
Secret Getaway


بسم الله الرحمن الرحيم

VITAMINS

BY

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Vitamins

Vitamins are organic compounds characterized by:

- Essential for normal health and growth.
- Essential for biological activity in the body.
- Present in food in very small concentration.
- Not enter in the tissue structure as carbohydrates, lipids and proteins.

- Act as catalysts and are not oxidized to give energy as carbohydrates, lipids and proteins.
- Deficiency of any vitamin in the body results in production of specific diseases.
- Many vitamin function as coenzymes.
- Not synthesized in the body by anabolic reaction, therefore should be taken in the diet.
- Some vitamin are present in food in the form of provitamins.

Provitamin

They are vitamin precursors.

Example:

- Carotenes are provitamin A.
- 7- dehydrocholesterol are provitamin D_3

Vitamer

When a vitamin is present in more than one chemical formula each is called a vitamers

Example:

- Vitamin A has Two vitamers A1 and A2.
- Vitamin D has two vitamers D2 and D3.
- Vitamin E has four vitamers alpha, beta, gama, delta.

Vitagen

These include both essential Amino acids and essential fatty acids.

Classification of vitamins

Vitamins can be classified according to their solubility and their function in metabolism into:

I- Fat soluble vitamins

II- Water soluble vitamins

I- Fat Soluble Vitamins

- **Vitamin A**
- **Vitamin D**
- **Vitamin E**
- **Vitamin K**

II-WATER SOLUBLE VITAMINS

I- B- complex

- **Thiamine (B_1)**
- **Riboflavin (B_2)**
- **Niacin (B_3)**
- **Folic acid**
- **Pyridoxine (B_6)**
- **Vitamin B_{12}**
- **Pantothenic Acid**
- **Biotin**

II- Non B- complex :

Vitamin C (ascorbic acid).

B- complex

a- Energy-releasing.

- **Thiamine (B_1)**
- **Riboflavin (B_2)**
- **Niacin (B_3)**
- **Biotin**
- **Pantothenic Acid**

b- Hematopoietic.

- **Folic acid**
- **Vitamin B_{12}**

c- Other.

- Pyridoxine (B6), pyridoxal, pyridoxamine

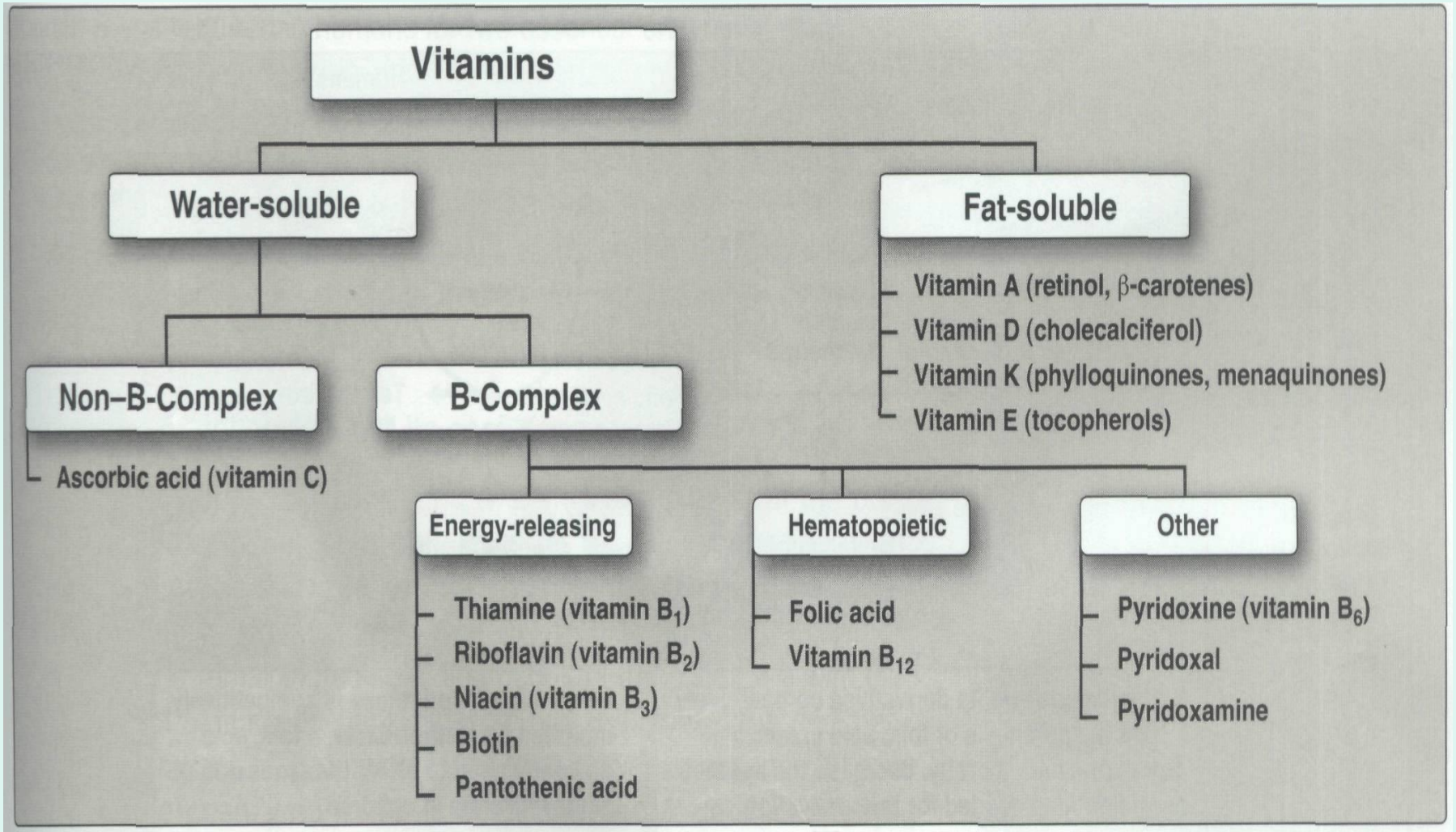


Figure 28.1
Classification of the vitamins.

	Fat soluble vitamins	Water soluble vitamins
Absorption	First into lymph and then into blood	Directly into blood
Storage	Stored in the liver and in fat	Not stored in the body (except vit B12)
Toxicity	Excess intake leads to toxic manifestation	Toxicity is rarely seen because they can be excreted in urine

RECOMMENDED DAILY ALLOWANCE (RDA)

Amount of the vitamin needed daily to maintain good nutrition in most healthy people.

FAT SOLUBLE VITAMINS

Objectives to learn:

- Chemistry
- Sources
- Biochemical functions
- Recommended daily allowance
- Deficiency manifestations [Hypovitaminosis]

VITAMIN A

Vitamin A

Synonyms:

- Anti-night blindness vitamin

Or

- Anti-xerophthalmic vitamin

Vitamin A

Structure:

- Vitamin A does not occur in plants, but many plants contain **carotenoids such as beta-carotene** that can be converted to vitamin A within the intestine and other tissues.

The term retinoids includes both natural and synthetic forms of vitamin A that may or may not show vitamin A activity.

RETINOIDS

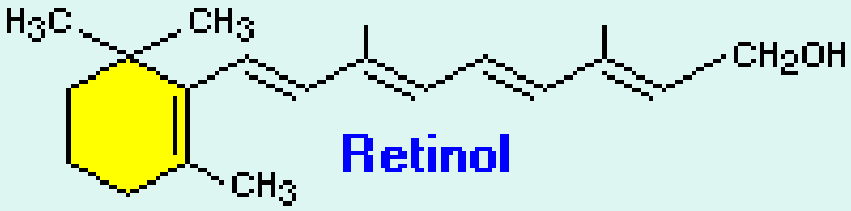
- A family of molecules that are related to retinol (vitamin A), are essential for vision, reproduction, growth, and maintenance of epithelial tissues. **Retinoic acid,** derived from oxidation of dietary retinol, mediates most of the actions of the retinoids, except for vision, which depends on **retinal,** the aldehyde derivative of retinol.

- **Retinol:** A primary alcohol containing a B-ionone ring with an unsaturated side chain. It is found in animal tissues as retinyl ester with long-chain fatty acids.

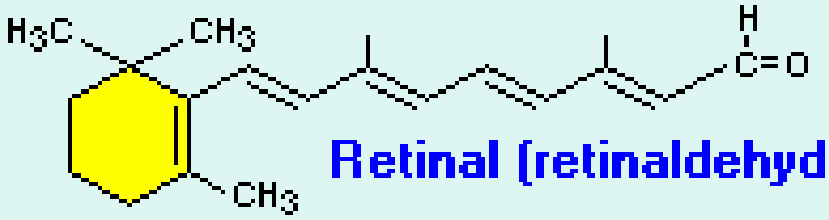
- **Retinal:** The aldehyde derived from the oxidation of retinol. Both are readily interconverted.

- B-carotene (provitamin A): It is present in plant foods, which can be oxidatively cleaved in the intestine to yield two molecules of retinal.

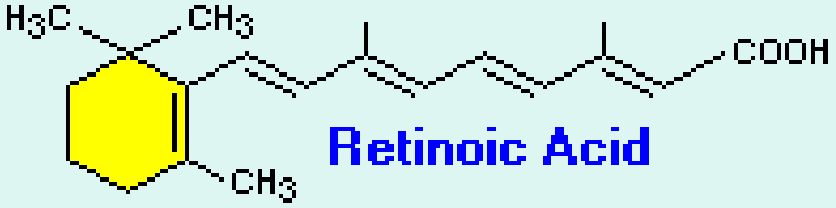
- **Retinoic acid:** The acid derived from oxidation of retinal. It cannot be reduced in the body so cannot give rise to retinol or retinal.



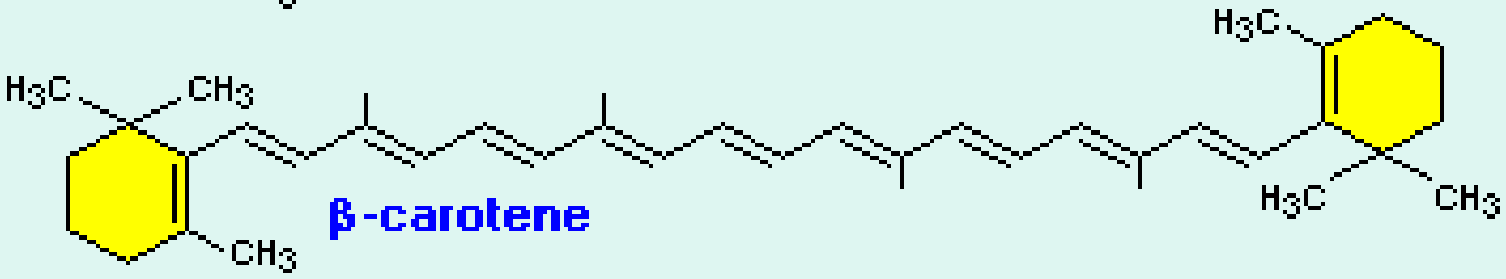
Retinol



Retinal (retinaldehyde)



Retinoic Acid



β-carotene

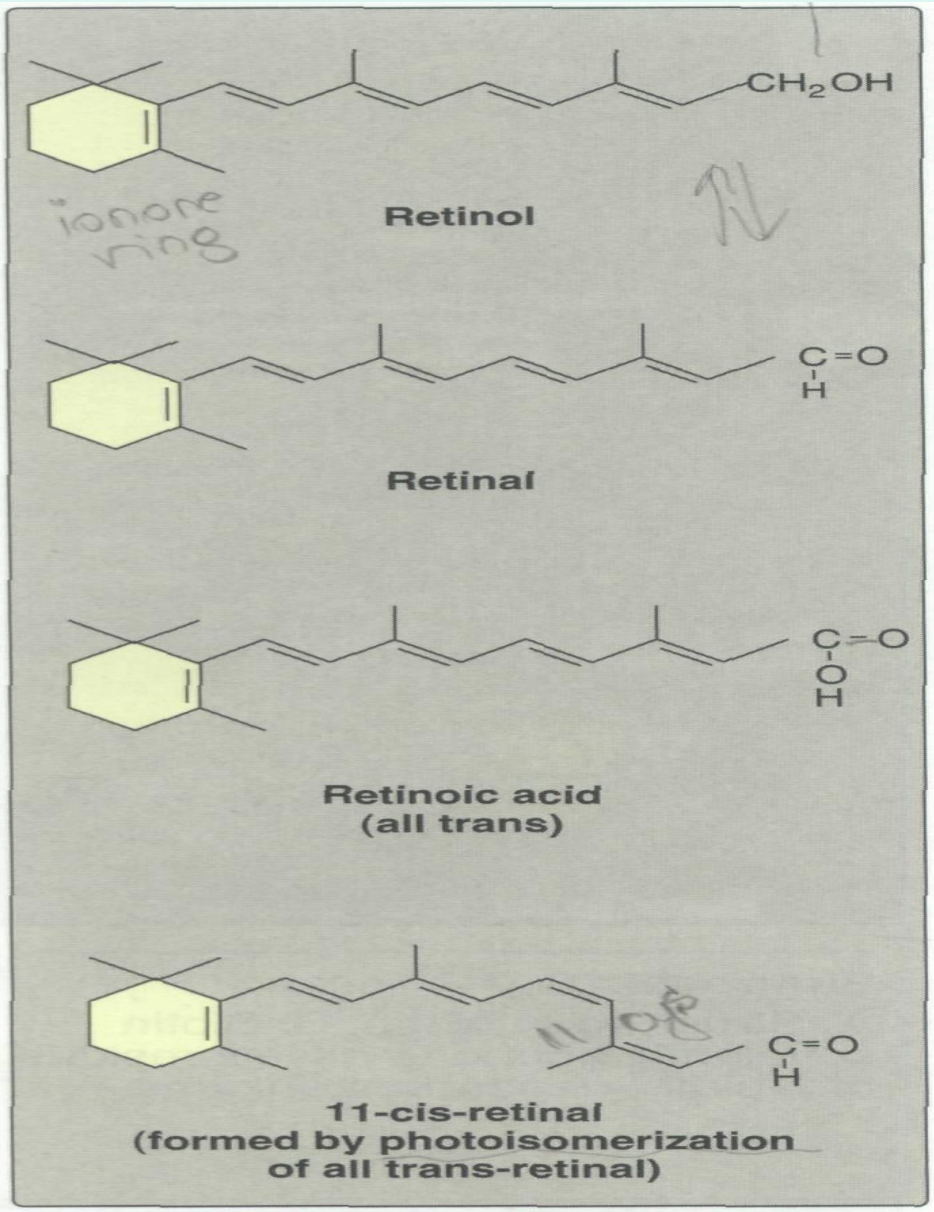


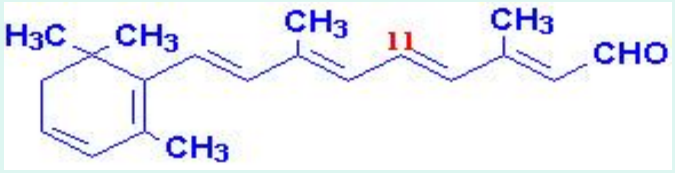
Figure 28.18
Structure of the retinoids.

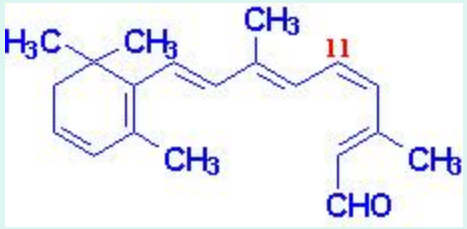
Vitamin A

Vitamin A consists of three biologically active molecules,

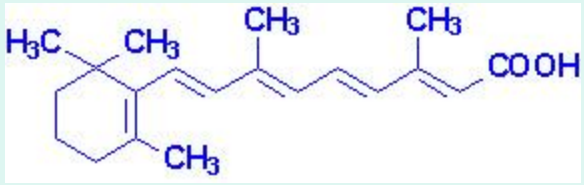
retinol, retinal (retinaldehyde) and **retinoic acid.**

- **All-*trans*-retinal** **11-*cis*-retinal**

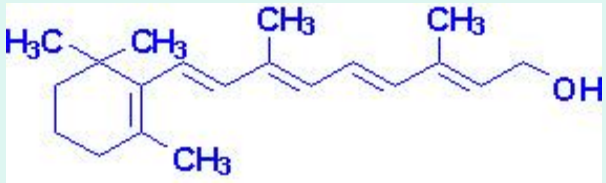




Retinoic Acid



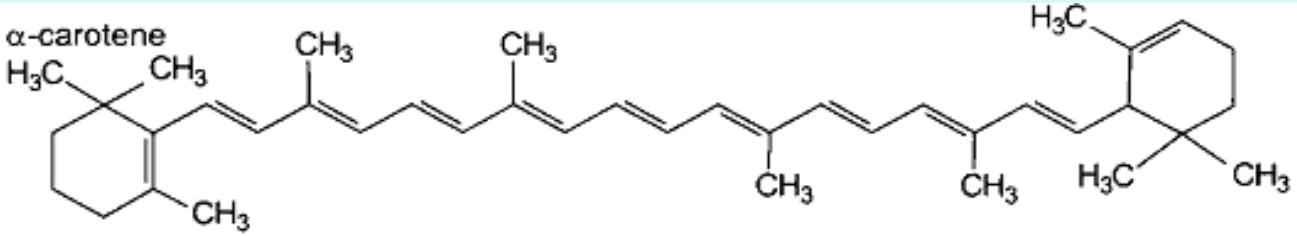
Retinol



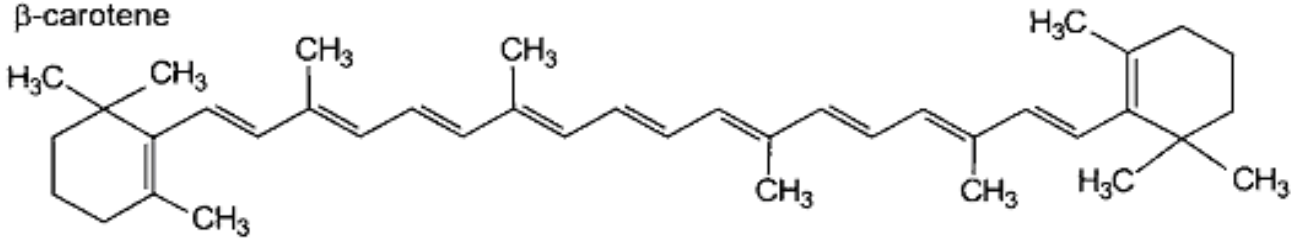
Chemistry of Vitamin A

- The provitamin or precursors of vit. A are carotenoids α, ß, ɣ carotene and cryptoxanthine containing ß -ionone ring.
- All carotenes are formed from two ring (A and B ring) connected together by 18 carbon atoms.
- A ring in all carotenes is ß -ionone ring.
- At the other B ring end there is:
- α-ionone ring in α-carotene.
- ß-ionone ring in ß-carotene.
- ɣ-ionone ring in ɣ-carotene.
- Hydroxy ß-ionone ring in cryptoxanthine.

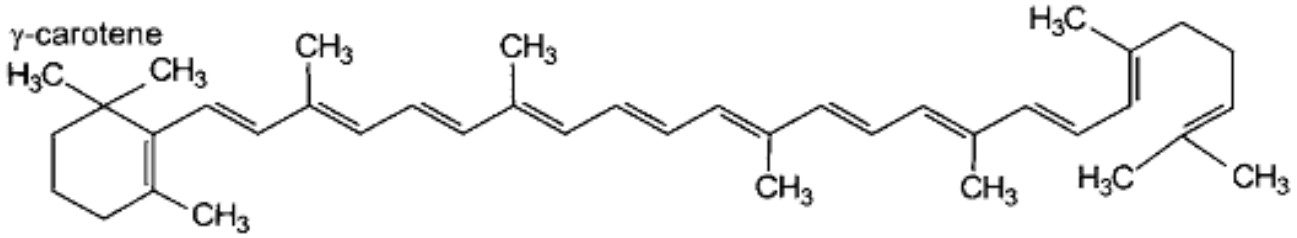
α-carotene



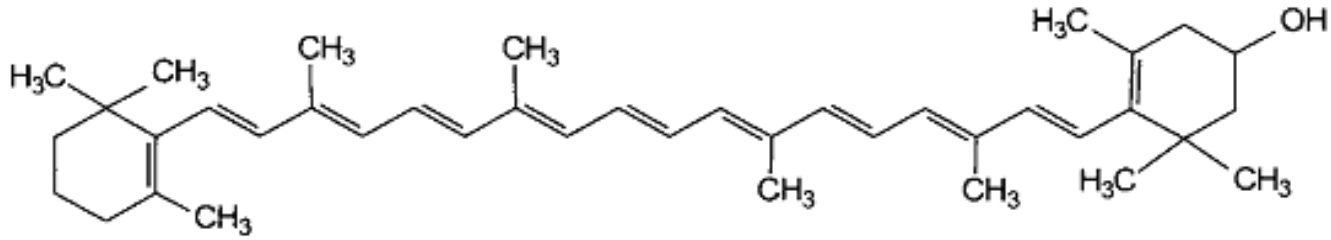
β-carotene



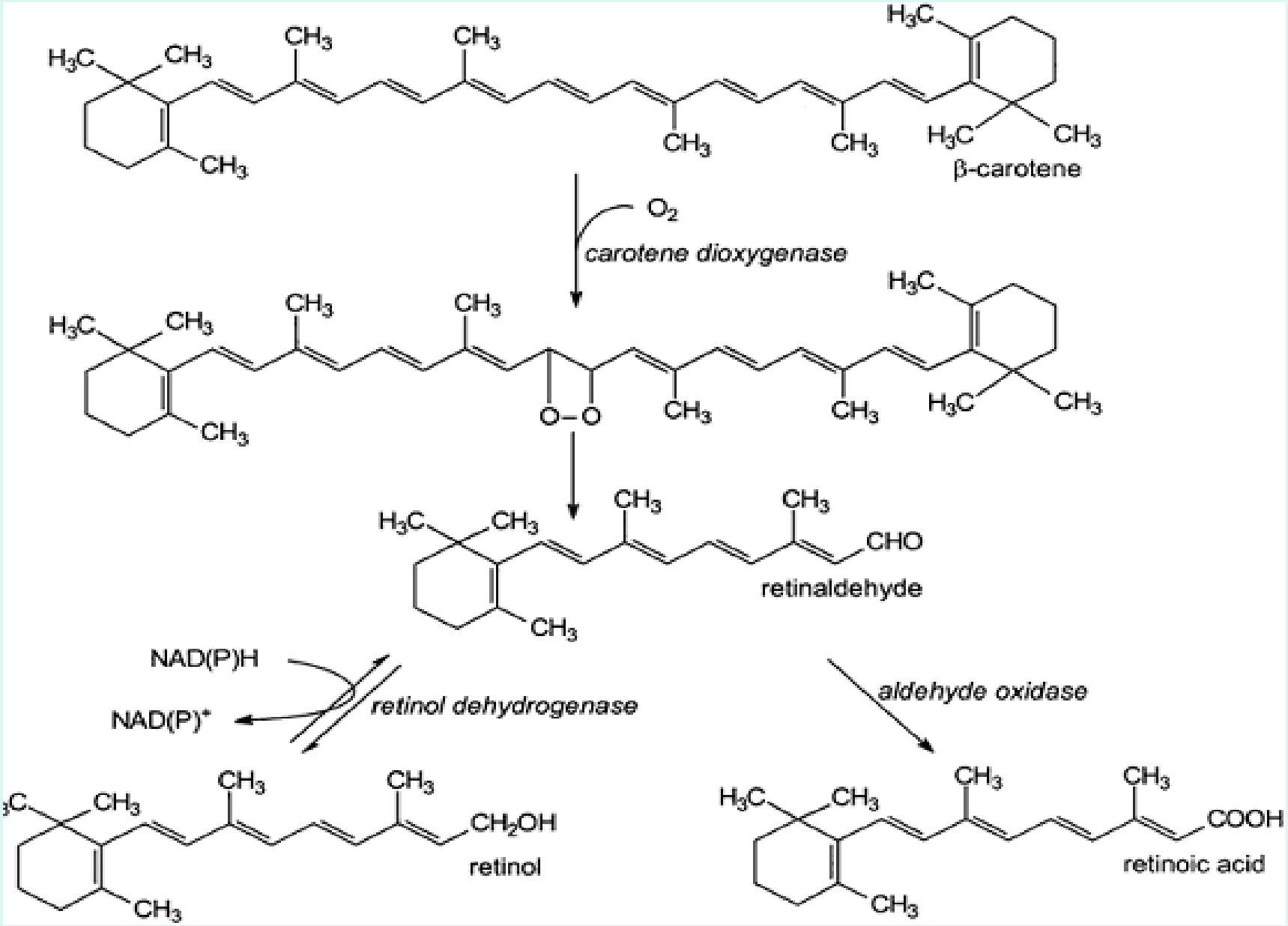
γ-carotene



β-cryptoxanthine (3-hydroxy-β-carotene)



- Carotenes by carotenase → give vitamin A aldehyde(retinal) by oxidation of the central double bond.
- Retinal by reduction → give vitamin A alcohol(retinol).
- ß-carotene is the most useful type give two molecules of vitamin A1(because it is asymmetrical molecule) while the other give only one molecule of vitamin A1.


β-carotene
O2
carotene dioxygenase
retinaldehyde
NAD(P)H
NAD(P)+
retinol dehydrogenase
aldehyde oxidase
retinol
retinoic acid

Absorption and transport of vitamin A

Transport to the liver:

- **Retinol esters present in the diet are hydrolyzed in the intestinal mucosa, releasing retinol and free fatty acids.**

- **Retinol derived from esters and from the cleavage and reduction of carotenes is reesterified to long-chain fatty acids in the intestinal mucosa and secreted as a component of chylomicrons into the lymphatic system.**
- **Retinol esters contained in chylomicrons are taken up by, and stored in, the liver.**

Release from the liver:

- **Retinol** is released from the liver and transported to extrahepatic tissues by the **plasma retinol-binding protein** (RBP).
- The complex attaches to specific receptors on the surface of the cells of peripheral tissues, permitting retinol to enter.

- Many tissues contain a **cellular retinol-binding protein** that carries retinol to sites in the nucleus where the vitamin acts in a manner analogous to steroid hormones.

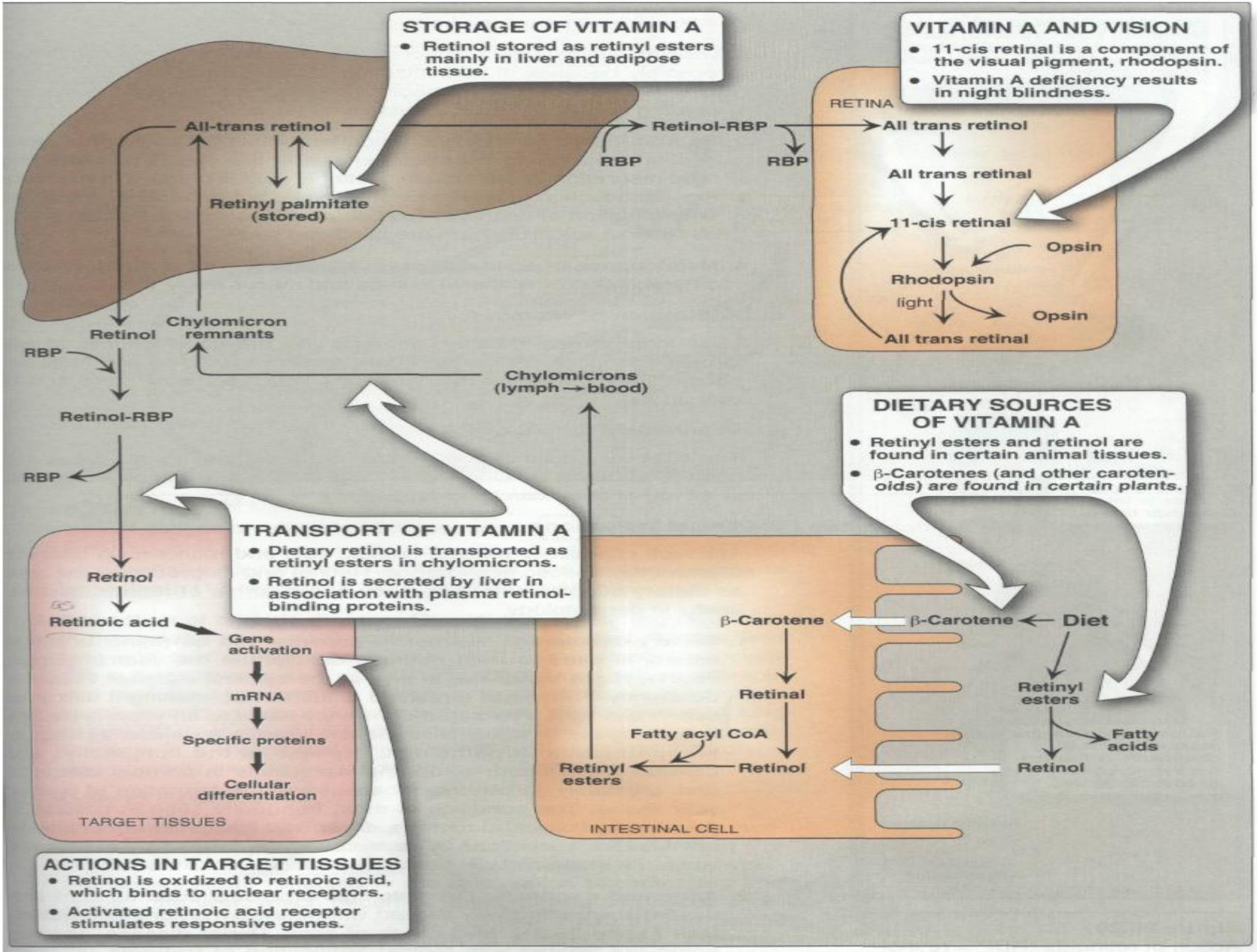


Figure 28.19
Absorption, transport, and storage of vitamin A and its derivatives. RBP = retinol-binding protein.

Mechanism of action of vitamin A

- Retinol is carried in the circulation on a retinol binding protein (RBP).

- The RBP complex attaches itself to specific receptors on the surface of cells of peripheral tissues permitting retinol to enter.

- Inside the cell, retinol is oxidized to retinoic acid. It may also have specific carriers inside some cells, cellular retinol binding protein (CRBP), that carries it to sites in nucleus.

- Retinoic acid binds with high affinity to specific receptor on nucleus. Then the activated receptors stimulate certain genes on the DNA and are transcribed into mRNA and then translated into specific proteins which increase cellular differentiation and regulate keratin genes.

- For example, retinoids control the expression of the keratin gene in most epithelial tissues of the body.
- The specific retinoic acid-receptor proteins are part of the superfamily of transcriptional regulators that includes the steroid and thyroid hormones and 1,25 dihydroxycholecalciferol.

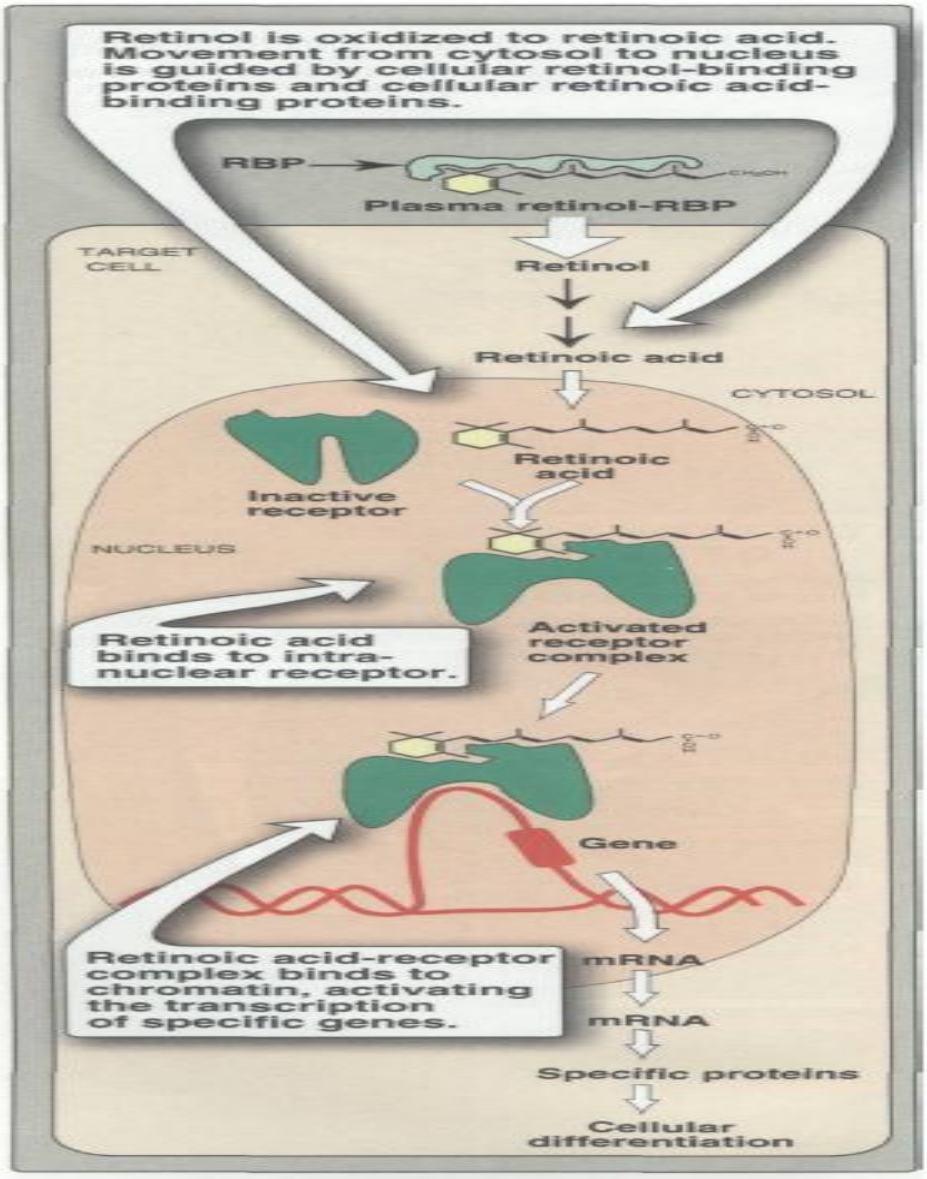


Figure 28.20
Action of retinoids (RBP = retinol-binding protein).

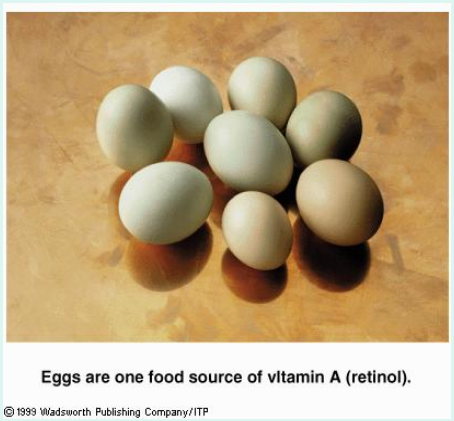
Distribution of vitamin A

- Liver, kidney, cream, butter, and egg yolk are good sources of preformed vitamin A.
- Yellow and dark green vegetables and fruits are good dietary sources of the carotenes, which serve as precursors of vitamin A.

SOURCES OF VITAMIN A

- **Preformed vitamin A (retinyl esters, free vitamin A):**

  Egg yolk, butter, milk, cod liver oil and liver



Eggs are one food source of vitamin A (retinol).

Provitamin A (β carotene)– Carrot, papaya, mangoes,tomatoes, pumpkin,

Requirement for vitamin A

The RDA for adults is 1000 retinol equivalents (RE) for males and 800 RE for females.

One RE = 1μg of retinol, 6 μg of β-carotene, or 12 μg of other carotenoids.

RECOMMENDED DAILY ALLOWANCE FOR VITAMIN A

Infants - 400 Retinol Equivalent (RE)

Children - 400 – 700 RE

Adults - Males - 1000 RE

- Females - 800 RE

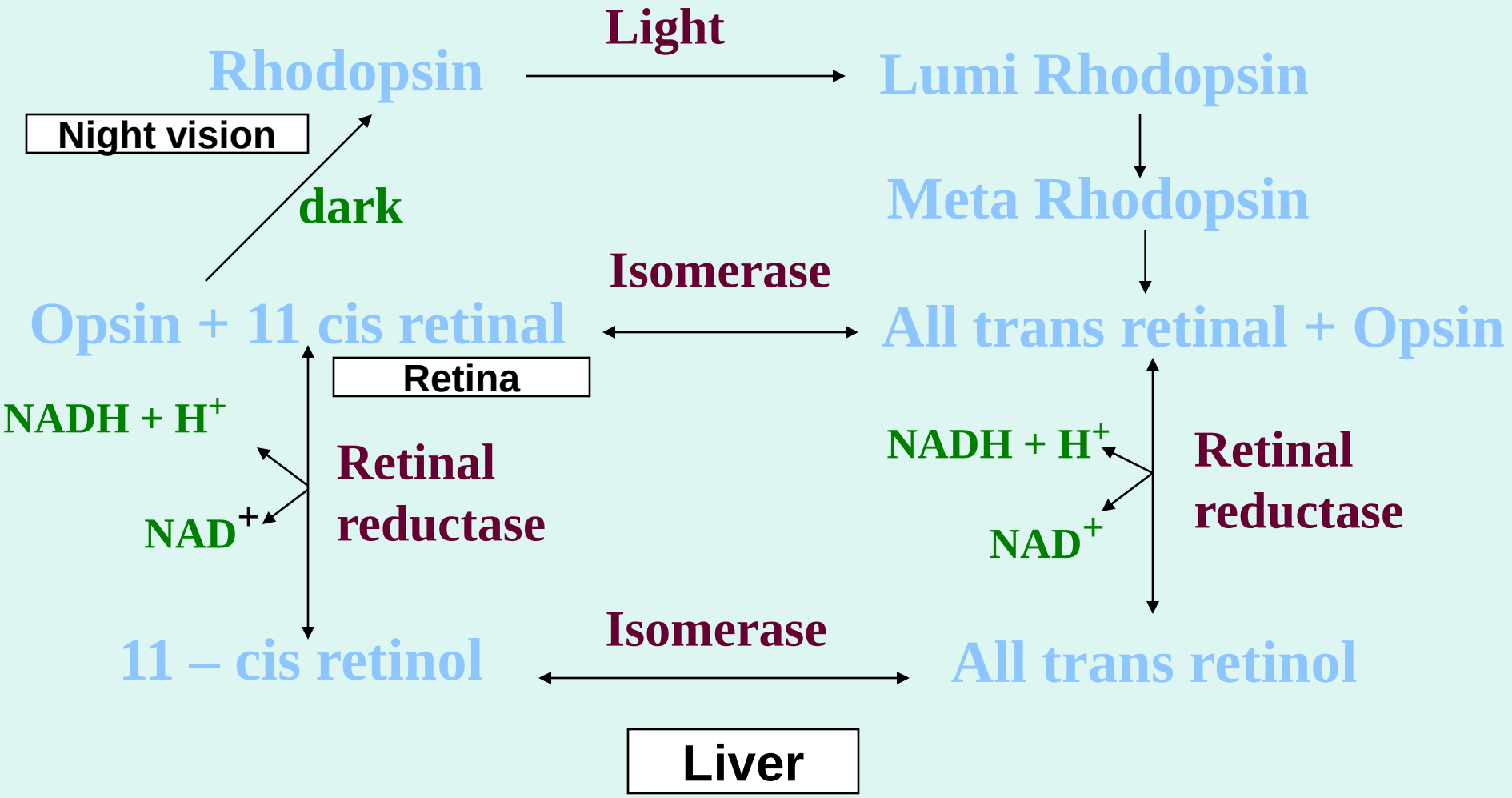
- Pregnancy - 1000 RE

- Lactation - 1200 RE

1 Retinol Equivalent = 1 micro gram of retinol (or) 6 micro gram of β carotene

FUNCTIONS OF VITAMIN A

1. Role in vision (Wald's visual cycle) Rhodopsin **is the visual pigment present in the retina of eye.It is made of opsin and retinal (vitamin A– 11 – cis retinal)**



Explanation of Wald's cycle:

- **Rhodopsin is a photosensitive pigment present in the rod cells and is involved in dim light vision.**
- **When light falls on the rod cells a series of reaction takes place converting the 11 –Cis retinal to Lumi then to meta rhodopsin and finally to All trans retinal.**

Regeneration of 11- cis –retinal:

- **can occur in the retina itself or may go to liver there it is converted to All trans retinol by retinal reductase and then isomerised to 11- cis retinol and carried to retina where it is oxidised to 11 cis retinal.**

- Vitamin A is essential for the differentiation and maintenance of epithelial cells [Retinoic acid] .
- Role in glycoprotein synthesis [Retinoic acid].
- Bone remodeling – Vitamin A is required for sulfation of the muco-polysaccahride in the matrix of bone.

- Essential for normal reproduction [Retinol]
- Retinoic acid is an important regulator of gene expression.
- May act as an antioxidant especially carotenoids, they trap peroxyl and free radicals

Additional Role of Retinol

- Retinol also functions in the synthesis of certain glycoproteins and mucopolysaccharides necessary for mucous production and normal growth regulation.

- This is accomplished by phosphorylation of retinol to **retinyl phosphate** which then functions similarly to dolichol phosphate

Functions of Vit A

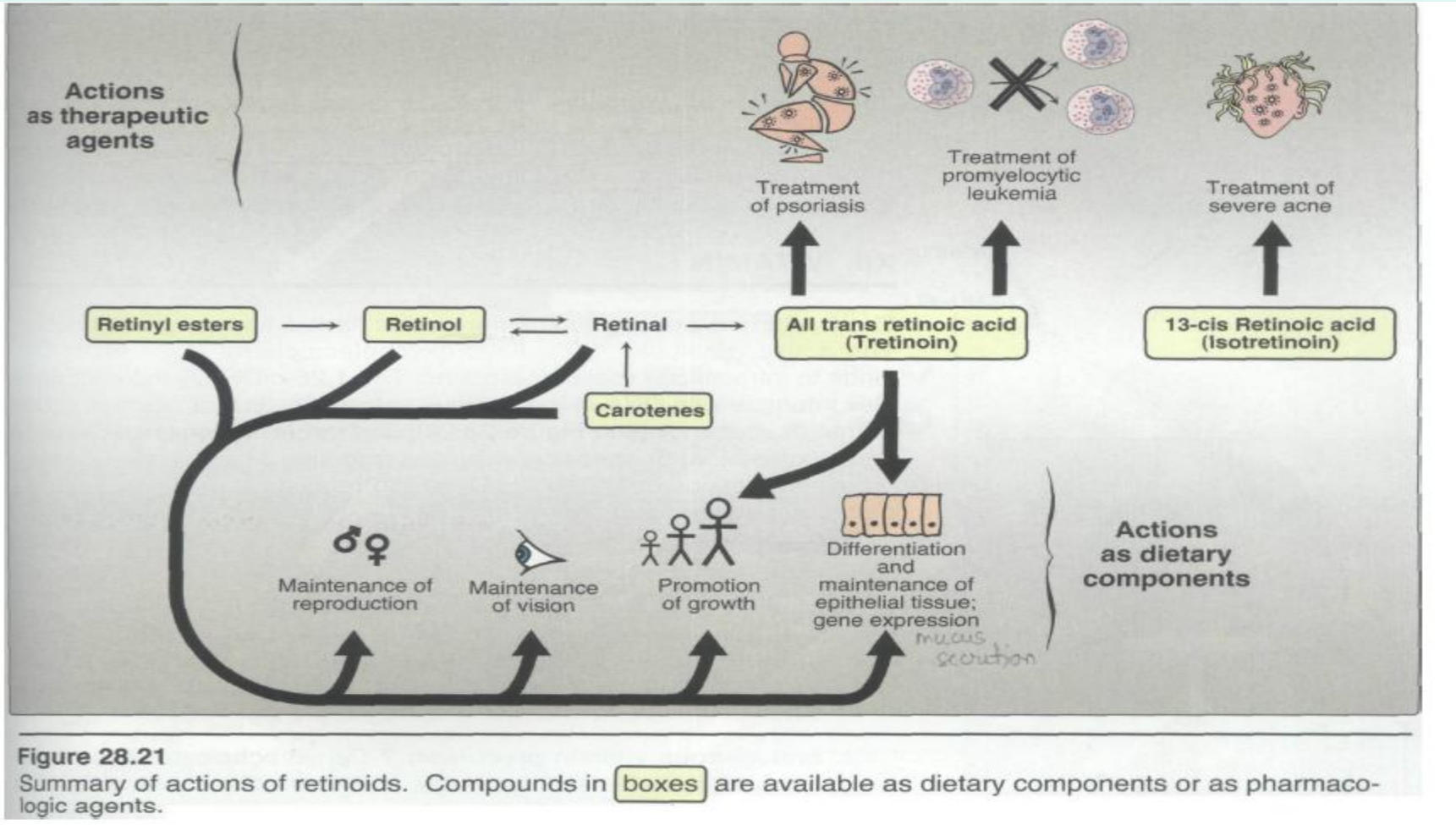


Figure 28.21
Summary of actions of retinoids. Compounds in boxes are available as dietary components or as pharmacologic agents.

Dietary deficiency

- Vitamin A, administered as retinol or retinyl esters, is used to treat patients deficient in the vitamin.
- **Night blindness** is one of the earliest signs of vitamin A deficiency. The visual threshold is increased, making it difficult to see in dim light.
- Prolonged deficiency leads to an irreversible loss in the number of visual cells.

- Severe vitamin A deficiency leads to **xerophthalmia,** a pathologic dryness of the conjunctiva and cornea.
- If untreated, xerophthalmia results in corneal ulceration and, ultimately, in blindness because of the formation of opaque scar tissue.

Clinical Significances of Vitamin A Deficiency

- Vitamin A is stored in the liver and deficiency of the vitamin occurs only after prolonged lack of dietary intake.
- The earliest symptoms of vitamin A deficiency are **night blindness**.
- Additional early symptoms include follicular hyperkeratinosis, increased susceptibility to infection and cancer and anemia equivalent to iron deficient anemia.
- Prolonged lack of vitamin A leads to deterioration of the eye tissue through progressive keratinization of the cornea, a condition known as xerophthalmia.

- The increased risk of cancer in vitamin deficiency is thought to be the result of a depletion in B-carotene.
- Beta-carotene is a very effective antioxidant and is suspected to reduce the risk of cancers known to be initiated by the production of free radicals. Of particular interest is the potential benefit of increased B-carotene intake to reduce the risk of lung cancer in smokers.

Vitamin A Deficiency Is a Major Public Health Problem Worldwide

- Vitamin A deficiency is the most important preventable cause of blindness. The earliest sign of deficiency is a loss of sensitivity to green light, followed by impairment to adapt to dim light, followed by **night blindness.**
- More prolonged deficiency leads to **xerophthalmia:** keratinization of the cornea and blindness.

- Vitamin A also has an important role in differentiation of immune system cells, and even mild deficiency leads to increased susceptibility to infectious diseases.
- Also, the synthesis of retinol binding protein is reduced in response to infection (it is a negative **acute phase protein**), decreasing the circulating concentration of the vitamin, and further impairing immune responses.

Deficiency disease

- Night blindness.
- Xerophthalmia.
- keratinization of skin.

Vitamin A Is Toxic in Excess

- There is only a limited capacity to metabolize vitamin A, and excessive intakes lead to accumulation beyond the capacity of binding proteins, so that unbound vitamin A causes tissue damage.

Symptoms of toxicity affect:

1. The central nervous system (headache, nausea, ataxia, and anorexia, all associated with increased cerebrospinal fluid pressure)
2. The liver (hepatomegaly with histologic changes and hyperlipidemia).
3. Calcium homeostasis (thickening of the long bones, hypercalcemia, and calcification of soft tissues).
4. The skin (excessive dryness, desquamation, and alopecia).

Toxicity of retinoids

- Excessive intake of vitamin A produces a toxic syndrome called hypervitaminosis A.
- Amounts exceeding 7.5 mg/day of retinol should be avoided.
- Early signs of chronic hypervitaminosis A are reflected in the skin, which becomes dry and pruritic, the liver, which becomes enlarged and can become cirrhotic, and in the nervous system, where a rise in intracranial pressure may mimic the symptoms of a brain tumor.
- Pregnant women particularly should not ingest excessive quantities of vitamin A because of its potential for causing congenital malformations in the developing fetus.

References:

1. Lippincott's review of biochemistry, 3rd edition.
1. Biochemistry Stryer 5th edition.
2. Harper,s Biochemistry 28 edition.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Retinoic Acid Has a Role in the Regulation of Gene Expression and Tissue Differentiation

- A major role of vitamin A is in the control of cell differentiation and turnover. All-*trans*-retinoic acid and 9-*cis*-retinoic acid (Figure 44–1) regulate growth, development, and tissue differentiation; they have different actions in different tissues. Like the thyroid and steroid hormones and vitamin D, retinoic acid binds to nuclear receptors that bind to response elements of DNA and regulate the transcription of specific genes. There are two families of nuclear retinoid receptors: the retinoic acid receptors (RAR) bind all-*trans*-retinoic acid or 9-*cis*-retinoic acid, and the retinoid X receptors (RXR) bind 9-*cis*-retinoic acid. Retinoid X receptors also form dimers with vitamin D, thyroid, and other a nuclear acting hormone receptors. Deficiency of vitamin A impairs vitamin D function because of lack of 9-*cis*-retinoic acid to form receptor dimers, while excessive vitamin A also impairs vitamin D function, because of formation of RXR-homodimers, meaning that there are not enough RXR available to form heterodimers with the vitamin D receptor.

Retinoic Acid Has a Role in the Regulation of Gene Expression and Tissue Differentiation