



"اللَّهُمَّ لَا سَهْلَ إِلَّا مَا جَعَلْتَهُ سَهْلًا، وَأَنْتَ تَجْعَلُ الْحَزْنَ إِذَا شِئْتَ سَهْلًا"



Vitamin A

Biochemistry Team 437

Color index:
Doctors slides
Doctor's notes
Extra information
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Neuropsychiatry block



Objectives

- What are Fat-soluble vitamins?
- The Biochemistry and types of vitamin A
- Absorption and transport of vitamin A
- Functions
- Functions in the visual cycle
- Deficiency and diseases

Vitamin Definition and Function

What are vitamins?

Are, **Non-caloric**¹ **Essential** Organic compounds present in small quantities in different types of food and are required in very small amounts².

Function

- They help in various biochemical processes in cell
- Most act as coenzymes³
- Important for growth and maintaining good health

Classification

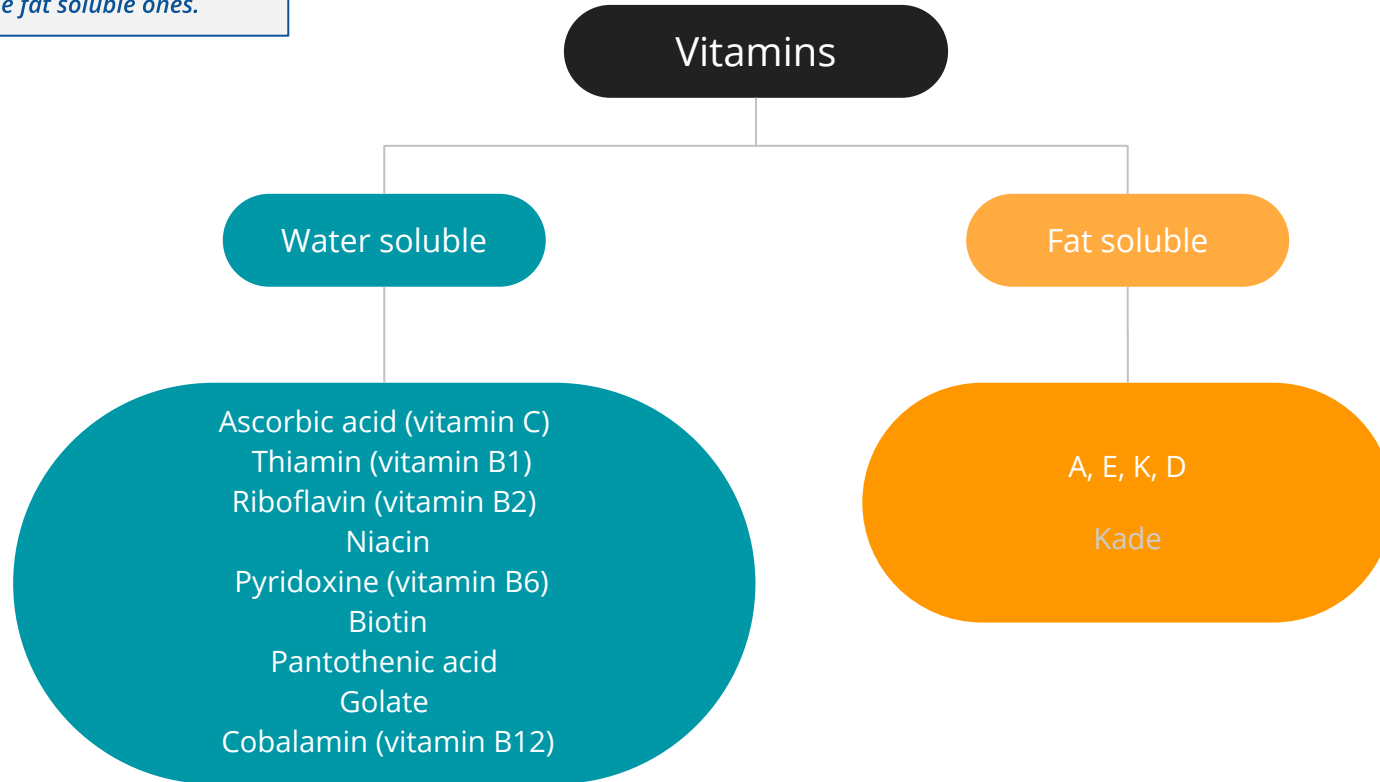
Vitamins are classified based on their solubility.

- 1- Do not provide energy if consumed.
- 2- Required in very small amounts but are very vital for the body function. If this quantity was not met, we develop deficiencies and diseases
- 3- Molecules that are required by certain enzymes to carry out catalysis.

Vitamin Classification



The water soluble vitamins will come up in another lecture and then we have to memorize them, for now memorize the fat soluble ones.



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.



- 1- Since they can be stored, it is rare to develop deficiencies but more likely to develop toxicity than water soluble vitamins which cannot be stored.
- 2- Toxicity requires the intake of large amounts of the enzyme for a long time.



- Vitamins in general are classified based on their solubility
- Vitamin A is a fat soluble vitamin and is classified based on its source and metabolic activity.



Vitamin A

Vitamin A from animal sources (Preformed)

Vitamin A from plant sources (Provitamin)

Preformed forms of Vitamin A are called **Retinoids**.
"already formed"

There are three retinoids that are:

- metabolically active (meaning they can be used directly by the body)
- and found in animal products (liver, kidneys, cheese) :
- **retinol** – alcohol form (can be converted to other forms)
- **retinal** or retinaldehyde – aldehyde form (essential in vision)
- **retinoic acid** – acid form (for skin and bone growth)

Provitamin compounds are called **Carotenoids**.

Provitamins cannot be used directly and have to be modified by the body first.

Two main carotenoids are:

- **(b-carotene)** "which comes from carrots"
- **cryptoxanthin**

Carotenoids can yield retinoids when metabolized in the body (They are from plant sources).

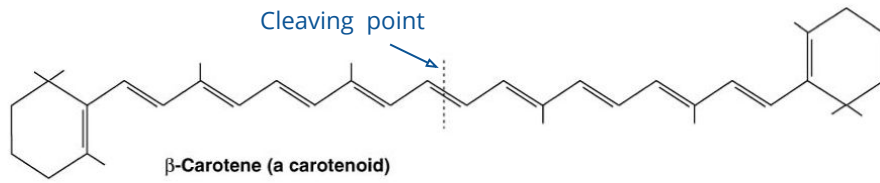
One molecule of b-carotene can be cleaved into two molecules of retinal in the intestine.

*The difference between the three retinoids is in the functional group and each of them has a different function

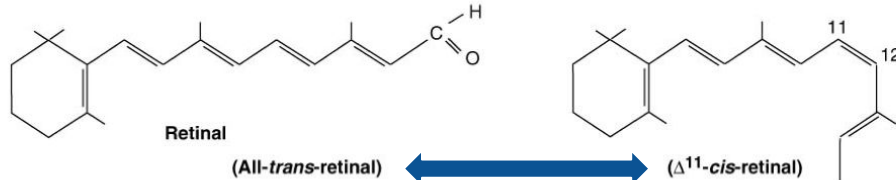
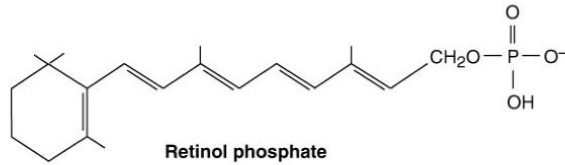
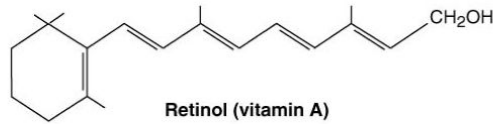
- Retinol can be converted to retinal
- Retinal can be converted to retinol again or to retinoic acid
- Retinoic acid is not converted to anything

If someone was vitamin A deficient, he is advised to increase his intake of animal sources and not plants why?

Even though the plant resource gives us more molecules of retinal "two molecules for each B-carotene", the retinal is found to be 12 times less efficient in function.



- Each β -carotene will split into 2 Retinols
- Retinol is the type that is stored in our body



- Retinal has two types, all-trans-retinal and 11-cis-retinal.
- The difference between the two types is the configuration around the 11th double bond.
- 11-cis retinal has a cis configuration "bent" around its 11th carbon, whereas All-trans-retinal has a straight form.

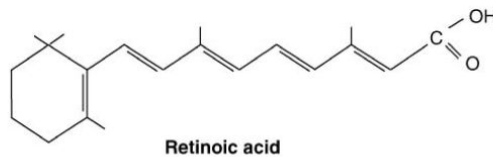


Figure 28.2. Structures of vitamin A and related compounds.

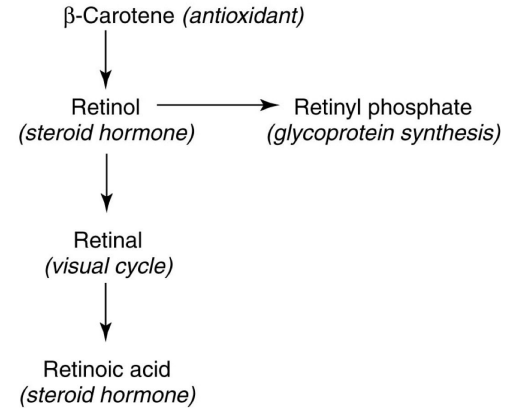


Figure 28.3. Vitamin A metabolism and function.

- The two forms can be converted into each other.
- This interconversion is very important in the visual cycle.

Functions of Vitamin A



- **Vision:** Vitamin A is a component of the visual pigment rhodopsin. Retinal “The aldehyde form” is bound to the protein opsin. (Retinal + Opsin = Rhodopsin)
- **Growth:** Vitamin A deficiency causes loss of appetite. Slow bone growth. Affects CNS.
- **Reproduction:** Retinol and retinal are essential for normal reproduction.¹
- **Maintenance of epithelial cells:** Essential for normal differentiation of epithelial tissues and mucus secretion ³.

Functions of Vitamin A

- 1- Supports spermatogenesis in male and prevent fetal resorption in female.
- 2- Especially for t-lymphocytes, People with deficiencies are more prone to infections.
- 3- Dry skin is one of the very early signs of vitamin A deficiency

Vision

Gene
Transcription

Immune
Function²

Embryonic
development and
reproduction¹

Bone
metabolism

Skin health and
antioxidant
activity

- Essential role in vision and normal cell differentiation
- Deficiency is the most significant cause of **blindness** in the developing world
Can be reversible with increased intake of vitamin A in the early stages.
- Large doses over a prolonged period of time can produce intoxication and eventually lead to liver disease
Because it is stored in stellate cells in the liver, toxicity leads to enlargement of the liver, and cirrhosis.
- Excessive carotenoids intake can result in **reversible** yellowing of the skin, but appears to be harmless

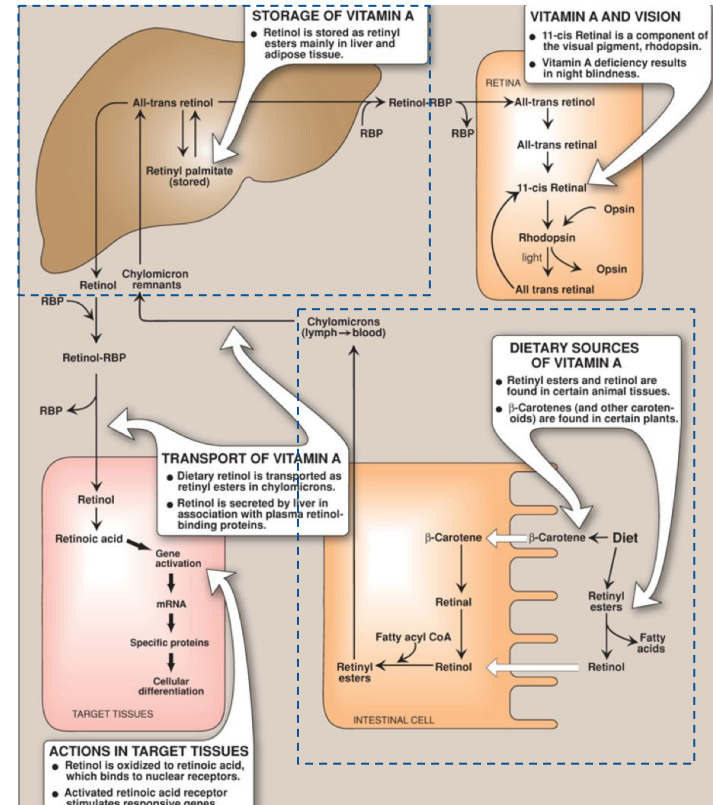
Vitamin A Metabolic Pathway

1- Dietary Source

- From animal sources we get retinyl esters and retinol
- From the plants we get the B-carotene form
- The body stores them in their performed form, mainly retinyl esters

2- Storage

- In the cytoplasm, We convert the retinyl ester coming from the diet into retinol by removing a fatty acid
- Retinol and b-carotene go into the intestinal epithelial cells, where the B-carotene is also converted to retinol.
- Then the retinol is re-esterified to long chain fatty acids to make retinyl esters by the enzyme fatty acyl coA, and secreted as a component of chylomicrons into the blood.
- Retinyl esters contained in chylomicron remnants are taken up by the liver where they are converted into all trans retinol and then to retinyl palmitate (retinol + palmitic acid) which is a **retinyl ester**, the form that is stored in the liver.



Vitamin A Metabolic Pathway

3- Transport

- When the tissues require vitamin A, they are transported from the liver to the blood as retinol by retinol binding protein (RBP).
- Remember, vitamin A is fat soluble, so we can't transport it through the blood without a carrier.
 - From the intestine into the blood: by chylomicrons
 - From the liver to the tissues: by retinol binding protein

*When someone is vitamin A deficient, they are prescribed zinc along with it, why?
Zinc is an important compound in the making of retinol binding protein*

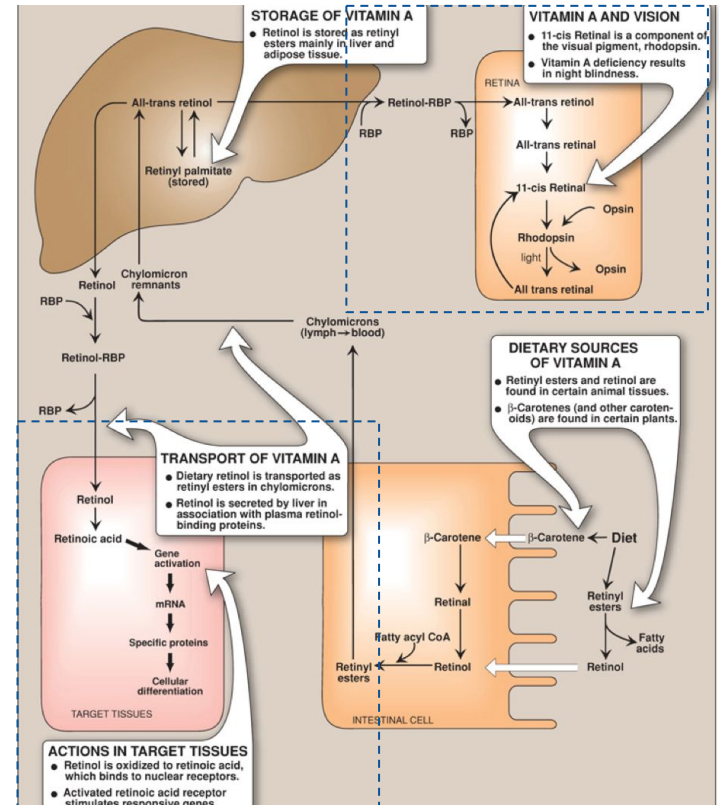
4- Vitamin A in tissue:

a) in the retina:

- All trans retinol is converted to all trans retinal and then to 11-cis retinal, which binds to opsin and becomes rhodopsin “photosensitive pigment in the retina”
- When rhodopsin absorbs light, the 11-cis retinal is converted back to all trans retinal and dissociates from opsin. And that is how the visual cycle happens

B) in other tissues “Discussed more in the next slide”

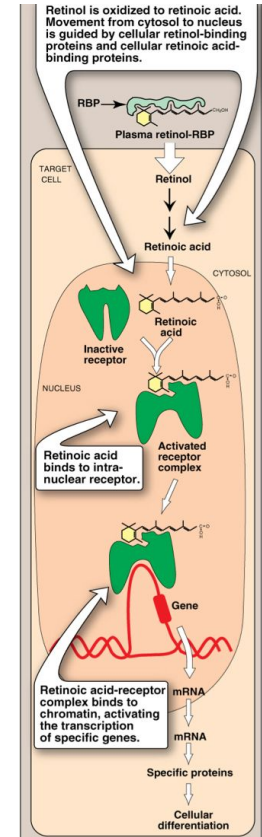
- Retinol is oxidized into retinoic acid, which binds to nuclear receptors to act as a steroid. And modifies gene transcription.



Vitamin A Metabolic Pathway

More details about retinol in tissues:

- Retinol is converted to retinoic acid in the cytosol.
- Then it enters the nucleus and is carried by retinoic acid binding protein which is present in the nucleus.
“not the same as RBP that is present in blood”
- Then it binds to the intra nuclear retinoid receptors and activates them.
- The activated receptor complex then binds to chromatin to activate the transcription of specific genes.



Vitamin A Metabolic Pathway

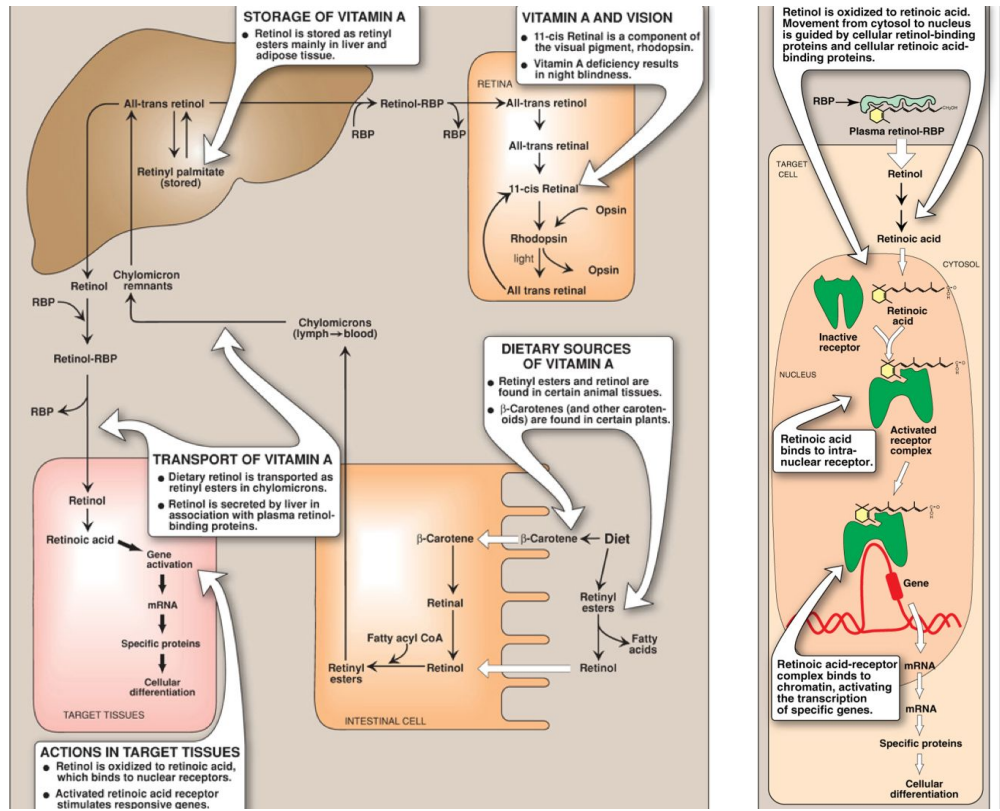
Team 435

لما احنا ناكل لحم مثلا ، ناخذ من اللحم Retinyl ester "الخاص بالحيوان" هذا الاستر بيخسر و يتحول الى Retinol fatty acid 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 إذا ركب بيروح عبر lymphatic system و يتحول هناك الى All trans retinol ، و يتخزن في الكبد علي 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 لللايبتيلال تيشو راح يتحول الى RETINOIC ACID مو retinal لأنه زي ما قلنا لو ترجع ورا الريتينال يشتغل للرؤية و الريتينوك اسيد يشتغل لصحة الجلد .

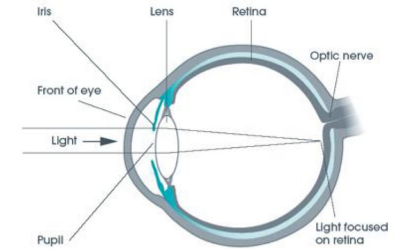
المهم .. الريتينوك اسيد بيلصق بالريسيتور الموجود باللايبتيلال اللي هو retinoic acid receptor عشان يسويه أكتيفيشن . هذا الكومبلكس اللي هو الأسيد و الرسبتور بيرتبط بال chromatin و يسوي ترانسكريبشن لجين معين .



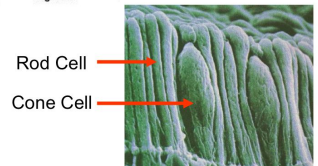
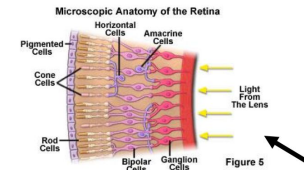
Role of Vitamin A in Vision

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.
- 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 “works in dim light”.
- Cone cells process color image “works in bright light”.
- Rods and cones have disks that contain rhodopsin, with a transverse section of this disk, we find a transmembrane protein “opsin” making a complex with 11-cis retinal, this complex is called rhodopsin.



Structure of the eye



Structure of the rods and cones

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) “Opsin + 11-cis retinal = rhodopsin”.
- 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 “a process called **bleaching**”.
- 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.

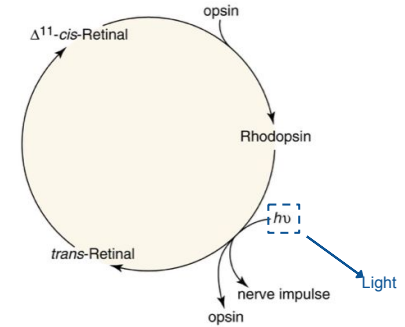
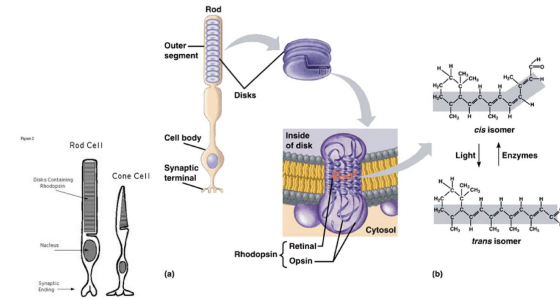


Figure 28.4. Role of vitamin A in vision.

- When rhodopsin reacts with light, 11-cis form is converted into the trans form, which dissociates from opsin.
- When there is no light, the trans form turns into 11-cis retinal again and bind to opsin again and so on. This process is called bleaching in the visual cycle.

Role of Vitamin A in Vision

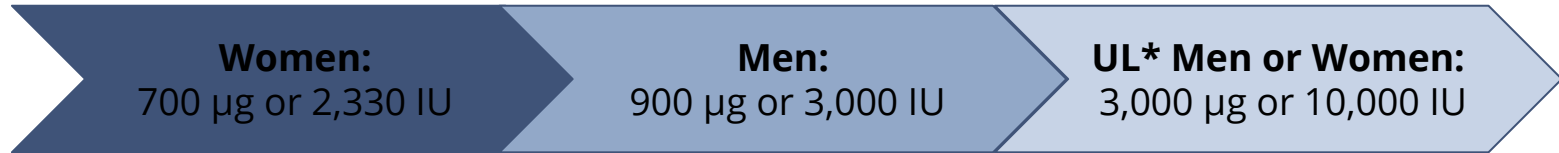


Dark Adaptation time

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

- Bright light depletes rhodopsin (**photobleaching**)
- Sudden shift from bright light to darkness causes difficulty in seeing **why?** Because when you go from bright light all your rhodopsin is bleached so it will take few seconds to mins depending on amount of Vitamin A to regenerate your rhodopsin so in that time you won't be able to see **temporary**
- 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 "dark adaptation time" is increased in vitamin A deficiency

Recommended Dietary Allowance (RDA) Vitamin A for Adults



UL= upper limit

Why do we have UL? because there is a risk of toxicity,

Vitamin A Deficiency and Diseases

**Nyctalopia
(night blindness)**

Patient cannot see
in low light or near
darkness
conditions

One of the earlier
signs of vitamin A
deficiency

Xerophthalmia

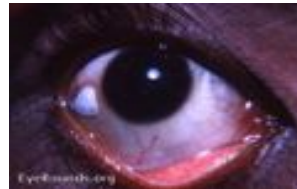
Dryness of the
conjunctiva and
cornea



Bitot's spots

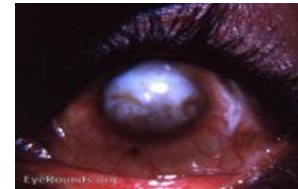
Localized
increased
thickness of
the conjunctiva

Deposition of keratin
in localized spots



Keratomalacia

Prolonged
xerophthalmia
leads
to drying and
clouding of cornea



**Complete
blindness**

In severe
deficiency

- Functions of vitamin A: vision, growth, reproduction, maintenance of epithelial cells.
- In the retina, Vitamin A in the form of retinal binds to a protein called opsin to make rhodopsin and iodopsin.
- When these pigments are exposed to light, bleaching occurs and signals are transmitted to brain through optic nerve.
- Retinal is converted back to its original form to start another cycle.
- Vitamin A deficiency causes diseases: nyctalopia, xerophthalmia, bitot's spots, keratomalacia, complete blindness.
- Vitamin A supplementation may cause toxicity.

MCQs:

1- Which one of the following is fat soluble vitamin?

A-ascorbic acid. **B**-biotin. **C**-riboflavin. **D**-retinoids.

2- One molecule of b-carotene can be cleaved into two molecules of in the

A-retinal, intestine. **B**-retinol, liver. **C**-retinal,liver. **D**-retinol, intestine.

3- Excessive carotenoids intake lead to skin discoloration in what color?

A-yellow. **B**-orange. **C**-blue. **D**-red.

4- In the retina opsin bind with to form rhodopsin.

A-11 cis retinal. **B**-11 cis retinol. **C**-all trans retinal. **D**-all trans retinol.

5- Vitamin A is stored in the liver and adipose tissue in the form of ?

A-all trans retinol. **B**-retinyl palmitate. **C**-retinoic acid. **D**-none of them.

Girls team

- رهنف الشننننر
- شهد النبرن
- مننرة المسعد
- أرنوانة العقنل
- رننار النرنبن
- رزان الزهرانن
- لنان المناع
- مشاعل القحطانن
- العنود المنصور
- لنلن الصبأع
- لننا الرحنة
- عبئر العبد النبار

Boys team

Team leaders

- رهام الحلبن
- معاذ الحمود



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