

Chapter 77

Chronic Selenosis in Ruminants

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Introduction

The first conclusive identification of spontaneous selenium (Se) toxicity was reported by the South Dakota and Wyoming Agricultural Experiment Stations (Beath *et al.*, 1934; Franke and Potter, 1934). These laboratories popularized a model of selenosis in which spontaneous selenosis in grazing animals takes one of three forms: acute selenosis, chronic selenosis "of the alkali disease type" and chronic selenosis "of the blind staggers type."

Acute selenosis is characterized by sudden death with few signs, or by gastroenteritis, myocardial necrosis, pulmonary edema, and hepatic and renal necrosis (Blodgett and Beville, 1987; MacDonald *et al.*, 1981; Smyth *et al.*, 1990). Acute selenosis is of limited relevance under range conditions as plants which accumulate sufficient Se to be acutely toxic are extremely unpalatable. As noted by Beath (1920), "when cattle were placed in enclosures on *Astragalus* they would not touch the plant at all and after a few days could not be kept inside the fence." In our experience, near-acutely toxic seleniferous feedstuffs fed in confinement rapidly produce conditioned aversion in mammals and waterfowl.

"Alkali disease" (AD) in horses and cattle is characteristically manifested by alopecia and hoof dystrophy after prolonged consumption of non-accumulator plants (Olson, 1978). Most features of spontaneous AD have been reproduced by feeding either seleniferous vegetation or inorganic Se salts (Miller and Williams, 1940; Olson and Embry, 1973; James *et al.*, 1994; Raisbeck *et al.*, 1995). While not as prevalent as previously claimed, this condition occurs with some regularity and can be economically very important in localized areas (Raisbeck *et al.*, 1993).

"Blind staggers" (BS) purportedly results from ingestion of Se-accumulating weeds (Beath, 1982) and presents as blindness, circling, headpressing, dysphagia and paralysis. There are only two original reports of BS (Draize and Beath, 1935; Rosenfeld and Beath, 1946). There are no well-documented reports of BS resulting

from controlled feeding experiments with either seleniferous plants or purified Se compounds. There is compelling evidence to question whether BS was actually related to Se (O'Toole *et al.*, 1996) yet the myth of massive mortalities seems permanently fixed in both the scientific and popular literature (Anonymous, 1991).

Much of the early dogma does not agree with the experience of ranchers and veterinarians in this area. Critical re-evaluation of Se toxicity in grazing livestock and wildlife was begun in 1989.

Controlled Feeding Studies

Purified selenium compounds in cattle

Most experimental data regarding selenosis in grazing animals was derived from inorganic Se salts (Miller and Williams, 1940; Glenn *et al.*, 1964; Olson and Embry, 1973) whereas the predominant form in palatable vegetation is thought to be selenomethionine (Olson, 1978). Knowledge of the chronic toxicity of the latter in ruminants is scant, but there is evidence in other species (Heinz *et al.*, 1988) that it differs quantitatively and qualitatively from inorganic Se salts. The toxic effects of L-selenomethionine (SEMET) and Na_2SeO_3 were compared in cattle.

Details of trial diets and animals are in Chapter 53. Steers were observed daily for signs of illness; blood was collected at 21d intervals for CBC, clinical pathology and Se determination by a fluorometric method (Raisbeck *et al.*, 1996). At termination of the trial, steers were euthanized and tissues taken for Se analysis.

Both principles and controls gained weight and appeared clinically healthy throughout the 120d feeding study. Controls gained slightly but non-significantly more than steers receiving 25ppm Se as Na_2SeO_3 at 84, 105 and 120d. There were no abnormalities attributable to Se in blood urea nitrogen, serum creatinine, creatinine kinase, alkaline phosphatase, aspartate aminotransferase, bilirubin, glucose, albumin, total protein, blood hemoglobin, or CBC. In contradiction to early reports (Franke and Potter, 1934; Draize and Beath, 1935), there were no changes in the erythron that might indicate anemia.

Plasma Se concentrations increased more rapidly and were generally more labile than blood Se levels (Fig. 77.1). This suggests that whole blood is a better index of long-term Se status than plasma or serum in mammals. Blood Se concentrations plateaued between 60-80d. Blood glutathione peroxidase was non-significantly *decreased* in steers receiving 0.8mg/kg Se as Na_2SeO_3 . Significantly higher blood Se concentrations resulted from SEMET than from corresponding dosages of NaSeO_3 . Tissue Se concentrations, with the exception of liver, were also significantly greater in the SEMET group than the SeO_3^- group (Fig 77.2).

One steer that received 0.8mg/kg Se as SEMET had grossly visible semicircular ridges and grooves parallel to the coronary band at necropsy. Both steers fed 0.08mg/kg, 1/2 steers fed 0.28 Se/kg as SEMET and 1/2 steers fed 0.8 mg Se/kg as

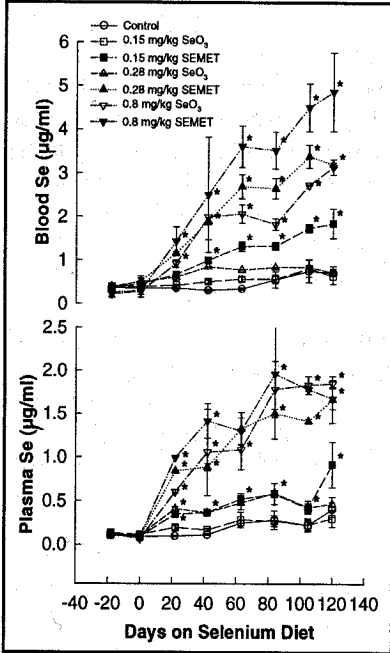


Fig. 77.1. Blood and plasma Se concentrations in steers fed three dosages of Na₂SeO₃ or SEMET. Asterisks denote significantly greater than controls ($P < 0.05$).

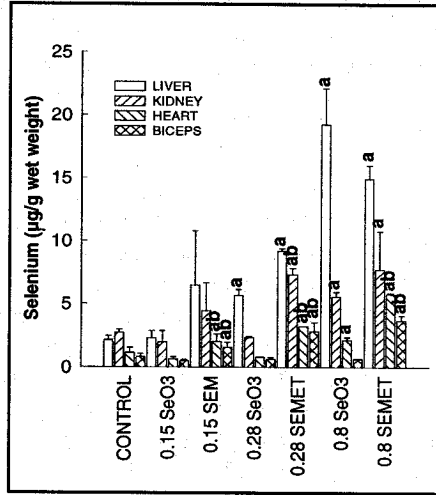


Fig. 77.2. Tissue concentrations in steers fed Na₂SeO₃ or SEMET. **a** indicates significantly different than controls, **b** greater than the corresponding Na₂SeO₃ group ($P < 0.05$).

Na₂SeO₃ had histologic lesions of dyskeratosis similar to those described in Chapter 76. Selenium deposition in hooves from these steers and from field cases with AD show a distinct morphologic relationship to necrotic lesions (Fig. 77.3) and varied by more than 10x. This is consistent with Se deposition in the hoof as keratin is formed.

A steer given 0.8mg Se/kg/d as SEMET *via* gelatin capsules for 4mos developed higher blood Se levels (≈ 7 ppm) than steers fed a similar amount in their daily ration (≈ 4.5 ppm), and his blood glutathione peroxidase activity declined precipitously from over 1,000 to 280mM/s/L just at the onset of clinical signs.

Antelope

It has been proposed that grazing species native to the Great Plains are genetically resistant to selenosis (Beath, 1982). Four pronghorn antelope fed a 15ppm Se diet prepared from seleniferous hay for more than 150d did not develop any clinical, morphologic or biochemical changes attributable to Se. The Se-treated group gained less than controls, but this was attributed to feed refusal rather than a direct

Se-toxic effect. They did, however, exhibit significantly decreased primary antibody response to hen egg albumin (Raisbeck *et al.*, 1996).

Blood and tissue Se concentrations were roughly equivalent to those of steers fed 0.28mg Se/kg/d as Na₂SeO₃ or 0.15mg Se/kg/d as SEMET, and were greater than previously suggested to be diagnostic of selenosis in this species (Williams, 1982). This observation reinforces the contention that tissue concentrations alone are not definitive evidence of selenosis (O'Toole and Raisbeck, 1997).

Cattle

To correlate biomarkers of experimental selenosis with naturally seleniferous hay, twelve 2yr-old steers were divided into three groups and housed in concrete pens. After a 60d acclimation period on normal hay, each group was fed a ration ground from seleniferous and non-seleniferous grass hay containing 3.33, 5.00 or 6.66ppm Se and balanced with corn and cottonseed meal to be isocaloric and isonitrogenous for 167d. Blood Se concentrations increased in a dose-related manner in all groups, and plateaued at 0.5, 0.8 and 1.4ppm, respectively. There were no significant differences in rate of gain between groups, nor did any steers exhibit clinical evidence of disease. Regression of blood concentration vs. dietary concentration yielded [blood]=0.2701*[hay]-0.449.

Field Study

To validate the experimental feeding trials under field conditions, four grazing sites were selected to represent the spectrum of Se concentrations available in eastern Wyoming and western Nebraska (Raisbeck *et al.*, 1997). Two (A and B) were mine reclamation projects suspected to be marginally high in Se. One (E) was a semi-improved pasture with a history of AD. The last (D) was known to contain merely adequate Se and served as a control. None contained any indicator plant species and all contained a few facultative accumulator specimens. Dietary botanical composition was determined by observing eating habits for 4hrs in the morning and evening at semi-monthly intervals. Representative 500g samples of grazed vegetation were collected onto dry ice at monthly intervals and frozen at -70°C until analyzed. Selenium concentrations were averaged by plant species, collection date and site (species mean). Selenium intake (dietary mean) was calculated from species means on the basis of the percentage of each plant species consumed.

Previous reports indicate that forage Se peaks in late spring. In this study Se concentrations peaked later in the growing season, typically in August. This discrepancy may be due to the fact that our samples were deliberately biased toward what cattle consumed rather than randomized to represent the biomass, or it may reflect site-specific differences in botany and geology between South Dakota and Wyoming. Possibly as a result of unusually lush growing conditions, the highest dietary mean Se concentrations were less than 1.0ppm at all sites except E, which

reached nearly 8.0ppm. None of the cattle at any site developed overt signs of selenosis. Sites A, B and E each had individual forage samples that exceeded 2.0ppm, but only on site E did species mean concentrations exceed 2.0ppm. At the latter, several species mean concentrations approached 10ppm, and individual samples often exceeded 20ppm. Blood Se concentrations remained below 0.5ppm except at site E, where blood Se peaked at slightly more than 2.0ppm and showed much greater variability than in the other groups (Fig. 77.4). Regression of dietary forage concentrations against blood concentrations yielded a similar slope but lower constant ($[\text{blood}] = 0.2816 * [\text{grass}] + 0.0871$) than steers fed seleniferous hay.

Summary

The most distinctive *chronic* toxic effect of Se in large ruminants is dyskeratosis, manifested as a particular pattern of hair loss and hoof dysplasia ("alkali disease") (Chapter 76). Decreased primary antibody response (Chapter 53) is not sufficiently specific to be diagnostically useful. This group has not recognized the syndrome termed BS or identified any lesions that might cause blindness and neurologic derangement in any animal fed any form of Se experimentally. In more than 40 field investigations since 1989, selenosis as an etiologic factor in any putative cases of BS has not been confirmed. As suggested by James *et al.* (1994) and Raisbeck *et al.* (1993), the most common etiologies of BS in seleniferous areas of the Great Plains are sulfur-induced polioencephalomalacia and lead poisoning.

Many summaries of early selenosis research describe infertility as a subclinical

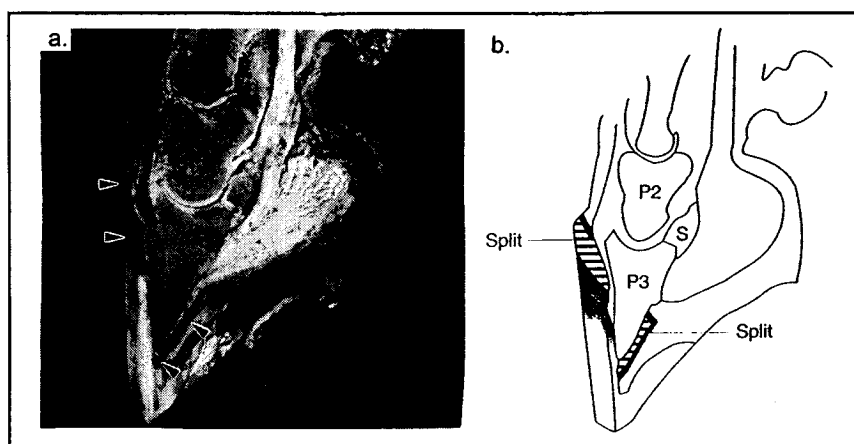


Fig. 77.3. a. Hoof from horse with alkali disease. Note crack in wall (▶). b. Schematic of same hoof. Note variation in Se concentration. Highest concentrations (darkest shading) correspond with defects (hatched) in hoof wall and in sole.

but major source of economic loss in "alkalied" livestock (Beath, 1982). Experimental studies in lab animals (Willhite, 1993), sheep (Panter *et al.*, 1995), cattle (Yeager, 1995) and non-human primates only produced infertility at maternally toxic doses. Veterinarians involved with early selenosis investigations hypothesized that the reported infertility was secondary to the crippling effects of selenosis and starvation (Tucker, 1996). A limited number of studies of ranches with histories of both reproductive failure and AD have revealed animals that were extremely Cu deficient as well as extremely high in Se. Intervention with Cu supplementation for 2yrs on one such premise increased pregnancy rates from less than 80% to nearly 100%. Given the geologic co-occurrence of Se and S in the Great Plains, it is possible that infertility attributed to Se by early studies was confused by S-induced Cu deficiency. Controlled experiments are needed to test this hypothesis.

Although ruminants are capable of synthesizing SEMET from toxic concentrations of SeO_3^- (Raisbeck and Belden, unpublished), dietary SEMET produced markedly higher tissue Se concentrations in ruminants than did Na_2SeO_3 . This is presumably a result of nonspecific substitution for methionine in protein. These results suggest that Se from forages accumulates in a fashion more similar to SEMET than SeO_3^- at normal to low-toxic dietary concentrations. Selenomethionine is less cytotoxic than SeO_3^- (Spallholz, 1994) but must be metabolized to a reactive form to cause cell death. Although AD has been produced with inorganic Se salts, it was most likely the result of prolonged exposure to seleniferous forages or SEMET. Conversely, acutely lethal lesions such as myocardial necrosis are more likely due to exposure to inorganic salts or accumulator plants. Possibly, this is because the relatively low toxicity of the former permits Se to accumulate to locally toxic concentrations in keratinized tissues without first triggering feed aversion, severe illness and anorexia or death.

Acknowledgments

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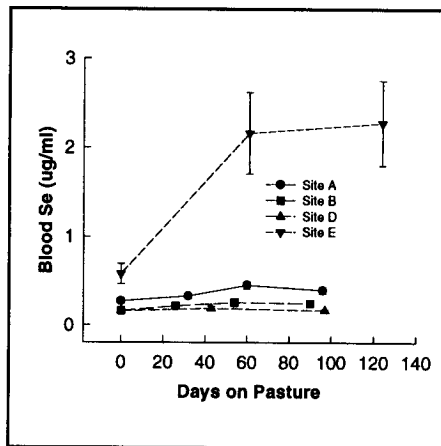


Fig. 77.4. Blood Se concentrations (mean \pm sd) in cattle grazing pastures with varying Se concentrations. Site E is significantly greater ($P < 0.05$) at all times.

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