

SPHINGOLIPIDS AND MYELIN STRUCTURE

The background features a dark blue gradient with a subtle pattern of white stars and dots. Overlaid on this are several technical diagrams. In the top right, there is a large circular diagram with concentric rings and a scale from 0 to 210. In the bottom right, there is a smaller circular diagram with dashed lines and arrows. In the bottom left, there is another circular diagram with solid lines and arrows. The overall aesthetic is scientific and technical.

OUTLINES

- Objectives.
- Background.
- Key principles.
- Take home messages.

OBJECTIVES

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

- Recognize the Sphingolipids class of lipids as regard their chemical structure, tissue distribution and functions.
- Be familiar with the biochemical structure and function of myelin.
- Learn the basics of biosynthesis of sphingolipids.
- Be introduced to Sphingolipidosis.

SPHINGOLIPIDS: BACKGROUND

- Essential component of membranes.
- Abundant in nervous tissue.
- Also exist extra-nervous tissue:

e.g. Receptors for:

Cholera toxins

Diphtheria toxins

Viruses.

SPHINGOLIPIDS: BACKGROUND

- Regulation of growth and development.
- Very antigenic:
 - Blood group antigen
 - Embryonic antigen
 - Tumor antigen
- Cell transformation.

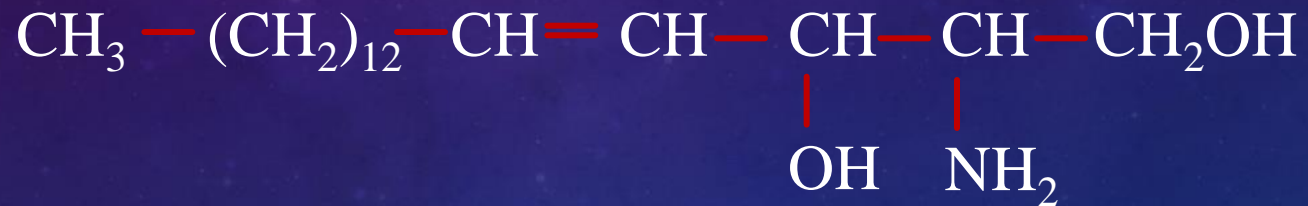
KEY PRINCIPLES

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

The background features a blue gradient with a field of small white dots. Several circular diagrams are overlaid: a large one in the top right with degree markings (0, 90, 100, 110, 120, 130, 140, 150, 160, 170, 180, 190, 200, 210, 220) and arrows, and smaller ones in the top left, bottom left, and bottom right, some with dashed lines and arrows.

SPHINGOLIPIDS: STRUCTURE AND TYPES

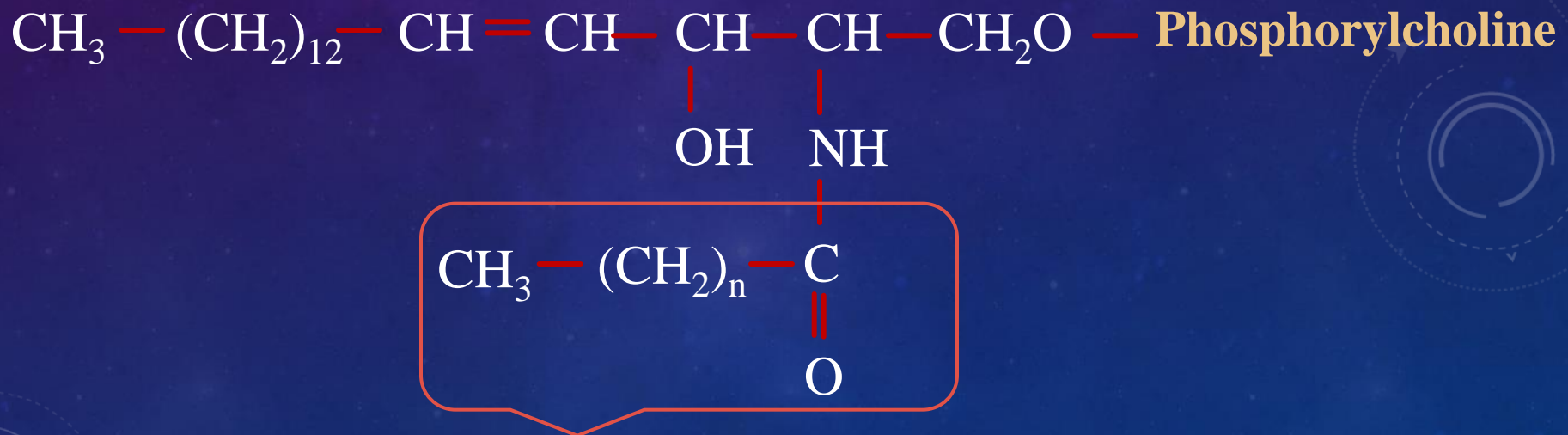
SPHINGOSINE



Long chain, unsaturated amino alcohol

SPHINGOMYELIN

Sphingomyelin = Ceramide + Phosphorylcholine

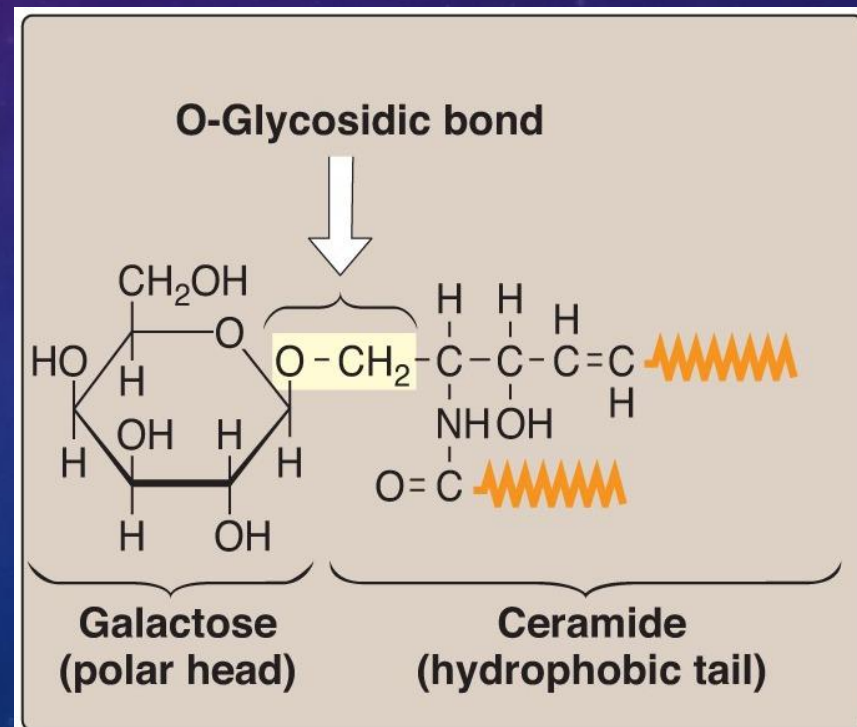


Long chain fatty acid

CEREBROSIDES

Cerebrosides = Ceramide + Monosaccharides

e.g. Galactocerebroside.



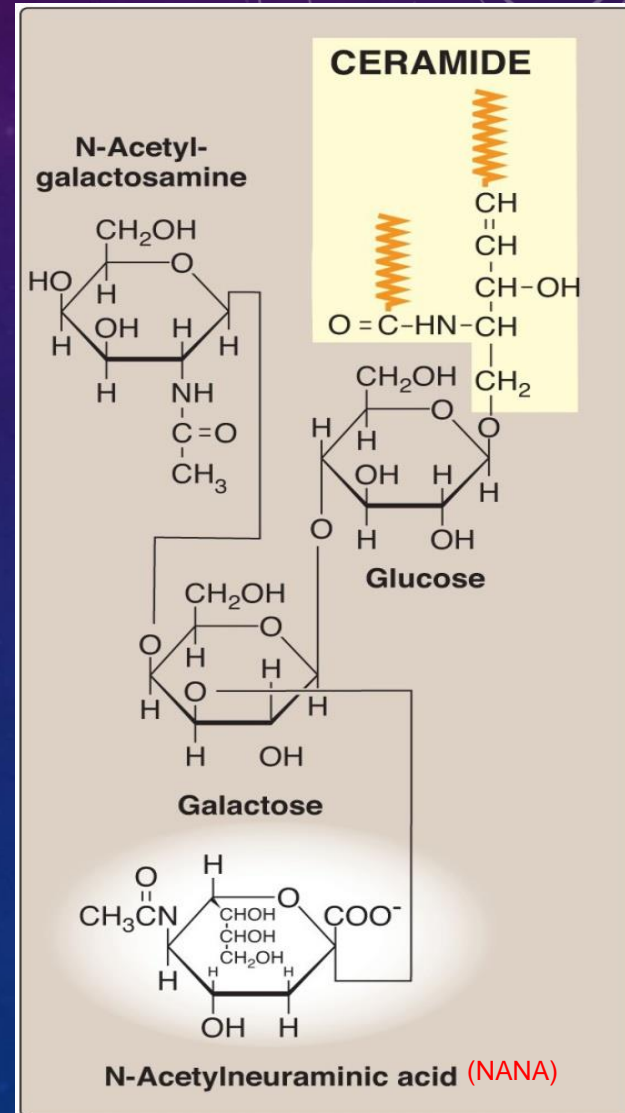
GANGLIOSIDES

Gangliosides = Ceramide oligosaccharides

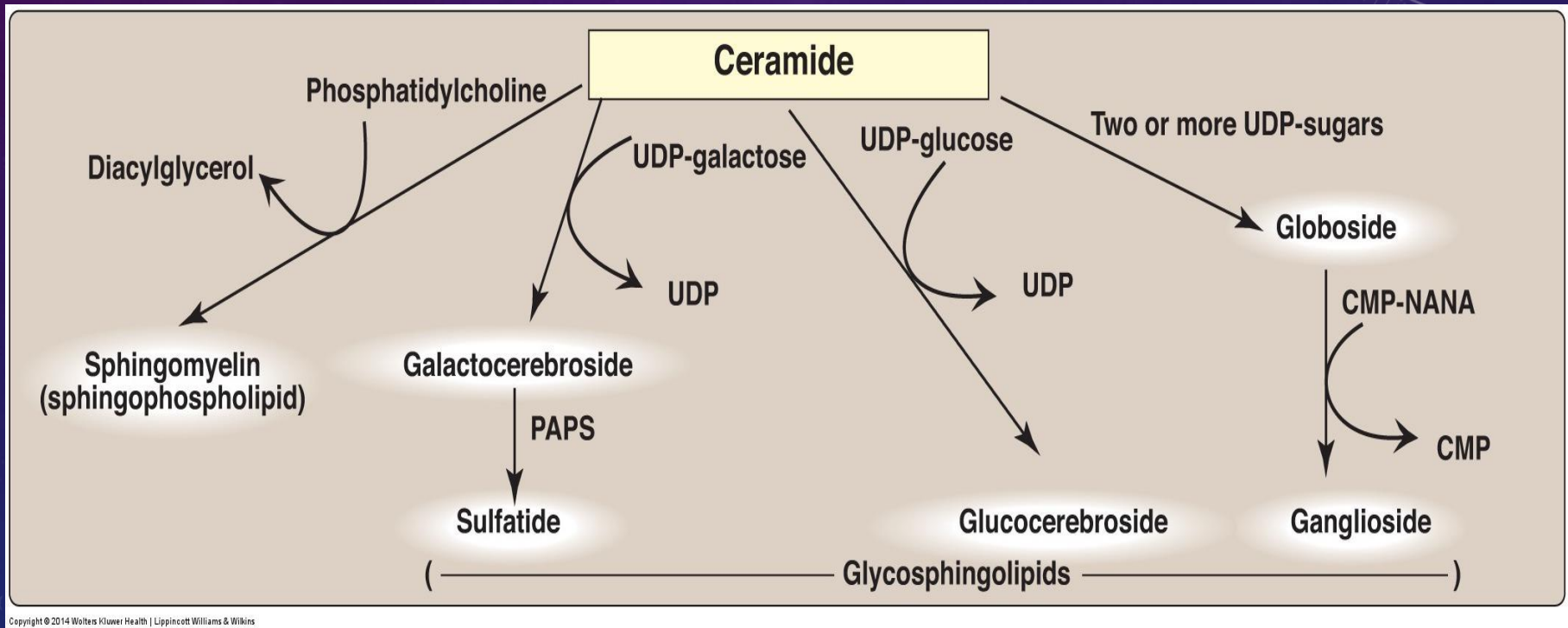
+

NANA

e.g. 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

Fatty acid of Sphingomyelin:

Myelin sheath:

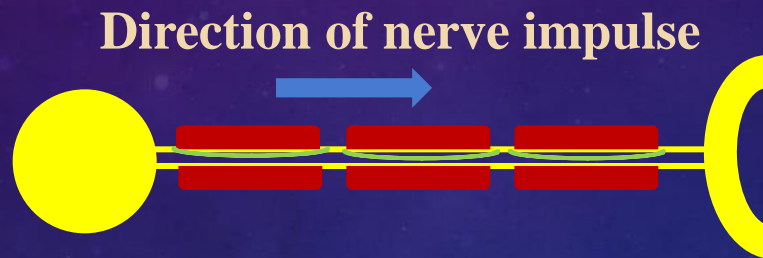
Very long chain fatty acids

Lignoceric 24:0

Nervonic 24:1(15)

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.

SPHINGOLIPIDOSES

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

SPHINGOLIPIDOSES

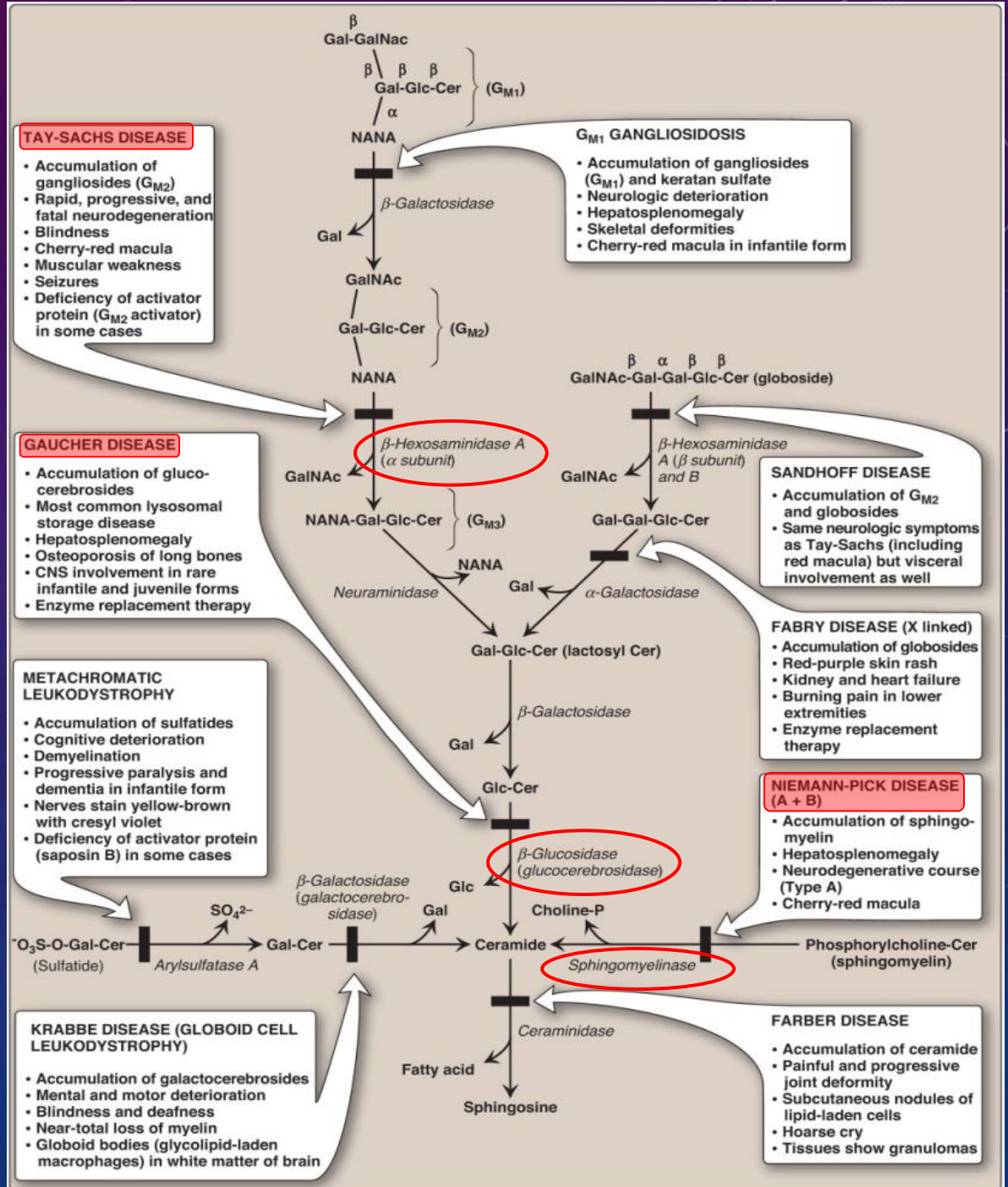
- **Diagnosis:**

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

- **Treatment:**

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

SPHINGOLIPIDOSES

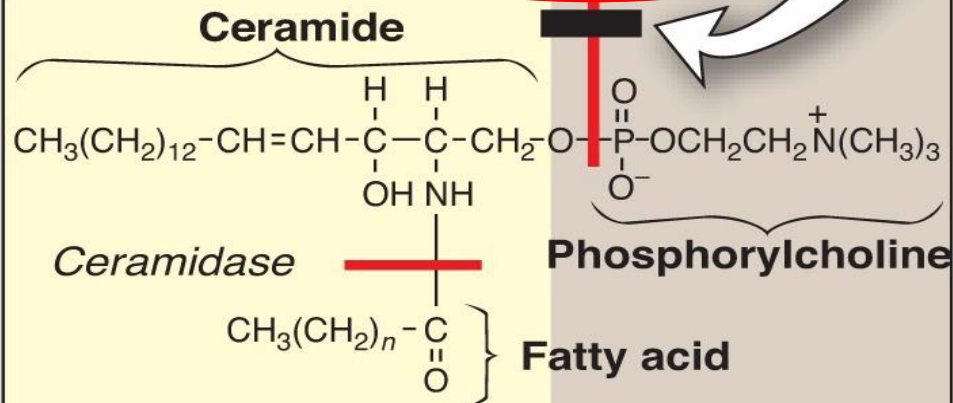


NIEMANN-PICK DISEASE

NIEMANN-PICK DISEASE

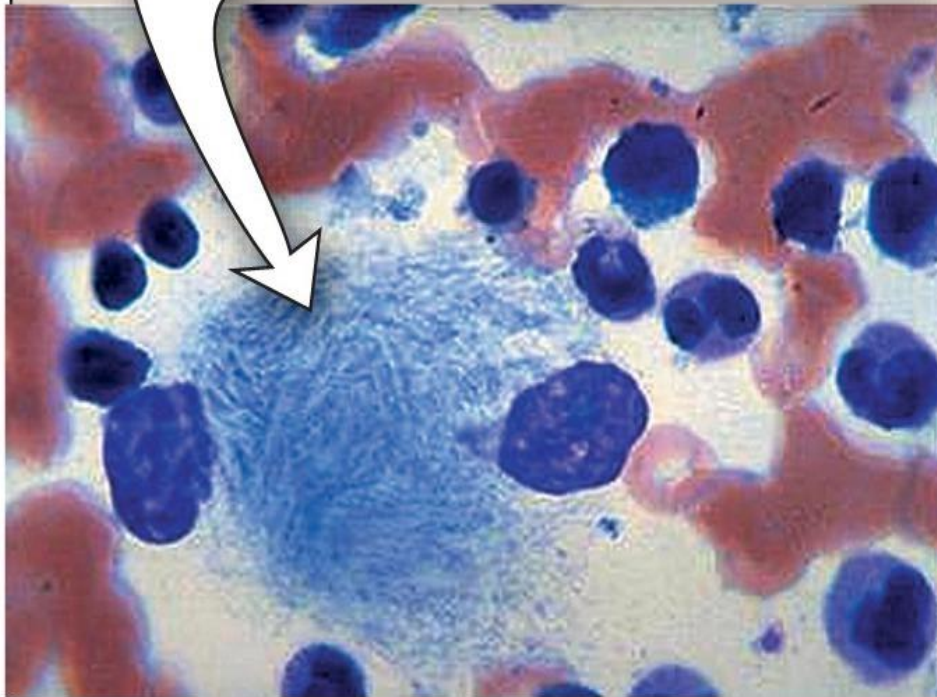
- *Sphingomyelinase* deficiency
- Enlarged liver and spleen filled with lipid
- Severe intellectual disability and neurodegeneration (Type A)
- Death in early childhood (Type A)

Sphingomyelinase



GAUCHER DISEASE

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



TAKE HOME MESSAGES

- Sphingolipids are complex lipids that includes sphingophospholipids and glycolipids.
- Ceramide is the precursor of all sphingolipids.
- Sphingolipids are present mainly in nerve tissue, but they are also found 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 degeneration of sphingolipids.

REFERENCE

Lippincott Illustrated Review of Biochemistry, 6th edition, 2014,
Unit 3, Chapter 17, Pages 201-218.