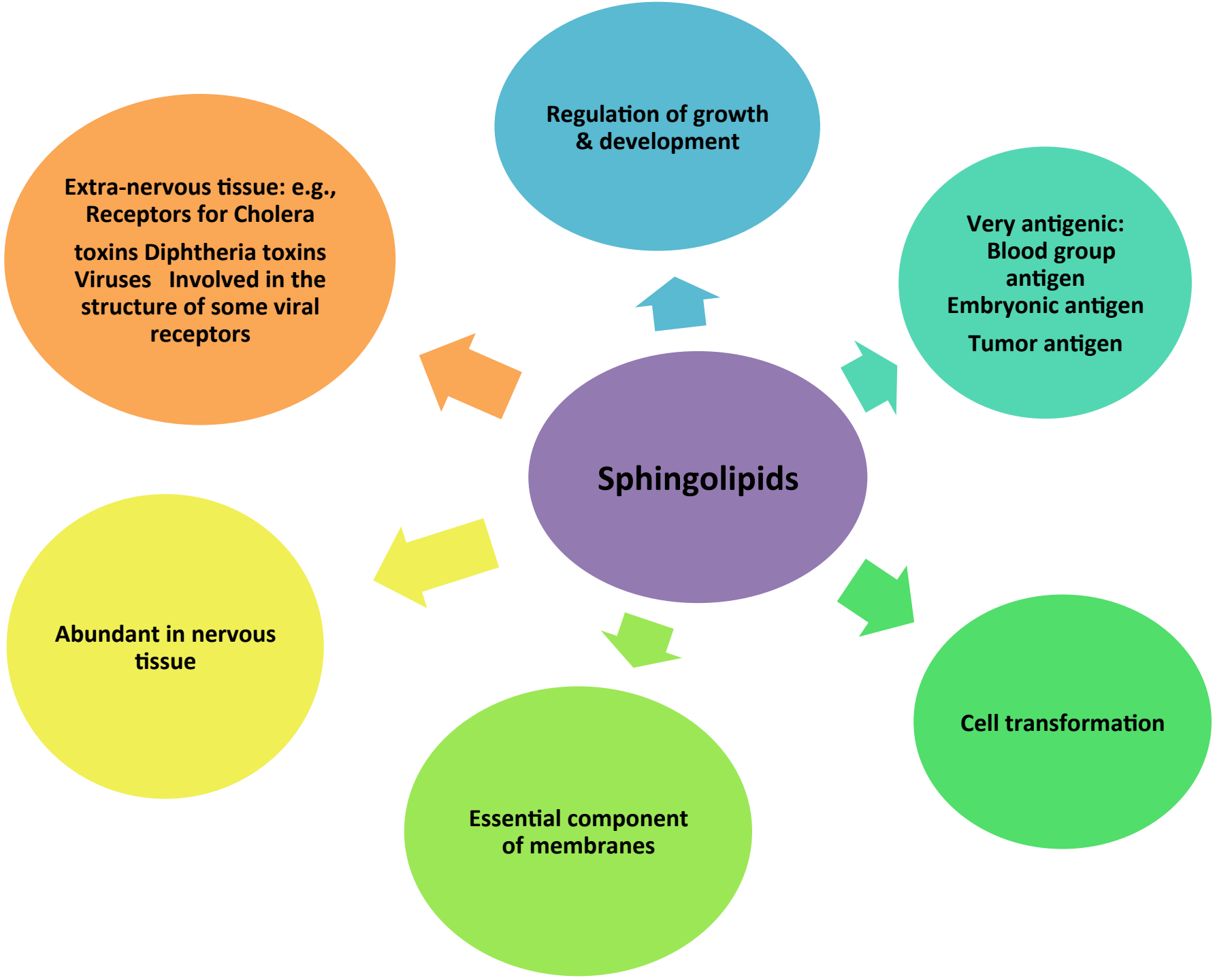
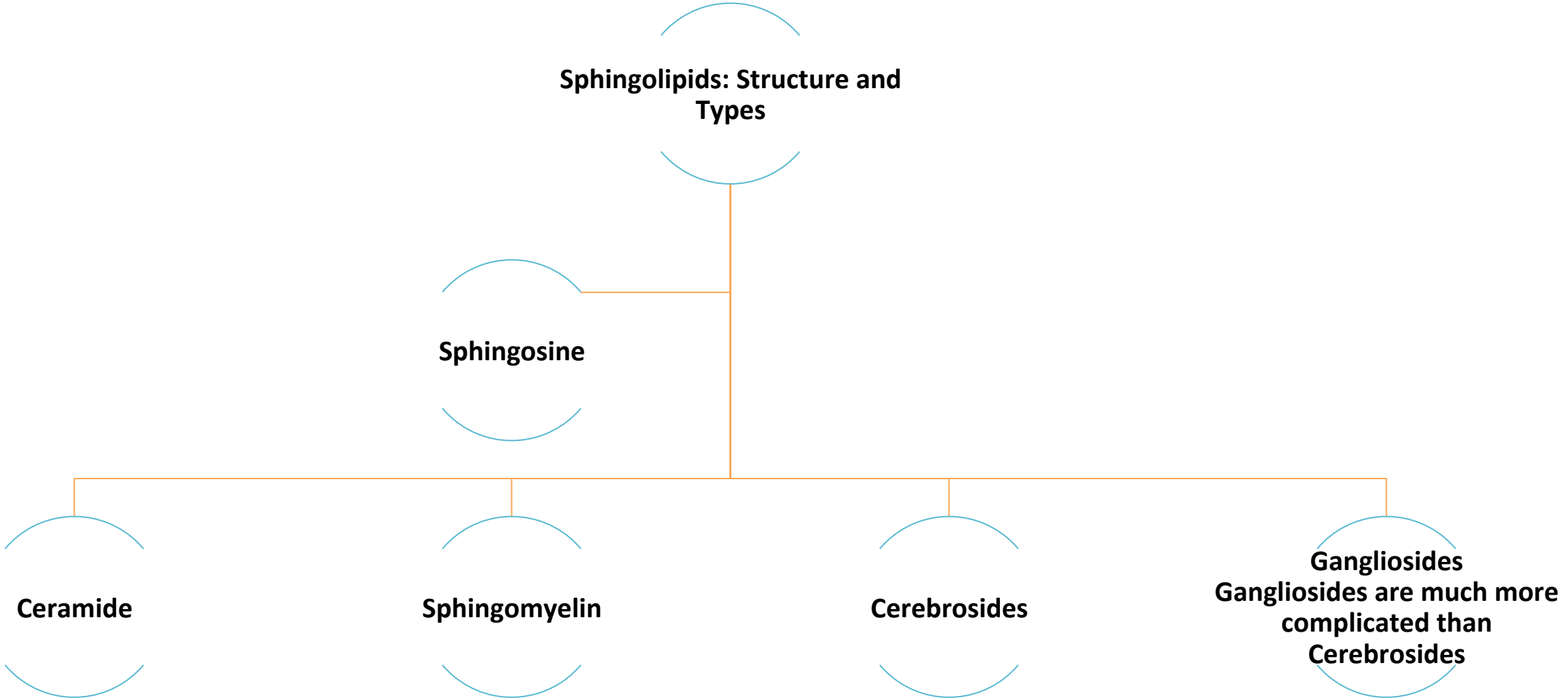
Biochemistry
Team 434

Sphingolipids and Myelin Structure

Biochemistry434@gmail.com

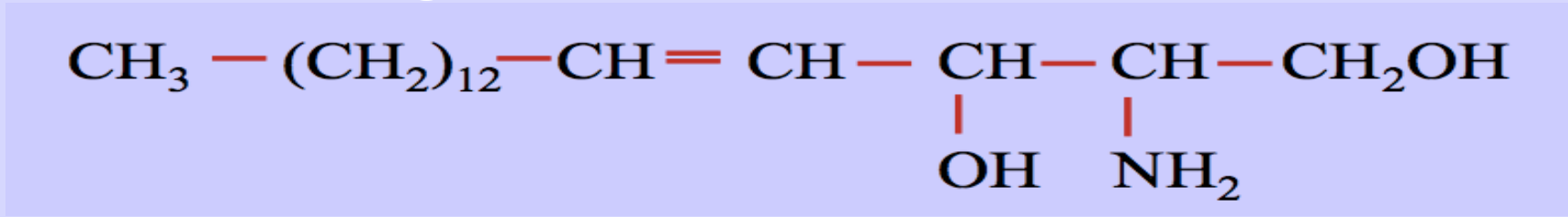

Regulation of growth & development
Extra-nervous tissue: e.g., Receptors for Cholera
toxins Diphtheria toxins Viruses Involved in the structure of some viral receptors
Very antigenic: Blood group antigen Embryonic antigen
Tumor antigen
Sphingolipids
Abundant in nervous tissue
Cell transformation
Essential component of membranes


Sphingolipids: Structure and Types
Sphingosine
Ceramide
Sphingomyelin
Cerebrosides
Gangliosides
Gangliosides are much more complicated than Cerebrosides

Structure and Types

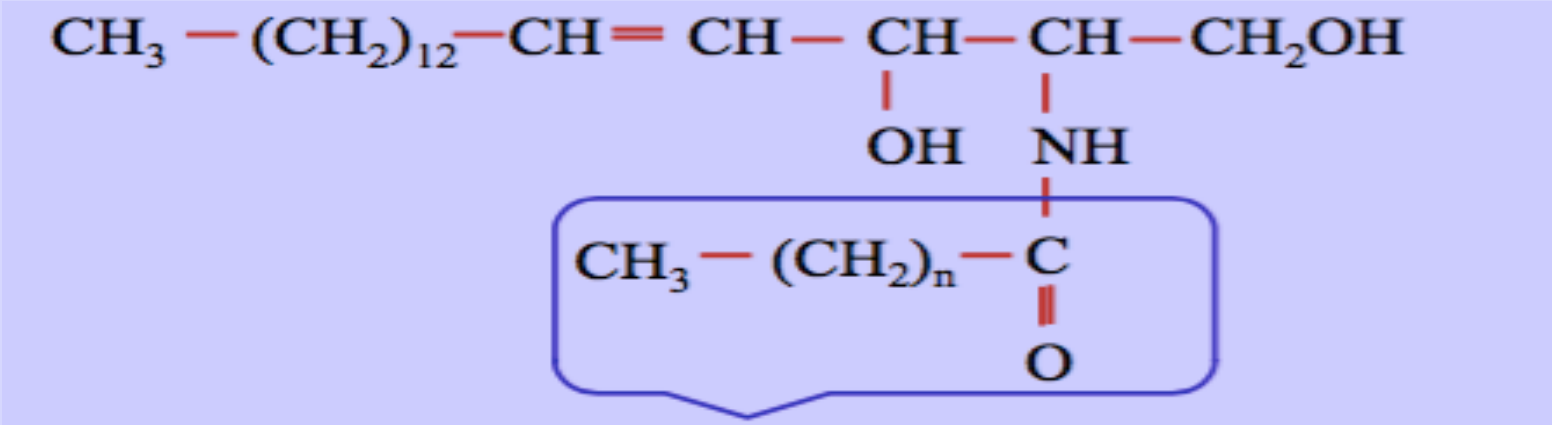
Sphingosine

Long chain, unsaturated amino alcohol



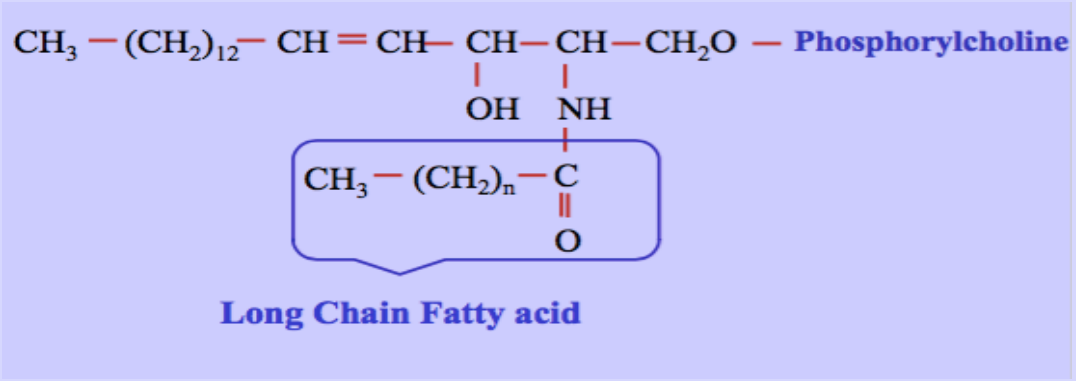
We don't have to memorize the structures.

Ceramide = Sphingosine + fatty acid



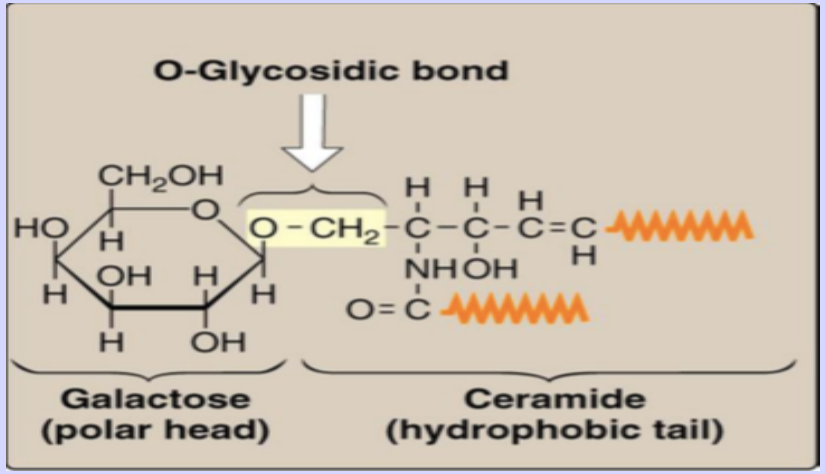
The chain may reach 24 carbons so it is really long

Sphingomyelin = Ceramide + Phosphorylcholine



Cerebrosides = Ceramide + Monosaccharides

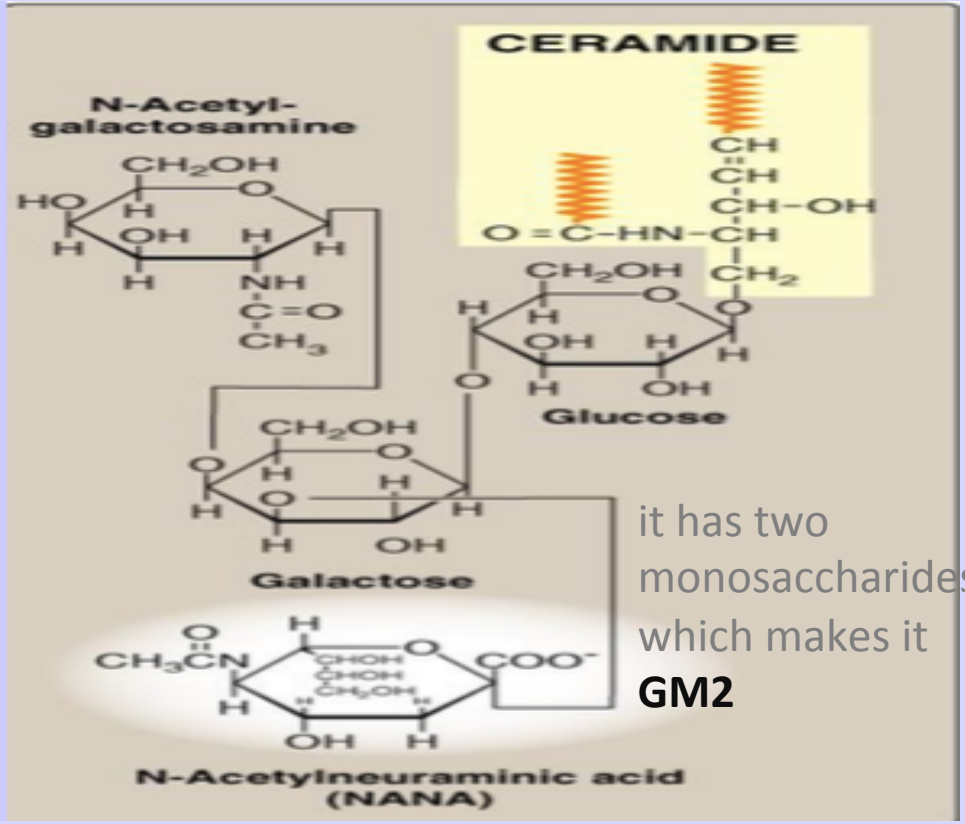
From the word cerebro we know how abundant this substance is –in the CNS-.



Gangliosides = Ceramide oligosaccharides + NANA

Gangliosides : each segment added has a specific function

Oligosaccharides: saccharide polymer containing a small number (typically three to nine) of simple sugars (monosaccharides).

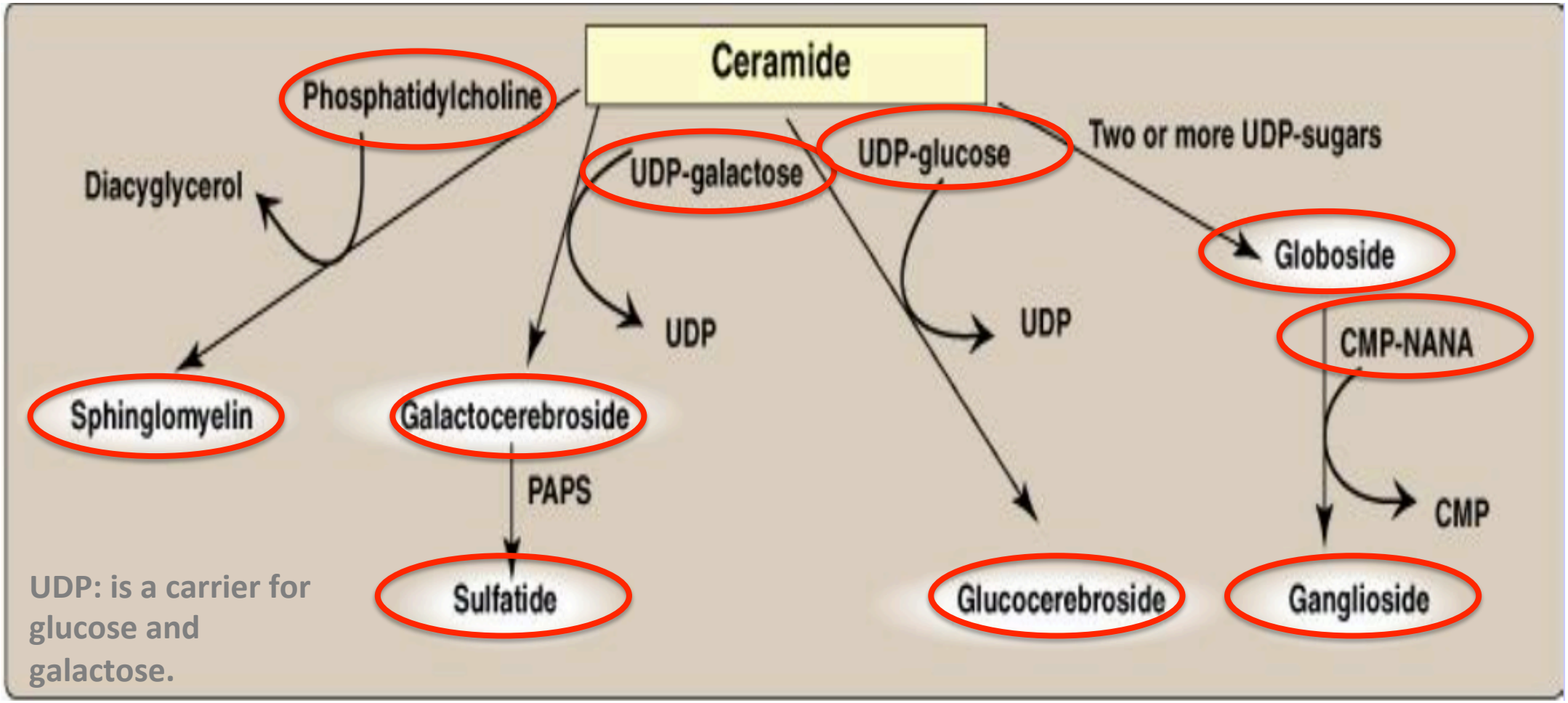


it has two monosaccharides which makes it **GM2**

We don't have to memorize the structures.

Sphingolipids' Synthesis

Ceramide added to it phosphatidylcholine >
And then removal of diacyglycerol
will form: sphinglomyelin.
And so on for the others.



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**
- **Fatty acid of Sphingomyelin: Myelin sheath:**
- **Very long chain fatty acids:**
- **Lignoceric 24:0 saturated**
- **Nervonic 24:1 unsaturated**

0: stands for the number of double bond, it equals 0 so it's saturated
1 means that it is unsaturated

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**

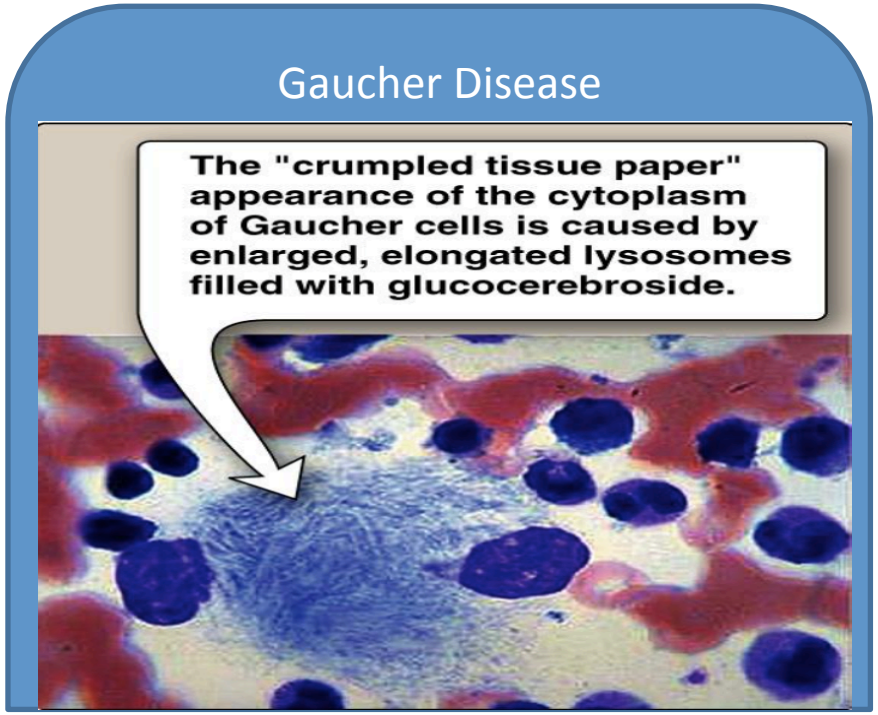
Diagnosis:

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

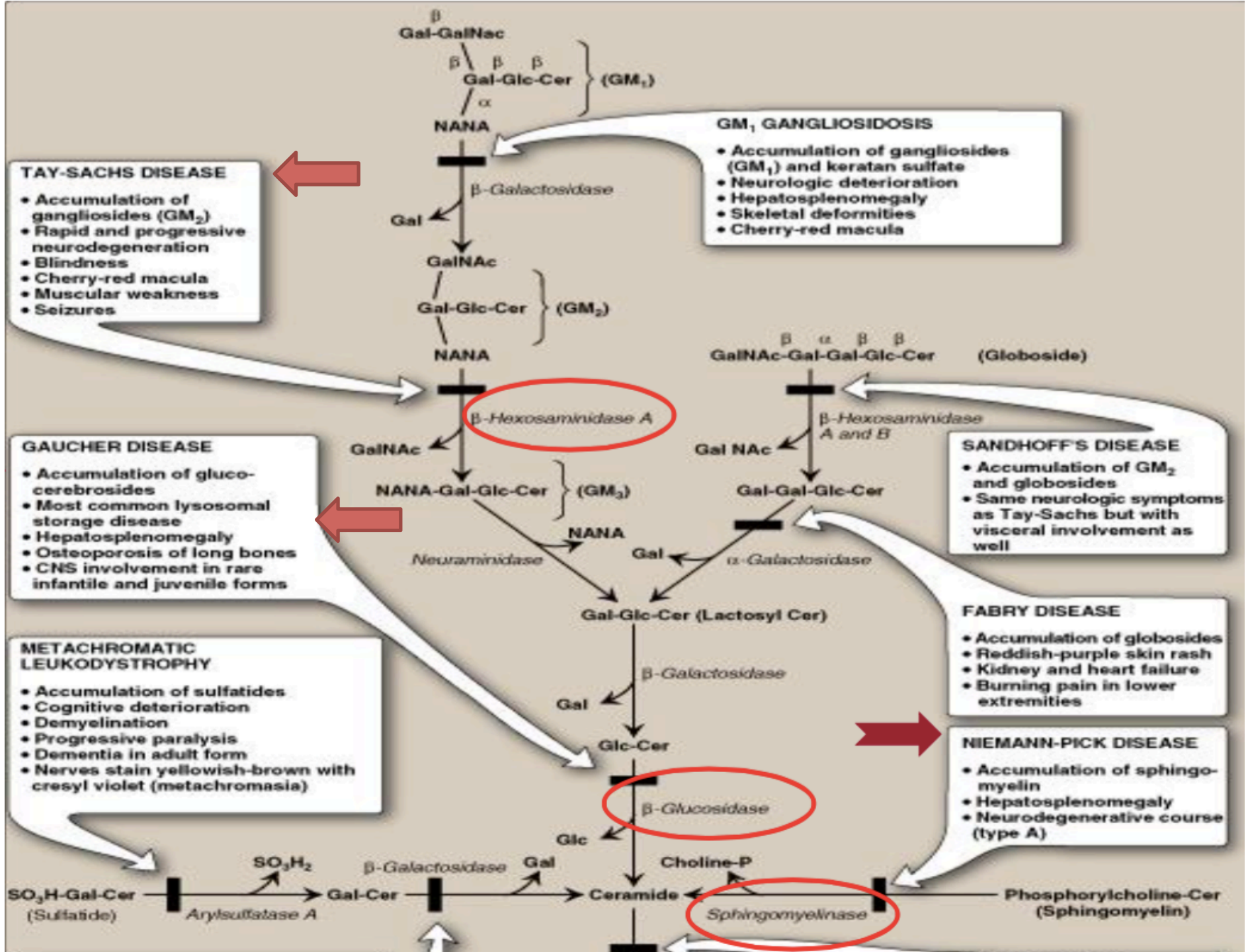
Treatment:

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

Cultured fibroblasts or peripheral leukocytes or any cell has a nucleus. Remember we can't use RBC



The defect here is in the enzyme responsible for degradation substances so the neurons become filled with unwanted substances
Mostly autosomal recessive ((focus in families carrying this disease))


Gal-GalNac
Gal-Glc-Cer
(GM1)
NANA
β-Galactosidase
Gal
GalNAc
Gal-Glc-Cer
(GM2)
NANA
β-Hexosaminidase A
GalNAc
NANA-Gal-Glc-Cer
(GM3)
Neuraminidase
NANA
Gal-Glc-Cer (Lactosyl Cer)
β-Galactosidase
Gal
Glc-Cer
β-Glucosidase
Glc
Ceramide
GalNAc-Gal-Gal-Glc-Cer
(Globoside)
β-Hexosaminidase A and B
Gal NAc
Gal-Gal-Glc-Cer
α-Galactosidase
Gal
Choline-P
Phosphorylcholine-Cer
(Sphingomyelin)
Sphingomyelinase
SO3H-Gal-Cer
(Sulfatide)
Arylsulfatase A
SO3H2
Gal-Cer
β-Galactosidase
Gal
TAY-SACHS DISEASE
• Accumulation of gangliosides (GM2)
• Rapid and progressive neurodegeneration
• Blindness
• Cherry-red macula
• Muscular weakness
• Seizures
GM1 GANGLIOSIDOSIS
• Accumulation of gangliosides (GM1) and keratan sulfate
• Neurologic deterioration
• Hepatosplenomegaly
• Skeletal deformities
• Cherry-red macula
GAUCHER DISEASE
• Accumulation of gluco-cerebrosides
• Most common lysosomal storage disease
• Hepatosplenomegaly
• Osteoporosis of long bones
• CNS involvement in rare infantile and juvenile forms
SANDHOFF'S DISEASE
• Accumulation of GM2 and globosides
• Same neurologic symptoms as Tay-Sachs but with visceral involvement as well
FABRY DISEASE
• Accumulation of globosides
• Reddish-purple skin rash
• Kidney and heart failure
• Burning pain in lower extremities
NIEMANN-PICK DISEASE
• Accumulation of sphingo-myelin
• Hepatosplenomegaly
• Neurodegenerative course (type A)
METACHROMATIC LEUKODYSTROPHY
• Accumulation of sulfatides
• Cognitive deterioration
• Demyelination
• Progressive paralysis
• Dementia in adult form
• Nerves stain yellowish-brown with cresyl violet (metachromasia)

TAY-SACHS DISEASE:

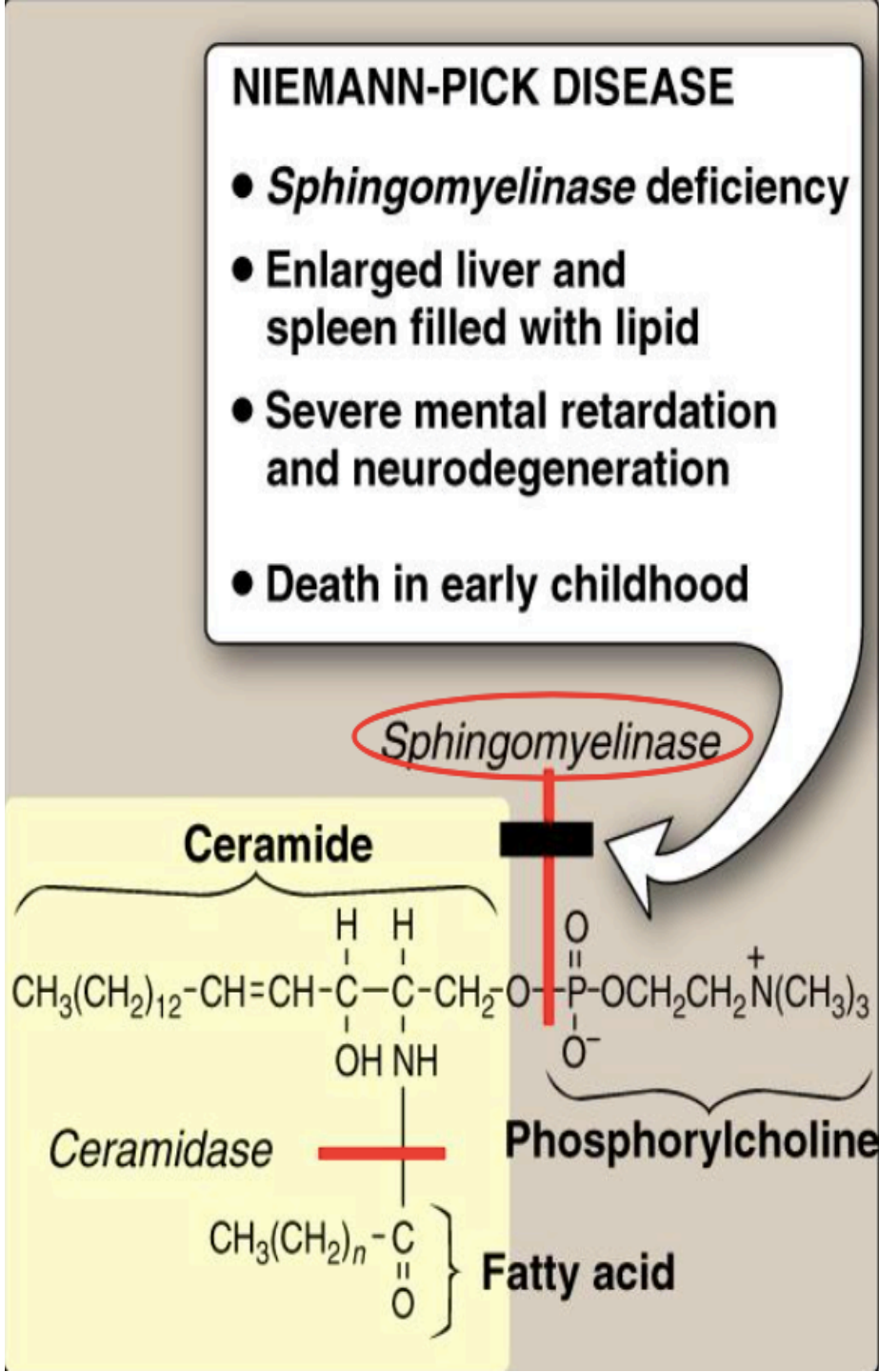
- accumulation of gangliosides (GM2)
- rapid and progressive neurodegenration.
- blindness.
- cherry-red macula.
- muscular weakness.
- seizures.

NIEMANN-PICK DISEASE:

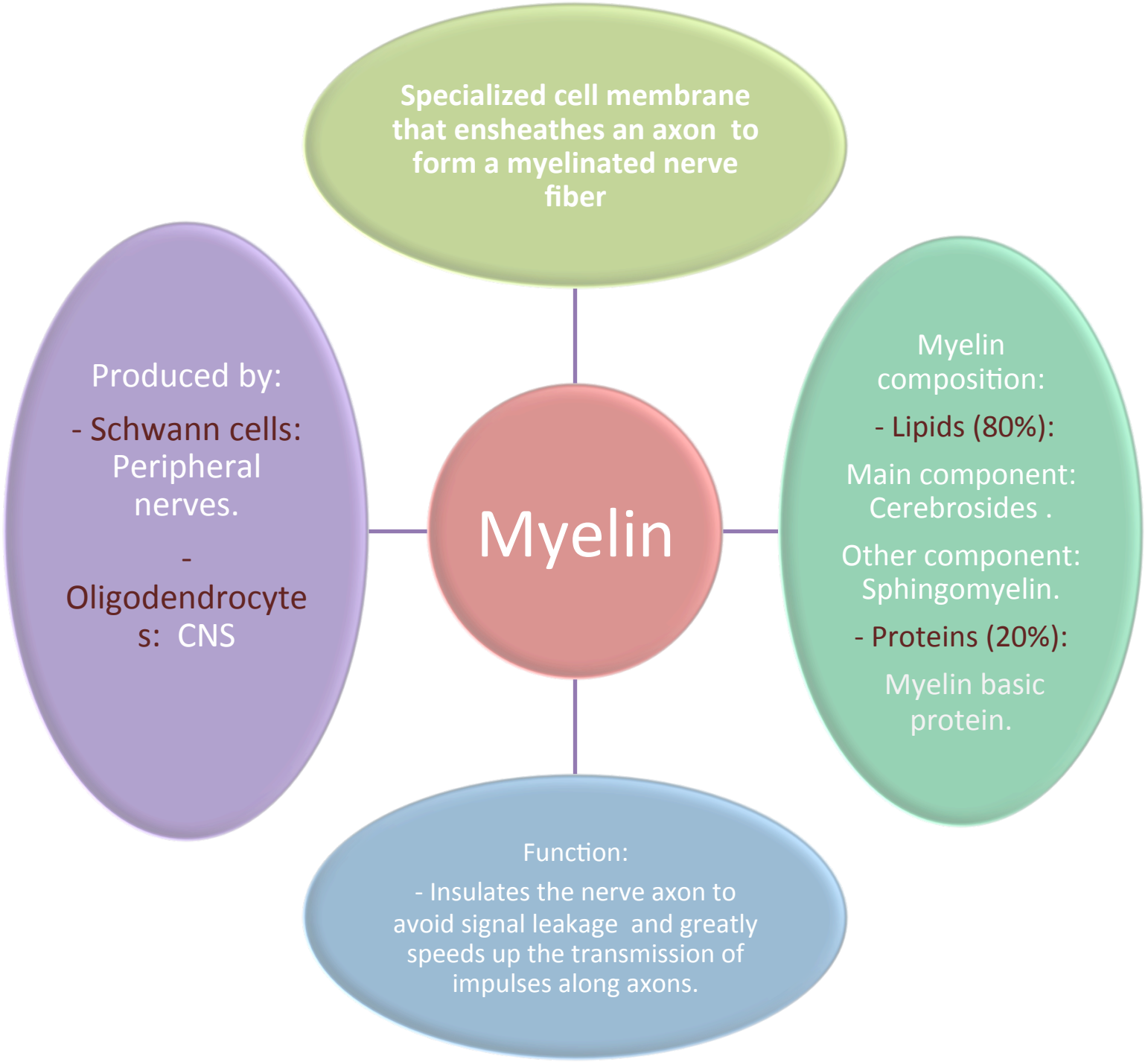
- accumulation of sphingomyelin.
- hepatosplenomegaly.
- neurodegerative course (type A).
- Death in early childhood.

GAUCHER DISEASE:

- accumulation of glucocerebrosides.
- most common lysosomal storage disease.
- hepatosplenomegaly.
- osteoprosis of long bones.
- CNS involvement in rare infantile and juvenile form.



Summary


Specialized cell membrane that ensheathes an axon to form a myelinated nerve fiber
Produced by:
- Schwann cells: Peripheral nerves.
- Oligodendrocytes: CNS
Myelin
Myelin composition:
- Lipids (80%):
Main component: Cerebrosides .
Other component: Sphingomyelin.
- Proteins (20%):
Myelin basic protein.
Function:
- Insulates the nerve axon to avoid signal leakage and greatly speeds up the transmission of impulses along axons.

Summary


TAY-SACHS Disease:
● β -HexosaminidaseA deficieny.
●Accumulation of gangliosides (GM2).
●Rapid and progressive neurodegeneration.
●Blindness, cherry-red macula, muscular weakness, seizures.
Sphingolipidosis
(genetic disease due to defective degradation of sphingolipids).
GAUCHER Disease:
● β -Glucosidase deficiency.
●Accumulation of Gluco-cerebrosides.
●Most common lysosomal storage disease.
●Hepatosplenomegaly.
●Osteoporosis of long bones.
NIEMANN-PICK Disease:
●Sphingomyelinase deficiency.
●Accumulation of sphingo-myelin.
●Hepatosplenomegaly.
●Severe mental retardation &neurodegeneration.
●Death in early childhood.

MCQs

1) Patient with sphingomyelinase enzyme deficiency is most likely to develop

A- Gaucher disease
B- Farber disease
C- Tay-Sachs disease
D- Niemann-pick disease

2) the main component of the myelin is :

A- Cerebrosides
B- Galactocerebroside
C-Sphingomyelin
D- Gangliosides

3) 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

4) The precursor of all sphingolipids is:

A- Phosphorycholine
B- Ceramide
C- Phospholipids
D- Sphingosine

5) Which ONE of the following will attach to ceramide in order to form Gangliosides?

A- Monosaccharides
B- Oligosaccharides+NANA
C- Phosphorycholine

6) Which ONE of the following is NOT a diagnostic procedure for Sphingolipidosis:

A- Histologic examination
B- Measurement of enzyme activity
C- PCR
D- DNA analysis

1- D
2- A
3- A
4- B
5- B
6- C

Biochemistry
Team 434

Done by:

Ghaida almasaad
Hanouf almuhanna
Mishael husain
Sara aljasser
Reema alhammad

https://www.youtube.com/watch?v=7h0lkds_d5E&feature=youtu.be

Biochemistry434@gmail.com