Mineral imbalance and ruminant health

A field study in the Netherlands

At a time when there is mounting biochemical evidence for the essential nature of correct trace-element balance to neuronal activity and resistance to neurodegenerative disease there is a paucity of research on how trace element dietary status effects livestock animals. With threats like TSEs fully in public view it is astounding that the care of animals and how their diet might expose them to such neurodegenerative and possibly transmissible diseases is largely ignored. While genetic status of an animal is an important consideration in this molecular age, it remains a fact that the phenotype of an animal is what is important and diet remain the single most critical regulator, aside from genetic information, that determines what that phenotype will be. On this background, Betty Stikkers' experiments on the role of trace-elements in sheep health are likely to provide interesting and important information. As these experiments are supported by a panel of international and experienced research scientists and it is important that these experiments continue.
*Dr. David R. Brown**

The sudden death of 3 Shetland sheep with neurological disorders en the death of 2 Shetland sheep with scrapie is the reason we have started this study.
The neurological disorders were linked to acute Cu def and in our search for a solution we came in contact with Dr. Stewart Telfer from Leeds University in the UK.
It has long been known that molybdenum is involved in copper deficiency but it is now becoming clear that, when combined with sulphur, it actually causes the symptoms which we call copper deficiency. When molybdenum and sulphur are present in the rumen the bacteria combine them to form thiomolybdates (MoSn). These compounds must combine with copper and once they have done so the copper present in copper-thiomolybdate is no longer available to the animal.
If thiomolybdate does not find copper in the rumen it passes through into the blood and tissues where it seeks out the most available forms of copper and in attaching to it makes it unavailable to the animal. Once it has taken out all of the amino acid copper present in the plasma it next comes to the copper metallo-enzymes and when it extracts the copper from these it stops them from working. The animal continues to produce the enzymes but as quickly as it does so thiomolybdate moves in to deactivate them. It is this deactivation of copper enzymes that causes the clinical symptoms of copper deficiency not the lack of copper. So even when an animal has adequate levels of total copper it can still show symptoms, which we know as copper deficiency, including infertility, poor coat, and (in sheep and deer) swayback.

Autopsy of the scrapie sheep learned that brains were totally deteriorated.
Inquiry learned that the 2 animals were not protected against Cu def and they ate ¾ of a salt lick in just 6 month time. Analyses of the lick learned that the animals consumed a total of 82.500 mg manganese in this period. The lick contained 11.000 mg of manganese per kilo. The animals showed neurological disorders, were wasting and apathetic.

In collaboration with scientists from England, Sweden and Finland we started this study to elucidate the effects of manganese supplementation.
All fodder and mineral products were to be analysed before feeding and only normal available products were to be used.

Analyses of mineral supplements, salt lick and hay

Al analyses are showing a different content as labelled.
Salt lick did not contain 7500 mg, manganese per kilo but 9.263 mg and 16.327 mg per kilo.
The mineral bucket did not contain 900 mg manganese but 1.319; not 400 mg of iron but 994 mg.
This bucket also contains 3.315 mg of sulphur, not labelled.
Hay of 2003 contained 1.301 mg. of iron against 386 mg in 2004.

Groups

There are 3 groups of animals, all the same age. Group 1 and 2 had the same father and were until the start of this study never protected from Cu def. Group 3 have had some protection as lamb or at the age of 6 month. At the start of the experiment the animals were 10 month old.
(to prevent Cu. def. the animals are given a glass bolus with copper, cobalt and selenium)

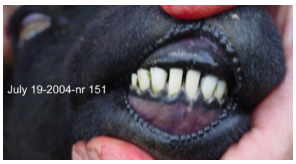
Group 2 received a bolus 2 month after the start of the study.

So far the study has provided us with the following information:

	Group 1 deficiënt	Group 2 not deficient	Control group
Weight at beginning of study	15,7 kg average	15,75 kg average	25,5 kg average
Weight after 1,5 year	30,25 kg average	40 kg average	39,25 kg average
Increase in weight	91,25%	142,5%	54,35%
Use salt lick in 1,5 year	6 kg	0,5 kg	

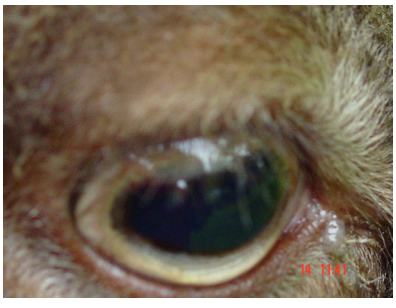
We noticed that the deficient group is consuming the lick frequently (daily) the non def. group is not.

- The development of the teeth is interesting, animals that were protected for Cu def as young lamb, 3 month (2 animals) are having a normal set of teeth, the rest is degenerated.



- The lack of muscles in the deficient group is significant

- As the experiment progressed we noticed striking changes.
  For instance, when we fed hay with high levels of iron and manganese we noticed that the animals displayed rapid movements with their tongues over their lips causing slight salivation, they didn't drink much water in spite of the hay, they have a stiff gait and seem depressed and quite lethargic. When changing fodder and reducing iron levels they showed different behaviour. Note, not the stiff gait.
  Also very interesting to see was the miosis in the sheep. Miosis is a constriction of the pupil of the eye, resulting from a normal response to an increase in light or caused by certain drugs or pathological conditions.



Interesting detail: Mn levels in scrapie blood is elevated, we see elevated Mn levels in blood of Cu def. sheep in de sheep.

Betty Stikkers
b.stikkers@shetlandsheep.nl

**Dr. David Brown is professor in Biochemistry at the University of Bath and a member of the Spongiform Encephalopathy Advisory Committee, SEAC, that advises the UK government on issues to do with BSE and variant CJD.*

References:

1.Discuss a re-evaluation of the TSE enigma and explore the role of environmental factors in prion diseases
Susan Haywood and David R. Brown.
Veterinary Times Jan 27 2003

2.Myocardial cytochrome c oxidase activity in Swedish Moose (Alces alces .L) affected by molybdenosis
Frank A, Wibom R, DanielssonR
Sci Total Environment 2002 ;121-129

3.Feed consumption and weight development in Experimental copper and chromium deficiency and additional molybdenum supplementation in goats.
Frank A, Anke M, Danielsson R.
Sci Total Environ 2000;249:133-142.

4.Experimental copper and chromium deficiency and additional molybdenum supplementation in goats. II. Concentrations of trace and minor elements in liver, kidneys and ribs, haematology and clinical chemistry.
Frank A, Danielsson R, Jones B.
Sci Total Environ 2000;249:143-170.

5.The mysterious disease in Swedish moose. Concentrations of trace and minor elements in liver, kidneys and ribs, haematology and clinical chemistry. Comparison with experimental molybdenosis and copper deficiency in the goat.
Frank A, Danielsson R, Jones B.
Sci Total Environ 2000;249:107-122.

6.Molybdenosis leading to type 2 diabetes mellitus in Swedish moose.
Frank A.
In: Skinner HCW, Berger AR editors. Geology and Health: Closing the Gap. New York, Oxford: Oxford University Press 2003;79-81.

7.Molybdenum-associated Pituitary Endocrinopathy in Sheep Treated with Ammonium Tetrathiomolybdate.
Haywood S, Dincer Z, Jasani B, Loughran MJ.
J Comp Pathol 2004;130:21–31.

8. Normal prion protein has an activity like that of superoxide dismutase
Brown DR, Wong BS, Hafiz F, Clive C, Haswell SJ, Jones IM
Biochem J 1999 Nov 15;344(Pt 1):1-5

9. A Case for the Role of Copper Deficiency in "Mad-Cow Disease and Human Creutsfeldt-Jakob Disease.
William H. Dresher, Ph.D., P.E.,Geoffrey Greetham, Ph.D., F.I.M. and Brenda J. Harrison, Ph.D.
Innovations CDA December 2001

10.Copper Converts the Cellular Prion Protein into a Protease resistant Species That Is Distinct from the Scrapie Isoform*
Received for publication, October 23, 2000, and in revised form, November 29, 2000
Published, JBC Papers in Press, January 18, 2001, DOI 10.1074/jbc.M009666200
Elena Quaglio, Roberto Chiesa, and David A.Harris
From the Department of Cell Biology and Physiology, Washington University School of Medicine, St.Louis, Missouri 63110

11.Consequenses of manganese replacement of copper for prion protein function and proteinase resistance
David R. Brown, Farida Hafiz, Leslie L. Glasssmith, Boon-Seng Wong, Ian M. Jones, Christine Clive and Stephen J. Haswell.
The EMBO Journal Vol. 19 no 6 pp. 1180-1186 2000

12. Copper deficiency or molybdenum toxicity? Diagnosis and treatment requires a new perspective.
Telfer S.B. Kendall N.R., Illingworth D.V., Mackenzie A.M.

13. Metal imbalance and compromised antioxidant function are early changes in prion disease.
Alana M. Thackray, Robert Knight, Stephen J. Haswell, Raymond Bujdoso and David R. Brown
Biochem J (2002) 253-258