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Ovine White-Liver Disease (OWLD). Trace Elements in Liver

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Ulvund, M. J.: Ovine white-liver disease (OWLD). Trace elements in liver. Acta vet. scand. 1990, 31, 297–307. – Trace elements in liver were examined in vitamin B_{12} deficient lambs which developed ovine white-liver disease (OWLD), in cobalt/vitamin B_{12} supplemented lambs on the same pastures as well as clinically healthy, but sometimes subclinical B_{12} deficient lambs on other pastures (H). Liver Co was marginal to deficient in both OWLD lambs (S lambs) and H lambs. Supplementation with B_{12} or Co elevated liver Co. Liver copper was significantly lower in OWLD lambs than in the H lambs, and Co/B_{12} supplementation on pasture generally had no significant effect on the contents. Dosing lambs on OWLD pastures with copper oxide needles (SCuO), however, resulted in high/toxic liver Cu. Dosing with Co, Se and Cu glass boluses resulted in adequate liver Cu, except for 1 lamb with toxic amounts indicating dissolution and absorption of the bolus. OWLD lambs had significantly lower liver molybdenum than H lambs, and Co/B_{12} supplementation elevated values, while CuO treatment depressed them. Liver zinc, manganese and selenium are also reported.

sheep; cobalt/vitamin B_{12} deficiency; trace element interferences; copper.

Introduction

An interaction between cobalt and copper has been detected in ovine white-liver disease (OWLD). Although the Cu content in OWLD pasture grass was poor (*Ulvund & Pestalozzi* 1990b), Cu supplementation or Cu treatment of already affected lambs worsened the OWLD condition (*Ulvund* 1990c, d). Serum Cu was generally higher in OWLD lambs than in cobalt/vitamin B_{12} supplemented lambs grazing the same pastures, and B_{12} treatment of affected lambs lowered Cu values (*Ulvund* 1990c, d). Subclinically B_{12} deficient lambs on other pastures (H) also had higher serum Cu than Co/B_{12} supplemented controls on these pastures.

There are few earlier reports on trace elements in the liver of OWLD lambs. Deficient liver Co values were found by *Richards & Harrison* (1981) and *Mitchell et al.* (1982). The same authors found normal liver Cu, while *Mason & McKay* (1983) reported low liver Cu in OWLD lambs.

The fact that B_{12} deficient lambs on some pastures develop OWLD while on other pastures they do not, together with the indication that Cu or other elements may be involved in the OWLD pathogenesis, necessitated the examination of trace elements in the livers of these lambs.

Materials and methods

Liver samples were collected from vitamin B_{12} deficient lambs which developed ovine white-liver disease (OWLD, S lambs), from lambs supplemented with cobalt, B_{12}, selenium or copper on the same pastures (SCo, SCo+, SB_{12}, SCopell, SCoSeCu, SSe lambs), and from clinically healthy, but sometimes

subclinically B_{12} deficient lambs on other pastures (H lambs). Survey and experimental design has been given earlier (*Ulvund & Pestalozzi* 1990a, *Ulvund* 1990a,d). Group symbols are explained in Tables 3–5.

Altogether 89 livers from 3 years of experiments (1982, 1984, 1985) were examined. During all years, liver samples were taken at slaughter at the end of the grazing period in September/October. One year (1982), single lambs from various groups were killed at regular intervals throughout the grazing season, and the livers were examined. The liver samples were frozen (÷ 20°C) within 2 h after slaughter/killing and forwarded to the performing laboratory.

The samples were examined by the following governmental laboratories: The Chemical Research Laboratory (CRL, Agricultural College of Norway, Ås-NLH), The National Veterinary Institute (NVI, Veterinærinstituttet, Oslo), and the National Veterinary Institute (SVA, Statens Veterinärmedicinska Anstalt, Uppsala, Sweden), as shown in Table 1.

Flameless atomic absorption spectrophotometry (AAS, grafite oven) was used by CRL to determine Co and Cu, Mn was determined by flame AAS, Mo by spectrophotometry, and total sulphur by spectrophotometric determination of turbidity ($BaSO_4$-suspension, *Halvorsen* 1989). NVI-Oslo used flame AAS for the determination of Cu and Zn, flameless AAS for the determination of Mo, and a fluorimetric or a hydride generator method for the determination of Se (*Norheim* 1989). At SVA-Uppsala, preparation and examination of the samples were performed according to *Frank* (1976) and *Frank & Petersson* (1983) using simultaneous multi-element analysis in a d. c. plasma-atomic emission spectrometer apparatus. The accuracy of the analytical values was checked by referring to certified values of elements in the National Bureau of Standards (NBS) Standard Reference Material, bovine liver SRM 1577. Blind parallels were included and the divergence in results as within acceptable limits.

Liver content of trace elements is sometimes given on dry weight basis (dw), sometimes on wet weight basis (ww). In comparing results given on different scales, an average of 30 % dry matter in the liver was used as recommended by others (*Frøslie* 1977).

Table 1. Chemical examination of liver samples from lambs stratified by year and date of slaughter, variables examined, and performing laboratory.

Year	Date of slaughter	Number of lambs	Variables	Performing laboratory
1982	Var.*	16	Co, Cu, Mo, Mn, total sulphur	CRL, Ås-NLH
1982	Oct. 11	22	Co, Cu, Mo, Mn, total sulphur	CRL, Ås-NLH
1984	Sept. 26	24	Co	SVA-Uppsala
1984	Sept. 26	24	Cu, Mo, Zn, Se	NVI-Oslo
1985	Oct. 8	27	Co, Cu, Fe, Mn, Zn	SVA-Uppsala
1985	Oct. 8	27	Se	NVI-Oslo

* Different dates of slaughter throughout the experimental period 1982.

Table 2. Liver Co, Cu, Mo, and Mn (mg/kg wet weight) in individual lambs slaughtered in 1982. The lambs were grazing OWLD pastures (S) or pastures where lambs have been growing well (H).

		Time slaughtered						
	Group	May 24	June 4	June 11	July 7	July 13	Aug. 11	Oct. 7
Co	S	0.014	0.028	<0.010	0.010	<0.010	0.011	0.021
	SB_{12}	0.038	0.057	0.039	–	0.059	0.045	–
	H	<0.010	0.013	0.021	–	–	0.022	–
Cu	S	23	15	12	4.6	8.9	5.6	3.6
	SB_{12}	47	7.5	10	–	2.8	2.7	–
	H	36	19	16	–	–	5.2	–
Mo	S	0.89	0.86	0.27	0.44	0.22	0.17	0.40
	SB_{12}	0.58	1.01	0.82	–	0.93	0.71	–
	H	0.94	0.33	0.79	–	–	1.09	–
Mn	S	3.5	2.9	3.1	3.3	4.8	2.5	4.1
	SB_{12}	2.9	2.9	3.1	–	2.1	1.7	–
	H	4.9	4.8	3.1	–	–	2.4	–

SB_{12}: Lambs grazing OWLD pastures, injected fortnightly with hydroxocobalamin (2 mg).

Localization of pellets in the forestomacs of dosed lambs was verified at slaughter.

Results

At the end of grazing, mean liver Co was below 0.025 mg/kg ww in both the unsupplemented S lambs (OWLD lambs) and the H lambs (Tables 3–5), and values were similarly low already from May (Table 2). Regular B_{12} injections of S lambs (SB_{12}) elevated liver Co throughout grazing (Table 2), and at slaughter these lambs had significantly higher liver Co than the S lambs ($p < 0.05$, Tables 3–5). Co supplementation (SCo, SCo+, SCopell) also elevated liver Co (Tables 3–5), as did dosing with CoSeCure pellets (Table 5), and Se dosing ($p < 0.025$, Table 5). The livers of the CuO dosed lambs were further depleted of Co ($p < 0.05$, Table 4).

Liver Cu is shown in Tables 2–5. Liver Cu was generally lower in S lambs than in H lambs. Values decreased evenly in all lambs already from pasture outlet in May (Table 2). At the end of grazing, the difference between the H and S lambs was significant ($p < 0.05$) in 1982 and 1985. Regular B_{12} injections or Co supplementation of S lambs had no significant effect on liver Cu.

Dosing 1 month old S lambs with CuO at pasture outlet resulted in toxic amounts of Cu in the liver at slaughter 4 months later (Table 4). CuO treatment of 2 lambs, 4–5 months old, affected with OWLD (*Ulvund* 1990d) resulted in elevation of liver Cu at slaughter 5 weeks later (Table 3). Dosing with CoSeCure elevated liver Cu to a smaller extent (Table 5). Se pellets seemed to have no effect on liver Cu.

Liver Mo is shown in Tables 2–4. The S lambs had the lowest means, and Co/B_{12} supplementation most often elevated the values. The difference between all values of the unsupplemented S lambs and the values of the SCo/SB_{12} lambs was significant ($p <$

Table 3. Liver Co, Cu, Mo, and Mn (mg/kg wet weight, mean ± sd) in lambs slaughtered on Oct. 11, 1982, and which had been grazing OWLD pastures (S) or pastures where lambs grew well (H). Three affected lambs were picked on Sept. 6 for treatment trials with copper and vitamin B_{12}.

Group	n	Co	Cu	Mo	Mn
S	2	0.024±0.002	2.9±0.1	0.38±0.01	4.3±1.0
S-CuO	1	0.039	96	0.17	4.1
S-CuO&B_{12}	1	0.022	74	1.14	2.7
S-B_{12}	1	0.030	1.6	0.71	3.5
SCo	6	0.081±0.025	3.5±1.2	0.66±0.19	4.0±0.5
SB_{12}	7	0.070±0.025	4.5±2.0	0.89±0.13	3.3±0.6
H	4	0.021±0.012	13±6.5	0.96±0.13	3.1

S : Lambs grazing OWLD pastures (OWLD lambs).
S-CuO : S lamb dosed (Sept. 6) with copper oxide needles (2 g).
S-CuO&B_{12} : S lamb dosed (Sept. 6) with CuO and vitamin B_{12} (2 mg).
S-SB_{12} : S lamb dosed (Sept. 6) with B_{12}.
SCo : Lambs grazing OWLD pastures fertilized with Co.
SB_{12} : Lambs on OWLD pastures injected fortnightly with B_{12}.
H : Lambs growing well on other pastures.
n = number of lambs examined.

0.001). CuO treatment significantly depressed liver Mo (Tables 3–4, $p < 0.05$). The highest liver Mo was found in the H lambs. The difference between the H and unsupplemented S lambs was significant ($p < 0.05$) in 1982 and 1984.

Liver Zn is given in Tables 4–5. There was a tendency that S lambs had lower liver Zn than H lambs ($p < 0.001$ in 1985), and that B_{12} or Co treatment elevated values, while CuO treatment depressed them. The difference between the S and SCuO groups was significant ($p < 0.025$).

Liver Mn is given in Tables 2, 3 and 5. In

Table 4. Liver Co, Cu, Mo, and Zn (mg/kg ww) in lambs from various groups slaughtered on Sept. 26 1984. Four lambs were examined in each group (n = 4). Mean values ± sd are given.

Group	Co	Cu	Mo	Zn
S	0.021±0.010	14±5.4	0.87±0.42	38±9
SCo	0.026±0.007	6.2± 1.4	1.25±0.20	48±4
SB_{12}	0.066±0.010	10±4.3	0.96±0.23	40±4
SCopell	0.058±0.007	6.1±2.3	1.19±0.29	43±4
SCuO	0.006±0.002	250±46	0.40±0.07	22±3
H	0.024±0.009	21±11	1.42±0.12	43±4

SCopell: Lambs dosed with cobalt pellets on June 25.
SCuO : Lambs dosed with copper oxide needles on May 15.
SB_{12} : Lambs injected every third week with B_{12}.
For group symbols, see also Table 5.

Table 5. Liver Co, Cu, Fe, Zn and Mn (mg/kg ww, mean ± sd) in lambs from various groups, slaughtered Oct. 8 1985. Four lambs were examined in each group (n = 4), except in the SCo and SCoSeCu groups where n = 3.

Group	Co	Cu	Fe	Zn	Mn
S	0.013±0.004	4.2±0.6	236±18	36±5	3.0±0.5
SCo	0.043±0.011	7.3±3.2	171±39	40±4	3.0±0.4
SCo+	0.048±0.006	8.6±1.3	128±23	43±7	3.1±0.6
SCoSeCu	0.051±0.013	17±9.8	148±39	42±11	3.0±0.2
SSe	0.021±0.002	7.7±5.0	265±86	40±7	2.9±0.3
SB_{12}	0.077±0.010	6.7±3.1	242±36	43±3	2.8±0.3
H	0.009±0.006	18±11	119±17	47±3	4.0±0.5

S : Lambs grazing OWLD pastures.
SCo : Lambs grazing OWLD pastures fertilized with Co ($CoSO_4$, 1 kg/ha) in 1980, 1981 and 1982.
SCo+ : Lambs grazing OWLD pastures fertilized with Co (1 kg/ha) in 1980–1982, 1984 and 1985.
SCoSeCu : Lambs grazing OWLD pastures, dosed with cobalt-selenium-copper glass boluses on July 1.
SSe : Lambs grazing OWLD pastures, dosed with selenium pellets on July 1.
SB_{12} : Lambs grazing OWLD pastures, treated every third week with 2 mg hydroxocobalamin.
H : Lambs growing well on other pastures.

1985, liver Mn was significantly lower in the S lambs than in the H lambs ($p < 0.05$, Table 5), but this was not the case in 1982. Liver Fe is shown in Table 5. The S lambs had higher levels at slaughter than the H lambs ($p < 0.001$). Co supplementation reduced liver Fe ($p < 0.005$), while Se and B_{12} dosing did not.

Mean liver Se was between 0.12 and 0.16 mg/kg ww in all groups, except in the Se treated groups (SSe, SCoSeCu), where mean values were 0.46 and 0.25 mg/kg respectively. There were no significant differences between the S and H lambs, the overall mean value for the H lambs was 0.09 mg/kg, while it was 0.10 mg/kg for the untreated S lambs.

Mean values of total liver sulphur varied between 0.18 mg/kg ww and 0.25, with no differences between the groups. At slaughter, mean values in all groups were between 0.21 and 0.25 mg/kg ww.

All pellets and boluses were recovered in the forestomacs at slaughter, with one exception, where no CoSeCure bolus could be found (*Ulvund* 1990c).

Discussion

Liver Co in healthy lambs is reported to be about 0.15 mg/kg dw (0.05 mg/kg ww, *Smith* 1987), or between 0.1 and 0.3 mg/kg dw (0.03–0.9 mg/kg ww, *Robertson* 1971). In addition to amounts of Co in the liver, values of vitamin B_{12} in liver and blood (*Suttle* 1986) and of methylmalonic acid (MMA) in blood (*McMurray et al.* 1985) are used to evaluate the Co status of sheep. In our case, the liver Co of all S, SSe and SCuO lambs were deficient, and correlated well

with the low plasma B_{12} and elevated MMA seen in these lambs (*Ulvund* 1990b, c).

On average, the H grass had slightly higher Co content than the S grass (NS), but some years the Co content in H grass was lower (*Ulvund & Pestalozzi* 1990b), and the H lambs were subclinically B_{12} deficient (*Ulvund* 1990b). In spite of these conditions, the H lambs on average grew 17 kg more than the S lambs on pasture (*Ulvund & Pestalozzi* 1990a). It was surprising, therefore, that the livers from the H lambs contained just as little Co as the livers from the S lambs. The liver Co values of the S and H lambs are in accordance with the amounts found by others in both OWLD (*Richards & Harrison* 1981, *Mitchell et al.* 1982) and Co deficiency (*Robertson* 1971, *Schwan et al.* 1987, *Smith* 1987). The supply of Co through pasture grass must have been too scarce to enable the fast growing H lambs to build up liver reserves. The better growth and lack of clinical symptoms in them as compared with the OWLD lambs, as well as the deficient liver Co in both, support the hypothesis that cofactors participate to promote fulminant OWLD.

The most effective way to enhance liver Co was regular B_{12} injections, but treatment with Co pellets, CoSeCu boluses, or Co fertilization of pasture was almost equally effective. In the lambs grazing Co fertilized pastures, values were highest in 1982 and 1985, when Co fertilization was done the same year.

Liver Cu varies with breed, age, and composition of the diet, and individual variation may be considerable (*Davis & Mertz* 1987). In Norway, optimal liver Cu is recognized to be about 50 mg/kg ww, values between 50 and 150 mg/kg reflect a moderate Cu overloading, values above 150 mg/kg may be sufficient to explain a Cu induced haemolytic crisis, and the lower marginal level for a Cu sufficiency is 10 mg/kg ww (*Frøslie* 1977, *Søli* 1980). *Caple & McDonald* (1983) report Cu deficiency at liver Cu below 10 mg/kg dw (3 mg/kg ww).

The low liver Cu content seen in both the Co/B_{12} supplemented and the unsupplemented S groups probably reflects the lower amounts in the OWLD pasture grass (*Ulvund & Pestalozzi* 1990b). According to *Frøslie* (1977), adult healthy sheep from Rogaland, where the experiments were carried out, had lower mean liver Cu and larger range in individual values than sheep from other areas, and 15 % of the liver samples at slaughter had below 10 mg Cu/kg ww. The higher serum Cu seen in the earlier phase of OWLD, associated with liver damage, may also have caused depletion of liver stores (*Ulvund* 1990a).

In 3 lambs with severe OWLD in Tasmania, *Mason & McKay* (1983) found low liver Cu (0.6–8 mg/kg ww), and they claimed that the presence of normal serum Cu in spite of low liver contents was a feature of OWLD. *Mitchell* (1979) and *Mitchell et al.* (1982) found mean liver Cu 1.5 mmol/kg ww in OWLD lambs, as compared to values above 0.8 mmol/kg for normal lambs in the area. The OWLD lambs, however, showed large individual variations (0.12–5.7 mmol/kg), which may reflect varying duration of disease. Lambs with OWLD may thus have normal liver Cu in the early phase of disease, but low amounts later.

A moderate hepatic damage as well as a moderate elevation of serum Cu was seen in H lambs with subclinical B_{12} deficiency (*Ulvund* 1990a, b). H grass contained significantly more Cu than S grass (*Ulvund & Pestalozzi* 1990b). Although mean liver Cu was higher in the H lambs, possibly reflecting the higher Cu intake, these lambs showed great individual variation, and several had values below 10 mg/kg ww. The low

values may represent some degree of hepatic loss.

In Swedish unthrifty lambs with reported Co and Cu deficiency, liver Cu was on average 13 mg/kg ww (*Schwan et al.* 1987). In weaners affected with coast disease, a concurrent deficiency of Co and Cu in Australia, *Marston et al.* (1938) found very low liver Cu (2–3 mg/kg ww), but no significant alteration in serum Cu. Treatment with Cu alone had no effect on the progress of the disease, whereas treatment with Co permitted growth in some, but a combination of Co and Cu was necessary for complete recovery. Dosing with CuO needles resulted in toxic amounts of liver Cu in all S lambs of both the Rygja and the Dala breeds. *Whitelaw et al.* (1983), who also dosed CuO needles (2 g) to lambs at 3–5 weeks of age, found that these lambs grew well and had adequate liver Cu at weaning (463 mg/kg dw, i.e. 139 mg/kg ww). In another examination, *Whitelaw et al.* (1982) dosed CuO needles (1 g) at 5 weeks of age, and these lambs had mean liver Cu 255 mg/kg dw (77 mg/kg ww) at weaning. No signs of toxicity were detected. *Suttle* (1987) reported Cu toxicity in 1 out of 4 ewes, which had received 20 g CuO particles, but none of those receiving smaller doses showed any signs of toxicity. The livers of our lambs dosed with Cu on OWLD pastures seemingly had increased affinity for Cu.

In lupinosis of sheep, which occurs on Cu deficient pastures, *Gardiner* (1966b) found elevated serum Cu, and liver Cu was increased when the sheep were Cu supplemented. Alkaloids in *Heliotropium europaeum* may also damage the liver in such a way that it retains Cu (*Seaman* 1987). The high liver Cu obtained after CuO dosing in our lambs indicated that they had a similar hepatic damage (*Ulvund* 1990e).

When Co and Se were dosed together with the Cu (SCoSeCu), liver Cu was lower. Values were also lower than those reported by others in dosing experiments. *Driver et al.* (1986) dosed CoSeCu glass boluses to 7 months old Cu deficient lambs, and found mean liver Cu between 211 and 136 mg/kg dw (63–41 mg/kg ww) in the dosed, as compared to 32 mg/kg dw (9.6 mg/kg ww) in the undosed, 5 months after dosing. *Allen et al.* (1984) also found higher liver Cu in lambs 3–7 months after dosing with Cu glass boluses, mean values in the treated and control groups were 108 and 56 mg/kg ww respectively.

Dissolution rate of the glass bullets vary (*Trengrove & Hudson* 1985), but complete dissolvement has not been described. The liver of the lamb which had no CoSeCure bullet at slaughter contained 307 mg Cu/kg ww, 0.05 mg Co/kg and 0.69 mg Se/kg. The values indicate dissolvement and absorbtion of the bullet, and increased affinity for Cu in the liver.

Cu retention in the liver is influenced by dietary Mo, Zn, Cd, Fe and Ca (*Davis & Mertz* 1987). OWLD grass had significantly lower Mo content than H grass (*Ulvund & Pestalozzi* 1990b). Normal liver Mo in sheep is often 2–4 mg/kg dw (0.6–1.2 mg/kg ww), and the content is not only influenced by the amount in the diet, but also by dietary sulphate (*Mills & Davis* 1987). As the sulphur content in the OWLD grass did not differ from the H grass (*Ulvund & Pestalozzi* 1990b), the low liver Mo found in the S lambs may reflect lower Mo intakes, and/or liver damage and leakage. Co/B_{12} supplementation of S lambs increased liver Mo to values which were similar to those found in the H lambs, and to values found in healthy lambs from eastern Norway (*Frøslie & Norheim* 1976), results indicating that prevention of liver damage enabled the liver to store more Mo.

Frøslie & Norheim (1976) found no difference in liver Mo between healthy lambs with low and high liver Cu respectively, but sheep dead of chronic Cu poisoning had lower liver Mo than sheep surviving the Cu accumulation, a pattern indicating that a decrease in liver Mo may occur in the terminal state of Cu poisoning. The results may indicate leakage from a damaged liver, and may thus be in accordance with the condition of our OWLD lambs.

Low intake of Mo favours the accumulation of Cu in the liver, and can lead to chronic Cu poisoning (*Søli* 1980, *Davis & Mertz* 1987, *Mills & Davis* 1987). The low Mo intake may therefore also be an important factor explaining the increased affinity for Cu in the liver of our lambs. *Spais et al.* 1966) found that Mo favoured the liver storage of Co, but that sulphate inhibited it. Low dietary Mo may therefore have favoured Co depletion as well as Cu accumulation.

The fact that increased Cu intake depresses liver Mo was clearly demonstrated in our SCuO lambs, as also reported by (*Spais et al.* 1966).

S grass had significantly lower Zn content than H grass (*Ulvund & Pestalozzi* 1990b), which probably explains the lower liver Zn values seen in the unsupplemented S lambs. All values were, however, within the range reported for normal lambs from eastern Norway (*Frøslie & Norheim* 1976). In Sweden, values about 30 mg/kg ww are normally found (*Schwan* 1987). Normal values of liver Zn in lambs in Western Australia were above 100 mg/kg ww, and 28 OWLD lambs had 133 mg/kg ww (*Richards & Harrison* 1981). A fall in serum Zn is indicative of Zn deficiency in lambs (*Suliman et al.* 1988). As serum Zn was normal in all our lambs (*Ulvund* 1990a), a Zn deficiency can probably be ruled out in the OWLD pathogenesis.

CuO treatment lowered liver Zn, which is in accordance with the Cu/Zn competitive mechanism (*Bremner et al.* 1976, *Søli* 1980). The interaction seen between Co and Zn, resulting in elevation of liver Zn after Co/B_{12} dosing, may indicate a certain degree of leakage of Zn from a damaged liver, and that prevention of this damage by Co/B_{12} increases liver retention of Zn as well.

S grass had significantly lower Mn contents than H grass (*Ulvund & Pestalozzi* 1990b), but this was not reflected in liver Mn contents. There is therefore reason to believe that the Mn was more easily absorbed or stored in the OWLD lambs. The lack of constant differences between S and H lambs regarding liver Mn, however, probably indicates that Mn plays no role in the etiology of OWLD. The values within all groups were regarded as normal, as liver Mn of healthy sheep is given to be 8–10 mg/kg dw (2.4–3 mg/kg ww, *Hurley & Keen* 1987).

S grass had significantly higher Fe contents than H grass (*Ulvund & Pestalozzi* 1990b), and the higher liver Fe found in the S lambs, may be due to higher intakes. The values may, however, also indicate a further similarity between OWLD and coast disease. In 12 weaners with coast disease, the liver on average contained about twice as much Fe (740 mg/kg ww) as normal sheep of the area (300 mg/kg ww, *Marston et al.* 1938). High liver Fe has also been found in pure Co deficiency (*Robertson* 1971). The lowered liver Fe seen in the SCo, SCo+ and SCoSeCu lambs, but not in the SB_{12} lambs, is probably due to the fact that high dietary intakes of Co may interfere with intestinal Fe absorption (*Morris* 1987).

Liver Se was judged to be adequate to marginal in our lambs (*Caple & McDonald* 1983, *Frøslie et al.* 1980). Results indicate that

OWLD had no effect on liver Se, which is in accordance with findings by *Richards & Harrison* (1981) and *Andrews et al.* (1964). Increased liver Se was found after dosing with Se pellets (*Andrews et al.* 1974). In our case, dosing with Se pellets was more effective in raising liver Se than dosing with CoSeCu glass boluses. Lack of effect of Se on liver Cu, as observed in the present study, was also reported by *Gardiner* (1966a). The slight increase of liver Co seen after Se dosing has not been reported by others, is difficult to explain, and is dealt with elsewhere (*Ulvund* 1990e).

Generally the OWLD livers contained increased lipid (*Ulvund* 1990e), and this may have affected the comparisons to some extent.

The lack of difference in liver Co between OWLD lambs and normally growing lambs on other pastures (H lambs) is intriguing, but correlates to some extent with earlier findings regarding plasma B_{12}, and further supports the hypothesis that cofactors are necessary for the fulminant development of OWLD. Based on liver Cu and Mo, a role of the Cu/Mo relationship in the OWLD pathogenesis can so far not be excluded.

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Sammendrag

Kvitleversjuke (kobolt/vitamin B_{12} mangel) hos lam. Sporstoffinnhold i leveren.

Sporstoffinnholdet i leveren ble undersøkt hos vitamin B_{12}-deficitte lam som utviklet kvitleversjuke (OWLD, S-lam), hos lam som gikk på de samme beitene men ble dosert med kobolt/-vitamin B_{12}, og hos klinisk friske som gikk på andre beiter, men som enkelte år var subklinisk B_{12} deficitte (H-lam). Koboltinnholdet i leveren var marginalt til deficitt både hos lam med kvitleversjuke (S) og H-lam. Behandling med vitamin B_{12} eller ekstra tilskud av kobolt økte innholdet av Co i leveren. Innholdet av kopper var signifikant lavere hos OWLD affiserte lam, og Co/B_{12} behandling av lam på disse beitene så ikke ut til å øke innholdet. Dosering med kopperoksydnåler resulterte i svært høye/toksiske nivå av Cu i leveren. Dosering med kobolt/selen/kopper glassboli resulterte i adekvat kopperinnhold, bortsett fra ett lam som hadde toksiske mengder, noe som tydet på oppløsning og absorbsjon av bolus. Lam med kvitleversjuke hadde signifikant lavere innhold av molybden i leveren enn H-lamma, og Co/B_{12} behandling resulterte i økning av innholdet, mens kopperbehandling førte til en senkning. Innholdet av sink, mangan og selen er også oppgitt.

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