

Review On Copper Deficiency In Domestic Ruminants

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Summary: The purpose of this review is to give an overview on the general conditions of copper deficiency and to highlight its preventive strategies. Copper deficiency is either a complete lack of the element in the diet or its presence in a very low amount in the animal tissue. Copper deficiency manifests itself in young ruminants as a herd problem of unthriftiness, progressive loss of weight, changes in hair coat color or texture of wool, neonatal ataxia in lambs and kids, chronic lameness, and terminal anemia. The problem occurs worldwide including the east African countries as a primary or secondary deficiency associated with environmental and animal factors. Although heavy mortalities occur in affected areas, the major loss is due to failure of animals to thrive. Copper deficiency develops annually in about 0.9% of the cattle population in the United Kingdom. Enzootic ataxia may affect up to 90% of a lamb flock in a badly affected area and most lambs die of inanition. In falling disease, up to 40% of cattle in affected herd may die. The problem can be prevented by several methods of copper supplementation, including feeding salt with 0.5-2.0% additional copper as copper sulfate, injecting a commercial preparation of copper, dosing with gelatin capsules containing copper wires, adding copper tablets to water and fertilizing pastures with copper.

Keywords: copper, deficiency, enzootic ataxia/swayback, ruminant

INTRODUCTION

Copper deficiency is an endemic disease of ruminants worldwide, which causes a problem of economic importance in Australia, New Zealand, and the United States. It causes, licking sickness, or liksucht of cattle in Holland, and falling disease of cattle in Australia.^[17] Enzootic ataxia or sway back of newborn domestic ruminants and particularly of small ruminants is a widespread disease often observed in East African countries.^[6] In animals, copper deficiency is mainly a disease of ruminants, which can be either primary or secondary. Primary deficiency occurs in areas with copper deficient soils resulting in forage or grass deficient in copper. Secondary deficiency in ruminants is generally caused by antagonists present in forage that reduce Cu absorption. It is well documented that high dietary concentrations of Mo, S and Fe reduce Cu status in ruminants. Although, studying the role of Cu in immune responses and disease resistance is made complex because of the numerous interactions that occur between Cu and other minerals, in several immune studies Cu deficiency was induced by feeding high concentrations of Mo or Fe.^[24] Historically, copper deficiency has been associated with several syndromes or abnormalities and clinical signs of deficiency can present as a large array of adverse effects. Reduced growth rates, decreased feed conversion, lameness, poor immune function, sudden death, achromotrichia, and impaired reproductive function are commonly encountered with copper deficiency. Copper deficiency is uncommon in sheep and goats. They are more efficient at absorbing Cu from the diet than other ruminants such as cattle. Each ruminant species seem to have subtle variations in the ability to absorb adequate (or excess) Cu from dietary sources. There also exist some wide variations among animals of the same species, breed, or herd. Intestinal parasites have a marked effect on Cu metabolism

in small ruminants. Therefore, in making a diagnosis of Cu deficiency in these species, someone should be certain that, they are relatively free of parasites for a period before sampling to determine Cu status. Before measures can be undertaken to correct primary or secondary copper deficiencies, it is necessary to assess the mineral status of forages and of the grazing animals as well as their production responses to mineral supplementation.^[14] Mineral status of grazing animals in Ethiopia and other African countries has received very little attention. This may be due partly to the fact that the methodology of mineral nutrition studies, especially of trace elements, is rather complicated and signs of marginal mineral deficiencies are not easily detected but frequently it is mistakenly assumed that the grazing animal will obtain its mineral needs from the pasture. Mineral deficiencies, even if marginal, can result in depression of animal performance. Sub clinical mineral deficiencies are often widespread and are responsible for unestimated, but probably great, economic losses in livestock production. An earlier mineral study in Ethiopia indicated probable widespread copper and zinc deficiencies, and although much more information on the supplies of essential minerals for livestock is required, it is very likely that mineral deficiencies contribute to the poor performance of livestock in Ethiopia.^[13] Therefore, the objective of this review is to give an overview on the general condition of copper deficiency in domestic ruminants and to highlight its prevention and control strategies for recommendation.

ETIOLOGY

The etiology of copper deficiency in grazing ruminants has been clarified by a number of recent discoveries and included the low availability of copper in lush grazed pasture compared with conserved forage, the inhibitory effects on

absorption of small increases in herbage molybdenum and sulfur, the antagonism from iron ingested in soil; and the wide genetic variation in copper absorption between different breeds of sheep.^[25] Copper deficiency occurs when the diet contains an abnormally low amount of copper (primary copper deficiency) or when copper absorption or metabolism is adversely affected (secondary copper deficiency). If inadequate amounts of copper are available to tissues in the form of essential metalloenzymes, the signs of copper deficiency may occur. Primary copper deficiency can occur in milk fed animals or pastured animals in copper deficient areas.^[23] Secondary copper deficiency occurs in the face of apparently adequate dietary levels with a variety of conditioning factors such as high dietary levels of molybdenum, sulfates, zinc, iron, or other compounds. The most common conditioning factor is a dietary excess of molybdenum. In certain instances, ruminants with excess dietary sulphur in the presence of low molybdenum intake will also have reduced copper absorption.^{[14], [10]} The cause of copper deficiency in clinical cases is often multifactorial and can be difficult to quantify as unknown factors may also cause clinical expression of copper deficiency in ruminants to be manifested as a variety of syndromes.^[14] Under normal circumstances only about five percent of the copper present in the diet is absorbed through the lining of the gut in to the blood stream. If high level of molybdenum or sulphur are present this poor rate of absorption is roughly halved again.^[12]

EPIDEMIOLOGY

Occurrence

Copper deficiency is endemic in ruminants worldwide and causes a disease of economic importance that may be severe enough to render large areas of otherwise fertile land unsuitable for grazing by ruminants of all ages, but primarily young, growing ruminants. It is also estimated that characteristic clinical signs of Copper deficiency develop annually in about 0.9% of the cattle population in the United Kingdom.^[19] In some surveys, the lowest level of serum copper was in heifers being reared as heifer replacements. Although heavy mortalities occur in affected areas, the major loss is due to failure of animals to thrive. Enzootic ataxia may affect up to 90% of a lamb flock in a badly affected area and most of these lambs die of inanition. In falling disease, up to 40% of cattle in affected herd may die.^[8]

Geographical Distribution

Primary copper deficiency: The disease caused by a Primary deficiency of copper in ruminants are enzootic ataxia of sheep in Australia, New Zealand, and the United States, licking sickness, or liksucht of cattle in Holland, and falling disease of cattle in Australia.^[17] Enzootic ataxia of newborn domestic ruminants and particularly of small ruminants is a widespread disease often observed in East Africa. It is characterized by very low blood copper levels and sometimes by histological lesions characteristic of a severe copper deficiency. This disease observed and described by various authors in Kenya, Ethiopia and Djibouti seems to be closely associated with the pedogeological area of the Rift Valley. Climatic conditions and geomorphological characteristics of this area, particularly the molybdenum and sulphur excess in this volcanic region,

seem to account for the marked clinical signs of this mineral deficiency.^[6]

Secondary copper deficiency: The disease caused by secondary copper deficiency due to high dietary intake of molybdenum and sulphates are listed in table (1).

Table 1: Secondary copper deficiency associated disease in different countries of the world.

Disease	Country	Species affected	Copper level in liver	Probable conditioning factors
Swayback	Britain, United states	Sheep	low	Unknown
Renguerra	Peru	Sheep	Low	Unknown
Peat	Britain	Sheep and Cattle	Unknown	molybdenum
Scouring disease	Holland	cattle	Unknown	Unknown
Peat scours	New Zealand	Cattle	Low	molybdenum
Peat scours	Britain	Cattle	Unknown, low level in blood	Unknown
Peat scours	Canada	Cattle	Unknown	molybdenum
Salt sick	United states(Florida)	Cattle	Unknown	Unknown
'pine'(unthrift)	Scotland	Calves	Low	Unknown

Source:^[17]

The syndromes characterised by diarrhoea or unthriftiness, 'yellow calf,' of nursing calves, occurs on Hawaii's rangeland where copper content of forages range from 2.6 to 11.8 mg/kg and the molybdenum less than 1 to 39 mg/kg. Swayback of lamb in the United Kingdom has been classed as secondary copper deficiency but no conditioning factors have been determined. While swayback is a naturally occurring disease caused by a primary deficiency of copper, identical lesions occur experimentally by feeding molybdenum and sulphate to the ewes. There is some evidence that heavy lime dressing of a pasture may predispose to a sway back. A wasting disease similar to peat scours and preventable by the administration of copper and, unthriftiness ('pine') of calves occur in the United Kingdom but in both instances, the copper and molybdenum intakes are normal.^[17]

PREDISPOSING FACTORS

Season of the year and Soil characteristics

Both primary and secondary copper deficiency occur most commonly in spring and summer coinciding with the lowest level of copper in pasture. Large monthly variations occur in the serum level of copper in both beef and dairy cattle, and are commonly correlated with the rainfall; the high the rain fall, the lower the copper level.^[5] Problems usually occur after summer when rains produce rapid growth in the pasture. Rapidly growing plants contain low levels of copper.

Deficiencies can also develop in animals grazing pastures with adequate copper levels if there are high levels of certain other trace elements. For example, the molybdenum content may be highest in the autumn when rains stimulate a heavy growth of legume.^[7] The level of copper is generally low in areas of high rainfall and leached soils, and often in peat soils and those derived from granite. Where soil copper is less than 2.2 ppm there is a risk of copper deficiency in livestock. In general, there are two types of soils on which copper deficient plants are produced. Sand soils, poor in organic matter and heavily weathered, such as occur on the coastal plains of Australia, and in marine and river silts, are likely to be deficient in copper as well as other trace mineral element, especially cobalt. The second groups of soils are 'peat' or muck soils more commonly associated with important copper deficiency in United States, New Zealand, and Europe. Such soils may have an absolute deficiency of copper, but more commonly the deficiency is relative in that copper is not available and the plants grown on the soils do not contain adequate amount of the element. The cause of the lack of availability of the copper is uncertain, but is probably the formation of insoluble organic copper complexes. An additional factor is the production of secondary copper deficiency on these soils due to their high content of molybdenum.^[3]

Pregnancy and Lactation

Chronic copper deficiency in pregnant ewes and does may produce a metabolic disorder in their lambs and kids called enzootic ataxia. In goats, this deficiency also causes sway back in the fetuses. This deficiency results in hind limb ataxia and apparent blindness in lambs up to about 3 months of age. Based on liver copper, diets containing copper of 4.4 or 4.6 mg/kg DM, did not meet the requirement of either Angus heifers or Simmental heifers during gestation and lactation and growth period.^[9] During gestation the copper concentration increases progressively in the ovine and bovine fetal liver and decreases in the maternal liver. The developing bovine fetus obtain its copper by placental transfer and at birth the liver concentration is high and decline postnatally to adult levels within the first few months. Placental transfer is less efficient in sheep, and lambs are commonly born with low liver reserves, making the neonatal lambs susceptible to copper deficiency. In copper deficient cattle the accumulation of liver copper in the fetus continues independently of the dam's liver copper until the fetus is about 180 days, then a gradual decline in the fetal liver copper occurs. The liver copper concentration in fetuses from dams on a copper adequate diet continue to increase and decline at 180 days of gestation. All of this indicates an increase in copper requirement by the dam during pregnancy. Colostrum is rich in copper, allowing the newborn with its preferential ability to absorb copper to increase hepatic stores. Later the copper content of milk declines rapidly so that it is usually insufficient to meet the requirement of the suckling neonates for copper.^[18]

Age, Breed, and Species of the Animal

Calves on dam fed on deficient diets may show signs at 2-3 months of age. As a rule the sign are sever in calves and yearling, less sever in 2 year olds, and of minor degree in adults. Enzootic ataxia is primarily a disease of suckling lambs whose dams receive insufficient dietary copper. Ewes with a normal copper status take some time to loss their

hepatic reserve of copper after transfer to copper deficient pasture and do not produce affected lambs for the first 6 months. The occurrence of the disease in sucklings, and its failure to appear after weaning, points to the importance of fetal store of copper and the inadequacy of milk as a source of copper – when it is the sole source of nourishment.^[17] There are marked genetic differences in copper metabolism between breeds of sheep. The Welsh Mountain ewe can absorb copper 50% more efficiently than the Scottish black face and the Texel cross black face 145% more efficiently than pure black face lambs. The susceptibility to, or protection from the effects of copper deficiency and copper poisoning, is influenced from birth by genetic effects. These affect copper status of the lamb at birth, through the maternal environment controlled by the dam's own genes. Later in life, the animals own genes become the predominant influence determining of its copper status on any given nutritional regimen. These genetic differences have physiological consequences reflected in differences in the incidence of sway back, both between and within breeds and in effects on growth and on reproduction. The differences observed are due to genetic differences in the efficiency of absorption of dietary copper. Breeds show wide variation in their susceptibility to sway back ; the incidence of sway back may vary from 0-40% between breeds within one flock, and the incidence according to breed type is closely related to the differences in the concentration of copper in the liver than in blood. There are significant differences in the copper requirements and tolerance between goats and sheep.^[17]

Presence (interference) of other Substances

Number of factors influences the copper absorption; conditions like gastric acidity, the base content of diet and intestinal secretions have an influence on copper absorption. Addition of large amount of calcium carbonate and ferrous sulphide to the diet markedly reduce the assimilation of copper by reducing the solubility of copper and formation of insoluble copper sulfide respectively. Under the influence of high molybdenum and sulphate intake, copper utilization is affected. Absorption of copper is lowered and excretion of copper from the body is increased.^[19]

Availability of Copper in the diet

Foodstuff vary considerably in the amount of copper they contain and, more importantly, on its availability to the animal once eaten. Fresh grass, especially lush, well fertilized swards low in copper and rich in protein (and therefore also rich in sulphur) often has much less available copper than conserved fodder. It is also thought that molybdenum has less of antagonistic effect on copper availability in hay than in fresh grass.^[12]

ECONOMIC IMPORTANCE

Production and Productivity

Reproductive failure is commonly observed in mammals fed Cu-deficient diets. The anemia, hemorrhages, and mortality of embryos are probably caused by defects in red blood cells and connective tissue formation during early embryonic development. Growth is severely affected by copper deficiency. The copper containing metalloenzyme cytochrome C oxidase is the terminal oxidase in the electron transport chain and important in energy production by

mitochondria. Copper deficiency also results in anemia which may affect growth by limiting oxygen transport. Cattle deficient in the element can suffer significant production losses.^[1]

Morbidity and Mortality

It is estimated that characteristic clinical signs of Copper deficiency develop annually in about 0.9% of the cattle population in the United Kingdom. In some surveys, the lowest level of serum copper was in heifers being reared as heifer replacements. Although heavy mortalities occur in affected areas, the major loss is due to failure of animals to thrive. Enzootic ataxia may affect up to 90% of a lamb flock in a badly affected area and most of these lambs die of inanition. In falling disease, up to 40% of cattle in affected herd may die.^[17]

PATHGENESIS

Decreased copper absorption: a variety of conditions can decrease copper absorption from the gastrointestinal tract (large intestine in sheep and small intestine in cattle). Excess dietary molybdenum can lead to the formation of sparingly soluble cupric molybdates in the rumen that are not absorbed from the intestine. The addition of excess sulfur or sulfates in the diet and/or water can result in the formation of insoluble copper thiomolybdates in the rumen. It is important to note that at low sulfur concentrations in the diet excess molybdenum has a minimum effect on decreasing copper absorption. Excessive calcium in the diet, particularly in the form of limestone, decreases copper absorption. Overgrazing, with the subsequent ingestion of excess soil also decreases copper absorption. The precise pathophysiology of most of the copper deficiency syndromes is not known. However, the central role of copper in preventing cellular oxidative damage and its role in iron and sulfur metabolism are probably important.^[14]

Osteoporosis: the osteoporosis that occurs in some natural cases of copper deficiency is caused by the depression of osteoblastic activity. There is a marked overgrowth of cartilage, especially at costochondral junctions and in metatarsal bones. There is also an impairment of collagen formation. When the copper deficiency is secondary to dietary excess of molybdenum and sulfate, the skeletal lesions are quiet different and characterized by widening of the growth palate and metaphysis and osteoblastic activity.^[18]

Infertility: the infertility seen with secondary copper deficiency may be due to excess circulating oxythiomolybdates which interfere with the release of luteinizing hormone.^[14]

Diarrhea: the pathogenesis of copper deficiency in causing diarrhea is uncertain and there is little evidence that a naturally occurring copper deficiency will cause diarrhea. There are no histological changes in gut mucosa, although villous atrophy is recorded in sever, experimentally produced cases. Diarrhea is a major clinical finding in secondary copper deficiency associated with molybdenosis.^[18]

Myocardial degeneration of falling disease may be a terminal manifestation of anemic anoxia, or be due to

interference with tissue oxidation. In this disease, it is thought that the stress of calving and lactation contribute to the development of heart block and ventricular fibrillation when there has already been considerable decrease in cardiac reserve.^[18]

Anemia: the known importance of copper in the formation of hemoglobin accounts for the anemia in copper deficient animals. The presence of hemosidrin deposits in tissue of copper deficient animals suggests that copper is necessary for the reutilization of iron liberated from the normal breakdown 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 unless there is a marginal copper deficiency, such as occurs in peat scours in New Zealand. The usual relationship in New Zealand between copper deficiency and postpartum hemoglobinuria is unexplained.^[18]

CLINICAL SIGNS

Ruminants grazing in copper deficient country do not receive all the copper they require. Initially signs are not obvious, as the animals draw on their liver reserves. When liver supplies are exhausted, - signs may become obvious.^[7] The clinical findings which are common in young ruminants include a herd problem of unthriftiness and progressive loss of weight, changes in hair coat color or texture of wool, neonatal ataxia in lambs and kids, chronic lameness and terminal anemia.^[18]

In Cattle

Typical deficiency symptoms include: rough, discolored hair coats, winter coats that are slow to shed, decreased conception rates, increased days open, hoof problems, depressed immunity, anemia, reduced growth rate and, in some cases diarrhea and a loss of pigment from the colored hair especially around the eyes giving the animal a bespectacled appearance. This does not show up in cattle with white hair around the eyes.^[15]



Figure 1: An example of a calf displaying a rough, discolored hair coat typical of copper deficiency
Source:^[15]

In Sheep

The most obvious sign of copper deficiency is swayback in young lambs. Congenital swayback is characterized by stillbirth and the birth of small and weak lambs, which may show fine tremors of the head. Less severely affected lambs

are bright, incoordination with characteristic weakness of hind limbs, which results in swaying or stumbling gait. The lambs are often fine banded and dull coated. A delayed form of the disease is occasionally seen in older lambs, sometimes initiated by gathering and handling.^[20]

Loss of pigmentation in black-woolled sheep: as there is usually a wide variation in susceptibility to copper deficiency between individuals within any flock, normal pigmentation in one or two marker black sheep does not guarantee copper sufficiency among the white-woolled individuals. Other conditions can occasionally cause loss of pigmentation. Secondary crimping and steeliness of wool are also poor guides to copper deficiency because they are not solely caused by lack of copper and experts cannot consistently differentiate between steely and doggy wool. Copper deficiency is rarely the cause of the poorly crimped wool often seen in Western Australia.^[11] The other clinical sign associated with copper deficiency in sheep are osteoporosis and bone fractures in young lambs and lambs may be more susceptible to neonatal diseases than copper sufficient lambs, but ill thrift is not a consistent feature of copper deficiency in sheep.^[20]



Figure 2: Paralysis of hind causes the typical swayback symptom in lamb
Source^[21]

In Goats

Uncoordinated movement in the newborn ruminant has been recognized and given local names such as “swayback”, and “lamcruis”. Loss of muscular coordination leading to uncoordinated movements, paresis of the hind legs, impossibility to suckle, spasmodic contraction, generalized tremor and convulsions are observed clinical signs. Examination of body temperature showed decrease of this parameter in kid goats with clinical manifestation. The clinical symptoms of hypothermia, tachycardia and increase in respiratory rate in kid goats with enzootic ataxia were observed. The hypothermia could have occurred because of morphological changes in brain substance thus giving rise to thermoregulatory mechanism disturbance. The increase in respiratory rate and tachycardia are compensation of registered decrease of haemoglobin levels and erythropenia in kid goats with enzootic ataxia.^[16]



Figure 3: Paralysis of hind quarter causes the typical swayback symptom in goat kids
Source^[21]

CLINICAL PATHOLOGY AND PHASES OF DEFICIENCY

The development of a deficiency can be divided into four phases. These are depletion, deficiency (marginal), dysfunction and disease. During the depletion phase, there is loss of copper from any storage site, such as liver, but the plasma concentration of copper may remain constant. With continued dietary deficiency, the concentration of copper in the blood decline during the phase of marginal deficiency. However, it may be some time before the concentrations or activities of copper containing enzymes in the tissue begin to decline and it is not until this happen the phase of dysfunction is reached. There may be a further lag before the changes in cellular function are manifested as clinical disease.^[18] The laboratory evaluation of copper status of farm animals is difficult because the biochemical values are often difficult to interpret and correlate with the clinical state of the animal. This is particularly true when only an individual animal is being evaluated. The evaluation of the copper status of herd or flock is usually easier. For many years the laboratory diagnosis of copper deficiency in cattle and sheep centered on the determination of serum or plasma copper and liver copper.^[4]

Hepatic and Serum or Plasma Copper Level

The primary site of copper reserves is the liver. Normal liver copper concentrations in cattle are approximately 60 to 120 µg/g (ppm) and in sheep 80 to 200 µg/g on a dry weight basis. Hepatic copper concentrations as high as 250 µg/g are not unusual in ruminants fed supplements (the concentration may exceed 350µg/g in sheep). Blood copper concentrations can be maintained near normal until hepatic copper concentration falls to bellow 35 ppm, at which time the serum copper concentration invariably begins to decline.^[22] The tissues of young animals (neonates) contain variable amounts of copper compared to adults of the same species. In sheep, serum and liver copper concentrations are the same for lambs (1 week of age) and adults. The plasma copper levels in lambs are low at birth, but rise to adult values by 1 to 7 days of age. Plasma copper levels in the bovine neonate are lower than in mature cattle. In the bovine neonate, hepatic copper concentration changes little from birth to maturity; however, copper distribution in the liver is quite variable in the neonate. Because of these differences, interpretation of neonatal serum copper concentrations is difficult.^[14]

Ceruloplasmin

The difficulty of interpreting plasma levels of copper led to the estimation of plasma levels of copper protein complexes, especially Ceruloplasmin. Ceruloplasmin contains greater than 95 % of the circulating copper in normal animals. There is a high significant correlation between plasma copper level and plasma ceruloplasmin activity, which is a less complicated and more rapid procedure than plasma copper. The regression analysis indicates a strongly positive correlation coefficient of ceruloplasmin with serum of cattle and sheep of 0.83 and 0.92, respectively. The correlation between serum ceruloplasmin activity and hepatic copper concentrations in cattle was only 0.35, indicating an unreliable relationship. Normal plasma ceruloplasmin in sheep is in the range of 45-100 mg/l. Normal levels of serum ceruloplasmin activity in cattle range from 120 to 200mg/l. The mean copper and ceruloplasmin levels are higher in plasma than serum; the percentage of copper associated with ceruloplasmin is less in serum (55%) than in plasma (66%). In experimental copper deficiency in calves, rapid decrease occur in plasma ceruloplasmin activity at least 80 days before overt clinical sign of deficiency.^[17]

Erythrocytedismutase activity

The measurement of the activity of Erythrocyte super oxide dismutase (ESOD), a copper containing enzyme is now being evaluated as a procedure for the diagnosis of copper deficiency. The activity of this enzyme decreases more slowly than plasma or liver copper in copper deficient animals and may be more correlated with the presence of imminence of hypocuprosis. In marginal deficiency ESOD value ranges from 2 to 5 μ /mg hemoglobin, and in functional deficiency the value is below 2.^[18]

NECROPSY FINDINGS

The characteristic gross findings in copper deficiency of ruminants are those of anemia and emaciation. Hair and wool abnormalities may be present. Extensive deposition of hemosidrin can cause darkening of the liver, spleen and kidney in most cases of primary copper deficiency, and in the secondary form of the copper status is sufficiently low. In lambs, there may be osteoporosis and long bone fractures. Osteoporosis is less evident in cattle but can be confirmed radiographically and histologically. In naturally occurring secondary copper deficiency in cattle, associated with high dietary molybdenum and sulfate, there is widening of the growth palate due to abnormal mineralization of the primary spongiosa, resulting in a grossly rachitic appearance to the bones.^[17] In swayback, the prominent lesion is absence or destruction of the white matter of the cerebral hemispheres. The changes in the white matter occur as small foci of gelatinous softening, or cavitations and collapse of the cerebral hemispheres. The large motor neurons of the red and vestibular nuclei are commonly rounded and swollen and usually show chromatolytic changes. In addition, demyelination in the motor tracts (ventral and dorsal portions of the ventrolateral column) of the white matter of the spinal cord has been reported. In a few extreme cases, and in most cases of swayback, the myelin loss also involves the cerebrum, where there is destruction and cavitations of the white matter. There is a marked internal hydrocephalus in such cases and the convulsions of the cerebrum are almost obliterated. Acute cerebral edema with marked brain swelling are cerebral herniation, reminiscent of

polioencephalomalacia, may also accompany the more typical myelopathy and multimodal cerebral leukomalacia in lambs with hypocuprosis. The most significant finding in enzootic ataxia is the degeneration of axon and myelin within the cerebellar motor tracts in the spinal cord, a change only evident at the microscopic level. Chromatolysis of neurons in a variety of locations within the central nervous system is usually detectable. In enzootic ataxia, lesions are limited to the large neurons of the brainstem and spinal cord. However, many goats with enzootic ataxia also have well defined lesions in the cerebellum, including patchy cerebellar hyperplasia, necrosis and loss of Purkinje cells and depletion of the granule cell layer.^[2] In falling disease, the heart is flabby and pale. There is generalized venous congestion and the blood may appear watery. The liver and spleen are enlarged and dark. Histological examination reveals atrophy of the cardiac muscle fibers and considerable cardiac fibrosis. Deposits of hemosidrin are present in the liver, spleen and kidney. Necropsy examination should include assay of copper in viscera. The level of copper in liver are usually low, in secondary copper deficiency there may be a high level of copper in the kidney, and high level of molybdenum in the liver kidney and spleen.^[18]

DIAGNOSIS

Diagnosis of copper deficiency should be based on clinical signs, history, blood serum copper levels, and liver copper levels. Forage analysis for copper, molybdenum, iron and sulfate and water analysis for sulfate also help diagnose and plan supplementation. The liver is the best measure of current copper status, except in the fetus or newborn. The fetus stores copper in its liver at the expense of the dam. In late pregnancy, it is normal for the cow's serum and liver copper levels to decline drastically. Blood serum is a more reliable and consistent measure of copper status than is whole blood. But neither reflects dietary intake unless the liver is severely depleted of its copper stores. Low serum copper indicates that almost all of the liver copper storage has been used. When the serum copper reaches normal levels, the only way to determine copper reserve status is by liver biopsy.^[1]

Visual indicators

Swayback in lambs and falling disease in cows can be diagnosed with a high degree of certainty. While depigmentation of the hair around the eyes in cattle and of black wool in sheep indicates copper deficiency is likely, it is not certain as similar symptoms occasionally result from other causes. Use as many other indicators as possible to make sure of your diagnosis.^[11]

Laboratory tests

Blood samples and Hepatic copper evaluation: When using blood samples for copper determination, serum or plasma is normally preferred. Plasma copper concentration is usually about 5% greater than an identical serum copper concentration. Normal serum copper is 0.7 to 1.2 ppm (μ g/ml). Serum or plasma copper concentrations of 0.4 ppm or less are considered as evidence of frank deficiency. Values of 0.4 to 0.7 ppm are marginal and are difficult to interpret. Hepatic copper concentration is the preferred diagnostic sample and is easily secured at necropsy. Hepatic copper values less than 35 ppm DMB are considered

deficient. However, surgical biopsy is necessary for live patients, and, since laboratories generally require 1 g or more of tissue, a biopsy instrument with an internal diameter of 3 to 5 mm is necessary.^[14] Guides for interpreting laboratory results are included in Table (2)

Table 2: Tissue Copper Concentrations

Clinical Signs	Serum Copper (ppm)	Liver Copper (wet weight, ppm)
Deficient	0.2–0.4	0.5–10.0
Marginal	0.4–0.7	5–25
Normal	0.7–1.1	25–550
Toxic	> 1.2	250–800

Source:^[11]

Brain and spinal specimen: In the case of swayback in lambs and kids, specimen of brain and spinal cord should also be examined.^[7]

Pasture analyses: Pasture analyses for copper and molybdenum concentrations provide only a rough guide to the copper status of sheep and cattle grazing them. Pastures with less than 2.5-ppm copper are sometimes deficient for sheep and cattle. Above 4-ppm copper, they are not deficient, provided molybdenum levels are less than 1.5 ppm (normal for Western Australian agricultural areas). The likelihood of copper deficiency can be assessed using levels of copper, molybdenum and sulphur in plants. Pasture with copper levels between 3 ppm and 4 ppm have seldom caused copper deficiency in stock in Western Australia. However, with higher pasture molybdenum and sulphur levels the copper concentration needed to give an adequate supply to sheep and cattle rises.^[11] Copper level in forage samples conducted during USDA forage audit 1991 is shown in table (3).

Table 3: Copper levels in forage samples

Percent of forage samples	copper level
49.7%	marginal
14.3 %	deficient
36.0%	adequate

Source^[15]

Almost 64% of all forage samples ranged from marginal to severely deficient in copper.

Dosed versus not dosed comparisons: In the absence of clear-cut clinical symptoms, the most convincing evidence of a copper deficiency is a response to treatment with copper. That is, treating some animals then comparing them with the other untreated animals from the same flock or herd. Both groups must be run together under identical conditions. A minimum of 25, with preferably more animals in each group, is usually needed to detect small but economically important differences in live weight.^[11]

DIFERENTIAL DIAGNOSIS

A combination of serum and liver copper and serum molybdenum, are major diagnostic aids in distinguishing between copper deficiency and the other diseases. Several disease complexes that are herd and flock problems in cattle and sheep may resemble both primary and secondary copper deficiency. The emphasis is on many animals being affected

at about the same time, with a chronic debilitating disease complex, under the same dietary and seasonal circumstances.^[18]

Cattle

Unthriftiness and progressive weight loss may be due to protein-energy malnutrition and examination of the diet will reveal the cause. Changes in hair-coat color, in young growing cattle are caused only by copper deficiency. Chronic lameness, in young growing cattle may be caused by a calcium, phosphorus and vitamin D imbalances, which is determined by examination of the diet and radiography of long bones. The radiographic changes in cattle with secondary copper deficiency consists of widened irregular epiphseal plate with increased bone density in the metaphysic and metaphyseal lipping. Chronic diarrhea, in young cattle may be due to intestinal parasitism and fecal examination and response to therapy are diagnostic. Diarrhea in a group of adult cattle by on pasture known to high in molybdenum is probably due to secondary copper deficiency and response to therapy are diagnostic. Winter dysentery of cattle, salmonellosis, coccidiosis and mucosal disease are acute diseases characterized by diarrhea but are accompanied by other signs and clinicopathological findings which facilitate their identification. Many poisons particularly, arsenic, lead and salt, causes diarrhea in ruminants but there are usually additional diagnostic signs and evidence of access to the poison. Assay of feed and tissue helps to confirm a diagnosis of poisoning. Falling disease occurs only in adult cattle and must be differentiated from other causes of sudden death.^[18]

Sheep and Goats

Unthriftiness and abnormal wool or hair, as flock or herd problem are characteristics of copper deficiency in sheep and goats which must be differentiated from protein-energy malnutrition, intestinal parasitism cobalt deficiency and external parasites. Lameness in-group of lambs, several weeks of age must be differentiated from nutritional osteodystrophy due to calcium, phosphorus and vitamin D deficiency or imbalances, stiff lamb disease, due to enzootic muscular dystrophy. Neonatal ataxia, caused by congenital sway back and enzootic ataxia in new born lambs and kids due to maternal copper deficiency must be differentiated from border disease of newborn lambs, characterized by an out break of new born lambs with hairy fleece and tremors, cerebellarhypoplasia (daft lamb disease) and hypothermia.^[18]

TREATMENT AND PREVENTION

Treatment of copper-deficient animals is usually possible, and the prognosis is guarded to good, depending on the severity of the lesions. When excess molybdenum, sulfate, and other factors leading to secondary deficiency are present, they can be overcome to some extent by increasing dietary copper or by injecting copper.^[14] Several methods have been used to supplement copper, including feeding salt with 0.5-2.0% additional copper (as copper sulfate), injecting a commercial preparation of copper, dosing with gelatin capsules containing copper wires, adding copper tablets to water, and fertilizing pastures with copper.^[1]

Fertilizers

The residual effectiveness of fertilizer copper is well established. One application of 0.8 to 2.5 kg/ha copper (3.3.

to 10 kg/ha copper sulphate), according to soil type, will supply copper to sheep and cattle for at least 20 years. A second application of 0.5 kg/ ha copper (2 kg/ha copper sulphate) 10 years after the first is probably unnecessary, but may be regarded as good insurance. Where too much molybdenum has been applied, extra copper fertilizer may not be effective in correcting the induced copper deficiency; since it can occur even when soil and plant, copper levels are high.^[11]

Injection

Injectable copper glycinate (30% copper by weight) is given to adult cattle at the rate of 400 mg (120 mg copper) subcutaneously. Calves are given 100 to 200 mg of copper glycinate (30 to 60 mg of copper), depending upon their age. One injection may be effective as a treatment/supplement for up to 4 to 6 months in cases of primary copper deficiency. However, in cases of excess molybdenum, sulfates, and/or sulfur, repeat injections may be necessary. Injections of copper glycinate frequently result in large swellings, granulomas, or abscesses and may be cosmetic considerations for some cattle. The reactions can be minimized by using sterile technique and using the subcutaneous tissue of the brisket as the injection site.^[14]

Licks, drenches, and drinking water

Copper sulphate can be supplied through licks and drinking water, but the dose rates cannot be controlled. Some animals can get too much and risk toxicity while others, especially with licks, may get too little. Drenches only have a brief effect and are not recommended for the treatment of copper deficiencies. Sheep are highly susceptible to copper toxicity and care should be taken whenever supplementing livestock.^[11]

Administration via the Pasture

The most important goal of copper supplementation is to provide adequate dietary amounts without over supplementing or risking toxicity.^[14] Although it is common to find that veterinarians favour only the 'direct' administration of copper to the animal, it is evident that under 'normal' conditions, grazing animals obtain all the copper they need from the pastures and fodder crops they consume. In view of this, as well as the cost and trauma of most forms of copper treatment, it is natural to feel that more consideration should be given to managing pastures in such a way to produce fodders that have adequate copper and which are not at the same time, enriched with any copper antagonists. Administration of copper via the pasture would be most sensible when the pasture itself is also likely to respond to the copper but it would be inadvisable where high Mo or S levels in the pasture are responsible for inducing copper deficiency or under extensive pastoral regimes where the treatment cost would be prohibitive.^[21]

Copper oxide needles

Another method of copper supplementation involves the oral administration of copper oxide needles (fine rods, 1 to 10 mm long) placed in gelatin capsules, which dissolve in the reticulo-rumen and liberate the CuO wires. These wires reside in the reticulum and abomasum and slowly release copper for absorption. These boluses are currently available in the U.S. (Copasure) and contain either 25 g or 12.5 g per bolus. The usual recommended dosage is 25 g per animal

500 pounds or greater. One 12.5 g bolus is recommended for calves and the usual dose is 2 to 4 g for ewes and does, which is an extra label recommendation for sheep and goats. The copper oxide needles are thought to provide copper supplementation for 4 to 12 months.^[14]

CONCLUSION AND RECOMMENDATION

Copper deficiency is endemic in ruminants worldwide and causes diseases of economic importance. Copper deficiency observed and described by various authors in domestic ruminants of Kenya, Ethiopia and Djibouti seems to be closely associated with the pedogeological area of the Rift Valley. Climatic conditions and geo-morphological characteristics of this area, particularly the molybdenum and sulphur excess in this volcanic region, seem to account for the marked clinical signs of this mineral deficiency in the region. It is known that many factors can trigger the development of copper deficiency syndromes in the domestic ruminants. These includes interference of other Substances in copper metabolism, Pregnancy and lactation and being reared under hand feed systems in which the animals have got inadequate level of copper in the diet and in the free rang grazing land where the soil is peat or leached, or there is heavy rain fall that facilitate rapid growth of the pasture. It was estimated that there are about 0.9% morbidity in the cattle population of United Kingdom, Enzootic ataxia may affect up to 90% of a lamb flock in a badly affected area, and most of these lambs die of inanition. In falling disease, up to 40% of cattle in affected herd may die. Although heavy mortalities occur in affected areas, the major loss is due to failure of animals to thrive. Copper deficiency in domestic ruminants like all other nutritional deficiency problems, have its own typical feature; that is its rapid response to copper supplementation, which ease the diagnosis of the condition. To prevent the economic loss due to hypocuprosis, early treatment of positive animal is necessary and prevention of the reproductive failure, retarded growth and enzootic ataxia of newborn has to be achieved through proper nutritional programs during gestation. Based on this conclusion the following points are forwarded as recommendation. Since there are no well researched documents on copper deficiency of ruminants in Africa, particularly in Ethiopia, intensive studies should be done to quantify its effect on livestock production and productivity and on the cost benefit of the available treatment and prevention methods.

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