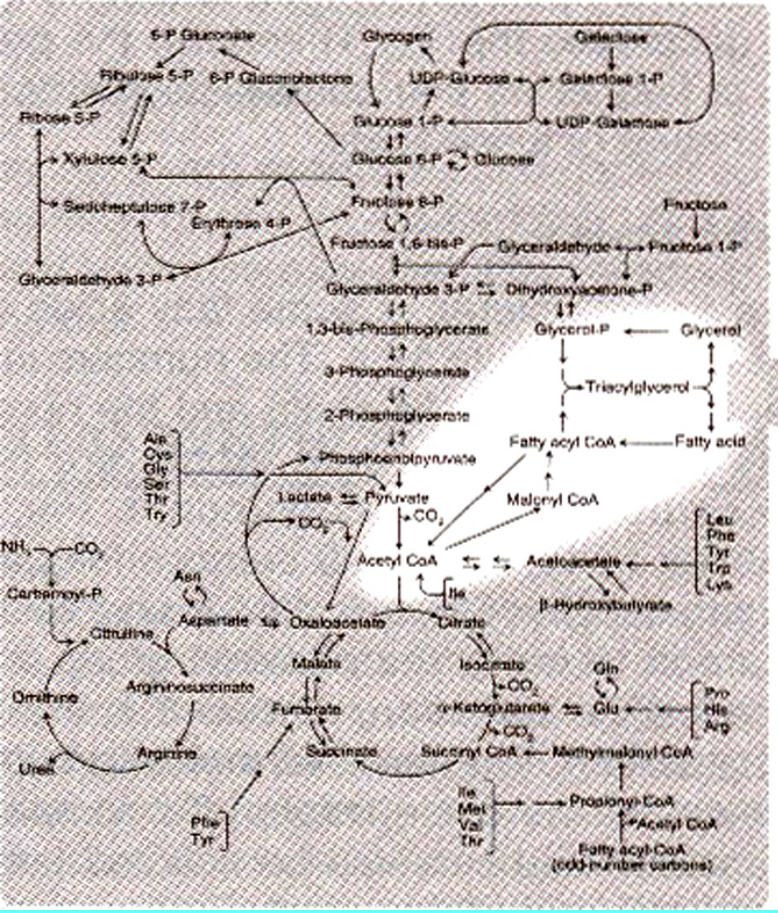
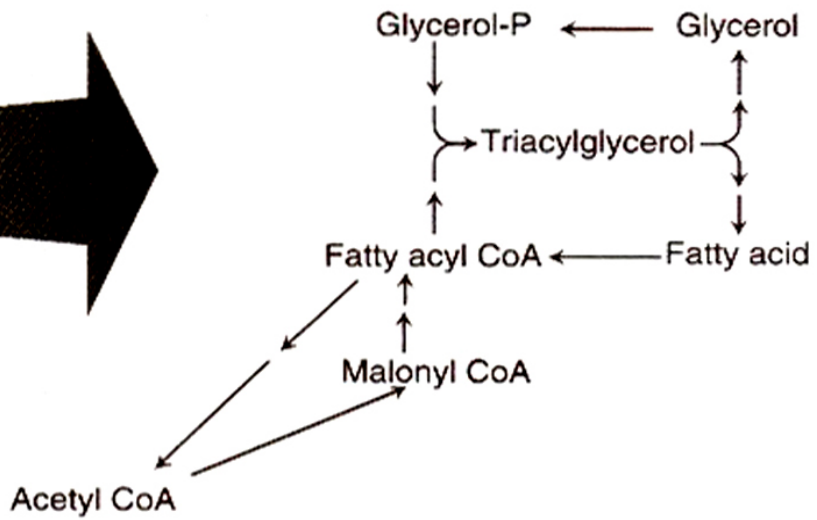




Fatty acids exist in the body free (unesterified) or as acyl ester in more complex molecules. Esterified fatty acids in the form of triacylglycerol serve as the major energy reserve of the body. The metabolic pathways of fatty acids synthesis and degradation and relation to carbohydrate metabolism is shown above.

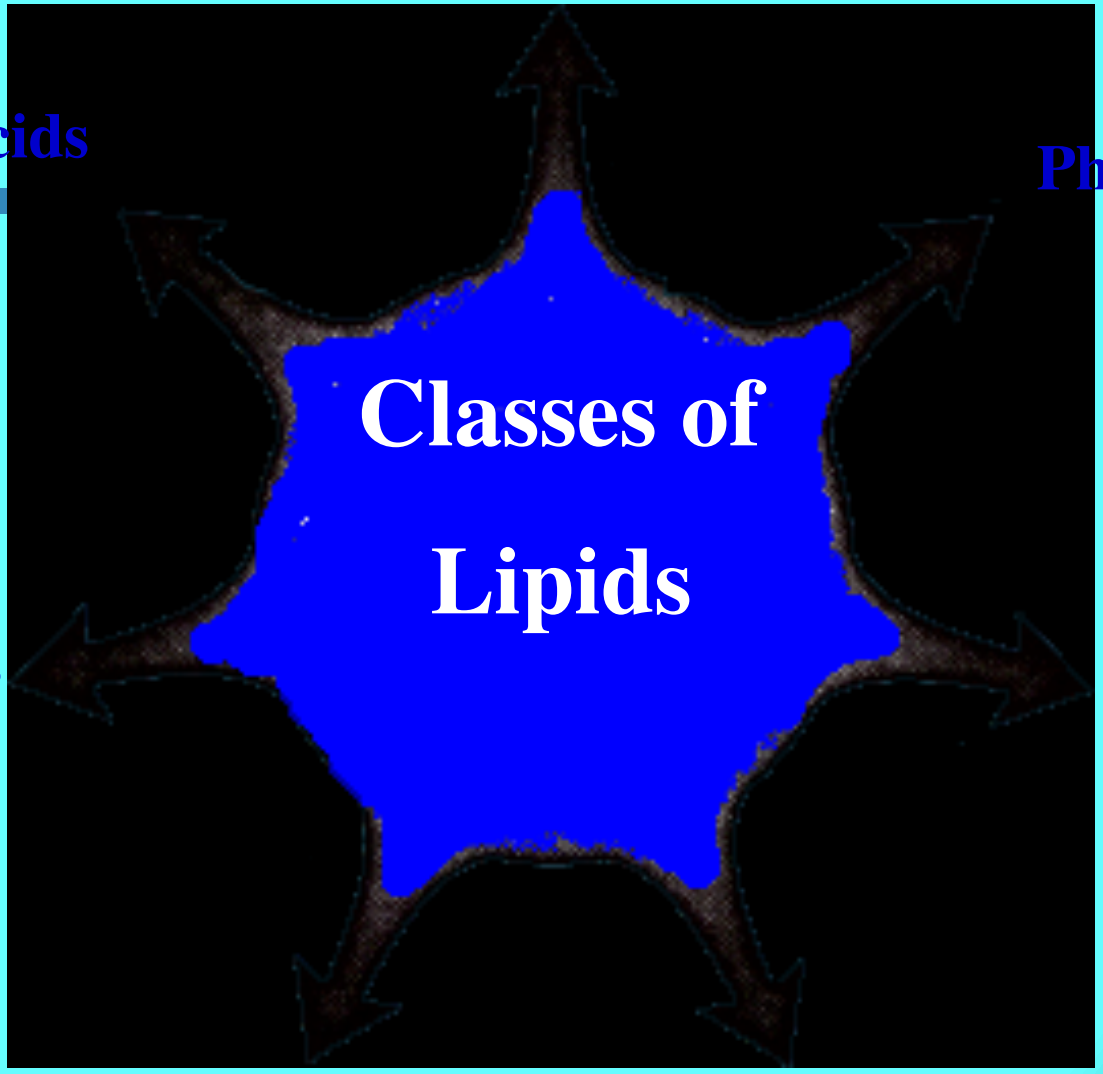
Metabolism of Dietary Lipids

Lipids are water-insoluble organic molecules, they are found compartmentalized or transported by plasma in association with proteins. A hydrophobic barrier that permits partitioning of the aqueous content of cells. They also provide a major source of energy. In addition they provide many functions, for example some fat soluble vitamins have regulatory or coenzyme functions, prostaglandins and steroids are important in the body's homeostasis. Some deficiencies or imbalances can lead to clinical problems such as atherosclerosis

Triacylglycerol

Fatty acids

Phospholipids



Glycolipids

Sphingolipids

Steroids

Vitamins A,D,E,K

Classification and Function of Lipids

Lipid Class	Functions
fatty acid	metabolic fuel, metabolic intermediate, membrane anchor
acylglycerol	fatty acid storage and transport, metabolic intermediate, regulation
phospholipid	membrane structure, signal transduction, storage of arachidonate, membrane anchor
sphingolipid	membrane structure, surface antigen, signal transduction
ketone body	metabolic fuel
polyisoprene	metabolic intermediate, regulation, cofactors & vitamins, membrane anchor
sterol	membrane structure, hormones, detergents, vitamins

FATTY ACIDS ARE SYNTHESIZED AND DEGRADED BY DIFFERENT PATHWAYS

- Fatty acids synthesis is not simply a reversal of the degradative pathway. Rather, it consists of a new set of reactions, again exemplifying the principle that *synthetic and degradative pathways in biological systems are usually distinct.*
- Synthesis takes place in the *cytosol,* in contrast with degradation, which occurs in the mitochondrial matrix.
- Intermediates in fatty acid synthesis are covalently linked to the sulfhydryl groups of an *acyl carrier protein (ACP),* whereas intermediates in fatty acid breakdown are bonded to coenzyme A.
- The enzymes of fatty acid synthesis in higher organisms are joined in a *single polypeptide chain* called *fatty acid synthase.* In contrast, the degradative enzymes do not seem to be associated.

FATTY ACIDS ARE SYNTHESIZED AND DEGRADED BY DIFFERENT PATHWAYS

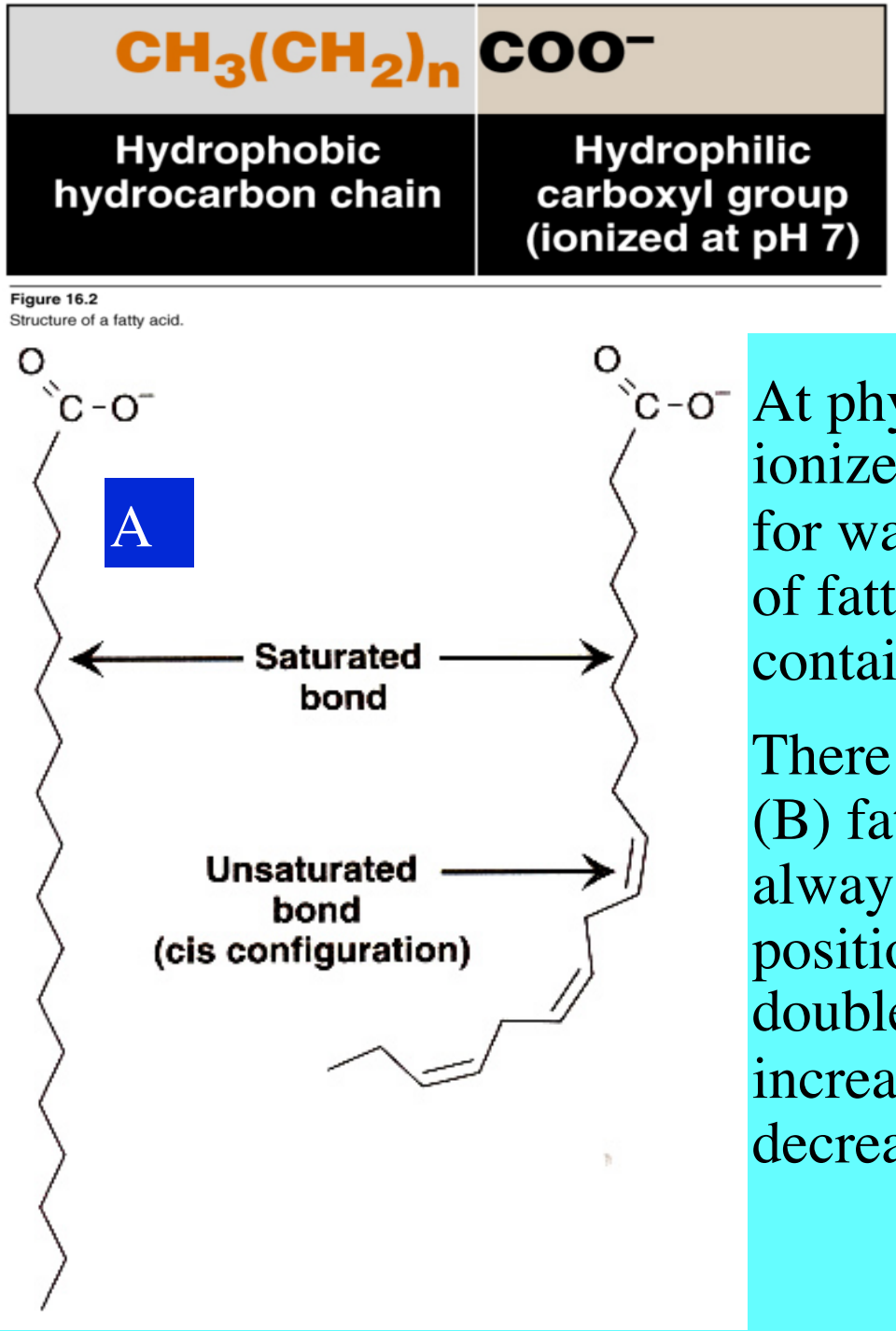
- **The growing fatty acid chain is elongated by the *sequential addition of two-carbon units* derived from acetyl CoA. The activated donor of two-carbon units in the elongation step is *malonyl-ACP.* The elongation reaction is driven by the release of CO_2.**
- **The reductant in fatty acid synthesis is *NADPH*, whereas the oxidants in fatty acid degradation are NAD^+ A and *FAD*.**
- **Elongation by the fatty acid synthase complex stops upon formation of *palmitate* (C_{16}). Further elongation and the insertion of double bonds are carried out by other enzyme systems.**

PHYSIOLOGICAL ROLES OF FATTY ACIDS

- Building blocks of phospholipids and glicolipids.
- Modification of proteins by covalent binding which targets them to membrane locations
- Fuel molecules (triacylglycerol)
- Serve as hormones and ultracellular messenger

Structure

A fatty acid consists of a hydrocarbon chain with a terminal carboxyl group and a methyl group at the other end.



At physiological pH the carboxyl group is ionized. This anionic group has an affinity for water (amphipathic nature). About 90% of fatty acid in plasma is esterified contained in lipoproteins.

There are saturated (A) and unsaturated (B) fatty acid. Double bonds are nearly always in cis configuration produce kink at position. Three carbon intervals after the double bonds. Melting temperature increases with length and double bonds decreases Tm.

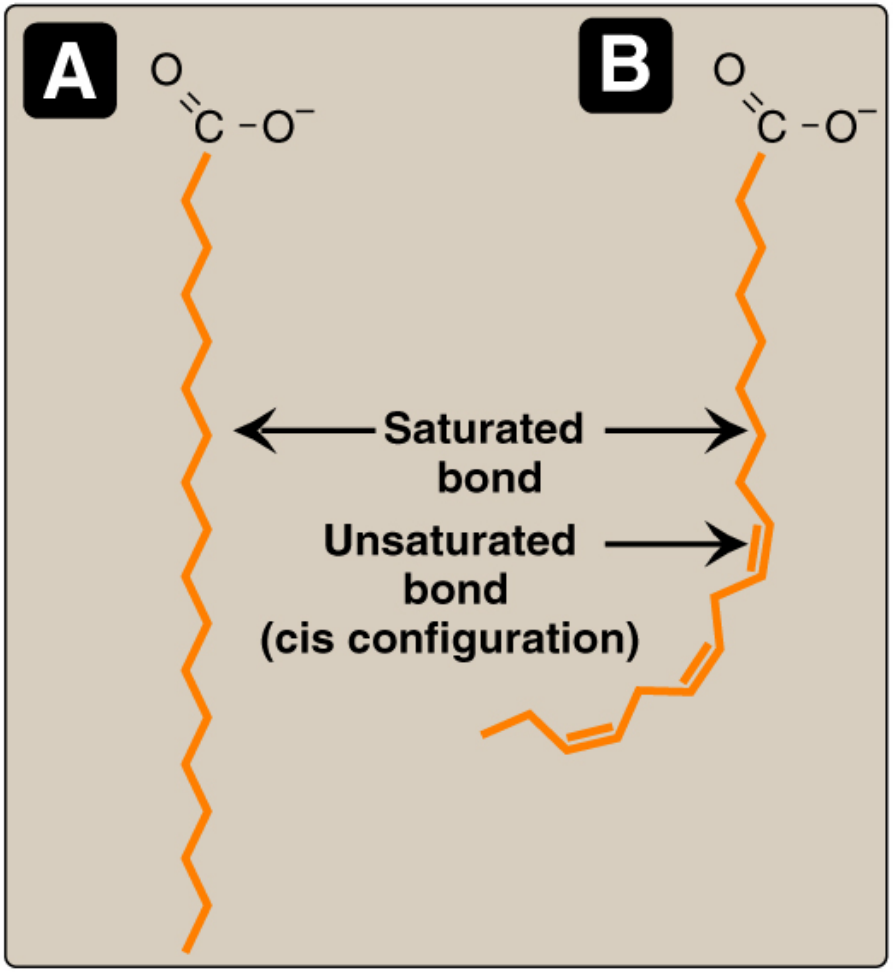
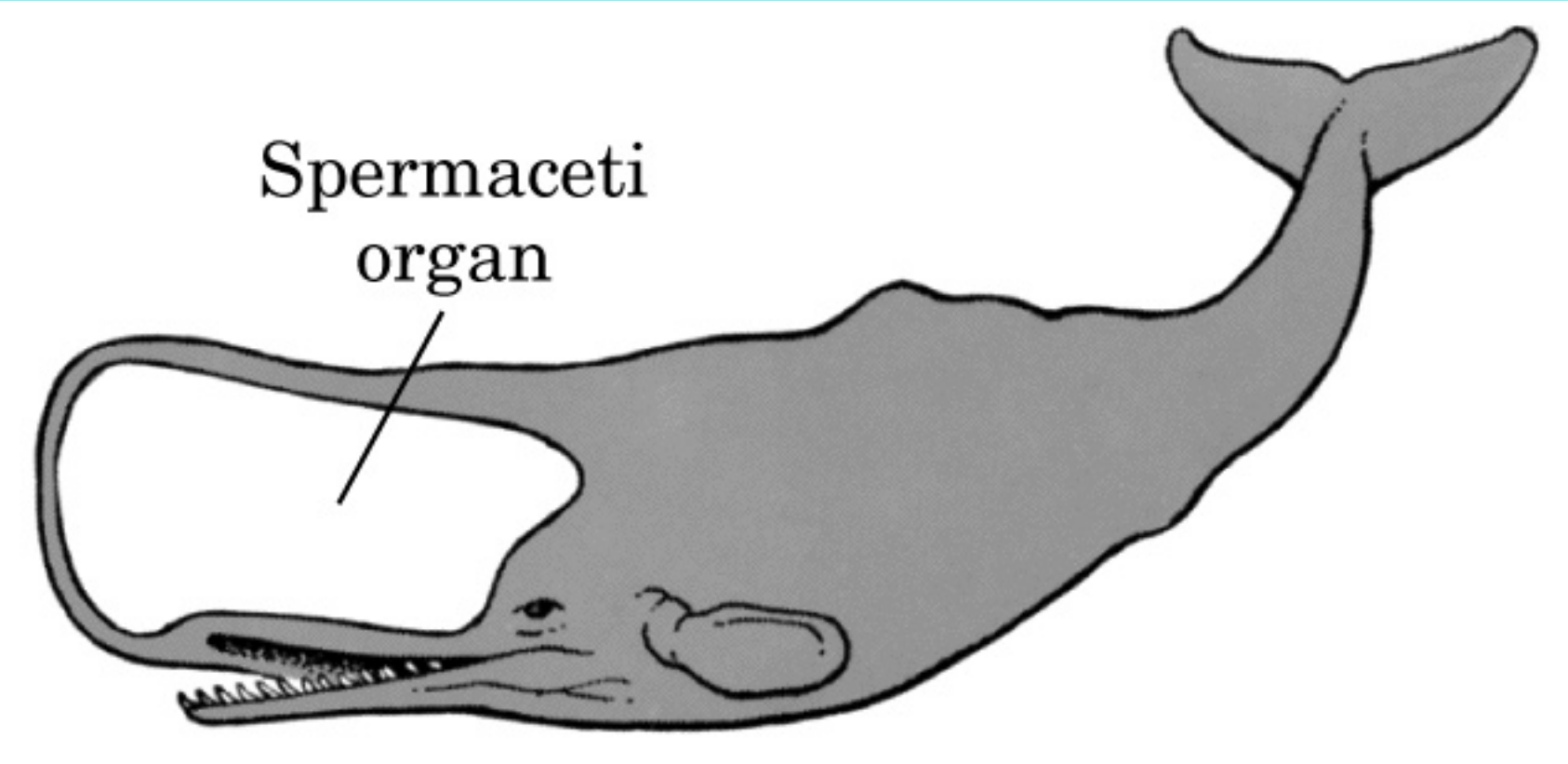


Figure 16.3
A saturated (A) and an unsaturated (B) fatty acid. [Note: Cis double bonds cause a fatty acid to "kink."]

NOMENCLATURE

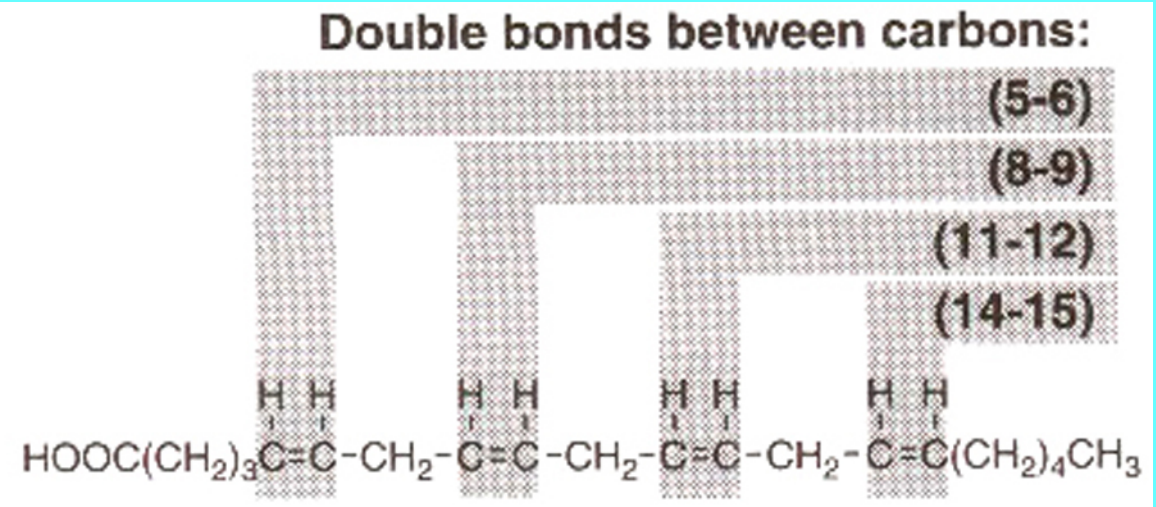
- Derived from parent hydrocarbon
- oic - e
- C_{18} - octadecanoic acid
- with one = octadecenoic acid
- with two= octadecadienoic acid


Spermaceti
organ

SOME FATTY ACIDS OF PHYSIOLOGIC IMPORTANCE

COMMON NAME	STRUCTURE	FUNCTIONAL SIGNIFICANCE
Formic acid	1	
Acetic acid	2:0	
Propionic acid	3:0	
Butyric acid	4:0	Fatty acids with chain lengths of 4–10 carbons
Capric acid	10:0	are found in significant quantities in milk
Palmitic acid	16:0	
Palmitoleic acid	16:1(9)	Structural lipids and triacylglycerols primarily
Stearic acid	18:0	contain fatty acids of at least 16 carbons
Oleic acid	18:1(9)	
Linoleic acid	18:2(9,12)	Essential fatty acid
Linolenic acid	18:3(9,12,15)	Essential fatty acid
Arachidonic acid	20:4(5, 8, 11, 14)	Precursor of prostaglandins
Lignoceric acid	24:0	Component of cerebrosides
Nervonic acid	24:1(15)	

Common names and structures of some fatty acids are listed. Carbons are numbered beginning with the carboxylic carbon as 1. The next number refers to the number of double bonds it has



and the numbers in parenthesis refers to the carbon where the double bonds exist. The carbon to which the carboxyl group is attached is also called the α carbon followed by the β and γ and finally the methyl carbon is called the ω carbon regardless of the length of chain..

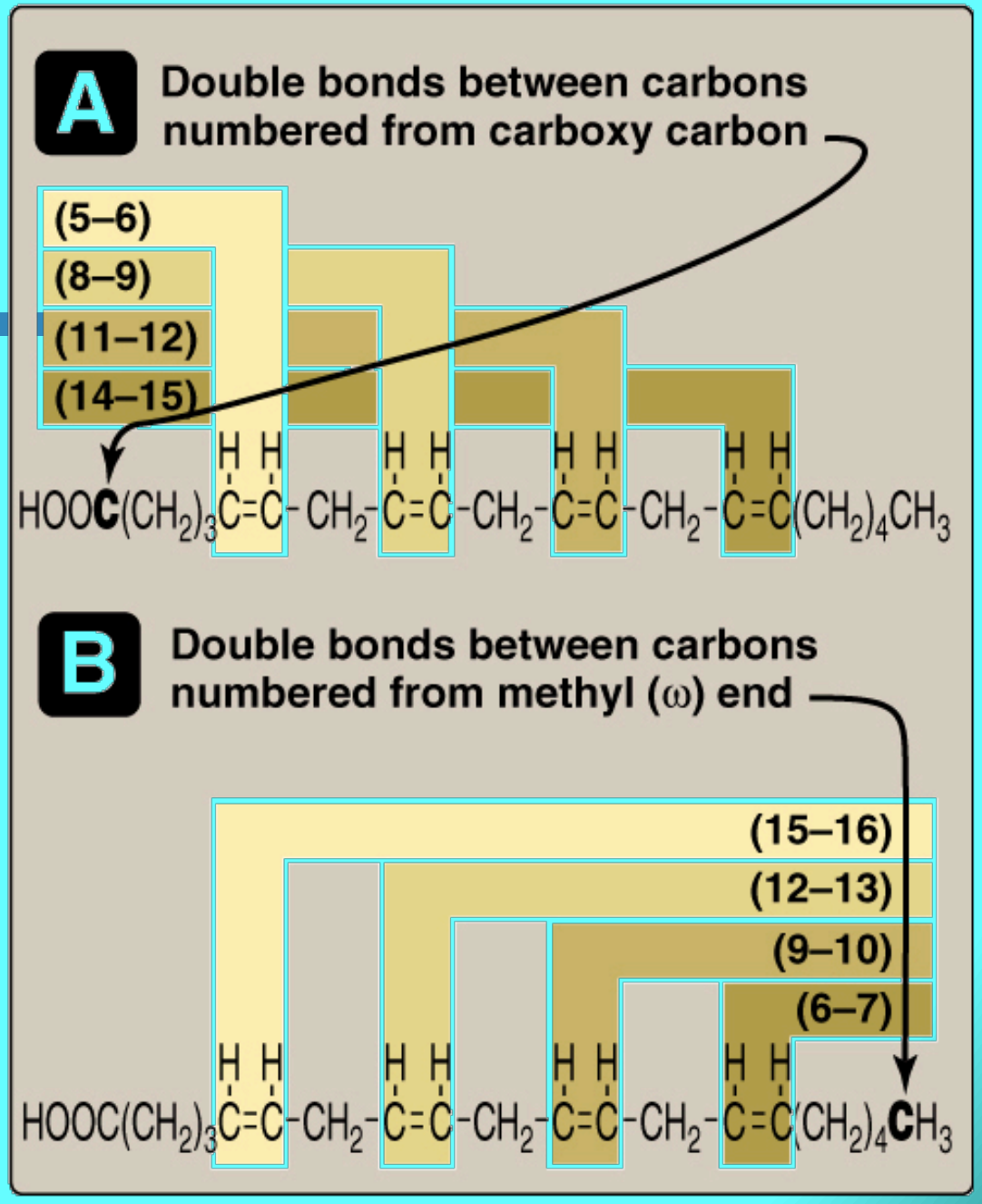


Figure 16.5

Arachidonic acid, illustrating position of double bonds.

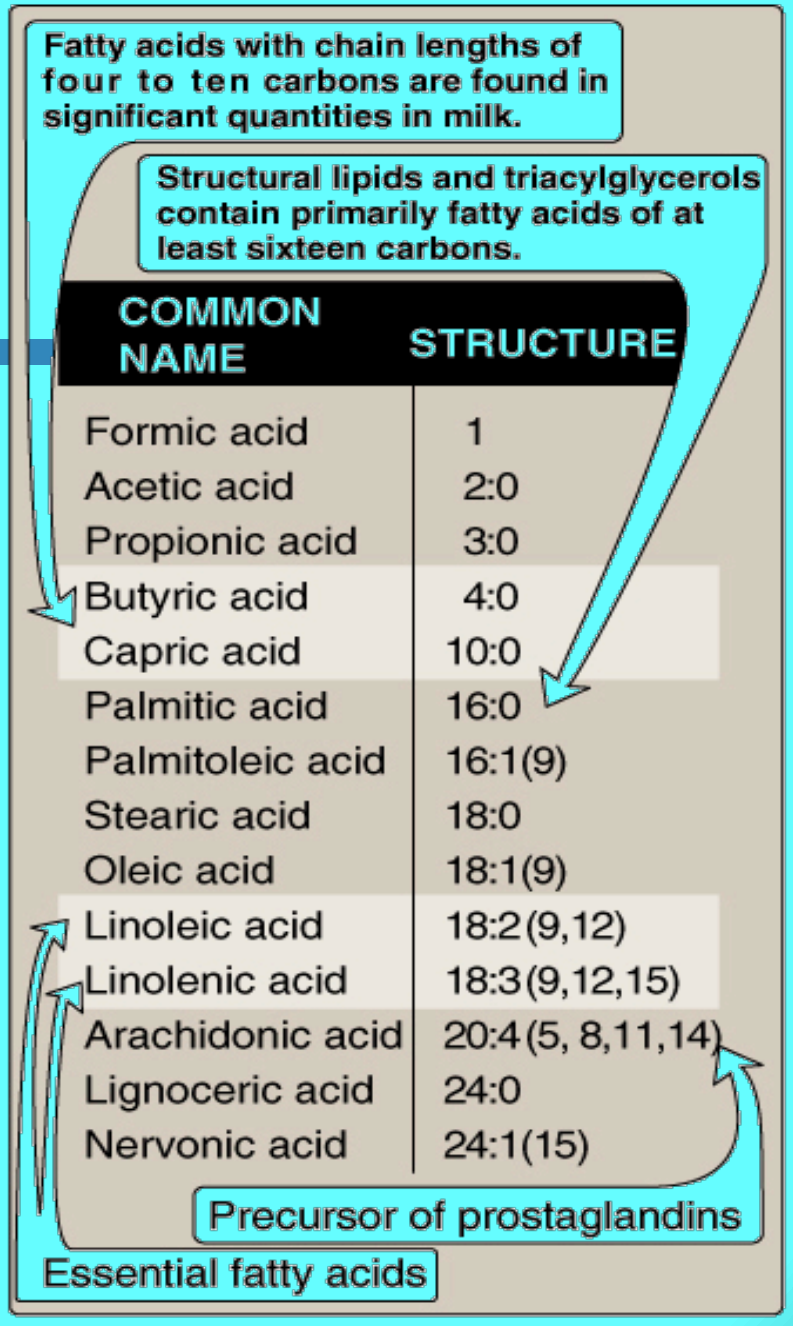
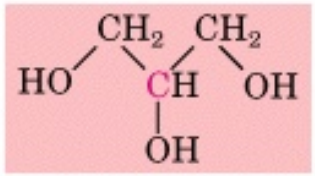
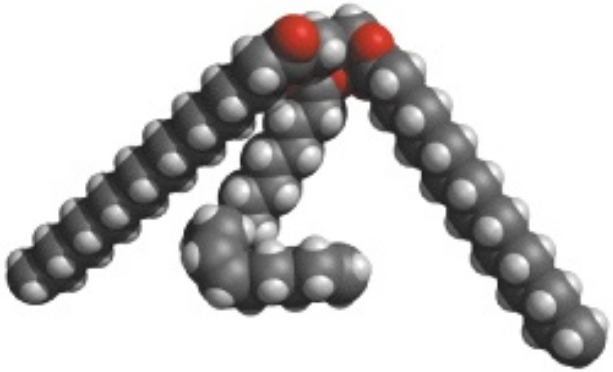
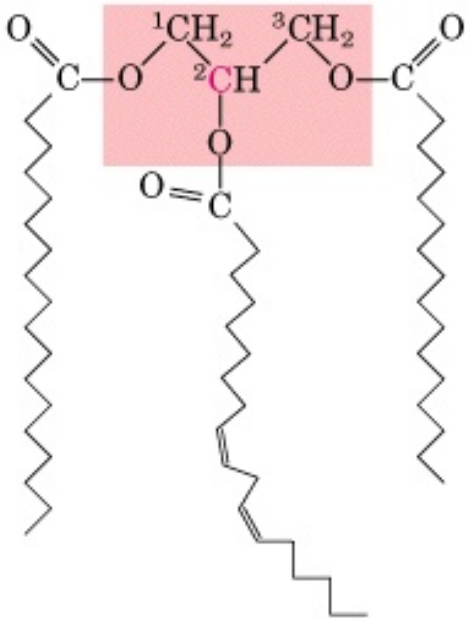


Figure 16.4
Some fatty acids of physiologic importance.

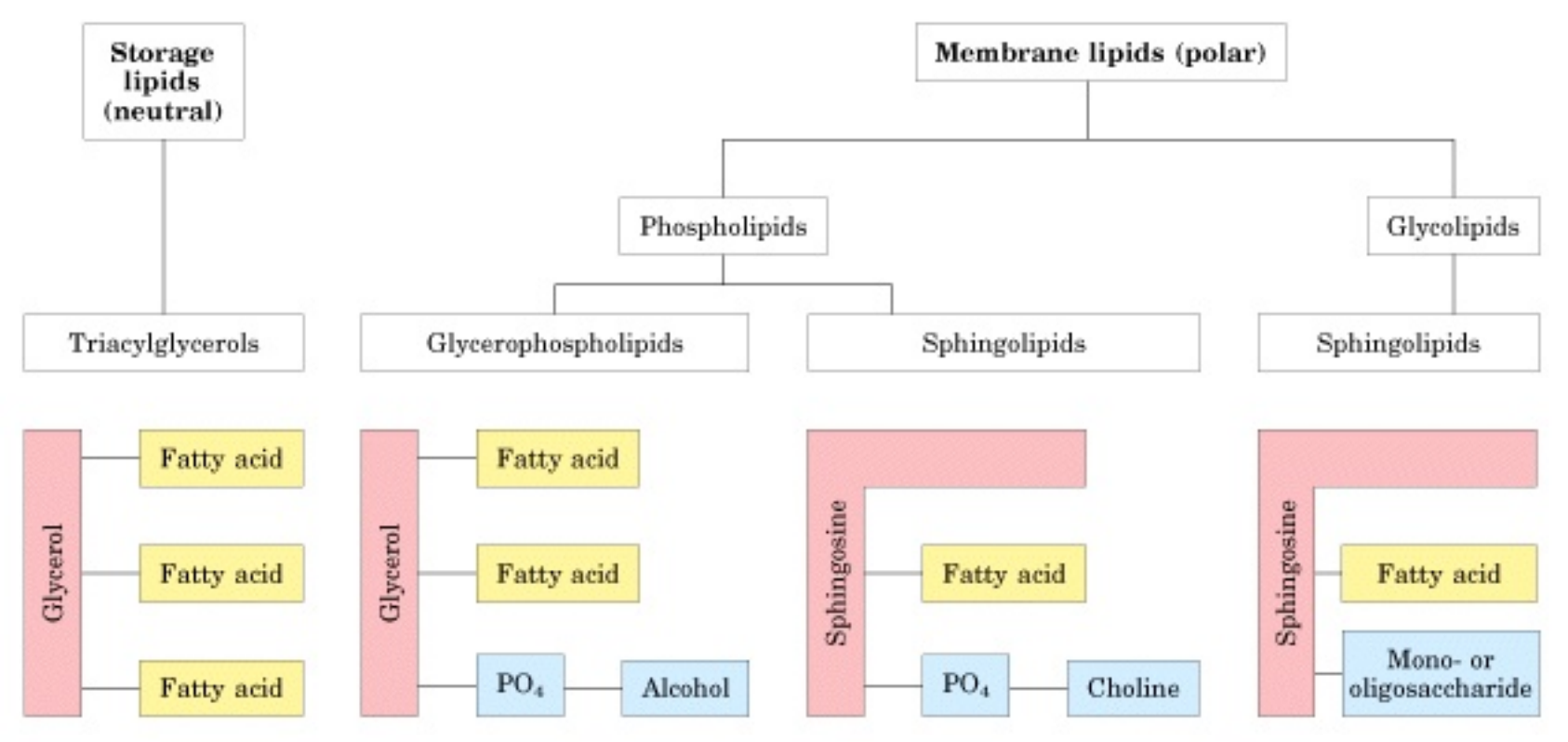


Glycerol

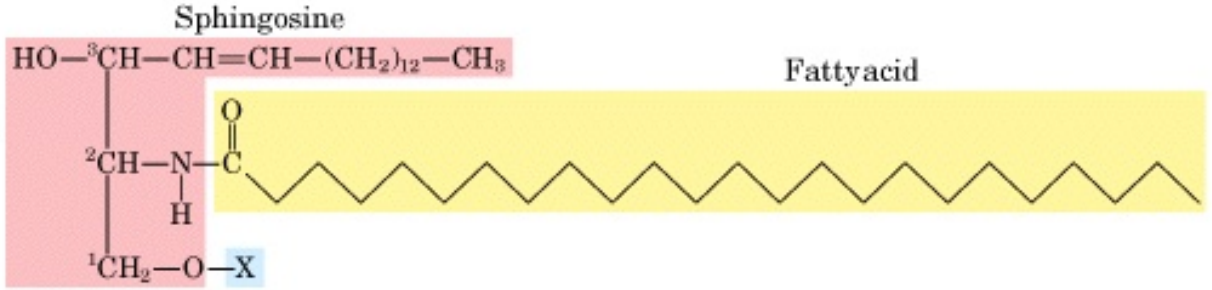


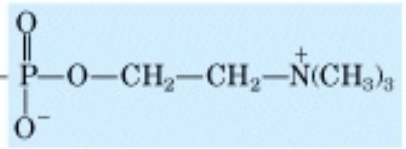
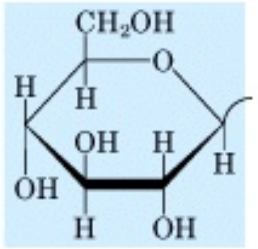
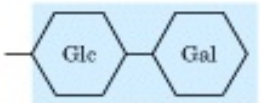
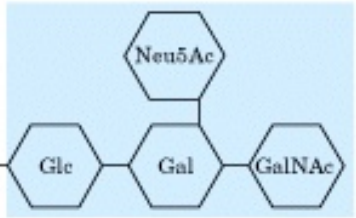


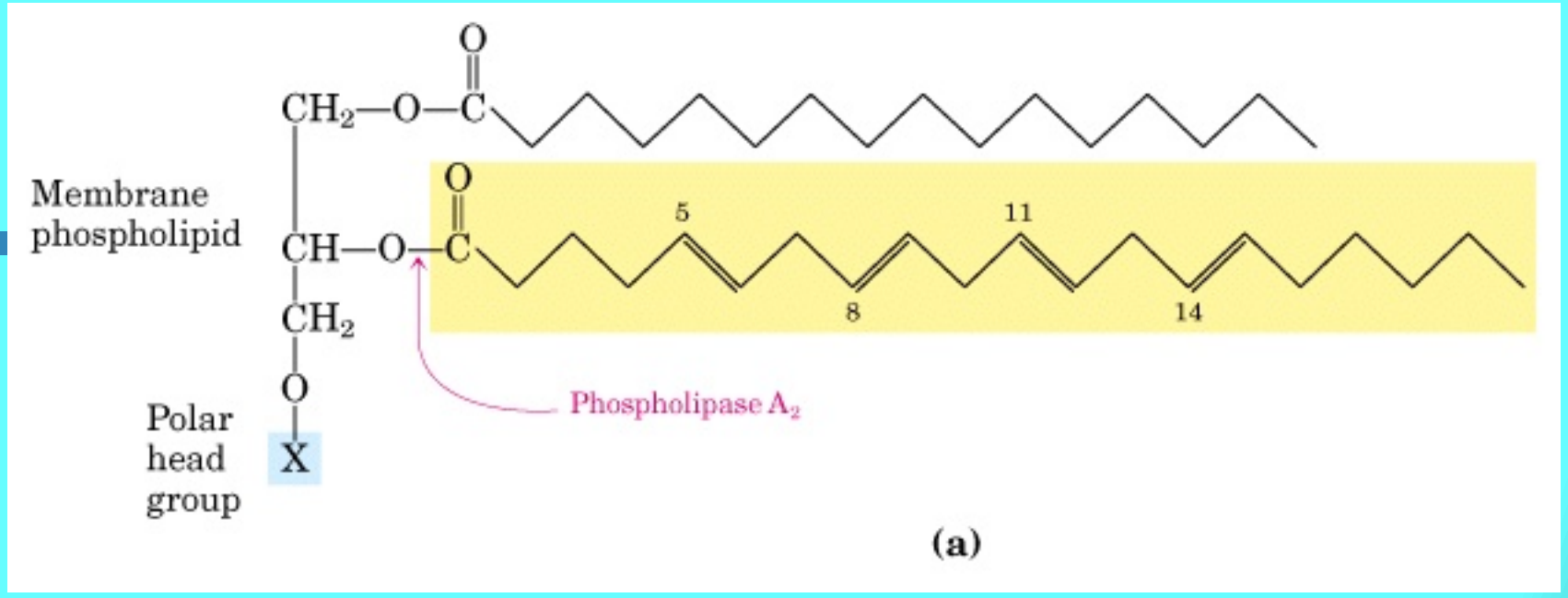
1-Stearoyl, 2-linoleoyl, 3-palmitoyl glycerol,
a mixed triacylglycerol

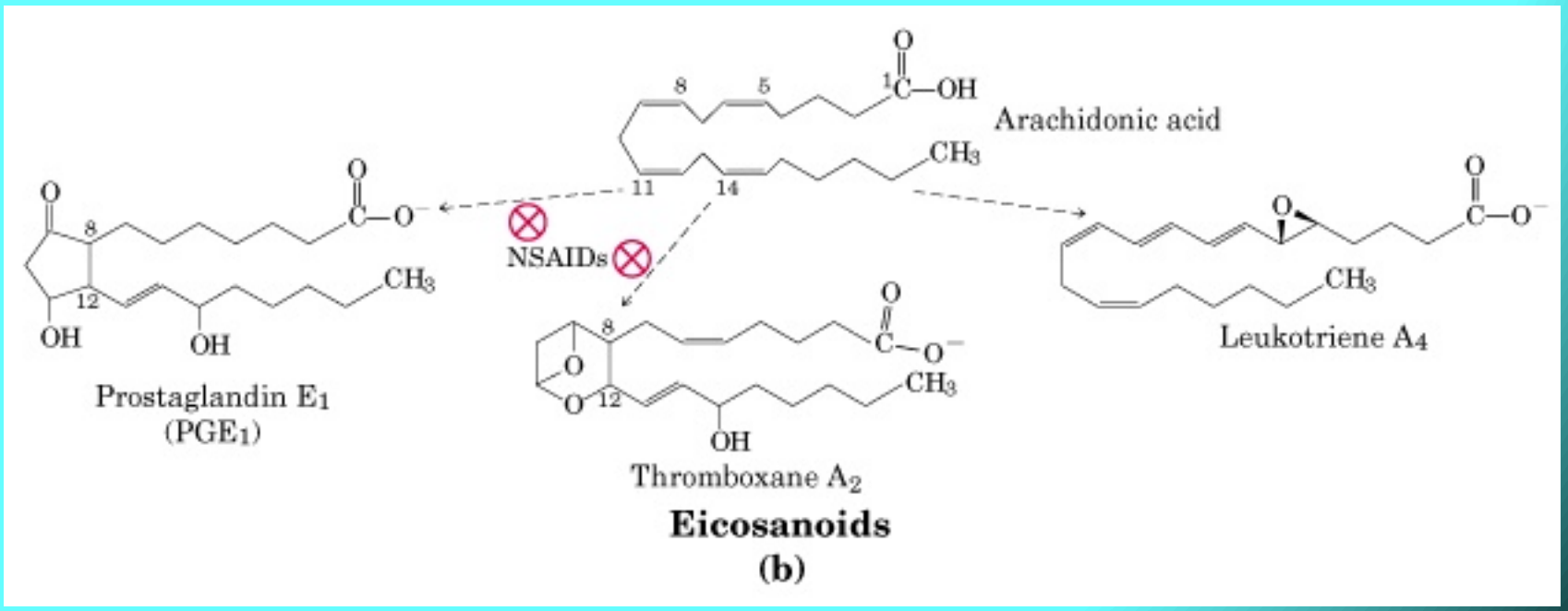

Storage lipids (neutral)
Membrane lipids (polar)
Phospholipids
Glycolipids
Triacylglycerols
Glycerophospholipids
Sphingolipids
Sphingolipids
Glycerol
Fatty acid
Fatty acid
Fatty acid
Glycerol
Fatty acid
Fatty acid
PO4
Alcohol
Sphingosine
Fatty acid
PO4
Choline
Sphingosine
Fatty acid
Mono- or oligosaccharide

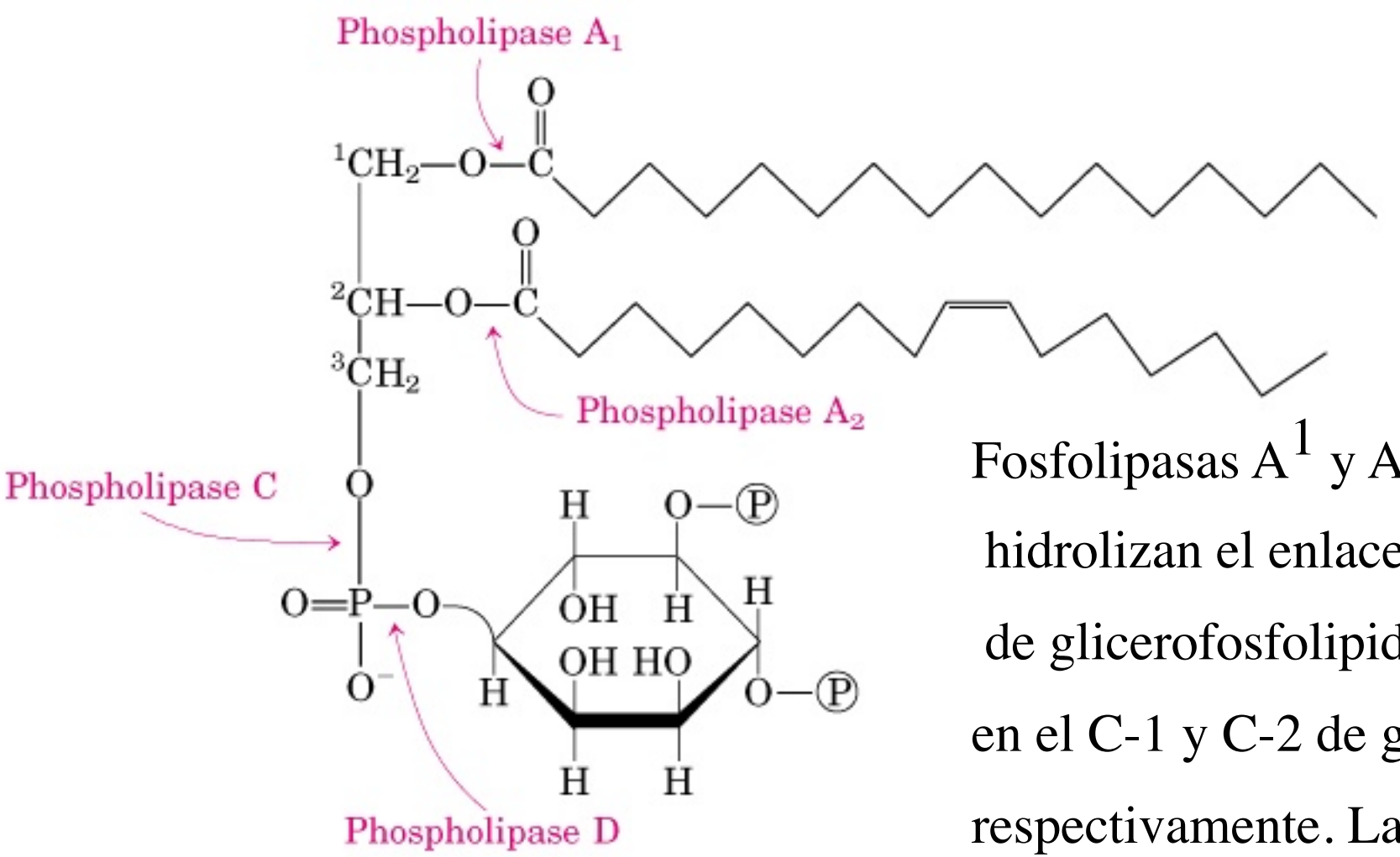
Sphingolipid (general structure)



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	

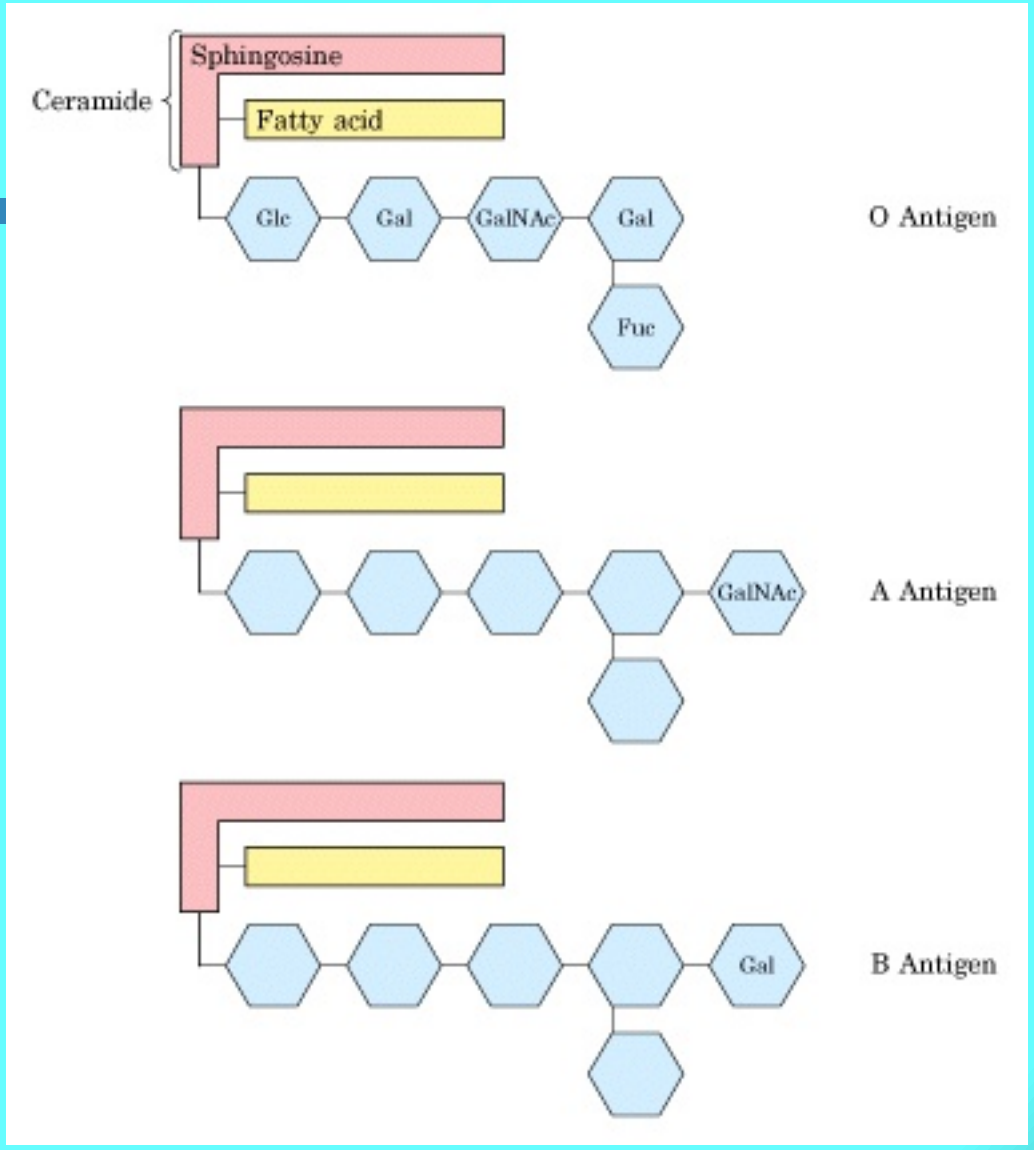

Membrane phospholipid
Polar head group
X
Phospholipase A2
5
8
11
14
(a)

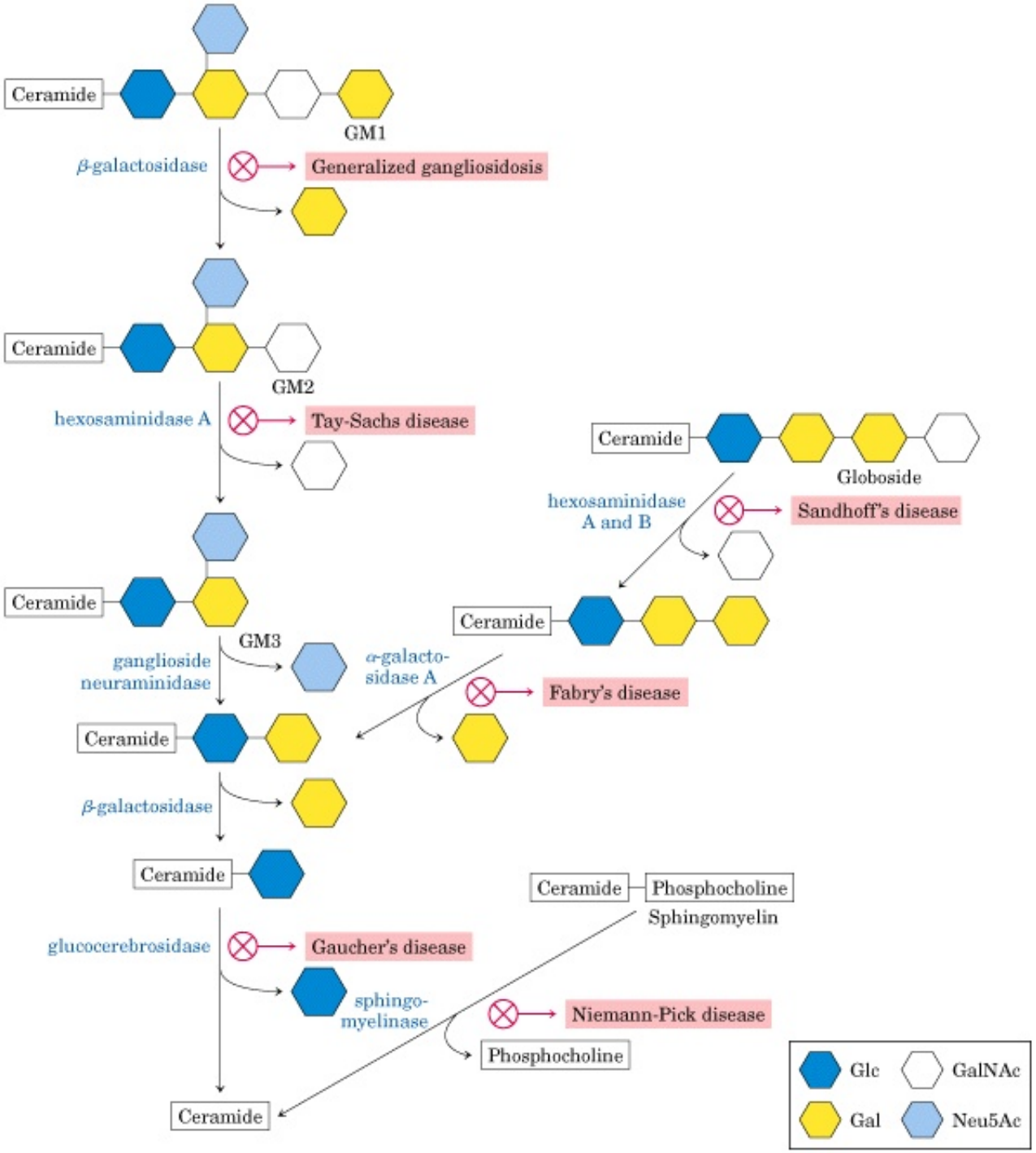

Arachidonic acid
NSAIDs
Prostaglandin E1 (PGE1)
Thromboxane A2
Leukotriene A4
Eicosanoids
(b)

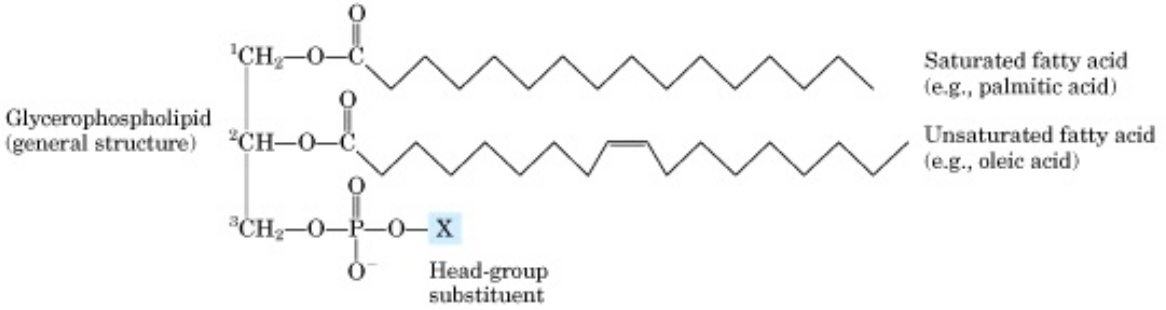


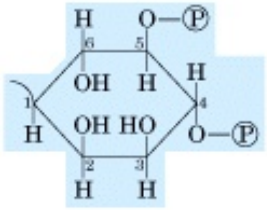
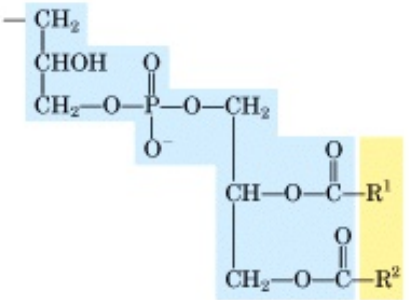
Fosfolipasas A^1 y A^2 hidrolizan el enlace ester de glicerofosfolipidos en el C-1 y C-2 de glicerol, respectivamente. Las C y D

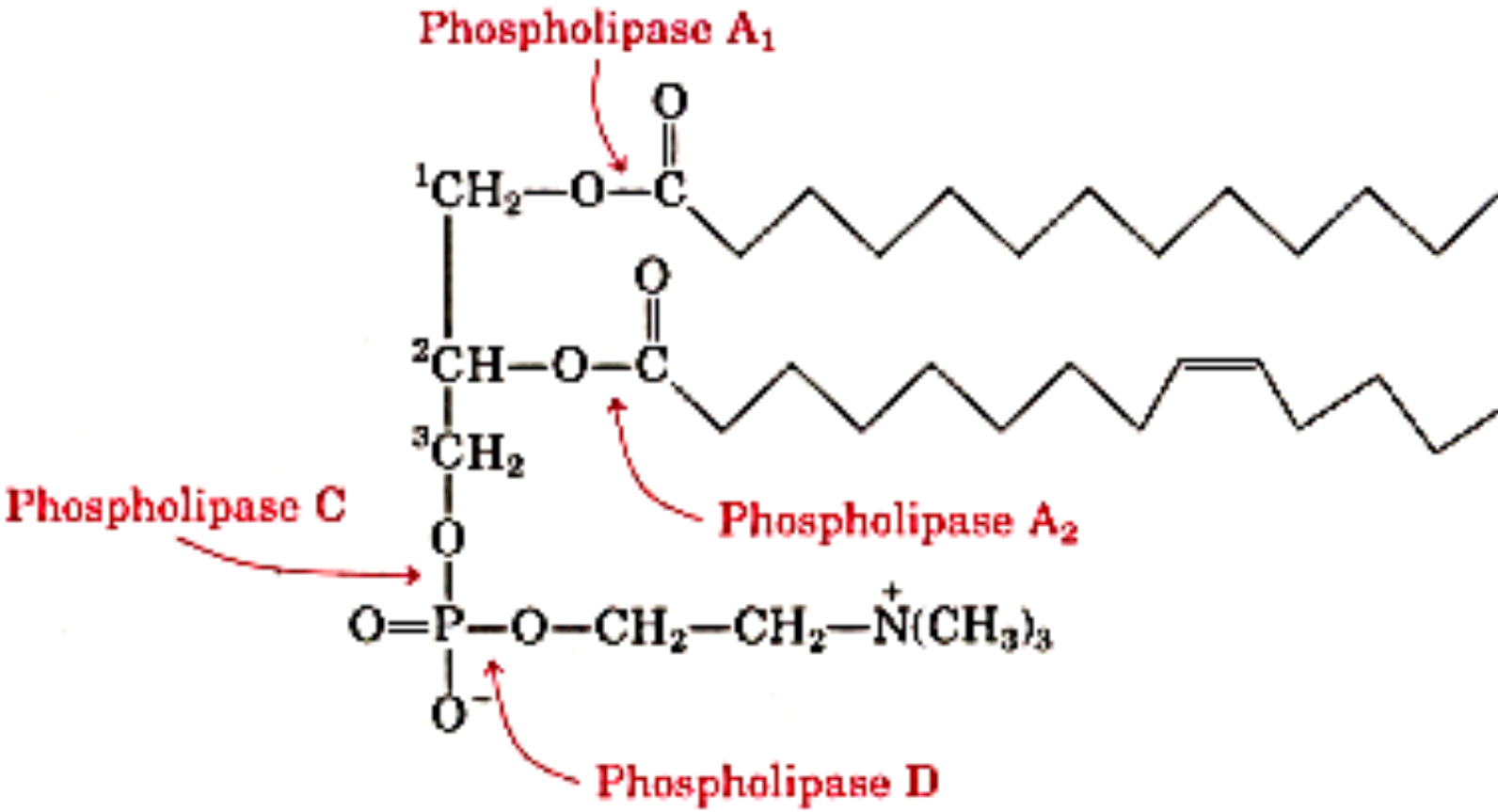
Cada una rompe un enlace fosfodiester. Algunas fosfolipasas solo actuan en un tipo de glicerofosfolipido, como fosfatidilinositol o fosfatidilcolina.

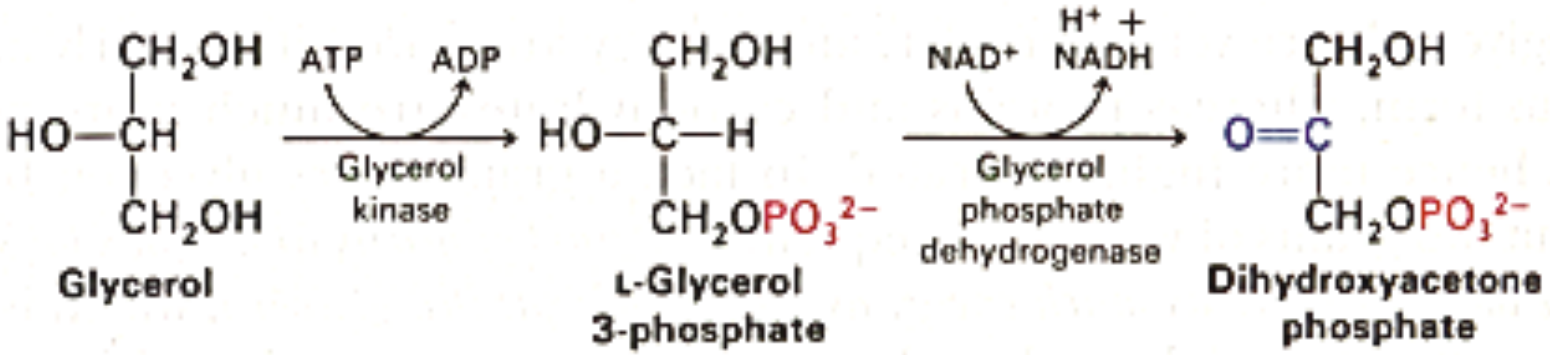

Ceramide
Sphingosine
Fatty acid
Glc
Gal
GalNAc
Gal
Fuc
O Antigen
GalNAc
A Antigen
Gal
B Antigen

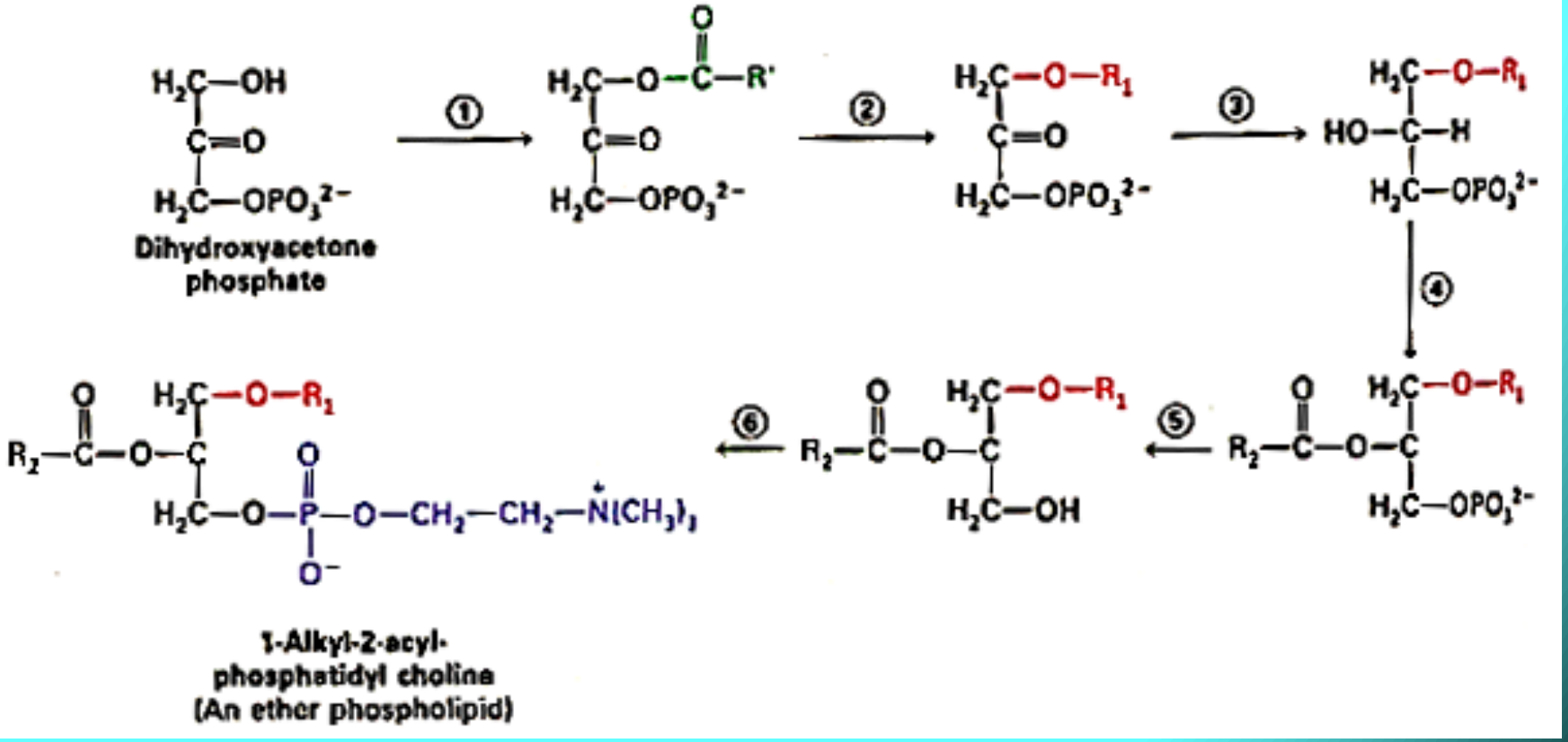

Ceramide
GM1
β-galactosidase
Generalized gangliosidosis
Ceramide
GM2
hexosaminidase A
Tay-Sachs disease
Ceramide
Globoside
hexosaminidase A and B
Sandhoff's disease
Ceramide
GM3
ganglioside neuraminidase
α-galacto-sidase A
Fabry's disease
Ceramide
β-galactosidase
Ceramide
Ceramide
Phosphocholine
Sphingomyelin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



Name of glycerophospholipid	Name of X	Formula of X	Net charge (at pH 7)
Phosphatidic acid	—	—H	−1
Phosphatidylethanolamine	Ethanolamine	$-CH_2-CH_2-\overset{+}{N}H_3$	0
Phosphatidylcholine	Choline	$-CH_2-CH_2-\overset{+}{N}(CH_3)_3$	0
Phosphatidylserine	Serine	$-CH_2-CH(COO^-)-\overset{+}{N}H_3$	−1
Phosphatidylglycerol	Glycerol	$-CH_2-CH(OH)-CH_2-OH$	−1
Phosphatidylinositol 4,5-bisphosphate	*myo*-Inositol 4,5-bisphosphate		−4
Cardiolipin	Phosphatidyl-glycerol		−2


Phospholipase A1
Phospholipase C
Phospholipase A2
Phospholipase D


CH2OH
HO—CH
CH2OH
Glycerol
ATP
ADP
Glycerol kinase
CH2OH
HO—C—H
CH2OPO3 2−
L-Glycerol 3-phosphate
NAD+
H+ + NADH
Glycerol phosphate dehydrogenase
CH2OH
O=C
CH2OPO3 2−
Dihydroxyacetone phosphate


H2C—OH
C=O
H2C—OPO3 2−
Dihydroxyacetone phosphate
①
H2C—O—C—R'
②
H2C—O—R1
③
HO—C—H
④
⑤
⑥
R2—C—O—C
O
O⁻
H2C—O—P—O—CH2—CH2—N(CH3)3
1-Alkyl-2-acyl-phosphatidyl choline (An ether phospholipid)