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Ovine White-Liver Disease (OWLD). Changes in Blood Chemistry

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Ulvund, M.J.: Ovine white-liver disease (OWLD). Changes in blood chemistry. Acta vet. scand. 1990, 31, 277-286. – Changes in blood chemistry were examined in vitamin B_{12} deficient lambs which developed ovine white-liver disease (OWLD), and were compared with values of cobalt/B_{12} supplemented lambs on the same pastures, as well as clinically healthy, but sometimes B_{12} deficient, lambs on other pastures (H). In the OWLD group, signs of hepatic damage were seen concurrently with reduction in weight gain, or 1-3 weeks before, and comprised elevation of serum glutamate dehydrogenase (GLDH) and decrease of phospholipid and cholesterol. Drop of plasma glucose and elevation of γGT also came in the earlier phase of the disease. All other blood changes developed later, and were partly regarded as reflections of the inappetence or hepatic injury. The changes included a drop in packed cell volume (PCV) and mean corpuscular volume (MCV), elevation of serum iron, and reduction of total serum protein and urea. Generally Co/B_{12} supplementation prevented hepatic damage and normalized blood values. The clinically healthy H lambs also showed signs of hepatic damage, especially one year when they were B_{12} deficient, indicating that simple B_{12} deficiency causes a moderate liver damage as well. For diagnostic purposes, clinical pathology is recommended mainly on a flock basis.

sheep; cobalt/vitamin B_{12}.

Introduction

It has long been unclear whether ovine white-liver disease (OWLD) is a simple cobalt deficiency, or a hepatotoxic disease in Co/vitamin B_{12} deficient lambs *(Sutherland et al.* 1979, *Mitchell et al.* 1982). In Norway, OWLD occurred in Co/B_{12} deficient lambs, but Co/B_{12} deficient lambs on other pastures did not develop OWLD *(Ulvund* in press).

Signs of liver damage reflected in elevation of liver enzymes in the blood have been reported during the early phase of OWLD *(Sutherland et al.* 1979). However, in experimentally induced Co deficiency, signs of liver damage also appeared before drop in plasma glucose *(Mac Pherson et al.* 1976). Some authors have discussed the possibility of presence of hepatotoxins in the feed used in the experiments performed by *Mac Pherson et al. (Sutherland et al.* 1979), but later *Fell* (1981) and *Fell et al.* (1985) also reported hepatic damage in sheep fed Co deficient diet.

There are few reports on changes in blood chemistry in lambs which develop OWLD as well as in lambs with simple Co deficiency. It was therefore of importance to examine OWLD lambs, lambs with simple B_{12} deficiency on other pastures, as well as Co/B_{12} supplemented lambs on either pastures regarding blood chemistry.

Materials and methods

The materials comprised 458 twin lambs of the Dala and Rygja breeds with the overall distribution of haemoglobin (Hb) phenoty-

pes: HbA 60%, HbAB 30%, HbB 10%. Survey of pastures and lamb groups is given *(Ulvund & Pestalozzi* 1990). Pasture outlet varied between May 10 and 20, when the lambs were about 1 month old. Blood was sampled at outlet, and at intervals of 3-4 weeks until the end of the experimental period in September/October. Lamb groups, number of lambs sampled within each group, and variables examined are given in Table 1. Data on serum Cu, plasma methyl malonic acid (MMA) and vitamin B_{12} are reported elsewhere *(Ulvund* 1990a, b).

Packed cell volume (PCV) was in 1983-1986 determined by centrifugation at 12,000 xG for 10 minutes in a Cellocrit 2 microhaematocrit centrifuge (AB L. Ljungberg & Co, Stockholm). Otherwise, PCV, number of red and white blood cells (RBC, WBC) and mean corpuscular volume (MCV) were estimated with a Coulter counter (model ZF with Ht-unit, Coulter Electronics, England),

Table 1. Number of lambs blood sampled within each group every year, and variables examined. In addition, PCV and plasma glucose were examined in all samples.

Year	Number of lambs sampled within each group		Parameters examined
1981	6 S	6 SCo	RBC, MCV, WBC, Hb, tot.serum prot.,
	6 SCoSO4	6 SB_{12}	Fe, SDH, γGT
1982	6 S	6 SB_{12}	RBC, MCV, WBC, Hb, tot.serum prot.,
	4 SCo		phospholipids, cholesterol, urea, Fe, Zn, γGT, GLDH, bilirubin
1983	16 S	4 H	phospholipids, triglycerides,
	4 SCo	4 HCopell	cholesterol, urea, tot.serum prot.,
	4 SB_{12}		Fe, γGT, GLDH, bilirubin
1984	5 S	5 SB_{12}	cholesterol, urea, Fe, GLDH
	5 SCuO	5 SCopell	
	5 SCo	5 H	
1985	4 S	4 SB_{12}	tot.serum prot., Fe, GLDH, serum
	4 SSe	4 SCopell	electrophoresis
	4 SCo	4 SCoSeCu	
	4 SCo+	4 H	
1986	6 S	6 H	cholesterol, γGT, GLDH
	6 SCo	6 HCo	
	6 SCo+	6 HColick	
	6 SColick		

S : Lambs grazing OWLD pastures.
H : Lambs grazing control pastures.
SCo : Lambs grazing moderately Co fertilized S pastures.
SCo+ : Lambs grazing heavily Co fertilized S pastures.
HCo : Lambs grazing Co fertilized H pasture.
SCoSO4 : Dosed weekly with cobalt sulphate by mouth.
SB_{12} : Injected every 2 or 3 weeks with vitamin B_{12}.
SCuO : Dosed with copper oxide needles.
SCopell : Dosed with cobalt pellets.
SSe : Dosed with selenium pellets.
SCoSeCu : Dosed with cobalt-selenium-copper glass boli.
SColick : Access to cobalt-enriched salt lick on OWLD pasture.
HColick : Access to cobalt-enriched salt lick on control pasture.

according to the manual. Hb was estimated in a haemoglobinometer (Coulter Electronics). Zone electrophoresis of serum was performed with the Gelman Serum Protein Electrophoresis System. Beckman microzone chamber (Micro Zone Cell, Beckman Instr. Inc. Palo Alto) with cellulose acetate membranes (Sepraphore 3, Gelman Instr. Comp., Michigan) was used. Total serum protein (TSP) was determined by the biuret method *(Wootton* 1974). Plasma glucose was estimated by a colorimetric method with o-toluen in acetic acid (Glucorapid test, Med-Kjemi, Høn, Norway). The samples from 1986 were examined by the Peridochrom Glucose GOD-PAP method (enzymatic colorimetric, Boehringer Mannheim GMBH Diagnostica test kits).

Following analyses were performed with Boehringer test kits: Sorbitol dehydrogenase (SDH, UV-method), L-γ-glutamyltransferase (γGT new, colorimetric), glutamate dehydrogenase (GLDH, UV), free cholesterol (CHOD-PAP, enz. col.), monotest cholesterol (CHOD-PAP, enz. col.), phospholipids (enz. col.), bilirubin (col.), triglycerides (Neutral Fat, fully enz. UV), urea (enz. UV), and non esterified fatty acids (col.).

Precinorm® U, Precilip® E.L., Precipath® E (Boehringer) and Seronorm® (Nyegaard & Co, A/S, Oslo) were used as quality control.

The estimations were performed in a photometer with interference filters (Kemion RP 90, Finland) at a constant temperature according to instructions.

Serum iron (SI) was examined as recorded by *Øverås* (1974). Serum zinc was determined by atomic absorption spectrophotometry according to manual (Unicam SP 90, Unicam Instr. Ltd., Cambridge).

Blood samples were collected from 08.30 a.m. and onwards. PCV, Hb, RBC, WBC and MCV were estimated shortly after return to the laboratory. Serum/plasma samples were frozen (-20°C), and enzymes were examined within the next days or weeks.

Statistical testing of differences was done by Student's t-test.

Results

Serum enzymes

GLDH varied greatly throughout grazing (Tables 2-3). During May and early June, mean values were similar in all groups, and most often between 3 and 14 U/l. During July-October, all unsupplemented lambs on OWLD pastures (S lambs) had GLDH above 15 U/l at one or more samplings, and mean values were most often above 30. The vitamin B_{12} supplemented group (SB_{12}) had lowest GLDH during all years. Mean values for the other groups were in between those 2, but always so that the H lambs had higher means and larger sd than the Co/B_{12} supple-

Table 2. Serum glutamate dehydrogenase (GLDH, U/l, 1983), means±sd. Four lambs were sampled in each group (n = 4), except in the S group where n = 16 in May-July. For group explanation, see legend of Table 1.

	Sampling dates					
Groups	May 9	June 7	June 28	July 26	Aug. 23	Oct. 4
S	5±3	6±3	23±23	64±60	65±39	54±27
SCo	6±5	14±13	14±8	9±2	7±3	13±16
SB_{12}	5±3	3±2	7±4	9±7	6±4	11±9
H	10±6	7±3	18±11	32±26	34±17	59±45
HCopell	13±9	32±40	23±22	39±45	76±55	93±94

Table 3. Serum GLDH, U/l, 1986, means±sd. Six lambs were sampled in each group. For group explanation, see legend of Table 1.

	Sampling dates				
Groups	May	June	Aug.	Sept.	Oct.
S	5±4	14±11	34±35	37±9	-
SCo	4±2	7±5	7±4	20±35	-
SCo+	6±3	14±8	17±15	9±6	-
SColick	6±6	17±14	8±5	9±4	-
H	6±5	19±21	70±97	63±53	62±67
HCo	11±16	9±6	10±9	8±3	12±13
HColick	5±3	16±11	28±22	35±31	27±25

mented S lambs. Mean GLDH of the H lambs varied between 8 and 93 in July-October, and application of Co sometimes resulted in lower concentration.

Individual γGT values also varied greatly. Results from 1986 are shown (Table 4). Generally, during 4 years, mean values for the S lambs were above 35 U/l during July-September, while the other groups were below. The percentage of S lambs with values >40 during July-September varied between 17 and 100. Several H lambs (up to 50%) had γGT values above 40 during this period. Lambs with severe clinical OWLD might as well have low γGT as high.

Individual SDH values varied between 2 and 32 U/l throughout grazing, with mean values for all groups between 4 and 16 U/l, and no specific differences between the groups.

Blood cell values

During 4 years (1982-1984, 1986), mean PCV values dropped in the unsupplemented S groups to between 26 and 32% in August-September, while the Co/B_{12} supplemented S lambs and H lambs had values of 32-38%. The differences between the S and SB_{12} groups were significant ($p<0.05$) during 2 years (1982, 1983), as was the difference between the unsupplemented and Co supplemented S groups in 1986.

Mean Hb values, RBC and WBC counts were within normal ranges, and there were no significant differences between the groups. Within the untrated S group there was a larger individual variation in Hb as lambs with severe OWLD sometimes had values between 4.34 and 6.21 mmol/l, while the Co/B_{12} supplemented S lambs had values above 6.21.

Table 4. Serum γ glutamyltransferase (γGT, U/l, 1986), means±sd. Six lambs were sampled in each group. For group explanation, see legend of Table 1.

Groups	May	June	Aug.	Sept.	Oct.
S	53±14	43±10	66±27	57±27	-
SCo	42±4	37±6	31±3	38±11	-
SCo+	43±18	35±6	27±3	30±4	-
SColick	39±9	44±7	34±4	34±3	-
H	49±14	33±7	33±7	40±7	40±14
HCo	46±11	36±5	33±8	33±5	31±4
HColick	51±13	36±7	36±6	37±5	34±3

During August and October 1981, mean MCV in the S and SB_{12} groups varied between 29 and 30, and 34 and 33 f* respectively ($p<0.001$), while values for the other groups were in between. Severely affected lambs often had lower MCV than the Co/B_{12} suppelemented ones. Mean corpuscular haemoglobin concentration (MCHC, g/100 ml) was most often 34-36% within all groups. Mean corpuscular haemoglobin (MCH) ranged between 10 and 13 pg. In late August and in September 1981, the unsupplemented S lambs had significantly lower MCH (<11 pg) than the Co/B_{12} supplemented ($p<0.001$-0.025). A similar tendency was seen in September 1982 (NS).

Serum proteins

Mean total serum protein (TSP) increased from between 47 and 66 g/l in May-June in all groups, to 60-75 g/l in mid July. From that time, values were unchanged, or increased to 70-80 in October. During August-October 1982-1983, the S lambs had lower mean values (≤ 70) than the SCo/SB_{12} lambs ($p<0.05$). The difference was also significant between the S and H lambs in August-October 1983.

Mean albumin content was 391-609 µmol/l in all groups throughout the grazing period. The albumin/globulin ratios showed no differences between the groups.

Plasma glucose

The general pattern of mean plasma glucose is illustrated in Fig. 1. The S lambs usually had the lowest mean values during July-October, while the H lambs had the highest. The differences between S and H lambs were significant in July and August 1983, and July 1984 ($p<0.05$). In 1986, however, all H groups had low mean plasma glucose during August-October (2.8-3.7 mmol/l).

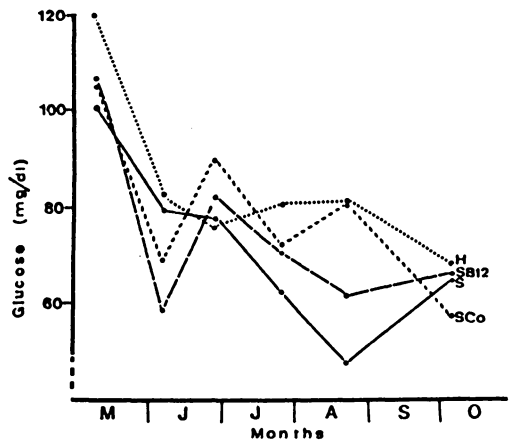

Figure 1. Mean plasma glucose (mg/dl) in 14 unsupplemented (S) and 4 B_{12} supplemented lambs (SB_{12}) grazing OWLD pastures, in 4 lambs grazing Co fertilized OWLD pastues (SCo), and in 4 lambs (H) grazing disease free pastures, 1983.

Serum lipids

Mean serum phospholipid (SPL) decreased in all lambs from 2.3-3.1 mmol/l in May, to 1-1.7 in late June. One year (1982), the S lambs had mean SPL below 1.4 mmol/l, while the SCo and SB_{12} lambs had values above 1.4 during July to October ($p<0.05$). In 1983, the S lambs had mean SPL below 1.1 mmol/l, whereas the other groups had values above (NS).

Mean total cholesterol fell in all groups from 2.3-4.3 mmol/l in May, to 0.9-2.0 in June-July. The S groups had the most abrupt fall, and mean values for this group were below 1.2 through August-October, while the SCo, SB_{12} and H lambs had mean values above 1.4. The differences between the S and SB_{12} lambs were significant ($p<0.01$) at all sampling dates in July-October 1982, August-October 1983, and August 1984. Six lambs with severe OWLD in September had a mean of 0.8±0.2 mmol/l. The amount of free cholesterol showed no significant difference between groups.

*fl = 10^{-15} liter

Mean serum triglyceride varied in all groups between 0.8 and 1.1 mmol/l in May, and fell to around 0.3 in June, with further decrease to between 0.1 and 0.2 on the last sampling. There were large individual differences within the groups, and no significant group differences were noted.

Serum urea

Mean serum urea concentration increased from 3-6 mmol/l in May to above 9 in June-July each year. Later, it remained on that level in the H, SCo + and SB_{12} lambs, or increased slightly, while a decrease occurred in the S lambs (below 9 mmol/l). The H lambs always had the highest values at the end of season (12-13 mmol/l). The differences between the S and H lambs were significant ($p<0.05$) in August-October 1983 and September 1984, as were the differences between the S and Co/B_{12} supplemented S lambs in September-October 1982 and August-October 1983.

Serum iron (SI)

SI varied between 6.5 and 118 µmol/l in May. By mid June, mean values for all groups were 32-47 µmol/l. As stagnation of growth was obvious in the S lambs in August-September, mean SI was above 36, whereas mean values in the other groups remained below. Some severely affected lambs had SI between 41 and 54 µmol/l. The SB_{12} group generally had the lowest SI (25-32 µmol/l).

Serum zinc

Serum Zn varied greatly, but were within normal limits, and there were no differences between the groups. Mean values for all groups and dates were between 15.3 and 24.2 µmol/l.

Total serum bilirubin (TSB)

Mean TSB rose from 1.7-2.0 mmol/l in May to 3.5-3.8 in July in all groups, with means between 2.3 and 3.7 throughout August-October. No differences between groups were observed.

Discussion

Serum enzymes

Elevation of serum enzymes indicating hepatic damage was found in OWLD (S lambs) as well as in simple B_{12} deficiency (H lambs). In acute OWLD, elevations of serum aspartate transaminase (AST) and γGT have been found *(Sutherland et al.* 1979, *Mason & McKay* 1983). *MacPherson et al.* (1976) found abnormal alkaline phosphatase (AP) and AST values 26-28 weeks after introduction of Co deficient diet to 50 kg wethers. *Hannam et al.* (1980), however, reported that AST and AP was not affected by the B_{12} status, but few lambs were sampled, and untreated lambs had in fact higher means and larger sd as compared with B_{12} treated, indicating hepatic dysfunction in some.

GLDH has not earlier been examined in OWLD or simple Co deficiency. GLDH is concentrated in ovine hepatocytes. Normal amount in plasma of adult sheep is below 10 U/l, and the enzyme is recommended in measuring hepatic necrosis *(Alemu et al.* 1976). It is unstable, and *Schmid & von Forster* (1985) reported loss of activity after 7 days by ÷ 20°C.

GLDH amounts above 15 U/l indicating hepatocyte damage were noted in individual S lambs 1-3 weeks before reduction in weight increase, but most often concurrently, and the elevation came before or at the same time as lowering of plasma glucose, serum total cholesterol and phospholipid. Severity of illness in later phase was not always correlated

with GLDH increase. Mean GLDH in 6 lambs with severe OWLD in October was 36 U/l (range 8-85). One lamb with severe OWLD eutanized in early July, however, had 887 U/l.

The elevated GLDH values seen annually in the H lambs, and especially pronounced in 1986, correlated nicely with the B_{12} state of these lambs *(Ulvund* 1990a). The H lambs were in ecellent condition during all years, but growth was less in 1986 than during the other years *(Ulvund & Pestalozzi* 1990), and the lambs were B_{12} deficient and had MMA accumulation *(Ulvund* 1990a). The correlation between reduced growth and increased serum GLDH was not always found on individual basis, as lambs with high serum GLDH did not differ particularly in lw from the others within the group.

Rise in γGT is related to cholestasis or bile duct damage *(Ford* 1974), and the enzyme is stable up to 1 month by ÷20°C *(Cornelius* 1980). At pasture outlet, our lambs had mean values between 32 and 55 U/l, and 53% had values above 40. Two to 4 weeks later, mean values were reduced to 28-44, and 24% had values >40. This is in accordance with *Pauli* (1983), who found that lambs acquire high γGT amounts from colostrum. In our case, the colostral amounts may have masked early increases due to hepatic damage.

Individual S lambs often showed γGT amounts >40 concurrently with growth stop in the earlier phase of the disease, but among 8 lambs with severe OWLD in August-October, only 3 had values >40. There was no correlation on individual basis between high γGT and reduced lws in the H lambs.

Normal serum γGT in 3 months old grazing lambs was reported to be 44 U/l by *Braun et al.* (1978), while *Thomas* (1986) reported 45 U/l for clinically normal weaners, and 60 for clinically poor. In acute OWLD, *Sutherland et al.* (1979) found mean γGT amounts to be 117 U/l, and 72 in chronic. Elevated γGT values has also been found in OWLD by others *(Weensvoort et al.* 1975, *McLoughlin et al.* 1984, *Mitchell et al.* (1982).

High serum SDH should be a good predictor of liver cell damage in sheep *(Alemu et al.* 1976). Normal serum SDH in lambs is low (<3 U/l), the enzyme is unstable, and reduced activity is seen after 2 day's storage at ÷20°C *(Schmid & von Forstner* 1985). Elevated SDH values (>10 U/l) were found in most lambs with OWLD *(Weensvoort et al.* 1975, *Mason & McKay* 1983, *Mitchell et al.* 1982). Under our conditions, however, there was no correlation between high SDH and OWLD, as elevated values were seen in all groups. Freezing may have reduced peak amounts.

Blood cell values

Judged by estimated PCV and TSP *(MacFarlane* 1975), dehydration was not typical for our OWLD condition, although occasional lambs were dehydrated. Nine of our lambs with severe OWLD had a mean PCV of 27%±6 at the last sampling, and range in TSP in 4 of these was 46-80 g/l. Lowered PCV and TSP are reported in experimental Co deficiency *(MacPherson et al.* 1976, *Hannam et al.* 1980), and in chronic hepatitis, a disease similar of identical to OWLD *(Weensvoort et al.* 1975).

Anaemia was not a clear feature of our lambs. However, Hb values down to 4.90 mmol/l were seen in lambs that had been affected for weeks. This is in accordance with observations in OWLD *(Weensvoort et al.* 1975, *Sutherland et al.* 1979). Such decrease in Hb may reflect low feed intake *(MacFarlane* 1975). In Co deficiency *(Gawthorne et al.* 1966, *Fell* 1981) as well as in OWLD *(Sutherland et al.* 1979), the anaemia, when present, has been classified as normocytic and

normochromic. In our case, the MCV fall (down to 25 fl) may be due to fewer immature cells being released from bone marrow, as an increase in the M/E ratio was found *(Ulvund & Øverås* 1980). Reduced MCH, as compared with the values in Co/B_{12} supplemented lambs, may indicate a slight hypochromic condition, although not classified as a hypochromic microcytic anaemia.

There was no affinity of disease to specific Hb types. No effort was made to correlate blood parameters to Hb types.

Plasma glucose

All our lambs showed a general glucose drop in June-July, similar to that recorded by *Lindsay & Leat* (1975) in normal lambs, and associated with decreasing milk intake and increasing intake of roughage. A further drop in S lambs most often occurred during the same week as stop in weight gain was noted. Lambs with severe OWLD often had plasma glucose between 2.2 and 3.3 mmol/l, although 9 severely affected lambs in September-October had mean value 3.8 mmol/l.

Plasma glucose falls during fasting in normal lambs *(Lindsay & Leat* 1975). In Co deficiency, lowered plasma glucose is also due to the inability to metabolize propionic acid *(Smith* 1987). *Mac Pherson et al.* (1976) reported lowered glucose values in Co deficient wethers. Under Co sufficient conditions, the lambs start to produce their own B_{12} from about 1 month of age, when they become ruminants. The milk B_{12} concentration falls abruptly during the first 48 h after lambing, and later provides little B_{12} to the lamb *(Halpin & Caple* 1982). The glucose drop seen at 2-3 months of age may therefore also be associated with insufficient B_{12} production during a period of intense growth and heavy needs.

The lambs which were treated fortnightly with 2 mg hydroxocobalamin grew faster than those treated every third week *(Ulvund & Pestalozzi* 1990). Below 3 months of age, the lambs treated every third week had lowered plasma glucose 3 weeks after last treatment, while older lambs showed no such drop in glucose after 3 weeks. This pattern was also seen by *Mac Pherson et al.* (1976). *Hannam et al.* (1980) found that lambs injected with 2 mg hydroxocobalamin at pasture outlet, at 1 month of age, and on soil highly prone to the occurrence of Co deficiency, had higher plasma glucose than untreated lambs 4-5 months later. Under their conditions, the B_{12} injection may perhaps have triggered better appetite and uptake of sufficient Co to produce more B_{12} in the rumen.

It is interesting to note that the H lambs had reduced plasma glucose in 1986, when they were B_{12} deficient throughout the grazing period.

Serum lipids

The general decrease of serum lipids seen in all our lambs from pasture outlet and onwards corresponds to conditions in normal lambs. The amount of lipids normally rises to a maximum at 20 days of age, and declines to adult level at weaning *(Leat* 1967). The rise is due to intake of fat through the milk, the decrease is due to reduced milk intake.

Individual S lambs showed further reduction of serum phospholipid (SPL) concurrently with growth stagnation, in some cases 1-3 weeks before, which may reflect either reduced milk intake or early hepatic damage. There are few reports on the relation between SPL and liver function in animals *(Cornelius* 1980).

Cholesterol is produced and esterified in the liver, and in hepatic disease, esterification is depressed *(Cornelius* 1980). *Hannam et al.* (1980) found mean values between 1.5 and

1.9 mmol/l in 19-22 weeks old B_{12} treated lambs, as compared to 1.4 in Co deficient, and related the decrease to reduced food intake. In our lambs, reduction was found in the esterified portion, and may be due to both reduced food intake and hepatic damage.

Serum urea

Reduced urea concentration may be an indication of reduced protein intake, reduced protein catabolism, or hepatic insufficiency *(Finco* 1980). *Hannam et al.* (1980) found depressed serum urea in 19 weeks old Co deficient lambs when compared with B_{12} treated ones, and *Smith & Marston* (1970) found higher excretion of faecal nitrogen in Co deficient sheep than in Co/B_{12} supplemented. The low serum urea in our OWLD lambs may be due to a combination of all these factors.

Serum iron

The increase in SI observed in normal lambs at 6 weeks of age *(Hidiriglou & Jenkins* 1971) correlates well with the May values seen in all our lambs. Elevation of SI may reflect liver damage *(Kaneko* 1980). Increased SI was found in some lambs with chronic hepatitis *(Weensvoort et al.* 1975). The rise seen in our OWLD lambs may be due to liver damage.

Lambs developing OWLD showed early signs of liver damage as well as lowering of plasma glucose, but subclinically B_{12} deficient lambs on other pastures also showed some degree of hepatic injury and glucose drop. Co/B_{12} supplementation prevented hepatic damage and normalized blood values.

References

Alemu P, Forsyth GW, Searcy GP: A comparison of parameters used to access liver damage in sheep treated with carbon tetrachloride. Canad. J. comp. Med. 1976, *41,* 420-427.

Braun JP, Rico AG, Benard P: Tissue and blood distribution of gammaglutamyl transferase in the lamb and in the ewe. Res. Vet. Sci. 1978, *25,* 37-40.

Cornelius CE: Liver function. In: Kaneko JJ (ed.): Clinical Biochemistry of Domestic Animals, 3rd ed, Academic Press, London 1980, p 201-257.

Fell BF: Pathological consequences of copper deficiency and cobalt deficiency. Phil. Trans. B, 1981, *294,* 153-169.

Fell BF, Hesketh JE, Lough AK, Duncan WRH, Mackie WS: Observations on the central nervous system of sheep deficient in cobalt (vitamin B_{12}). In: Mills CF, Bremner I, Chesters JK (eds): Trace Elements in Man and Animals, Tema 5. Proc. 5th. Int. Symp. CAB, London 1985, p 263-265.

Finco DR: Kidney function. In: Kaneko JJ (ed): Clinical Biochemistry of Domestic Animals, 3rd ed., Academic Press, London 1980, p 338-394.

Ford EJH: Activity of gamma-glutamyl transpeptidase and other enzymes in the serum of sheep with liver or kidney damage. J. comp. Path. 1974, *84,* 231-243.

Gawthorne JM, Somers M, Woodliff HJ: Cobalt deficiency anaemia in sheep. Aust. J. exp. Biol. med. Sci. 1966, *44,* 585-588.

Halpin CG, Caple IW: Vitamin B_{12} nutrition of foetal and newborn lambs. Proc. Aust. Soc. Anim. Prod. 1982, *14,* 658.

Hannam RJ, Judson GJ, Reuter DJ, McLaren LD, McFarlane JD: Effect of vitamin B_{12} injections on the growth of young merino sheep. Aust. J. agric. Res. 1980, *31,* 347-355.

Hidiriglou M, Jenkins KJ: Serum levels of magnesium, iron and zinc in normal and dystrophic sheep. Canad. J. anim. Sci. 1971, *51,* 803-806. 1971.

Kaneko JJ: Iron Metabolism. In: Kaneko JJ (ed.): Clinical Biochemistry of Domestic Animals. 3rd. ed., Academic press, London 1980, p 649-668.

Leat WMF: Plasma lipids of newborn and adult ruminants and of lambs from birth to weaning. J. agric. Sci. 1967, *69,* 241-246.

Lindsay DB, Leat WMF: Carbohydrate and Lipid Metabolism. In: Blunt MH (ed.): The Blood of Sheep. Composition and Function. Springer Verlag, Berlin 1975, p 45-56.

MacFarlane WV: Distribution and Dynamics of Body Fluids in Sheep. In: Blunt MH (ed.): The Blood of Sheep. Composition and Function. Springer Verlag, Berlin 1975, p 1-22.

MacPherson A, Moon FE, Voss RC: Biochemical aspects of cobalt deficiency in sheep with special reference to vitamin status and a possible involvement in the aetiology of cerebral necrosis. Br. vet. J. 1976, *132,* 294-308.

MacPherson A, Moon FE, Voss RC: The influence of cobaltdeficient diets on housed sheep. Vet. Rec. 1977, *101,* 231.

Mason RW, McKay RM: Ovine white liver disease. Aust. vet. J. 1983, *60,* 219-220.

McLoughlin MF, Rice DA, Taylor SM: Liver lesions resembling ovine white liver disease in cobalt deficient lambs. Vet. Rec. 1984, *115,* 325.

Mitchell PJ, McOrist S, Thomas KW, McCausland P: White liver disease of sheep. Aust. vet. J. 1982, *58,* 181-184.

Pauli JV: Colestral transfer of gamma glutamyl transferase in lambs. N. Z. vet. J. 1983, *31,* 150-151.

Schmid M, von Forstner: Laboratory testing in veterinary medicine diagnosis and clinical monitoring. Boehringer Mannheim GmbH, Mannheim 1985, 253 pp.

Smith RM: Cobalt. In: Mertz W (ed.): Trace Elements in Human and Animal Nutrition. 5th ed. Vol. 1. Academic Press, London 1987, 143-183.

Smith RM, Marston HR: Some metabolic aspects of vitamin B_{12} deficiency in sheep. Brit. J. Nutr. 1970, *24,* 874-891.

Sutherland RJ, Cordes DO, Carthew GC: Ovine white liver disease - an hepatic dysfunction associated with B_{12} deficiency. N. Z. vet. J. 1979, *27,* 227-232.

Thomas KW: The effect of thiaminase-induced subclinical thiamine deficiency on growth of weaner sheep. Vet. Res. Comm. 1986, *10,* 125-141.

Ulvund MJ: Ovine white-liver disease (OWLD). Vitamin B_{12} and methyl malonic acid (MMA) estimations in blood. Acta vet. scand. 1990a, 31, 267-275.

Ulvund MJ: Ovine white-liver disease (OWLD). Serum copper and effects of copper and selenium supplementation. Acta vet. scand. 1990b, 31, 287-295.

Ulvund MJ, Pestalozzi M: Ovine white-liver disease (OWLD) in Norway. Clinical symptoms and preventive measures. Acta vet. scand. 1990, 31, 53-62.

Ulvund MJ, Øverås J: Chronic hepatitis in lambs, a conditon resembling ovine white liver disease in New Zealand. N. Z. vet. J. 1980, *28,* 19.

Wennsvoort P, Herweyer CH, Wensing TH: Occurrence, diagnosis and course of chronic hepatitis in weaned lambs of a flock of Texel sheep. T. Diergeneesk., 1975, *16,* 864-874.

Wooton IDP: Microanalysis in Medical Biochemistry. 5th ed. Churchill Livingstone, Edinburg & London 1974, 307 pp.

Øverås J: A comparison between hay fed and grass silage fed sheep with special reference to serum iron, total iron-binding capacity and transferrin saturation. Nord. Vet.-Med. 1974, *26,* 545-555.

Sammendrag

Kvitleversjuke (kobolt/vitamin B_{12} mangel) hos lam. Klinisk patologi.

Vitamin B_{12}-deficitte lam som utviklet kvitleversjuke (OWLD) ble undersøkt klinisk-patologisk, og verdiene ble sammenliknet med resultatene hos kobolt/B_{12} doserte lam på de samme beitene, og klinisk friske, men noen ganger B_{12}-deficitte, lam på andre beiter (H). Økning av serum glutamat dehydrogenase (GLDH) og nedsatt fosfolipid- og kolesterolnivå forekom enten samtidig med reduksjon i tilvekst, eller 1-3 veker før, når lamma var 8-10 veker gamle. Fall i plasma glukose og økning av γGT kom også i den tidlige fasen av sjukdommen. Alle andre forandringer i blodbildet kom senere, og ble hovedsakelig vurdert som en følge av nedsatt matlyst og leverskade. Forandringene omfattet fall i PCV og MCV, stigning i serumjern, og reduksjon av serumprotein og urea. Dosering med Co/B_{12} forhindret leverskade og normaliserte blodverdiene. H-lamma viste også tegn på en viss leverskade, spesielt da de var B_{12}-deficitte, noe som indikerer at det ved simpel B_{12} mangel også er en moderat leverskade. Ved diagnostiske undersøkelser anbefales klinisk kjemi gjennomført på flokkbasis.

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