



Important Doctors slides  
Extra Information **Doctors notes**



# Biochemistry

## Vitamin A & Visual Cycle

[Editing file](#)

# OBJECTIVES

By the end of this lecture, the students should be able to:

- understand the function and transport of vitamin A.
- To know the role of vitamin A in vision and deficiency can lead to blindness

Background of the lecture:

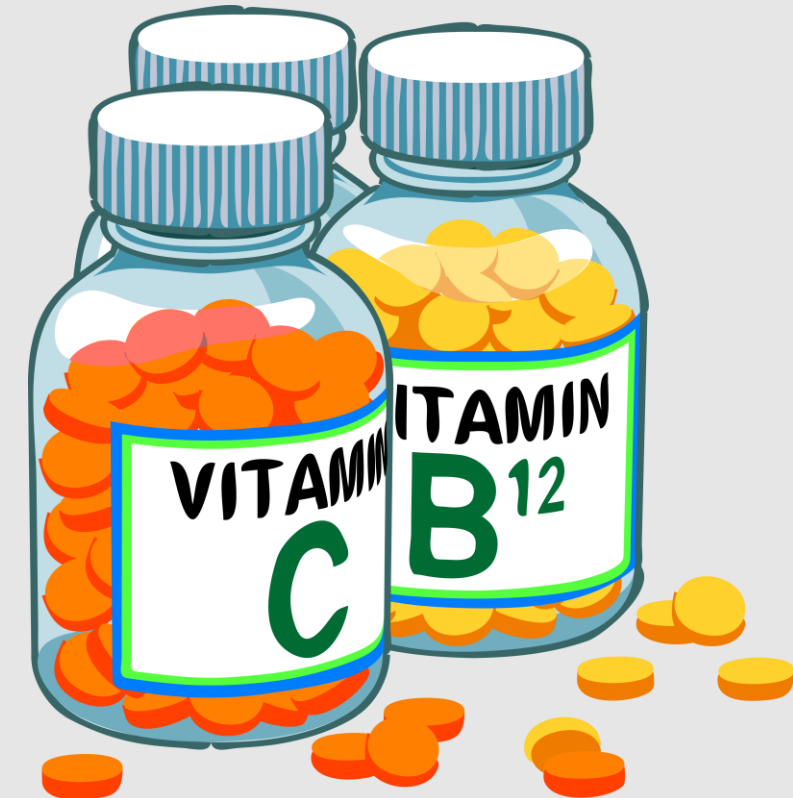
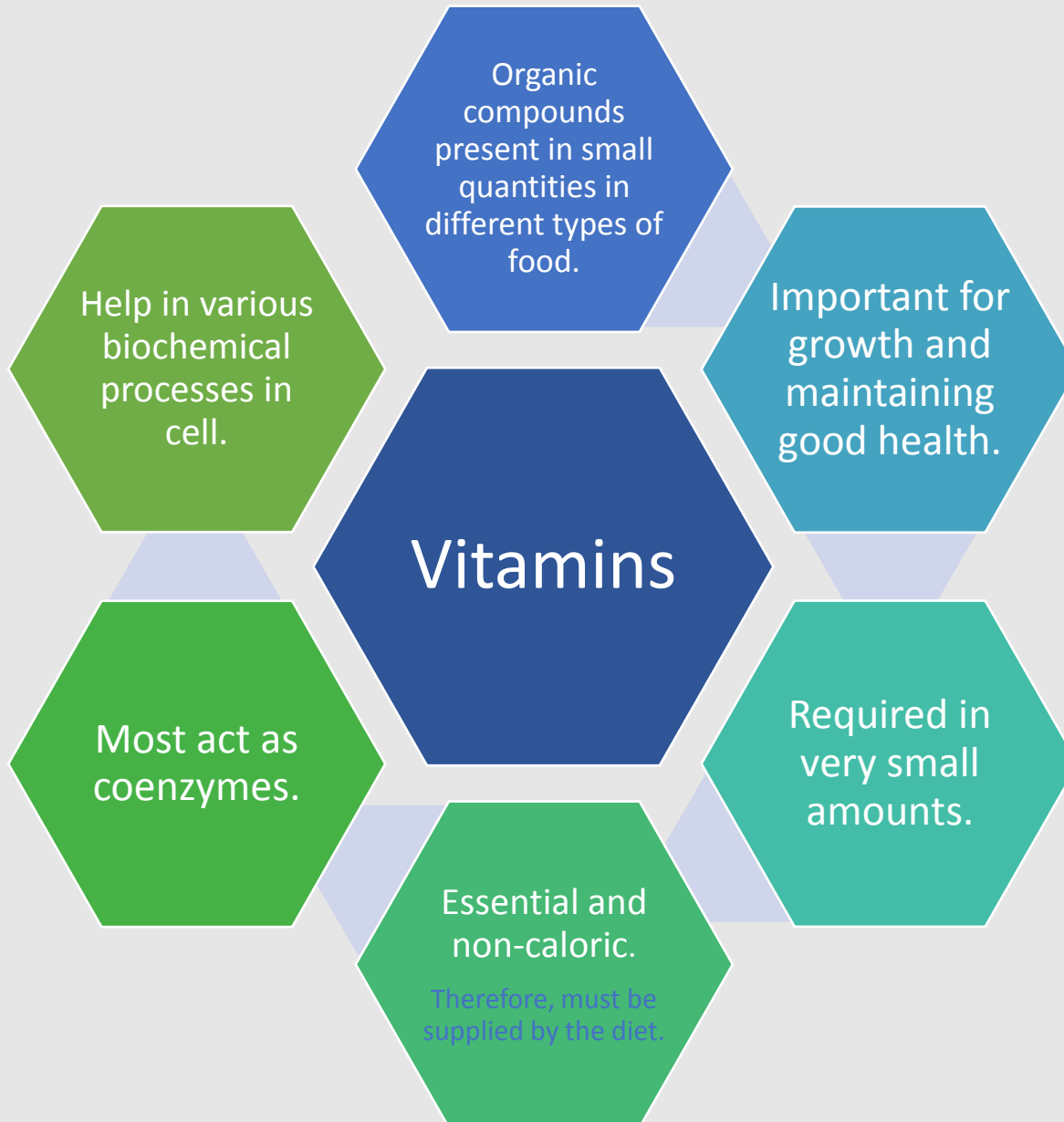
Vitamin A is often used as a collective term for several related biologically active molecules. The term retinoids includes both natural and synthetic forms of vitamin A that may or may not show vitamin A activity. The retinal family of molecules that are related to retinol (vitamin A), are essential for vision, reproduction, growth, and maintenance of epithelial tissues. Retinal is a component of visual pigment and derived from oxidation of dietary retinol, responsible for vision.

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

# Vitamins

"The word vitamin came from 2 words: Vital and minerals"

Interesting introductive video



(we need Vitamin A in very small amounts. If the person didn't get them he'll be having deficiency diseases, they're helping in growth and maintaining body physiology so they don't provide calories)

Vitamins are indirect source of energy. They help the body to obtain enough energy from the other sources (fats, carbohydrates ...)

# Vitamins - Classified Based on Solubility:

## Fat-soluble vitamins

- A,D,E and K

They are released, absorbed, and transported with dietary fat (not excreted by urine) and excess use can accumulate and cause toxicity.

Mnemonic: KADE (Name of a girl)

Fat soluble vitamins are stored inside the body while water soluble are not so developing vitamin deficiency in water soluble is more prominent

\* Please don't just memorize the number of the vitamin, memorize the name of it so when you are asked in the exam you don't get confused

## Water-soluble vitamins

- ascorbic acid (vitamin C)
- thiamin (vitamin B1)
- riboflavin (vitamin B2)
- Niacin (Vitamin B3)
- pyridoxine (vitamin B6)
- biotin
- pantothenic acid
- folate
- cobalamin (vitamin B12)

They are readily excreted in urine and the toxicity is rare. But their deficiency can occur quickly

# 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.

they're stored in other tissues as well but in very small amounts. They can cross the membrane and stay in the body, their deficiency is commonly developed. And they are not needed in daily amounts thus rarely get deficient

because the liver is a big organ and can provide vitamins (as they are stored in it) when the person's not taking them for that day.



# Vitamin A:

## Vitamin A from animal sources (Preform)

“Preform: means already formed” and it’s the main source

- Three preformed compounds called **retinoids** “which are the other 2 forms (with aldehyde > retinal, with acid > retinoic acid)”
- that are metabolically active and found in animal products:
  1. **retinol** – alcohol form found in animal tissue (can be converted to other forms)
  2. **retinal or retinaldehyde** – aldehyde form derived from the oxidation of retinol (essential in vision)
  3. **retinoic acid** – acid form derived from the oxidation of retinal (for skin and bone growth)
- ✓ can not be reduced back or converted to retinol or retinal, they have experienced this by giving only retinoic acid to mice and when they grow up they were blind and sterile since they don’t have the other types

## Vitamin A from plant sources (Pro-vitamin)

“Pro-vitamin: means that this form is not metabolically active . It get activated in the body”  
This source is mainly available in carrots and yellow or orange fruits and vegetables .

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

# Forms Vitamin A

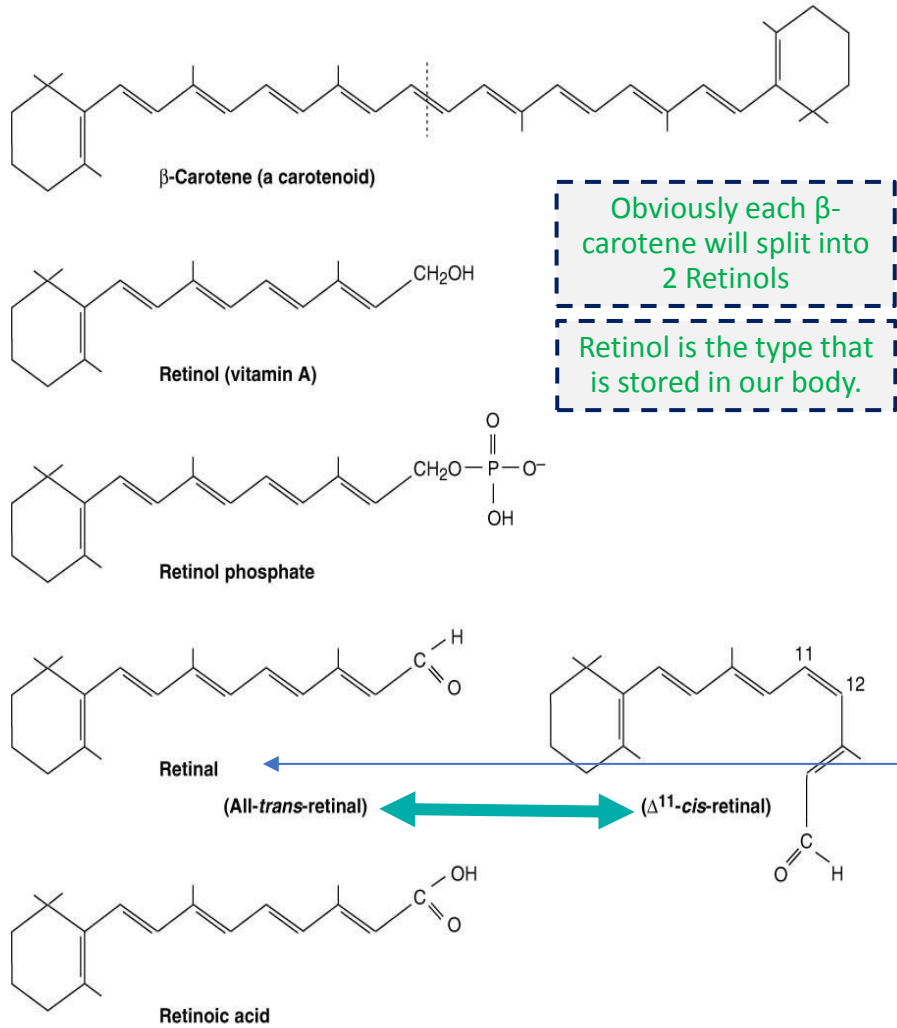


Figure 28.2. Structures of vitamin A and related compounds.

Textbook of Biochemistry With Clinical Correlations, Sixth Edition, Edited by Thomas M. Devlin. Copyright © 2006 John Wiley & Sons, Inc.

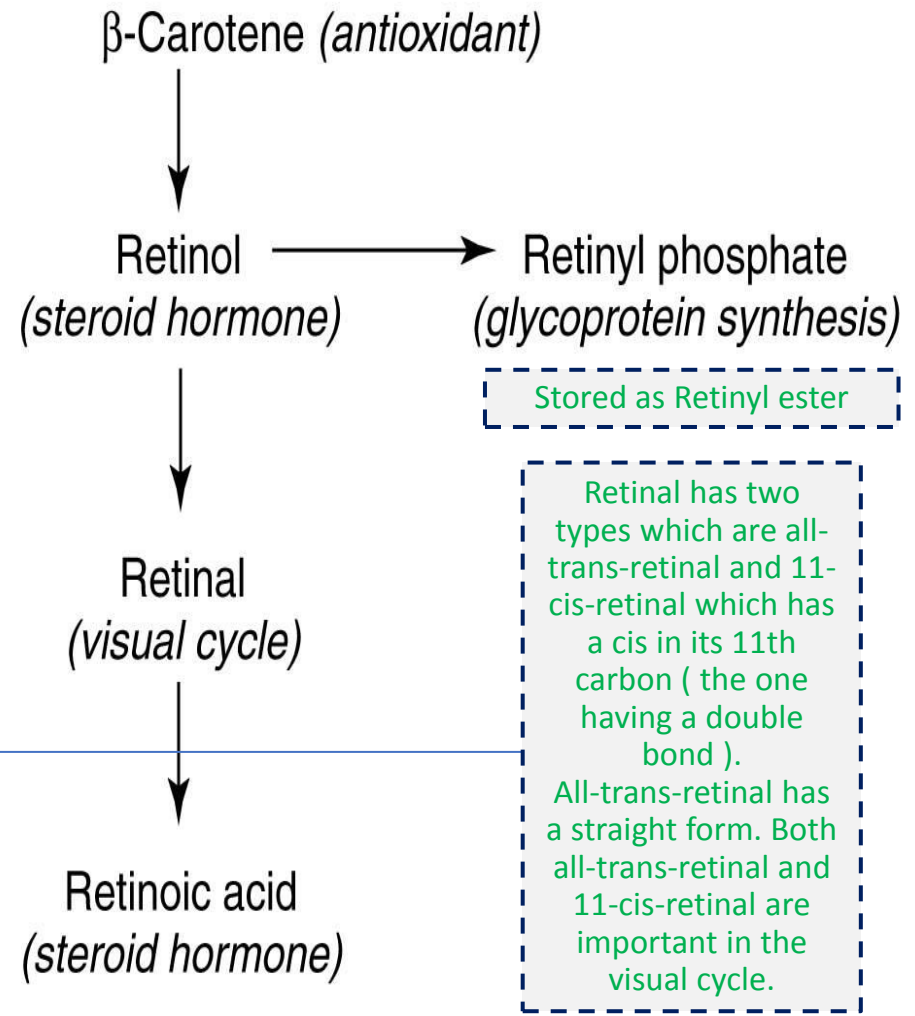


Figure 28.3. Vitamin A metabolism and function.

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# Functions of 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.

Vitamin A exert its function through gene processing within the nucleus ..





# Extra Notes about Vitamin A:

## Large doses:

there are specialized cells in the liver called stellate cells or the ito cells which store Vitamin A – 80-90% of Vitamin A get stored here) so if there is an excessive stimulation, it will lead to toxicity, and there are acute toxicity symptoms like (diarrhea, blindness, nausea) and chronic symptoms like (pruritus, increased cranial pressure which mimics the symptoms of a brain tumor) but this is caused by synthetic forms, so for example when you eat too much carrots your skin's pigmentation will change but as soon as you reduce or stop eating them your skin will go back to it's normal color.

Vitamin A Controls the production of B-carotene (so if retinoic acid is deficient it will lead to overproduction of B-carotene, and if there's a toxicity it will lead to less production of B-carotene).

(increases the immunity, sometimes it is written as anti-infective vitamin so it prevents infections)

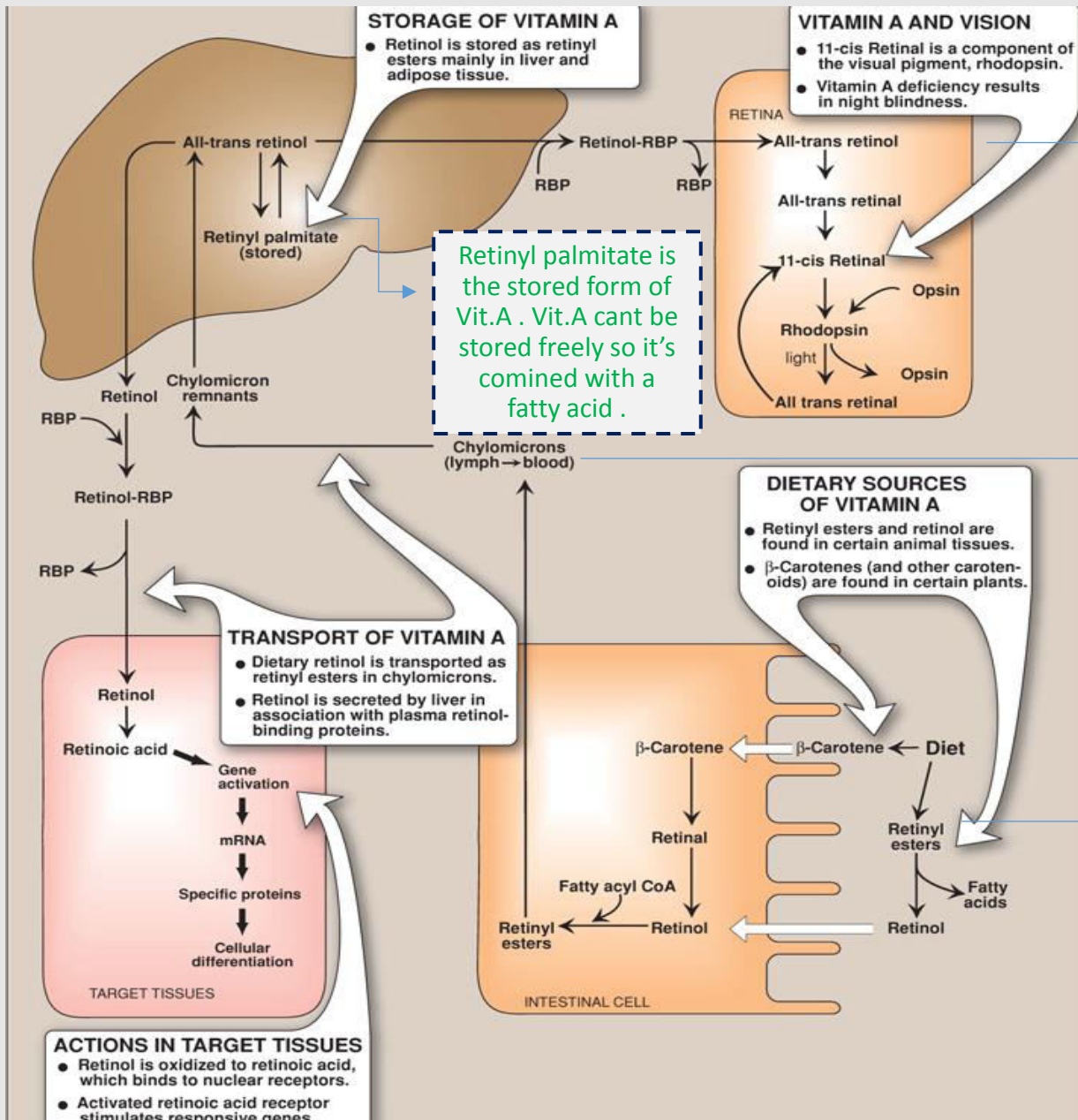


# Vitamin A "Metabolic pathway"



شرحنا لكم الباثواي هنا:

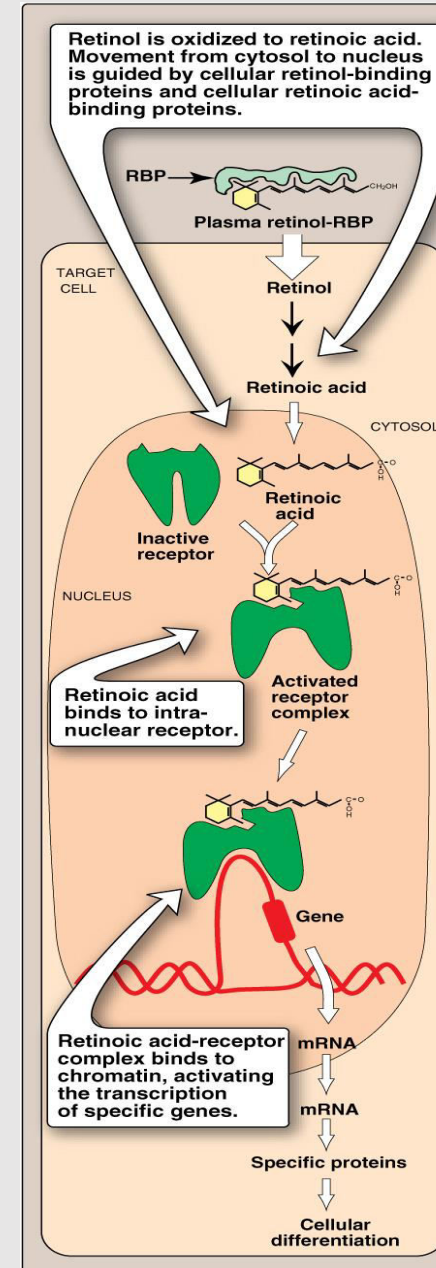
مهم في الصورة يحفظ الصورة التي تم تخزينها في كل مكان سواء من كبد او ادبيوس تيشو وغيره



Retinol is converted to Retinal in the eyes , and to retinoic acid in other tissues .

It carries the fat through the body . (Transporter)

When we eat meat from animal source , our bodies will be supplied with retinyl ester that is exclusive for animals . So , this ester when it enters the body it will be converted to RETINOL to enter the intestine , then it will be converted again to Retinyl ester that is exclusive for human . Which will go to the liver and be stored there .



When we eat vitamin A in the "pre" form the fatty acid gets removed and it becomes a free retinol in order to be absorbed in intestine , after absorption it get combined to fatty acid again and get transported to the liver by chylomicrons ..

RBP takes retinol to the targeted tissue within the blood, then ONLY retinol goes inside and gets converted into retinoic acid which will go to the nucleus and bind to specific receptors (retinoid receptors / RAR) there and makes it active which will affect gene transcription.

# Explanation for Vitamin A pathway in the Body : (Previous slide) 435 team

لما احنا ناكل لحم مثلا ، نأخذ من اللحم Retinyl ester "الخاص بالحيوان" هذا الاستر بيخسر واحد fatty acid و يتحول الى Retinol. هذا الريتينول بيدخل الأمعاء و يتفاعل مع Acetyl CoA عشان يرجع و يسوي لنا ريتينايل استر و لكن هذه المرة الخاص بالإنسان وليس الحيوان ! هذا الاستر بيركب على Chylomicron لأنه طبعاً ما يقدر يتمشى بالجسم لحاله لأنه hydrophobic فيحتاج ترانسبورتير . المهم اذا ركب بيروح عبر lymphatic system للكبد و يتحول هناك الى All trans retinol ، و يتخزن في الكبد على هيئة retinyl palmitate ، و يضل هناك إلى ما تحتاجه الأعضاء . مثلا العين تحتاجه الحين ، بيتحول مرة ثانية إلى trans retinol بحيث انه يشيل الفاتي أسيد اللي كانت لاصقة فيه و يركب التاكسي حقه اللي بيوصل العين ، اللي هو (RBP (Retinol binding protein ، التاكسي بيوصله للعين ثم يروح . إذا وصل الريتينول للعين بيتحول هناك إلى ريتينال ، which is the active form in the eyes .

✓ إذا مثلا في عضو ثاني غير العين يحتاج ريتينول زي epithelial tissue ؛ وش بيصير ؟؟؟  
بيسافر الريتينول من الكبد بنفس الطريقة و يركب التاكسي اللي هو RBP و اذا وصل للابيثيليا تيشو راح يتحول الى RETINOIC ACID مو retinal لأنه زي ما قلنا لو ترجع ورا الريتينال يشتغل للرؤية و الريتينويك اسيد يشتغل لصحة الجلد .  
المهم .. الريتينويك اسيد بيلصق بالرسبتور الموجود بالابيثيليا اللي هو retinoic acid receptor عشان يسوي له أكتفیشن . هذا الكومبلكس اللي هو الأسيد و الرسبتور بيرتبط بال chromatin و يسوي ترانسكريبشن لجين معين .

# 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.

It's a cyclical process so there are molecules which stay there.

**Input:** Light.

**Output:** Nerve impulse

Vitamin A (Retinal) combine with "opsin" in order to make the pigment photosensitive

## Retina

is a light-sensitive layer of cells at the back of the eye where an image is formed.

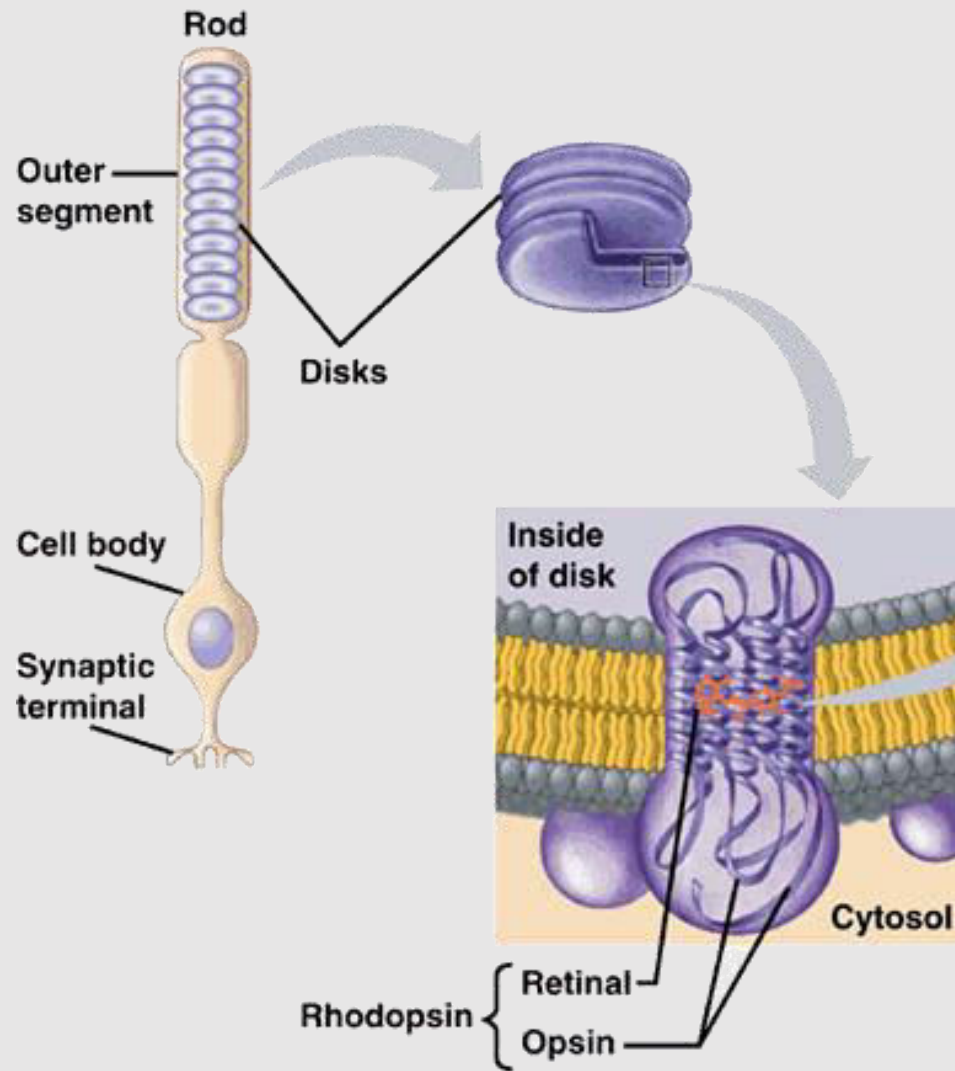
Retina consists of: Rod and cone cells (photosensitive cells).

Rod cells process black & white image. (they have rhodopsin)

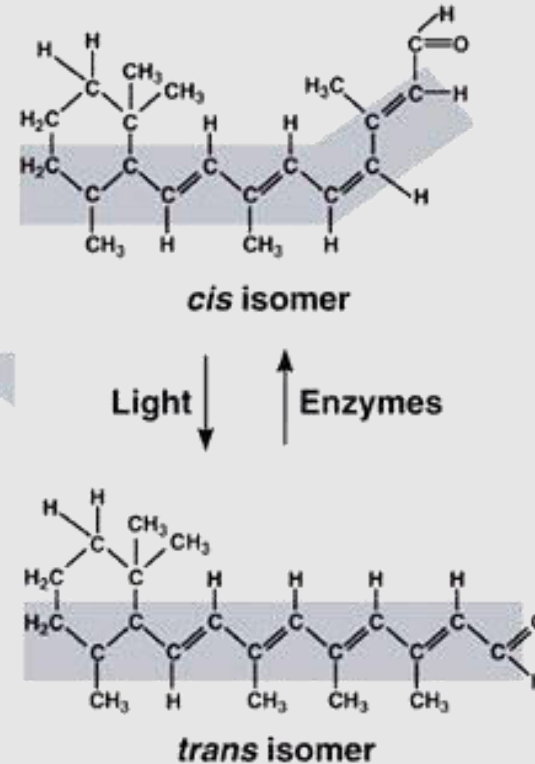
Cone cells process colored image.

(they have three types of iodopsin for colored vision: red, green and blue.)

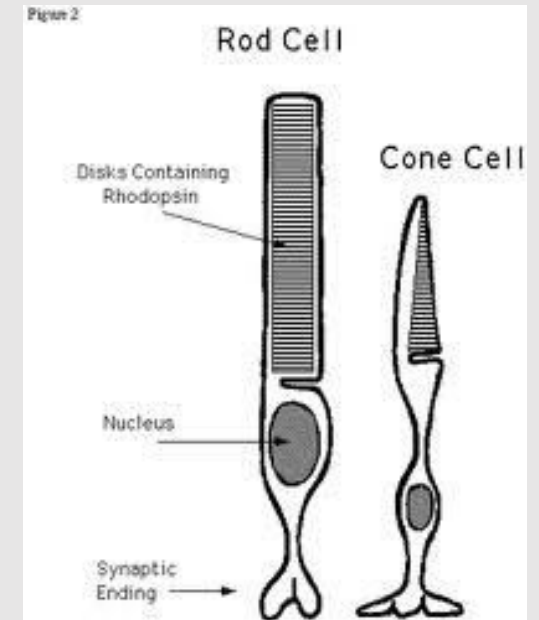
# Rhodopsin and retinal structures



(a)



(b)



Rods and cones have disks that contain rhodopsin. If we take a transverse section from these disks we will see a transmembrane complex (opsin is a transmembrane protein and it makes a complex with the aldehyde form (11-cis-retinal) of Vitamin A. Then in presence of light it gets converted into the isomerized form or straight form which is all-trans-retinal.

# Role of Vitamin A in Vision

- ✓ Normal vision depends on the retina and on adequate vitamin A.
- ✓ First discovered by George Wald 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.

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

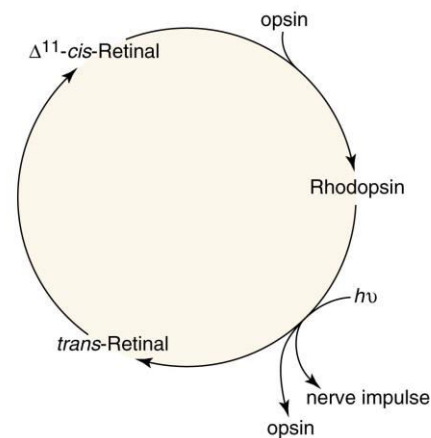


Figure 28.4. Role of vitamin A in vision.

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So rhodopsin is the molecule being used (by light) and regenerated (by enzymes).

# Role of Vitamin A in Vision

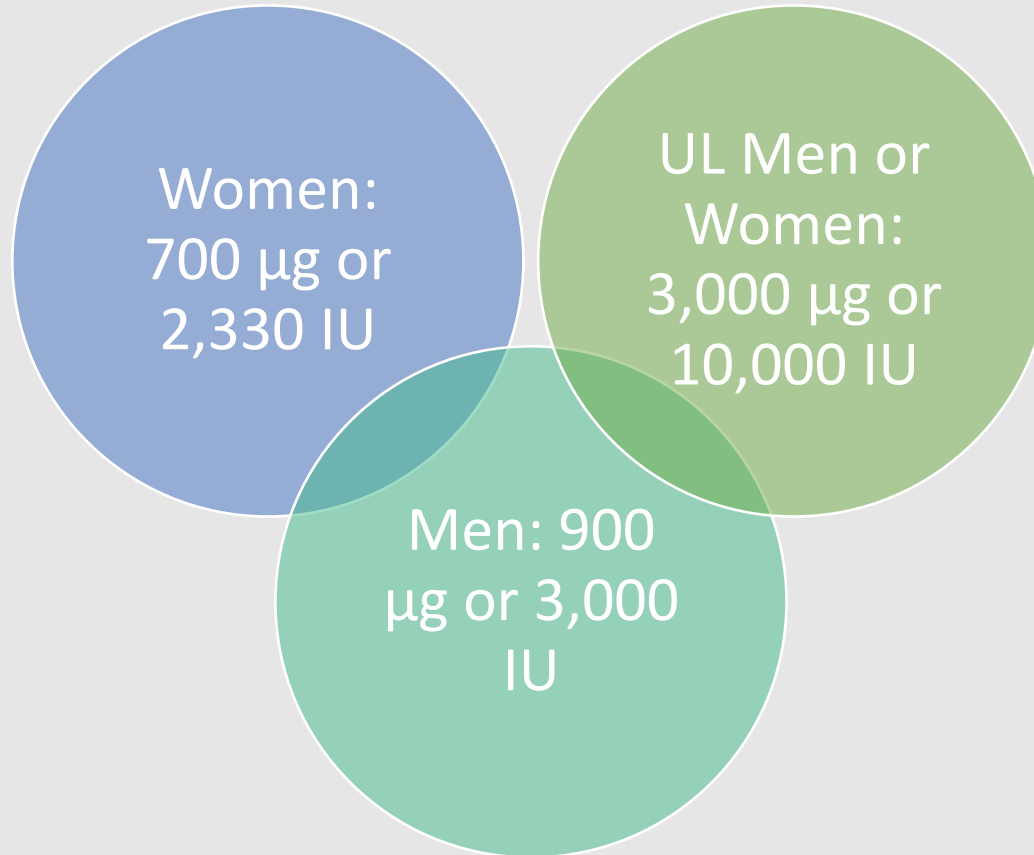
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## Dark Adaptation time

It is the time needed to regenerate rhodopsin, it depends on the amount of Vitamin A, so for example if you have a high amount of Vitamin A, adaptation will be faster, and if we have low amount of Vitamin A, adaptation will be prolonged. And if there isn't Vitamin A at all > night blindness occur

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



(because it causes toxicity symptoms, so molecules that do not have toxicity symptoms will not have upper limit)

Upper limit in men or women 3000μg or 10,000 IU .  
Above this they will have toxicity.



# Vitamin A Deficiency and Diseases



**Xerophthalmia**  
dryness of the conjunctiva and cornea.



**Bitot's spot**  
localized increased thickness of the conjunctiva.



**Keratomalacia**  
prolonged xerophthalmia leads to drying and clouding of cornea.

**Nyctalopia**  
(night blindness):  
patient cannot see in low light or near darkness conditions.

**Vitamin A associated diseases**

**Complete blindness**  
(in severe deficiency).

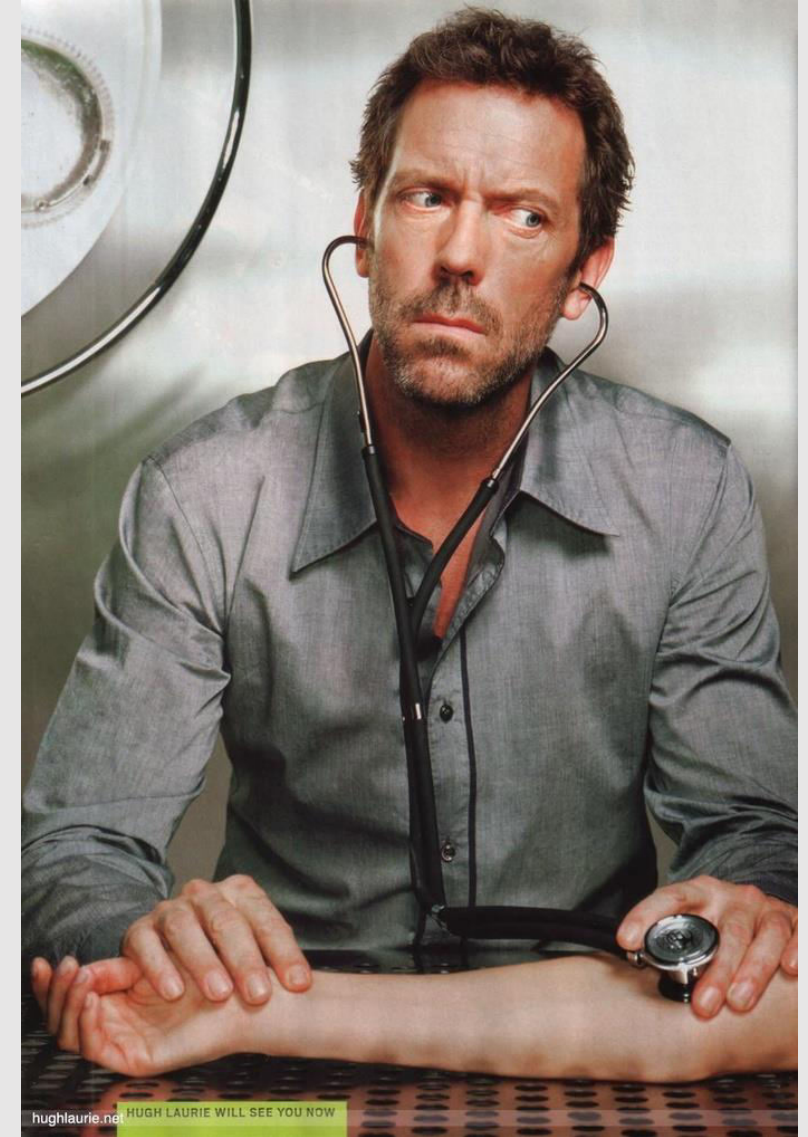
**Xerophthalmia:** (Vitamin A affects gene transcription and one of the genes is (repressors I think) so when there is a deficiency in Vitamin A, too much of carotene is being produced. So in the lacrimal gland, instead of secreting fluids it gets keratinized so it stops producing lacrimal fluid which leads to dryness of the cornea)

**Nyctalopia:** is one of the first signs of vitamin A deficiency. Visual threshold increases leading to the difficulty in seeing in dim light.  
**Xerophthalmia:** most effects children and people in tropical areas. And it could lead to permanent blindness.

# Take home messages

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

Good luck doctors



# Quiz

1) Which ONE of the following is a fat soluble protein?

- a) Vitamin B12
- b) Vitamin B6
- c) Vitamin C
- d) Vitamin E

2) Which of the is the plant source of vitamin A ?

- a) Pyridoxine
- b) Retinoids
- c)  $\beta$ -carotene
- d) Biotin

3) Which ONE of the following best describes Xerophthalmia ?

- a) Localized increased thickness of the conjunctiva.
- b) Inability see in low light or near darkness conditions
- c) Dryness of the conjunctiva and cornea.
- d) None of the above

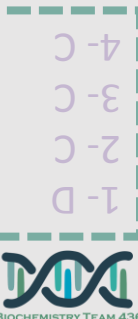
4) Excessive carotenoid intake lead to skin discoloration but in what colour ?

- a) Blue
- b) Red
- c) Yellow
- d) Pink

Q : Describe the role of vitamin A in vision and visual cycle?

Q : List the functions of vitamin A ?

[Suggestions and recommendations](#)





# TEAM MEMBERS



BIOCHEMISTRY TEAM 436



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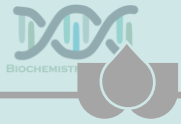


Mohammad Almutlaq

Rania Alessa

  
**THANK  
YOU**

**FOR CHECKING  
OUR WORK**



**PLEASE CONTACT  
US IF YOU HAVE  
ANY ISSUE**



• Lippincott's Illustrated Reviews Biochemistry 6<sup>th</sup> E



<https://www.youtube.com/watch?v=nnCrnWOiKG4>



Don't forget to review the notes



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