

## Recent progress in exploring the essentiality of the ultratrace element cadmium to the nutrition of animals and man

Manfred Anke, Wolfram Dorn, Mario Müller, Mathias Seifert

Institute of Nutrition and Environment, Faculty of Biology and Pharmacy, Friedrich Schiller University Jena, D-07743 Jena, Germany

### Abstract

Cadmium-poor nutrition ( $< 15 \mu\text{g Cd/kg}$  feed dry matter (DM)) did not affect feed intake and growth rate, while it affected reproduction performance. Intrauterinally cadmium-depleted kids were often phlegmatic, too lazy to eat and drink, and died of muscle weakness. With oral application of the control feed ( $300 \mu\text{g Cd/kg DM}$ ), they slowly regained their mobility. Feeding them  $65 \mu\text{g Cd/kg}$  feed DM prevented myasthenia. The normative cadmium requirement of goats (and animals in general) amounts to  $< 20 \mu\text{g/kg}$  diet DM. The daily requirement of humans might be  $< 3 \mu\text{g}$ .

**Keywords :** cadmium, essentiality for animals, geological influences, intake by man, foodstuffs

### Introduction

Cadmium is well known as a toxic element. Its essentiality is disputed. Smith [1] noted that, although a specific function for cadmium is not known, this metal is a good candidate for essentiality. First results regarding the essentiality of cadmium in goats and rats were published 1977 [2, 3, 4]. In rats, cadmium supplementation ( $50$  to  $100 \mu\text{g/kg}$  feed dry matter, DM) increased the growth rate in one experiment, whereas in other examinations it did not influence the development.

Better evidence of the essentiality of cadmium is available after ten repetitions of cadmium deficiency experiments with growing, pregnant and lactating goats and their kids, and the discovery of a cadmium-specific carboanhydrase in the diatom *Thalassia sira weissflogii* [5], which is involved in acquiring inorganic carbon. On the other hand, cadmium mimics the in-vivo effects of estrogen in the uterus and mammary glands of rats [6]. Women with estrogen contraceptives excreted significantly more cadmium

with the faeces than those without such contraceptives [2].

Informations to material and methods are given bei Anke et al., Res. Trace Elemens, 16 : 2005.

### *Essentiality of cadmium for animals*

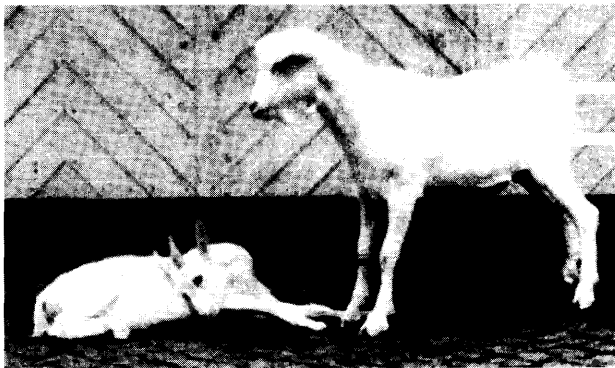
The essentiality of cadmium was investigated systematically in control goats with  $300 \mu\text{g Cd/kg}$  feed DM, and in corresponding cadmium-deficient animals with  $< 15 \mu\text{g/kg}$  feed DM (Table 1). Cadmium-poor nutrition did not have any effect on feed intake ( $629$  and  $644 \text{ g/day}$ , respectively). Live weight gain ( $18.2$  and  $16.8 \text{ kg}$  by day 91 of life, respectively) was not affected by cadmium-poor nutrition, whereas cadmium deficiency had a significant effect on first insemination, rate of abortion and number of services per gravidity. The cadmium-poor nutrition of mothers affected the activity of the kids. The intrauterinely cadmium-depleted kids were often very phlegmatic, moved very little, were too lazy to eat and drink, and had problems holding their heads erect (Figure 1). The symptoms of impaired mobility occurred at different times of the lactation period. Of nine kids (6 males, 3 females) from cadmium-deficient goats, all showed clinical deficiency symptoms in the form of muscular weakness about 6 weeks after weaning. Subsequently, six of the cadmium-deficient kids died. The last three survivors were then given the feed of control animals,

Address correspondence to :

Manfred Anke, Am Steiger 12,  
D-07743 Jena, Germany  
E-mail : carmengalambos@hotmail.com  
TEL : ++49 3641 448536  
FAX : ++3641 448536

with 300  $\mu\text{g Cd/kg DM}$  matter, by means of an esophageal tube, and slowly regained their mobility and achieved their normal body weight. Myasthenia also occurred due to nutrition depletion in lactating goats, and, without cadmium supplementation, led to death. Feeding cadmium (65  $\mu\text{g/kg feed DM}$ ) prevented the occurrence of cadmium-deficiency symptoms [2, 7, 8, 9].

The liver, muscles, heart, kidneys and cerebrum of cadmium-deficient goats were examined with regard to their ultrastructure. Primarily, the mitochondria appeared to be damaged and their size increased, with degenerative changes especially in mitochondria of the liver and kidneys. Christolysis and enlargements were also detected. The mitochondria were only detectable because of their double membrane and detectable isolated cristae - changes which could not be found in other organs. Within these organs, the considerable increase in regularly arranged cristae



**Figure 1** Left : cadmium-deficient kid ; right : control kid

was impressive. There were also striking reductions in the contractile apparatus of the cardiac and skeletal muscles. Such findings point to reduced protein synthesis or, in lactating goats, to increased protein mobilization from muscles. This hypothesis might explain the reduction of the contractile system, but not the increased mitochondrial size. Such hyperplasia was found when there was an insufficiency of mitochondria, and might represent compensatory hypertrophy [8, 9, 10].

The normative cadmium requirement of goats and animals amounts to  $< 20 \mu\text{g/kg DM}$ . Primary cadmium deficiency is not to be expected in animals, as the normal intake is considerably above this range [11].

#### *Influence of the geological origin of the soil on the cadmium content of the vegetation*

The acid weathering soils of granite rock transferred most cadmium into the food chain in Germany and Europe, whereas the more neutral soils of Muschelkalk, Keuper and loess and humus-rich boglands produce a significantly cadmium-poor flora (Table 2). The cadmium content in the flora may increase twentyfold in the vicinity of non-ferrous metal smelteries and cadmium producing and processing plants [12, 13].

#### *Cadmium intake by humans*

The cadmium intake by adult Germans with mixed diets has decreased by about  $> 10\%$  over the last 12 years and is quite low. In Mexico, the cadmium con-

**Table 1** Influence of Cd-poor nutrition on feed intake, growth, reproduction, mortality and milk performance

Parameter		Control goats	Cd-deficient goats	p <sup>2)</sup>	% <sup>1)</sup>	
Cd-content of the feed	$\mu\text{g/kg DM}$	$< 300$	$< 15$	$< 0.001$	$< 5$	
Feed intake	First year of life	687	679	$> 0.05$	99	
	Adult goats	629	644	$< 0.05$	102	
Growth	Birth weight	$< 1.6 \text{ kg}$	5	$< 0.05$	-	
	Live weight	91 <sup>st</sup> day	18.2	16.8	$> 0.05$	92
	Live weight	101 <sup>st</sup> -268 <sup>th</sup> day	86	78	$> 0.05$	91
Reproduction performance	Success of first insemination	%	73	46	$< 0.001$	-
	Conception rate	%	85	72	$> 0.05$	-
	Abortion rate	%	0	12	$< 0.01$	-
	Service per gravidity		1.2	2.2	$< 0.001$	-
	Sex ratio (female = 1)		1.4	1.5	$> 0.05$	-
Mortality	Kids	7 <sup>th</sup> to 91 <sup>th</sup> day	8	43	$< 0.001$	-
	Adult goats	1 <sup>st</sup> and 2 <sup>nd</sup> year	30	41	$< 0.001$	-
Milk performance	Amount of milk	ml/day	1010	730	$< 0.001$	72
	Milk of 4% fat	ml/day	882	581	$< 0.001$	66
	Fat	g/day	35	23	$< 0.001$	66
	Protein	g/day	28	22	$< 0.001$	79

%<sup>1)</sup> Control goats = 100 %, Cadmium deficiency goats = x %; p<sup>2)</sup> = Significance level, Student test

**Table 2** Influence of the geological origin of the site on the relative cadmium contents of the flora in Central Europe

Geological origin of the site	Relative index
Granite weathering soils	100
Rotliegende weathering soils	90
Boulder clay	86
Phyllite weathering soils	82
Slate weathering soils (Devonian, Silurian, Culm)	81
Gneiss weathering soils	79
Bunter weathering soils	75
Alluvial riverside soils	71
Diluvial sands	70
Muschelkalk weathering soils	69
Keuper weathering soils	67
Loess	60
Bogs, peat soils	52

**Table 3** Cadmium intake by German and Mexican adults with mixed and ovo-lacto-vegetarian diets depending on time and gender ( $\mu\text{g}/\text{day}$ ) ( $n^2 = 1750$ )

Form of diet, country	Women		Men		Fp <sup>1)</sup> p	%	
	s	x	s	x			
Mixed diet (MD)	Germany (G) 1.	12	8.4	10	9.1	< 0.001	119
	Germany 4.	6.2	9.2	12	8.7		130
	Germany 8.	4.4	7.1	8.8	5.1		124
	Mexico (M) 8.	2.7	4.8	5.8	3.3		< 0.001
Vegetarian (V)	Germany 8.	6.8	11	17	13	< 0.001	155
Fp	MDG 1.: MDG 8.	< 0.001					-
p	MDG 8.: MDM 8.	< 0.001		< 0.001			
	MDG 8.: VG 8.	< 0.001		< 0.001			
%	MDG 1.: MDG 8.	85		88			
	MDG 8.: MDM 8.	68		66			
	MDG 8.: VG 8.	155		193			

Fp<sup>1)</sup> = Significance level in one- or multifactorial variance analysis; n<sup>2)</sup> = Number

**Table 4** The cadmium contents of foods ( $\mu\text{g}/\text{kg}$  dry matter) and beverages ( $\mu\text{g}/\text{L}$ ) (n 1506)

Vegetable foods		Animal foods		Beverages	
Sugar-rich products	2.5-5.0	Cheese	1.0-5.0	Drinking water	0.5
Starch	5.0-10	Infant formulas	1.0-10	Brandy	0.9
Fruits	5.0-40	Marine fish	2.0-25	Cola, lemonade	1.0
Bread, cake	10-55	Sausage	3.0-28	Wine	1.0
Prepared cereals, flour	5-50	Meat	2.0-20	Beer	1.2
Vegetables	13-550	Curd, milk	4.0-10	Juice	1.4
Herbs, spices	500-1800	Kidneys, cattle	800	Advokaat	1.6

sumption is one third lower than in Germany, and ovo-lacto-vegetarians eat 50 to 90% more cadmium than people with mixed diets (Table 3). Their higher cadmium intake is only partly due to their higher dry matter consumption. Vegetable foodstuffs contain more cadmium than animal foodstuffs (except kidney and liver).

On average, the cadmium intake in Germany and Japan is similar [10, 14, 15, 16, 17].

#### *Cadmium contents of foodstuffs and beverages*

The cadmium contents of the foodstuffs examined were comparable with results of recent studies carried out in Europe and Japan [18, 19] (Table 4). In Europe, sugar and sugar-rich products, starch, as well as milk and dairy products contain 1 to 10  $\mu\text{g}$  Cd/kg dry matter (DM). The cadmium contents of fruits, meat, marine fish and sausage deliver, on average 2 to 30  $\mu\text{g}$  Cd/kg DM to the food chain of Europeans. Bread, cake, prepared cereals, and flour are relatively rich in cadmium, storing 10 to 50  $\mu\text{g}$  Cd/kg DM.

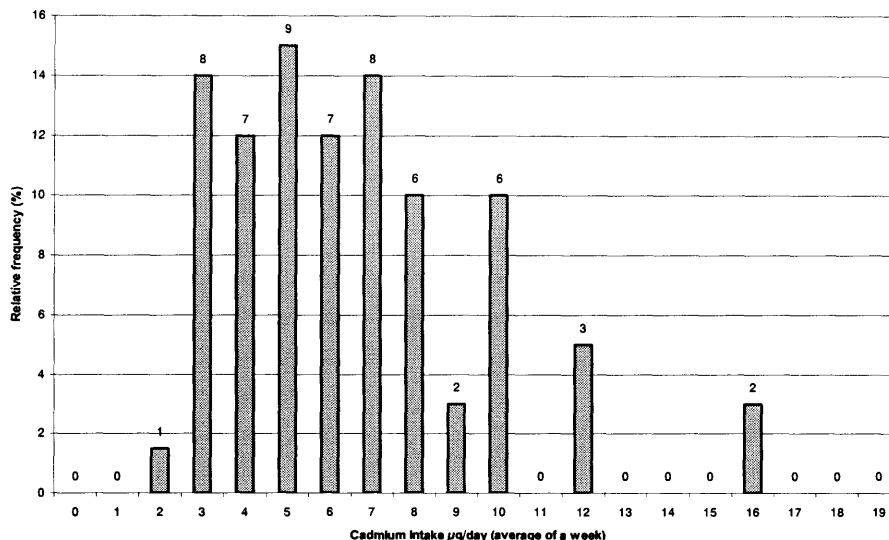


Figure 2 Frequency distribution of the daily cadmium intake by women

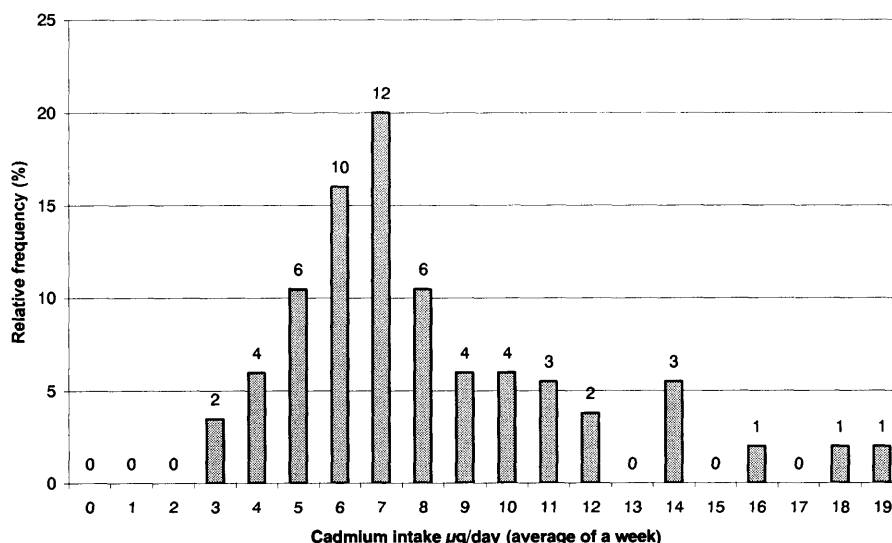


Figure 3 Frequency distribution of the daily cadmium intake by men

Vegetables contain extremely different cadmium levels. Pulses (beans, peas, lentils) store only 10 to 25 µg Cd/kg DM. Red and white cabbage, sauerkraut, asparagus, cauliflower, tomatoes, potatoes and mixed mushrooms deliver 30 to 100 µg cadmium to the food chain, whereas cucumber, kohlrabi, carrots and especially lettuce provide 100 to 600 µg Cd/kg DM. Herbs (chive, parsley, dill) accumulate between 500 and 2000 µg Cd/kg DM.

Beverages in Germany are relatively poor in cadmium, containing between 0.5 and 1.6 µg Cd/L.

Discussion

On the average of a week, the German test subjects consumed 2 to 16 µg Cd/day (women) and 3 to 9 µg

Cd/day (men), respectively (Figures 2, 3). These cadmium intakes are far from harmful. In case of cadmium being essential for man, the normative requirement may be > 3 µg Cd/day, while that of animals is < 20 µg/kg feed dry matter.

References

- 1) Smith HA: Cadmium. In: Frieden E (editor): Biochemistry of the Essential Ultra Trace elements. Plenum Press, New York, London; 1984: pp. 341-366.
- 2) Anke M, Hennig A, Groppe B, Partschefeld M, Grün M: The biochemical role of cadmium. In: Kirchgessner M (editor): Trace Element Metabolism in Man and Animal TEMA-3, Technische

- University München, Freising-Weihenstephan, Germany, 1997 : pp. 540-548.
- 3) Anke M: Essentiality of cadmium in goats. In: Anke M, Schneider H-I, editors. Cadmium - Symposium. Friedrich-Schiller-University, Jena, Germany ; 1977 : pp. 193-194.
  - 4) Schwarz K, Spallholz JE: The potential essentiality of cadmium. In: Anke M, Schneider H-J, editors. Cadmium-Symposium, Friedrich Schiller University Jena, Germany ; 1977 : pp. 188-194.
  - 5) Westerkamp C, Brown NE, Goldblatt P: A cadmium enzyme from a marine diatom. *Nature* ; 435 : 42, 2005.
  - 6) Johnson MD, Kenney N, Stoica A, Hilakivi-Clarke L, Singh B, Chepko G, Clarke R, Sholler PF, Lirio AA, Foss C, Reiter R, Trock B, Paik S, Martin MB: Cadmium mimics the in vivo effects of estrogen in the uterus and mammary gland. *Nature Med* ; 9 : 1081-1083, 2003.
  - 7) Anke M, Schmidt A, Groppe B: Die Bedeutung kleinster Kadmiummengen für das Tier. *Mengen- und Spurenelemente* ; 4 : 482-489, 1984.
  - 8) Anke M, Groppe B, Schmidt A, Kronemann H: Cadmium deficiency in ruminants. In: Anke M, Baumann W, Bräunlich H, Brückner C, Groppe B, editors. 5. Spurenelement-Symposium Univ. Leipzig and Jena ; 1986 : pp. 937-946.
  - 9) Anke M, Groppe B, Schmidt A: New results on the essentiality of cadmium in ruminants. In: Hemphill DD (editor): *Trace Substances in Environment Health - 21*, University of Missouri, USA ; 1987 : pp. 556-566.
  - 10) Anke M, Müller R, Dorn W, Seifert M, Müller M, Gonzales D, Kronemann H, Schäfer U: Toxicity and essentiality of cadmium. In: Ermidou-Pollet S, Pollet S, editors. 2nd International Symposium on Trace Elements in Human: New Perspectives, Athens, Greece ; 2000 : pp. 343-362.
  - 11) Anke M: Essential and toxic effects of macro, trace and ultratrace elements in the nutrition of animals. In: Merian E, Anke M, Ihnat M, Stoeppler M, editors. *Elements and their Compounds in the Environment*. 2<sup>nd</sup> Edition. Wiley-VCH Verlag GmbH and Co. KGaA, Weinheim, Germany ; 2004 : pp. 305-341.
  - 12) Anke M, Groppe B, Kronemann H: Relations between the cadmium content of soil, plant, animal and humans. In: Momcilovic G (editor): *Trace Elements in Man and Animal - 7*, IMI, Zagreb, 1990 : pp. 26-10 - 26-11.
  - 13) Anke M, Gleis M, Müller M, Seifert M, Anke S, Gunstheimer G: Environmental cadmium pollution and its health effects in Germany. In: Nogawa K, Kuracki M, Kasuya M, editors. *Advances in the Prevention of Environmental Cadmium Pollution and Countermeasures*. Eiko Laboratory, Kanazawa, Japan ; 1999 : pp. 68-72.
  - 14) Anke M, Müller M, Trüpschuch A, Müller R: Intake and effects of cadmium, chromium and nickel in humans. *J. Commodities* ; 41-63, 2002.
  - 15) Anke M, Gleis M, Müller M, Seifert M, Anke S, Gunstheimer G: Environmental cadmium pollution and its health effects in Germany. In: Nogawa K, Kurachi M, Kasuya M, editors. *Eiko Laboratory Kanazawa, Ishikawa, Japan* ; 1999 : pp. 68-72.
  - 16) Kawada T, Suzuki S: A review on the cadmium content of rice, daily cadmium intake, and accumulation in the kidneys. *J. Occup. Health* ; 40 : 264-269, 1998.
  - 17) Kikuchi Y, Nomiyama T, Kumagai N, Dekio F, Uemura T, Takebayashi T, Hishiwaki Y, Matsumoto Y, Sano Y, Hosoda K, Watanabe S, Sakurai H, Omae K: Uptake of cadmium in meals from the digestive tract of young non-smoking Japanese female volunteers. *J. Occup. Health* ; 45 : 43-52, 2003.
  - 18) Müller M, Anke M, Hartmann E, Illing-Günther H: Oral cadmium exposure of adults in Germany. 1. Cadmium content of foodstuffs and beverages. *Food Add. And Cont.* ; 13 : 359-378, 1996.
  - 19) Kikuchi Y, Nomiyama T, Kumagai N, Uemura T, Omae K: Cadmium concentration in current Japanese food and beverages. *J. Occup. Health* ; 44 : 240-247, 2002.