بسم الله الرحمن الرحيم

Sphingolipids and Myelin Structure

By

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Outlines

Objectives

Background

Key principles

Take home message

Objectives

- **By the end of this lecture, the students should be able to:**

1- recognize the Sphingolipids class of lipids as regard their:

- **Chemical structure**
- **Tissue distribution and functions**

2- be familiar with the biochemical structure of myelin

3- learn the basics of biosynthesis of sphingolipids

4-be introduced to 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

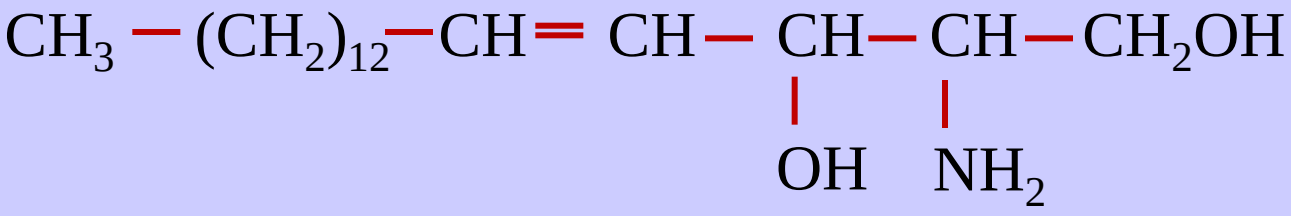
Ceramide = **Sphingosine + fatty acid**

Sphingomyelin = **Ceramide + Phosphorylcholine**

Cerebrosides = **Ceramide + Monosaccharides**

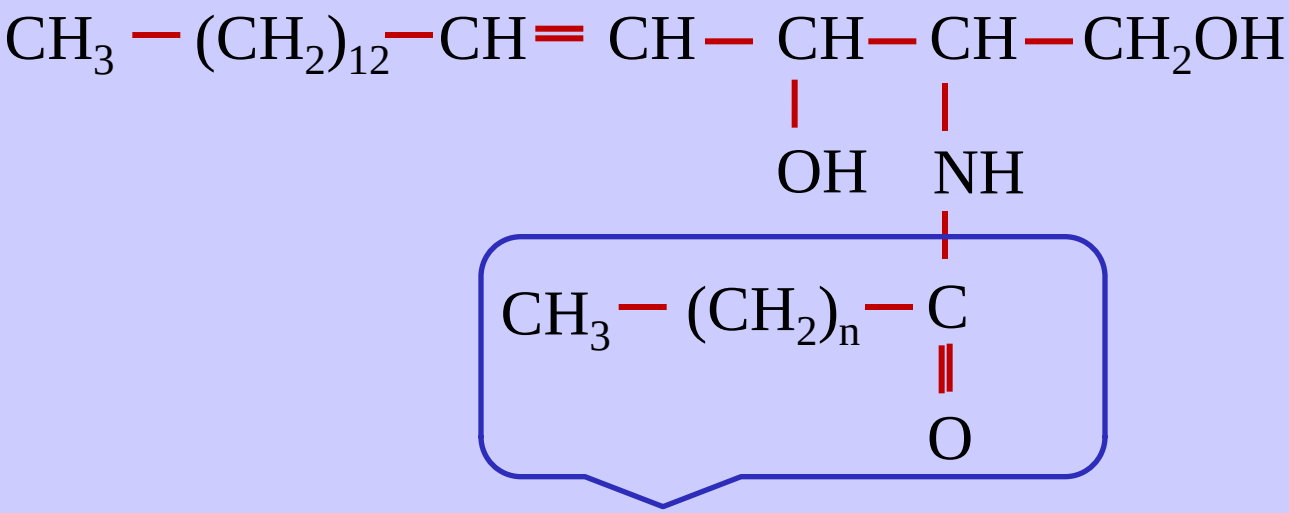
Gangliosides = **Ceramide oligosaccharides + NANA**

Sphingosine



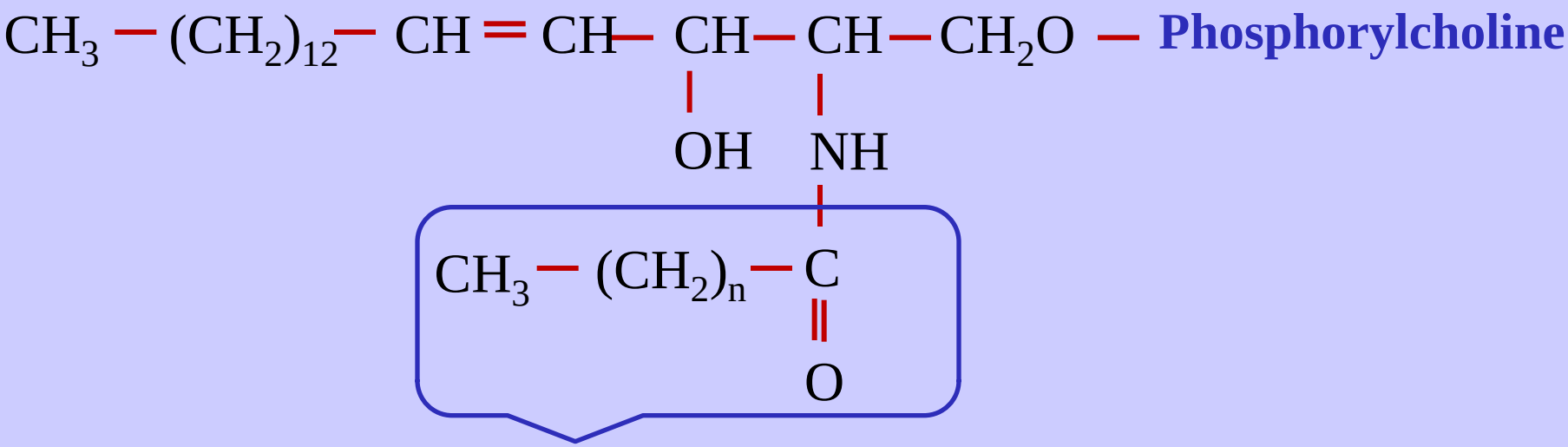
Long chain, unsaturated amino alcohol

Ceramide



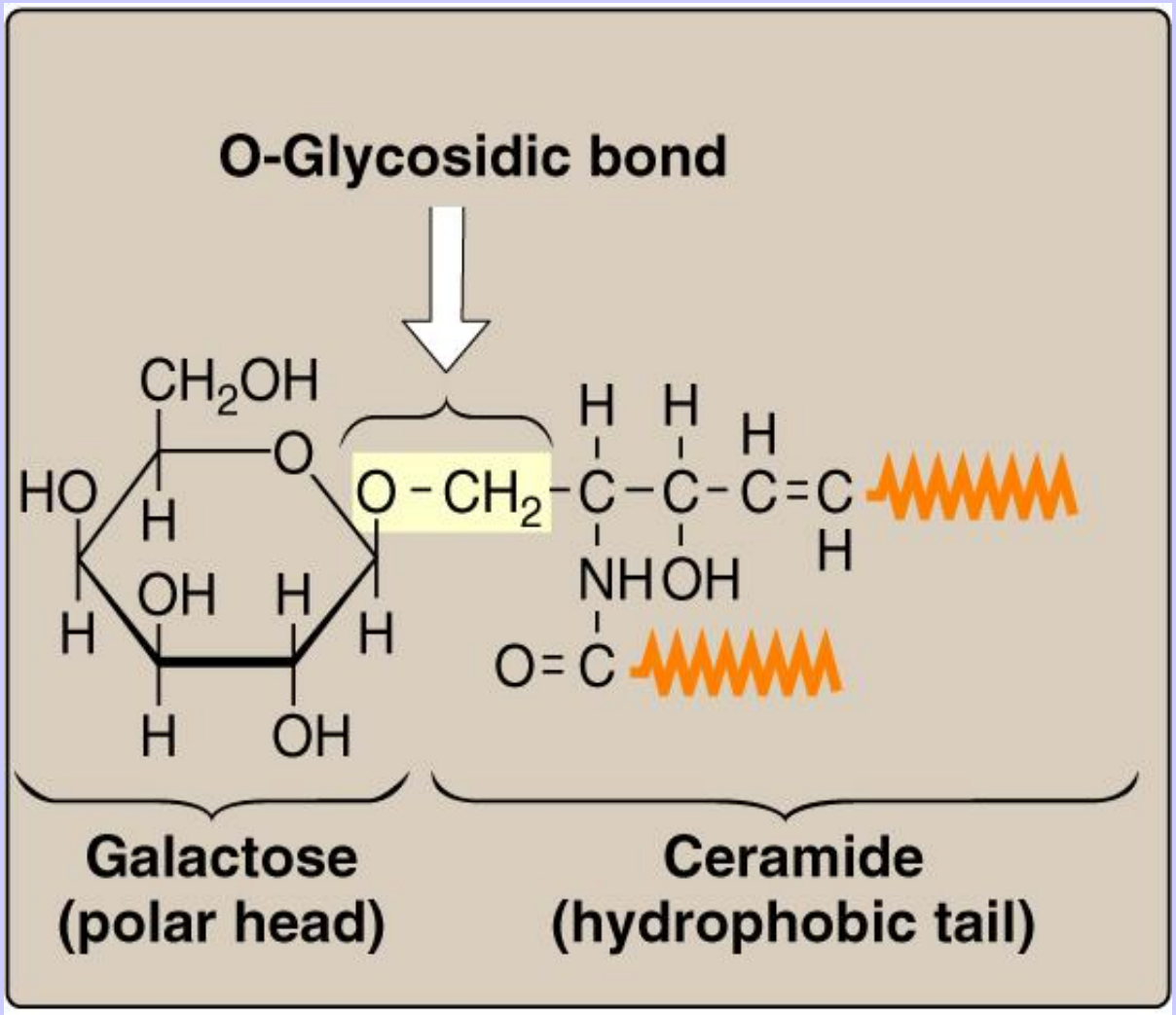
Long Chain Fatty acid

Sphingomyelin



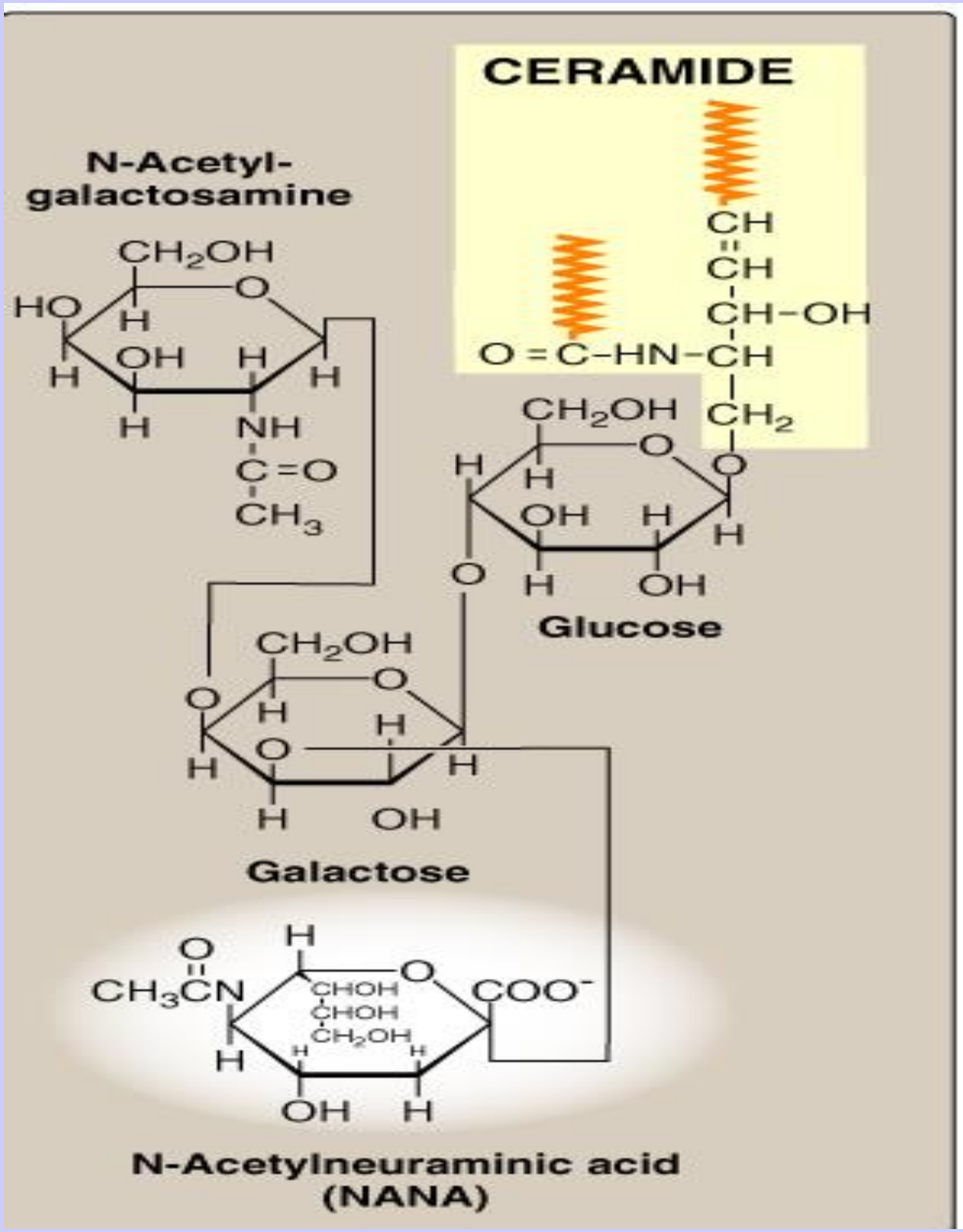
Long Chain Fatty acid

Galactocerebroside

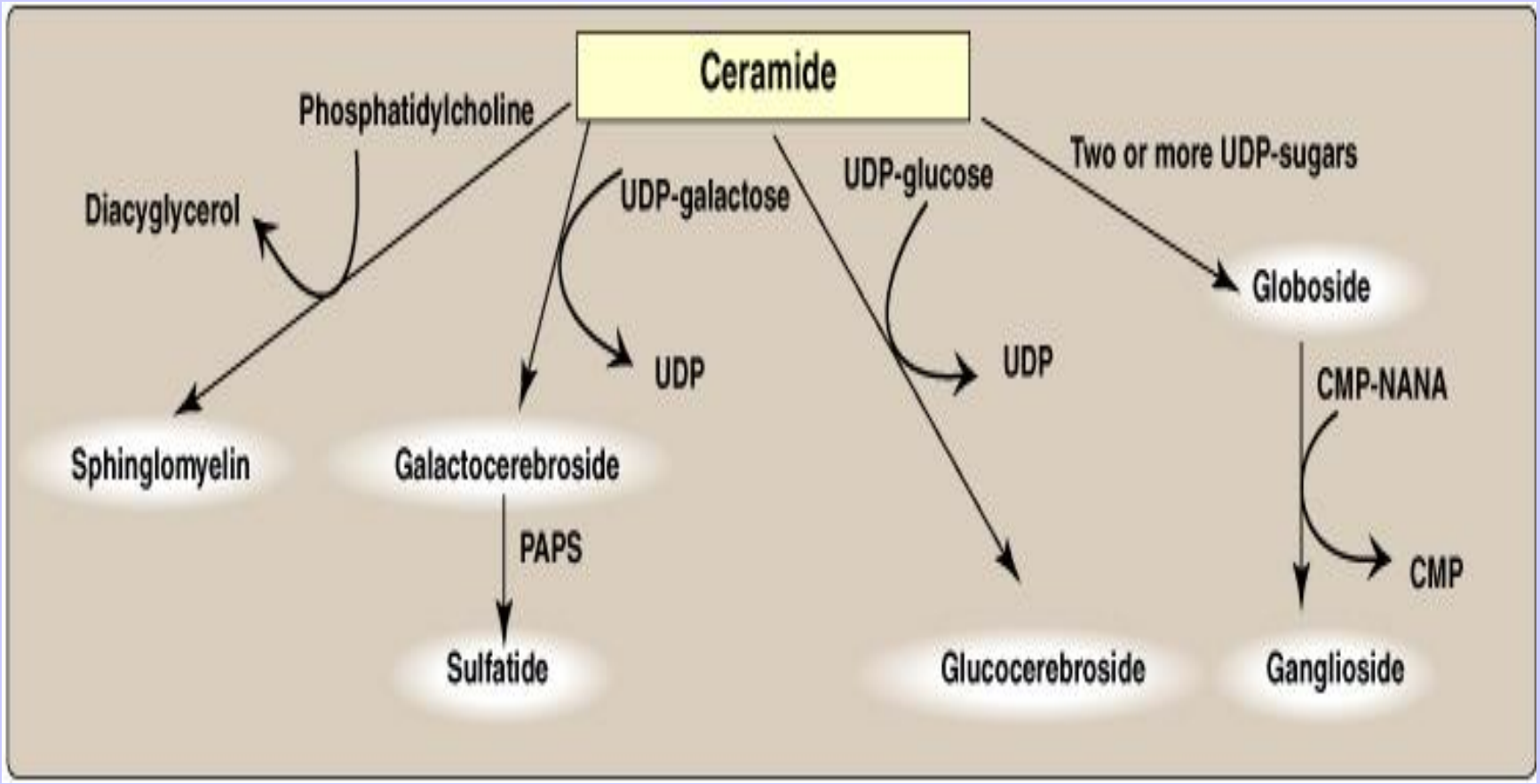


Gangliosides

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%):	**Main component:** Cerebrosides **Other component:** Sphingomyelin
Proteins (20%):	e.g., Myelin basic protein

Myelin Structure

CONT'D

Fatty acid of Sphingomyelin:

Myelin sheath:

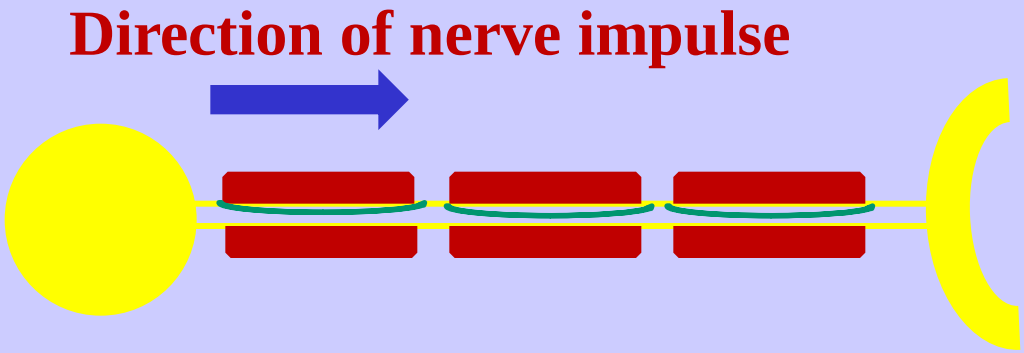
Very long chain fatty acids:

Lignoceric 24:0

Nervonic 24:1

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:

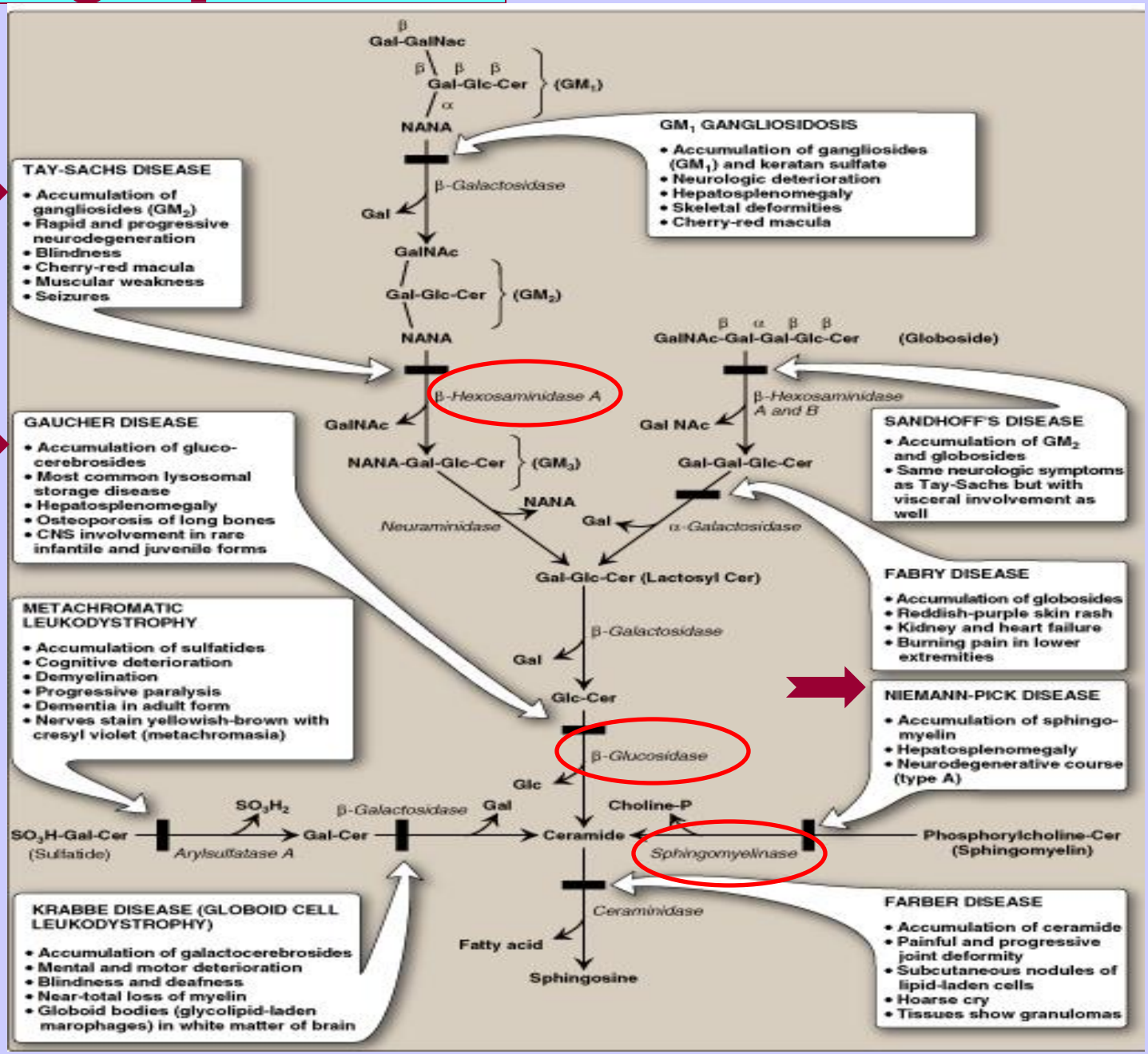
- Measure enzyme activity
  - Cultured fibroblasts or peripheral leukocytes
  - Cultured amniocytes (prenatal)
- Histologic examination
- DNA analysis

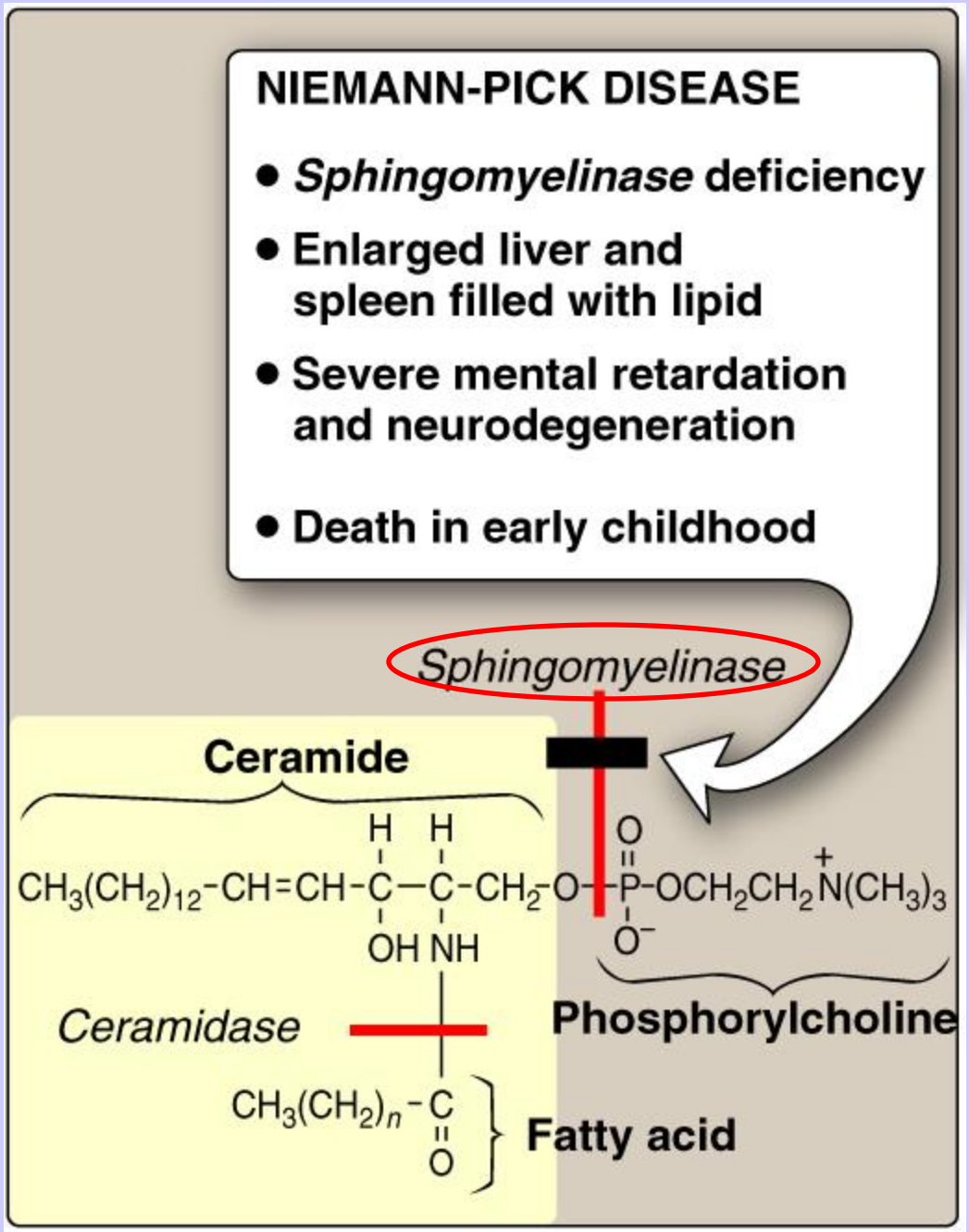
Treatment:

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

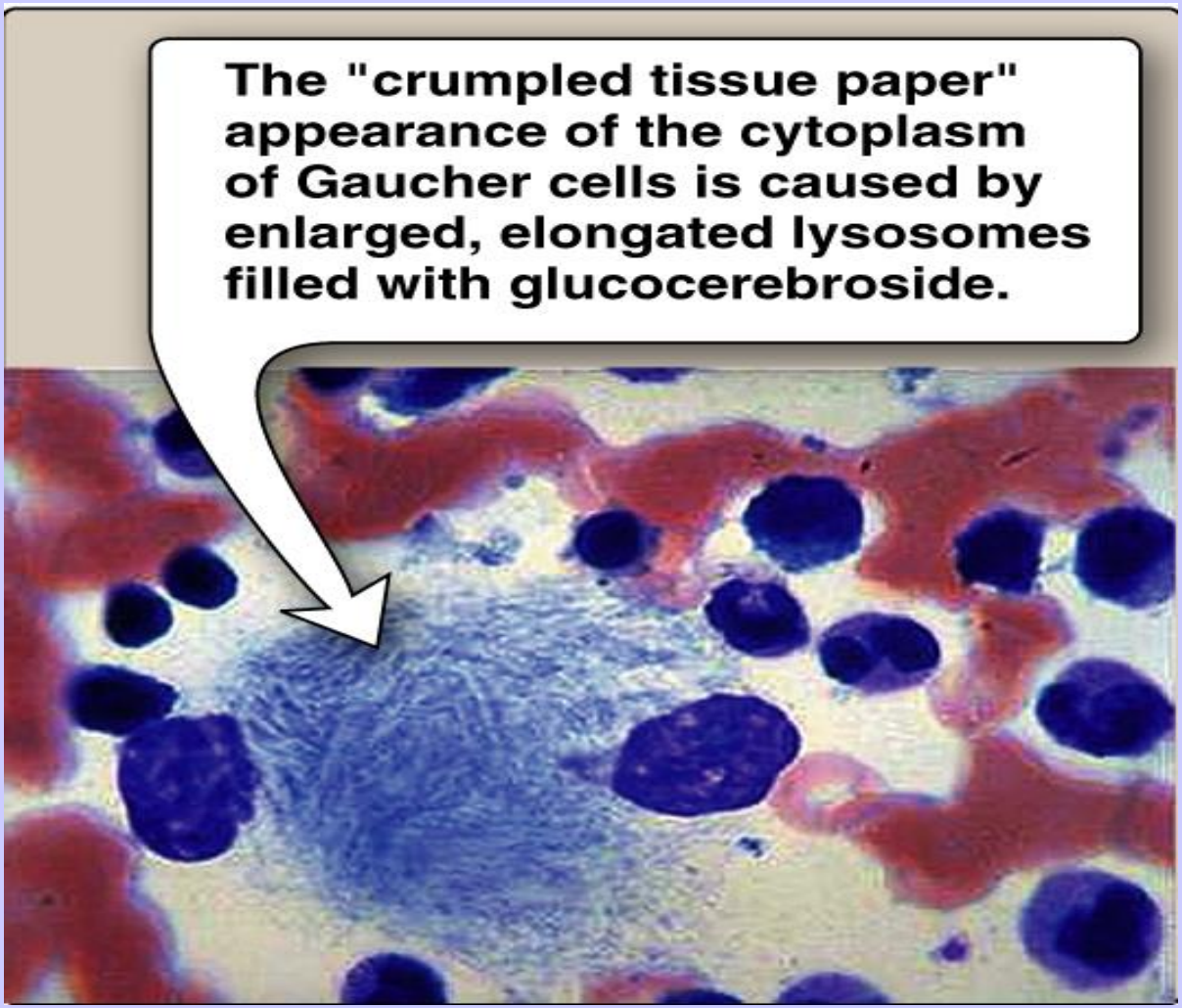
Sphingolipidosis

CONT'D




NIEMANN-PICK DISEASE
• Sphingomyelinase deficiency
• Enlarged liver and spleen filled with lipid
• Severe mental retardation and neurodegeneration
• Death in early childhood
Sphingomyelinase
Ceramide
CH3(CH2)12-CH=CH-C(H)(OH)-C(H)(NH)-CH2-O-P(=O)(O-)-OCH2CH2N+(CH3)3
Phosphorylcholine
Ceramidase
CH3(CH2)n-C(=O)
Fatty acid

Gaucher Disease



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.

Take Home Message CONT'D

- 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