High Dietary Cadmium on Zinc Absorption and Metabolism in Calves Fed for Comparable Nitrogen Balances[1] (37708)

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In substantial amounts, cadmium (Cd) is highly toxic to animals (1), with one effect as an antimetabolite to essential trace elements including zinc (Zn) (2). Dietary Cd reduces feed intake and ^{65}Zn absorption in growing calves (3). However, Zn absorption is homeostatically controlled and closely related to the level of energy intake, nitrogen balance, and protein deposition (4). This suggests that the reduced Zn absorption, associated with dietary Cd, might be caused by the indirect Cd effect of reduced feed intake and protein deposition (as measured by nitrogen balance).

This experiment was primarily designed to determine whether dietary Cd decreases Zn absorption through an indirect effect on feed intake and nitrogen balance. A further objective was to study the effect of Cd on tissue ^{65}Zn distribution.

Methods and Materials. Eleven intact male Holstein calves, averaging initially 86 kg in weight and 109 days of age, were fed either a control diet (5) (8.5 ppm Zn) or the same diet with 350 ppm Cd for 14 days. In an attempt to keep the groups in a similar nitrogen balance, feed intake of controls was restricted to about 20% less than that voluntarily consumed by Cd-fed calves. The amount of feed given controls was based on consumption of Cd-fed animals the previous day. An oral tracer ^{65}Zn dose (597.4 μCi) was administered at the beginning of day 8, with total feces and urine collected for 7 days. The calves were killed 7 days after dosing, and the following tissue samples were taken for analysis: heart, apex; liver, lower center of reticular impression area; lung, center cross-section area; spleen, half; kidney, left; testicle, left; muscle, semitendinosus; rib, twelfth; small intestine (SI) 1, first 1.8 m; SI 2, second 1.8 m; SI 3, middle 1.8 m; SI 4, last 1.8 m; large intestine, middle 0.9 m; rumen wall, left aspect of dorsal sac; abomasum, fundic; abomasum, pyloric; and omasum, laminae. All samples, except the rib, were ground before stable Zn and ^{65}Zn analysis.

^{65}Zn analyses were made with an automatic gamma test-tube changer with NaI(Tl) well crystal. Feed, fecal, and urinary nitrogen were determined by the Kjeldahl method. Fecal, feed and tissue Zn analyses were determined by atomic absorption spectrophotometry following nitric–perchloric–sulfuric wet ashing of samples.

Results. When 350 ppm Cd was added to the diet, there was a sudden drop in feed consumption (Fig. 1). As planned, feed and nitrogen intake was 26% higher in Cd-fed calves (Table I), yet control calves had a slightly higher (not significant at 10% level) nitrogen retention (Table I). Nitrogen balance and nitrogen intake were highly correlated ($r = 0.89$, $p < 0.01$). However, the correlation between nitrogen balance and ^{65}Zn retention was far smaller ($r = 0.25$).

In sharp contrast to the lack of a major effect on nitrogen balance, dietary Cd greatly reduced ^{65}Zn retention (Table I, Fig. 2A). During the 7 days after dosing 71.7% of the dose was excreted via feces in Cd-fed calves compared to 42.8% for controls (Fig. 2A). The effect of dietary Cd on fecal ^{65}Zn was greater on day 2 than any other day (Fig. 2B). The 350-ppm dietary Cd lowered ^{65}Zn in all 19 tissues and blood by at least 57%. Although quite variable, the Cd effect on

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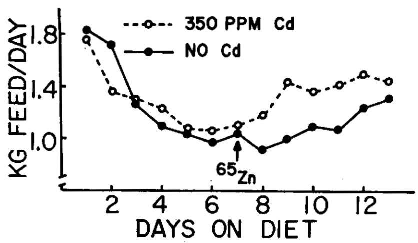

FIG. 1. Effect of 350 ppm dietary Cd on daily feed consumption.

^{65}Zn retention was highly significant ($p < 0.01$) for all tissues and blood (Table II). The smallest reductions were in rumen wall (57%), kidney (59%), and liver (62%). Dietary Cd had far larger effects on ^{65}Zn in whole blood (86%), rib (86%), muscle (77%), and testicle (75%) (Table II). In most tissues, Cd had little effect on stable Zn, with the only significant differences being decreases in round muscle ($p < 0.05$) and rumen wall ($p < 0.01$) and an increase ($p < 0.05$) in small intestine 4 (Table III). However, in agreement with earlier studies, liver Zn was increased (not significant at 5% level) in Cd-fed animals (6).

Discussion. As observed previously (3), feeding 350 ppm Cd greatly reduced ^{65}Zn absorption and tissue retention. Earlier studies had shown that reduced feed intake lowered ^{65}Zn absorption, which was closely related to protein deposition and nitrogen balance, apparently functioning through the homeostatic control mechanism (4). Since similar nitrogen balances were maintained for the two groups of calves, it was clearly established that Cd has a substantial effect on ^{65}Zn absorption above and beyond any indirect influence on protein deposition. Whether the Cd reduces Zn absorption through an indirect effect within the intestine or is controlled by changes in other tissues that are reflected back to the absorption site has not been established.

The low correlation between nitrogen balance and ^{65}Zn retention in this study compared to much higher correlations in the studies of Stake *et al.* (4) in large part probably was due to the small range in feed consumption.

Dietary Cd reduced nitrogen balance more than feed intake, indicating less efficient feed utilization. In agreement with previous studies, the greatly decreased net ^{65}Zn absorption was an important factor in the reduced tissue ^{65}Zn content of Cd-fed animals. The highly variable effect of Cd feeding on ^{65}Zn

TABLE I. Effect of Dietary Cd on N Intake, N Balance, and ^{65}Zn Retention 7 Days After a Single Oral ^{65}Zn Dose.

	Control	350 ppm Cd	SE[a]
Body weights at dosing (kg)	87.1	85.0	
Feed intake (g/day)[b]	1112.6	1378.9	
N intake (g/day)[b]	30.7	38.7	6.2
N in feces (g/day)[b]	5.0	11.3*	0.8
N in feces (% of intake)[c]	14.3	37.4**	7.0
N in urine (g/day)[b]	21.7	26.4***	1.2
N in urine (% of intake)[c]	71.8	66.6	16.2
N balance (g/day)[b]	4.1	1.1	6.0
^{65}Zn retention (% of dose)	57.2	28.3*	2.7

[a] Standard error; $n = 5.5$.
[b] For a 6-day period following ^{65}Zn dosing.
[c] Percentage for each calf averaged.
* Significant at 1% level.
** Significant at 10% level.
*** Significant at 5% level.

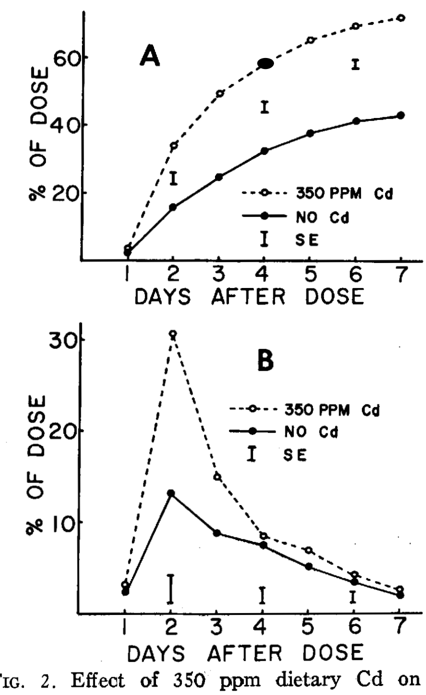

FIG. 2. Effect of 350 ppm dietary Cd on fecal ^{65}Zn excretion following a single oral dose: (A) accumulative total, (B) daily rate.

in different tissues indicates that the Cd has an important influence on metabolism of Zn after absorption. In comparison to the influence on ^{65}Zn, the effects on stable Zn are minor. Thus, it appears that labile Zn is the fraction most affected by dietary Cd.

Summary. Intact male Holstein calves were fed a purified diet (8.5 ppm Zn) with and without 350 ppm Cd in amounts to provide approximately equal nitrogen balances. The added Cd reduced ^{65}Zn absorption, showing that the earlier established effect on Zn absorption was not due to the indirect influence on feed intake and nitrogen balance. Whether the Cd effect was caused by changes at the tissue or intestine level was not established. However, Cd had a major influence on ^{65}Zn metabolism after absorption, as indicated by a differential influence on ^{65}Zn in several tissues.

TABLE II. Effect of Dietary Cd on Tissue ^{65}Zn 7 Days After a Single Oral ^{65}Zn Dose.

Tissue	% of ^{65}Zn dose/kg of fresh tissue			Reduction due to Cd feeding (%)
	No Cd[a]	350 ppm Cd	SE[b]	
Liver	2.99	1.13	0.29	62
Kidney	1.59	0.65	0.15	59
Spleen	2.00	0.67	0.17	69
Heart	1.40	0.42	0.12	70
Lung	1.28	0.37	0.10	71
Testicle	0.92	0.23	0.07	75
Muscle (round)	0.31	0.07	0.02	77
Rib cartilage	0.16	0.03	0.01	81
Rib shaft	0.86	0.12	0.07	86
Rumen wall	1.62	0.69	0.18	57
Omasum	1.92	0.69	0.17	64
Abomasum				
Fundic	0.91	0.29	0.08	68
Pyloric	0.91	0.27	0.11	70
Small intestine				
1	1.42	0.43	0.15	70
2	1.32	0.43	0.11	67
3	1.22	0.44	0.12	66
4	1.45	0.42	0.14	71
Large intestine	1.16	0.33	0.13	72
Whole blood				
Day 2	0.17	0.023	0.018	86
Day 4	0.16	0.023	0.014	86
Day 7	0.15	0.024	0.013	84

[a] All were significant at the 1% probability level.
[b] Standard error; $n = 5.5$.

TABLE III. Effect of Feeding 350 ppm Dietary Cd on Stable Zn Content in Calf Tissues.

Tissue	Zinc in dry tissues (ppm)		SE[a]
	No Cd	350 ppm Cd	
Liver	122	166	22.2
Kidney	79	89	4.2
Spleen	94	93	3.2
Heart	81	81	4.0
Lung	83	82	2.2
Testicle	66	64	4.3
Muscle (round)	88*	76	3.6
Rib cartilage	37	38	6.5
Rib shaft	94	79	9.7
Rumen wall	118**	100	3.5
Omasum	151	153	4.4
Abomasum fundic	81	78	3.7
Abomasum pyloric	58	78	9.5
Small intestine			
1	85	86	5.4
2	89	92	6.0
3	92	93	4.6
4	91*	104	3.2
Large intestine	64	60	8.7
Av of above tissues	87.5	89.5	
Whole blood			
Day 2	2.8	2.5	0.1
Day 4	3.2	2.7	0.5
Day 7	2.7	2.3	0.5

[a] Standard error; $n = 5.5$.
* Significant at the 5% probability level.
** Significant at the 1% probability level.

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1. Powell, G. W., Miller, W. J., Morton, J. D., and Clifton, C. M., J. Nutr. 84, 205 (1964).
2. Miller, W. J., J. Dairy Sci. 53, 1123 (1970).
3. Powell, G. W., Miller, W. J., and Blackmon, D. M., J. Nutr. 93, 203 (1967).
4. Stake, P. E., Miller, W. J., and Gentry, R. P., Proc. Soc. Exp. Biol. Med. 142, 494 (1973).
5. Neathery, M. W., Rachmat, S., Miller, W. J., Gentry, R. P., and Blackmon, D. M., Proc. Soc. Exp. Biol. Med. 139, 953 (1972).
6. Bunn, C. R., and Matrone, G., J. Nutr. 90, 395 (1966).

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