

VEIN BATCH 2027



Sub: Molecular المادة:

Lecture: 8 المحاضرة:

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Edited: تعديل:



Lipids of biological importance- 4

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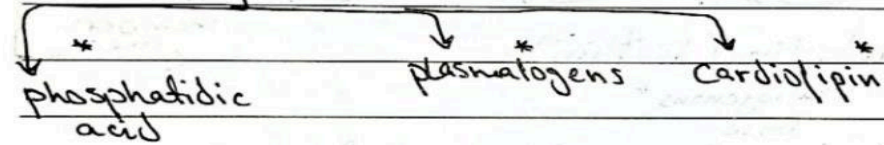
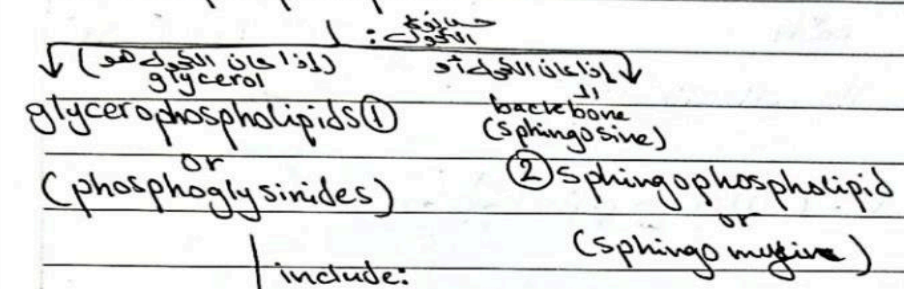
Complex (compound) lipids

- Complex lipids are formed of:
 - simple lipids
 - **PLUS** other substances such as:
 - Phosphate radical/ group → phospholipids
 - carbohydrates → glycolipids
 - Proteins → lipoprotein

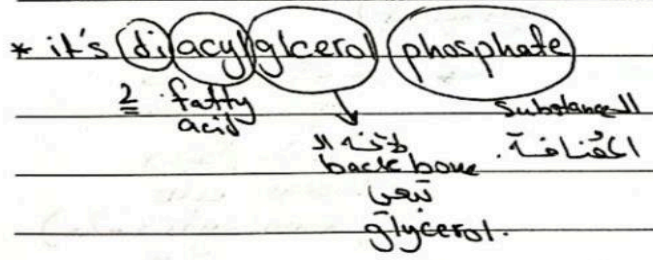
Lipids "3"

Complex lipids = Simple lipid + other substance.

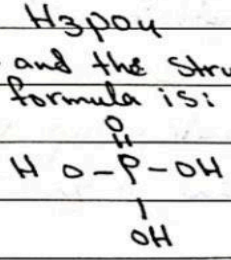
① phospholipids



والتي هي أبداً نوع من الـ parent molecule *



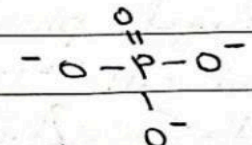
* note: ↳ the molecular formula of phosphoric acid:



وهي تتكون من الـ OH

التي هي الـ ionized (يعني كذالك H و تسعة على الـ (-)) في الماء السالبي

وهي في جزيء الـ polar و بالتالي water soluble.



I. Phospholipids

Structure:

- Phosphate group + alcohol (joined via ester bond) + FA
- There are two classes of phospholipids (according to alcohol):
 - those that have glycerol as a backbone → glycerophospholipids
 - those that contain sphingosine → sphingophospholipids

A-Glycerophospholipids: There are 9 types & include:

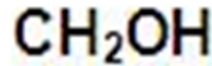
- Phosphatidic acid and its esters with one alcohol
- Plasmalogens
- Cardiolipin

*ما في داعي تحفظ ال chemical structure لكل واحد بس
بدك تكون عارف المكونات تبعته (زي ال ATP مثلا بتكون من
ribose/adenine/triphosphate بس ما كان مطلوب شكله)

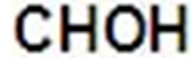
Simple lipids

Primary carbons

1

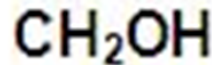


2



Secondary carbon

3

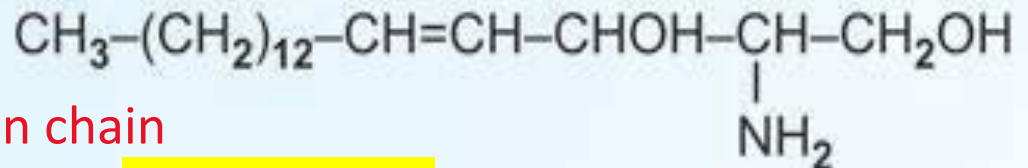


I. Glycerol :

- It is the simplest form of **trihydric** alcohol
- It is commercially known as glycerin: $\text{CH}_2\text{OH}.\text{CHOH}.\text{CH}_2\text{OH}$
- Glycerol is the main component of neutral fats
- Since the glycerol contains three hydroxyl groups, it has the ability to combine with three FA through an **ester bond**.
- These FA may be the same to give simple triacylglycerols (TAG) or different to give mixed triacylglycerols.
- The most common FAs which may enter in the structure of neutral fats are palmitic, stearic and/or oleic acids.

Sphingosine:

- amino alcohol
- has an unsaturated hydrocarbon chain
- long chain



Sphingosine: an amino alcohol with 18C

1- Phosphatidic acid: (الأب الروحي لل phosphoglyceride)

- Simplest phosphoglyceride & is the precursor of the other members of this group

→ (acyl means Fatty acid)

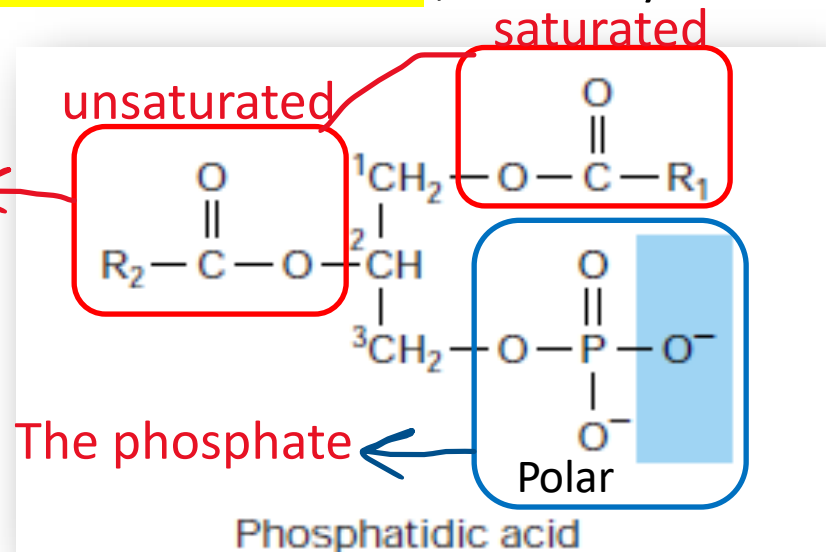
- It is diacylglycerol phosphate:

– It consists of glycerol to which are esterified :

- (1) a fatty acid, **usually saturated** at the 1- position
- (2) a fatty acid , **usually unsaturated** at the 2- position, and
- (3) phosphate at the 3-position

Phosphatidic acid is an **intermediate in metabolism** ; little may be found in cell membranes.

The Diacyl ←



The phosphate ←

وبما انه يحتوي على FA (hydrophobic) و

phosphate (hydrophilic) اللي علاقتهم بالماء

عكس بعض ف هاض المركب يعتبر Amphipathic

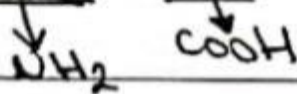
(لو ناسي معناها ارجع لليكشر 5 سلايد 18)

parent molecule is phosphatidic acid

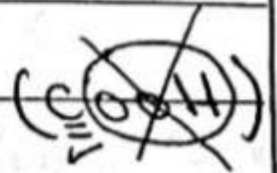
other members

* choline: with positive charge & 3 OH groups.

* serine: amino acid (monomer of proteins)



decarboxylation of it gives:



* ethanolamine: HO-CH₂-CH₂-NH₂



alcohols

2- Phosphatidylcholine (lecithin):

*اسمه الثاني مهم جدا, و متوقع جدا نشوفه بالامتحان

- The phosphate group of phosphatidic acid is esterified to the alcoholic group of the nitrogenous base

هو charged ammonium compound وهو شبيه بال amino acids وبنحتاجه بال acetylcholine اللي هو neurotransmitter

- It is the most abundant phospholipid in the cell membrane

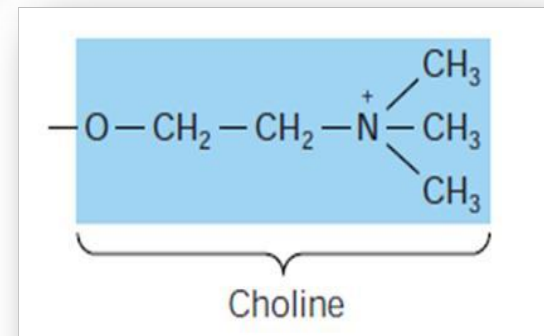
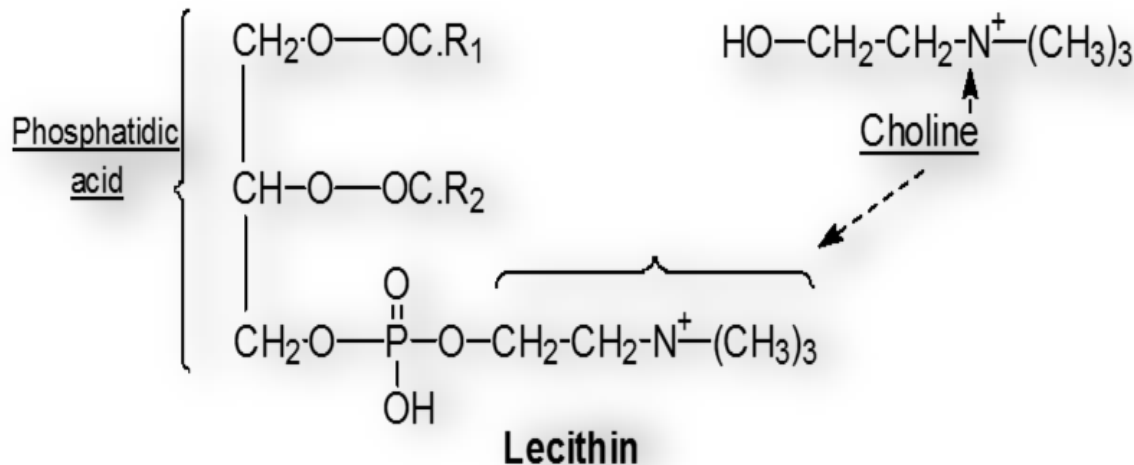
- Represents a large proportion of body's stores of choline

*مهم للامتحان

أهم مكون لل lung surfactant (مادة موجودة في الرئتين بتتكون بالشهر الأخير في حياة الجنين بنهاية الحمل)

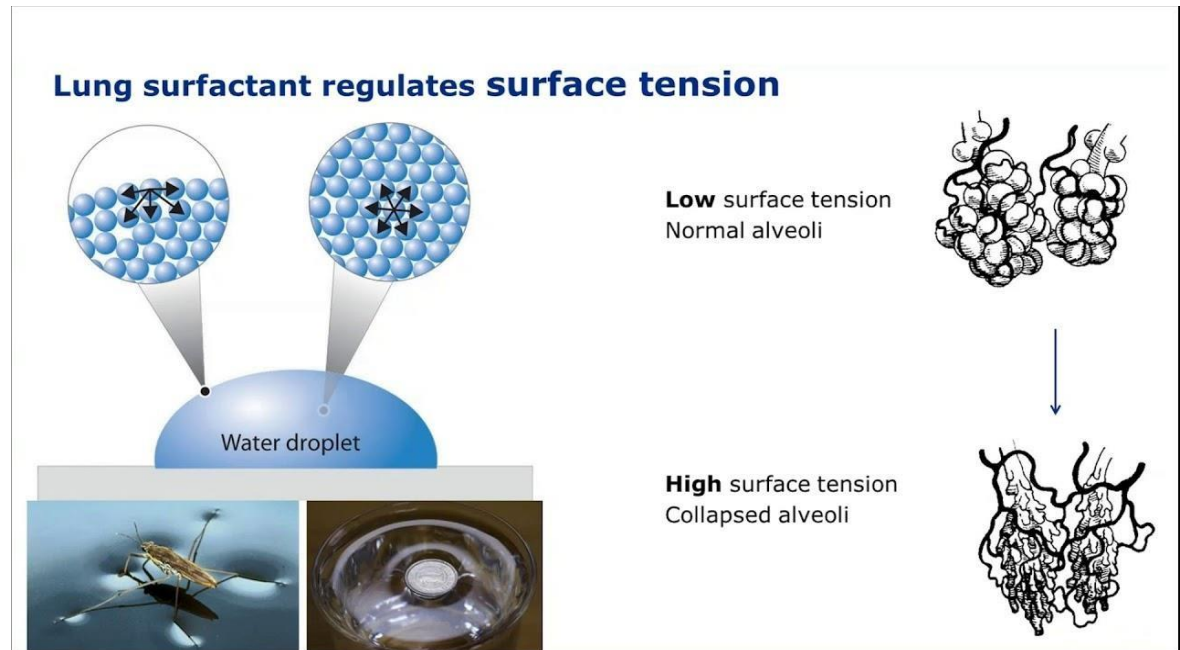
- Dipalmitoyl lecithin (two C₁₆ palmitic FA) is the chief lung surfactant. Its deficiency leads to respiratory distress syndrome in premature infants

نسبة ال lecithin لل Sphingomyelin لازم تكون 2:1.. ولو كانت أقل هاض يعني عنا deficiency , اللي ممكن يكون سببها الولادة المبكرة قبل ما يتكون ال lung surfactant



Lung surfactant

- ↓ surface tension in alveoli → Prevents collapse of lung alveoli
- Constituents: **dipalmitoyl lecithin**, phosphatidyl glycerol, Sphingomyelin, cholesterol and surfactant proteins A, B and C
- As foetus matures, more lecithin is synthesized
- Low levels of surfactant leads to respiratory distress syndrome (RDS)



2 phosphatidylcholine (lecithin).

these members are:

"nitrogenous" base

* it's important in cell membrane & blood plasma.

- phosphatidic acid
- esterification
- phosphate group
- choline

lung surfactant

lipid + protein
alveolar cells (pneumocytes - 2)

expiratory & inspiratory

* Don't forget: phospholipid which is found in lung surfactant called "dipalmitoyl lecithin"

glycerol

to be not attached by

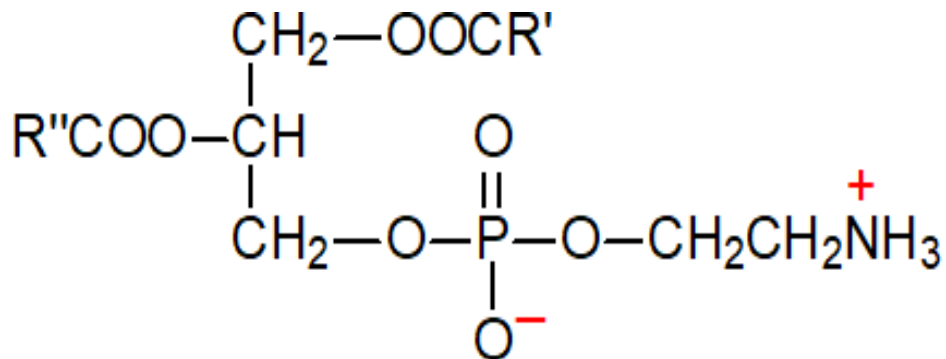
palmitic acids (saturated)

which is found in lungs.

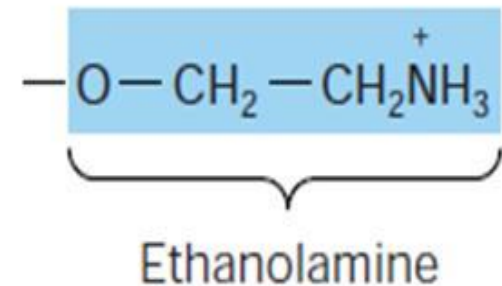
3-Phosphatidylethanolamine (Cephalin):

- The phosphate group of phosphatidic acid (PA) is esterified with the alcoholic group of the nitrogenous base **ethanolamine**
- It is the **next common to lecithin in cell membranes** and in blood plasma

الlecithin هو most common
وبعده مباشرة بيحي الcephalin



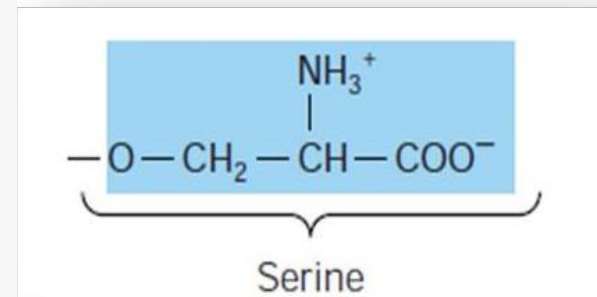
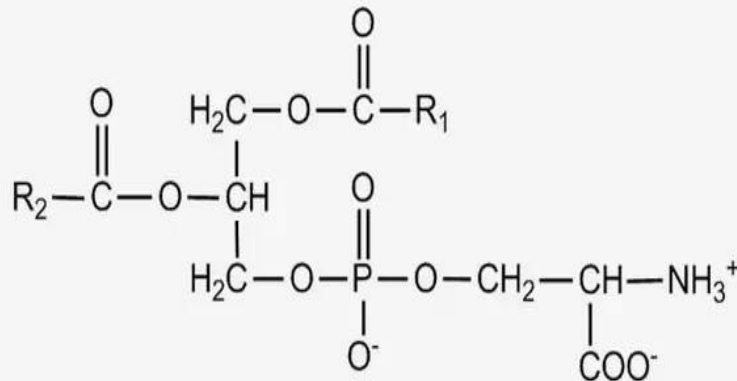
phosphatidylethanolamine



4- Phosphatidylserine:

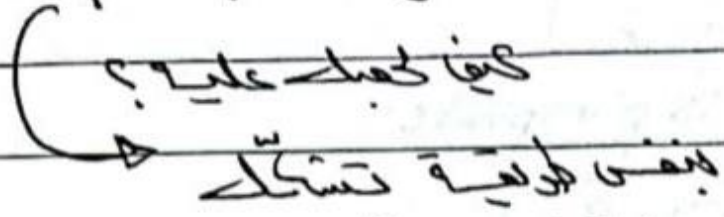
- The phosphate group of phosphatidic acid (PA) is **esterified with** the alcoholic group of the amino acid **serine**
- It is found in cell membranes.

PHOSPHATIDYLSERINE



3

phosphatidylethanolamine (cephalin).

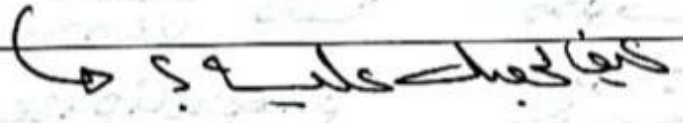


esterification
 phosphate group
 phosphatidic acid

ethanolamine : ٢٥

4

phosphatidylserine.

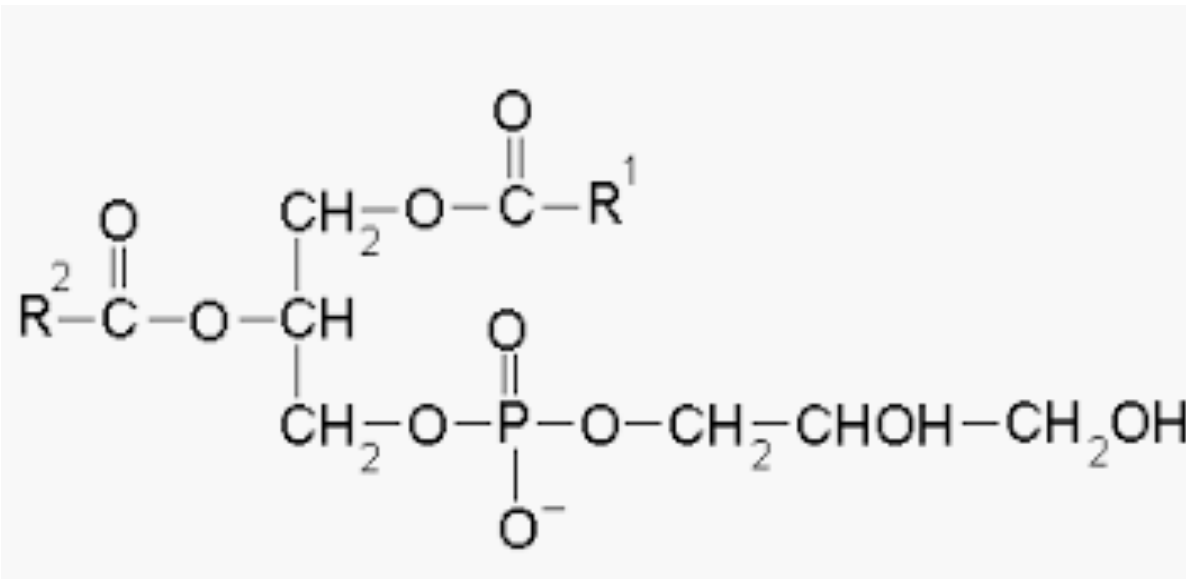


phosphate group
 esterification
 Serine
 phosphatidic acid

5- Phosphatidylglycerol:

- The phosphate group of phosphatidic acid was esterified with the alcoholic group of glycerol
- It forms part of the lung surfactant.

بس ال lecithin هو الأهم ←



5

phosphatidyle glycerol.

(lung surfactant) (أنتج في الرئة)

phosphatidylcholine (di palmitoyl)

phosphatidylcholine
(di palmitoyl)

تحلل

المنتجات

hydrolyzed
product

(product) (المنتجات)

2 glycerol

2 fatty acid
(saturated)

1 phosphate group.

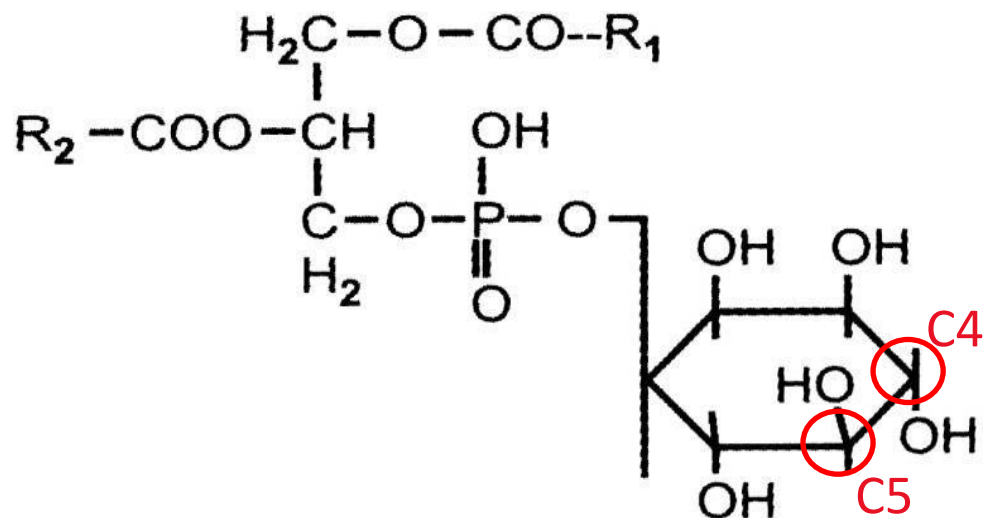
6-Phosphatidylinositol (lipositol):

- The phosphate group of phosphatidic acid is **esterified with** the alcoholic group of **inositol**
- It is found in cell membranes, especially nuclear membrane

اضافة PO₃ على C4,5

- **Phosphatidylinositol 4,5 bisphosphate** found in the plasma membrane is important in the mediation of the action of some hormones

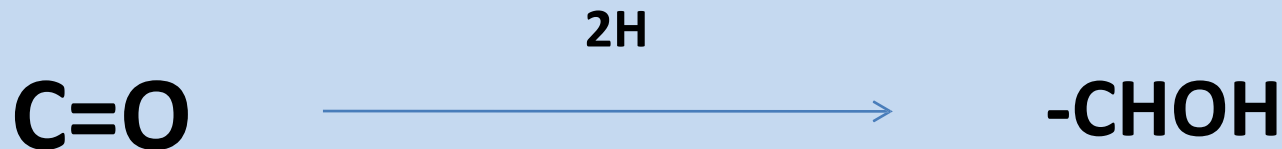
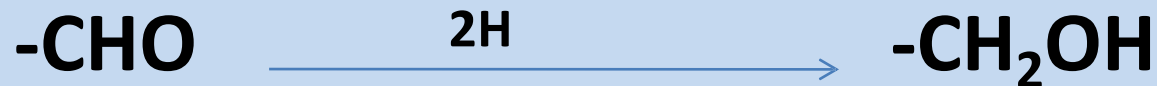
مهم ك 2nd messenger حيث بتفرزه الخلية
لما يدخل هرمون أو اشي يآثر عالخلية



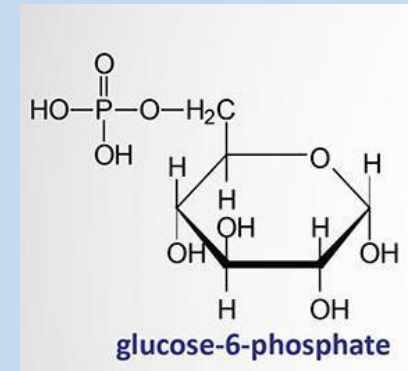
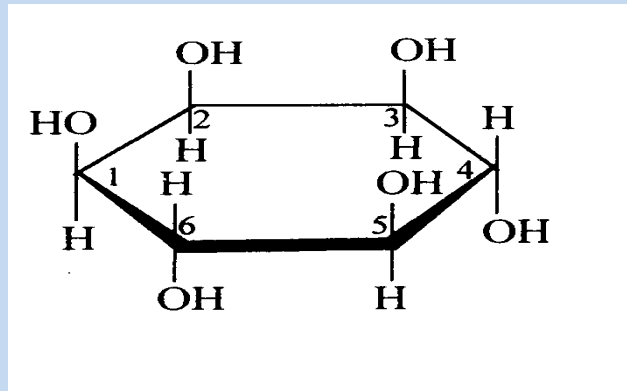
Which carbon?

5-Sugar alcohols

- Reduction of monosaccharides produce the corresponding alcohols
- They are produced by hydrogenation of aldoses and ketoses

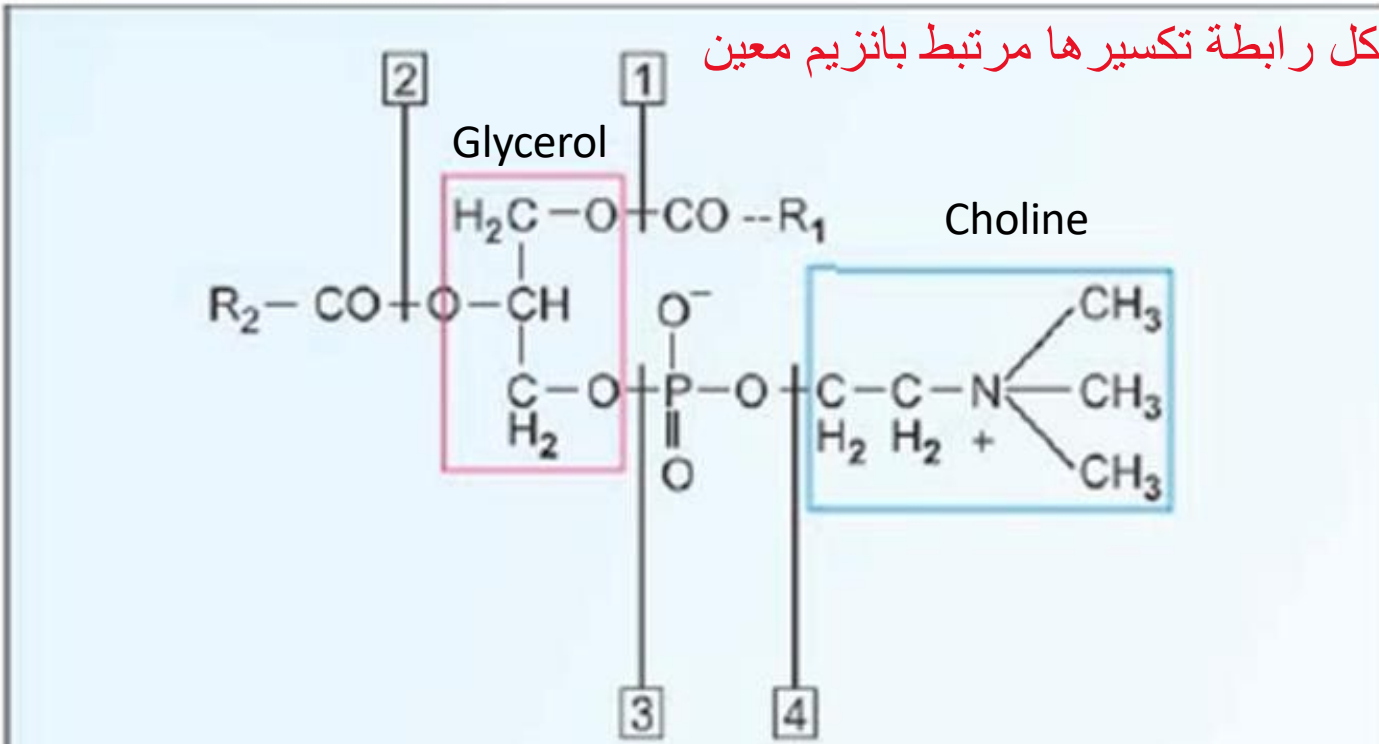


- **Myo-inositol:**



- Sugar alcohol synthesized from glucose-6-phosphate (G-6-P). It is abundant in brain and other mammalian tissues (in humans most inositol is synthesized in the kidneys)
- it is found in animal tissues in the free state as well as in the form of the phospholipid
 - It is a constituent of certain phospholipids and hence its role in the mobilization of fats from the liver (lipotropic action i.e. encourages the export of fat from the liver)
- It forms phosphatidyl inositol that enters in structure of plasma membranes and **can serve as a second messenger in action of some hormones (i.e. mediates cell signal transduction in response to a variety of hormones)**
- ❖ **Second messengers** are intracellular signaling molecules released by the cell in response to exposure to extracellular signaling molecules—the **first messengers**.

Hydrolysis of glycerolphospholipids



- 1 = site of action of phospholipase A1 (PLA1)
- 2 = site of action of phospholipase A2 (PLA2)
- 3 = site of action of phospholipase C (PLC)
- 4 = site of action of phospholipase D (PLD)

PLD is not present in humans, only in plants

Snake venom contains enzyme with PLA2 activity: converts PL in RBCs to lysophospholipids

لما أفعى تلدغ شخص بصير عنده تكسر بكريات الدم الحمراء.. وهاض بسبب احتواء انيابها على

PLA2 لأنه يحوّل ال lecithin ل lysophospholipid

7-lysophospholipids:

- **Phospholipase A2** is an enzyme that removes the fatty acid in the 2- position of phospholipids → forming a lysophospholipid (contain one acyl radical):
 - e.g., from lecithin we get lysolecithin.

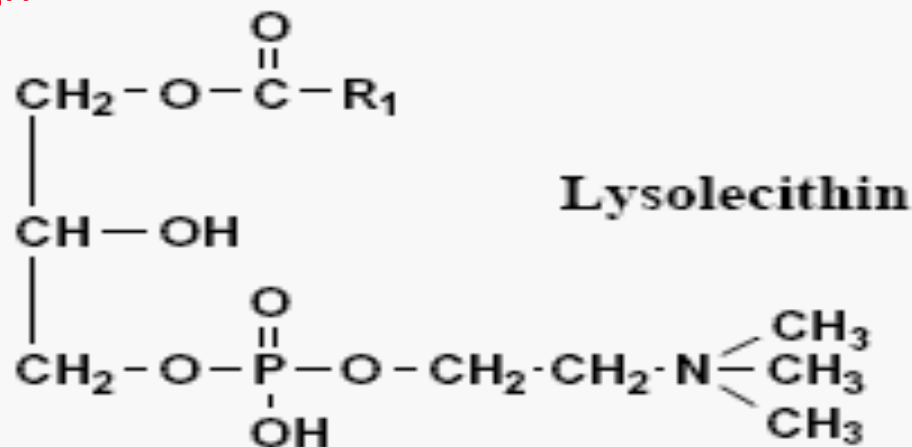
Lysophospholipids are intermediates in metabolism

They are produced in the blood by the action of snake venom, where they produce hemolysis

Lysolecithin has been implicated in some of their effects in promoting atherosclerosis

مهم لامتحان

Effects low density lipoprotein (LDL/ high cholesterol) and platelets aggregation



6

phosphatidylinositol (lipositol).

في نون 4 و 5 في ال 9 انا

phosphatidylinositol 4,5 bis phosphate.

(لحين 2 phosphate group في C4 + C5)

و يقتر وجوده في ال Cell membrane

المessenger action of some hormones.

7

lysophospholipids

Snake Venom ال
phospholipase ال
A2

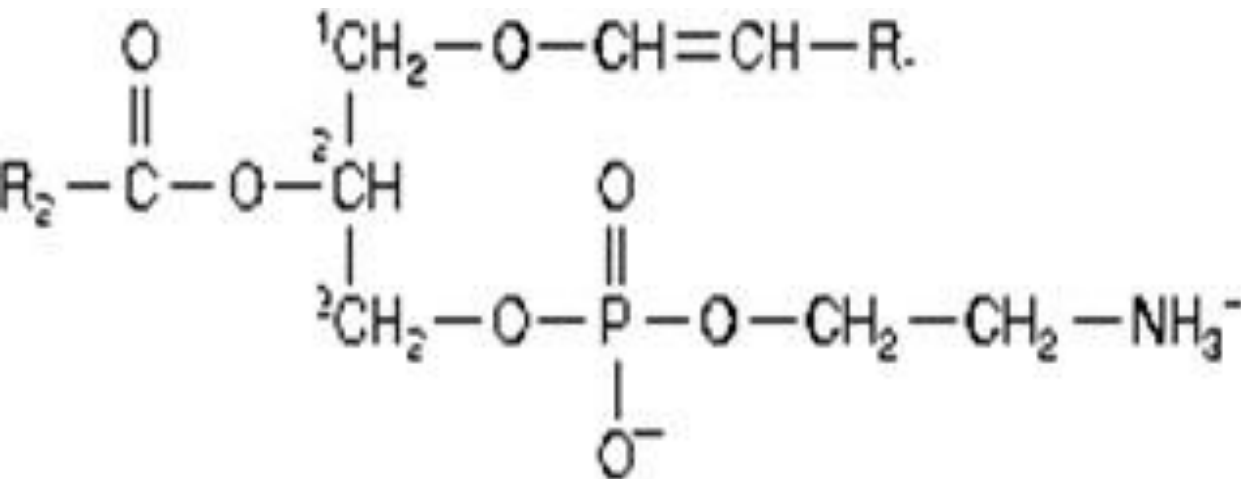
حلوة
فقد ال f.a بقا
ببب enzyme ال
phospholipase A2.

ال اول من نوع ال f.a
فنا ال PL و تتكسر ال
lysophospholipid

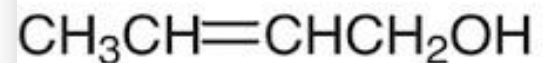
وهذا الكي كبت ال RBCs و يبي hemolysis
و كمان كبت ال PL ال جودة ال plasma و ال كبت ال
عملية ال Coagulation (تخثر ال دم) كبت ال bleeding.

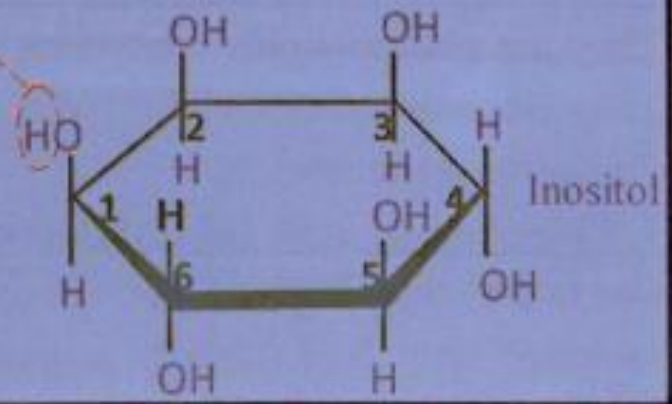
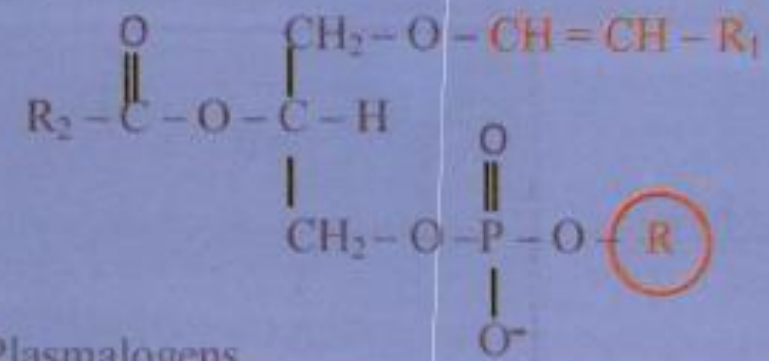
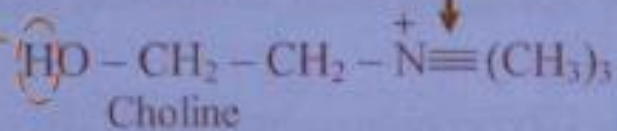
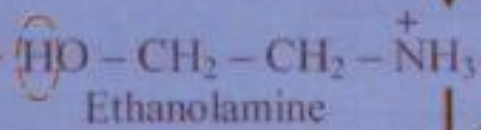
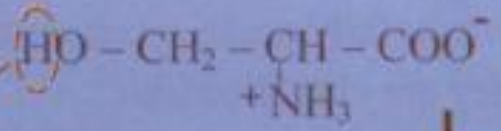
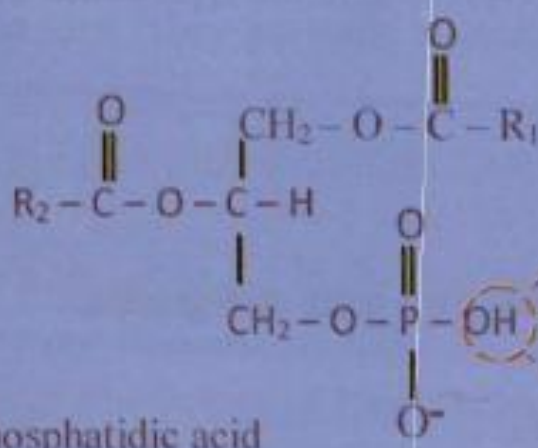
8- Plasmalogens:

- These are similar to cephalins, but the fatty acid in the 1- position is replaced by a fatty alcohol, usually unsaturated-
- The phosphate is usually esterified to ethanolamine; however it may also be esterified to choline or inositol
- **Plasmalogens** are found in cell membranes, especially in muscles and brain (10% of the phospholipids of brain and muscle are plasmalogens)



Example of fatty alcohol





CO₂

3 CH₃

Phosphatidic acid

Serine

Ethanolamine

Choline

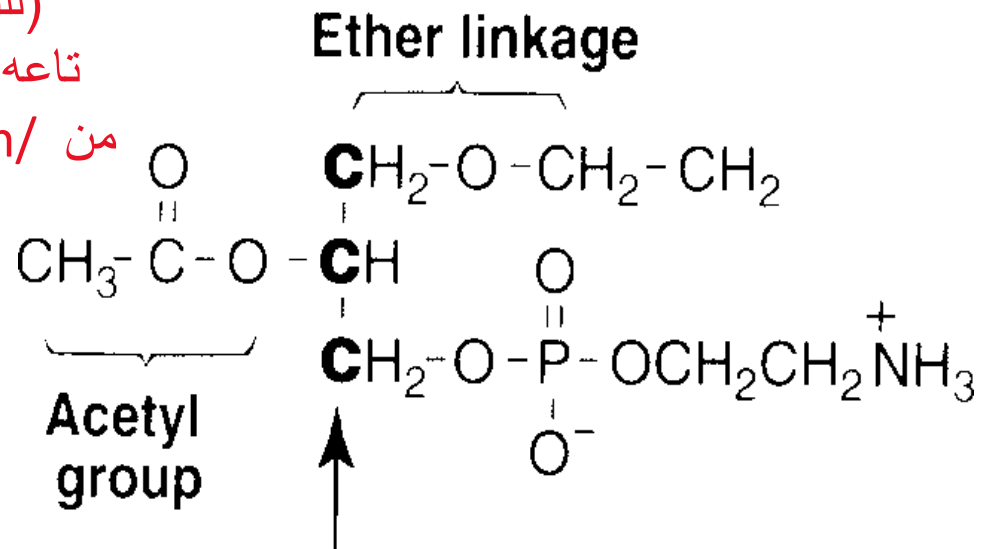
Inositol

- **Platelet-activating factor (PAF)** is a choline plasmalogen in which position 1 contains saturated palmityl alcohol and position 2 contains acetic acid

(للتذكير.. أبسط أنواع الـ FA والـ function)

تأهه mediator of leukocytes functions

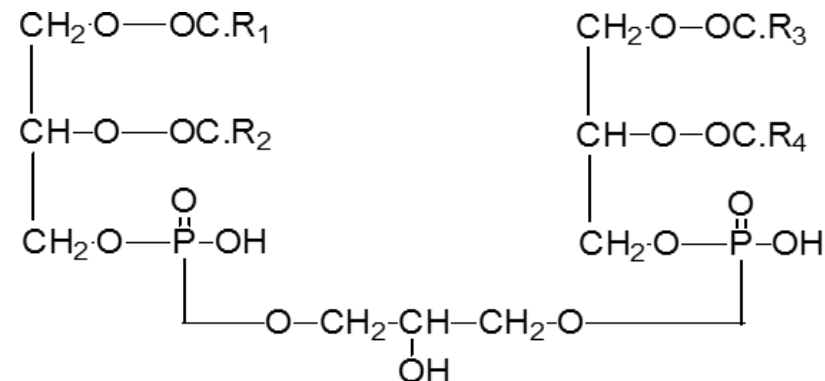
من inflammation / platelet aggregation / (anaphylaxis)



Function: mediator of many leukocyte functions, platelet aggregation, inflammation and anaphylaxis.

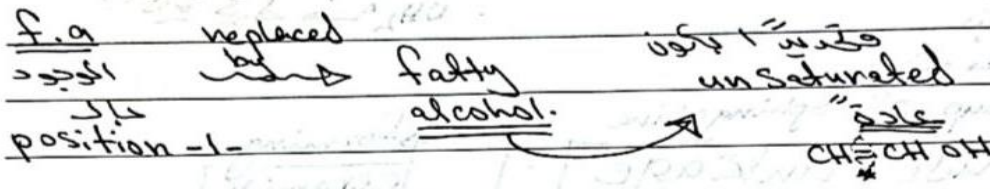
9-Diphosphatidylglycerol (Cardiolipin):

- **Two** molecules of phosphatidic acid **esterified through** their phosphate groups to an additional molecule of **glycerol**
- This is the only phospholipid that is **antigenic** *مهم للامتحان*
- It is an important **component of** the inner **mitochondrial membrane** (accounts for 20% of mitochondrial lipids) & bacteria
- Decreased cardiolipin levels or alterations in its structure or metabolism cause mitochondrial dysfunction in pathological conditions including heart failure & Barth syndrome
- **Barth syndrome** (cardioskeletal myopathy): **genetic defect** in coding for tafazzin, an enzyme involved in the biosynthesis of cardiolipin

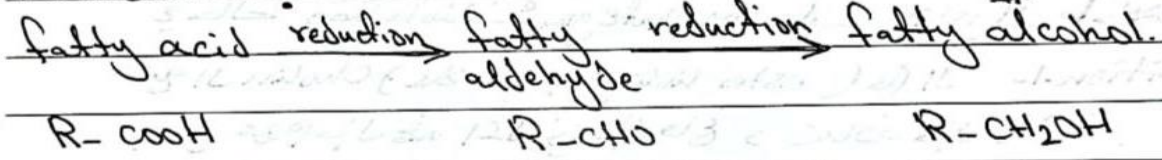


8 plasmalogens. * [phosphate group to ethanolamine]

cephalin



remember!



Cholin or inositol // phosphate group // it is also

position -1- : Saturated f.a (palmitic alcohol)
 " -2- : acetic acid.

PAF

9 diphosphatidylglycerol (cardiolipin).

what are the hydrolytic product of it?

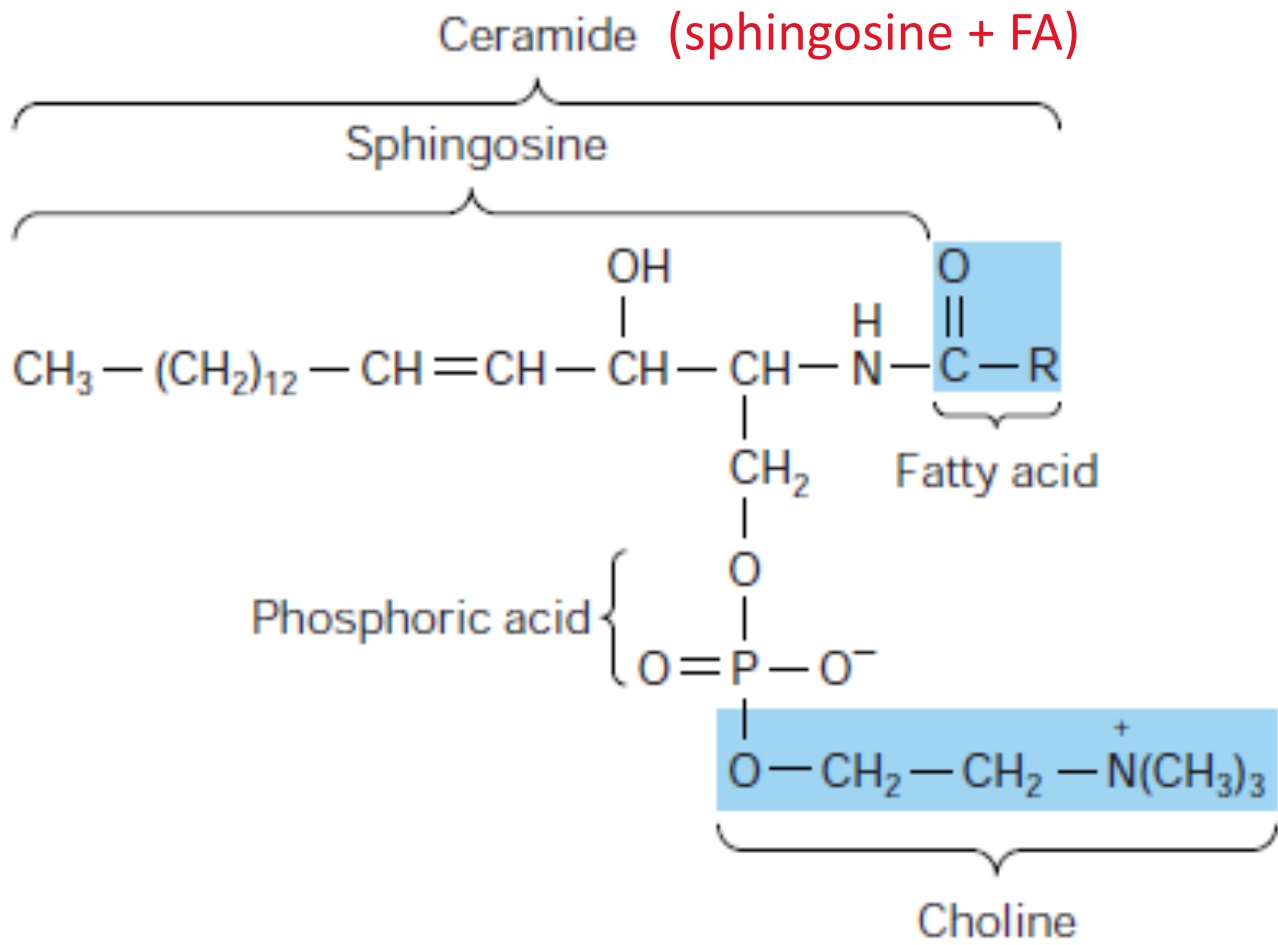
- 3 glycerol.
- 4 f.a
- 2 phosphate group.

note: antibodies antipl syndrom

(حال وحيات)

B- Sphingophospholipids (Sphingomyelin):

- The **backbone** of sphingomyelin is the amino alcohol sphingosine rather than glycerol
-
- A long chain FA is attached to the amino group of sphingosine through an amide linkage, producing a ceramide, which can also serve as a precursor of glycolipids
- A phosphate is esterified to the 1- position of sphingosine and choline is esterified to the phosphate
- Sphingomyelin is found in cell membranes, **especially in lungs** (form part of lung surfactant) and brain (myelin sheath)
- * → which is present more in surfactant? **lecithin**

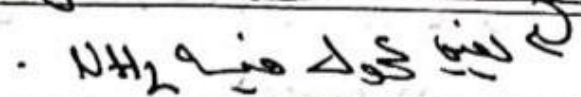


sphingomyelin

* Sphingophospholipids (Sphingo myelin)

↳ the backbone of it sphingosine (amino alcohol)

* FA chain
long chain



amino group of sphingosine

by [amide linkage]

forming

ceramide

phosphate group

position-1- choline (ester linkage)

...



Solubility of phospholipids

They are
amphipathic

- The presence of nonpolar groups → make them soluble in fat solvents
- The presence of polar groups (phosphate, choline, serine, ethanolamine, and inositol) → makes them water soluble, forming micelles (very fine emulsion) in water

- The presence of both nonpolar and polar groups enables PLs to facilitate **emulsification** of other insoluble fats

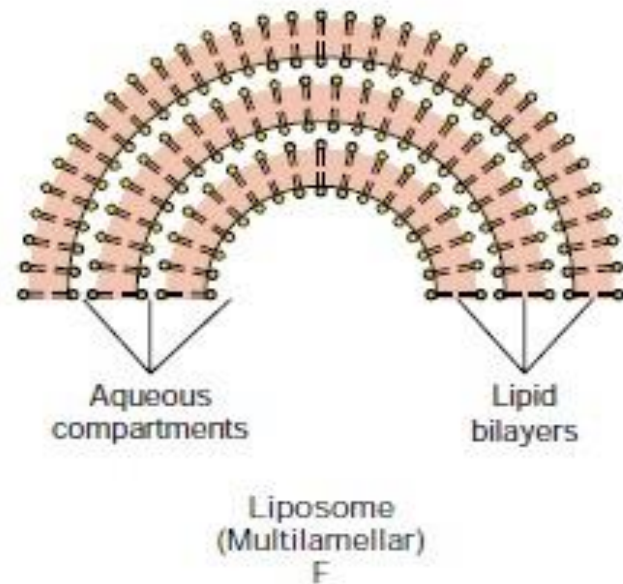
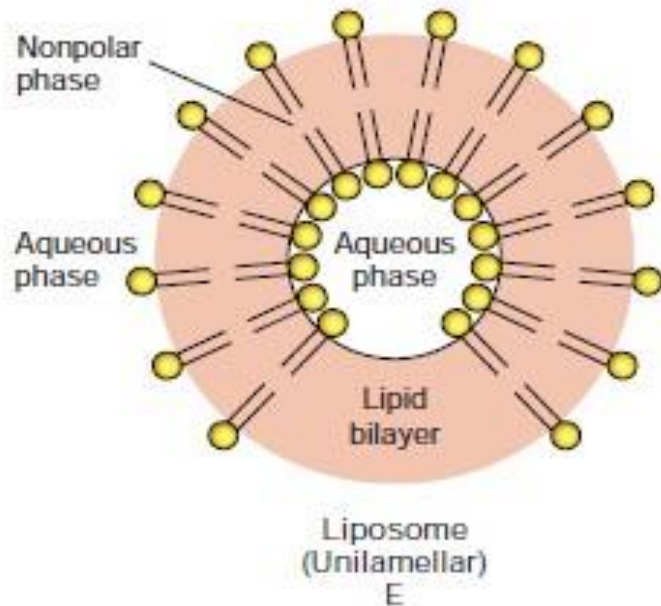
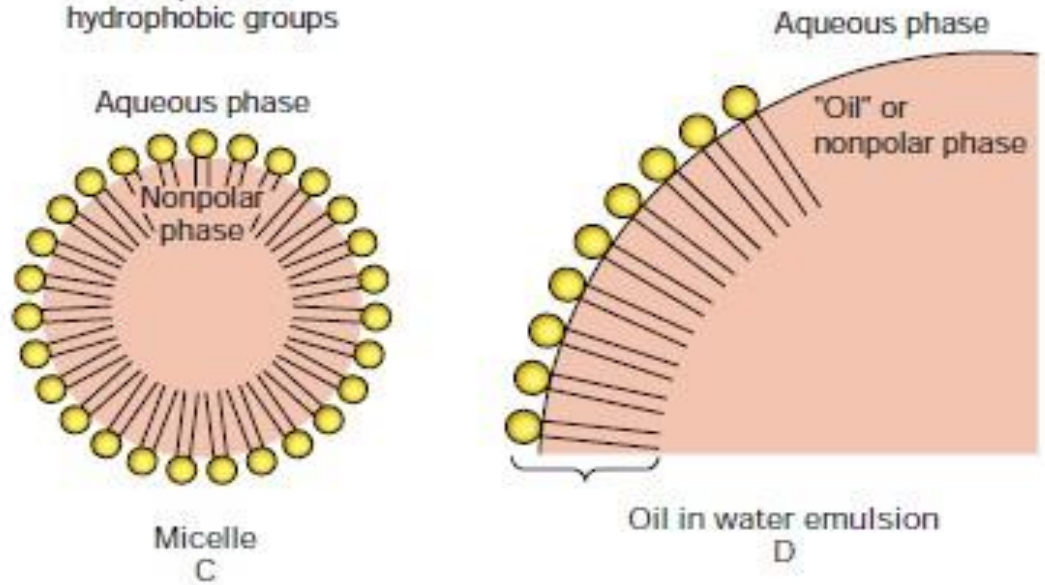
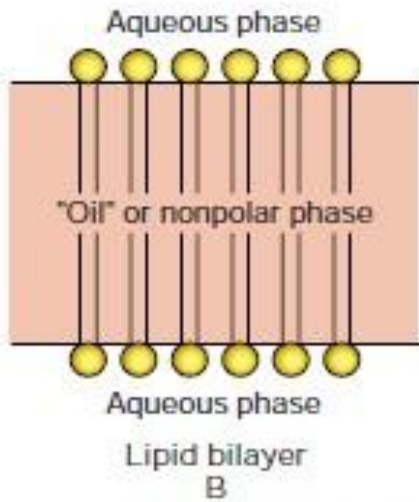
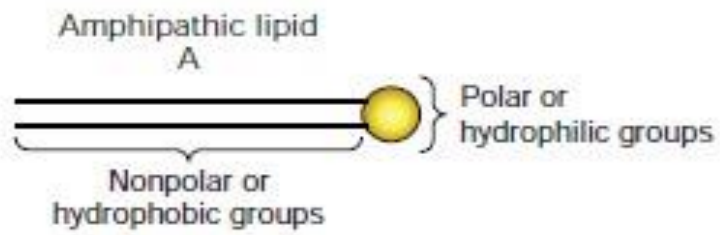
↓
الاستحلاب (تكسير ال lipids من big
(smaller molecules ل molecules)

- The PL molecules are arranged around the emulsion particles so that the nonpolar groups are towards the lipid phase, and the polar groups are towards the surrounding aqueous phase

وهي العملية هي التي بتساعد بترتيب ال molecules بالشكل اللي بنعرفه
(ال polar لبرا وال nonpolar لجوا)

وهاض ال فوائد صيدلية كثير.. في بعض أدوية ال chemotherapy مثلا زي
ال doxorubicin, فال liposomal doxorubicin أفضل واحسن فهو أقل toxicity وإله
effect أحسن.. فبشكل عام ال liposomal drugs مهمة

- This is important in the formation of the plasma lipoproteins and in the digestion and absorption of triacylglycerols



II Glycolipids

- Glycolipids are lipids containing a carbohydrate radical
- They also contain glycerol backbone ما فيهم sphingosine and are, therefore, classified with sphingomyelin as sphingolipids
- They are widely distributed in every tissue of the body, particularly in nervous tissue such as brain + outer part of cell membrane

Types:

1. Cerebrosides:

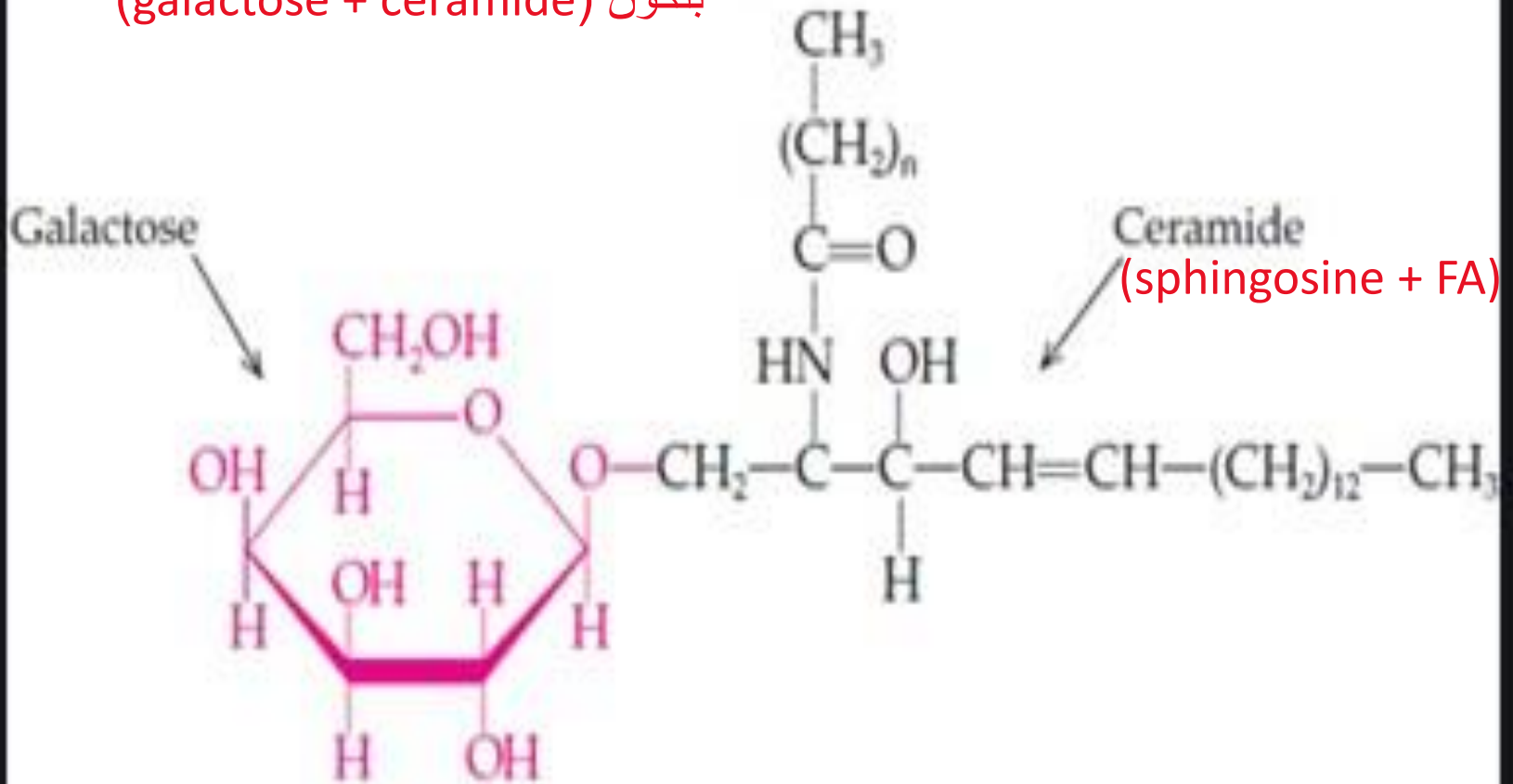
- These consist of sphingosine, FA (usually 24 carbon lignoceric, cerebronic, or nervonic acid), and galactose or glucose.

↓
اللي بحتوي على
galactose موجود بكثرة
بالnervous system

↓
اللي بحتوي على glucose
موجود بكثرة خارج
النervous system

- The FA is connected to the amino group of sphingosine in amide linkage
- The sugar is connected to the primary alcohol group of sphingosine in **β -glycosidic linkage**
- **Galactocerebrosides** predominate in nervous tissue
- **Glucoerebrosides** predominate in extra-neural tissues

*الstructure مش حفظ بس احفظ من ايش
بتكون (galactose + ceramide)

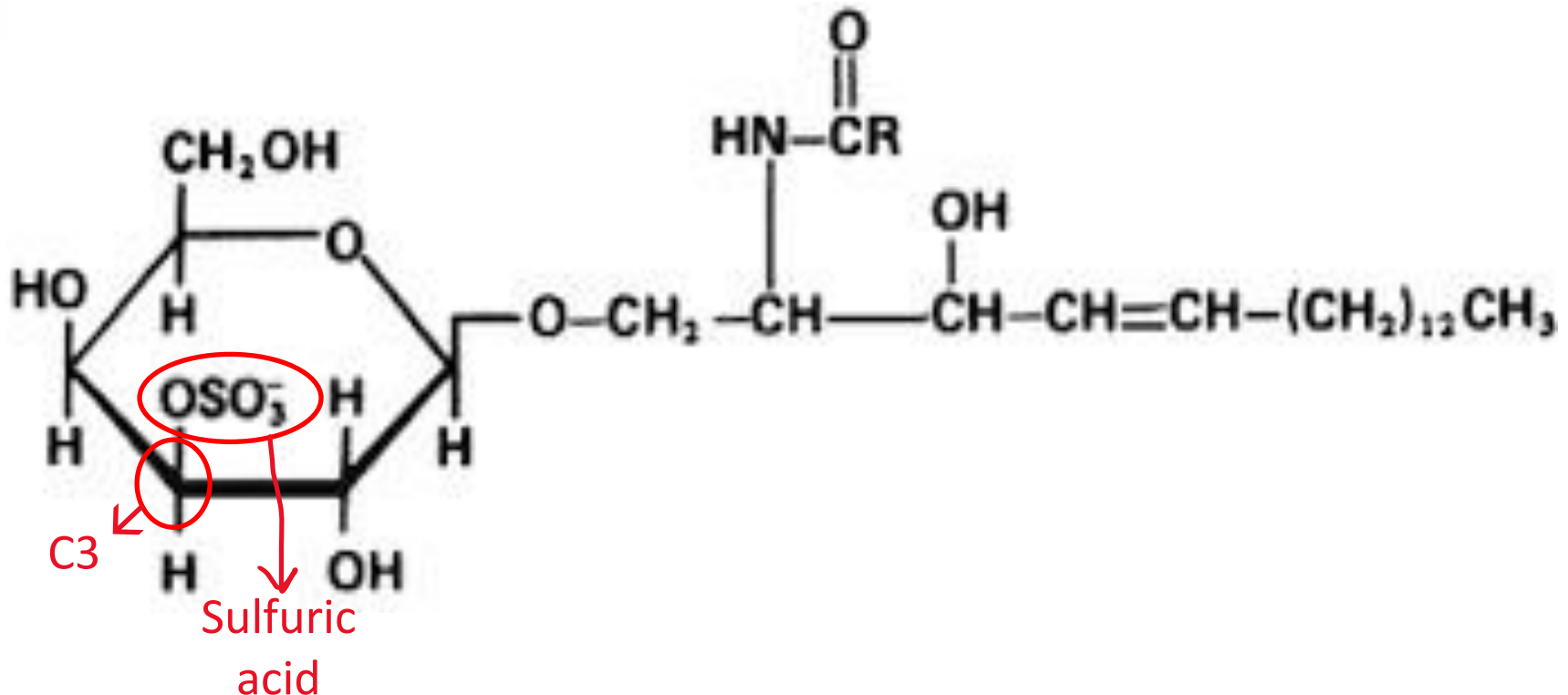


Galactocerebroside

2. Sulpholipids:

- Sulpholipids, or sulphatides, are galactocerebrosides in with sulfuric acid @C3 in galactose

الفرق الوحيد بينه وبين الgalactocerebrosides انه هاض معه sulfuric acid



3. Globosides (ceramide oligosaccharides)

- These are cerebrosides in which the sugar is replaced by an oligosaccharide chain (hexose/ hexosamine) that **does not include a sialic acid as a component**
- Found in cell membrane

4. Gangliosides

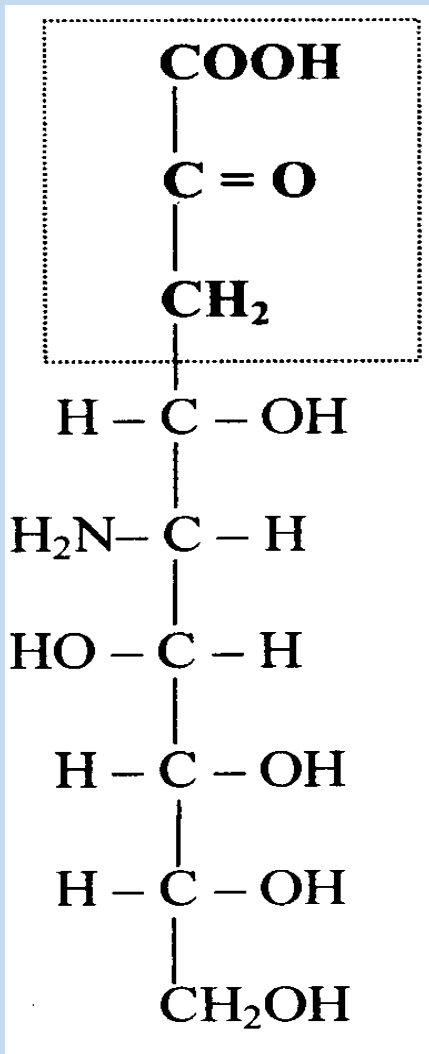
- They are found in the ganglion cells of central nervous system (CNS)
- They are similar to Globosides but **contain a sialic acid (N-acetylneuraminic acid) as a component.**

الثنين نفس الاشئ تماما.. بس الفرق انه ال globosides ما فيها sialic acid
(وفي حال إنك ناسئ ائش هو ال sialic acid فالسلائدئ الجائات عشان يذكروك)

"ركزوا بالدراسة على النقاط هاي اللي بكون فيها اشئ مش موجود بغيرها.. لأنه هاي اللي بنحب
نجيبها بالامتحان" , the doctor said

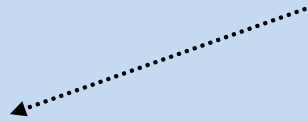
2-Amino sugar acids

- Formed by addition of acids to aminosugars
- They are occurring in glycoproteins, glycolipids
- Examples include neuraminic acid (pyruvic acid and mannosamine)
- Neuraminic acid is unstable and so, it is present in an acetylated form called sialic acid (NANA)

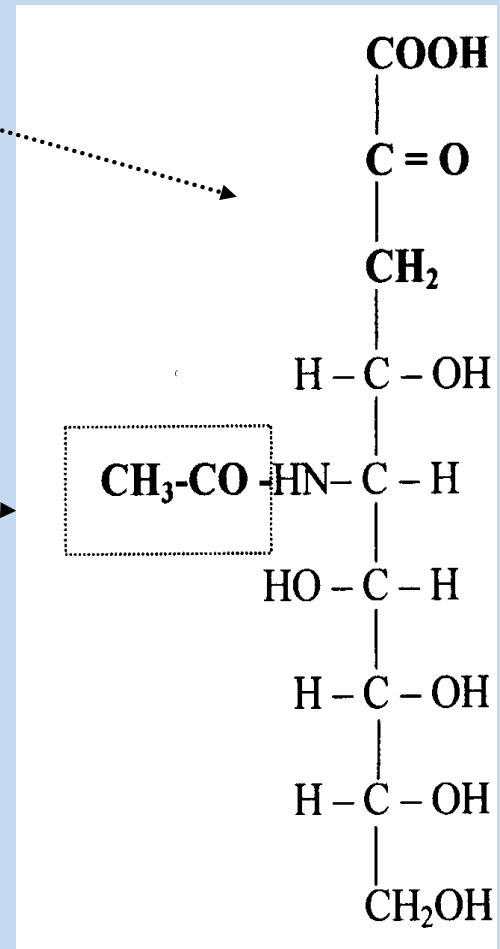
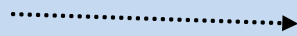


Neuraminic acid

Pyruvic acid



Acetyl group

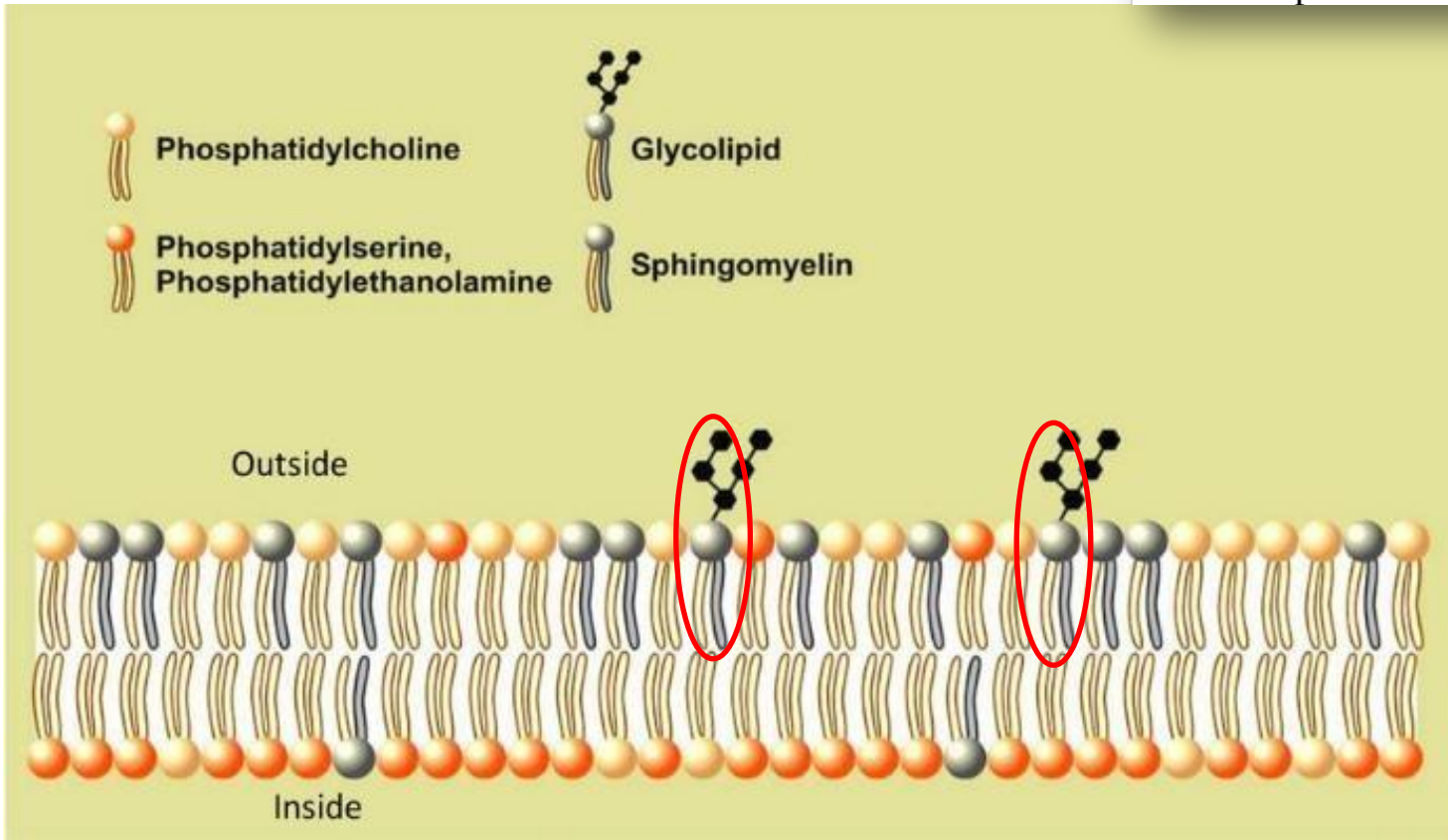
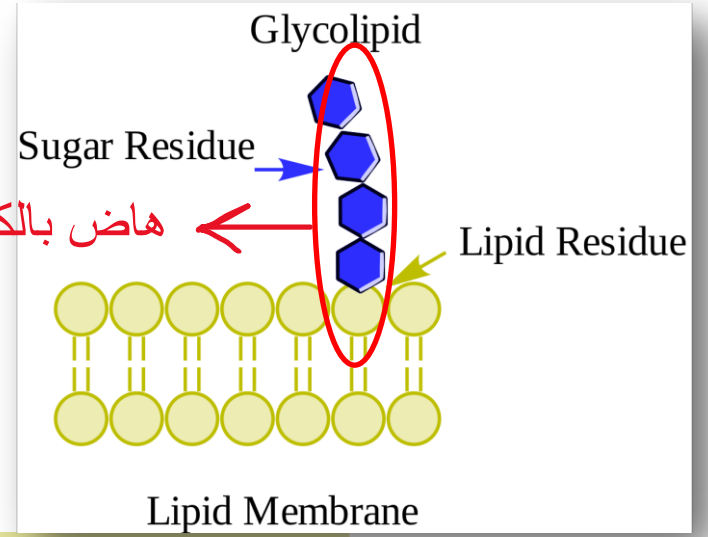


**N-Acetyl neuraminic acid
(NANA)
(Sialic acid)**

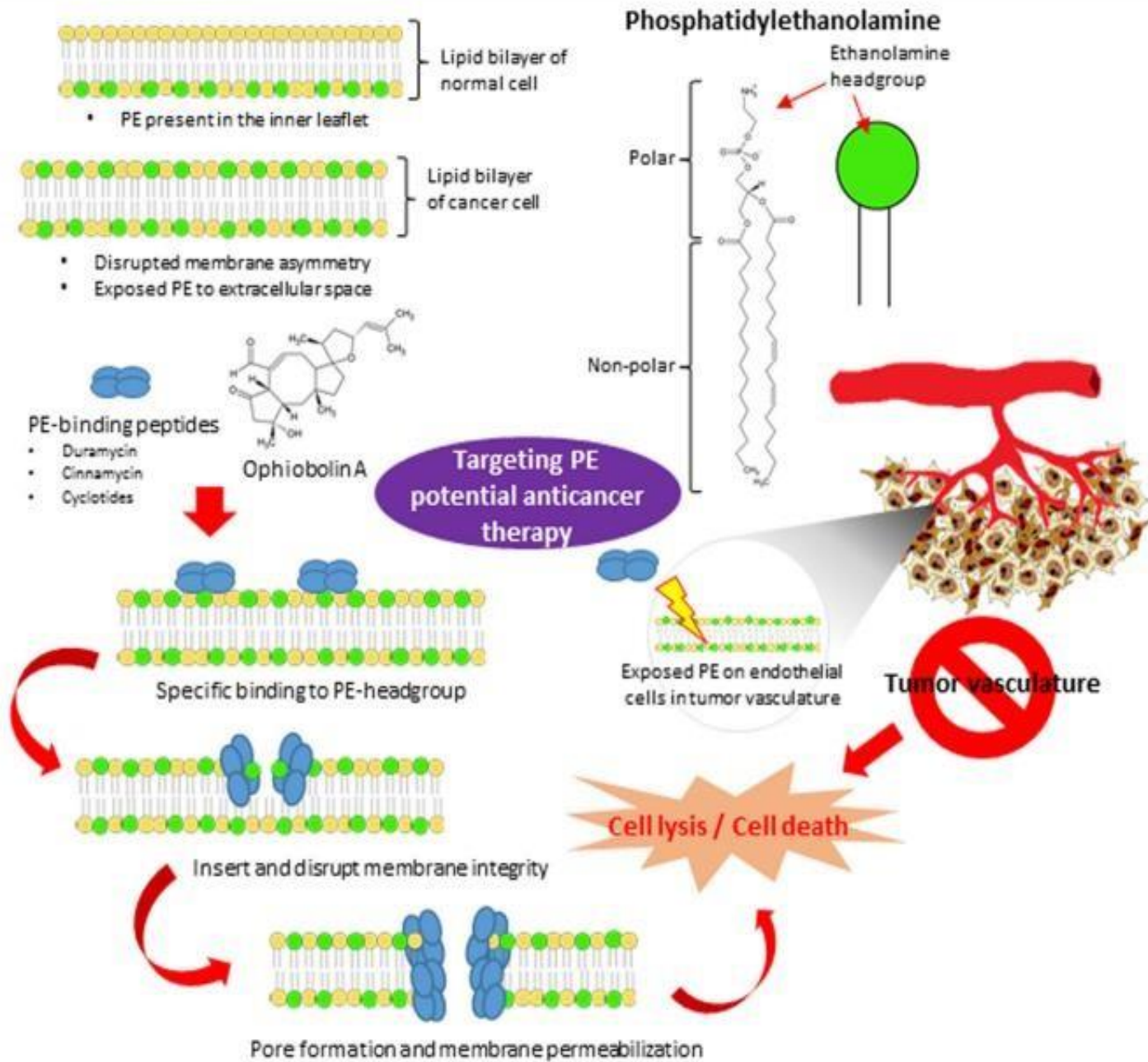
- Glycolipids are found in cell membranes, especially in myelin sheath
- In the plasma membrane (outer leaflet), the CHO radical of glycolipids projects outside the cell and may have a receptor function (for some toxins and viruses, cellular connections)
- CHO radicals of gangliosides and globosides are **antigenic**; they form the blood group antigens, certain tumor antigens
- Malignant cells show marked changes in the composition of glycolipids in cell membranes

الموجودة بالسطح الخارجي للـ plasma membrane الهـم أهمية كبيرة بالجسم وضـد
 cancer مثلـا لأنه همـه المسؤـولين عن الـ cell to cell connection و تواصل الخلايا مع بعضها ,
 لأنه المكونات الموجودة بالـ cell wall للـ cancer cells مثلـا بتختلف كليـا عن الـ الموجودة بالـ normal
 cells , فالـ researches حاليا بتشتغل على آلية استهدافها للعلاج

هاض بالكامل هو ال glycolipid



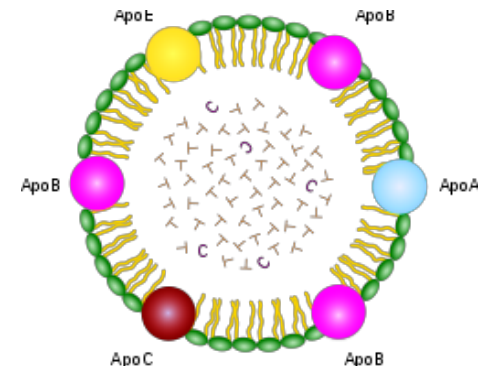
For info only



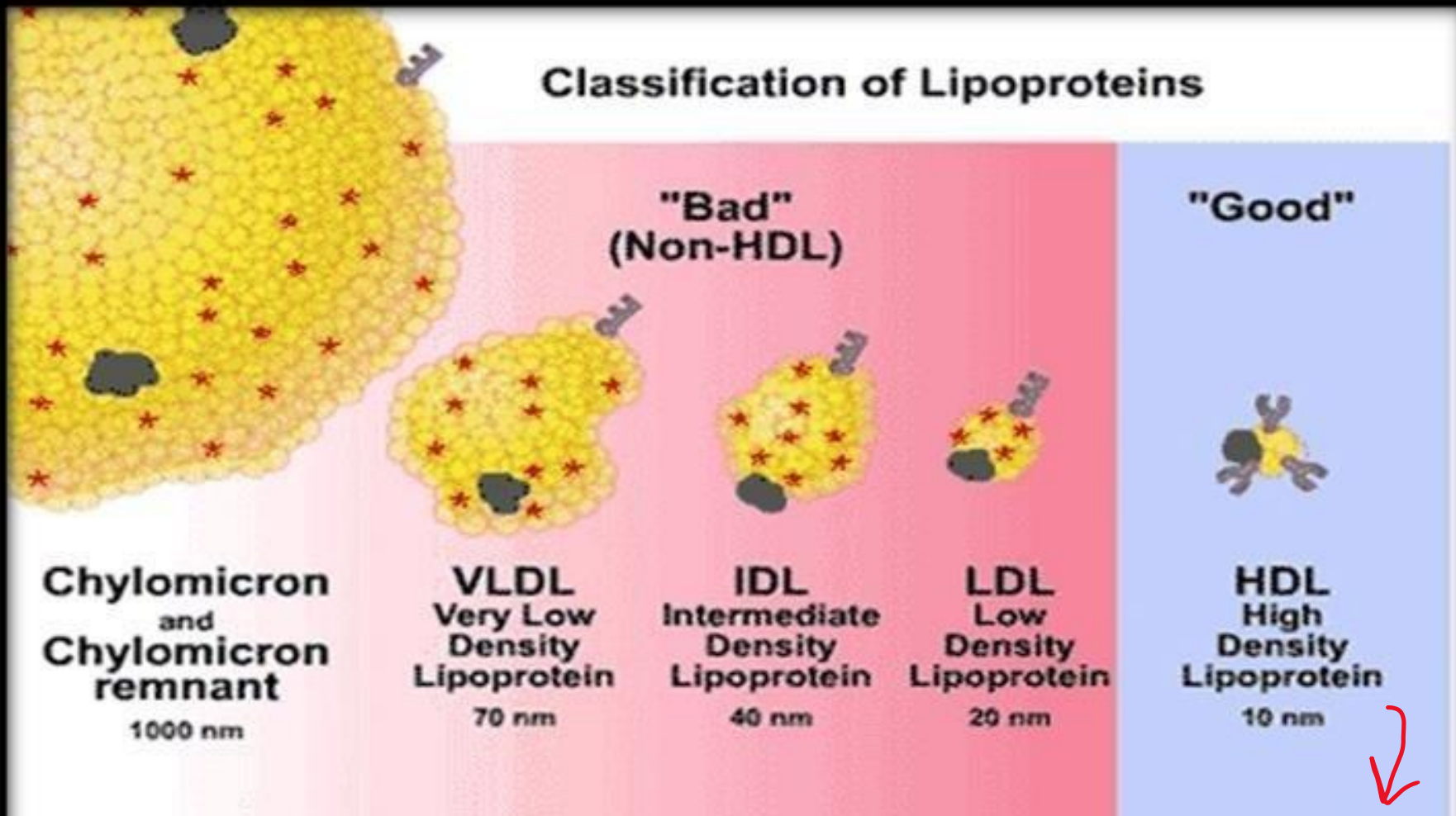
III Lipoproteins

وهاض الاشي بساعد بنقل المواد بحيث انها ما تختلط بسوائل الجسم , فال lipoproteins هي اللي بتغلف ال lipids وبتنقلها

- Lipoproteins are arranged as:
 - lipid part to the interior of the molecule → (Mainly TAG)
 - protein part to the exterior of the molecule
- This gives the structure a property of its solubility in water (lipoproteins are water-soluble)
- Used to transport lipids in plasma



Classification of Lipoproteins



ليش good؟ لأنه فيه كمية protein عالية بالإضافة لأنه يستخدم في نقل ال cholesterol لل liver و وجوده بمستوى عالي بحمي الشخص من ال Atherosclerosis (تصلب الشرايين)

Derived lipids

- These lipids are derived from both simple & compound lipids.

أي اشي بنتج من تكسير ال simple lipids

1- Alcohols: These are.

- Glycerol. It is the backbone of glycerol phospholipids.
- Higher alcohols. → Found in waxes E.g. myricyl alcohol
- Sterols: as cholesterol, ergosterol. Their esters with fatty acids are waxes
- Vitamins: as vit. A (retinol) & D
- Sphingosine: This alcohol as previously mentioned in sphingomyelin & Glycolipids

2- Fatty acids

3- Substances associated with lipids

These substances are present in association with lipids.

- **Vitamins:** vitamins E & K & D are fat soluble & are associated with food fat (fat soluble vitamins)
- **Carotenoids:** important precursors of vitamin A