MEDICAL CHEMISTRY
BIOCHEMISTRY

University Of Fallujah

College Of Medicine

Lecture : Lipid-2-

Stage : 1st Stage

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Department: Chemistry and Biochemistry department

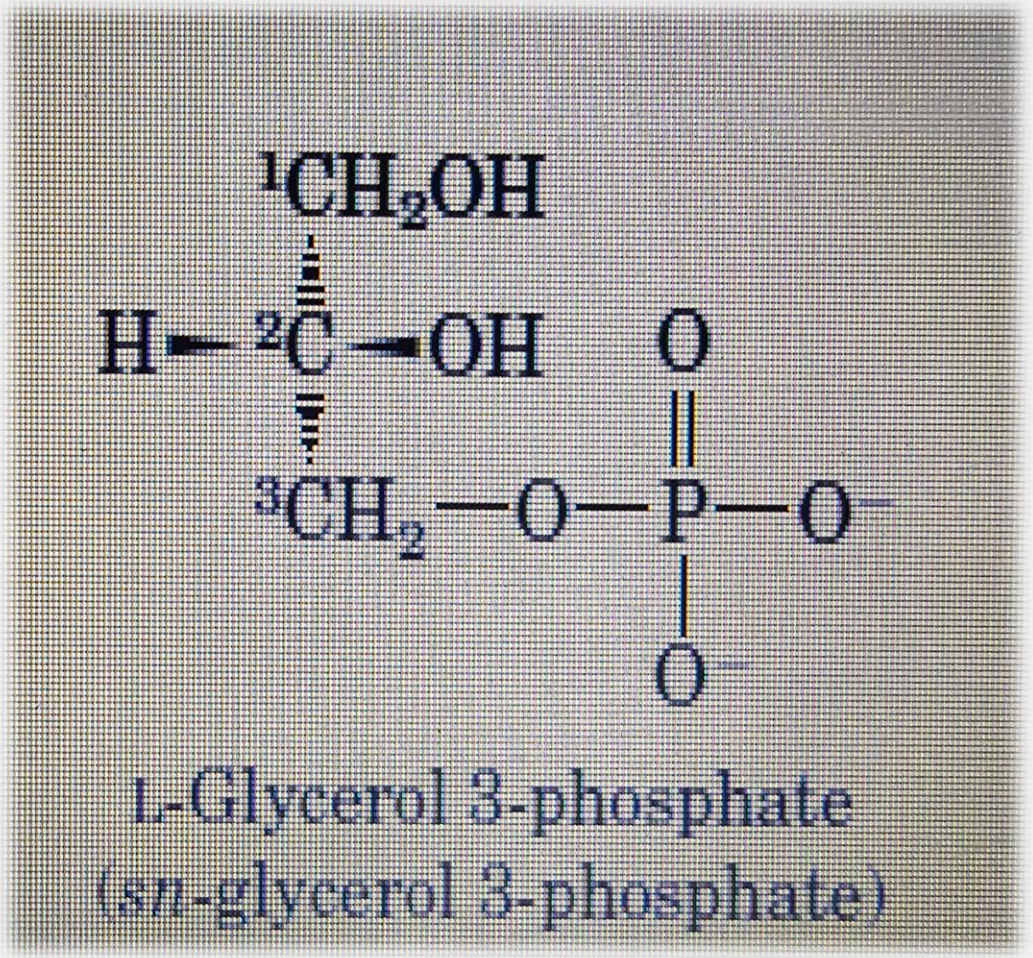
Date: 16/ 4/ 2026

Learning Objective :

- Identify and differentiate the basic chemical structures of glycerophospholipids, sphingolipids, and cholesterol.
- Classify different types of lipids, including lipoproteins (chylomicrons, VLDL, LDL, HDL), eicosanoids, and steroid hormones.
- Correlate enzyme deficiencies with the pathophysiology of specific lipid storage diseases, such as Tay-Sachs and Niemann-Pick.

LIPID

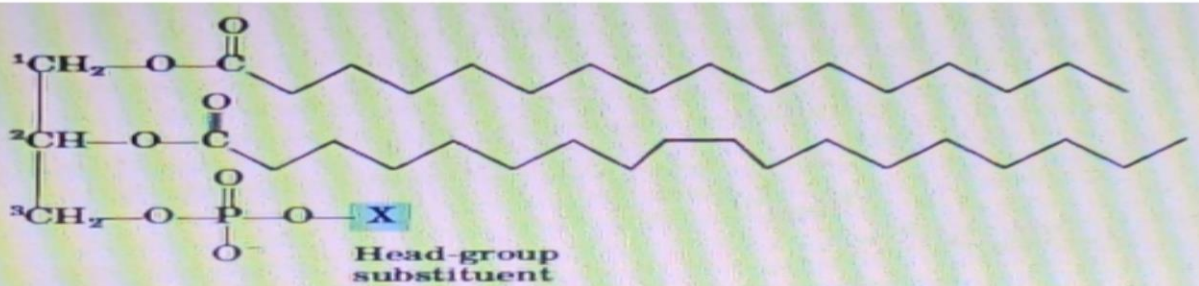
- What is Glycerophospholipids ?
- Glycerophospholipids are membrane lipids in which two fatty acids are attached in ester linkage to the first and second carbons of glycerol, and a highly polar or charged group is attached through a phosphodiester linkage to the third carbon. Glycerol is prochiral; attachment of phosphate converts it into a chiral compound.

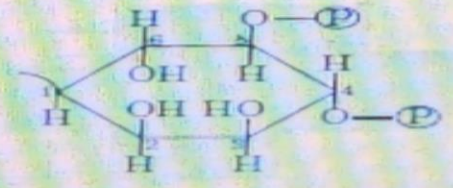
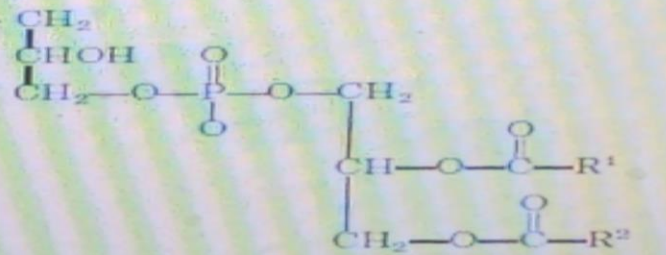


COMMON GLYCEROPHOSPHOLIPIDS

- **The Common Glycerophospholipids :**
- Glycerophospholipids are named as derivatives of phosphatidic acid. Examples: phosphatidylethanolamine, phosphatidylcholine (lecithin), phosphatidylserine, phosphatidylglycerol, phosphatidylinositol 4,5-bisphosphate, and cardiolipin.

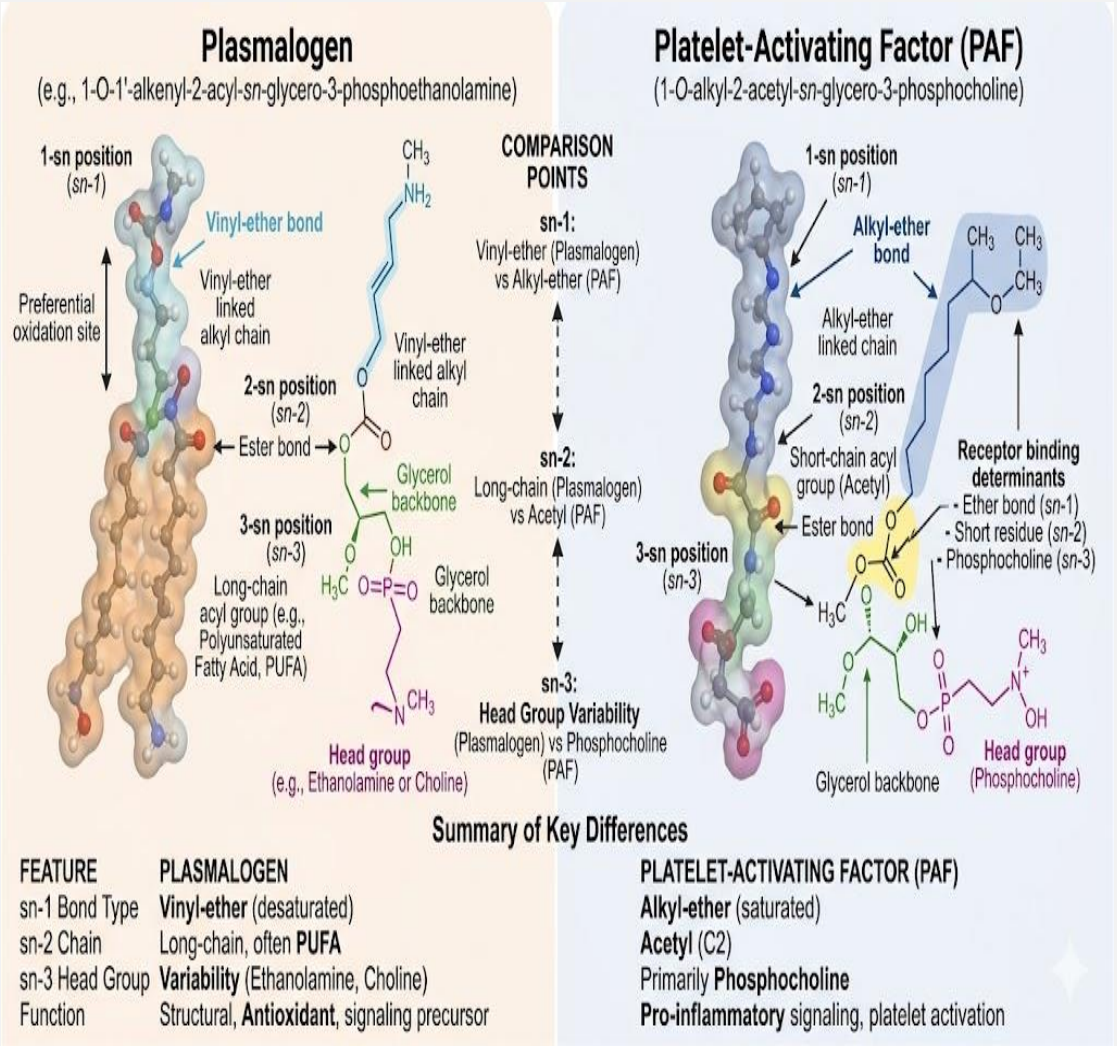
Glycerophospholipid (general structure)



Name of glycerophospholipid	Name of X	Formula of X	Net charge (at pH 7)
Phosphatidic acid	—	—H	−1
Phosphatidylethanolamine	Ethanolamine	$-CH_2-CH_2-\overset{+}{N}H_3$	0
Phosphatidylcholine	Choline	$-CH_2-CH_2-\overset{+}{N}(CH_3)_3$	0
Phosphatidylserine	Serine	$-CH_2-\underset{\displaystyle COO^-}{\underset{|}{CH}}-\overset{+}{N}H_3$	−1
Phosphatidylglycerol	Glycerol	$-CH_2-\underset{\displaystyle OH}{\underset{|}{CH}}-CH_2-OH$	−1
Phosphatidylinositol 4,5-bisphosphate	*myo*-Inositol 4,5-bisphosphate		−4
Cardiolipin	Phosphatidyl-glycerol		−2

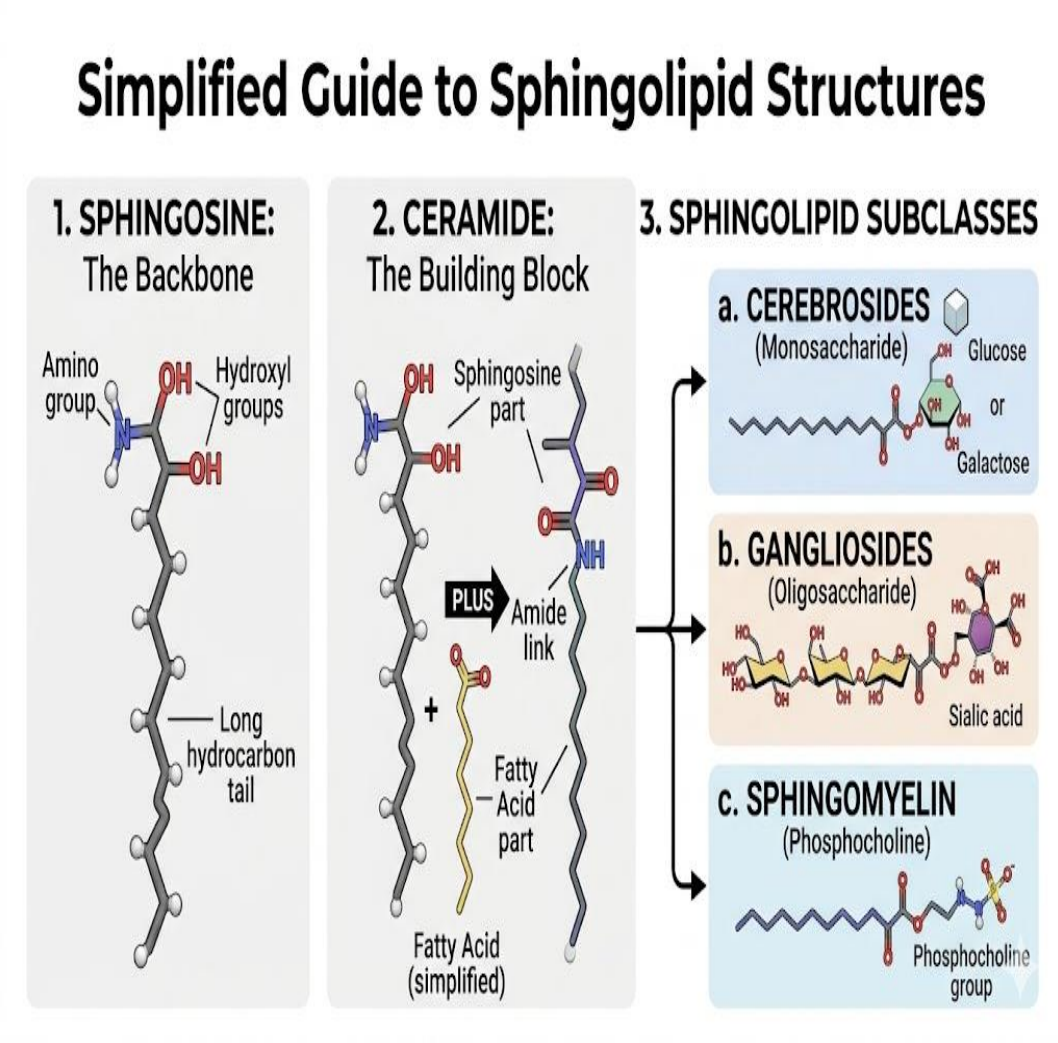
ETHER LIPIDS AND PLASMALOGENS

- **What are Ether Lipids and Plasmalogens:**
  - Some animal tissues contain ether lipids. where one acyl chain is attached to alycerol in ether linkage. Plasmalogens contain a double bond between C-1 and C-2. Platelet-activating factor (PAF) is an ether lipid that acts as a potent molecular signal.



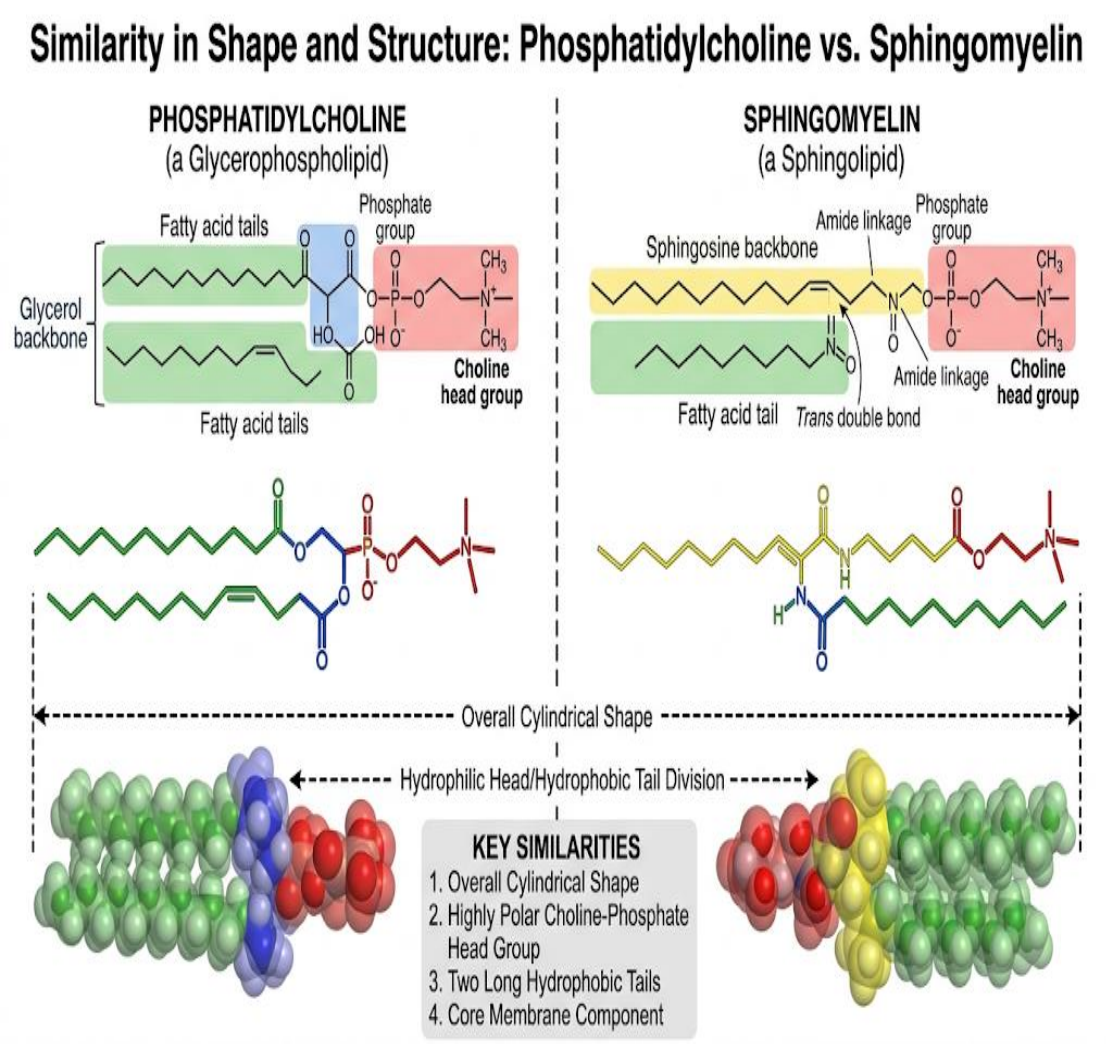
SPHINGOLIPIDS - SPHINGOSINE AND CERAMIDE

- **What are the Sphingolipids – Sphingosine and Ceramide :**
- Sphingolipids are composed of sphingosine (a long-chain amino alcohol), a long-chain fatty acid, and a polar head group. When a fatty acid is attached in amide linkage to the –NH2 on C-2, the resulting compound is ceramide, the structural parent of all sphingolipids.



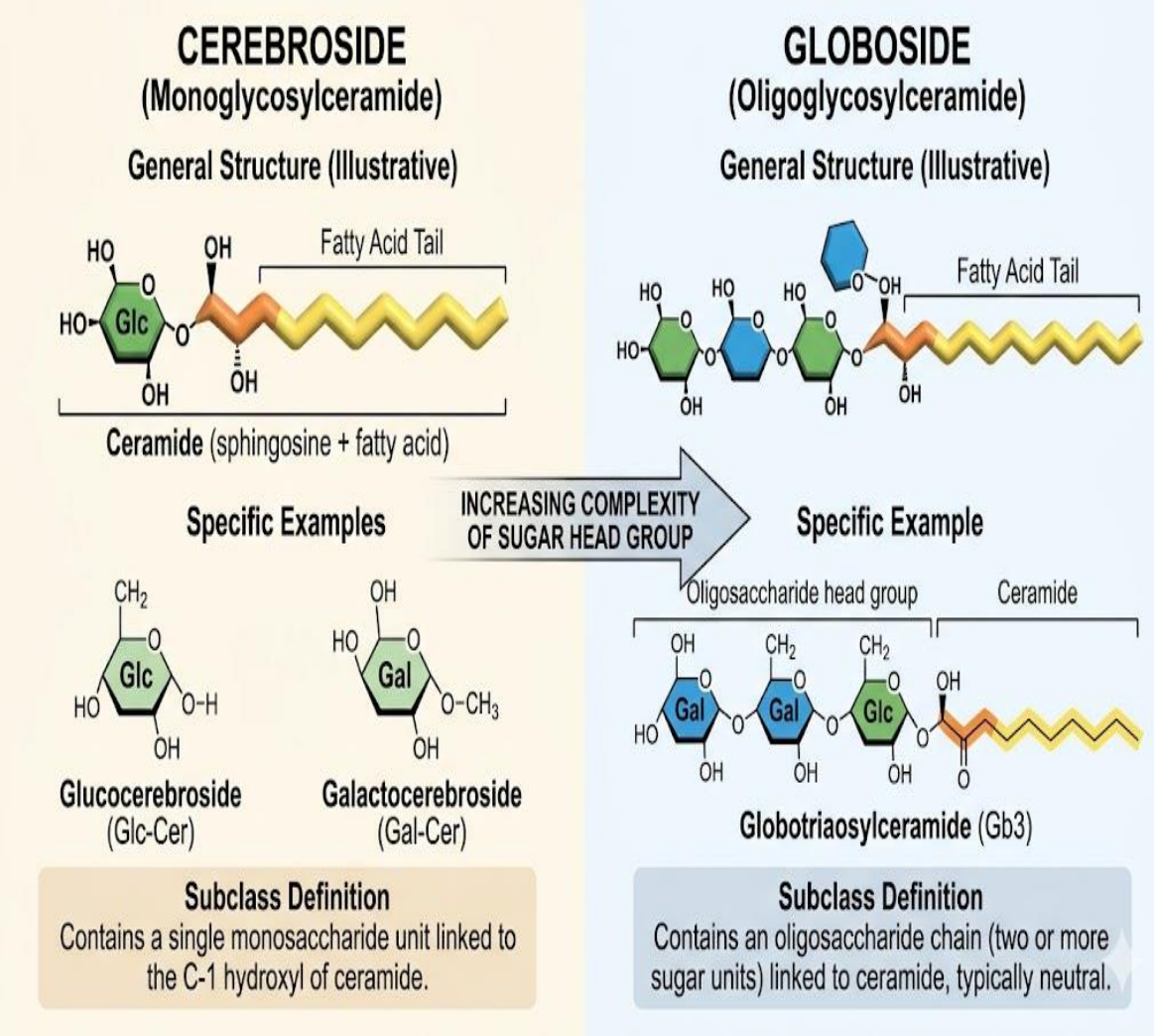
SPHINGOMYELIN

- **What is Sphingomyelin :**
  - Sphingomyelin: Sphingomyelins contain phosphocholine or phosphoethanolamine as their polar head group and are therefore classified as phospholipids. They resemble phosphatidylcholines and have no net charge. Sphingomyelins are present in plasma membranes and are especially prominent in myelin.



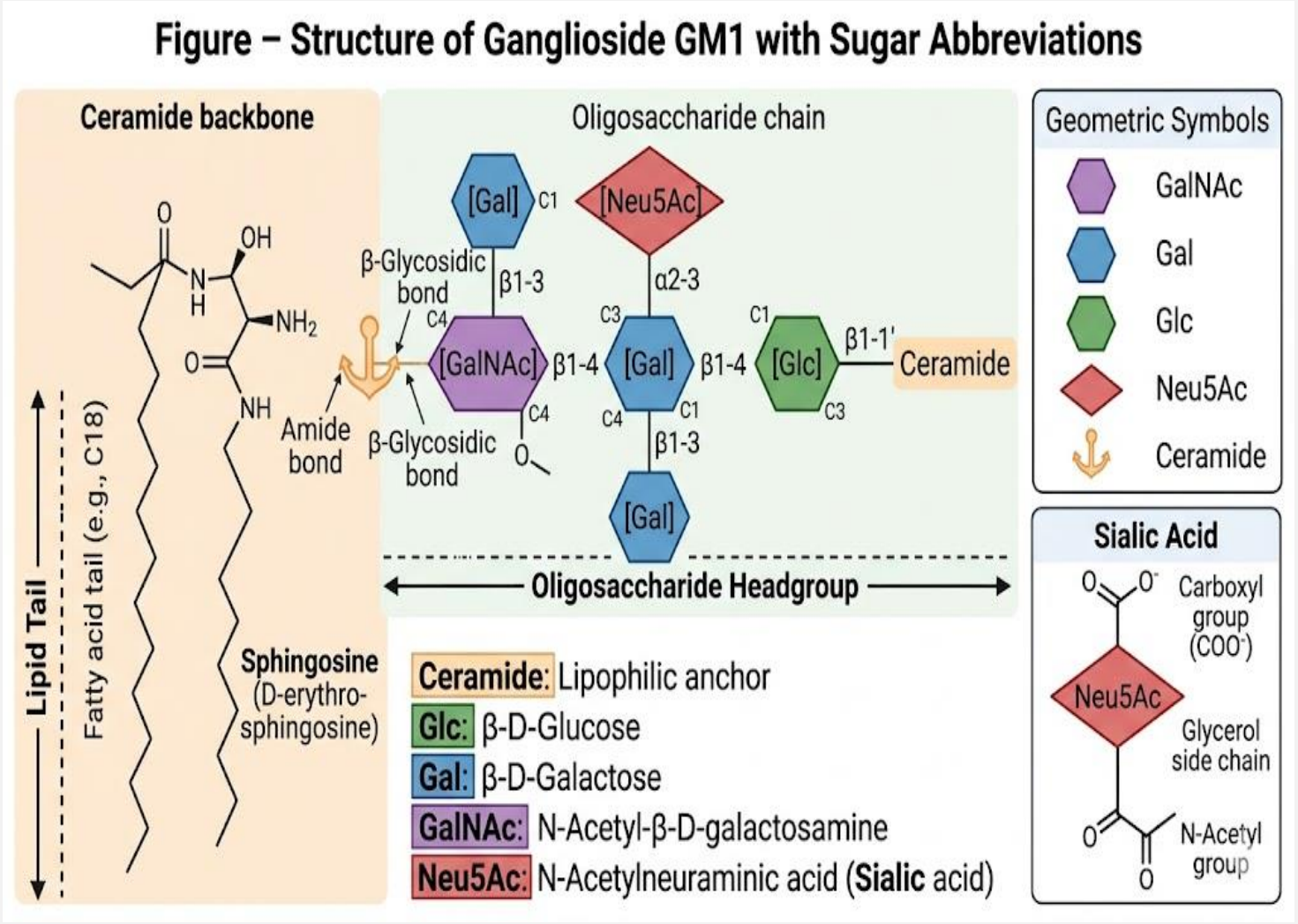
GLYCOSPHINGOLIPIDS - CEREBROSIDES AND GLOBOSIDES

- **Glycosphingolipids – Cerebrosides and Globosides :**
  - Glycosphingolipids occur on the outer face of plasma membranes. Cerebrosides have a single sugar (galactose in neural tissue, glucose in non-neural tissues). Globosides have two or more neutral sugars and are called neutral glycolipids (no charge at pH 7).



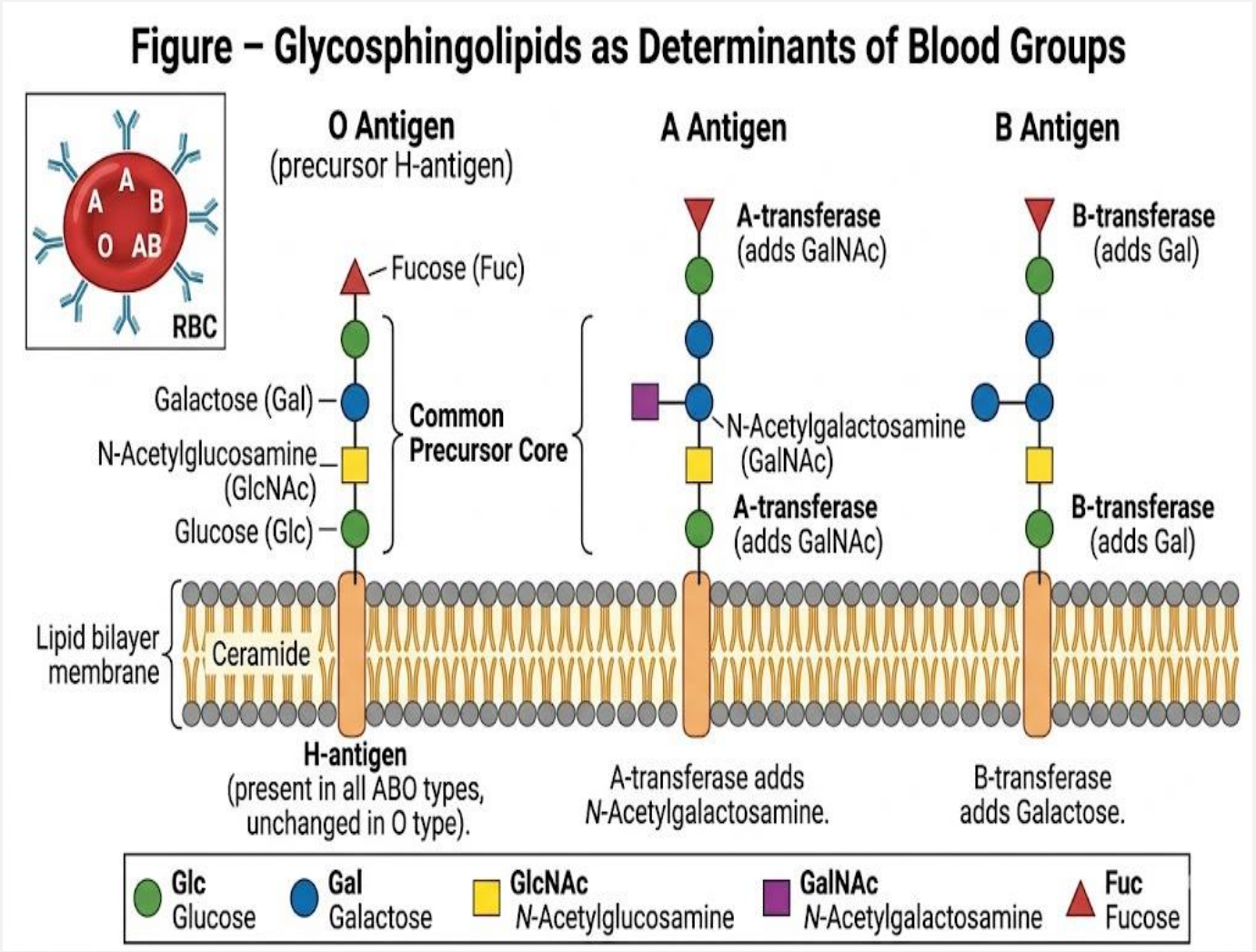
GANGLIOSIDES

- **Gangliosides :**
- Gangliosides are the most complex sphingolipids, with oligosaccharide head groups and one or more residues of N-acetylneuraminic acid (sialic acid), which gives them a negative charge at pH 7. They are classified as GM, GD, GT, GQ based on the number of sialic acid residues.



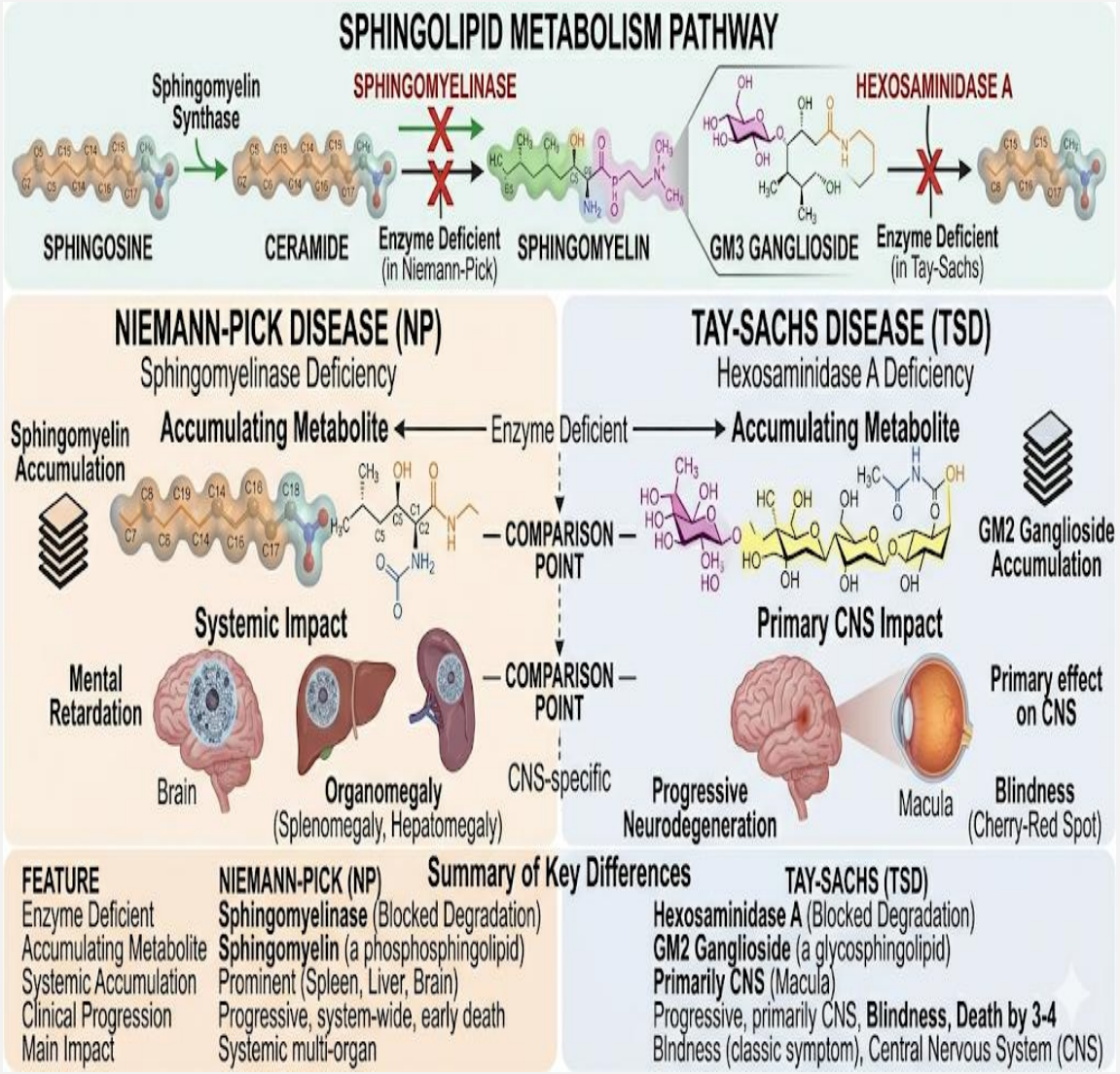
BIOLOGICAL RECOGNITION - BLOOD GROUPS AND GANGLIOSIDES

- **Blood Groups and Gangliosides :**
  - The carbohydrate moieties of certain sphingolipids define the human blood groups (O, A, B). Gangliosides are concentrated on the outer cell surface, where they present recognition points. Their kinds and amounts change during embryonic development and tumor formation.



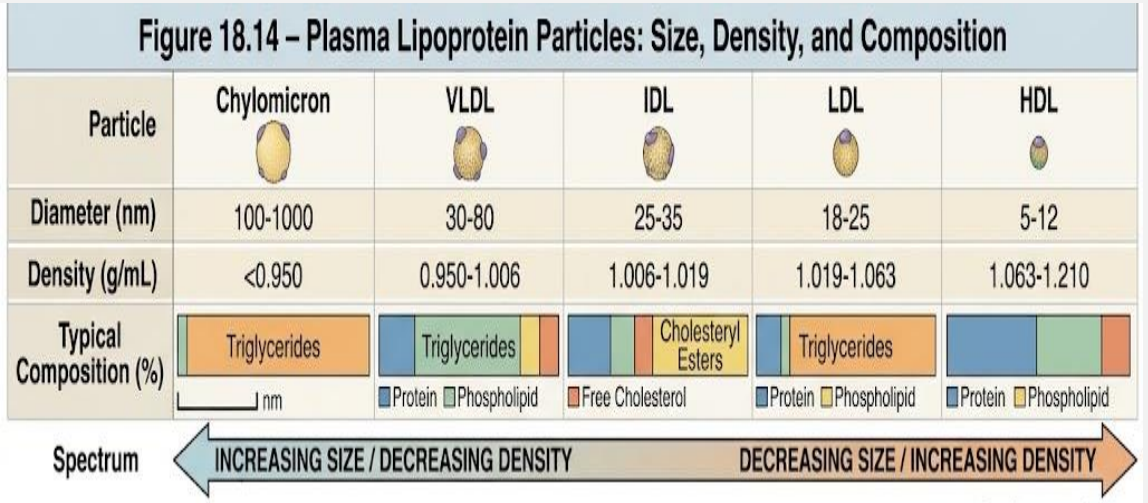
LYSOSOMAL DEGRADATION AND SPHINGOLIPIDOSES

- **Lysosomal Degradation and Sphingolipidoses :**
  - Specific lysosomal enzymes degrade membrane lipids. Defects cause accumulation of partial breakdown products.
  - Niemann-Pick disease: deficiency of sphingomyelinase → sphingomyelin accumulates in brain, spleen, liver → mental retardation, early death.
  - Tay-Sachs disease: deficiency of hexosaminidase A → GM2 ganglioside accumulation → progressive retardation, blindness, death by age 3-4.



PLASMA LIPOPROTEINS - OVERVIEW AND COMPOSITION

- **Overview and Composition:**
  - The plasma lipoproteins are spherical macromolecular complexes of lipids and proteins (apolipoproteins). The lipoprotein particles include chylomicrons, chylomicron remnants, very-low-density lipoproteins (VLDLs), VLDL remnants, also known as intermediate-density lipoproteins (IDLs), low-density lipoproteins (LDLs), high-density lipoproteins (HDL) and lipoprotein (a) (Lp[a]). They differ in lipid and protein composition, size, density (Fig. 18.14), and site of origin. Lipoproteins function both to keep their component lipids soluble as they transport them in the plasma and to provide an efficient mechanism for transporting their lipid contents to (and from) the tissues.



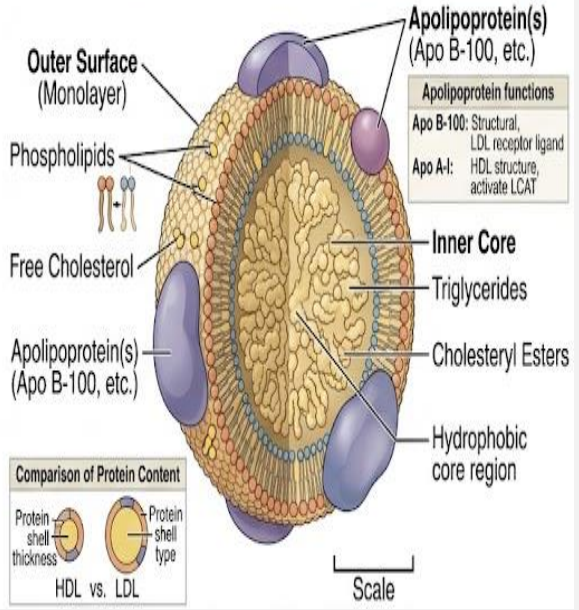
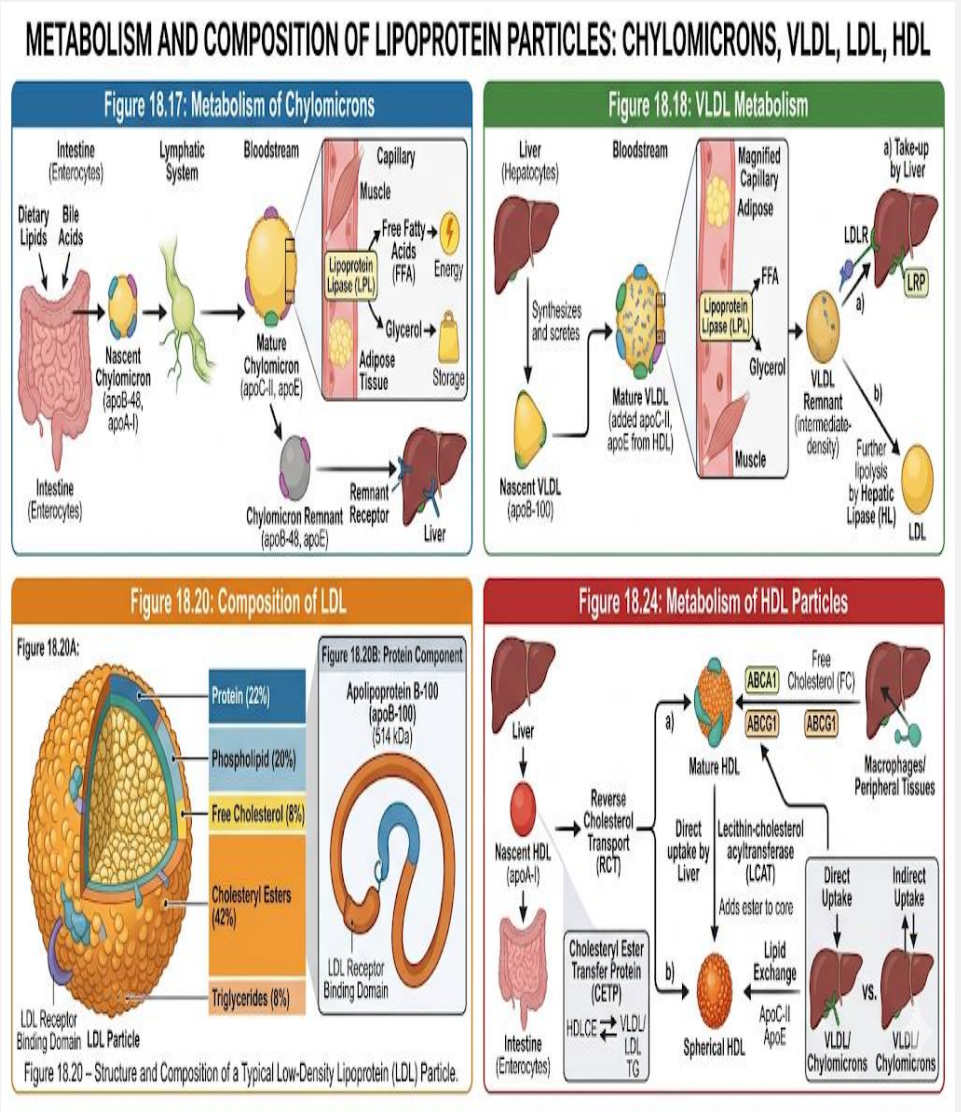


Figure 18.15 – Structure of a Typical Lipoprotein Particle

CHYLOMICRONS, VLDL, LDL, AND HDL

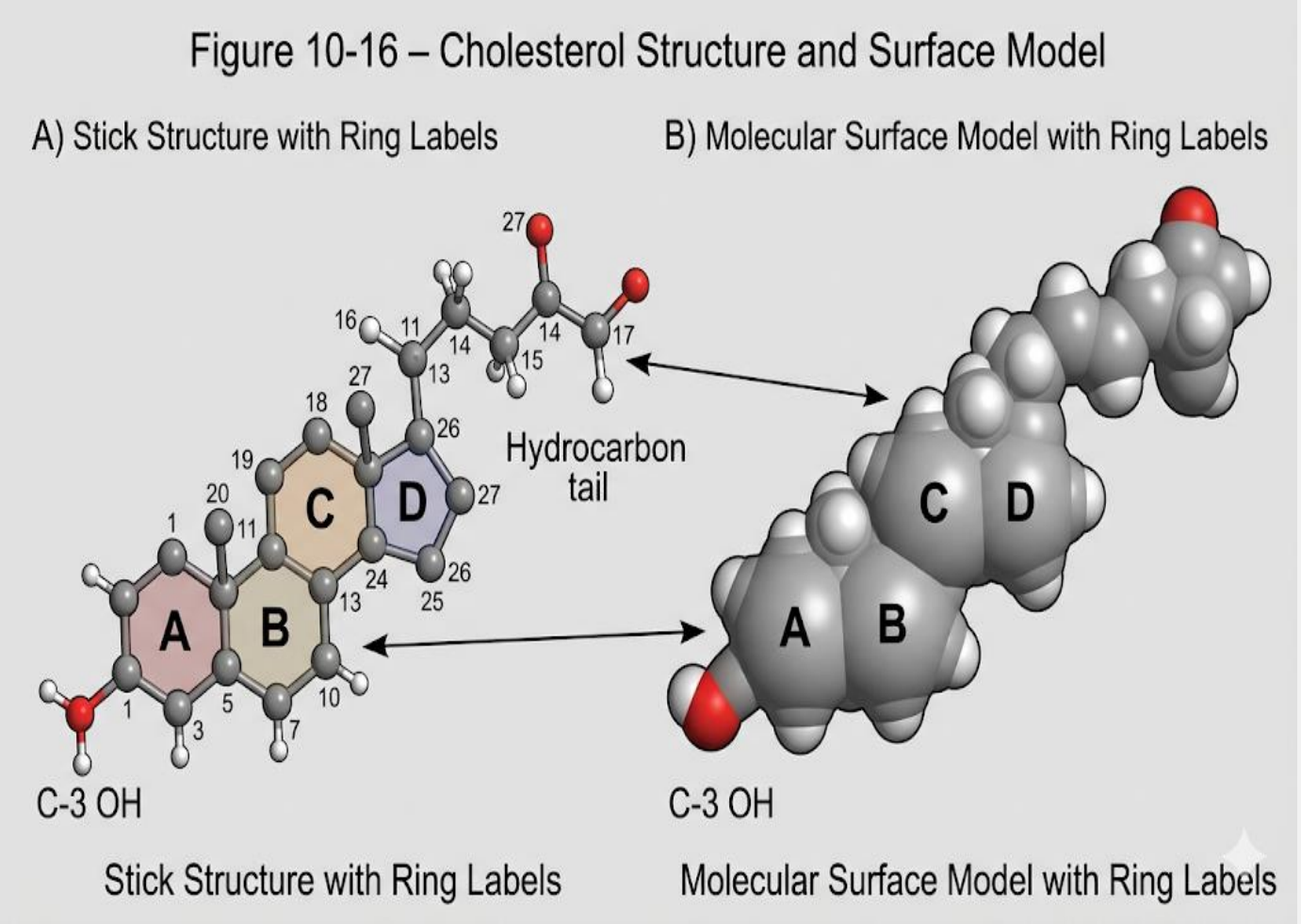
- **Key Features:**

- Chylomicrons are assembled in intestinal mucosal cells and carry dietary (exogenous) TAG, cholesterol, fat-soluble vitamins, and cholesteryl esters to the peripheral tissues. Apo B-48 is unique to chylomicrons. VLDLs are produced in the liver and are composed predominantly of endogenous TAG (~60%), and their function is to carry this lipid from the liver to the peripheral tissues. VLDLs contain apo B-100. With modifications, VLDL is converted in the plasma to LDL. LDL particles contain a high concentration of cholesterol and cholesteryl esters (about 70% of plasma cholesterol is in LDL). HDL particles are formed in the blood by the addition of lipid to apo A-1, an apolipoprotein made and secreted by the liver and intestine. HDL serves as a circulating reservoir of apo C-II and apo E and mediates reverse cholesterol transport (RCT).



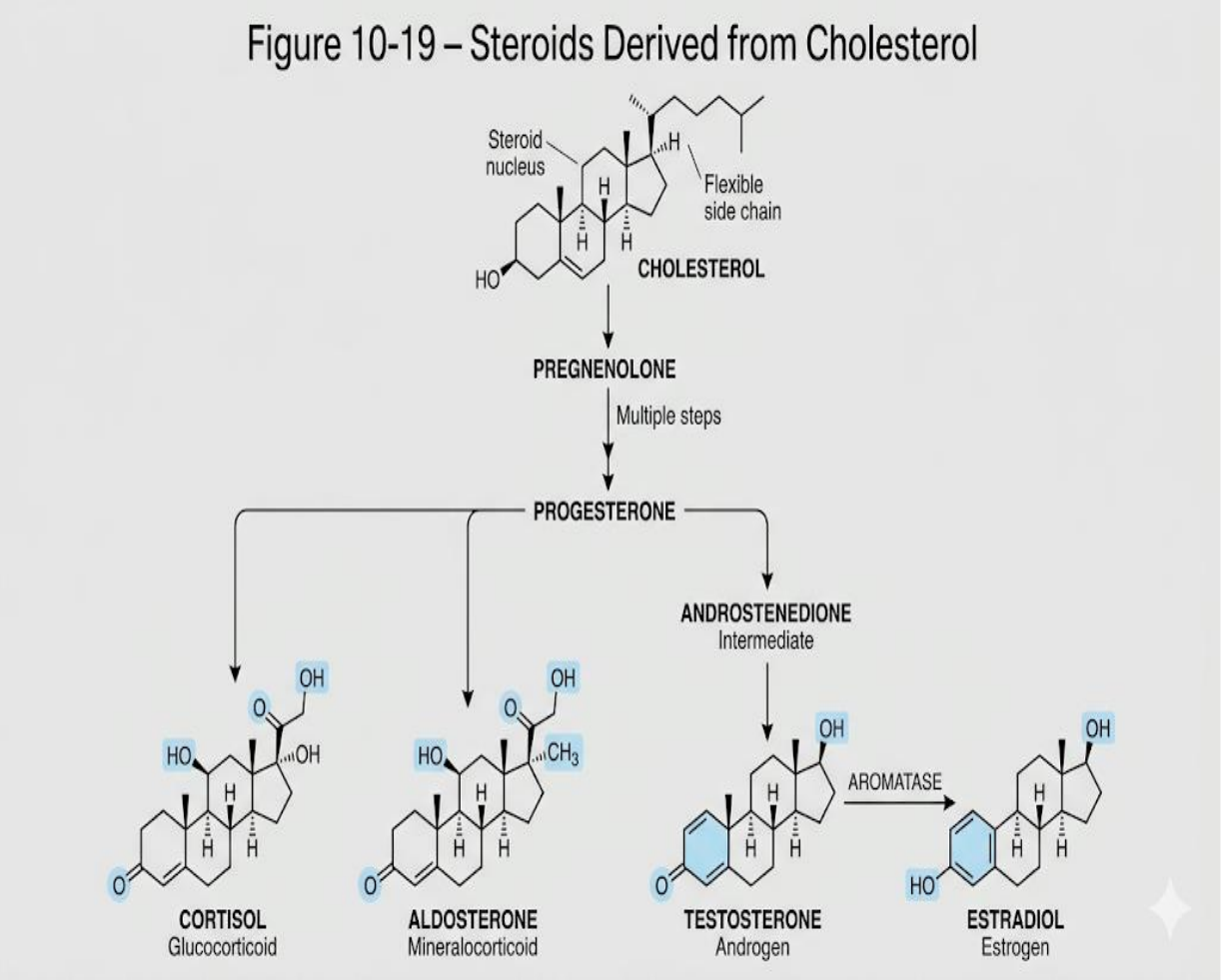
STEROLS - CHOLESTEROL

- **Sterols – Cholesterol :**
  - Sterols are structural lipids in eukaryotic membranes. Cholesterol is the major animal sterol. It is amphipathic: a polar hydroxyl group at C-3 and a nonpolar hydrocarbon body (steroid nucleus with four fused rings and a side chain at C-17).



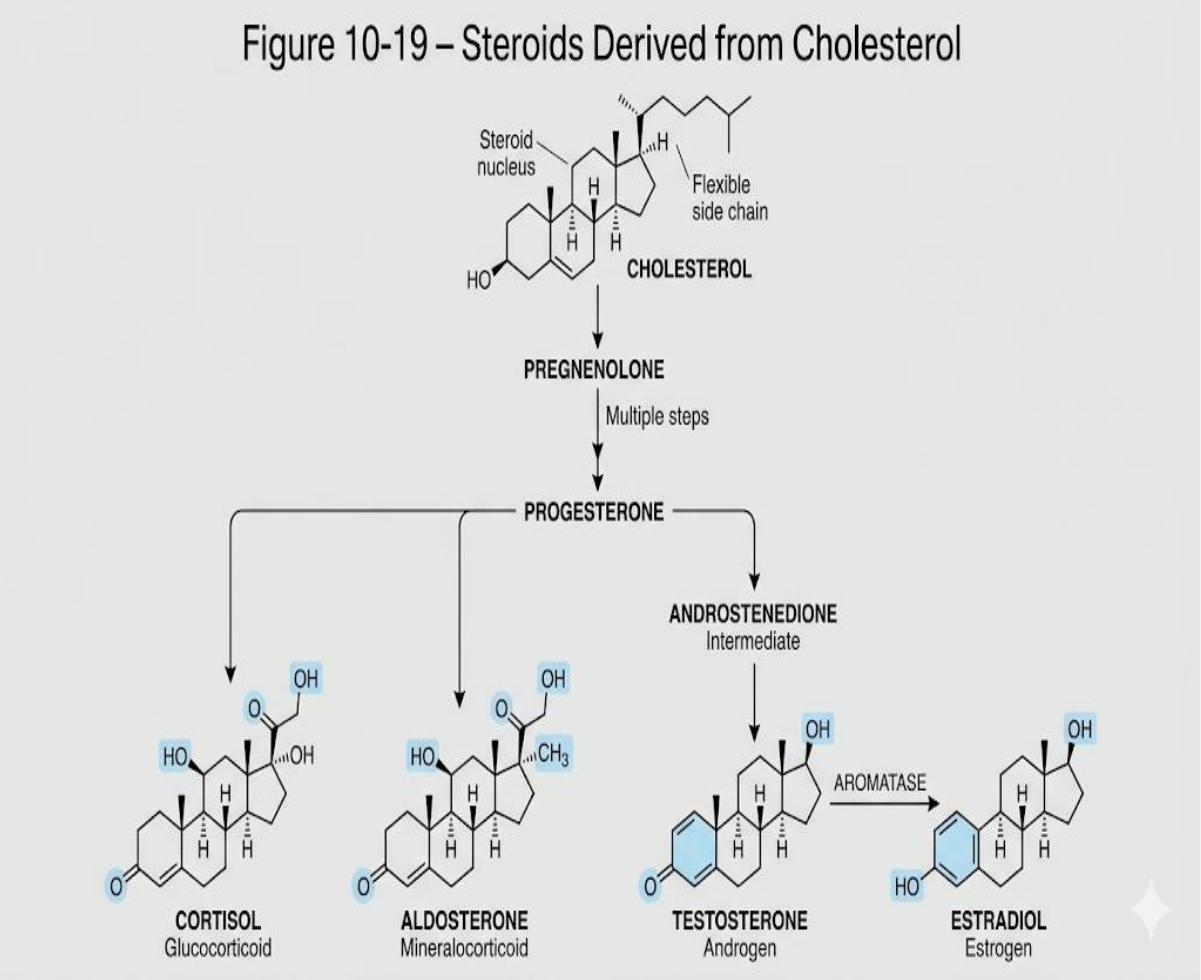
STEROIDS - DERIVED FROM CHOLESTEROL

- **Steroids – Derived from Cholesterol:**
  - Steroids are oxidized derivatives of sterols; they have the sterol nucleus but lack the alkyl chain on ring D. Steroid hormones travel in blood on protein carriers, enter cells, bind nuclear receptors, and trigger changes in gene expression.



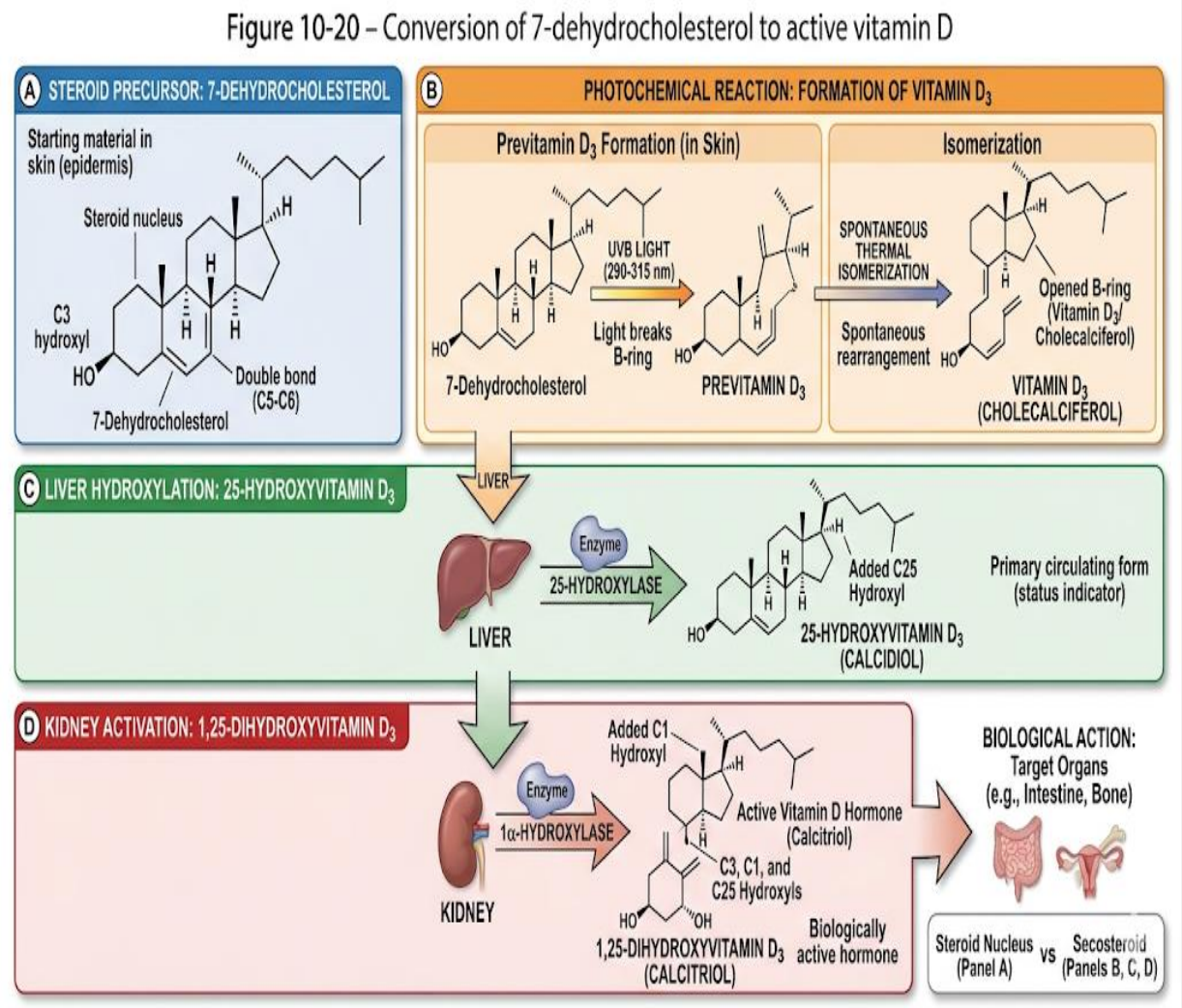
SEX HORMONES AND ADRENAL CORTEX HORMONES

- **Sex Hormones and Adrenal Cortex Hormones :**
  - Testosterone (male sex hormone) is produced in testes. Estradiol (female sex hormone) is produced in ovaries and placenta. Cortisol regulates glucose metabolism; aldosterone regulates salt excretion. Prednisolone and prednisone are synthetic antiinflammatory steroids.



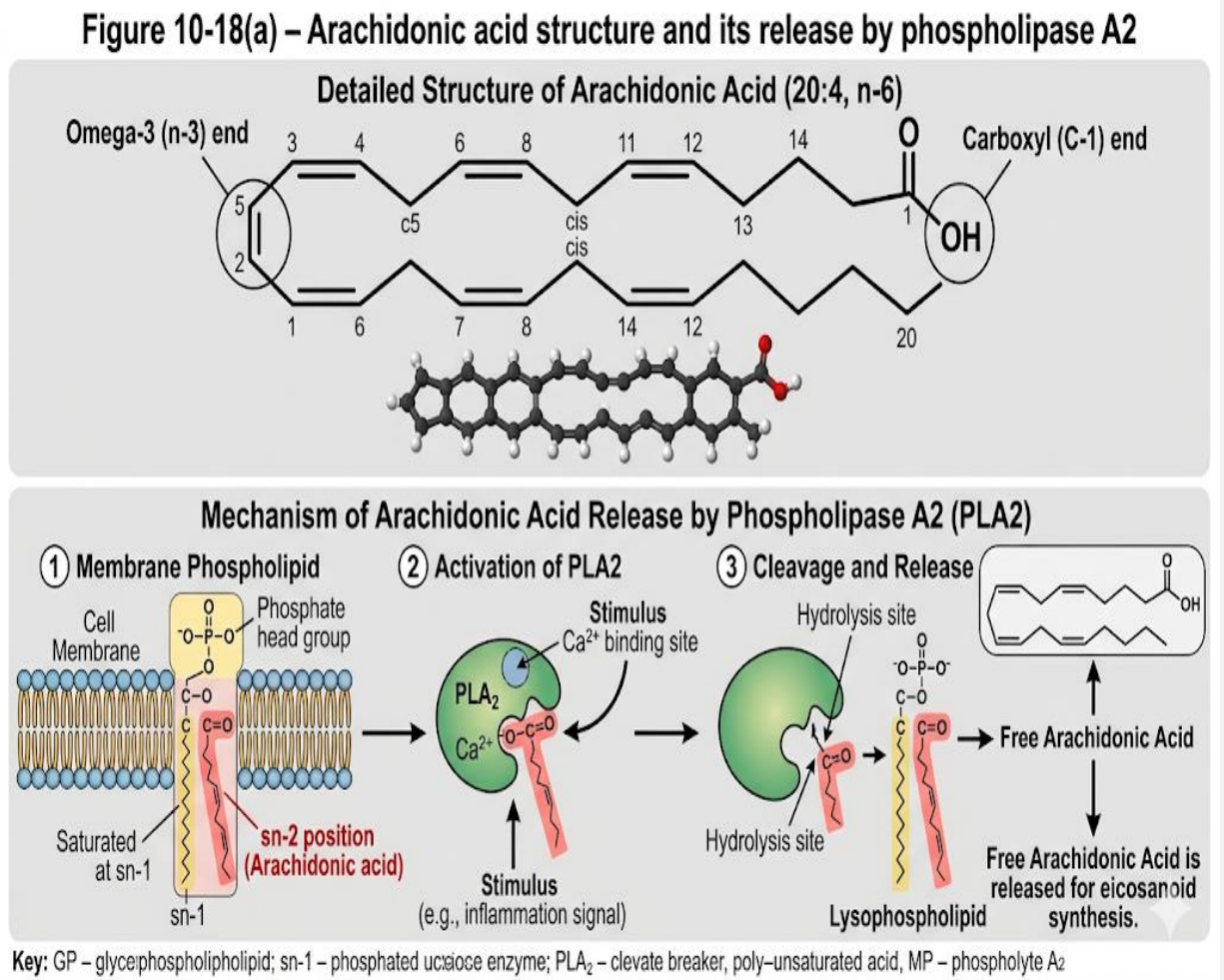
VITAMIN D AS A HORMONE PRECURSOR

- **Vitamin D as a Hormone Precursor :**
  - Vitamin D3 (cholecalciferol) is formed in skin from 7-dehydrocholesterol by UV light. It is converted in liver and kidney to 1,25-dihydroxycholecalciferol, a hormone that regulates calcium uptake in intestine and calcium levels in bone. Deficiency causes rickets.



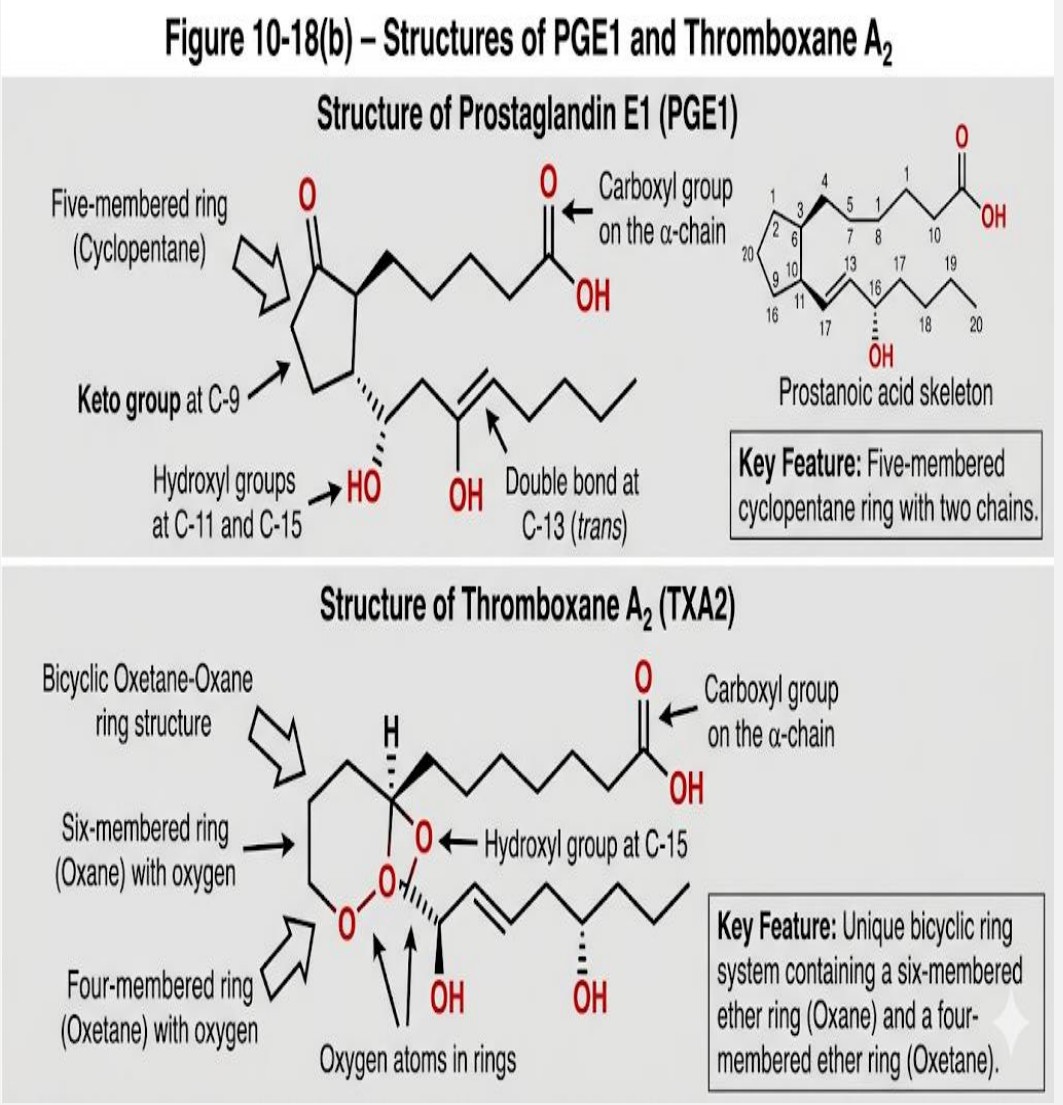
EICOSANOIDS

- **Eicosanoids – Introduction and Arachidonic Acid:**
  - Eicosanoids are paracrine hormones derived from arachidonic acid (20:4 Δ5,8,11,14). Three classes: prostaglandins, thromboxanes, and leukotrienes. They are involved in inflammation, fever, pain, blood clotting, and asthma.



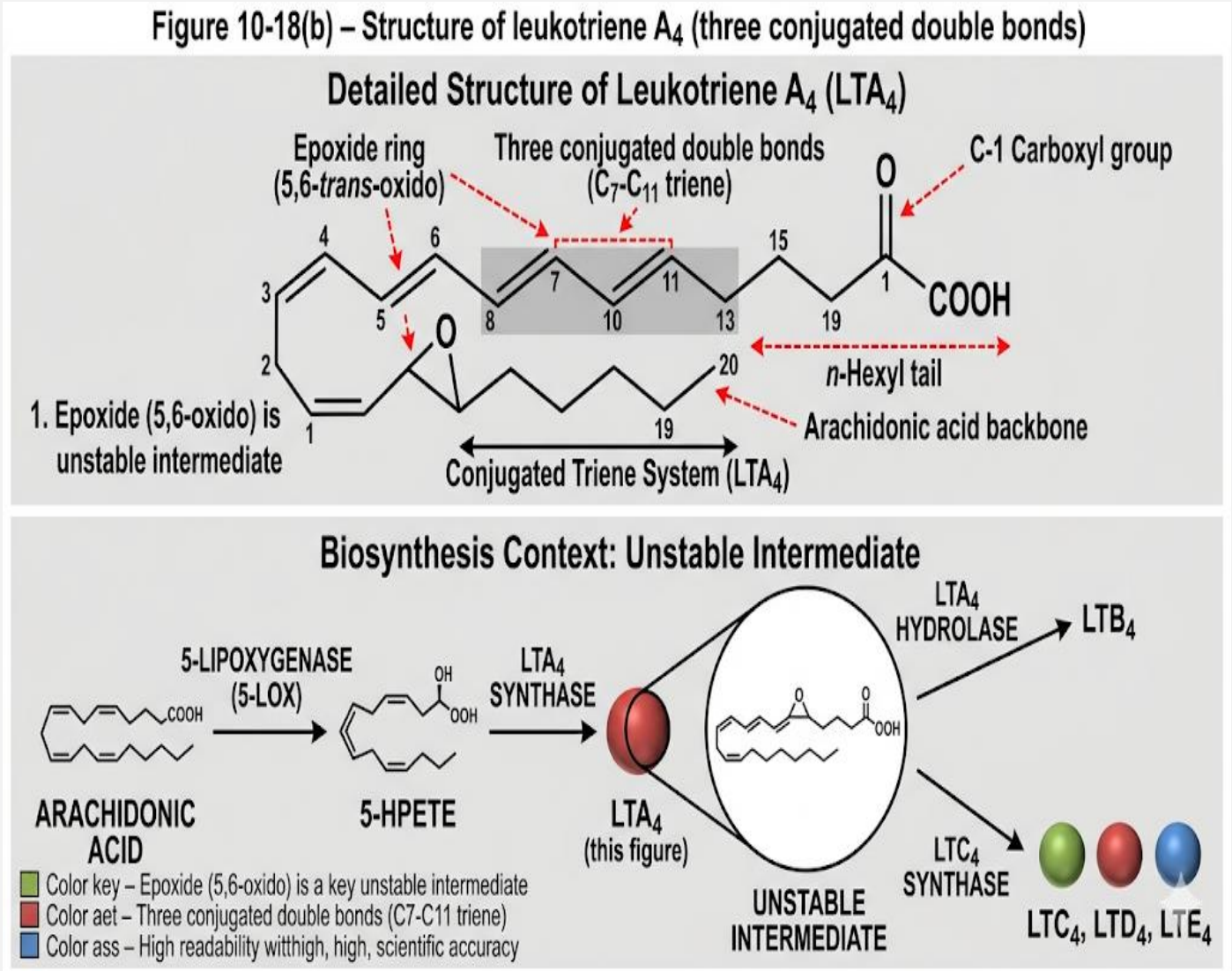
PROSTAGLANDINS AND THROMBOXANES

- **Prostaglandins and Thromboxanes :**
  - Prostaglandins contain a five-membered ring; they regulate cAMP synthesis, stimulate uterine contraction, and cause fever, inflammation, and pain. Thromboxanes have a six-membered ring with an ether; they are produced by platelets and promote blood clot formation. NSAIDs (aspirin, ibuprofen) inhibit cyclooxygenase (COX), blocking their synthesis.clotting, and asthma.



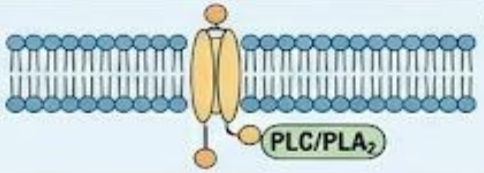
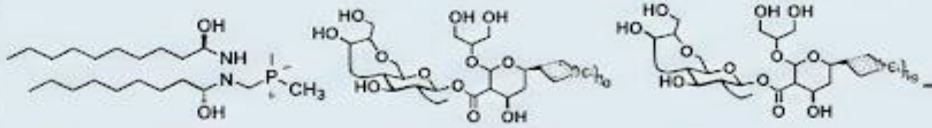
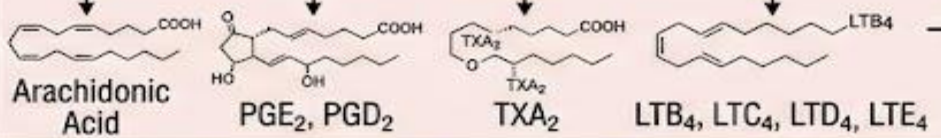
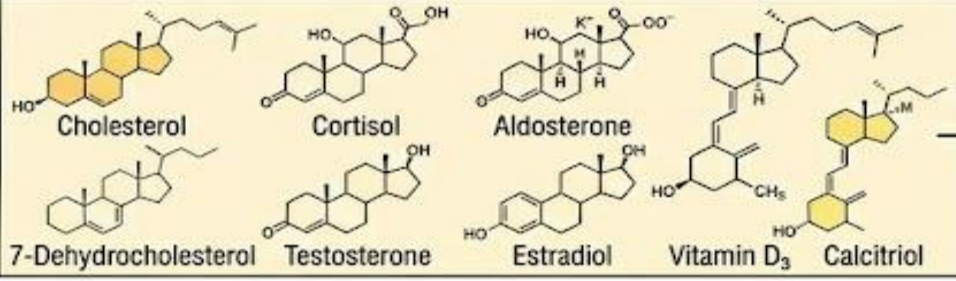
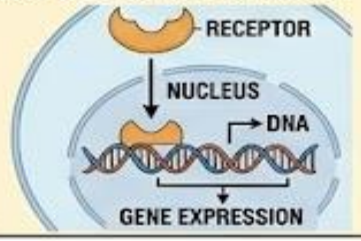
LEUKOTRIENES

- **Leukotrienes:**
  - Leukotrienes contain three conjugated double bonds. They induce contraction of airway smooth muscle. Overproduction causes asthmatic attacks. Antiasthmatic drugs such as prednisone target leukotriene synthesis.



CLINICAL SUMMARY AND REFERENCES

MAJOR LIPIDS: STRUCTURE, METABOLISM, AND CLINICAL SIGNIFICANCE (TABLE FORMAT)

	LIPID CLASS & FUNCTION	CHEMICAL STRUCTURES & PATHWAYS	CLINICAL SIGNIFICANCE / DISORDERS	MECHANISMS & REGULATION
	PHOSPHOLIPIDS & MEMBRANES Membrane Structure & Signaling (Glycerophospholipids & Sphingomyelins)	 $PIP_2/PC \rightarrow PLC/PLA_2$; $IP_3 \rightarrow DAG$; Arachidonic Acid	Disorders of Signaling & Storage	Regulated by PLC/PLA_2
SPHINGOLIPIDS	**SPHINGOLIPIDS:** Sphingomyelin & Glycosphingolipids	 Sphingomyelin; Cerebrosides; Gangliosides	**Lysosomal Storage Diseases (Sphingolipidoses):** Tay-Sachs Disease (Deficiency: Hexosaminidase A) & Niemann-Pick Disease (Deficiency: Sphingomyelinase)	Metabolic intermediates for further signaling
LIPID SIGNALING (EICOSANOIDS)	**EICOSANOIDS:** Arachidonic Acid Derivatives: COX & LOX Pathways	CYCLOOXYGENASE (COX) PATHWAY; LIPOXYGENASE (5 PATHWAY;  Arachidonic Acid; PGE_2, PGD_2; TXA_2; LTB_4, LTC_4, LTD_4, LTE_4	**Pathophysiology:** Inflammation, Pain, Fever (PGs); Platelet Aggregation, Vasoconstriction (TXAs); Bronchoconstriction, Asthma (LTs)	**Pharmacological Regulation:** NSAIDs (Aspirin, etc.) block COX-1/COX-2; LT receptor antagonists (Montelukast) / 5-LOX Inhibitors (Zileuton)
STEROIDS & VITAMIN D	**Steroids** (Cholesterol, Hormones) & Vitamin D	 Cholesterol; Cortisol; Aldosterone; 7-Dehydrocholesterol; Testosterone; Estradiol; Vitamin D_3; Calcitriol	**Steroid Mechanism of Action** 	**Calcitriol regulation:**  **Calcitriol regulation:** Increases serum calcium


THANK YOU
FOR YOUR
ATTENTION