

PHOSPHOLIPIDS METABOLISM

❖ The chemical structure and types of phospholipids: (in introductory module of biochemistry)

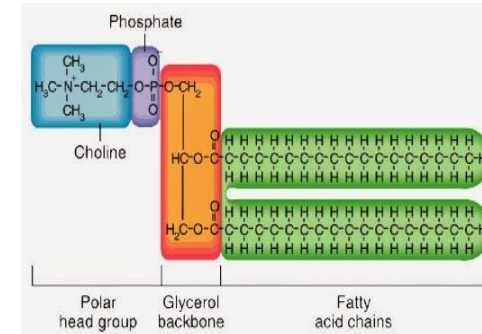
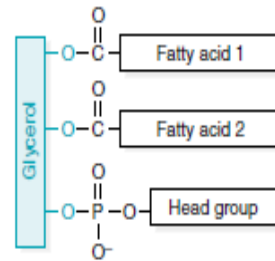
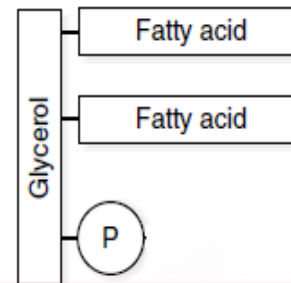
Alcohol, Fatty acid, and phosphoric acid.

1. Glycero-phospholipids: Glycerol alcohol

1. Phosphatidic acid. **(Parent)**
2. Lecithin (phosphatidylcholine).
3. Cephalin (phosphatidylethanolamine).
4. Phosphatidylinositol
- 5- Cardiolipin

2- Sphingo phospholipids

• **Sphingomyelin.**



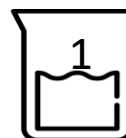
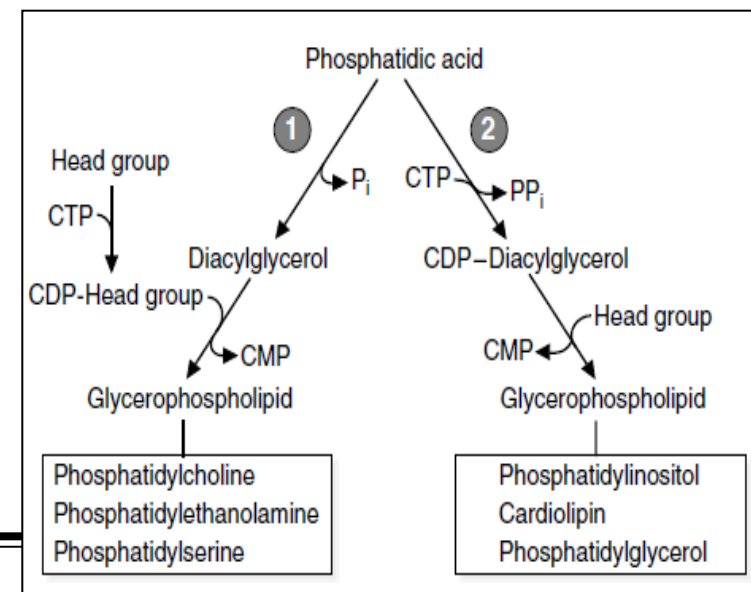
SYNTHESIS OF PHOSPHOLIPIDS CONTAINING GLYCEROL

- Glycerol 3-phosphate reacts with fatty acyl CoA to form phosphatidic acid.
- Two different pathways to add a head group to the molecule

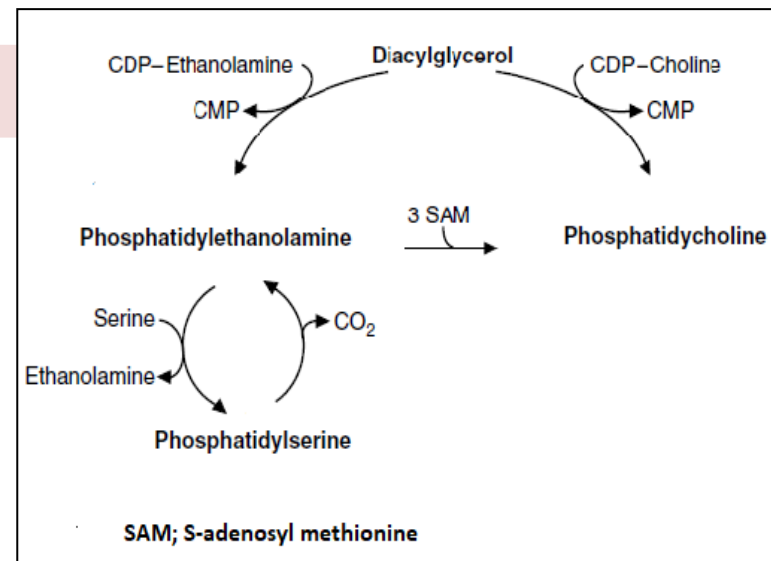
❖ In the first pathway:

Phosphatidic acid is cleaved by a **phosphatase** to form **diacylglycerol (DAG)**.

- DAG then reacts with an **activated head group**.

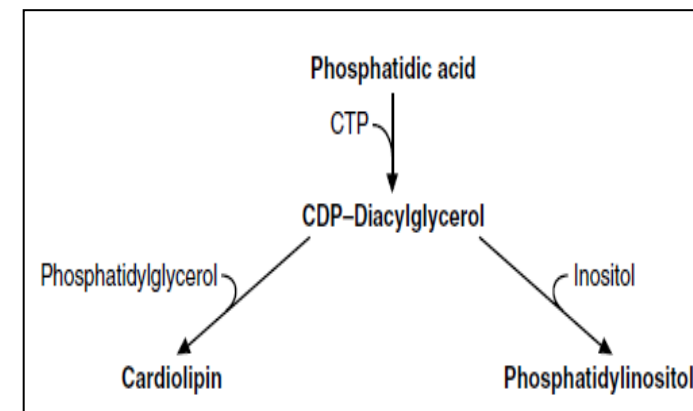


- In the synthesis of **phosphatidylcholine**, the head group **choline** is activated by combining with **CTP** to form **CDP-choline**. **Phosphocholine** is then transferred to **carbon 3** of **DAG**, and **CMP** is released.
- **Phosphatidylethanolamine** is produced by a similar reaction involving CDP-ethanolamine.
- **Phosphatidylserine** is produced by a reaction in which the **ethanolamine** moiety of phosphatidylethanolamine is **exchanged for serine**.
- **Phosphatidylserine** can be converted back to **phosphatidylethanolamine** by a **decarboxylation reaction**.
- **Phosphatidylethanolamine** can be **methyalted** to form **phosphatidylcholine** (through **3 methylation steps**). S-adenosyl methionine (SAM) is the methyl donor.



❖ In the second mechanism:

- **Phosphatidic acid** reacts with **CTP** to form **CDP-diacylglycerol**.
- **CDP-diacylglycerol** reacts either with **phosphatidylglycerol** (which itself is formed from the condensation of CDP-diacylglycerol and glycerol 3-phosphate) to produce **cardiolipin** or with **inositol** to produce **phosphatidylinositol**.
- **Phosphatidylinositol** can be **phosphorylated** to form **phosphatidylinositol 4,5-bisphosphate (PIP2)**, which is a **component of cell membranes**. In response to **signals** such as the **binding of hormones to membrane receptors**, PIP2 can be cleaved to form the second messengers: diacylglycerol and inositol tri-phosphate.

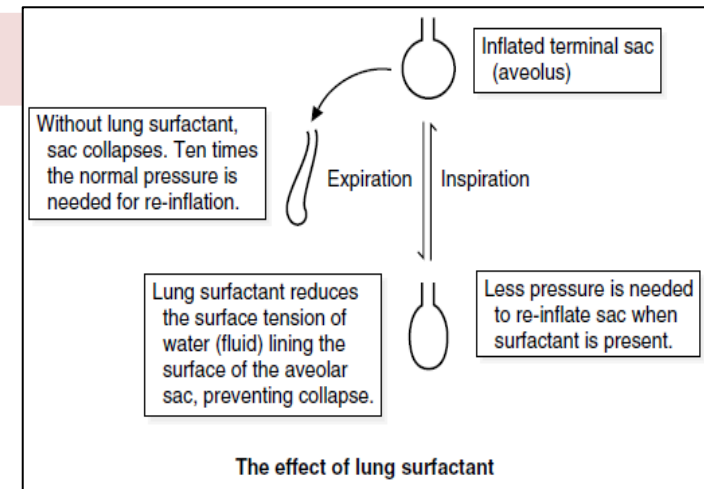


Clinical significance:

Respiratory distress syndrome (RDS):

Neonatal defect in synthesis of the **phospholipids Dipalmitoyl Phosphatidyl choline (Dipalmitoyl lecithin, Lung surfactant)**

Lung surfactant **decreases** the **surface tension** in the lung alveoli. So, it **prevents adherence** of the inner surfaces of the lung at the **end of expiration**

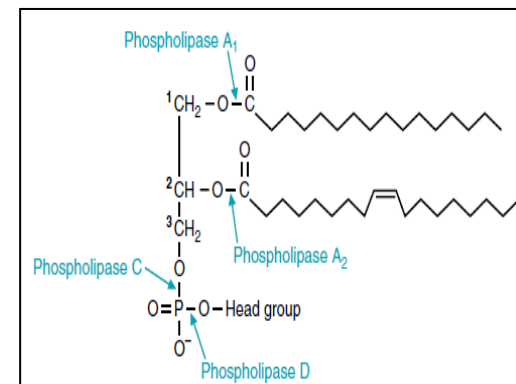


Neonatal respiratory distress syndrome (RDS):

- RDS in premature infants is associated with **insufficient surfactant production** and/ or **secretion**.
- RDS is preventable if prematurity can be avoided by appropriate management of high-risk pregnancy.
- **Lung prematurity** of the fetus determined by the ratio concentrations of **phosphatidylcholine (lecithin)** to **sphingomyelin** in the amniotic fluid (value of 2 or more indicates lung maturity).
- The administration of synthetic **corticosteroids 48 to 72 hours before delivery** of a fetus of less than 33 weeks of gestation in women who have toxemia of pregnancy, diabetes mellitus, or chronic renal disease **may reduce the incidence or mortality of RDS by stimulating fetal synthesis of lung surfactant**.
- The administration of **one dose of surfactant into the trachea of the premature infant immediately after birth** may transiently improve respiratory function but does not improve overall mortality.

➤ **Phospholipases** located in **cell membranes** or in **lysosomes** degrade **glycerophospholipids**.

- **Phospholipase A1** removes the **fatty acyl** group on **carbon 1** of the glycerol moiety.
- **Phospholipase A2** removes the **fatty acid** on **carbon 2**. The fatty acid attached to C2 in cell membrane phospholipids is usually an **unsaturated fatty acid**, which is frequently **arachidonic acid**. It is removed in response to signals for the **synthesis of eicosanoids**. Phospholipase A2 is inhibited by glucocorticoids, e.g., cortisol.
- The bond joining **carbon 3** of the glycerol moiety to **phosphate** is cleaved by **phospholipase C**.
- Hormonal stimuli activate phospholipase C, which hydrolyzes PIP2 to produce the second messengers DAG and inositol trisphosphate (IP3).
- The bond between the phosphate and the head group is cleaved by **phospholipase D**, producing **phosphatidic acid** and the **free alcohol of the head group**.



❖ Phospholipidosis

Lysosomal storage disorder characterized by excess accumulation of phospholipids in tissues (Kidney, lung, liver).

- It may be **inherited or acquired**.
- In acquired phospholipidosis, some drugs bind to phospholipids and inhibit their hydrolysis by lysosomal phospholipases. This condition is reversible after discontinuation of drug treatment.