

# **SPHINGOLIPIDS AND MYELIN STRUCTURE**

# 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 Sphingolipidoses.

# BACKGROUND

**There are two classes of phospholipids based on the backbone:**

- Glycerol (from glucose).
- Sphingosine (from serine and palmitate).

# BACKGROUND (*Cont'd...*)

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

e.g. Receptors for:

Cholera toxins

Diphtheria toxins

Viruses.

# BACKGROUND (*Cont'd...*)

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

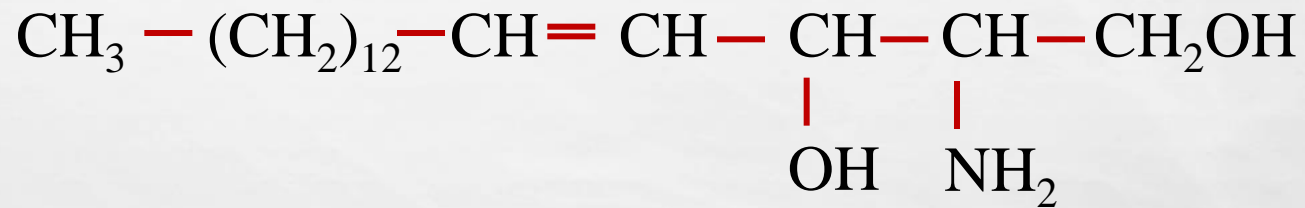
# KEY PRINCIPLES

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

# **SPHINGOLIPIDS: STRUCTURE AND TYPES**



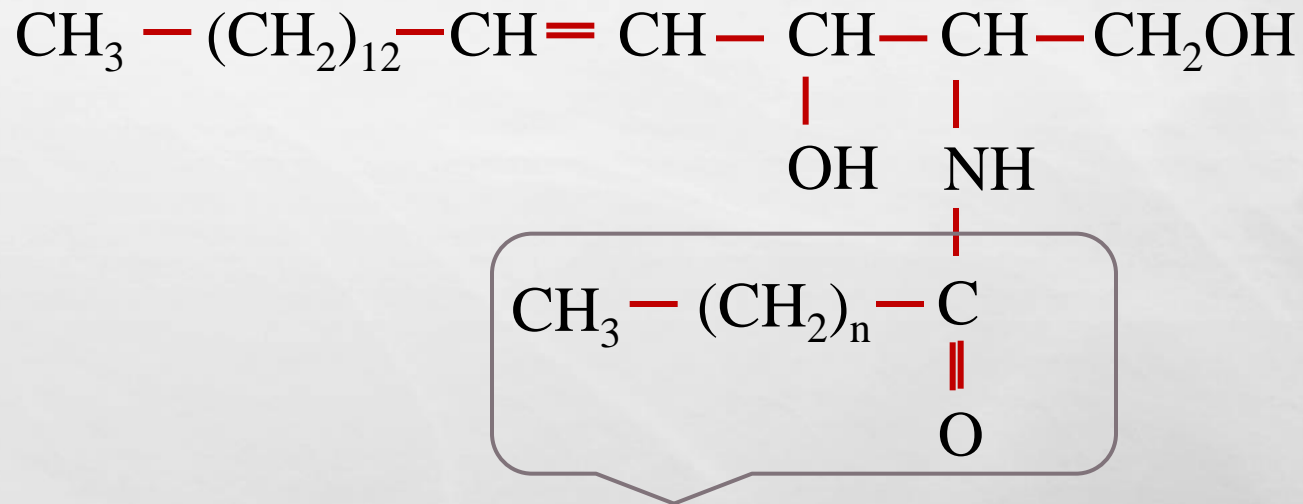
# SPHINGOSINE



Long chain, unsaturated amino alcohol

# CERAMIDE

**Ceramide** = Sphingosine + Fatty acid

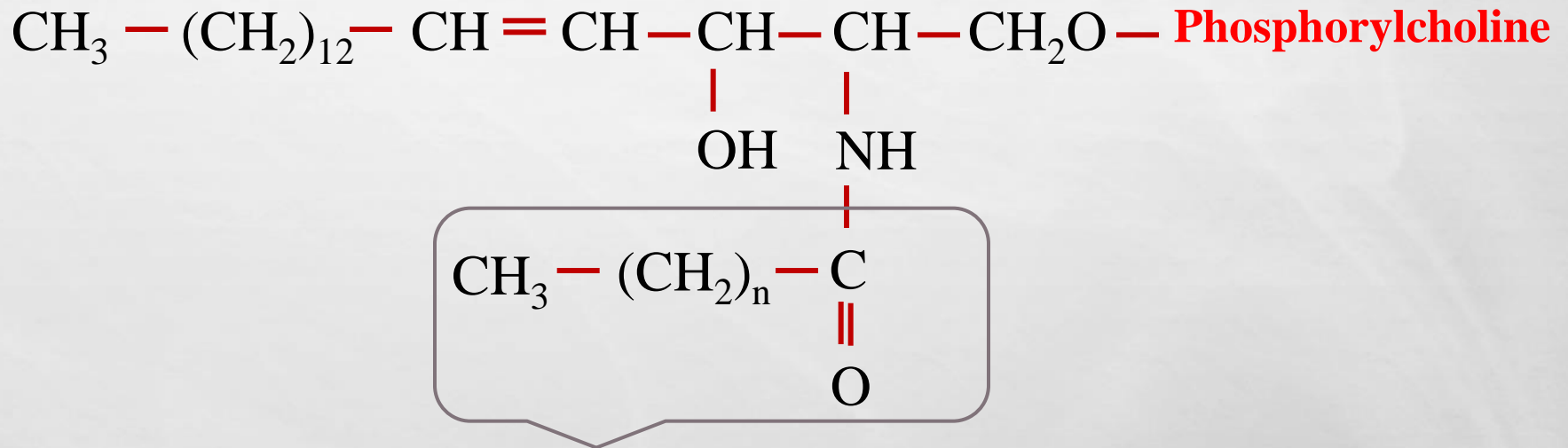


Long chain fatty acid

- *Ceramide play a key role in maintaining the skin's water-permeability barrier.*
- *Decreased ceramide levels are associated with a number of skin diseases.*

# SPHINGOMYELIN

**Sphingomyelin** = Ceramide + Phosphorylcholine



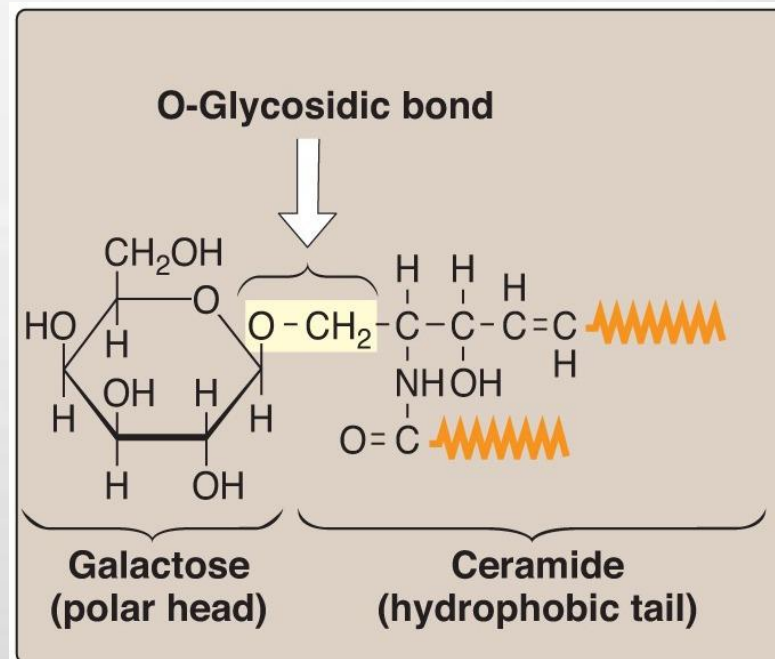
Long chain fatty acid

- Sphingomyelin is the only significant sphingolipid in humans*

# CEREBROSIDES

**Cerebrosides = Ceramide + Monosaccharides**

e.g. Galactocerebroside.



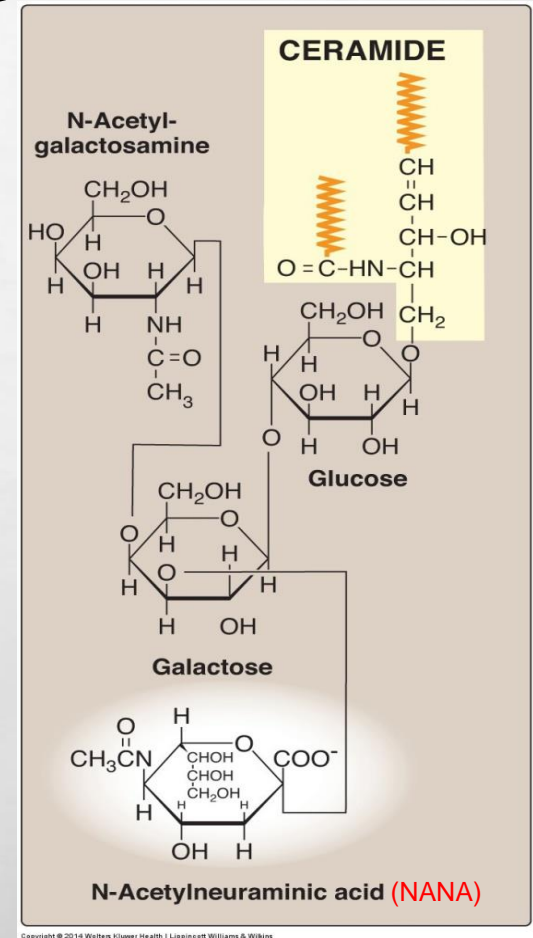
# GANGLIOSIDES

Gangliosides = Ceramide oligosaccharides

+

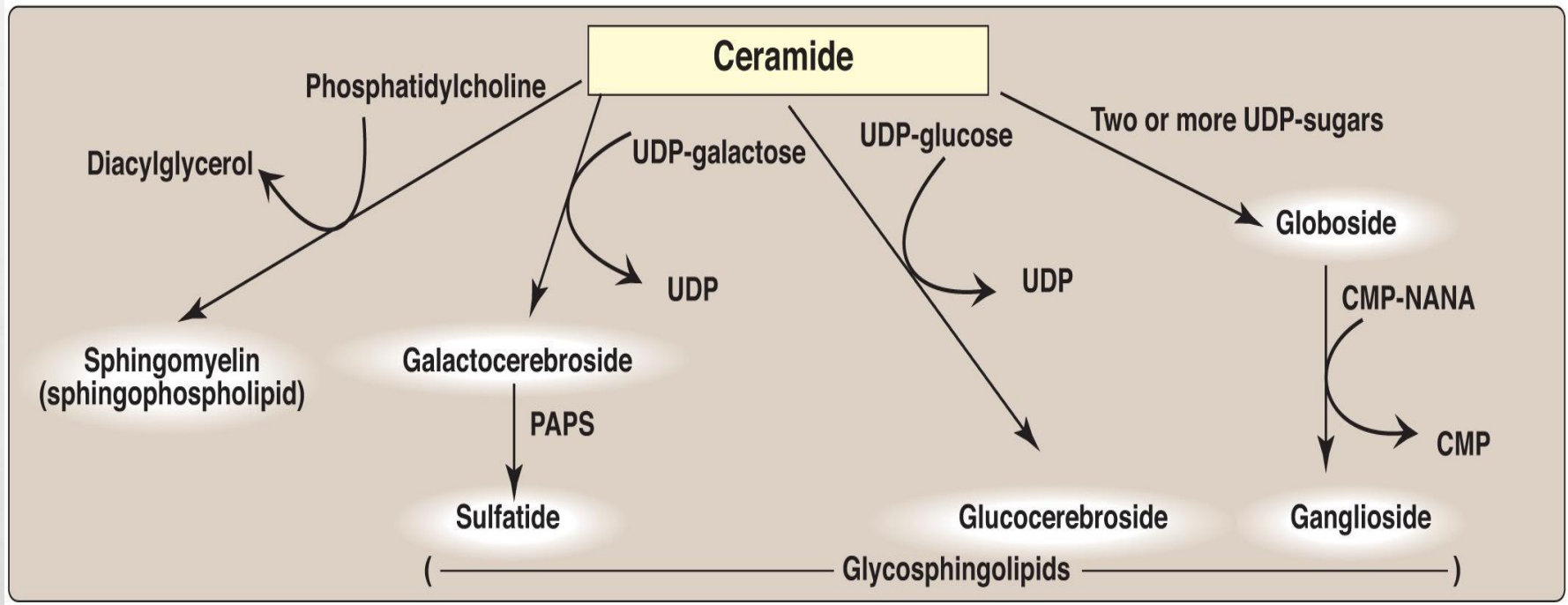
NANA

e.g.  $G_{M2}$ .



- For  $G_{M2}$ : G=ganglioside; M=mono molecule of NANA; 2=the monomeric sequence of the carbohydrate attached to the ceramide

# 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

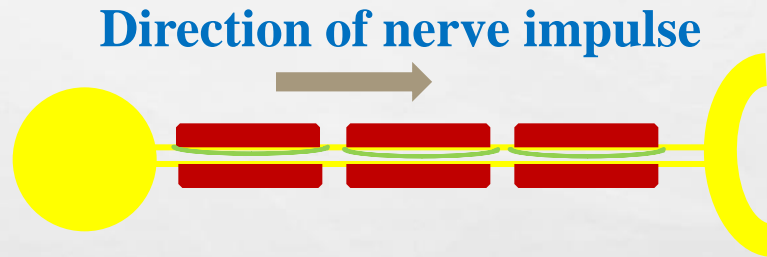
Lignoceric 24:0

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

- 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**.

# SPHINGOLIPIDOSES (*Cont'd...*)

- Synthesis (**Normal**); Degradation (**Defective**).
  - Substrate accumulates in organs..
  - Progressive, early death.
  - Phenotypic and genotypic variability.
  - Autosomal recessive (**mostly**).
  - Rare, **Except in** Ashkenazi Jewish.
- *Usually only a single sphingolipid accumulates in the involved organs in each disease*

# SPHINGOLIPIDOSES (*Cont'd...*)

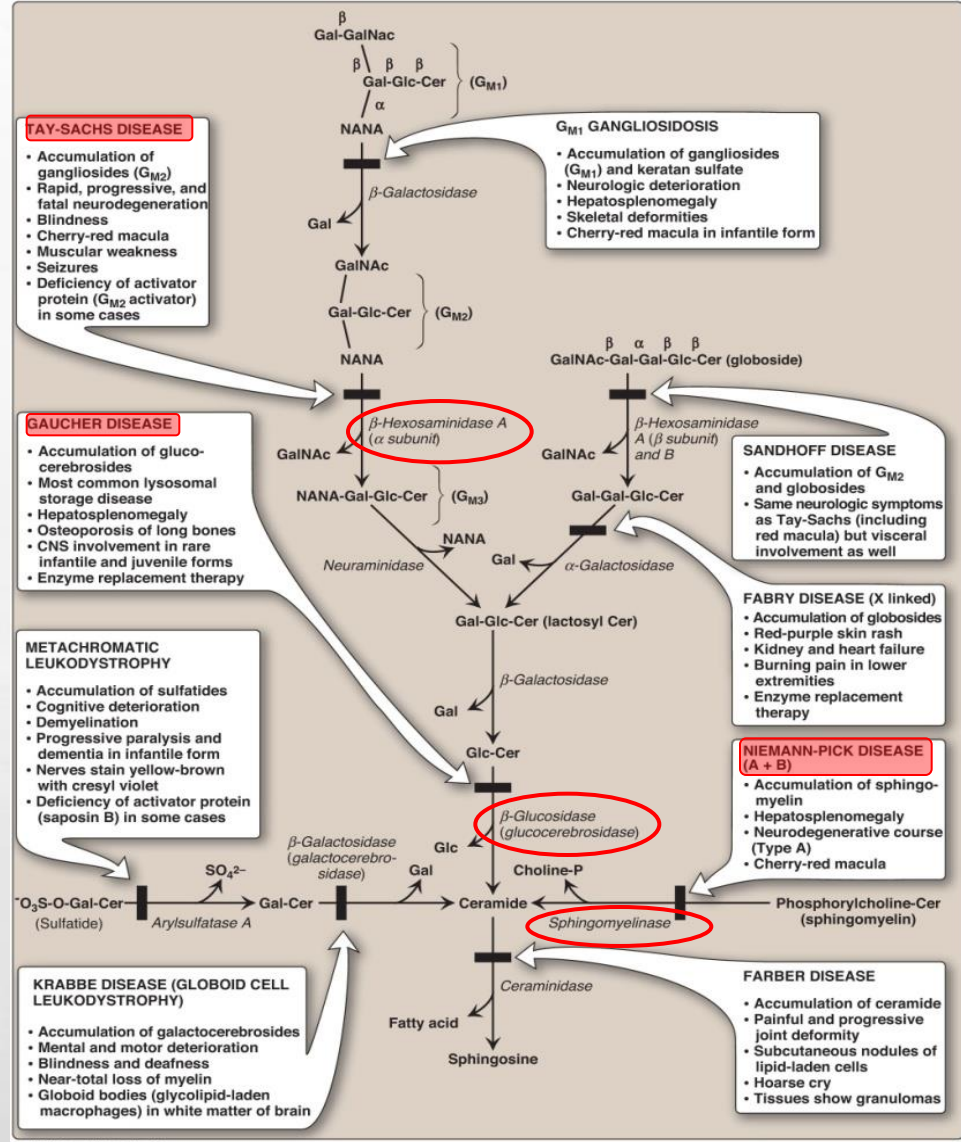
- **Diagnosis:**

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

- **Treatment: e.g. for Gaucher disease:**

- Replacement Therapy (e.g. recombinant human enzyme).
- Bone marrow transplantation.

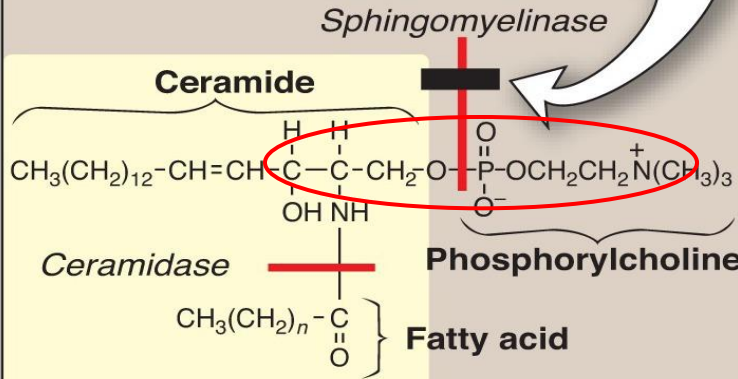
# SPHINGOLIPIDOSES



# NIEMANN-PICK DISEASE

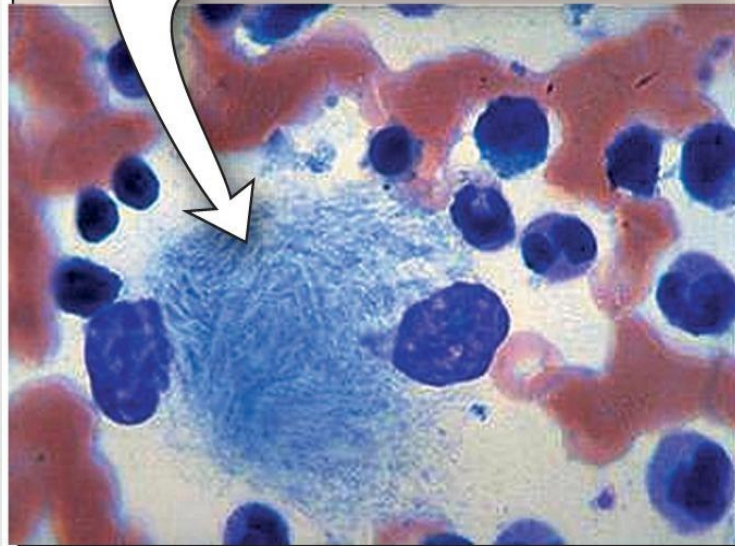
## NIEMANN-PICK DISEASE

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



# 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.
- Sphingolipidoses are rare genetic diseases due to defective degeneration of sphingolipids.



# REFERENCE

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