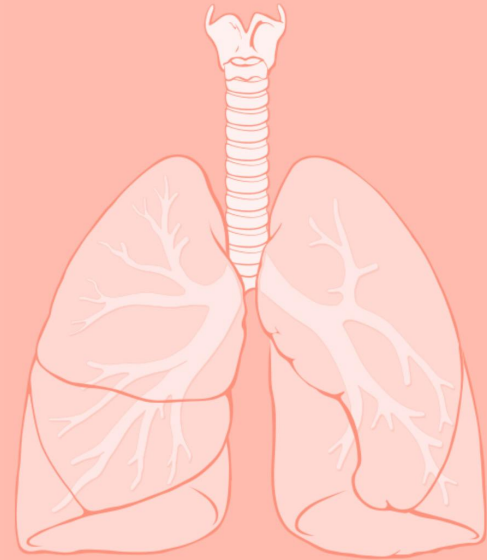


# Phospholipids of Clinical Significance



*Color index :*





*Main text*

**IMPORTANT**

*Extra Info*

*Drs Notes*

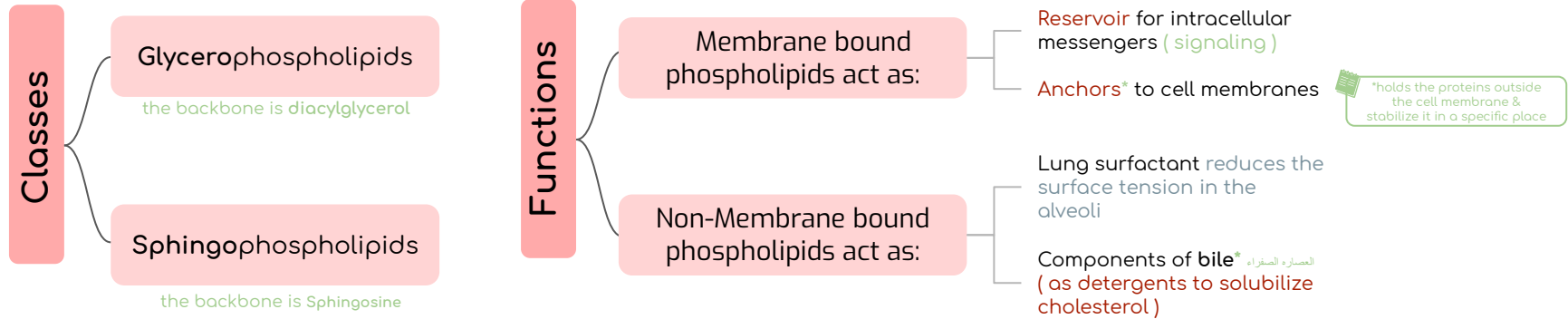
## Objectives:

-  Identify the types and functions of phospholipids
-  Discuss the physiological importance of phospholipids
-  Understand the role of glycerophospholipids in lung surfactant and their clinical implications in respiratory distress syndrome (RDS)
-  Identify the classes and physiological functions of phospholipase enzymes

# Phospholipids

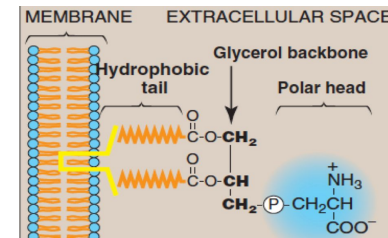
**Definition:** Phospholipids are amphipathic the polar part is ( ionic compounds ) that contain an alcohol group attached either to: A) Diacylglycerol B) Sphingosine and the non polar part is ( lipid )

- phospholipids are the major lipids of cell membrane



**Properties:**

- Their hydrophobic (non-polar) portion is attached to the membrane  
it consist of long chain of fatty acid
- Their hydrophilic (polar) portion extends outward interacting with the aqueous environment



 amphipathic = hydrophobic+hydrophilic

# Glycerophospholipids (Phosphoglycerides)

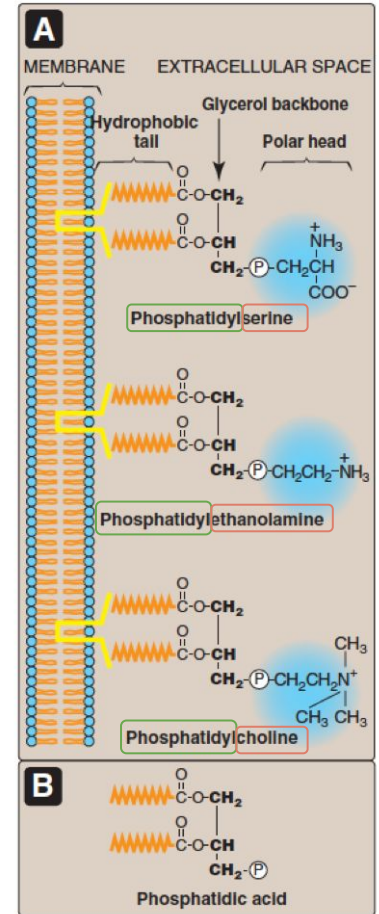
- Contain glycerol (Backbone)
- A **major** class of phospholipids
- All contain **phosphatidic acid**, (PA) (simplest) It's formed from (polar head without alcohol + glycerol backbone)
- (PA) is the simplest phospholipid (precursor)

Phospholipids are derived from PA such as:

You have to memorize all the PA derivatives & their functions

Remember : Getting Early Calls Is Sweet

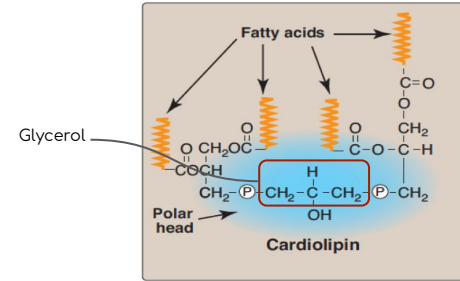
Glycerol + PA	→ Phosphatidyl <u>g</u> lycerol (P <u>G</u> )	Lung surfactant
Ethanolamine + PA	→ Phosphatidyl <u>e</u> thanolamine (P <u>E</u> ) (cephalin)	membrane fusion during cell division
Choline + PA	→ Phosphatidyl <u>c</u> holine (P <u>C</u> ) (lecithin)	Lung surfactant
Inositol + PA	→ Phosphatidyl <u>i</u> nositol (P <u>I</u> )	Cell signaling
Serine + PA	→ Phosphatidyl <u>s</u> erine (P <u>S</u> )	Cell signaling & blood clotting



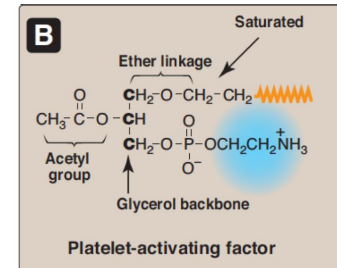
# Some examples of Glycerophospholipids

	Cardiolipin	Platelet activating factor (PAF)
Structure	Two molecules of PA joined to an additional molecule of glycerol through PO <sub>4</sub> groups	In other phosphoglycerides, the fatty acids are attached to glycerol by Ester linkages, while in PAF: 1. it is bound by an Ether linkage 2. it has an acetyl group at carbon No.2 #Team 437 & drs note
Location	In the inner mitochondrial membrane	Binds to cell surface receptors
Function	maintenance of respiratory complexes of electron transport chain	Triggers thrombotic and acute inflammatory reaction it plays a role in hypersensitivity

Cardiolipin



Platelet activating factor (PAF)

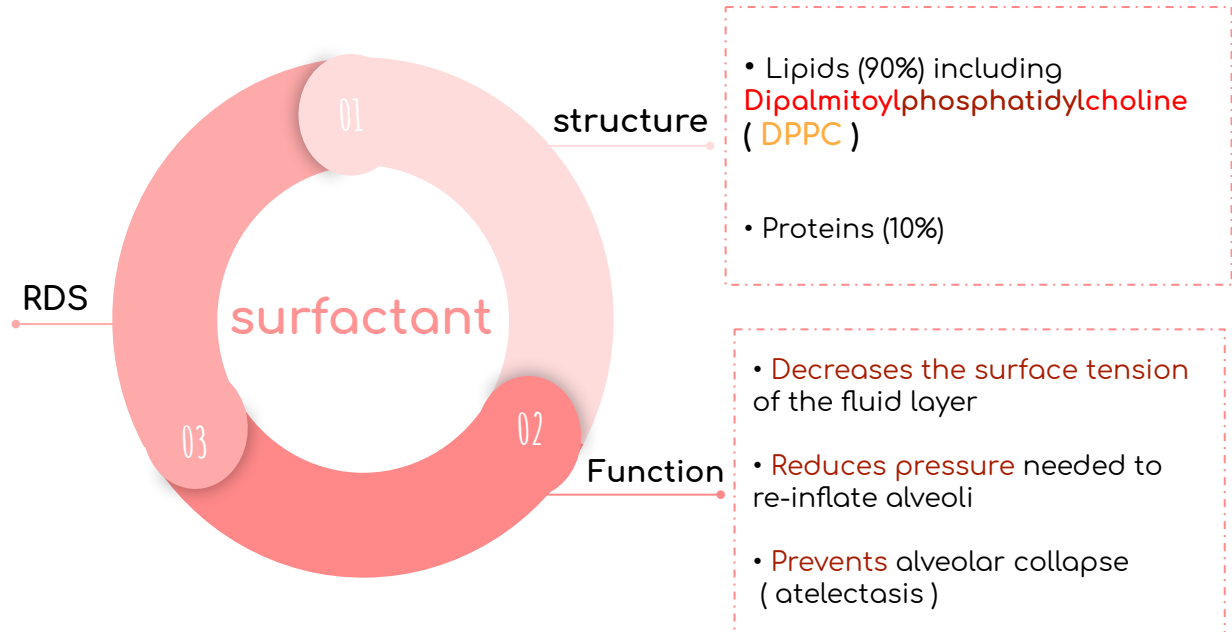


# Role of PC in lungs surfactant

- Alveolar cells of the lungs are lined by the extracellular fluid layer
- Alveolar cells secrete **DPPC** (a major lung surfactant)

## Respiratory distress syndrome (RDS)

- In **preterm infants** due to deficiency of lung surfactant
- A major cause of neonatal death
- **Treatment:** Glucocorticoids to mother to **promote lung maturation** (increase the production of surfactant)
- In **adults** due to damaged alveoli by **infection** or **trauma**



# Role of PI in

## 1) cell signaling

- Plays important role in intracellular signaling
- PI is part of calcium-phosphatidylinositol system

## 2) Membrane protein anchoring

- Anchoring of proteins to membranes through carbohydrate-PI bridge
- Anchoring proteins can be cleaved by phospholipase C enzyme

more explanation in the next slide

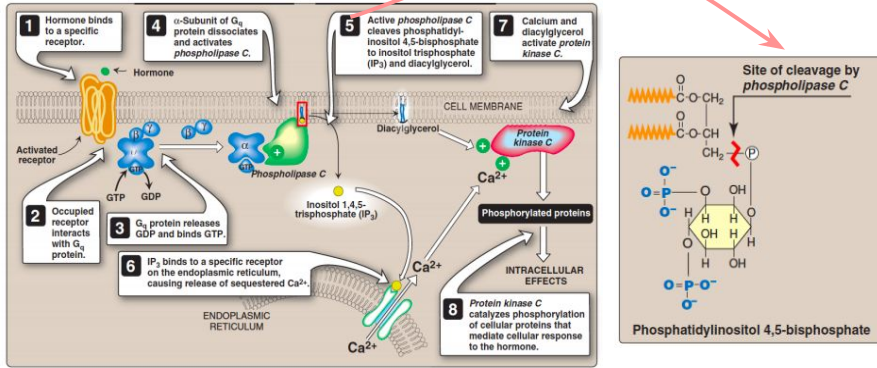


Figure 17.8  
Role of inositol triphosphate and diacylglycerol in intracellular signaling.

Examples of Anchoring proteins :

Alkaline phosphatase

on the surface of small intestine

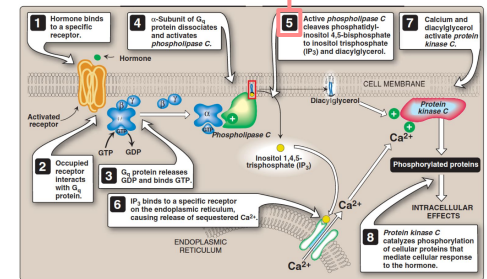
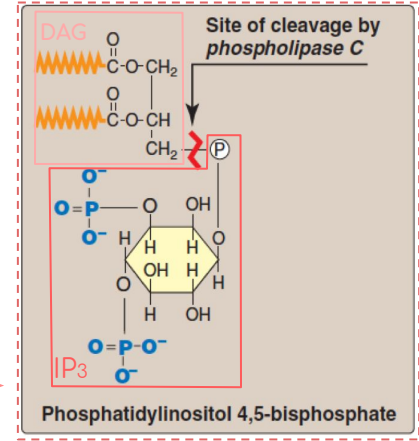
Acetylcholine esterase

on postsynaptic membrane of neurons

You need to know the following:  
- Functions of PI  
- Examples of anchoring proteins  
- How to cleave

# Role of PI in 1) cell signaling

- 1 A specific Ligand “first messenger” (hormone or neurotransmitter), binds to G-protein coupled receptors.
- 2,3 Receptor interacts with G-protein, stimulates its release of GDP and replaces it with GTP, therefore activating it.
- 4  $\alpha$ -subunit disassociate from G-protein,  $\alpha$ -subunit binds to Phospholipase C activating it in the process.
- 5 Phospholipase C breaks phosphatidylinositol 4,5-bisphosphate into Inositol trisphosphate (IP3) + diacylglycerol (DAG) .
- 6 IP3 “second messenger” binds to Endoplasmic Reticulum (ER), a major store of Calcium ions, causing the release of Calcium ions.
- 7 Protein Kinase C responds to second messengers, in this case they're Calcium from ER and signals from DAG.
- 8 Protein Kinase C phosphorylates proteins in response to the signals from DAG and IP3  
(remember that kinase proteins function in phosphorylating proteins).
- 9 Intracellular effect and response.





# Sphingophospholipids

You need to know the following:  
-Functions  
-Examples

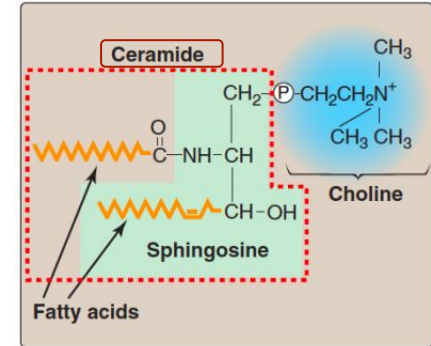
- A long-chain **fatty acid** attached to **sphingosine** ( sphingosine is a backbone )
- Example: **Sphingomyelin**
- Sphingomyelin is an important component of myelin that protects and insulates nerve fibers

- what is the simplest Sphingophospholipids ? Ceramide
- what is the simplest phospholipid ? phosphatidic acid



- sphingosine (green box) + fatty acid ( palmitic acid ) = **ceramide** (dashed box)
- sphingosine (green box) + fatty acid + choline = **Sphingomyelin**

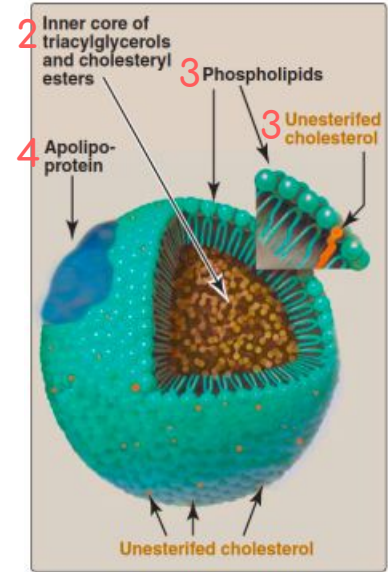
Choline here with phosphate so ( choline + phosphate = phosphorylcholine )



# Phospholipids in lipoprotein particles

1. The **outer** core of lipoprotein particles is hydrophilic
2. The **inner** core of triacylglycerols & cholesteryl esters ( hydrophobic )
3. The outer core contains phospholipids and free cholesterol which is Unesterified "polar"  
→ Allows transport of core lipids in aqueous ( water ) plasma
4. Apolipoprotein are proteins that transport lipids by binding to them

free cholesterol = Unesterified cholesterol



**Figure 18.14**  
Structure of a typical lipoprotein particle.

# Phospholipases

- Phospholipids are degraded by ? phospholipase enzymes
- phospholipase Present in ? all tissues including **pancreatic juice**
- ✦ Glycerophospholipids are degraded by? .....→ Phospholipase A1, A2, C, D (more details in the next slide)
- ✦ **Sphingo**phospholipids are degraded by? .....→ **Sphingo**myelinase

## Function of phospholipases

there is a contentious remodeling for phospholipids we call it deacylation; which means remove the fatty acid and reacylate it with another one)

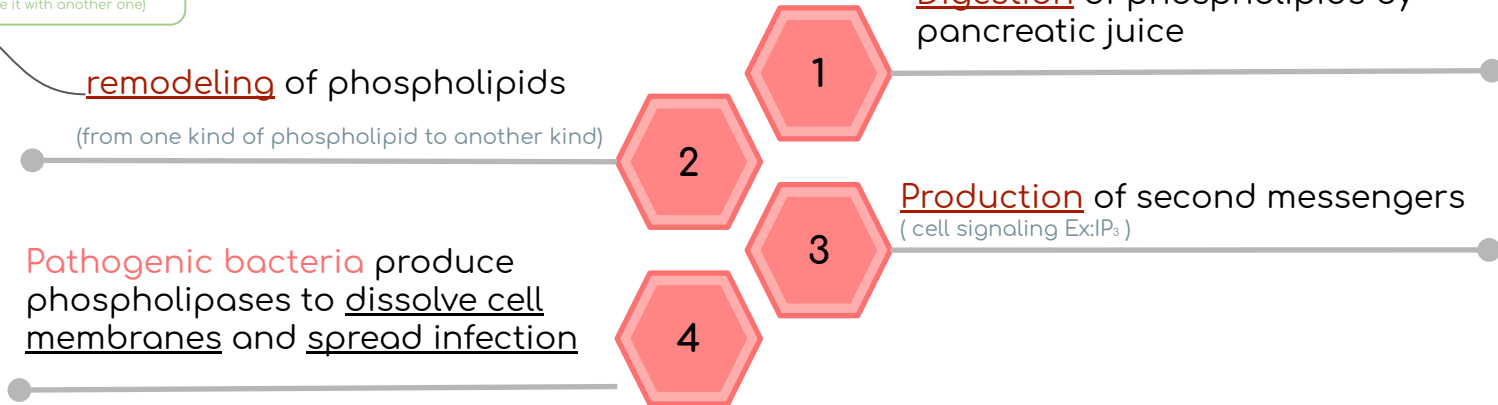
remodeling of phospholipids

(from one kind of phospholipid to another kind)

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

Digestion of phospholipids by pancreatic juice

Production of second messengers  
(cell signaling Ex:IP<sub>3</sub>)



# Phospholipase<sup>(1)</sup>

type  
A1

## Location

- Mammalian Tissues

type  
A2

## Location

- Mammalian Tissues
- Pancreatic juice<sup>(2)</sup>
- Pancreatic secretions
  - are especially rich in the Phospholipase A2 proenzyme<sup>(3)</sup>
  - it is **activated by trypsin**<sup>(4)</sup> and requires bile salts for activity
- Snake and bee venoms سموم الثعابين و النحل

## Mechanism

- **Acting on** : Phosphatidylinositol (PI)
- **Releases** : arachidonic acid (the precursor of prostaglandins)
- **Inhibited by** : Glucocorticoids
  - Eg: cortisol

type  
C

## Location

- Liver lysosomes
- $\alpha$ -toxin of clostridia<sup>(5)</sup> and other bacilli

## Mechanism

- membrane-bound phospholipase C
- **Activated by** : PIP<sub>2</sub> system
  - thus , plays role in producing : 2nd messengers

type  
D

## Location

- Plants tissue

1- There are four major of Phospholipase classes, termed A, B, C and D  
2- Pancreatic juice : the clear alkaline digestive fluid secreted by the pancreas  
3- proenzyme or zymogen : are inactive enzyme precursors that require biochemical change to become active.  
4- Trypsin : is an enzyme that helps us digest protein.  
5- clostridia : type of bacteria

# Take Home Messages



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



Non Membrane-bound phospholipids function as lung surfactant and as detergent in the bile

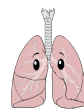


Phospholipases are enzymes that degrade phospholipids



They are important for remodeling of phospholipids

# Summary



## Phospholipids

### Characteristic

Amphipathic

polar,  
ionic compound

Major lipids of the  
cell membrane

Attached with  
alcohol group

### Classified

#### Glycerophospholipids

##### simplest phospholipid (precursor)

PS

Function :  
-Cell signaling  
-Blood clotting

PE

Function :  
Play a role in  
membrane fusion

PC

Function :  
Lung surfactant

PI

Function :  
Cell signaling

PG

Function :  
Lung surfactant

##### Examples

#### Cardiolipin

structure :

2 molecules of PA

location :

the inner  
mitochondrial  
membrane

function :

maintenance of  
respiratory complexes  
of electron transport  
chain

#### Platelet activating factor (PAF)

location :

Binds to cell surface  
receptors

function :

Triggers thrombotic and acute  
inflammatory reaction

##### Catalyzed by :

#### Degradation

Phospholipases  
A1, A2, C, D

Result :

-Glycerol  
-fatty acid  
-phosphate  
-alcohols

#### Sphingophospholipids

##### Structure :

fatty acid  
+sphingosine

##### Example:

Sphingomyelin

Function: protects  
and insulates nerve  
fibers

##### Degradation :

Characterized by  
Sphingomyelinase

# Quiz

Q1 :Phosphatidylglycerol is involved in which of the following ?

- |                    |                   |                     |                    |
|--------------------|-------------------|---------------------|--------------------|
| A ) cell signaling | B ) cell division | C ) lung surfactant | D ) blood clotting |
|--------------------|-------------------|---------------------|--------------------|

Q2 :A doctor expected that a pregnant woman will give birth early ,What should give the mother to avoid the collapse of the child's lungs ?

- |                        |                     |             |            |
|------------------------|---------------------|-------------|------------|
| A ) inhaled surfactant | B ) glucocorticoids | C ) calcium | D ) NSAIDs |
|------------------------|---------------------|-------------|------------|

Q3 : Phospholipase type A2 Inhibited by ?

- |                      |             |                 |                     |
|----------------------|-------------|-----------------|---------------------|
| A ) arachidonic acid | B ) trypsin | C ) PIP2 system | D ) Glucocorticoids |
|----------------------|-------------|-----------------|---------------------|

Q4 : what is the simplest Sphingophospholipids ?

- |                       |              |                   |                 |
|-----------------------|--------------|-------------------|-----------------|
| A ) Phosphatidic acid | B ) Ceramide | C ) Sphingomyelin | D ) sphingosine |
|-----------------------|--------------|-------------------|-----------------|

Q5 : Anchoring proteins can be cleaved by ?

- |                     |                      |                     |                      |
|---------------------|----------------------|---------------------|----------------------|
| A ) phospholipase C | B ) phospholipase A2 | C ) phospholipase D | D ) phospholipase A1 |
|---------------------|----------------------|---------------------|----------------------|

## SAQs :

Q1: What is the major component of alveolar surfactant does pneumocyte type II secrete ?

Q2: give two examples of sphingophospholipids ?

Q3: Explain the Mechanism phospholipase C ? And where can be found ?

★ MCQs Answer key:

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

★ SAQs Answer key:

1) Dipalmitoylphosphatidylcholine

2) Ceramide, Sphingomyelin

3) membrane-bound phospholipase C  
Activated by PIP<sub>2</sub> system, thus plays role in producing 2nd messengers

Girls team:



Boys team:



قد يكون السطر الذي حَرَمَ عينيكَ النومَ ليلةً  
شفاءً لَداءِ أَرَقِّ العليل ليالٍ طوال

Rania Almutiri

Alia Zawawi

 Norah Alshathry

Reem Alamri


Renad Alhomaidi

Norah Alasheikh

 Fatimah Alhelal

 Manal Altwaim

Abdullaziz Alrabiah

 Hamad Almousa

 Omar Alsuliman

Bassam Alasmari

Homoud Algadheb


Abdullah Alanzan

Abdullah Almazro

Ahmad Alkhayatt

Abdullaziz Alomar

Mishal Alhamed

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