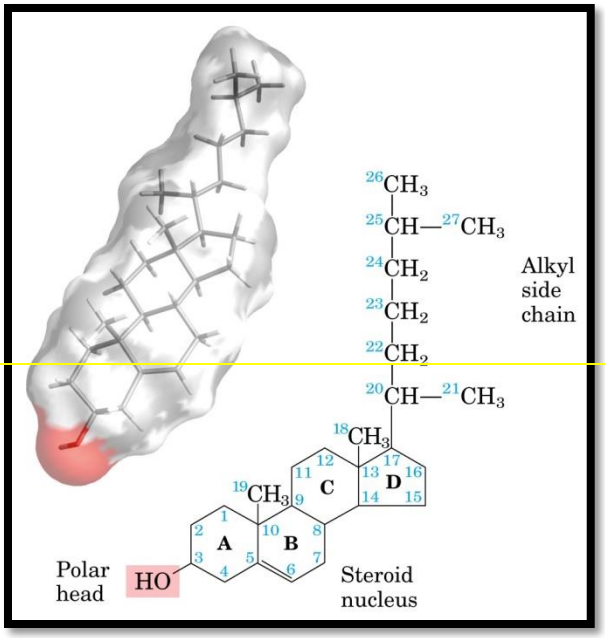
- **Sphingolipids**:

  sphingosine backbone to which are attached a long-chain fatty acid & a polar alcohol.

- **Sterols**:

  a lipid containing the steroid nucleus

  (4 fused hydrocarbon rings).



Storage lipids (neutral)

Membrane lipids (polar)

Phospholipids

Glycolipids

Triacylglycerols

Glycerophospholipids

Sphingolipids

Glycerol

Fatty acid

Fatty acid

Fatty acid

Glycerol

Fatty acid

Fatty acid

PO_4

Alcohol

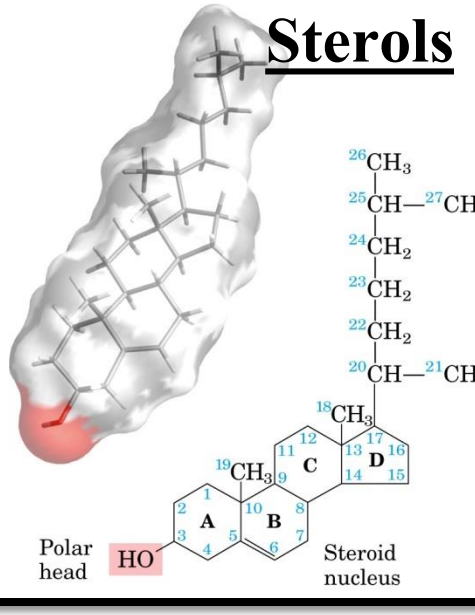
Sphingosine

Fatty acid

PO_4

Choline

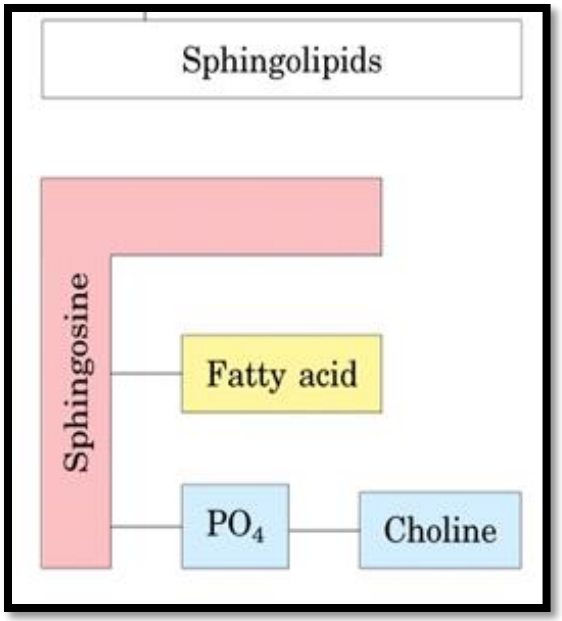
Sterols

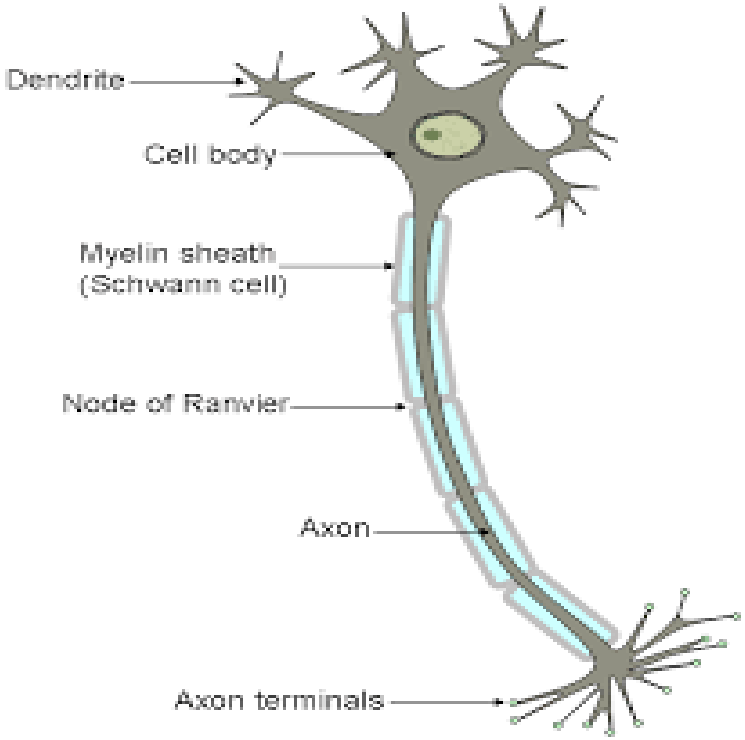


Sphingolipids subclasses

1. Sphingomyelin:

- Contain phosphocholin or phosphoethanolamine as their polar head group.
- Present in the plasma membrane (neurons).

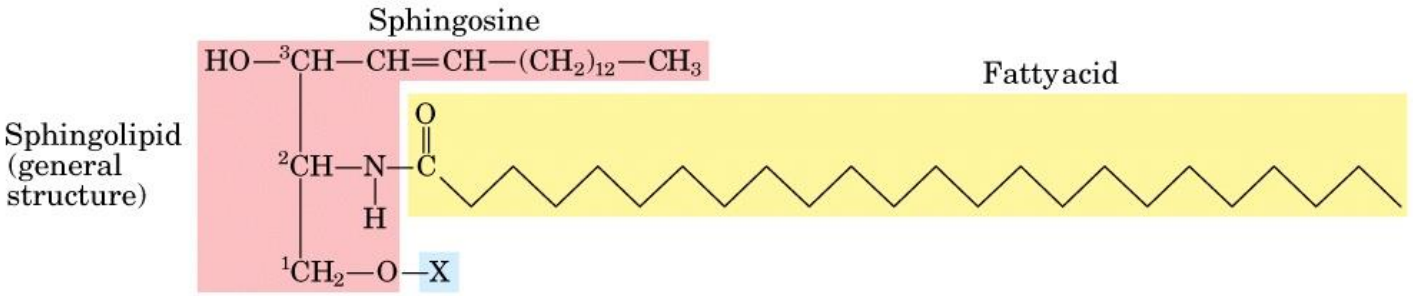




Sphingolipids subclasses

2. <u>Glycosphingolipids</u>:

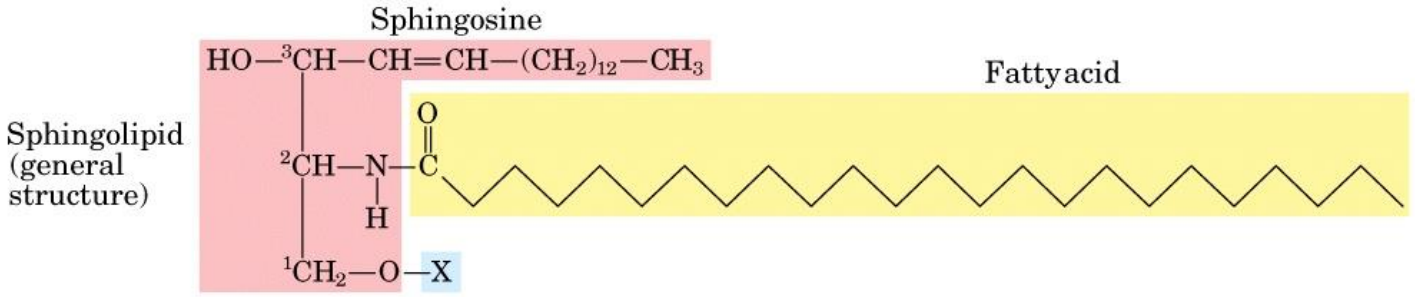
- Do not contain phosphate, have head groups with one or more sugars connected directly to the ceramide moiety.
- Occur largely in the outer face of plasma membrane
- *Cerebrosides*:



Sphingolipids subclasses

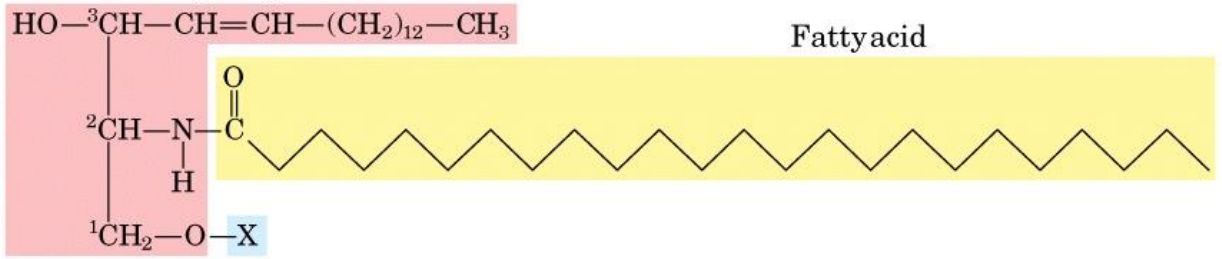
3. Gangliosides:

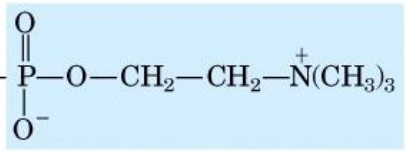
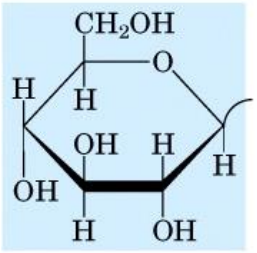
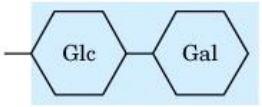
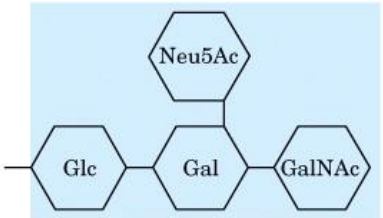
- complex sphingolipids
- Polar head groups are oligosaccharides & one or more residues of N-Acetyneuraminic acid.



Sphingosine

Sphingolipid (general structure)

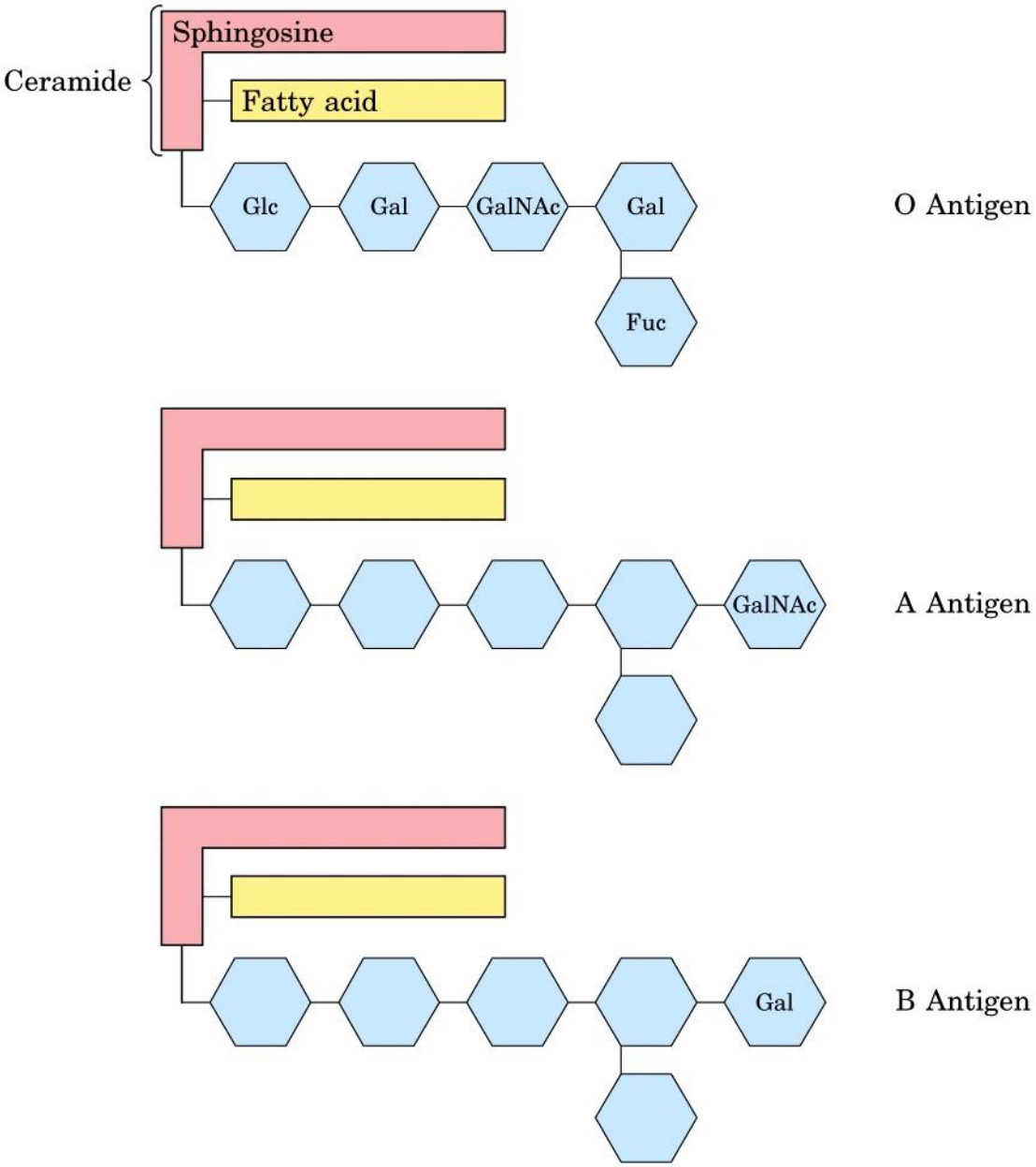


Name of sphingolipid	Name of X	Formula of X
Ceramide	—	—H
Sphingomyelin	Phosphocholine	
Neutral glycolipids Glucosylcerebroside	Glucose	
Lactosylceramide (a globoside)	Di-, tri-, or tetrasaccharide	
Ganglioside GM2	Complex oligosaccharide	

Importance of Sphingolipids

- plasma membranes of neurons
- recognition sites

Importance of Sphingolipids



Phospholipids & sphingolipids are degraded in Lysosomes

Phospholipase A1

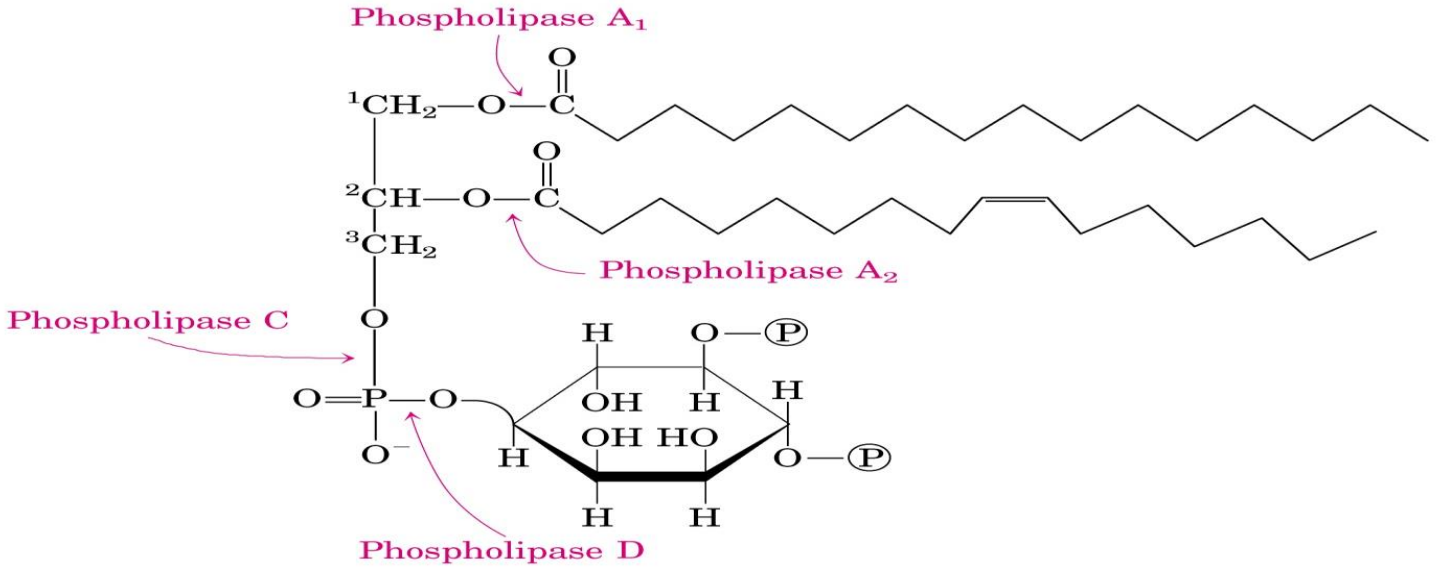
Hydrolyzes the ester bonds of intact glycerophospholipids at C1 of glycerol.

Phospholipase A2

Hydrolyzes the ester bonds of intact glycerophospholipids at C2 of glycerol.

Phospholipase C & D

Split one of the diester bonds in the head group.

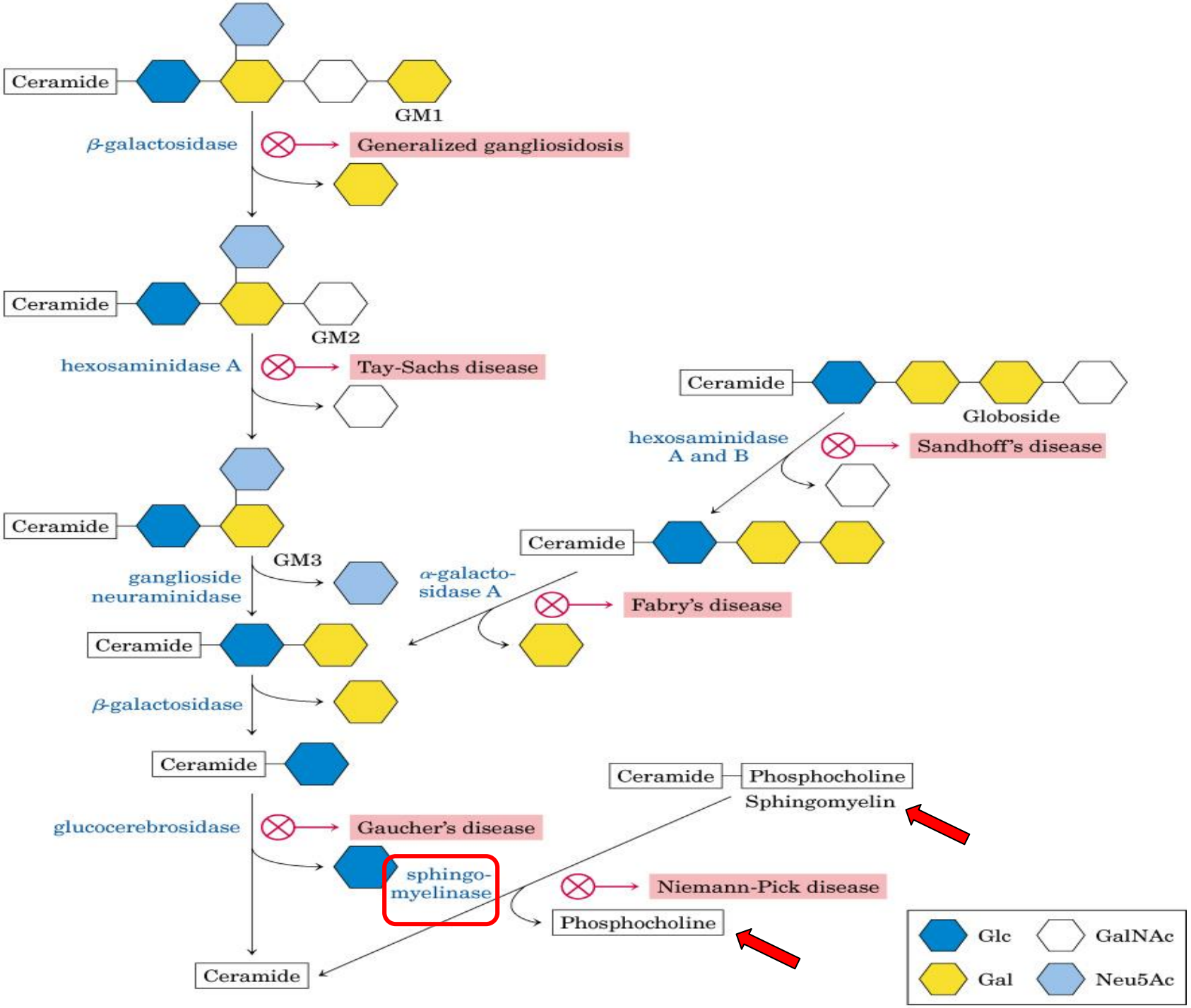


Inherited human diseases resulting from abnormal accumulations of membrane lipids

❖**Gangliosides** are degraded by lysosomal enzymes that catalyze the stepwise removal of sugar units, to yield a ceramide.

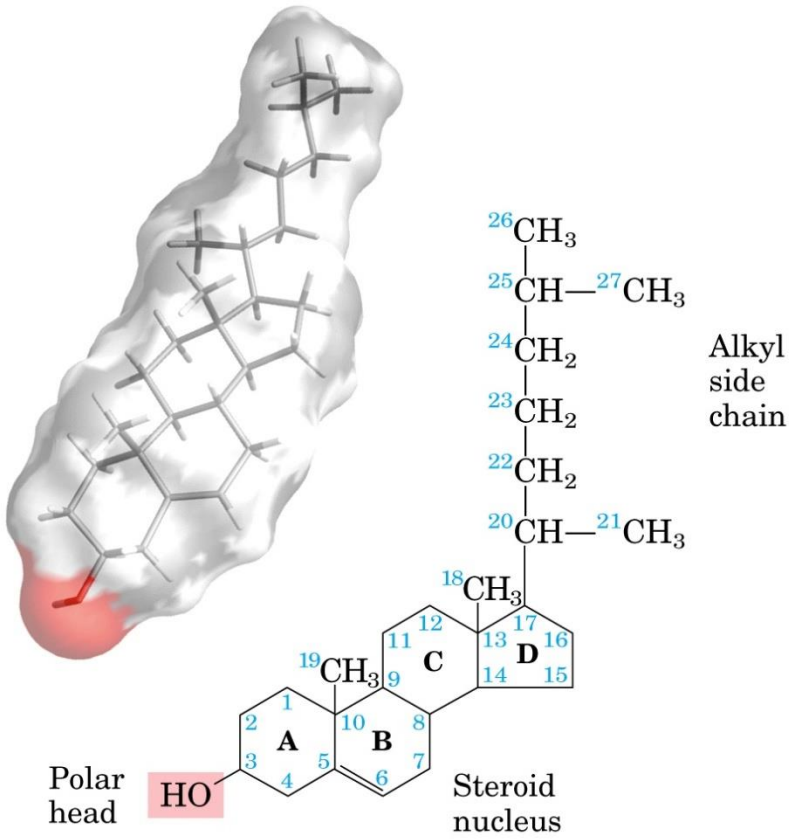
❖A **Genetic Defect** in any of these enzymes leads to the accumulation of these gangliosides in the cell with severe medical consequences.

Niemann-Pick disease:


Ceramide
GM1
β-galactosidase
Generalized gangliosidosis
Ceramide
GM2
hexosaminidase A
Tay-Sachs disease
Ceramide
GM3
ganglioside neuraminidase
Ceramide
β-galactosidase
Ceramide
glucocerebrosidase
Gaucher's disease
sphingo-myelinase
Ceramide
Ceramide
Globoside
hexosaminidase A and B
Sandhoff's disease
Ceramide
α-galacto-sidase A
Fabry's disease
Ceramide
Phosphocholine
Sphingomyelin
Niemann-Pick disease
Phosphocholine
Glc
GalNAc
Gal
Neu5Ac

Sterols

- Contain the steroid nucleus (consisted of four fused rings).
- The major sterol in animal tissue is **cholesterol** which is amphipathic.



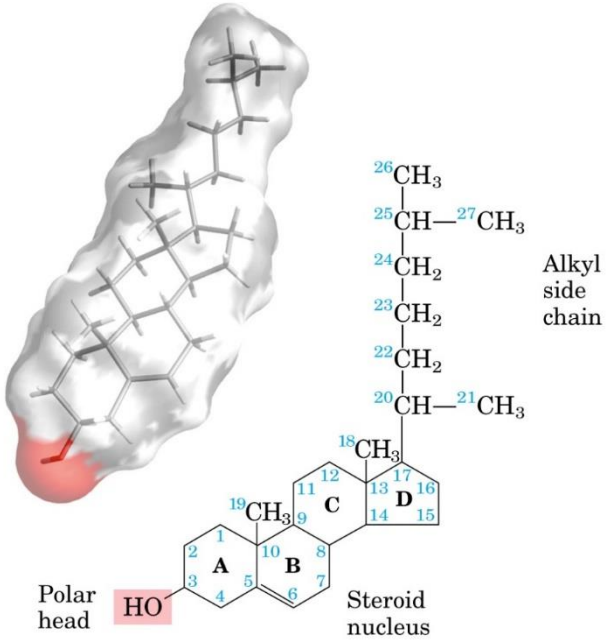
Sterols

- **Functions**:

1. **Structural** lipids
2. **Precursors**

-Steroid hormones

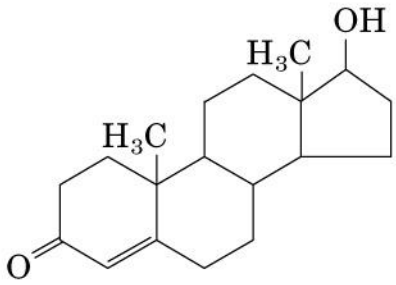
-bile acids



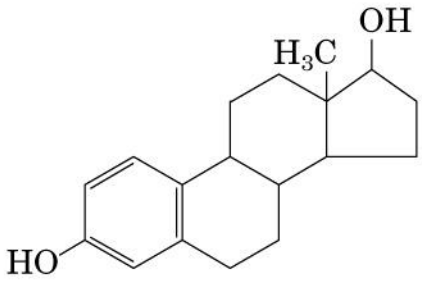
Steroid Hormones

Classes:

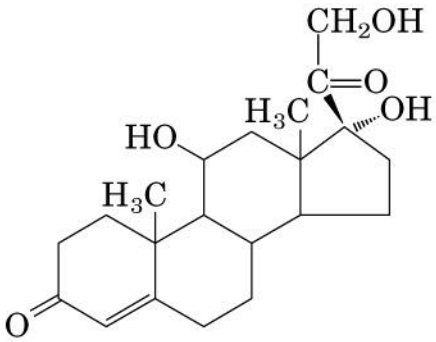
1) Glucocorticoids: adrenal cortex
   decrease inflammation & increase resistance to stress
2) Mineralocorticoides: adrenal cortex
   maintain water & salt balance
3) Estrogens: adrenal cortex & gonads
   Maturation & function of female secondary sex organs
4) Androgens: adrenal cortex & gonads
   Maturation & function of male secondary sex organs
5) Progestines: ovaries & placenta
   pregnancy



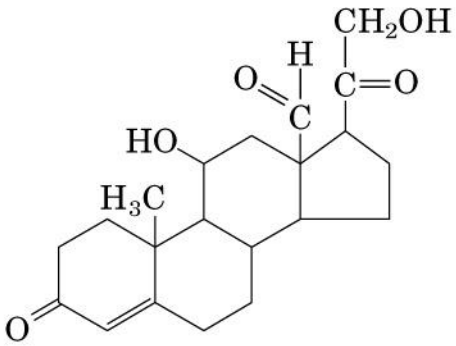
Testosterone



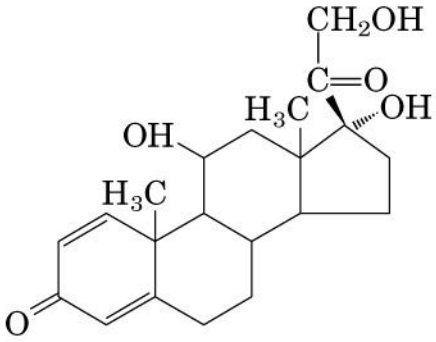
Estradiol



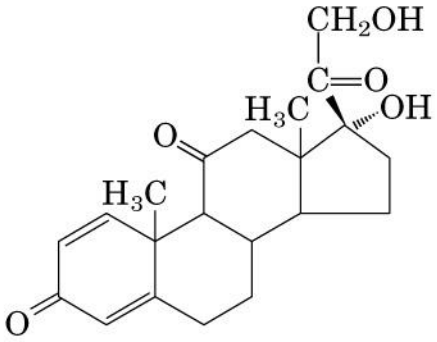
Cortisol



Aldosterone



Prednisolone



Prednisone

Lipids as Signals, Cofactors, and Pigments

- signals (hormones)
- intracellular messengers
- enzyme cofactors
- pigment molecules
- Specialized lipids

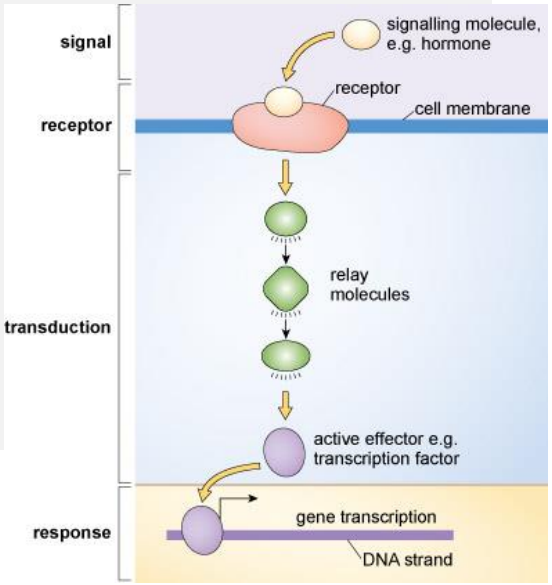
Phosphatidylinositols as intracellular signals

- Act several levels to regulate cell structure & metabolism

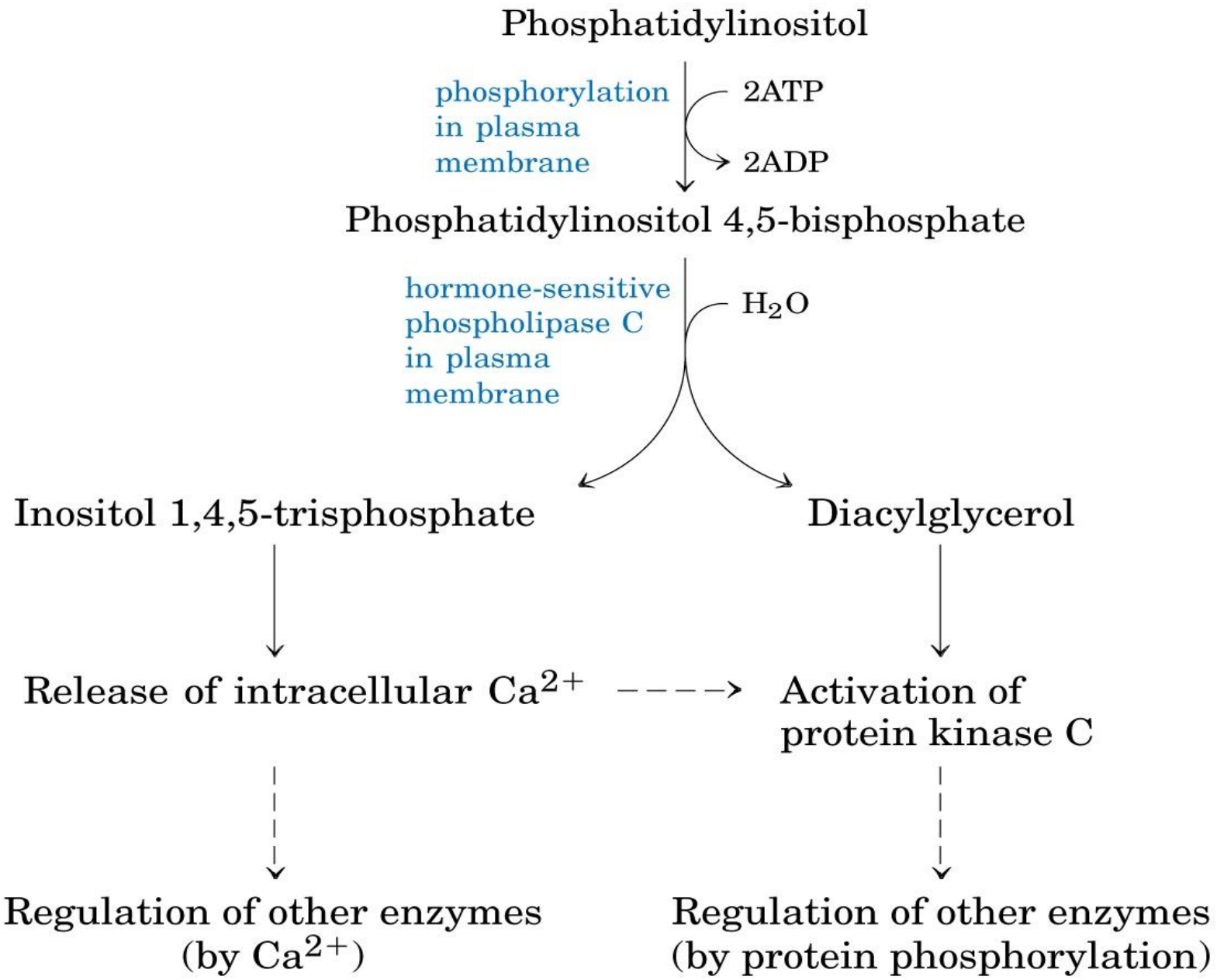
- **Phophatidylinositol 4,5 bisphosphate** serves as:

  1. **specific binding site** for certain cytoskeletal proteins & some soluble proteins (membrane fusion during exocytosis).

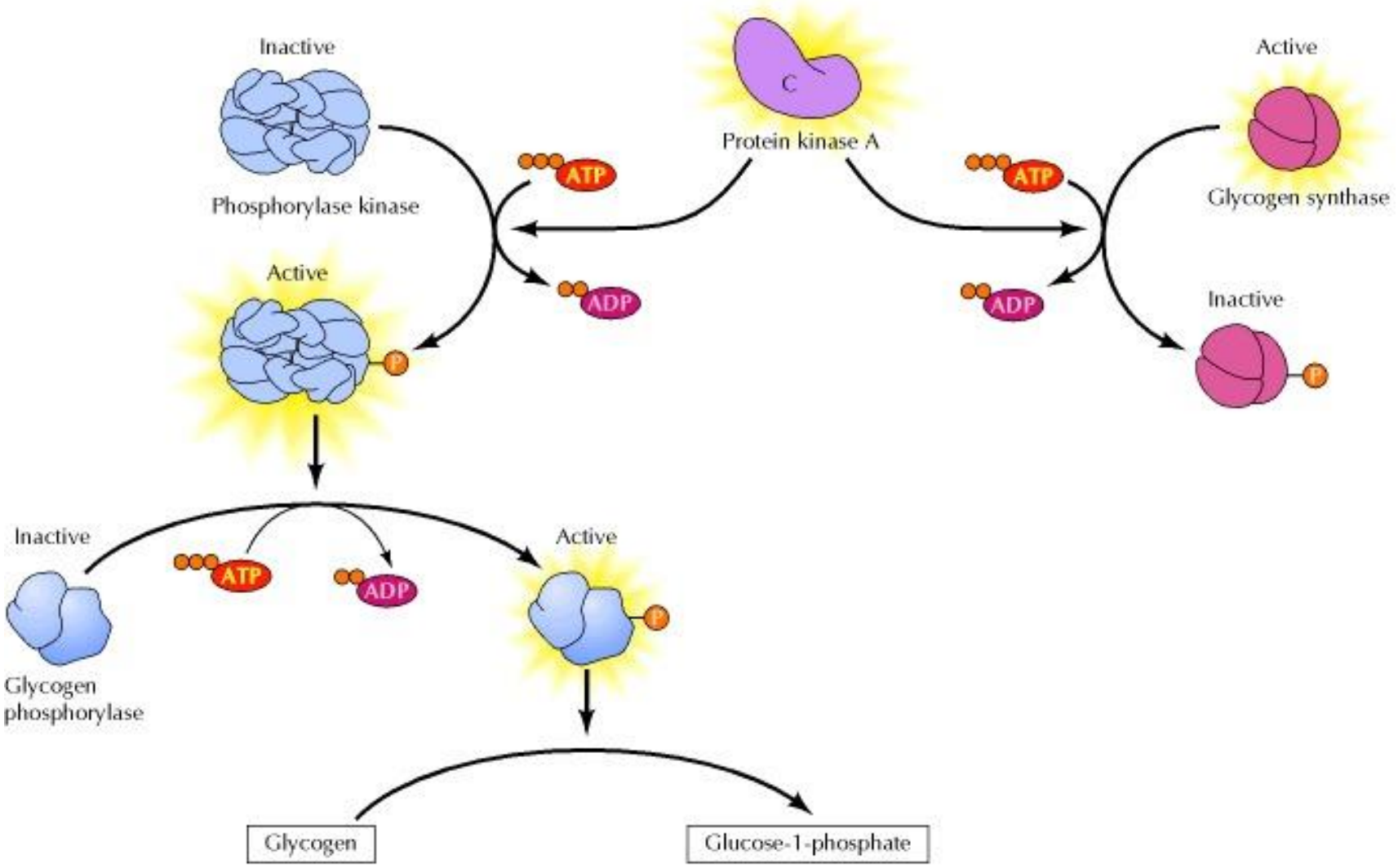
  2. **reservoir of messenger molecules** that are released inside the cell in response to extracellular signals.



Intracellular signals



Regulation of glycogen metabolism by protein kinase A



Eicosanoids

carry messages to nearby cells

a. derivatives of arachidonic acid

b. paracrine hormones

c. **<u>Functions</u>**:

reproduction, inflammation, fever, injury pain, blood clot formation, blood pressure regulation, gastric acid secretion.

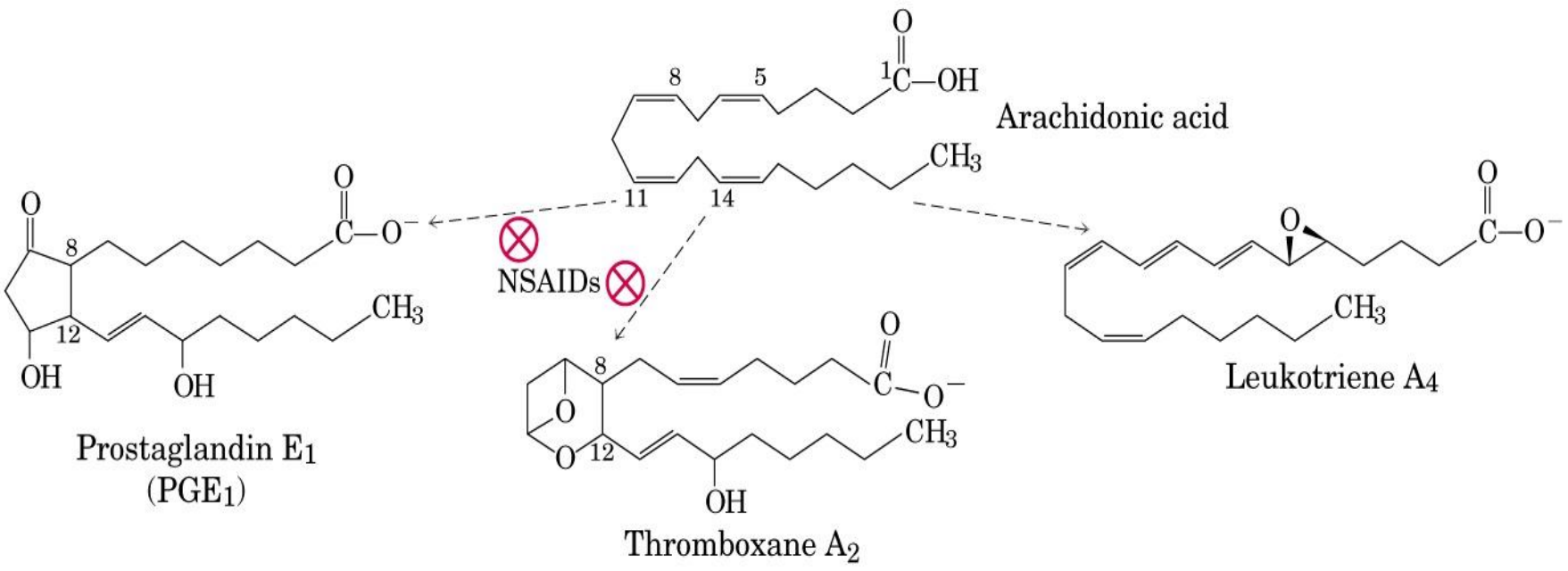
d. **<u>3 classes</u>**:

prostaglandins

thromboxanes

leukotrienes

Eicosanoids



Eicosanoids

(b)

1. Prostaglandins

- Regulate the synthesis of cAMP.

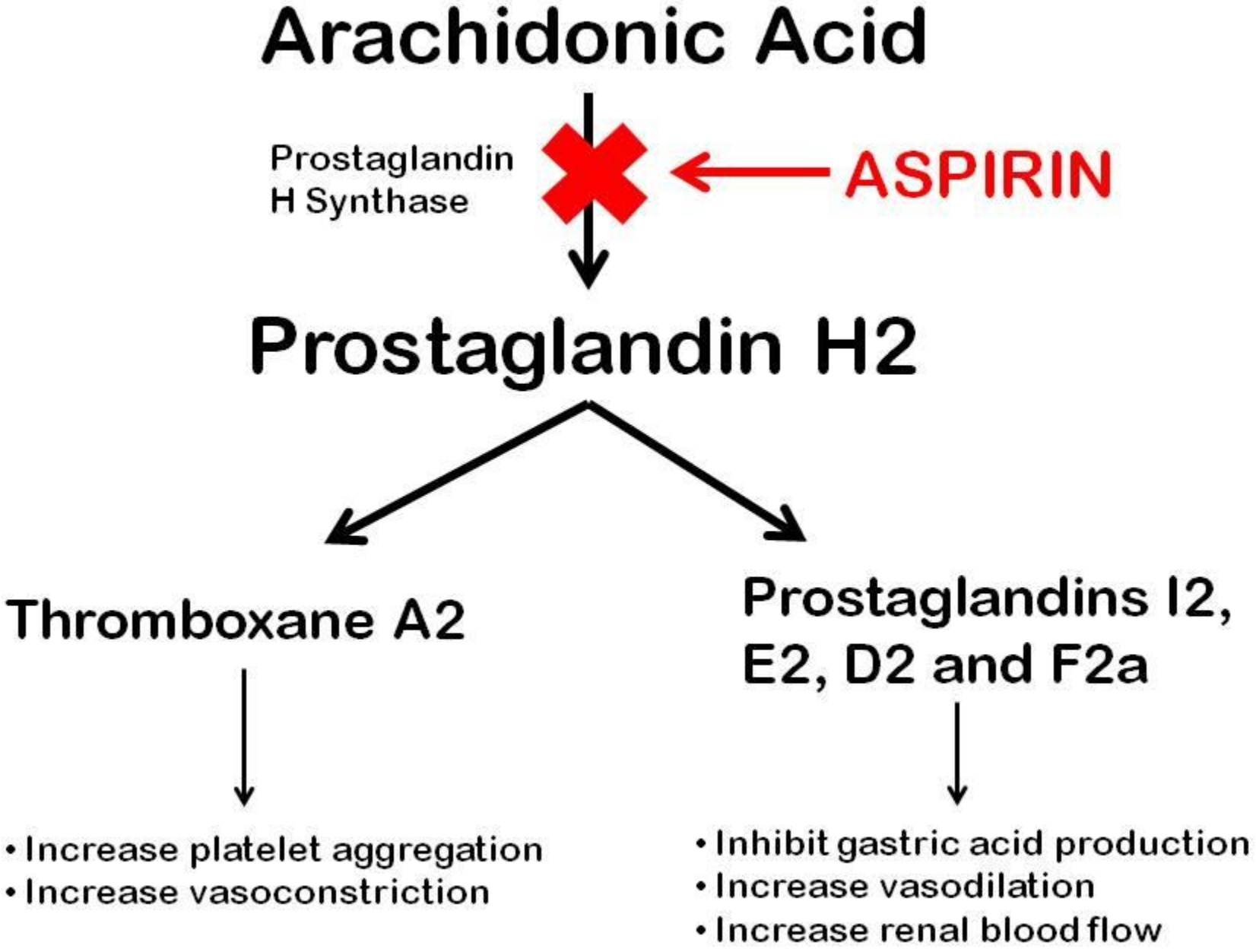
- Affect a wide range of cellular & tissue functions:

- contraction of smooth muscles of uterus during labor
- affect blood flow to specific organs, wake-sleep cycle, responsiveness to hormones.
- elevate body temperature & cause inflammation & pain.

2. Thromboxanes

- Produced by **platelets**.
- Act in the:
  - formation of blood clots.
  - reduction of blood flow to the site of a clot.
- Synthesis is **inhibited** by nonsteroidal anti-inflammatory drugs (NSAIDs) –aspirin, ibuprofen, and meclofenamate.

  inhibit the enzyme prostaglandin H2 synthase.


Arachidonic Acid
Prostaglandin H Synthase
ASPIRIN
Prostaglandin H2
Thromboxane A2
Prostaglandins I2, E2, D2 and F2a
• Increase platelet aggregation
• Increase vasoconstriction
• Inhibit gastric acid production
• Increase vasodilation
• Increase renal blood flow

3. Leukotrienes

- found first in **leukocytes**
- powerful biological signals.
- **Function**:
  Contraction of smooth muscles lining lung airways

- Overproduction causes - asthmatic attacks
  - anaphylactic shock
- Antiasthmatic drugs inhibit leukotriene synthesis.
  - prednisone

Vitamin D & A are hormone precursors

Vitamin D

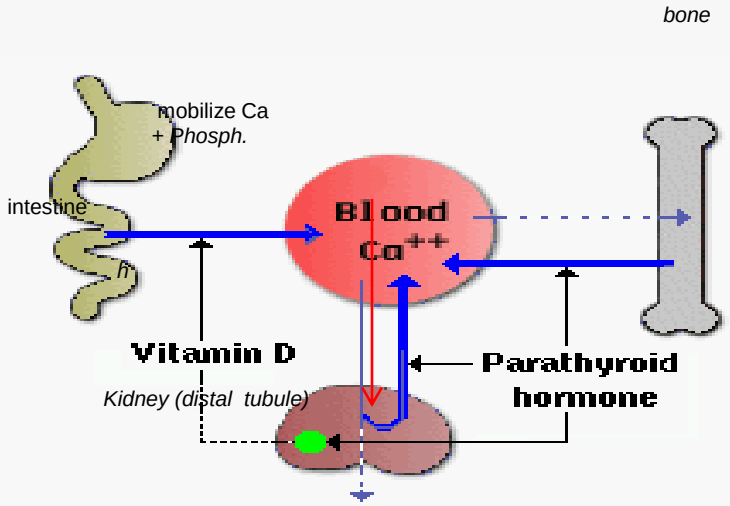
- Formed in the skin from 7-dehydrocholesterol in a photochemical reaction driven by UV

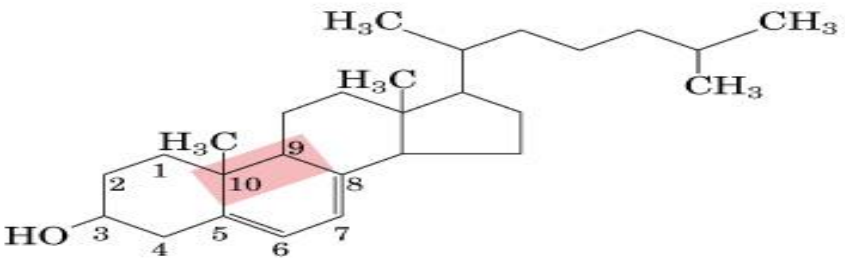
- **Biologically active** form of vitamin D :
  - Regulates Ca uptake in the intestine
  - Regulates Ca levels in kidney & bone
  - Regulates Ca and P metabolism.

Deficiency of vitamin D leads to:

defective bone formation

(***Rickets Disease***)

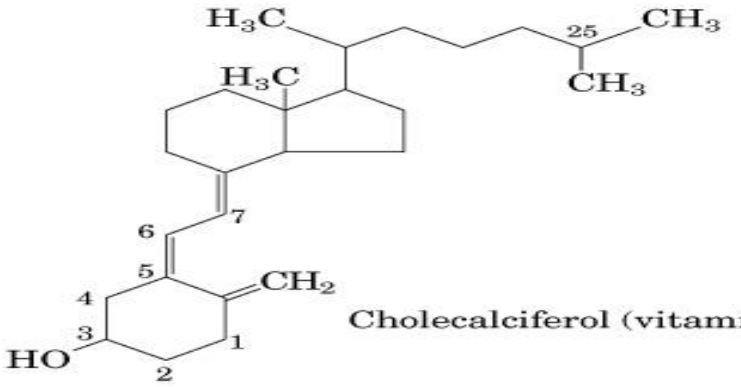




7-Dehydrocholesterol

UV light

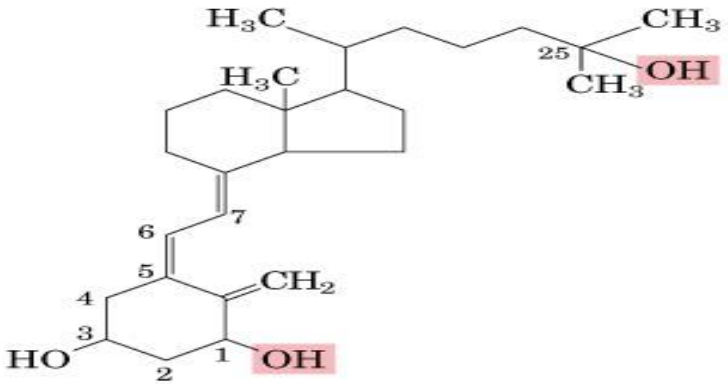
2 steps (in skin)



Cholecalciferol (vitamin D_3)

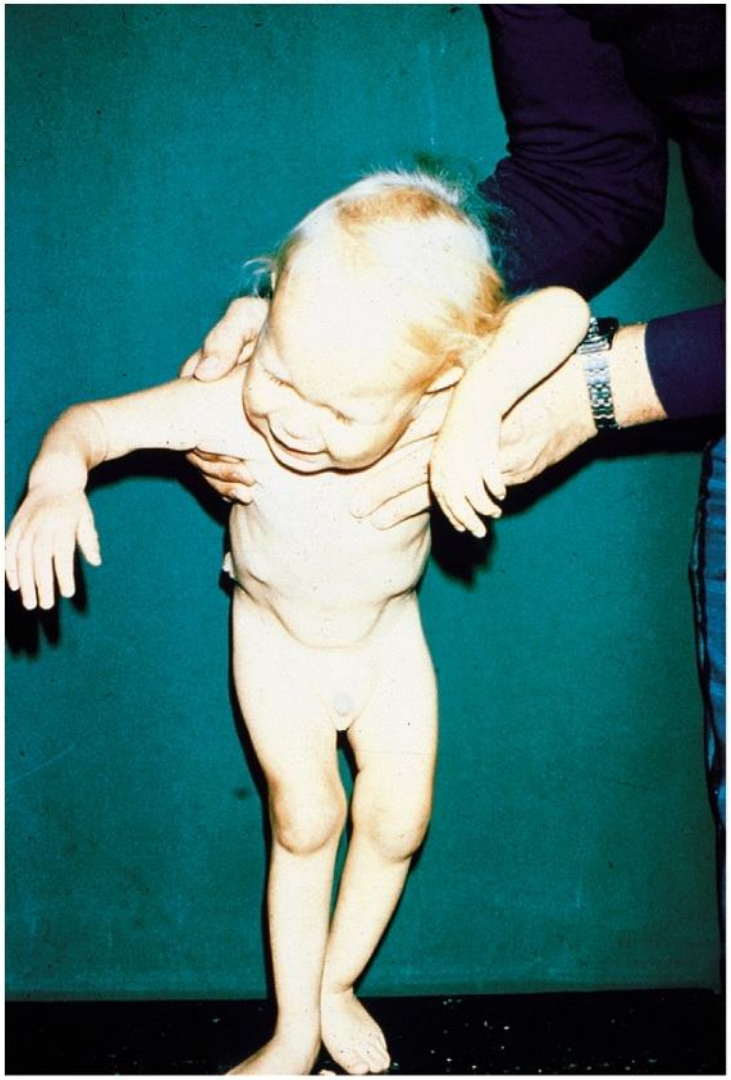
1 step in the liver

1 step in the kidney

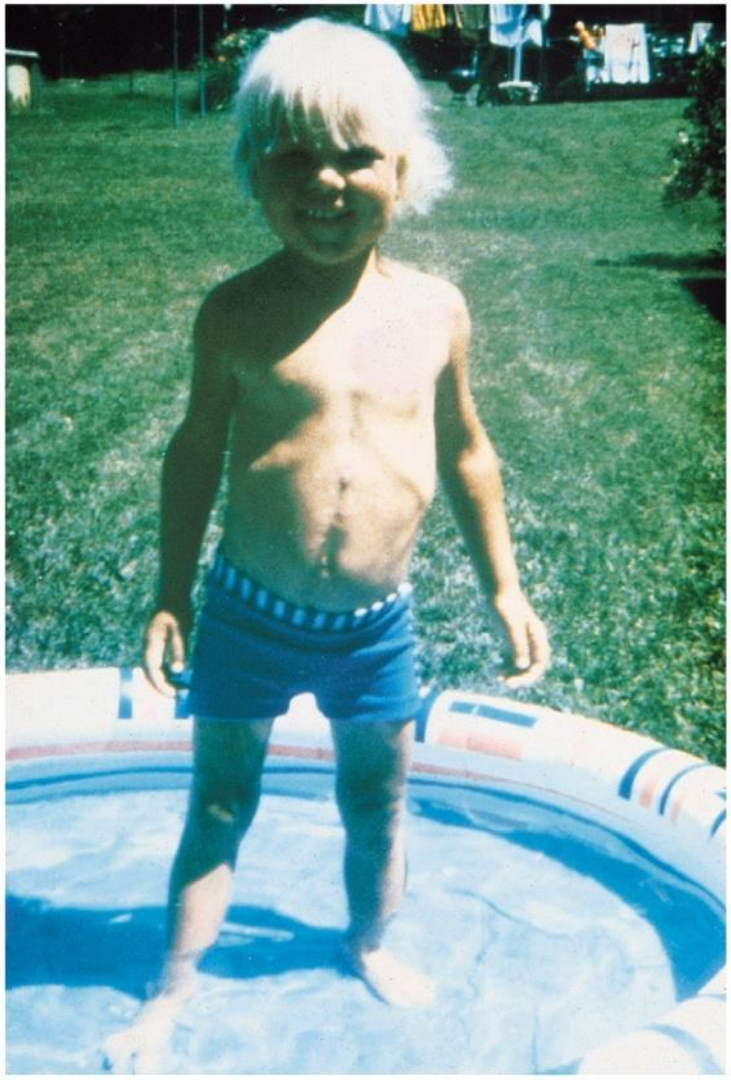


1,25-Dihydroxycholecalciferol
(1,25-dihydroxyvitamin D_3)

(a)



Before vitamin D treatment



After 14 months of vitamin D treatment

(b)