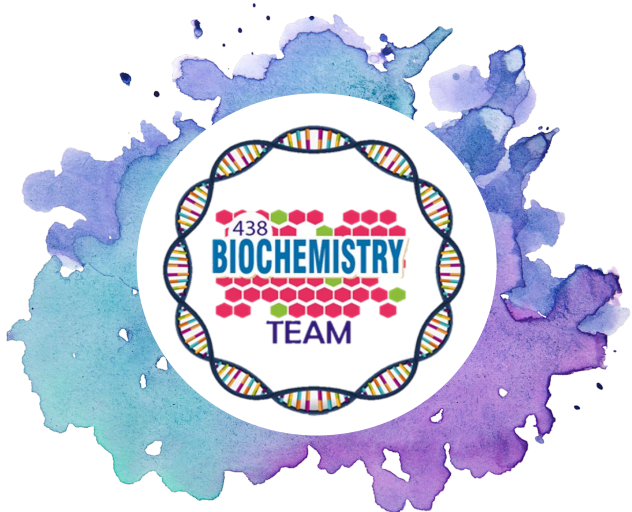
editing file

Respiratory Block

PHOSPHOLIPIDS OF CLINICAL SIGNIFICANCE

Color Index:

- Original content
- Important
- Extra info, Dr's notes
- Only in girls' slides
- Only in boys' slides



Objectives:

Slide No. 3	Identify the types and functions of phospholipids
Slide No. 3	Discuss the physiological importance of phospholipids
Slides (4-7)	Understand the Types, functions and role of glycerophospholipids in cell signaling, protein anchoring, lung surfactant and their clinical implications in respiratory distress syndrome (RDS)
Slides (10,11)	Identify the classes and physiological functions of phospholipase enzymes

★ **Objectives:** 1) Identify the types and functions of phospholipids
2) Discuss the physiological importance of phospholipids

Phospholipids

What are phospholipids?

- ★ Major lipids of cell membranes
- ★ polar, ionic compounds that
- ★ contain an alcohol group attached either to:
  - Diacylglycerol → Glycerophospholipids
  - Sphingosine → Sphingophospholipids

Classes

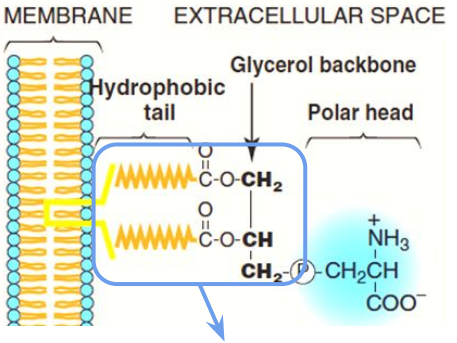
Phospholipids

- Hydrophilic (polar) — interacting with the aqueous environment
- Hydrophobic (non-polar) — attached to the membrane.

* Function: selectivity in permeability (only lipid soluble can cross)

Properties

Amphipathic



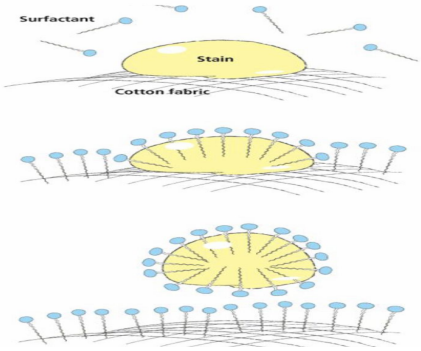
★ Functions

★ **Membrane-bound** phospholipids:

- Reservoir for intracellular messengers (signaling)
- Anchors to cell membranes

★ **Nonmembrane-bound** phospholipids:

- Lung surfactant
- Components of bile (as detergents to solubilize cholesterol)



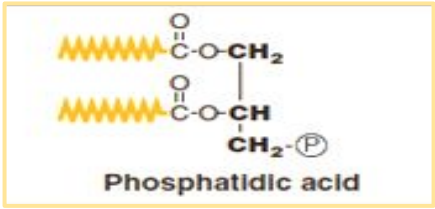
435 team

What is a detergent?
A molecule with a nonpolar end that attaches to the lipid, and a polar end that attaches to water. Because of this property, it can solubilize lipid in water."as Shown in the picture"

(مثل مساحيق الغسيل عندما تقوم بتذويب البقع الدهنية)

Glycerophospholipids

"Also called phospho**glycerides**"

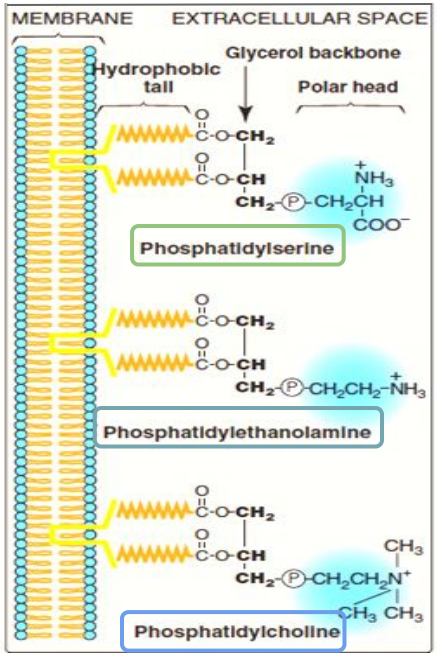


- A major class of phospholipids
- Contain glycerol (Backbone)
- All contain (derived from) **phosphatidic acid** -> PA is the simplest phospholipid (precursor)

★

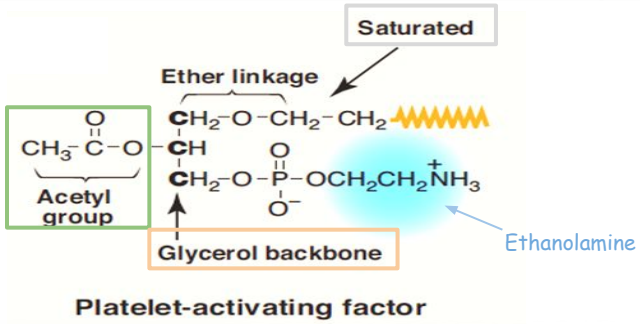
Serine + PA	Phosphatidylserine (PS)	Cell signaling - Blood clotting
Ethanolamine + PA	Phosphatidylethanolamine (PE) (cephalin)	Play a role in membrane fusion
Choline + PA	Phosphatidylcholine (PC) (lecithin)	Lung surfactant
Inositol + PA	Phosphatidylinositol (PI)	Cell signaling
Glycerol + PA * by phosphodiester bond	Phosphatidylglycerol (PG)	Lung surfactant

★ not the only function but the most abundant

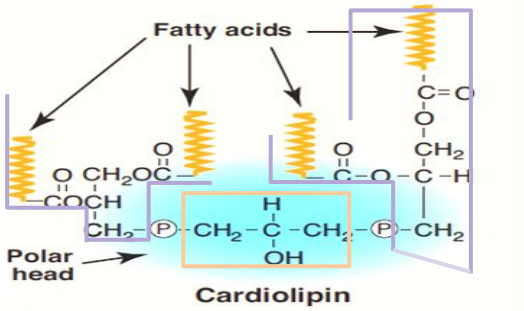


Some examples

	Platelet activating factor (PAF)	Cardiolipin
structure	Other phosphoglycerides, the fatty acids are attached to glycerol by **Ester** linkages, **while in PAF:** • it is bound by an **Ether** linkage • it has an acetyl group at carbon No.2 Team 437	**2** molecules of **PA** + additional molecule of glycerol → through **PO4** groups
location	Binds to cell surface receptors * of platelets (mainly) or other cells	the inner mitochondrial membrane.
function	• Triggers thrombotic and acute inflammatory reaction (hypersensitivity) (which can cause tissue damage) • activates platelets to aggregate	maintenance of respiratory complexes of electron transport chain



Platelet-activating factor



Cardiolipin

★ **Objective:** Understand the role of glycerophospholipids in lung surfactant and their clinical implications in RDS

Role of PC in lung surfactant

Alveolar cells of lungs

- lined by the extracellular fluid layer.
  (with tendency to develop surface tension)
- Type 2 alveolar cells secrete

lung surfactant complex

1. lipids (90%)

- Dipalmitoylphosphatidylcholine **(DPPC)** (the major)
- Other: PG.

2. proteins (10%)

help in distributing the surfactant in between the water molecules, preventing them from sticking together (reduce the surface tension).

Function of surfactant

Decreases the surface tension of the fluid layer:

- ➔ reduces the pressure needed to re-inflate the alveoli.
- ➔ prevents alveolar collapse (atelectasis)

Respiratory distress syndrome (RDS)

adults

Due to damaged alveoli
➔ by infection,trauma. or smoking

preterm infants

due to deficiency of lung surfactant

Major cause of neonatal death.

Treatment:
Glucocorticoids to mother to promote lung maturation.

How to assist the lung maturity of the fetus by : target for the Amniotic fluid and measure the ratio of DPPC and sphingomyelin.
علاقة الاثنين عكسية بحيث الجنين يصنع واحد اكثر من الثاني.

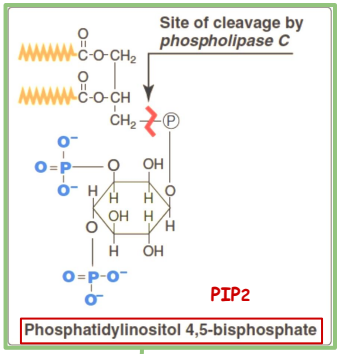
★ **Objective:** Understand the role of glycerophospholipids in cell signaling, protein anchoring

Role of PI

1 Intracellular signaling

- part of calcium-phosphatidyl inositol system

"In the membrane it is phosphorylated at tow positions."



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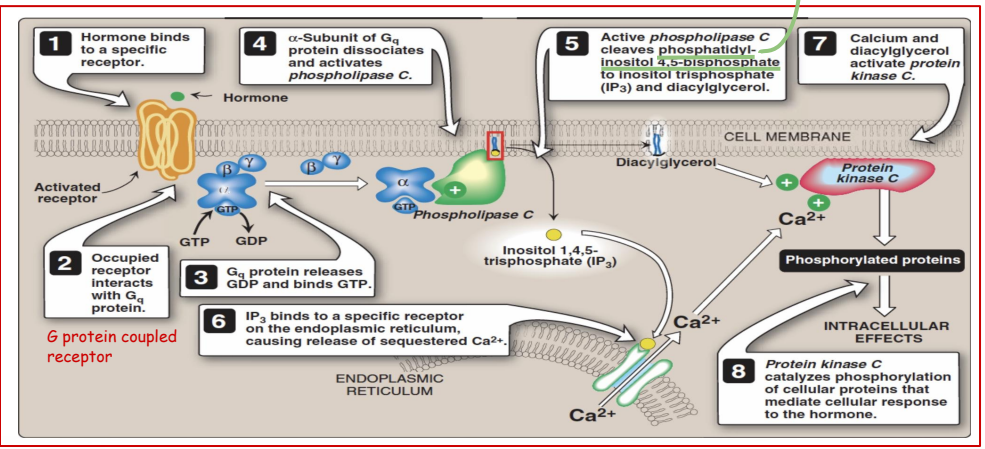


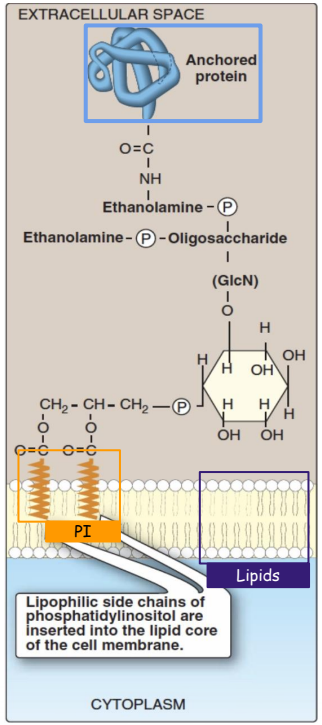
2 Protein anchoring to membranes

Attaching of protein to the embedded lipid.

by carbohydrate-PI bridge

★ can be cleaved by phospholipase C enzyme

Common proteins that are anchored	
Protein	**location**
Alkaline phosphatase	surface of small intestine
Acetylcholine esterase	postsynaptic membrane of neurons



Sphingophospholipids

1 Structure:

A long-chain fatty acid attached to sphingosine

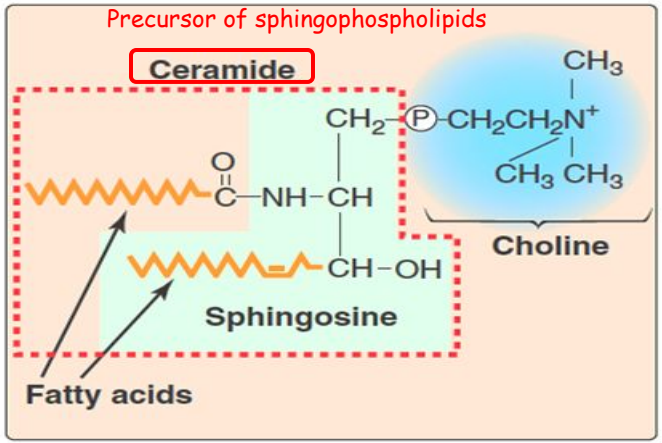
2 Example:

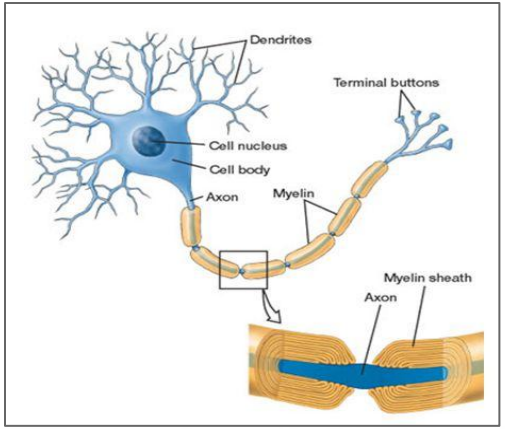
Sphingomyelin

3 Importance:

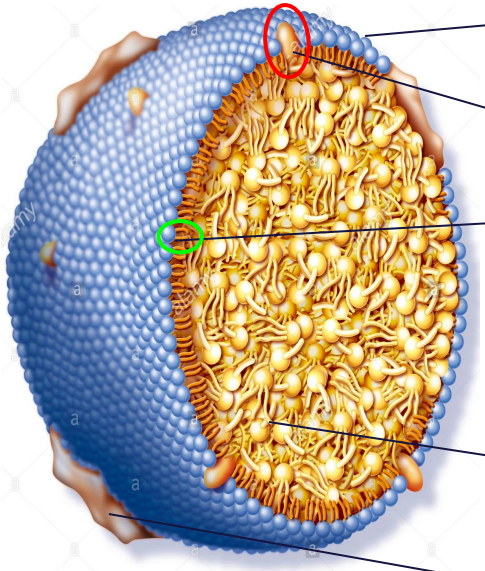
An important component of **myelin** that **protects** and **insulates** nerve fibers

→ ↑ conduction velocity





Phospholipids in lipoprotein particles



The outer core of lipoprotein particles is hydrophilic

Contains phospholipids & **free cholesterol** (Unesterified) "polar"

➔ Allows transport of core lipids in aqueous plasma

Inner core of triacylglycerols & cholesteryl esters

Apolipoprotein

★ **Objective:** Identify the classes of phospholipase enzymes

PHOSPHOLIPASES

Degradation of phospholipids

- Phospholipase A1 ,A2, C, D
  - Degradation of **Glycero**phospholipids
- **Sphingo**myelinase
  Present in lysosomes especially hepatocytes (liver)
  - Degradation of **sphingop**hospholipids

Present in

- All tissues including pancreatic juice

involved in **signal transduction** , generating **phosphatidic acid** and **choline** from **phosphatidylcholine** and **diacylglycerol**

***Slide 12 summarize important things in this figure**

PHOSPHOLIPASE A_2

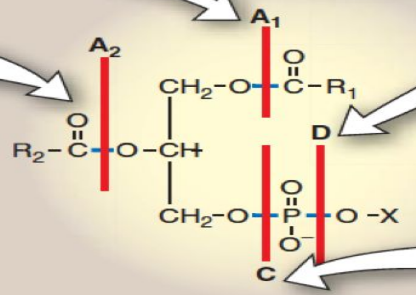
- *Phospholipase A_2* is present in many mammalian tissues and pancreatic juice. It is also present in snake and bee venoms.
- *Phospholipase A_2*, acting on phosphatidylinositol, releases arachidonic acid (the precursor of the prostaglandins).
- Pancreatic secretions are especially rich in the *phospholipase A_2* proenzyme, which is activated by *trypsin* and requires bile salts for activity.
- *Phospholipase A_2* is inhibited by glucocorticoids (for example, cortisol).

PHOSPHOLIPASE A_1

- *Phospholipase A_1* is present in many mammalian tissues.

PHOSPHOLIPASE D

- *Phospholipase D* is found primarily in plant tissue.



PHOSPHOLIPASE C

- *Phospholipase C* is found in liver lysosomes and the α-toxin of clostridia and other bacilli.
- Membrane-bound *phospholipase C* is activated by the PIP_2 system and, thus, plays a role in producing second messengers.

signaling

★ **Objective:** Identify physiological functions of phospholipase enzymes

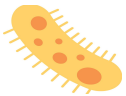
Functions of phospholipases

Digestion of phospholipids by pancreatic juice

remodeling of phospholipids

(from one kind of phospholipid to another kind)

Production of second messengers



Pathogenic **bacteria produce** phospholipases to **dissolve cell membranes** and **spread infection**

Phospholipids

GlyceroPhospholipids

Precursor

PA

Functions

- **signaling**
- **surfactant**
- **Components of bile**

Degraded by

Phospholipase

A1

location

Mammalian Tissues

A2

location

- **Pancreatic juice** (activated by trypsin)
- Mammalian tissues
- Snake and bee venoms

Mechanism

- Acting on : **PI**
- Releases: **arachidonic acid.**
- Inhibited by: **Glucocorticoids**

C

location

- **Liver lysosomes**
- a-toxin of clostridia and other bacilli

Mechanism

- Activated by: **PIP2 system**
- producing: **2nd messengers**

D

location

Plant tissue

SphingoPhospholipids

Degraded by

Sphingomyelinase

Functions

- **protection**
- **insulation** of nerve fibers

Precursor

Ceramide

Take home message

- Phospholipids are complex lipids that perform important physiological functions in the body
- **Membrane-bound** phospholipids are involved in cell signaling, protein anchoring and myelin protective functions
- **Nonmembrane-bound** phospholipids function as lung surfactant and as detergent in the bile
- Phospholipases are enzymes that degrade phospholipids
- They are important for remodeling of phospholipids

Quiz

MCQs

Q1: Which of the following is the function of phosphatidylcholine?
a) Cell signaling **b)** Lung surfactant **c)** Membrane fusion **d)** Blood clotting

Q2: Glycerophospholipids are degraded by?
a) phospholipase A3 **b)** phospholipase B **c)** phospholipase E **d)** Phospholipase C

Q3: Which one of the following is the simplest phospholipids?
a) Phosphatidic acid **b)** Phosphatidylserine **c)** Phosphatidylcholine **d)** Sphingomyelin

Q4: Which one of the phospholipases below present in snake and bee venoms?
a) Phospholipase A_1 **b)** Phospholipase A_2 **c)** Phospholipase C **d)** Phospholipase D

Q5: Which of the following enzymes degrade sphingomyelin?
a) Phospholipase A_1 **b)** Phospholipase A_2 **c)** Sphingomyelinase **d)** Phospholipase D

Q6: Nonmembrane - bound phospholipids are involved in?
a) Lung surfactant **b)** Myelin protective functions **c)** Cell signaling **d)** Protein anchoring

SAQs

Q1: An infant, born at 28 weeks' gestation, rapidly gave evidence of respiratory distress. What would the clinical laboratory and imaging results that supported the diagnosis of infant respiratory distress syndrome?.

Q2: List the functions of phospholipids

Q3: What is the lung surfactant composed of ? and what its role ?

★ MCQs Answer key:

1) B 2) D 3) A 4) B 5) C 6) A

★ SAQs Answer key:

1) The concentration of DPPC in the amniotic fluid would be expected to be lower than that of a full-term baby.

2) 1-Reservoir for intracellular messengers (signaling) 2-Anchors to cell membrane 3- Lung surfactant 4 • Components of bile

3) 90% lipids (including DPPC) and 10% proteins , its role to decrease the surface tension of fluid layer and to reduce pressure and to prevent (atelectasis)

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★ تعرف إلى الله في الرخاء يعرفك في الشدة واعلم أن ما أخطأك لم يكن ليصيبك وما أصابك لم يكن ليخطئك واعلم أن النصر مع الصبر وأن الفرج مع الكرب وأن مع العسر يسرا

438 BIOCHEMISTRY TEAM

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