Diseases associated with deficiencies of trace mineral nutrients

Introduction

The trace elements are involved as component parts of many tissues, and one or more enzyme activities and their deficiency leads to a wide variety of pathological

Pathophysiology of trace element deficiency

The physiological basis of trace element deficiency is complex. Some elements are involved in a single enzyme, some in many more, and a lack of one element may affect one or more metabolic processes.

There are wide variations in how individual animals respond clinically to lowered blood or tissue levels of a trace element. The susceptibility to clinical disease may be a function of the stage of physiological development at which they occur, genetic differences within a species, and interrelationships with other trace elements.

A dietary deficiency does not necessarily lead to clinical disease. Several factors predispose the animal to clinical disease and they include:

1. The age at which the deficiency occurs (for example fetal lambs are highly susceptible to demyelination due to copper deficiency in late fetal life)
2. Differences in genotype requirements
3. Discontinuous demands for trace elements because of changes in environment
4. The challenge of infections, diet, and production demands
5. Individual variations in response to the deficiency, the use of alternative pathways by the body in the face of a deficiency
6. Size of the functional reserves.

The ingestion of soil can have a profound effect on trace element nutrition and metabolism. Geochemical surveys can assist in the identification of areas in which livestock are exposed to excessive ingestion or deficiencies of trace elements. The dose-response trial will continue to play a significant role in the delineation of trace element deficiencies because it is often difficult to determine the role of individual trace elements. A dose-response trial can be defined as the application of a test and a control substance to a group, or replicates, of individuals and the measurement of the response to the treatment. A deficiency of one trace element may result in clinical disease, which may be indistinguishable from a deficiency of more than one trace element. Many of the trace element deficiencies may produce non-specific as well as specific effects.

Laboratory diagnosis of mineral deficiencies

The diagnosis of mineral deficiencies, particularly trace element deficiencies, will depend heavily on the interpretation of the biochemical criteria of the trace element status. This is because deficiencies of any one or more of several trace elements can result in non-specific clinical abnormalities, such as loss of weight, growth retardation, anorexia, and inferior reproductive performance. The interpretation of biochemical criteria of trace element status are governed by three important principles: relationship with intake, time, and function.

1 . Relationship between the tissue concentrations of a direct marker and the dietary of the intake element
2. Non-storage criteria can be divided into indicators of acute and chronic deficiency
3. A deficiency can be divided into four phases: depletion, deficiency (marginal), dysfunction, and clinical disease.

Depletion is a relative term describing the failure of the diet to maintain the trace element status of the body. and it may continue for weeks or months without observable clinical effects when substantial body reserves exist.

deficiency, which is marked by biochemical indications that the homeostatic mechanisms are no longer maintaining a constant level of trace elements necessary for normal physiological function.

dysfunction. There may be a further lag period, the subclinical phase, before the changes in cellular function are manifested as clinical disease.

clinical disease The biochemical criteria can be divided, according to the phase during which they change, into indicators of marginal deficiency and dysfunction. The rate of onset of clinical disease will depend on the intensity of the dietary deficiency, the duration of the deficit and the size of the initial reserve. If reserves are non-existent, as with zinc metabolism, the effects may be acute and the separate phases become superimposed.

The definitive etiological diagnosis of a trace element deficiency will depend on the response in growth and health obtained following parenteral treatment or supplementation of the diet. The strategies for preventing trace element deficiencies include regular analysis of the feed and soil .and monitoring samples from herds and flocks to prevent animals from entering the zone of marginal trace element deficiencies.

COBALT DEFICIENCY

Cobalt deficiency is a disease of ruminants ingesting a diet deficient in cobalt, which is required for the synthesis of vitamin B12. The disease is characterized clinically by in appetence and loss of body weight. Some effects on reproductive performance in sheep have been reported.

ETIOLOGY

The disease is caused by a deficiency of cobalt in the diet which results in a deficiency of vitamin B12.

EPIDEMIOLOGY

1-Occurrence

Cobalt deficiency occurs in Australia, New Zealand, the UK, North America, and occurs in many other parts of the world . Cattle are slightly less susceptible than sheep, and lambs and calves are more affected than adults. Although the disease occurs most commonly in ruminants at pasture in severely deficient areas, sporadic cases occur in marginal areas, especially after long periods of stable feeding. Bulls, rams, and calves are the groups most commonly affected, dairy cows kept under the same conditions may develop a high incidence of ketosis.

2-Risk factors

Dietary and pastures containing less than 0.07 and 0.04 mg/kg DM result in clinical disease in sheep and cattle, respectively. Variations in the cobalt content of pasture occur with seasonal variations in pasture growth and with drainage conditions. The increased incidence of the disease, which has been observed in the spring, may be related by rapidly growing grasses of the pasture, which have a lower cobalt content than legumes.

Primary cobalt deficiency occurs only on soils which are deficient in cobalt.

PATHOGENESIS

Cobalt is unique as an essential trace element in ruminant nutrition because it is stored in the body in limited amounts only and not in all tissues. In the adult ruminant, its only known function is in the rumen and it must, therefore, be present continuously in the feed.

The effect of cobalt in the rumen is to participate in the production of vitamin B12 (cyanocobalamin), and compared with other species the requirement for vitamin B12 is very much higher in ruminants.

The essential defect in cobalt deficiency in ruminants is an inability to metabolize propionic acid. A key biochemical pathway for propionic acid from rumen fermentation. The clinical and pathological signs of cobalt deprivation are preceded by characteristic biochemical changes in tissues and fluids of the body.

As soon as depletion begins, the concentration of cobalt and vitamin B12 fall in rumen fluid and serum .

hypothesis suggests that the high level of fructan may initiate hepatic lipodystrophy, leading to hepatic insufficiency, growth reduction and ovine white liver disease .

The pathological changes in lambs grazing cobalt- deficient pastures are related to blood concentrations of vitamin B12, methylmalonic acid, and homocysteine, and lesions are confined mainly to the liver and brain Hepatic encephalopathy associated with cobalt deficiency and white liver disease has been described in lambs.

CLINICAL FIN DINGS

1 -No specific signs are characteristic of cobalt deficiency.

2 -A gradual decrease in appetite.

3 - Loss of body weight, emaciation, and weakness, and these are often observed in the presence of abundant green feed.

4 -Pica is likely to occur, especially in cattle.

5 -There is marked pallor of the mucous membranes and affected animals are easily fatigued.

6 -Growth, lactation, and wool production are severely retarded, and the wool may be tender or broken.

7- In sheep, severe lacrimation with profuse outpouring of fluid sufficient to mat the wool of the face is one of the most important signs in advanced cases.

8 -Signs usually become apparent when animals have been on affected areas for about 6 months and death occurs in 3-12 months after the first appearance of illness, although severe wasting may be precipitated by the stress of parturition or abortion.
9 -Cobalt deficiency in pregnant ewes can result in decreased lambing percentage, increased percentage of stillbirths.

CLIN ICAL PATH OLOGY
1-Serum and hepatic cobalt and vitamin B12 concentrations
2-Hematology
Affected animals are anemic, but their hemoglobin and erythrocyte levels are often within the normal range because of an accompanying hemoconcentration. The anemia is normocytic and normochromic.
There is also a decrease in cellularity of the bone marrow in cobalt-deficient sheep. It is not repaired by the administration of vitamin B12 or by the parenteral administration of cobalt.

Differentiated diagnosis
Cobalt deficiency must be differentiated
from other causes of 'ill-thrift'
1 –Copper deficiency
2 -Internal parasitism
Careful necropsy or fecal examination will determine the degree of helminthes Infestation.
3-Johne's disease In sheep.
4-General nutrition deficiency(protein and energy)

TREATMENT
Cobalt and vitamin B12 affected animals respond satisfactorily to oral dosing with cobalt or the IM injection of vitamin B12.
1- Oral dosing with cobalt sulfate 1 mg cobalt/d in sheep and can be given in accumulated doses at the end of each week. Intervals of 2 weeks between dosing are inadequate for the best possible response.
2- Monthly dosing of lambs with oral doses of 300 mg cobalt is sufficient greatly to reduce deaths and permit some growth at suboptimal levels.
3- injection of 1 mg provides protection to lambs for 14 weeks.

Cobalt toxicity
Overdosing with cobalt compounds is led to toxic signs of loss of weight, rough hair coat, listlessness, anorexia, and muscular incoordination appear in calves at dose rates of about 40-45 mg of elemental cobalt per 50 kg BW/d.
Sheep appear to be much more resistant to the toxic effects of cobalt than are cattle.

Control Dietary supplementation with cobalt.

IODINE DEFICIENCY

Iodine deficiency may be due to deficient iodine intake or secondarily conditioned by a high intake of calcium, diets consisting largely of Brassica spp., or gross bacterial pollution of feed stuffs or drinking water. A continued intake of a low level of cyanogenetic glycosides, e.g. in white clover, is commonly associated with a high incidence of goitrous offspring. The most common cause of iodine deficiency in farm animals is the failure to provide iodine in the diet.

PATHOGENESIS

Iodine deficiency results in a decreased production of thyroxine and stimulation of the secretion of thyrotropic hormone by the pituitary gland. This commonly results in hyperplasia of thyroid tissue and a considerable enlargement of the gland. Most cases of goiter of the newborn are of this type. The primary deficiency of thyroxine is responsible for the severe weakness and hair abnormality of the affected animals. Although the defect is described as hairlessness, it is truly hypoplasia of the hairs, with many very slender hairs present and a concurrent absence and diminution size of hair follicles.

A hyperplastic goiter is highly vascular and the gland can be felt to pulsate with the arterial pulse and a loud murmur may be audible over the gland. Colloid goiter is less common in animals and probably represents an involutional stage after primary hyperplasia.

Other factors, particularly the ingestion of low levels of cyanide, exert their effects by inhibiting the metabolic activity of the thyroid epithelium and restricting the uptake of iodine. Thiocyanates and sulfocyanates are formed during the process of detoxication of cyanide in the liver and these substances have a pronounced depressing effect on iodine uptake by the thyroid

Some pasture and fodder plants, including white clover, rape and kale, are known to have a moderate content of cyanogenetic glucosides. These goitrogenic substances may appear in the milk and provide a toxic hazard to both animals and man. The inherited form in cattle is due to the increased activity of an enzyme that deiodinates iodotyrosines so rapidly that the formation of thyroxine is inhibited.

Iodine is an essential element for normal fetal brain and physical development in sheep. A severe iodine deficiency in pregnant ewes causes reduction in fetal brain and body weight from 70 days of gestation to parturition. The effects are mediated by a combination of maternal and fetal hypothyroidism, the effect of maternal hypothyroidism being earlier than the onset of fetal thyroid secretion There is also evidence of fetal hypothyroidisms, and absence of wool growth and delayed skeletal maturation near parturition.

CLINICAL FINDINGS

loss of condition, decreased milk production, and weakness might be anticipated, these signs are not usually observed in adults. Loss of libido in the bull, failure to express estrus in the cow, and a high incidence of aborted, stillborn or weak calves have been suggested as manifestations of hypothyroidism in cattle, whereas prolonged gestation is reported in mares, ewes, and cows. A high incidence of stillbirths and weak, newborn animals is the most common manifestation of iodine deficiency.

Partial or complete alopecia and palpable enlargement of the thyroid gland are other signs that occur with varying frequency in the different species

Affected foals have a normal hair coat and little thyroid enlargement, but are very weak at birth

In most cases, they are unable to stand without support and many are too weak to suck. Excessive flexion of the lower forelegs and extension of lower parts of the hindlegs has also been observed in affected foals.

Defective ossification has also been reported, the manifestation is collapse of the central and third tarsal bones leading to lameness and deformity of the hock.

In cattle, the incidence of thyroid enlargement in adults is much lower than in horses and the cardinal manifestations are gross enlargement of the thyroid gland and weakness in newborn calves.

Adult sheep in iodine-deficient areas may show a high incidence of thyroid enlargement . Newborn lambs manifest weakness, extensive alopecia, and palpable, if not visible, enlargement of the thyroid glands.

Goats present a similar clinical picture, except that all abnormalities are more severe than in lambs. The degree of alopecia varies from complete absence of hair, through very fine hair, to hair that is almost normal. Auscultation and palpation of the jugular may reveal the presence of a murmur and thrill, the 'thyroid thrill', due to the increased arterial blood supply of the glands

the primary clinical signs of iodine deficiency in goats is birth of dead , weak , or premature kids with a scant haircoat and goiter is typical of dietary iodine deficiency

CLINICAL PATHOLOGY

Several criteria have been used for the laboratory diagnosis of iodine deficiency in sheep.

They include thyroid weight, lamb thyroid to body weight ratio, comparisonof serum T4 (serum thyroxine) concentrations in lamb and dam (T4 concentrations are lower in the lamb than in the dam when iodine deficiency is present, serum T4 concentrations

in the ewe and pasture iodine concentrations Estimations of iodine levels in the blood and milk are reliable indicators of the thyroxine status of the animal. Organic or protein -bound iodine is estimated in serum or plasma and used as an index of circulating thyroid hormone, provided access to exogenous iodine in the diet, or as treatment, is adequately controlled.

There may be between-breed differences in blood iodine levels but levels of 2.4-14 µg of protein-bound iodine per 100 mL of plasma appear to be in the normal range. In ewes, an iodine concentration in milk of below 8 µg /L indicates a state of iodine deficiency. milk iodine content should be greater than 300 µg /L.

Differential diagnosis list

• Weak calf syndrome

• Abortion

• Congenital defects.

• Hypothyroidism

TREATMENT

Treatment of neonates with obvious clinical evidence of iodine deficiency is usually not undertaken because of the high case fatality rate. When outbreaks of iodine deficiency occur in neonates, the emphasis is usually on providing additional iodine to the pregnant dams.

The recommendations for control can be adapted to the treatment of affected animals.

CONTROL

The recommended dietary intake of iodine for cattle is 0.8-1 .0 mg/kg DM of feed for lactating and pregnant cows, and 0.1-0.3 mg/kg DM of feed for no pregnant cows and calves.

ZINC DEFICIENCY (PARAKERATOSIS

ETIOLOGY

Pigs

A zinc deficiency in young, growing pigs can cause parakeratosis. the etiology of parakeratosis in swine is that an excess of dietary calcium (0.5-1 .5%) can favor the

development of the disease, and the addition of zinc to such diets at levels much higher (0.02% zinc carbonate.

Ruminants

A primary zinc deficiency due to low dietary zinc in ruminants is rare but does occur. Many factors influence the availability of zinc from soils, including the degree of compaction of the soil, and the nitrogen and phosphorus concentration. The risk of zinc deficiency increases the soil pH rises above 6.5 and as fertilizatio with nitrogen and phosphorus increases.

A secondary zinc deficiency include the consumption of Immature grass, which affects digestibility, the feeding of late-cut hay, which may be poorly digestible, and the presence of excessive dietary sulfur.

PAT HOGENESIS

Zinc is a component of the enzyme carbonic anhydrase, which is located in the red blood cells and parietal cells of the stomach, and is related to the transport of respiratory carbon dioxide and the secretion of hydrochloric acid by the gastric mucosa.

Zinc is also associated with RNA function and related to insulin, glucagon, and other hormones.

It also has a role in keratinization, calcification, wound healing, and somatic and sexual development.

Because it has a critical role in nucleic acid and protein metabolism a deficiency may adversely affect the cell mediated immune system.

A zinc deficiency results in a decreased feed intake in all species, and is probably the reason for the depression of growth rate in growing animals and body weight in mature animals.

Failure of keratinization resulting in parakeratosis, loss and failure of growth of wool and hair and lesions of the coronary bands probably reflect the importance of zinc in protein synthesis.

There are lesions of the arteriolar walls of the dermis. The bones of zinc- deficient ruminants reveal abnormal mineralization and reduction of zinc concentration in bones.

Retarded testicular development occurs in ram lambs, and complete cessation of spermatogenesis suggests impairment of protein synthesis.

CLINICAL FINDINGS

Ruminants

In the naturally occurring disease in cattle, in severe cases, parakeratosis and alopecia may affect about 40% of the skin area. The lesions are most marked on the muzzle, vulva, anus, tail head, ears, backs of the hindlegs, kneefolds, flank, and neck.

Most animals are below average body condition and are stunted in growth .

Experimentally produced cases exhibit the following signs:

1- Poor growth

2- A stiff gait

3- Swelling of the coronets, hocks, and knees

4- Soft swelling containing fluid on the anterior aspect of the hind fetlocks

5- Alopecia

6- Wrinkling of the skin of the legs, scrotum and on the neck and head, especially around the nostrils.

7- Hemorrhages around the teeth

8- Ulcers on the dental pad.

In goats, hair growth, testicular size, and spermatogenesis are reduced, and growth rate is less than normal. the case fatality rate is high. There is a marked delay in wound healing.

The natural disease in sheep is characterized by loss of wool and the development of thick, wrinkled skin. Wool-eating also occurs in sheep and may be one of the earliest signs noticed in lambs after being on a zinc- deficient diet for 4 weeks. Induced cases in lambs have exhibited reduced growth rate, salivation, swollen hocks, wrinkled skin and open skin lesions around the hoof and eyes.

On severely deficient experimental diets, other clinical signs in young rams are:

-Drooling copious amounts of saliva when ruminating

- Parakeratosis around eyes, on nose, feet, and scrotum

- Shedding of the hooves

- Dystrophy and shedding of wool, which showed severe staining

- Development of a pungent odor.

In naturally occurrin g cases in rams the animals stood with their backs arched and feet close together.

CLINICAL PATHOLOGY

Skin scraping Laboratory examination of skin scrapings negative results, but skin biopsy will confirm the diagnosis of parakeratosis. Zinc in serum and hair Serum zinc levels may have good diagnostic value.

NECROPSY FINDINGS

Necropsy examinations are not usually performed, but histological examination of skin biopsy sections reveals a marked increase in thickness of all the elements of the epidermis.

DIFFERENTIA DIAGNOSIS

1-Sarcoptic mange may resemble parakeratosis, but is accompanied by much itching and rubbing. The parasites may be found in skin scrapings. Treatment with appropriate parasiticides relieves the condition.

2-Exudative epidermitis is quite similar in appearance, but occurs chiefly in unweaned pigs. The lesions have a greasy character that is quite different from the dry, crumbly lesions of Para keratosis. The mortality rate is higher.

3- photosensitization , vitamin A deficiency

TREATMENT

In outbreaks of parakeratosis in swine, zinc should be added to diet immediately at the rate of 50 mg/kg DM (200 mg of zinc sulfate or carbonate per kg of feed). The calcium level of the diet should be maintained at between 0.65 and 0.75 % .

The injection of zinc at a rate of 2-4 mg/kg BW daily for 10 days is also effective. Zinc oxide suspended in olive oil and given 1M at a dose of 200 mg of zinc for adult sheep and 50 mg of zinc for lambs will result in a clinical cure within 2 months. The oral administration of zinc at the rate of 250 mg zinc sulfate daily for 4 weeks resulted in a clinical cure of zinc deficiency , in goats in 12-14 weeks.

SELENIUM AND OR VITAMIN E DEFICIENCIES

the synonym (nutritional muscular dystrophy , white muscle disease)

Etiology

It is a non inflammatory degenerative disease of skeletal and cardiac muscles. The selenium- and vitamin E-responsive or deficiency diseases of farm animals are caused

by diets deficient in selenium and/or vitamin E, with or without the presence of conditioning factors such as an excessive quantity of polyunsaturated fatty acids in the diet,unaccustomed exercise and rapid growth in young animal.

Biological functions of selenium and vitamin E

Glutathione peroxidases and tissue peroxidation Selenium is biochemical component of the enzyme glutathione peroxidase (GSH-PX). The activity of the enzyme in erythrocytes is positively related to the blood concentration of selenium in cattle, sheep, horses, and pigs and is a useful for the diagnosis of selenium deficiency and to determine the selenium status of the tissues of these animals. Selenium is also a component of thyroid gland hormones.

Plasma GSH-PX protects cellular membranes and lipid- containing organelles from peroxidative damage by inhibition and destruction of endogenous peroxides, acting in conjunction with vitamin E to maintain integrity of these membranes.

Selenium also facilitates significant changes in the metabolism of many drugs .

For example.

selenium functions to counteract the toxicity of several metals such as arsenic, cadmium, mercury, copper, silver, and lead.

The Selenium important in, phagocytosis, all the immune response and are important mediators of immune and reproductive function.

Vitamin E

Vitamin E is an antioxidant that prevents oxidative damage to sensitive membrane lipids by decreasing hydroperoxide formation.

The vitamin has a central role in protection of cellular membranes from lipoperoxidation, especially membranes rich in unsaturated lipids, such as mitochondria, endoplasmic reticulum, and plasma membranes. Interrelationships between selenium and vitamin E An important interrelationship exists between selenium, vitamin E and the sulfur-containing amino acids in preventing some of the nutritional diseases caused by their deficiency.

EPIDEMIOLOGY

Enzootic nutritional muscular dystrophy (NMD)

Occurrence

This muscular dystrophy occurs in all farm animal species, but most commonly in young, rapidly growing calves, lambs, goat kids, and foals born from dams that have been fed for long periods, usually during the winter months, on diets low in selenium

and vitamin E It is an important cause of mortality in goat kids from birth to about 3 months of age. The disease is not well recognized in adult horses, but sporadic cases of dystrophic myodegeneration are recorded in horses from 5 to 10 years of age.

The disease also occurs in grain-fed yearling cattle Outbreaks of severe and fatal NMD have occurred in heifers, at the time of parturition so that selenium deficiency may have a role in retained placenta , mastitis and other diseases, which were previously on a diet deficient in both selenium and vitamin E. Myopathy and hepatic lipidosis in weaned lambs deficient in vitamin E without concurrent selenium deficiency has been described. In foals commonly signs associated with nutritional muscular dystrophy: stiffness and muscular weakness, dysphagia and myalgia, depression and anorexia without evidence of infectious disease, and poor suckle reflex.

There are two major syndromes of myopathy:

1- An acute form: myocardial dystrophy, which occurs most commonly in young calves and lambs and occasionally foals

2- A sub acute form: skeletal muscular dystrophy, which occurs in older calves and yearling cattle.

PATHOGENESIS

The antioxidant roles of selenium and vitamin E. Dietary selenium, sulfur containing amino acids and vitamin E act synergistically to protect tissues from oxidative damage which is selenium-dependent, functions by detoxifying lipid peroxides and reducing them to non- toxic hydroxy fatty acids.Vitamin E prevents fatty acid hydroperoxide formation. vitamin E protects cellular membranes from lipoperoxidation, especially membranes rich in unsaturated lipids, such as mitochondric, endoplasmic reticulum and plasma membranes.Diets low in selenium and/or vitamin E do not provide sufficient protection against the 'physiological' lipoperoxidation that occurs normally at the cellular level.selenium has a sparing effect on vitamin E and is an efficient prophylactic against muscular dystrophy of calves and lambs at pasture, but does not prevent muscular dystrophyin calves fed on a diet containing cod liver oil.

Nutritional muscular dystrophy:-

Diets deficient in selenium and/or vitamin E permit widespread tissue lipoperoxidation leading to hyaline degeneration and calcification of muscle fibers. Unaccustomed exercise can accelerate the oxidative process and precipitate clinical disease. Muscle degeneration led to the release of enzymes, such as lactate dehydrogenase and creatine phosphokinase, the last of which is of importance in diagnosis. Degeneration of skeletal muscle is rapidly and successively followed by invasion of phagocytes and regeneration. In calves, lambs, and foals, the major muscles involved are skeletal, myocardial and diaphragmatic.

The myocardial and diaphragmatic forms of the disease occur most commonly in young calves, lambs, and foals, resulting in acute heart failure, respiratory distress, and rapid death.

The skeletal form of the disease occurs more commonly in older calves, yearling cattle, and older foals and results in weakness and recumbence, is usually less severe and responds to treatment. Acute NMD results in the liberation of myoglobin into the blood, which results in myoglobin urea.

CLINICAL FINDINGS

Acute enzootic muscular dystrophy:-

1 - Affected animals may collapse and die suddenly after exercise without any other premonitory signs.

2 - The excitement associated with the hand-feeding of dairy calves may precipitate peracute death.

3 – In calves under close observation, a sudden onset of dullness and severe respiratory distress, accompanied by a frothy or bloodstained nasal discharge, may be observed in some cases.

4 - Affected calves, lambs, and foals are usually in lateral recumb ency and may be unable to sternal recumbency .

5 - The heart rate is usually increased up to 200/min and often with arrhythmia, the respiratory rate is increased up to 60-72/min and loud breath sounds are audible. The temperature is usually normal or slightly elevated.

6 - Affected animals commonly die 6-12 h after the onset of signs in spite of therapy.

7 -Outbreaks of the disease occur in calves and lambs in which up to 15 % of susceptible animals . may develop the acute form and the case fatality approaches 100%.

Subacute enzootic muscular dystrophy:-

1- The most common form in rapidly growing calves, 'white muscle disease' and in nursing lambs from birth to 4 weeks of age, 'stiff-lamb disease'.

2- Affected animals may be found in sternal recumbence and unable to stand ,If they are standing, the obvious signs are stiffness, trembling of the limbs, weakness.

3-The gait in calves is accompanied by rotating movements of the hocks and in lambs a stiff, goosestepping gait.

4- Muscle tremor is evident if the animal is forced to stand for more than a few minutes.

5-On palpation the dorsolumbar, gluteal and shoulder muscle masses may be symmetrically enlarged and firmer than normal.

6- Most affected animals retain their appetite and will suck if held up to the dam or eat if hand-fed.

7- Major involvement of the diaphragm and intercostal muscles causes dyspnea with labored and abdominal-type respiration.

8-The temperature in the normal range but there may be a transient fever (41°C, 105°F) due to the effects of myoglobinemia and pain. The heart rate may be elevated .

9- Following treatment, affected animals usually respond in a few days and within3-5 days they are able to stand and walk unassisted.

10-In some cases, the upper borders of the scapulae protrude above the vertebral column and are widely separated from the thorax. This has been called the'flying scapula' .

11- the toes are spread and there is relaxation of carpal and metacarpal joints or knuckling at the fetlocks and standing on tip-toe, inability to raise the head, difficulty in swallowing inability to use the tongue and relaxation of abdominal muscles.

12- Choking may occur when the animals attempt to drink.

13-Clinical signs occur within 1 week and consist of stiffness, recumbency, myoglobinuria, hyperpnea, and dyspnea. Severe cases may die within a few days and some are found dead without premonitory signs.

Subcapsular liver rupture in lambs

has been associated with vitamin E deficiency in lambs usually under 4 weeks of age , Affected lambs collapse suddenly, become limp, and die within a few minutes or several hours after the onset of weakness.

Clinical pathology Increased plasma levels of creatine kinase, serum aspartate transaminase activity. Low blood (serum) levels of selenium and vitamin E. serum glutathione peroxidase activity.

Not :the serum alkalin phosphatase activity is laboratory test is not very helpful in diagnosis of white muscle disease (nutritional myodegeneration) of calves because does not indicate muscle damage

Necropsy findings Bilaterally symmetrical pale skeletal muscle, pale streaks in myocardial muscle. Hyaline degeneration of affected muscle. Diagnostic confirmation

Low selenium and vitamin E in diet and tissues, increased creatine kinase and muscle degeneration.

Differential diagnosis list

Acute muscular dystrophy in calves and yearlings:

• Haemophilus somnus septicemia

• Pneumonia.

Subacute enzootic muscular dystrophy:

• Musculoskeletal diseases

polyarthritis, traumatic or infectious myopathies (blackleg), osteodystrophy,

and fractures of long bones

Diseases of the nervous system:

spinal cord compression, Haemophilus somnus meningoencephalitis and myelitis, organophosphatic insecticide poisoning

Diseases of the digestive tract:

carbohydrate engorgement resulting in lactic acidosis, shock, dehydration and weakness.

• Muscular dystrophy in lambs and

kids: Enzootic ataxia and swayback

Treatment Vitamin E selenium parenterally. it is recommended that a combined mixture of selenium and IX-tocopherol be used in treatment.

Nutritional muscular dystrophy

For treatment of NMD in calves, lambs, and foals a mixture containing 3 mg selenium (as sodium or potassium selenite) and 150 IU/mL of DL-IX-tocopherol acetate, given 1M at 2 mLl45 kg BW is recommended. One treatment is usually sufficient.

Animals with severe myocardial involvement will usually not respond to treatment and the case mortality rate is about 9 0 % .

Control Selenium and vitamin E supplementation of diet, strategic oral and/or parenteral vitamin E and selenium to pregnant dams or young animals on pasture.

COPPER DEFICIENCY:

- ETIOLOGY

Copper deficiency may be primary , when the intake in the diet is inadequate, or secondary (conditioned) when the dietary intake is sufficient but the utilization of the copper by tissues is impeded.

- Primary copper deficiency:

The amount of copper in the diet may be inadequate when the forage is grown on deficient soils or on soils in which the copper is unavailable.

Secondary copper deficiency:

In secondary copper deficiency, the amount of copper in the diet is adequate, but conditioning dietary factors interfere with the utilization of the copper.

A high molybdenum intake can induce copper deficiency even when the copper content of the pasture is quite high and a higher copper intake can overcome the effect of the molybdenum , also Zinc, iron, lead, calcium carbonate and Dietary inorganic sulfate are also conditioning factors. the administration of selenium to sheep on copper-deficient pastures increases copper absorption and improves the growth rate of lambs. The use of zinc sulfate for the control of facial eczema may cause a depression of plasma copper.

Risk factors :

Several factors influence the plasma and tissue concentrations of copper , particularly in ruminants, including :

1- Age of animal 2- Demands of pregnancy and lactation

3- Stage of growth,4- Mineral composition of feed

5- Season of the year,6- Soil characteristics and its mineral composition

7- Breed of animal ,8- Concentration of minerals, such as sulfur and molybdenum, which can interfere with the availability of copper.

-PATHOGENESIS:

1-Effects on tissues.

The consequences of hypocuprosis include a failure of copper metalloenzymes, many of which form part of the antioxidant defense system such as copper/zinc superoxide dismutase (Cu/Zn SOD) , ceruloplasmin, and cytochrome oxidase activity Copper , as well as other essential trace elements, is an atypical antioxidant because it functions indirectly. Copper is a catalytic cofactor for Cu/Zn SOD and ceruloplasmin. Cu/Zn SOD catalyzes dismutation of the superoxide an ion Copper deficiency can affect the antioxidant defense system resulting in oxidative damage to cellular components. The activity of Cu/Zn SOD and glutathione peroxidase is decreased in animals with copper deficiency.

2-Chromosomal abnormalities

The association between copper deficiency and DNA damage in cattle has been examined copper deficiency in cattle is associated with an increase in the frequency of chromosomal aberrations as well as in DNA migration.

3-Wool

The straightness and stringiness of this wool is due to inadequate keratinization ، probably due to imperfect oxidation of free thiol groups. Provision of copper to such sheep is followed by oxidation of these free thiol groups and a return to normal keratinization within a few hours.

4-Body weight:

In the later stages of copper deficiency ، the impairment of tissue oxidation causes interference with intermediary metabolism and loss of condition or failure to grow .

5-Diarrhea:

The pathogenesis of copper deficiency in causing diarrhea is uncertain and there is little evidence that a naturally-occurring primary copper deficiency will cause diarrhea. There are no histological changes in gut mucosa, although villous atrophy is recorded in severe, experimentally produced cases. Diarrhea is usually only a major clinical finding in secondary copper
deficiency associated with molybdenosis.

6-Anemia

The known importance of copper in the formation of hemoglobin accounts for the anemia in copper deficiency. The presence of hemosiderin deposits in tissues of copper-deficient animals suggests that copper is necessary for the reutilization of iron liberated from the normal break down of hemoglobin. There is no evidence of excessive hemolysis in copper-deficiency states. Anemia may occur in the later stages of primary copper deficiency, but is not remarkable in the secondary form.

7-Bone

The osteoporosis that occurs in some natural cases of copper deficiency is caused by the depression of osteoplastic activity, Copper deficiency in foals causes severe degenerative disease of cartilage characterized by breaking of articular and growth plate cartilage.

8- Connective tissue

Copper is a component of the enzyme lysyl oxidase, secreted by the cells involved in the synthesis of the elastin component of connective tissues and has important functions in maintaining the integrity of tissues such as capillary beds, ligaments ،and tendons.

9-Heart

The myocardial degeneration of falling disease may be a terminal manifestation of anemic anoxia, or be due to interference with tissue oxidation.

10-Blood vessels.

Experimentally produced copper deficiency has also caused sudden death due to rupture of the heart and great vessels in a high proportion of pigs fed a copper deficient diet.

11. Pancreas:

Lesions of the pancreas may be present in normal cattle with a low blood copper status. The lesions consist of an increase in dry matter content and a reduction in the concentrations of protein and copper in wet tissue.

12-Nervous tissue

Copper deficiency halts the formation of myelin and causes demyelination in lambs ،probably by a specific relationship between copper and myelin sheaths.

13-Immune system:

Copper is an essential trace mineral with an import ant role in the immune response but the precise mechanism is not well understood. Copper deficiency results in decreased humoral and cell-mediated immunity, as well as decreased non-specific immunity regulated by phagocytic cells, such as macrophages and neutrophil, The decreased resistance to infection in sheep is responsible for treatment with copper and genetic selection.

- Copper -molybdenum-sulfate relationship:

The interaction between copper , molybdenum, and sulfur in ruminant nutrition is unique in its effects on health and production. Copper, molybdenum, and sulfur from organic or inorganic sources can combine in the rumen to form an un absorbable triple complex, copper tetrathiomolybdate and deplete the host tissues of copper. It is proposed that thiomolybdates form in the rumen from the reaction of dietary molybdenum compounds with sulfides produced from the reduction of dietary sulfur compounds by rumen bacteria. The thiomolybdates reduce the absorption of dietary copper from the intestine and also inhibit a number of copper-containing enzymes, including ceruloplasmin, cytochrome oxidase and superoxide dismutase.

Copper utilization :

Sulfate and molybdate can interfere with mobilization of copper from the liver ، inhibition of copper intake by the tissues ، inhibition of copper transport both into and out of the liver and inhibition of the synthesis of copper-storage complexes.

Hepatic storage: -

The copper status of the liver depends on whether the animals are receiving adequate dietary copper. With adequate dietary levels, the liver copper levels are less in the presence of molybdate and sulfate.

CLINICAL FINDINGS: -

The general effects of copper deficiency are the same in sheep and cattle,

General syndrome:

- Primary copper deficiency :

Primary copper deficiency causes un thriftiness, loss of milk production, and anemia in adult cattle. The coat color is affected red and black cattle changing to a bleached rusty red and the coat itself becomes rough and staring calves grow poorly and there is an increased tendency for bones to fracture, particularly the limb bones and the scapula. Ataxia may occur after exercise, with a sudden loss

of control of the hind limbs and the animal falling or assuming a sitting posture. Itching and hair-licking are also recorded as manifestations of copper deficiency in cattle Although diarrhea may occur, persistent diarrhea is not characteristic of primary copper deficiency and its occurrence should arouse suspicion of molybdenosis or helminthiasis.

Secondary copper deficiency This syndrome includes the signs of primary copper deficiency, except that anemia occurs less commonly, probably due to the relatively better copper status in the secondary state, anemia being largely aterminal sign in primary copper deficiency.

-Falling disease

The characteristic behavior in falling disease is for cows in apparently good health to throw up their heads, bellow, and fall Death is instantaneous in most cases, but some fall for a few minutes with intermittent bellowing and running movement attempts to rise. Rare cases show signs for up to 24 h or more. These animals periodically lower their heads and pivot on the front legs Sudden death usually occurs during one of these episodes .

- Peat scours ('teart)

Persistent diarrhea with the passage of watery , yellow-green to black feces with an inoffensive odor occurs soon after the cattle go on to affected pasture, in some cases within 8-10 days. The feces are released without effort, often without lifting the tail. Severe debilitation is common' although the appetite remains good, slight anemia. The hair coat is rough and Apoor, thin haircoat with hair depigmentation is manifested by reddening or gray flecking especially around the eyes, in black cattle.

- Unthriftiness (pine) of calves :

The earliest signs are a stiffness of gait and unthriftiness. The epiphyses of the distal ends of the metacarpus and metatarsus may be enlarged and resemble the epiphysitis of rapidly growing calves deficient in calcium and phosphorus vitamin D

- Swayback and enzootic ataxia in lambs and goat kids:

These diseases have much in common Swayback is the only authentic manifestation of a primary nutritional deficiency of copper . The incidence can vary greatly among breeds of sheep reflecting the genetic differences in copper metabolism both between and within breeds of sheep. Enzootic ataxia affects only unweaned lambs and young kids. In severe outbreaks, the lambs may be affected at birth, but most cases occur in the 1-2-month age group The first sign to appear in enzootic ataxia is incoordination of the hind limbs, appearing when the lambs are driven. Respiratory and cardiac rates are also greatly accelerated by exertion. As the disease progresses, the incoordination becomes more severe and may be apparent after walking only a few yards. There is excessive flexion of joints, knuckling over of the fetlocks, wobbling of the hind quarters and finally falling.

Necropsy findings

Anemia, emaciation, hemosiderosis, osteodystrophy, demyelination in enzootic ataxia, myocardiopathy.

Diagnostic confirmation

Low serum and hepatic copper and response to treatment.

Differential diagnosis list

Copper deficiency must be differentiated from herd problems associated with the following clinical findings:

- Unthriftiness due to intestinal parasitism
- Malnutrition due to energy-protein deficiency
- Lameness caused by osteodystrophy due to calcium, phosphorus, and vitamin D imbalance
- Anemia
- Neonatal ataxia in lambs (congenital swayback and enzootic ataxia) from border disease; cerebellar hypoplasia (daft lamb disease); hypothermia; meningitis
- Sudden death due to other causes .

Treatment Copper sulfate orally; copper glycinate parenterally.

Control Provide source of copper by oral dosing or dietary supplementation in feed or on pasture. Parenteral administration of copper at strategic times. Copper oxide needles orally for prolonged effectiveness. Genetic selection. Removal of sulfates from water supply.

animals with copper toxicity should be treated with 50 to 100 mg ammonium molybdare and 0.5 to 0.10 g sodium sulfate daily.