

بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

Sphingolipids and Myelin Structure

By

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Outlines

Objectives

Background

Key principles

Take home message

Objectives

Sphingolipids:

Chemical structure

Tissue distribution and functions

Biochemical structure of myelin

Biosynthesis of sphingolipids

Sphingolipidosis

Sphingolipids: Background

- **Essential component of membranes**
- **Abundant in nervous tissue**
- **Extra-nervous tissue:**
 - e.g., Receptors for**
 - Cholera toxins**
 - Diphtheria toxins**
 - Viruses**

Sphingolipids: Background

CONT'D

- **Regulation of growth & development**
- **Very antigenic:**
 - Blood group antigen**
 - Embryonic antigen**
 - Tumor antigen**
- **Cell transformation**

Key Principles

- **Chemical Structure of sphingolipids**
- **Types:**
 - **Glycosphingolipids (Glycolipids)**
 - **Sphingophospholipids e.g., Sphingomyelin**
- **Myelin structure and function**
- **Sphingolipidosis**

Sphingolipids: Structure and Types

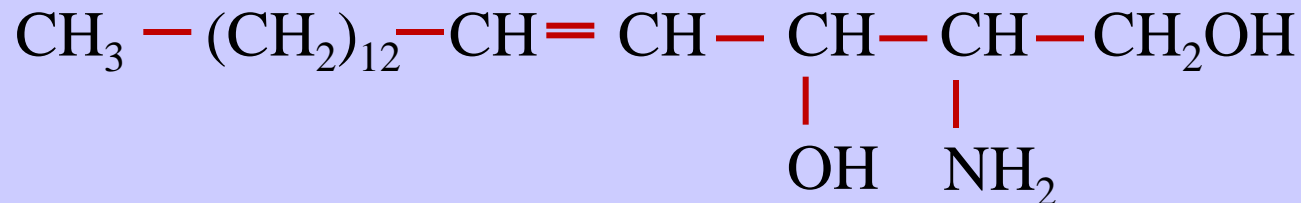
Ceramide = Sphingosine + fatty acid

Sphingomyelin = Ceramide + Phosphorylcholine

Cerebrosides = Ceramide + Monosaccharides

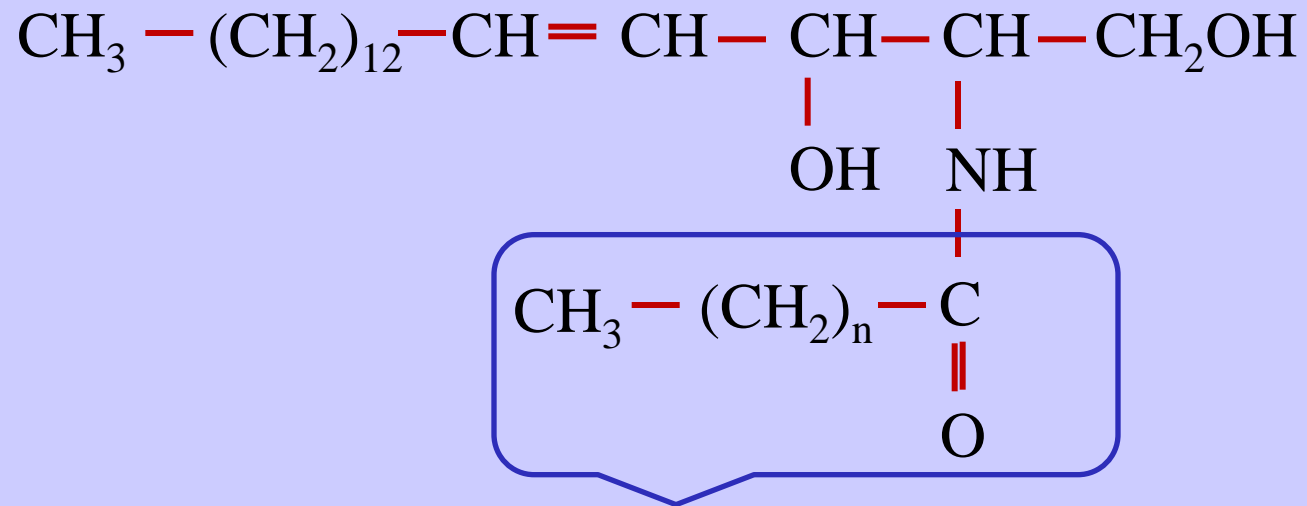
Gangliosides = Ceramide oligosaccharides + NANA

Sphingosine



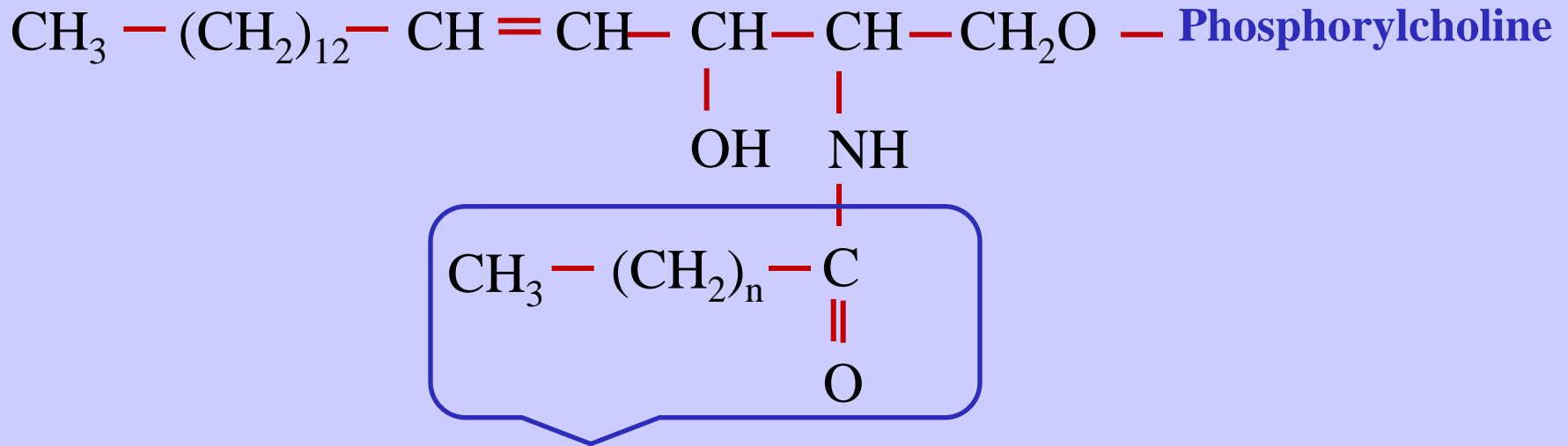
Long chain, unsaturated amino alcohol

Ceramide



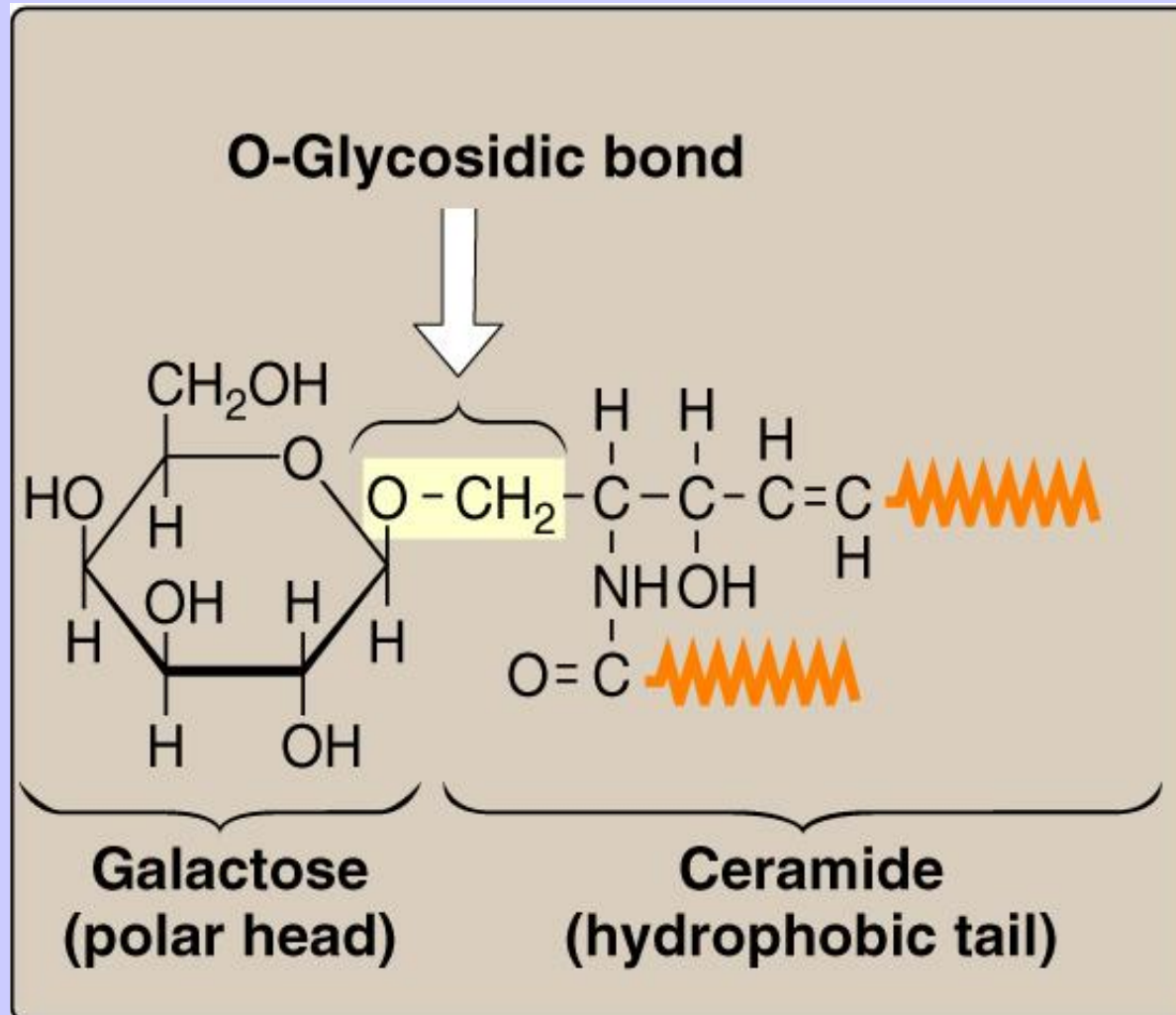
Long Chain Fatty acid

Sphingomyelin



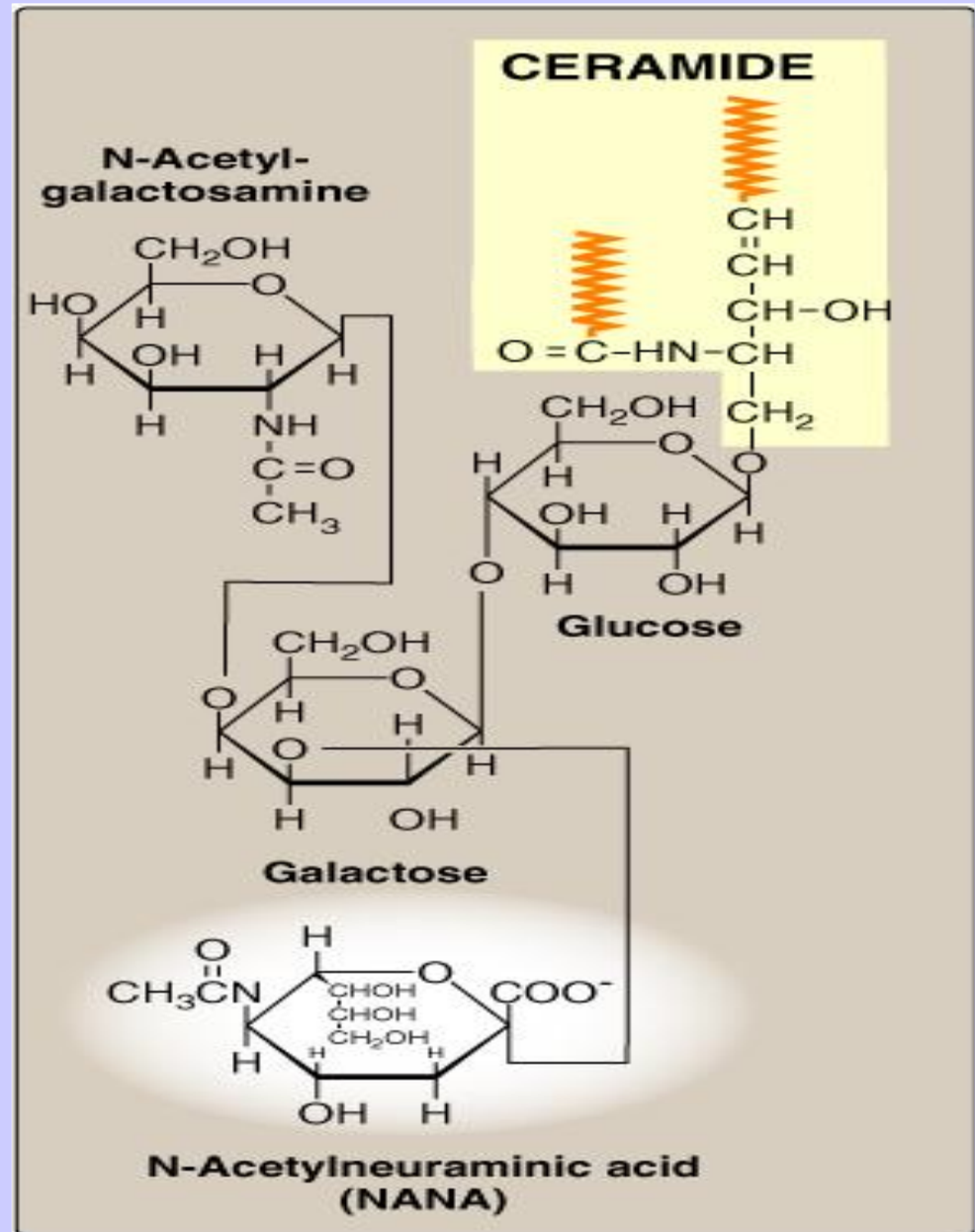
Long Chain Fatty acid

Galactocerebroside

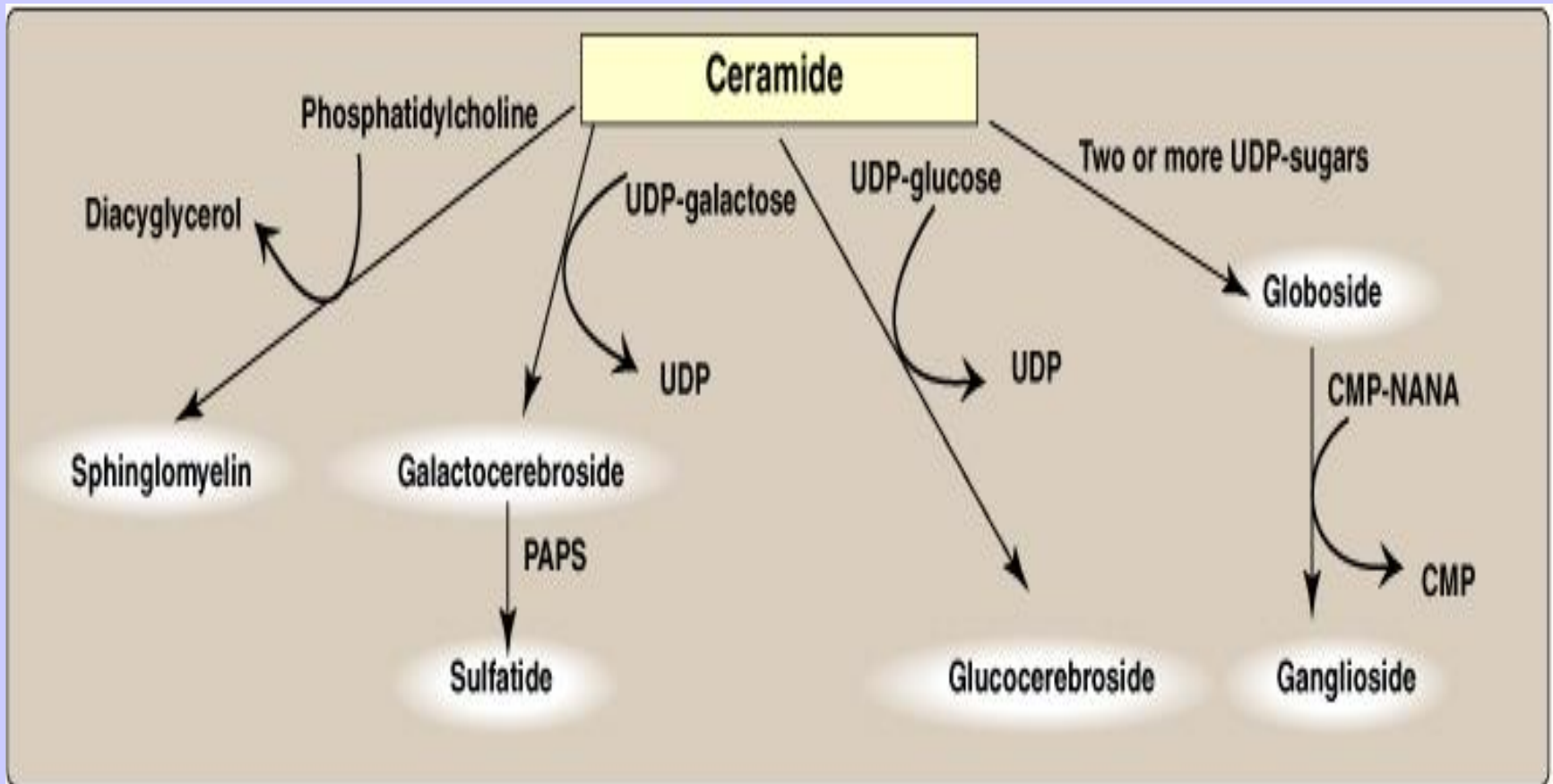


Gangliosides

G_{M2}



Sphingolipids' Synthesis



Myelin Structure

Myelin is a specialized cell membrane that ensheathes an axon to form a myelinated nerve fiber

Myelin is produced by:

Schwann cells:	Peripheral nerves
Oligodendrocytes:	CNS

Myelin composition:

Lipids (80%):	Mainly glycolipids (cerebrosides) plus sphingomyelin
Proteins (20%):	e.g., Myelin basic protein

Myelin Structure

CONT'D

Fatty acid of Sphingomyelin:

Myelin sheath:

Very long chain fatty acids:

Lignoceric 24:0

Nervonic 24:1

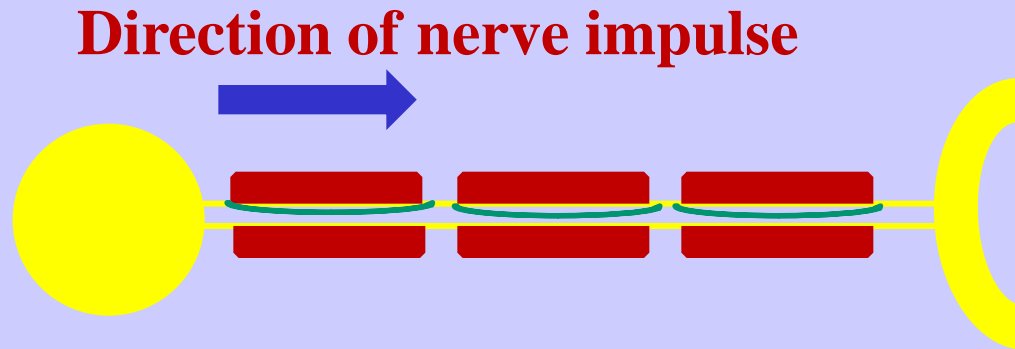
Gray matter:

Long chain fatty acid

Stearic 18:0

Myelin Structure and Function

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



Multiple sclerosis:

Neuro-degenerative, auto-immune disease

Breakdown of myelin sheath (demyelination)

Defective transmission of nerve impulses

Sphingolipidosis

- **Synthesis (Normal); Degradation (Defective)**
- **Substrate accumulates in organs**
- **Progressive, early death**
- **Phenotypic and genotypic variability**
- **Autosomal recessive (mostly)**
- **Rare, Except in Ashkenazi Jewish**

Sphingolipidosis

CONT'D

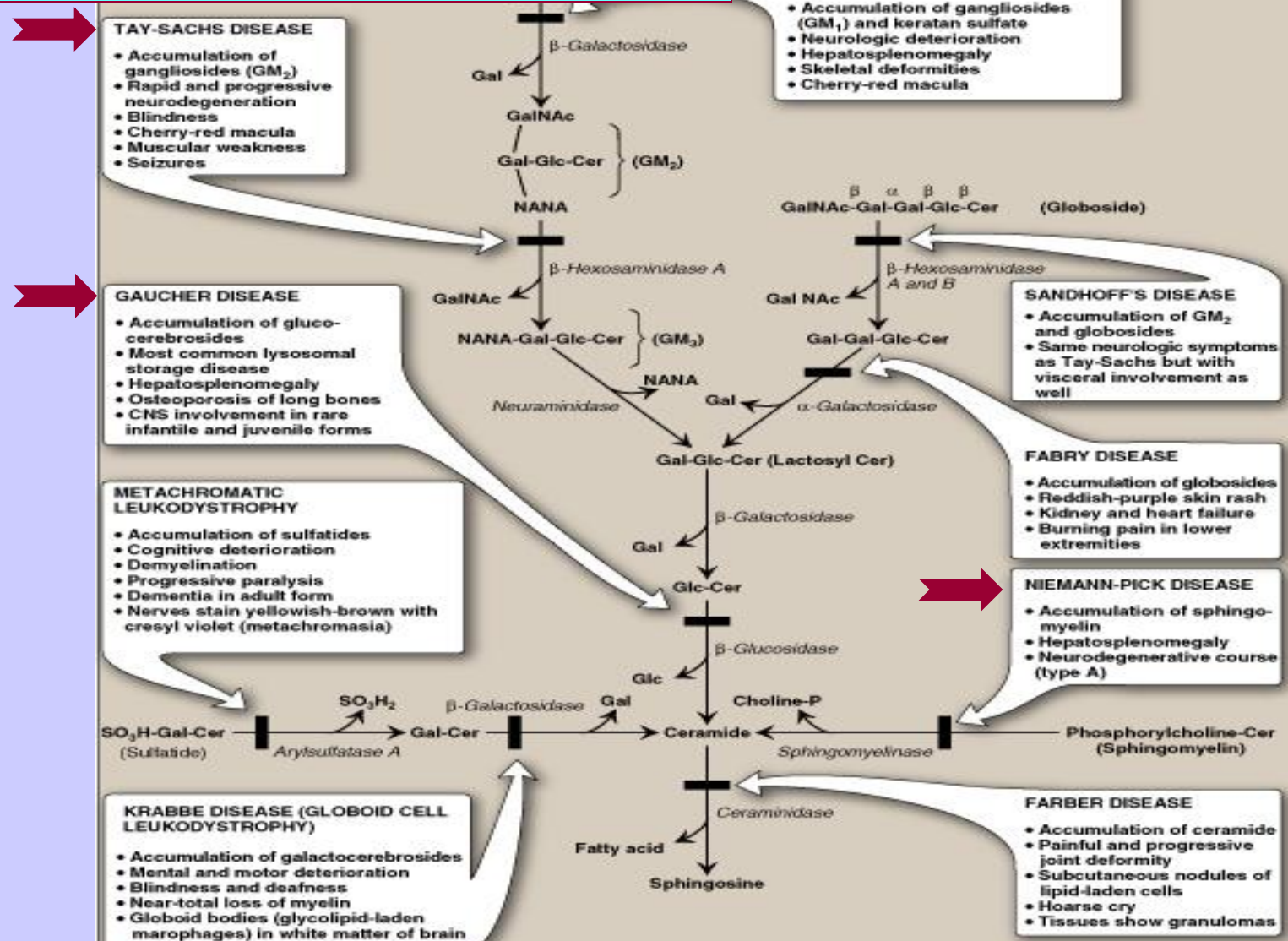
Diagnosis:

- **Measure enzyme activity**
 - Cultured fibroblasts or peripheral leukocytes**
 - Cultured amniocytes (prenatal)**
- **Histologic examination**
- **DNA analysis**

Treatment:

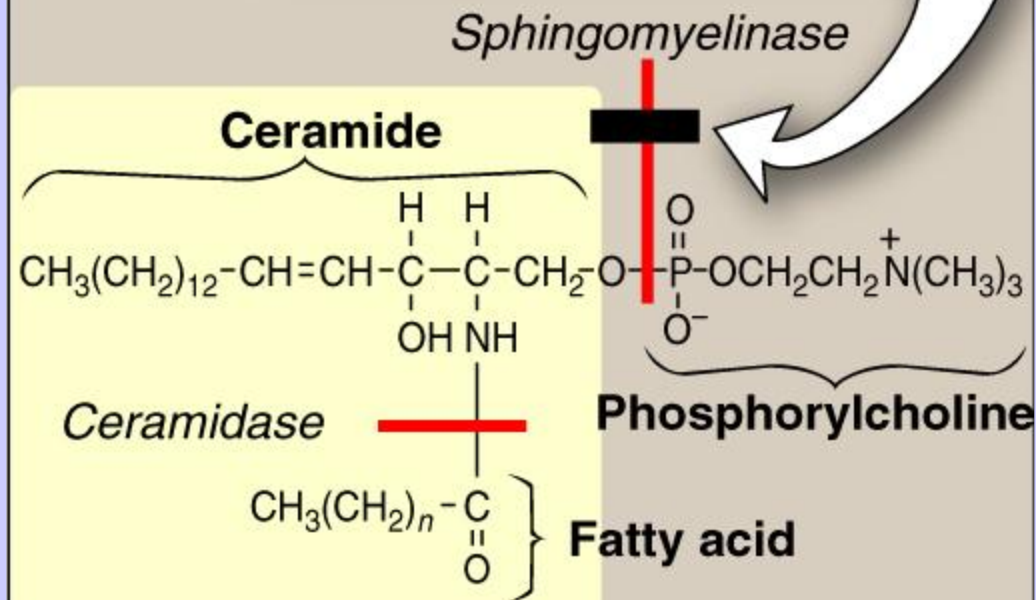
- **Replacement Therapy:**
 - Recombinant human enzyme**
- **Bone marrow transplantation: Gaucher disease**

CONT'D



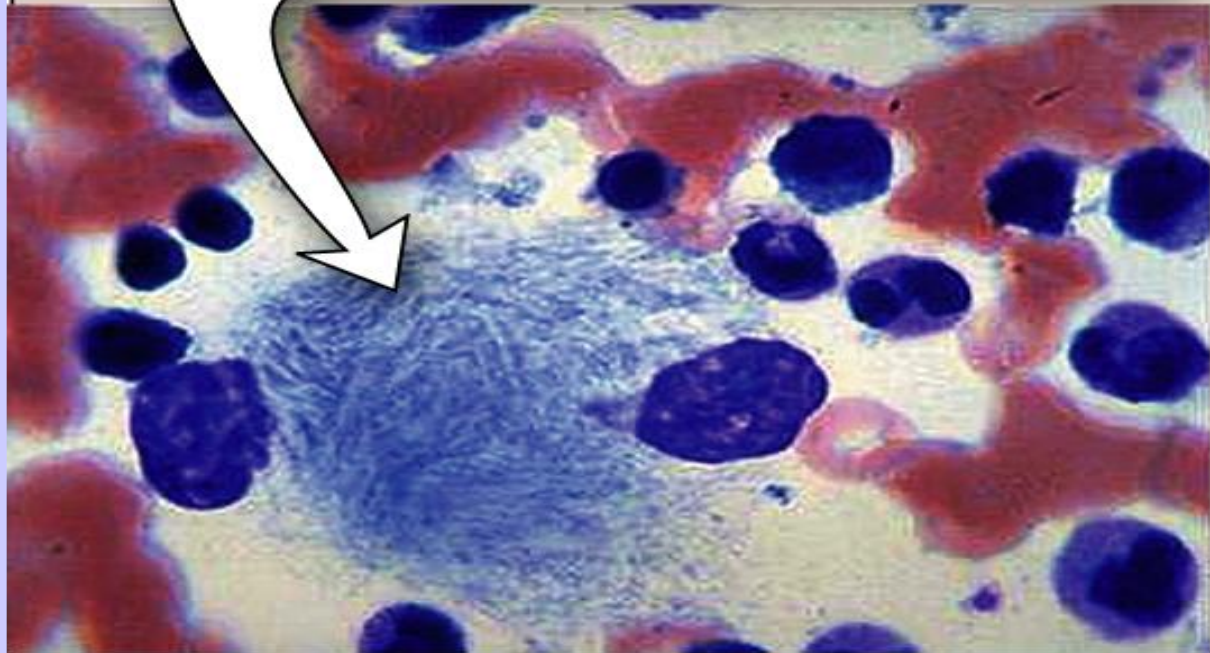
NIEMANN-PICK DISEASE

- *Sphingomyelinase* deficiency
- Enlarged liver and spleen filled with lipid
- Severe mental retardation and neurodegeneration
- Death in early childhood



Gaucher Disease

The "crumpled tissue paper" appearance of the cytoplasm of Gaucher cells is caused by enlarged, elongated lysosomes filled with glucocerebroside.



Take Home Message

- Sphingolipids are complex lipids that includes sphingo-phospholipids and glycolipids
- Ceramide is the precursor of all sphingolipids
- Sphingolipids are present mainly in nerve tissue, but they are found also extra-neural.
- Myelin sheath insulates the nerve axon to avoid signal leakage and speed up impulse transmission
- Sphingolipidosis are rare, genetic diseases due to defective degradation of sphingolipids

Thank you