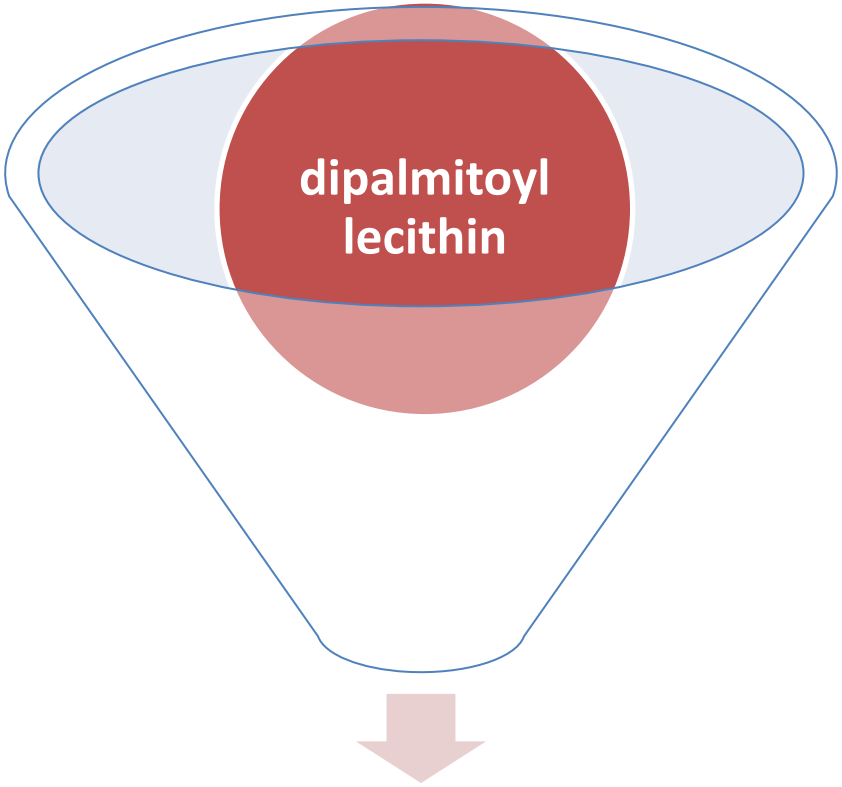
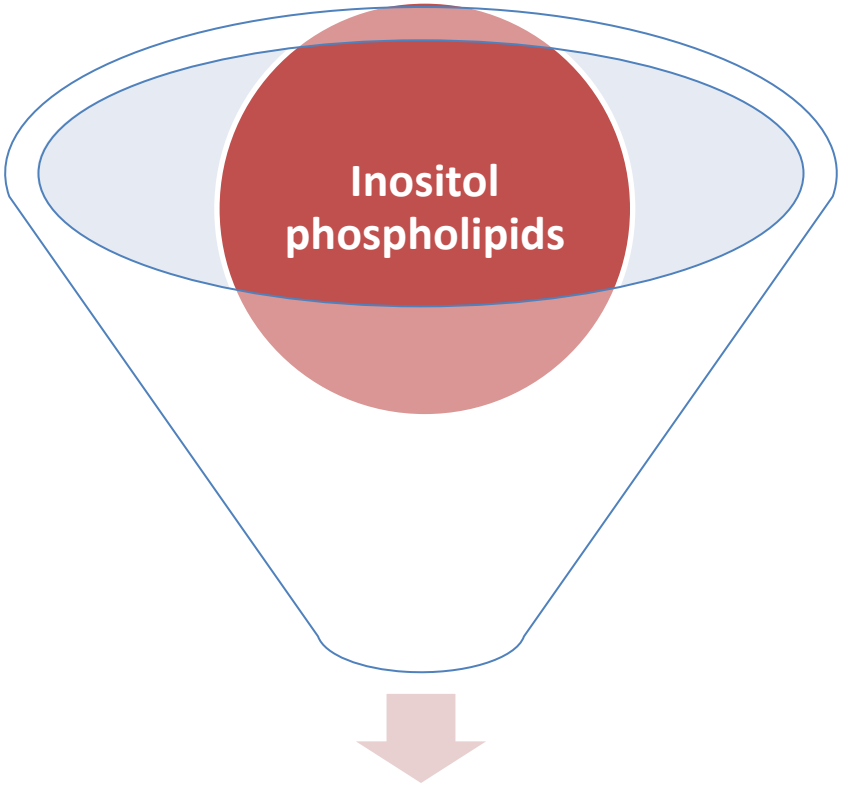
Metabolism of complex lipids

Dr. Ahmed Jalal AL-Bayati

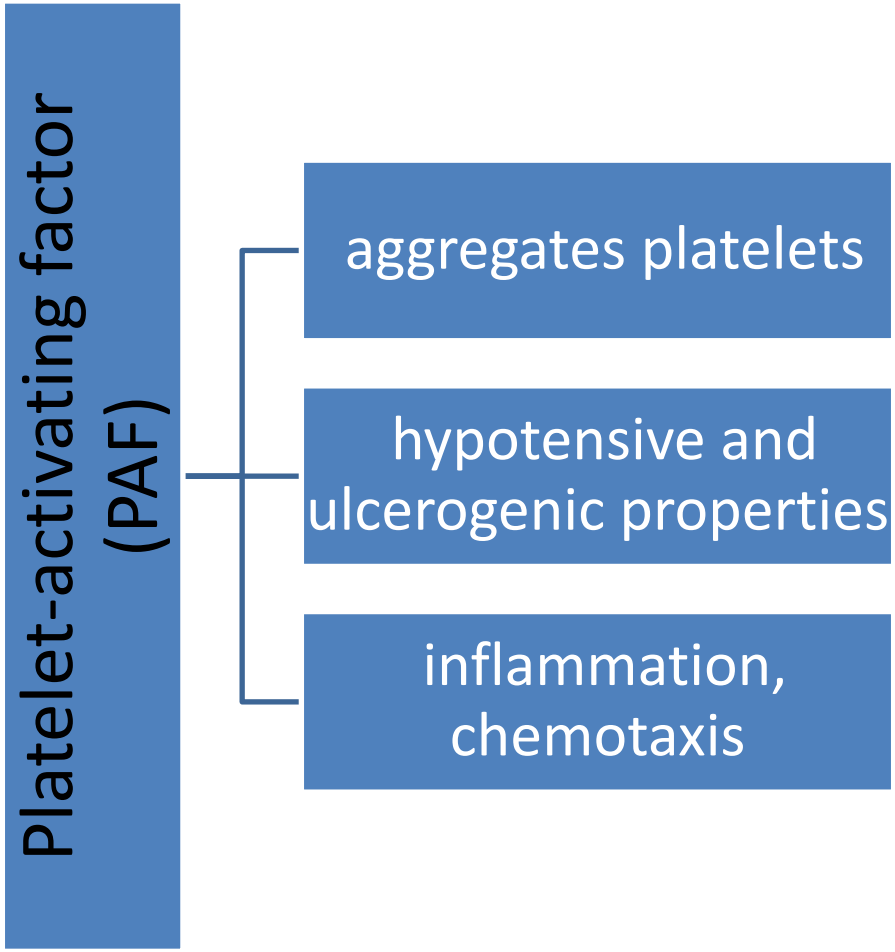
- **Acylglycerols** constitute the majority of lipids in the body. **Triacylglycerols** are the major lipids in fat deposits and in food, and their roles in lipid transport and storage and in various diseases such as obesity, diabetes, and hyperlipoproteinemia.
- The **amphipathic** nature of **phospholipids** and **sphingolipids** makes them ideally suitable as the main lipid component of cell membranes.

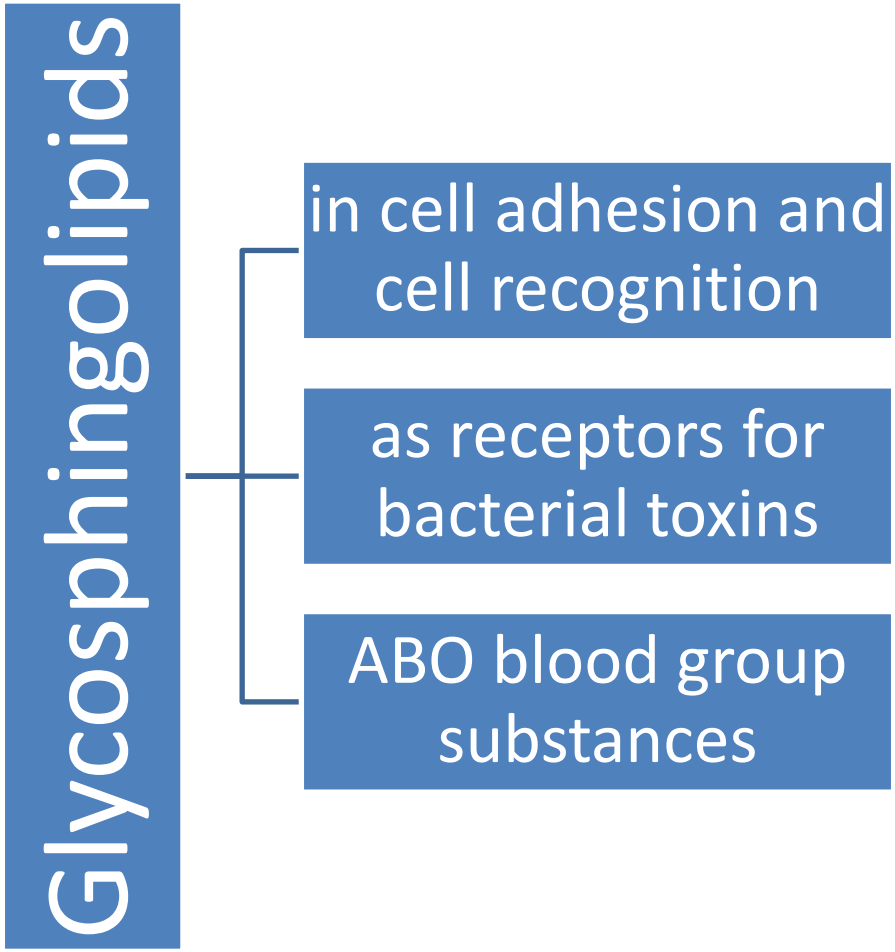


lung surfactant



hormone second messengers

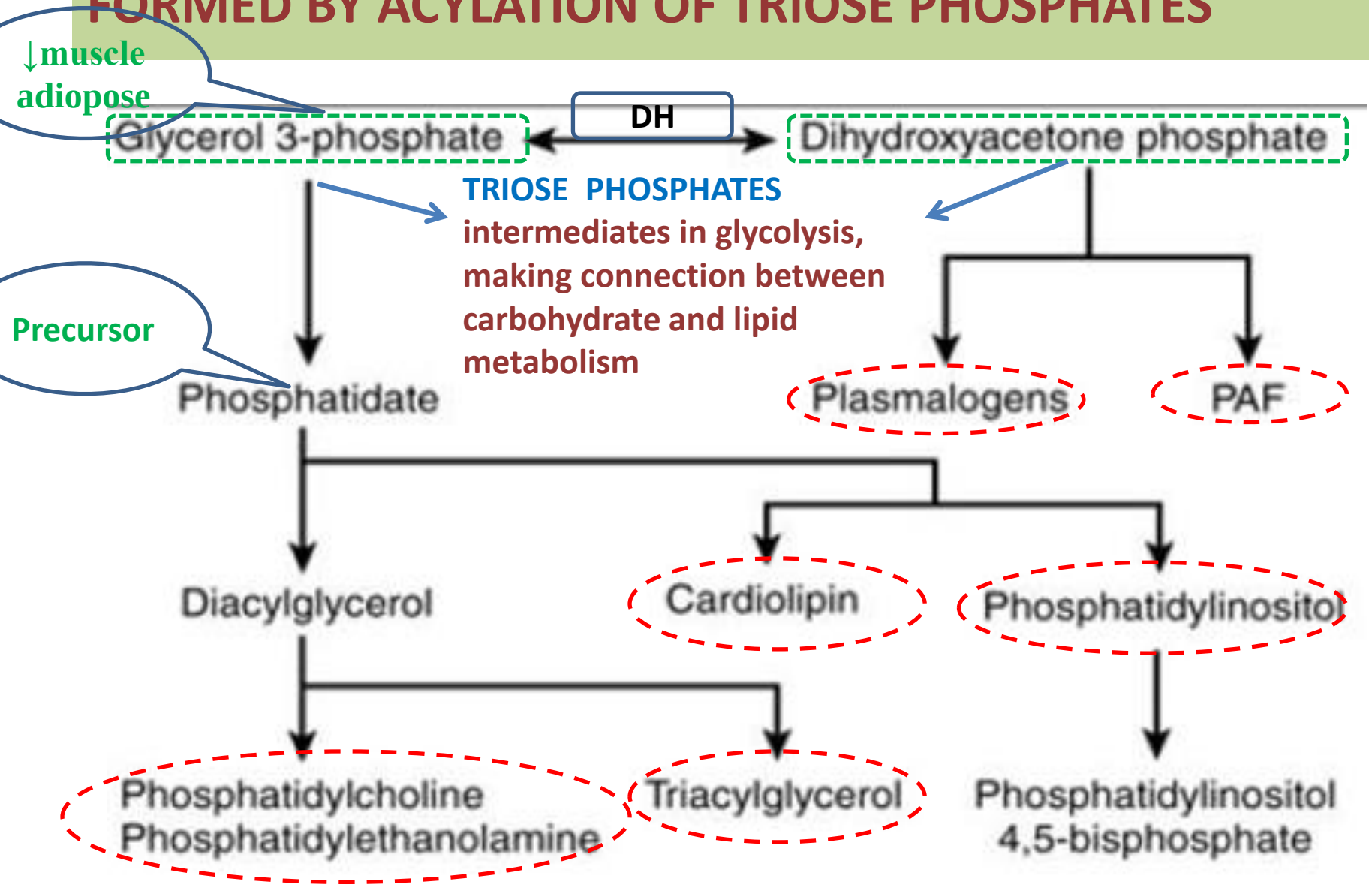

Platelet-activating factor (PAF)
aggregates platelets
hypotensive and ulcerogenic properties
inflammation, chemotaxis

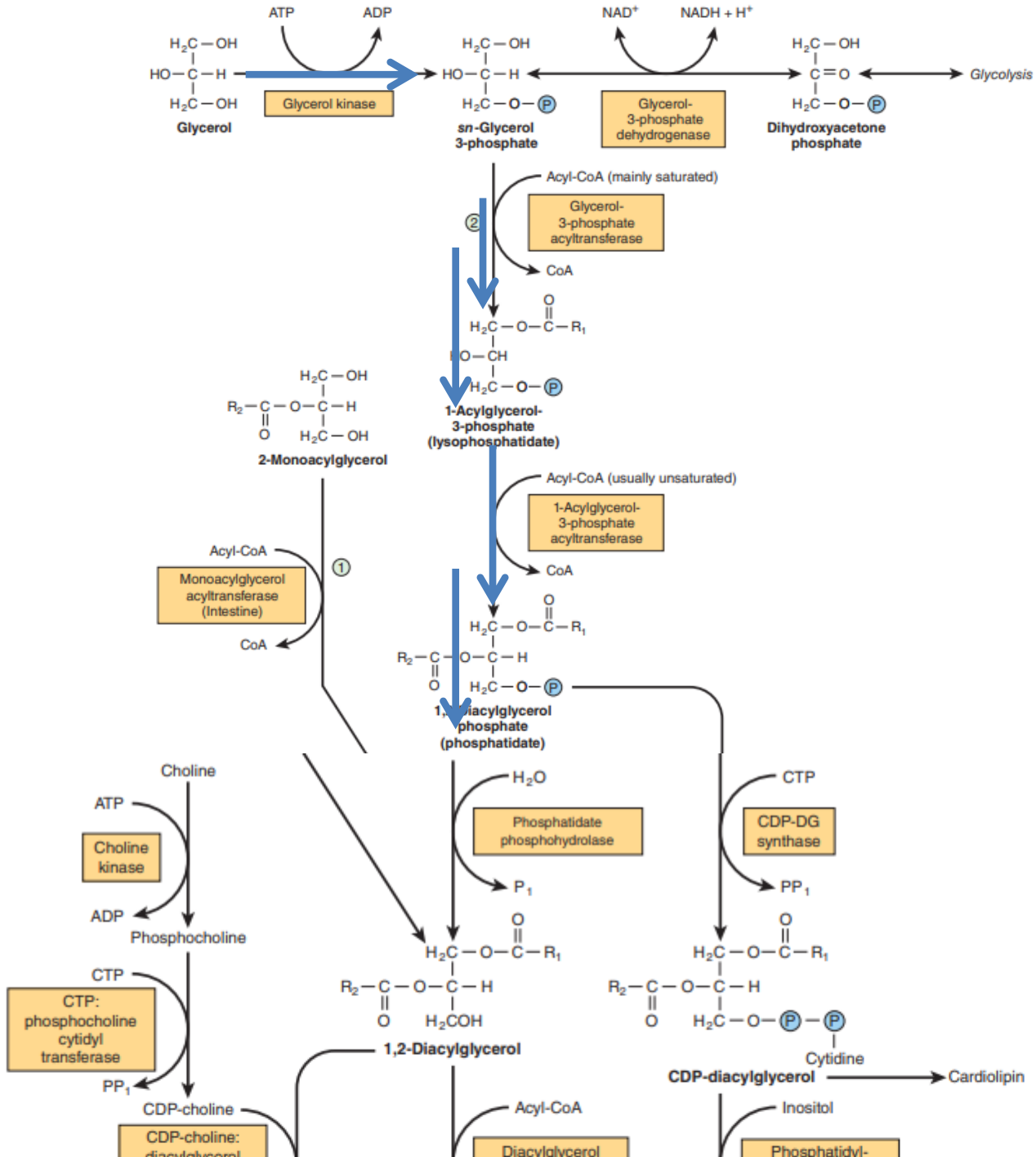

Glycosphingolipids
in cell adhesion and cell recognition
as receptors for bacterial toxins
ABO blood group substances

lipolysis

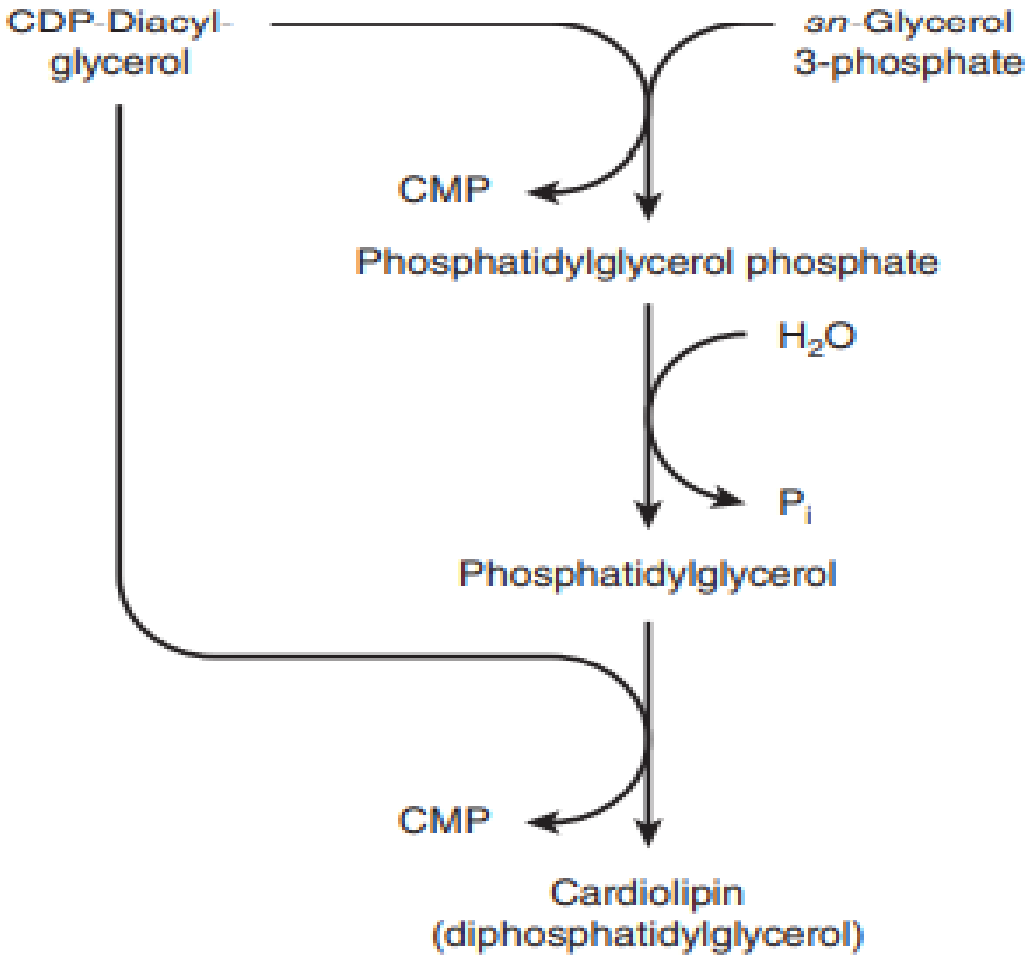
- Triacylglycerols must be hydrolyzed by a **lipase** to their constituent fatty acids and glycerol
- **free fatty acids** into the plasma, where they are found combined with serum albumin . followed by free fatty acid uptake into tissues (including liver, heart, kidney, muscle, lung, testis, and adipose tissue, but not readily by brain)
- utilization of glycerol depends upon whether such tissues have the enzyme **glycerol kinase,** which is found in significant amounts in liver, kidney, intestine, brown adipose tissue, and the lactating mammary gland.

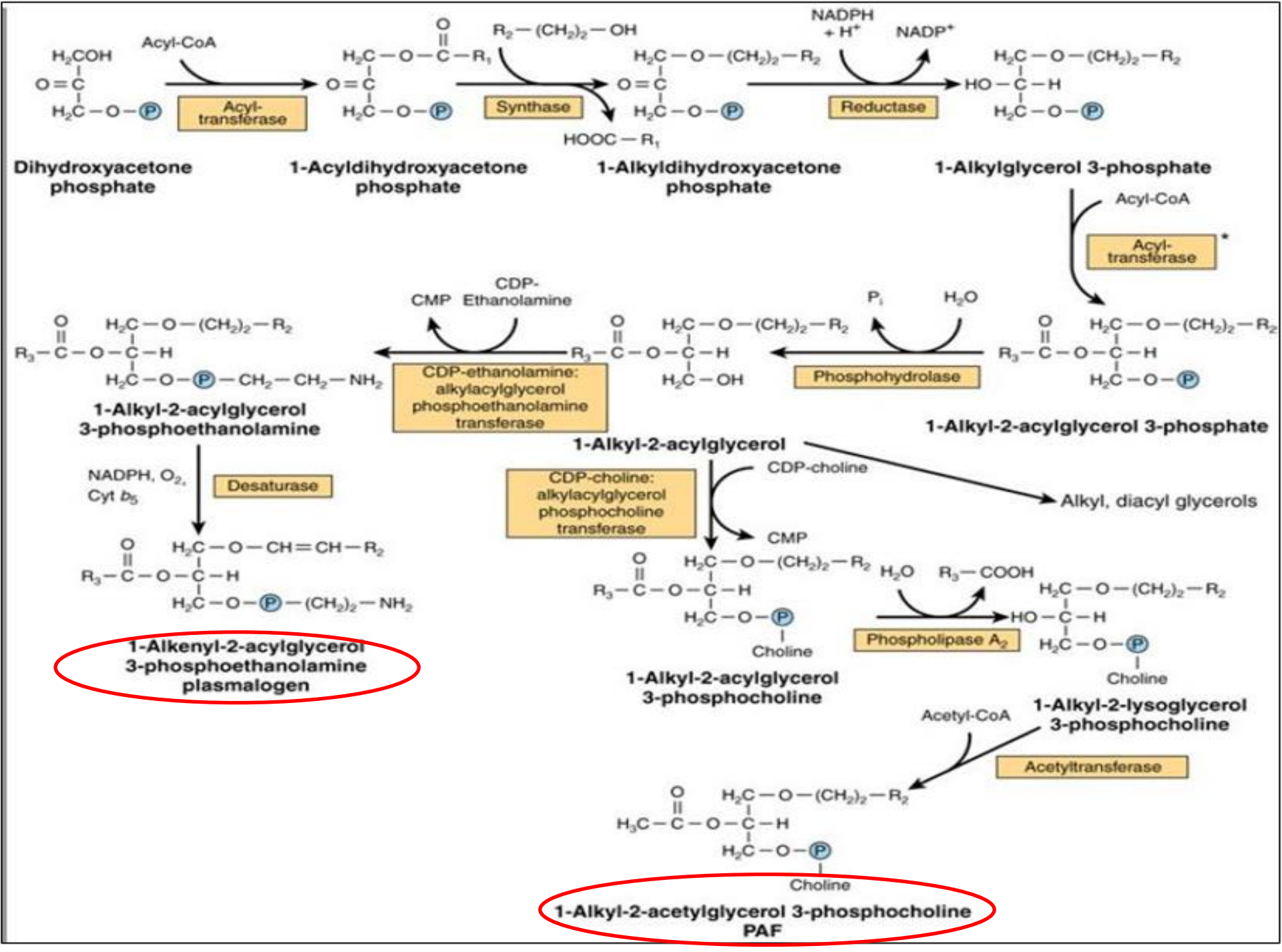
TRIACYLGLYCEROLS & PHOSPHOGLYCEROLS FORMED BY ACYLATION OF TRIOSE PHOSPHATES



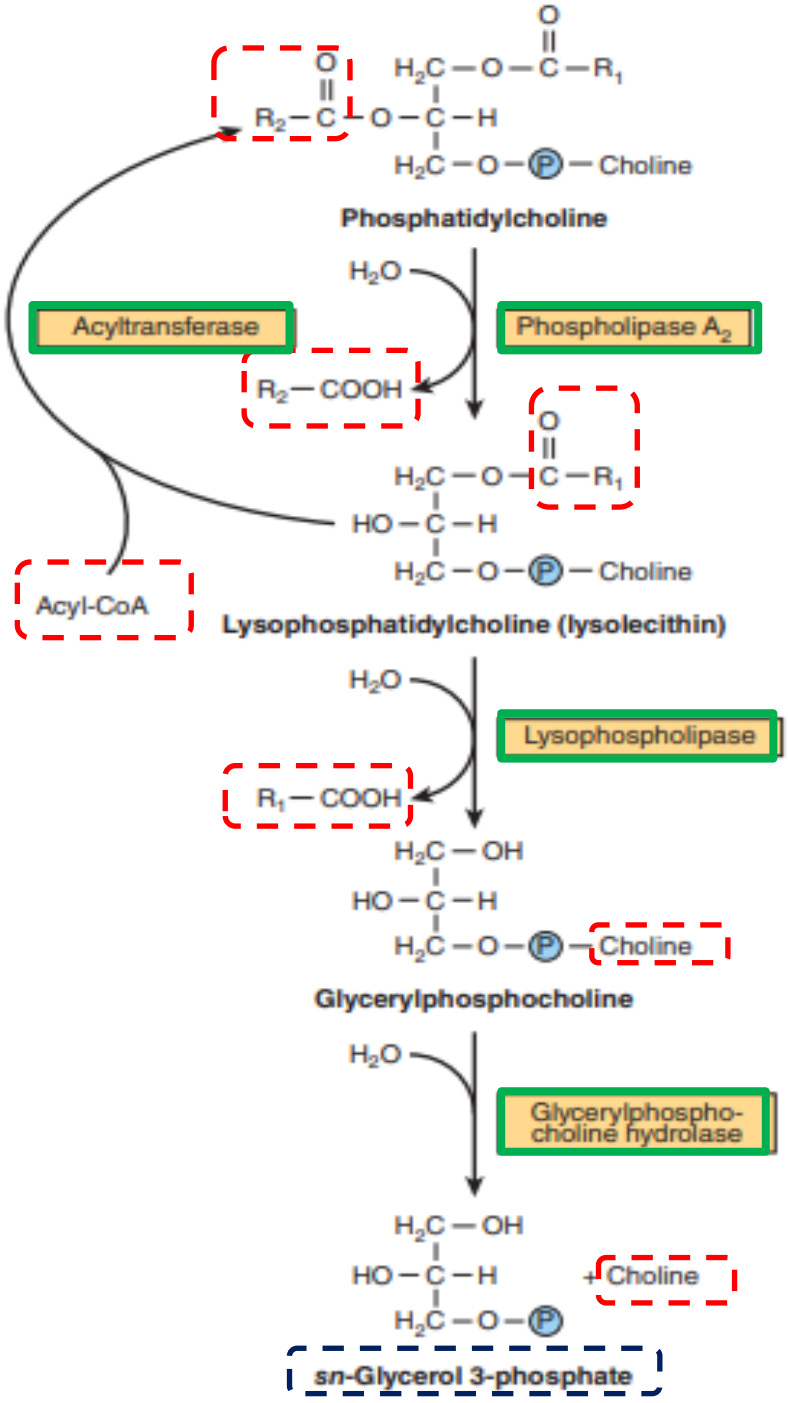

ATP
ADP
NAD+
NADH + H+
Glycerol kinase
Glycerol-3-phosphate dehydrogenase
Glycolysis
Glycerol
sn-Glycerol 3-phosphate
Dihydroxyacetone phosphate
Acyl-CoA (mainly saturated)
Glycerol-3-phosphate acyltransferase
CoA
1-Acylglycerol-3-phosphate (lysophosphatidate)
2-Monoacylglycerol
Acyl-CoA (usually unsaturated)
1-Acylglycerol-3-phosphate acyltransferase
Acyl-CoA
Monoacylglycerol acyltransferase (Intestine)
Phosphatidate (phosphatidate)
Choline
ATP
Choline kinase
ADP
Phosphocholine
CTP
CTP: phosphocholine cytidyl transferase
PP1
CDP-choline
CDP-choline:
H2O
Phosphatidate phosphohydrolase
P1
1,2-Diacylglycerol
CTP
CDP-DG synthase
PP1
Cytidine
CDP-diacylglycerol
Cardiolipin
Acyl-CoA
Inositol
Diacylglycerol
Phosphatidyl-

Biosynthesis of cardiolipin.

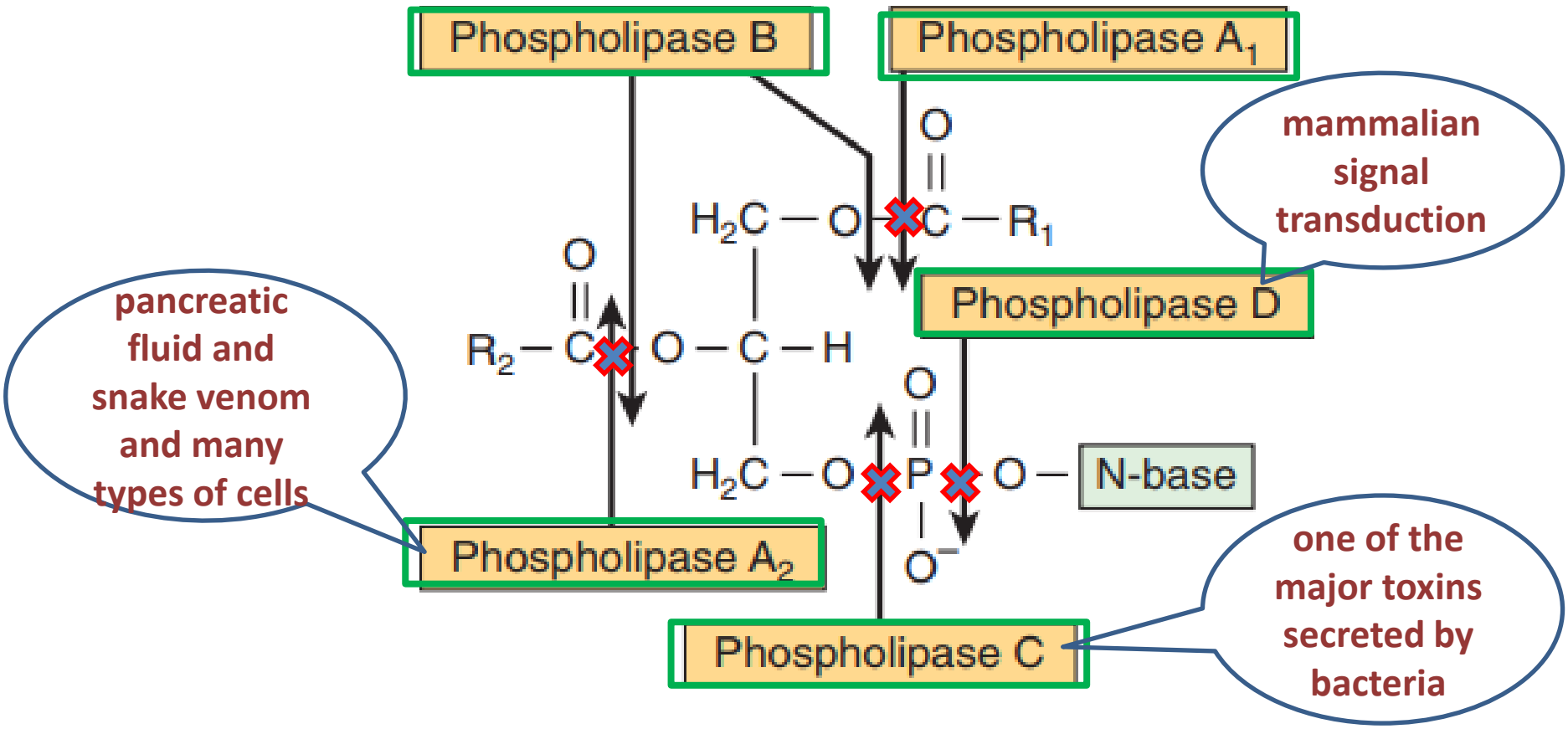



Acyl-CoA
Acyl-transferase
Dihydroxyacetone phosphate
1-Acyldihydroxyacetone phosphate
Synthase
HOOC — R1
NADPH + H+
NADP+
Reductase
1-Alkyldihydroxyacetone phosphate
1-Alkylglycerol 3-phosphate
Acyl-CoA
Acyl-transferase
1-Alkyl-2-acylglycerol 3-phosphate
Pi
H2O
Phosphohydrolase
CDP-Ethanolamine
CMP
CDP-ethanolamine: alkylacylglycerol phosphoethanolamine transferase
1-Alkyl-2-acylglycerol 3-phosphoethanolamine
1-Alkyl-2-acylglycerol
CDP-choline
CDP-choline: alkylacylglycerol phosphocholine transferase
CMP
Alkyl, diacyl glycerols
NADPH, O2, Cyt b5
Desaturase
1-Alkenyl-2-acylglycerol 3-phosphoethanolamine plasmalogen
1-Alkyl-2-acylglycerol 3-phosphocholine
H2O
R3 — COOH
Phospholipase A2
Choline
1-Alkyl-2-lysoglycerol 3-phosphocholine
Acetyl-CoA
Acetyltransferase
Choline
1-Alkyl-2-acetylglycerol 3-phosphocholine
PAF

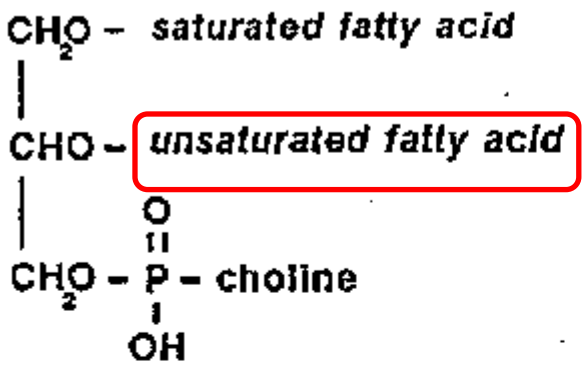
Degr of g


Phosphatidylcholine
H2O
Acyltransferase
Phospholipase A2
R2—COOH
Acyl-CoA
Lysophosphatidylcholine (lysolecithin)
H2O
Lysophospholipase
R1—COOH
Glycerylphosphocholine
H2O
Glycerylphospho-choline hydrolase
+Choline
sn-Glycerol 3-phosphate

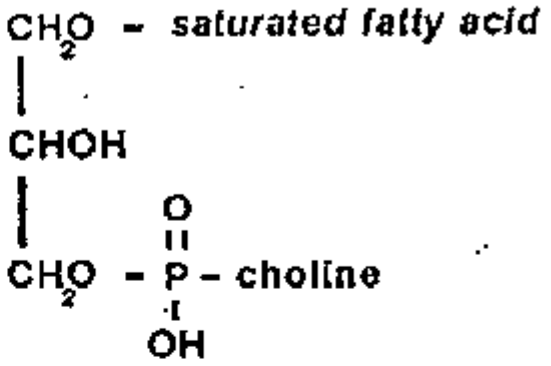
Phospholipases



LECITHIN



LYSOLECITHIN

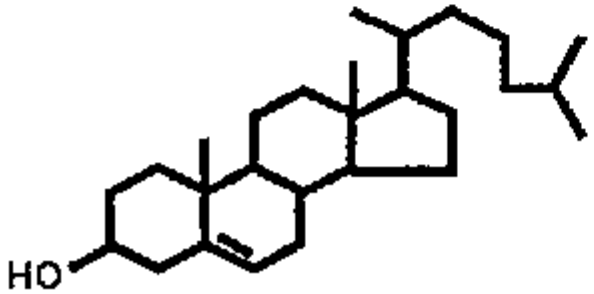


Phospholipase A2

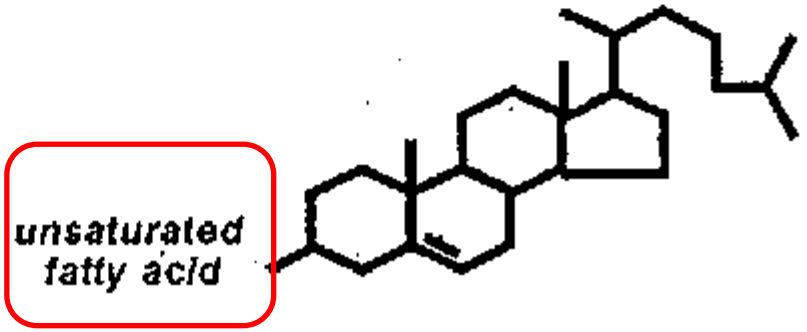
LCAT

Transacylase

CHOLESTEROL



CHOLESTERYL ESTER

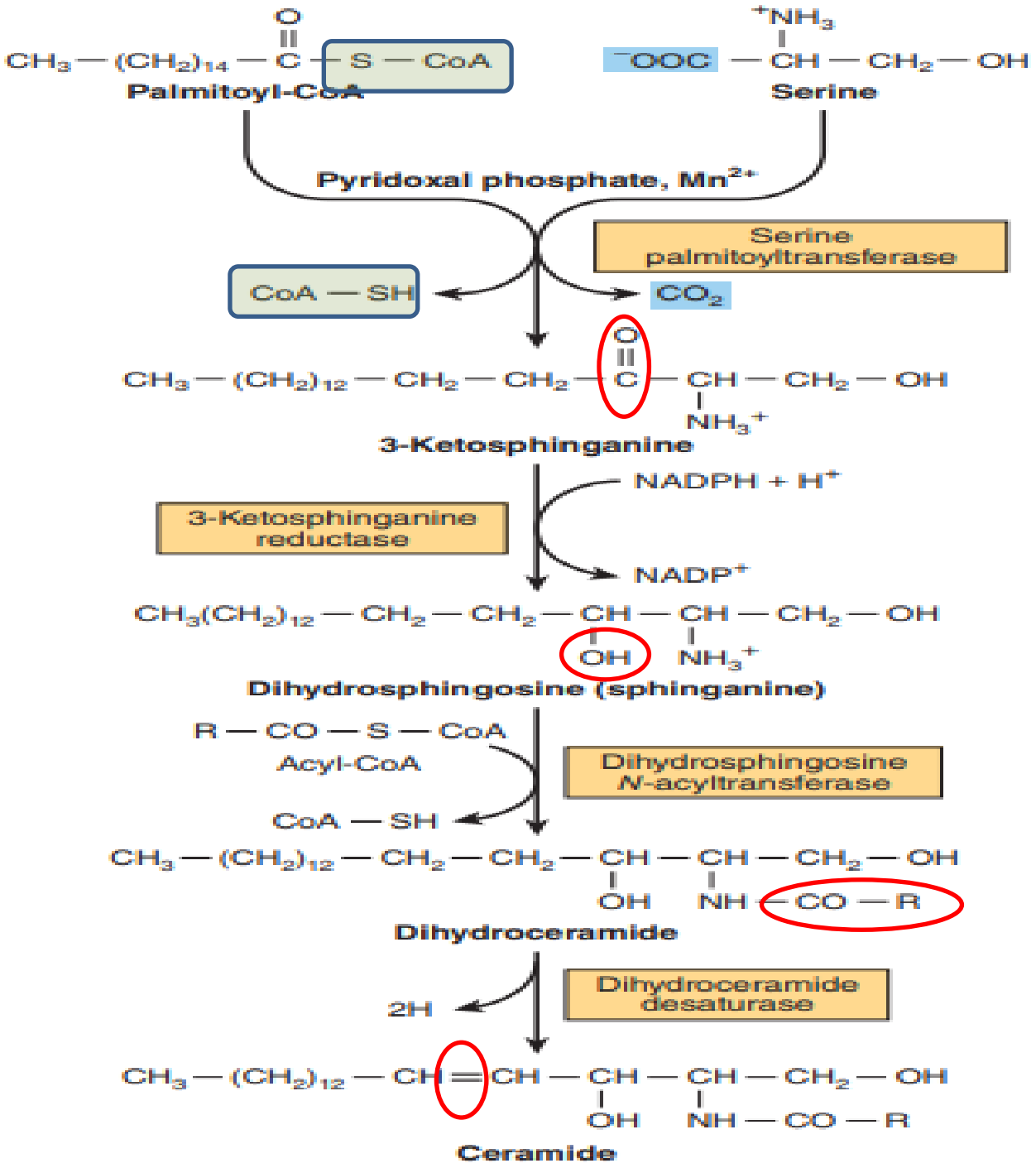


The incorporation of fatty acids into lecithin occurs in three ways

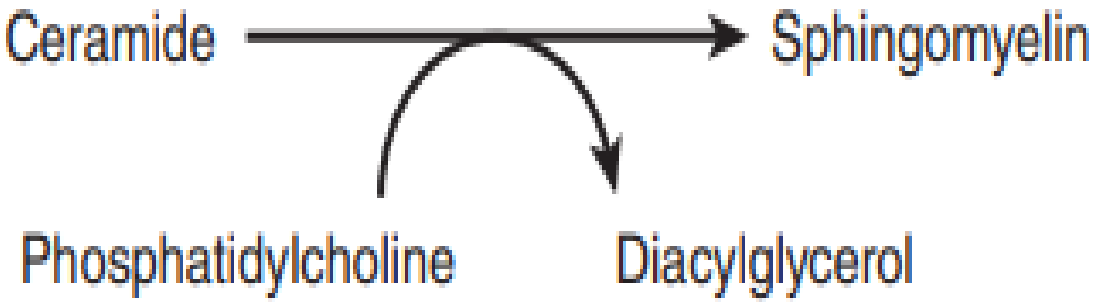
- by complete synthesis of the phospholipid.
- by transacylation between cholesteryl ester and lysolecithin.
- by direct acylation of lysolecithin by acyl-CoA.

Thus, a continuous exchange of the fatty acids is possible, particularly with regard to introducing essential fatty acids into phospholipid molecules.

- **Ceramide** is synthesized in the **endoplasmic reticulum** from the amino acid **serine.** Ceramide is an important
- signaling molecule (second messenger)
- **(apoptosis)** programmed cell death
- **cell cycle**
- **cell differentiation and senescence.**

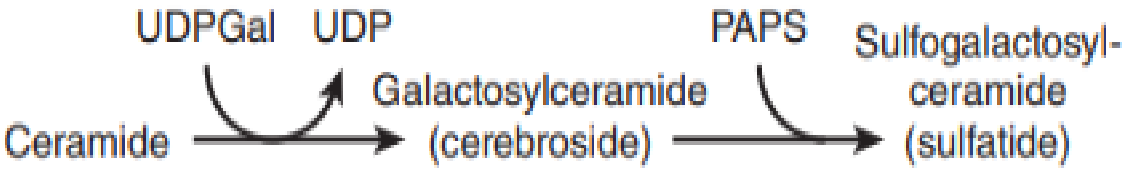

Palmitoyl-CoA
Serine
Pyridoxal phosphate, Mn2+
Serine palmitoyltransferase
CoA — SH
CO2
3-Ketosphinganine
NADPH + H+
3-Ketosphinganine reductase
NADP+
Dihydrosphingosine (sphinganine)
R — CO — S — CoA
Acyl-CoA
Dihydrosphingosine N-acyltransferase
CoA — SH
Dihydroceramide
2H
Dihydroceramide desaturase
Ceramide

Sphingomyelins



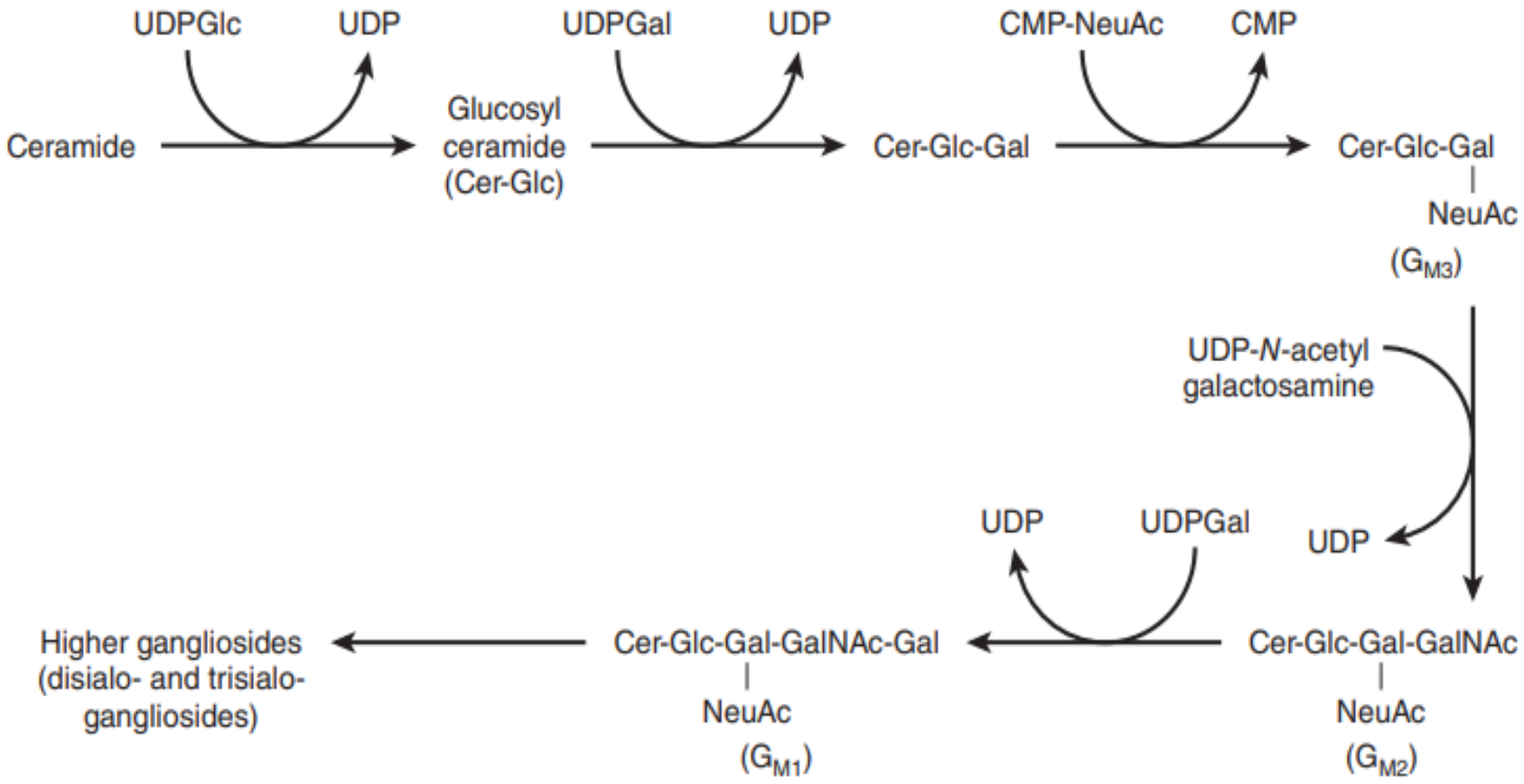
Glycosphingolipids

- The simplest glycosphingolipids **(cerebrosides)** are **galactosylceramide (GalCer)** and is a major lipid of **myelin.**



Glycosphingolipids

- whereas GlcCer is the major glycosphingolipid of **extraneural tissues** and a precursor of most of the more complex glycosphingolipids
- **Gangliosides** are synthesized from ceramide by the stepwise addition of activated sugars (eg, UDPGlc and UDPGal) and a **sialic acid,** usually *N*-acetylneuraminic acid . A large number of gangliosides of increasing molecular weight may be formed. Most of the enzymes transferring sugars from nucleotide sugars (glycosyl transferases) are found in the Golgi apparatus.


UDPGlc
UDP
Ceramide
Glucosyl ceramide (Cer-Glc)
UDPGal
UDP
Cer-Glc-Gal
CMP-NeuAc
CMP
Cer-Glc-Gal
NeuAc
(G_{M3})
UDP-*N*-acetyl galactosamine
UDP
UDP
UDPGal
Cer-Glc-Gal-GalNAc
NeuAc
(G_{M2})
Cer-Glc-Gal-GalNAc-Gal
NeuAc
(G_{M1})
Higher gangliosides (disialo- and trisialo-gangliosides)