Diseases associated with deficiency of fat-soluble vitamins

Vitamin A deficiency
(Hypovitaminosis - A)

A deficiency of vitamin A may be caused by an insufficient supply of the vitamin in the ration or its defective absorption from the alimentary canal. In young animals, the manifestations of the deficiency are mainly those of compression of the brain and spinal cord. In adult animals, the syndrome is characterized by night blindness, corneal keratinization, pityriasis, defects in the hooves, loss of weight and infertility.

Congenital defects are common in the off spring of deficient dams. Vitamin A may also provide a protective effect against various infectious diseases and enhance many facets of the immune system.

Etiology

Vitamin A deficiency may be primary disease, due to an absolute deficiency of vitamin A or its precursor carotene in the diet, or a secondary disease in which the dietary supply of the vitamin or its precursor is adequate, but their digestion, absorption, or metabolism is interfered with to produce a deficiency at the tissue level.

Epidemiology

- **Primary vitamin A deficiency**

Primary vitamin A deficiency is of major economic importance in groups of young growing animals on pasture or fed diets deficient in the vitamin or its precursors.

In the UK, primary vitamin A deficiency occurs in housed cattle fed a ration containing little or no green forage .

Ruminants on pasture Primary vitamin A deficiency occurs in beef cattle and sheep on dry range pasture during periods of drought.

Clinical vitamin A deficiency does not always occur under these conditions because hepatic storage is usually good and the period of deprivation not sufficiently long for these stores to reach a critically low level.

Young sheep grazing natural, drought stricken pasture can suffer serious depletion of reserves of the vitamin in 5-8 months, but normal growth is maintained for 1 year at which time clinical signs develop.

Adult sheep may be on a deficient diet for 18 months before hepatic stores are depleted and the disease becomes evident.

Secondary vita m i n A deficiency

May occur in cases of chronic disease of the liver or intestines because much of the conversion of carotene to vitamin A occurs in the intestinal epithelium and the liver is the main site of storage of the vitamin.

Highly chlorinated naphthalenes interfere with the conversion of carotene to vitamin A and animals poisoned with these substances have a very low vitamin A status.

The intake of inorganic phosphorus also affects vitamin A storage, low phosphate diets facilitating storage of the vitamin.

This may have a sparing effect on vitamin A requirements during drought periods when phosphorus intake is low and an exacerbating effect in stall-fed cattle on a good grain diet.

Pathogenesis

Vitamin A is essential for the regeneration of the visual purple necessary for dim light vision, for normal bone growth and for maintenance of normal epithelial tissues.

Deprivation of the vitamin produces effects largely attributable to disturbance of these functions. The same tissues are affected in all species.

There is a difference in tissue and organ response in the different species and particular clinical signs may occur at different stages of development of the disease.

The major pathophysiological effects of vitamin A deficiency are as follows.

Night vision

Ability to see in dim light is reduced because of interference with regeneration of visual purple.

Cerebrospinal fluid pressure

An increase in CSF pressure is one of the first abnormalities to occur in hypovitaminosis-A in calves. It is a more sensitive indicator than ocular changes and, in the calf, it occurs when the vitamin A intake is about twice that needed to prevent night blindness.

hyppvitaminosis A causes increased cerebrospinal fluid pressure accompanied by papillary edema and at times central nervous system signs.

The increase in CSF pressure is due to impaired absorption of the CSF due to reduced tissue permeability of the arachnoid villi and thickening of the connective tissue matrix of the cerebral dura mater. The increased CSF pressure is responsible for the syncope and convulsions, which occur in calves in the early stages of vitamin A deficiency.

Bone growth

Vitamin A is necessary to maintain normal position and activity of osteoblasts and osteoclasts. When deficiency occurs there is no retardation of endochondral bone growth, but there is incoordination of bone growth in that shaping, especially the finer molding of bones, does not proceed normally.

Epithelial tissues

Vitamin A deficiency leads to atrophy of all epithelial cells, but the important effects are limited to those types of epithelial tissue with a secretory as well as a covering function.

The secretory cells are without power to divide and develop from undifferentiated basal epithelium.

In vitamin A deficiency these secretory cells are gradually replaced by the stratified, keratinizing epithelial cells common to non-secretory epithelial tissues. This replacement of secretory epithelium by keratinized epithelium occurs chiefly in the salivary glands, the urogenital tract (including placenta but not ovaries or renal tubules.

These changes in epithelium lead to the clinical signs of placental degeneration, xerophthalmia and corneal changes.

Embryological development

Vitamin A is essential for organ formation during growth of the fetus.

Immune mechanisms

The effects of vitamin A and β-carotene on host defense mechanisms have been uncertain and controversial for many years.

Clinical findings

In general, similar syndromes occur in all species, but because of species differences in tissue and organ response, some variations are observed. The major clinical findings are set out below.

Night blind ness

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

Xerophthalmia

True xerophthalmia, with thickening and clouding of the cornea, occurs only in the calf. In other species a thin, serous mucoid discharge from the eyes occurs, followed by corneal keratinization, clouding and sometimes ulceration, and photophobia.

Changes in the skin

A rough, dry coat with a shaggy appearance and splitting of the bristle tips in pigs is characteristic.

Heavy deposits of bran-like scales on the skin are seen in affected cattle. Dry, scaly hooves with multiple, vertical cracks are another manifestation of skin changes and are particularly noticeable in horses.

Body weight

Under natural conditions, a simple deficiency of vitamin A is unlikely to occur and the emaciation commonly attributed to vitamin A deficiency may be largely due to multiple deficiencies of protein and energy. Although in appetence, weakness, stunted growth and emaciation occur under experimental conditions of severe deficiency.

Reproductive efficiency

Loss of reproductive function is one of the major causes of loss in vitamin A deficiency. Both the male and female are affected. In the male, libido is retained but degeneration of the germinative epithelium of the seminiferous tubules causes reduction in the number of motile, normal spermatozoa produced.

In the female, conception is usually not interfered with, but placental degeneration leads to abortion and the birth of dead or weak young. Placental retention is common.

Nervous system

Signs related to damage of the nervous system include:

Paralysis of skeletal muscles due to damage of peripheral nerve roots

Encephalopathy due to increased intracranial pressure.

Blindness due to constriction of the optic nerve canal. These defects occur at any age but most commonly in young, growing animals and they have been observed in all species except horses.

Congenital defects

These have been observed in piglets and calves. In calves, the defects are limited to congenital blindness due to optic nerve constriction and encephalopathy. In piglets, complete absence of the eyes (anophthalmos), or small eyes (microphthalmos), incomplete closure of the fetal optic fissure, degenerative changes in the lens and retina, and an abnormal proliferation of mesenchymal tissue in front of and behind the lens are some of the defects encountered.

Other diseases

Increased susceptibility to infection is often stated to result from vitamin A deficiency. The efficacy of colostrum as a preventive against diarrhea in calves was originally attributed to its vitamin A content, but the high antibody content of colostrum is most important.

Anasarca. Edema of the limbs and brisket have been associated with vitamin A deficiency in feedlot cattle, especially steers.

The edema can be extensive, include all four limbs, ventral body wall and extending to the scrotum.

Clinical pathology

Plasma vitamin A

Vitamin A levels in the plasma are used extensively in diagnostic and experimental work. Plasma levels of 20 µg/dL are the minimal concentration for vitamin A adequacy.

Plasma retinol

Some information on the plasma retinol values in stabled Thoroughbred horses is available.

Plasma carotene

Plasma carotene levels vary largely with the diet. In cattle, levels of 150 µg /dL are optimum and, in the absence of supplementary vitamin A in the ration, clinical signs appear when the levels fall to 9 µg /dL.

Hepatic vitamin A

A direct relationship between plasma and hepatic levels of vitamin A need not exist since plasma levels do not commence to fall until the hepatic stores are depleted.

Cerebrospinal fluid

CSF pressure is also used as a sensitive indicator of low vitamin A status. In calves, normal pressures of less than 100 mm of saline rise after depletion to more than 200 mm.

Differential diagnosis list

Cattle

- Polioencephalomalacia
- Hypomagnesemic tetany
- Lead poisoning
- Rabies
- Meningoencephalitis
- Peripheral blindness due to bilateral ophthalmitis.

TREATMENT

Vitamin A

Animals with curable vitamin A deficiency should be treated immediately with vitamin A at a dose rate equivalent to 10-20 times the daily maintenance requirement. As a rule, 440 IU/kg BW is the dose used.

Parenteral injection of an aqueous rather than an oily solution is preferred, The response to treatment in severe cases is often rapid and complete, but the disease may be irreversible in chronic cases.

Calves with the convulsive form due to increased CSF pressure will usually return to normal in 48 h following treatment.

Cattle with the ocular form of the deficiency and that are blind will not respond to treatment and should be slaughtered for salvage.

Control

Dietary requirement

The minimum daily requirement in all species is 40 IU of vitamin A/kg BW, which is a guideline for maintenance requirements, In the formulation of practical diets for all species, the daily allowances of vitamin A are commonly increased by 5 0-100% of the daily minimum requirements, During pregnancy,lactation, or rapid growth.

The amounts of the vitamin to be added to the ration of each species to meet the requirements for all purposes should be obtained from published recommended nutrient requirements of domestic animals.

Supplementation method

The method of supplementation will vary depending on the class of livestock and the ease with which the vitamin can be given. In pigs, the vitamin is incorporated directly into the complete ration, usually through the protein supplement. In feedlot and dairy cattle receiving complete feeds, the addition of vitamin A to the diet is simple. In beef cattle, which maybe fed primarily on carotene-deficient roughage during pregnancy, it may not be possible to supplement the diet on a daily basis.

Parenteral injection An alternative method to dietary supplementation is the 1M injection of vitamin A at intervals of 50-60 days at the rate of 3000-6000 IU/kg BW. Under most conditions, hepatic storage is good and optimum plasma and hepatic levels of vitamin A are maintained fur up to 50-60 days.

Oral vitamin A

The oral administration of a single bolus of vitamin A at a dose of 2.8 mg/kg BW **.**

VITAMIN K DEFICIENCY

A primary deficiency of vitamin K , is unlikely under natural conditions in domestic animals because of the high content of substances with vitamin K activity in most plants and the substantial synthesis of these substances by microbial activity in the alimentary canal.

Sporadic cases may occur when impairment of the flow of bile reduces the digestion and absorption of this fat-soluble vitamin.

Experimentally produced vitamin K deficiency in piglets is manifested by hypersensitivity, anemia, anorexia, weakness, and a marked increase in prothrombin time. The minimum daily requirement for newborn pigs is 5 µg/kg BW and the minimum curative injection dose is four times larger.

A hemorrhagic disease of recently weaned pigs from 6 to 15 weeks of age is considered to be associated with vitamin K deficiency. Affected pigs fail to grow, become pale, develop large subcutaneous hematomas and exhibit lameness and epistaxis. Excessive and fatal hemorrhage following routine castration may occur in pigs from 30 to 40 days of age, but not at 15-20 days of age.

Subcutaneous massive hemorrhage is more common in pigs at 40-70 days of age. Prothrombin time and activated partial thromboplastin time are prolonged along with decreased levels of vitamin K-dependent factors II, VII, IX, and X.2 At necropsy, hemorrhages are extensive in the muscles of the hind limbs, forelimbs, and axillary and mandibular region.

Vitamin K, or vitamin K2, given at a dose of 3 mg/kg BW 1M as a single dose will restore the blood coagulation defects to normal. Vitamin K3 added to the feed at a rate of 25 mg/kg for 4 days was also effective.

The cause of the vitamin K deficiency was considered to be related to the use of antibacterial drugs in the feed but this has not been substantiated.

The most important therapeutic use of vitamin K in domestic animals is in sweet clover poisoning where toxic quantities of coumarin severely depress the pro thrombin levels of the blood and interfere with its clotting mechanism. Industrial poisons used in rodent control which contain anticoagulants of the coumarin type, e.g. warfarin, cause fatal hypothrombinemia;

warfarin is a vitamin K antagonist. warfarin therapy results in a deficiency of vitamin K in the liver. warfarin therapy results in a deficiency of factors II,VII,IX, and of

protein C. the effect of warfarin therapy on coagulation (prolongation of the prothrombin time)due to inhibition of factor VII and protein C.

vitamin K is an effective antidote. For warfarin - induced anticoagulation in the horse, the administration of 300-500 mg of vitamin Kl SC every 4-6 h until the prothrombin time retums to baseline values is recommended.

Diseases associated with deficiencies of water soluble vitamins

Water-soluble vitamins, including vitamin C and the B complex, are of minor importance in ruminants (except for vitamin B complex ,because of their synthesis in the alimentary tract of these animals.

Vitamin requirements were defined as the smallest dietary amount necessary to prevent clinical signs of deficiency.

It was demonstrated that even when fed a vitamin-free diet, the synthesis of B complex vitamins by the rumen microflora was sufficient to avoid deficiencies. Consequently, it was concluded that a dietary supply of B-complex vitamins was unnecessary in ruminants.

Niacin requirements per feed unit are higher with high-energy feeds. Niacin increases the number of ruminants protozoa and in cows with clinical or subclinical ketosis, repeated doses of niacin lead to a rapid decrease of non -esterified fatty , acids. Dietary supplementation of niacin at 6 mg/d, have improved milk production.

Biotin supplementation of 20 mg/head per day in early lactation can result in improved hoof horn health.

Folic acid is essential for cell division and growth for protein synthesis and may increase milk .

Vitamin B12 requirements are usually met by ruminal microflora synthesis if the dietary supply cobalt is adequate. High concentrate diets can modify bacterial synthesis of the vitamin and metabolic utilization of propionate increases the demand for Vitamin B12.

Thiamin, nicotinic acid, riboflavin, pantothenic acid, pyridoxine, biotin, and folic acid are all synthesized by microbial activity.

Nicotinic acid and vitamin C are synthesized by other means. The young calf or lamb, in the period before ruminal activity begins, is likely to receive inadequate supplies of these vitamins and deficiency states can be produced experimentally.

In the pre-ruminant stage, colostrum and milk are good sources of the water-soluble vitamins, ewes' milk being much richer than cows' milk. The production of signs of deficiency of the B vitamins in horses by the feeding of deficient diets has raised some doubts as to the availability of the B vitamins synthesized in the large intestine in this species.

Vitamin C is synthesized by all species and is not an important dietary essential in any of the domestic animals. Synthesis occurs in tissues and, although blood levels fall after birth, in the newborn calf they begin to rise again at about 3 weeks of age.

A dermatosis of young calves has been associated with low levels of ascorbic acid in their plasma and responds to a single injection of 3 g of ascorbic acid. A heavy dandruff, followed by a waxy crust, alopecia and dermatitis commences on the ears and spreads over the cheeks, down the crest of the neck and over the shoulders. Some deaths have been recorded, but spontaneous recovery is more usual.

Thiamin deficiency
(Hypothiminosis)

The disease caused by deficiency of thiamin in tissues is characterized chiefly by nervous signs.

Etiology

Thiamin deficiency may be primary, due to deficiency of the vitamin in the diet, or secondary, because of destruction of the vitamin in the diet by thiaminase.

A primary deficiency is unlikely under natural conditions because most plants, especially , seeds, yeast, and milk contain adequate amounts.

Thiamin is normally synthesized in adequate quantities in the rumen of cattle and sheep on a well-balanced roughage diet. The degree of synthesis is governed to some extent by the composition of the ration, a sufficiency of readily fermentable carbohydrate causing an increase of synthesis of most vitamins of the B complex and a high intake in the diet reducing synthesis.

Microbial synthesis of thiamin also occurs in the alimentary tract of monogastric animals and in young calves and lambs, but not in sufficient quantities to avoid the necessity for a dietary supply, so that deficiency states can be readily induced in these animals with experimental diets.

Epidemiology

One of the best examples of secondary thiamin deficiency is inclusion of excess raw fish in the diet of carnivores, resulting in destruction of thiamin because of the high content of thiaminase in the fish.

A thiaminase-induced subclinical thiamin deficiency causing sub optimal growth rate of weaner lambs has been described.

Higher levels of thiaminase activity were present in the feces and rumen contents of lambs with poor growth rate compared with normal lambs .

The evidence indicates that the thiamin deficiency is a primaly one associated with deprivation of feed during transportation to the preembarkation feedlots. The low feed

intake and failure of the ruminal microbes to adapt, thrive and synthesize a net surplus of thiamin during.

Pathogenesis

The only known function of thiamin is its activity as a co-carboxylase in the metabolism of fats, carbohydrates and proteins and a deficiency of the vitamin leads to the accumulation of endogenous pyruvates.

Although the brain is known to depend largely on carbohydrate as a source of energy, there is no obvious relationship between a deficiency of thiamin and the development of the nervous signs which characterize it.

paliencephalomalacia is caused by a thiamin deficiency in grain – fed young cattle.

focal or laminar areas of necrosis in the gray matter of the cerebral cortex may be seen grossly or microscopically with polioencephalomalacia.

increased CSF pressure is often markedly elevated with polioencephalomalacia

There are other prodromal indications of deficiency disease. For example, there is a decrease in erythrocyte precursors and in erythrocyte transketolase.

Additional clinical signs also in the circulatory and alimentary systems, but their pathogenesis cannot be clearly related to the known functions of thiamin. Subclinical thiamin deficiency due to thiaminases in the alimentary tract is associated with low erythrocyte transketolase activities and elevated thiamin pyrophosphate effects, which may explain the poor growth rate .

Clinical findings

Bracken fern (Pteridium aquilinum) and horsetail (Equisetum arvense) poisoning in the horse Incoordination and falling and bradycardia due to cardiac irregularity, are the cardinal clinical signs of bracken fern poisoning in the horse.

These signs disappear after the parenteral administration of thiamin. Similar clinical effects occur with horse, tail swaying from side to side occurs first, followed by pronounced incoordination, including crossing of the forelegs and Wide action in the hind legs.

When standing, the legs are placed well apart and crouching and arching of the back are evident. Muscle tremor develops and eventually the horse is unable to rise.

Clonic convulsions and opisthotonos are the terminal stage.

Appetite is good until late in the disease when somnolence prevents eating.

Temperatures are normal and the heart rate slow until the terminal period when both rise to above normal levels.

The greatest danger is when the immature plants are cut and preserved in meadow hay.

Lambs 1-3 days old placed on a thiamin -deficient diet show signs after 3 weeks.

Somnolence, anorexia, and loss of condition occur first, followed by tetanic convulsions.

Treatment

In clinical cases the injection of a solution of the vitamin produces dramatic results (5 mg/kg BW given every 3 h) . The initial dose is usually given IV followed by 1M injections for 2-4 days. An oral source of thiamin should be given daily for 10 days and any dietary abnormalities corrected.

parenteral administration of thiamin is the usual treatment for poliioencephalacia

CONTROL

The daily requirement of thiamin for mono gastric animals is, in general, 30-60 µg/kg BW. The addition of yeast, cereals, grains, liver, and meat meal to the ration usually provides adequate thiamin.

Biotin (Vitamin H) Deficiency

(Hypobiotinosis)

Biotin or vitamin H, has several important biochemical functions. It is a cofactor in several enzyme systems involved in carboxylation and trans carboxylation reactions and consequently has a significant effect on carbohydrate metabolism, fatty acid synthesis, amino acid deamination, purine synthesis, and nucleic acid metabolism. Biotin is found in almost all plant and animal materials and, being required in very small quantities, is unlikely to be deficient in diets under natural conditions, especially as microbial synthesis occurs in the alimentary tract.

Cattle

Biotin is now considered a significant factor in lameness of cattle. Biotin is important for the differentiation of epidermal cells which are required for normal production of keratin and hoof horn tissue. Biotin also acts as a co-factor in carboxylase enzymes and is an important factor in both gluconeogenesis and fatty acid synthesis. Significant differences in the fatty acid profile of horn tissue of cattle with claw lesions have been observed.

Biotin supplementation reduces clinical white line disease, reduces horn lesions, and improves horn quality by strengthening the intercellular cementing material between keratinocytes. Improved hoof integrity in intensively managed dairy cows has occurred following biotin supplementation.

A long period of supplementation is required before the effect of the vitamin on hoof health care is expressed. In addition, there may be improved milk production, milk composition, and cow fertility with biotin Supplementation .

Skin lesions also develop in affected gilts and sows. There is gradual alopecia, particularly over the back, the base of the tail, and the hindquarters. The hairs are more bristly than normal and break easily. The alopecia is accompanied by a dryness of the skin.

Folic acid deficiency(Hypofolicosis)

Folic acid (pteroylglutamic acid) is necessary for nucleic acid metabolism and its deficiency in humans leads to the development of pernicious anemia. A dietary source is necessary to all species and an adequate intake is provided by pasture.

Although naturally occurring deficiencies have not been diagnosed positively in domestic animals, folic acid has numerous and complex interrelationships with other nutrients and the possibility of a deficiency playing a part in inferior animal performance should not be overlooked. The vitamin has a particular interest for equine nutritionists.

(Hypocyanocobal).

Vitamin B12 deficiency is unlikely to occur under natural conditions other than because of a primary dietary deficiency of cobalt, which is an important disease in many countries of the world.

Although microbial synthesis of the vitamin occurs in the rumen in the presence of adequate cobalt and in the intestines of other herbivores such as the horse, it is probably a dietary essential in the pig and young calf. Animal protein is a good source. A deficiency syndrome has been produced in young calves on a synthetic ration. Signs include anorexia, cessation of growth, loss of condition, and muscular weakness.

The daily requirement under these conditions is 20-40µg of vitamin B12.