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Ovine White-Liver Disease (OWLD). Vitamin B_{12} and Methyl Malonic Acid (MMA) Estimations in Blood

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Ulvund, M.J.: Ovine White-liver disease (OWLD). Vitamin B_{12} and methyl malonic acid (MMA) estimations in blood. Acta vet. scand. 1990, 31, 267-275. - At pasture outlet, mean plasma vitamin B_{12} varied between 210 and 1,200 pmol/l in 1 month old lambs, 19% of them had values below 250 pmol/l. In those put on OWLD pastures, mean values dropped after 2-4 weeks, and mostly stayed below 150 pmol/l throughout grazing. Plasma methylmalonic acid (MMA) rose above 5 µmol/l 2-8 weeks after outlet, and above 15 µmol/l 4 weeks later. Reduced growth occurred 3-8 weeks after plasma B_{12} dropped below 150 pmol/l, and 4-6 weeks after MMA rose above 5 µmol/l. Clinical OWLD was most often associated with plasma B_{12} < 150 pmol/l and MMA > 15 µmol/l. Cobalt fertilization of pastures induced satisfactory plasma B_{12}/MMA values for 3 succeeding years. Elevated plasma B_{12} was found 3 weeks after Co pellet dosing. The use of Co lick resulted in large individual variations in plasma B_{12}/MMA.
The control lambs, which were healthy and grew well on pastures which some years contained marginal/deficient cobalt, had plasma B_{12}/MMA values which varied considerably. One year values indicated functional Co deficiency, but none developed OWLD, and growth was satisfactory, but less than other years. In these lambs, high MMA was not always associated with low B_{12}, or depressed growth. OWLD occurred in Co/B_{12} deficient lambs, but Co/B_{12} deficient lambs on other pastures did not develop OWLD.

sheep; cobalt/vitamin B_{12} deficiency; plasma vitamin B_{12}; plasma methyl malonic acid (MMA).

Introduction

Vitamin B_{12} is synthesized by rumen microbes from dietary cobalt, and a Co deficiency in ruminants is in fact a deficiency in B_{12} (*Smith 1987*). Methylmalonic acid (MMA) is an intermediate in the conversion of propionic acid to succinate. The conversion requires the vitamin B_{12} dependant enzyme methylmalonyl CoA mutase, and when the supply of B_{12} in scarce, MMA accumulates in the tissues, urine and blood (*Marston et al.* 1961, *Gawthorne* 1968, *Rice et al.* 1987). The measurement of MMA is therefore a useful diagnostic test for B_{12} deficiency, and held together with B_{12} estimations, it is possible to distinguish between various states of Co deficiency (*McMurray et al.* 1985).

It has been unclear whether ovine white-liver disease (OWLD) is a simple Co deficiency, or a hepatotoxic disease in Co/B_{12} deficient lambs. The disease has been described from various countries, including Norway (*Ulvund & Øverås* 1980, *Ulvund & Pestalozzi* 1990a). Examinations revealed that OWLD was associated with pasture grass containing marginal to deficient Co during the first months of grazing. Similar Co values were, however, also found some years in control pastures, where clinically healthy lambs gained 13 kg more than the OWLD affected ones during 3.5 months of grazing *(Ulvund & Pestalozzi* 1990b). It therefore became important to examine blood from lambs on these pastures for vitamin B_{12} and MMA.

Materials and methods

Altogether 458 twin lambs of the Dala and Rygja breeds were included during a 6 year study (1981-86). Experimental design has been described elsewhere *(Ulvund & Pestalozzi* 1990a, *Ulvund* 1990). Pasture outlet varied between May 10 and 20, when the lambs were about 1 month old. The lambs grazed with their dams throughout the experimental period. Lambs designated S were put on OWLD pastures, which were either moderately (SCo) or heavily (SCo+) fertilized with Co, or not Co fertilized (S). H lambs grazed disease free control pastures, which some years had marginal to deficient Co contents. Prophylactic measures and symbols used are given in Table 1.

Vitamin B_{12} in plasma was estimated with the vitamin B_{12} (^{57}Co) Radioassay Kit (Becton Dickinson) by NORLAB, Oslo, Norway. Altogether 376 samples from the 1982 and 1984-1986 grazing seasons were examined. Plasma MMA estimations of 511 samples from the same years were performed by the Veterinary Research Laboratories, Stormont, Belfast. High resolution capillary gas chromatography (GC) was used for separation, flame ionization for detection *(McMurray et al.* 1986).

Results

The results of the vitamin B_{12} estimations are shown in Table 2. Mean plasma B_{12} varied between 210 and 1,200 pmol/l at the first sampling in May, and 19 out of 101 lambs (19%) had values below 250 pmol/l, varying from 7% (1985) to 22% (1986). During all years, mean values in the S lambs dropped after 2 weeks on pasture, and usually remained below 150 pmol/l.

Co fertilization of pastures (SCo) induced higher mean plasma B_{12} throughout grazing, but values were reduced during the second and third year after last fertilization, and after 4 years mean values were below 155 pmol/l in June and September. The lambs which were regularly injected with vitamin B_{12} (SB_{12}) had very high plasma values, with mean values above 1,000 pmol/l. The lambs dosed with cobalt pellets (SCopell) showed elevated values 3 weeks after dosing (July). In the lambs which had admittance to cobalt

Table 1. Explanation of lamb group symbols used in the experiments. Lambs designated S were grazing OWLD pastures (at Særheim), while those grazing disease free pastues at Høyland were designated H.

Symbol	Explanation
S	Not treated.
SCo	S lambs grazing OWLD pastues fertilized with Co ($CoSO_4$, 1 kg/ha) in 1980, 1981 & 1982.
SCo+	S lambs grazing OWLD pastures fertilized with Co (1 kg/ha) in 1980, 1981, 1982, 1985 & 1986.
SB_{12}	Injected with hydroxocobalamin (2 mg) every second (1982, 1985) or third week (1984) from pasture outlet (mid May, 1982, 1984) or end of June (1985) to mid September, starting with the half dose (1 mg) on the first injection.
SCopell	Dosed on July 1 with cobalt pellets, but moved from OWLD pastures (S) onto control pastures (H) in mid August.
SColick	Lambs grazing OWLD pastures having access to Co enriched salt lick.
H	Lambs grazing control pastures 15 km apart.
HCo	Lambs grazing H pastures fertilized with Co (2 kg/ha) in 1986.
HColick	H lambs having access to Co enriched salt lick.

Table 2. Plasma vitamin B_{12} (pmol/lx10^2), mean values ± sd, in lambs from various groups sampled at different years and throughout grazing. Number of lambs are given (n), exceptions are indicated (lifted). For explanation of groups, see Table 1. Number of weeks since last injection of vitamin B_{12} are given (in brackets).

Group	Year	n	May	June	July	August	September	October
S	1982	3	6.1±4.0^{4}	1.4±0.8	0.8±0.2	0.8±0.1	0.7±0.2	1.3±0.6^{2}
	1984	5	7.6±3.9	0.8±0.2	0.5±0.1	1.4±1.4	1.1±0.5	-
	1985	4	3.9±1.4	1.2±0.7	2.5±2.5	0.9±0.2	-	5.6±5.0
	1986	6	3.4±1.1	0.5±0.1	-	0.5±0.1	0.4±0.0	-
SCo	1982	3	4.8±2.6	9.0±4.4	24±7.0	30±13	30±3.0	30±1.3
	1984	5	3.6±1.2	2.9±2.0	1.5±0.5	1.9±0.3	4.7±1.3	-
	1985	4	5.8±2.7	10±3.4	10±3.3	4.3±2.0	-	10±2.6
	1986	6	4.8±2.9	0.9±0.2	-	-	1.6±0.6	-
SB_{12}	1982	3	6.5±6.7	3.4±1.0(2)	1400±13(2)	110±170(2)	13±6(1)	9±5(3)
	1984	5	2.1±1.0	3.2±0.3(3)	12±4(1)	680±530(3)	17±9(3)	-
	1985	4	3.4±1.6	0.6±0.1	14±4(1)	117±6(1)	-	29±7(2)
Scopell	1985	4	5.4±2.9	0.8±0.1	9.1±4.3^{3}	1.6±0.4^{3}	-	6.5±1.5^{2}
Scolick	1986	6	11±7.8	4.5±2.7	-	2.9±2.3	2.8±1.3	-
H	1984	5	5.5±2.6	2.1±0.8	2.6±1.2	4.6±1.8	2.2±1.1	-
	1985	4	6.1±1.7	1.8±1.1	2.4±1.1	2.0±0.8	-	2.5±1.5
	1986	6	12±12	0.9±0.2	-	0.8±0.2^{3}	0.8±0.1	-
HCo	1986	6	5.6±3.8	-	-	-	35±11	-
HColick	1986	6	11±4.9	-	-	3.9±2.6	4.7±2.1	-

salt lick (SColick), mean plasma B_{12} was about 300 pmol/l throughout grazing.

In the controls (H lambs), plasma B_{12} varied considerably, and was especially low in 1986. Co fertilization of H pastures, as well as use of Co lickstone, resulted in an increase.

Plasma MMA is shown in Table 3. The S lambs showed increasing values from June/July each year. The SCo lambs had low MMA values during the year of fertilization, but during the second and third year a moderate increase took place in individual lambs in July-October. A significant MMA increase occurred during the fourth year after Co fertilization. Refertilizing half of the SCo pasture in 1985 and 1986 (SCo+) yielded lambs with very low plasma MMA. The use of Co lickstone and Co pellets usually resulted in low plasma MMA. The SB_{12} lambs had very low plasma MMA throughout the experimental period.

The H lambs showed a wide range in individual values, especially in 1984 and 1986, whereas only 1 lamb had MMA above 5 µmol/l i 1985. The highest value found among H lambs was 148 µmol/l (Table 4). Three H lambs sampled on June 1 1982, had the following B_{12}/MMA values (pmol/l-µmol/l): 108-9, 119-44 and 62-47.

All individual MMA estimations are plotted against the B_{12} values in Figure 1. MMA amounts of 5 µmol/l and above were usually associated with B_{12} contents below 250 pmol/l, and most lambs with MMA >15 µmol/l had B_{12} amounts less than 150 pmol/l.

Table 3. Plasma MMA (µmol/l), mean values±sd, in lambs from various groups sampled at different years and throughout grazing. Number of lambs are given (n), exceptions are indicated (lifted). For explanation of groups, see Table 1.

Group	Year	n	May	June	July	August	September	October
S	1982	6	0.8±0.5	4.1±3.4	50±13	110±61	140±129[3]	24±13[3]
	1984	5	1.0±1.1	7.7±3.1	11±3.7	48±49	43±56[4]	-
	1985	5	0.4±0.3	-	12±8	3.5±3.5[4]	-	1.4±1.2
	1986	6	2.5±2.5	45±23[4]	-	98±41	97±35	-
SCo	1982	4	1.4±0.4	1.4±1.2[5]	1.0±0.3	0.9±0.6	1.2±0.8	0.8±0.5
	1984	5	1.0±1.0	4.0±2.2	7.2±3.4	5.8±3.9	1.5±1.0	-
	1985	5	1.0±0.8	-	0.9±0.6	1.9±2.3[4]	-	6.8±4.5
	1986	6	5.0±1.2	5.5±5.2[5]	-	24±23	15±14	-
SCo+	1985	5	0.6±0.2	-	0.4±0.2	2.0±0.2	-	2.1±0.6
	1986	6	2.8±2.4[5]	0.2±0	-	1.4±1.6[5]	1.9±1.2	-
SB_{12}	1982	5	0.9±0.3[6]	0.7±0.5	1.3±0.6[6]	1.7±2.2	0.8±0.9	1.1±0.4
	1984	5	1.5±1.7	1.4±0.4	0.9±0.8	4.2±5.3[4]	0.3±0.5	-
	1985	5	0.5±0.2	-	0.3±0.3	21±1.2	-	2.3±0.9
SCopell	1985	4	1.2±0.6	4.0±1.6	0.9±0.1	32±26[3]	-	5.1±1.2[2]
SColick	1986	6	1.5±2.2	3.4±3.7	-	3.3±3.0	3.8±2.9	-
H	1984	5	3.6±4.3	12±15	38±63	29±39	13±11	-
	1985	5	0.7±0.6	-	1.7±2.3	1.0±0.5[4]	-	3.8±4.7
	1986	6	0.8±1.5	8.6±0.2	-	13±8.6	16±11	-
HCo	1986	6	1.1±1.0	1.2±1.3	-	2.9±1.5	1.7±1.2	-
HColick	1986	6	3.2±3.1	4.7±4.6	-	1.9±2.0	2.5±1.9	-

Table 4. Individual values of plasma vitamin B_{12} (pmol/l) and MMA (µmol/l) in control lambs (H) throughout grazing (1984).

	Sampling dates									
Lamb	May 15		June 12		July 9		Aug. 13		Sept. 25	
no	B12 -	MMA	B12 -	MMA	B12 -	MMA	B12 -	MMA	B12 -	MMA
1	403 -	<1	115 -	3	346 -	3	572 -	3	343 -	1
2	321 -	11	208 -	37	414 -	25	586 -	22	289 -	23
3	537 -	4	210 -	12	164 -	148	245 -	98	102 -	23
4	499 -	<1	335 -	2	253 -	5	484 -	4	259 -	2
5	985 -	2	183 -	4	123 -	8	303 -	20	115 -	14

Discussion

Both microbiological and radioassay methods have been used for B_{12} determination. Although results have correlated well *(Millar & Penrose* 1980), comparison of results from various investigations should be made with some caution *(Millar* 1982). Values may vary within a group of sheep, and between days in the same sheep *(Findlay* 1972).

At pastuer outlet, when our lambs were about 1 month old, mean plasma B_{12} values were satisfactory. According to *Halpin & Caple* (1982), colostrum provides the essential source of B_{12} to the newborn lamb during

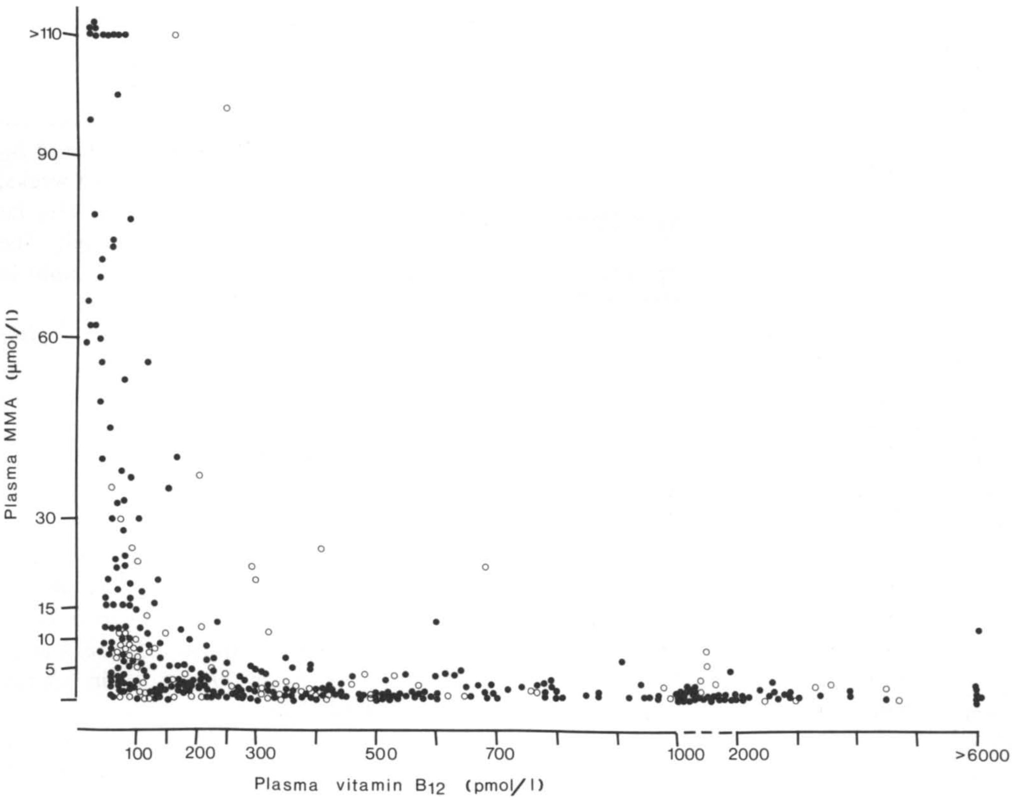

Figure 1. Individual plasma MMA results versus plasma vitamin B_{12} values in unsupplemented and Co/B_{12} supplemented S lambs grazing OWLD pastures (•), and control lambs (H) grazing disease free pastures (○).

48 h after birth. They found that plasma B_{12} was lowest at 2 weeks of age (0.4 μg/l, 295 pmol/l), and increased linearly, exceeding 1 μg/l (740 pmol/l) after 37 days.

In our case, reduced weight gain appeared in the S lambs after 6-12 weeks on pasture, and additional symptoms of OWLD were seen 2-4 weeks later *(Ulvund & Pestalozzi* 1990a). The S lambs showed a close correlation between drop of plasma B_{12}, rise of MMA, and reduced growth. In 1982, reduced growth was noted already from early July *(Ulvund & Pestalozzi* 1990a). Reduced mean plasma B_{12} (142 pmol/l) was seen 6 weeks earlier, after only 2 weeks on pasture, and at the same time, 2 lambs had plasma MMA above 5 μmol/l. Clinical symptoms like lethargy, eye discharge etc. were observed 3-4 weeks after growth reduction had been noted, and almost 2 months after the initial lowering of plasma B_{12}.

In 1984, the condition of the S lambs was better than in 1982, and reduced growth was not noted until end of July *(Ulvund & Pestalozzi* 1990a). During the 6 preceding weeks, plasma B_{12} was below 100 pmol/l in all, all had MMA values >5 μmol/l, and 1 had MMA value >15 during the last 2 weeks. From mid August to end of September, when clinical symptoms were obvious, mean plasma B_{12} was below 138 pmol/l, and most MMA values were above 15 μmol/l. The lambs with the highest plasma MMA by mid June ended up as the smallest ones 3 months later.

In 1985, reduced growth in the S group was noted on July 22. Plasma B_{12} was very low 6 weeks earlier, and on July 22, 3 out of 4 lambs had MMA >5 µmol/l, 1 had MMA value >15 µmol/l. During August-October, MMA values were low, although the lambs had OWLD symptoms, but the condition was not so serious as in 1982 and 1986.

In 1986, initial flattening of the live weight curve was also noted on July 22. The S lambs had very low plasma B_{12} 3 weeks earlier, and all had plasma MMA above 15 µmol/l. That year, the lambs were particularly severely affected. On September 1, mean lw was 28 kg, while the SColick lambs were 13 kg heavier. The low initial plasma B_{12} seen in 1986 may have rendered them particularly susceptible. Generally, all untreated S lambs with plasma B_{12} below 250 pmol/l at outlet ended up among the smaller within the group.

The correlation between low plasma B_{12}/elevated MMA values and reduced growth was not so obvious in the H lambs. The H lambs were in good clinical condition during all years, but showed some annual variations in lw increase, and Co supplementation promoted growth to some (NS) extent *(Ulvund & Pestalozzi* 1990a). In 1986 the H lambs grew less than in other years, and were on average 4 and 6 kg lighter in mid September than in 1984 and 1985 respectively. But althouth they had mean plasma B_{12} values below 90 µmol/l for more than 2 months, they gained 13 kg more than the S lambs which had similar B_{12} amounts. Average growth (g/day) in the S lambs was for example 46 in July and ÷100 in August, while corresponding rates in the H lambs were 257 and 136 respectively.

The results in the S lambs correlate to some extent with the findings of *Caple & McDonald* (1983). According to them, liver B_{12} reserves decline until rumen microorganisms become established 20-30 days after birth. If pastures contain insufficient Co for adequate B_{12} synthesis, production losses due to B_{12} deficiency become apparent after 6-8 weeks, and clinical signs of OWLD may develop later if the deficiency is severe enough. The lack of clinical symptoms in the H lambs in 1986 is, however, difficult to explain.

Reduced growth was noted 3-8 weeks after plasma B_{12} dropped below 150 pmol/l in our S lambs. In clinical B_{12} deficiency of weaned lambs, plasma B_{12} is often reported to be below 150-240 pmol/l *(Andrews & Stevenson* 1966, *Fraser* 1982, *Russel et al.* 1975), while in moderate, marginal or uncertain B_{12} deficiency values may be below 330-370 pmol/l *(Andrews & Stevenson* 1966, *Millar & Lorenz* 1979, *Fraser* 1982). *MacPherson et al.* (1976) noted loss of appetite 5 weeks after plasma B_{12} fell below 295 pmol/l in healthy wethers of 40-70 kg.

Lambs affected with OWLD in New Zealand had 187 pmol/l of plasma B_{12} (range 70-520), while clinically unaffected on the same properties had 142 pmol/l (40-310), and control lambs grazing other pastures had 1,600 pmol/l (400-4000, *Sutherland et al.* 1979). In the OWLD lambs with high B_{12} values, a leakage of B_{12} from a damaged liver was suggested. In 38 lambs from farms with OWLD problems in Northern Ireland, mean plasma B_{12} was 138 pmol/l *(McLoughlin et al.* 1984), while mean amounts between 90 and 220 pmol/l were found in OWLD lambs in Australia *(Mitchell et al.* 1982).

On our OWLD pastures, reduced growth was associated with plasma MMA above 5 µmol/l together with B_{12} below 150 pmol/l, fulminant clinical OWLD most often with plasma B_{12} below 150, and MMA above 15. *McMurray et al.* (1985) considered MMA values below 5 µmol/l to be normal. B_{12}

amounts below 220 and MMA amounts below 15 were considered subclinical, while B_{12} amounts <220 combined with MMA >15 were considered clinical Co deficiency. B_{12}/MMA values indicating clinical Co deficiency were thus found in our OWLD lambs, but occurred in several healthy H lambs as well, both during 1984 and 1986.

Reduction of B_{12} or elevation of MMA did not seem to be associated with sex, breed or Hb-type. In the Co/B_{12} supplemented 5 lambs, growth increase was associated with low MMA contents and high B_{12} amounts. The SB_{12} lambs were among the better growing ones each year, and fortnightly injections yielded better growth than injections every third week *(Ulvund & Pestalozzi* 1990a). *Hogan et al.* (1973) injected B_{12} into lambs grazing Co deficient pasture at weaning, and found some effect on lw for at least 2 months. Larger doses than 1 mg did not increase growth rate proportionally, but they suggested that more frequent dosing than at monthly intervals with 1 mg, possibly could.

In our case, sampling of individual lambs at different intervals after B_{12} injection showed that the B_{12} was rather quickly removed from the blood. For example, on day 2 after injection (August), plasma B_{12} was 5540 pmol/l, on day 3: 3345 (June), on day 6: 1168 (May), and on day 10: 402 pmol/l (June). *Hannam et al.* (1980), who stated that B_{12} injection had no consistent effect on serum B_{12}, only made their first sampling 6 weeks after injection of 4 week old wethers. *Whitelaw & Russel* (1979) found that mean serum B_{12} in 2-3 months old lambs injected with 2 mg B_{12} was significantly higher than in the untreated controls for only 3-4 weeks. In 3 weekly injections of 1 mg into wethers (25-31 kg), *Millar & Albyt* (1984) found serum B_{12} values around 900-1000 pmol/l 1 week after injection, and 300-700 pmol/l 2 weeks after, which is largely in accordance with our results.

Our S lambs dosed with Co pellets were not sampled until 3 weeks after dosing, but had satisfactory B_{12} at the time. *Russell et al.* (1975) found an abrupt increase in plasma B_{12} 7 days after Co pellet dosing to 3 months old lambs. *Whitelaw & Russel* (1979) found that Co pellet dosed lambs maintained high plasma B_{12} over a period of 3 years, while *Millar & Albyt* (1984) reported that dosed lambs were not significantly different from undosed 14 weeks after the pellet administration. Due to scarce amounts of pasture grass in mid August 1985, the SCopell group was moved onto more lush grass on H pastures *(Ulvund & Pestalozzi* 1990a). The low plasma B_{12}/elevated plasma MMA seen 4 days later was probably due to sudden increased uptake of propionate precursors, as values were satisfactory 3 months after dosing (Tables 2 and 3).

Use of Co salt lick on the OWLD pastures resulted in larger range in individual plasma B_{12}/MMA than use of other types of Co/B_{12} supplementation, probably reflecting varying licking habits among the lambs. Effect on lw gain was, however, very good, except for 1 lamb with low initial plasma B_{12}, which gained 66 g/day less than average for the group. The salt lick contained extra Mn, Zn, I and Se as well *(Ulvund & Pestalozzi* 1990a), which may have had influence.

According to *Rice et al.* (1987), 38% of lambs with plasma B_{12} below 180 pmol/l had plasma MMA below 5 µmol/l, which should indicate that these lambs had no functional evidence of B_{12} deficiency. In our case, about 10% of all samples had such plasma B_{12}/MMA values. This percentage was, however, largest in June (28%), during the first month on pasture, before symptoms had developed.

A peculiar feature among the H lambs was the occurrence of elevated MMA values in individuals with B_{12} values fairly above 200 pmol/l (Fig. 1). Generally, high plasma MMA was not related to reduced lw in these lambs. Lambs number 2, 3 and 5, which had plasma MMA ≥ 14 µmol/l (Table 4), were among the better growing ones, with September mean lw 50 kg, as compared with 47 kg for the whole group. The elevated plasma MMA seen at start of grazing (Table 3), may reflect a high intake of soluble carbohydrates in lambs with very good appetite. The MMA accumulation may indicate lack of factors other than B_{12}, necessary in the propionate metabolism. Results suggest a big growth potential of the lambs.

The large difference in lw gain between the S and H lambs, especially in 1986 when both were deficient in B_{12} and showed MMA accumulation, together with the total lack of clinical symptoms in the H lambs, suggest that additional factors may be decisive as to whether the OWLD condition will develop or not. It was therefore of interest to examine the lambs from the various groups further regarding both blood and liver chemistry, as well as pathological changes.

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Sammendrag

Kvitleversjuke (kobolt/vitamin B_{12} mangel) hos lam. Vitamin B_{12} og methylmalon-eddiksyre (MMA) i blod.

Ved beiteslipp hadde 19% av de månedsgamle lamma plasma vitamin B_{12} under 250 pmol/l. Hos alle lam som ble satt på OWLD-beitene sank verdiene etter 2-4 veker, og var som regel under 150 pmol/l iløpet av beiteperioden. Plasma methylmalonsyre (MMA) steg over 5 µmol/l 2-8 veker etter slipp, og over 15 µmol/l 4 veker senere. Redusert tilvekst kom 3-8 veker etter at B_{12} var sunket under 150 pmol/l, og 4-6 veker etter at MMA steg til over 5 µmol/l. OWLD var som regel assosiert med plasma B_{12} uder 150 pmol/l og MMA over 15 µmol/l.

Koboltgjødsling av beitet ga tilfredsstillende plasma B_{12}/MMA hos lamma i 3 år etterpå. Ved dosering med koboltpellets var B_{12} forhøyet 3 veker senere. Bruk av kobolt saltslikkestein resulterte i store individuelle variasjoner i plasma B_{12}/MMA.

Kontrollamma varierte sterkt mhp plasma B_{12}/MMA. I 1986 indikerte verdiene funksjonell koboltmangel, men ingen utviklet OWLD, og veksten var tilfredsstillende, men noe mindre enn andre år. Hos disse lamma var ikke alltid høyt MMA korrelert til lavt B_{12}, eller til nedsatt vekst. OWLD forekom hos Co/B_{12} deficitte lam, men Co/B_{12} deficiette lam på andre beiter utviklet ikke OWLD.

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