# FAT SOLUBLE VITAMINS

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

# VITAMIN A

## CHEMISTRY

- All compounds with Vit A activity - retinoids

- Compounds with a Beta-Ionone ring & Polyisoprenoid hydrocarbon chain

- Compounds with Vit A activity

- Retinol
- Retinal
- Retinoic acid
- Beta Carotene: pro vitamin A

- Most common – all-trans-retinal - Vit A1
- Biologically imp – 11-cis –retinal

- ACTIVE FORM OF VITAMIN A IS PRESENT ONLY IN ANIMAL TISSUES
- In plant tissues - pro-vitamin A β carotene
- β carotene – 2 molecules of retinal joined
- As a source of Vit A , β carotene is only 1/6 $^{th}$ as effective as retinol

# SOURCES

- Animal sources – cod liver oil, shark liver oil, milk, butter, cream, cheese, egg yolk

- Plant sources – ***contain β carotene.***

  carrot ,papaya,mango, green leafy vegetables

- Cooking – VIT. A activity not destroyed

## RECOMMENDED DAILY ALLOWANCE

- Infants & children = 400 –600 µgm/day

- Men = 750 –1000 µgm/day
- Women = 750 µgm/day
- Pregnancy = 1000 µgm/day
- Lactation = 1200 µgm/day

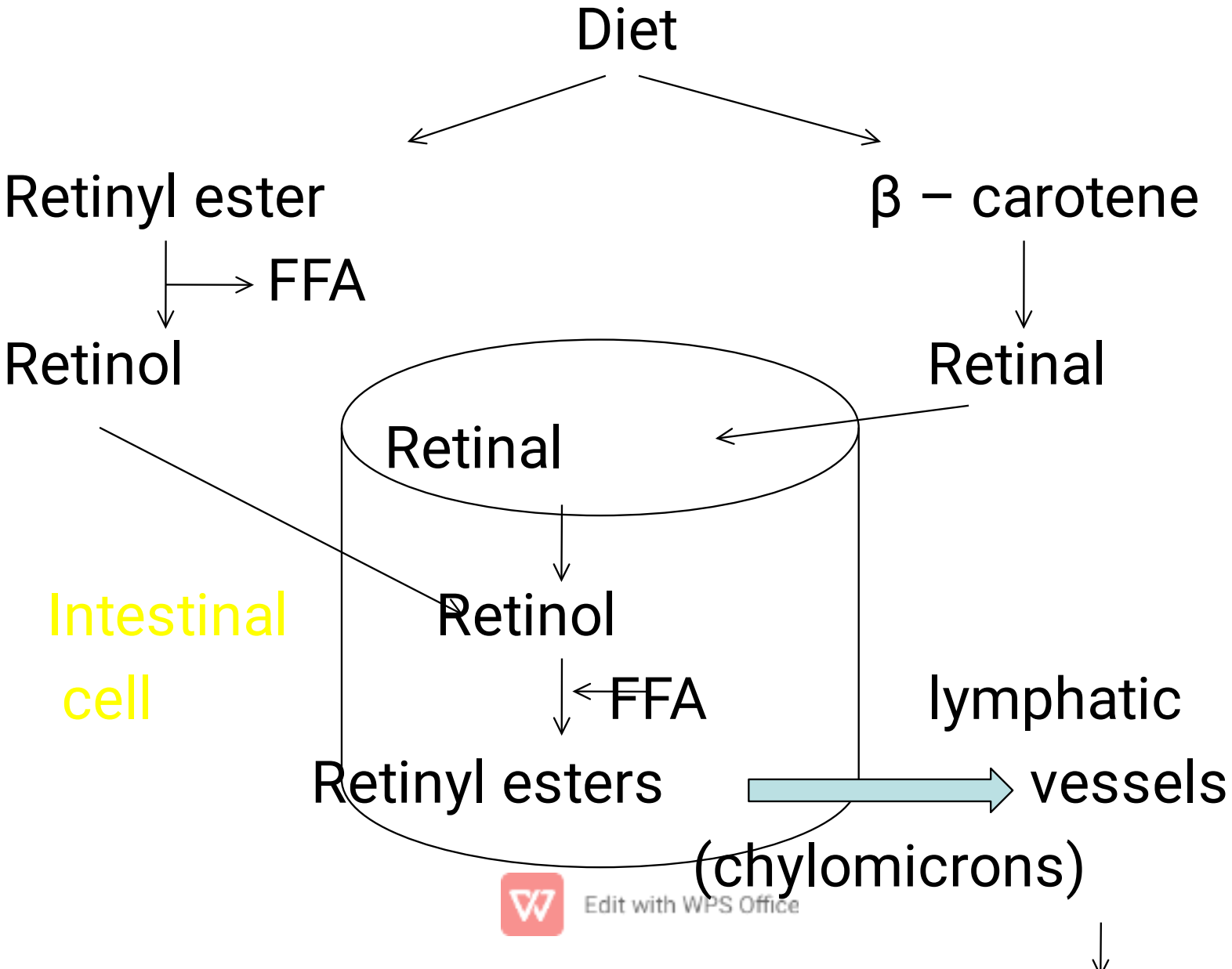
# Absorption & Storage

Retinol is absorbed from small intestine

Retinol esters present in diet are hydrolysed in the lumen and absorbed into intestinal epithelium

β- carotene is oxidatively cleaved by β carotene dioxygenase to 2 molecules of Retinal

In intestinal mucosa, Retinal is reduced to retinol by retinal reductase


Diet
Retinyl ester
β – carotene
FFA
Retinol
Retinal
Retinal
Intestinal cell
Retinol
FFA
lymphatic vessels
Retinyl esters
(chylomicrons)
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A small fraction of retinal is oxidized to retinoic acid

In the mucosal cell, retinol is re esterified with saturated FA & incorporated into chylomicrons – taken up by the liver - stored as retinol/retinyl palmitate

Absorption requires bile salts, takes place along with other fats

# TRANSPORT

- For transport, retinol  is bound to retinol binding protein (RBP)

- Tissue uptake

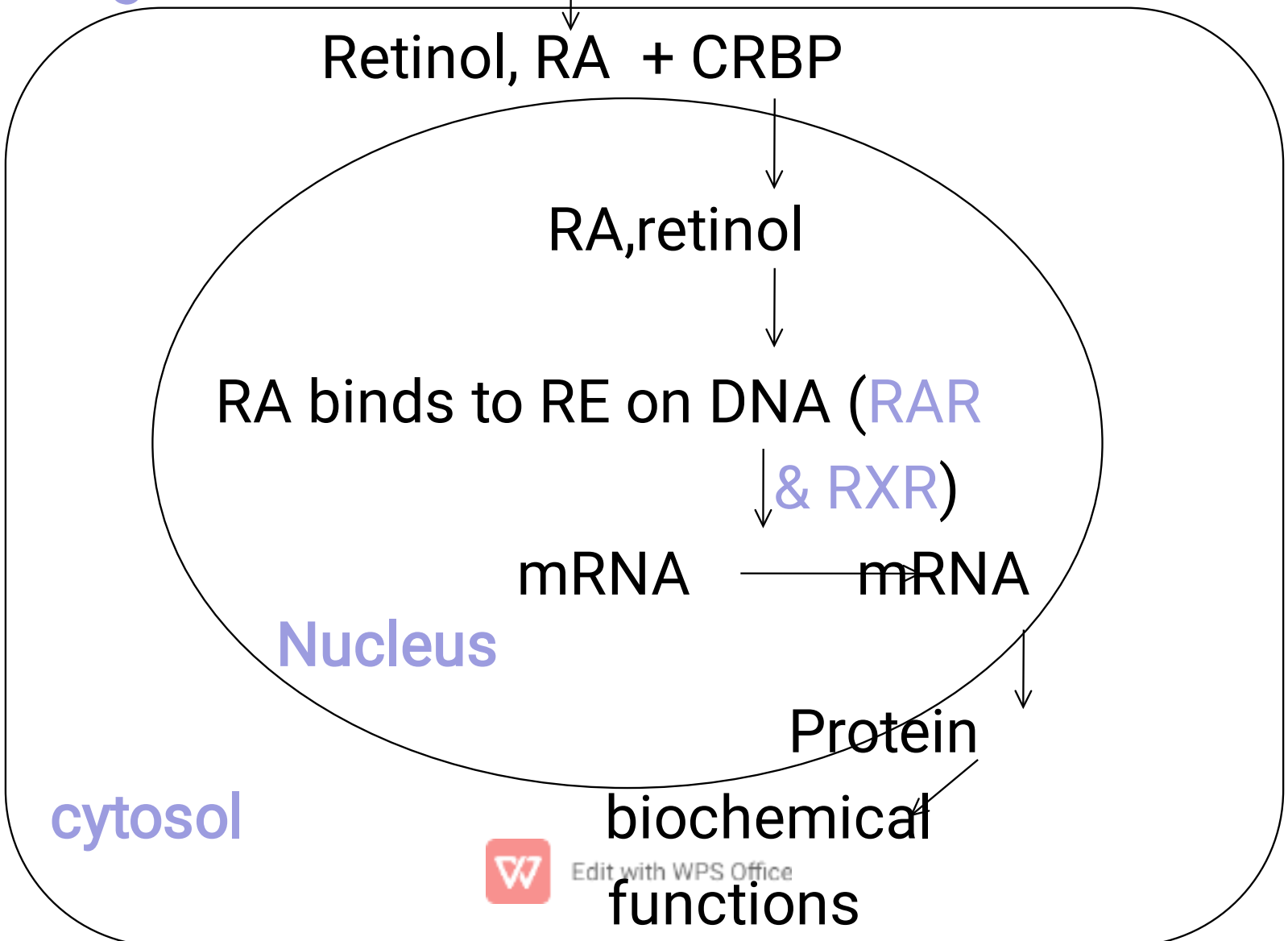
– Retinol – RBP complex binds to receptors on cell surface of peripheral tissues

- Retinol enters the cell

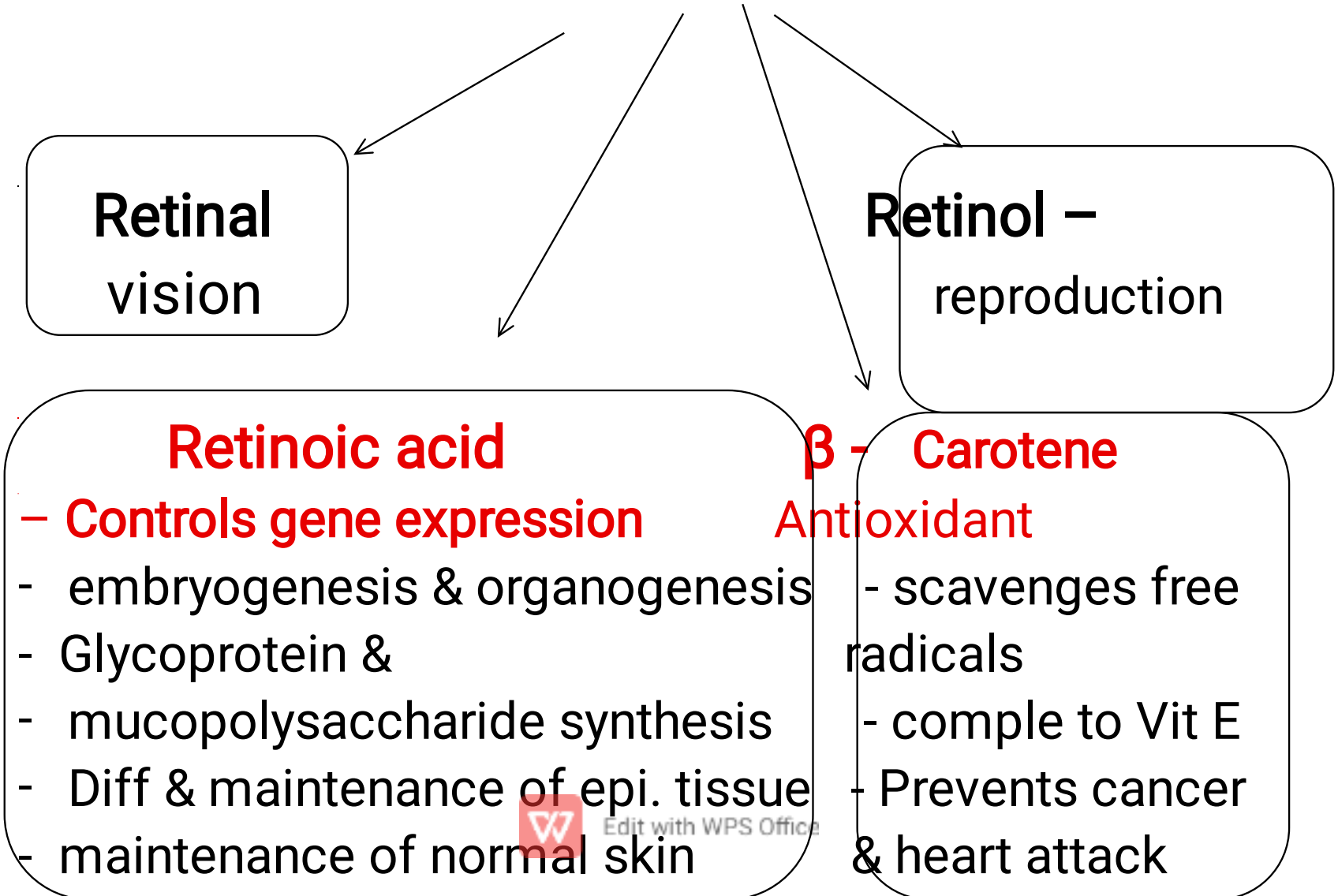
- In cytoplasm, vitamin binds to cellular retinoic acid binding protein (CRBP)

- Retinol & Retinoic acid  bound to CRBP bind to nuclear proteins – control expression of genes – synthesis of specific proteins- carry out biochemical functions of vitamin A

- Target cell



# BIOCHEMICAL ROLE OF VITAMIN A



# BIOCHEMICAL ROLE OF VITAMIN A

- Retinal – active form for normal vision
- Retinoic acid

– Growth, differentiation & maintenance of epithelial tissue

- mucus secretion
- maintenance of normal skin
- Gene expression

- Retinol

- for normal reproduction (supports spermatogenesis in the male)

# *VITAMIN A (RETINAL) IN VISION*

- Photosensitive cells in retina – Rods & Cones
- Rods – vision in dim light
- Cones – vision in bright light & color vision
- Visual Pigments in Retina –

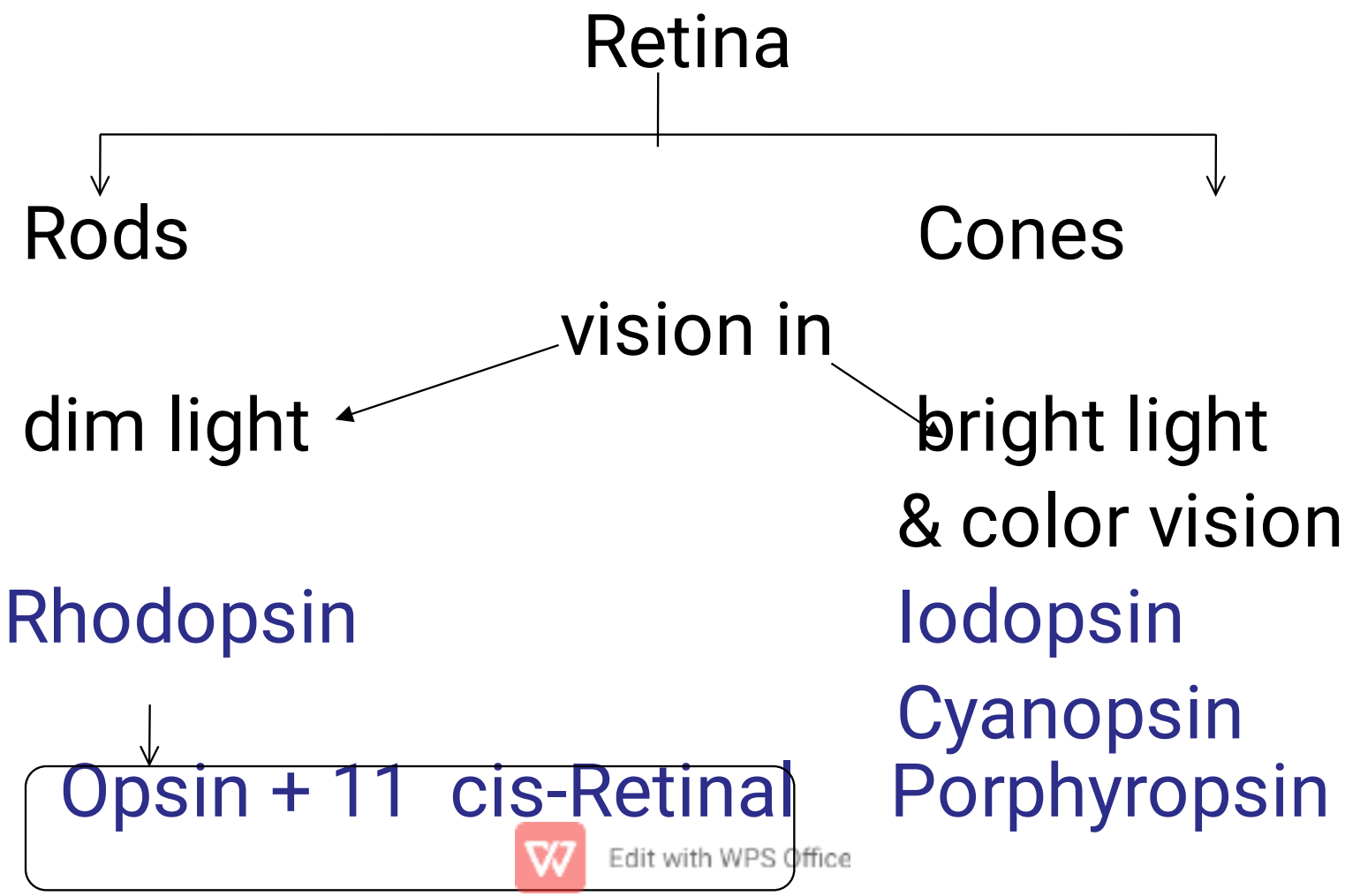
Rod cells - **Rhodopsin**

**Cone cells – Iodopsin - Green**

**- Cyanopsin - Blue**

**- Porphyropsin - Red**

# 1. RETINAL - VISION



- Rhodopsin is a membrane protein made up of opsin and 11 – cis retinal (prosthetic group)

- Rhodopsin has strong light absorption in visible range (400-700nm)

# In dark

↑ c GMP

↓

$Na^+/Ca^+$ ion channel open

↓

Influx of $Na^+/Ca^+$ ion

## Resting membrane potential

# Changes on light stimulus

- Rhodopsin is converted into several unstable intermediates and finally dissociates to opsin and all trans retinal.

# Photoexcitation of rhodopsin

Rhodopsin

↓

Bathorhodopsin

↓

Lumirhodopsin

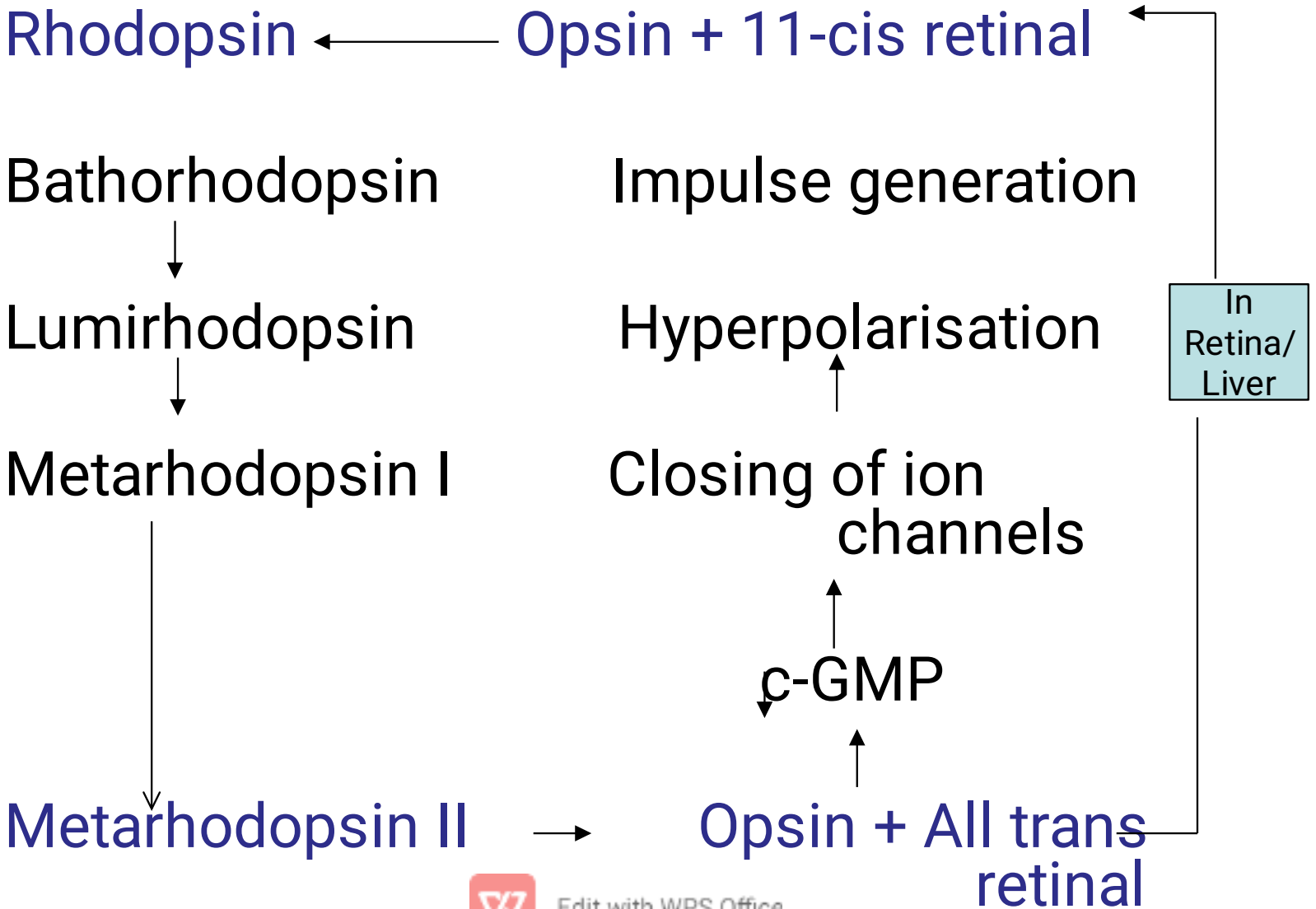
↓

Metarhodopsin I

↓

Metarhodopsin II → Opsin + All trans retinal

Visual cycle is completed when All trans retinal is isomerized to 11 cis retinal



# Termination of impulse

- ↑ cGMP ⟶ opening of $Na^+/Ca^+$ channel

  ↓

  membrane depolarization

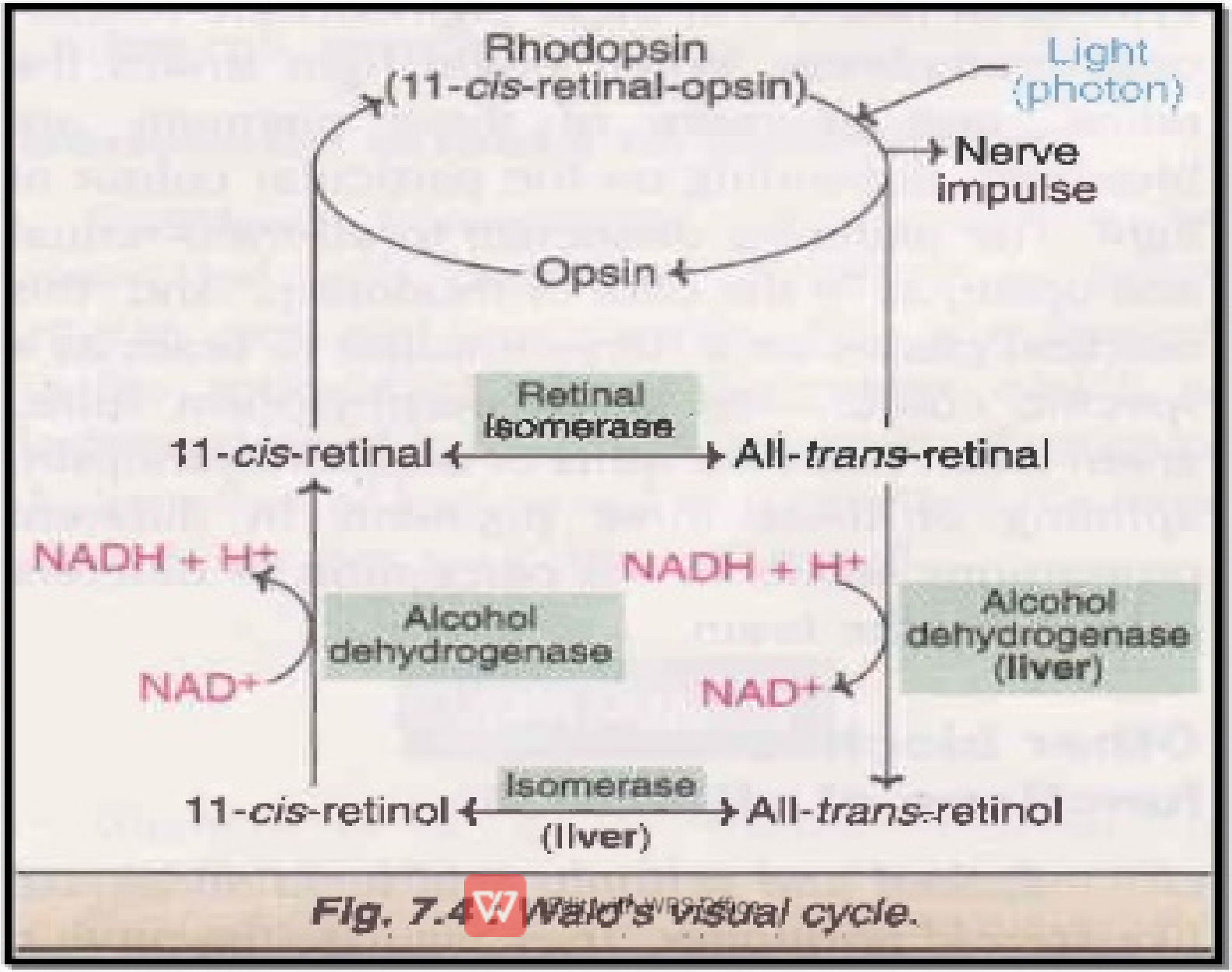
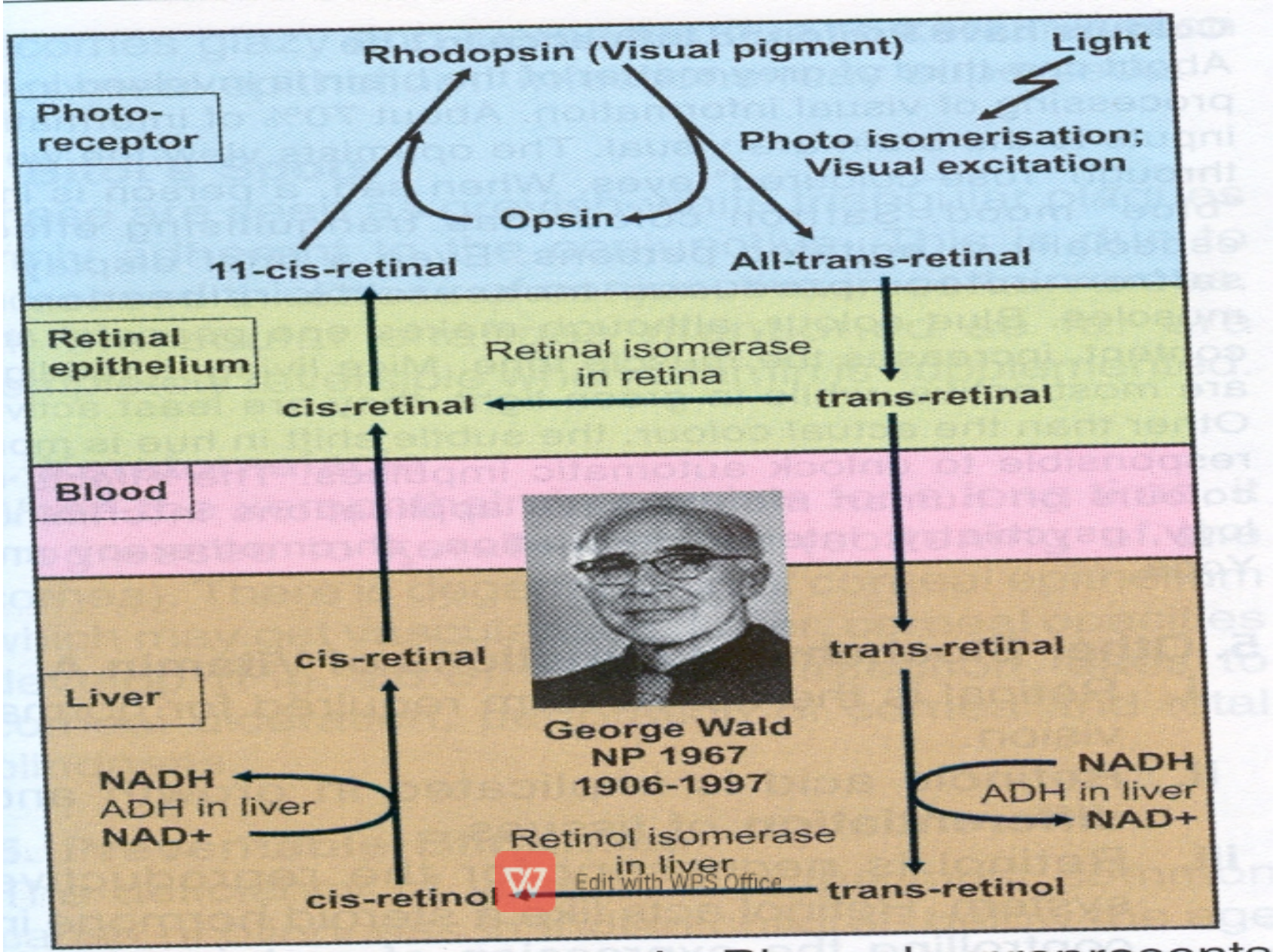



*Fig. 7.4 Wald's visual cycle.*

# *WALDS VISUAL CYCLE*

- The overall mechanism through which Vit.A functions in visual system is known as walds visual cycle /Rhodopsin cycle

- It is the cycle/reactions by which all trans retinal is reconverted to 11 cis retinal for regeneration of rhodopsin


Rhodopsin (Visual pigment)
Light
Photo-
receptor
Photo isomerisation;
Visual excitation
Opsin
11-cis-retinal
All-trans-retinal
Retinal
epithelium
Retinal isomerase
in retina
cis-retinal
trans-retinal
Blood
cis-retinal
trans-retinal
Liver
George Wald
NP 1967
1906-1997
NADH
ADH in liver
NAD+
NADH
ADH in liver
NAD+
Retinol isomerase
in liver
cis-retinol
trans-retinol
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# DARK ADAPTATION

Def: The time required for improved vision when one moves from bright light to a dark environment

Mechanism:

- Continued bright light depletes the rhodopsin stores
- there is difficulty in seeing
- Within a few minutes,Rhodopsin is regenerated
- Vision is improved

This is the time taken for resynthesis of Rhodopsin

- **In vitamin A deficiency , dark adaptation time is ↑**

## 2. Retinol

Required for

1. normal reproduction
2. Differentiation and maintenance of germinal epithelium.

# 3. RETINOIC ACID

## Controls Gene expression:

- Helps in embryogenesis and organogenesis.
- Glycoprotein synthesis
- Mucopolysaccharide synthesis
- Prevents collagen break down
- Prevents keratinization
- Supports growth & tissue differentiation
- Affects cellular & humoral immunity

- Maintenance of normal epithelium and skin
- Growth & development - Role in cell differentiation & cell division
- Formation of bone matrix & connective tissue

## 4. ( β – Carotene) ANTI OXIDANT FUNCTION

- Scavenges free radicals
- Complementary to vit. E
- Helps prevention of cancers
- May prevent heart attacks

# Causes of VITAMIN A deficiency

- ↓ intake
- ↓ absorption (obstructive jaundice)

- Malnutrition - ↓ RBP

- Liver cirrhosis - ↓ RBP synthesis

- Chronic nephrosis – excretion of RBP

# *1. Manifestations in Eye*

- **A. Nyctalopia (night blindness)**

- Visual acuity diminished in dim light
- Dark adaptation time ↑
- Can’t read or drive in poor light

- **B. Xerophthalmia**

- conjunctiva & corneal epithelium  dry & keratinised

- conjunctiva loses its transparency

- Cornea - dull & lusterless


Xerophthalmia

- C. Bitot’s spots

- White patches of keratinised epithelium on the sclera

- All these changes are completely reversible, if vitamin is supplemented


EyeRounds.org
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- **D. Keratomalacia**
- softening of cornea
- degeneration of corneal epithelium
- corneal ulcerations due to bacterial infections
- perforation of cornea

- **E.Total blindness**

# WHO classification

| | |
|---|---|
| XN | Night blindness |
| X1A | Conjunctival xerosis |
| X1B | Bitot's spot |
| X2 | Corneal xerosis |
| X3A | Corneal ulceration/keratomalacia (< $^{1}/_{3}$ corneal surface) |
| X3B | Corneal ulceration/keratomalacia (≥ $^{1}/_{3}$ corneal surface) |
| XS | Corneal scar |
| XF | Xerophthalmic fundus |

# KERATOMALACIA

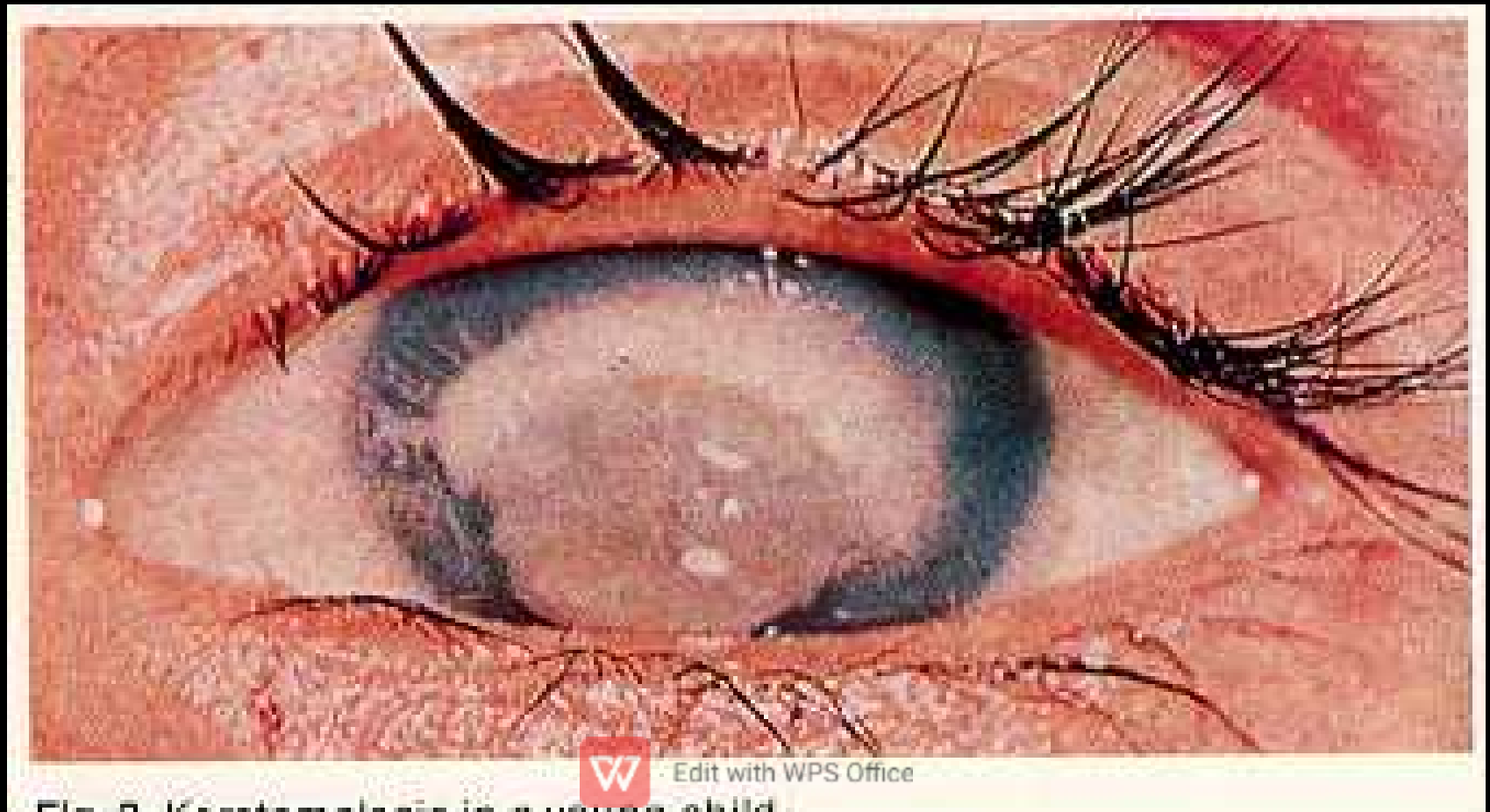
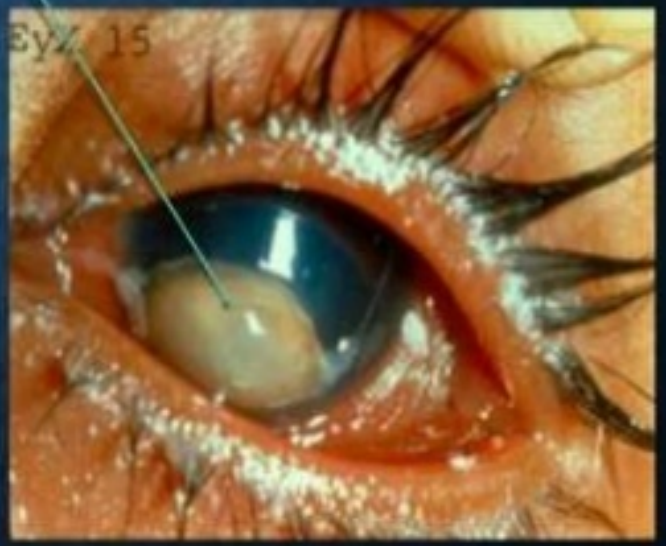




Fig. 3 Keratomalacia in a young child.

# Keratomalacia followed by Blindness



# Deficiency manifestations of Retinol and retinoic acid

## *Manifestations in skin& mucous membrane*

Phrenoderma – due to hyperkeratinisation of epithelium lining follicles – toad like rough skin

Keratinisation of epithelium lining GIT, respiratory tract & genitourinary tract

Keratinisation of urinary tract epithelium → urinary calculi

Skin changes → infections

# assessment of deficiency

- C/F +
- Vit.A level in serum ↓
- RBP level in serum ↓
- Dark adaptation time ↑

# HYPERVITAMINOSIS A

Due to high intake of vit. A

- Anorexia
- nausea
- vomiting
- Headache
- irritability (pseudo tumor cerebri)