Biochemistry
Team 434

PHOSPHOLIPID COMPOUNDS OF PHYSIOLOGICAL IMPORTANCE

Respiratory Block

COLOR INDEX: Red= Important Purple= Addition Orange= Explanation

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❖ *Objectives*

- **Selected members of phospholipids**
- **Physiological importance of phospholipids**
- **Phospholipases:**
  - Phospholipases A1, A2, C and D
  - Lysosomal phospholipase: Sphingomyelinase

Functions Of Phospholipids

membrane bound phospholipids

- structural:predominant lipids of cell membranes
- signaling:source of IP3 and DAG
- anchoring:attaching some proteins to membranes
- myelin sheath: insulator and speeds up transmission of nerve impulses

as if it has 2 hands one holds the membrane the other hand holds another structure ex:protein

which is about sphingomyelin + phospholipid +other components

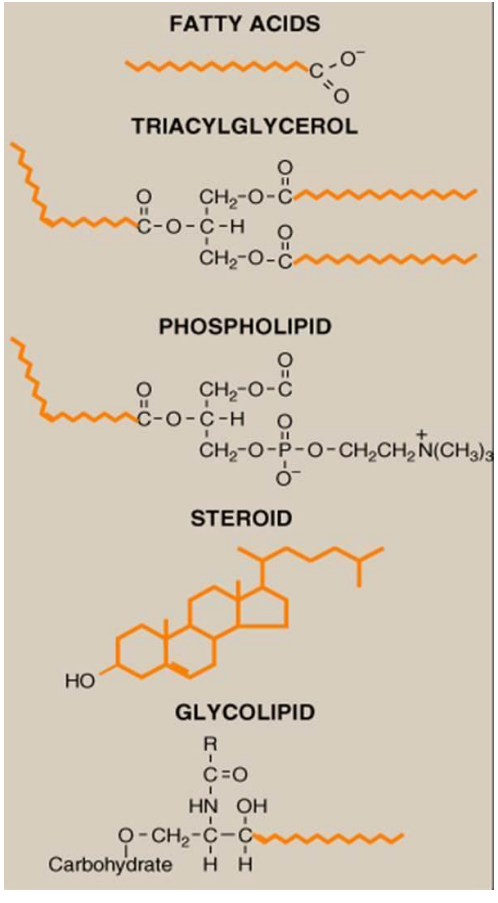
non membrane bound phospholipids

- easy reinflation of alveoli by air: lung surfactant
- detergent effect: essential component of bile solublize cholesterol,preventing gallstones
- emulsifying lipids,helping in lipids digestion
- structural: coat of lipoproteins

Background: lipid compounds

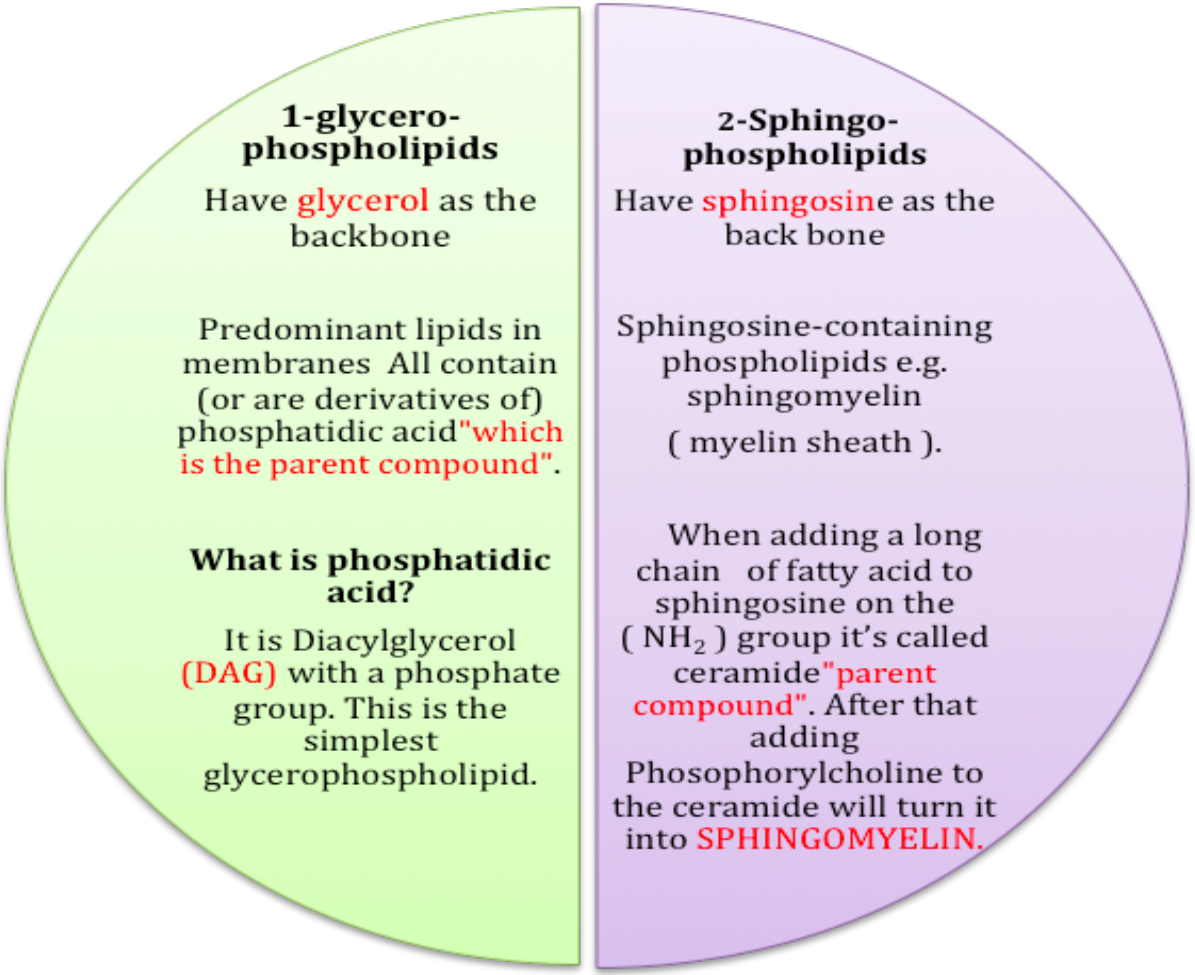
Heterogeneous group
Relatively water-insoluble except ketone bodies
Soluble in nonpolar solvents

Lipids compound: heterogeneous group



- **simple lipids**
  - fatty acids
  - ketone bodies
  - triacylglycerol
  - cholesterol
- **complex lipids**
  - phospholipids
    - 1-glycero-phospholipids: glycerol containing phospholipids
    - 2-sphingo-phospholipids: sphingosine containing phospholipids
  - lipoproteins
  - glycolipids

There are two classes of phospholipids:



❖ Phosphatidylcholine

We will talk about dipalmitoyl lecithin (DPPC) which is a major component of surfactant.

- Where is it synthesized and secreted?

In granular pneumocytes, aka:type II alveolar cells.

Makes up 65% of lung surfactant .

طبقه زي الفازلين
to prevent the alveolar from collapsing
"تفرقع" COLLAPSE = atelectasis

We have talked about the function of surfactant many times as it decreases surface tension. So now, let us jump to a pathologic process : Congenital Respiratory Distress Syndrome (CRDS): Surfactant is usually produced after 32 weeks of gestation"الحمل" (around 8 months). Premature infants are at increased risk of CRDS.
Instead of listing the information regarding CRDS, it would be better if we put it as a Q & A

What are the symptoms of CRDS?

Neonates would have difficulty breathing and since the surface tention is increased with the loss of surfactant, the alveoli may collapse & it may lead to death.

1) How can we diagnose this before birth?

We take a sample of the amniotic fluid & take the ration between lecithin (which is our friend that makes surfactant) and sphingomyelin. So we will do this: Lecithin (L) / Sphingomyelin (S) "L/S". The rule is that: a ratio of 2 and above means that the baby is OK.

2) A pregnant woman had an L/S ratio of 1. What drugs could help in her case?

- We can administer a beta 2 agonist that causes postponing of labor.
- We can give glucocorticoids shortly before delivery because it expresses some genes that help.

3) What is the treatment for the freshly born neonate with CRDS?

- We can give them surfactant. It is administered in the trachea.

❖ Phosphatidylinositol 4,5 bisphosphate

- **Hormone → G Protein coupled receptor** on cell membrane → **activation of Gq alpha subunit → Production of IP3 & DAG →mobilization of intracellular Ca → activation of protein kinase C cellular response**

- **The hormone could be Ach, ADH, or catecholamines.**
- **Phosphatidylinositol is digested to Diacylglycerol (DAG) and Inositol Triphosphate (IP3) by phospholipase C.**

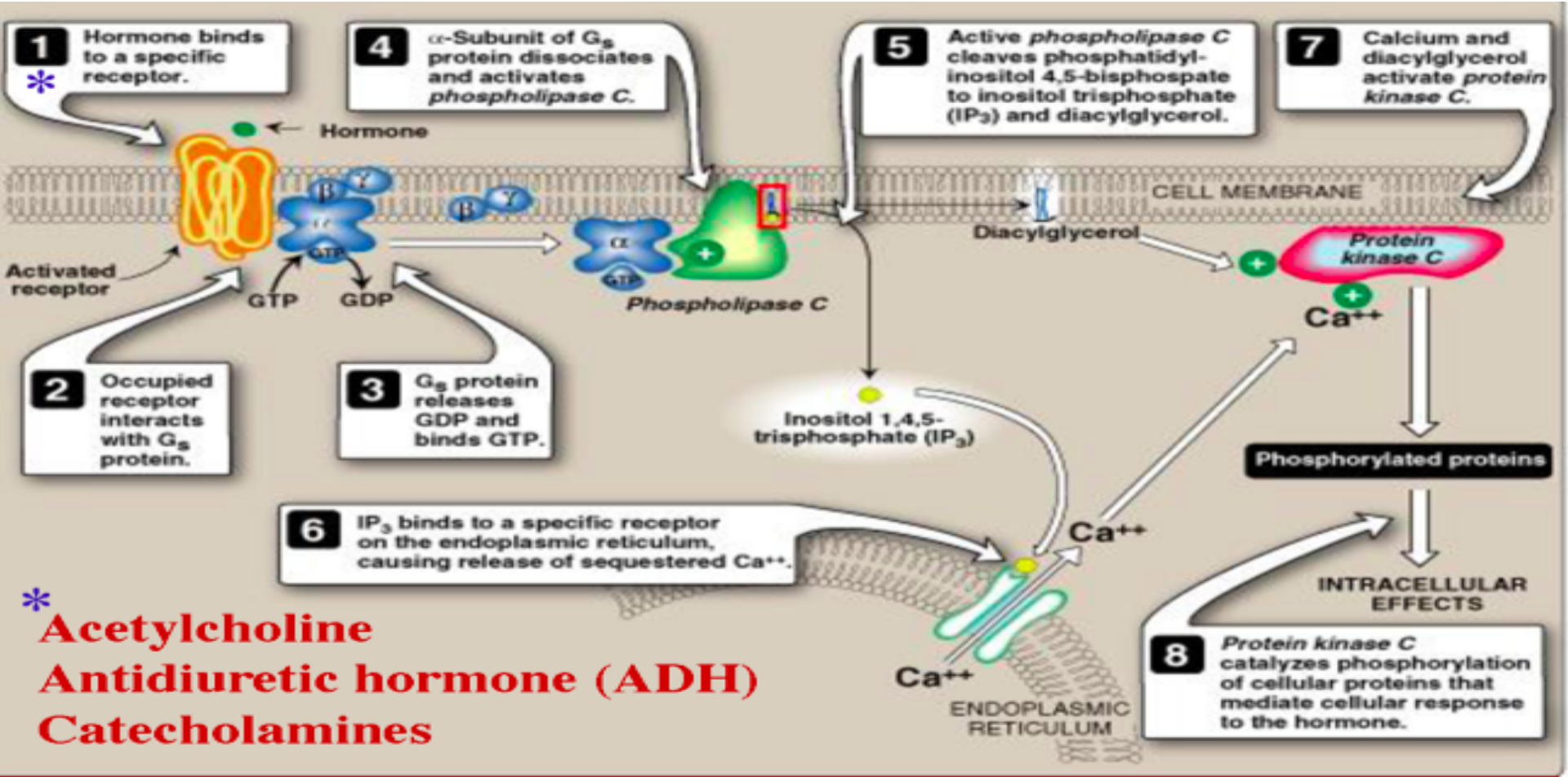
Anchoring "ربط" functions of PI: Anchoring of proteins to membranes via Carbohydrate-Phosphatidylinositol Bridge

Examples include: 1)**Ach Esterases** in the postsynaptic membrane. 2)**alkaline phosphate** which is found in the surface of small intestines.

These proteins can be cleaved from their attachment to the membranes

by **phospholipase C**

Intracellular Signaling by Inositol trisphosphate



Sphingo-phospholipids:

Sphingosine-containing phospholipids e.g. sphingomyelin (myelin sheath).

When adding a long chain of fatty acid to sphingosine on the (NH_2) group it's called ceramide. After that adding Phosophorylcholine to the ceramide will turn it into SPHINGOMYELIN.

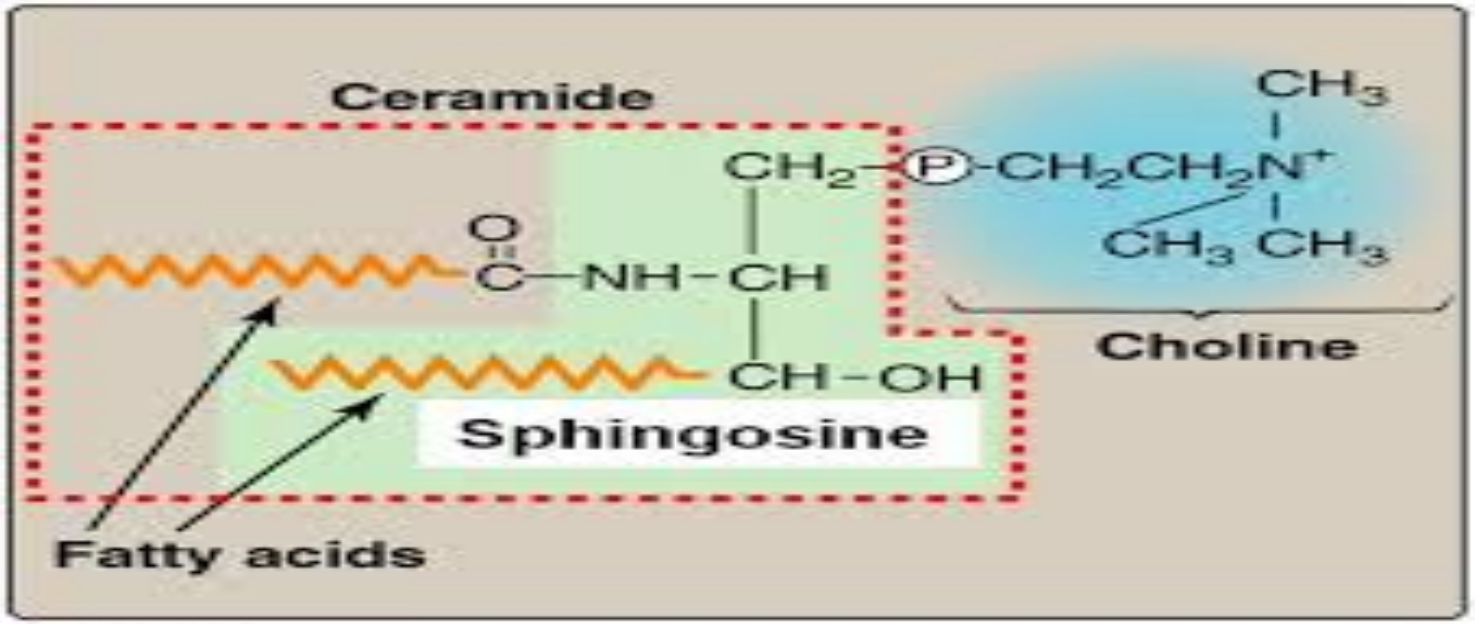
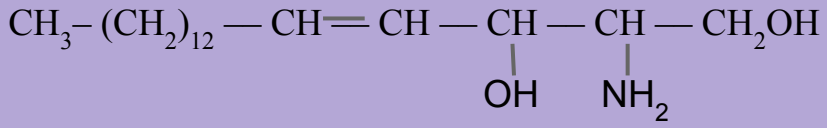
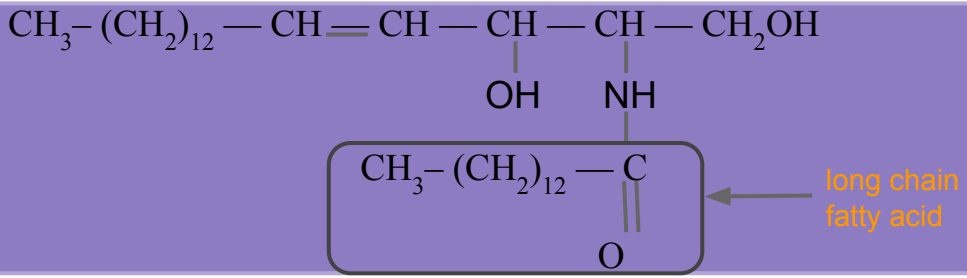


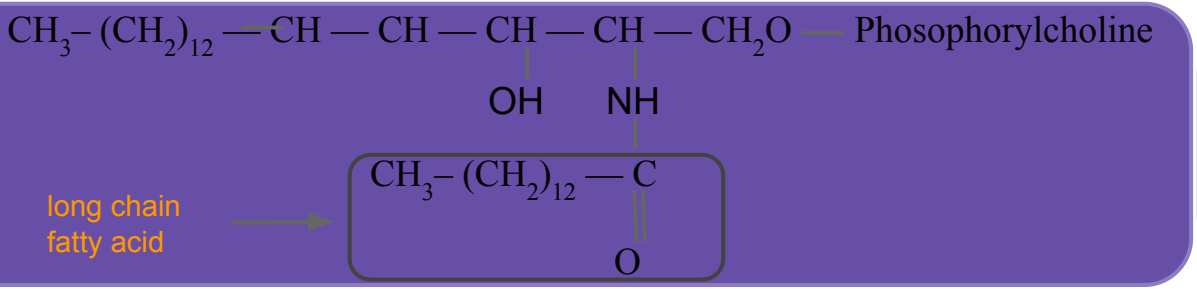
Figure 17.4
Structure of sphingomyelin, showing sphingosine (in green box) and ceramide components (in dashed box).

sphingosine: long chain, unsaturated amino acid.



Ceramide : Parent sphingolipid compound





Sphingomyelin

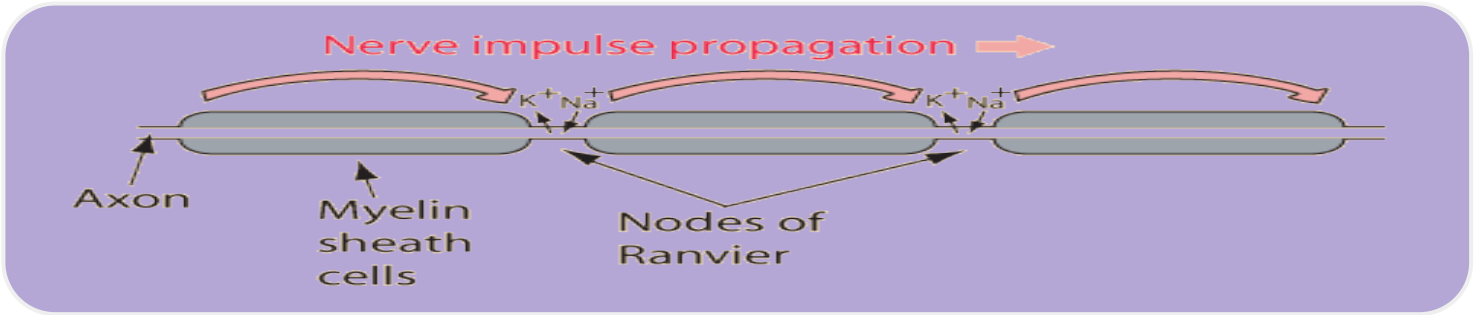
Structure & Function of Myelin Sheath

Myelin structure:

Lipids (80%) Proteins (20%)

A) Glycolipids (mainly)
B) sphingomyelin

Myelin sheath insulates the nerve axon to avoid signal leakage and greatly speeds up the transmission of impulses along axons.



Lipoprotein structure

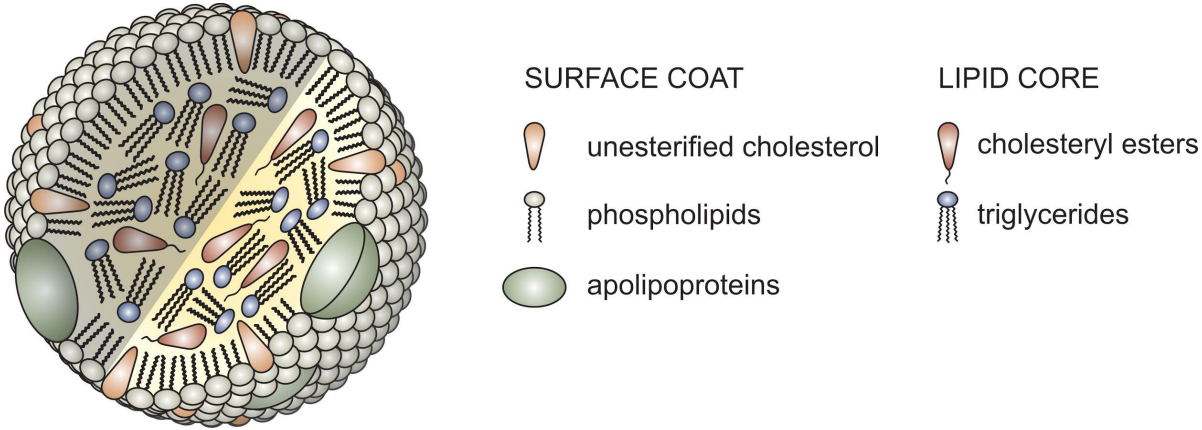
Outer part (surface coat) :

- apoproteins or apolipoproteins .
- phospholipids
- free cholesterol

(relatively hydrophilic, allowing transport of lipid particles of the core in the aqueous plasma)

Inner part (Lipid core) :

- according to the type of lipoproteins .
- different lipid components in various combinations.



Phospholipases

a group of enzymes that catalyze the cleavage of phospholipids. While some phospholipases possess substrate specificity for certain phospholipid species so it has remodeling and degradation functions.

❖ for glycerophospholipids

phospholipase A1 : present in many mammalian tissues .

Phospholipase A2 : acts on phosphatidylinositol to release arachidonic acid (the precursor of the prostaglandins) , present in pancreatic juice , snake and bee venoms and inhibited by glucocorticoids

they have them to degrade phospholipid in our body (virulence factor)

Phospholipase C: found in liver lysosomes and bacterial toxin, activated by PIP system.

phospholipase D : found primarily in plant tissue

cause they need to cleave PI 4,5 Bisphosphate to it component

❖ for sphingophospholipids

Lysosomal phospholipase :

-sphingomyelinase :

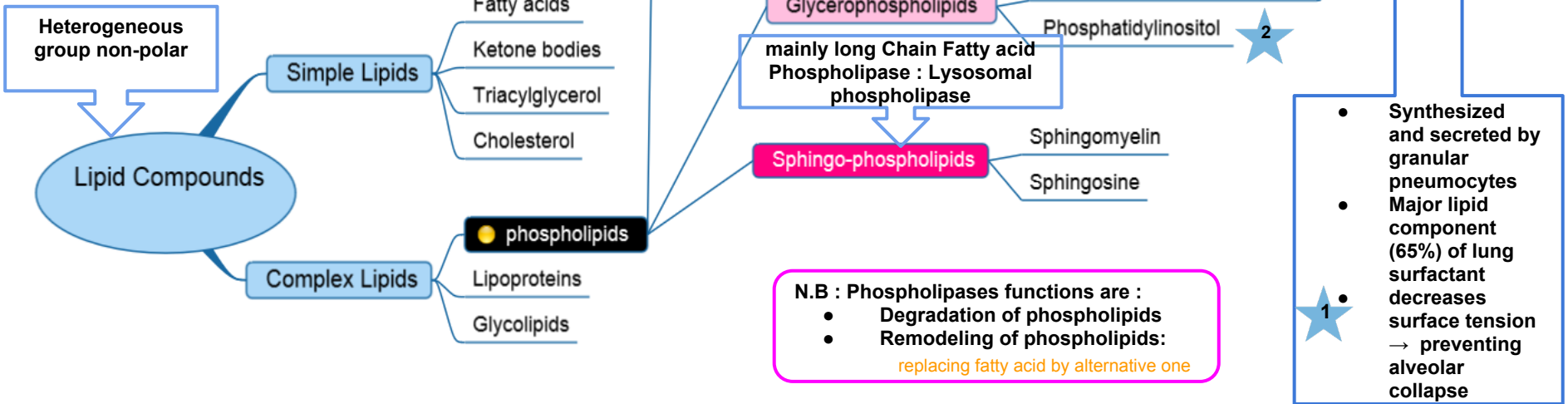
catalyze Sphingomyelin to produce→ ceramide + phosphocholine .

Summary

1 Congenital Respiratory distress syndrome (RDS) : Insufficient production of lung surfactant

2 Phosphatidylinositol System :

- Signal : Hormones or neurotransmitters
- receptor: G-protein coupled receptor
- Effects : - activation of phospholipase C.
  - Hydrolysis of phosphatidylinositol 4,5-bisphosphate
  - Production of IP3 (Ca2+) and DAG
  - Activation of protein kinase C .
- Response : Phosphorylation (either activation or inhibition of the enzyme)



MCQs

Many of these questions we took from 433 team, because these are very helpful:

Q1) Which one of the following has a signaling function:

A- Inositol trisphosphate C-Dipalmitoylecithin

B- Proteins D- ATP

Q2) Diabetic 35 week pregnant patient came to your clinic and you predicted that she will deliver prematurely which one of these test will make us sure that the baby has normal surfactant level:

a- manteaux test.

b- lecithin/sphingomeylin ratio

c- RAST test.

d- E.M.C test

Q3) phospholipids is transported in the circulation in the form of:

A- phospholipase A1 B- phospholipase A2

C- lipoprotein D- phospholipase c

Q4) which of following is responsible for remodeling and degradation of phospholipids:

a- sphingomyelin

b- lipoprotein

c- phospholipases

d- phosphatidic acid

Q5)The MAIN component of lung surfactant is:

A- cholesterol B- proteins

C- DPPC. D- Carbohydrates

Q6) lung surfactant are made of:

A- non membranebound phospholipid B- membrane bound phospholipid

C- phospholipase D D- phospholipase A2

Q7) All lipid compounds are lipid soluble except:

A- Ketone bodies
B- cholesterol
C- fatty acids
D- triacylglycerol

Q8) 28 week pregnant lady was going deliver her baby early, which one of these you should give her to prevent the low surfactant percentage:

A- VIT.D
B- Adrenalin
C- Intra tracheal administration of surfactant
D- Glucocorticoids

Q9) The anchor proteins can be cleaved from their attachment to the membranesby:

A- Phospholipase C
B- Phospholipase A2
C- Phospholipase A1
D- Phospholipase D

Q10) phospholipase A2 is inhibited by:

A- Trypsin
B- Glucocorticoids
C- fructose 1,6-bisphosphatase
D- Bacteria

Ans: 1-A 2-B 3-C 4-C 5-C 6-A 7-A 8-D 9-A 10-B

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