SPHINGOLIPIDS AND MYELIN STRUCTURE

Color Index:

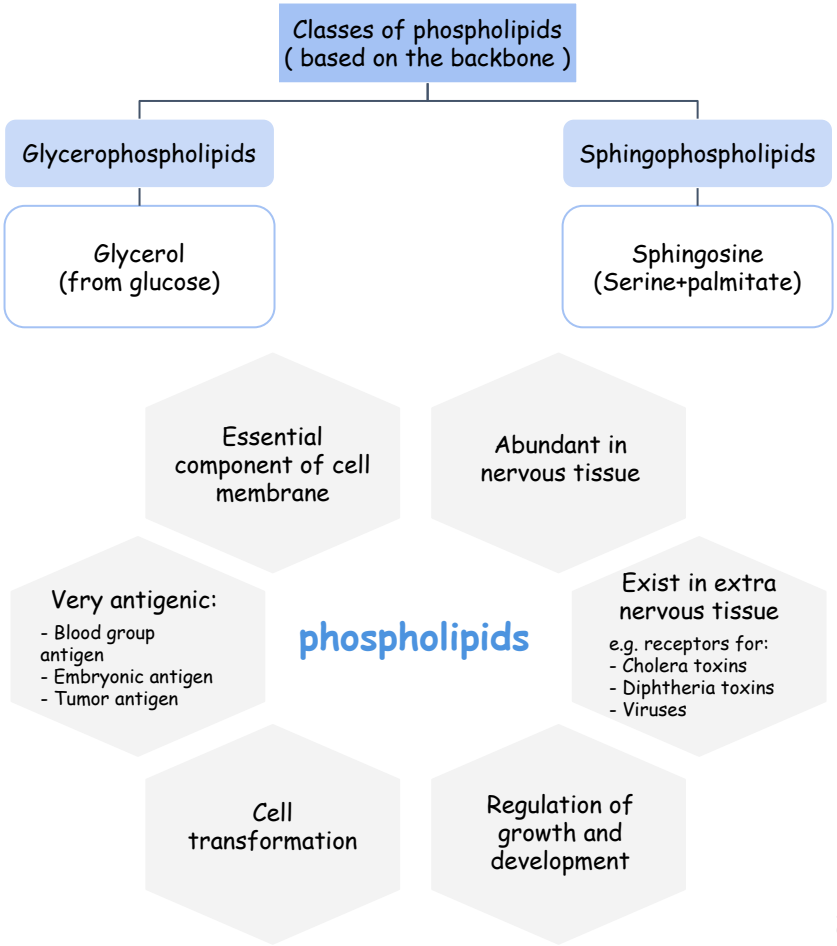
- Main Topic
- Main content
- Important
- Extra info, Drs' notes
- Only in girls' slides
- Only in boys' slides

Editing File

Objectives:

- 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 basis of biosynthesis of sphingolipids.
- Be introduced to sphingolipids .

Background



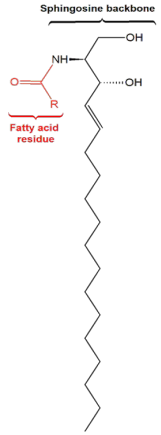
Sphingosine Structure

Sphingosin

Long chain, unsaturated amino alcohol

Sphingolipids

Ceramide:
Sphingosine + Fatty acid



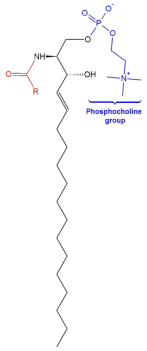
A Ceramide

- Play a central role in maintaining the skin's water permeability

- Decreased ceramide levels are associated with a number of skin diseases

Sphingophospholipids

Sphingomyelin:
Ceramide + phosphorylcholine

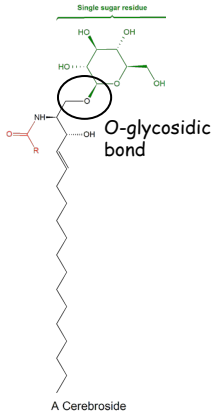


A Sphingomyelin

- Sphingomyelin is the only significant sphingolipid in humans

Glycosphingolipids

Cerebrosides:
Ceramide + Monosaccharide

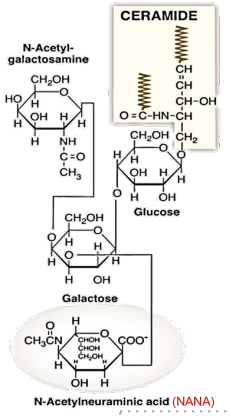


A Cerebroside

e.g. Galactocerebroside

Most common monosaccharide is galactose but also it could be glucose sometimes .

Gangliosides:
Ceramide + oligosaccharides + NANA



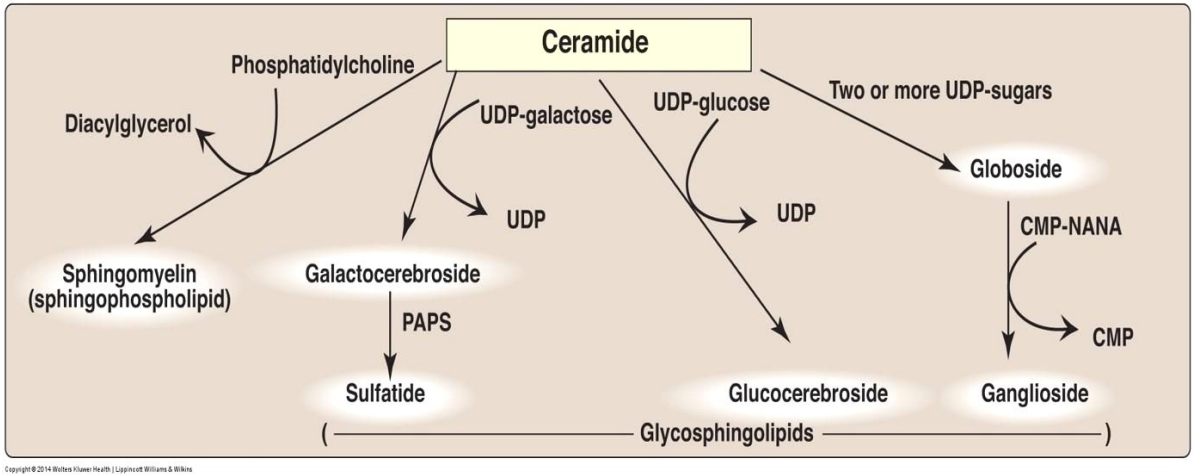
E.g. G_{M2}:

G= ganglioside;
M= mono molecule of NANA;
2= the monomeric sequence (position) of the carbohydrate attached to the ceramide

Could be D = di
Or T = tri
Or Q = Quad
Regarding the NANA

THIS SLIDE IS IMPORTANT!!

Sphingolipids' Synthesis

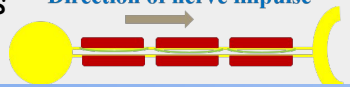


437 team

1. Phosphatidylcholine interacts with ceramide, diacylglycerol goes out and gives us sphingomyelin
2. Galactose is added to ceramide by the carrier UDP "uridine diphosphate", UDP goes out and we get galactocerebroside. We can modify it further by adding a sulfate group with the carrier PAPS, giving us sulfatide.
3. Glucose is added to ceramide by the carrier UDP, UDP goes out and we get glucocerebroside.
4. Two or more UDP sugars are added to ceramide and we get: globosides. If NANA was added to it by the carrier CMP "cytidine monophosphate", we get gangliosides

Myelin

Definition	Myelin is a specialized cell membrane that ensheaths an axon to form a myelinated nerve fiber
Production	• Oligodendrocytes ⟶ CNS • Schwann cells ⟶ PNS
Composition	1. Lipids (80%) : Main component: Cerebroside Other component: Sphingomyelin 2. Protein (20%) : e.g Myelin basic protein
Myelin Sheath	Is a very long chain of sphingomyelin fatty acid composed of : Lignoceric acid: 24:0 Nervonic acid 24:1 (15)
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
- Antibodies attacks Myelin basic protein

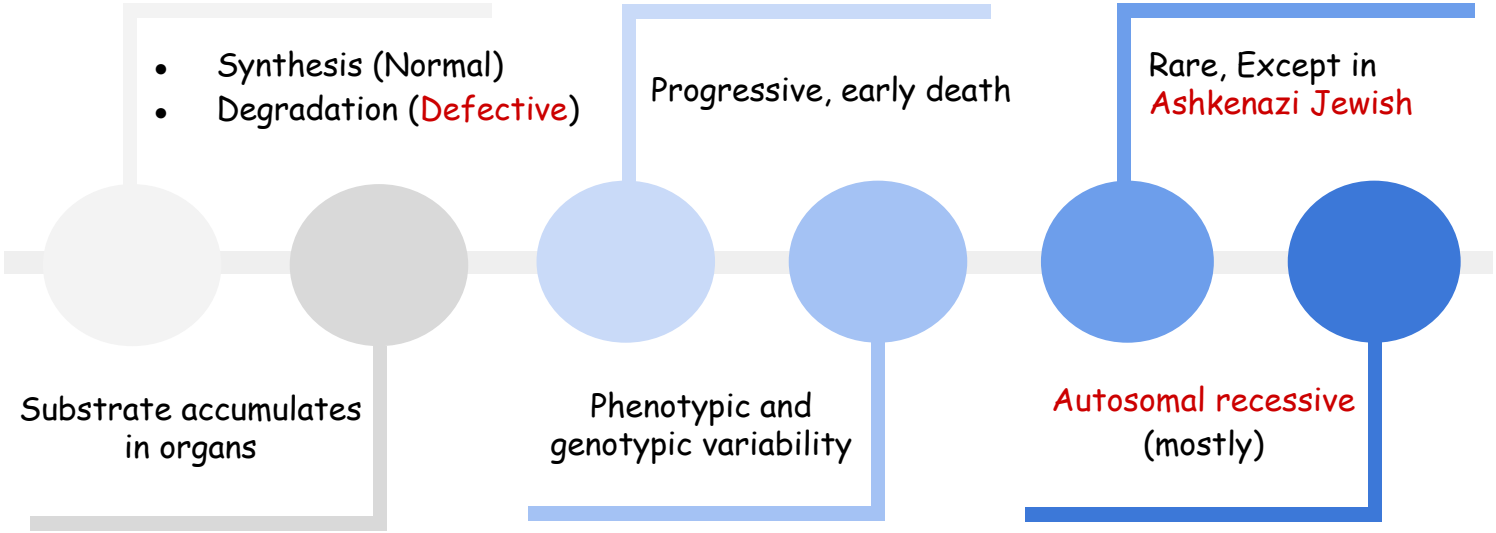
★

- 24: refers to the number of carbon atoms
- 1: is the number of double bonds
- 15: is the position of the double bond

- Lignoceric: 24 carbon atoms with 0 double bond.
- Nervonic: 24 carbon atoms with One double bond in the 15th carbon atom.

Sphingolipidoses

- A partial or total missing of a specific lysosomal acid hydrolase leads to accumulation of a sphingolipid.
- Lysosomal lipid storage diseases caused by these deficiencies are called **sphingolipidoses**.
- *Usually only a single sphingolipid accumulates in the involved organs in each disease*



Sphingolipidoses

The highlighted diseases are important

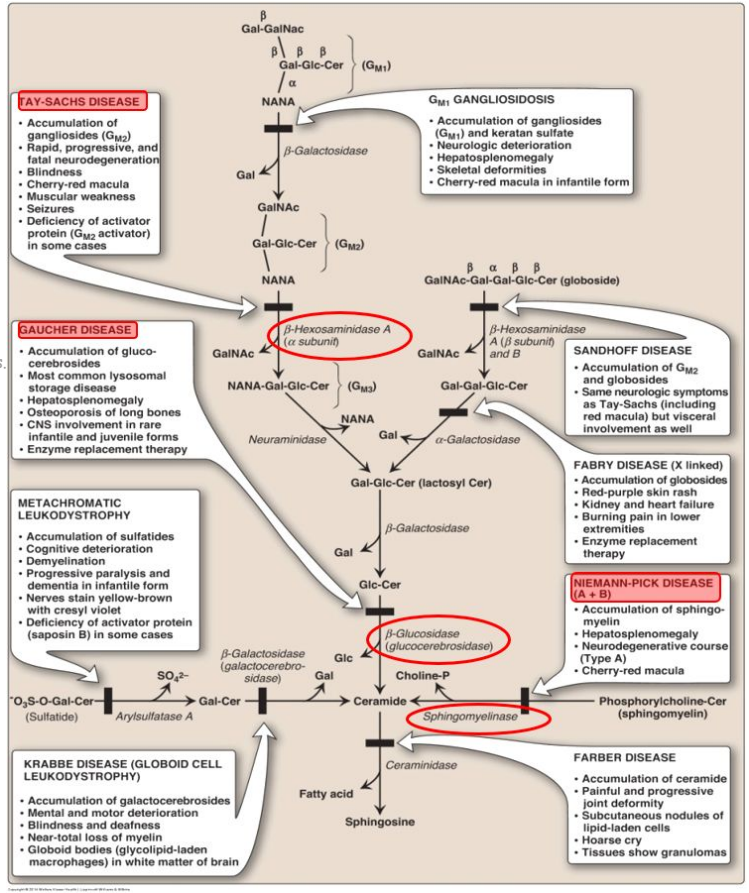
Diagnosis:

1. Measure enzyme activity:
   a. Cultured fibroblasts or peripheral leukocytes. Easy to culture (grow fast)
   b. Cultured amniocytes or chorionic villi (prenatal). This test is used ONLY when parents are affected or carriers.
2. Histologic examination.
3. DNA analysis. Specific, need to know the EXACT mutation

Treatment:

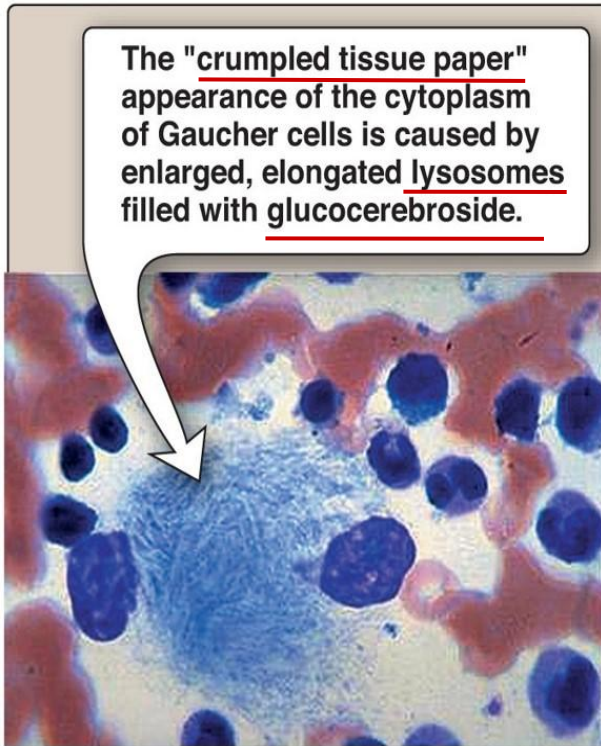
e.g. for Gaucher disease:

1. Replacement Therapy (e.g. recombinant human enzyme).
2. Bone marrow transplantation. To produce macrophages

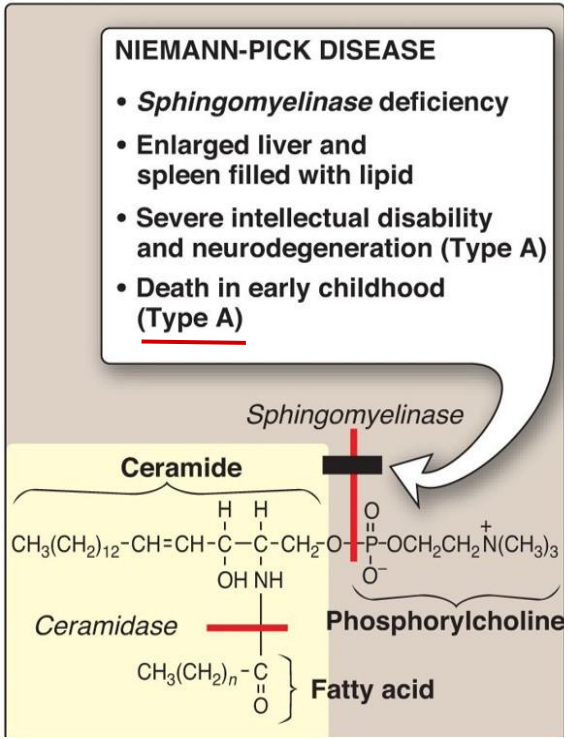


You will find a table that summarizes the 3 diseases in the summary slide

1 Gaucher Disease



2 Niemann-pick disease



Take Home Messages

- 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 also found extra-neural
- Myelin sheath insulates the nerve axon to avoid signal leakage and speed up impulse transmission
- Sphingolipidoses are rare genetic diseases due to defective degeneration of sphingolipids

Summary

Sphingolipids

Ceramide:
Sphingosine + Fatty acid

- Play a central role in maintaining the skin's water permeability
- Decreased ceramide levels are associated with a number of skin diseases

Sphingophospholipids

Sphingomyelin:
Ceramide + phosphorylcholine

- Sphingomyelin is the only significant sphingolipid in humans

Glycosphingolipids

Cerebrosides:
Ceramide + Monosaccharide

e.g. Galactocerebroside

Gangliosides:
Ceramide + oligosaccharides + NANA

E.g. G_{M2}:
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2= the monomeric sequence (position) of the carbohydrate attached to the ceramide

Myelin

Oligodendrocytes → CNS
Schwann cells → PNS

80% Lipids → Cerebroside
20% Proteins → Myelin basic protein

Myelin sheath:
Lignoceric → 24:0
Nervonic → 24:1 (15)

A specialized cell membrane ensheaths an axon to form a myelinated one

Myelin sheath → Insulation → Avoid signal leakage → Speed up transmission of impulses

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

Sphingolipidoses

TAY-SACHS DISEASE

- Accumulation of gangliosides (GM2).
- Deficiency of the enzyme β-Hexosaminidase.
- Rapid, progressive and fatal neurodegeneration.
- Cherry-red macula "red spot found in the retina"
- Muscular weakness.
- Seizures
- Deficiency of activator protein (GM2) in some cases.

GAUCHER DISEASE

- Accumulation of gluco-cerebroside .
- Deficiency of the enzyme β-glucosidase (glucocerebrosidase).
- Most common.
- Causes osteoporosis in long bones
- hepatosplenomegaly "in liver and spleen".
- Causes crumpled tissue paper appearance of the cytoplasm.
- Treated with replacement therapy and bone marrow transplantation.

NIEMANN-PICK DISEASE (A+B)

- Accumulation of sphingomyelin.
- Sphingomyelinase deficiency.
- hepatosplenomegaly
- Cherry-red macula .
- It has two types, A and B:

  - Type A is more severe because the enzyme has almost no activity, it causes severe intellectual disability and death in early childhood.

  -Type B is less severe, has a later onset and causes little to no neurodegeneration.

Quiz

MCQs :

Q1: Myelinated axons ...

a) Conduct action potentials slower than unmyelinated axons **b)** Do not have action potentials
c) Conduct action potentials faster than unmyelinated axons **d)** Are not electrically insulated

Q2: Lysosomal storage diseases occur when mutations cause defects in which of the following?

a) Sphingolipid biosynthesis enzyme **b)** Lysosome transformation
c) Sphingolipid degradation enzyme **d)** Formation of NANA derivatives

Q3: accumulation of gangliosides leads to which of the following diseases?

a) Multiple sclerosis **b)** GAUCHER disease
c) TAY SACHS disease **d)** NIEMANN-PICK disease

Q4: Myelin consists (80%) of lipids which of the following is the main component?

a) cerebroside **b)** sphingosine **c)** phospholipids **d)** sphingomyelin

Q5: which of the following is wrong regarding sphingolipidoses?

a) Rare **b)** Due to increasing the synthesis of sphingolipids
c) An autosomal recessive disease **d)** Progressive

Q6: Which one of the following is the only significant sphingolipids in humans?

a) sphingomyelin **b)** cerebroside **c)** gangliosides **d)** ceramide

SAQs :

Q1: Ceramide is the precursor to which lipids?

Q2: What is multiple sclerosis?

Q3: Mention the diseases produced by sphingolipidoses and the deficient enzyme of each.

★ **MCQs Answer key:**

1) C 2) C 3) C 4) A 5) B 6) A

★ **SAQs Answer key:**

1) Sphingomyelin and glycosphingolipids
2) It is a neurodegenerative autoimmune diseases that occurs by the breakdown of myelin sheaths (demyelination) which leads to defective transmissions .of impulses.
3) - TAY SACHS DISEASE (β-Hexosaminidase)
- Gaucher disease (β-glucosidase (glucocerebrosidase).
- Niemann-pick disease (sphingomyelinase)

Team members

Girls Team:

- Ajeed Al-Rashoud
- ★ Alwateen Albalawi
- Amira AlDakhilallah
- Arwa Al Emam
- Deema Almaziad
- Ghaliah Alnufaei
- Haifa Alwaily
- Leena Alnassar
- ★ Lama Aldakhil
- ★ Lamiss Alzahrani
- Nouf Alhumaidhi
- Noura Alturki
- Sarah Alkhalife
- Shahd Alsalamah
- Taif Alotaibi

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- Alkassem Binobai
- Naif Alsolais
- Omar Alyabis
- Rayyan Almousa
- Sultan Alhammad
- Tariq Alanezi

Team Leaders

Lina Alosaimi

Mohannad Alqarni

★ إنَّ الذي خلق التعثر خلق النهوض

438 BIOCHEMISTRY TEAM

We hear you