

MAY 2014  
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WK 14 092-273

WEDNESDAY  
 APRIL

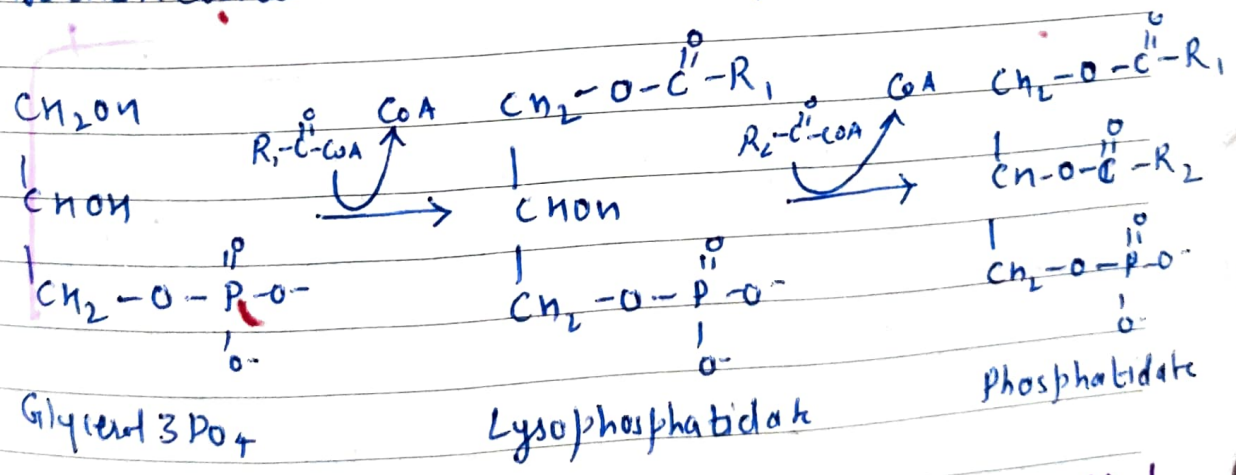
02

Phospholipid Biosynthesis

Familial hypercholesterolemia - a genetical disorder, people lacking the receptor have markedly elevated cholesterol level in the blood and cholesterol deposit on blood vessels and they are prone to childhood heart attack.

The first step in synthesis of both phospholipids for membranes and triacylglycerol for energy storage is the synthesis of phosphatidate (diacylglycerol 3-Phosphate).

Phosphatidate is synthesized in ER and outer mitochondrial membrane. Begins with glycerol 3-P.



These acylation is catalyzed by glycerol phosphate acyltransferase.

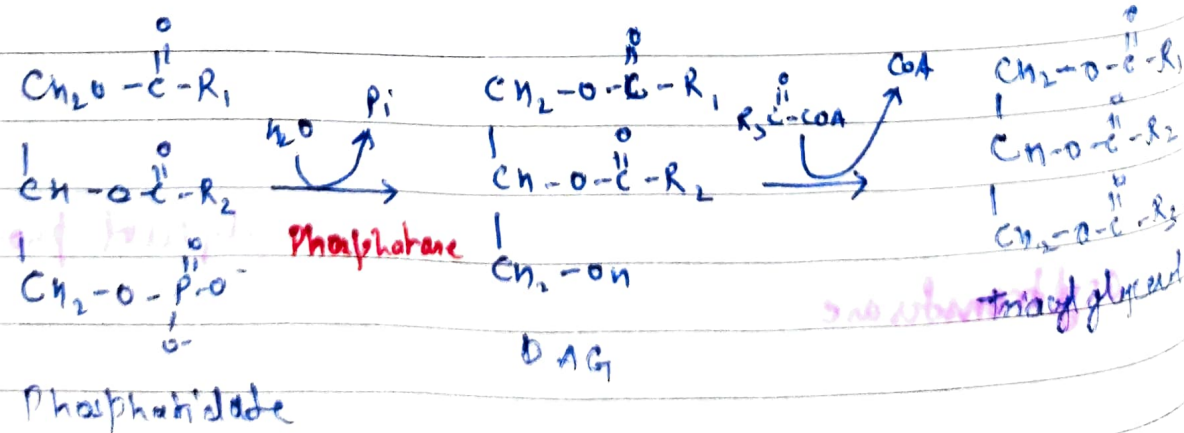
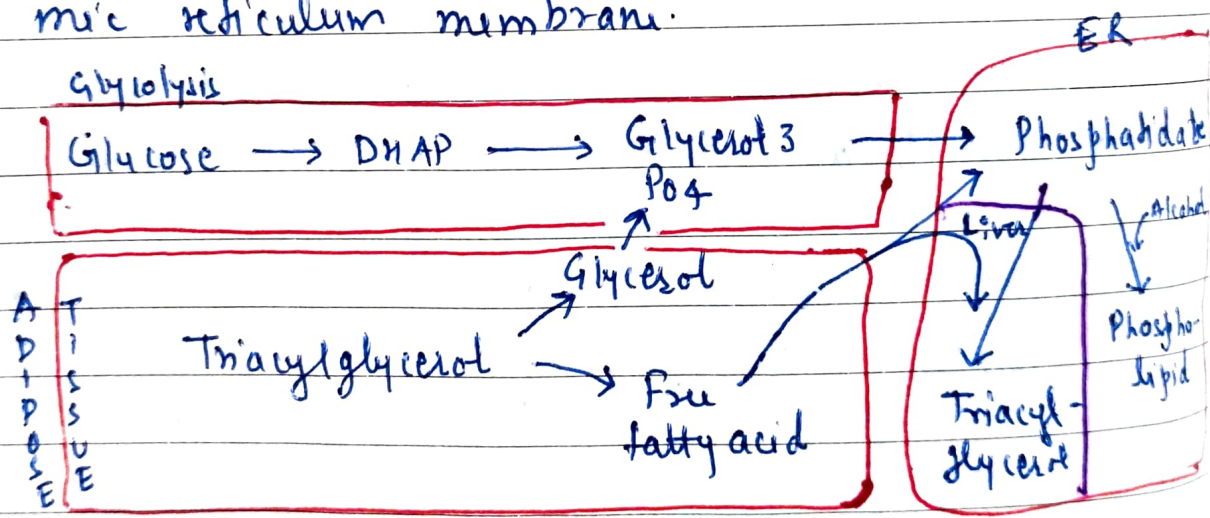
MAY

JUNE

→ In synthesis of ~~phosphatidate~~ triacylglycerol, phosphatidate is hydrolyzed by a specific phosphatase to give a diacylglycerol (DAG).

→ This intermediate is acylated to a triacylglycerol through the addition of a third fatty acid chain in a reaction that is catalyzed by diglyceride acyltransferase.

Both enzymes are associated in a triglycerol synthetase complex bound to endoplasmic reticulum membrane.



Phosphatidylinositol + 2ATP

↓ 2ADP

Phosphatidylinositol + 5 bisphosphate

DAG ← IP<sub>3</sub>

WK 14 094-271

FRIDAY  
APRIL

04

Membrane lipid synthesis continues in ER.

Phospholipid syntheses require the combination of DAG with an alcohol.

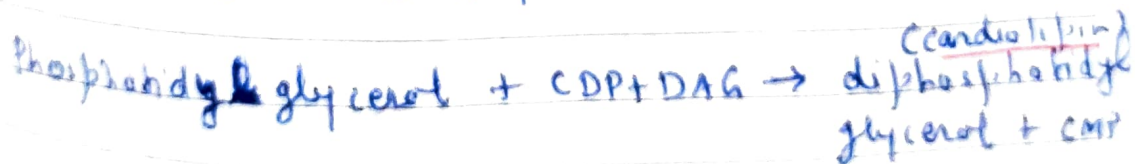
The de novo pathway starts with the reaction of phosphatidate with CTP to form activated DAG, cytidine diphospho diacylglycerol (CDP-DAG)



The activated CDP-DAG then reacts with hydroxyl group of an alcohol to form phosphodiester linkage

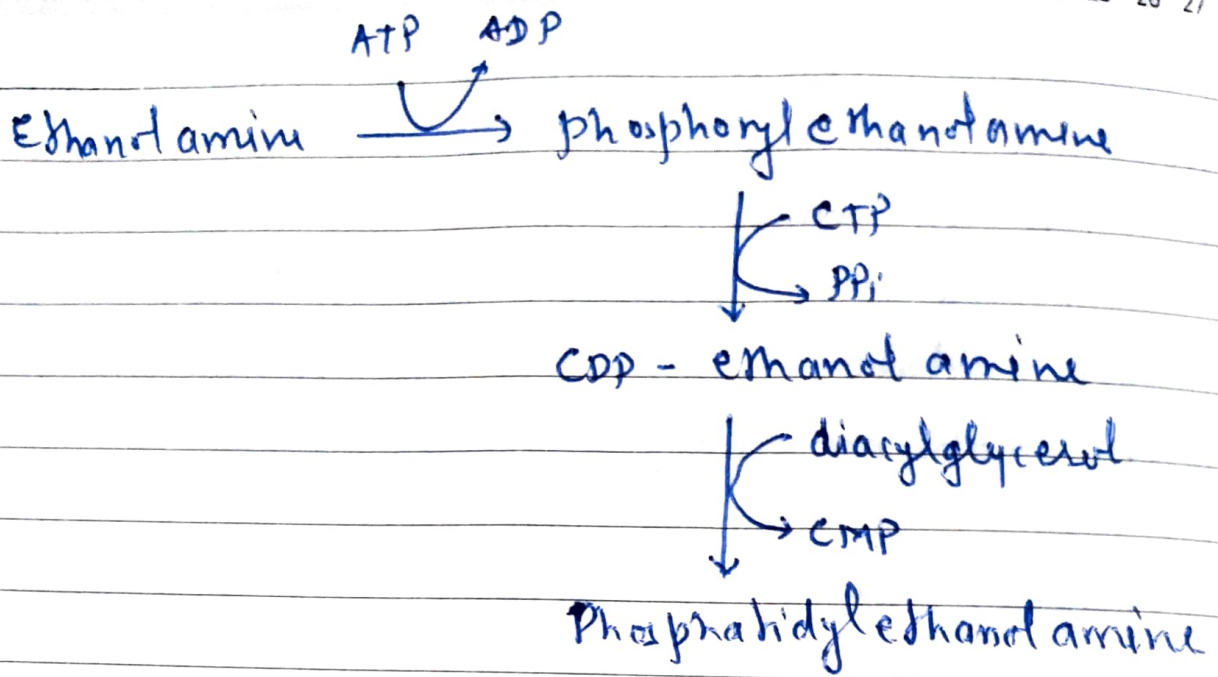


If the alcohol is phosphatidyl glycerol, the products are diphosphatidyl glycerol (cardiolipin) and CMP

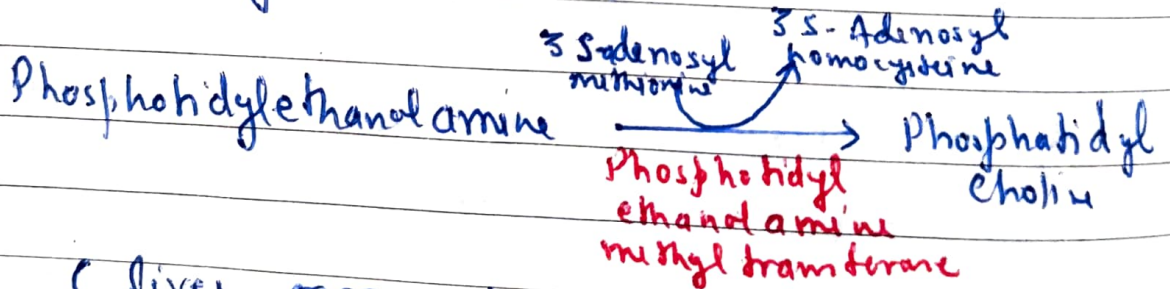


Phosphatidyl ethanolamine - A common phospholipid in mammals.

To activate the alcohol, ethanolamine is phosphorylated by ATP to form the precursor, phosphatidylethanolamine.



→ The most common phospholipid in mammals is phosphatidylcholine. Dietary choline is activated in a series of reaction analogous to those in the activation of ethanolamine.



(liver ~~organ~~ possesses this enzyme when dietary choline is insufficient)

06

SUNDAY

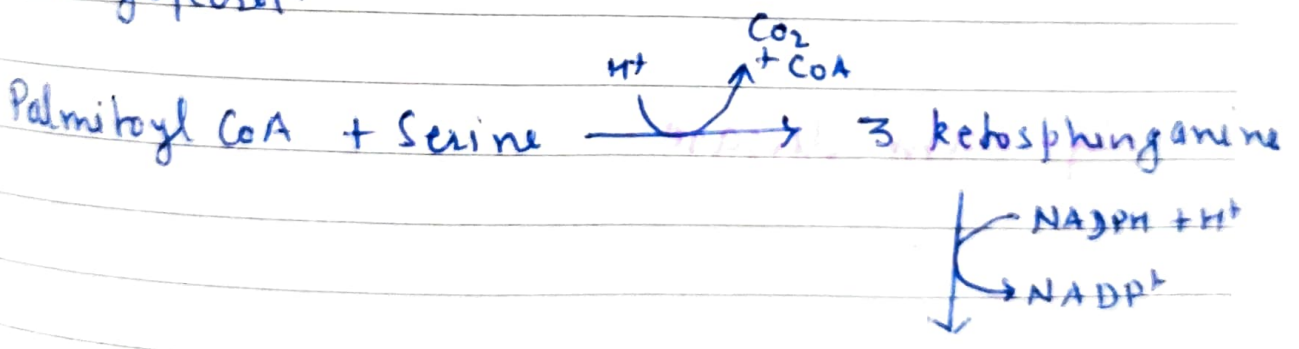
→ Phosphatidylserine makes up 10% of phospholipids in mammals. This phospholipid is synthesized in a base exchange reaction of serine with phosphatidylcholine or phosphatidylethanolamine.

Phosphatidylcholine + Serine → Choline + Phosphatidylserine  
 Phosphatidylethanolamine + Serine → ethanolamine + Phosphatidylserine

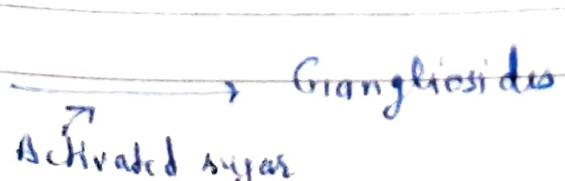
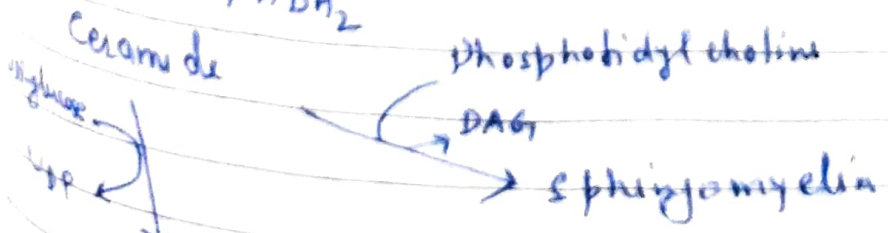
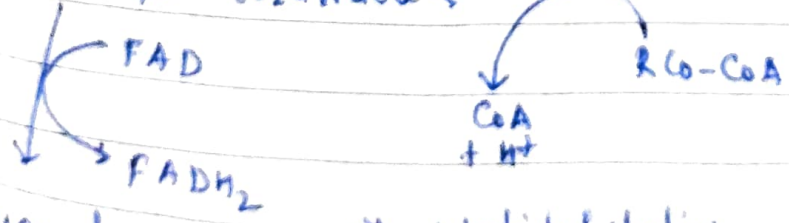
⇒ Phosphatidylserine is normally located in the inner leaflet of the Plasma membrane bilayer but is moved to the outer leaflet in apoptosis.

Sphingolipid

- Lipids found in the Plasma membrane of all eukaryotic cells, conc<sup>n</sup> is higher in CNS.
- The backbone of a sphingolipid is sphingosine rather than glycerol.



Dihydroceramide ← Dihydrosphingosine



Gangliosides are the most complex sphingolipids. In a ganglioside, an oligosaccharide chain is linked to the terminal hydroxyl group of ceramide by a glucose residue.

**Respiratory distress Syndrome** - Pathological condition resulting from a failure in the biosynthetic pathway for dipalmitoyl phosphatidylcholine. This phospholipid in conjugation with sp. proteins & other phospholipid, is found in the extracellular fluid that surrounds the alveoli of the lung.

Its function is to decrease the surface tension of the fluid to prevent lung collapse at the end of the expiration phase of breathing.

**Tay-Sachs disease** - Caused by a failure of lipid degradation: an inability to degrade gangliosides.

Gangliosides are found in high conc<sup>n</sup> in the nervous system, particularly in grey matter, where they constitute 6% of the lipids.

As a consequence, neurons become significantly swollen with lipid-filled lysosomes. An affected infant displays weakness and retarded psychomotor skills before 1 year of age. The child is demented and blind by age 2 and usually dies before age 3.