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Molybdenosis Leading to Type 2 Diabetes Mellitus in Swedish Moose

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Introduction

The "mysterious moose disease" also called "wasting disease" is affecting moose in a strongly acidified region of southwestern Sweden (Fig. 13.1). Chemical investigations of animals from the affected region have been performed since 1988 and several articles are already published (Frank et al. 1994, Frank 1998, Frank et al. 1999, 2000a, b, c, d).

The numerous clinical signs and necropsy findings have included diarrhea, loss of appetite, emaciation, discoloration and loss of hair, apathy, osteoporosis, and neurological signs such as behavioral and locomotor disturbances (Rehbinder et al. 1991, Stéen et al. 1993). Further findings were mucosal oedema, hyperemia, hemorrhages and lesions of the mucosa in the gastrointestinal tract, hemosiderosis of the spleen and liver, dilated flabby heart, alveolar emphysema, and uni- or bilateral corneal opacity. Not all the symptoms appear simultaneously in one and the same animal. About 150–180 affected animals have been reported annually since the late 1980s.

An increase in molybdenum (Mo) and a decrease in copper and cadmium (Cu, Cd) content in organ

Figure 13.1: The region of Älvsborg (shaded) in southwestern Sweden. Source: Frank, 1998. Reprinted with permission from the publisher

tissues (e.g., liver) are signs of a disturbed trace element balance found in affected animals (Frank 1998) (see Fig. 13.2). To confirm the findings and to elucidate the mechanisms leading to molybdenosis and Cu deficiency, experimental studies were performed in goats. The feeding studies were performed in a controlled laboratory environment and a semi-synthetic diet was supplied (Frank et al. 2000c). Despite considerable differences in species and living conditions between goat and moose, similar changes in trace element pattern and clinical chemical parameters were observed in both species. The study shows that the etiology of the moose disease is basically molybdenosis followed by Cu deficiency, inter alia (Frank et al. 2000a,b,d).

Mo is an essential trace element that controls the metabolism of Cu in ruminants. Increased Mo concentrations relative to Cu in feed results in Cu deficiency, whereas the converse leads to an accumulation of Cu, even to Cu poisoning (e.g., in sheep). In an acidified environment, the molybdate anion is adsorbed in the soil, contrary to positively charged metals. The presence of Mo and Cu in the environment is basically dependent mainly on geochemistry, influenced by numerous physical and chemical parameters (Selinus et al. 1996, Selinus and Frank 2000). The solubility and availability of Mo to plants increases with increasing pH (e.g., after liming).

In the rumen and intestine, molybdates are transformed to thiomolybdates (TTM), which, like sulfides, bind Cu. These insoluble compounds are excreted via the feces. Excess TTM is absorbed and transported by the blood and distributed to the tissues, where available Cu is bound as a TTM complex. This inactivation of Cu-containing enzymes causes severe lesions in the animals. The various clinical signs reflect functional disturbances caused by affected Cu-containing enzymes. Cu deficiency is also known to cause glucose intolerance.

On reaching the hypothalamus, TTM causes disturbances in the endocrine balance. The hypothalamus controls appetite, the thyroid gland, synthesis of sex hormones, gluconeogenesis, and so on, resulting in weight loss, emaciation, behavioral disturbances, lethargy, and disturbances in fertility and reproduction.

Normal insulin function requires sex hormones in both males and females. Deficiency of such hormones leads to insulin resistance, a condition that may cause increased insulin production, though the efficacy of insulin is depressed and glucose concentrations may increase in the body (hyperglycemia). The long-term elevated glucose levels result in non-insulin-dependent diabetes mellitus (NIDDM), also called type 2 diabetes (Frank et al. 1999, 2000b). The increased glucose concentrations will cause glycation of proteins. These products are easily detected in diabetic humans and domestic animals, and are known to cause lesions in diabetic humans, for example in blood vessels and eyes.

In cooperation with an American group, certain reaction products [furosine, pentosidine, and carboxymethyllysine (CML)], occurring after long-term hyperglycemia, were identified and estimated in tissues of affected moose. These have been found to be higher than in non-affected individuals (Frank et al. 1999, 2000b).

Our experimental goat study revealed the principal features of this complex moose disease. The new findings have increased our understanding of the "mysterious moose disease," making it possible to interpret the clinical signs and lesions of molybdenosis and Cu deficiency in this and probably the most sensitive ruminant, the moose. From the results it could be concluded that a suggested diagnostic test for the "mysterious moose disease" ought to include determination of hepatic trace elements (Mo, Cu, Fe) and investigation of characteristic clinical chemical parameters *decreasing* in blood serum or plasma, such as ceruloplasmin, thyroxine (T_4), Mg, P_{inorg}, and *increasing* parameters, such as insulin and urea. In red blood cells, decreasing activity has been found in the enzymes Cu, Zn-SOD (superoxide dismutase), and GSH-Px (glutathione peroxidase) (Frank et al. 2000a, b, d).

This is the first time diabetes mellitus has been demonstrated with the above method in wild ruminants. It is assumed that a considerable proportion of domestic ruminants reported dead from Cu deficiency/molybdenosis (11.3 million animals in 1970, WHO) were also affected by diabetes. The method opens up new diagnostic perspectives.

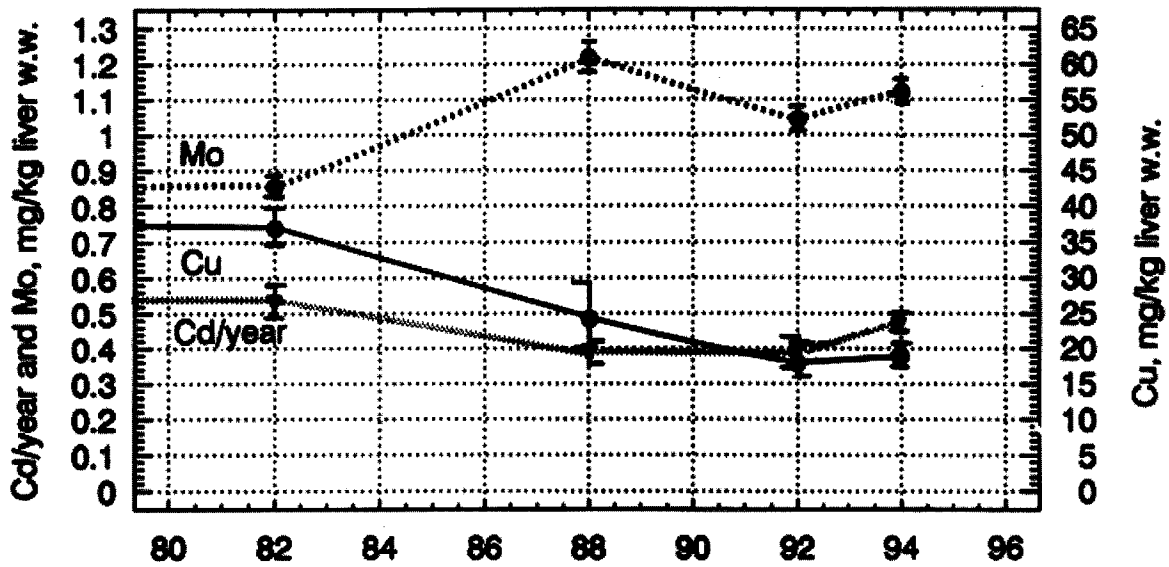

Figure 13.2: Molybdenum, copper and the average yearly cadmium uptake in the liver from moose yearlings in the southern part of Älvsborg region during 1982 through 1994. Median concentrations (median ± S.D.) are expressed in mg/kg on a wet wt. basis.
Source: Frank, 1998. Reprinted with permission from the publisher.

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