Biochemistry team

Phospholipid Compounds of Physiological Importance

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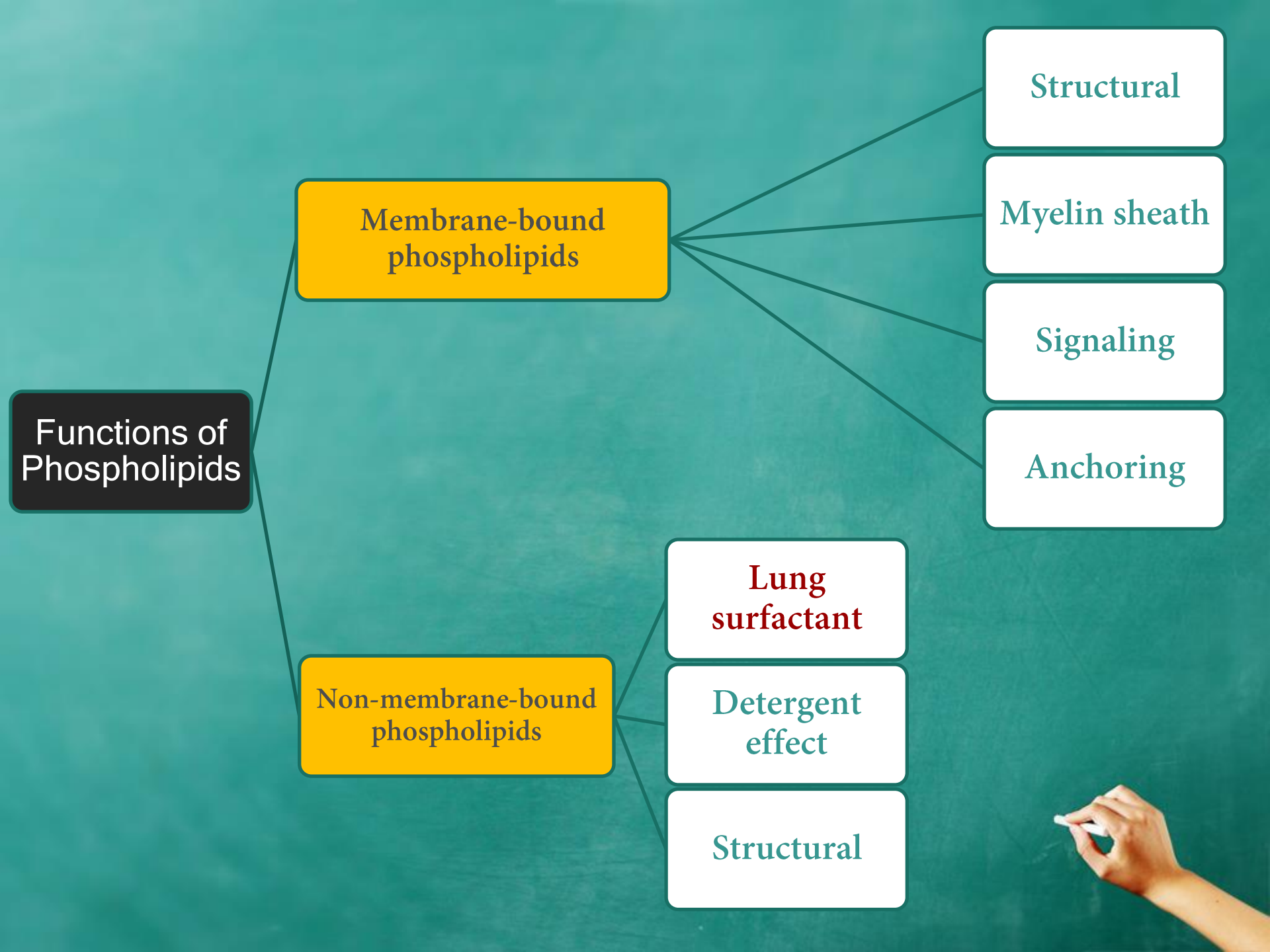
Objectives

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

- N. B
- We didn’t have to memorise any structure


Functions of Phospholipids
Membrane-bound phospholipids
Structural
Myelin sheath
Signaling
Anchoring
Non-membrane-bound phospholipids
Lung surfactant
Detergent effect
Structural

Functions of Phospholipids

(A)Membrane-bound phospholipids:

قسموها ع حسب الدور اللي تعمله الى :

1)Structural: Predominant lipids of cell membranes.

2)(تثبيت)Anchoring: Attaching some proteins to membranes.

3)Signaling: Source of IP3 and DAG.

4)Myelin sheath: insulator and speeds up transmission of nerve impulses.

(B) Non-membrane-bound phospholipids:

The main function is :(Lung surfactant)

Easy re-inflation of alveoli by air

قسموها ع حسب الدور اللي تعمله الى :

1)Detergent effect:

-Essential component of bile

-Solubilize cholesterol, preventing gall stones

-Emulsifying lipids, helping lipid digestion

2)Structural: Coat of lipoproteins

Background: Lipid Compounds

- Heterogeneous group(مجموعات غير متجانسه)
- Relatively water-insoluble Except (Ketone body)
- Soluble in non-polar solvents

Lipid Compounds: Heterogeneous Group

A. Simple Lipids:

- Fatty acids
- Ketone bodies
- Triacylglycerol
- Cholesterol

B. Complex Lipids:

- Phospholipids اللي بندرسه هالمحاضره
- Lipoproteins
- Glycolipids

Phospholipids

A. Glycerophospholipids:

- Glycerol-containing phospholipids

B. Sphingo-phospholipids:

- Sphingosine-containing phospholipids

Phospholipids

A. Glycerophospholipids:

1. Phosphatidylcholine (Lecithin)

e.g. Surfactant consist of , (Dipalmitoylecithin)

2. Phosphatidylinositol

Wich is do 2 important functions:

(1)Signaling (2)anchoring molecule

Phospholipids

A. Glycerophospholipids:

- **Parent Compound:**
  Phosphatidic acid

- **Members:**
  1. Phosphatidylcholine (Lecithin)
  e.g., (Dipalmitoylecithin) Surfactant

Phospholipids

A. Glycerophospholipids:

1. Dipalmitoylecithin (Lung surfactant)

- Synthesis and secretion: by granular pneumocytes

- Surfactant consist of:
- 1)Major lipid component (Dipalmitoylecithin65%) of lung surfactant
  2)(Remaining 35%: Other phospholipids, cholesterol & proteins)
- Function of Surfactant: decreases surface tension of fluid layer

-lining of alveoli, reducing the pressure needed for their inflation by air, and preventing alveolar collapse (atelectasis)

Congenital Respiratory distress syndrome (RDS):

- Insufficient production of lung surfactant
- (especially in pre-term babies) ⟶ neonatal death

Congenital Respiratory distress syndrome (RDS)

Pre-natal diagnosis by:

Lecithin/sphingomyelin (L/S) ratio in amniotic fluid

Ratio of **2 or above** indicates lung maturity and no RDS

(i.e., shift from sphingomyelin to lecithin synthesis by pneumocytes that normally occurs by 32 weeks of gestatioin)

Prevention:

- Glucocorticoids to the pregnant mother with low L/S ratio shortly before delivery

Treatment:

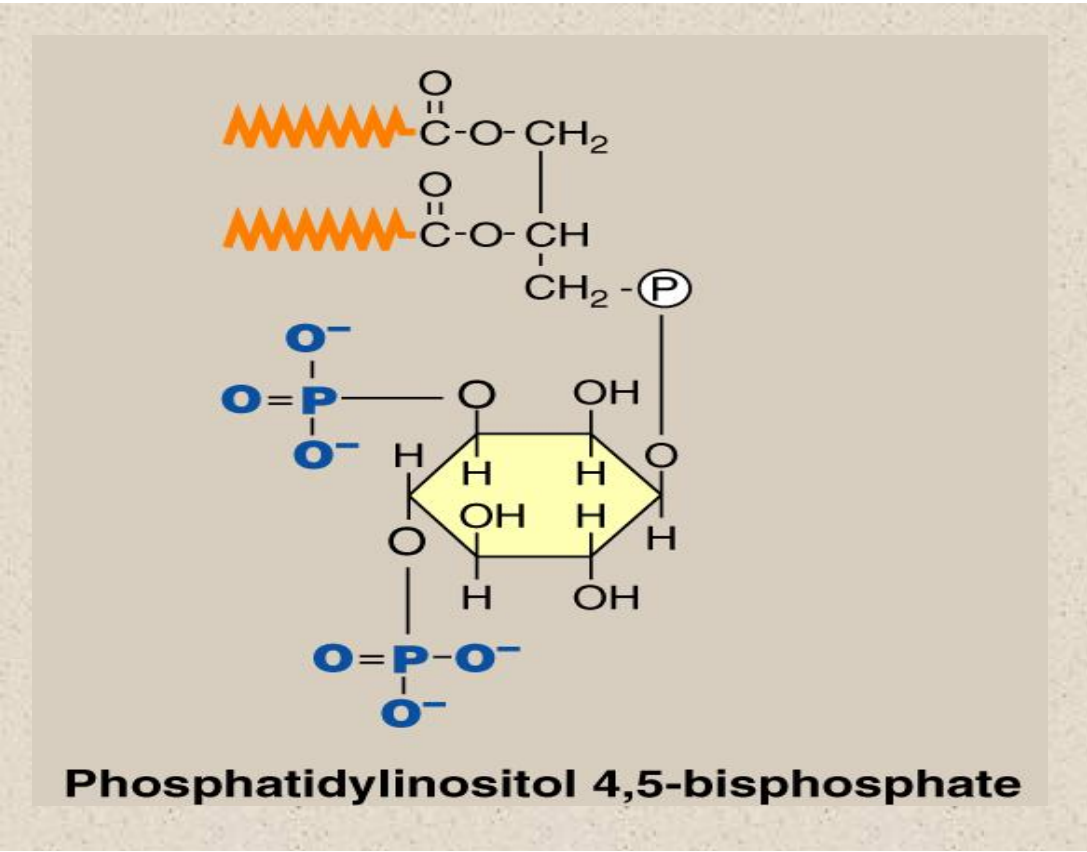
– Intratracheal administration of surfactant to pre-term infants with RDS

نشيك عالـ Ratio
قبل الولادة فلطلع قليل
تعني ان المولود بيجي
بـ RDS
فعمل على حل قبل
الولادة

Phospholipids

A. Glycerophospholipids:

2. Phosphatidylinositol 4,5 bisphosphate (PI)



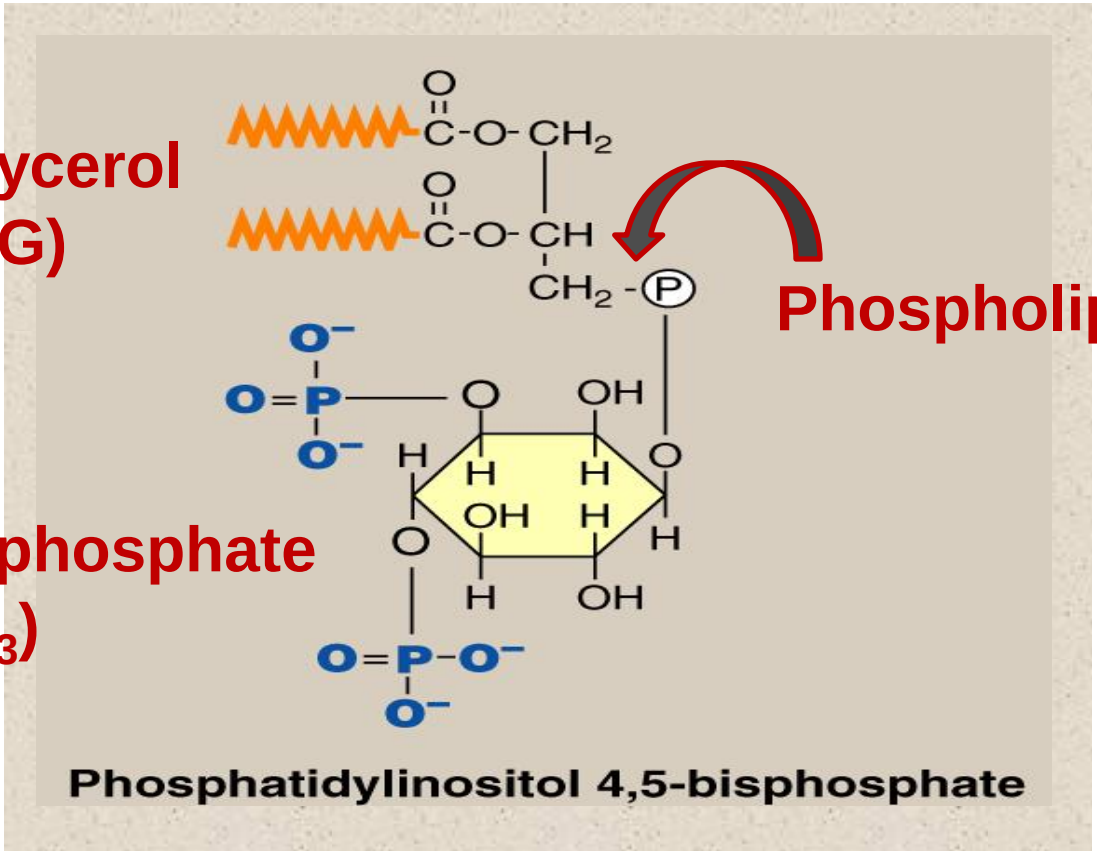
سلايد للتأمل فقط ^^

Calcium/Phosphatidylinositol System

Diacylglycerol (DAG)

Phospholipase C

Inositol Trisphosphate (IP_3)

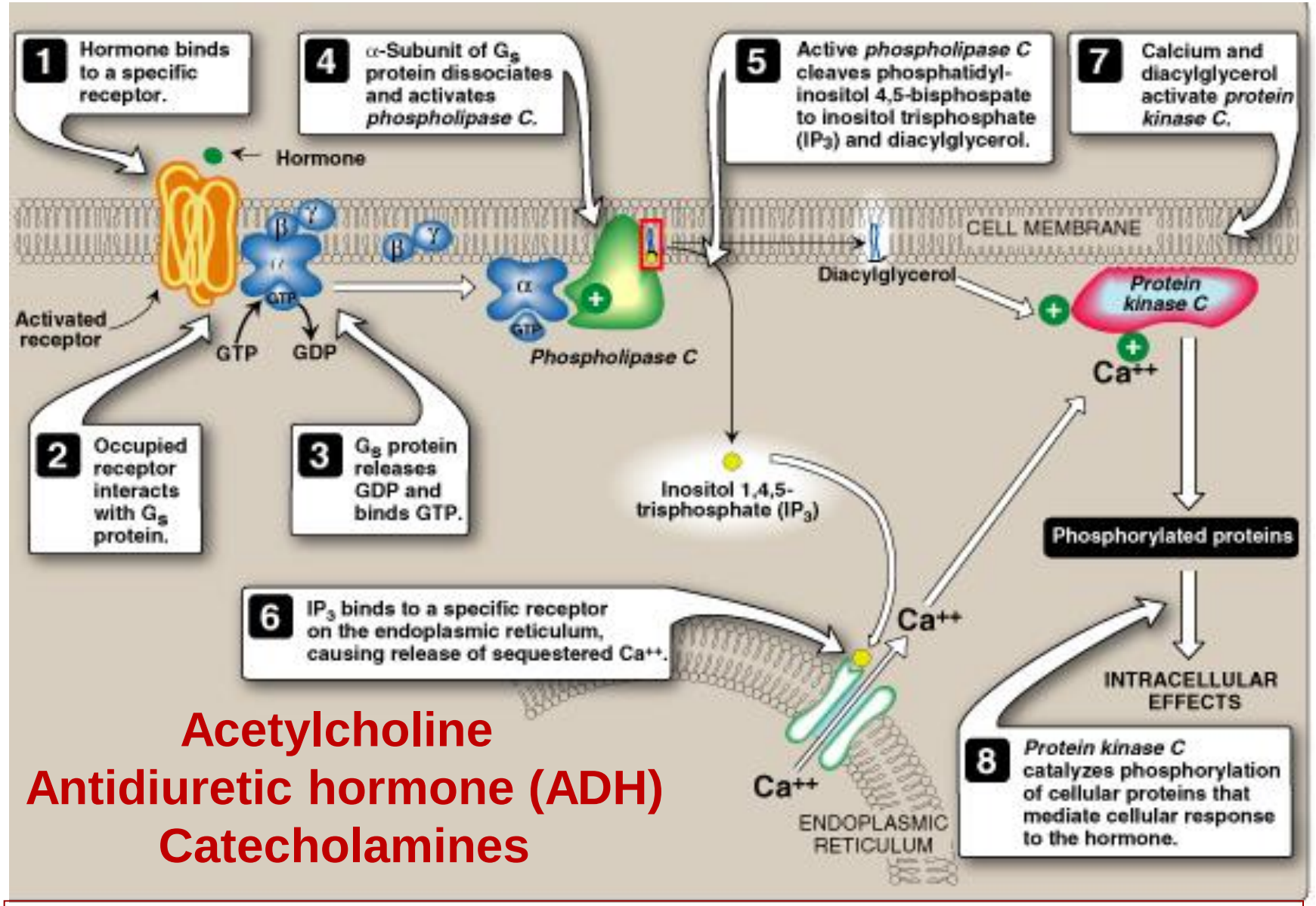


phospholipase C الـ
يكسر المركب لجزئين
(DAG + IP3)
من عند الكربون رقم 3

Phosphatidylinositol System

- **Signal:** Hormones or neurotransmitters
  e.g., Acetylcholine, antidiuretic hormone (V_1 receptor) and catecholamines (α_1 actions)
- **Receptor:** G-protein coupled receptor
- **Effects:**
  1) *Activation of phospholipase C
  2) Hydrolysis of phosphatidylinositol 4,5-bisphosphate
     Production of IP3 (Ca^{2+}) and DAG
  3) Activation of protein kinase C
  4) Phosphorylation of cellular proteins
  - *Please refer to activation of adenylyl cyclase and guanylyl cyclase for production of second messengers in other G-protein coupled signaling pathways*
- **Response:** Biological responses to hormones

هذا الكلام شرح للسلايد اللي بعدهـ



Acetylcholine
Antidiuretic hormone (ADH)
Catecholamines

Intracellular Signaling by Inositol trisphosphate

PI- Protein Anchoring

Anchoring of proteins to membranes
via
Carbohydrate-Phosphatidylinositol Bridge

Examples of anchored proteins:

1. **Alkaline phosphatase**
   (to the surface of small intestine)
2. **Acetylcholine esterase**
   (to postsynaptic membrane)

These proteins can be cleaved from
their attachment to the membranes
by **phospholipase C**

B. Sphingo-phospholipids:

Sphingosine-containing phospholipids:
e.g., sphingomyelin (Myelin sheath)

- **Sphingosine :**
- **Long chain, unsaturated amino alcohol**
  "amino because of amino group"

- **Ceramide: Parent Sphingolipid Compound :**

✓ **Long Chain Fatty acid**
✓ **Sphingosine + fatty acid = cermide**

- **Sphingomyelin :**

✓ **Long Chain Fatty acid**
✓ **Ceramide + Phosphorylcholine = sphingomyelin**

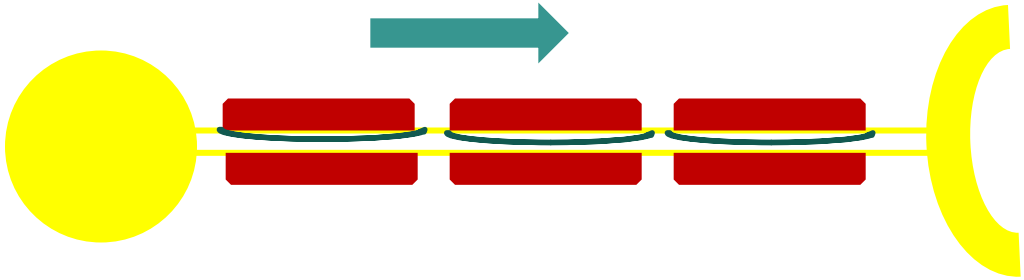
الدكتور قال
«ما
عليكش
فيها كثير
^^»

Structure & Function of Myelin Sheath

- **Myelin structure:**
  - Lipid 80%
    - Glycolipids "mainly"
    - Sphingomyelin
  - Protein 20%

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

Direction of nerve impulse



Lipoprotein Structure :

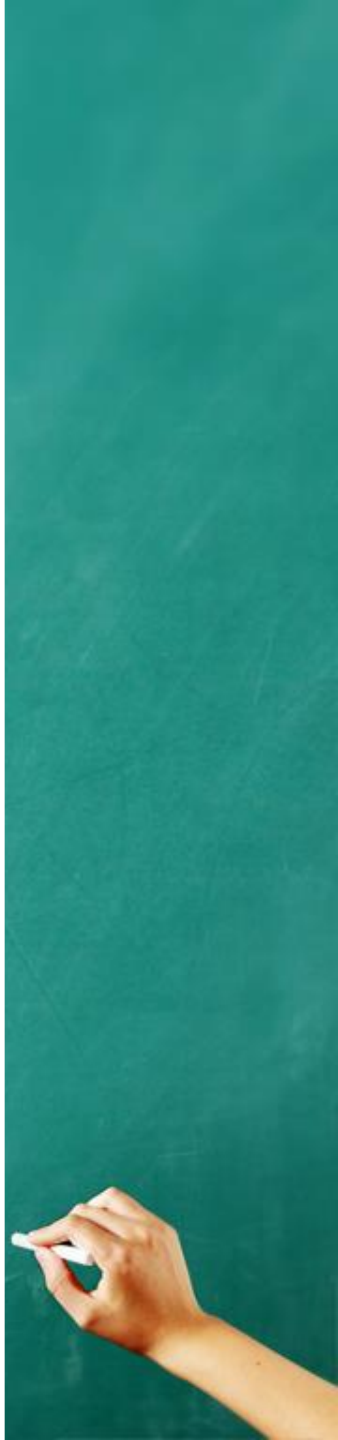
Outer part (coat):

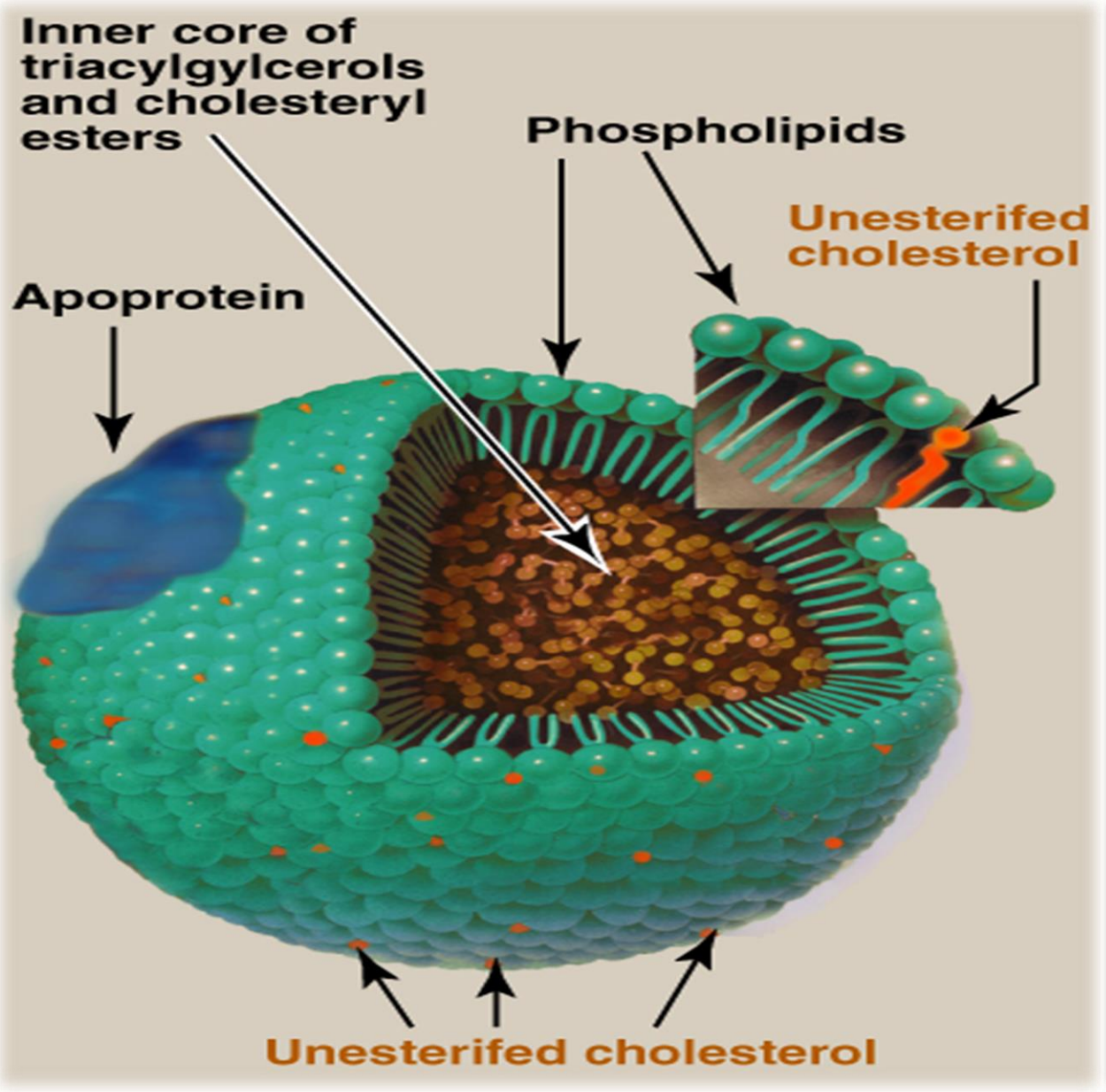
- Apoproteins or apolipoproteins
- **Phospholipids** (Why?)
- Free cholesterol

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

Inner part (core):

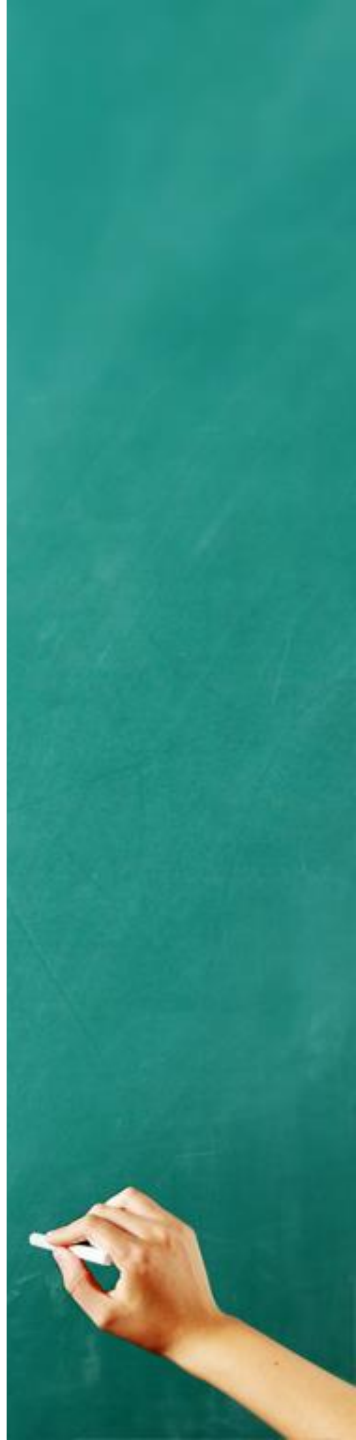
- According to the type of lipoproteins
- Different lipid components in various combinations




Inner core of triacylglycerols and cholesteryl esters
Phospholipids
Unesterifed cholesterol
Apoprotein
Unesterifed cholesterol

شرح للسلآيدين السآبقين :

- ✓ الـ lipoprotein لا يستطيع أن يتحرك في البلازما بسهولة لانه ما يذوب في الماء والبلآزما أغلبهآ مآء , لذلك وهذآ من بديع صنع الخالق فقد وضع الله سبحانه وتعالى حوله coat ليجعله يذوب جزئياً في الماء , وفي هذا الغطاء phospholipid ليشش ؟ لآنه الـ phospholipid يحتوي على رأس محب للمآء «hydrophilic head» و ذيل كاره للمآء «hydrophobic tail» , وضحت ☺ ؟



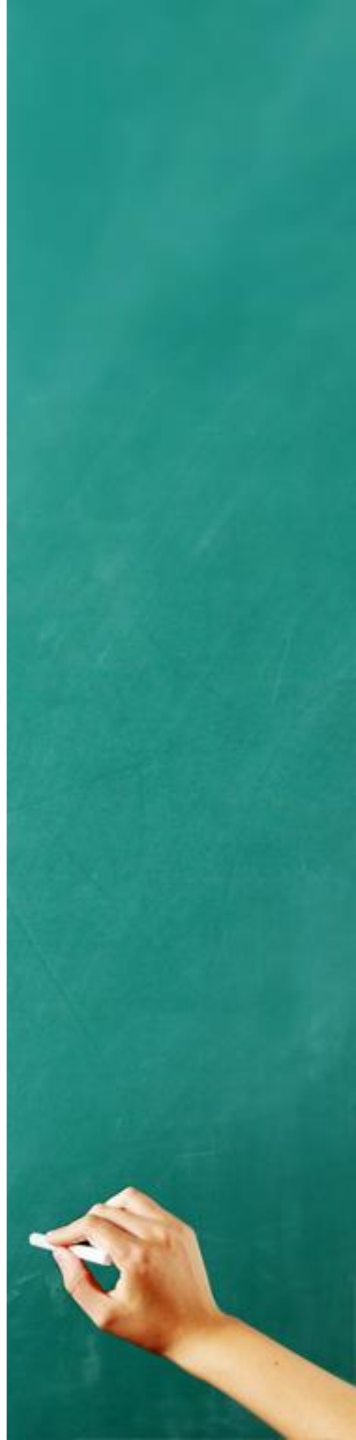
Phospholipases

(1) For glycerophospholipids:

- **Phospholipases A1, A2, C and D**
- **Present in all tissues and pancreatic juice**
- **Present in snake venoms and bacterial**
- **toxins**

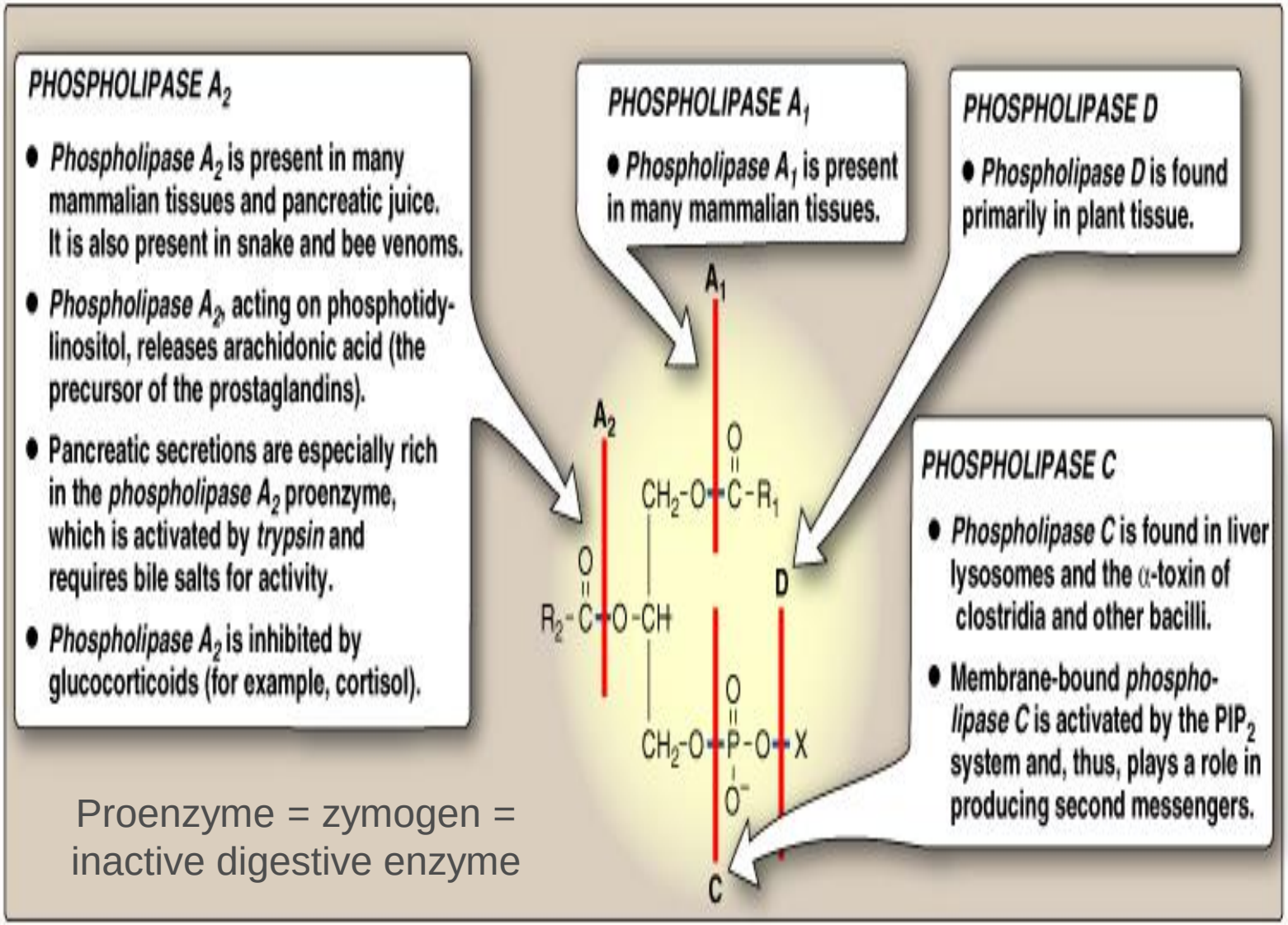
(2) For sphingophospholipids:

- **Lysosomal phospholipase**
- **Sphingomyelinase**
- **Sphingomyelin ⟶ Ceramide + Phosphocholine**



Glycero-phospholipases

الدكتور قال «مهم جداً إنك تعرف الكلام اللي بالصورة»



Proenzyme = zymogen = inactive digestive enzyme

Functions of Phospholipases

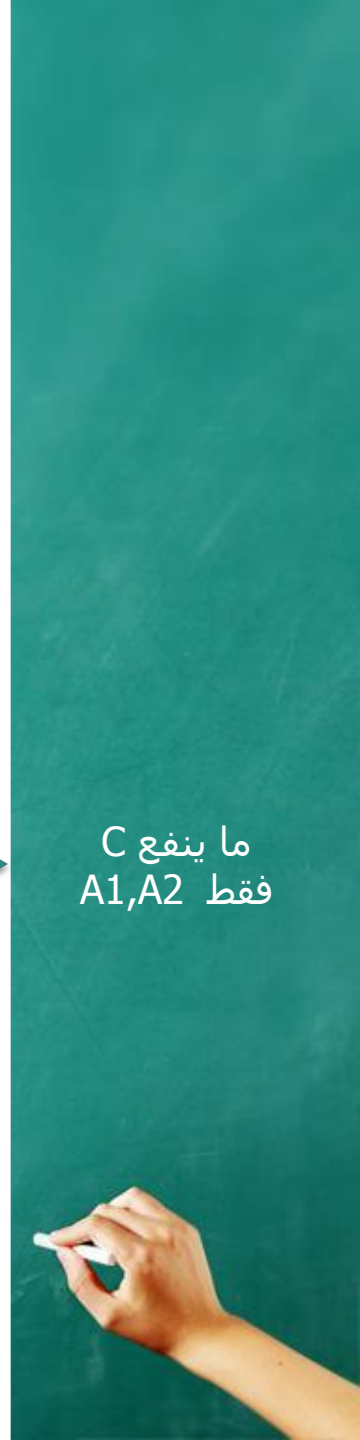
(1) Degradation of phospholipids :

- Production of second messengers
- Digestion of phospholipids by pancreatic juice
- Pathogenic bacteria degrade phospholipids of membranes and causing spread of infection

(2) Remodeling of phospholipids:

- Specific phospholipase removes fatty acid from phospholipid
- Replacement of fatty acid by alternative fatty acid using fatty acyl CoA transferase
  e.g., Binding of 2 palmitic acids in:
  Dipalmitoylphosphatidylcholine (DPPC)
  Binding of arachidonic to carbon 2 of PI or PC

ما ينفع C
فقط A1,A2



Take Home Message

- **Phospholipids are Complex lipids**

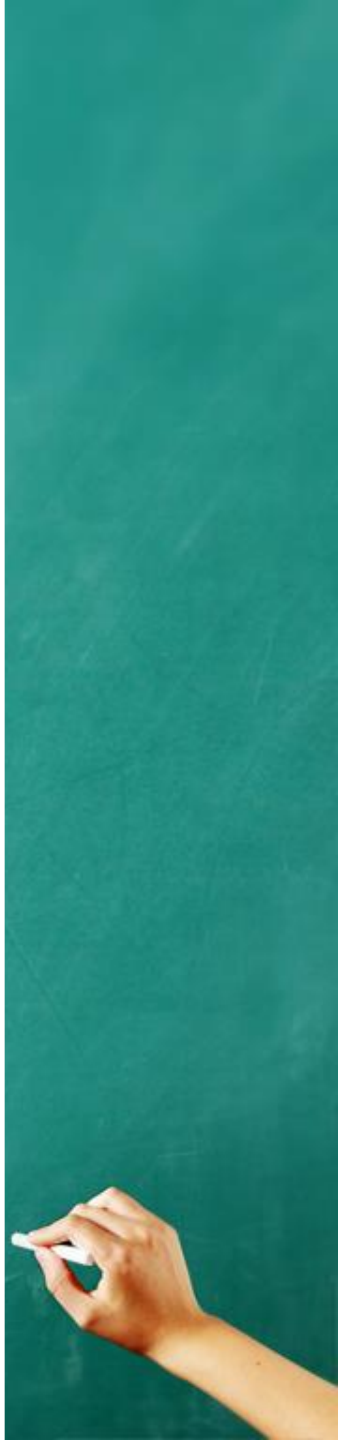
- **Phospholipids have important physiological functions:**

  A. Membrane-bound:

  Structural
  Signalling & anchoring: e.g., PI
  Myelin sheath: e.g., sphingomyelin

  B. Non-membrane bound:

  Structural: Lipoprotein coat
  Alveolar re-inflation: Lung surfactant
  Detergent effect: Phospholipids of bile



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Phospholipases:

Phospholipases A1, A2, C and D

Lysosomal Phospholipase: Sphingomyelinase

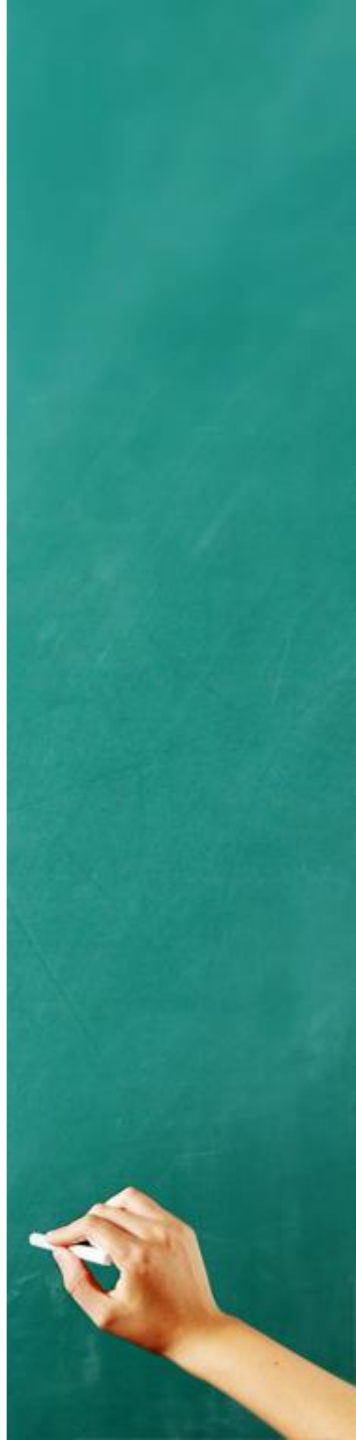
Function of phospholipases:

Degradation of phospholipids

e.g., production of second messengers

Remodeling of phospholipids

e.g., production of DPPC (lung surfactant)



Quiz

1) Pregnant mother with low L/S ratio what the complication of that ?
   A) DSR Syndrome.
   B) Insufficient production of lung surfactant.
   C) Pre-term babies
   D) Down Syndrome.

the answer is(B)

2) Pregnant mother with low L/S ratio what we shoud to do ?
   A) Give her Glucocorticoids shortly before delivery.
   B) Surgical intervention.
   C) Tell the mother to take supplements (Vitamins).
   D) Give her Glucocorticoids at 20 week.

the answer is (A)

3) What is the intracellular messenger produced by IP3?
   A) Diacylglycerol (DAG)
   B) Sphingomyelinase
   C) Inositol 1,4,5-Trisphosphate (IP3)

the answer is (A)

Quiz

4) Alkaline phosphatase in intestine is:

A) Phosphatidylinositol
B) Sphingomyelinase
C) physiolapase A2

the answer is (A)

5) Which of the following is the remodeling phospholipid in Dipalmitoylphosphatidylcholine which produce lung surfactant ?

A) Sphingomyelinase
B) physiolapase A2
C) Phosphlipase C

the answer is (B)

6) Which of the following is second messenger:

A) Inositol 1,4,5-Trisphosphate (IP_3)
B) COA
C) physiolapase C

the answer is (A)