

Fats

Fatty Acid

- Fatty acids exist “free” in the body
- Also found as fatty acyl esters such as triacylglycerol's.
- Low levels of free fatty acids occur in all tissues,
- Plasma free fatty acids (transported by serum albumin) are in route from their point of origin (triacylglycerol of adipose tissue or circulating lipoproteins) to their site of consumption (most tissues).

Fatty Acid

- **Functions**
- Free fatty acids can be oxidized by many tissues—particularly liver and muscle—to provide energy.
- Fatty acids are also structural components of membrane lipids, such as phospholipids and glycolipids.

Fatty Acid

- Fatty acids are attached to certain intracellular proteins
- Fatty acids are also precursors of the hormone-like prostaglandins
- Esterified fatty acids, in the form of Triacylglycerols stored in adipose cells, serve as the major energy reserve of the body.

Structure of fatty acids

$\text{CH}_3(\text{CH}_2)_n$	COO^-
Hydrophobic hydrocarbon chain	Hydrophilic carboxyl group (ionized at pH 7)

Structure of fatty acids

- A fatty acid consists of a hydrophobic hydrocarbon chain with a terminal carboxyl group

Structure of fatty acids

- At physiologic pH, the terminal carboxyl group ($-\text{COOH}$) ionizes, becoming $-\text{COO}^-$.
- This anionic group has an affinity for water, giving the fatty acid its amphipathic nature (having both a hydrophilic and a hydrophobic region). However, for long-chain fatty acids (LCFAs), the hydrophobic portion is predominant. These molecules are highly water-insoluble

Transportation in Plasma

- More than 90% of the fatty acids found in plasma are in the form of fatty acid esters (primarily triacylglycerol, cholesteryl esters, and phospholipids) contained in circulating lipoprotein particles
- Unesterified (free) fatty acids are transported in the circulation in association with albumin.

Types of fatty acids

- Fatty acid chains may contain no double bonds—that is, be saturated—or contain one or more double bonds—that is, be mono- or polyunsaturated.

melting temperature of Fats

- If the fatty acid has two or more double bonds, they are always spaced at three-carbon intervals.
- In general, addition of double bonds decreases the melting temperature (T_m) of a fatty acid, whereas increasing the chain length increases the T_m .
- Because membrane lipids typically contain LCFA, the presence of double bonds in some fatty acids helps maintain the fluid nature of those lipids.

Chain length

- the carbon atoms are numbered, beginning with the carboxyl carbon as carbon 1
- Carbon 2, the carbon to which the carboxyl group is attached, is also called the α -carbon, carbon 3 is the β -carbon, and carbon 4 is the γ -carbon. The carbon of the terminal methyl group is called the ω -carbon regardless of the chain length

Fatty acids with chain lengths of four to ten carbons are found in significant quantities in milk

Structural lipids and triacylglycerols contain primarily fatty acids of at least sixteen carbons.

COMMON NAME

STRUCTURE

Formic acid	1
Acetic acid	2:0
Propionic acid	3:0
Butyric acid	4:0
Capric acid	10:0
Palmitic acid	16:0
Palmitoleic acid	16:1(9)
Stearic acid	18:0
Oleic acid	18:1(9)
Linoleic acid	18:2(9,12)
α -Linolenic acid	18:3(9,12,15)
Arachidonic acid	20:4(5, 8,11,14)
Lignoceric acid	24:0
Nervonic acid	24:1(15)

Precursor of prostaglandins

Essential fatty acids

Essential fatty acids

- Linoleic acid → precursor of arachidonic acid → substrate for prostaglandin synthesis
- α -linoleic acid, the precursor of other ω -3 fatty acids important for growth and development

Desaturation of fatty acid chains

- Enzymes present in the ER are responsible for desaturating fatty acids. Desaturation reactions require NADH and O_2

- Humans have carbon 9, 6, 5 and 4 desaturases, but lack the ability to introduce double bonds from carbon 10 to the ω -end of the chain.
- This is the basis for the nutritional essentiality of the polyunsaturated linoleic and linolenic acids.

Storage of fatty acids as components of triacylglycerols

- Types of triacylglycerols:
- Mono-, di-, and triacylglycerols
- Consist of one, two, or three molecules of fatty acid esterified to a molecule of glycerol.
- Fatty acids are esterified through their carboxyl groups, resulting in a loss of negative charge and formation of “neutral fat.”

Difference between Fats & Oils

- Acyl-glycerol is solid at room temperature, it is called a “fat”; if liquid, it is called an “oil”

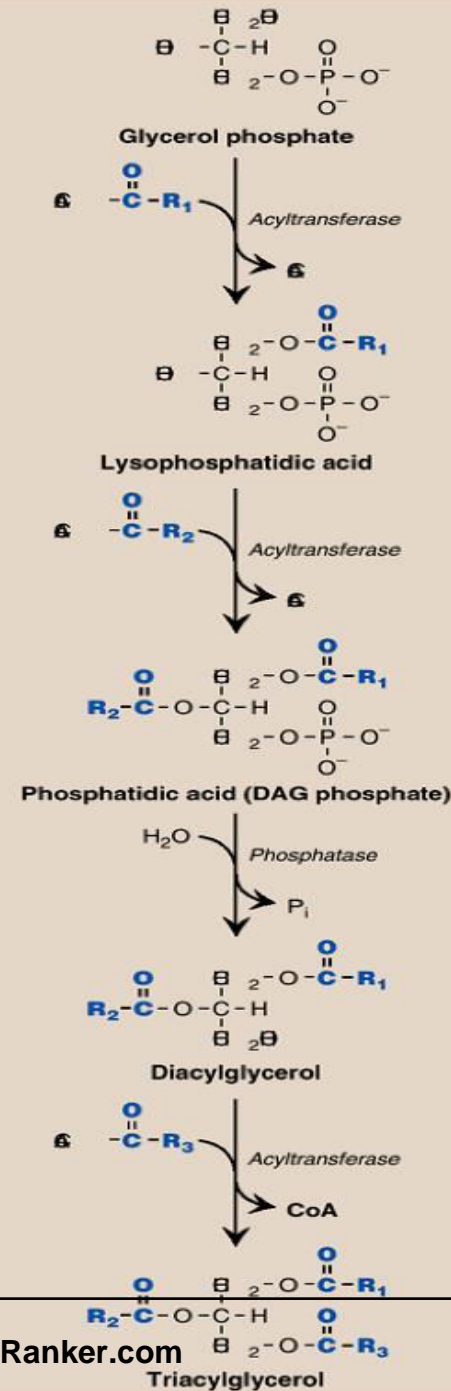
Structure of triacylglycerol (TAG)

- The three fatty acids esterified to a glycerol molecule are usually not of the same type.
- The fatty acid on carbon 1 is typically saturated, that on carbon 2 is typically unsaturated, and that on carbon 3 can be either.
- Recall that the presence of the unsaturated fatty acid(s) decrease(s) the melting temperature (T_m) of the lipid.

Storage of TAG

- within adipocytes
- Act as major energy reserve

Synthesis of TAG



Different fates of TAG in the liver and adipose tissue

- In adipose tissue, TAG Can be used as fuel when required
- Little TAG is stored in the liver, Instead, most is exported to different body parts Via Lipoproteins

Phospholipids

- Phospholipids are:
- Polar,
- Ionic compounds,
- composed of an alcohol, attached by a phosphodiester bond to either diacylglycerol or sphingosine
- Amphipathic

Structure of Phospholipids

- Hydrophilic head (Phosphate group + alcohol)
- hydrophobic tail (containing fatty acid chains)

Location of Phospholipids

- Mostly Commonly found in Cell membranes

Functions of Phospholipids

- Signal Transmission
- Surfactant (Makes breathing easy especially for new born)
- Bile
- Provide support to proteins in cell membrane

Types of phospholipids

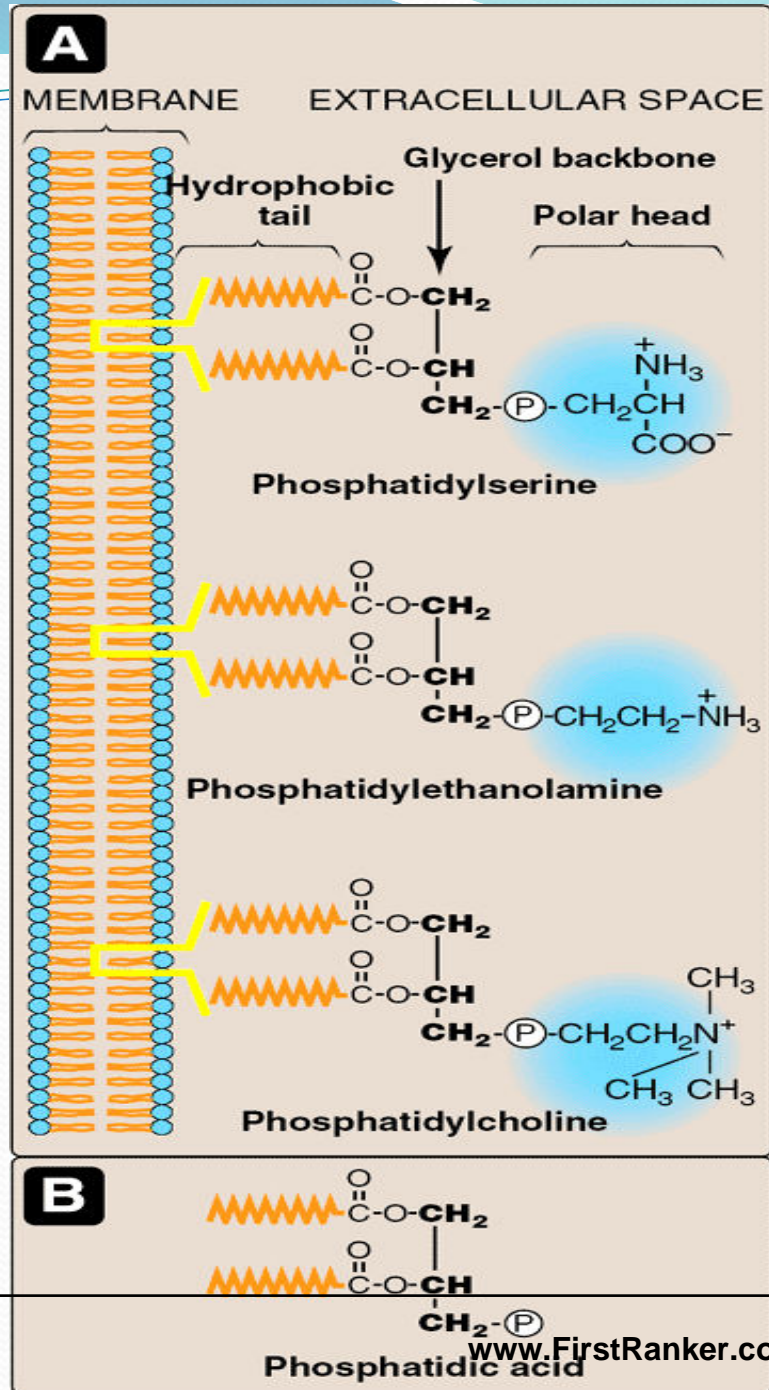
- 02 types
 - Glycerophospholipids
 - Sphingophospholipids

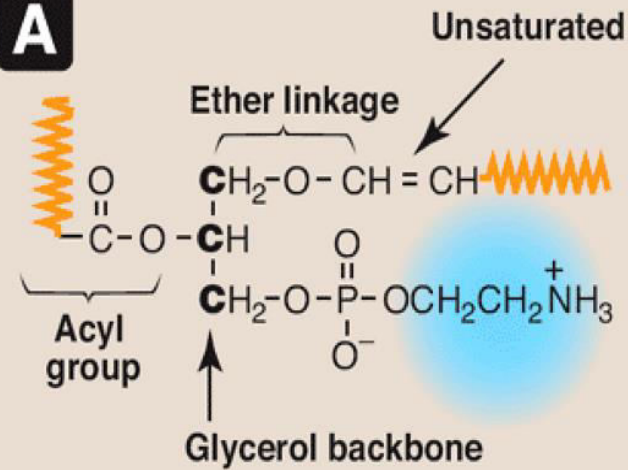
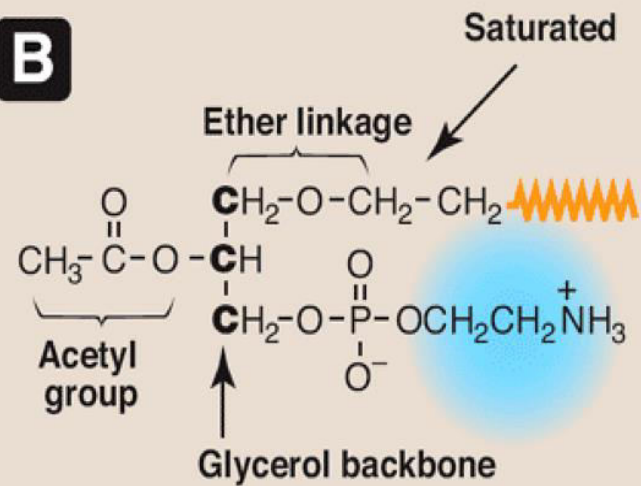
Glycerophospholipids

- Also known as phosphoglycerides
- Example: Phosphatidic acid is the simplest phosphoglyceride
- Phosphatidic acid is composed of diacylglycerol with a phosphate group on the third carbon
- precursor of the other Glycerophospholipids

Types of Glycerophospholipids

- Phosphatidylserine
- phosphatidylethanolamine (cephalin)
- phosphatidylcholine (lecithin)
- Phosphatidylinositol
- Phosphatidylglycerol



A**Phosphatidylethanolamine****B****Platelet-activating factor**

- Phosphatidylserine = Serine + PA
- phosphatidylethanolamine (cephalin) = Ethanolamine + PA
- phosphatidylcholine (lecithin) = Choline + PA
- Phosphatidylinositol = Inositol + PA
- Phosphatidylglycerol = Glycerol + PA

Cardiolipin:

- Two molecules of PA esterified through their phosphate groups to an additional molecule of glycerol is called cardiolipin
- Cardiolipin is found in bacteria and eukaryotes (inner mitochondrial membrane)

Importance of cardiolipin

- Cardiolipin is antigenic, and is recognized by antibodies raised against *Treponema pallidum*, the bacterium that causes syphilis

Plasmalogens

- When the fatty acid at carbon 1 of a glycerophospholipid is replaced by an unsaturated alkyl group attached by an ether linkage to glycerol

Examples of plasmalogens

- phosphatidylethanolamine (abundant in nerve tissue)
- Phosphatidylcholine (abundant in heart muscle)

Platelet-activating factor (PAF)

- Saturated alkyl group in an ether link to carbon 1 and an acetyl residue at carbon 2 of the glycerol
- synthesized and released by a variety of cell types

Functions of PAF

- It causes platelets to aggregate and degranulate, and neutrophils and alveolar macrophages to generate superoxide radicals

Sphingophospholipids: sphingomyelin

- Amino alcohol sphingosine, rather than glycerol
- **Ceramide**
 - A long-chain fatty acid is attached to the amino group of sphingosine through an amide linkage

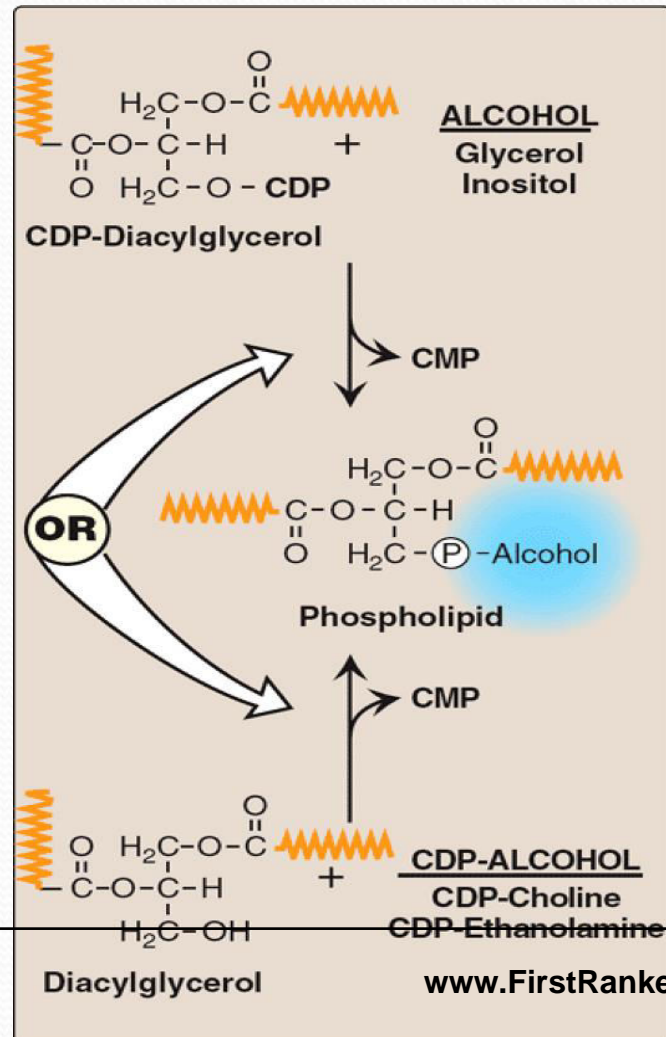
Sphingomyelin

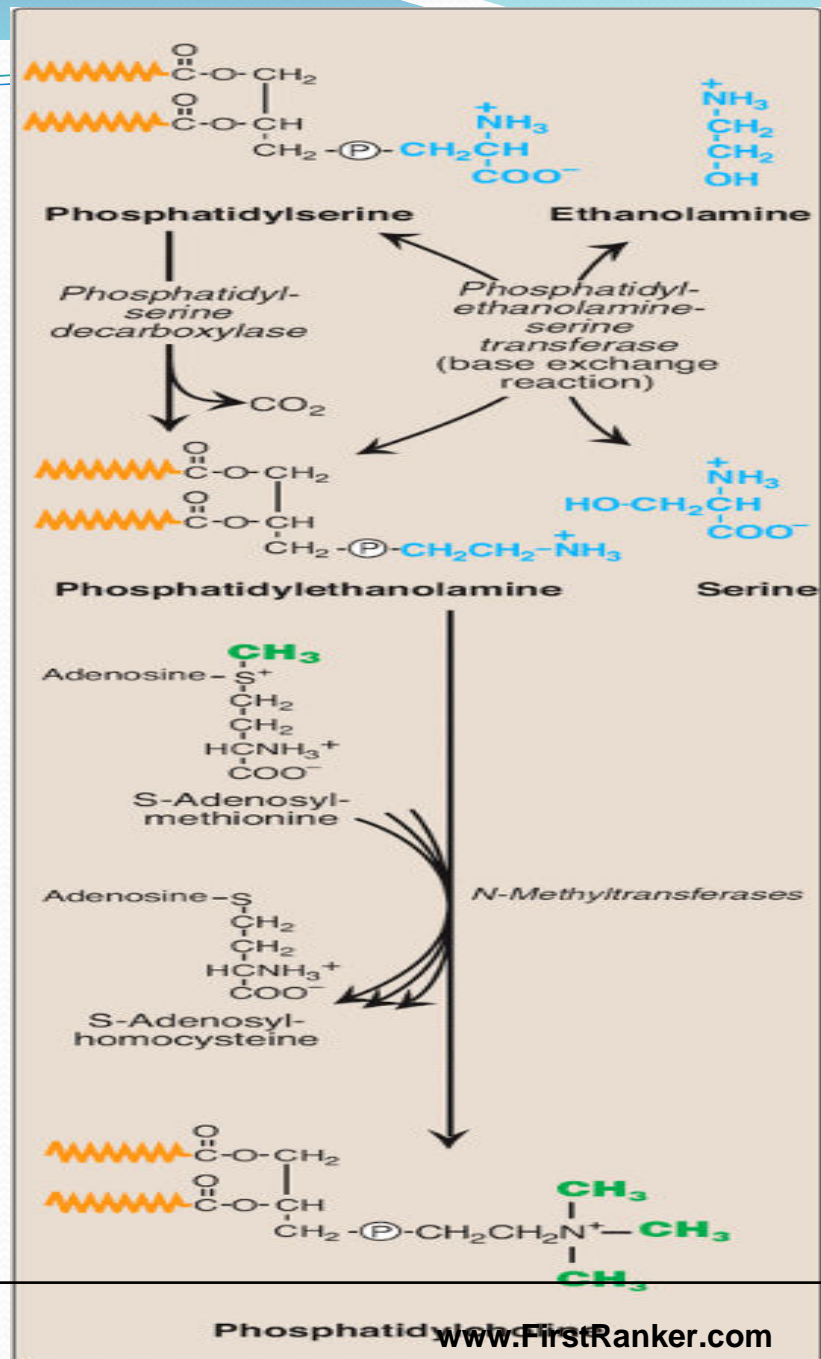
- The alcohol group at carbon 1 of sphingosine is esterified to phosphorylcholine

Functions

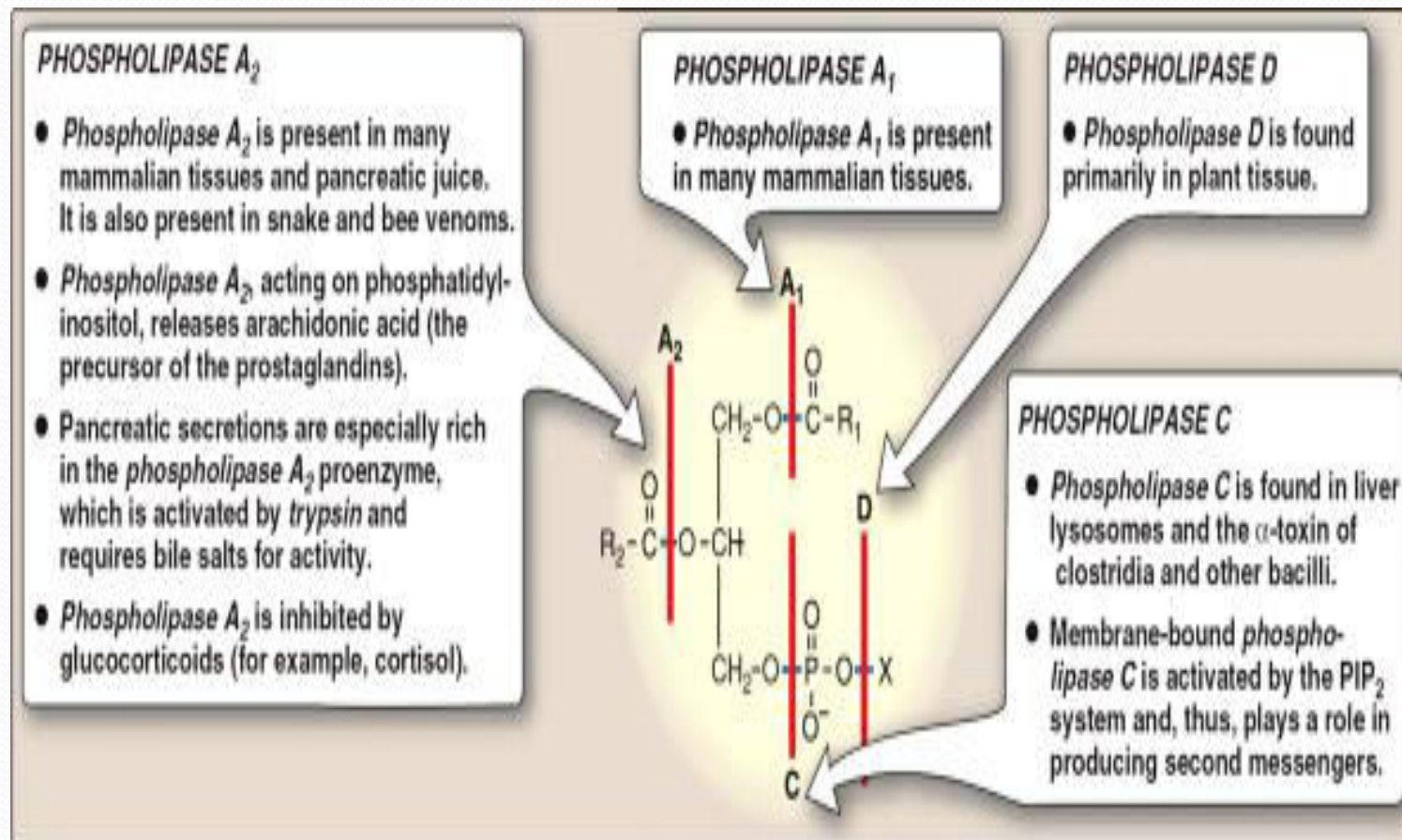
- Sphingomyelin is an important constituent of the myelin of nerve fibers

Phospholipid Synthesis

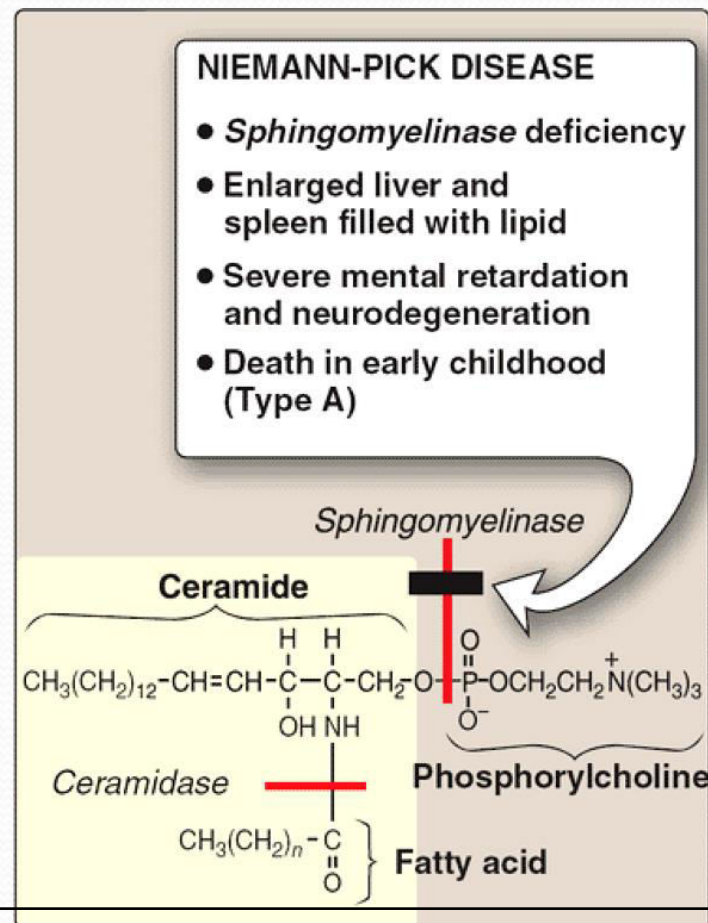




Degradation of Phospholipids



Niemann Pick Disease



Types of Niemann-Pick disease

- Niemann-Pick disease (Types A and B)
- Autosomal recessive disease
- Inability to degrade sphingomyelin
- The deficient enzyme is sphingomyelinase—a type of phospholipase C

- Type A—less than 1% normal activity
- lipid deposit in liver and spleen → Increase size of liver and spleen , Neuron-degeneration
- Type B—5% or more of normal activity
- little to no damage to neural tissue, but lungs, spleen, liver, and bone marrow are affected
- Mostly commonly affect jews

Degradation of Sphingomyelin

- Sphingomyelin is degraded by sphingomyelinase, a lysosomal enzyme that hydrolytically removes phosphorylcholine, leaving a ceramide.
- The ceramide is, in turn, cleaved by ceramidase into sphingosine and a free fatty acid

Significance of Ceramide & sphingosine

- Ceramides appear to be involved in the response to stress
- sphingosine inhibits protein kinase C

Prostaglandins

- Eicosanoids →

• Prostaglandins + thromboxanes + leukotrienes

Prostaglandins

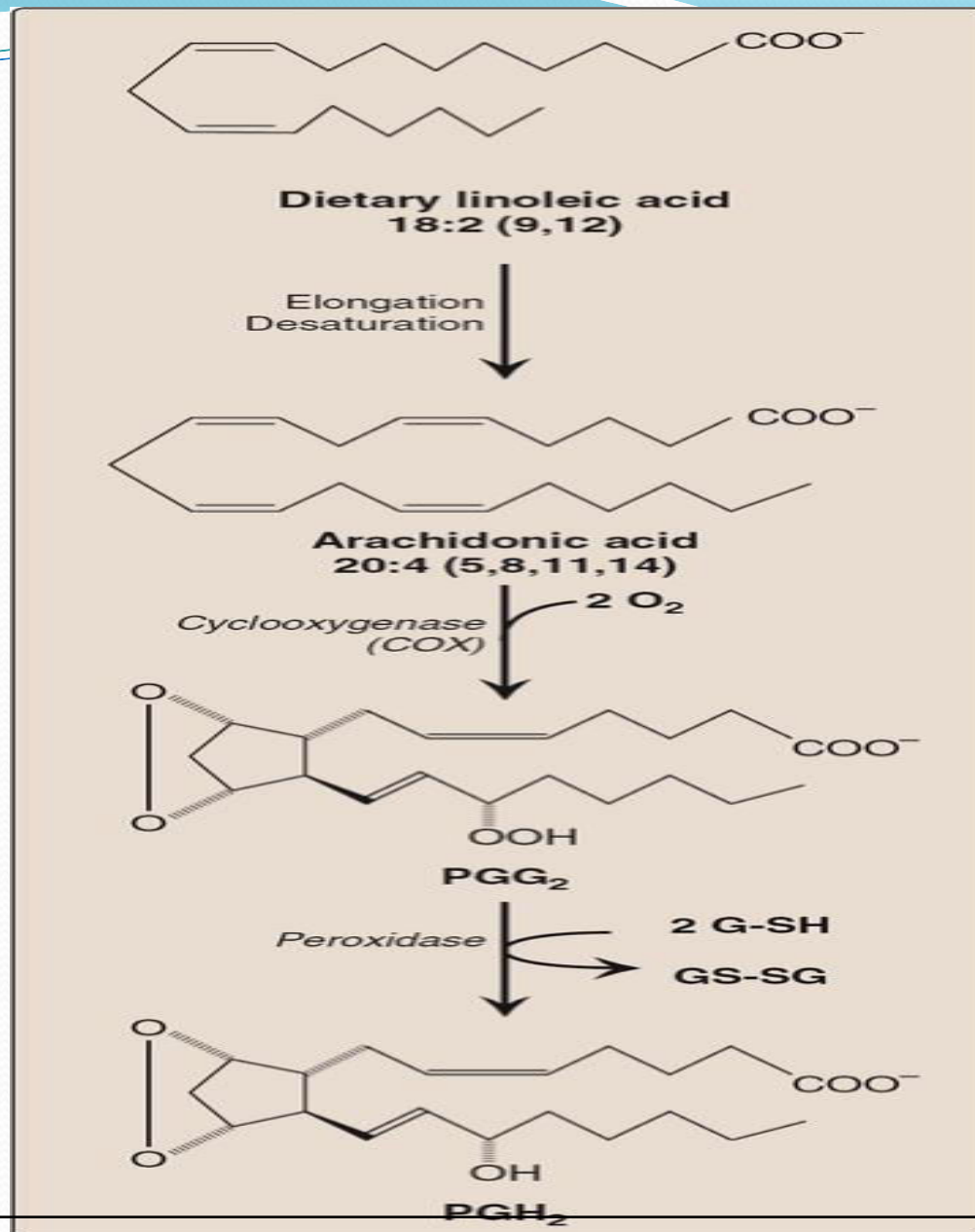
- Made from polyunsaturated fatty acids with 20 carbons

Prostaglandins differ from Hormones

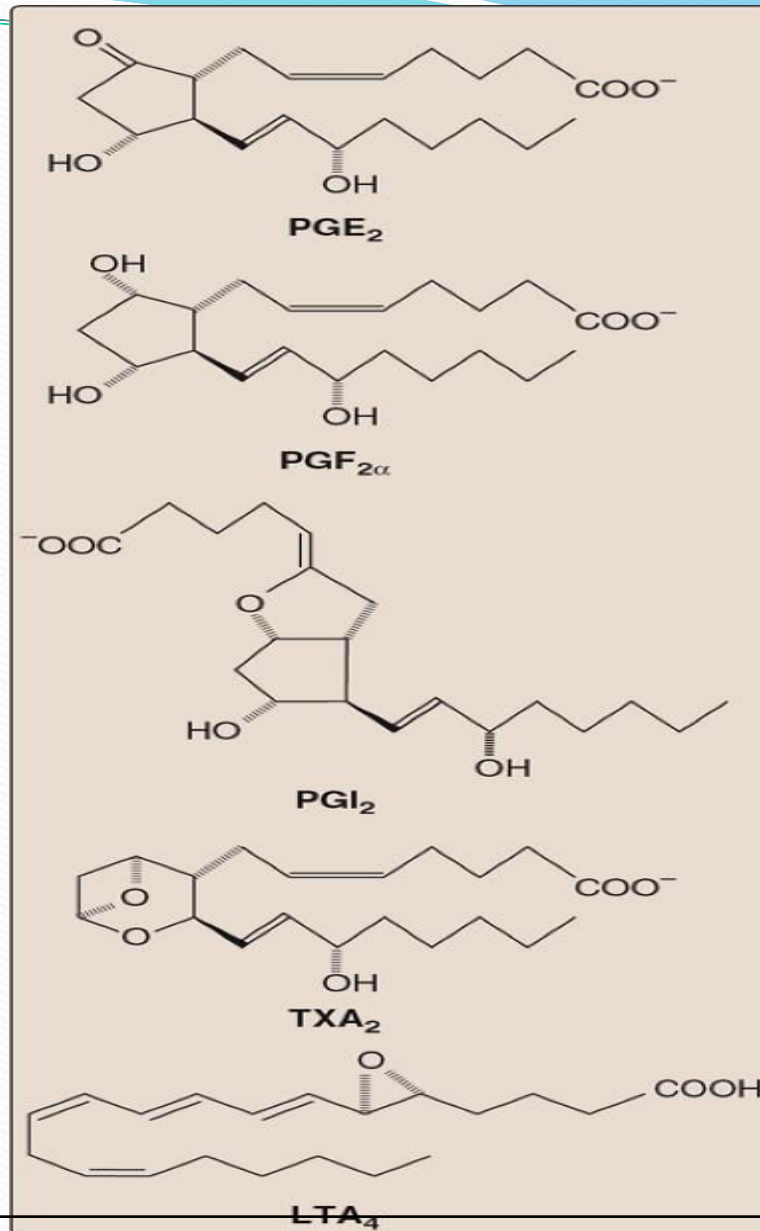
- produced in very small amounts
- Synthesis by All cells
- Act locally
- Not stored
- Rapidly metabolized to inactive products

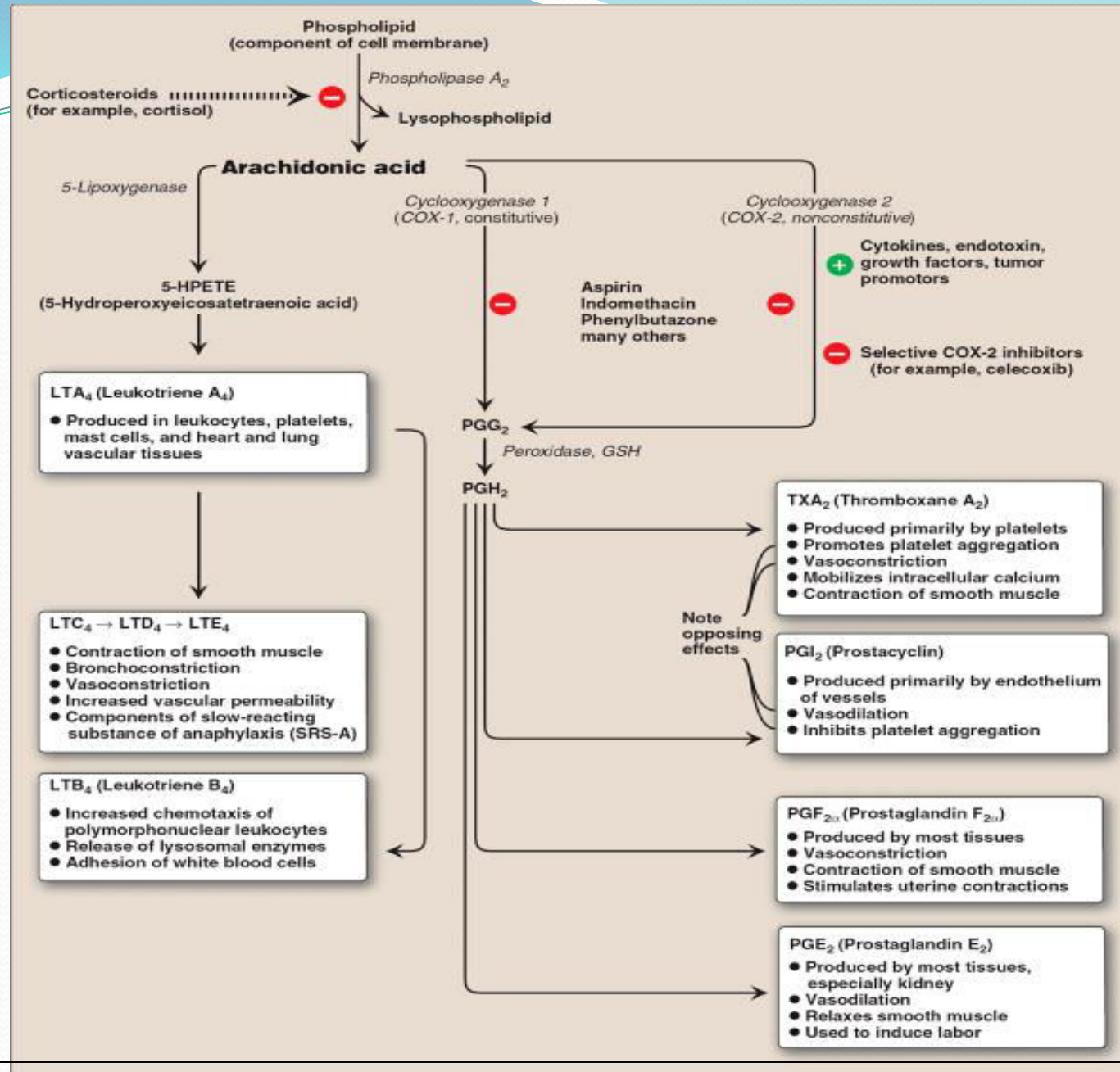
Synthesis of prostaglandins and thromboxanes

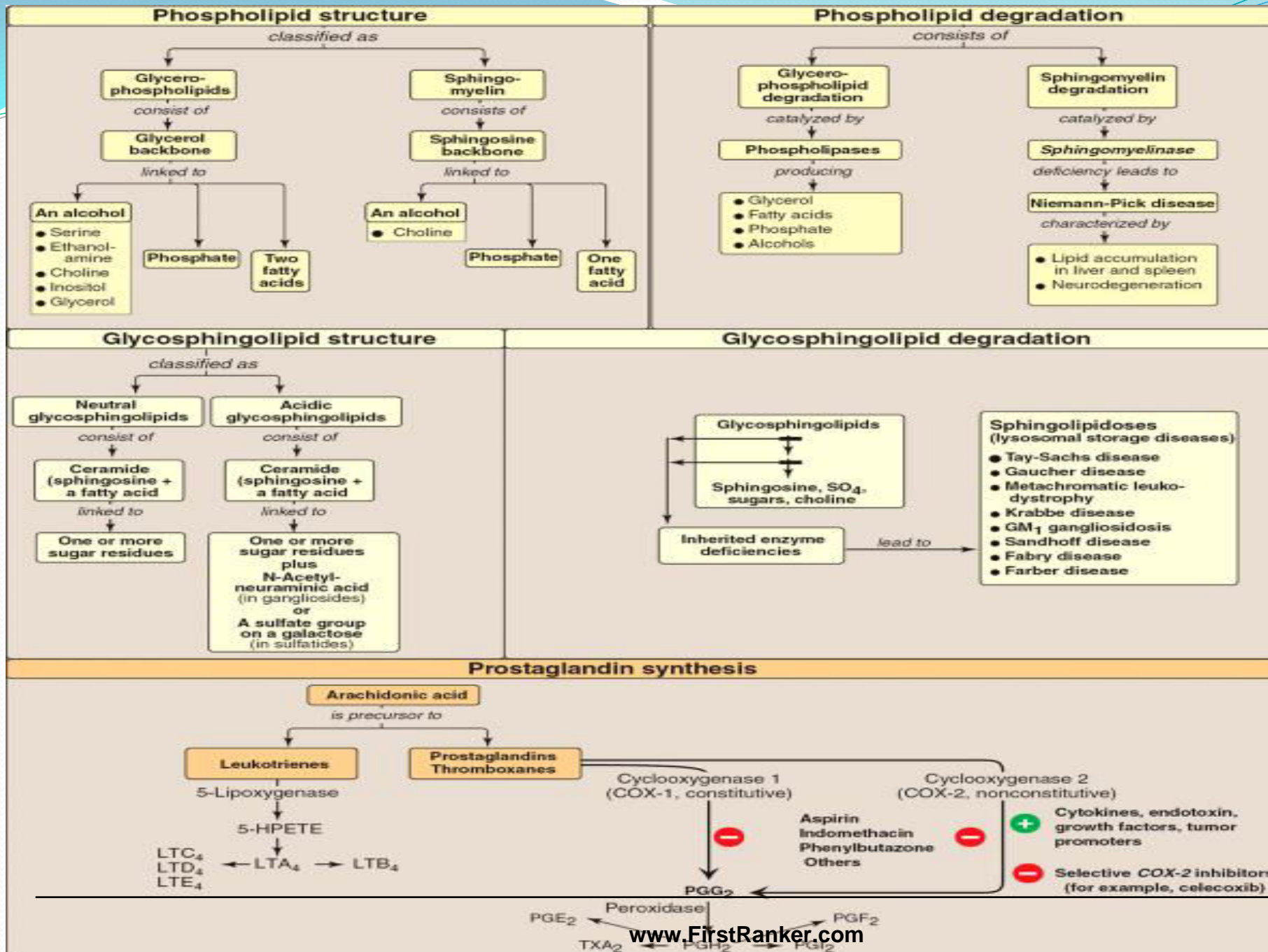
- From linoleic acid → arachidonic acid
- Arachidonic acid is released from membrane-bound phospholipids by phospholipase A₂



Types of PG







Glycolipids

- Also known as glycosphingolipids
- contain both carbohydrate and lipid components
- derivatives of ceramides in which a long-chain fatty acid is attached to the amino alcohol sphingosine

Functions

- essential components of:
 - All membranes
 - Nerve cells

Significance

- Glycosphingolipids are antigenic → a source of blood group antigens
- The carbohydrate portion of a glycolipid is the antigenic determinant
- serve as cell surface receptors for cholera and tetanus toxins

Structure of Glycosphingolipids

- glycosphingolipids differ from sphingomyelin in that they do not contain phosphate
- Polar head function is provided by a monosaccharide or oligosaccharide attached directly to the ceramide by an O-glycosidic bond

Types

- Neutral glycosphingolipids
- simplest neutral (uncharged) glycosphingolipids are the cerebroside

- Galactocerebroside—the most common cerebroside found in membranes
- Glucocerebroside

Location

- cerebroside predominantly in the brain and peripheral nervous tissue
- Ceramide oligosaccharides (or globosides) are produced by attaching additional monosaccharides (including GalNAc) to a glucocerebroside

Acidic glycosphingolipids

- negatively charged at physiologic pH → provided by N-acetylneuraminic acid (NANA) in gangliosides, or by sulfate groups in sulfatides.
- [NANA is also referred to as sialic acid.]

Ganglioside

- found in the ganglion cells
- Derivatives of ceramide oligosaccharides, and contain one or more molecules of NANA.

Classification of Lipids

- **1. Simple lipids:** Esters of fatty acids with various alcohols.
 - a. **Fats:** Esters of fatty acids with glycerol. **Oils** are fats in the liquid state.
 - b. **Waxes:** Esters of fatty acids with higher molecular weight monohydric alcohols.

Classification of Lipids

- **Complex lipids:** Esters of fatty acids containing groups in addition to an alcohol and a fatty acid.
 - a. **Phospholipids:** Lipids containing, in addition to fatty acids and an alcohol, a phosphoric acid residue.
 - 2 types Phospholipids
 - Glycerophospholipids
 - Sphingophospholipids

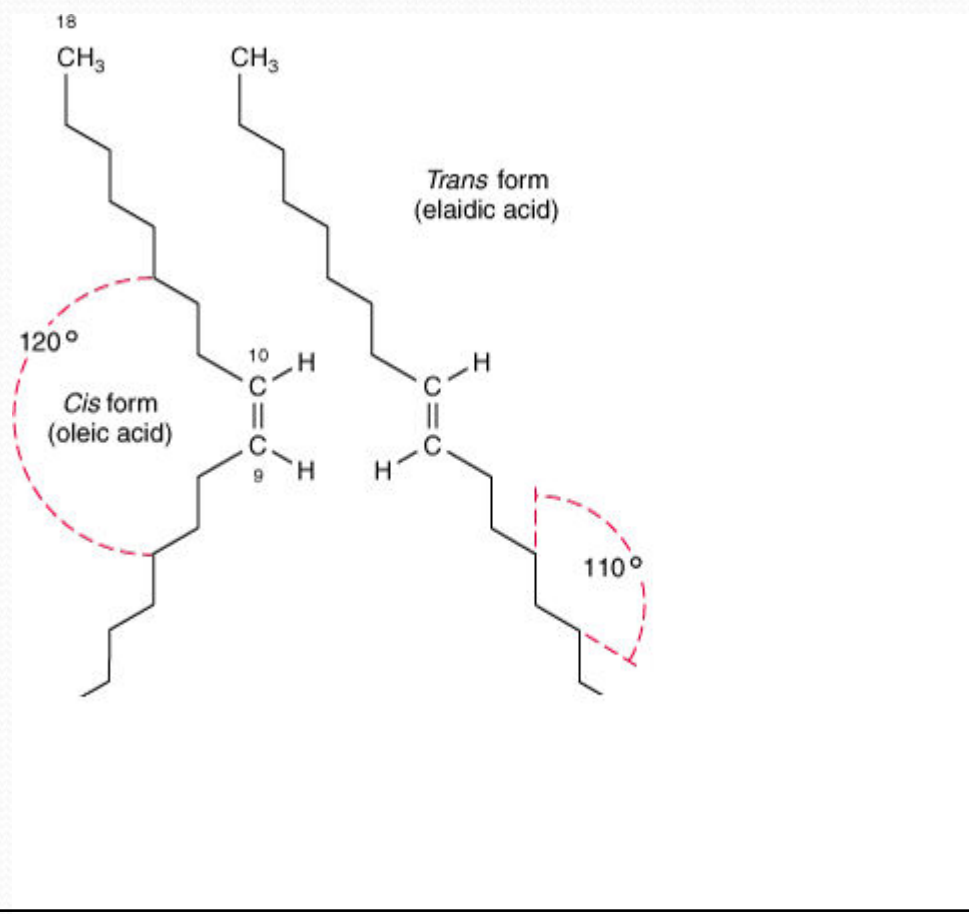
- b. **Glycolipids (glycosphingolipids):** Lipids containing a fatty acid, sphingosine, and carbohydrate.
- c. **Other complex lipids:** Lipids such as sulfolipids and aminolipids & Lipoproteins

- **Precursor and derived lipids:** These include fatty acids, glycerol, steroids, other alcohols, fatty aldehydes, ketone bodies, lipid-soluble vitamins, and hormones.

Difference between Cis & Trans

- If the acyl chains are on the same side of the bond, it is *cis*-, example: oleic acid.
- if on opposite sides, it is *trans*-, example: elaidic acid, the *trans* isomer of oleic acid

- Double bonds in naturally occurring unsaturated long-chain fatty acids are nearly all in the *cis* configuration, the molecules being "bent" 120 degrees at the double bond. Thus, oleic acid has an L shape, whereas elaidic acid remains "straight."



Clinical Significance

- Consumption of *trans* fatty acids → **not good health.**
- Previously in Margarine → Higher number of Trans FA.
- Now soft margarine low in *trans* fatty acids or containing none at all.