Reviews on the mineral provision in ruminants (XV): FLUORINE, CHROMIUM, NICKEL AND MOLYBDENUM METABOLISM AND REQUIREMENTS IN RUMINANTS

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CONTENT

LIST OF ABBREVIATIONS

Abbreviations	Unit	Description
BW	Kg	Body weight
DM		Dry matter
DMI	Kg	Dry matter intake

1 Functions and toxic effects in the body

1.1 Fluorine

Although F is known to be essential for the prevention of dental caries in man and normal growth in both rats and goats, no specific essential function of F is known in ruminants. Toxic concentrations of F impair ameloblast function of growing teeth, thereby affecting normal shape, abrasion and function of the teeth. Moreover, F toxicosis causes abnormal periosteal bone formation, giving rise to abnormal shape and structure of skeletal bones [86].

1.2 Chromium

Chromium is an essential component of the glucose tolerance factor[1] and increases the utilization of glucose and other metabolites by cells. However, not in all ruminants experiments an influence of Cr on glucose kinetics could be demonstrated. Biologically active Cr compounds, such as Cr tripicolinate or Cr nicotinate, decrease body fat stores, blood NEFA levels and increase muscling in sheep [19], reduce hepatic triacylglycerol accumulation in periparturient cows and increase milk yield in primiparous cows [54;62;63]. Chromium addition to lamb rations had only minimal and inconsistent effects on performance and immunology [22], although performance and immune response against respiratory and intestinal viruses were improved in transport-stressed calves in some cases [13;86]. Recently, Cr picolinate supplementation has been shown to reduce incidence of retention secundinarum in cows [90]. However, the relationship between various forms of stress, chemical form and dosage of Cr and the variability of biochemical and performance responses of ruminants make it difficult to define the circumstances under which ruminants will benefit from Cr supplementation [12;36;37;41;80;86;95].

1.4 Nickel

In calves[2], sheep and goats Ni deficiency causes decreased activities of ruminal urease and the activity of sorbite dehydrogenase (SDH) and alanine transaminase (ALAT) in serum and liver when compared to animals receiving sufficient amounts of Ni. Moreover, enzymes as carbon monoxide dehydrogenase and methyl-coenzyme-M-reductase, which are involved in ruminal volatile fatty acid production, also require Ni for proper function. Finally, sufficient amounts of Ni seem to be necessary for proper Ca and Zn metabolism [3;50;76;77;79]. However, a specific biochemical role for Ni has not yet been identified [86].

1.5 Molybdenum

Molybdenum is a component of nitrate reductase, xanthine oxidoreductase, sulfide oxidase and aldehyde oxidase [16;24;54]. In this way, it is i.a. involved in nitrate, purine and sulphur metabolism and possibly in celullolytic activity of ruminal bacteria [31;49].

[1] An organometallic molecule composed of Cr^{3+}, nicotinic acid, glutamic acid, glycine and cysteine, which is inactive without Cr [54].

[2] Effect on urease was only significant at a 10% crude protein diet, but not at crude protein levels of 12.3 and 14.5% [76].

2. Sources, distribution in the body and kinetics

2.1 Fluorine

Airborne F pollution can occur by volcanism, erosion of F-rich rocks and by industrial activities (aluminium and phosphorus plants, coal fueled electric power plants, steel and brick industries)[11;74;86], as shown by contamination of marsh and pastures in industrial areas [7]. However, deposition of airborne F onto plants contributes to F loading of animals rather than direct inhalation of F [8]. Occasionally F pollution has occurred as a result of topdressing with superphosphate [14]. Plants accumulate F in their leaves. In uncontaminated areas plants contain 2-30 ppm F [8;11]. After absorption, F is mainly transported in the plasma [86]. Within the body F is accumulated in the bones and teeth, the concentrations being higher in older animals [8]. Soft tissues contain only low F concentrations [86]. Placental transfer of F to the calf is limited [67], although fetal blood F concentrations can equal those of the dam (duration of exposure not reported). Within the fetus, selective F accumulation occurs in bone an teeth [70].

2.2 Chromium

Industrial and traffic exhaust are the most important sources of Cr and Ni. Normally, feedstuff Cr concentrations (ppm (DM)) range from 0.1-0.4 (grasses), 0.2-4.2 (legumes) and 0.01-0.6 (cereals) [86] or 0.1-5.0 ppm [61]. Besides this, Cr from soil can contribute to total Cr intake [86]. Dutch soils contain 50-164 ppm Cr (DM), whereas sludge can contain up to 820 ppm (DM) [89].
In Dutch slaughter cattle, both Cr and Ni concentrations are extremely low [18]. Selected data are given in Table 1. In Indian Barbari goats, Cr and Ni concentrations in blood and/or hair slightly differed due to physiological state [29]. Selected data are given in Table 2.

Table 1 Selected data on Cr and Ni concentrations in kidneys of Dutch slaughter cattle [18][a]

	ppm (fresh weight)
Cr	
Median	< 0.01
Range	<0.01 – 1.04
Ni	
Median	< 0.01
Range	<0.01 – 0.38

[a] means could not be calculated due to the large number of samples below detection limit

Table 2 Chromium and nickel concentrations in goat blood and hair [29]

	n	Blood		Hair
		µM		ppm
		Cr	Ni	
Pregnant goat	8	34.2	29.2	10.6
Non-pregnant goat	6	64.0	20.5	12.5
Male	7	81.7	20.7	14.0

2.3 Nickel

Normal Ni concentrations (ppm (DM)) in grasses are 0.13-1.1 , in legumes 1.2-2.7 and in cereals 0.2-0.3 [86]. In the blood, Ni is mainly transported bound to albumin [86]. In calves fed extra Ni, Ni mainly accumulated in the kidneys. Nickel accumulation not only depended

on Ni, but also on crude protein content of the diet[3] [76]. Selected data are given in Table 3. Similar Ni distribution data (not shown) were obtained from an experiment with lambs fed a single oral dose of ^{63}Ni [79].

Table 3. Tissue nickel accumulation in calves as influenced by dietary nickel and crude protein content [76]

Dietary crude protein (%)	10		14.5	
Dietary Ni (ppm)	0	5	0	5
Tissue Ni concentrations (ng/g DM)				
Liver	38	90	46	60
Kidney	48[a]	654[b]	46[a]	286[c]
Spleen	66	71	62	66
Lung	66	143	66	140
Heart	64	78	66	76
Muscle	54	65	46	49
Serum	2.4	5.6	2.5	3.6

[a.b.c] values within a row not dealing the same superscript are significantly different

In sheep from a Ni-contaminated area in the Norwegian-Russian border area, liver Ni concentrations were up to 0.01 µg/g wet weight, whereas kidney levels ranged from 0.01-0.10 µg/g wet weight[4] [73].

2.4 Molybdenum

Steel industries can cause airborne Mo emission. Besides this, soils of marine origin and in (uranium) mining areas can contain relatively high Mo concentrations [86;91]. Accidental poisoning has occurred from used motor oil [64]. Normal Mo concentrations in Dutch forages are low (0.9 – 5.4 ppm (DM) BLGG, Oosterbeek, The Netherlands). In severely contaminated areas, Mo concentrations of the grass can increase up to 90 ppm (DM) [88] or even 100 ppm [57]. On alkaline soils, Mo uptake by plants is higher than on acidic soils [57]. Together with S, Mo can form thiomolybdates in the rumen. These compounds depress Cu absorption from the gastrointestinal tract (Documentation report no. 40). Absorption of Mo mainly occurs in the abomasum [86], but also in the small intestine and the rumen (tri- and tetrathiomolybdates) and is hampered by sulphate ions [38;46;48;49]. Increasing the Mo content of the diet decreases the ruminal conversion of sulphate to sulphide [21]. After absorption most of the body Mo in cattle and sheep is found in liver and kidney (1.3-13.7 ppm (DM)(cattle) and 1.6-4.3 ppm (DM)(sheep)[5]). Muscle, lung, heart and bones contain lower levels (0.5-0.8 ppm (DM)(cattle) and 0.02-0.5 ppm (DM)(sheep)) [27;49;57;60]. In goats fed ^{99}Mo, most of the dose was recovered from the bones, the liver containing the next high concentrations [4]. Within the blood, Mo partition between erythrocytes and plasma differs according to Mo status. When Mo status is high, ± 80% of Mo is recovered from the plasma as Cu-thiomolydates. When Mo status is low, most of the blood Mo is found in the erythrocytes [49;52]. Molybdenum can cross the placental barrier [49] and accumulates in the pregnant uterus mainly in the second half of the pregnancy. Twin bearing sheep accumulate more Mo in their wombs than single bearing ewes. However, at term in both cases ± 40% of the Mo is recovered from the liver, whereas ± 50% of the Mo is recovered from the uterus itself [26].

[3] Maize/cottonseed hulls/cottonseed meal diet.
[4] Assuming DM contents of 24% (liver) and 18% (kidney) [75], these values correspond with up to 42 and 42-420 ng/g DM, respectively.
[5] Assuming DM % of 24 (liver), 18 (kidney), 29 (muscle), 14 (lung), 12 (heart) and 99 (bone) [75].

3. Absorption and metabolism

3.1 General

The apparent absorption of F from soil is reported to be < 10% [47]. However, F from soluble sources (e.g. NaF) is almost completely absorbed from the gastrointestinal tract. Fluorine absorption from F-rich hay is similar to that of soluble sources, whereas F absorption from rock phosphate and CaF_2 is lower. Quantitative data are lacking [86].
In cattle given inorganic Cr, Cr is found in glucose tolerance factor-like forms in the liver [94]. This could indicate for some metabolism of inorganic Cr, although the occurrence of small amounts of organically bound Cr in the diet cannot be excluded. In an experiment with cattle, 2-4% of a dose of ^{51}Cr-EDTA was excreted via the urine, indicating for some absorption of this compound. However, it was not clear as to what extent this compound was metabolized and biologically available [42]. No data on Ni absorption and metabolism in ruminants are available.

3.2 Differences in metabolism due to different sources

3.2.1 Differences in availability between sources

3.2.2.1 Fluorine

No suitable quantitative data on differences in F availability from different sources are available.

3.2.1.2 Chromium

Inorganic Cr compounds such as $CrCl_3$ and Cr_2O_3 are very poorly absorbed[6], whereas organically bound Cr, such as Cr nicotinate and Cr (tri)picolinate have higher absorption rates than inorganic ones (20-30 times) [54;86]. In an experiment with feeder calves, slight health differences[7] occurred between diets[8] enriched with either high-Cr yeast or chelated Cr [51]. On the other hand, CrEDTA chelate is hardly absorbed by adult ruminants [42], whereas some absorption occurs in milk-fed ruminants [86]. No more information is available on differences in Cr absorption between Cr sources.

3.2.1.3 Nickel

No suitable quantitative data on differences in Ni availability from different sources are available.

3.2.1.4 Molybdenum

Hexavalent Mo compounds like Mo trioxide, ammonium molybdate and Ca molybdate as well as Mo in herbage is rapidly absorbed. Tetravalent Mo compounds such as MoS_2 are poorly absorbed [49;57]. In the rumen, Mo forms thiomolybdates together with S (see Documentation report no. 40).

3.2.1.5 Discussion and conclusions

Due to a general lack of data and uncertainty about requirements no reliable conclusions concerning differences in availability and recommended sources can be drawn.

[6] This property underlying their use as inert markers of feed intake etc..
[7] Through one third of the experimental period, DMI was significantly higher in the chelated Cr group.
[8] Maize/soybean meal diets supplemented with 0.5 ppm Cr (DM); high-Cr yeast: Chemeast; chelated Cr: amino acid-chelated Cr (Metalosate)

3.3 Interactions influencing absorption and metabolism

3.3.1 Interactions of fluorine and aluminium, calcium, sodium chloride and fat

3.3.1.1 General

Although aluminium, calcium, sodium chloride and fat have been reported to reduce F absorption [54], no more details are given.

3.3.1.2 Cattle and goats

No experimental evidence is available on effects of dietary Al additions on F metabolism in cattle or goats.

3.3.1.3 Sheep

Although oral Al administration[9] has been reported to diminish F absorption from the gastrointestinal tract of sheep [9], insufficient data were provided to judge this effect.

3.3.1.4 Conclusion

Due to lack of data no conclusion can be drawn.

3.3.2 Molybdenum and sulfur

Increasing the S content of the diet of sheep can both decrease and increase Mo retention in the body [28;86].

3.4 Recycling

No data are available on recycling of either F, Cr or Ni in ruminants. Oral administration of tetrathiomolybdate to sheep has been demonstrated to increase biliary Mo excretion [25], whereas studies employing intravenous infusion of ^{99}Mo revealed secretion of Mo into the rumen of sheep [84].

3.5 Excretion

3.5.1 Fluorine

Dietary F is mainly excreted via the urine, fecal excretion accounting for 17-37% of total excretion[10] [34]. Urinary F increase with increasing F content of the feed. Selected data are given in Table 4.
However, feed F content does not seem to be the only determinant of urinary F concentrations. In growing cattle, a complex relationship between age, urinary fluorine concentration and F content of ration DM was calculated [68]:

$$R = 6.607 + 0.11178 \times A - 0.0020238 \times A^2 + 6.446 \times U - 0.01204 \times U^2 - 0.04871 \times A \times U$$

($r^2 = 0.74$)

in which:

[9] Probably from Al chloride or Al sulphate.
[10] Total of urinary and fecal F excretion.

R = F content of the ration (in ppm)
A= age (in months)
U = ppm F in urine.

Table 4. Selected data on the relationship between dietary and urinary F concentrations in cattle[a]

Ref.	D (years)[d]	n	Case description		Dietary F (ppm)	Urinary F (ppm)
[71;72]	1-3	88	Clinical fluorosis	Affected	99-953	34
		?		Healthy		8
[69]	1.5	4	F-loading experiment		10[b]	4
		4			62	15
		4			69	11
		4			68	20
[81]	2.5	5	F-loading experiment		[c]	2
		3				18
		6				23
		6				30
		4				37
		3				48
[83]	5.5	4	F-loading experiment		3-5	5
		4			23-25	17
		4			33-35	26
		4			43-45	29
		4			53-55	38

[a] specific gravity of the urine corrected to a value of 1.040; [b]rations consisted of low F hay (10 ppm F), high F hay (62 ppm F), low F hay + CaF_2 and low F hay + NaF, respectively; [c] groups received unsupplemented ration (F content not given) or 1.0, 1.2, 1.4 1.6 or 2.0 mg F/kg BW as NaF; [d] duration of the exposure

Bovine milk F concentrations depend on the F content of the feed (Table 4) [40], although opinions do not agree [86]. Values (µg F/kg) of 100-300 [33;86], 150 [1], 160 [83], 110 (non F-contaminated pastures) or 260 (F-contaminated pastures) [20] or up to 440 (40 ppm F as NaF added to the ration [83]) have been reported. Diagnostic limits for milk F concentrations are given in Table 5. Ewe milk is reported to contain 135 µg F/kg [92].

Table 5. Selected data on F content of bovine milk depending of the F content of the feed [40]

F content of feed (ppm)	Lactation number		
	1	2	3
	F content of milk (µg/kg)		
10	36	96	60
109	96	172	198

3.5.2 Chromium

As most Cr sources are extremely poorly absorbed, the feces is the main route of excretion [86]. Normal bovine milk is reported to contain 10 [1] or 15 µg Cr/kg [40].

3.5.3 Nickel

The majority of dietary Ni is excreted via the feces. In an experiment with lambs[11] fed a single oral dose of ^{63}Ni, at 72 hours post dosing 74 vs. 0.8% of dose (low Ni) or 65 vs. 2.0% of dose

[11] Dried skim milk/starch diet containing either 0.065 or 5.065 ppm Ni.

(high Ni) was excreted via feces and urine, respectively [79]. Bovine milk normally contains up to 36 µg Ni/kg [40]. The Ni excretion via the milk appears not to be influenced by dietary Ni supplementation when the dietary Ni amount increased from 365 to 1835 mg Ni/day[12], but colostrum contains approximately 100 µg Ni/kg[13] [40;86].

3.5.4 Molybdenum

In cattle and goats, Mo is mainly excreted via the feces, although excretion via the urine can also contribute to the elimination from the body [4;57;60;86]. Increasing the S content of the ration shifts the route of excretion from urine to feces. At low S intakes (1 g/day) urinary excretion of Mo in sheep can account for more than 50% of daily Mo excretion [28]. Bovine milk contains (µg Mo/kg) 31[14] [2], 42 [91], 50 [1;49], 18-120 [49], 20-150 [33], or in most cases < 100 [40], whereas caprine milk is reported to contain 12 [10] to 14 µg Mo/kg[15] [2]. Colostrum is reported to contain ± 1.5 times as much Mo as mature milk [40]. Increasing the dietary Mo content increases Mo content of the milk [40]. As an extreme example, lactating cattle fed a ration containing 200 ppm Mo had milk Mo concentrations of 2100 µg/kg [87]. At a low Mo content of the feed, almost all of the Mo is associated with xanthine oxidoreductase. However, an increase in dietary Mo does not result in a proportional increase in xanthine oxidoreductase activity [49]. Xanthine oxidoreductase activity in caprine milk is normally much lower than in bovine milk [16].
Ewe milk can contain <10 µg/L on pastures of low Mo content, but can increase to 1043 µg/L when the diet contains 25 mg Mo/kg [49]. On a maize silage/barley ration containing 0.9 ppm Mo (DM) ewe milk Mo concentration was 140µg/kg, whereas this value increased to 2700 µg/L when dietary Mo concentration was 40 ppm (DM) [93].

[12] As Ni carbonate.
[13] The same value is reported for commercial milk [33].
[14] 0.26 mg Mo/kg DM; assuming a DM content of bovine milk of 12% [45].
[15] 0.12 mg Mo/kg DM; assuming a DM content of caprine milk of 12% [56].

4. Requirements

4.1 Data on requirements

4.1.1 Fluorine

No data are available to calculate F requirements of ruminants, although F deficiency occurred in goats receiving rations < 0.3 ppm F (DM) [86].

4.1.2 Chromium

As yet, insufficient data are available to reliably assess Cr requirement of ruminants, although it is increased by stress (transport, infection, exercise) [54;86].

4.1.3 Nickel

The Ni requirement of goats is assessed to be at least 300-350 µg/kg DM. However, as ruminant feeds usually contain much more Ni[16], deficiencies are unlikely to occur [3].

4.1.4 Molybdenum

Data necessary to for factorial estimation of Mo requirements are incomplete. In ruminant sheep, both true Mo absorption and fecal endogenous Mo losses are reported to depend on the S content of the diet [28]. Selected data are given in Table 5. Sheep wool is reported to contain 34-36 µg Mo/kg [27].

Table 5. Selected data on fecal endogenous Mo losses and true Mo absorption in sheep as depending on dietary S intake (total DM intake 750 g/day) [28]

	S content (g/kg DM)	1.3	1.8	2.3	4.3
	Mo content (ppm (DM))				
Fecal endogenous loss (µg/d)	0.5	54	11	11	9
	4.8	540	93	19	17
True absorption coefficient (%)	0.5	84	58	53	47
	4.8	75	37	29	26

A ration containing 0.07 mg Mo/kg DM did not suffice to prevent Mo deficiency symptoms. On the other hand, mature goat milk containing 0.12 mg Mo/kg DM was sufficient for normal growth of the kids. Therefore, the minimum dietary Mo requirement of young goats is assessed to be approximately 0.10 mg/kg DM [2].

4.2 Conclusion

As insufficient data are available, factorial estimation of F, Cr and Ni requirements of ruminants is precluded.

[16] Not quantified; some more data in 8.

5 Allowances

As requirements cannot be calculated, the same is the fact for allowances.

6 Criteria to judge status

6.1 Fluorine

The sensitivity of ruminants to fluorosis declines with age [66]. Diagnosis of fluorosis is based on chemical analysis of F in bones and visual classification of tooth affection (the scale ranging from 0 (healthy) to 5 (severely affected). However, in contaminated areas values are usually high, thereby reducing the usefulness of this parameter (Van Dijk, PRI, personal communication). Normal values in bone ash range from 200-800 ppm. Bone F concentrations may not be sufficiently indicative of fluorosis when short-term peak loading occurs. Toxicity signs may then occur at relatively low bone F concentrations [11]. In the proximity of F-emitting industrial plants (Al- or P-processing industries) bone F concentrations up to 8700 ppm have been recorded [8]. Furthermore, both plasma and urinary F concentrations are positively related to dietary F intake [82]. However, urinary F concentrations are insufficiently informative about F retention in the body, whereas older animals excrete higher proportions of ingested F in the urine than do younger ones. Specific gravity of urine samples should be adjusted to 1.04 for comparative analyses [61]. On the other hand, plasma F concentrations show marked diurnal variation and respond to variations in dietary F intake very rapidly (within hours). This hampers the proper interpretation of plasma F values, mainly in acute cases [86]. Selected indicators of F status in dairy cattle together with diagnostic limits are given in Table 6.

Table 6. Selected indicators of F status in dairy cattle

Ref.	Indicator	Age	Normal	Chronic F toxicosis		Acute F toxicosis
	F concentration in	(years)		Threshold	severe	
[66]	Feed (ppm (DM))	All	< 15	30-40	>60	>250
	Tooth classification[a]	All	<1	2-3	4-5	
	Dry, fat-free bone (ppm)	2	401-714	1605-2130	3027-4206	
		4	706-1138	2379-3138	4504-6620	
		6	653-1221	2794-3788	5622-8676	
	Blood (µM)	All	<15.8	15.8-21.1	>26.3	
	Urine (ppm)	2	2.27-3.78	8.04-10.54	14.71-19.86	
		4	3.54-5.30	10.32-13.31	18.49-25.63	
		6	3.51-6.03	11.29-14.78	20.96-30.09	
	Milk (ppm)	All	<0.12	0.12-0.15	>0.25	
[61]	Feed (ppm)	All	10-20			>100[c]
		Young		30		
		Mature		40-50		
	Dry, fat-free bone (ppm)[b]	All	200-1800			>6000[c]
	Blood (µM)	All	<15.8			>26.3[c]
	Urine (ppm)	All	1-5			>14[c]
	Milk (ppm)	All	0.01-0.06			>0.08[c]

[a] incisors; [b] rib bone; [c] "toxic"; not clear if this means "acutely toxic"

6.2 Chromium

Information on suitable indicators of Cr status in ruminants is lacking. However, some data have been given [61;86]. Selected data are given in Table 7. One should be aware of the fact that Cr and Ni are abundant elements in the environment, whereas only traces are found in body fluids and tissues. Therefore, there is a real risk of contamination of samples, resulting in misinterpretations.

Table 7. Selected data on possible indicators of Cr status in cattle [61;86].

	Liver	Kidney	Milk	Serum
	ppm		µg/kg	µM
Normal	0.04-3.8	0.5-6.2	8-250	0.005-0.006
Toxic	> 10	> 15		

6.3 Nickel

No suitable information is available on indicators of Ni status in ruminants.

6.4 Molybdenum

For rough estimation of Mo toxicity risks, the Cu:Mo relationship can be used (see Documentation report no. 40). The Mo concentrations in blood plasma, milk and urine are reported to be fairly suitable indicators of Mo status [91]. Moreover, TCA-insoluble Cu concentrations in blood can be used to diagnose molybdenosis [44]. Liver Mo concentrations per se are not sufficiently reliable [49].

6.5 Conclusions

Due to lack of information, choosing suitable indicators for Cr and Ni status is virtually impossible. In case of F toxicosis, it is very important to judge both pathological (bone and tooth deformations) and biochemical indicators (acute: mainly urine; chronic: bone F). Plasma and urinary F concentrations are only valuable in acute cases.

7 Deficiency

7.1 Fluorine

In F deficiency, atrophy of thymus and endocrine glands, such as the thyroid, can be observed. Furthermore, liver fat dystrophy and inflammation of the gastrointestinal tract and the kidneys is reported [6].

7.2 Chromium

Chromium-deficient ruminants show a poor performance (low DMI and milk yield) and symptoms of ketosis [54].

7.3 Nickel

Nickel deficiency in goats is characterized by lower DMI, growth, milk fat yield, success of 1st insemination and increased rates of abortion, services per gravidity and deaths of lambs and their dams. Milk yield was slightly lower than in goats receiving sufficient amounts of Ni. Finally, in Ni-deficient goats damage of skin (parakeratotic lesions), hair and testicles, as well as dwarfism, reduced hemoglobin synthesis and lower Zn concentrations in blood, bones and milk suggest effects of Ni deficiency on Ca and Zn metabolism [3;5;85]. Liver Cu concentrations can also be lower in Ni-deficient lambs than in lambs fed sufficient amounts of Ni [78]. However, quantitative data are lacking.

7.4 Molybdenum

Molydenum deficiency in ruminants is extremely rare and in fact only observed under experimental circumstances. Normal European ruminant feeds contain sufficient amount of Mo, thereby excluding the possibility of Mo deficiency. Goats fed a semi-synthetic ration containing as few as 24 µg Mo/kg showed impaired growth and fertility (more inseminations per gravidity needed, more abortions, more stillbirths) than did goats receiving 533 µg/kg of ration [2].

7.5 Measures in deficiency cases

Fluorine deficiency is not known to occur in ruminants, so no specific treatment is necessary. As diagnosis of Cr or Ni deficiency is difficult and suitable supplementation sources are not well defined, no specific measures in cases of deficiency can be recommended. In cases of “incurable” ketosis determination of Cr indicators as suggested in Table 6 and, if very low, Cr supplementation might be considered at a rate of 0.2-1 mg Cr/kg feed from organically bound Cr [13].

8 Toxicity

8.1 Fluorine

As F is a cumulative poison, F toxicity is usually chronic. Acute fluorosis is characterized by diarrhea, excitement, stiffness, anorexia, reduced milk yield, excessive salivation, vomiting, incontinence, weakness, severe depression and heart failure. Fluorine concentrations in blood and urine are high [55;66].

Subacute and chronic fluorosis is characterized by poor dentition and tooth quality ("mottled teeth"), abnormal abrasion and dark discoloration of teeth in young animals (up to 30 months), lameness, stiffness and anemia. Periosteal hyperostosis and exostoses, for instance on ribs, may be observed. In advanced stages of chronic fluorosis, performance (DMI, milk yield, growth) will deteriorate [11;14;30;35;66]. In both cattle and sheep oocytes mutagenic effects of NaF have been reported [32].

For F, maximum tolerable levels are differentiated according to physiological state. For young and mature dairy cattle, 40 ppm is suggested [53]. However, 20-30 ppm is reported to cause decoloration of teeth in young animals [11]. For mature beef cattle (50 ppm), finishing beef cattle (100 ppm), breeding sheep (60 ppm) and finishing sheep (150 ppm) higher limits are suggested [11;53]. Related to BW, 50-70 mg/kg BW (single dose) or 6-20 mg/kg BW (for several days) should be acutely toxic [61]. The ingestion of 150-200 ppm F for 1 month to adult cattle only slightly decreased milk yield [82]. In the Netherlands, 25 ppm F (DM) for young cattle and 30-33 ppm F (DM) for mature cattle have been adopted as safe levels in feed [23]. As sheep and goats are less sensitive to fluorosis than are cattle, using the limits adopted for cattle also protects sheep and goats [23;74]. Finally, F toxicity is highest when soluble sources as NaF are fed, whereas sources as rock phosphate[17], CaF_2 and soil F are much less available [86].

8.2 Chromium

The acute lethal dose of hexavalent Cr for cattle is reported to be 600-800 mg/kg BW, whereas the chronic lethal dose for calves is 30-40 mg/kg BW. Diarrhea is the main toxicity symptom [17]. For Cr, maximum tolerable levels of 1000 ppm (chloride) and 3000 ppm (oxide) are suggested for cattle and sheep from interspecies extrapolation [53], but dietary concentrations > 1000 ppm (DM) are tolerated by livestock[18] [86]. In other species, hexavalent Cr (in Cr trioxide, chromates and bichromates) is said to be at least 5 times more toxic than trivalent ones [54]. For organically bound Cr, no maximum allowable concentrations are given.

8.3 Nickel

Normal Ni concentrations in grasses are 0.13-1.1 ppm (DM) [86]. Nickel deposition occurs in the vicinity of frequently used motorways and nickel processing plants. At a distance of 32 m from the roadside, Ni content of the grass was 1.3-2.8 ppm (DM), whereas corresponding values at 8 m form the roadside were 3.8-5.0 ppm (DM) [43]. However, also for Ni no toxicity data are available, although the main adverse effect of Ni is said to be reduced DMI [54]. A maximum tolerable level of 50 ppm is suggested for cattle and sheep [53].

8.4 Molybdenum

As Mo (in combination with S) is an inhibitor of Cu absorption from the intestines, the clinical signs of Mo toxicosis largely coincide with those of Cu deficiency [15]. Feeding 1.4 g of soluble molybdates/head/day caused severe diarrhea in dry cows, whereas 60 ppm Mo in the ration of young cattle disturbed normal intestinal function and bone metabolism, resulting

[17] Used as a P source in animal feeds.
[18] Not specified.

in stiff gait, lameness and fractures. Other clinical signs of Mo toxicosis are growth retardation, BW loss, anemia, loss of hair color, rough coat, low milk production and poor fertility. Sheep are thought to be more tolerant to Mo than are adult cattle [57;58;91]. Five-week old, possibly ruminating calves fed a semi-purified diet[19] and receiving drinking water containing either <1, 1, 8 or 53 ppm Mo had only slightly different liver Cu concentrations [39]. Under certain circumstances goats may be even extremely tolerant to Mo toxicosis, as a ration[20] containing 1000 ppm Mo was consumed for weeks without any signs of Mo toxicosis. The nature of this high tolerance is unclear [2]. On the other hand, grazing goats fed a ration containing 100 ppm Mo (DM)[21] developed severe symptoms of Mo toxicosis similar to those occurring in cattle [65]. In sheep lambs swayback may develop, whereas adult sheep may show alterations in the structure of the wool (see Documentation report no. 40) [57;59;88;91]. For both cattle and sheep, a maximum tolerable level of 10 ppm Mo is recommended [53]. Moreover, 5 ppm is also "clearly indicated as a threshold level" for cattle [91]. For goats this level might be substantially higher, but no clear evidence is available. In normal Dutch forages the threshold of 10 ppm is never exceeded. However, the Mo content of the ration has to be judged together with the S and Cu concentrations. Then, Mo levels much lower than 10 ppm may be detrimental to Cu supply to the animal (see Documentation report no. 40). Finally, both cattle (up to 100 ppm) and sheep (up to 174 ppm) have been proven to tolerate much higher levels of dietary Mo without clinical symptoms of Mo toxicity, even when Cu levels were low (2-3 ppm) and S levels were moderate (> 3 g/kg) [91]. As a conclusion, setting maximum tolerable levels solely for dietary Mo in ruminant rations is hardly possible or useful. The complex three-way interaction with Cu and S (see Documentation report no. 40) makes it necessary to consider all these three elements together, whereas other factors may be involved either.

8.5 Direct measures in toxicity cases

8.5.1 Fluorine

Skeletal and teeth alterations are essentially irreversible. Removal of affected animals from the F-polluted site is one of the most suitable methods in case of fluorosis. Moreover, the addition of concentrates containing $Al_2(SO_4)_3$ to the diet[22] may retard the progression of the disease [9;86].
Adaptation of the industrial processes responsible for the F pollution should be considered, but is often very expensive [8].

8.5.2 Chromium and nickel

Except providing other feed, no specific strategy for both Cr and Ni toxicity cases (if any) can be recommended.

8.5.3 Molybdenum

Removing the source of excess Mo is, of course, one of the most effective ways to combat Mo toxicosis. Oral adminstration of 2 g of copper sulphate/day for mature cows or 1 g of copper sulphate/day for young cattle were effective in controlling Mo toxicosis, but smaller supplements may be effective as well [57;86]. Adding copper sulphate to drinking water (0.2 g/L) for a short time is another possibility [91]. For more details, see Documentation report no. 40. As molybdenosis is usually less severe in dried forage, using meadows for hay production rather than for grazing will alleviate Mo toxicity problems [91].

[19] Barley/alfalfa/milk powder diet containing 13 ppm Cu and 2.9 g S/kg.
[20] Not specified.
[21] From ammonium molybdate.
[22] Not clear if 1% Al (from Al sulphate) or 1% Al sulphate should be added.

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