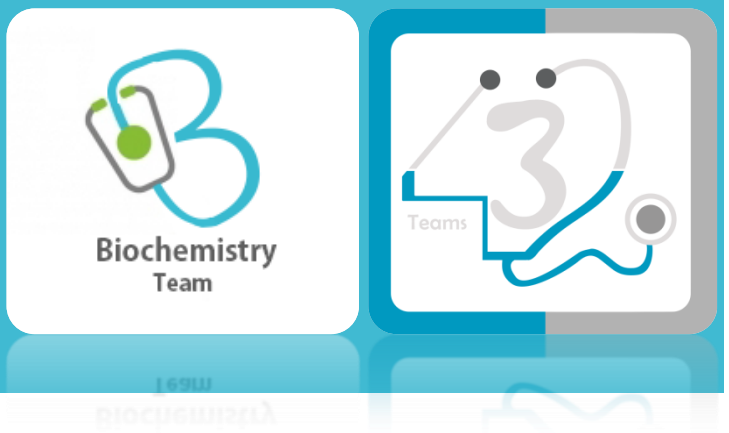
[lecture 1]

Sphingolipids and Myelin Structure



The Objectives

- Sphingolipids:
- Chemical structure
- Tissue distribution and functions
- Biochemical structure of myelin
- Biosynthesis of sphingolipids
- Sphingolipidosis

Red = Import-ant

Blue = explain

Green = addition notes

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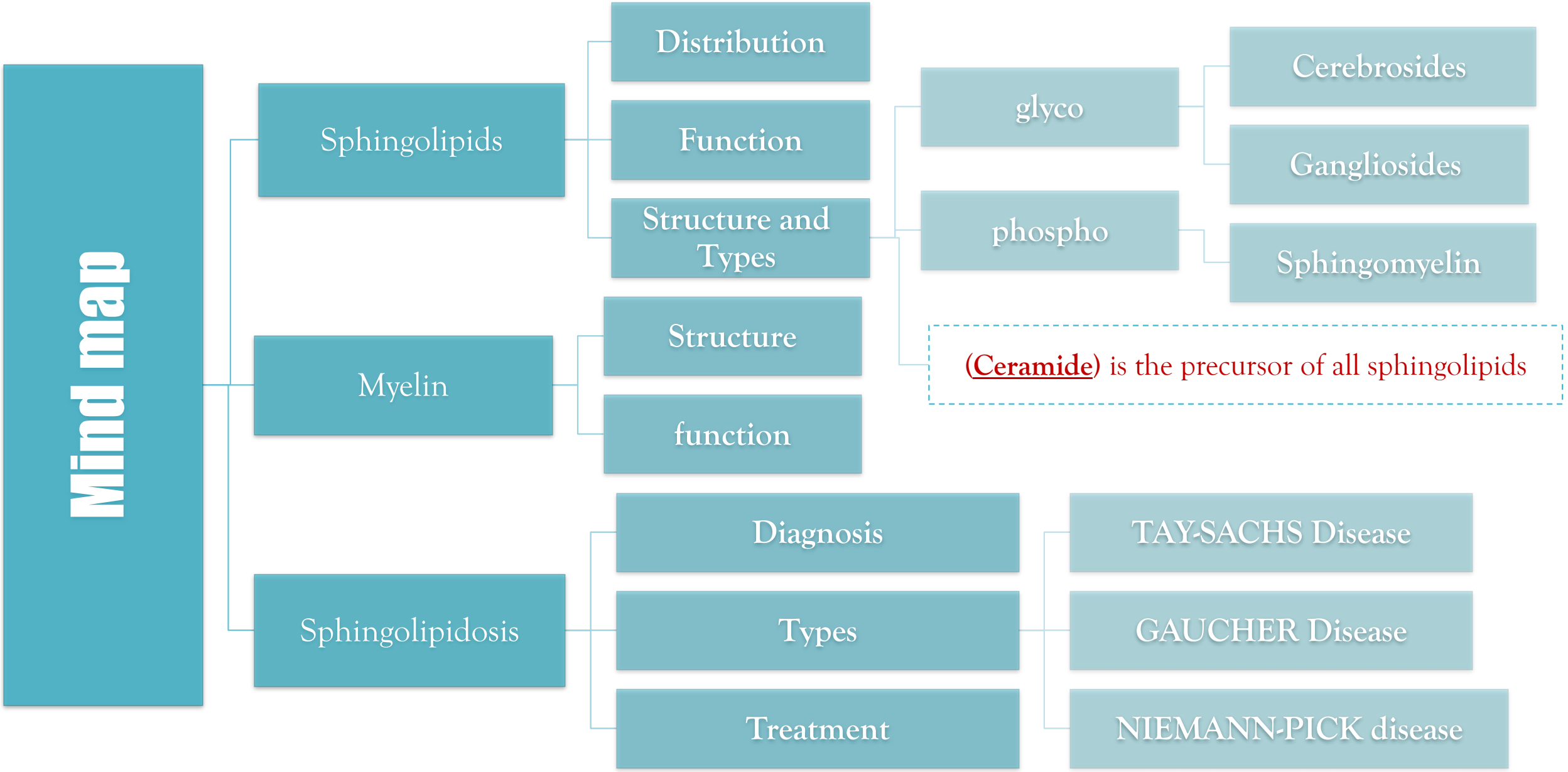

Mind map
Sphingolipids
Distribution
Function
Structure and Types
glyco
Cerebrosides
Gangliosides
phospho
Sphingomyelin
(Ceramide) is the precursor of all sphingolipids
Myelin
Structure
function
Sphingolipidosis
Diagnosis
Types
Treatment
TAY-SACHS Disease
GAUCHER Disease
NIEMANN-PICK disease

Sphingolipids: Background

1) **Essential component of membranes**
2) **Abundant in nervous tissue** (CNS is very rich in sphingolipids but they also can be found outside NS)
3) **Extra-nervous tissue:** * Receptors for : (means: sphingolipids are one of the components of these receptors)
   - Cholera toxins
   - Diphtheria toxins
   - Viruses
4) **Regulation of growth & development**
5) **Very antigenic**: (means: it will stimulate the immune system to release an antigens)
   - Blood group antigen
   - Embryonic antigen
   - Tumor antigen
6) **Cell transformation** (means: cells transformation into tumor cells and one of the causes is structural changes of the sphingolipids)

Sphingolipids: Structure and Types

sphingolipids Types:

- **Sphingophospholipids** — e.g., Sphingomyelin
- **Glycosphingolipids** — e.g. Glycolipids

Sphingosine + fatty acid = Ceramide

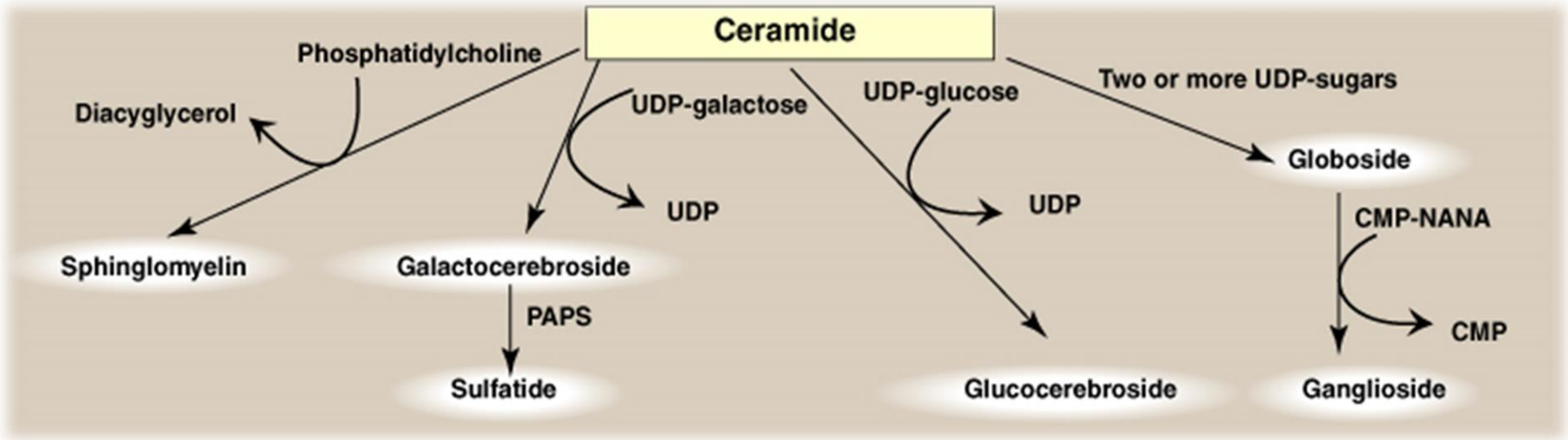
CERAMIDE is the parent compound for all sphingolipids family

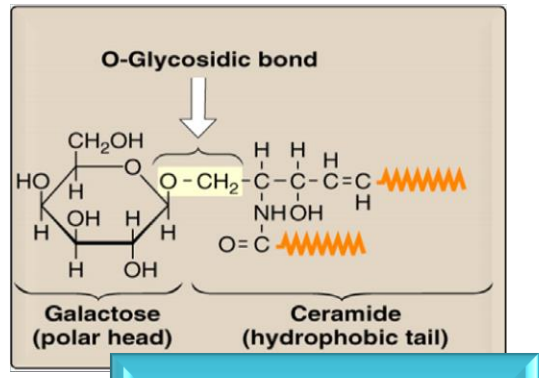
- Ceramide + Phosphorylcholine = Sphingomyelin
- Ceramide + Monosaccharides = Cerebrosides
- Ceramide + galactose = Galactocerebroside
- Ceramide oligosaccharides + NANA = Gangliosides

Sphingolipids' Synthesis

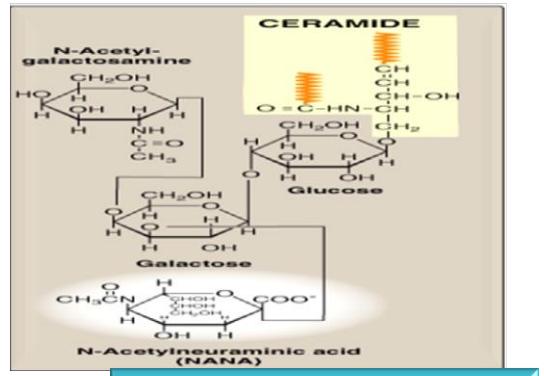
Not imp slide

We do not have to memories the structures

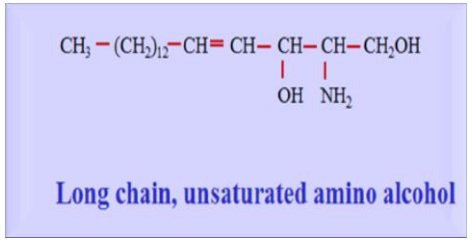




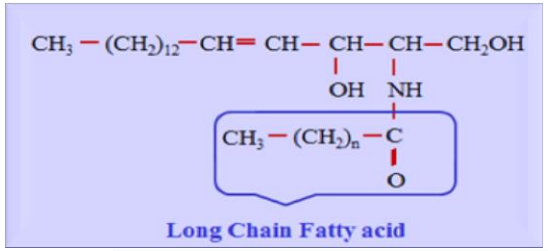
Galactocerebroside



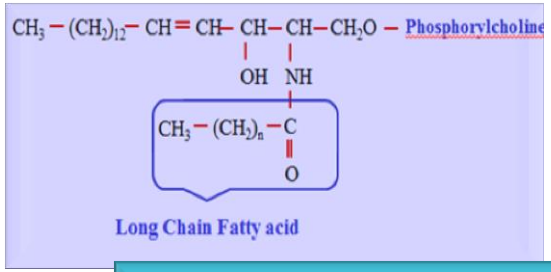
Gangliosides



Sphingosine



Ceramide



Sphingomyelin

Myelin Structure

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

Myelin Function

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

Myelin composition:

- Lipids (80%):
  - Main component: Cerebrosides
  - Other component: Sphingomyelin
- Proteins (20%):
  - e.g., Myelin basic protein

Myelin sheath:

Very long chain fatty acids:
Lignoceric 24:0
Nervonic 24:1

Multiple sclerosis:

Neuro-degenerative, auto-immune disease → Breakdown of myelin sheath (demyelination) → Defective transmission of nerve impulses

Myelin is produced by:
Schwann cells: peripheral nerves
Oligodendrocytes: CNS

Sphingolipidosis

- Synthesis (Normal); Degradation (Defective)
- Substrate accumulates in organs

The defect of enzymes cause stoppage of substrate degradation accumulation of substrate.

- Progressive, early death
- Phenotypic and genotypic variability
- Autosomal recessive (mostly)
- Rare, Except in Ashkenazi Jewish (mainly seen in communities with high consanguinity rates only marry one another, with no outside exposure)

*This group of diseases are also called lysosomal lipid storage disease because the substrate will accumulate in the lysosomes of the cells. (seen histologically)

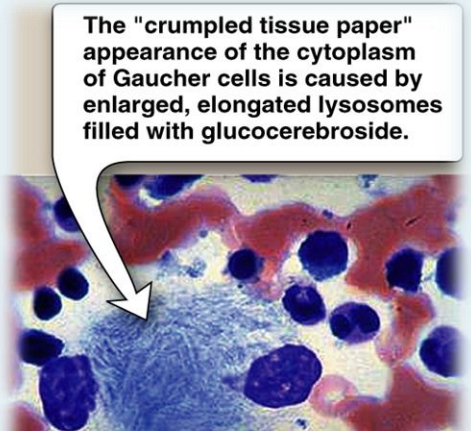
they are found in organs rich in reticular connective tissue like liver, kidney, spleen, and lymph nodes, as well as in bone marrow That's why these organs are the most affected in sphingolipidosis.

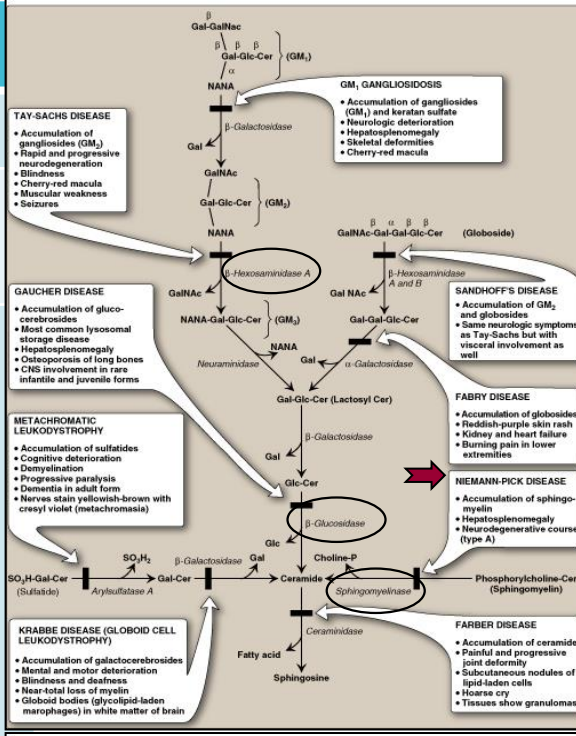
Diagnosis:

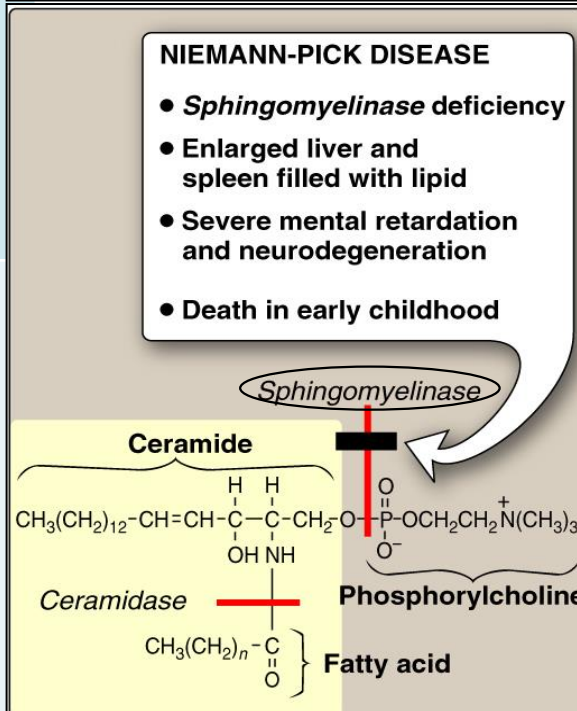
- Measure enzyme activity
  - Cultured fibroblasts or peripheral leukocytes
  - Cultured amniocytes (prenatal)
- Histologic examination
- DNA analysis

Treatment:

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

Types:	TAY-SACHS Disease	GAUCHER Disease	NIEMANN-PICK disease
Substrate	gangliosides (GM2)	glucocerebrosides	sphingomyelin
Defected Enzyme	Beta-Hexosaminidase A	Beta-Glucosidase (glucocerebrosidase)	Sphingomyelinase
Features	• Accumulation of gangliosides (GM2) • Rapid, progressive, and fatal neurodegeneration • Blindness • Cherry-red macula • Muscular weakness • Seizures	• Accumulation of glucocerebrosides • Most common lysosomal storage disease • Hepatosplenomegaly • Osteoporosis of long bones causing severe bone aches • CNS involvement in rare infantile & juvenile forms • Crumpled tissue paper appearance of cytoplasm under microscope	• Accumulation of sphingomyelin • Hepatosplenomegaly • Neurodegenerative course (type A)
More about it	Accumulation of gangliosides in the gangliocytes of retina → cherry-red macula → blindness		**Type A** o Acute disease o Sever deficiency of enzyme. o Which comes with neurodegernative effect (severe mental retardation) **Type B** o Chronic disease. o Mild deficiency of enzyme.





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

Qs..

Q1: which one of the folloing is a Sphingophospholipids :

a) Cerebrosides - b) Galactocerebroside - c) Sphingomyelin - d) Gangliosides

Q2: A 10-month-old male is brought to the pediatrician by his mother who is concerned about his lack of interaction. He was previously playful and happy but now hardly ever smiles. On exam, he is found to have poor muscle tone and a cherry-red macula. Deficiency of which enzyme is most likely?

a) Beta-Hexosaminidase A - b) Beta-Glucosidase - c) Sphingomyelinase

Q3: the main component of the myelin is :

a) Cerebrosides - b) Galactocerebroside - c) Sphingomyelin - d) Gangliosides

Q4: A defect in *Sphingomyelinase* enzyme will result in

a) TAY-SACHS Disease - b) GAUCHER Disease - c) NIEMANN-PICK disease - d) MS

Q5: in the CNS myelin produced by :

a) Schwann cells - b) astrocytes - c) macrophages - d) oligodendrocytes

Q6: A histological examination of a patient with an autosomal recessive disease revealed Crumpled tissue paper appearance of cytoplasm under microscope , what will be your diagnosis ?

a) TAY-SACHS Disease - b) GAUCHER Disease - c) NIEMANN-PICK disease - d) MS

Answers: q p o e e o

Biochemistry
Team

If you find any mistake, please contact us:)

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