Review on Copper's Functional Roles, Copper X Mineral Interactions Affecting Absorption, Tissue Storage, and Cu Deficiency Swayback of Small Ruminants

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Abstract: *This review describes the functional roles of copper and related enzymes targeting clinical manifestations of deficiency. These include osteoarthritis, aortic rupture in cattle, anaemia, swayback and recent studies on copper's immune function in combating infection. Factors affecting copper intakes, absorption and metabolism affecting copper storage are next portrayed in a logical sequence. Copper dietary mineral interactions are emphasized with interactions involving Fe-Cu, Fe- S – Cu, S- Cu, Cu- Mo- S and Zn- Cu. The role of high iron intakes inhibiting copper storage is of particular relevance to tropical environments and is discussed. Next, tissue Cu levels enzootic ataxia or swayback, goats and sheep blood copper levels and requirements for copper are put forward.*

Keywords: *Cu Functional roles; Cu mineral interactions; tissue Cu; Swayback*

1. INTRODUCTION

Functional roles of copper pertaining to deficiency

Copper (Cu) participates in many biological and biochemical body functions including erythropoiesis, cellular metabolism, membrane stability, collagen and elastin synthesis and immunobiological responses. The activities of the Cu containing enzymes namely cytochrome C oxidase (EC 1.9.3.1), superoxide dismutase (SOD) (EC 1.15.1.1), lysyl oxidase (EC 1.4.3.13), ceruloplasmin (EC 1.16.3.1) and tyrosinase (monophenol monooxygenase) (EC 1.14.18.1) are closely related to the functional roles of copper (Zatta and Frank 2007; Prohaska 2011).

Cytochrome C oxidase (EC 1.9.3.1) is required to generate ATP in the electron transport chain of cellular respiration (Zatta and Frank 2007; Prohaska, 2011). Consequently, cytochrome C oxidase activity reduces in Cu deficiency in tissues concerned with erythropoiesis (liver and bone marrow) (Williams et al. 1985), cell-mediated immune responses (spleen and thymus) (Prohaska et al. 1983) and myelin synthesis (Howell and Davison 1959). Thus, Williams et al. (1985) found that reduced cytochrome C oxidase activity in liver hepatocytes and bone marrow erythroid cells, contributing to impaired haem synthesis, as supporting evidence to explain the anaemia sometimes observed in Cu deficiency. Regarding the role of Cu in myelin lipid synthesis, Howell and Davison (1959) and Mills and Williams (1962) found lowered cytochrome C oxidase activity in degenerating nervous tissue to coincide with lowered brain Cu concentrations (<3.0 mg/kg DM) and the neuronal chromatolytic changes characteristic of enzootic ataxia.

Cytochrome C oxidase activity in the leucocytes of the white blood cells (Boyne 1978), or of the lymphocyte producing spleen and thymus gland, may diminish because of Cu deficiency (Prohaska et al. 1983). These findings coupled with Cu-Zn superoxide dismutase (EC 1.15.1.1) role in preventing peroxidative damage to the phagocytes provide suitable explanations of the role of Cu in immunity, The clinical findings of Woolliams et al. (1984), and Woolliams et al. (1986) agree with Cu's immunocompetent role. The mortality of lambs of selected low Cu lines, prone to respiratory infections by *Escherichia coli* and *Pasturella haemolytica*, was considerably reduced by Cu supplementation. Alternatively, amelioration occurred in specific pathogen free lambs succumbing to a pre haemolytic anaemia due to copper toxicity, when infected with *Mycobacteriun avium* implying a copper immunocompetency function or requirement (Suttle 2011).

Cu-Zn Superoxide dismutase (SOD) (EC 1.15.1.1), containing the prosthetic groups Cu for catalysis and Zn for stability, is required to prevent peroxidative damage to tissues such as aortic tissue, liver, circulating erythrocytes, leucocyte and myelin (Andrewartha and Caple 1980; Jones and Suttle 1981; Prohaska et al. 1983; Prohaska 1987, 2011; Nelson et al. 1992; Suttle 2011). Cu-Zn Superoxidase dismutase ability to convert circulating dismutase (O_2^-) to hydrogen peroxide (H_2O_2) originating from cellular metabolism ($O_2 \rightarrow O_2^-$) of microbicidal activity confers a protective function on the leucocytes ability to destroy invading microorganisms (Jones and Suttle 1981). Smith et al. (1981) and Prohaska (1987) have suggested that lowered Cu-Zn SOD activity in neurones and glial cells may contribute to increase lipid peroxidation of myelin in enzootic ataxia. Erythrocyte SOD activity tends to decline more slowly than liver or plasma Cu (Andrewartha and Caple 1980) and may be more valuable in monitoring chronic Cu deficiency (Suttle 1983).

The Cu dependent enzyme lysyl oxidase (EC 1.4.3.13) functions in synthesizing the elastin content of aortic tissue and in maintaining the stability and strength of bone collagen (Mills 1983; Davis and Mertz 1987). Diminished lysyl oxidase activity observed in Cu deficiency has been implicated in aortic rupture causing falling disease of cattle (Underwood and Suttle 1999), calcification of degenerating elastin in the abdominal aorta of rabbits (Hunt and Carlton 1965) and in the increased vascularity (venous stasis) sometimes observed in the cortex of swayback lambs (Schulz et al. 1951; Williams 1977). Osteoporotic changes sometimes found in Cu deficient lambs (Whitelaw et al. 1979) were evidently related to an impairment in lysyl oxidase activity causing defects in cross-linkages of polypeptides of bone collagen (Davis and Mertz 1987).

Ceruloplasmin (EC 1.16.3.1) (Cu oxidase) in its reduced form is required for the binding of Fe III tranferrin to plasma (Frieden 1971). Additionally, ceruloplasmin may also function as a transport protein used in the synthesis of cytochrome oxidase (EC 1.9.3.1) (Hsieh and Frieden 1975) and lysyl oxidase (EC 1.4.3.13) (Harris and Di Silvestro 1981). The Cu containing enzyme tyrosinase (EC 1.14.18.1) catalyses the conversion of tyrosine to melanin, a deficiency of which can result in the characteristic spectacled appearance in cattle and sheep (Mills 1983; Underwood and Suttle 1999).

Additional functions of copper include its roles in preventing pancreatic lesions in cattle and its requirement for prostaglandin synthesis. Fell et al. (1987) found that copper is required to prevent splitting and disorganization of the pancreatic basement acini membrane in cattle. Also deficient copper diets fed to rats resulted in diminished prostacyclin production and that was associated with increased aortic lipid peroxidation (Nelson et al. 1992).

2. ABSORPTION AND METABOLISM OF COPPER

Site of copper absorption

Limited information is available about the site of Cu absorption in ruminants. In general copper may be absorbed from the small and large intestines in sheep (Miller et al. 1988). Earlier studies (Grace 1975) suggested that the major site of Cu absorption in sheep to be the large intestine. This site of absorption has not been described for other species; the major site in man (Bush et al. 1955) and rats (Van Campen and Mitchell 1965) appears to be the stomach, and in the chicks (Starcher 1969) the deudenum. However, availability of Cu for absorption appears to vary throughout the alimentary tract. Price and Chesters (1985) assessed the availability of Cu in digesta from sheep given grass. The dried digesta, taken from different regions of the alimentary tract, was given to partially hypocuprimic rats and the availability of Cu in the digesta was determined by measuring the response in the activity of cytochrome C oxidase in the duodenal mucosa of the rats. The relative availability of Cu in the grass

(75%) was substantially higher in duodenal (43%) than in the ruminal (12%), or ileal (28%) contents of the dried extracts.

Copper absorption and homeostasis

At low or high copper concentrations absorption is mediated by an active or passive diffusional process (Bronner and Yorst 1985). Passage of copper through the intestinal mucosa may involve binding to certain transfer sites; firstly to an intracellular pool and then to plasma albumin on the serosal side (Cousins 1985). High zinc intakes can induce intestinal metallothionein synthesis which has a stronger affinity for copper thereby inhibiting further Cu absorption on the serosal transfer of copper to albumin (Hall et al. 1979; Mason, Woods and Poole 1986). On the serosal side copper is loosely bound to albumin ($\approx$ 5%) where it traverses to the liver. At the liver copper is found in two pools; one for storage and the other for ceruloplasmin synthesis and biliary excretion (Weber et al. 1982). Biliary endogenous excretion is low in ruminants and is incorporated into faecal losses (Camakaris 1987). Urinary losses are even lower and are usually about 1% administered oral dose (^{64}Cu) (Weber et al. 1982).Because of these low homeostatic control mechanisms found in ruminants, the storage capacity of the liver is substantial and long term which can prove beneficial in situations of high copper preceded by low copper intakes (Wiener and Woolliams 1983). Alternatively the storage capacity of the liver can prove harmful for breeds susceptible to copper toxicity (eg. Textel) (Weiner and Woolliams 1983).The main cellular storage fraction in the liver of sheep is the nuclear fraction (Saylor et al. 1980). In situations of copper toxicity metallothioneins are synthesized in the liver and kidneys to detoxify and excrete copper into bile and urine (Camakaris 1987; Evering et al. 1990). Of major importance is the synthesis and accumulation of Cu metallothionein in the kidney in its role of detoxifying and adaptation to copper loading in rats and sheep (Bremner and Young 1978; Evering et al. 1990).

3. FACTORS AFFECTING COPPER AVAILABILITY AND ABSORPTION IN RUMINANTS

There are many factors that can influence Cu absorption in ruminants. These factors include age, animal species, breed, type of diet, chemical form, and mineral interaction.

Age and form of copper

Copper absorption was much higher in milk fed pre-ruminant lambs (75 – 90%) than in post-weaned lambs and adult ewes (8 – 9%) (Suttle 1974, 1975; Grace and Watkinson 1988). The effect of age of sheep on the availability of dietary Cu was investigated by Suttle (1975) using [64]Cu. The apparent availability of Cu in lambs fell from 71% to 47% after 28 and 14 days, respectively, before weaning which was performed at 38-64 days of age. This change in Cu availability presumably coincided with the development of ruminal fermentation. The role of the rumen in reducing the availability of Cu was demonstrated by Suttle (1975) who showed that Cu administered to the abomasum of the lambs 42 days after weaning was absorbed with an efficiency of 21%, whereas for Cu administered into the rumen the availability was only 3.7%. Copper absorption was much higher in milk fed pre-ruminant lambs (75 – 90%) than in post-weaned lambs and adult ewes (8 – 9%) (Suttle 1974, 1975; Grace and Watkinson 1988). Furthermore, a group of lambs weaned at only 8% of Cu when 23 days old versus 75% for unweaned lambs at the same age. Copper absorption was higher from chelated amino acid complexes compared with inorganic feed sources (Pal et al. 2010). Cattle and sheep can absorb 60 – 80% of Cu from milk but less than 5% from herbage (Suttle 1983).

Animal species

Availability of Cu was calculated as 6.1% and 3.7% in sheep and deer respectively (Freudenberger et al. 1987). In cattle the availability was estimated approximately as 3.1% while the predicted value was 4.0% using equations based on sheep data, thus reflecting species differences in Cu availability (Suttle 1979). There are breed differences within sheep in efficiency of Cu absorption (Wiener et al. 1978). For example, Wooliams et al. (1982) using diets ranging from 12 to 20 mg Cu/kg DM showed Blackface x Texel lambs to retain more than twice as large a proportion of ingested Cu in the liver as pure Blackface lambs (12,7 vs 5.2%). The retention, from diets containing 4 or 9 mg Cu/kg DM, was calculated to be 4.2% for mature Blackface ewes and 7.3% from mature Welsh ewes (Wiener and Woolliams 1983)

4. MINERAL INTERACTIONS AFFECTING Cu INTAKES, DIGESTION AND METABOLISM

Iron-Copper

Pastures contaminated with soil in Britain and New Zealand account for high Fe intakes in ruminants of over several thousand parts per million (Suttle et al. 1975). The incorporation of 10% dry matter of Fe rich soils or of inert soil Fe oxides into feeds or silages; or feeding of saccharated Fe compounds to cattle and sheep always resulted in a rise of Fe with an accompanying decline in Cu in the liver (Suttle et al. 1975; Suttle et al. 1984; Phillippo et al. 1987; Grace and Lee 1990). Intakes of 500 mg/kg DM Fe or more tended to accelerate the decline in liver Cu to levels below 30 mg/kg DM. Lower dietary intakes of 150 mg/kg DM, as is found in some tropical forages or of 250 mg/kg DM in many agricultural foodstuffs (ARC 1980), may also severely exhaust liver Cu stores when imposed for a few months (Bremner et al. 1982).

The independent effects of Fe on Cu metabolism were also observed in sheep and goats. In grazing sheep highest Fe, but lowest Cu, were present in all tissues, especially the lung tissue, when Fe intakes of 247 and 827 mg/kg DM were compared (Grace and Lee 1990). These findings also agree with the inverse relationships of liver Fe and Cu reported for swayback prone breeds and swayback kids (Woolliams *et al.*, 1986; Ivan *et al.*, 1990). Ivan et al. (1990) suggested that the high Fe content (>500 mg/kg DM) found in herbage consumed by ataxic kids was related to the high Fe content of 859 mg/kg DM found in liver tissue. High proportions of farmed goats and swayback lambs and kids, with deficient blood Cu levels in Oman and Brazil were attributed to high dietary iron intakes associated with high liver Fe concentrations (Dos Santos et al. 2006; Osman et al. 2009; De Sousa et al. 2012). These effects were independent on the sulphate and Mo contents of the diets.

Iron-Sulphur

Suttle et al. (1991) linked their observed decline in liver Cu to the rise in ruminal sulphide levels when three Fe-rich soils were fed to cattle. They postulated that ruminal Fe sulphide could interchange for relatively insoluble Cu sulphide in the acid conditions of the abomasum. Bremner et al. (1978) found that when total S was reduced from 2.8 g/kg DM to 1.5 g/kg DM in controlled diets containing Fe at 100 mg/kg DM, there was actually a rise in plasma and liver Cu values. At 200 mgFe /Kg DM the reduction in S slowed the decline in liver Cu; but these effects were not evident at 500 or 800 mgFe /kg DM. They speculated that Fe could exert an effect on Cu that is independent of S, especially at high dietary Fe intakes.

Sulphur-Copper

Sulphur levels within the range of 2 to 4 g/kg DM, have been found to limit the availability of Cu (Suttle 1979). Methionine and especially cysteine, the main S organic forms present in plant protein have been shown to act independently of Mo in limiting Cu availability by 16 to 44% (Suttle 1970). However, S incorporated at 2 g/kg DM in the presence of 2.5 mg/kg DM Mo reduced the availability of Cu by approximately 40% in sheep. Microbially produced sulphide sequestered to the acid abomasum in the form of metal sulphides or thiomolybdate complexes may eventually produce unavailable CuS or Cu_2S (Mills 1985). Insoluble Cu complexes of a microbial nature may also form at lower down the alimentary tract (Bremner 1970).

Zinc-Copper

An imbalance of Cu metabolism may occur at moderate (100 mg/kg DM) or high Zn intakes (500 mg/kg DM). Towers et al. (1981) reported that cattle, marginally deficient in plasma Cu (<0.6 mg/L), when allowed to graze Cu sufficient pastures and having access to Zn treated water, 75% remained deficient compared with 22% for untreated controls. Mills (1974), and Ivan and Grieve (1975) noted that Zn intakes of 100 mg/kg DM depressed liver Cu stores. At above normal Zn intakes, the liver synthesizes Zn metallothionein binding protein (Bremner and Marshall 1974). Copper with a greater affinity for thionein S displaces Zn without Cu being readily released into the plasma. Such a device may serve as a protective function against Cu toxicity (Zervas et al. 1990).

Sulphur-Molybdenum-Copper

Apart from the formation of insoluble Cu sulphide in the rumen and lower down the abomasum (Underwood and Suttle 1999; Suttle 2010), S also limits the availability of Cu by its interaction with Mo (Dick et al. 1975). Ruminal microorganisms reduce sulphate to sulphide which could then

substitute in the molybdate anion (MoO_4^{2-}) to form a mixture of di-($MoO_2S_2^{2-}$), tri- ($MoOS_3^{2-}$) and tetra- (MoS_4^{2-}) thiomolybdates. The greater the degree of substitution the more limiting the availability of Cu by its interaction with Mo and S (El – Gallad et al. 1983; Bremner et al.1982; Osman, 1988).

Several authors have found Cu thiomolybdate complexes to be associated with the solid phase of digestion (Suttle 1983; Allen and Gawthorne 1987). In sheep Allen and Gawthorne (1987) suggested that tetrathiomolybdates complex copper to proteins of microbial and plant origin to limit the availability and absorbability of copper further down the intestine. In contrast di- and tri-thiomolybdates (Suttle 1983; Price et al. 1987; Osman 1988) and tetrathiomolybdates (Osman 1988) are only slowly formed and are likely to be absorbed into the systemic circulation. Oxythiomolybdates absorbed into the blood can form complexes with Cu in the plasma and other tissues (Suttle 1988; Osman 1988). These latter complexes promote the appearance in plasma of forms of copper and molybdenum that are insoluble in trichloracetic Acid (TCA- Insoluble Cu) (Osman 1988), and are closely associated with albumin (Mason, Woods and Poole 1986). Trithiomolybdates were more readily formed in sheep under rumen conditions, and, when infused in the duodenum, promoted an increase in TCA insoluble Cu in plasma with an accompanying decline in caeruloplasmin activity (EC 1.16.3.1) (Mason et al. 1982) An increase in TCA insoluble Cu in response to thiomolybdates administration to goats may be unavailable for uptake at the liver (Galbraith et al. 1997). There was a rapid clearance of albumin bound copper by the liver except in the presence of trithiomolybdate administered intravenously (Suttle 2011). However, when injected intravenously in sheep and deer, di-, tri- and tetrathiomolybdates produced an immediate drop in TCA-solubility in plasma Cu, the severity and clearance of which depended on both, the concentration and the degree of thio substitution of the complex (Osman 1988; Suttle 2011). Caeruloplasmin oxidases activity was not affected in any of the treatments. These latter findings explain the rise in plasma (or serum), but fall in liver copper, that sometimes occur with high molybdenum and sulphur intakes (Suttle 1975; Andrewartha and Caple 1980; Bremner and Young 1978). At increasingly high molybdenum intakes (15-45 mg/kg) there was a linear increase of Mo in serum, and liver while serum Cu and TCA insoluble Cu also increased (Pott et al. 1999). An increase in molybdenum can decrease liver Cu stores (Crosby et al. 2004) and, when combined with sulphate/sulphur, Mo can also increase kidney Cu levels, urinary and biliary Cu excretion (Marcilase et al. 1970; Gooneratne et al. 2011). In sheep, Bremner and Young (1977) demonstrated an increase in kidney Cu thionein proteins in its role to detoxify copper in copper poisoned sheep. The rise in TCA insoluble Cu however, after treatment for molybdenum toxicity in hepato copper toxic sheep using pharmacological doses of TTM does not inhibit Caeruloplasmin (Cp) oxidase (EC 1.16.3.1) activity or lower the Cp: TCA-soluble Cu, although promoting a transient rise in TCA insoluble Cu (Suttle 2008). In Norway copper toxicity in grazing sheep is endemic; treatment with tetra thiomolybdates produced minimal declines in Cu in Norwegian sheep with elevated liver copper concentrations in the autumn. Further studies are needed on TTM administration for the treatment of copper toxicity exposure in sheep and goats.

Serum and Tissue Copper Levels in sheep and goats in Relation to Cu Deficiency Swayback

Figure 1. *Swayback kid*

Swayback is a neurological disorder affecting lambs and kids at birth or postnatally up to six months of age. Clinical signs of the disease include an inability to stand at birth or hind limb ataxia progressing to quadriplegia in the delayed forms (Figure 1). The disease is identified pathologically as chromatolysis and necrosis of the large motor neurones of the brainstem and spinal cord of most affected animals (Barlow, 1993). Most normal plasma Cu for sheep and goats lie within the range 0.8 – 1.2 mg/L (Underwood and Suttle 1999), while serum levels below 0.65 are indicative of deficiency in grazing ruminants (McDowell and Arthington 2005). However, Underwood and Suttle (1999) suggested a critical Cu level of 0.5 mg/L or lower for plasma, because many sheep and goats grazing critically deficient areas have levels of between 0.2 – 0.3 mg/L without showing clinical signs of deficiency. Alternatively, levels of about 0.5 mg/L may affect growth rate (Osman et al. 2008) and disease proneness, whereas ataxia in small ruminants or bone abnormalities in cattle can manifest at levels of 0.2 mg/L (Whitelaw et al. 1982; Whitelaw 1985; Mohammed 1999).The microcytic hypochromic anaemia in swayback lambs, kids including apparently normal sheep is associated with serum copper levels below critical level (Schulz et al. 1951; Camenzind et al. 2003; Mohammed et al. 2014) (Figure 1).

Table 1 shows the levels of Cu found in various tissues as influenced by age, and deficiency in sheep and goats. In new-born lambs plasma or serum levels tend to be lower than in adult sheep (Rosero et al. 1984), due to the almost complete absence of ceruloplasmin (McCosker 1968).In kids minimal values of plasma Cu were found at birth (0.59 ± 0.054 mg/l) and maximum values after 4 day (0.86 ± 0.056 mg/l) (Osman et al. 2003). In the latter study kids at 7 month age had plasma Cu mean value of 1.17 ± 0.039 mg/l, which was higher than that of barren and pregnant does at that time. Conversely liver Cu levels in newborn lambs may be higher than those of their corresponding dams. Weiner and Field (1970) reported liver Cu Levels in dead one day old lambs of 128 mg/kg DM compared with 14.3 mg/kg DM in ewes. Whitelaw (1985) and Barlow (1991) stated that liver Cu levels found in many swayback lambs were below 10 mg/kg DM. However, the levels found in swayback kids may be higher (<20 mg/kg DM), as suggested by Merrall (1985) and Smith and Sherman (1994). In southern Brazil Santos et al. (2006) reported liver Cu levels of 45.8 mg/kg DM in swayback kids which concur with the finding by Mohammed (1999) in one swayback kid with a liver Cu level of 42 mg/kg DM.

In Trinidad, low liver Cu concentrations were reported in cattle from the North (13 mg/kg DM) and South (7 mg/kg DM) (Mohammed et al. 1994); and in swayback lambs (4.5 mg/kg DM) from the Central region (Mohammed et al. 1995). Deficient liver, kidney and brain tissue levels, in experimentally induced copper deficiency with clinical signs, in goats, are about 5.3 ± 2.5; 9.7 ± 3.6; and 6.4 ± 1.8 mg/kg DM, respectively (Haenlein and Anke 2011)

Although plasma Cu levels are variable during gestation, levels are consistently lower in ewes kept on Cu deficient diets (Suttle and Field 1969, 1970). These authors produced swayback lambs from ewes fed 10 mg Cu/kg DM, 5.3 g/kg sulphate and 25 mg/kg DM Mo, respectively. Liver, kidney and heart tissue Cu levels in mg/kg DM in swayback and normal control lambs were 7.1 and 10.9, 16.8 and 17.9, 8.9 and 12.3, respectively. Normal levels in the kidney cortex are between 12.7 and 19.0 mg/kg DM (Suttle 1986). Values below this range have been found in two Cu responsive conditions namely ataxia and pneumonic pasteurellosis.

Whitelaw et al. (1982) suggested that normal brain Cu levels between 9-12 mg/kg DM with a critical level of 6 mg/kg. Suttle and Field (1970) found brain Cu levels in swayback and normal control lambs to be 1.8 and 10.9 mg/kg DM, respectively. In goats Anke et al. (1973) reported a 40% reduction in brain Cu levels at clinical signs of deficiency (skeletal damage, growth rate). These findings accord with that of Mills and Williams (1962) that neuronal degeneration in the brainstem of ataxia lambs is coincident with a low threshold of cytochrome c oxidase activity at brain Cu levels below 3 mg/kg DM.

Table1. *Serum and Tissue Copper Levels in sheep and goats in Relation to Cu Deficiency Swayback*

Condition	Plasma mg/L	Liver	Kidney mg/kg DM	Brain	Comment/ Reference
Goats and Sheep Normal ranges	0.8 – 1.2		12.7 – 19.0	8 – 12	Underwood and Suttle, 1999

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Critical Level	0.50	(25 – 75)	12.7	6	McDowell and Arthington, 2005 Suttle, 1986;
Whitelaw et al., 1982					
New-born lambs	0.63, 0.5	-	-	-	
Adult sheep	1.02	-	-	-	McCosker, 1968
New-born lambs	0.24	-	-	-	
Growing lambs	0.15	207	-	-	Rosero et al., 1984b
Adult sheep	0.63	-	-	-	
Dead new-born lambs	-	128	-	-	
Adult sheep	-	14.3	-	-	Weiner and Field, 1970
Stillborn lambs	-	<15	-	-	Adamson, Shaw and Dover, 1983
New-born lambs from					
ewes on 2 mg Cu/kg DM	-	8.2	-	5.4	51.8% of other lambs
ewes on 24 mg Cu/kg DM	-	66	-	10	developed delayed swayback. Lewis, Terlecki and Parker, 1974
Normal kids and lambs	-	50	14	11	
Swayback kids (25) and					
lamb (1)	-	19	13	5	Ivan et at., 1990. Congenital and neonatal swayback
New-born lambs from					
ewes on 1.2 mg Cu/kg DM	-	7.1	16.8	-	
ewes on 11.2 mg Cu/kg DM	-	10.9	17.9	-	
					Suttle and Field, 1969a
Swayback lambs	-	-	-	1.8	
Normal lambs	-	-	-	10.9	
					6 congenital and 1 delayed. Suttle and Field, 1970
Abattoir					
Goats and sheep	0.33	11.9	-	-	
Ataxic kids and lambs	0.24	7.3	-	-	
					Hedger, Howard and Burdin, 1964
Lambs affected by swayback					
and other diseases	-	6	10.2	4.1	Wooliams et al., (1986a)
Swayback kids		<10	-	-	Inglis, Gilmour and
Cu treated adults - 4 g Cu	-	32	12.5	-	Murray (1986)
Untreated adults	-	30	12.4	-	
Normal goats		86	-	-	Hennig, Anke, Groppel
Cu Deficient goats	-	3.3	-	-	and Ludke (1974)
Cu deficient goats		8.9	11.2	12.1	Anke et al., (1973)
	-				
Normal lambs		109 ± 13	13 ± 2	8 – 19	Howell and Davison
Swayback lambs	-	17 ± 4	16± 2	1.4 – 5.4	(1959)
Swayback lambs	< 0.4	5			Mohammed et al 1995
Swayback lambs	< 0.4	4-8			De Sousa et al; (2012)

Seasonal serum and tissue Cu levels in goats and sheep particularly in the tropics

Marked seasonal related changes in blood plasma Cu have been reported by Gromadzka-Ostrowsk et al. (1986) over a three year investigation in primitive goats. In a study of Khan et al. (2007) seasonal variations in plasma Cu were detected in grazing goats in southern region of Punjab in Pakistan, where levels were higher in winter than in summer seasons. These variations could be attributed to the higher Cu levels in forage during winter than in summer, although no such difference was detected in feeds. Goats had their dietary Cu requirements fulfilled with the free supplement of salt lick all year. However, only lactating goats were marginally Cu deficient in summer. An increase in plasma Cu in June (hot season) compared with October/November (cool season) in goats in Oman (Osman et al. 2003) was suggested by authors to be related to generous supply of Cu rather than a genuine effect of season. However, there was a prevalence of swayback among kids born to grazing goats in summer in Oman rather than at other time (Ivan et al. 1990) suggesting the natural influence of season on Cu status.

Seasonal variation in forage Cu concentrations were also reported. Comparisons of locations were reported by Tartour (1975) who did not find differences in serum Cu levels of sheep and goats, among regions in Western Sudan. In Saudi Arabia, Ali and Al-Noim (1992) found differences in serum Cu between grazing and intensively reared sheep at two locations. A high prevalence of plasma Cu deficiency in sheep and goats have been reported across districts in Kashmir valley (Yatoo et al 2013). Liver Cu levels found in normal goats of Kenya and sheep of Ethiopia were between 9 - 18 and 16 - 51 mg/kg DM, respectively (Faye et al. 1991).

Copper requirements and levels in tropical grasses

Feeds and forages containing 7 – 11 mg.kg DM Cu are considered adequate for all classes of sheep (NRC 2007). ARC (1980) requirements for adult, pregnant and lactating ewes are between 4.4 and 8.6 mg/kg DM. Recommended daily allowances for the lactating goat is 8 – 10 mg/kg DM (Kessler 1991; Meschy 2000). However, dietary Cu levels over 30 mg/kg DM can cause chronic Cu poisoning in sheep (McDowell and Arthington 2005). In Trinidad, Youssef and Brathwaite (1987) and Mohammed (1999) found 50% of grasses had Cu levels below 5 mg/kg DM, which is associated with uncomplicated serum Cu deficiency in sheep (Suttle et al. 1991) and goats (Smith and Sherman 1994). Further, McDowell et al. (1977), Youssef et al. (1987, 1999) and Cerrillo-Soto et al. (2004) reported that grasses, shrubs and browse in Trinidad, Latin American Countries, and North Mexico had high Fe (> 500mg/kgDM) concentrations that can induce dietary copper insufficiency (Phillippo et al. 1987). However, most grasses had low Mo (< 1mg/kgDM) and S (< 2 g/kgDM) levels. Hence occurrence of Cu deficiency swayback in kids and lambs from grass-fed dams in Trinidad is probably caused by the low Cu levels present in local grasses, with some interference because of high Fe, but not of other minerals such as Mo and sulphur.

5. CONCLUSION AND RECOMMENDATION

During the past several years research on causes copper disorders in ruminants has focused on the important dietary interactions of copper X molybdenum X sulphur or tetrathiomolybdate formation affecting absorption and metabolism. In tropical environments where Fe overload may likely affect liver copper status emphasis should include measurements of several Fe metabolites that could be associated with TCA soluble Cu and TCA insoluble Cu including Caeruloplasmin (Cp) oxidase (EC 1.16.3.1). These metabolites may include serum iron, total iron binding capacity (TIBC) or unsaturated iron binding capacity (UIBC) or serum transferrin (TRF), percent transferrin saturation (TS%, percent iron saturation), and ferritin.

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