
بسم الله الرحمن الرحيم

Neurosciences Module

2nd Year MBBS (2022-2023)

Phospholipids Synthesis And Degradation

Biochemistry

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By the end of this lecture we will be able to know-

- Lipid definition , classification
- Phospholipids , types , chemical structure
- Biomedical importance
- Synthesis and degradation
- Sphingomyelin lipidosis


KEEP
CALM
AND
ACTIVATE PRIOR
KNOWLEDGE

LIPIDS

Chemically they are various types of esters of different alcohols.

In addition to alcohol and fatty acids, some of the lipids may contain phosphoric acid, nitrogenous base and carbohydrates.

CLASSIFICATION OF LIPIDS

L. Simple Lipids

II. Compound Lipids: (Phospholipids)

III. Derived Lipids

(a) phospholipids: They have fatty acid , glycerol, a phosphoric acid, a nitrogenous base and other substituents.

Examples:

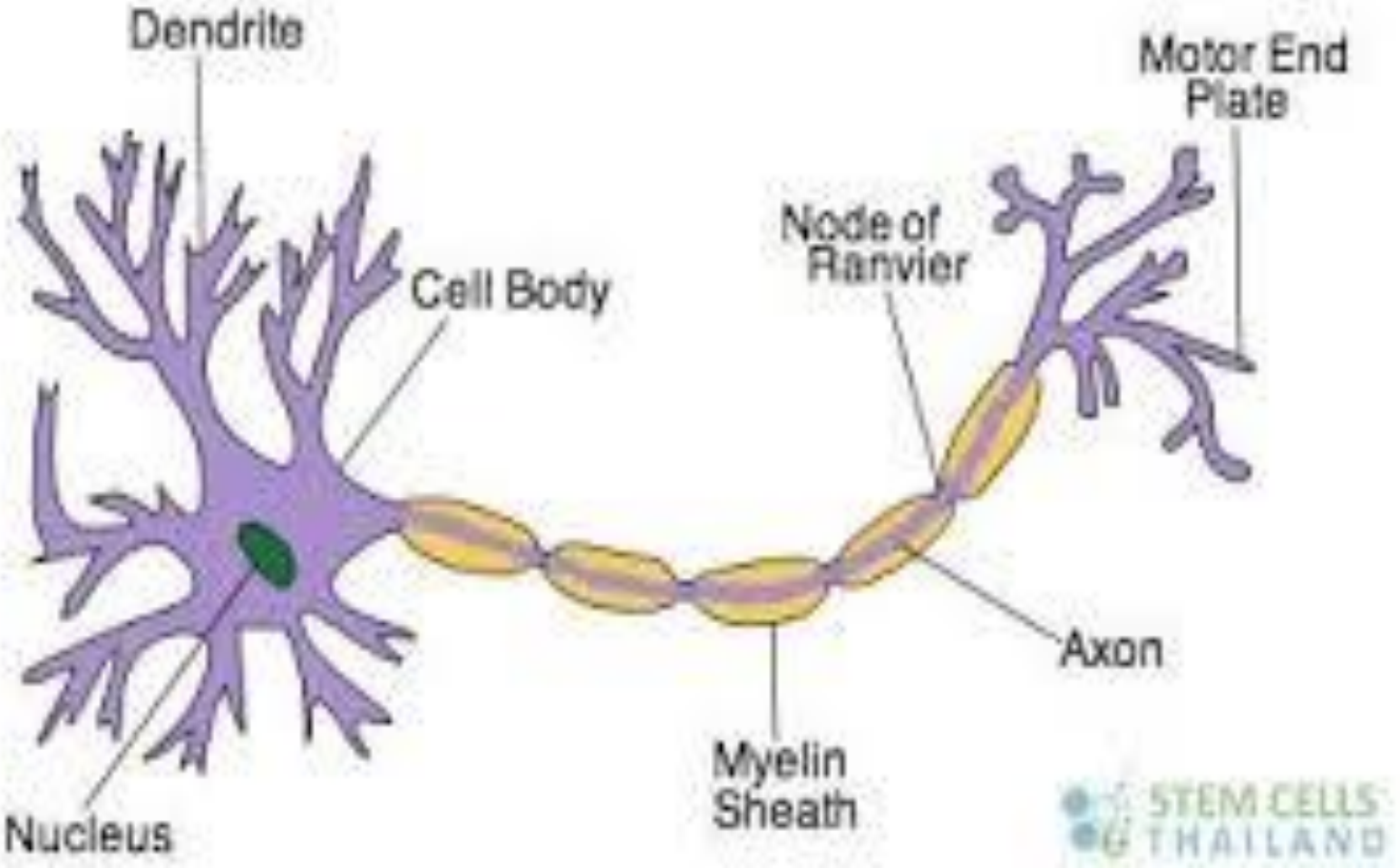
- **Lecithin,**
- **inositols** ,
- **serine,**
- **Cardiolipin,**
- **Plasmalogens and PAF,**
- **sphingomyelins**.

BIOMEDICAL IMPORTANCE

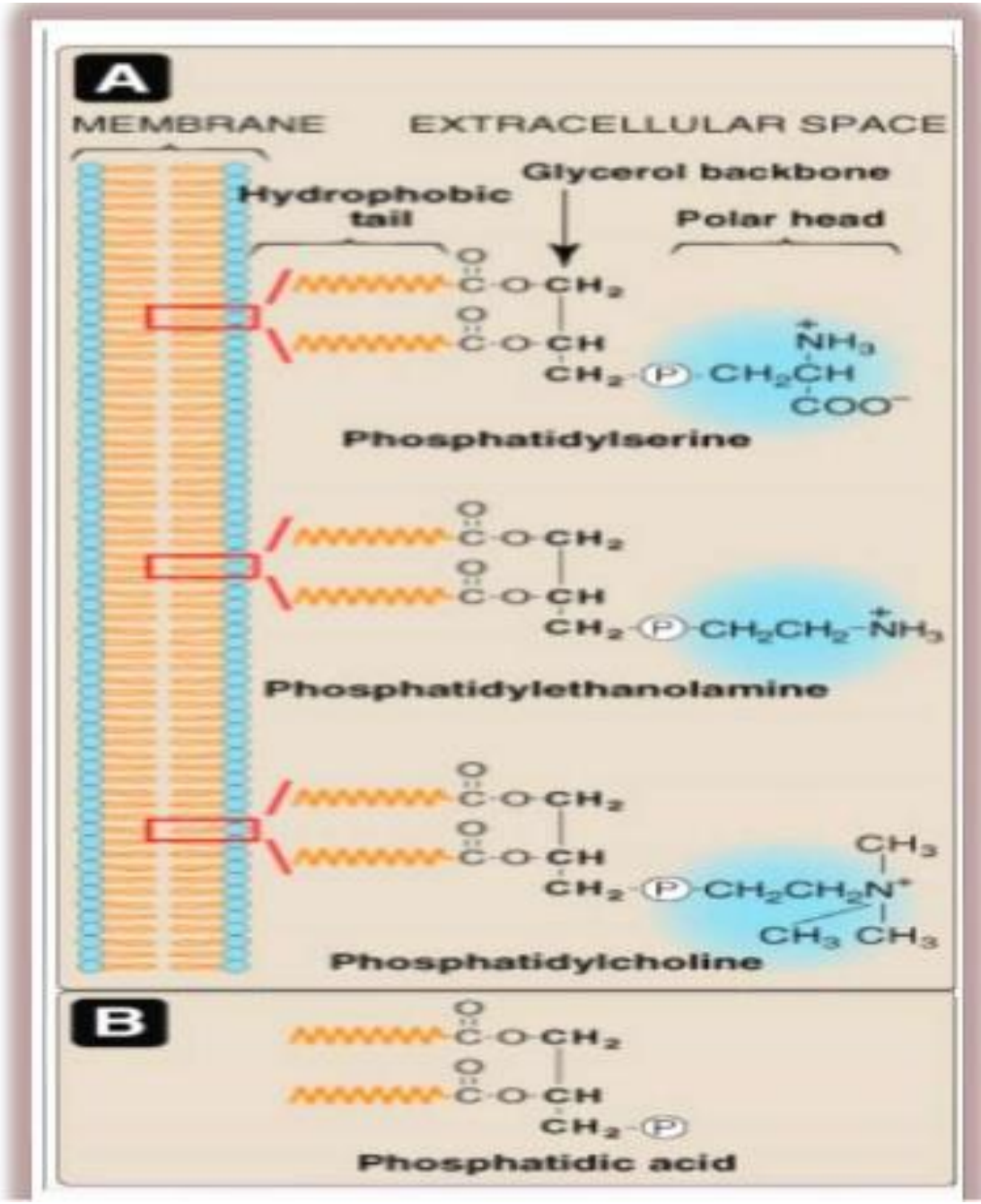
- Lipids are important dietary fuel in the body.
- Can be stored in the body in almost unlimited amount.
- Some deposits exert an insulating effect.
- May provide padding and protect the organs.
- Necessary for vitamins like A, D, E and K.
- Constituents of many natural membranes.
- Lipoproteins act as carriers.
- building biological active materials.
- Essential fatty acids.
- Nervous system is particularly rich in lipids.


THE ADVENTURES of
NED THE NEURON

Structure of a Neuron



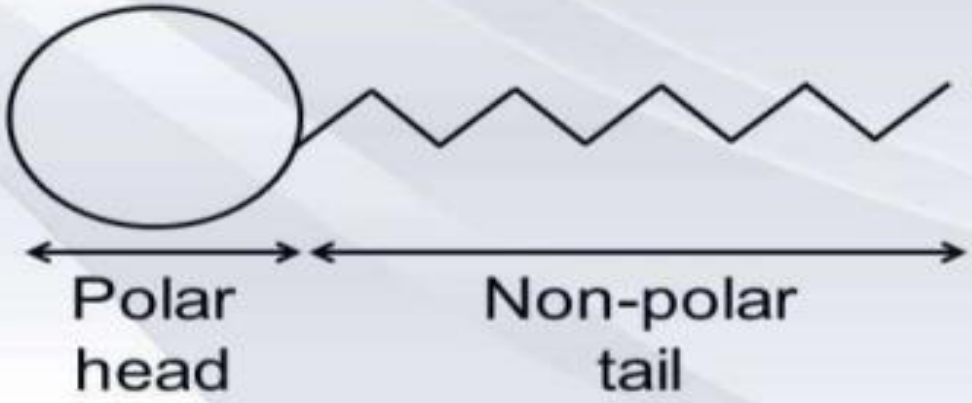
Phosphilipids



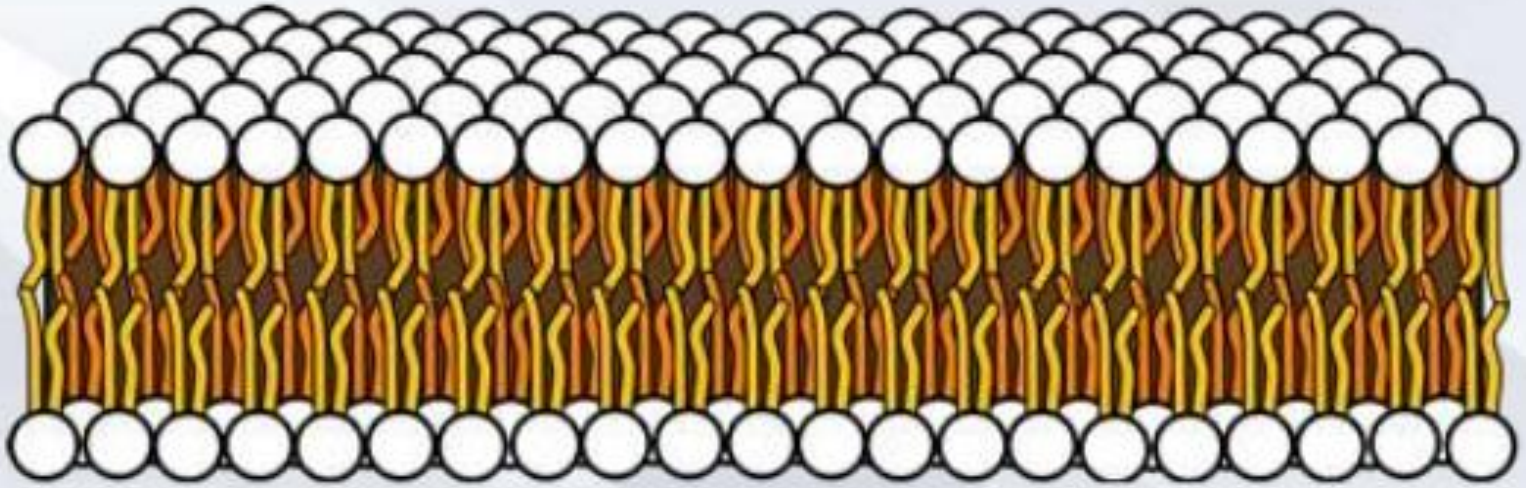
PHOSPHOLIPIDS

Phospholipids are amphipathic

A part of the molecule is polar and a part non-polar



Amphipathic lipids can form bilayers since non-polar tails attract each other



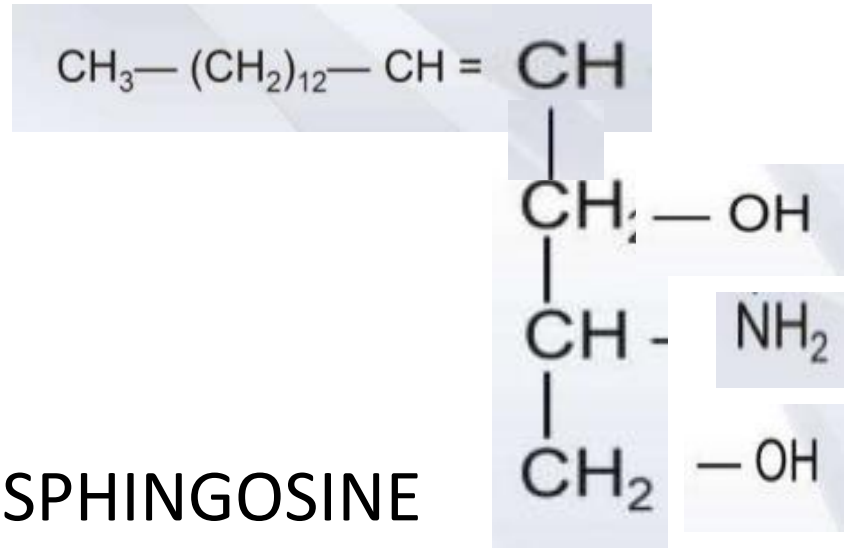
Lipid bilayers constitute the basic structure of membranes

PHOSPHOLIPIDS

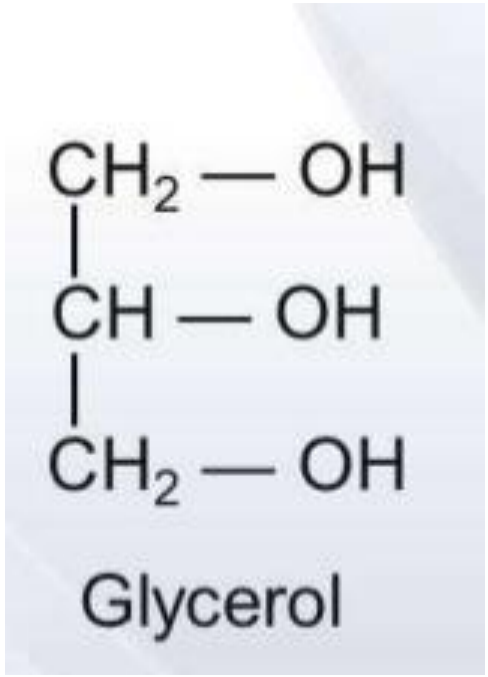
Phospholipids include: (i) glycerophospholipids and (ii) sphingophospholipids

In glycerophospholipids, the alcohol is glycerol

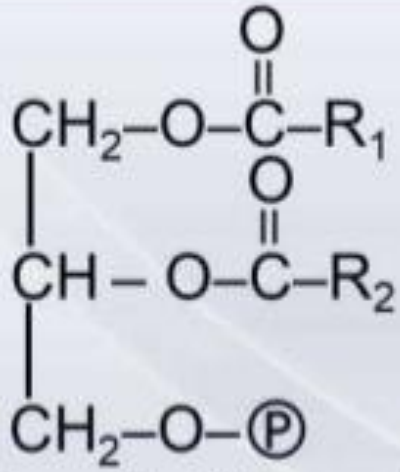
In sphingophospholipids, the alcohol is sphingosine



SPHINGOSINE



Glycerophospholipids may be considered to be derivatives of phosphatidic acid

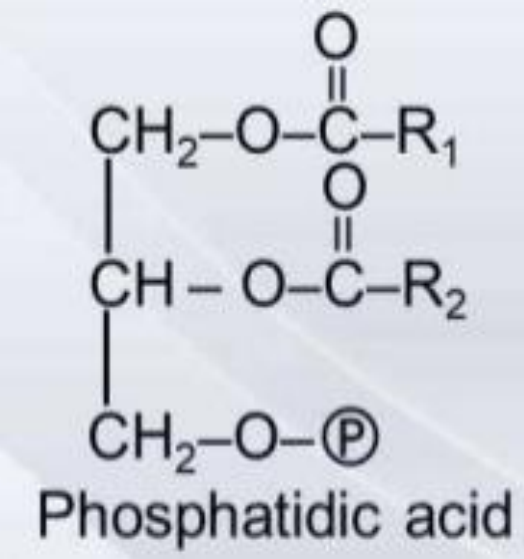


Phosphatidic acid

Phosphatidic acid is 1,2-Diacylglycerol-3-phosphate

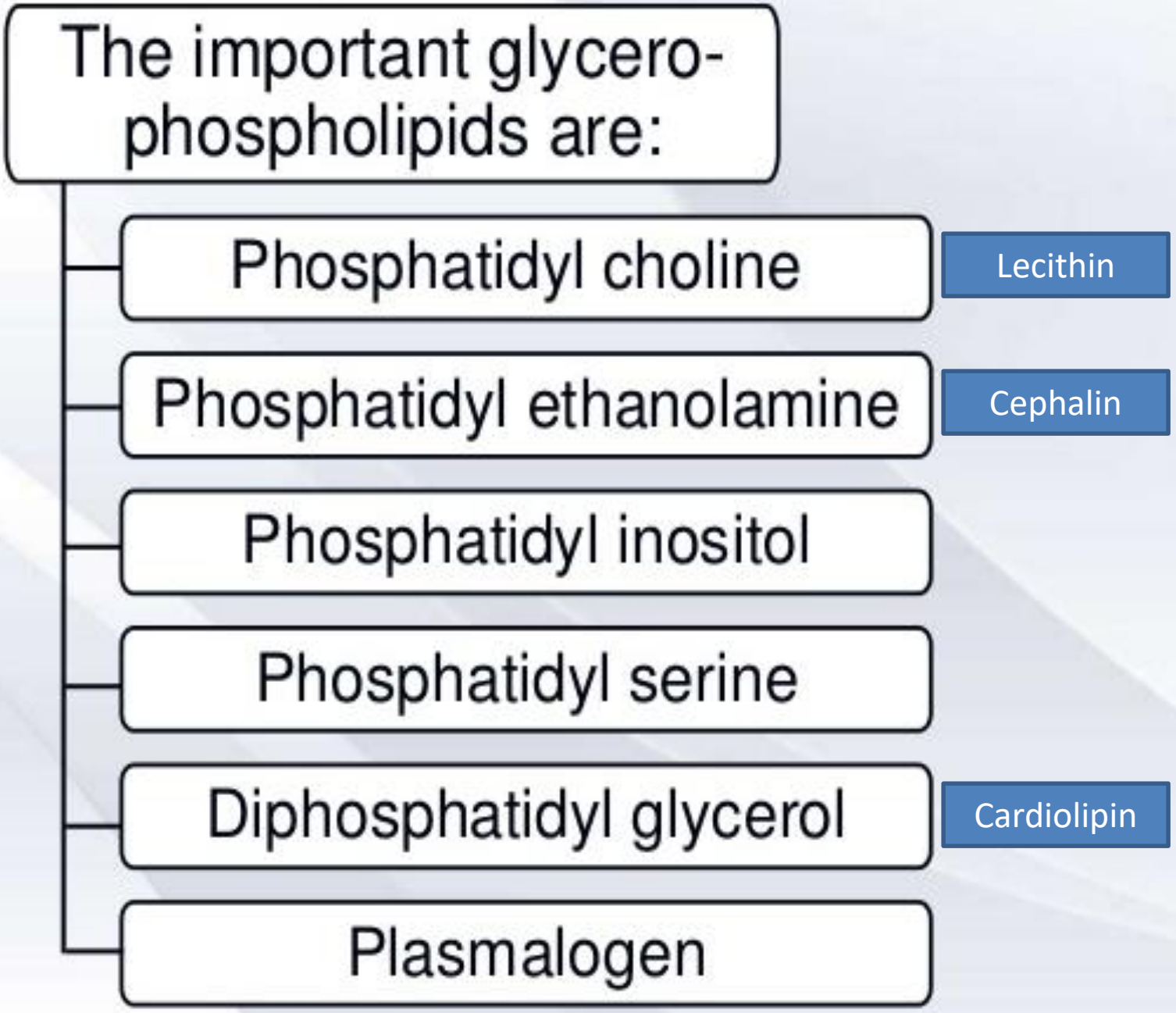
The glycerophospholipids generally have:

- A saturated fatty acid at position 1
- An unsaturated fatty acid at position 2



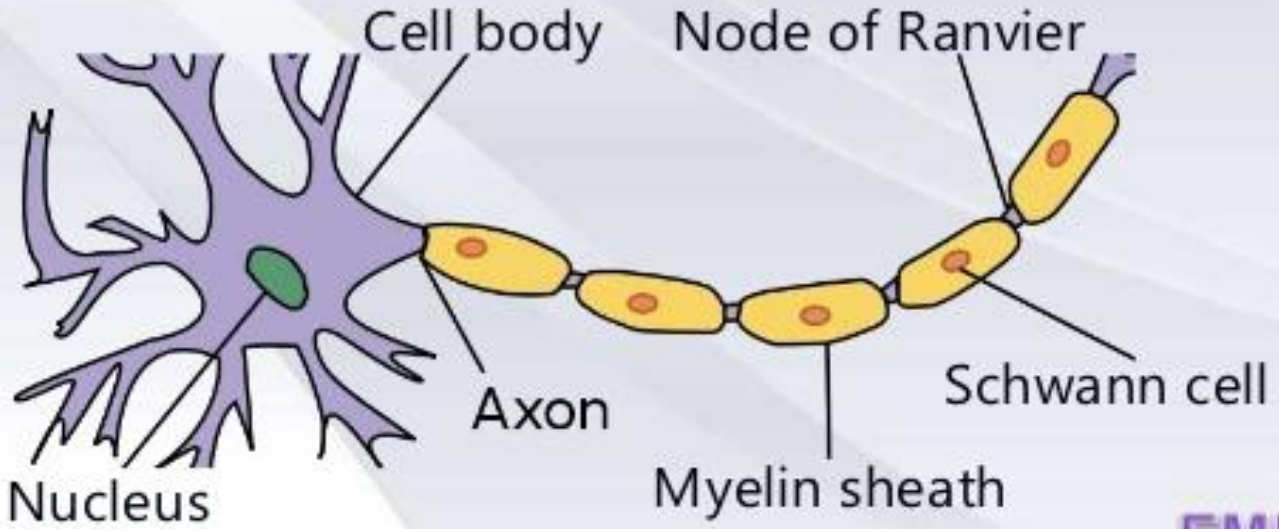
Phosphatidic acid

The fatty acids at position 1 and position 2 are in a continuous state of flux


The important glycero-phospholipids are:
Phosphatidyl choline
Lecithin
Phosphatidyl ethanolamine
Cephalin
Phosphatidyl inositol
Phosphatidyl serine
Diphosphatidyl glycerol
Cardiolipin
Plasmalogen

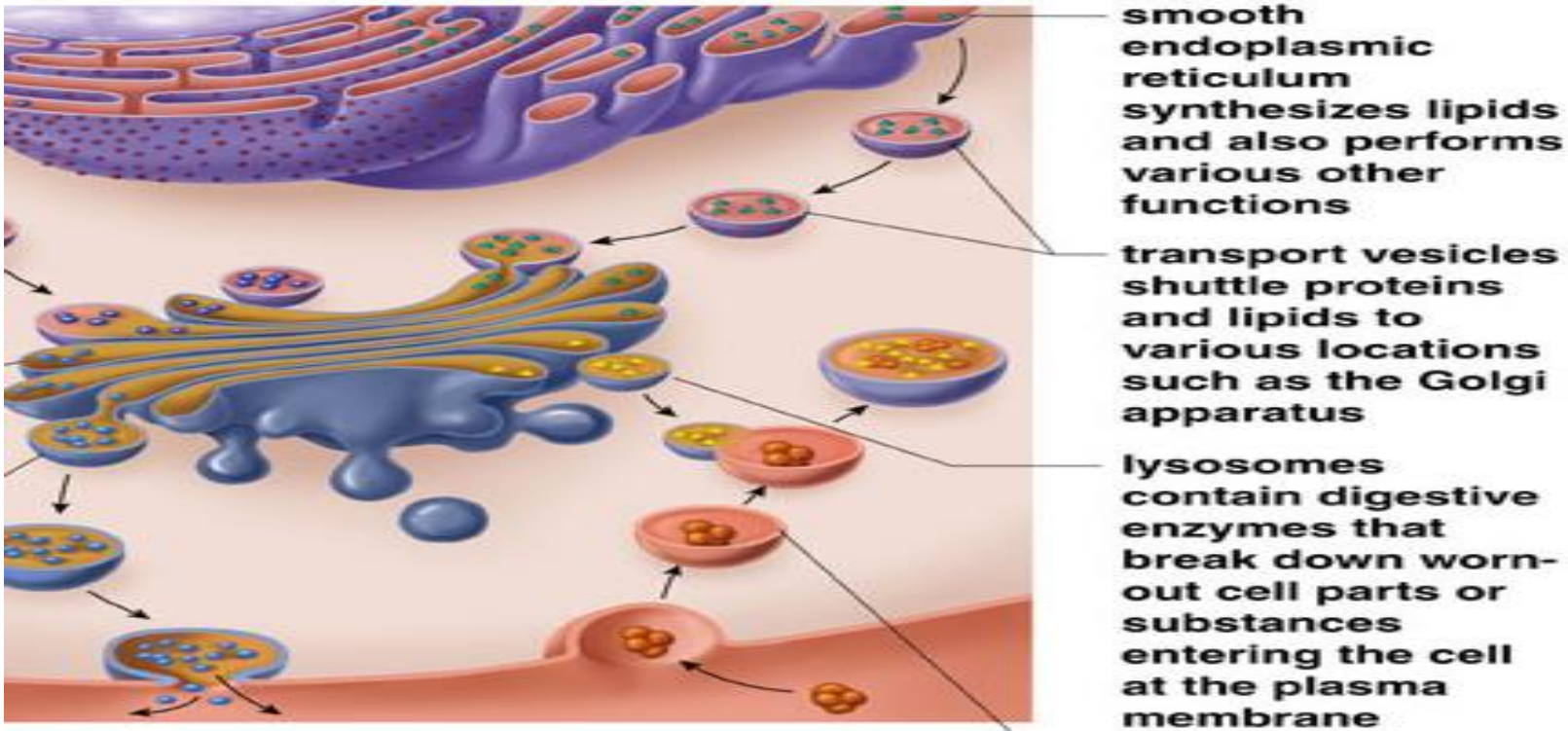
The only phosphosphingolipid is sphingo-myelin

Sphingomyelin is found predominantly in myelin sheath

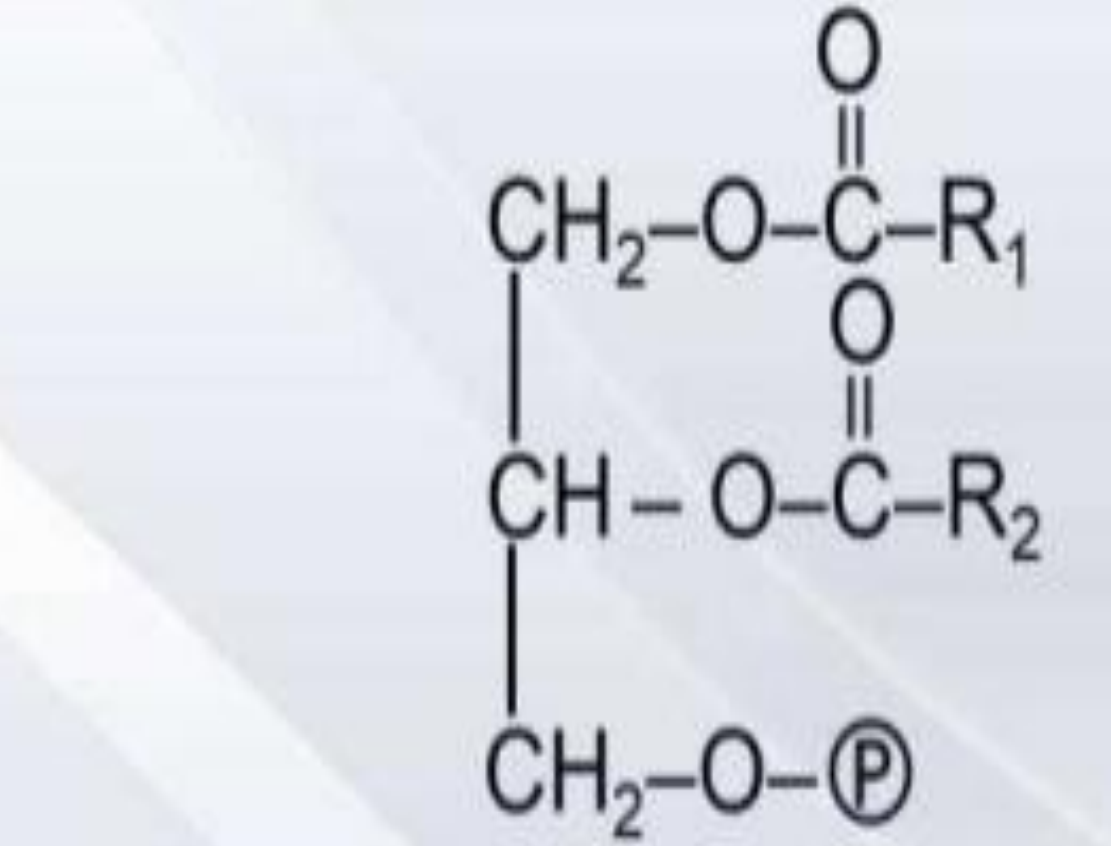


SYNTHESIS OF PHOSPHOLIPIDS

- Mostly phospholipids are synthesized in the smooth endoplasmic reticulum (ER). From there, they are transported to the Golgi apparatus and then to membranes of organelles or the plasma membrane and secreted from the cell by exocytosis.

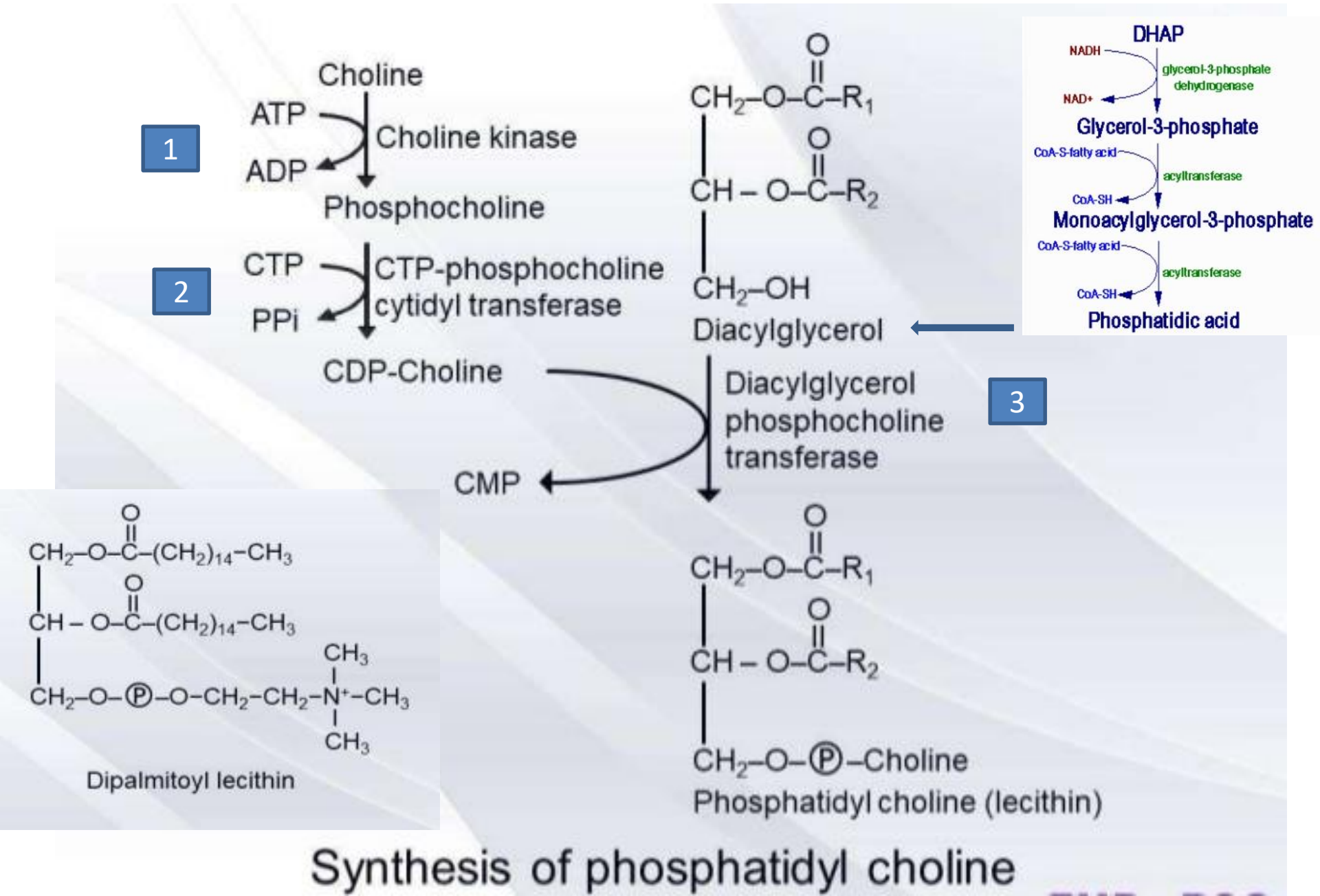


Phosphatidic acid



Phosphatidic acid

Lecithin synthesis



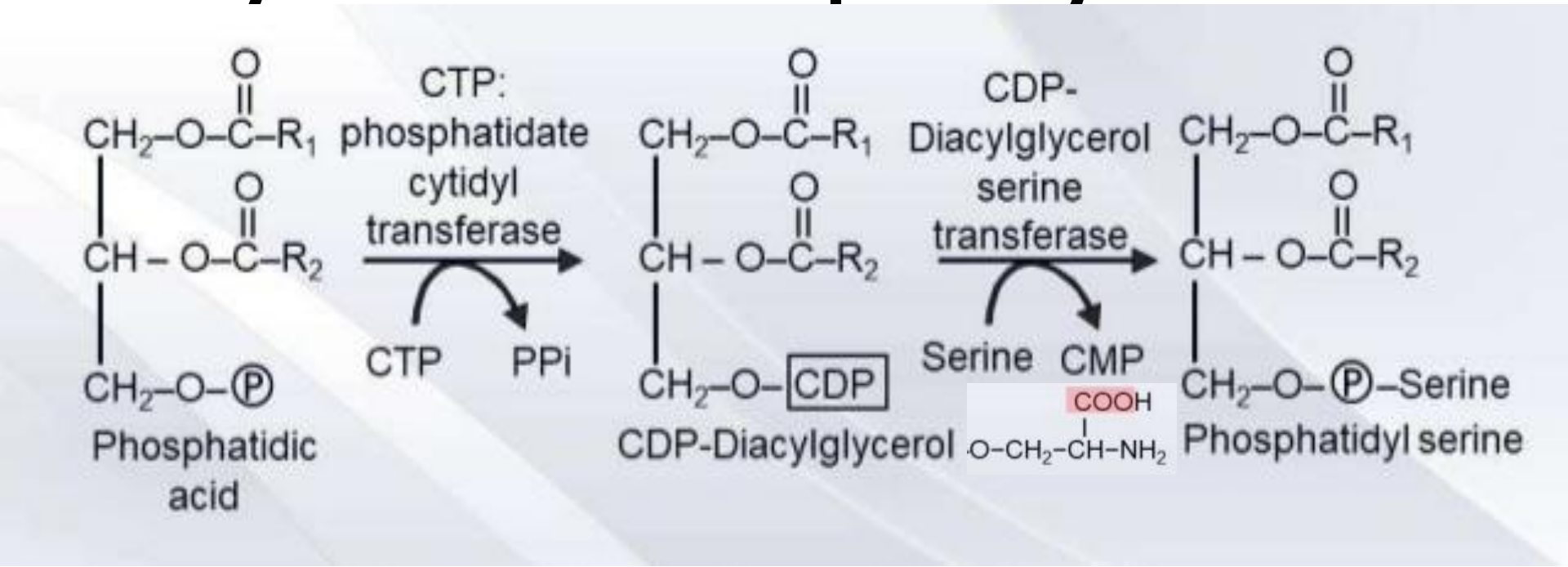
Synthesis of phosphatidyl choline

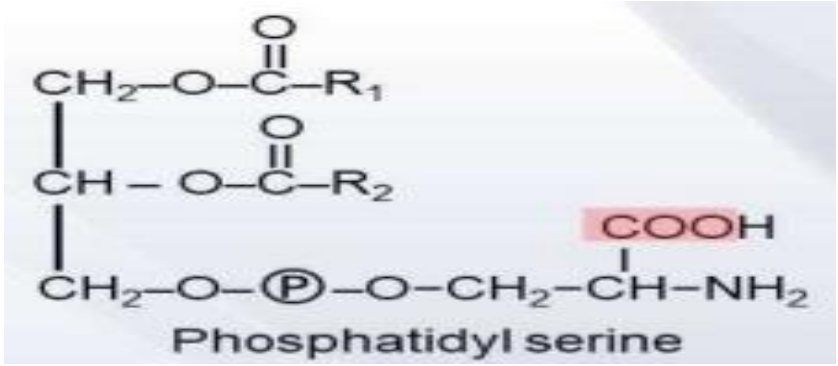
Dipalmitoyl lecithin has palmitate at both position 1 and position 2

Dipalmitoyl lecithin is a component of lung surfactant

Lung surfactant lowers surface tension at the air/liquid interface in the alveoli

Synthesis of Phosphatidyl Serine



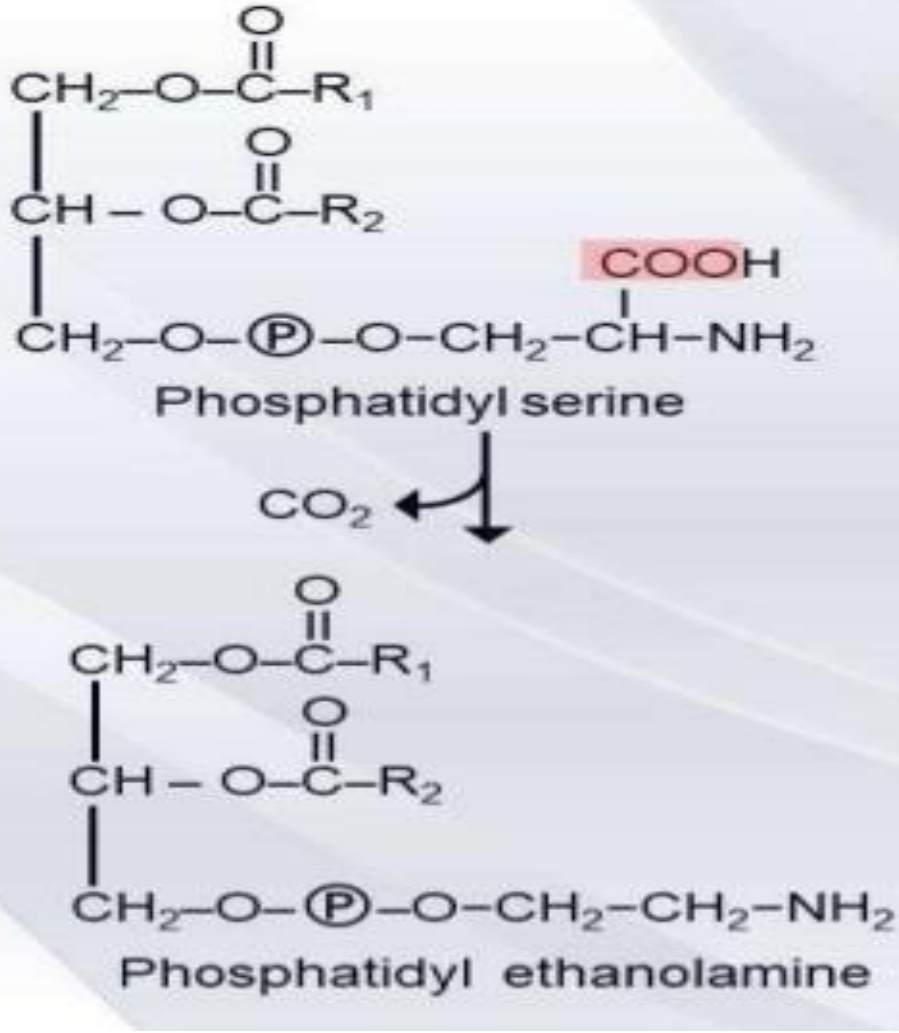


Glycerophospholipids can undergo inter-conversion

Serine residue of phosphatidyl serine can be decarboxylated to ethanolamine

This converts phosphatidyl serine into phosphatidyl ethanolamine

Phosphatidyl Ethanolamine synthesis



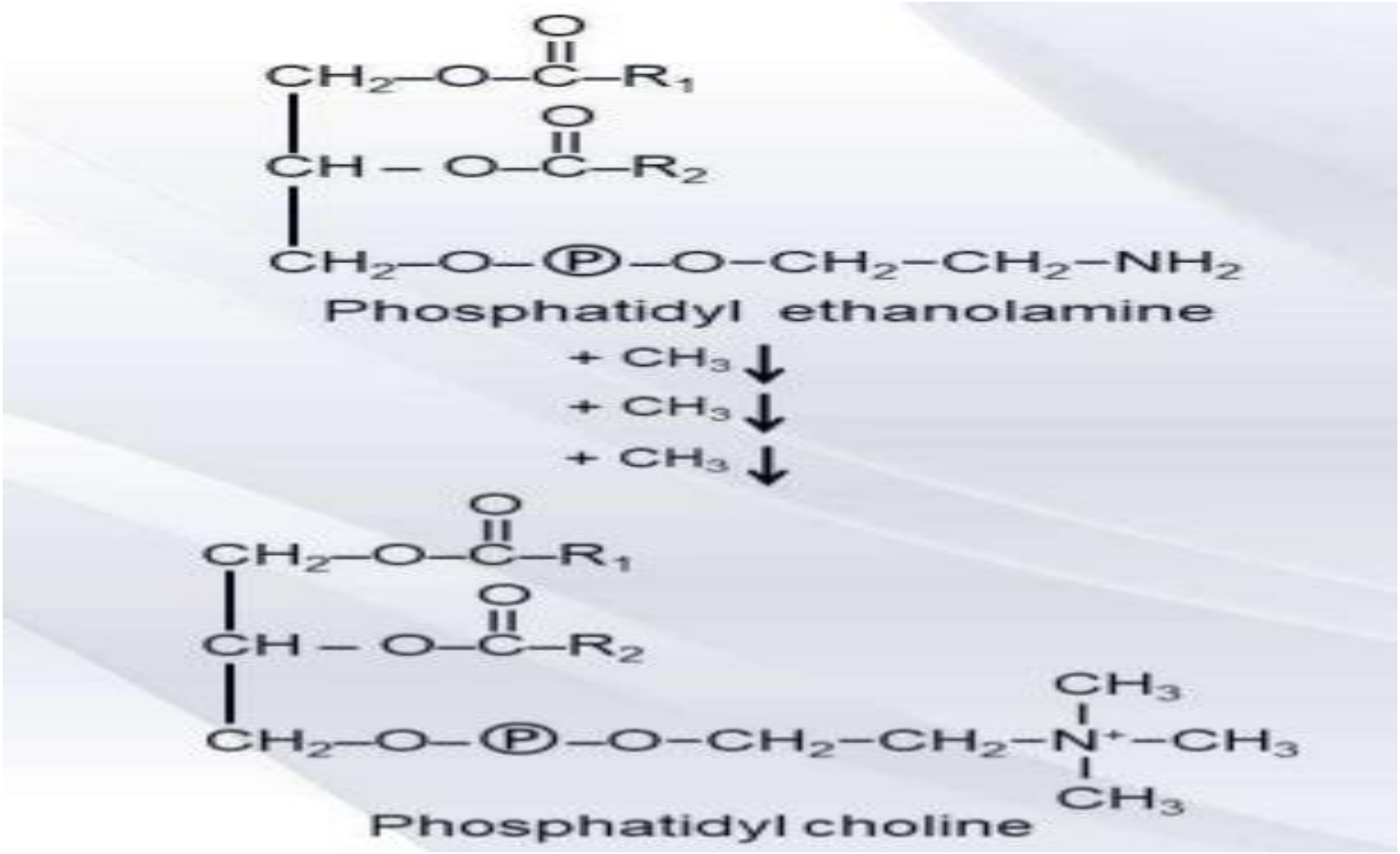
Conversion of phosphatidyl ethanolamine into choline

Ethanolamine residue of phosphatidyl ethanolamine can be methylated

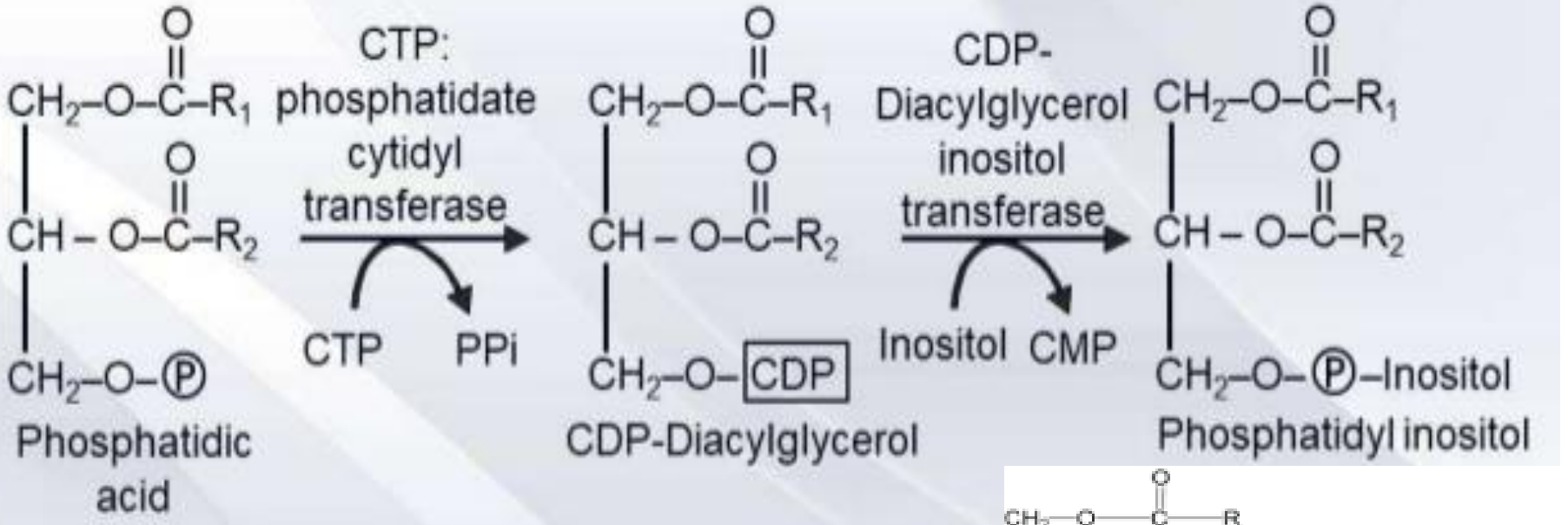
Addition of three methyl groups converts ethanolamine into choline

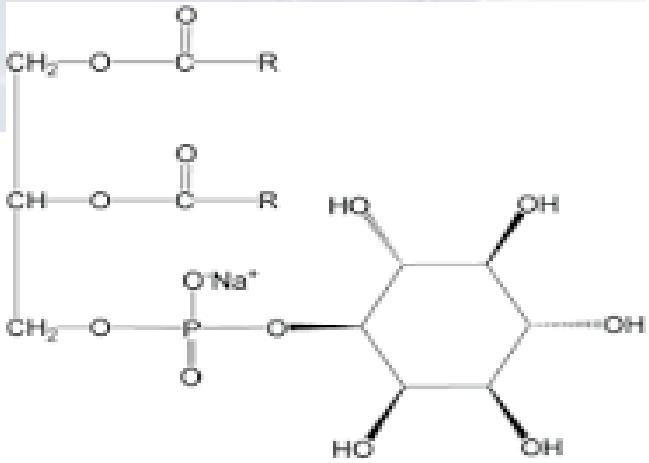
Thus, phosphatidyl choline can be formed from phosphatidyl ethanolamine

Conversion of phosphatidyl ethanolamine into choline



Synthesis of phosphatidyl inositol





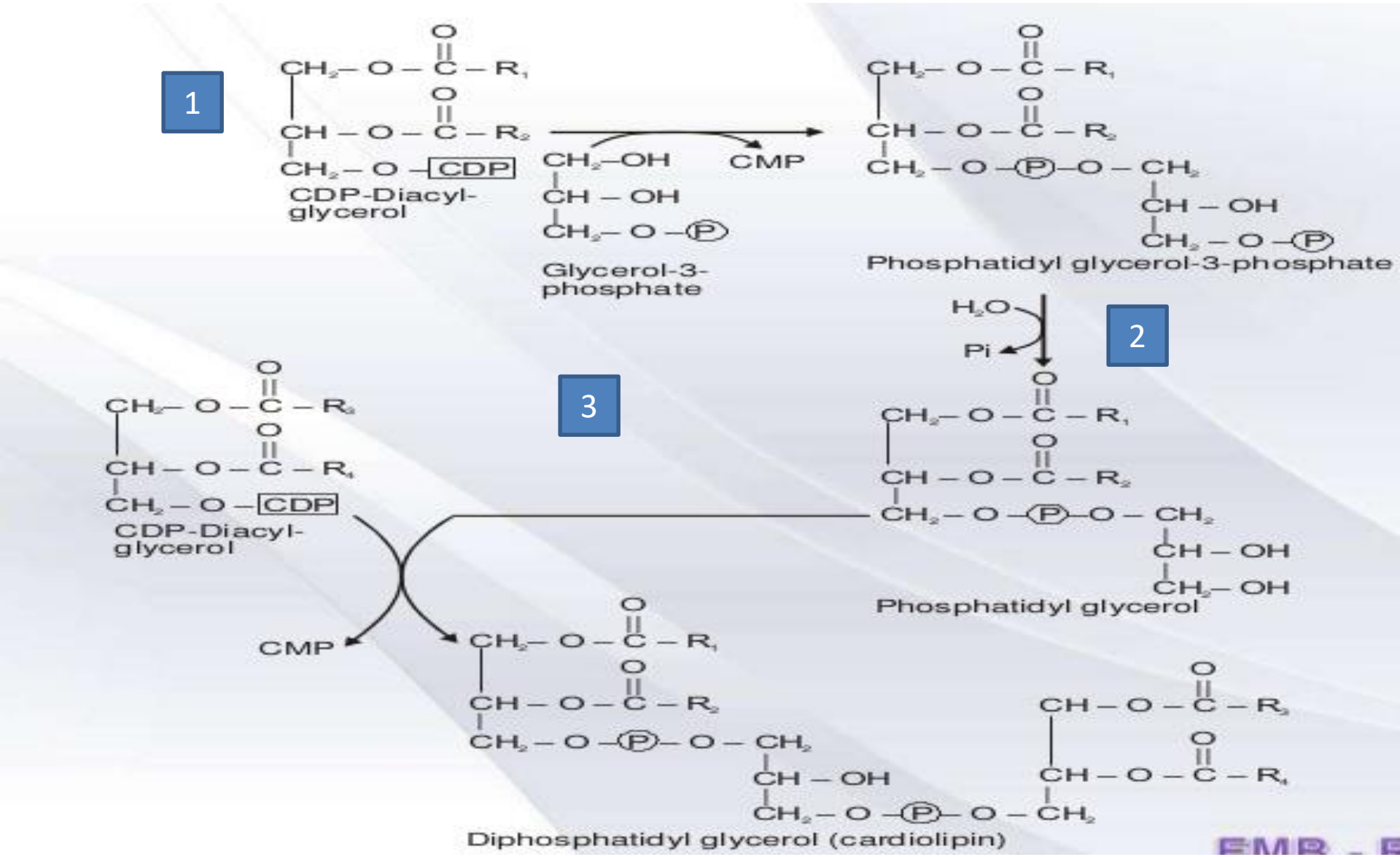
Synthesis of cardiolipin

Cardiolipin is diphosphatidyl glycerol

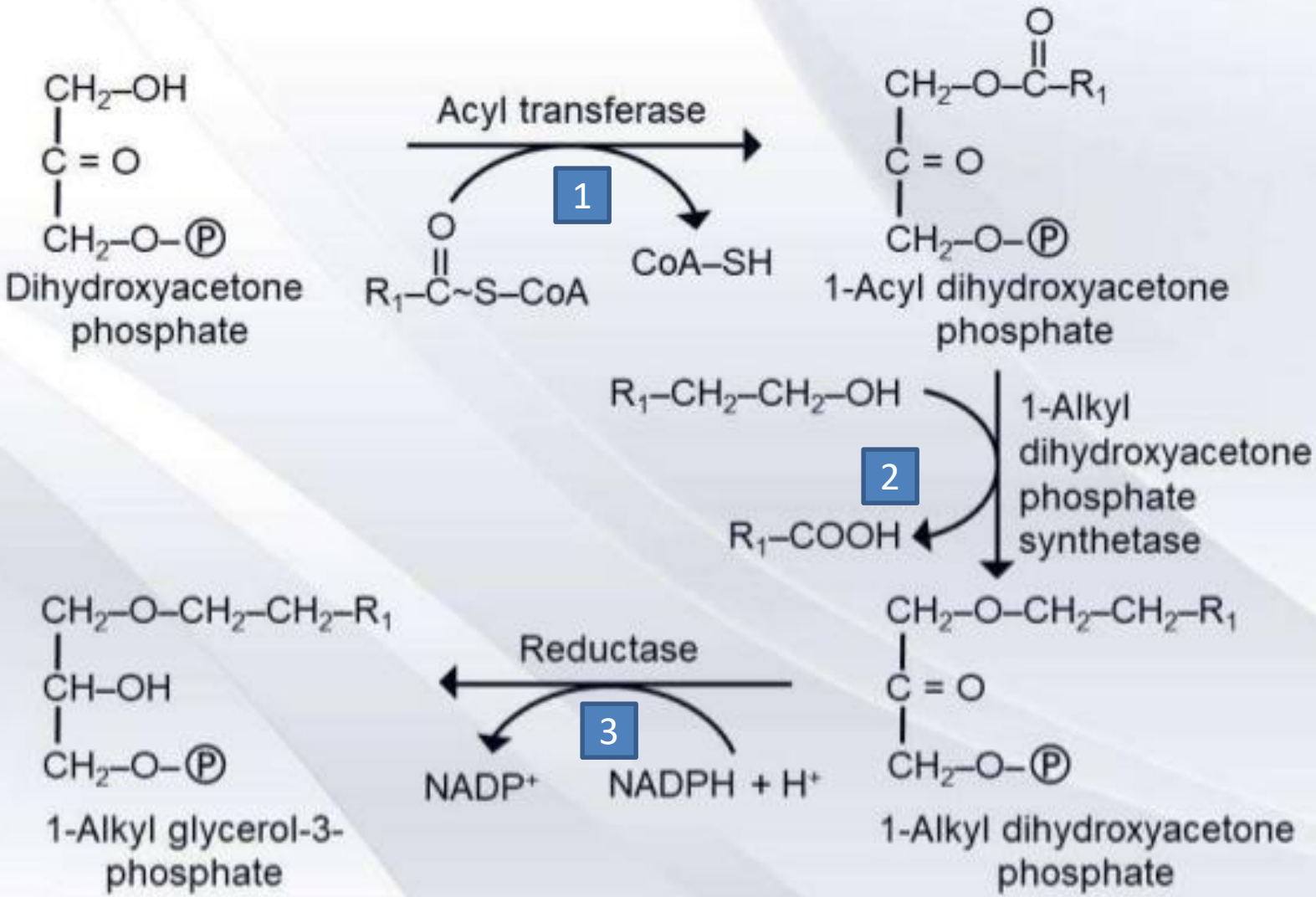
It is found only in mitochondria where it is synthesized from:

- Two molecules of CDP-diacylglycerol
- One molecule of glycerol-3-phosphate

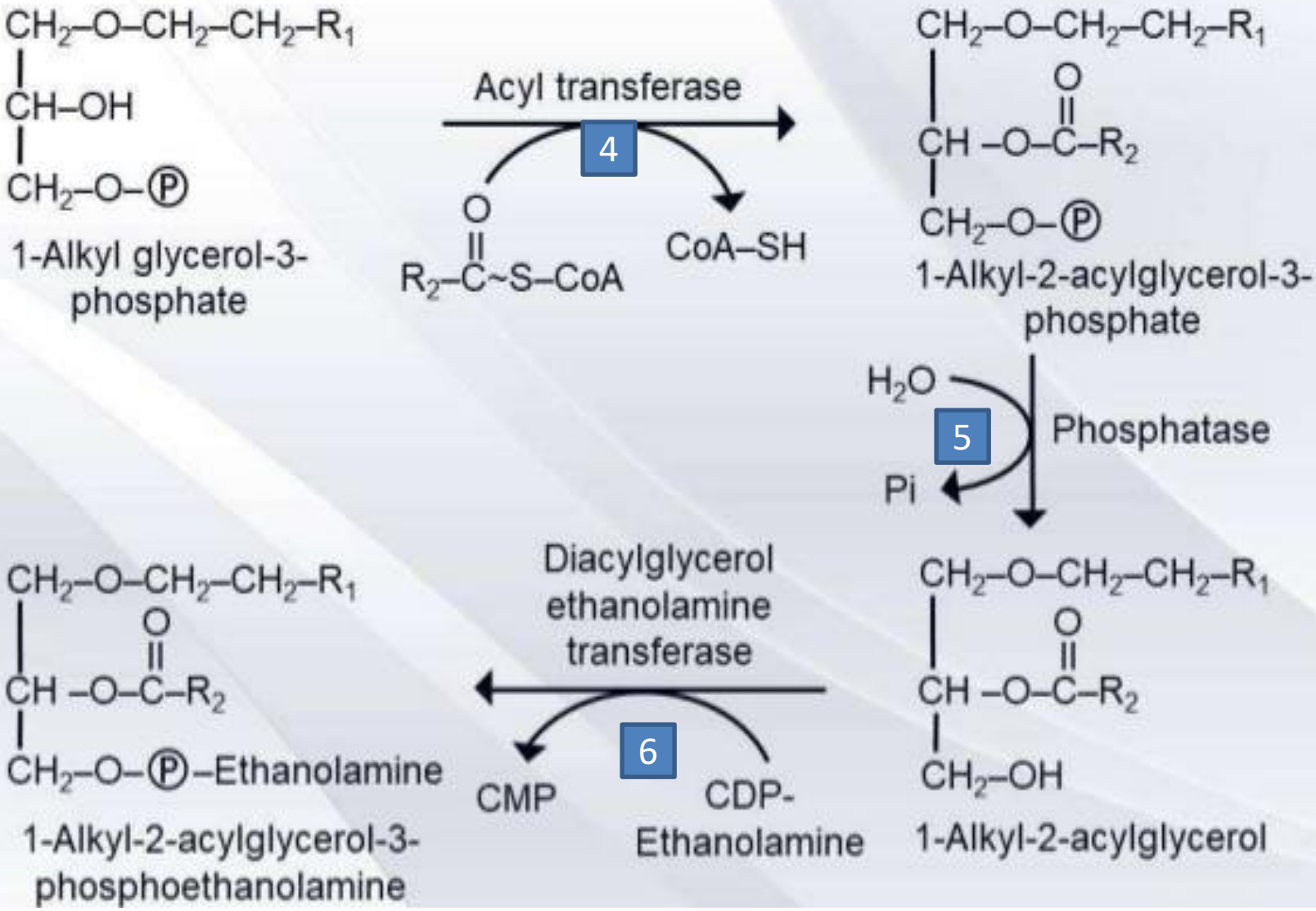
Synthesis of cardiolipin



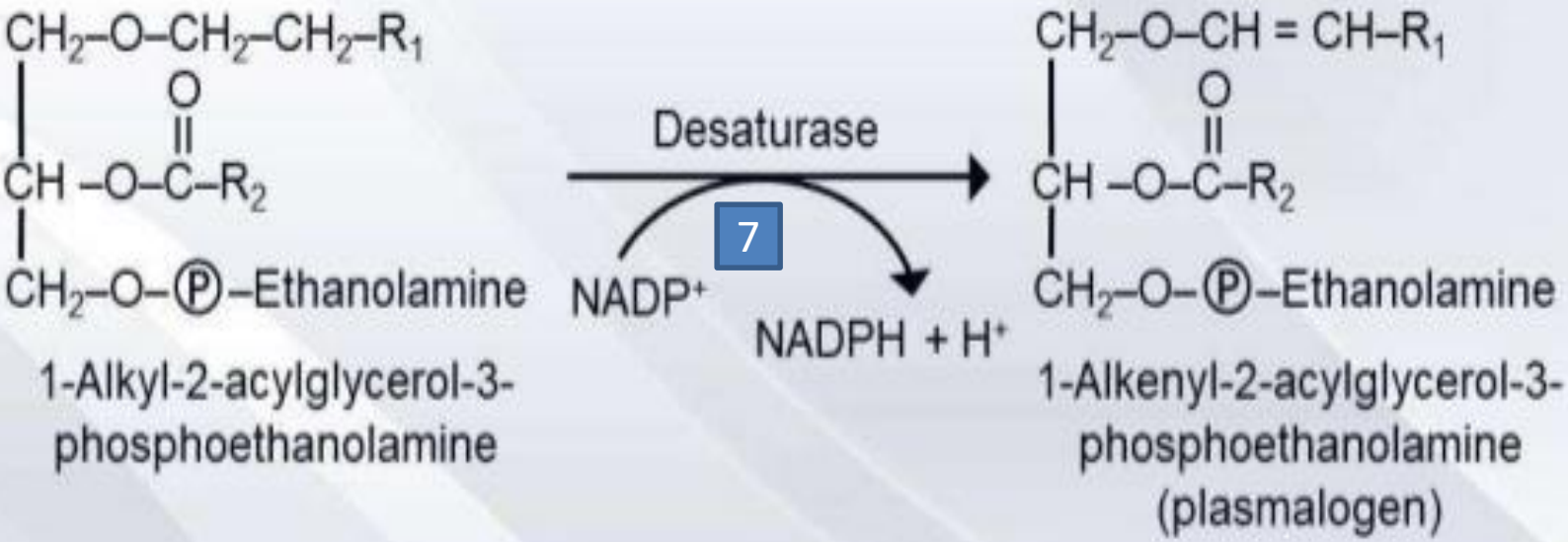
Synthesis of plasmalogen



Synthesis of plasmalogen



Synthesis of plasmalogen



Synthesis of plasmalogen

In some plasmalogens, ethanolamine is replaced by choline or serine

Ethanolamine plasmalogen is present in myelin

Choline plasmalogen is abundant in cardiac tissue

Serine plasmalogen is present in retina and white matter

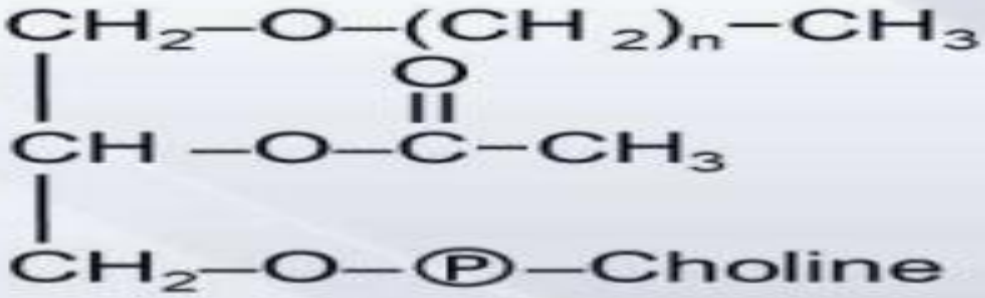
PAF

Platelet activating factor (PAF) is a specific type of plasmalogen

It has an alkyl group (generally 16-carbon) at position 1

The acyl group at position 2 is acetate

Phosphocholine is present at position 3



1-Alkyl-2-acetylglycerol-3-phosphocholine
(platelet activating factor)

PAF is released by several types of cells in response to a variety of stimuli

It is a very powerful chemical mediator

It mediates inflammatory reaction, hypersensitivity and anaphylactic shock

PAF causes platelet aggregation, vasodilatation and bronchoconstriction

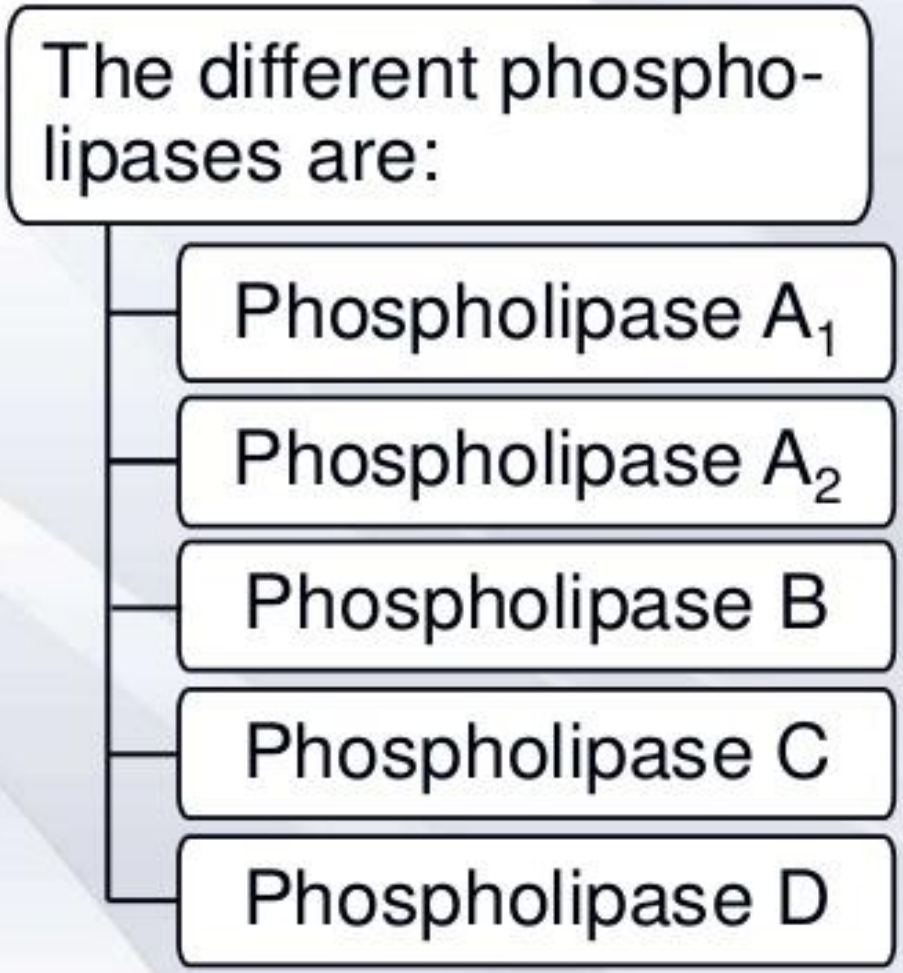
Catabolism of glycerophospholipids

Glycerophospholipids are hydrolysed by phospholipases

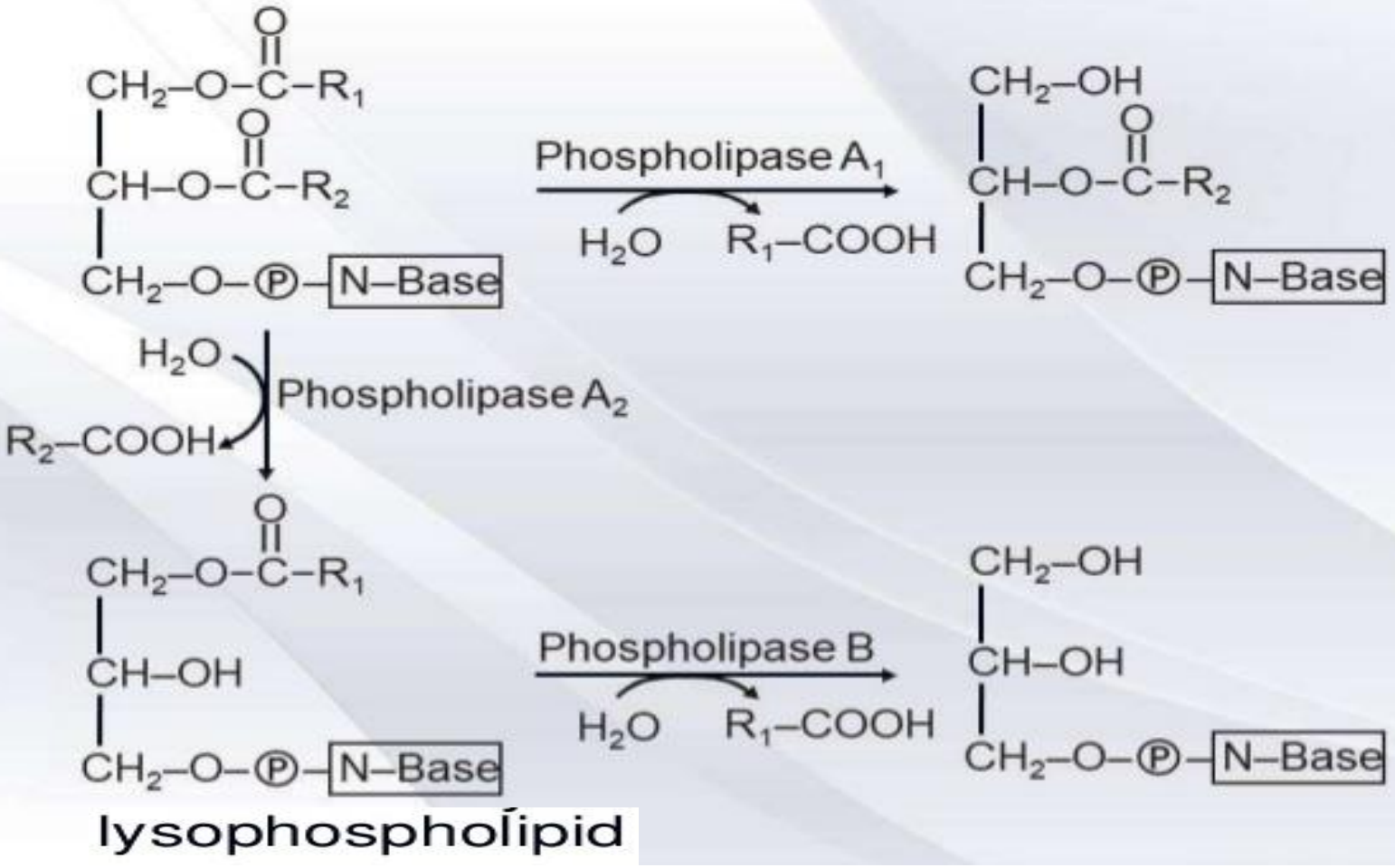
There are several different phospholipases

Each phospholipase acts on a specific bond

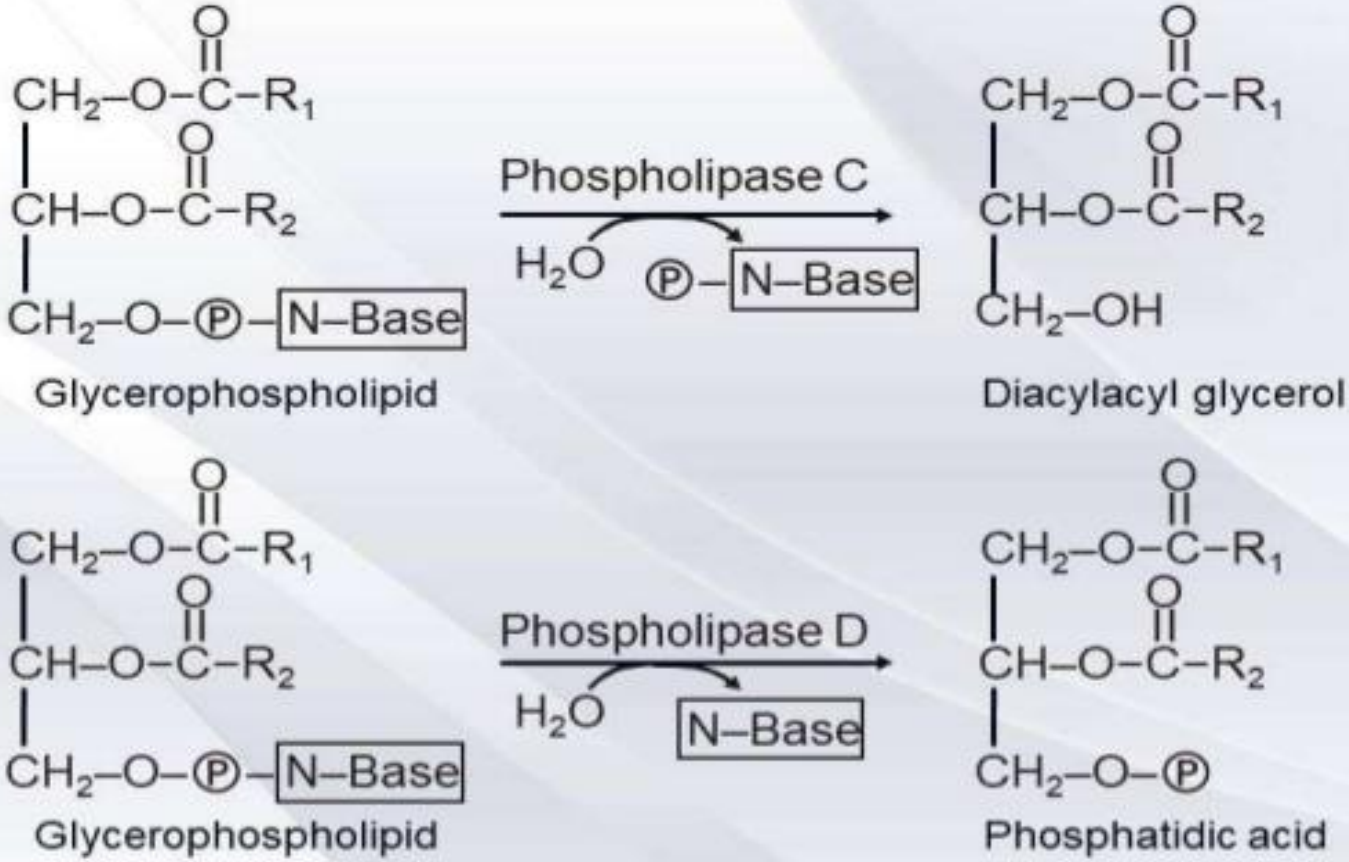
ENZYMES INVOLVED



ENZYMES INVOLVED



ENZYMES INVOLVED

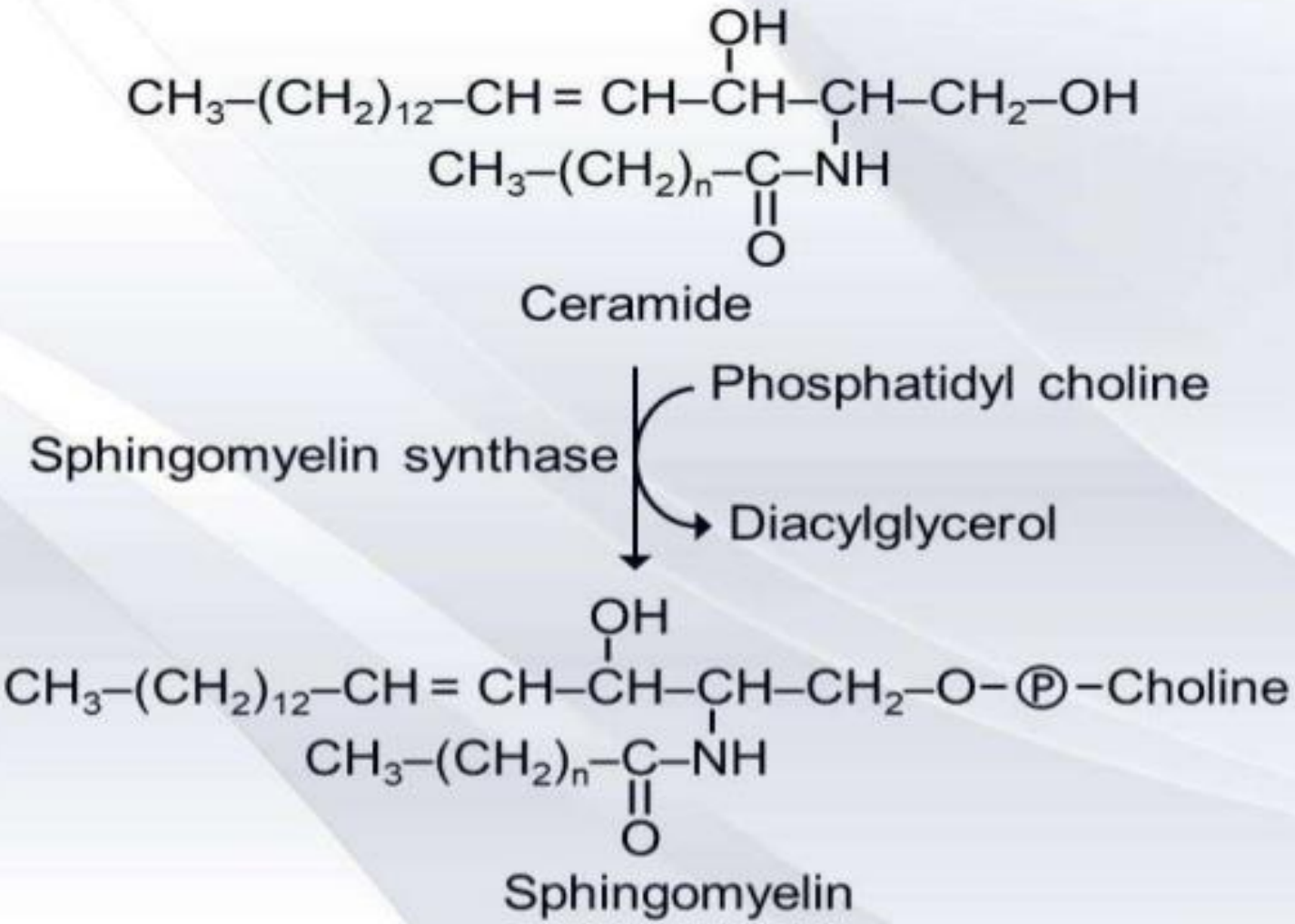


Synthesis of sphingomyelin

Sphingomyelin is synthesized from ceramide and phosphatidyl choline

Ceramide is acyl sphingosine

SYNTHESIS OF SPHINGOMYELIN

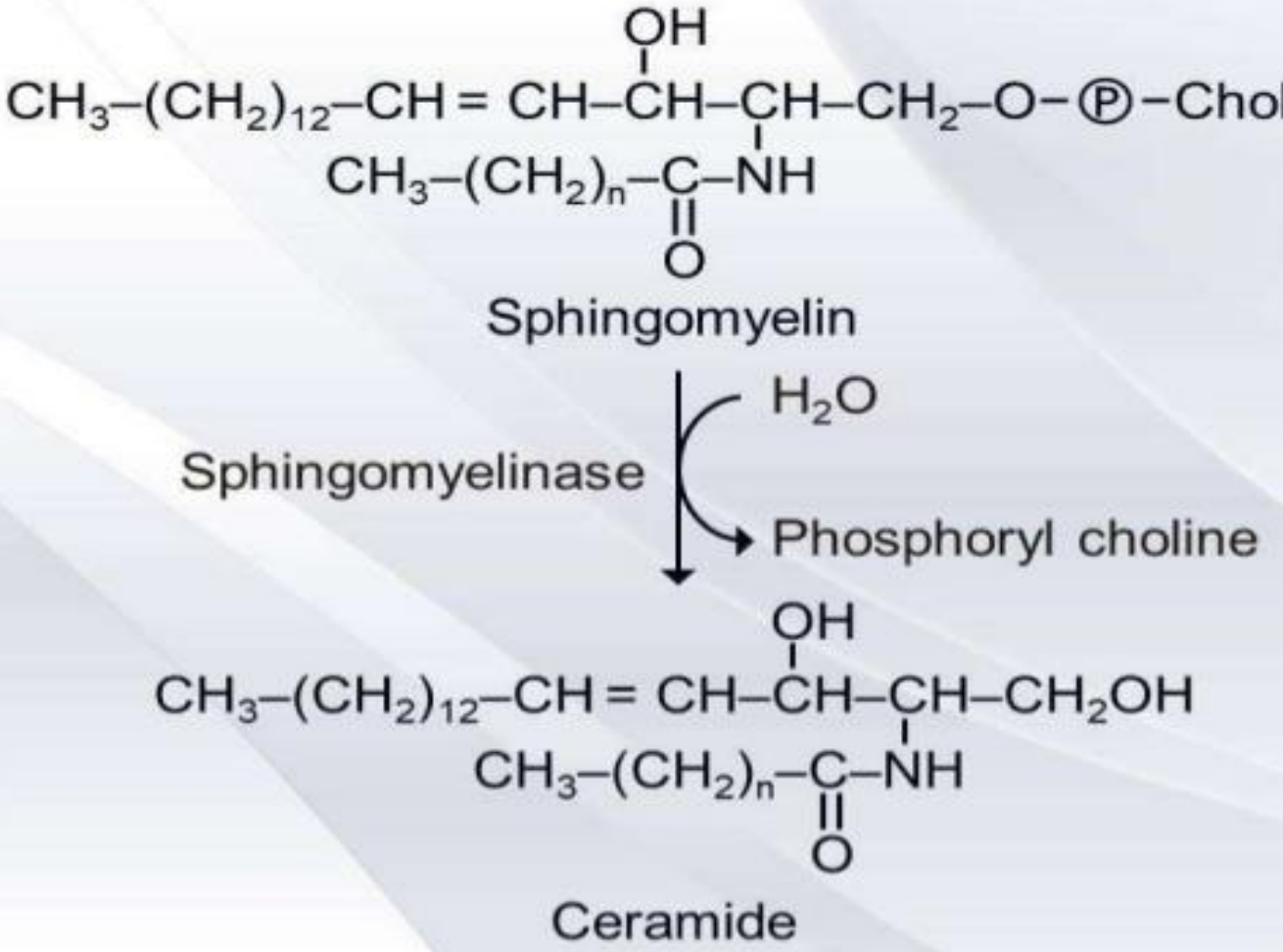


Catabolism of sphingomyelin

Sphingomyelin is catabolized by lysosomal sphingomyelinase

Sphingomyelin is hydrolysed into ceramide and phosphoryl choline

CATABOLISM OF SPHINGOMYELIN



Sphingomyelin lipidosis

Niemann Pick disease

Due to impaired degradation of sphingomyelin caused by deficiency of enzyme sphingomyelinase

- So sphingomyelin got accumulated in spleen, liver ,brain and bone marrow. It is a congenital disease.
- Autosomal recessive in nature
- There are 2 types: A and B
- Type A: more common present in 1/40000 population
- Type B: present in 1/80000 population
- More common in Jewish population

Niemann Pick disease :

Clinical manifestation

- Type A: there is progressive mental retardation, hepatosplenomegaly because of progressive accumulation of sphingomyelin. Children die within 2 years of life
- Type B: there is no involvement of brain but sphingomyelin is present in excessive amount in liver, spleen, and bone marrow. Death occurs within 20 years of life.

Lipotropic factors and fatty liver

Fatty liver is a condition in which large amounts of fat accumulate in the liver

This can later lead to serious disease

Some phospholipids have a role in prevention of fatty liver

Liver is the site for several pathways of lipid metabolism

Most of the major lipids can be synthesized and catabolized in the liver

Triglycerides are synthesized in liver, and are transported out of liver as VLDL

Lipotropic factors are the compounds required for transport of lipids out of liver

The lipotropic factors are choline, methionine and betaine

Their deficiency causes abnormal accumulation of triglycerides in liver

Normally, triglyceride content of liver is not more than 5% of liver weight

When it exceeds 5%, the condition is known as fatty liver

Excessive fat deposition in liver may cause inflammation of liver cells

Inflammation of liver cells may lead to their destruction

This may be followed by formation of scar tissue in liver (fibrosis)

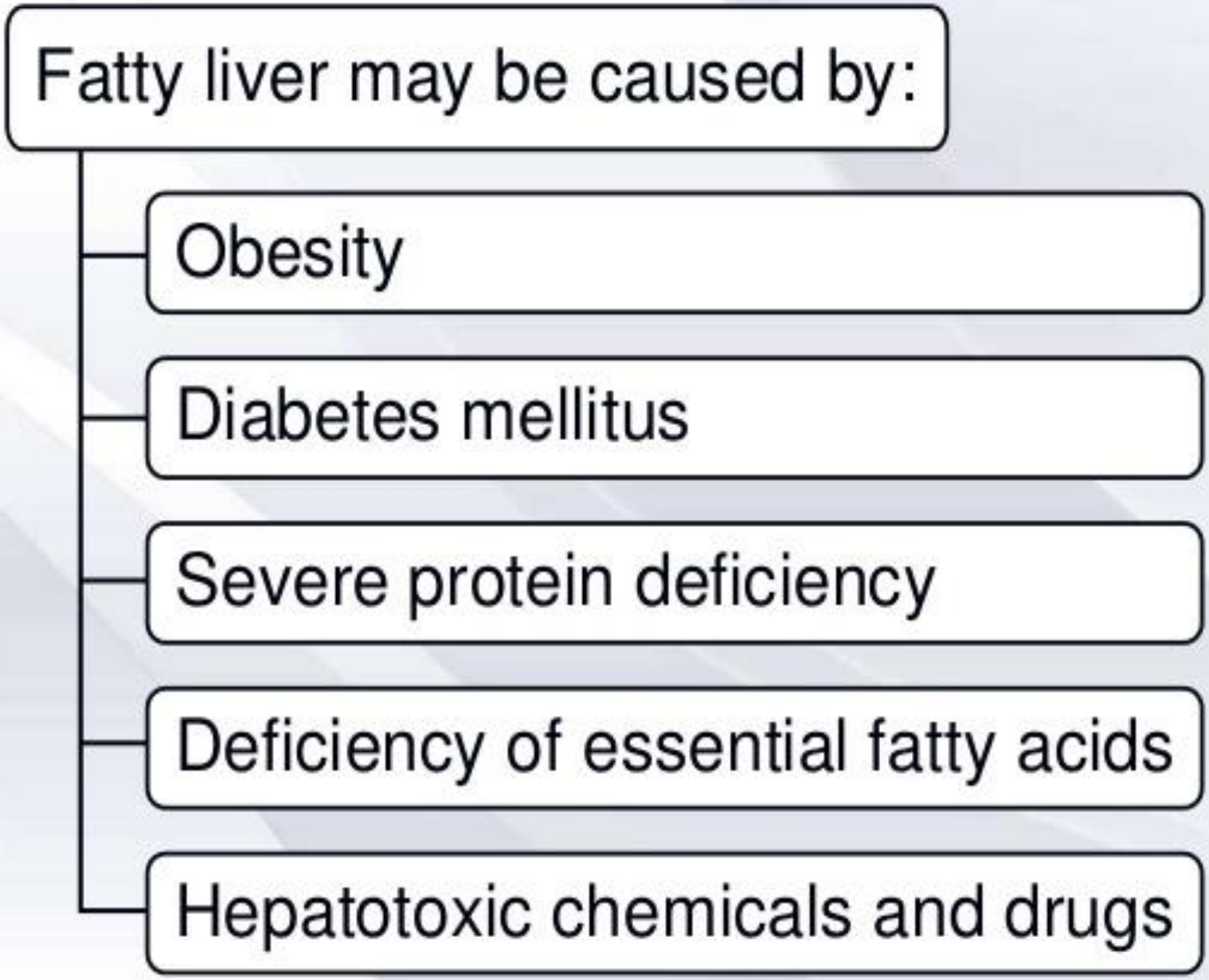
Extensive replacement of liver cells by fibrous tissue results in cirrhosis of liver

Normal liver: Fat less than 5%

Fatty liver: Fat more than 5%

Fibrosis: Formation of scar tissue

Cirrhosis: Hardening of liver tissue


Fatty liver may be caused by:
Obesity
Diabetes mellitus
Severe protein deficiency
Deficiency of essential fatty acids
Hepatotoxic chemicals and drugs

Chronic alcoholism is the most important cause of fatty liver and cirrhosis of liver

With a calorific value is 7 kcal/gm, alcohol (ethanol) is rich in energy

After ingestion of alcohol, oxidation of glucose and fatty acids decreases

Alcohol becomes the preferred source of energy

Since fatty acids are not oxidized, they are esterified with glycerol to form triglycerides

Increased synthesis of triglycerides in liver leads to their accumulation in liver

This causes fatty liver (specially when lipotropic factors are deficient)

Mechanisms by which fatty liver is caused are:

- Interference in phospholipid synthesis
- Disruption of intracellular membranes
- Interference in the synthesis of VLDL
- Interference in the release of VLDL

ROLE OF LECITHIN IN FATTY LIVER

Choline acts as a lipotropic factor as it is required to form lecithin

Lecithin is a component of lipoproteins that help in transport of lipids from liver

Lecithin is also the major component of membranes

Lecithin deficiency may disrupt endoplasmic reticulum membrane

Apoprotein component of lipoproteins is synthesized on endoplasmic reticulum

Disruption of membranes can disturb VLDL synthesis in liver

ROLE OF LECITHIN IN FATTY LIVER

Betaine and methionine act as lipotropic factors indirectly

They provide methyl groups for the synthesis of choline

Essential fatty acids also help in the transport of lipids

They are required for the synthesis of phospholipids

Fatty acid at C_2 of glycerophospholipids is usually an essential fatty acid

ROLE OF LECITHIN IN FATTY LIVER

Essential fatty acids also help in the transport of lipids

They are required for the synthesis of phospholipids

Fatty acid at C_2 of glycerophospholipids is usually an essential fatty acid

ANY QUESTIONS

dr.nabi 65@gmail.com

- CHATTERJEA BIOCHEMISTRY
- LIPPINCOTT BIOCHEMISTRY
- HARPERS BIOCHEMISTRY
- SATYANARAYANA BIOCHEMISTRY
- INTERNET

Thank you