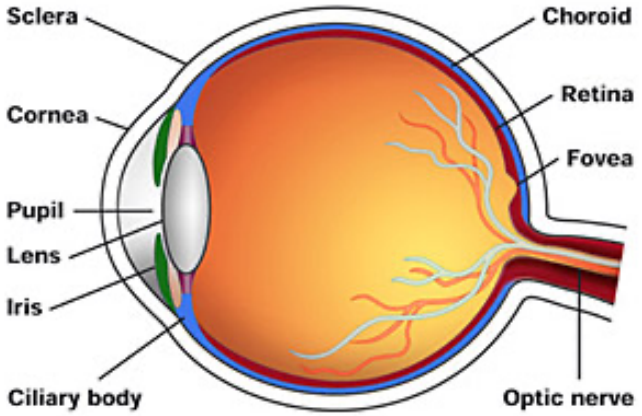
Vitamin A
& Visual Cycle



Neuropsychiatry Block
Dr. Usman Ghani
Biochemistry

1 Lecture

Objectives

By the end of this lecture the Second Year students will be able to:

- Identify the types of vitamin A and their functions.
- Discuss the transport and metabolism of vitamin A.
- Comprehend the role of vitamin A in visual cycle
- Correlate the deficiency of vitamin A with vision impairment and blindness

Overview

- Fat-soluble vitamins
- Biochemistry and types of vitamin A
- Absorption and transport
- Functions
- Functions in the visual cycle
- Deficiency and diseases

Vitamins

- Organic compounds present in small quantities in different types of food
- Help in various biochemical processes in cell
- Most act as coenzymes
- Important for growth and maintaining good health
- Essential
- Non-caloric
- Required in very small amounts

Vitamins - Classified Based on Solubility

- **Fat-Soluble Vitamins**
  - A, D, E, and K
- **Water-Soluble Vitamins**
  - ascorbic acid (vitamin C)
  - thiamin (vitamin B_1)
  - riboflavin (vitamin B_2)
  - niacin
  - pyridoxine (vitamin B_6)
  - biotin
  - pantothenic acid
  - folate
  - cobalamin (vitamin B_{12})

Fat-soluble Vitamins

- Stored in the liver and adipose tissue
- Excess may accumulate and cause toxicity
- Cases of toxicity with vitamin A and D have been reported
- Do not need to be consumed each day due to storage in the body
- Absorbed slowly with fats
- Diseases due to deficiency are rare as large amounts are stored in the body

Vitamin A from animal sources (Preformed)

- Three preformed compounds called retinoids that are metabolically active and found in animal products
  - retinol – alcohol form

  (can be converted to other forms)
  - retinal or retinaldehyde – aldehyde form

  (essential in vision)
  - retinoic acid – acid form

  (for skin and bone growth)

Vitamin A from plant sources (Provitamin)

- Carotenoids (β-carotene) and cryptoxanthin can yield retinoids when metabolized in the body
- These are from plant sources
- One molecule of β-carotene can be cleaved into two molecules of retinal in the intestine

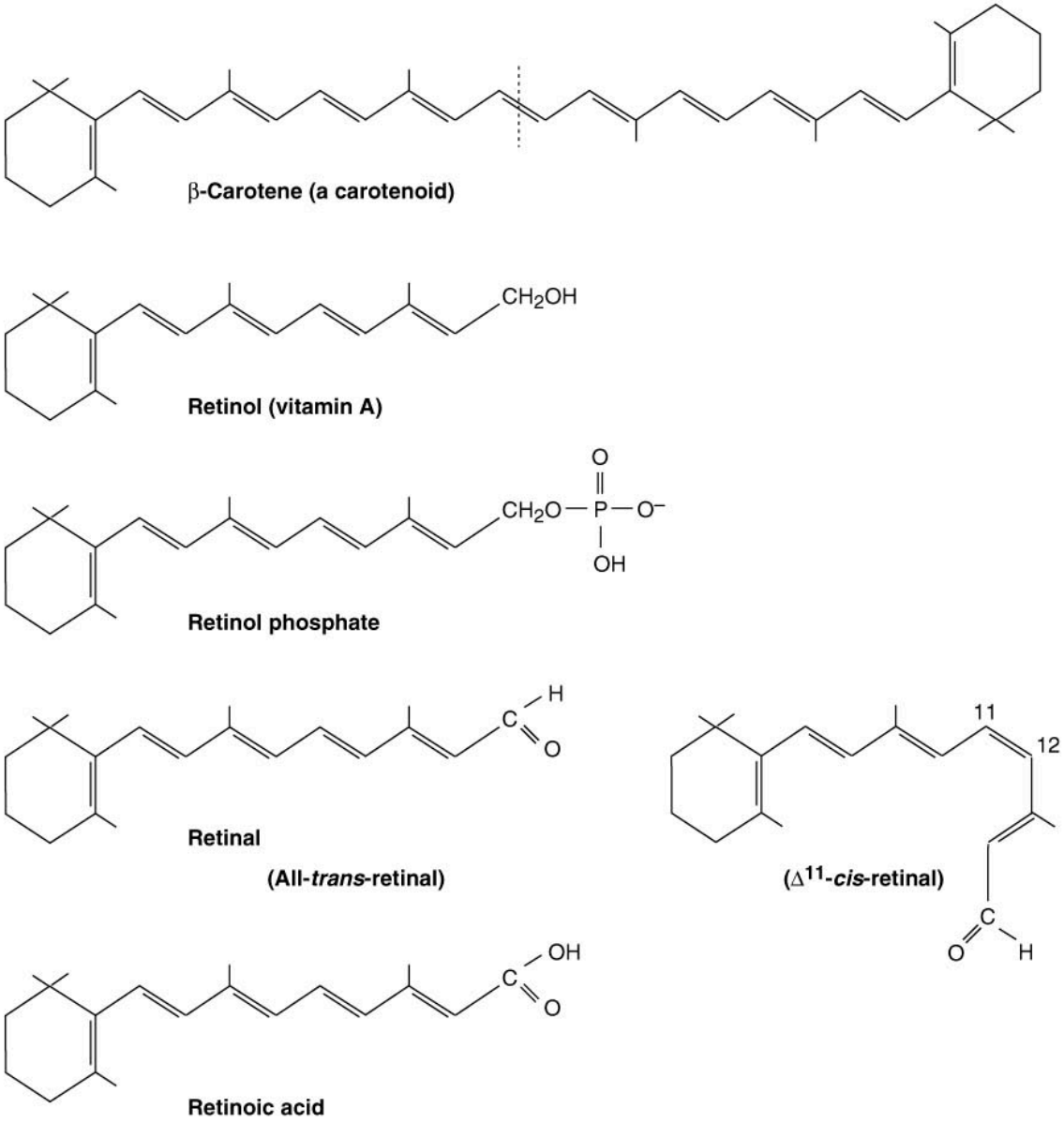
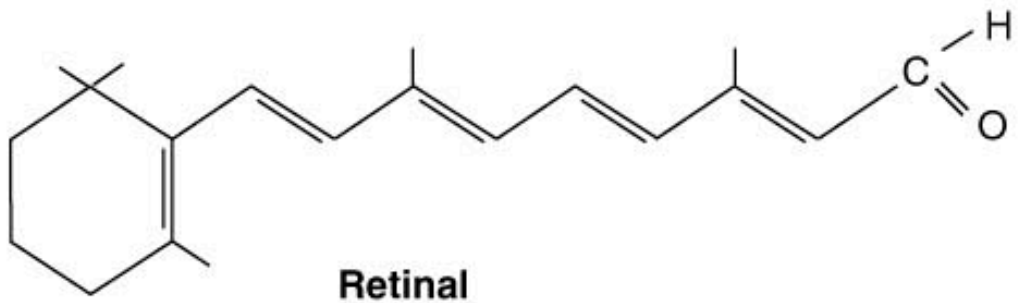
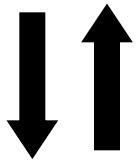


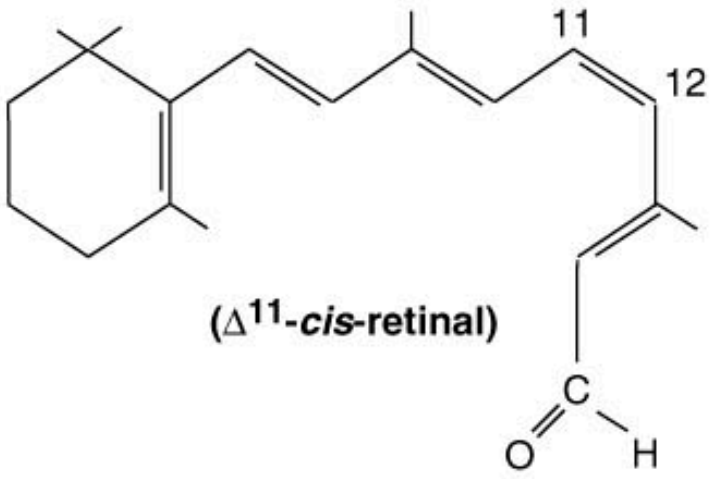
Figure 28.2. Structures of vitamin A and related compounds.



Retinal

(All-*trans*-retinal)





(Δ^{11}-*cis*-retinal)

Functions of Vitamin A

- Vision: Vitamin A is a component of the visual pigment rhodopsin. Retinal is bound to the protein opsin
- Growth: Vitamin A deficiency causes:
  - Loss of appetite
  - Slow bone growth
  - Affects CNS
- Reproduction: Retinol and retinal are essential for normal reproduction
- Maintenance of epithelial cells: Essential for normal differentiation of epithelial tissues and mucus secretion

Functions of Vitamin A

- Vision
- Gene transcription
- Immune function
- Embryonic development and reproduction
- Bone metabolism
- Skin health
- Antioxidant activity

Vitamin A

- Essential role in vision and normal cell differentiation
- Deficiency is the most significant cause of blindness in the developing world
- Large doses over a prolonged period of time can produce intoxication and eventually lead to liver disease
- Excessive carotenoids intake can result in yellowing of the skin, but appears to be harmless

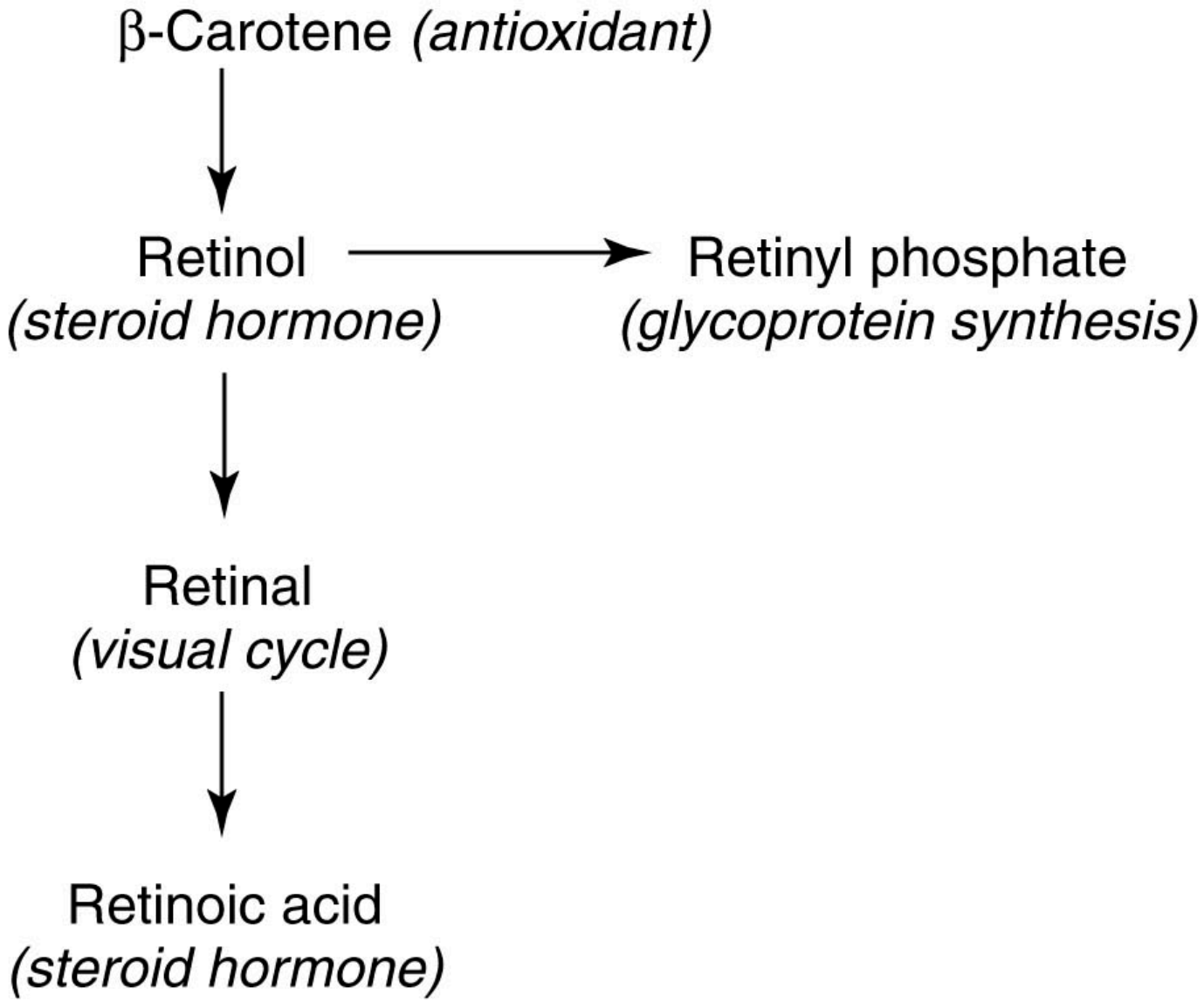
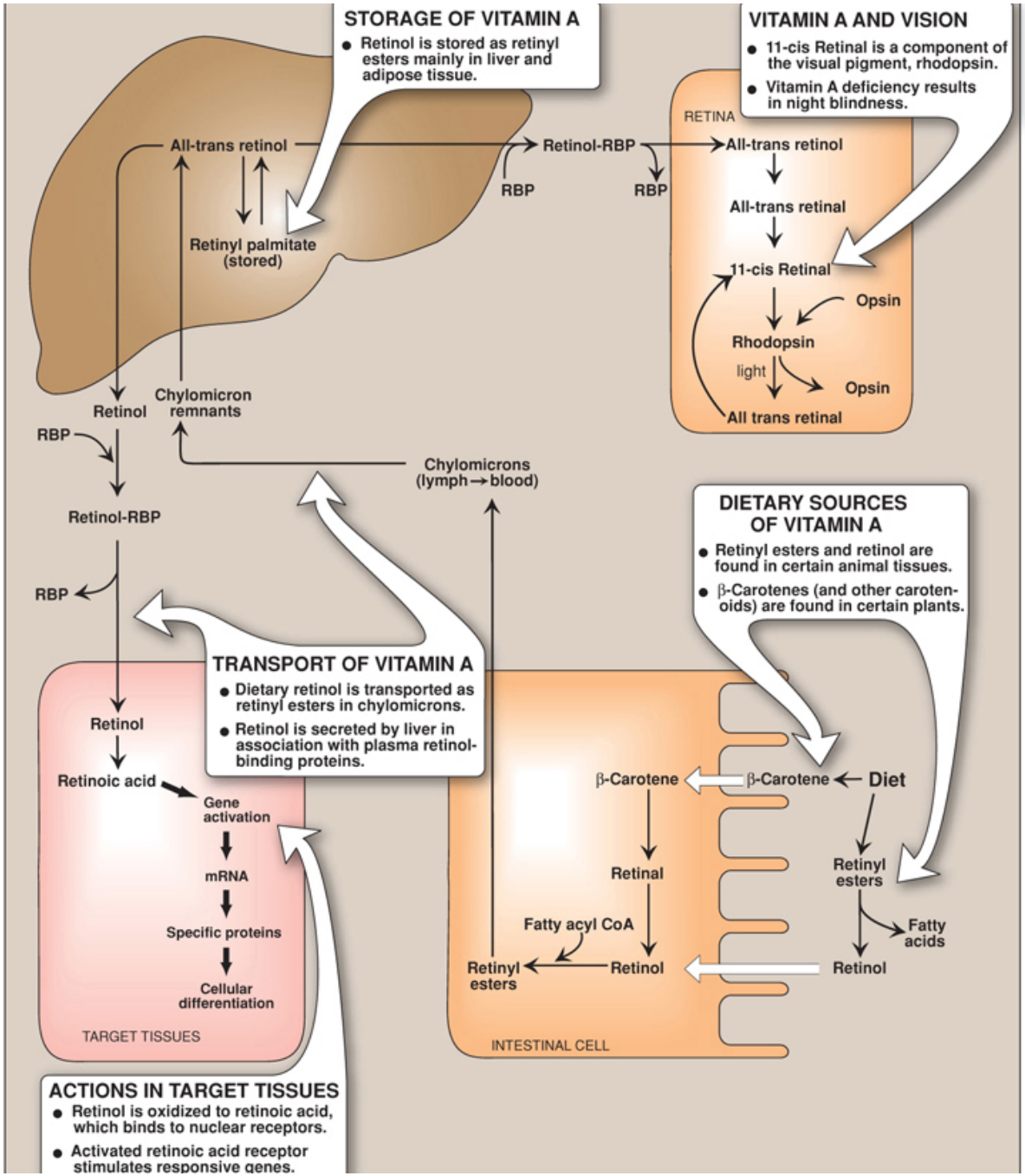
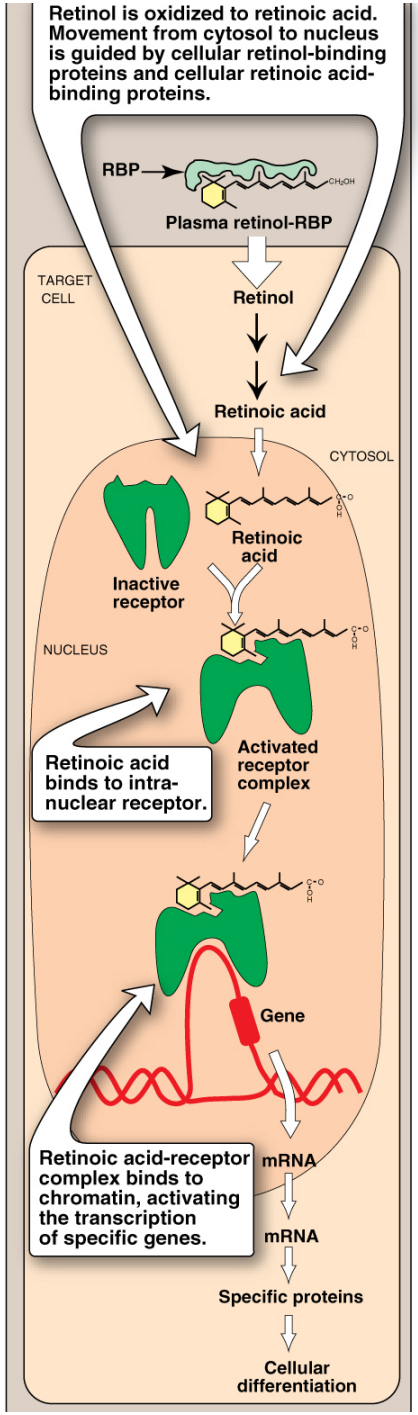


Figure 28.3. Vitamin A metabolism and function.


STORAGE OF VITAMIN A
Retinol is stored as retinyl esters mainly in liver and adipose tissue.
VITAMIN A AND VISION
11-cis Retinal is a component of the visual pigment, rhodopsin.
Vitamin A deficiency results in night blindness.
All-trans retinol
Retinol-RBP
RBP
RBP
Retinyl palmitate (stored)
RETINA
All-trans retinol
All-trans retinal
11-cis Retinal
Opsin
Rhodopsin
light
Opsin
All trans retinal
Retinol
Chylomicron remnants
RBP
Chylomicrons (lymph → blood)
Retinol-RBP
RBP
DIETARY SOURCES OF VITAMIN A
Retinyl esters and retinol are found in certain animal tissues.
β-Carotenes (and other carotenoids) are found in certain plants.
TRANSPORT OF VITAMIN A
Dietary retinol is transported as retinyl esters in chylomicrons.
Retinol is secreted by liver in association with plasma retinol-binding proteins.
Retinol
Retinoic acid
Gene activation
mRNA
Specific proteins
Cellular differentiation
TARGET TISSUES
β-Carotene
β-Carotene
Diet
Retinal
Retinyl esters
Fatty acids
Fatty acyl CoA
Retinyl esters
Retinol
Retinol
INTESTINAL CELL
ACTIONS IN TARGET TISSUES
Retinol is oxidized to retinoic acid, which binds to nuclear receptors.
Activated retinoic acid receptor stimulates responsive genes.


Retinol is oxidized to retinoic acid. Movement from cytosol to nucleus is guided by cellular retinol-binding proteins and cellular retinoic acid-binding proteins.
RBP
CH2OH
Plasma retinol-RBP
TARGET CELL
Retinol
Retinoic acid
CYTOSOL
Retinoic acid
Inactive receptor
NUCLEUS
Activated receptor complex
Retinoic acid binds to intra-nuclear receptor.
Gene
Retinoic acid-receptor complex binds to chromatin, activating the transcription of specific genes.
mRNA
mRNA
Specific proteins
Cellular differentiation

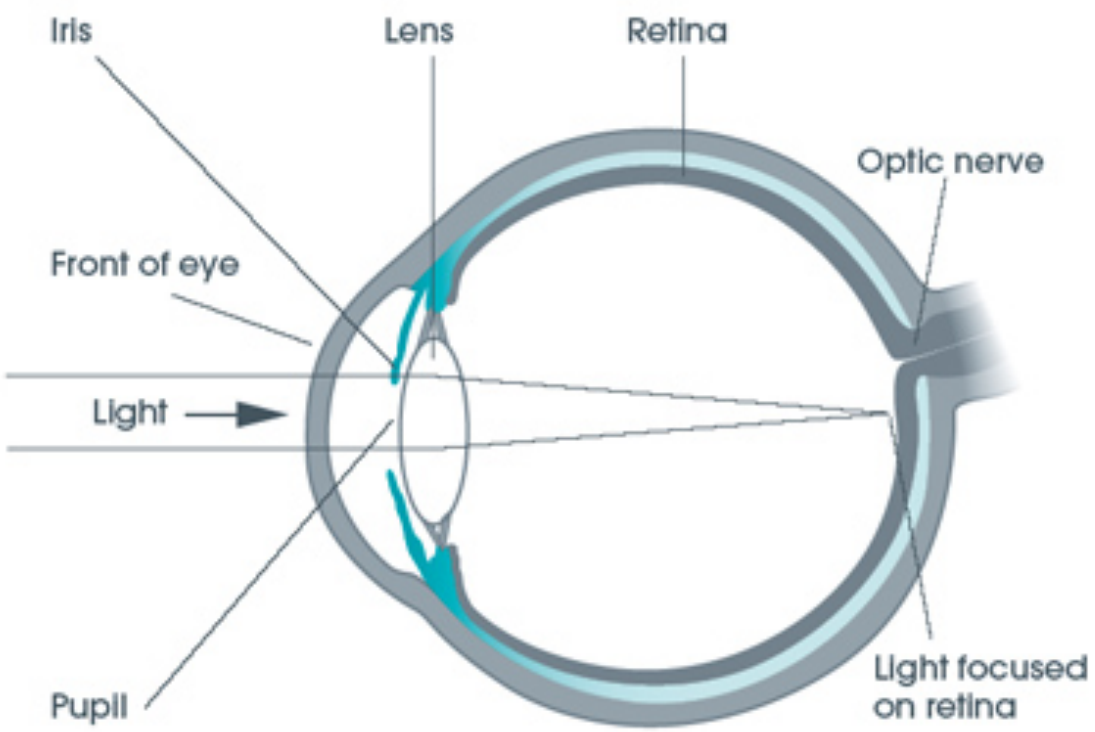
Role of Vitamin A in Vision

Visual Cycle

- A process by which light impacting on the retina of the eye is converted to an electrical signal
- The optic nerve carries the electrical signal to the brain (nerve impulse)
- The brain processes the signal into an image

Role of Vitamin A in Vision

- Retina is a light-sensitive layer of cells at the back of the eye where an image is formed
- Retina consists of: Rod and cone cells (photosensitive cells)
- Rod cells process black & white image
- Cone cells process color image


Iris
Lens
Retina
Optic nerve
Front of eye
Light
Pupil
Light focused
on retina

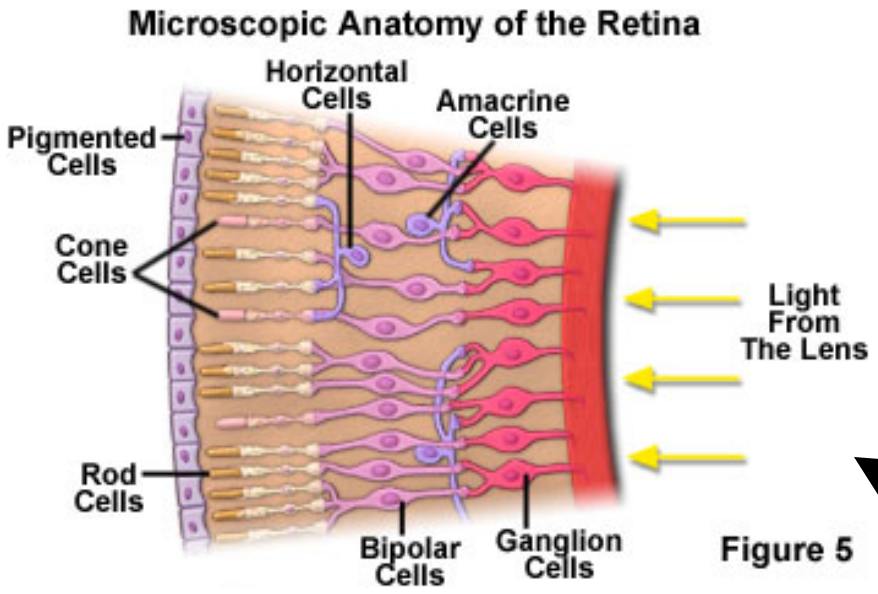
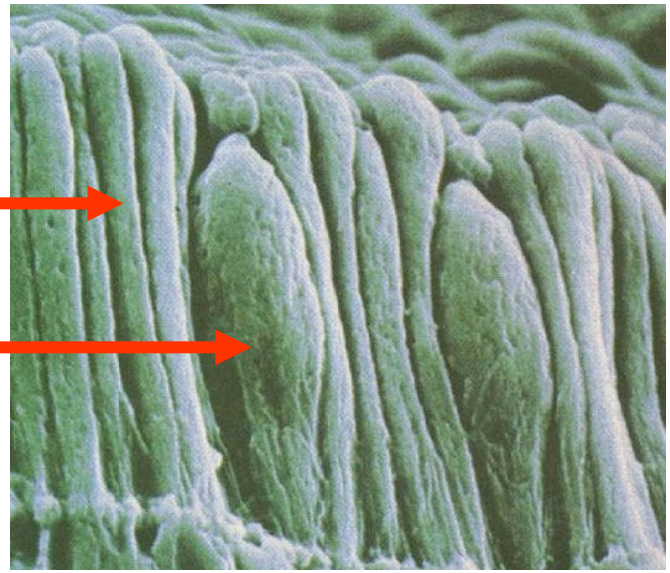
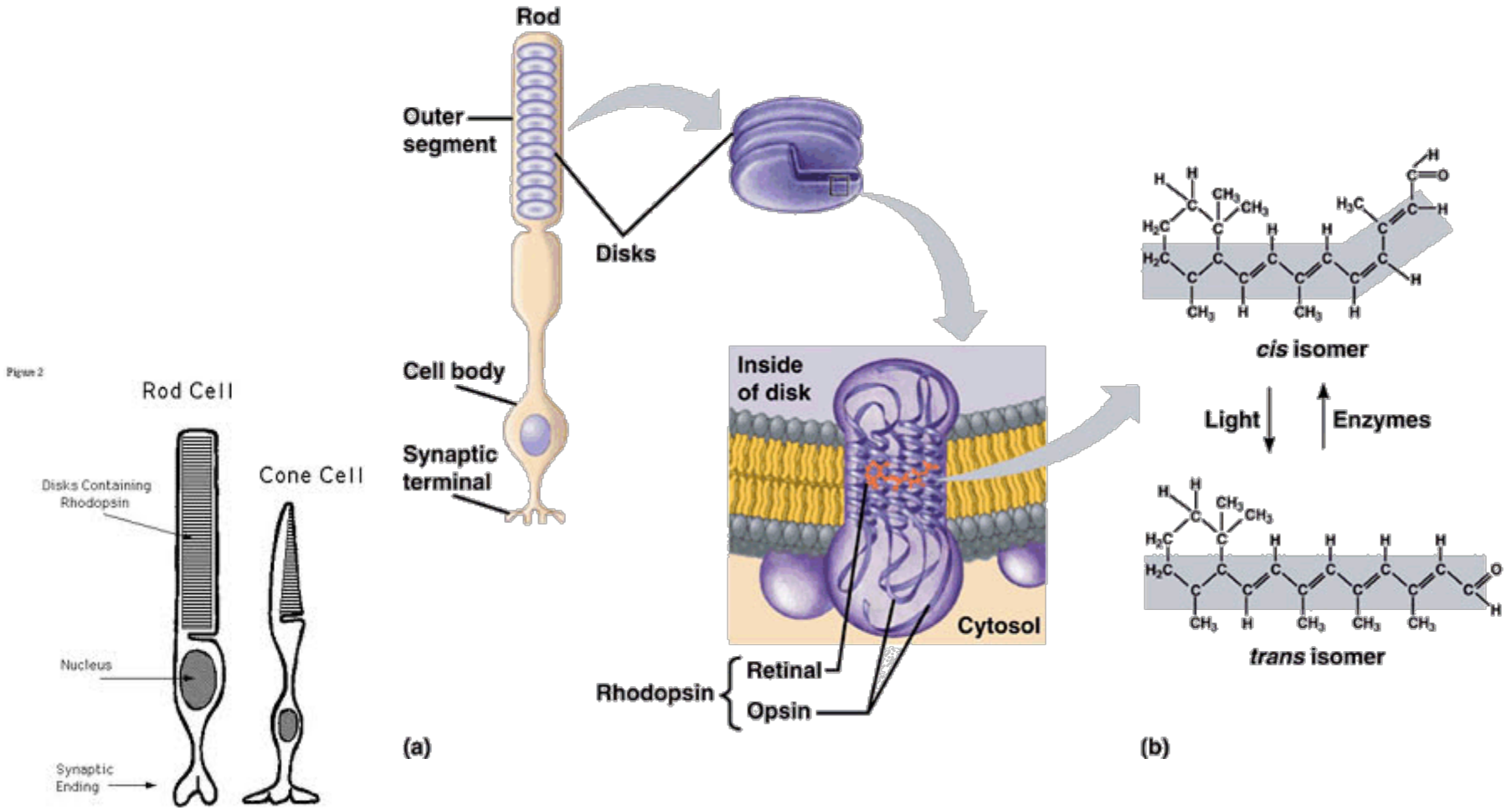

Microscopic Anatomy of the Retina
Horizontal Cells
Amacrine Cells
Pigmented Cells
Cone Cells
Light From The Lens
Rod Cells
Bipolar Cells
Ganglion Cells

Figure 5


Rod Cell
Cone Cell

Rhodopsin and retinal structures



Role of Vitamin A in Vision

- Normal vision depends on the retina and on adequate vitamin A
- First discovered by George Ward in 1967 (a Nobel Laureate)
- In the retina, vitamin A in the form of retinal binds to a protein called opsin to make rhodopsin (in rod cells) and iodopsin (in cone cells)
- Rhodopsin and iodopsin are light-sensitive pigments

Role of Vitamin A in Vision

- When stimulated by light vitamin A isomerizes from its bent ‘cis’ form to a straighter ‘trans’ form and detaches from opsin
- The opsin molecule changes shape, which sends a signal to the brain via optic nerve and an image is formed
- Most retinal released in this process is quickly converted to trans-retinol and then to cis-retinal, to begin another cycle

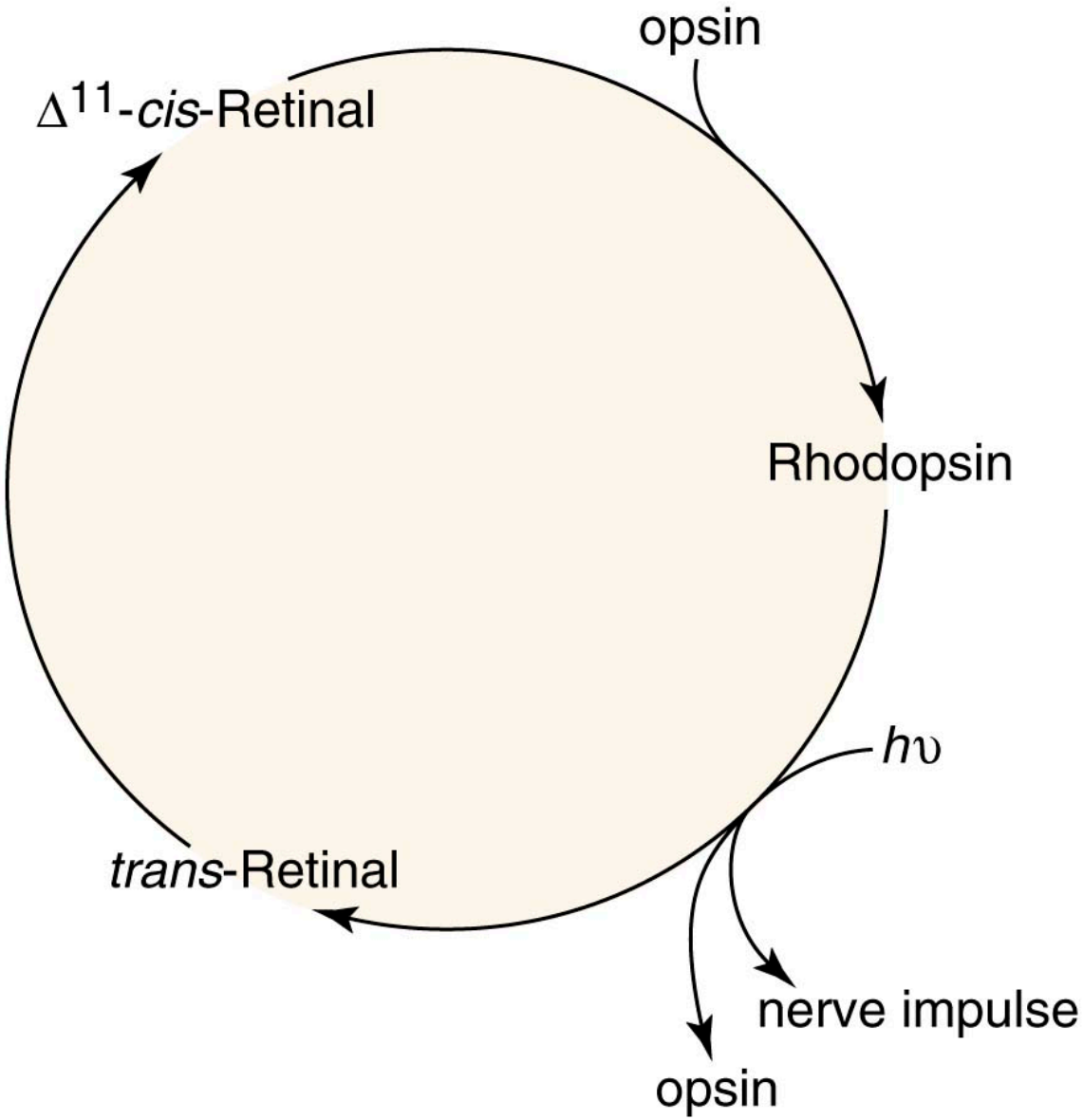


Figure 28.4. Role of vitamin A in vision.

Role of Vitamin A in Vision

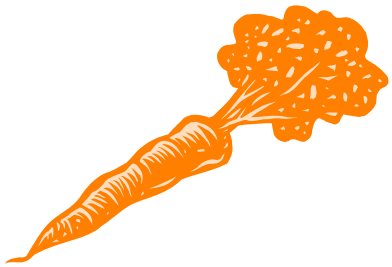
Dark Adaptation time

- Bright light depletes rhodopsin (photobleaching)
- Sudden shift from bright light to darkness causes difficulty in seeing
- Rhodopsin is synthesized in a few minutes and vision is improved in the dark

Role of Vitamin A in Vision

- The time required to synthesize rhodopsin in the dark is called dark adaptation time
- It is increased in vitamin A deficiency

Recommended Dietary Allowance (RDA)
Vitamin A for Adults



- **Women: 700 µg or 2,330 IU µg**
- **Men: 900 µg or 3,000 IU**
- **UL Men or Women: 3,000 µg or 10,000 IU**

Vitamin A Deficiency and Diseases

- Nyctalopia (night blindness): patient cannot see in low light or near darkness conditions
- Xerophthalmia: dryness of the conjunctiva and cornea
- Bitot's spots: localized increased thickness of the conjunctiva

Vitamin A Deficiency and Diseases

- Keratomalacia: prolonged xerophthalmia leads to drying and clouding of cornea

- Complete blindness (in severe deficiency)

Take-home message

- Vitamin A plays a major role in visual cycle and color vision.
- Its deficiency can lead to vision impairment and blindness.

References

Lippincott's Biochemistry, 5th Edition
pp 381-384, Lippincott Williams & Wilkins
New York, NY, USA.