

VITAMIN A DEFICIENCY, HYPOVITAMINOSIS A, NIGHT BLINDNESS

A deficiency of vitamin A may be caused by insufficient supply of the vitamin A and its precursors in the rations or its defective absorption of vitamin A from alimentary tract, and characterized clinically: -

In young growing animals, the disease characterized mainly by those of compression of the brain and spinal cord (blindness, encephalopathy, paralysis).

In adult animals, the disease is characterized by night blindness, corneal keratinization, pityriasis, defects in hooves, loss of weight, increase susceptibility to infection and suppression of immunity, and infertility with congenital defects in the offspring of deficient dams.

ETIOLOGY:

I- Primary vitamin A deficiency:

Primary vitamin A deficiency is due to an absolute vitamin A or its precursors (carotene) in the diet:

① - **In case of animals at pastures** usually receive adequate supplies of the vitamin A, except during prolonged droughts. The signs of hypovitaminosis A does not occur except after feeding for long time on droughts because hepatic storage of vitamin A is usually good. The hepatic storage must be depilated firstly to reach a critical level, this period may be extended for 5 – 8 months in young sheep, maintaining normal growth rate, and clinical signs develop at 1 year. In adult sheep, may be on deficient diet for 18 months before hepatic storages are depleted and the disease becomes evident. Cattle may be lived on deficient diet for 5 – 18 months before the clinical signs appear. In beef calves may live for 6 – 8 months on deficient diet, before the clinical signs appear. In pigs, the clinical signs appear after 4 – 5 months on deficient diet. Adult horses may remain clinically normal for as long as 3 years on deficient ration.

species	The time on deficient ration before clinical signs becomes evident	species	The time on deficient ration before clinical signs becomes evident
Yong sheep	1 year	Beef-calves	6 – 8 months
Adult sheep	18 months	Pigs	4 – 5 months
Adult cattle	5 – 18 months	Horses	3 years
Growing feedlot cattle	6 – 12 months		

② - In case of animals indoors:

A. When fed prepared diets deficient in vitamin A or its precursors without adequate supplementation, such a diet of dried sugar beet pulp, concentrates, and poor-quality hay.

- B. When feeding on rations their vitamin A and its precursors are already destructed or oxidized. Vitamin A and its precursors readily oxidized particularly in the presence of unsaturated fatty acids, storage for prolonged time, pelleting of the ration may cause serious loss up to 32 % of vitamin A in the original feedstuff, as well as heat, light, and mineral mixes are known to increase rate of vitamin A supplements in commercial rations; 47 % - 92 % of vitamin A content of the ration may be destructed in ration after one week exposure to the trace minerals, high relative humidity, sunlight, and warm temperature.
- C. When the ration consists mainly of grains and hay, as all grains contains negligible amounts of vitamin A and its precursors, except yellow corn (*yellow corn may loss its carotene content by long storage*), and the hay is a poor source in vitamin A. as hay loss its carotene content by sun and dryness.

N.B

- In feedlot cattle, the vitamin A deficiency is most common in **steers (males)** fed the same ration (that deficient in vitamin A) as **heifers** which may remain clinically normal. It is suggested that **sexual dimorphism** may be due to the production of vitamin A by the corpus luteum of the heifers.

③-Maternal vitamin A deficiency:

- Dams (cow, ewe, and does, and in sow) that fed diet deficient on vitamin A or its precursors, or that feed only green fodders without supplementation with vitamin A (animal source or ester form), will result in congenital hypovitaminosis A (in calves, lambs and kids, and only to limited extent in piglets), because the status of the dam is reflected in that of the fetus, as well as the carotene content in green feed and the alcoholic form of vitamin A (present in green feed, plant form of vitamin A; RETANOL) do not pass through placenta to the fetus during pregnancy so feeding green feed to pregnant dams will lead to congenital hypovitaminosis A in offspring. The ester form of vitamin A (Animal form, RETANAL) can pass through placenta. Vitamin A (2 forms) and carotene will increase the vitamin A and carotene content on colostrum, which will be taken by the neonates and rise their hepatic storage.

II- Secondary vitamin A deficiency: in which the vitamin A or its precursors in the diet is adequate, but their digestion, absorption, or metabolism is interfered with to produce a deficiency at tissue level. Such in: -

1. In chronic diseases of the liver because the liver is the main site of storage of the vitamin A
2. In chronic diseases of intestine because much of the conversion of carotene to vitamin A occur in the intestinal epithelium.
3. Poisoning with highly chlorinated naphthalene because it interferes with the conversion of carotene to vitamin A, and animal poisoned with this substance has very low level of vitamin A status.

4. The intake of inorganic phosphorous will affect vitamin A storage, low phosphorous diet facilitates the vitamin A storage, and phosphorous deficiency may lower the efficiency of carotene conversion.
5. Additional factors which may increase the requirement of vitamin A include high environmental temperature, a high nitrate content of the feed which reduce the carotene conversion to vitamin A, and rapid gain.
6. The continuous ingestion of mineral oils, which may occur when using oils in preventing bloat in cattle, may cause depression of plasma carotene and vitamin A status in cattle. The deleterious effect of using oils in cattle is unlikely under the conditions in which oils is ordinarily used because of the short period for which the oil is used and the high vitamin A and carotene intake.

PATHOGENESIS:

The functions of vitamin A:

1. Vitamin A is essential for the regeneration of the visual purple (Rhodopsin) necessary for dim light vision.
2. Vitamin A is essential to maintain normal position and activity of osteoblast and osteoclast cells i.e. coordination of bone growth and finer molding of the bones.
3. Vitamin A is essential for normal epithelium tissue especially covering and secretory epithelium.
4. Vitamin A is important for maintenance of cerebrospinal fluid pressure (CSF).
5. Vitamin A is essential for organ formation during growth of the fetus.
6. Vitamin A may afford protection against infections by influencing both specific and non-specific host defense mechanisms through enhancing polymorphonuclear neutrophil functions.

N.B

Rhodopsin, or **visual purple**, pigment-containing sensory protein that converts light into an electrical signal. It is required for vision in dim light and is located in the retina of the eye—specifically, within the tightly packed disks that make up the outer segment of the retina's photoreceptive rod cells, which are specially adapted for vision under low-light conditions. It is made up of opsin (a colorless protein) and 11-cis-retinal (11-cis-retinaldehyde), a pigmented molecule derived from vitamin A. When the eye is exposed to light, the 11-cis-retinal component of rhodopsin is converted to all-trans-retinal, resulting in a fundamental change in the configuration of the rhodopsin molecule. The change in configuration initiates a phototransduction cascade within the rod, whereby light is converted into an electrical signal that is then transmitted along the optic nerve to the visual cortex in the brain.

① - Night vision:

- In vitamin A deficiency, the ability to see in dim light is reduced (resulting in night blindness), because of interference with regeneration of visual purple.

②- Cerebrospinal fluid pressure:

- In hypovitaminosis A in calves, an increase in CSF pressure occurs. The increase in CSF pressure is one of the first and more sensitive indicator than ocular changes in the calves. It occurs when vitamin A intake is twice that needed to prevent night blindness.
- The increase in the CSF pressure is because of: -
 - Impairment of absorption of CSF due to reduction in tissue permeability of the arachnoid villi.
 - Thickening of the connective tissue matrix of the cerebral dura matter.
- The increase in CSF pressure is responsible for the syncope and convulsions, which occur in calves in early stages of vitamin A deficiency.
- The syncope and convulsion of hypovitaminosis A may occur spontaneously or after an excitation and exercise. It is suggested that the CSF pressure is increased in sub-clinical hypovitaminosis A and the excitation and exercise make further increases in the CSF pressure to the convulsion levels.

③- Bone growth:

- Vitamin A is essential to maintain normal position and activity of the osteoblasts and osteoclasts. So, during hypovitaminosis A, there is incoordination between bone growth and the shaping of the bone that resulting in the finer molding of bone does not produced normally.
- In most locations this has little effect but may cause serious damage to the nervous system (because the thickening and malformation in bone of the skull and vertebral column).
- The abnormal bone growth of the cranial cavity and vertebral column will lead to:
 - A. Overcrowding of the cranial cavity that lead to distortion and herniation of the brain, and an increase in CSF pressure up to 4 to 6 times than normal, that will lead to the characteristic nervous signs of vitamin A including papilledema (*Papilledema is a serious medical condition where the optic nerve at the back of the eye becomes swollen, causing serious damage to vision*), incoordination, and syncope.
 - B. Compression on the cerebellum that lead to herniation of cerebellum into foramen magnum, causing weakness and ataxia.
 - C. Constrictions of the cranial nerve canals in which cranial nerves pass leading to compression, twisting, and lengthening of the cranial nerves, particularly optic and facial nerves causing blindness and facial paralysis.
 - D. Abnormal bone growth of the vertebral canal that lead to compression and herniation of the spinal cord into intervertebral foraminae results in damage to nerve roots and localizing signs referable to individual peripheral nerves (most of them motor and their dysfunction causing paralysis).

4 - Epithelium tissues:

- As vitamin A is essential to maintain health and integrity of epithelium tissues, particularly covering and secretory epithelium.
- Vitamin A deficiency leads to atrophy of the all epithelium cells but the important effects are limited to those types of epithelium tissue with a secretory and covering function, as the secretory cells are become without power to divide and develop from undifferentiated basal epithelium. So the secretory epithelium tissues are gradually replaced by stratified, keratinizing, non-secretory epithelium tissue. This replacement of the secretory epithelium occurs chiefly in: -
 - A. Salivary glands (squamous metaplasia of the interlobular ducts of parotid salivary gland)
 - B. Urogenital tract, including placenta (placental degeneration) and testicles (reduction in normal spermatogenesis) but not ovaries and renal tubules.
 - C. Paraocular glands and cornea (corneal changes and xerophthalmia).
 - D. Teeth (causing disappearance of odontoblasts from enamel organ).
 - E. Thyroid gland (with marked reduction of thyroxine).

5 - Embryological development:

- Vitamin A is essential for organ formation during fetal growth. So, during vitamin A deficiency, multiple congenital defects (congenital hypovitaminosis A) occurs in the offspring when there is maternal vitamin A deficiency. The congenital defects including: -
 - A. Blindness with dilated pupils in calves (because of constriction of the optic nerve canal with thickening of the dura matter resulting in ischemic necrosis of the optic nerve and optic disc edema resulting in blindness), nystagmus, and retinal dysplasia.
 - B. Weakness and incoordination.
 - C. Thickening of the occipital bones and sphenoid, and doming of the frontal and parietal bones with compression of the brain.
 - D. Increase in CSF pressure in the newborns.

6 - Immune mechanisms:

- The effects of vitamin A and β -carotene on the host defense mechanisms are uncertain and controversial for many years.
- It is possible that vitamin A and β -carotene afford protection against infections (bacterial, or viral, or rickettsial, or parasitic) by influencing both specific and non-specific host defense mechanisms via enhancing polymorphonuclear neutrophil function (but this is influenced by physiological status of the animal such as lactation, also).

CLINICAL FINDINGS:

Generally, hypovitaminosis A causes similar syndromes in all species, but some variations were observed among the species because of species differences in tissue and organ response. The major clinical findings are: -

① - **Night blindness (Nyctalopia):**

- * Inability to see in dim light (moonlit night, twilight), this the earliest and important diagnostic sign in all species, except in the pig in which it is not evident until plasma vitamin A levels are very low.

② - **Xerophthalmia:**

- * *Xerophthalmia* means excessive dryness of the cornea and conjunctiva (eye) because of the eye fails to produce tears. The condition is usually caused by vitamin A deficiency and is followed by thickening and cloudiness of the cornea (corneal keratinization).
- * *True xerophthalmia* (dryness of the eye and thickening and clouding of cornea, corneal keratinization) occurs in calves. In the other species, there is a thin mucoid ocular discharge followed by corneal keratinization, clouding and sometimes corneal ulceration and photophobia.

③ - **Changes in skin:**

- * The changes of skin in case of vitamin A deficiency include: -
 - In cattle, there are heavy deposits of bran-like scales on the skin (**Pityriasis**).
 - Dry, scaly hooves with multiple vertical cracks are seen, particularly in horses.
 - Excessive skin keratinization is usually observed in *chlorinated naphthalene poisoning* (secondary vitamin A deficiency) in cattle.
 - In pigs, there is a rough, dry coat with a shaggy appearance, and splitting of the bristle tips usually observed in hypovitaminosis A.

④ - **Effect on bodyweight:**

- * **Under the field conditions (natural)**, vitamin A deficiency is often observed in will or good-conditioned animals (such as fattening bulls), although severe vitamin A deficiency leads to inappetence, weakness, stunted growth, and emaciation, **experimentally**.

⑤ - **Effect on reproductive performance:**

- * Vitamin A deficiency causes loss of reproductive efficiency in both male and female as:
 - **In male with hypovitaminosis A:** there are retained libido, with reduction in the number of motile, normal spermatozoa because of the degeneration of the germinative epithelium of the seminiferous tubules (reduction in spermatogenesis). In rams may leads to reduction in testicular size.
 - **In female with hypovitaminosis A:** the conception rate is not affected but the degeneration of the placental epithelium may lead to abortion, stillbirth, or production of weak young, or young with anomalies, or causing retained placenta (common).

6-Nervous manifestations:

The nervous signs related to hypovitaminosis A due to the damage of the nervous system include:

1. Paralysis of the skeletal muscles due to damage of the peripheral nerve roots.
 2. Encephalopathy (syncope and convulsions) due to increased intracranial pressure.
 3. Blindness due to constriction of the optic nerve canal that causing ischemic necrosis of the optic nerve.
- ✱ These defects occur at any age but most commonly in young, growing animals, and have been observed in all species except horses.

A. **Paralytic form:** the nervous signs are abnormal bone growth of the cranial cavity with compression and herniation of cerebellum into foramen magnum.

1. The nervous signs in this form include abnormalities in gait due to weakness and incoordination (ataxia). The hindlegs are usually affected firstly and fore-legs later. Complete limb paralysis occurs in the terminal stage.
2. In pigs, there are stiffness of the legs initially, with stilted gait or flaccidity, knuckling of the fetlock and sagging of the hindquarter.

B. **Encephalopathy with convulsions:**

- i. These signs are common in beef or fattening calves at 6 – 8 months of age when they suffered from hypovitaminosis A (primary vitamin A deficiency due to insufficient vitamin A intake such taken concentrated without vitamin A supplement or without green fodders).
- ii. Encephalopathy is due to increase in the CSF pressure.
- iii. The encephalopathy is manifested by syncope and convulsions which may be occurred spontaneously or after excitation or exercise or handling; the animal collapse (syncope), and during lateral recumbency a clonic-tonic convulsion will occur, lasting for 10 – 30 seconds with ventroflexion of the head and neck, sometimes opisthotonos and commonly tetanic closure of the eyelids and retraction of the eyeballs. Death may occur during the convulsion or the animal will survive and lie quietly for several minutes as if paralyzed, before another episode of convulsion occurs. Some calves may hyperesthetic to touch or sounds. The affected calves are usually not blind and menace reflex may be slightly impaired or hyperactive. The case fatality rate in this form may reach to 25 %.
- iv. The prognosis usually excellent as the treatment will cure the condition in 48 hours but the convulsions may continue for 48 hours following treatment.

B. **Ocular form with blindness:**

- a. This form usually occurs in yearling cattle (12 – 18 months old) and up to 2 – 3 years of age or more.

- b. The affected animal shows night blindness initially, then followed by complete blindness of both eye during daylight, with ocular abnormalities including both pupils are widely dilated and fixed, and will not respond to light.
- c. Exophthalmos and excessive lacrimation may occur in some cases.
- d. Menace reflex is completely absent while the palpebral and corneal reflexes are present.
- e. Examination of the affected eyes with ophthalmoscope reveals optic disc edema (papilledema), some loss of usual brilliant color of the tapetum, varying degree of peripapillary retinal detachment, papillary and peripapillary retinal hemorrhages, and disruption of the retinal pigment epithelium.
- f. The CSF pressure is increased in these animals but not as high as in the calves with convulsions, but the convulsions may be occurred in these animals if they exposed to excitation such in case of forced to walk, or if loaded onto a vehicle for transportation. These animals are usually aware of its surroundings and usually eat and drink normally, unless placed in unfamiliar surroundings.
- g. The prognosis in the ocular form is unfavorable and treatments is ineffective because of the degeneration of the optic nerves.

7- Congenital defects in newborns:

- These had been observed in piglets and calves with maternal hypovitaminosis A.
- These defects include abortion, stillbirth, and weak offspring unable to stand or suck, or production of offspring have congenital anomalies such as
 - a. *In calves*: the defects are limited to congenital blindness due to optic nerve canal constriction and encephalopathy.
 - b. *In piglets*: the defects include complete absence of eyes (anophthalmos), or small eyes (microphthalmos), incomplete closure of the optic fissure, degeneration of the lens and retina of the eyes, cleft palate, accessory ears, malformations of legs, cardiac or renal defects, diaphragmatic hernia, aplasia of genitalia, herniation of spinal cord, hydrocephalus, generalized edema, stillbirth, or very weak piglets.

8- Increase susceptibility to infections.

CLINICAL PATHOLOGY:

- * **Plasma vitamin A level**: the level of vitamin A in the plasma is used extensively in diagnostic and experimental works.

		Plasma vitamin A level	Plasma carotene level
Normal level		25 – 60 µg/dL	150 µg/dL
Minimal level		20 µg/dL	< 9 µg/dL
Papilledema (early sign of hypovitaminosis A)		< 18 µg/dL	
Experimentally	Loss of body weight	8.87– 18. 05 µg/dL	
	Ataxia and blindness	4.87 – 8.88 µg/dL	
	convulsions	< 4.88 µg/dL	

✱ **Hepatic levels of vitamin A and carotene:**

- This can be estimated by liver biopsy.
- The level of vitamin A in the plasma does not reduce till complete depletion of hepatic level of vitamin A.

Hepatic level	Vitamin A level	Carotene level
Normal	60 µg/dL	4 µg/dL
Critical or Deficient (signs of deficiency)	2 µg/dL	0.5 µg/dL

The levels of vitamin A and carotene are reduced in case of infections, and at the last 3 weeks of pregnancy in cattle because of large amounts of vitamin A and carotene is being secreted in colostrum.

✱ **CSF pressure:**

- Estimation of the CSF pressure is also used as a sensitive indicator of low vitamin A status.

	Normal pressure	Deficiency (in ≤ 7 µg/dL)
in calf	< 100 mm of saline	> 200 mm
In pigs	80 – 145 mm	> 200 mm

NECROPSY FINDINGS:

✱ Gross changes:

- No gross changes could be observed, except decrease in the size of the cranial vault and the vertebrae, and compression and injury of the cranial and spinal nerve roots.

✱ Microscopical changes:

- Atrophy of the photoreceptor layer of retina.
- Squamous cell metaplasia of the interlobular ducts of parotid salivary glands, is strongly suggestive of hypovitaminosis A in pigs, calves, and lambs. This change is transient and disappears within 2 – 4 weeks after intake of vitamin.
- Abnormal epithelial cell differentiated could be observed in trachea, esophagus, rumen mucosa, preputial lining, pancreatic ducts, and urinary epithelium.
- Increased incidence of pituitary cysts in cattle.

DIFFERENTIAL DIAGNOSIS:

The diagnosis of vitamin A depend upon:

1. History: green feeds or vitamin A supplements are not being provided.
2. Night blindness, and changes of eyes such as papilledema, blindness. As well as, syncope, and convulsions or ataxia -.
3. Level of vitamin A in plasma and liver.
4. Response to vitamin A therapy.

The convulsion form due vitamin A deficiency must be differentiated from:

1. **Polioencephalomalacia (thiamin deficiency):** characterized by sudden onset blindness, head pressing, usually in grain-fed animals but also in pastured animals that ingested an excess of sulfate in water.

2. **Hypomagneseemic tetany:** occurs commonly in dairy cattle on pasture or calves fed milk during cold atmospheric condition, characterized by hyperesthesia, champing of jaws, clonic-tetanic convulsions, normal eyes, loud tachycardia, and response to magnesium therapy.
3. **Lead poisoning:** all ages could be affected with the same signs, characterized by sudden blindness, tonic-clonic convulsions champing of jaws, head pressing and rapid death.
4. **Rabies:** all age groups could be affected, sporadic cases, history of biting from rabies animal, gradual progressive ascending paralysis, ataxia, inability to swallow, normal eyes, death within 4 – 7 days.

TREATMENT:

- Treatment of hypovitaminosis A should be immediately in case of curable form such as calves with convulsions due to increase in CSF pressure (response within 48 hours after treatment) but in cattle with ocular form (blindness) will not respond to treatment (irreversible damage of the optic nerve) and should be slaughtered for salvage.
- Using oily or aqueous solution of vitamin A, **at dose rate of 440 IU/kg BW** (10 – 20 times more than daily requirements).

CONTROL:

1-Dietary daily requirement:

Vitamin A	
Minimal daily requirement (MDR)	40 IU/ kg BW
Pregnancy, lactation, growing	50 – 75 % increases than MDR
1 IU of vitamin A = 0.3 µg of Retinol.	
5 – 8 µg of β-Carotene = 1 IU of Retinol.	

2-Supplementation of the vitamin A: this depend upon the species and the ease of vitamin; the most effective and economical method is supplementation of the vitamin in feed or with the protein daily or at regular intervals (when the daily dietary supplement is not applied in case of beef cattle, which fed primarily on carotene-deficient roughages during pregnancy)

3-Parenteral vitamin A injection: an alternative method to dietary supplementation is the IM injection of vitamin A at intervals of 50 – 60 days at the rate of 3000 – 6000 IU/kg BW. This for good hepatic storage, and optimum plasma and hepatic levels of vitamin A for 50 – 60 days. In pregnant beef cattle, the last injection should not be more than 40 – 50 days before parturition to insure adequate level of the vitamin A in the colostrum. Ideally, the last injection should be given 30 days before parturition.

4- Oral vitamin A administration is also used at a dose rate of 2.8 mg/kg BW as a single bolus during drought or dry season is effective in control of vitamin A deficiency and rise the level of vitamin A in milk of such animals.