DISEASES CAUSED BY DEFICIENCIES OF WATER-SOLUBLE VITAMINS

- Water-soluble vitamins include vitamin B complex and vitamin C.
- The members of vitamin B complex include:
    1. Thiamin or thiamine (B_1).
    2. Nicotinic acid (niacin).
    3. Riboflavin.
    4. Pantothenic acid.
    5. Pyridoxine (B_6).
    6. Biotin.
    7. Folic acid (pteroylglutamic acid).
    8. Cyanocobalamin (B_{12}).
- All members of vitamin B complex *except nicotinic acid* are synthesized by the microbial activity in the forestomach and large intestine in ruminants and horses, while nicotinic acid and vitamin C (Ascorbic acid) can be synthesized in the tissues by other means. Furthermore, colostrum and milk of these animals are considered good sources (sheep's milk is much richer than cow's milk in vitamin B complex) for these vitamins during pre-ruminant periods. So, these vitamins are of minor importance in herbivores animals (except B12, as previously mentioned).

THIAMIN(E) DEFICIENCY, HYPOTHIAMINOSIS, POLIOENCEPHALOMALACIA IN RUMINANTS, NUTRATIONAL CEREBROCORTICAL NECROSIS IN RUMINANT, BRAKEN FERN OR HORSTAIL POISONING IN HORSES.

Thiamin (or Vitamin B_1) deficiency occurs in all species of animals, particularly young, due to primary thiamin deficiency (rare), or secondary thiamin deficiency (more common), and characterized clinically by nervous signs.

ETIOLOGY & EPIDEMIOLOGY:

A-Primary thiamin deficiency:

primary thiamin deficiency is due to inadequate thiamin in the diet of the animals, this form is unlikely under natural conditions because: -

1. most plants (particularly, seeds and yeast), animal source proteins, colostrum, and milk contain adequate amount of thiamin.

2. Thiamin is usually synthesized in adequate quantities in the rumen of the cattle and sheep and in the large intestine in horses, when they fed high quality roughage in diets.
    a. The degree of synthesis in ruminants is governed, to some extent, by the composition of ration; a sufficiently of readily fermentable carbohydrate causing an increase of synthesis of most vitamins of B complex, while high the high intake of diet reducing the synthesis.
    b. The disease is most common in feedlots sheep and cattle which are being fed concentrate rations in intensive production, also recorded in cattle fed molasses with minimal quantity of roughages.
3. The microbial synthesis of thiamin occurs in the alimentary tract of the monogastric animals, and in young ruminants during pre-ruminant stage (but insufficient quantities as in adults, so these animals can be readily induced thiamin deficiency experimentally).
4. Thiamin deficiency occurs in sheep being subjected to live expert from *Australia* to the *Middle East* due to the deprivation of feed and water (or reduction in feed and water) during transportation and the pre-embarkation of feedlots. The low feed intake and alteration of rumen environment (failure of rumen microbes to adapt and thrive) will lead to deficiency in synthesize of thiamin, and consequently thiamin deficiency develops.

B-Secondary thiamin deficiency:

Secondary thiamin deficiency is more common than the primary thiamin deficiency, particularly in young of farm animals. Secondary thiamin deficiency occurs because of destruction of thiamin content of the diet by thiaminase enzymes (thiaminase type-I & thiaminase type-II), as in case: -

1. In carnivores, excess of raw fish in the diet because the high content of thiaminase in fish.
2. In horses, secondary thiamin deficiency occurs due ingestion of excessive quantities of *braken fern* and *horsetail* plants (also, ingestion large quantities of turnips without grains) because of the high thiaminase content of these plants. *These plants are unpalatable to horses and poisoning is rarely occurs at pasture, but may be danger when immature plants are cut and preserved in meadow hay.*
3. In ruminants (sheep and cattle) and horses administration of large daily doses of pyrimidine containing structural analogs of thiamin such as amprollium (orally or intraperitoneal administration).
4. In sheep and cattle, ingestion of excessive quantities of sulfur (as sulfate) in the diet or water (sulfur or sulfate toxicity, *this produce polioencephalomalacia without any changes in thiamin content in sheep and cattle* i.e. not respond to thiamin therapy.

5. Destruction of thiamin content in the GIT by bacterial thiaminases, which are produced by thiaminase-producing bacteria in rumen and intestine (producing thiaminase type-I and thiaminase-type II).
6. Feeding moldy feed containing certain spp. of fungi, which also producing thiaminase enzymes.

PATHOGENESIS:

The function of the thiamin:

1. The main function of the thiamin is its activity as a co-carboxylase enzyme (pyruvate dehydrogenase) (co-enzyme or co-factor) in the metabolism of fats, carbohydrates and protein i.e. vitamin B1 (thiamine) is co-enzyme for pyruvate dehydrogenase, an essential enzyme for aerobic metabolism. In the absence of thiamine, the conversion of pyruvate to acetyl-CoA is inhibited and pyruvate cannot enter the *Kreb's cycle*.

Pyruvates (of fat, Cho, and protein) $\frac{co-pyurvate\ dehydrogenase}{co-carboxylation}$ ***acetyl-CoA***

1- Thiamin is important for erythrocyte precursors and in erythrocyte transketolase (important for pentose phosphate pathway and energy production).

So, thiamin deficiency leads to:

A. Impairment of the metabolism of carbohydrate with accumulation of endogenous pyruvates.

B. Low erythrocyte transketolase activities and elevation of thiamin pyrophosphate effects which lead to poor growth rate in subclinical thiamin deficiency in lambs and calves.

- The brain depends largely on carbohydrate as a source of energy, particularly cerebral cortex (cerebral cortex has specific requirement for oxidative metabolism of glucose). So, the characteristic nervous signs of thiamin deficiency may be attributed to the development to polioencephalomalacia due to abnormalities of carbohydrate metabolism and accumulation of pyruvates that lead to edema and necrosis of the brain (astrocytes). In this context, ***there are auto-fluorescent spots observed under UV 365 nm illumination (diagnostic and pathognomonic sign for thiamin deficiency) that corresponding to the production of auto-fluorescence substance in mitochondria in cerebrocortical neurocytes, suggesting impairment of carbohydrate metabolism in brain.***

CLINICAL FINDINGS:

In cattle:

1. The disease may cause sudden death or the animal may be found dead without any premonitory signs, particularly in beef cattle in pasture.
2. Sudden onset of blindness.

3. Nervous signs include, which may occur in episodes in early stage and later may be continuous:
    a. walking aimless.
    b. Ataxia (incoordination).
    c. Head pressing.
    d. Muscular tremors, particularly on the head, ear twitching, champing of the jaws and frothy salivation.
    e. Animal is difficult to be handle or move.
    f. Convulsions (clonic-tetanic convulsions) which may occur in episodes in first stage, and within several hours become continuous with limb tetanic.
4. Finally, recumbency occurs, with marked opisthotonos, nystagmus (vertical or horizontal), dorsal strabismus due to stretching of the trochlear nerve (is common).
5. Dysphagia.
6. Grinding teeth.
7. Body temperature is normal, but may be slightly elevated due to the muscular activity during nervous signs.
8. Heart rate may be normal, subnormal or elevated.
9. The rumen movement is normal for several days (this of important for distinguishing the thiamin deficiency from lead poisoning in which rumen is static).
10. Menace reflex is absent, palpebral reflex is normal, pupil of normal size and respond to light (pupillary light reflex).
11. Death of the animal if there is no rapid treatment and recover is more common in elder ages.

In sheep and goats

1. Sudden blindness.
2. Nervous signs include:
    a. Wander or aimless movements, sometimes in circle, or stand motionless.
    b. Head pressing.
    c. Within a few hours, animal become recumbent with opisthotonos, extension of limbs, hyperesthesia, with periodic colonic-tonic convulsions.
    d. Nystagmus.
    e. Occasionally animal shows unilateral localizing signs including circling and spasmodic deviation of the head.
3. In goats, the early signs may be excitability with elevation of the head.

In horses:

1. Incoordination and falling; firstly, swinging from side to side, followed by pronounced incoordination with crossing of the forelimbs and wide action in the hindlimbs and falling.

2. When the animal in standing, the legs are placed well apart and arching of the back
3. Bradycardia, except in late stage may be elevated and ECG shows myocardial insufficiency.
4. Muscle tremor develops and eventually the horse is unable to stand.
5. Colonic convulsions and opisthotonos are the terminal stage.
6. Appetite is good till late stage of the disease when somnolence (sleepiness) prevents eating.
7. Body temperature is normal, except in late stage when it is above normal.

CLINICAL PATHOLOGY:

1-Blood thiamin level:

	Blood thiamin levels
Normal level	8 – 10 µg/dL
Deficient condition	2.5 – 3 µg/dL

2-Blood pyruvic acid level (pyruvate):

	s pyruvic acid level
Normal level	2 – 3 µg/dL
Deficient condition	6 – 8 µg/dL

3-Blood transketolase activity: is decreased.

NECROPSY FINDINGS:

Gross lesions:

The gross lesions of thiamin deficiency are inconsistent and may be subtle or not obvious particularly in the early stage of the condition, but the following features may be recognized especially in severe cases, as:

1. Swelling of the brain with flattening of gyri of the brain, and coning of cerebellum due to its herniation into foreman magnum.
2. Slight yellowish discoloration of the affected cortical tissue.
3. Examination of the affected brain under ultraviolet illumination (365 nm wavelength): showing autofluorescent spots or bands in the cerebral cortex (evident on the meningeal and cut surfaces of brain) due to cerebrocortical necrosis.
4. In advanced stage of the disease, the affected cerebrocortical tissue contains *macroscopic cavitation*, sometimes sufficient to result in apposition (ابدال/تبديل) pia meninge to the white matter.
5. *In horses with braken fern or horsetail poisoning*, the main lesions are only signs of congestive heart failure and congestion of intestine and liver.

Microscopic lesions:

In early stage, there are:

- Necrosis of cerebrocortical neurons, and the affected neurons are shrunken and have homogenous eosinophilic cytoplasm.
- Sometimes cortical spongiosis may occur in case of severely affected cases.
- Vessels cells undergo hypertrophy and hyperplasia.

In later stage, there are:

- The affected cortical tissue undergoes cavitation because of macrophage infiltrations and necrotic tissue is removed.
- In case of sulfur toxicity in cattle, there are multifocal vascular necrosis, hemorrhage, and parenchymal necrosis in the deep gray matter of the brain.

TREATMENT:

The treatment should be as quickly as possible to obtain a satisfactory recovery.

1. Thiamin injection (as thiamin HCl):
    a. at a dose rate 10 mg/kg BW, every 6 or 8 hours/ day (tid or qid), for 3 – 5 days, and the first dose must be injected slowly IV, while subsequent doses administered IM.
    b. Or thiamin may be used at dose rate 5 mg/ kg BW, every 3 hours, for 2 – 4 days, and the first dose must be injected slowly IV, while subsequent doses administered IM.

    -When the vitamin is given within a few hours after the onset of clinical signs, a good response commonly occurs within 1 – 6 hours and complete recovery can occur within 24 hrs. sheep and goats commonly respond within 1 – 2 hours after thiamin injection.

    -Failure to thiamin response is due to diffuse cortical and subcortical necrosis or due to sulfur toxicity.
2. An oral thiamin HCl should be given daily for 10 days, particularly when the suspected cause is thiaminases in alimentary tract as thiamin HCL does not affected by intestinal thiaminases. Oral dose of thiamin HCl is 1 g for goat and lamb/day, 5 g/day for calf and sheep.
3. Remove any dietary abnormalities.
4. Dexamethasone injection at dose rate 1 – 2 mg/kg BW/day, IM or SC, for 2 – 3 days to reduce cerebral edema.
5. Symptomatic treatment for control nervous signs when the convulsions or excitation is pronounced (sedatives or tranquilizers).

CONTROL & PREVENTION:

1. The daily requirement of thiamin in diet is 30 – 60 µg/kg BW, and diet must contain 3 – 10 mg/ kg DM.
2. Sufficient good quality roughages.
3. Avoid excess of sulfur in feed and water as well as other causative factors contributing in causing thiamin deficiency.

RIBOFLAVIN DEFICIENCY (HYPORIBOFLAVINOSIS)

Riboflavin deficiency is rare in domestic animals under natural conditions, because of:

1. The green plants (pastured animals), and animal protein (omnivorous and carnivores) are considered good and adequate sources of riboflavin.
2. Riboflavin can be synthesized in sufficient quantities by alimentary tract microflora in all species.
3. Colostrum and milk are good sources in case of young.

The function of riboflavin:

Riboflavin is an essential vitamin for cellular oxidation processes in all animals.

CLINICAL SIGNS IN CASE OF EXPERIMENTAL RIBOFLAVIN DEFICIENCY IN CALVES:

1. Anorexia.
2. Poor growth rate.
3. Diarrhea.
4. Excessive salivation and areas of hyperemia in develop in the oral commissures, on edge of lips and around navel.
5. Excessive lacrimation without ocular lesions.
6. Alopecia.

TREATMENT:

By riboflavin administration.

NICOTINIC ACID (NIACIN) DEFICIENCY (HYPONIACINOSIS)

- Nicotinic acid or niacin is high in the most of animal feeds and can be synthesized in the tissues. So, nicotinic acid deficiency is rare under natural conditions in animals, except in pigs fed ration high in corn as the corn has a low level of niacin and a low content of tryptophan, a niacin precursor.
- The oral supplementation of niacin in the diet of pre-parturient dairy cattle may lead to an increase in serum inorganic phosphorous and a decrease in serum potassium, calcium, and sodium levels.

Function of niacin:

- Nicotinic acid is essential for normal carbohydrate metabolism.

CLINICAL SIGNS OF NIACIN DEFICIENCY IN PIGS:

1. Anorexia.
2. Severe diarrhea.
3. Dirty yellow skin with a severe scabby dermatitis and alopecia.
4. Posterior paralysis occurs.

NECROPSY FINDINGS:

- ***Gross lesions:*** Hemorrhages in the gastric and duodenal walls, congestion and swelling of the small intestinal mucosa, and ulcers in large intestine are characteristic and closely resemble those of necrotic enteritis caused by salmonella spp.
- ***Microscopical lesions:*** there is severe mucoid degeneration followed by local necrosis in the wall of cecum and colon.

TREATMENT & CONTROL IN PIGS:

- Oral administration of niacin at dose rate 100 – 200 mg/day.
- Daily requirement of niacin for mature pigs are 0.1 – 0. 4 mg/kg BW, while in growing pigs 0.6 – 1 mg/kg BW.
- In pig's ration, niacin should be added, particularly in corn-based rations.

PYRIDOXINE (VITAMIN B_6) DEFICIENCY (HYPOPYRIDOXINOSIS)

- Pyridoxine deficiency is rare to be occur in animals under natural conditions.
- Experimentally, pyridoxine deficiency can be induced in pigs and calves and cattle. The affected animal may show anorexia, poor growth, apathy, dull coat and alopecia, anemia, and periodic epileptiform convulsions.
- In clinical pathological examination, there is anemia (microcytic, hypochromic anemia) with poikilocytosis and bone marrow abnormalities.

PANTOTHENIC ACID DEFICIENCY (HYPOPANTOTHENOSIS)

- Pantothenic acid is an essential dietary component in all animal species other than ruminants, which able to synthesize it in the rumen.
- Under natural conditions, deficiency of pantothenic acid is recorded only in pigs on corn-based rations.
- Experimentally induced pantothenic acid deficiency in calves (also in pigs) is manifested by anorexia, reduction in growth, dermatitis under the lower jaws, rough hair coat, alopecia, excessive nasal mucus, and death, (dermatitis develops with dark brown exudation collection about eyes, diarrhea, and incoordination with spastic, goose-stepping gait is characteristic in pigs). At necropsy, there secondary pneumonia, demyelination in the spinal cord and peripheral nerves, and softening and congestion of cerebrum, and dermatitis.
- Treatment of hypopantothenosis in pigs is done by using calcium pantothenate 500 µg/kg BW/ day and used as feed additive as 10 – 12 g/ton of ration.

BIOTIN DEFICIENCY (HYPOBIOTINOSIS)

Biotin is found in almost all plants and animal materials, as well as biotin can be synthesis in the alimentary tract (microbial synthesis). So, the deficiency of biotin is unlike to be occurred under natural conditions, except in swine.

Functions of biotin:

- It is a cofactor in several enzyme systems involved carboxylation and trans-carboxylation reactions, so, it has a significant effect on carbohydrate metabolism, fatty acid synthesis, amino acid deamination, purine synthesis, and nucleic acid metabolism.
- Biotin is essential for maintaining and improve the hoof horn material in horses and pigs.

ETIOLOGY:

- In swine, the deficiency of biotin occurs when the animals fed on diets-based on cereals with low available biotin content. Continuous feed sulfonamides or antibiotics may induce deficiency. Feeding large quantities of uncooked egg white causes biotin deficiency in pigs and pets because the egg white contains an antivitamin to biotin called avidin.

CLINICAL FINDINGS:

- Biotin deficiency in pigs causes alopecia, dermatitis, lameness due to painful cracking of soles and the walls of hooves.
- The dietary supplementation of horses with 10 – 30 mg biotin/day for 6 – 9 months is considered to be effective as an aid in the treatment of weak horn hoof, as the biotin supplementation improve and maintain the hoof horn quality in horses (it is necessary to use continuous dietary supplementation with biotin at a daily dose 20 mg in horses).

FOLIC ACID (PTEROYLGLUTAMIC ACID) DEFICIENCY (HYPOFOLICOSIS)

- Natural occurring deficiency of the folic acid has not been diagnosed in domestic animals, but folic acid has numerous and complex interrelationships with other nutrients. So, folic acid is considered an essential dietary nutrient for all animal species and humans.
- Permanently stabled horses and horses in training may require additional daily oral folic acid.

Function of the folic acid:

- The folic acid (*pteroylglutamic acid*) is necessary for nucleic acid metabolism, so it is important in organ formation during pregnancy.
- It is important for erythropoiesis, particularly in humans as its deficiency lead to pernicious anemia.

CHOLINE DEFICIENCY (HYPOCHOLINOSIS)

- Choline is a dietary essential for pigs and newborn calves (but not older calves).
- Addition of choline in ration of feedlot steers increase daily gain.

Function of choline:

1. Choline is important for synthesis of acetylcholine.
2. It is important for synthesis phospholipids (cell membrane).
3. Choline acts as lipid transport (lipoproteins), especially in hepatocytes (used in treatment of fatty degeneration and fat-cow syndrome).
4. Choline acts as methyl-group donor or methyl metabolism (homocysteine reduction).

CLINICAL FINDINGS IN CHOLINE DEFICIENCY:

In newborn calves:

- Calves fed on a synthetic choline-deficient diet from the second day of life develop an acute syndrome in about 7 days as marked weakness, inability to get up. Labored or rapid breath, and anorexia. The recovery occurs after choline administration.

In pigs:

- Ataxia, enlarged and tender hocks, anorexia, with fatty degeneration of the liver.

ASCORBIC ACID DEFICIENCY, (VITAMIN C DEFICIENCY)

- Vitamin C (Ascorbic acid) is synthesized in all animal species in their tissues from glucose molecules as they have ***gulonolactone oxidase*** enzyme, while humans, other primates, Guinea pigs, and bats are unable to synthesis vitamin C as the are lack on ***gulonolactone oxidase*** which catalyze the last step in biosynthesis of ascorbic acid in the tissues. So, vitamin C is not dietary essential in any of domestic animals, although its blood levels fall after birth., in the newborn calves, the ascorbic acid levels begin to rise again at about 3 weeks of age.
- A type of dermatosis was recorded in young calves associated with low level of vitamin C in their plasma.
- Administration of high doses of ascorbic acid orally is used in horses to counteract the effect of stress and minimize the effects of infections. *The daily administration of 4.5 – 20 g of ascorbic acid results in significant increases in the plasma level while a single oral dose of 20 g of ascorbic acid does not result any increase in the plasma level of the vitamin.*

Function of the ascorbic acid:

1. Vitamin C is important for synthesis of collagen.
2. Vitamin C acts as antioxidant by donating electrons to various enzymatic and non-enzymatic reactions in the body.
3. Vitamin C is important for iron absorption.
4. Vitamin C is important for wound healing.
5. Vitamin C is important for immune system.

DERMATITIS ASSOCIATED WITH LOW LEVEL OF VITAMIN C IN YOUNG CALVES:

CLINICAL FINDINGS:

1. Heavy depositions of dandruff over the skin, followed by a waxy crust, alopecia, and dermatitis lesions begin on the ears and spread over the cheeks, down the crest of the neck, and over shoulders.
2. Sometimes death is occurred, but spontaneous recovery is more usual.

TREATMENT:

- Spontaneous recovery is usual but over the time, and for rapid treatment and response of such condition using a single injection of 3 g of ascorbic acid.