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CHANGES IN SERUM MAGNESIUM LEVELS
OF RUMINANTS, AS INFLUENCED BY ABRUPT
CHANGES IN THE COMPOSITION OF THE DIET
EFFECT OF ORAL ADMINISTRATION OF VARIOUS
INORGANIC AND ORGANIC COMPOUNDS ON THE
SERUM-MAGNESIUM LEVEL

By

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In healthy ruminants the serum Mg level varies very little, the value remains about 2.3 to 2.8 mg per 100 ml and is generally not markedly influenced by pregnancy or parturition. By tetany, however, the serum Mg level may drop to values of about 0.5 mg per 100 ml or lower. This low serum Mg level associated with hypocalcaemia, as a criterion of the disease, was for the first time demonstrated by *Sjollema* (1928). Since then studies on etiological factors in relation to hypomagnesaemic tetany have been carried out on a larger scale, especially by Dutch and British research workers. A comprehensive review covering most of the known theories concerning the cause of disorders associated with hypomagnesaemia has been given by *Rook & Storry* (1962).

It is now an accomplished fact that tetany generally develops in connection with sudden changes in the manner of feeding, sometimes by stall-feeding, but much more frequently by changing from stall- to grass-feeding. Hypomagnesaemia without tetany has been produced already in 1932, when *Kruse et al.* succeeded in making rats hypomagnesaemic by reducing the Mg intake. The importance of a deficiency of available Mg in the fodder in relation to development of tetany in cows was demonstrated

experimentally by *Ender et al.* (1949), by inducing hypomagnesaemia and hypomagnesaemic tetany in cows using Mg deficient diets low in calories. *Blaxter et al.* (1954) have induced hypomagnesaemia in calves by feeding diets low in Mg, and *McAleese & Forbes* (1959) produced hypomagnesaemia in lambs on similar diets.

During the winter seasons 1960/61 and 1961/62 the author has performed feeding experiments with Mg deficient diets to lactating cows in collaboration with S. Tollersrud at the veterinary research station Wøyen (u.d.). The feeding was as normal as possible except for the Mg content which ranged from 3 to 5 g daily, proportional to the lactation volume (milk yield ranging from 12 to 21 kg a day). The results from 36 experiments were: 30 cases of hypomagnesaemia with serum Mg levels below 1 mg per 100 ml. Similar low serum Mg levels have been obtained by *Rook* (1961, 1963) using daily rations supplying about 1.5 g of magnesium daily to cows.

The results mentioned above support the theory that hypomagnesaemic tetany must be a consequence of deficient absorption of magnesium. In practical farming, however, it is hardly probable that the reduced absorption is caused by such sweeping changes in the nutritional Mg-content. When hypomagnesaemic tetany occurs as a result of underfeeding, *Swan & Jamieson* (1956) did not suppose deficient Mg supply to be the reason. When the disease develops shortly after the cows have been turned to pasture, it is likewise improbable that the fall in serum Mg may be due to deficient Mg intake. All scientists who have studied this problem agree with *Sjollem* (1932) that the Mg content in tetany prone pasture grass is generally not much lower than in pastures on which no diseases have been recorded. Accordingly, the disease is considered to be due to a conditioned Mg deficiency. *Blakemore & Stewart* (1934) even claimed to have found a higher Mg content in tetany prone pasture than in normal grass.

At the British Veterinary Association's Conference on Hypomagnesaemia in London 1960, *Ender* stressed the problem of nutritional factors responsible for hypomagnesaemia, the condition which he had already explained as a typical prodromal symptom leading to tetany (*Ender* 1957). The fact that real starving of cows leads to attacks of hypomagnesaemia even when Mg supplements are given is shown by *Halse* (1948). When cows

are turned out on the highly dressed pastures, however, they are not starving. Nevertheless, experience has shown, and it has been verified by experiments that the number of cows attacked by hypomagnesaemic tetany on these pastures increases with increased fertilization. That particularly dressings with excess of nitrogen, potassium and sulphur, as $(\text{NH}_4)_2\text{SO}_4 + \text{K}_2\text{SO}_4$, has proved to give a rather tetany prone pasture grass is demonstrated by *Bartlett et al.* (1954) *Ender et al.* (1957), *Huidsten et al.* (1959), and others.

According to *Rook & Balch* (1958) and *Kemp et al.* (1961), a higher absorption coefficient for magnesium in cows has been found in experiments carried out during the stall-feeding period than during periods feeding rapidly growing ryegrass. The problem, however, is to answer how it comes that these special pastures are able to decrease the Mg absorption coefficient in grazing cows to such a high degree that pathological serum Mg levels may be observed. Based upon studies on the chemical composition of tetany prone pasture grass in relation to normal pasture grass, many theories have been advanced during the last years to solve this problem. *Sjollema* (1930, 1931) pointed to the extremely high protein content of the pasture as a contributory causal factor. Other research workers have given support to the same theory, *Udall* (1947), *White* (1953) and *Kemp* (1960). According to the changed levels of N, Ca, Mg, Mn, K, Na, P, S, Cl, NO_3 and SO_4 in the tetany prone grass, many theories have been proposed concerning the influence of a surplus or a shortage of one or more of these elements upon the availability of dietary Mg, *Brower & Vliert* (1951), *Brower* (1952), *Oyaert* (1953), *Sjollema* (1954), *Sjollema et al.* (1955), *Rook & Balch* (1958, 1962), *Kemp* (1959), *Fontenot et al.* (1960), *Meyer & Steinbeck* (1960), and others. Many research workers have also stressed the importance of an abnormal interrelationship between the various elements with special regard to K/Ca, K/Mg, Na+K, Ca+K and K/Ca+Mg as contributory factors, *Brower & Vliert* (1951), *Colby & Frye* (1951), *Kemp & t'Hart* (1957), *Smyth et al.* (1958). Consideration has also been paid to the alkali alkalinity of the pasture, *Brower et al.* (1951), *Rook & Wood* (1960).

Many of these hypotheses have been denied: *Marr* (1958) could not find the alleged influence of protein, K, NO_3 and Mn. *Kemp* (1959) did not agree with the supposed influence of sodium and *v. d. Horst & Hendriks* (1958) did not believe in the

importance of the K/Ca+Mg ratio. Other hypotheses which have been launched include the influence of changes in the environmental temperature to cold, wet and windy weather, *Allcroft* (1947); the effect of fear, *Platner* (1950), *Platner & Hosko* (1953), *Hegsted et al.* (1956); the importance of excitement, *Mershon & Custer* (1958); forced exercise, *Udall* (1947); and the character of the grass whether coarse-fibred or not, *Larvor & Brochart* (1960), *Larvor, Brochart & Ladrat* (1960). Administration of vitamin D has been supposed to have a curing effect upon Mg deficiency, but according to *Blackburn et al.* (1957), *Line et al.* (1958), *Allcroft* (1960) and *McTaggart* (1960) this seems improbable.

The hypothesis of metabolic disturbances in the intestine as initiating factors by this disease was first advanced by *Sjollem & Seekles* (1929) and in the following years expanded by *Sjollem* (1932), *Green* (1939) and *Seekles* (1948). *Head & Rook* (1957) have explained this anomaly as a consequence of a fall in ultrafiltrable Mg demonstrated in the intestine of the cows when transferred to grass feeding.

The same authors, *Head & Rook* (1955) observed an increase in the ammonia content of rumen liquor on the transfer of ruminants to grass feeding and reported a fall in serum Mg following the introduction of ammonium salts into the rumen. They concluded that inadequate absorption of Mg could probably be associated with a high ruminal ammonia production, but the mechanism was not understood. *Simesen* (1957) launched the hypothesis that the high ammonia content would render Mg less soluble producing magnesium ammonium phosphate in the rumen. *Field et al.* (1958), however, maintained: "until direct measurements of Mg absorptions are made, the effect of ammonia on Mg absorption will remain uncertain".

The possibility of the presence of unknown toxic factors in the young grass has been stressed by several research workers, *Green* (1939), *Rosenberger et al.* (1961) and infection with *fasciola hepatica* is propounded as a causal factor by *Sinclair* (1960).

In 1961 *Burt & Thomas* advanced the hypothesis that an excess of citrate in the herbage may lead to hypomagnesaemia.

OWN INVESTIGATIONS

The experiments published in 1957 by *Ender et al.* concerning hypomagnesaemia and tetany induced in lactating cows by turning them out on a pasture heavily dressed with ammoniumsulphate and potassiumsulphate, have been continued during the last years, and analytical investigations of the pasture grass have been carried out. As seen from Table 1 hardly any difference was found between the percentage of Mg in the highly

Table 1. Analyses of air-dried pasture grass sampled on the first day of grazing.

	Highly dressed pasture		Normally dressed pasture		per cent Mg	per cent protein
	per cent Mg	per cent protein	per cent Mg	per cent protein		
		average		average		
1958	0.180		34.8			
	0.184		35.0			
	0.192		36.4			
	0.175	0.183	37.1	35.8		
1959	0.180		32.5			
	0.165		31.9			
	0.165		30.0			
	0.190		31.9			
	0.185		31.5			
	0.195	0.173	32.5	31.7		
1960	0.103		33.1			
	0.112	0.108	31.3	32.2	0.150	18.7
1961	0.115		27.7			
	0.130	0.123	27.7	27.7	0.117	16.0

dressed and the normally dressed pasture grass, whereas the protein content was very high in the nitrogen dressed pasture at the time of outlet. Equal relations were found between the average values calculated during the grazing period from start to attacks of tetany (Table 2), and on the days of attacks (Table 3).

Despite the fact that the protein content in springtime grass usually is high, the tetany prone pasture grass showed a content nearly twice as high as the normally dressed pasture grass. Amounts of Norwegian feed units in the pasture grass were calculated according to analyses performed at the State Agri-

Table 2. Mean values of Mg and protein in pasture grass sampled during the grazing period from start to attacks of tetany.

		Tetany producing pasture		Normally dressed pasture	
		per cent Mg	per cent protein	per cent Mg	per cent protein
1958	30/5—4/6	0.187	36.1		
1959	20/5—1/6	0.143	27.8		
1960	18/5—9/6	0.115	26.2	0.190	17.2
1961	27/5—1/6	0.104	23.0	0.113	12.2
	19/5—27/5	0.132	27.1	0.127	13.8

cultural Chemical Control Station in Oslo and found to be from 0.67 to 0.69 f.u. per kg dried matter in both samples. The tetany prone grass thus represented a very badly balanced diet with regard to the ratio between feed units and protein.

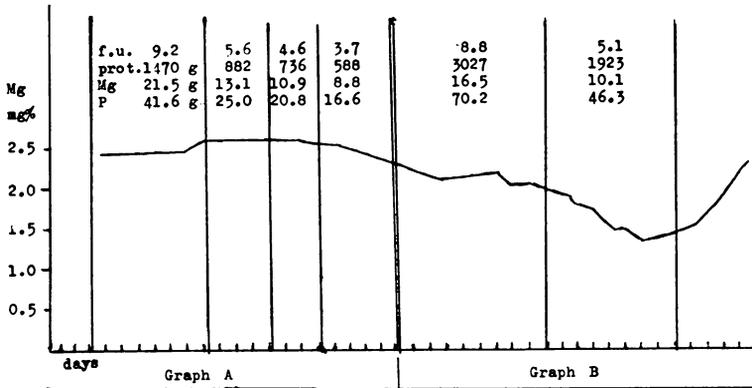
By examining the cows' manner of eating and by weighing them twice daily, the food intake was found to be almost normal. However, when forced to eat the unbalanced grass as their only diet, the cows were unable to regulate the relative intake of protein and f.u. Grass enough to cover the feed unit requirement represents a protein content of about three times the requirement, whereas cows unable to consume notably more protein than usual by stall feeding have to suffer from deficiencies in feed units and reduced intake of minerals.

Based upon controlled indoor feeding, experiments have been performed to test the influence of this reduction in calories combined with the still rather high excess of protein upon the serum Mg level. A similar reduction in fodder having a normal protein/f.u. ratio was performed as a basis for comparison (Graph 1). The two experiments were performed in succession, using the same six cows in the lactation period as test animals.

The preliminary feeding was fresh cut, normally topdressed grass ad libitum. On an average, each cow consumed 9.2 f.u. and 1471 g protein, i.e. 11 per cent of feed units and 60 per cent of protein above the theoretical requirement, and about 20 g of Mg a day. The serum Mg level was controlled by daily analyses during ten days and found normal all the time. During the following days the cows were underfed by exposing them to

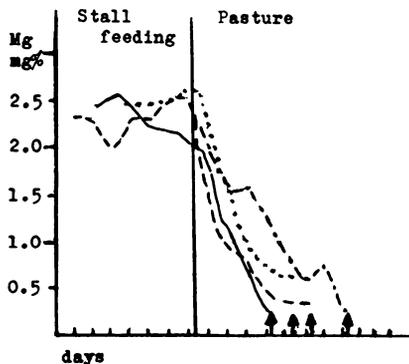
Table 3. Analyses of air-dried pasture grass sampled on the day of tetany attacks.

	Normal pasture				Tetanyproducing pasture				average values
	1 a	2 a	3 a	4 a	1 b	2 b	3 b	4 b	
% Ca	0.605	0.606	0.456	0.539	0.435	0.364	0.486	0.333	0.405
% Mg	0.150	0.122	0.104	0.117	0.125	0.107	0.130	0.115	0.119
% P	0.220	0.250	0.255	0.251	0.266	0.397	0.520	0.413	0.399
% S	0.216	0.241	0.231	0.194	0.452	0.367	0.359	0.455	0.408
% S (SO ₄)	0.047	0.088	0.068	0.048	0.260	0.125	0.076	0.178	0.160
% Na	0.022	0.009	0.007	0.010	0.023	0.013	0.019	0.012	0.017
% K	2.50	2.50	2.20	2.20	2.40	3.25	3.80	3.15	3.14
% N (NO ₃ ⁻)	0.015	< 0.01	0.01	< 0.01	0.102	0.048	0.086	0.025	0.065
% protein	12.2	12.9	11.6	13.4	19.5	24.2	27.5	27.7	24.7
p.p.m. Cu	6.0				6.9				
p.p.m. Mn	32				835				
p.p.m. Cr	0.11				1.0				
p.p.m. Sr	16				20				
p.p.m. Ba	9.4				21				
p.p.m. Ti	4.3				54				
p.p.m. Li	1.3				4.7				
p.p.m. Pb	1.1				5.4				
p.p.m. Ni	0.27				4.0				
p.p.m. Mo	0.87				< 0.3				
p.p.m. Co	< 0.3				< 0.3				
p.p.m. Sn	< 1.1				< 1.1				
p.p.m. V	< 1.1				1.8				



Graph 1 A and B. Average serum Mg levels recorded for six lactating cows when exposed to reduced intake of fodder.

- A: Cows exposed to a fodder normally balanced as to feed units and proteins.
- B: The same cows exposed to diets with normal amounts of feed units and the high protein content which is found in tetany prone pasture grass.



Graph 1 C. Serum-Mg-levels recorded in four cows attacked by tetany on highly dressed pasture.

gradually smaller daily rations of grass, and blood samples were drawn every morning to examine the serum Mg level. Calculated with respect to the feed unit content the food was reduced to 68 per cent of the requirement for the first four days, to 56 per cent for the next three days, and to 45 per cent for the last five days. Although the intake of Mg was only about 9 grammes per day during the last period, no noticeable effect upon the serum Mg level was observed in the course of these

twelve days with reduced, normally balanced fodder. The feeding was then increased to a normal level with respect to calories, and simultaneously a considerable excess of protein was given in the form of herring-meal and casein to make the protein/f.u. ratio equal to what is found in tetany prone pasture grass. On an average, the cows received per diem about 8.8 f.u. and 3027 g of protein, i.e. a surplus of 6 per cent of f.u. and about 200 per cent of protein. This feeding, which corresponds to a daily intake of 16.5 g magnesium, was given for nine days. In one cow the serum Mg level fell to 1.3 mg per cent, while the other five cows had normal serum Mg levels. From this time on $\frac{1}{3}$ of the mixed daily ration was taken away, bringing about a reduction in the amount of feed units to 65 per cent of the requirement, the protein, however, was still in an excess of 120 per cent, despite the reductions. After this change of diet, the daily rations supplied about 10 g magnesium. On the fourth day, the effect of this reduction upon the serum Mg levels was obvious and within six days the mean value had fallen from 2.0 to 1.3 mg Mg in 100 ml serum. The highest individual fall was found to be from 2.0 to 1.15 mg per cent Mg, whilst the least affected cow had a decrease from 2.0 to 1.85 mg per cent Mg. The lowest estimated serum Mg value, i.e. 0.7 mg per cent, was found in the cow that had already reached the level of 1.3 mg per cent at the beginning of the underfeeding period. The period lasted for eight days, and then the f.u. content of the daily rations was again increased to levels above the requirement by giving a surplus of fresh cut grass, by which the daily supply of protein simultaneously amounted to 130 per cent above the requirement. Exposed to this feeding the serum Mg values normalised within four days.

As no supplements of minerals were given during this experiment, the Mg intake decreased in accordance with the reduction of the fodder supply. Nevertheless, by using concentrates containing convenient amounts of Mg, it has been possible to avoid great differences in daily Mg intake between the two underfeeding periods. The values are presented in Graph 1.

The decrease in serum Mg caused by the artificial feed unit deficient and protein rich fodder was obvious, but the serum Mg level fell slowly and not at all in the same dangerous way as is seen by attacks of grass tetany (Graph 1 C). Because of the cows' difficulties in maintaining the serum Mg level at its normal level

by this unbalanced feeding, however, the abnormal ratio between protein and feed units may contribute to the proneness of the grass to produce tetany. The cows are brought into a labile state and are in an extremely susceptible condition in the face of variations. The decisive effect, however, must be produced by some other factor giving the impetus to the attack. This factor (or factors) was looked for by analysing the tetany prone pasture grass with regard to minerals and trace elements. The results are given in Table 3.

All analysed grass constituents, the amount of which was higher than the normal level, were taken into account and experiments were carried out to test the effect of dietary supplements of the same constituents on the serum Mg and Ca level.

Organic compounds supposed to have some influence on the Ca and Mg metabolism, because of their content of special nitrogen compounds, were also examined.

The animals in these experiments were healthy lambs and sheep with normal serum Mg levels, and they were fed diets having a normal or relatively high content of protein. Most of the tests were carried out as short time experiments by administering one or two relatively large doses of the mineral salts through stomach tubes for one or more days. Supplements to be tested during a longer period were given mixed into the concentrates. Blood samples for Ca, Mg and P analyses were drawn several times on each day during the experiments and on the following 8—10 days.

A survey of the results is presented in Table 4. The largest individual decreases in serum Mg were found in ewes dosed Na_2HPO_4 alone or combined with NaHCO_3 , but also dosages of K_2HPO_4 , $\text{K}_2\text{HPO}_4 + \text{Na}_2\text{SO}_4$, Na_2SO_4 or K_2SO_4 had a great effect. Simultaneously, the serum Ca value dropped to subnormal levels. $(\text{NH}_4)_2\text{HPO}_4$ had a similar effect, but too high doses seem to be toxic. Both of the ewes given $(\text{NH}_4)_2\text{SO}_4$ died without decreases in the serum Mg level. In one single experiment dosage of MnCl_2 seemed to have a pronounced influence as the serum Mg level fell about 0.9 mg per cent. Three other experiments, however, using the same MnCl_2 dosage, did not confirm this result.

The strikingly reducing effect of CaCO_3 upon serum Mg is also worth mentioning but, because of the simultaneous increasing effect upon serum Ca, no attention has been paid to CaCO_3 as a tetanygenic factor.

Table 4. The influence on serum Ca, P and Mg of peroral doses of mineral salts or organic compounds administered to sheep on normal diets.

Supplement	Daily doses g	The state of the sheep	Days from partum	Diet		Days of dosing	Provoked changes in serum mineral values mg/100 ml			Remarks
				f. u.	g prot.		△ Ca	△ P	△ Mg	
$\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$	330	non-pregnant		1.2	128	1	-2.6	+6.0	-1.2	
	330	"		1.5	280	1	-3.6		-0.6	dead
	188	"		1.2	128	1	-2.4	+3.8	-0.1	
	188	"		1.5	280	1	-3.7	+5.0	-0.3	
	75	pregnant	25	0.85	120	6	4.5	+3.4	-0.1	
	75	"	20	0.85	120	4	-5.1	+1.0	-0.4	dead
	75	"	33	0.85	120	6	-3.7	+7.0	-0.8	
	75	"	18	0.85	120	6	-3.3	+2.5	-0.4	
	75	"	27	0.85	120	6	-3.9	+7.2	-1.1	
	75	lactating	8	0.85	120	6	-5.8	+3.8	-1.5	
	75	"	10	0.85	120	6	-5.8	+5.2	-2.3	
	75	"	1	0.85	120	6	-2.9	+2.4	-1.2	
							-3.9	+4.2	-0.8	average 12 exp.
							-5.8	+7.2	-2.3	max.
$\text{Na}_2\text{HPO}_4 \cdot 12\text{H}_2\text{O}$ + NaHCO_3	190	non-pregnant		1.2	128	1	-1.1	+3.0	-0.5	
	+ 56	"		1.2	128	1	-2.3	+6.3	-0.8	
						-1.7	+4.7	-0.65	average 2 exp.	
						-2.3	+6.3	-0.8	max.	
$\text{NaH}_2\text{PO}_4 \cdot \text{H}_2\text{O}$	125	non-pregnant		1.2	128	1	-2.2		-0.7	
	125	"		1.5	280	1	-2.2		-0.1	
	85	"		1.2	128	1	-1.8		-0.4	
	85	"		1.5	280	1	-1.7		-0.4	
	40	lamb		grass		1	-2.1		-0.1	
	40	"		grass		1	-3.5		-0.5	
							-2.3		-0.4	average 6 exp.
						-3.5		-0.7	max.	
$(\text{NH}_4)_2\text{HPO}_4$	105	non-pregnant		1.2	128	1	-1.3	+3.1	-0.2	
	105	"		1.2	128	1	-1.8	+6.0	-0.8	
	150	"		1.5	280	1	-3.5		+0.3	dead
	65	lactating	8	1.2	128	1	-2.6	+8.2	-0.5	
	65	"	27	1.2	128	1	-0.9	+3.9	-0.3	
							-2.1	+5.3	-0.3	average 5 exp.
							-3.5	+8.2	-0.8	max.

K_2HPO_4	90	non-pregnant	1.5	280	1	-1.5	-0.6
	90	"	1.2	128	1	-2.3	-0.3
	90	"	1.2	128	1	-1.8	0
	90	"	1.2	128	1	1.5	-0.3
	90	lactating	1.2	128	1	-1.0	-0.6
	110	non-pregnant	1.2	128	1	-1.0	-2.2
	110	"	1.2	128	1	-2.1	0
							average 7 exp.
							max.
K_2HPO_4 + Na_2SO_4	60	non-pregnant	1.2	128	1	-1.6	-0.3
	+ 75	"	1.2	128	1	-0.7	-0.8
	70	"	1.2	128	1	1.5	+2.3
	+ 100	"	1.2	128	1	-1.7	+1.0
	30	lamb	0.8	73	1	-1.3	+0.6
	+ 30	"	0.8	73	1	+0.7	+2.0
							average 6 exp.
							max.
Na_2SO_4	105	non-pregnant	1.5	280	1	-2.7	+0.4
	105	"	1.5	280	1	-1.7	+2.2
	140	"	1.5	280	1	-0.6	+3.8
	75	"	0.85	120	1	-0.4	0
	75	"	hay		1	-1.2	-1.3
	75	lactating	0.85	120	1	-0.3	+5.1
	75	"	0.85	120	1	-2.2	+1.2
	81	lamb	0.8	73	1	-1.1	0
	81	"	0.8	73	1	-2.0	-0.8
	81	"	0.8	73	1	-1.0	-0.4
						average 10 exp.	
						max.	
K_2SO_4	129	non-pregnant	1.5	280	1	-0.3	-0.2
	129	"	1.5	280	1	-0.2	-0.6
	200	"	1.2	128	1	-1.1	-0.7
	77	lamb	grass		1	-0.4	+0.5
	77	"	grass		1	-1.0	+0.6
	100	"	0.8	73	1	-0.8	0
	100	"	0.8	73	1	-1.1	+3.8
							average 7 exp.
							max.
$(NH_4)_2SO_4$	75	non-pregnant	1.2	128	1	-1.9	+0.6
	75	"	1.2	128	1	0	+0.7

Table 4 (continued).

Supplement	Daily doses g	The state of the sheep	Days from parturition	Diet		Days of dosing	Provoked changes in serum mineral values mg/100 ml			Remarks
				f. u.	g prot.		Δ Ca	Δ P	Δ Mg	
CaCO ₃	50	non-pregnant		1.2	128	1	+1.6	+1.1	-0.9	
	50	"		1.2	128	1	+2.5	+1.4	-0.4	
	50	"		1.2	128	1	+4.0	-1.8	-0.3	
	50	"		1.2	128	1	+2.9	+0.4	-0.4	
	100	"		1.2	128	1	+1.9	-1.0	-1.0	
	100	"		1.2	128	1	+1.6	-1.0	-1.0	
	100	"		1.2	128	1	+1.3	+0.2	-0.8	
	100	"		1.2	128	1	+3.0	+1.2	-0.7	
	70	"		1.2	128	1	+2.0	-1.1	-0.7	
	70	pregnant	85	0.85	100	1	+3.1	-3.7	-0.9	
	55	"	9	0.85	120	1	+2.3	-1.0	-0.8	
	55	"	7	hay		1	+2.7	-3.6	-1.2	
							+2.4	-0.7	-0.8	average 12 exp.
							+4.0	-3.6	-1.2	max.
MnCl ₂ ·4H ₂ O	26	non-pregnant		1.2	128	1	-0.5	-2.5	-0.3	
	60	pregnant	60	1.2	128	1	-1.5	-2.9	-0.3	
	26	lamb		0.8	73	1	-1.2	0	-0.9	
	26	"		0.8	73	1	-0.5	+0.1	-0.4	
(NH ₄) ₆ Mo ₇ O ₂₄	0.2	non-pregnant		1.2	128	1	+0.9	+0.2	+0.3	
	0.2	"		1.2	128	1	-1.9	+1.7	+0.3	
FeCl ₂ ·4H ₂ O	30	pregnant	55	1.2	128	3	-3.0	-4.3	+0.6	
	30	"	50	1.2	128	3	-0.7	-1.8	+0.4	
	30	"	50	1.2	128	1	-0.3	-2.5	-0.4	
FeCO ₃	20	pregnant	20	1.2	128	1	-1.3	-2.9	+0.2	average 4 exp.
	20	"	20	1.2	128	1	-3.0	-4.3	+0.6	max.
	20	"	25	1.2	128	2	-1.0	-0.3	-0.2	
	20	"	25	1.2	128	2	-1.3	0	+0.5	
CuSO ₄ ·5H ₂ O	0.6	non-pregnant		1.2	128	1	-2.2	+1.3	+1.2	
	0.6	"		1.2	128	1	-1.5	+0.3	+0.5	average 3 exp.
NaCl	30	pregnant	30	1.2	128	1	-2.2	+1.3	+1.2	max.
	20	lamb		0.8	73	10	-2.4	+1.5	+0.5	
Na ₂ SO ₃ ·7H ₂ O	20	lamb		0.8	73	10	-0.6	-1.5	+0.5	
						-0.5	-1.3	+0.3		
									None ¹⁾	

Na ₂ S	2-4	lamb				0.8	73	4	None
	2-4	"				0.8	73	4	"
	6-8	"				0.8	73	5	"
	6-8	"				0.8	73	5	"
	10-14	"				0.8	73	14	"
	10-14	"				0.8	73	14	"
	16	"				0.8	73	1	"
Na ₂ S ₂ O ₃	20-30	"				0.8	73	14	"
	20	non-pregnant				1.2	128	1	"
	40	lactating	23			1.5	280	1	"
KNO ₃	40	"	28			1.5	280	1	"
	0.1	non-pregnant				1.2	128	4	"
	0.1	"				1.2	128	4	"
Na-phytate	260	non-pregnant				1.2	128	1	"
	260	"				1.2	128	1	"
	15	"				1.2	128	1	" 1)
	25	"				1.2	128	1	" 1)
	30	"				1.2	128	1	" 1)
	15	lactating	28			1.2	128	6	" 1)2)
	20-25	"	20			1.2	128	2	" 1)2)
Urea	25-45	"	60			1.2	128	40	" 1)2)
	25-60	"	45			1.2	128	40	" 1)2)
	25-60	pregnant	60			0.8	136	20	" 1)2)
	25-80	"	70	hay				24	" 2)
	3-4	lamb				0.8	73	15	" 1)
	3-4	"				0.8	73	10	" 1)
	Methionine	4-30	pregnant	90			1.1	347	4
15-30		"	35			1.1	347	7	" 1)
6-30		pregnant	120			1.1	347	7	" 1)
4-30		"	90			1.1	347	7	" 1)
12-40		"	70			1.1	347	8	" 2)
3-6		"	70			1.1	347	5	" 1)
3-6		"	30			1.1	347	5	" 2)
Dihydrobenzene-di-sulfonic acid Na	3-15	non-pregnant				1.1	347	7	"
	3-15	"				1.1	347	7	"
	30	lamb				0.8	73	3	" 1)
Cysteinehydrochloride	4-8-12 tablets	lamb				0.8	73	30	" 1)
	4-8-12	"				0.8	73	30	" 1)
	4-8-12	"				0.8	73	30	" 1)
Cystin	2000-8000 I.U.	pregnant	66			0.8	112	43	" 3)
Thiourea	3-4	lamb				0.8	73	15	" 1)
	3-4	"				0.8	73	10	" 1)
									dead

1) The P level was unsteady, but without any special tendency.

2) The Ca level was unsteady with decreasing tendency in the beginning, but normalized quickly.

3) The Ca level increased in proportion to the quantity of vitamine given.

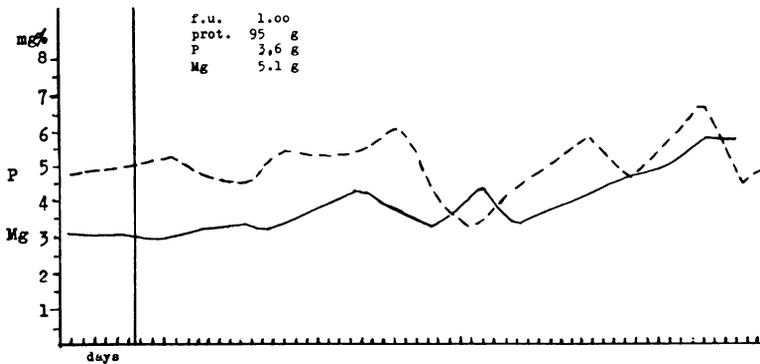
The other salts which were tested had no remarkable influence upon the serum Mg level, nor had the organic compounds.

The fact that urea may exert a toxic effect is shown in an experiment with a ewe which was fed hay and urea only. The ewe died under violent tetanic symptoms and tympania, but without any changes in the serum Mg level. Urea dosed in moderate quantities as a supplement to other concentrates produced no toxic effect, nor did it influence the serum Mg level.

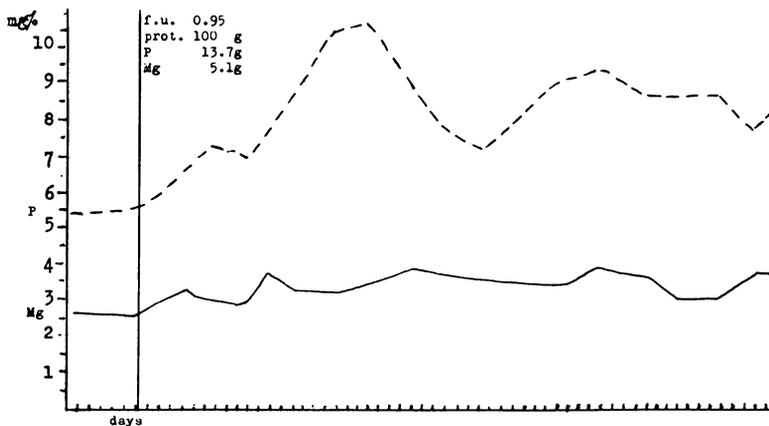
With a view to the pronounced serum Mg reducing effect of excess of phosphate in diets normally balanced as to the Mg content, another experiment was carried out in order to study how far the magnesium absorption would be disturbed when the magnesium intake simultaneously was relatively high. Two ewes, A and B, were fed diets equal in feed units and protein. Both diets supplied 5 g Mg per day, the P contents, however, were respectively 3.6 g and 13.7 g a day. The diets were given for seven weeks, and inorganic P and Mg in serum were continuously determined by analyses. A steady rise in the levels of serum Mg was observed for ewe A with no changes in the serum phosphorus levels (Graph 2 A). In ewe B, however, serum phosphorus increased considerably, whereas the expected rising tendency in serum Mg was rather limited (Graph 2 B).

Analyses have shown that the large number of concentrates usually given as protein supplements vary considerably as to the P content. This may perhaps be the reason why the different protein concentrates do not interfere with serum Mg to the same extent. In order to test this experimentally, two groups of sheep were exposed to high protein feeding, one group being fed P rich herring meal and the other receiving whale meat meal which contained only small quantities of P. The concentrates were given in protein-equivalent quantities up to six times the protein requirement. During the first 18 days, no further supplements were given. During the following 12 days 20 g of MgO was added daily, and then, during the last days, the supplement of MgO was augmented to 30 g daily.

The large excess of protein given as whale meat meal, containing only 1.5 g of P daily, did not noticeably influence the serum Mg level during the period of normal Mg support, 1.2 g daily, nor did it seem to interfere with the serum Mg increasing effect of MgO supplements. The same quantity of protein given as herring meal, with the high amount of 14.5 g of P daily, was



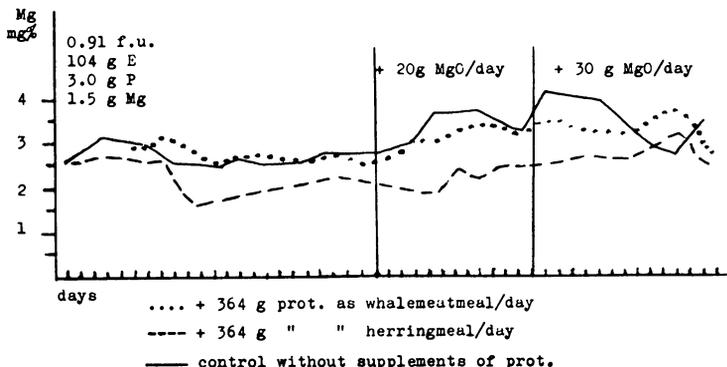
Graph 2 A. Serum Mg and P levels recorded in ewe A fed a diet high in Mg and normal in P.



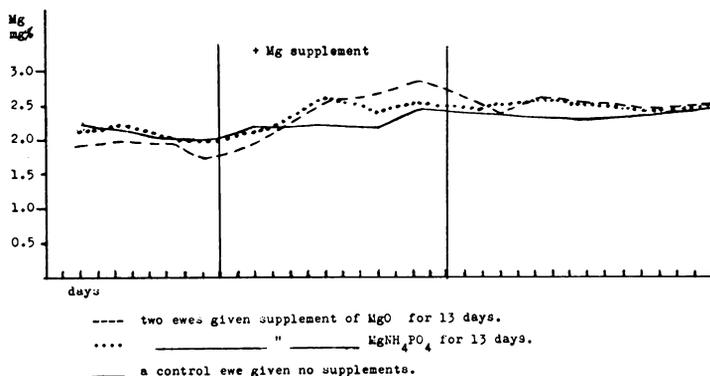
Graph 2 B. Serum Mg and P levels recorded in ewe B fed a diet high in Mg and high in P.

found to have a pronounced decreasing effect on the serum Mg level during the first 18 days when the dietary supply of Mg was 1.4 g daily and MgO as a supplement to the same diet did not increase the serum Mg level even in the neighbourhood of what was found in the first group (Graph 3).

No hypothesis has been advanced concerning the reaction mechanism between phosphorus and magnesium metabolism. According, however, to the theoretical possibility of phosphate adhering to magnesium in a complex salt as MgNH_4PO_4 , this salt has been compared with MgO as a metabolic Mg supplier. MgNH_4PO_4 and MgO in Mg equivalent amounts were dosed on



Graph 3. Serum Mg levels in sheep given normal diets supplemented with high amounts of protein and MgO.

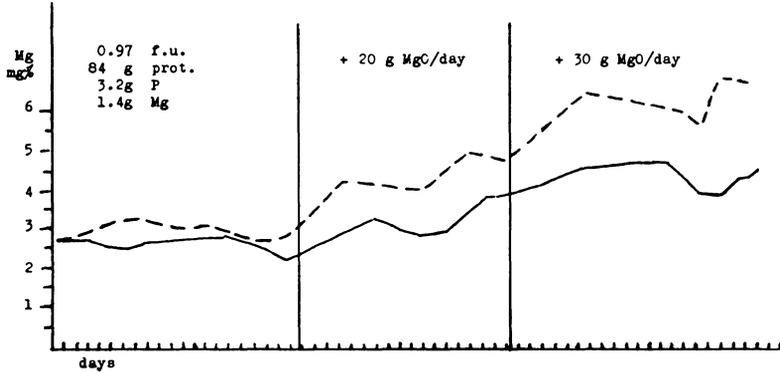


Graph 4. Average serum Mg levels recorded in ewes given equal doses of Mg as MgO and Mg NH₄PO₄ respectively.

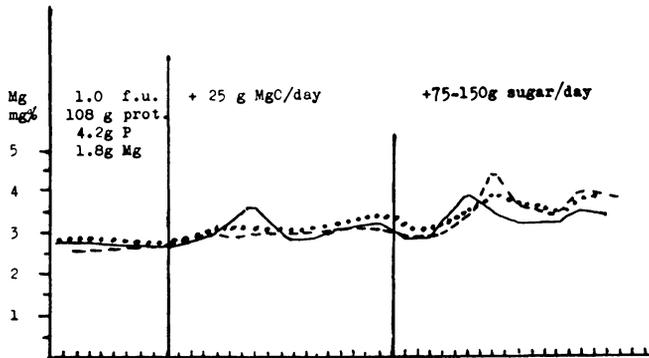
a parallel basis for 13 days to two groups of sheep fed high amounts of protein. A third group of sheep which received 1.5 g Mg daily served as control. The low Mg dosages (only 7 g/day) were perhaps responsible for the merely slight differences between control animals, on the one side, and the animals which were dosed MgO and MgNH₄PO₄, on the other. The tendency, however, towards higher Mg absorption was more pronounced in animals receiving MgO than in those which were dosed with MgNH₄PO₄ (Graph 4).

A conspicuous increase of the serum Mg level was observed by giving normally fed sheep 20 g MgO or more daily (Graph 5).

By multiplying the dietary amount of carbohydrates by supplying sucrose, the serum Mg level increased still more (Graph 6). The degree of reaction, however, appears to be of an individual nature.



Graph 5. Serum Mg levels in normally fed sheep given supplements of MgO.



Graph 6. Serum Mg levels in normally fed sheep given supplements of MgO and carbohydrates.

DISCUSSION AND CONCLUSION

With regard to the serum Mg reducing tendency and the tetany prone effect of the early pasture grass highly toppedressed with $(\text{NH}_4)_2\text{SO}_4$ and K_2SO_4 , our studies justify the assumption that the abnormally high protein content of such grass, although normal in feed units, plays an important part among the factors causing changes in the serum Mg levels of ruminants.

The majority of the cows used in our experiments were of the "Rödkoll" breed, with an average live weight of about 500 kg.

Daily amounts of calories and protein advised for the maintenance of such cows, according to *Breirem* (1959), are 3.5 Norwegian feed units and 260 g protein. By milk production each kg of milk (4.0 per cent) requires 0.4 N.f.u. and 60 g protein. With a daily milk production of 15 kg the total amounts advised will be 9.5 N.f.u. and 1.160 kg protein per day, corresponding to a N.f.u./protein ratio of 8.2. As long as the cows are fed indoors, no difficulties are encountered in supplying the correct ratio of protein and feed units. When the cows are turned out, however, and are bound to eat pasture grass as their only feed, this ratio will be considerably changed. This is particularly pronounced if the highly dressed pastures are used. The N.f.u./protein ratio in this pasture grass amounts only to about 2.1, and grass giving the required 9.5 N.f.u. contains the high amount of about 4.50 kg protein. As long as the cows can manage to eat enough grass to cover their requirement to feed units, the described experiments show that the serum Mg level will not decrease notably despite the high protein content. However, as soon as they are no longer capable of eating these very large quantities of protein, they are forced to reduce the consumption of grass. As seen from Graph 1, a temporary underfeeding with grass of normal feed unit/protein ratio does not affect the cows very much. They accommodate by decreasing in weight and especially in milk production, and remain healthy with a normal Mg level, despite a fall in the dietary supply of Mg to about 10 g daily. The same decreases in f.u. and dietary Mg, however, seem to have a greater influence when the protein content of the diet is not simultaneously below the requirement, but is still available in large excess, as is the fact when the intake of grass from the tetany prone pasture is reduced. The high protein content of grass will stimulate milk production despite the reduction in f.u. and minerals, and a cow exposed to this unbalanced feeding will, therefore, be counteracted in bringing about the sufficient reduction in milk production. Consequently, the ability of maintaining normal Mg balance will be thwarted, but if nothing else happens, this is not proposed to produce any forms of tetany. The reduction in serum Mg proceeds slowly and not at all in the serious way observed in connection with attacks of tetany. Cows brought into this hypomagnesaemic condition will, however, be much more susceptible to attacks of tetany than "normal" cows. When cows are in "normal" conditions abrupt variations in diets or environment

provoking moderate short-time decreases in the serum Mg- and Ca-levels, will usually be of no importance to the health. These already hypomagnesaemic cows, however, are unable to stand up against similar decreases in the serum Mg- and Ca-levels and consequently the risk of attacks of tetany will be increased. As seen from Table 4, it is evident that particularly phosphates and sulphates of sodium and potassium may be able to produce this drop in Mg as well as in Ca, if they are present in excess. These facts, combined with the analytical findings of higher contents of P, S and K, and to some extent Na in the tetany prone grass than in normally dressed pasture grass, justify the mentioning of these elements as contributory factors. Phosphates or sulphates, separate or in co-operation, may be suggested as tetany releasing elements, thus possessing a typical "trigger effect". Although this proposal seems to be well motivated, these compounds may hardly be considered as the only "trigger elements" releasing tetany. Other, not yet tried, elements, inorganic as well as organic, may very likely exert similar effects. The "trigger effect", however, is only a secondary cause to tetany, the *sine qua non* is undoubtedly the labile, hypomagnesaemic condition preparing the way for attacks of tetany. The influence of environmental conditions may also be taken into consideration as contributing factors.

Etiological studies are going on continually and grass extracts from tetany prone pasture and rumen juice from tetany cows are being analysed and tested in order to study the Mg absorption in relation to hypomagnesaemic tetany.

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SUMMARY

During a period of four years in succession samples of grass from tetany prone pastures, topdressed with large amounts of ammonium sulphate and potassium sulphate, have been analysed throughout the tetany season each year, and the results have been compared with the analytical data obtained from corresponding samples of grass collected from normally dressed pastures. The content of Mg and Ca and the feed unit value of the tetany prone grass differed very little from the normal. The protein content, however, was exceptionally high, and rather great differences were found in the content of P, S, K, Na and

the trace elements. Several feeding experiments have been carried out in order to test the hypomagnesaemic and/or the tetanygenic effect of these compounds as dietary supplements to ruminants. The feeding was performed under exact daily control and the experiments were supported by daily serum mineral analyses. Experiments carried out with diets containing protein and feed units in the same ratio as found in the highly topdressed pasture grass, proved that this unbalanced ratio undoubtedly played an important role in the hypomagnesaemia inducing effect of the grass. As long as the fodder was given in amounts high enough to cover the feed units requirements, the level of serum Mg remained unchanged. The falling tendency of the serum Mg level was, however, evident when the fodder rations were reduced to amounts insufficient to cover the feed unit requirements of the cows — a situation often met with for shorter periods during pasturing. Hypomagnesaemia was produced within 3—4 days, whereas a similar reduction of a normally balanced fodder to cows had no serum Mg reducing effect in the course of twelve days.

Of other factors coming into play, especially K_2HPO_4 , Na_2HPO_4 , K_2SO_4 and Na_2SO_4 proved to influence the serum mineral balance. Oral applications of large doses of these substances to healthy sheep, produced neither pronounced hypomagnesaemia nor tetany. The initial drop in the levels of serum Mg and particularly serum Ca were, however, so remarkable that tetany very probably would have been provoked if the animals had been in a hypomagnesaemic state when the experiment started.

Experiments and results have been closely discussed. The conclusion has been drawn that the tetany prone effect of the heavily ammoniumsulphate dressed pastures could not possibly be conditioned by one single factor in the grass. A more possible explanation seems to be an unpropitious interaction of more active compounds present at the same time:

The first step in the development of the disorder, i. e. the hypomagnesaemic condition, seems principally to be due to the unproportionately high content of protein in relation to the feed unit value of the grass. Owing to the fact that the quantity of dietary protein is in excess even if the feed unit content does not cover the theoretical requirements, the milk production remains high and the cows are hampered in their efforts to accommodate to those reductions in food intake uneventfully happening to occur on pasture. The next step, the convulsion of tetany, however, depends upon other, co-operating factors able to disturb the Ca-balance at the very moment when the serum Mg is already low. According to the serum Mg- and Ca-reducing effect brought about by diets supplemented with alkaliphosphates and -sulphates, the author inclines to the view that the extremely high content of P, S, K and to some extent also of Na found in the tetany prone pasture grass, may be the background for this effect of the grass. Temperature, rainfall and other environmental factors have also been taken into consideration as influencing the appetite and the absorptioncoefficient.

ZUSAMMENFASSUNG

Variationen im Blutmagnesiumgehalt bei Wiederkäuern verursacht von plötzlichen Änderungen in der Zusammensetzung des Futters. Die Wirkung oraler Beigabe anorganischer und organischer Stoffe auf den Magnesiumgehalt des Blutes.

Im Laufe einer vierjährigen Periode wurde das Gras von einer Weide, welche stark mit Ammoniumsulphat und Kaliumsulphat gedüngt war und auf der häufig Tetanie festgestellt wurde, von Anfang des Weideganges bis zum Ausbruch der Tetanie kontinuierlich analysiert. Die Ergebnisse wurden mit Proben von einer normalgedüngten Weide verglichen.

Der Futterwert des Grases und der Gehalt an Mg und Ca wich nicht weiter von den Werten des normalgedüngten Grases ab. Der Proteingehalt war dagegen sehr hoch, und für die Gehalte an P, S, K, Na und Spurenelementen wurde eine relativ grosse Abweichung festgestellt. Eine Reihe von Fütterungsversuchen werden beschrieben in welchen diese Abweichungen in Diäte eingeführt wurden die im voraus genau berechnet waren. Der eventuelle hypomagnesaemische oder tetaniegene Effekt dieser Diäte wurde durch eine tägliche Kontrolle des Serummineralgehaltes untersucht. Versuche mit einem Futter dessen Protein- und Futterwert den Werten des Grases der Tetanie-Weide entsprach zeigten, dass dieses schlecht abgestimmte Verhältnis zweifellos für die Erklärung des hypomagnesaemischen Effektes eine grosse Rolle spielt. Der grosse Proteinüberschuss störte nicht die Mg-Bilanz wenn das Futter in so grossen Mengen verabreicht wurde, dass es im übrigen suffizient war. Der Serum-Mg-Gehalt zeigte jedoch eine deutlich abfallende Tendenz als die Futtermenge herabgesetzt wurde, wodurch der Futterbedarf nicht mehr ganz gedeckt wurde, was bei frühem Weidegang in kürzeren Perioden oft der Fall ist. Die Analysen zeigten deutlich Hypomagnesaemie nach 3 bis 4 Tagen. Bei normal abgestimmten Futter zeigte eine entsprechend verminderte Futtermenge nach dem Verlauf von 12 Tagen noch keine Reaktion.

Bei den übrigen geprüften Stoffen zeigte es sich, dass besonders eine Beigabe von K_2HPO_4 , Na_2HPO_4 , K_2SO_4 und Na_2SO_4 grossen Einfluss auf die Mineralstoffbilanz ausübten. Keiner der Stoffe verursachte jedoch Tetanie bei Schafen, welche sich im voraus in normaler Bilanz befanden. Der Fall sowohl in den Serum-Ca als auch in den Serum-Mg Werten war aber so gross, dass eine Tetanie höchst wahrscheinlich eingetroffen wäre bei einer im voraus niedrigen Mg-Bilanz.

Die Versuchspläne und Ergebnisse werden eingehend diskutiert, und der Verfasser konkludiert diese dahin, dass der tetaniegene Effekt, welcher in stark ammoniumsulphatgedüngten Weidegras festgestellt ist, nicht auf einen einzelnen Komponenten sondern auf ein ungünstiges Zusammentreffen verschiedener Faktoren zurückgeführt werden kann.

Die erste Stufe im Krankheitsverlauf — die Hypomagnesaemie scheint in erster Reihe von dem im Verhältnis zum Futterwert unverhältnismässig hohen Proteingehalt herzurühren. Weil ein Protein-

überschuss vorhanden ist — auch wo der Futterbedarf nicht gedeckt ist — setzt die Milchproduktion fort, weshalb die Kühe sich den zufälligen Reduktionen in der Futterraufnahme, welche immer bei frühem Weidegang eintreten werden, nicht anpassen können. Die zweite Stufe des Verlaufes — die Tetanie — ist darauf zurückzuführen, dass ausser dem geringen Mg-Niveau auch die Ca-Bilanz gestört ist.

Der Verfasser ist der Meinung, auf Grund der Ergergebnisse welche bei einer Fütterung mit normalem Futter nach Zusatz eines Überschusses an Alkali-Phosphat und -Sulphat erreicht wurden, dass besonders der grosse Gehalt an P, S, K und zum Teil Na im ammoniumsulphatgedüngten Weidegras diesen Effekt erklären kann. Temperaturänderungen, Niederschläge und Wetteränderungen wurden als mitwirkende Ursachen berücksichtigt, weil diese zweifellos den Appetit der Kühe und die Aufnahmefähigkeit des Organismus beeinflussen.

SAMMENDRAG

Variasjoner i drøvtyggenes serum-magnesium-speil i tilknytning til plutselige forandringer i førets sammensetning. Undersøkelse av serum-Mg-speilet etter orale tilskudd av forskjellige uorganiske og organiske komponenter.

Gjennom en fire års periode er prøver av gras fra sterkt ammon-sulfat + kaliumsulfat-gjødslet tetani-beite blitt analysert kontinuerlig fra beiteslipp til tetaniutbrudd, og resultatene er blitt sammenlignet med tilsvarende analyser av prøver fra normalgjødslet beite.

Grasets førenhetsverdi og dets innhold av Mg og Ca avvek ikke i særlig grad fra det som ble funnet i normalgjødslet gras. Proteininnholdet var derimot meget høyt og en relativt stor avvikelse ble funnet med hensyn på innhold av P, S, K, Na og sporelementer. En rekke føringsforsøk er beskrevet, hvor disse avvikelser er innført i på forhånd nøyaktig beregnede dietter, og deres eventuelle hypomagnesiumiske eller tetanigene effekt er blitt undersøkt ved daglig kontroll av serum mineral speilet. Forsøk med før hvis protein- og førenhetsverdi tilsvarte tetani-beitegrasets, viste at dette dårlig avbalanserte forhold utvilsomt må spille en stor rolle når det gjelder å forklare grasets hypomagnesiumiske effekt. Det store proteinoverskudd forstyrret ikke Mg-balansen så lenge føret ble gitt i så store mengder at det ellers var fullverdig, men serum Mg-speilet viste tydelig fallende tendens da tilførselen ble nedsatt så førenhetsverdien ikke lenger fullt ut dekket behovet, noe som ofte forekommer i kortere perioder ved tidlig beiteslipp. Analysene viste tydelig hypomagnesiumemi etter 3—4 døgn, mens samme nedslag i normalt avbalansert før ikke ga noen reaksjon i løpet av 12 døgn.

Av de øvrige stoffer som ble prøvet, ble særlig tilskudd av K_2HPO_4 , Na_2HPO_4 , K_2SO_4 og Na_2SO_4 funnet å ha betydelig innflytelse på mineralbalansen. Ingen av stoffene fremkalte tetani på sauer som på forhånd var i normal balanse, men fallet i så vel serum Ca som serum Mg verdiene var så stort at tetani høyst sannsynlig ville ha inntruffet hvis Mg-balansen på forhånd hadde vært lav.

Forsøksoppleggene og resultatene er inngående diskutert og forfatteren er kommet til den konklusjon at den tetanigene effekt som er påvist i sterkt ammonisulfat-gjødslet beitegras ikke kan tilskrives en enkelt komponent, men må skyldes et uheldig samspill mellom flere tilstedeværende komponenter:

Første trinn i sykdomsutviklingen, den hypomagnesemiske tilstand, synes i første rekke å skyldes grasets uforholdsmessig høye proteininnhold i forhold til førenhetsverdien. Ved at proteinet er i overskudd også når førenhetsbehovet ikke er dekket, holdes melkeproduksjonen oppe og kuene kan ikke tilpasse seg de tilfeldige reduksjoner i fóropptak som alltid vil forekomme ved tidlig beiteslipp. Annet trinn i utviklingen, tetani, er et resultat av at også Ca-balansen svikter samtidig med at Mg-nivået er lavt. Ut fra de resultater som er oppnådd ved fóring med normalt fórtilsatt overskudd av alkali-fosfat og -sulfat er forfatteren av den oppfatning at det ammonisulfatgjødslete beitegrasets store innhold av P, S, K og til dels Na i særlig grad kan forklare denne effekt. Temperaturomslag, nedbør og andre forandringer i værforholdene er også tatt i betraktning som medvirkende årsaker, da det utvilsomt influerer på kuenes appetitt og organismens oppsugningsevne.

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