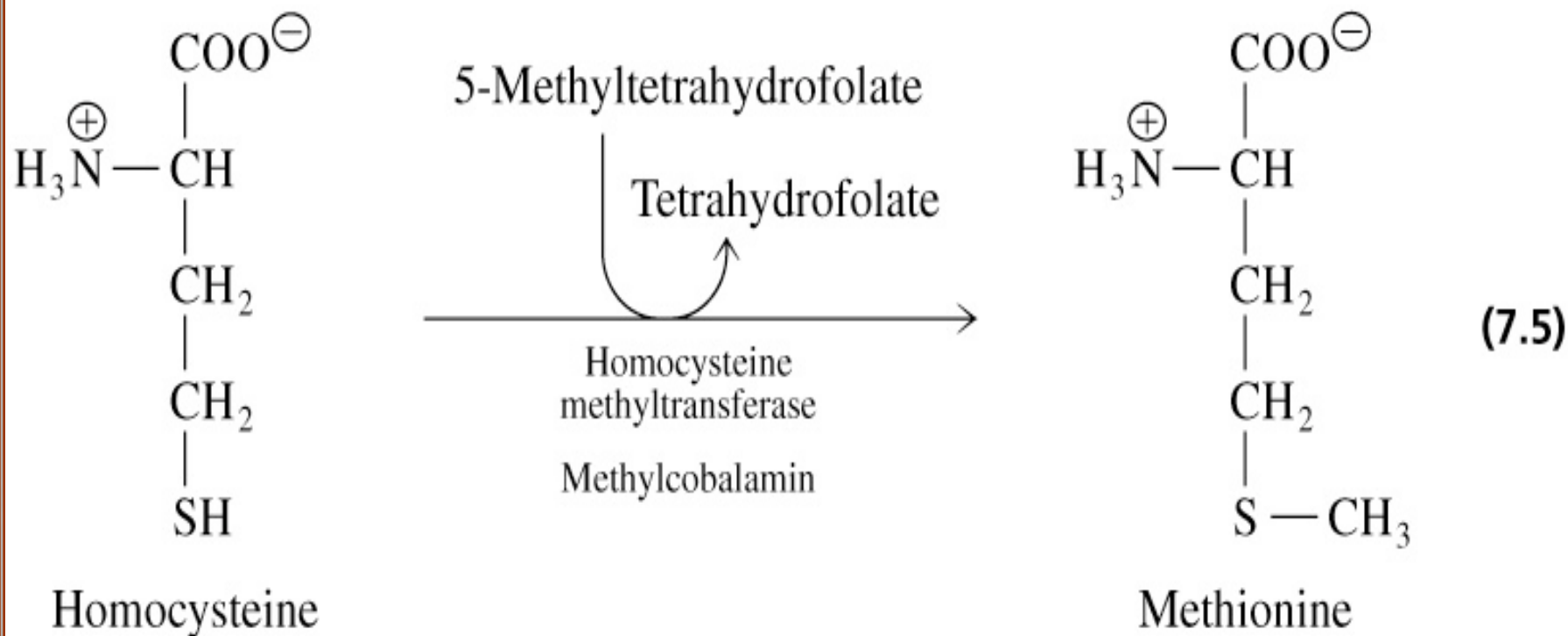


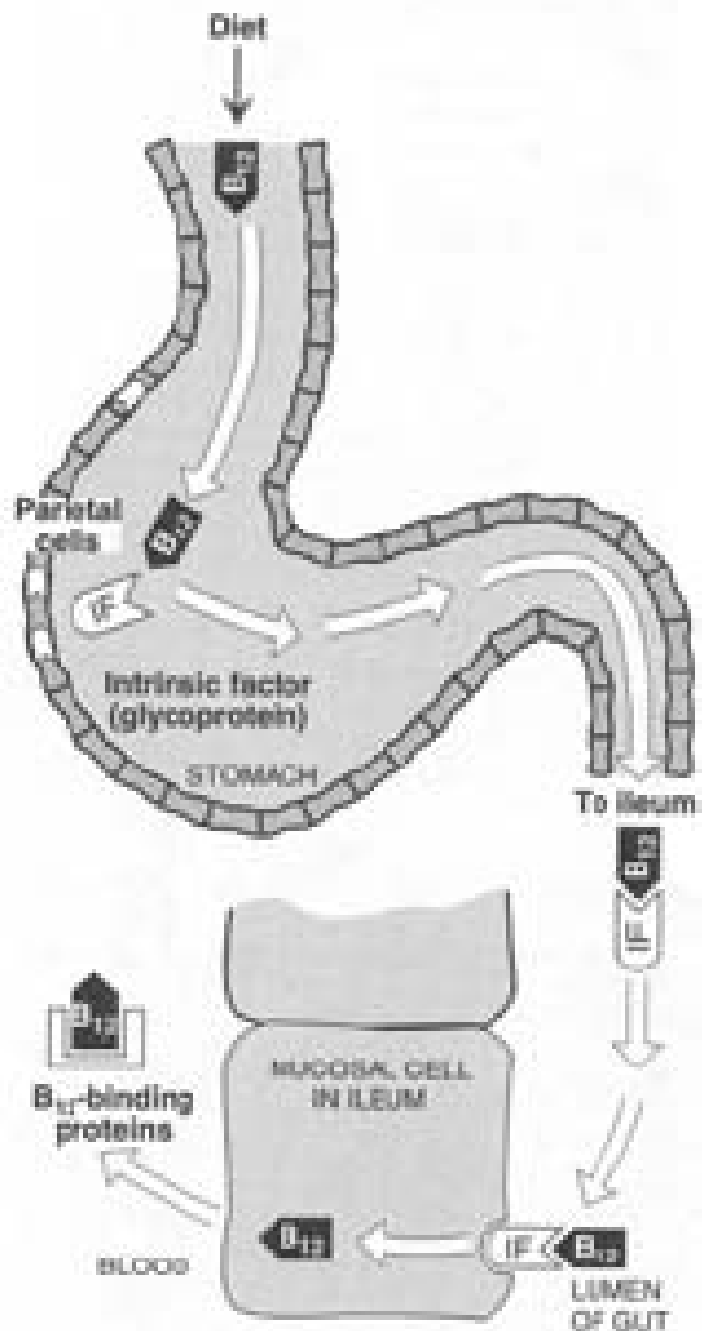
# Methylcobalamin participates in the transfer of methyl groups



# Can't let it loose on it's own:

$B_{12}$  is chaperoned into our bodies by a glycoprotein called Intrinsic Factor.

Deficiencies can occur due to a lack of the intrinsic factor: This is called Pernicious Anemia.



Why anemia? Let me tell you.

# B12 is Important in Two Reactions

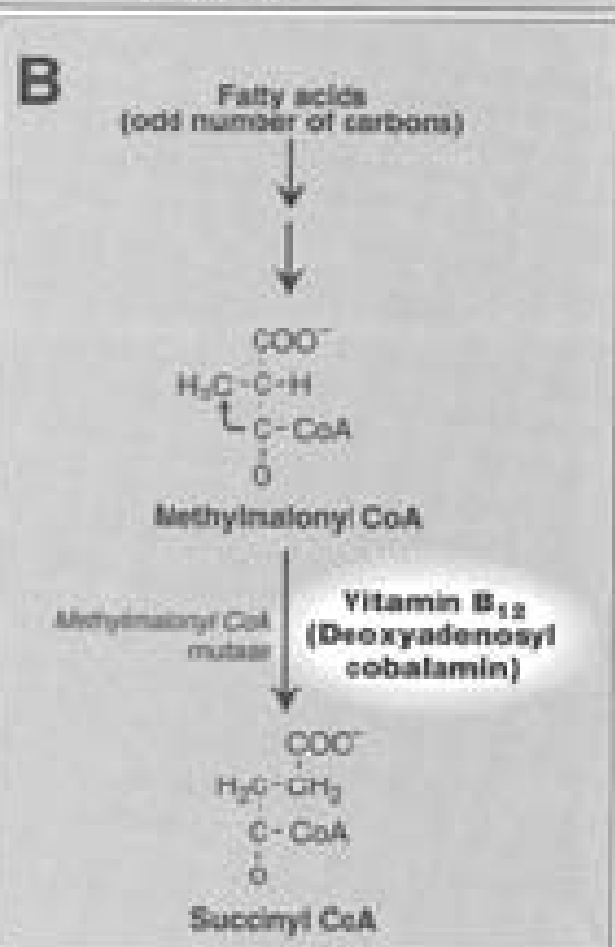
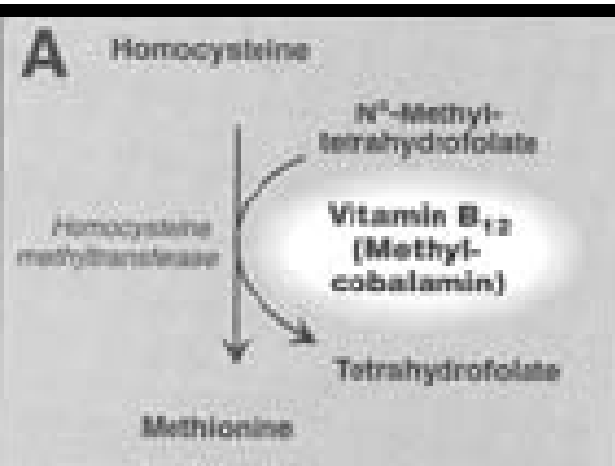
1. Catabolism of odd number fatty acid chains
2. Synthesis of methionine from homocysteine


The anemia comes from the methionine synthesis: Folate becomes trapped in the N5-methyl THF form.

Usable THF is depleted and BAM!

Anemia from no dTTP.

There can also be neurological symptoms in B12 deficiencies: myelin.





# 10 - Vitamin C (Ascorbic Acid)

# Ascorbic acid (Vitamin C)

- Vitamin C is an important antioxidant, reacting with reactive oxygen species
- And regenerating vitamin E from its reduced, radical form.
- Deficiency of vitamin C causes scurvy, characterized by connective tissue degradation
- Poor healing, bleeding, tooth loss, bone pain, heart failure
- Milder cases: fatigue, irritability, increased severity of respiratory tract infections

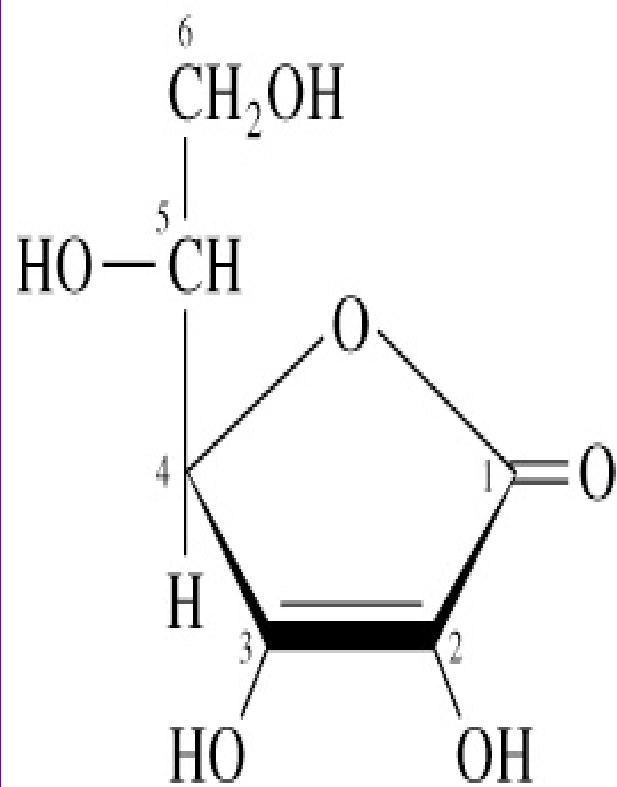
# Ascorbic Acid

- *Vitamin C*; anti-scorbutic vitamin (scurvy)
- Structure is reminiscent of *glucose*
- Produced in plants from glucose via the uronic pathway
- The enzyme gulonolactone oxidase converts gulonolactone to ascorbic acid
- Exists in the enolic and ketonic forms
- Sources: citrus fruits, tomatoes, green peppers, strawberries, cantaloupe, cabbage, turnips, peas, lettuce and asparagus

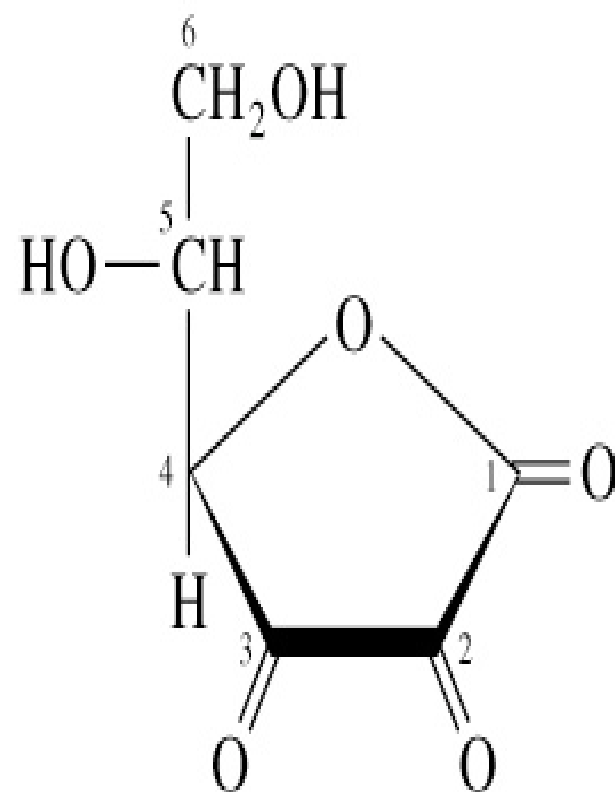
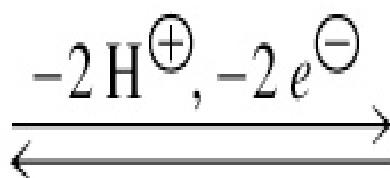


# Vitamin C: a vitamin but not a coenzyme

- ❖ Most animals make vitamin C, but humans do not have this ability. It is obtained through fruits and vegetables
- ❖ Ascorbic acid is required for the hydroxylation of proline in collagen
- ❖ Ascorbic acid is a cofactor for prolyl 4-hydroxylase. A reducing reagent for hydroxylation of collagen
- ❖ Deficiency leads to the disease scurvy
- ❖ Most animals (not primates) can synthesize Vit C



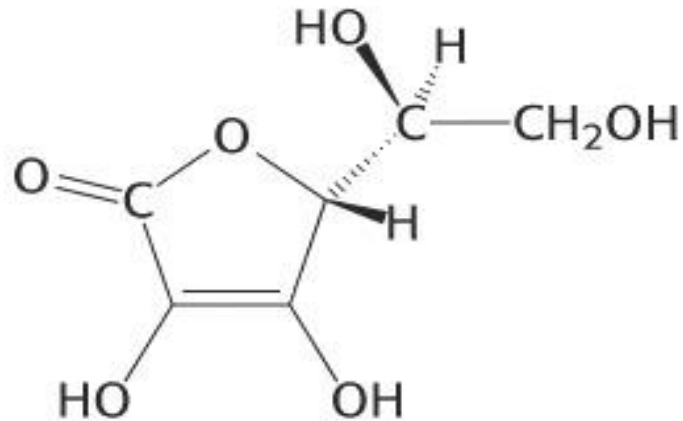
Ascorbic acid



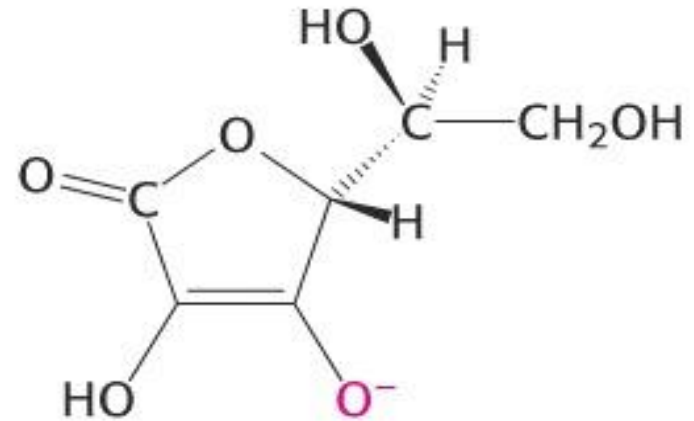
Dehydroascorbic acid



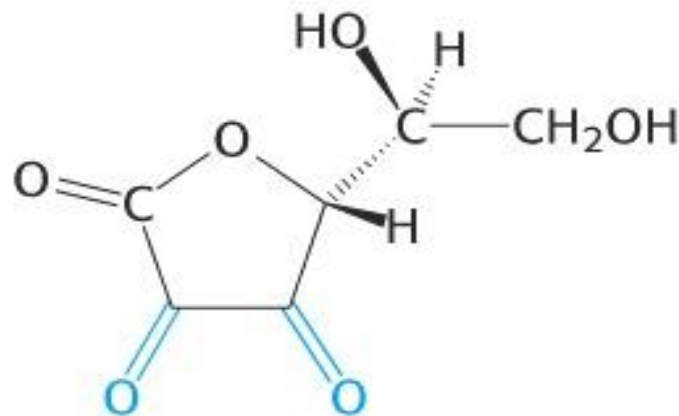
# Ascorbic acid (Vitamin C)



**Ascorbic acid**



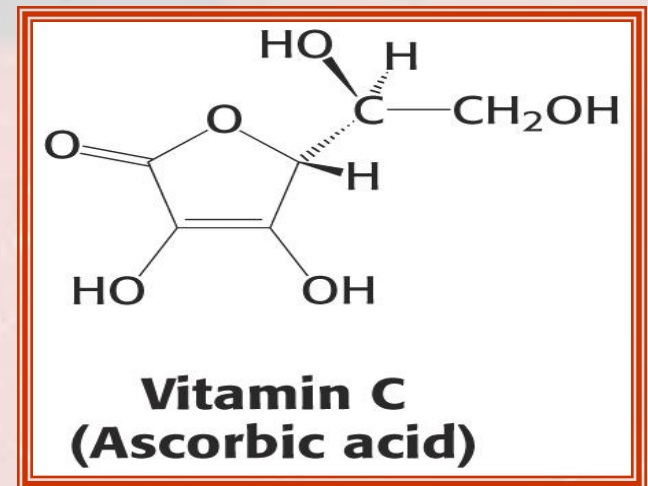
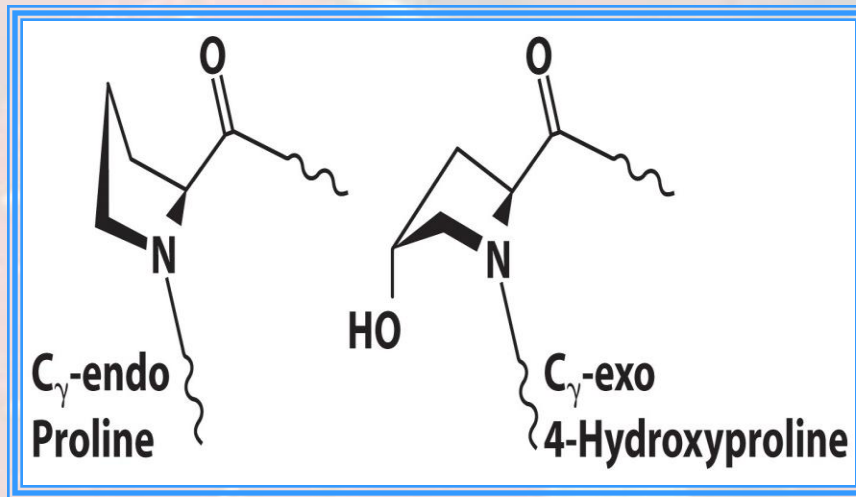
**Ascorbate**



**Dehydroascorbic acid**

# Ascorbic acid (Vitamin C)

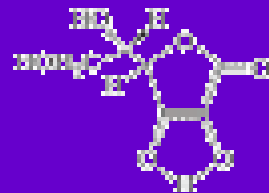
## A cofactor for prolyl 4-hydroxylase



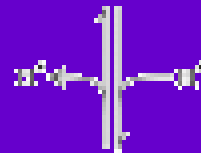
- ✓ Gly-X-Y repeats in collagen have Pro or 4-Hyp at X and Y.
- ✓ Hydroxylation stabilizes the C<sub>γ</sub>-exo conformation which is required in collagen structure
- ✓ And also enhances hydrogen bonding that stabilizes the helix

# Vitamin C

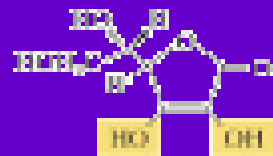
Ascorbic Acid, Effect on the stability of Iron in Food  
Figure 14.66



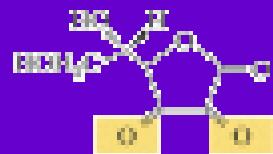
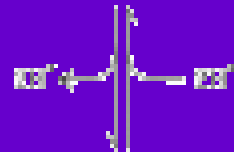
L-Ascorbate Iron radical



Reducing agent



Ascorbate anion (Vitamin C)



Dihydroxy-L-ascorbate anion

# Ascorbic Acid

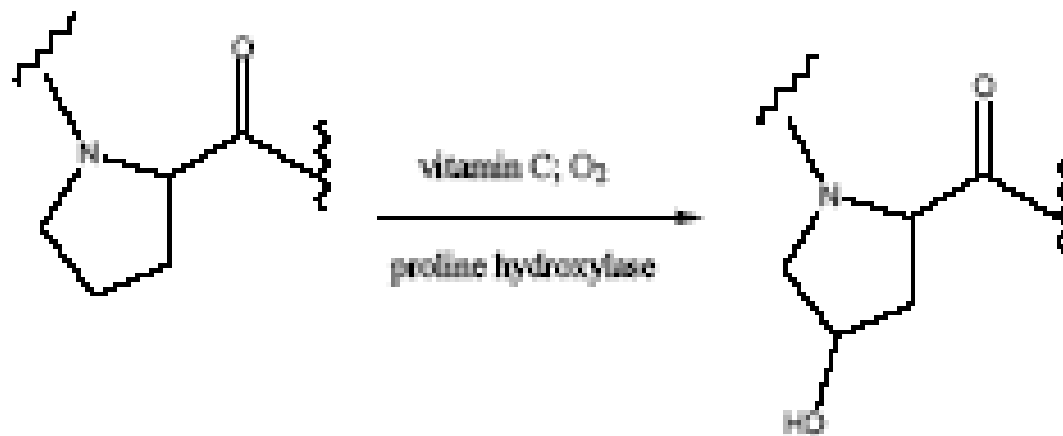
- Biochemical functions:
  - Production and maintenance of collagen
    - Proline -----hydroxyproline
    - Lysine ----- hydroxylysine
  - Mitochondrial electron-transport chain (cytochrome C)
  - Metabolism of tyrosine
    - Tyrosine ----- p-hydroxyphenylpyruvic acid---- 2,5-dihydroxyphenylacetic acid (homogentisic acid)

# Ascorbic acid

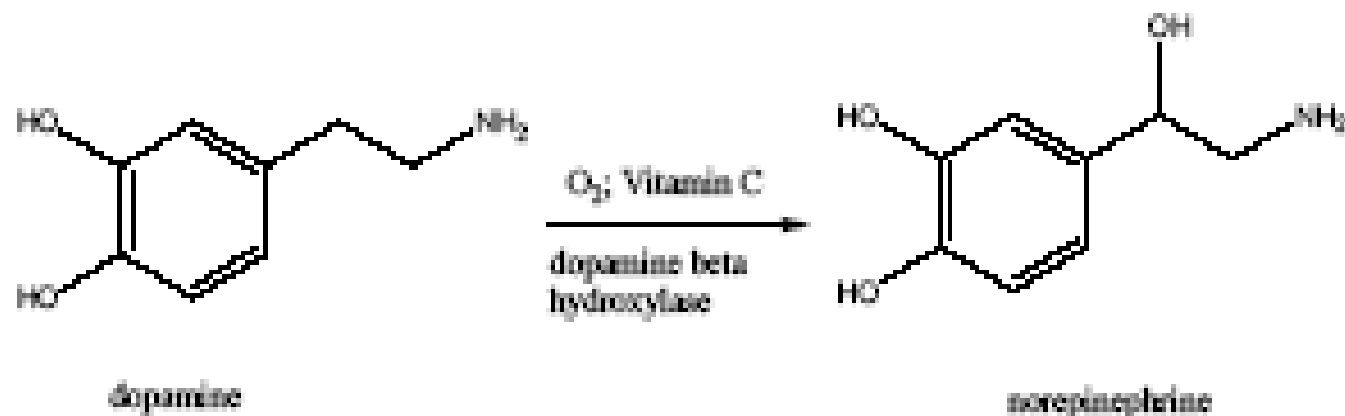
- conversion of folic acid to THFA
- hydroxylation reactions of cholesterol to cholic acid
- hydroxylation of tryptophan to 5-hydroxytryptophan
- regulation of cholesterol biosynthesis in the adrenal gland
- aids in the absorption and utilization of iron
- antioxidant properties may inhibit formation of nitrosamines during digestion of protein

# Ascorbic Acid - Functions

Proline hydroxylase: (collagen formation)



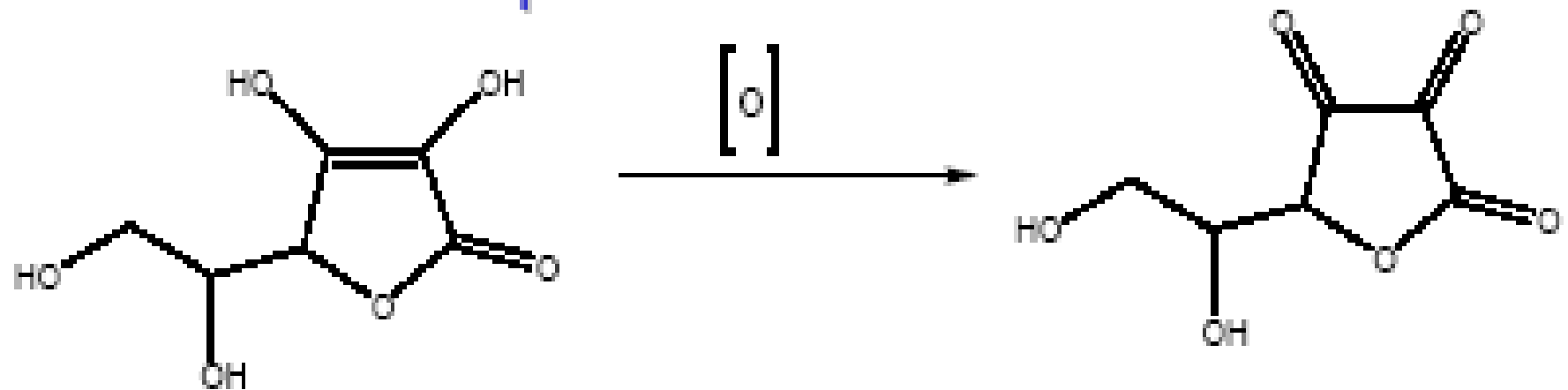
Dopamine-beta hydroxylase ( neurotransmitter formation)





# Anti-oxidant properties of vitamin C:

helps prevent damage to cellular proteins and DNA



- Normal metabolic processes in the cell lead to the generation of reactive oxidizing agents such as superoxide
- Superoxide can react with and damage protein and DNA, leading to cellular changes that can lead to premature aging and cancer Vitamin C reacts with superoxide, thus preventing this damage

# Ascorbic acid

- requirements:
  - children: 30 mg
  - adults: 40 –80 mg
  - pregnancy: 100 mg
- therapeutic uses
  - scurvy
  - idiopathic methemoglobinemia
- questionable use: common cold

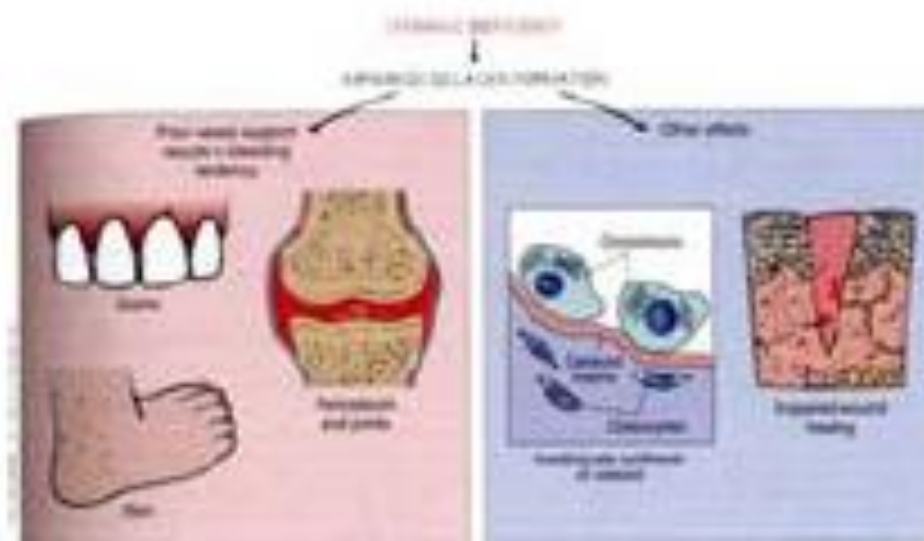
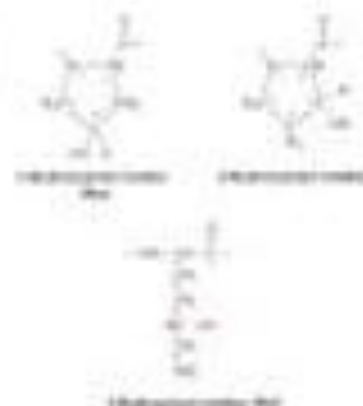
# Ascorbic acid

- deficiency: scurvy
  - hemorrhage from mucous membranes, mouth and GIT, skin and muscles
  - gingivitis: swelling, tenderness, redness and ulceration of gums
  - loosening or loss of teeth
  - swelling of joints
  - rarefaction of bones and dentine

# Example 1: Nutrition

## Scurvy

- Vitamin C deficiency
- Inactive prolyl and lysyl hydroxylase
- Impaired collagen synthesis
- Skin lesions, vascular fragility, poor wound healing and bone and joint disease



The background of the slide is a close-up photograph of several ripe, red strawberries. The strawberries are covered in small, light-colored seeds (achenes) and have green leafy tops. The image is slightly out of focus, creating a soft, naturalistic backdrop for the text.

# Lipid Soluble Vitamins

# **Lipid Vitamins**

## **(Fat soluble vitamins)**

- ❖ Four lipid vitamins: A, D, E, K
- ❖ All contain rings and long, aliphatic side chains
- ❖ All are highly hydrophobic
- ❖ The lipid vitamins differ widely in their functions



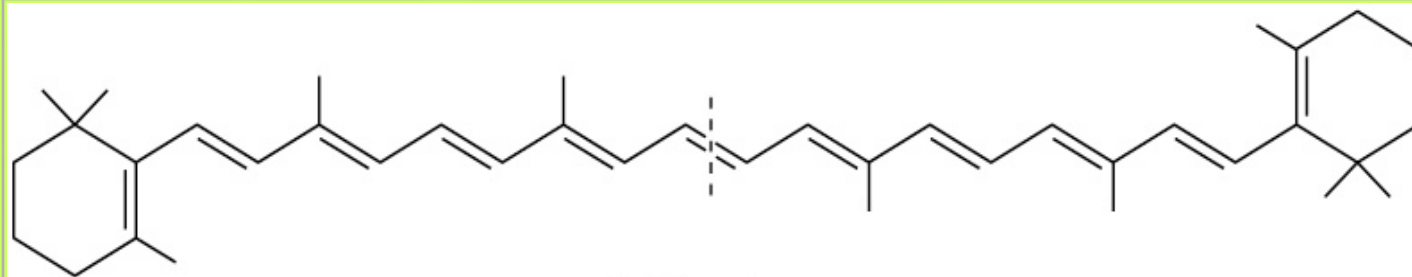
The background of the slide is a close-up photograph of several ripe, red strawberries. The strawberries are covered in small, yellowish seeds (achenes) and have green leafy tops. The image is slightly out of focus, creating a soft, naturalistic backdrop.

*I = Vitamin A*

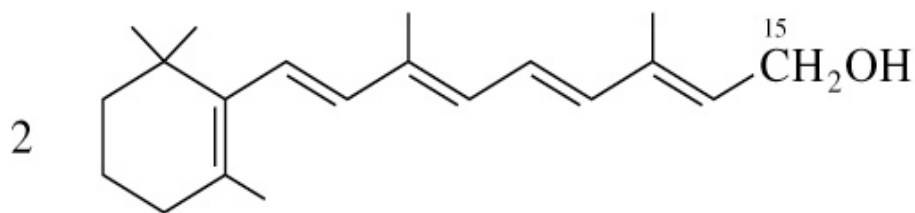
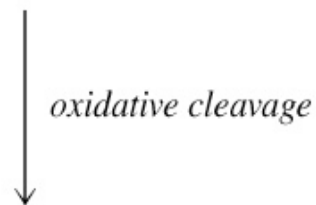
# A. Vitamin A (Retinol)

- ❖ Vit A is obtained from liver, egg yolks, milk products or b-carotene from yellow vegetables
- ❖ Vit A exists in 3 forms: alcohol (retinol), aldehyde and retinoic acid
- ❖ Retinol and retinoic acid have roles as protein receptors
- ❖ Retinal (aldehyde) is a light-sensitive compound with a role in vision

# Formation of vitamin A from b-carotene



$\beta$ -Carotene



Vitamin A  
(retinol form)

# Vitamin A

## ❖ Forms

- ❖ retinol, retinal, retinoic acid = retinoids;  
carotenoids

## ❖ Functions

- ❖ Vision, cell development and health, immunity

## ❖ Food sources

- ❖ Preformed vitamin A: liver, milk, egg yolks
- ❖ Beta-carotene: yellow/orange fruits and  
vegetables

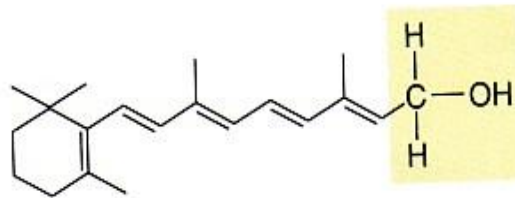
## ❖ Retinal Binding Protein (RBP)



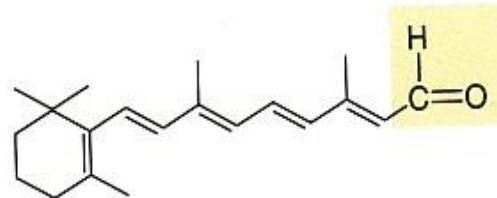
**Retinol**

**Retinal**

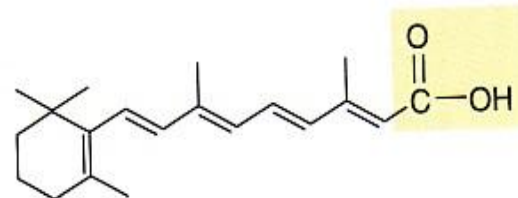
**Retinoic acid**



**Retinol**



**Retinal**



**Retinoic acid**

**Figure 9.4**

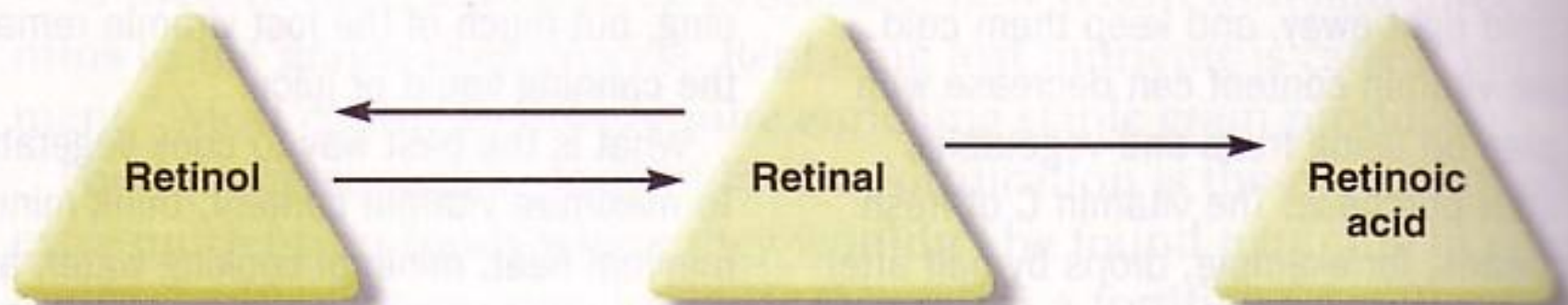
**Forms of vitamin A.** Retinol is the alcohol form of vitamin A, retinal is the aldehyde form, and retinoic acid is the acid form.

**Alcohol form**

**Aldehyde form**

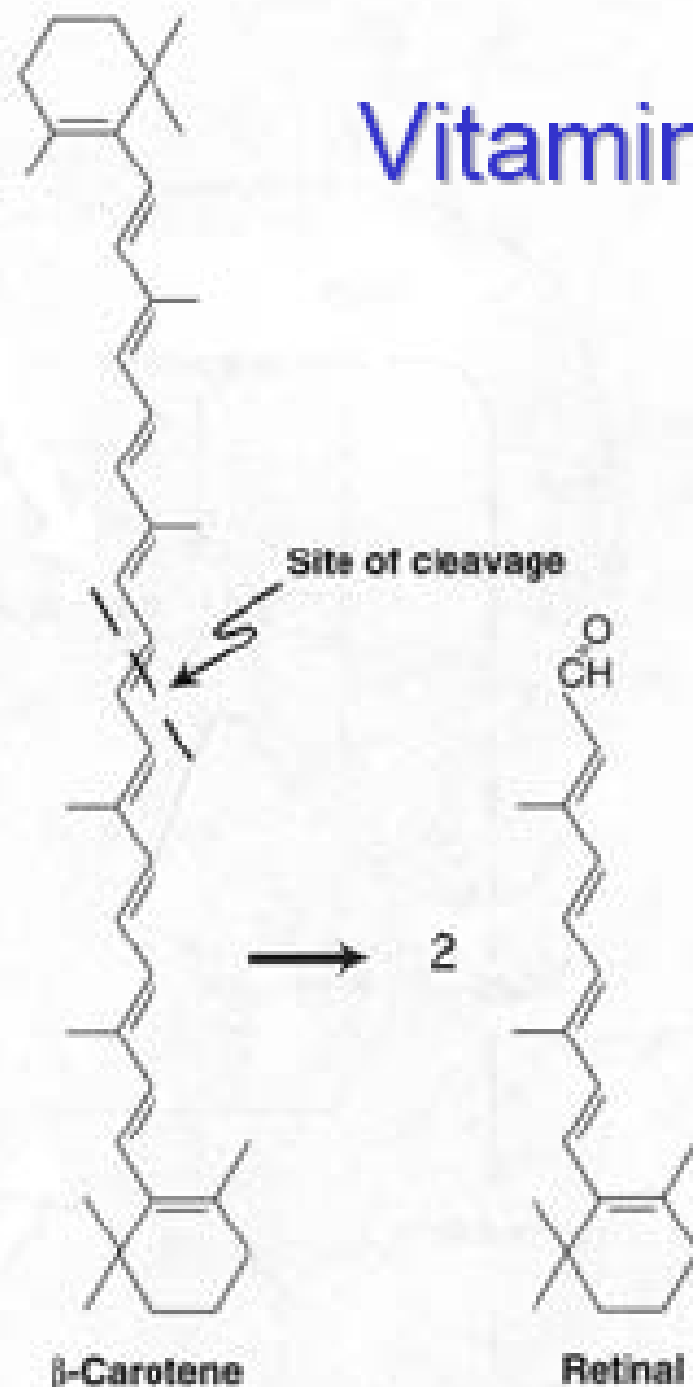
**Acid form**

## VITAMIN A INTERCONVERSIONS





# Vitamin A: Retinoids



Usually derived from beta carotene.

Used as a hormone and in vision

Fat Soluble: Too much can be toxic!

Variety of forms:  
can be converted in the diet, but each is unique in pharmacology.



Retinal



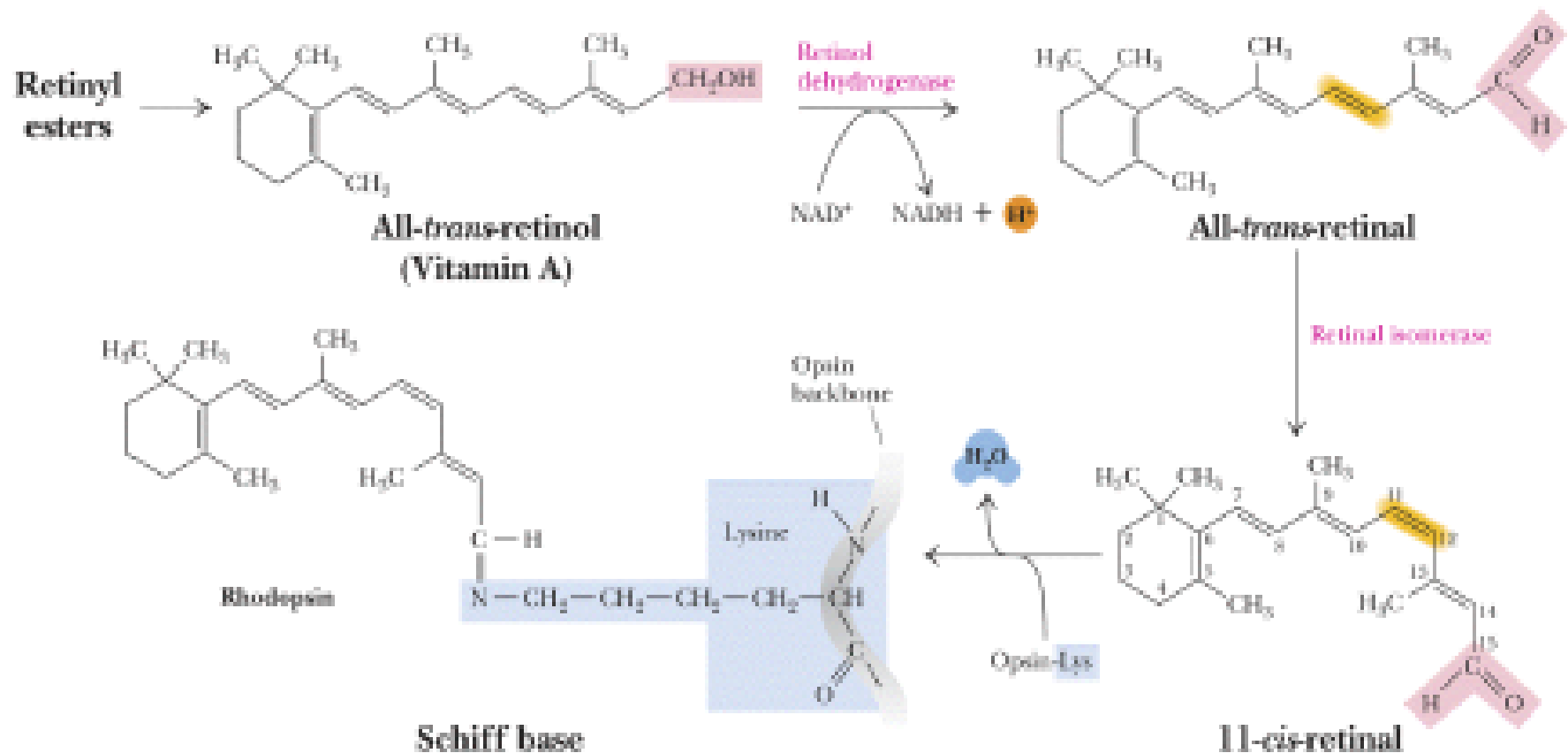
Retinal

Retinoic acid  
(all trans)11-cis-retinal  
(formed by photoisomerization  
of all trans-retinal)

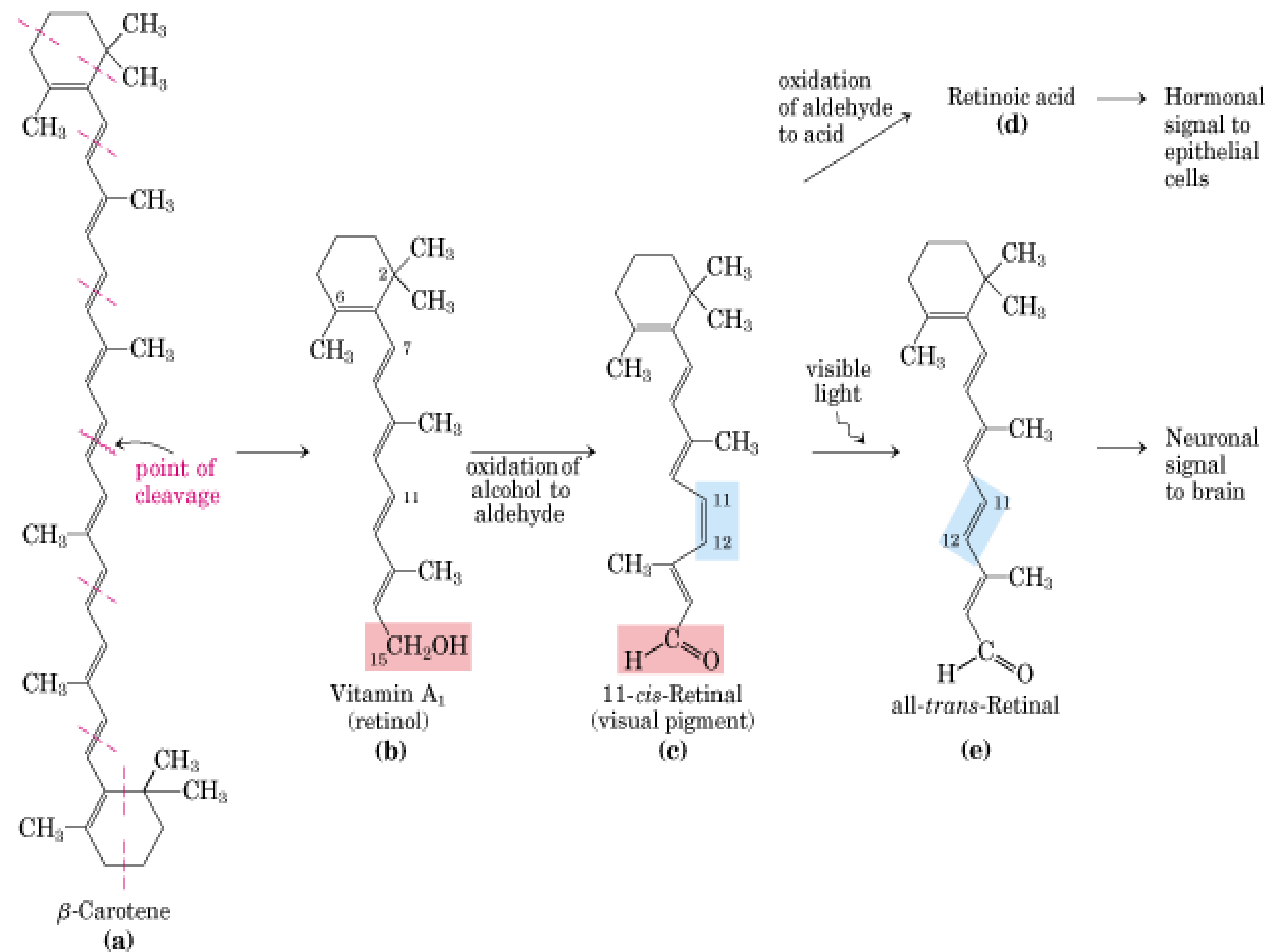
# Vitamin A

Garrett/Grisham, Biochemistry with a Human Focus

Figure 14.31



ADH in fetus makes retinoic acid



# **Roles of Vitamin A in Body**

## ❖ Vision

- ❖ cornea and retina

- ❖ rhodopsin=opsin + retinal

## ❖ Protein Synthesis and Cell Differentiation

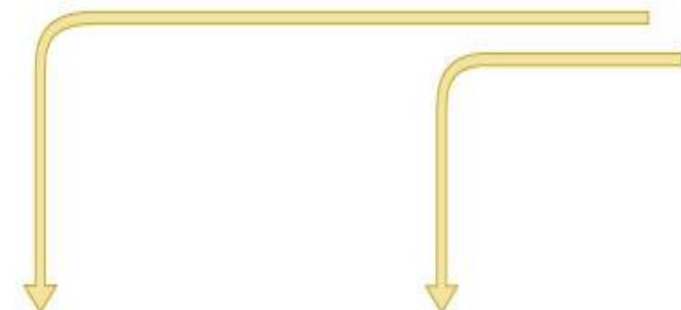
- ❖ Maintains healthy cells in mucous membranes

## ❖ Reproduction and Growth

- ❖ retinol participates in sperm development

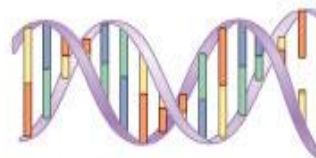
- ❖ vitamin A supports normal fetal development

- ❖ Vitamin A participates in dismantling of bone during growth

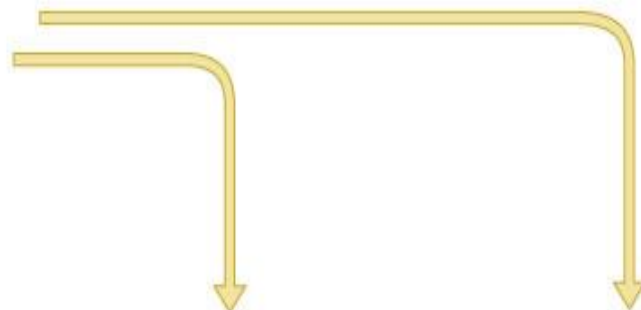
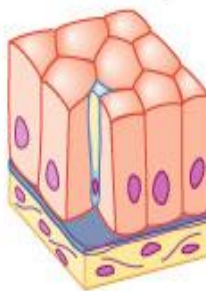


Vision

Cell differentiation



Immunity

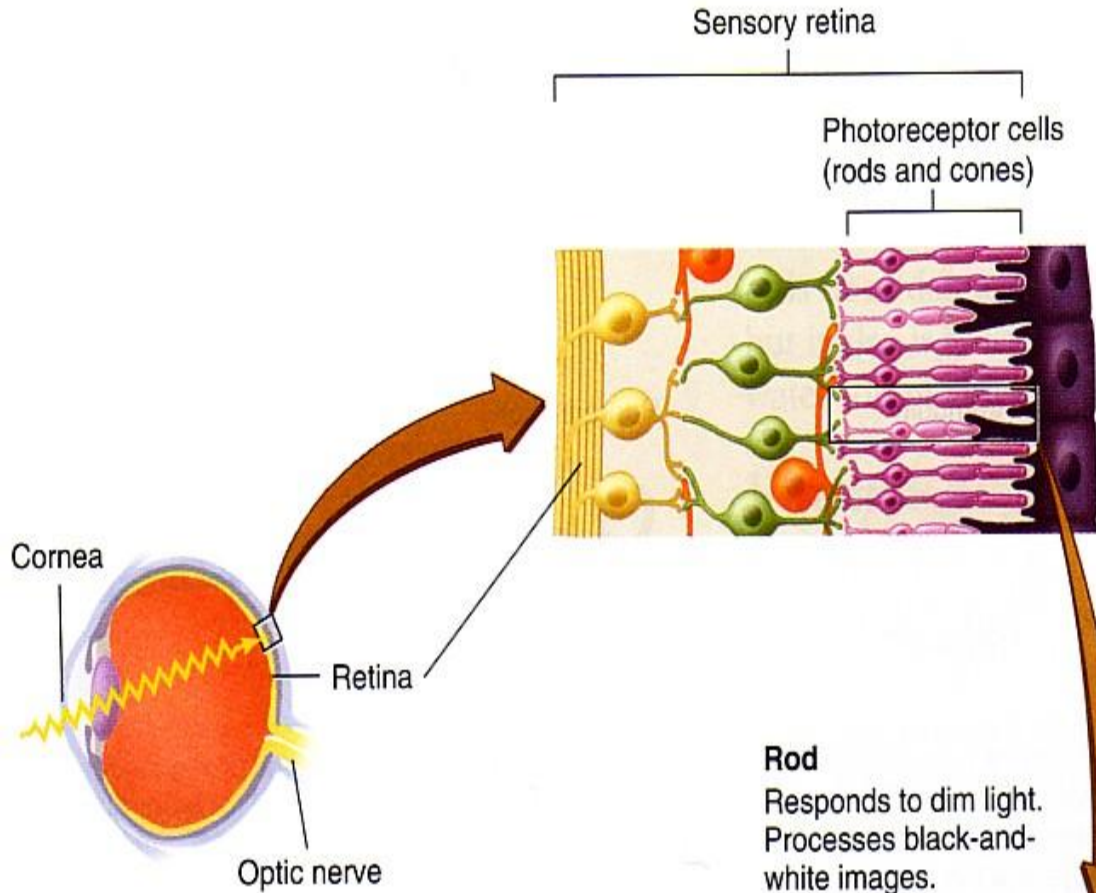


Reproduction

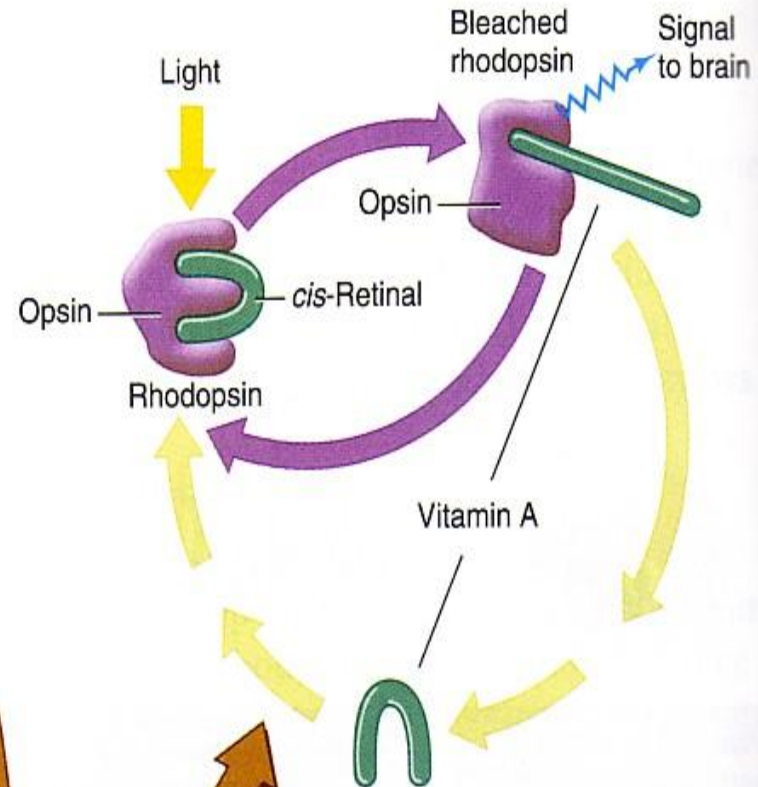
Growth



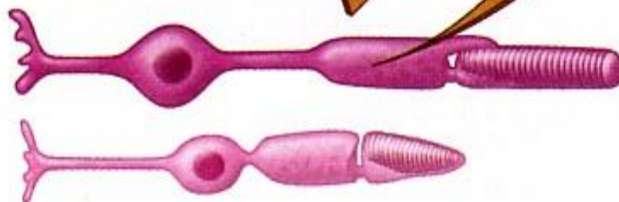
## STRUCTURE OF RETINA



## VISUAL CYCLE IN RETINA



**Rod**  
Responds to dim light.  
Processes black-and-white images.

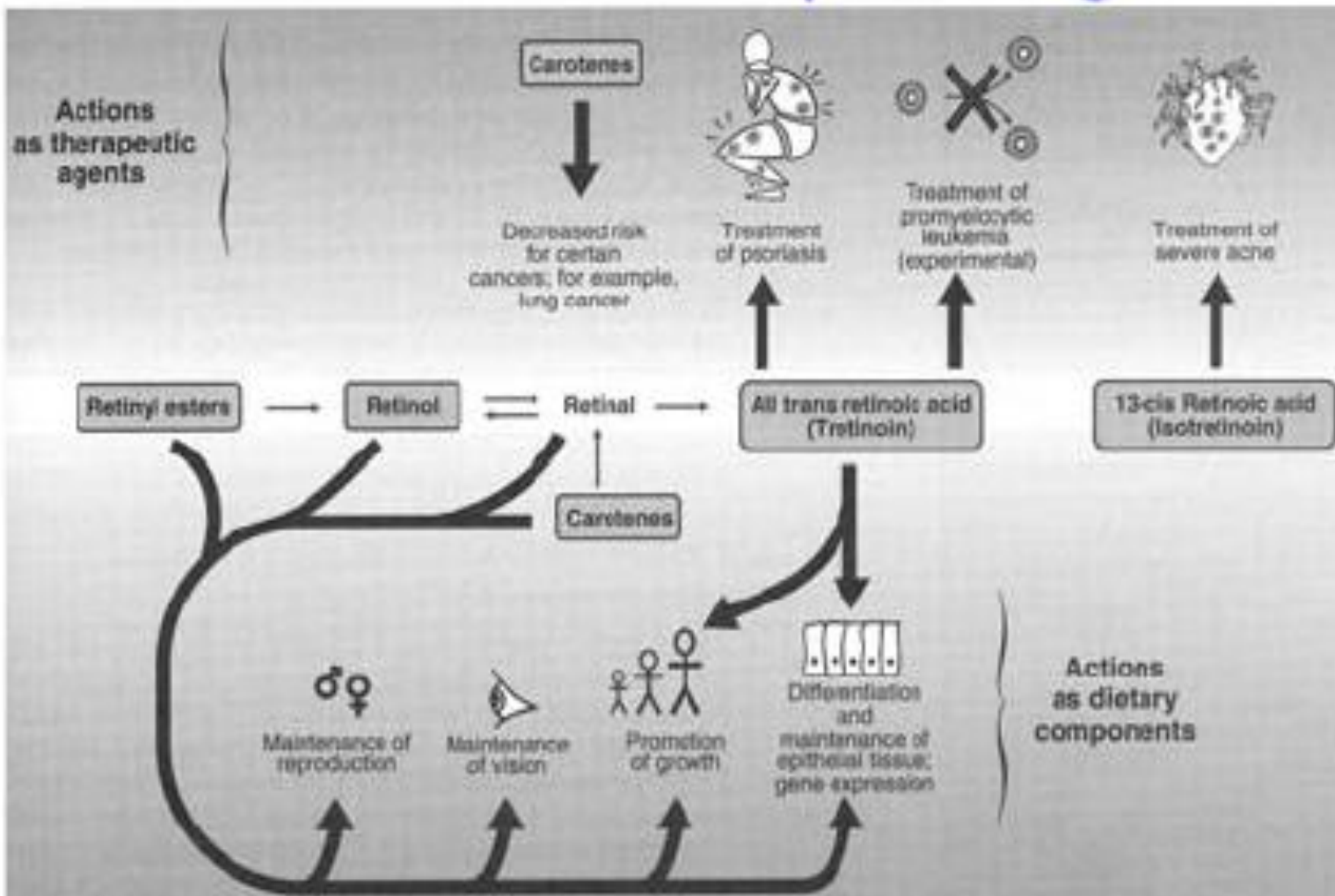


**Cone**  
Responds to bright light.  
Translates light to color images.





# Also used as a therapeutic agent

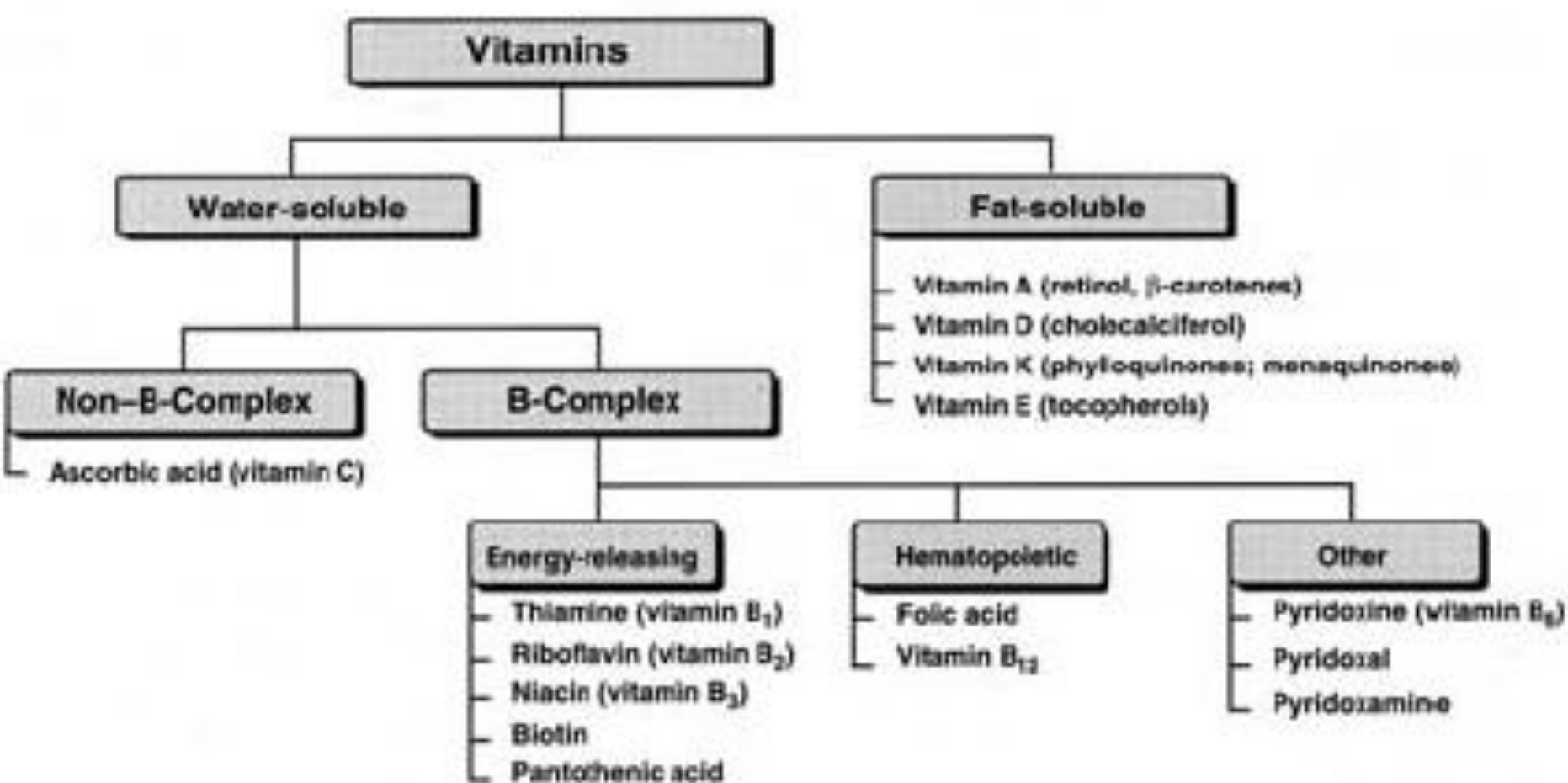


# Vitamin A in Foods

- ✓ Recommendations: RDA: in RAE Men=900  $\mu\text{g}$ ; women=700  $\mu\text{g}$ ; preg=770  $\mu\text{g}$ ; lact=1,300  $\mu\text{g}$
- ✓ Retinoids in animal foods; vitamin A precursors, carotenoids in plants
- ✓ The Colors of Vitamin A Foods
  - ✓ dark leafy greens; rich yellow or deep orange vegetables and fruits
- ✓ Vitamin A-Poor Fast Foods
- ✓ Vitamin A-Rich Liver
  - ✓ don't eat too much too often: pregnant women

# Vitamin A

Vitamin A: liver, kidney, dairy, egg yolk,  
Carotenes: yellow and dark green vegetables and fruits



# Vitamin A Deficiency

- Infectious Diseases
  - Measles in children in developing countries
- Night Blindness
  - retina does not receive enough retinal to regenerate the visual pigments bleached by light
- Blindness (Xerophthalmia)
  - lack of vitamin A in cornea; major cause of childhood blindness in the world
- Keratinization
  - less goblet cells; some cells secrete keratin;



# Retinoic acid and limb development in chick embryos



Normal wing development



Retinoic acid added to growing wing bud (note symmetry).

# Vitamin A Toxicity

- Children are sensitive to
- Beta-Carotene
  - in food may cause yellow skin
  - in supplements may act as a prooxidant, promoting cell division and destroying vitamin A
- Birth Defects
  - 10,000 IU during pregnancy lead to birth malformation
- Not for Acne
  - Accutane is different than vitamin A



The background of the slide is a close-up photograph of several ripe, red strawberries. The strawberries are covered in small, yellowish seeds (achenes) and have green leafy tops. The image is slightly out of focus, creating a soft, naturalistic backdrop.

# *II- Vitamin D*

# Vitamin D

- ✓ A group of related lipids involved in control of Ca<sup>2+</sup> utilization in humans
- ✓ Vitamin D<sub>3</sub> and 1,25-dihydroxycholecalciferol

