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Diseases and Disorders of Trace Elements Deficiency in Farm Animals: An Illustrated Review

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ABSTRACT

This review was written to emphasize the clinical importance of the trace elements selenium (Se), copper (Cu), cobalt (Co), iodine (I), iron (Fe), zinc (Zn) and manganese (Mn) in farm animals especially camels, cattle, sheep and goats. The deficiency of Se can have major economic effects by lowering fertility, causing placental retentions, and increasing the risk of metritis and mastitis. Se contributes to the development and function of cytotoxic T cells, natural killer cells and helper T cells in the immune system. The Cu is a co-factor in numerous enzymatic processes that include the synthesis of collagen, maturation of red blood cells, the production of energy, the formation of hormones, and the defense against oxidative damage. When excessive amounts are present, it can be extremely risky. The Co is required for the formation of vitamin B_{12} by rumen microorganisms; thus, Vitamin B_{12} insufficiency is the result of Co deficiency. Co deficiency results in anemia that is both normochromic and normocytic, as well as anorexia, loss of body condition, and wasting of muscles. Decreased weight gain, photosensitivity and lacrimation, scaly ears, wool discoloration, cardiovascular diseases, and cerebrocortical necrosis are all indications of Co deficiency. Iodine deficiency is a common cause of disorders ranging from goiter to metabolic and neurological disorders. These disorders may occur from the embryonic stage until adolescence. Iodine deficiency in ruminants causes goiter, particularly in young animals, and consequently lowers the chance that lambs and newborns will survive. Animals may develop an iodine shortage for two reasons: low iodine intake and goiterogenic substance consumption. Fe is essential for several catalytic events, oxidative metabolism, oxygen transport, and cell proliferation. It functions as a cofactor for several proteins and enzymes required for the metabolism of oxygen and energy as well as for many of other vital functions. Zn is regarded to be necessary for the functioning of many proteins, important enzymes, and transcription factors because they bind to Zn. Mn plays a crucial role in the production and activation of several enzymes. It is involved in the metabolism of glucose and lipids, and it accelerates the synthesis of proteins, vitamin C, and vitamin B. Ultimately, even if trace elements are only needed in little quantities, their lack can result in many diseases and disorders in livestock, leading to significant financial losses Therefore, balanced diets are required to prevent such affections in camels, cattle, sheep and goats.

Key words: Animals, Diseases, Pathophysiology, Ruminant, Trace elements.

INTRODUCTION

Major elements principally calcium, phosphorus and magnesium are present in considerable amounts in tissues, very important for the living organism and their deficiency can lead to several life-threatening diseases (Tharwat et al. 2024a,b). However, trace elements, or trace minerals, although also very important, are found in small levels in living tissues. Some of them are known to be nutritionally essential, while others are deemed nonessential despite the fact that the evidence for their necessity is only suggestive or incomplete. The main role of trace elements is as catalysts in enzyme systems; iron (Fe) and copper (Cu), for example, are metallic ions that take part in oxidation - reduction

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reactions in energy metabolism. As a component of myoglobin and hemoglobin, iron is essential for the oxygen-transport process. All trace elements are toxic if consumed in sufficient quantities for extended periods of time. For certain important trace elements, there is a significant difference between toxic intakes and appropriate intakes to meet physiological needs; for other elements, the difference is considerably smaller. Zinc (Zn), Fe, selenium (Se), Cu, fluoride, cobalt (Co), iodine (I), manganese (Mn) and molybdenum are widely recognized as trace elements (National Research Council 1989).

All species require trace elements in small quantities, and they are crucial to many biological processes. Moreover, an overabundance or shortage of these elements can greatly influence metabolism and overall, well-being. The presence of trace minerals plays a role, in the health and productivity of animals influencing physiological functions as well. Their deficiency results in numerous forms of pathogenic issues and metabolic abnormalities, which lowers animal productivity (Abdelrahman et al. 2022). Deficiency of trace elements lead to pica or depraved appetite in farm animals and may lead to decreases in productivity and terminate by death (Tharwat and Al-Hawas 2024; Tharwat et al. 2024c).

Factors like dietary quality, mineral availability and mineral utilization have an impact on both the production and reproductive capacity of male and female ruminant animals. The impact of a particular element on metabolism can be evaluated through the four stages that define the progression of deficiency. The first stage, known as early depletion, is limited to alterations in the element metabolism. The second stage, known as the compensating metabolic phase, is identified by alteration in the element-dependent function. These changes can be compensated by alternative system, unless external stress is occurred. The third stage, metabolic deficiencies, involves alterations in the most important metabolic processes (nucleic acids, proteins, carbohydrates, and fats). The fourth stage, known as clinical deficiency, represents the appearance of clinical symptoms, the progression of the disease, and ultimately, lead to mortality (Mertz 1981).

A variety of proteins and enzymes containing trace minerals, like Zn, Cu, Fe, Mn, Co, I and Se play a role in controlling growth productivity, reproductive functions and overall, well-being, through various physiological processes. Insufficient amounts of these minerals result in a reduction in performance. To address this, dairy animal diets are formulated with trace mineral supplements to prevent these deficiencies, as stated in numerous articles (Chen et al. 2021).

The contribution of trace elements to the antioxidative function is one of their most significant functions. This particular function is most effective under stress (Tomlinson et al. 2008). In a healthy animal, the antioxidant system opposes the harmful impacts of free radicals by producing several molecules that prevent cells and metabolites from damage. Nevertheless, when subjected to prolonged stress, the production of free radicals might surpass the capacity of the antioxidant system to counteract them, resulting in oxidative damage to the lipids, carbohydrates, and proteins present in cells (Miller 1981). Therefore, a lack of minerals may be linked to many situations of stress.

Following, the deficiency of the most important trace elements Se, Cu, Co, I, Fe, Zn, and Mn in camels, cattle, sheep and goats will be discussed in details.

Selenium deficiency

Se is a trace element that has an essential role in the health and performance of animals. Se supplementation acts with vitamin E as an antioxidant agent in the health regulation of transition dairy cattle (Xiao et al. 2021). Its insufficiency can lead to financially significant consequences such as lower fertility, placental retention and an increase of mastitis and metritis incidence (Eulogio et al. 2012). The decrease in embryonic death during the first month of gestation is thought to be the cause of the increased fertility when Se is administered. In the immune system, Se contributes to the development of cytotoxic T cells, helper T cells natural and killer cells (Petrie et al. 1989). Disorders in the prenatal stage caused by a Se deficiency change the quality of milk produced by cows (Horky 2015). Se contributes to the defense against the formation of hydroperoxides which resulting from cellular metabolism (Sordillo 2016). This biological function occurs via selenoproteins, including, iodothyronine deiodinases, glutathione peroxidase (GSH-PX) and thioredoxin reductases, where selenium serves as a structural part (Brigelius-Flohé and Maiorino 2013).

Se is a biological constituent of glutathione peroxidase enzyme (GSH-PX). This enzyme activity in erythrocytes exhibits a positive correlation with the blood concentration of selenium in cattle. This association is important in diagnosing Se deficiency and measuring the Se level. Plasma GSH-PX prevents lipid-containing organelles and cellular membranes from damage caused by oxidation by hindering and annihilating endogenous peroxides. It works in coupling with vitamin E to protect the safety of these membranes. Lipid peroxides and hydrogen peroxide have the ability to induce irreversible denaturation of crucial cellular proteins, resulting in necrosis and degeneration. GSH-PX promotes the collapse of hydrogen peroxide and certain organic hydroperoxides formed by glutathione. The reliance of GSH-PX activity on the existence of Se provides a rationale for the interdependent link of vitamin E, selenium and sulfur-containing amino acids in mammals. Vitamin E functions as an antioxidant by reducing the generation of hydroperoxides, thereby protecting membrane lipids from oxidative damage. Vitamins play a crucial role in protecting cellular membranes against lipoperoxidation, particularly membranes that contain high levels of unsaturated lipids, such as endoplasmic reticulum and mitochondria, plasma membranes (Smith 2015; Constable et al. 2017).

Several diseases in farm animals are linked to Se or vitamin E insufficiency, typically in collection with predisposing factors such unaccustomed exercise, dietary polyunsaturated fatty acids and rapid development in growing animals. Muscular dystrophy and retained fetal membranes are major cattle diseases. They are known as Se/vitamin E-responsive diseases because they can be stopped by feeding enough of both nutrients (Mehdi and Dufrasne 2016). Vitamin E/Se deficiency causes nutritional myopathy, which causes skeletal muscle, heart muscle, and hepatic necrosis (white muscle disease) (Helmer et al. 2021).

It was reported that Se deficiency triggers programmed cell death, inflammatory responses and mitochondrial dynamic imbalance in calf liver (Wang et al. 2022). More recently, Se deficiency was found to induces inflammation, apoptosis, necroptosis, cause oxidative stress and induce pathological lesions in the intestine, lungs, spleen and kidneys of calves and pigs (Li et al. 2020; Lei et al. 2023; Lei et al. 2023; Mu et al. 2023). Se Deficiency was also reported to promote oxidative stress-induced mastitis Pathways in dairy cow (Zhang et al. 2022). Huang et al. (2023) have also found that organic Se is highly effective compared to inorganic Se in upgrading the antioxidant capacity and immune status of beef cattle. It was reported also that Se shortage-induced oxidative stress leads to myocardial injury in neonatal calves by activating apoptosis, inflammation and necroptosis (Lei et al. 2023). In a trial to prevent transition period mastitis, Khan et al. (2024) have found that the bovine immune status and anti-inflammatory antioxidant responses were enhanced with rumen-protected amino acids, vitamins and trace minerals. Moreover, the immunological and nutritional properties of milk/colostrum and the health of the offsprings under heat stress conditions were greatly improved through the injection of antioxidant trace minerals/vitamins into peripartum cows (Yadav et al. 2024).

Etiology and clinical findings

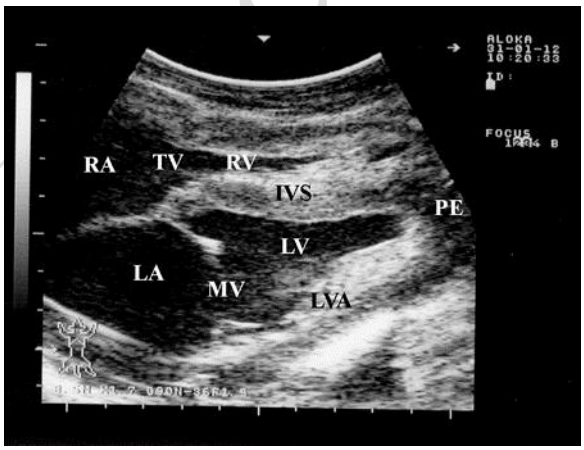
Farm animals with SE- and vitamin E-deficient diets, with or without conditioning factors such as high polyunsaturated fatty acids, develop Se- and vitamin E-responsive diseases (Constable et al. 2017). Acute enzootic muscular dystrophy affects the cardiac muscle muscles of farm animals, while subacute enzootic muscular dystrophy affects the skeletal muscles (Tharwat et al. 2013).

Acute enzootic muscular dystrophy

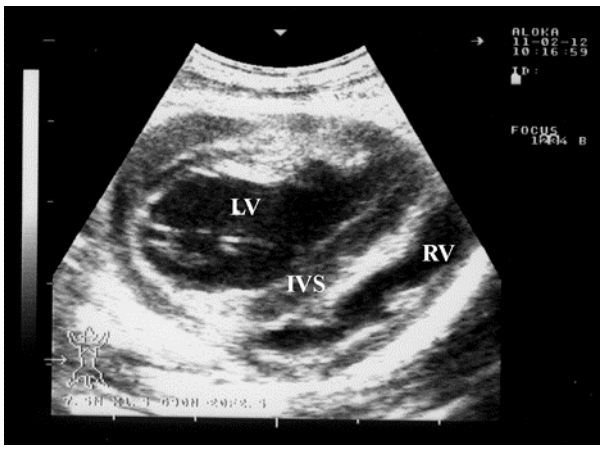
Animals that are affected may have unexpected collapse and death during exercise, without any previous indications (Fig. 1). The excitement linked to the act of hand-feeding dairy calves might potentially lead to sudden and severe mortality. In closely monitored calves, sudden start of drowsiness and intense difficulty in breathing, along with the presence of blood-tinged or frothy nasal discharge, may be seen in certain cases. Calves and lambs that are affected typically lie on their side and may not be able to lie on their chest even with help (Fig. 2). In some times, arrhythmia is observed and the respiration is increased to 60-72/min and raucous breath noises are audible across the lung areas. The temperature tends to be normal or a bit elevated. Despite treatment, affected animals die 6-12 h after symptoms appear. In lambs and calves, up to 15% of highly liable animals can experience the acute form and the morality approaches 100% (Pugh and Baird, 2002). The myocardium is more echogenic on ultrasound (Fig. 3). The acute form of Se/vitamin E deficiency raises serum cardiac troponin I (cTnI) significantly compared to healthy animal (Fig. 4) (Tharwat et al. 2013).

Fig. 1: Five kids with cardiac nutritional muscular dystrophy. Kids on the left were admitted dead while the one on the right was alive.

Fig. 2: Acute enzootic muscular dystrophy in lambs. Affected lambs are admitted in lateral recumbency and unable to assume sternal recumbency even when assisted.



A



B

Fig. 3: Diagnostic ultrasound in acute form of selenium deficient animals. Image A shows increased echogenicity of the myocardium in a camel calf image B shows increased echogenicity of the cardiac muscle in a goat kid. RA = right atrium, TV = tricuspid valve, LA = left atrium, RV = right ventricle, LV = left ventricle, IVS = interventricular septum, MV = mitral valve, PE = pericardial effusion, LVA = left ventricular wall.

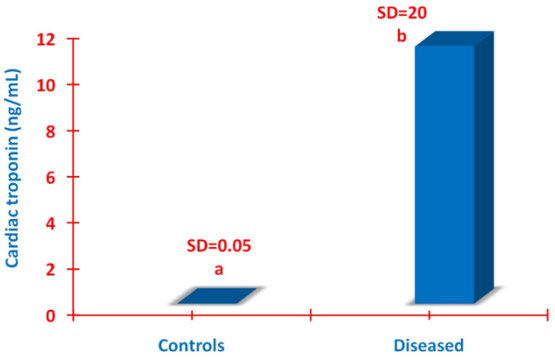


Fig. 4: Comparative (mean±SD) values of cardiac troponin I in goat kids with cardiac nutritional muscular dystrophy compared to healthy controls. [a,b] Different letters indicate a significant difference (P=0.017) (Tharwat et al. 2013).

Fig. 5: Different presentations for selenium/vitamin E deficiency. Image A shows a camel calf with nutritional muscular dystrophy. Image B shows nutritional muscular dystrophy in a 30-day old goat kid. Note the dilated anal opening. Image C shows a lamb with nutritional muscular dystrophy. Image D shows Stiffness in a goat kid with nutritional muscular dystrophy. Image E shows 2 lambs with nutritional muscular dystrophy. Image F shows 2 goat kids with nutritional muscular dystrophy.

Subacute enzootic muscular dystrophy

Rapidly growing calves and young lambs have the most common form, white muscle illness or stiff-lamb disease where affected animals try to stand but are sternal recumbent. Standing animals show stiffness, limb trembling, and in almost cases, disability to stand more than few minutes (Fig. 5). Standing for longer than a few minutes causes muscle tremor. Gluteal, dorsolumbar and shoulder muscles may be symmetrically larger and stiffer on examination. Most damaged animals still eat if hand-fed or suck close to the dam. Dyspnea with abdominal-type breathing results from diaphragm and intercostal muscle

involvement. Usually normal, however myoglobinemia and discomfort can cause a temporary fever (41°C). Heart rate may be high, but rhythmic abnormalities are rare. Following therapy, animals normally recover in 3-5 days and can stand and walk alone. Toes may be spread, carpal and metacarpal joints relaxed, fetlocks knuckled, standing on tiptoe, disability to elevate the head, difficulties swallowing, lake tongue mobility, and abdominal muscle relaxation (Smith and Sherman 2009). Ultrasonography shows an increased echogenicity of the myocardium and of thigh muscle (Fig. 6).

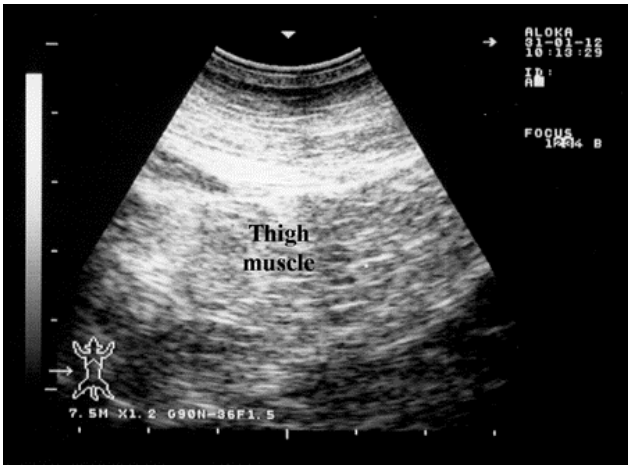


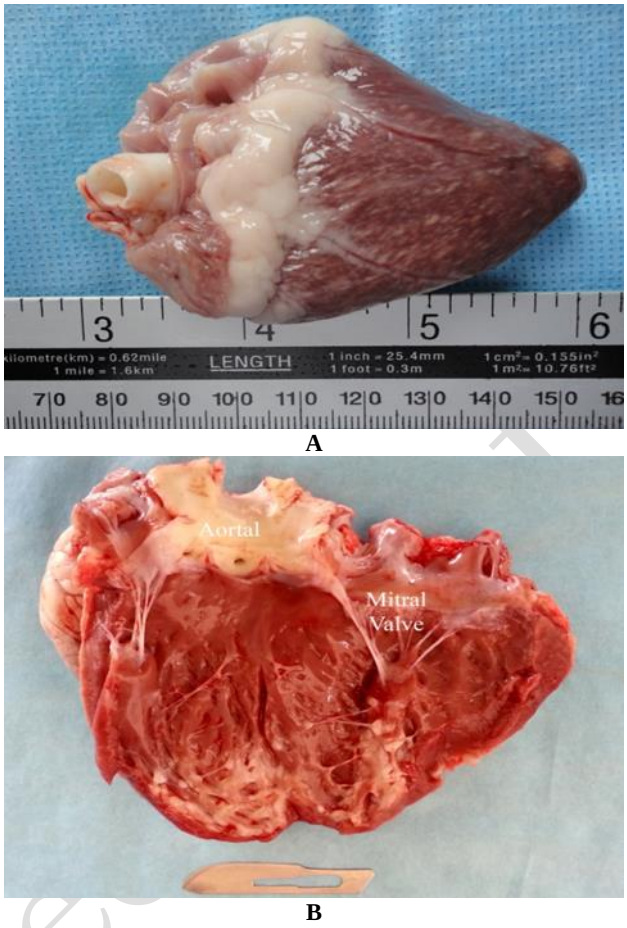
Fig. 6: Ultrasonography in a camel calf with nutritional muscular dystrophy. Image shows increased echogenicity of the thigh muscle.

Necropsy findings

The muscle lesions' physical appearance is consistent. Skeletal muscle groups affected are bilaterally symmetrical and have localized gray or white necrosis and degeneration. These streaks may involve a significant group of muscle fibers that run through the middle of the apparently normal muscle or as a peripheral boundary. Friable and edematous muscle may mineralize (Fig. 7). Lung congestion and edema are prevalent. In calves with myocardial involvement, white deterioration is evident under the left ventricle endocardium. Lesions may affect the papillary muscles and interventricular septum and are gritty like calcification. The diaphragm is radially striated due to broken bundles. Muscle lesions in all species appeared non-inflammatory histologically. Following, coagulation necrosis, hyaline degeneration and different degrees of mineralization are detected (Fig. 8) (Scott 2015).

Treatment

Treatment should include SE and alpha-tocopherol. Alpha-tocopherol is accessible in several pharmacological forms. A mixture of 3mg Se (as sodium or potassium selenite) and 150 IU/mL alpha-tocopherol acetate given IM treats nutritional muscular dystrophy in calves. One treatment typically works. In extensive cardiac involvement, 90% of animals die without therapy. However, all in-contact calves need preventative treatment. Subacute skeletal muscular dystrophy animals may stand and walk unassisted within a week after treatment (Constable et al. 2017).



A

B

Fig. 7: Necropsy finding in kids with cardiac nutritional muscular dystrophy. Degenerative changes on the epicardium (**A**) and under the endocardium (**B**) are detected.

Copper deficiency

Cu is vital for survival and a co-factor in hundreds of enzymatic activities that form red blood cells, energy, hormones, collagen, and defend against oxidative damage. Ensuring Cu adequate supplementation is challenging in ruminants due to the complexity of Cu metabolism in these species (López-Alonso and Miranda 2020). However, excess Cu is harmful, thus biological organisms have developed homeostatic mechanisms to recruit, transport, and eliminate Cu and reduce its harmful impacts (Mercer 2001). Most animals, including humans, have efficient Cu store regulation mechanisms, protecting them against excess dietary Cu (de Romaña et al. 2011).

Unlike other animals, ruminants lack effective Cu regulation systems, and chronic Cu toxicity, notably in sheep, has been reported globally (National Research Council 2005). Due to their adaption to grazing Cu-deficient pastures with antagonistic minerals including sulphur, molybdenum, and Fe, ruminants may be more sensitive to Cu toxicosis (Suttle 2010). Ruminants store excess Cu in the liver via lowering bile Cu excretion because they have poor homeostatic control over Cu absorption. Ruminants do not adjust Cu excretion in the bile and accumulate excessive hepatic Cu when exposed to Cu amounts above physiological needs (National Research Council 2005; Suttle 2012). It was found that blood Cu levels may not confirmatory reflect the actual Cu levels of the herd, and it cannot predict Cu status during

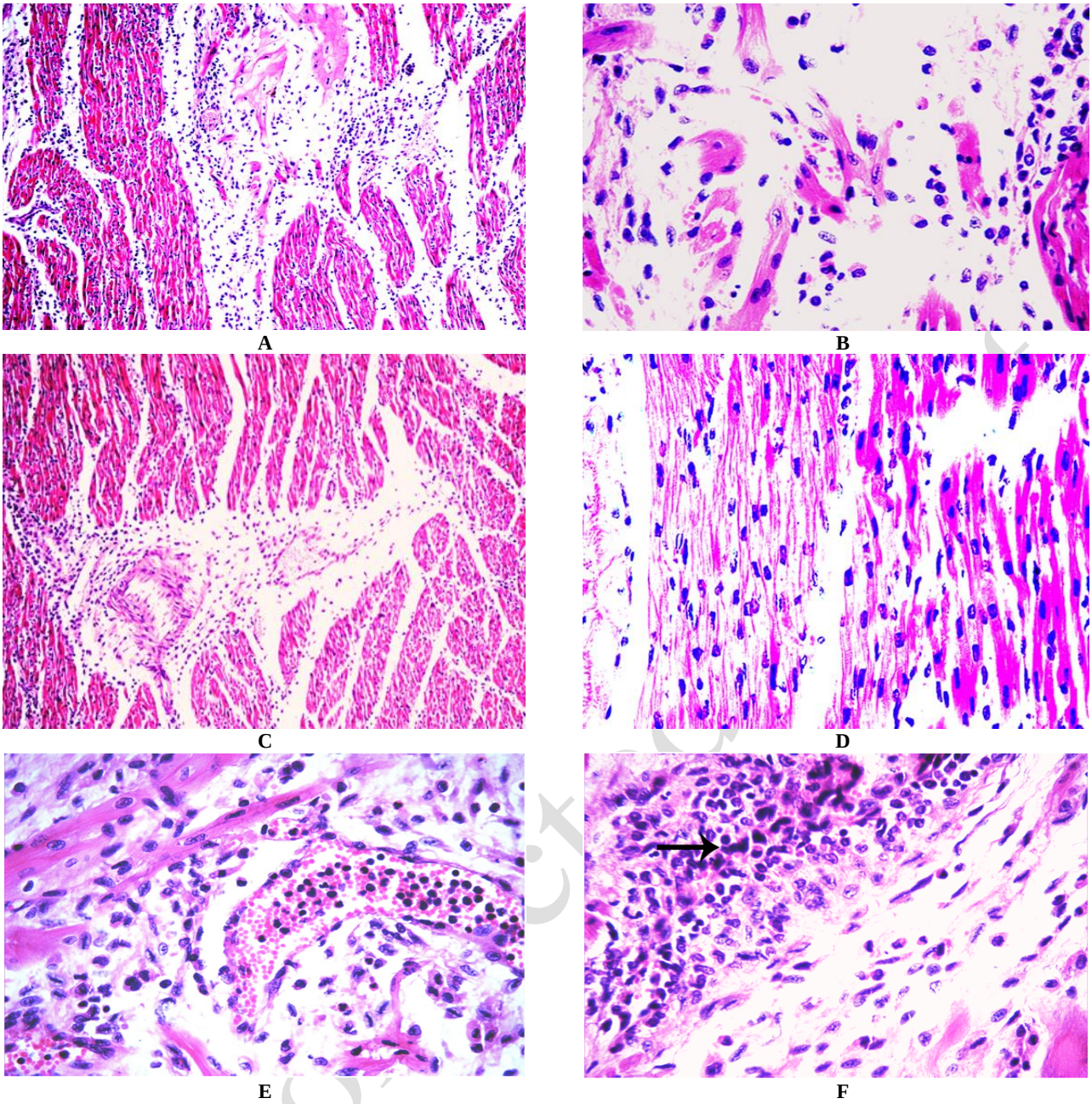


Fig. 8: Histopathological findings in goat kids with nutritional muscular dystrophy. Image A shows severe myocardial muscles degeneration that represented by hydropic, granular as well as hyaline degeneration. Image B shows Zenker's necrosis of the heart muscles. Image C shows severe myocardial degeneration, necrosis with mononuclear inflammatory cells infiltration in a goat kid. Image D shows myocardial necrosis (nuclear pyknosis, Karyorrhexis and karyolysis) in a goat kid with cardiac nutritional muscular dystrophy. Image E shows histopathological findings in goat kids with cardiac nutritional muscular dystrophy. The necrotic muscles are replaced by mononuclear cells. Image F shows calcified plaques (arrow) in between the muscles and sub-endocardium. Images A, C, E ×200; Images B, D, F ×400.

inflammation and stress. Opposite, evaluation of hepatic Cu status is the most practical indicator of Cu storage (Postma et al. 2023).

Etiology

The deficiency of Cu may be primary, when the uptake in the diet is insufficient when the forage is grown on deficient lands, typically sandy or weathered soils, or areas in which the Cu is unobtainable. Deficiency of Cu may be secondary that is the predominant form where the amount of Cu in the diet is enough, but other factors (mainly sulfur, molybdenum and Fe; but also lead calcium, Zn, Mn and carbonate are risk factors) intervene with the utilization and availability of Cu (Pugh and Baird 2002; Scott 2015; Constable et al. 2017; Thorndyke et al. 2021).

Clinical signs

Primary copper deficiency

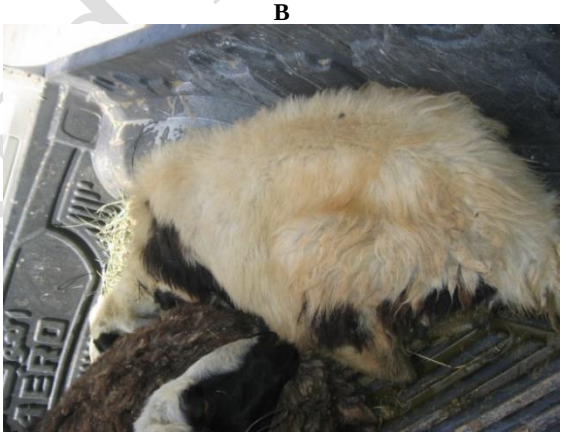
Primary Cu deficiency leads to decreased milk production, unthriftiness, anemia, coat color changes, causing red and black to change to rusty red, and the coat becoming staring and rough (Fig. 9). Severe deficiency in nutrients leads to poor neonate growth, increased bone fracture risk, ataxia after exercise, and infertility in cattle. Coarse, depigmented hair, and infertility have been linked to Cu deprivation (Constable et al. 2017).

Fig. 9: Copper deficiency in camels. The coat color is affected, red and black camels changed to a bleached, rusty red and the coat itself becomes rough and staring.

A

B

C



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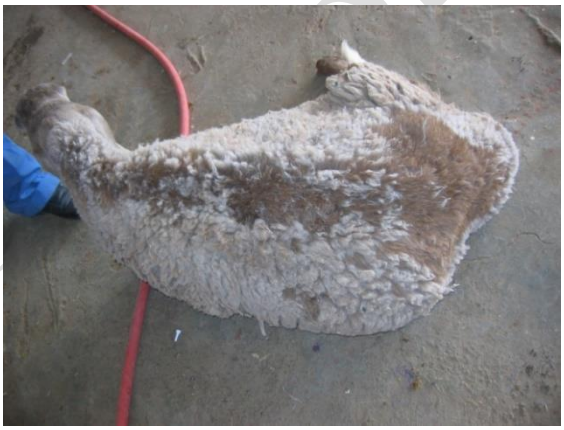
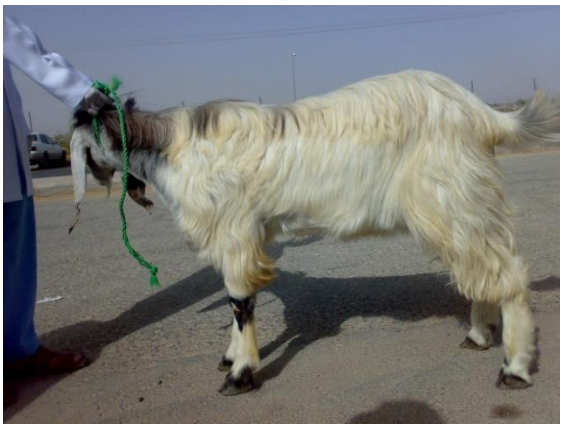


E



F

Fig. 10: Copper deficiency in 5 sheep (A - E) and a goat (F). Fine wool becomes limp, glossy and loses its crimp, developing a straight, steely appearance. Black wool shows depigmentation to gray or white, often in bands coinciding with the seasonal occurrence of copper deficiency.

General syndrome in sheep and goats

Wool abnormalities are the first signs of marginal copper deficiency, with fine wool becoming limp and glossy, and black wool depigmenting to gray or white (Fig. 10). Extreme deficiency may cause anemia, scouring, unthriftiness, and infertility, with enzootic ataxia being the major manifestation in lambs. Clinical findings include retardation of growth, diarrhea, delay to marketing, and

increased mortality in sheep, with lambs showing the most common symptoms (Laven and Smith 2008).

Secondary copper deficiency

This syndrome includes symptoms of primary Cu deficiency, with anemia being less common due to better secondary copper status. Diarrhea is generally associated with primary copper deficiency, possibly due to a conditioning factor reducing copper availability. Anemia is a terminal sign in primary copper deficiency (Helmer et al. 2021). For example, the acuteness of the diarrhea is proportional to the level of intake of molybdenum (Fig. 11).

Fig. 11: Chronic diarrhea in a camel suffering from copper deficiency.

Cerebrospinal swayback is only congenital in profound Cu deficiency. Born dead or weak, affected lambs cannot stand or suck. Compared to enzootic ataxia, spastic paralysis and incoordination are more noticeable. Blindness occurs occasionally. The cerebral white matter undergo softening and cavitation, most likely occurs about day 120 of gestation (Draksler et al. 2002). Delayed or progressive spinal swayback starts to develop weeks post birth with clinical signs and lesions appearing 3-6 weeks of age (Fig. 12).

Fig. 12: Swayback disease in 3 goat kids. Incoordination and erratic movements are evident in all kids.

Enzootic ataxia only affects un-weaned lambs. In acute attacks, neonates may be affected at parturition, although most instances occur between 1-2 months. As age increased, paresis severity reduces. Lambs diagnosed at birth or in the first month collapse within 3-4 days. Survival is higher in older lambs, but they always have hindquarter ataxia and atrophy (Laven and Smith 2008; Tharwat et al. 2024d). The first symptom appeared in enzootic ataxia is in-coordination of the hind legs visualizing when the lambs are just born (Fig. 13). Exertion also significantly increases heart and respiratory rates. The incoordination increases with the development of the disease and might be observed even after a short distance of walking. There is excessive joint flexion, fetlock knuckling, hindquarter wobbling, and finally falling (Laven and Smith 2008).

A

B

Fig. 13: Enzootic ataxia in goats (**A** & **B**). Incoordination of the hindlimbs, excessive flexion of joints, knuckling over of the fetlocks, wobbling of the hindquarters and finally falling are apparent in both animals. The hindlegs are affected first and the lamb may be able to drag itself about in a sitting posture.

Necropsy findings

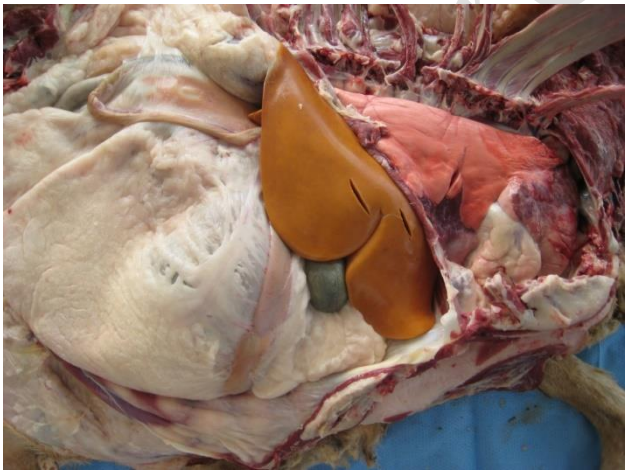
The pathology of Cu deficiency, or hypocuprosis, is often non-specific and not very informative. The histological changes observed are not unique and do not clearly distinguish the condition from other causes. In severe cases, diarrhea may be present, accompanied by villous atrophy in the jejunal and duodenal regions. However, this pathological finding is indiscernible from the changes caused by gastrointestinal parasites. The anemia associated with Cu deficiency resembles Fe deficiency anemia, characterized by macrocytic and

hypochromic red blood cells. Additionally, natural outbreaks of Cu deficiency have been reported to include cardiac lesions, such as fibrosis of the myocardium (Draksler et al. 2002).

Treatment and prevention

Cu deficiency can be easily treated with parenteral injections of the element or single oral dosages. Whether administered subcutaneously or intramuscularly, chelates of Cu combined with tetra-acetic acid, ethylene diamine, glycine or methionine may cause intolerable "cold" abscesses at the injection site in animals that are reaching market weight. Several months of protection can be obtained with Cu oxide particles, which are more effective than serial injections. With oral and parenteral supplements, deficiencies and disorders can be prevented to varied degrees of accuracy and duration (Smith and Sherman 2009). Acute Cu toxicosis can be instantiated by extra dosage via the injection route and is manifested by hemolysis and jaundice (Fig. 14).

A



B

Fig. 14: Acute copper toxicity in a sheep. The animal was admitted with a history of copper repeated overdosing and in a downer state (**A**). Necropsy findings revealed icteric hepatic parenchyma (**B)**.

Cobalt deficiency

Co is a crucial trace element in the formation of vitamin B_{12} by rumen microorganisms (González-Montaña et al. 2020; Silva et al. 2020). Thus, secondary Co shortage results in a vitamin B_{12} deficiency. Ruminant animals require a dietary uptake of Co for the formation of the essential vitamin B_{12} by rumen microorganisms. Vitamin B_{12}-dependent enzymes in mammals, methylmalonyl-CoA mutase and 5-methyltetrahydrofolate homocysteine-methyltransferase, are essential for converting propionate to succinate and methionine, respectively (NRBC, 2016). Inability to change succinate to propionate is the initial manifestation of Co deficiency (Kennedy et al. 1991). Ruminal function disorders can lead to vitamin B_{12} deficiency, even with adequate Co supplementation in the diet, due to dysfunction in the ruminal microbiota (Helmer et al. 2021). It was reported that Co-containing fertilizers must be supplied to the forages and soil. Animal feed derived from the Co-containing supplements are supplied to the animals, to satisfy the nutritional demands of livestock (Khan et al. 2023). It was found also that cattle with uterine torsion had low serum Zn levels, and offspring born to these animals had elevated serum Co levels (Kazama et al. 2023).

Clinical signs

Co deficiency, a condition causing unthriftiness and death, can be severe and prolonged, affecting young animals, particularly lambs, and predisposing sheep to white liver disease, photosensitization, blindness, and convulsions (Mitchell et al. 1982). Co deficiency symptoms include weight loss, anorexia and poor growth, with severe cases causing rapid weight loss, fatty liver, and anemia in ruminants in pastures lacking quality mineral supplements (Tokarnia et al. 2010). Early stages of the disease cause rough hair (Fig. 15), discolored mucous membranes, fatigue, retarded growth, lactation, and wool production in sheep and goats. Severe lacrimation with profuse fluid mating the face is a crucial sign in advanced cases (Pugh and Baird 2002; Scott 2015) (Fig. 16). Co nutrition in sheep can be assessed by determining vitamin B_{12} concentration in blood plasma or serum. Blood samples from weaned lambs or adult sheep are best for assessment. Co intake is the main determinant of vitamin B_{12} synthesis in the rumen, but natural analogues are also synthesized in sheep and cattle. (Mills 1981).

Treatment and prevention

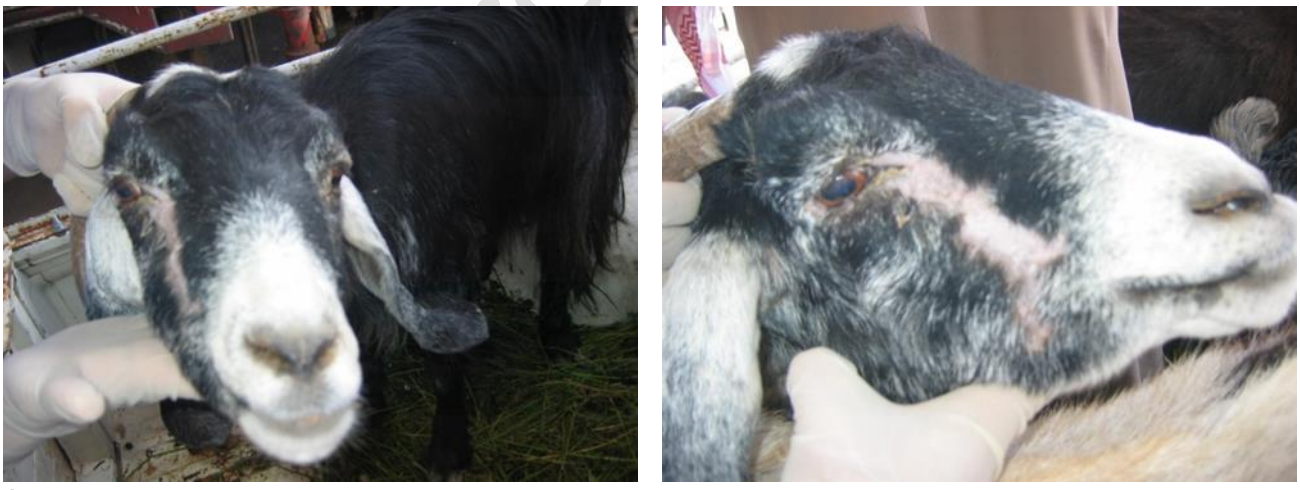
Parenteral administration of vitamin B_{12} is recommended for prompt treatment of diseased animals, providing adequate vitamin B_{12} for 3 months. Co pellets can be used for prompt treatment, depending on cost effectiveness and time period (Pugh and Baird 2002). Co deficiency can be prevented through various supplements like drenches, licks, sprays, fertilizer top-dressing, pellets, and vitamin B_{12} injections. Regular oral dosing is necessary for optimal effectiveness. Salt licks or mineral mixes containing cobalt should provide 0.05mg $CoSO_4$ per sheep daily, but may not be effective if animals fail to lick. Pasture top-dressing and an annual application of 350g $CoSO_4$ per hectare are recommended (Scott 2015).

Iodine deficiency

I deficiency disorders, which can occur from fetal age to puberty, cause a wide range of diseases including goiter, metabolic and neurological disorders. (Constable et al. 2017). I deficiency in ruminants, particularly in newborns,

A **B** **C** **D**

Fig. 15: Cobalt deficiency in goats (**A - C**) and sheep (**D**). Growth and wool production are severely retarded, and the wool may be tender or broken.



A **B**

Fig. 16: Cobalt deficiency in a goat. Severe lacrimation is observed causing hair detachment below both eyes (**A**). Image **B** shows a close-up view.

can lead to goiter and negatively impact the survival rate of kids and lambs (Davoodi et al. 2022). Goiter is a disease caused by I deficiency in animals and also in humans resulting from low I intake and feeding on goiterogenic factors (Clark et al. 1998). I deficiency occurs in mountainous and low-height regions due to soil lack, seasonal changes, and rainfall which leaches I from the soil (Zicker and Schoenherr, 2012). Goats, ruminants, show signs of deficiency due to selective food consumption and increased I requirements. To prevent congenital goiter, I is recommended in diets and sodium thyroxine treatment is effective treat I deficiency in the herd (Davoodi et al. 2022).

Clinical signs

Although decreased milk supply, loss of condition and weakness are expected, adults rarely show symptoms. I shortage most often causes stillbirths and weak newborns. Other indications include partial or entire alopecia and thyroid gland enlargement, which vary by species (Fig. 17 and Fig. 18). Thyroid gland enlargement can be congenital in calves, adult sheep, newborn lambs, and goats. Affected calves have a thick neck, partial alopecia, and palpable gland enlargement. Newborn lambs and goats show weakness, extensive alopecia, and palpable gland enlargement. Alopecia can range from complete absence to almost normal hair (Fig. 19).

Necropsy findings

Thyroid enlargement is an adaptive response to I deprivation, indicating I deficiency. Chronic I deficiency can cause thyroid gland to reach 0.79 g/kg BW without stillbirths. I supplementation reduces thyroid weight without reducing calf mortality or stillbirths (Smith and Sherman 2009; Davoodi et al. 2022).

Treatment and prevention

Congenital goiter is preventable through inorganic I supplements, slow-release boluses, and iodized poppyseed oil. Organic goitrogens can be bypassed by using low glucosinolate content cultivars and by-products. In areas with I deficiency in goats and sheep's forage and diet, I is advised to be added to the meal to prevent congenital goiter. (Scott 2015; Smith 2015; Constable et al. 2017; Davoodi et al. 2022).

Iron deficiency

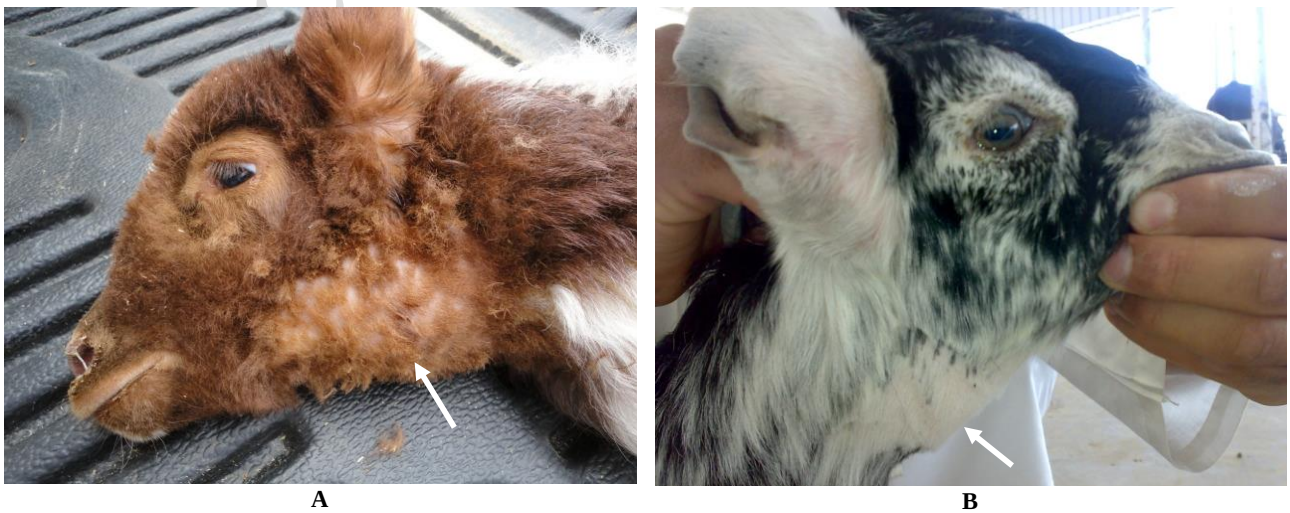
Fe is an element found in living organisms serves a role, in transporting oxygen supporting metabolic processes, and facilitating catalytic reactions. The divalent ferrous (Fe^{2+}) and the trivalent ferric (Fe^{3+}) are the 2 most common iron forms (Yiannikourides and Latunde-Dada 2019).

Etiology and clinical findings

Circulating erythrocytes hold two-thirds of body iron reserves, while remaining stores are found in spleen, liver and bone marrow. Fe deficiency leads to decreased serum Fe and increased Fe-binding capacity, resulting in microcytic, hypochromic erythrocytes. Laboratory findings include decreased packed cell volume, hemoglobin concentration, and echinocytosis. Newborn animals often experience Fe deficiency when they depend on their

A **B**

Fig. 17: Goiter in an adult goat (**A**). Image **B** shows a close-up view (red arrow).



A **B**

Fig. 18: Goiter in a lamb (**A**) and in a kid (**B**) (white arrows).

Fig. 19: Iodine deficiency in sheep. Partial alopecia is apparent in all cases.

mothers' milk as the Fe stored in their livers is not enough to support blood production for more than 2- 3 weeks. (Constable et al. 2017). Fe deficiency is not commonly seen in sheep and goats because they can get Fe, from the forages and grains they eat. Newborn animals mainly depend on colostrum for their Fe needs. The deficiency of Fe is a rare problem in adults, except in animals suffering from excessive parasitism (Pugh and Baird 2002). Fe deficiency is linked to chronic blood loss, parasitism, bleeding gastrointestinal lesions, and hemostatic defects. It's not the sole cause of anemia, except in neonates raised on cement or in barns. Veal calves may experience modest anemia, possibly due to congenital iron deficiency (Smith 2015). Pica and changes in hair color are observed in some cases suffered from Fe deficiency. Main clinical manifestations include inappetence, weight loss and the mucous membranes appear pale (Fig. 20).

Treatment and prevention

Treatment typically involves giving each calf an injection of 1g of iron either as Fe dextran or 0.5–1.0g of polygalactofuranose. Vitamin B_{12} is also commonly administered at doses ranging from 5–10mg/kg body weight. To prevent this condition, it is recommended to provide a milk substitute, with an iron concentration of 25–30mg/kg DM. This helps maintain the calf appetite and growth while ensuring the meat is light in color, ideal for production. The Fe level is carefully balanced to achieve blood hemoglobin levels without myoglobin production. Most milk substitutes used for calf rearing contain Fe content less than milk (Smith and Sherman 2009; Scott 2015; Constable et al. 2017).

Zinc deficiency

One of the most significant trace elements for animal health is Zn. It binds to many proteins, enzymes, and transcription factors, which may depend on it. Zn is involved in numerous life-sustaining metabolic reactions. The most crucial include oxygen usage, cellular respiration, free radical sequestration, DNA and RNA expression, lipid peroxidation protection and cell membrane integrity. Zn is a trace element that is a central component of metalloenzymes, lactate dehydrogenase, carboxypeptidase, and RNA and DNA polymerases (Sloup et al. 2017). A primary Zn deficiency in ruminants due to inadequate Zn intake is unusual but occurs. Zn availability from soils depends on soil compaction, nitrogen, and phosphorus concentrations. Zn deficiencies increase with soil pH above 6.5 and phosphorus and nitrogen fertilizer. Multiple conditions may deplete ruminants' Zn supply and induce secondary deficiencies (Constable et al. 2017).

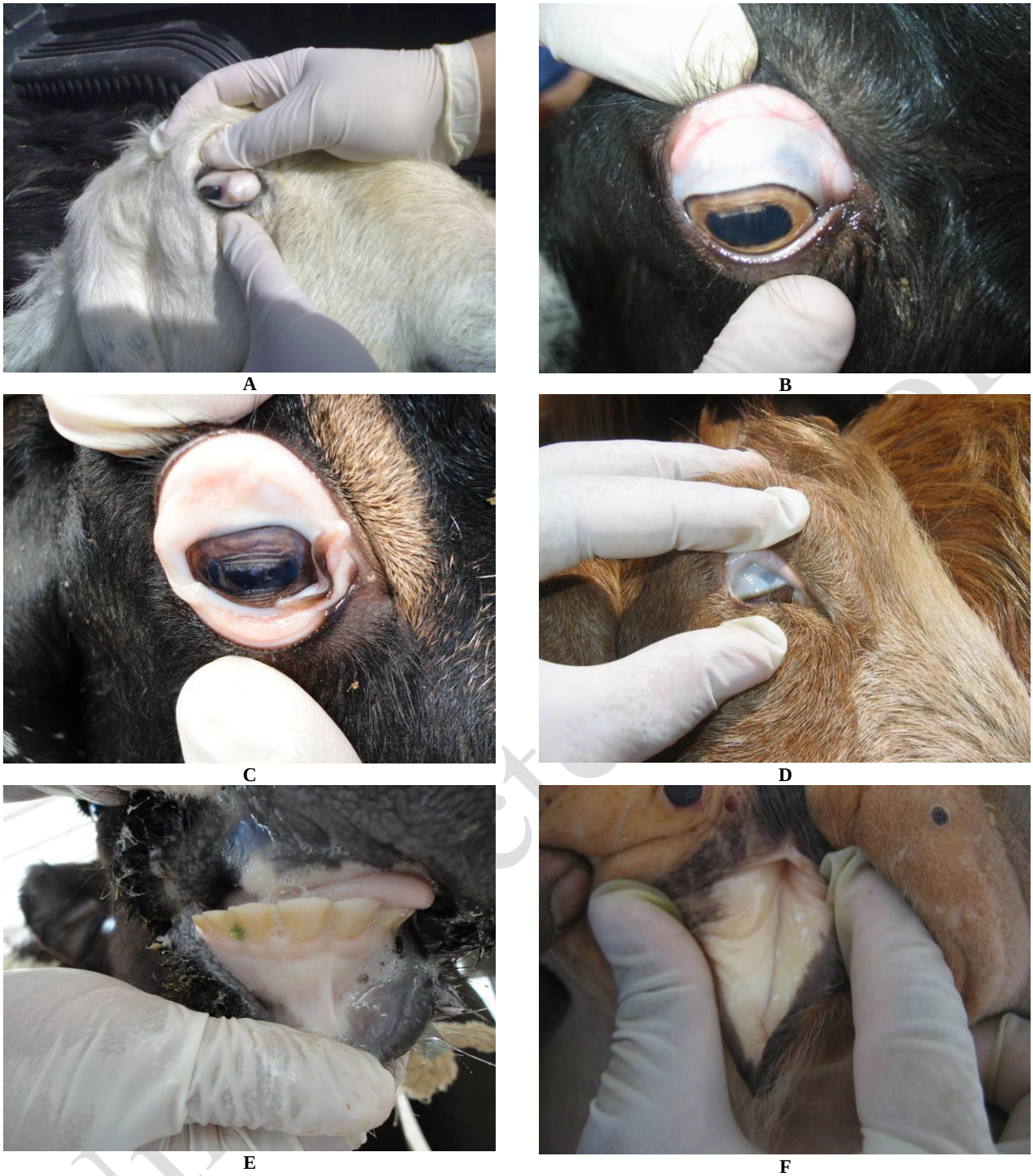


Fig. 20: Iron deficiency anemia in sheep (**A**), goats (**B, C, D**) and cows (**E, F**). The conjunctival, oral, oral and vulval mucous membranes are severely pale.

Several investigations proposed the importance of Zn in male fertility. The impact of Zn on sperm motility has been investigated in many invertebrate and vertebrate and species (Allouche-Fitoussi and Breitbart 2020). In cattle, it was found that Zn supplementation within the normal ranges for Zn status improves the quality of sperms but without altering the in vitro fertilization performance (Galarza et al. 2020). In addition, when bull semen was processed with Zn nanoparticles, a benefic effect was found suggesting Zn nanoparticles improve bovine gametes quality without affecting pregnancy rate (Jahanbin et al. 2021).

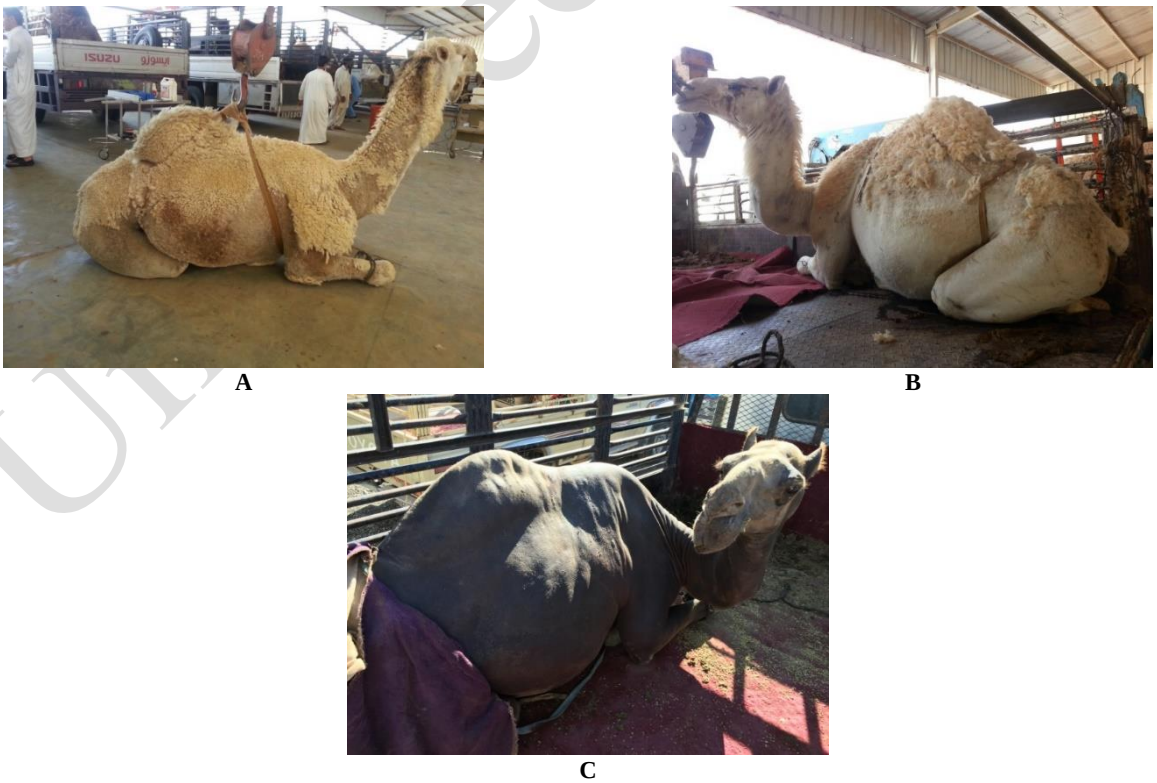
Clinical findings

In cattle, alopecia and parakeratosis may affect 40% of the skin over the vulva, muzzle, tail-head, anus, backs of the hindlegs, ears, neck, flank and knee-folds. Stunted in growth and decreased body weights are also observed in most animals. One of the earliest symptoms in lambs after feeding a Zn-deficient diet for four weeks was the wool eating. Impaired testicular growth and complete stop of spermatogenesis is one of the most important effects in sheep. Signs of Zn deficiency in small ruminants include parakeratosis, dermatitis, inappetence, decreased milk

production, slow growth, poor feed utilization, decreased hair growth on head and legs, poor growth, swollen joints, increased susceptibility to foot rot, impaired vitamin A metabolism, reduced testicular development, increased vitamin E requirements and decreased reproductive performance (Pugh and Baird 2002). The natural disease in sheep is manifested by the development of thick, wrinkled skin and loss of wool (Fig. 21). Complete or partial alopecia is one of the common symptoms of Zn deficiency in dromedary camels (Fig. 22).

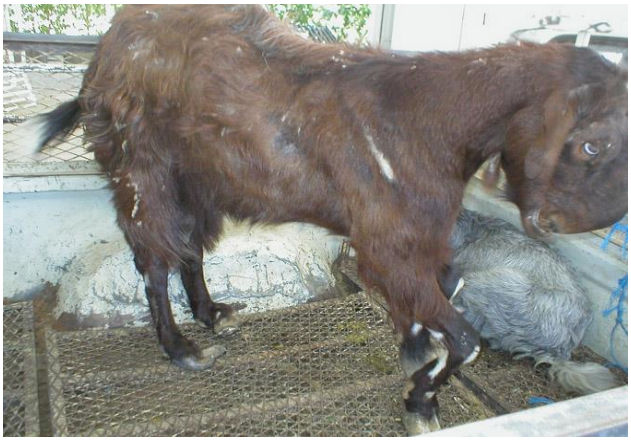
A **B** **C**

Fig. 21: Zinc deficiency lesions in a sheep. The disease is characterized by loss of wool and the development of thick, wrinkled skin (**A, B**) and keratinization under the tail (**C**).



A **B** **C**

Fig. 22: Partial or complete loss of wool in zinc deficiency camels. Differential diagnosis includes iodine deficiency, manage and ringworm.



A

B

Fig. 23: Manganese deficiency in 2 goats. Various skeletal abnormalities are present. The bones are shorter and weaker than normal and there are signs of joint pain, hopping gait, and reluctance to move.

Treatment and prevention

Administration of Zn orally at the dose of 250 mg Zn sulfate daily for four weeks led to a clinical improvement of Zn deficiency in goats in 12-14 weeks. For large animals, the feeding of Zn sulfate (2 - 4 g/day) is advisable as a rapid measure followed by the using of a Zn-containing fertilizer. Intra ruminal Zn pellet has been demonstrated in sheep; only it was efficient for seven weeks and was not be valuable on the long-term. The creation of SC depots of Zn by the injection of Zn oxide or Zn metal dust has been reported. A soluble bolus containing Zn, Co, and Se was able to edit induced Zn shortage in sheep. The bolus provided the daily needs of the sheep for Zn with no harmful effect on their Cu status, although high-dose Zn impaired Cu absorption in cattle that are provided extra Cu in the diet (Smith and Sherman 2009; Scott 2015; Constable et al. 2017).

Manganese deficiency

Mn is an essential element in the body and is obtained principally from water and food. It is absorbed through the digestive tract and then transferred to organs rich in the mitochondria (especially the pancreas, liver and pituitary). Mn is also involved in the activation and synthesis of several enzymes (e.g., transferases, oxidoreductases, lyases, isomerases, hydrolases and ligases), metabolism of lipids and glucose, acceleration in the formation of vitamin C, protein, and vitamin B, regulation of the endocrine, catalysis of hematopoiesis; and improvement in immune function. In addition, Mn metalloenzymes including arginase, glutamine synthetase, phosphoenolpyruvate decarboxylase and Mn superoxide dismutase also contribute to the reduction of oxidative stress towards free radicals (Li and Yang 2018; Hindman 2023).

Clinical findings

The common syndromes are congenital limb deformities, dry coat, poor growth and loss of coat color in calves, and infertility in adult cattle. In newborn calves, deformities include enlarged joints, fetlocks knuckling and twisting of the legs. Dietary deficiency of Mn may cause bone deformities (congenital and acquired) and infertility. The bones of lambs are weaker and shorter than normal and there are signs of hopping gait, joint pain and no desire to move (Fig. 23). Congenital bony malformations in calves include doming of the foreheads, joint laxity, dwarflike appearance due to the short long bones and superior brachygnathia. In cattle, it is manifested by failure to conceive, slowness to exhibit estrus, by decreased size of one or both ovaries and weak estrus (Constable et al. 2017). Mn deficiency during pregnancy can result in abortion or birth of small, weak, paralyzed or deformed neonates (Smith 1986).

Conclusion

Although required by very low amounts, deficiency of trace elements leads to several diseases and disorders in farm animals and subsequently huge economic losses. Therefore, balanced diets are required to prevent such affections in animals particularly camels, cattle, sheep and goats.

Author contribution

MT: conceived, designed the review framework, collected date, wrote the manuscript draft and prepared figures. TA and MM: edited and revised the manuscript draft. All authors re-read, revised and approved the final manuscript version for publication.

Conflict of interest

The authors declare that there is no conflict of interest.

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