

Vitamin A





BC.8.1,

Describe Biochemical role of vitamins in the body
& Explain manifestations of their deficiency

Specific Learning Objective

The learner will be able to Explain

Active forms

Sources

RDA

Role of Vitamin A in vision and Wald's visual cycle

Deficiency manifestations

Management of deficiency

Prevention of deficiency

May 2022

What are the sources of vitamin A.

Enumerate the biochemical role and

Deficiency manifestations of vitamin A

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Blindness

Major public health problem



1/3 rd of World's blind poulation
reside in India

40% of blindness is preventable

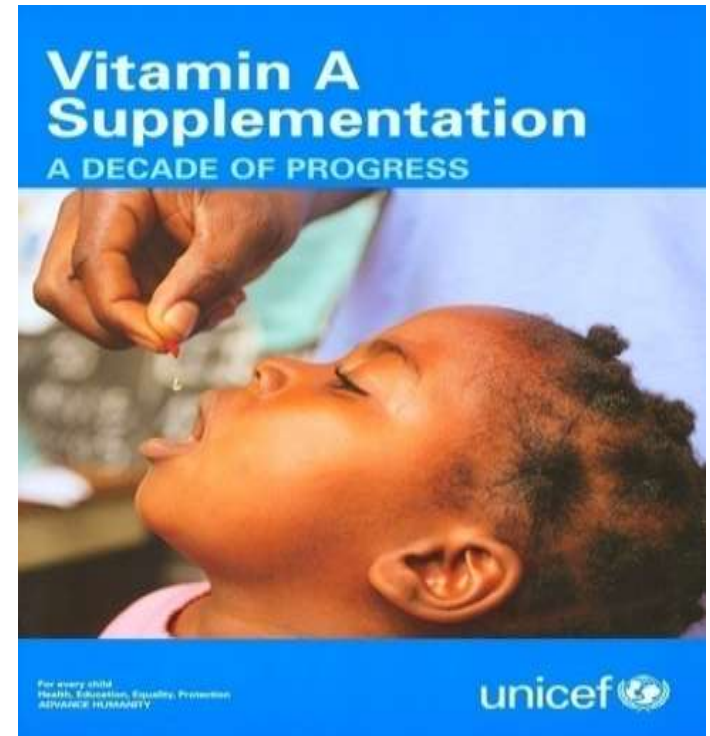
Vitamin A deficiency (VAD) is the world's
leading cause of **preventable** childhood
blindness(below 5 yrs)

- About 250,000 to 500,000 malnourished children in the developing world go blind each year from a deficiency of vitamin A
- Around half of them die within a year of becoming blind

Vit:A supplementation Programmes by UNICEF Nutrition international,WHO

- Vitamin A supplementation in Preschool children of low & middle income group in 70 countries was associated with a 12% reduction in mortality rate.

Vitamin A supplements available in capsule & drops form included with national immunization days (NIDs) for polio eradication or measles.



- Vitamin A supplementation not the best long-term solution for vitamin A deficiency
- food fortification,
- improved food distribution programs, crop improvement, such as for fortified rice are more effective in eradicating vitamin A deficiency.

Vitamin A Supplementation Schedule for Indian Children

Age	Dose	Frequency
6 months to 11 months	1,00,000 IU	Once
12 months to 5 years	2,00,000 IU	Every 6 months

Sources



Egg yolk



Fish



Milk

Vitamin A Rich Foods



Green Leafy
Vegetables



Cod liver oils



Pumpkin



Mango

Fig 11.1: Food Sources of Vitamin A

RDA

Children (upto 9 yrs) : **400–650 µg/day**

Men :**1000 µg/day**

Women :**850 µg/day,**

Pregnancy : **900 µg/day,**

Lactation:**950 µg/day**

Vitamin A

- Fat soluble
- Active form only in Animal tissues
- Pro vitamin A (**Beta carotene**) in plant tissues

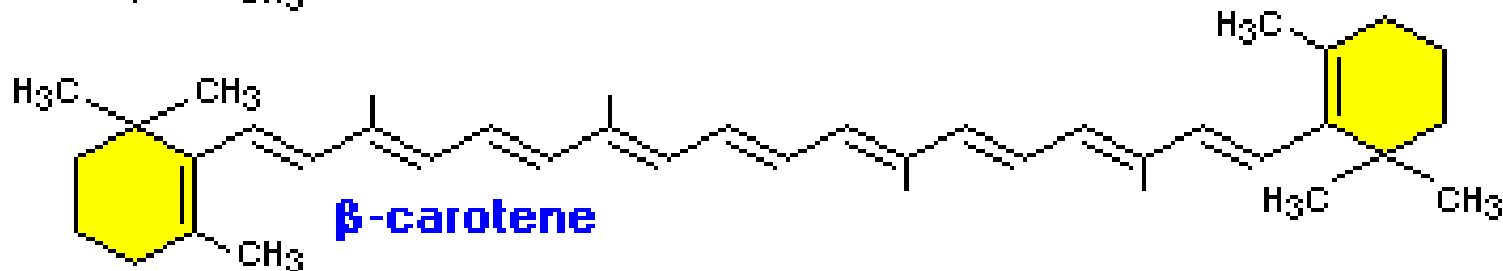
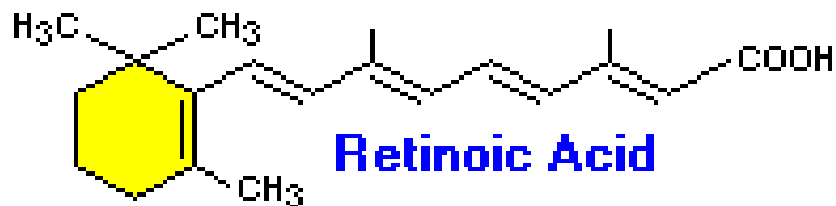
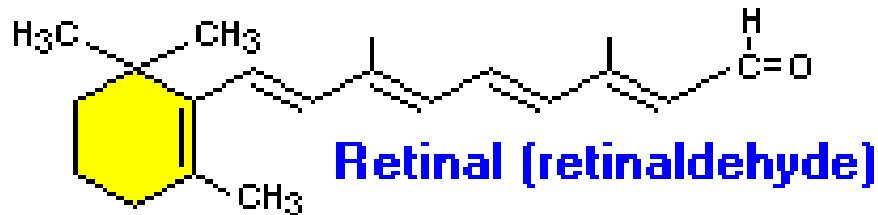
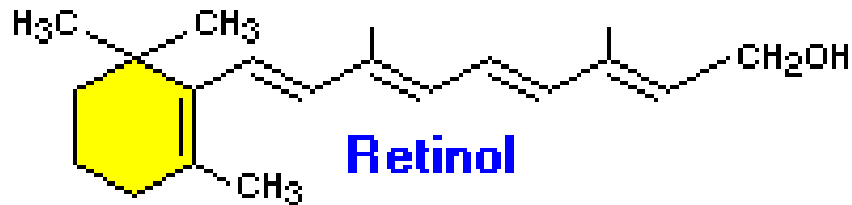
Retinoids

Compounds with Vitamin A activity .

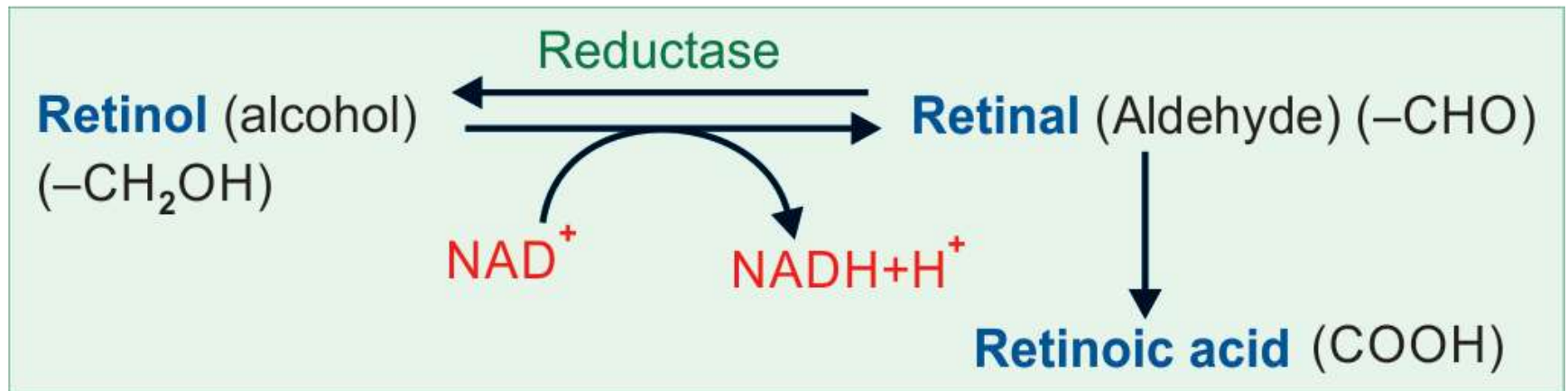
Polyisoprenoid with beta-ionone ring

- 1)Retinol(Alcohol form)
- 2)Retinal(Aldehyde form)
- 3)Retinoic acid(Acid form)

Vitamin A Different Forms



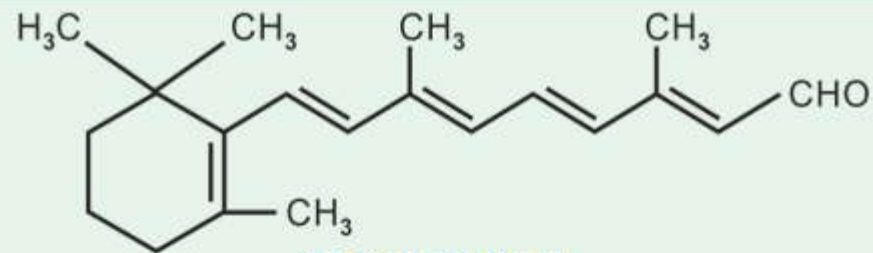
Interconversion of vitamin A molecules.



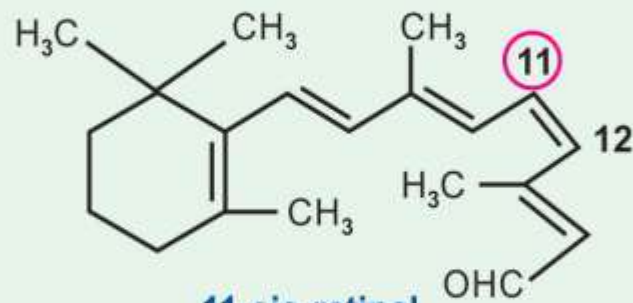
Isomeric forms of Vitamin A

All –trans Retinal (VitaminA1)

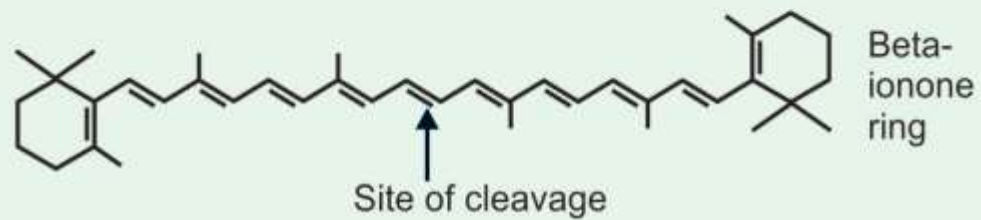
11-Cis Retinal (Vitamin A2) in Fish oil
(Biologically important compound)



All-trans-retinal



11-cis-retinal



Beta-carotene

Beta-ionone ring

Absorption

(Intestine with fats, require B.S)

Beta-carotene

↓ Dioxygenase

Retinal

↓ retinal reductase(NADH/NADPH)

Retinol

↓ Absorption to intestinal cell

Esterified with FA → Chylomicrons → Liver

(RE)

(Stored as Retinol Palmitate)

Transport

Liver  Peripheral tissues

As Trans retinol by RBP (Retinol binding protein)

Vit A deficiency-----RBP 

Uptake by tissues

R-RBP complex

bind to receptors on retina, skin, gonads & other tissues



RBP return

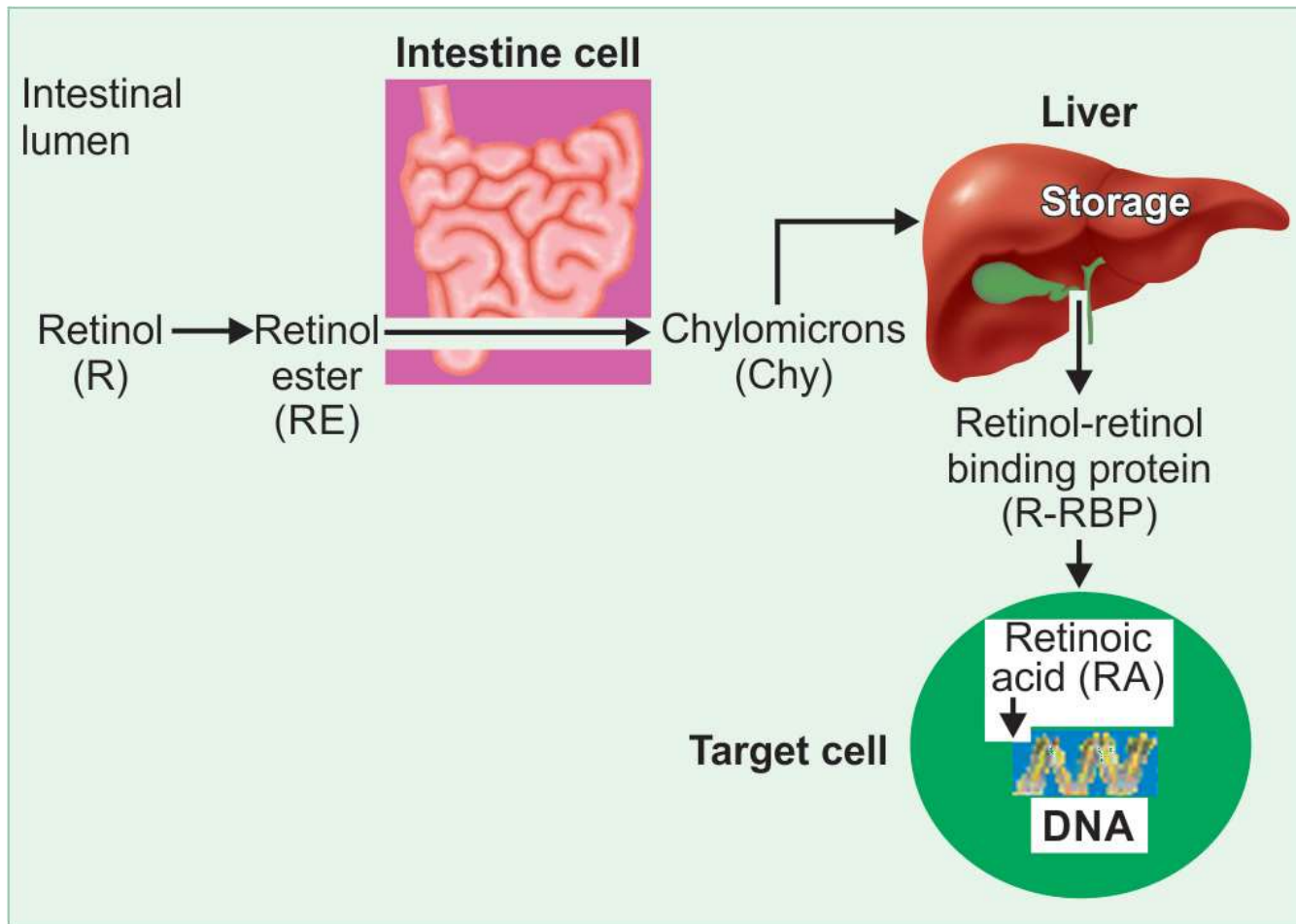
Inside cytoplasm Retinol bind to **CRBP**
(cellular retinoic acid binding protein)



HRE of DNA



Gene activation



Biochemical Role of Vitamin A in Vision

- 1)Wald's visual cycle
- 2)Dark adaptation mechanism
- 3)Dim light vision
- 4)Color vision

Other functions of Vit A

Gene regulation

Immunological system

Reproductive system

Antioxidant function

Effect on skin

Wald's Visual Cycle

Whole cycle of changes in Rhodopsin on exposure to light & its regeneration is known as Wald's visual cycle

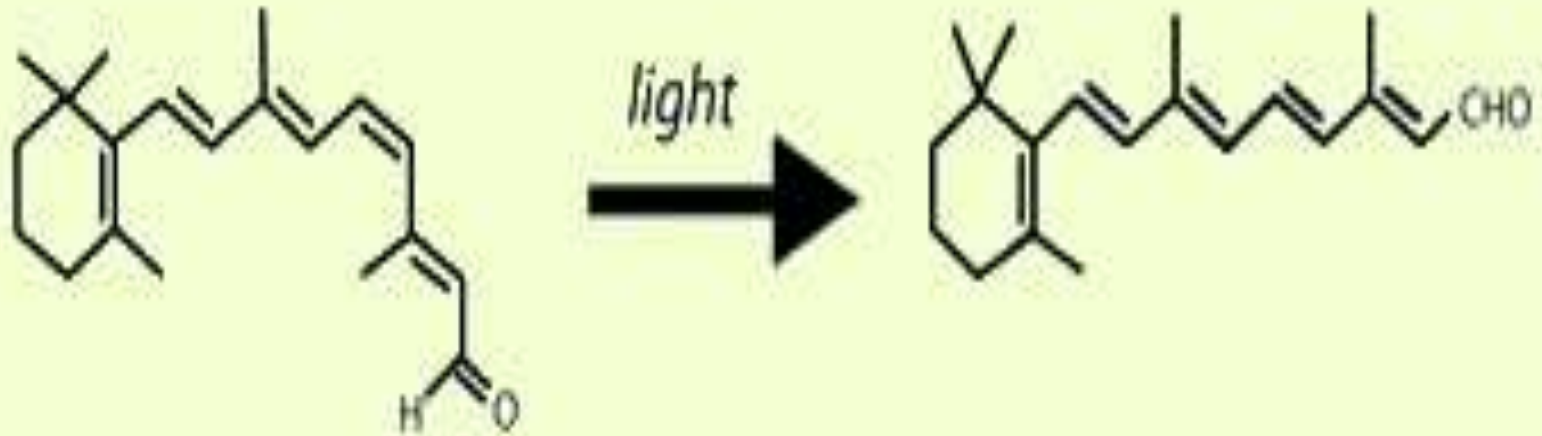
Wald's visual cycle

Photoisomerisation

A) Nerve impulse generation

B) Regeneration of 11-cis Retinal

Photo isomerisation



11-*cis* retinal

all-*trans* retinal

A) Nerve impulse generation

Rhodopsin-pivotal role

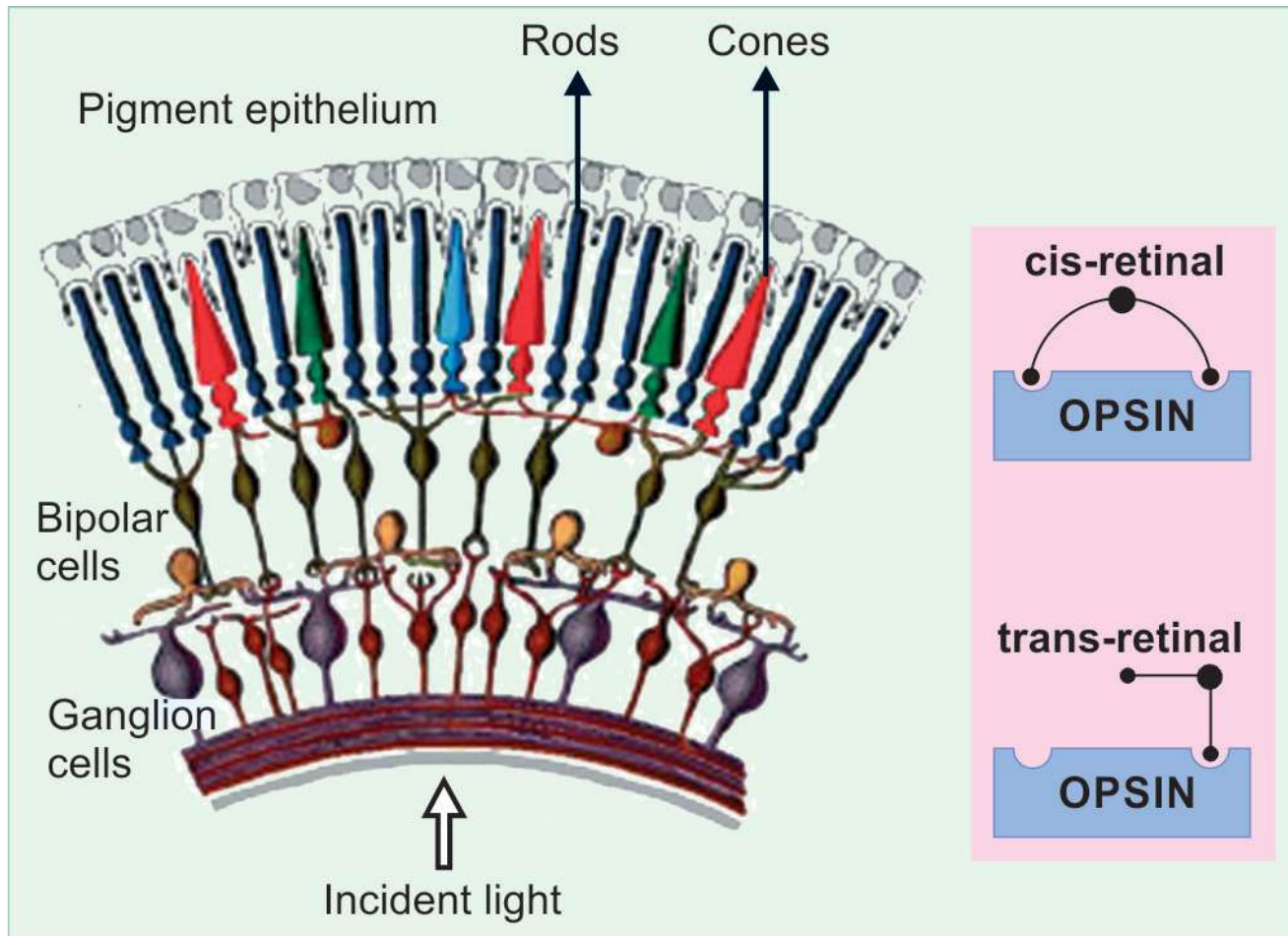
Opsin (protein part) and 11 -cis-retinal

Membrane protein in photoreceptor cells of retina.

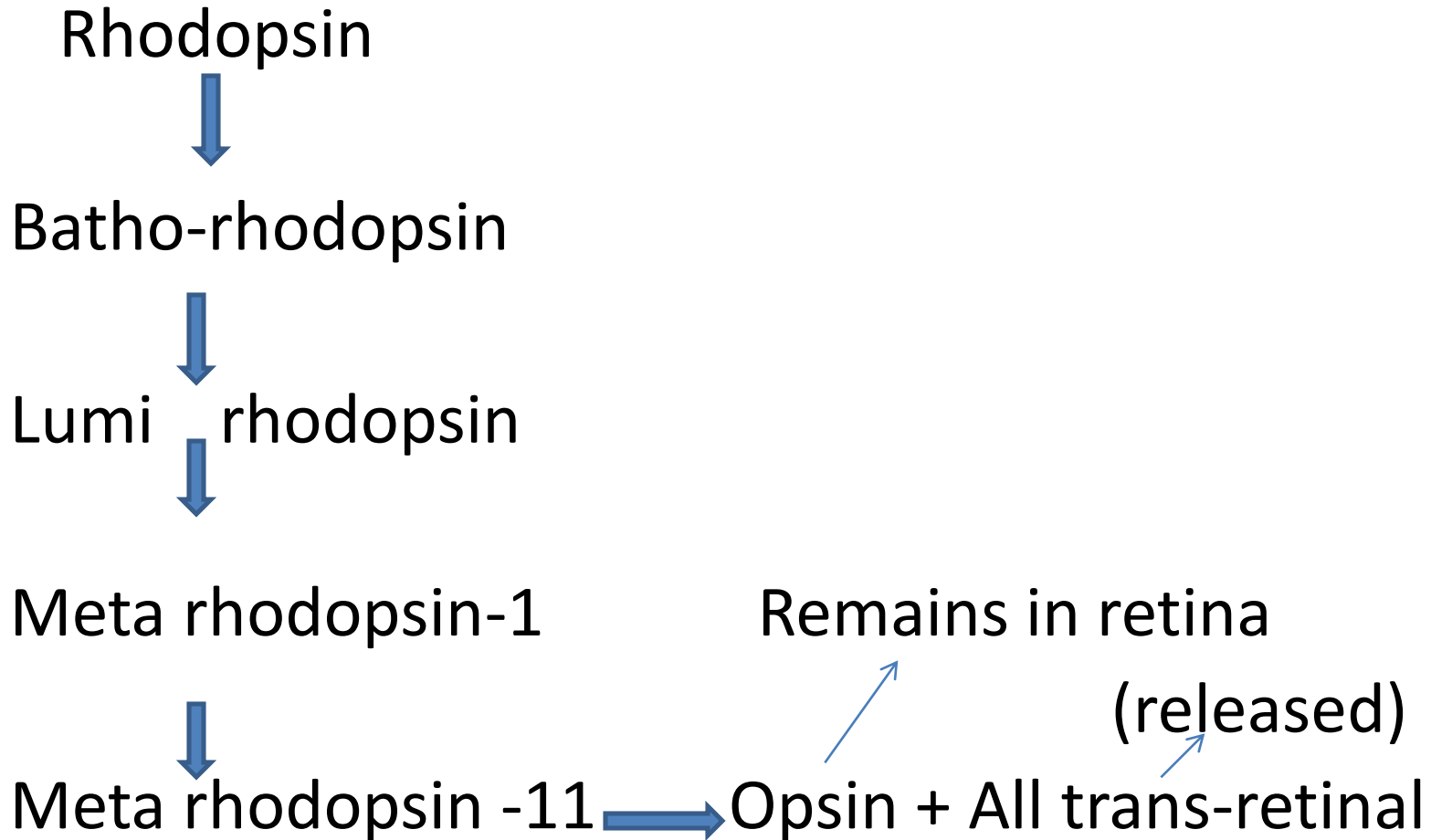
Visual pigments are G protein coupled receptors

Transducin is the G protein in retina

Retina Structure



Unstable intermediates

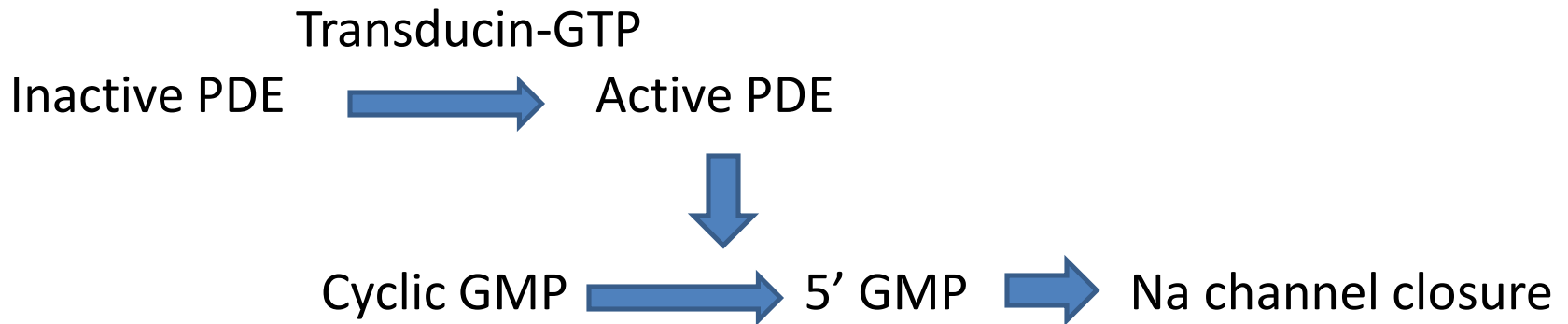


Nerve impulse

Bleaching of Rhodopsin & release of
All-trans retinal & Opsin activates G protein
Transducin.

Transducin activated by GTP binding

Nerve impulse



This triggers a nerve impulse in retina which is transmitted by **optic nerve to Brain**

Signal is terminated by **rhodopsin kinase** which phosphorylate the activated rhodopsin & inactivate it.

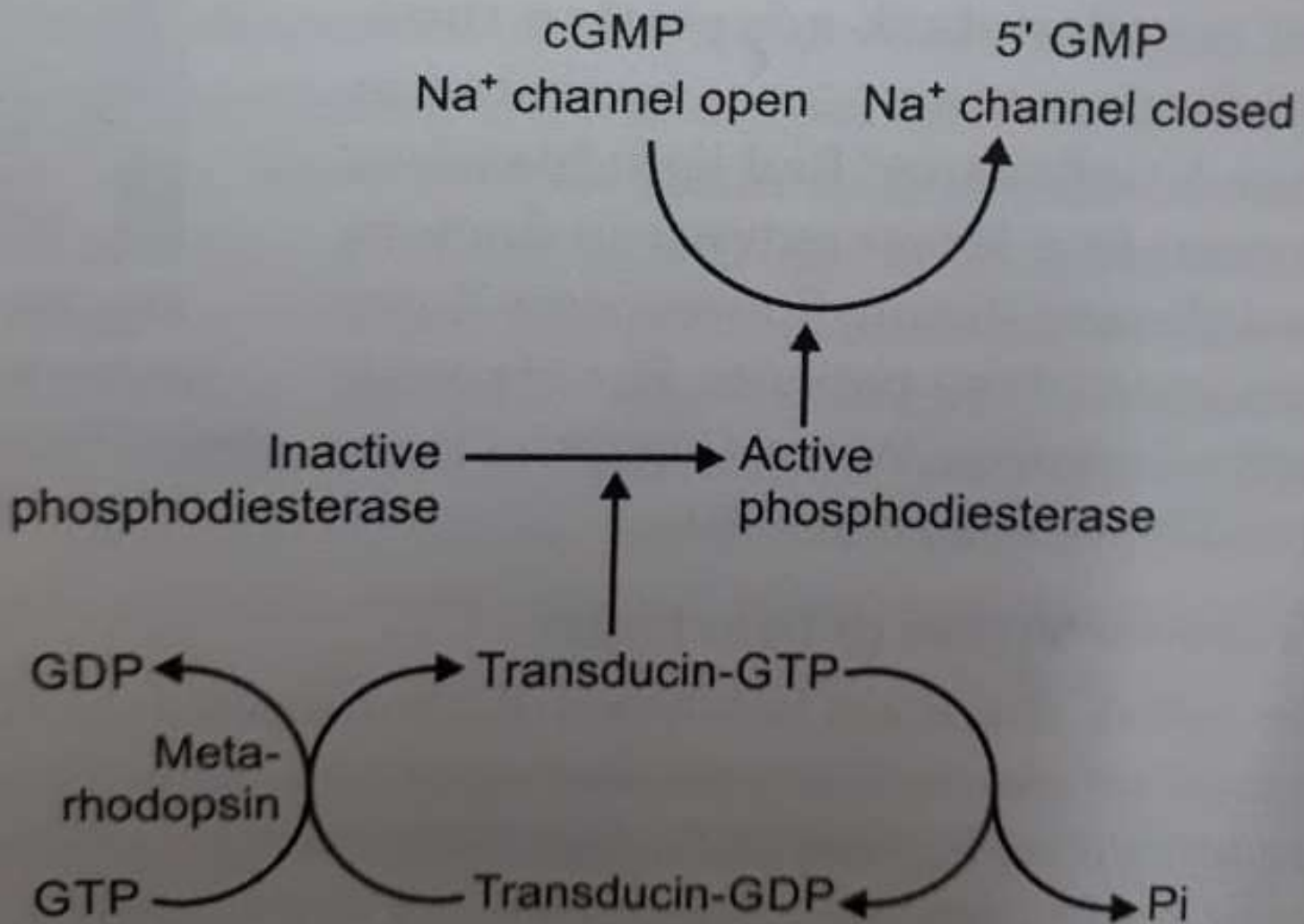
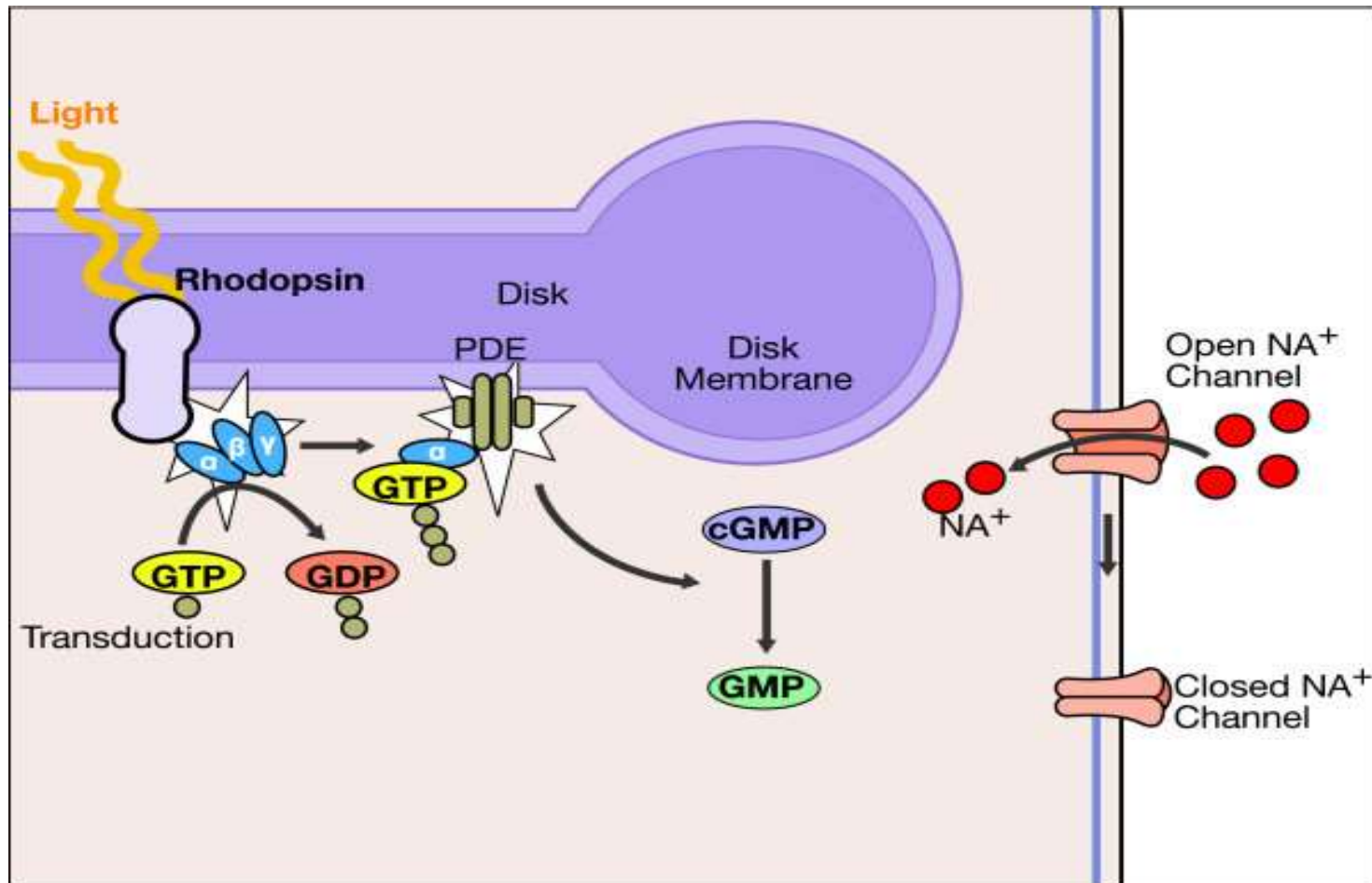


Fig. 28.10: Photoexcitation leads to activation of G-protein.

Phototransduction & Membrane hyperpolarisation



B. Regeneration of 11-cis retinal in retina

Opsin remains in retina

All trans-retinal enter blood circulation

In dark

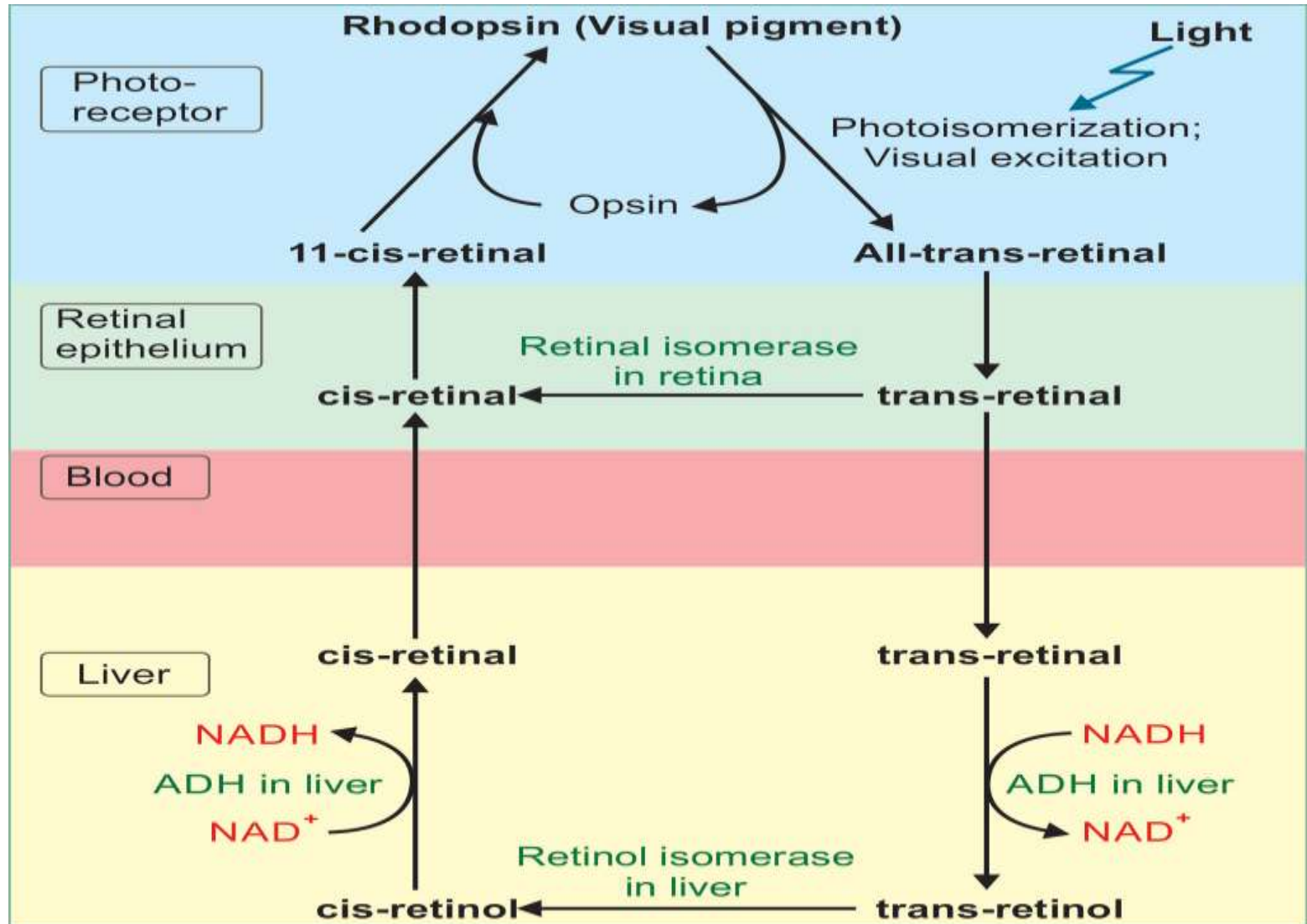
Retinal isomerase in retina

All trans-retinal  11-cis retinal

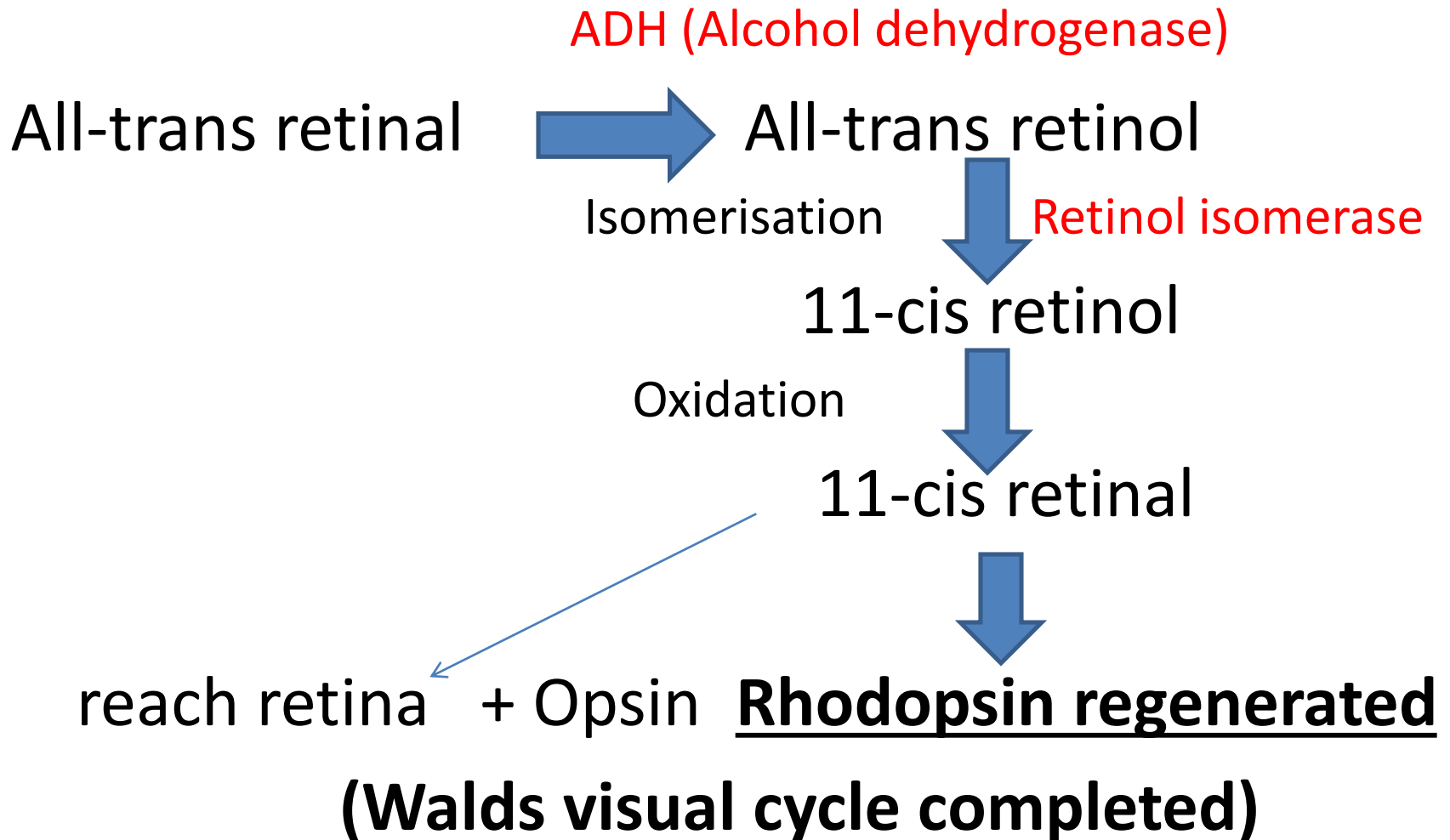
+Opsin 

Rhodopsin Regenerated

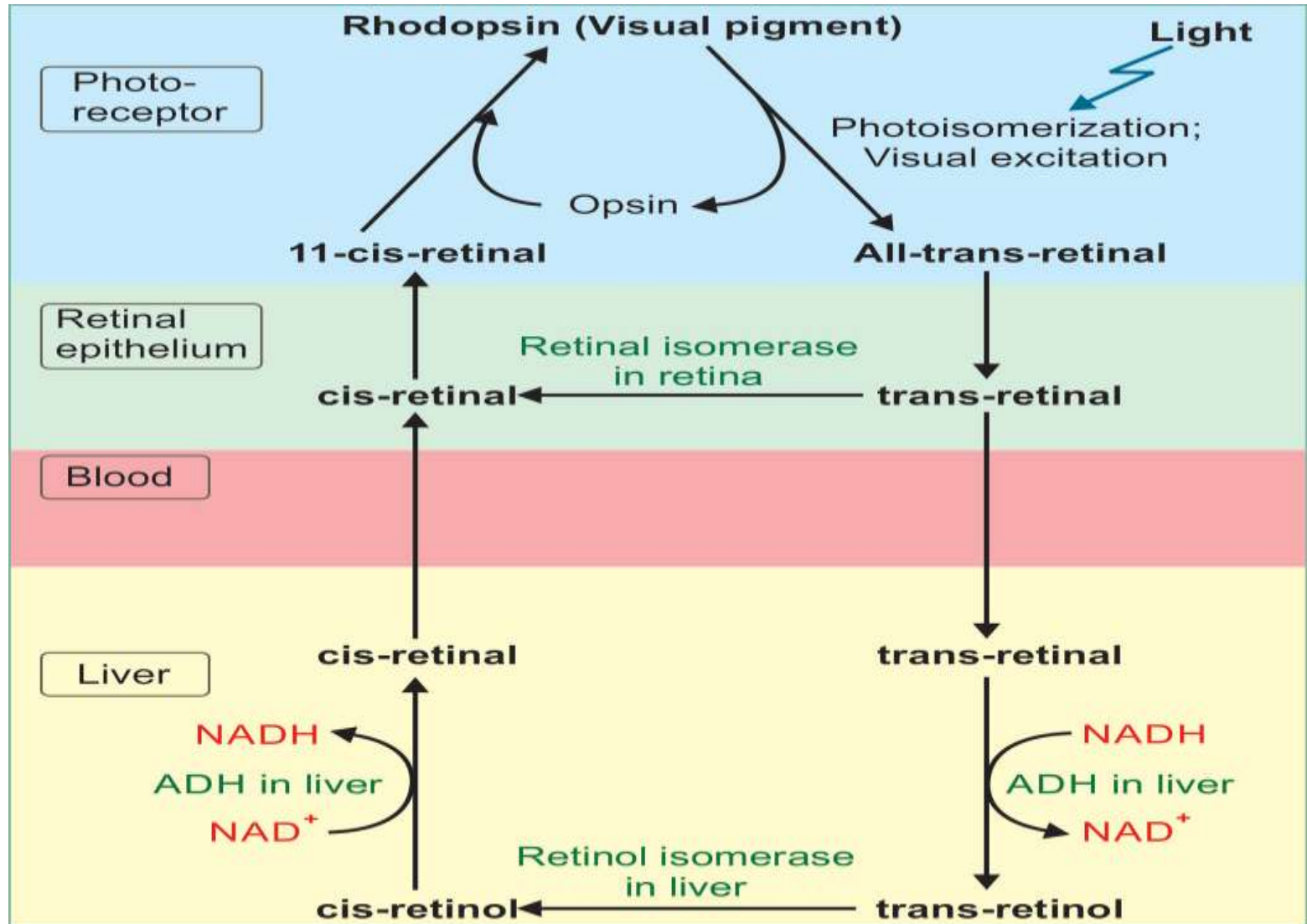
Wald's Visual Cycle



11 cis retinal regeneration in Liver



Wald's Visual Cycle



Dark Adaptation mechanism

Bright light deplete stores of rhodopsin in rods.

After a few mts rhodopsin is resynthesised & vision improved

This period is called **Dark adaptation time**

In Vitamin A deficiency (Cis retinal) Dark adaptation time increased.

- Rods for Dimlight vision
- Cones for vision in bright light & Color vision

Rods for Dimlight vision

In humans one eye contain 120 million rods

Each rod contain one 120 million molecules of rhodopsin

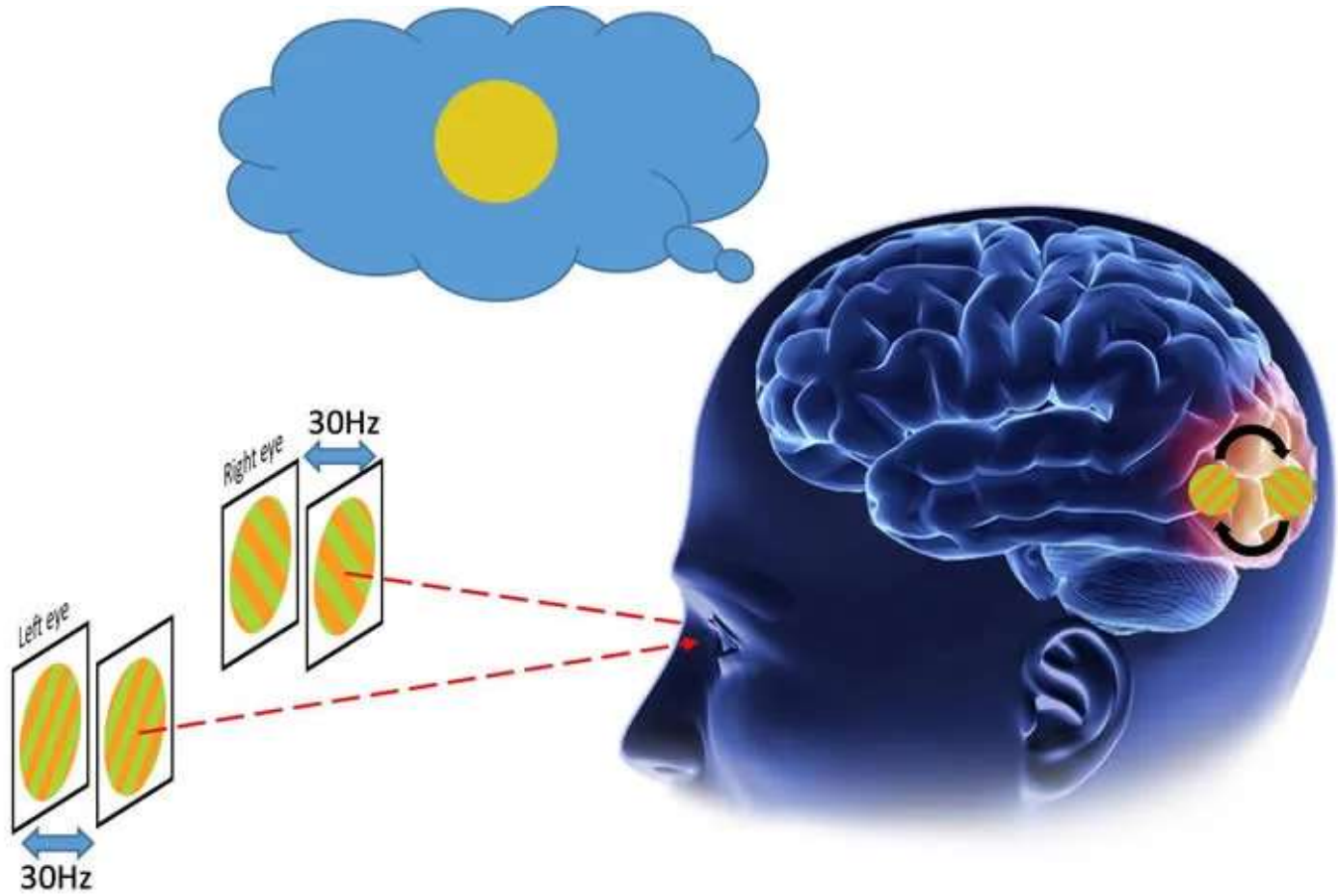
Cats & Owls eye contain more rods



Cones for vision in bright light & Color vision



70% of information input to brain is visual



Colors have profound influence in life



Effect of colors in human mood

Sad person---Blue mood (increase muscle tone)

Tranquilising effect-----Saffron color(muscle relaxation)

Optimism-----Rose color

Applications of color

----in Criminology, Psychiatry,interior
decoration,chromotherapy,Yoga

One eye-----6 million cones

Conopsin

- Cyanopsin-----Blue sensitive
- Iodopsin-----Green
- Porphyropsin-----Red

Reduction in cone or cone proteins---color blindness

Other biochemical functions

1) Gene expression & tissue differentiation

All trans retinoic acid (RAR receptor) &
9 cis retinoic acid (RXR receptor)
act like steroid hormones.

RXR form dimer with Vit D receptor.

Vit A deficiency impair Vit D function

2)Immunological System

Retinoic acid in differentiation of T cells to regulatory T cells

3)Reproductive system

Retinol necessary for normal reproduction

4)Anti oxidant property

Carotenoids in fresh vegetables are natural antioxidants.

Reduce cancer incidence

Beta carotene supplements prevent
Cardio vascular diseases

5)Effect on Skin

Retinoic acid Promotes growth & differentiation
of epithelial cells

Maintain normal epithelium & skin

Vitamin A deficiency

1)Primary Cause

Inadequate intake of fruits & Vegetables

2)Secondary cause

- a)Obstructive jaundice (defective lipid absorption)
- b)Liver cirrhosis(less RBP Synthesis)
- c)Chronic nephrosis(loss of RBP through urine)
- d)Chronic alcoholism

Vit A -Defeciciency manifestations

1)Eye manifestations

Night Blindness or Nyctalopia

Bitot's Spots

Xerophthalmia

Keratomalacia

Preventable Blindness

2)Other manifestations

Skin and Mucous Membrane Lesions,

Growth retardation

Reduced immunity against infections.

1: Eye manifestations

- a) Nyctalopia
- b) Bitot's spots
- c) Xerophthalmia
- d) Keratomalacia

a) Nyctalopia

- Night blindness
- Visual acuity diminished in dim light
- Dark adaptation time increased

b) Bitot's spots

Triangular
White
Grayish
plaques



c)Xerophthalmia

- Dry,thick ,wrinkled conjunctiva
- Keratinisation of corneal epithelium



Progress to

d) Keratomalacia

Softening of cornea
Corneal opacity
Bacterial infection
Ulceration,
perforation of Cornea



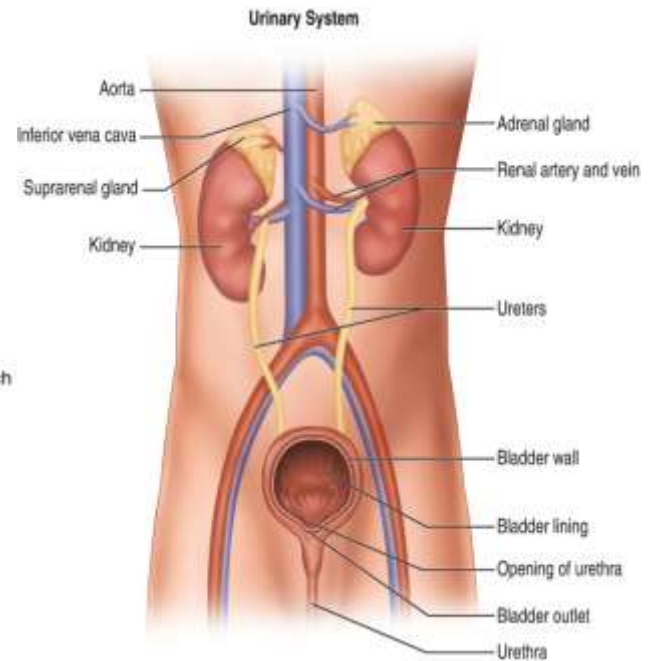
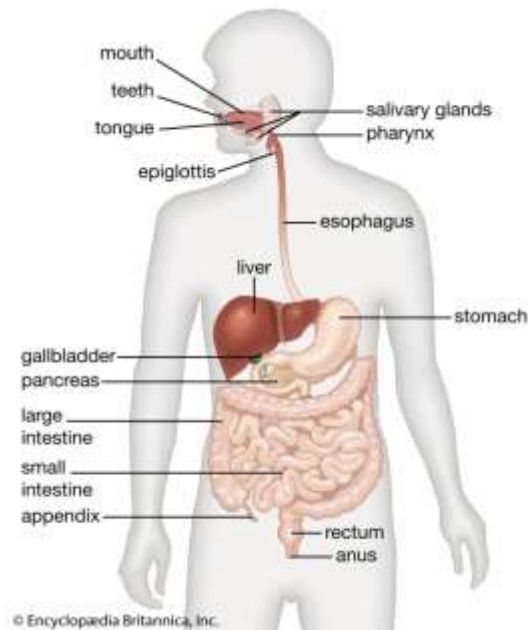
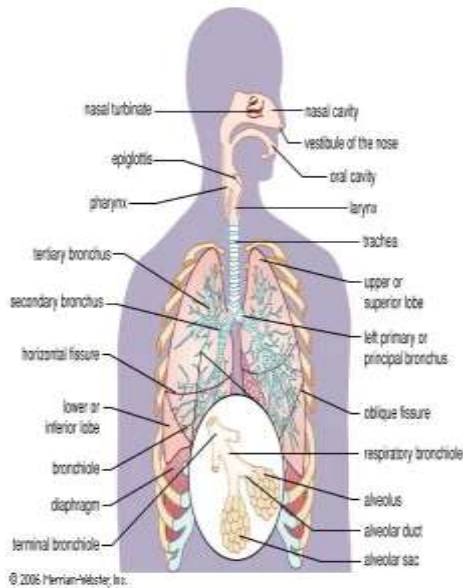
TOTAL BLINDNESS

2.Skin &Mucous membrane lesions

- Follicular Hyperkeratosis—cause rough skin
- Increased skin infections



Keratinising metaplasia of RT,GIT,UT



Acne

- Most common disease of skin
- Seen in 85% teen agers
- In Endocrine disorders

Isotretinoin(13-cis retinoic acid), synthetic variant of Vit A reduce sebaceous secretions, prevent acne formation

Also used to treat Sqamous cell carcinoma of skin

Vit A deficiency also cause

Growth retardation, Failure of skeletal growth
(defective synthesis of chondroitin sulphate)

Defecency management

In Defecency states Vitamin A given as capsules or injections

Therapeutic dose is 20-50 times higher than RDA

All-transretinoic acid used in treatment of promyelocytic leukemia. Causes remission.

Assessment of Vit A deficiency

Dark adaptation test

Serum RBP Estimation

Serum Vit A Estimation

(Carr & Price reaction, blue color measured by spectrophotometry)

Normal blood level-----25-50 $\mu\text{g}/\text{dl}$

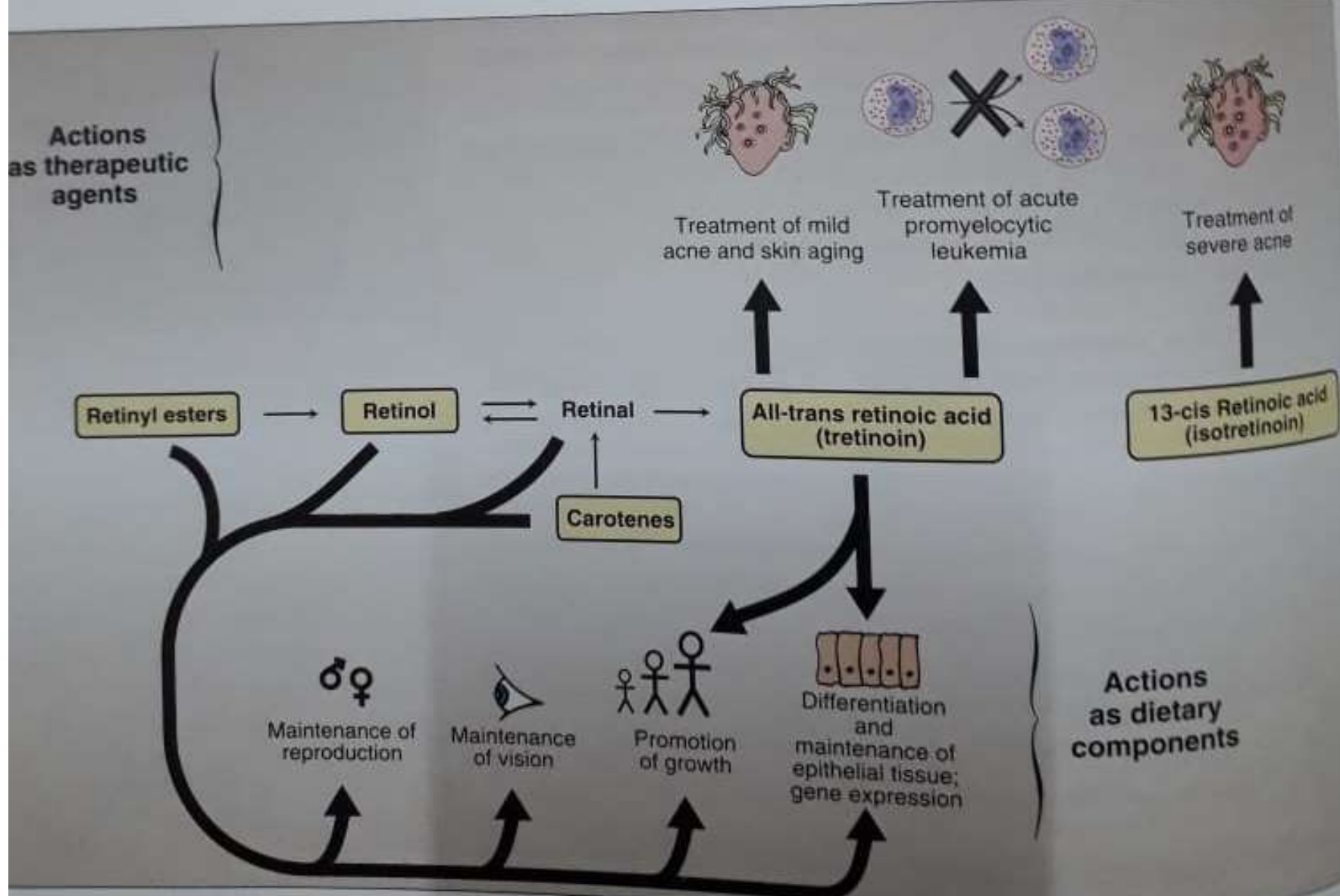


Figure 32.21

Hypervitaminosis

- Excessive intake can lead to toxicity since the vitamin is stored.
- Symptoms of toxicity are anorexia, irritability, headache, drowsiness and vomiting, **increased intracranial tension.**
- Sometimes swelling over long bones **(bony exostosis)** may occur with painful bones. Enlargement of liver is also seen in children.

Active forms

Sources

RDA

Vitamin A in vision and Wald's visual cycle

Deficiency manifestations

Management of deficiency

Prevention of deficiency

