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Effect of Milk on Mercury Absorption and Gut Retention in Rats

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The digestive tract is the main route of entry of heavy metals into the body in conditions of environmental exposure. In such circumstances the body burden of metals will primarily depend upon age and diet, i.e. factors which greatly influence intestinal absorption of metals (NORDBERG et al. 1978). Very high intestinal absorption and oral toxicity of metals is a specific feature of metal metabolism in neonates (KOSTIAL et al. 1978). For some metals like cadmium or mercury the high absorption in suckling rats was found to be associated with a high gut retention (KOSTIAL, RABAR et al. 1979; KOSTIAL, KELLO et al. 1979; SASSER and JARBOE 1977). From the "gut compartment" the main fraction of the metal is eliminated from the body at the age of weaning and a smaller fraction enters into other parts of the body and increases the body burden of metals (KOSTIAL et al. 1979). The significance of the high gut retention of some metals in sucklings is not yet known. It might be associated, at least for cadmium, with decreased intestinal activity (HIETANEN 1978), enteropathies etc. (RICHARDSON and FOX 1974).

Milk diet was assumed to be one of the factors influencing high absorption of metals in neonates since older rats on milk diet also show increased whole body retention after oral administration of several metals (KOSTIAL et al. 1978).

The purpose of this work was to determine whether milk diet also increases gut retention after oral administration of mercury in older rats. This would indicate that the high gut retention is not specific for the absorption of some metals in sucklings but that it might be associated with milk diet. We also wanted do determine whether changing the diet from milk to rat's diet - a procedure similar to weaning-influences the gut and carcass retentions of ^{203}Hg in older rats.

MATERIAL AND METHODS

Animals. The experiments were performed on six week old female albino rats. In the first experiment 27 rats received radioactive mercury orally and in the second 27 rats received radioactive mercury intraperito-

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neally. All animals were kept in plastic cages throughout the experiments which lasted nine days. At the end of each experiment rats were killed and the gut i.e. total gastrointestinal tract distal to the diaphragm was removed. The carcass and the gut were put into containers for radioactivity determination.

Diet. Rats received milk or rat's diet and water ad libitum. In the first and the second experiment rats were divided into 7 groups according to the dietary treatment as presented in Table 1.

TABLE 1

Experimental design

GROUP	No. of rats	Dietary treatment (days) Before ^{203}Hg administration		After ^{203}Hg administration	
		Milk	Rat's diet	Milk	Rat's diet
1	6	-	3	-	6
2	3	3	-	1	5
3	3	3	-	2	4
4	3	3	-	3	3
5	3	3	-	4	2
6	3	3	-	5	1
7	6	3	-	6	-

Group 1 was on rat's diet, and group 7 on milk throughout the experiment. Rats in groups 2 to 6 were all on milk diet three days before radioisotope administration. On the first day after ^{203}Hg administration rats from group 2 were transferred from milk to rat's diet till the end of the experiment. The same procedure, i.e. transfer from milk diet, to rat's diet was performed for group 3 on the second, group 4 on the third, group 5 on the fourth and group 6 on the fifth day after ^{203}Hg administration.

Radioisotope administration and determination of radioactivity. Inorganic mercury (^{203}Hg) was supplied from the Radiochemical Center, Amersham, England as a chloride with a specific activity of about 0.5 mCi/mg Hg. The oral dose contained 2 μCi in 1 ml and the intraperitoneal dose contained 1 μCi in 0.5 ml.

The radioactivity was determined six days after ^{203}Hg administration in the gut-free carcass (C) and in the gut (G). All measurements were performed in a two-crystal scintillation counter, "Tobor", Nuclear Chicago, connected to a single channel analyzer. The results were

corrected for radioactive decay and geometry of the samples and were expressed as percentages of the administered dose. The whole body (WB) values were calculated as the sum of the radioactivity retained in the gut-free carcass and in the gut (C+G). The gut retention was also expressed as the per cent of the whole body radioactivity (Gx100/C+G). The group results are presented as the arithmetic mean and standard error of the mean which was calculated from the range (EVANS 1955).

RESULTS

Mercury retention in the whole body, carcass and gut after oral administration. The lowest whole body and carcass retentions were found in animals on rat's diet (group 1) and the highest in rats on milk (group 7) as shown in Table 2.

TABLE 2

The influence of diet on ^{203}Hg retention six days after a single oral administration (means±SEM)

Dietary treatment group	No. of rats	Gut-free carcass (C)	Gut (G)	Whole body WB (C+G)	G%WB $\frac{Gx100}{C+G}$
		(per cent dose)			
1	6	0.59 0.07	0.06 0.004	0.64 0.07	8.97 1.09
2	3	0.75 0.12	0.09 0.01	0.84 0.13	11.44 1.40
3	3	0.83 0.12	0.12 0.03	0.95 0.14	12.70 1.00
4	3	0.56 0.08	0.10 0.04	0.65 0.11	14.11 3.02
5	3	1.10 0.38	0.18 0.02	1.28 0.40	15.73 3.12
6	3	1.94 0.55	0.60 0.15	2.54 0.54	25.64 7.83
7	6	1.35 0.21	1.36 0.12	2.71 0.30	52.04 4.27

The values of groups 2 to 5 were similar or only slightly higher than in animals on rat's diet. Only rats in group 6, i.e. in animals which were transferred from milk to rat's diet one day before killing, showed higher whole body and carcass retentions, similarly to rats which were maintained on milk diet throughout the experiment.

The gut retention values ranged by a factor of 23 between groups in relation to the dietary treatment. Highest values were observed in group 7, i.e. in animals which were only on milk. Rat's diet supplied within one to four days after mercury administration could prevent or reduce the high gut and carcass retentions of ^{203}Hg in rats which were on milk at the time of mercury administration.

Mercury retention in the whole body, carcass and gut after intraperitoneal administration. The results presented in Table 3 show little changes in ^{203}Hg retention in relation to dietary treatment.

TABLE 3

The influence of diet on ^{203}Hg retention six days after a single intraperitoneal administration (means±SEM)

Dietary treatment group	No. of rats	Gut-free carcass (C)	Gut (G)	Whole body WB (C+G)	G%WB $\frac{Gx100}{C+G}$
		(per cent dose)			
1	6	55.03 1.16	3.16 0.24	56.51 1.46	5.57 0.33
2	3	62.95 3.43	3.82 0.42	63.44 1.82	5.70 0.28
3	3	60.49 2.50	4.02 0.18	64.51 2.54	6.25 0.31
4	3	56.84 3.94	3.52 0.50	60.36 4.40	5.77 0.63
5	3	59.04 0.91	3.02 0.39	62.06 1.30	4.85 0.59
6	3	57.07 1.06	4.07 0.07	61.14 1.08	6.66 0.10
7	6	57.49 2.08	6.84 0.51	64.33 2.30	10.63 0.61

The highest gut retention in group 7 is most probably the result of a higher retention of the endogenous fraction of mercury in animals which were on milk diet throughout the experiment.

DISCUSSION

Milk diet causes increased carcass and gut retention of ^{203}Hg when administered orally and little changes when administered intraperitoneally indicating that milk primarily influences the absorption and retention of mercury in the gut. The high percentage of the whole

body radioactivity which is retained in the gut of older rats after oral ^{203}Hg administration (about 50%) is similar to the high gut retention of mercury in suckling rats (KOSTIAL, RABAR et al. 1979). When rats are fed on rat´s diet about two times less mercury is absorbed into the gut-free carcass and about 23 times less mercury is retained in the gut wall than in animals on milk diet.

Although we do not know the site of mercury retention in the gut, we may assume that it is located in the small intestine as found for ^{141}Ce (INABA and LENGEMANN 1972) and cadmium (SASSER and JARBOE 1977) in sucklings. The significance of rat´s diet in removing cerium or cadmium from the gut wall in sucklings was pointed out previously. It was assumed that solid diet accentuates the extrusion of cells from the villi where the metal is deposited in sucklings (INABA and LENGEMANN 1972, SASSER and JARBOE 1977). This theory might also be applicable to older rats but even in sucklings it is not likely to be the only mechanism by which solid diet enhanced elimination of some metals from the gut compartment.

Rat´s diet has a higher content of several essential elements than milk and it is known that essential elements might interact in the absorption process of other metals. Rat´s diet might also produce ligands which have a higher affinity for metals than ligands in the gut wall or ligands produced during the digestion of milk. For this hypothesis mercury from the gut compartment should be accessible for interaction with essential elements or ligands in the luminal content.

We can conclude that milk diet increases gut retention of orally administered mercury in older rats which is similar to findings in sucklings and also that rat´s diet can remove mercury and possibly other metals from the gut and prevent their absorption several days after an oral dose.

SUMMARY

The retention of ^{203}Hg was studied six days after a single oral or intraperitoneal administration to six week old female albino rats fed rat´s diet or milk. After oral administration rats on milk diet had a two times higher retention of mercury in the gut-free carcass and a 23 times higher retention in the gut than animals on rat´s diet. Changes in diet had very little influence on mercury retention after intraperitoneal administration. The higher gut and carcass retentions of mercury in animals on milk diet could be prevented or reduced by transferring rats from milk diet to rat´s diet several days after an oral dose of mercury.

These results might be relevant for interpreting high gut and carcass retention after oral administration of some metals in suckling and changes which occur at weaning.

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