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Chronic and Multigeneration Toxicities of Small Concentrations of Cadmium in the Diet of Rats[1]

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Groups of rats were fed a basal diet that contained 80 μg/kg cadmium and 97 mg/kg zinc or the basal diet with additions of cadmium chloride to yield concentrations of cadmium of 100 and 125 μg/kg. Four generations of offspring were produced by sequential feeding on the same diets given to the original parental groups. No significant effects of either amount of added cadmium on growth, mortality, systolic blood pressure, or the induction of grossly or microscopically evident pathemas were detected. The one significant change attributable to feeding of the diet containing 125 μg/kg cadmium was a progressive decrease in the mean number of litters per female in the generations of dams for the F_2 through F_4 generations of offspring. Although no lesions of the testes were reported by the pathologists, this low reproductive success is believed to have been due probably to a failure of fertilization rather than to a toxic effect by cadmium on embryos and fetuses. The results of the study suggest that persons eating a diet containing reasonable amounts of zinc-rich foods, such as oatmeal, bran, oysters, herrings, and liver, could withstand toxic actions from a modest increase in the daily exposure to cadmium arising from enhanced occupational or environmental concentrations of that metal.

Cadmium has been recognised to constitute an occupational hazard since the middle of the 17th century, when cadmium fume was reported to have been responsible for attacks of diarrhea, vomiting, and other gastrointestinal upsets among workers in foundries (Stockhusen, 1656). During the succeeding centuries, there has been a slow growth of interest in the biologic effects of this metal as its toxicity has increased in importance in proportion to its enlarged use in various industries (Sovet, 1858; Wheeler, 1876; Alsberg and Schwartze, 1919; Friberg, 1948; Lane and Campbell, 1954; Lucis *et al.*, 1969; Goyer *et al.*, 1972; Lauwerys *et al.*, 1974). Experimental studies of the toxic effects of this metal seem to have begun in the early part of the 19th century, but the first respectable experimental study was that by Marmi (1867). This investigator found that administration of cadmium salts to animals resulted in gastroenteritis, with anorexia and emaciation, subpleural hemorrhages, pulmonary infarcts, fatty change of the liver and the heart, and diffuse inflammation of the kidneys. Much of the experimental study of the toxic effects of cadmium since that time has been related to its effects on the cardiovascular system, especially so since Schroeder and his coworkers (Schroeder and Vinton, 1962; Schroeder, 1964; Schroeder *et al.*, 1966) with the rat and Thind and

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associates (Thind *et al.*, 1970, 1973; Thind, 1974) with the rabbit and the dog found that hypertension followed administration of cadmium to the animals. However, Porter *et al.* (1974, 1975) have reported that they could not induce hypertension by the same schedule of doses of cadmium used by Schroeder *et al.* (1966). Ohanian *et al.* (1978) have found that strains of rats selected for their propensities to develop hypertension when fed a diet containing 4% of NaCl differed also in their susceptibilities to induction of hypertension by cadmium. A genetic factor may be involved in establishing the difference between the results obtained by Schroeder *et al.* (1966) and by Porter *et al.* (1974, 1975) in ostensibly identical experiments.

In addition to its hypertensive effect, cadmium has been found to produce gonadal injury in both sexes of rats (Kar *et al.*, 1959; Gunn *et al.*, 1963) and to induce the development of facial deformities in fetuses of the hamster (Ferm and Carpenter, 1967) and the rat (Chernoff, 1973). Barr (1973) found a genetic effect on facial malformation in the presence of cadmium similar to that on the hypertensive response to the metal.

METHODS

Because much of the research performed previously has been done by adding cadmium compounds to either diets or water that had been specially prepared to contain very little of that metal, this study was undertaken to compare rats fed a standard commercial diet and given ordinary tap water with those fed the same basal diet with added cadmium chloride and watered from the same source. Such a procedure was thought to model an occupational or environmental exposure to cadmium more faithfully than the more rigorously quantitative method.

The daily intake of cadmium by an average person, largely in food, has been estimated (Schroeder and Balassa, 1961; Guthrie, 1973) to be between 4 and 104 μg. These figures correspond with a mean daily dose of between 0.067 and 1.73 μg/kg on the assumption that the human population consists of equal numbers of 50-kg females and 70-kg males. Accidental or occupational exposures to cadmium would be superimposed on this basal intake of this metal. Accordingly, we chose as our basal diet ground rat chow (Wayne Lab-Blox), to which we added either 32.6 or 73.4 μg/kg cadmium chloride. The basal diet contained about 80 μg/kg cadmium, so that the three diets supplied to our rats daily doses of cadmium of about 4.4, 5.5, and 6.9 μg/kg of body wt. Because of the known biologic interactions of zinc and cadmium (Parizek, 1957; Parizek *et al.*, 1969; Parzyck *et al.*, 1978), the concentration of zinc in the basal diet was determined; it amounted to 97 $\pm$ 4.6 mg/kg ground chow.

Three groups of rats, 25 males and 25 females in each, were caged in sexual pairs at a body weight of about 125 g. These rats constituted the F_0 generation. When the females were seen to have been impregnated upon examination of their vaginas, they were separated from the males until the young had been weaned and the females had had rest periods of about 3 weeks. They were then reunited with their original mates. After birth of the first litters, the number of pairs in the F_0 generation was reduced to 20.

Upon weaning, two sexual pairs from each litter were caged and fed the same diet as their parents. The remaining young of each litter were killed and examined

for gross abnormalities. Gross lesions were prepared for microscopic examination, to enable precise identification of the pathemas. At sexual maturity of the offspring, the total number of pairs of each generation on each diet was reduced to 40 or less for logistic reasons. F_1, F_2, F_3, and F_4 generations were produced by this general method.

In addition to the pathologic studies outlined above, rats in the F_4 generations of the three groups of rats were matched as closely as possible on the basis of their systolic pressures at the end of the exposure period and were studied carefully for the occurrence of gross and microscopic lesions in the heart, the lungs, and the kidneys. This group of necropsies included 10 rats fed the basal ration, 7 fed the diet with the smaller concentration of added cadmium, and 6 fed the diet containing the larger concentration of the added metal.

The diets were analyzed for cadmium and zinc by atomic absorption spectrometry (Berman, 1967). Blood pressures were estimated by use of the Arteriosonde 1010 with the special cuff and pressure transducer for application to the rat's tail (Rowberg *et al.*, 1969). This method has been found to yield measurements of the systolic pressure of the rat that agreed almost precisely with those obtained by direct arterial puncture. We attempted to measure diastolic pressure also by this method, but the results were so erratic that this variable will not be discussed.

The rats were weighed and examined weekly for general condition and for externally detectable lesions. The systolic blood pressure was measured monthly when both personnel and time were available. At parturition and weaning, records were made of the numbers of abortions and of false pregnancies in each dietary group, of the numbers of litters, of still and live births, of pups born with deformities, of pups alive at weaning, and of the weight of each litter.

RESULTS

Birth and weaning data for the four generations of offspring from the F_0 generation are summarized in Table 1. The only significant differences in this table are those between the numbers of litters per female among the group of rats fed the diet with the highest concentration of cadmium and those among the other two groups. These differences were particularly striking for the F_3 and the F_4 generations, but were significant for the F_2 generations also. Production of litters by females in the group of rats fed the diet to which 73.4 μg/kg cadmium had been added for the F_4 generation was only one-half that for the F_3 generation, which in turn was about three-fourths that for the F_2 generation. In this group of rats there was apparently a progressive effect on fertility in the succeeding generations. In this regard, the reader should recognize that the data for the numbers of litters per female in this table for a particular generation actually pertain to the preceding generation whereas the other data in the table pertain to the listed generation. Although there was a tendency for the mean weight of the pups at weaning to decrease progressively as the concentration of cadmium fed to the dams increased, the differences between the mean weights of litters in corresponding generations never reached the level of significance.

Figure 1 summarizes the growth and mortality experiences of the F_0 and the F_1 generations. For clarity of the figure, only the data pertaining to the rats fed the diets containing the lowest and the highest concentrations of cadmium have been

TABLE 1

BIRTH AND WEANING DATA FOR THE F_1–F_4 GENERATIONS

	Basal diet				Basal diet + 32.6 $\mu g CdCl_2$/kg of diet				Basal diet + 73.4 $\mu g CdCl_2$/kg of diet			
	F_1	F_2	F_3	F_4	F_1	F_2	F_3	F_4	F_1	F_2	F_3	F_4
No. of pseudopregnancies	1	4	9	4	1	0	7	2	0	1	9	1
No. of abortions	0	1	3	1	0	0	2	2	0	5	1	1
Litters/females	24/25	36/40	41/56	31/41	24/25	38/40	41/59	35/41	25/25	30/40	29/54	10/36
No. of stillbirths	9	20	27	32	3	34	26	29	12	40	27	34
No. of live births	219	349	330	250	274	352	331	273	278	270	237	318
No. born with deformities	0	1	1	0	0	0	1	0	0	0	1	0
Mean weight at birth (g)	7.1	6.6	6.9	6.8	6.6	6.7	6.8	6.9	6.9	6.4	6.6	6.9
Percentage weaned	96.3	85.1	94.5	84.4	94.9	88.1	97.3	92.7	95.7	90.1	92.8	80.5
Mean weight at weaning	43.9	44.5	43.2	31.5	40.6	42.5	37.0	34.3	41.7	46.0	34.5	31.7

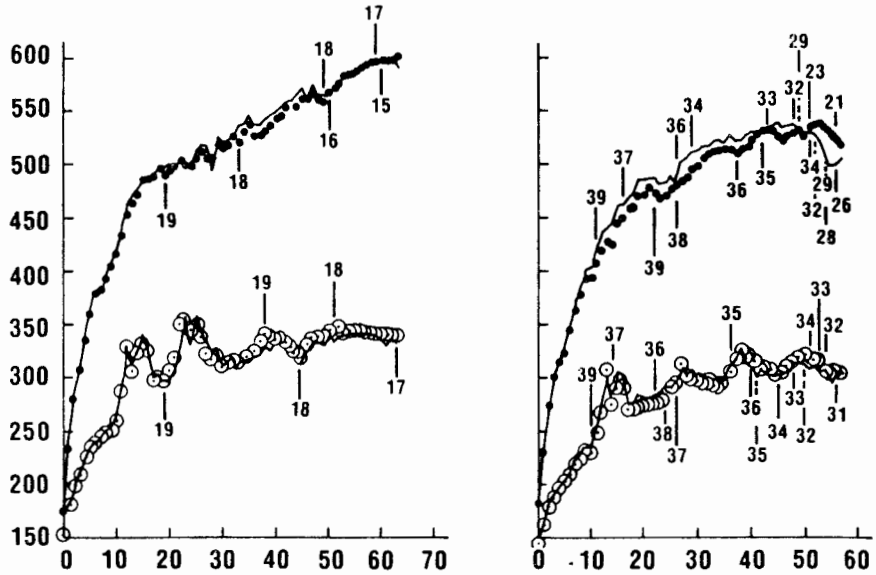

FIG. 1. Growth and mortality experiences of rats of the F_0 and F_1 generations fed the basal diet and the basal diet with an addition of 73.4 μg/kg cadmium chloride. Left panel: F_0 generation. Right panel: F_1 generation. Abscissas: weeks on the diet. Ordinates: body weights (g). Continuous lines: rats fed the basal diet. Dots and circles: rats fed the diet containing 125 μg/kg cadmium. Dots: males. Circles: females. Numbers below the lines represent the numbers of rats remaining alive on particular days from groups of 20 (F_0) or 40 (F_1) fed the basal diet; those above the lines give the same information for rats fed the diet having the highest concentration of cadmium.

plotted. The growths and mortalities of the groups of rats given the various diets in these two generations did not differ to any appreciable extent. The growth and mortality experiences of the F_2 and F_3 generations during shorter periods of observation are summarized in Table 2, which includes also information for the F_0 and F_1 generations for comparison. This table indicates that the concentrations of cadmium that were added to the rats' diets had no consistent effects on growth or mortality in either sex, but the females seemed to be slightly less likely to die during our periods of observation than the males.

Figure 2 summarizes the courses of the systolic blood pressures of the F_0 and the F_1 generations during consumption of the diets containing 80 and 125 μg/kg cadmium. As in Fig. 1, the data for the rats fed the diet containing 100 μg/kg cadmium were not plotted, to keep the figure from being cluttered confusingly. No consistent effect on the systolic pressure by the increased concentration of cadmium is visible in this figure. When the systolic pressures of the successive generations at sexual maturity are considered, as in Table 3, the later generations appear to have experienced some heightening of their general levels of pressure. The relation of the elevation to the concentration of cadmium in the ration is not clear, however.

Gross observation at necropsy of 276 rats from various generations of the three dietary groups revealed that 59/93 of those fed the diet with the lowest concentration of cadmium seemed normal, that 76/93 fed the diet to which the lower concentration of cadmium chloride had been added appeared to be normal, and that 62/90 fed the diet to which the higher concentration of cadmium chloride had

TABLE 2

EFFECTS OF CADMIUM ON GROWTH AND MORTALITY OF PARENTAL RATS

Generation	Weeks of observation	Concentration of cadmium in diet (μg/kg)	Mean body weights				Percentage mortality	
			Male		Female			
			Initial	Final	Initial	Final	Male	Female
F_0	64	80	169	591	181	332	25	15
		100	175	613	152	334	25	25
		125	175	602	153	340	15	10
F_1	58	80	190	505	143	308	35	22.5
		100	184	522	140	310	20	15
		125	183	521	145	307	47.5	20
F_2	20	80	326	524	205	299	13.8	18.3
		100	321	523	209	286	13.6	15.3
		125	319	522	207	296	17.3	25.9
F_3	20	80	434	521	274	326	14.6	12.2
		100	426	520	273	331	11.9	2.6
		125	407	504	268	323	12.2	2.4

been added seemed normal. In all groups, the most common diagnoses of gross pathemas were pneumonia, ovarian cysts, and tumors in the intestine. Fibrotic tumors of the breast were found in a few females of the F_0 generation; similar tumors were not found in any generation of offspring.

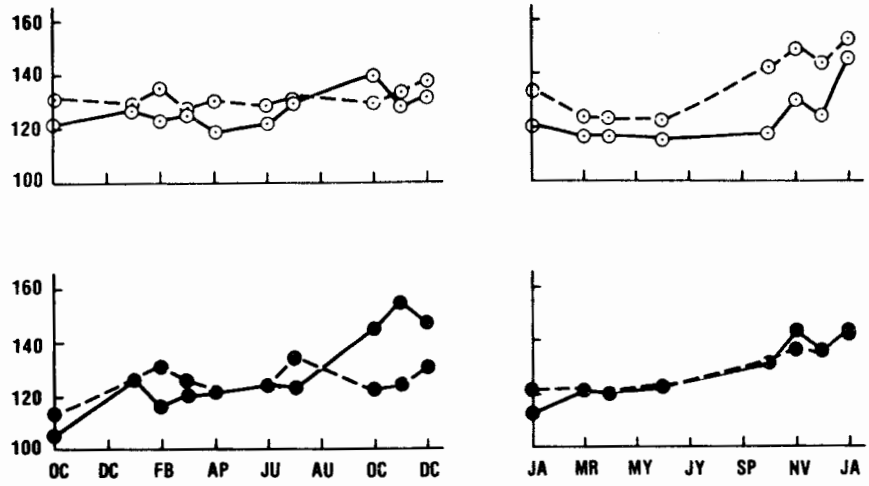

FIG. 2. Systolic blood pressures of rats of the F_0 and F_1 generations fed the basal diet and the basal diet with an addition of 73.4 μg/kg cadmium chloride. Left panels: F_0 generation. Right panels: F_1 generation. Abscissas: JA, January; FB, February; MR, March; AP, April; MY, May; JU, June; JY, July; AU, August; SP, September; OC, October; NV, November; DC, December. Ordinates: systolic blood pressure (mm Hg). Continuous lines: rats fed the basal diet. Broken lines: rats fed the diet containing 125 μg/kg cadmium. Dots: males. Circles: females.

TABLE 3

HYPERTENSION AMONG FIVE GENERATIONS OF RATS FED CADMIUM-CONTAINING DIETS

Generation	Dietary concentration of cadmium (μg/kg)	Males			Females		
		No.	No. with BP > 150	No. with BP > 160	No.	No. with BP > 150	No. with BP > 160
F_0	80	20	0	0	20	0	0
	100	20	0	0	20	0	0
	125	20	0	0	20	1	0
F_1	80	40	0	0	40	0	0
	100	40	0	0	40	1	0
	125	37	0	0	37	0	0
F_2	80	56	1	0	56	12	7
	100	55	0	0	53	5	1
	125	45	4	3	45	8	7
F_3	80	41	8	0	41	3	1
	100	42	10	3	39	6	0
	125	41	14	2	41	15	4
F_4	80	8	1	1	8	3	1
	100	12	1	1	12	3	1
	125	12	3	1	12	4	0

Tables 4 and 5 summarize, respectively, the microscopic findings in small series of male and of female rats of the F_0 generation. All grossly and microscopically recognizable changes were considered to be either minor in degree or the results of spontaneous diseases known to occur within the colony of rats. Because the incidence of these changes were not above those in the profile of diseases that occurred spontaneously in the colony, we doubt that any of these morphologic abnormalities can be attributed to the cadmium in the diets.

Twenty-three rats selected from various groups of the F_4 generation on the basis of their systolic pressures just before necropsy were studied carefully for possible vascular pathemas in heart, lung, and kidneys. Three rats on the diet containing 80 μg/kg cadmium with systolic blood pressures of 100 mm Hg were paired with 2 from each of the other dietary groups with the same systolic pressure. Three rats fed the diet containing 80 μg/kg cadmium with systolic pressures of 140 (2 rats) and 144 (1 rat) mm Hg were paired with 3 from the group fed the diet containing 100 μg/kg with identical pressures. Three rats from the group fed the diet with the lowest concentration of cadmium with systolic pressures of 160 mm Hg were paired with a rat with a systolic pressure of 158 mm Hg from the group fed the diet that contained 125 μg/kg and with one from each group fed the diets with added cadmium chloride with systolic pressures of 160 mm Hg. One rat from the group fed the basal diet with a systolic pressure of 190 mm Hg was paired with 3 rats from the group fed the diet with the highest concentration of cadmium with systolic pressures of 180 mm Hg.

Four of the ten rats fed the diet containing the lowest concentration of cadmium were judged to be completely normal. One had plasma cell myelomata in all organs

TABLE 4

INCIDENCE OF MORPHOLOGIC CHANGES IN MALE RATS EXPOSED TO CADMIUM IN THEIR DIETS FOR 14 MONTHS

	Concentration of Cd in the diet (μg/kg)		
	80	100	125
Heart			
1. Focal macrophages	1/5	—	—
2. Necrotic muscle fibers, focal macrophages	—	—	1/5
Lung			
1. Perivascular granuloma	1/5	—	—
2. Giant cell granuloma	—	1/6	—
3. Bronchopneumonia	1/5	—	1/5
4. Purulent bronchopneumonia	—	3/6	—
5. Intraalveolar macrophages	1/5	—	1/5
Liver			
1. Parasitic granuloma	1/5	—	—
Kidney			
1. Nephrosclerosis, tubular dystrophy	5/5	5/6	5/5

examined (heart, kidneys, liver, spleen, and lungs). One had multiple bronchiogenic abscesses in its lungs and another had peribronchial lymphocytic infiltration into its lungs and focal calcification of an important artery, with subintimal edema and focal myocarditis, in the wall of the left ventricle. Three of these rats (2 males and a female) had a few sclerosed glomeruli within their kidneys; 2 of the same rats had a few areas of thyroidization within their kidneys and slight interstitial nephritis. The mean systolic pressure of these 10 rats was 139 ± 30.8 mm Hg.

The 7 rats fed the diet containing 100 μg/kg cadmium had a mean systolic pressure of 135 ± 25.0 mm Hg; 2 of them were judged to be entirely normal. One had a subpleural granuloma with cholesterol clefts and areas of brown pigmentation within the epithelial cells of the proximal tubules of its kidneys. Another had sclerotic glomeruli and areas of thyroidization, associated occasionally with slight infiltration of round cells into the interstitial tissue, within its kidneys and a minute area of infiltration by mononuclear cells into the endocardium of the left ventricle. One had a benign papillary adenoma, several areas of thyroidization, and some sclerosis of the glomeruli within its kidneys. The 2 remaining rats had brown pigmentation of the epithelia of their proximal tubules; one of these rats had slight hydronephrosis, with several calcified areas, and the other had slight interstitial nephritis with several areas of thyroidization.

The 6 rats from the group fed the diet containing the largest concentration of cadmium had a mean systolic pressure of 151 ± 39.9 mm Hg. Two of these rats were entirely normal. One had pneumonia with consolidation, and several areas of thyroidization within its kidneys. Two others had focal areas of accumulation of macrophages within alveoli of the lungs and areas of thyroidization, with interstitial fibrosis and glomerular sclerosis, within their kidneys. The last rat in this

TABLE 5

INCIDENCE OF MORPHOLOGIC CHANGES IN FEMALE RATS EXPOSED TO CADMIUM IN THEIR DIETS FOR 14 MONTHS

	Concentration of Cd in the diet (μg/kg)		
	80	100	125
Lung			
1. Giant cell granuloma	1/5	—	—
2. Purulent bronchopneumonia	1/5	—	—
3. Intraalveolar macrophages	1/5	—	—
Kidney			
1. Nephrosclerosis, tubular dystrophy	—	1/5	2/5
2. Colloid cysts	1/5	—	—
Ovaries			
1. Abscess	—	1/5	—
2. Fibrosis	—	2/5	—
3. Cyst	—	—	1/5
4. Periovarian cyst	—	—	1/5
Uterus			
1. Pigment-laden macrophages	—	1/5	—
2. Endometritis	—	—	1/5
Pituitary			
1. Colloid cysts with pigmented macrophages	—	1/5	—
2. Old and recent hemorrhages	—	—	1/5

group had a few minute areas of thyroidization, with interstitial fibrosis, within its kidneys.

When the pathemas found in rats matched on the basis of their blood pressures are compared, the rats with systolic pressures below 145 mm Hg and those with systolic pressures of or above 160 mm Hg being considered separately, 4 in the group with the lower systolic pressures (2 from the group fed the basal diet and one from each of the other dietary groups) were judged to have completely normal hearts, lungs, and kidneys whereas only 2 rats in the group with the higher range of systolic pressures (one each from the groups fed the basal diet and fed that with the larger concentration of added cadmium) were considered to have normal hearts, lungs, and kidneys.

One rat fed the basal diet in the group with the lower systolic pressures had multiple bronchiogenic abscesses within its lungs and 2 had minor sclerotic changes in the glomeruli of their kidneys, with slight interstitial nephritis also in one of these animals. The last rat in this group from those fed the basal diet had mild inflammatory changes in its heart and lungs. One of the five rats fed the diet that contained 100 μg/kg cadmium included within this group had normal heart and lungs but had minor inflammatory changes in its kidneys. Another of these rats had normal heart and lungs but had hydronephrosis, with multiple calcifications, within its kidneys. A fourth had a normal heart and nothing more within its kidneys than increased pigmentation of the epithelium lining the proximal tubules, but had

a subpleural granuloma and cholesterol clefts within its lungs. The fifth rat from this dietary group had slight inflammatory changes in both its heart and its kidneys. The second rat with a systolic pressure in the lower range from the group fed the diet that contained 125 μg/kg cadmium had pneumonia with consolidation within its lungs and several areas of thyroidization within its kidneys.

In the group of rats with systolic pressures of or above 160 mm Hg, one of four from the group fed the basal diet had diffuse infiltration of myelomatous cells into not only the heart, the lungs, and the kidneys but also the liver and the spleen. The remaining 2 rats fed the basal diet had normal hearts and lungs, but had minor inflammatory changes in their kidneys (focal areas of thyroidization and a few sclerosed glomeruli). The 2 rats in this group from those fed the diet that contained 100 μg/kg cadmium had normal hearts and lungs, but had minor inflammatory changes within their kidneys. One of these rats had also a benign adenoma in one kidney. Of the 3 rats with lesions in this group from those fed the diet with 125 μg/kg cadmium, one had normal heart and lungs but had minor inflammatory changes in its kidneys. The remaining 2 rats from this dietary group both had minor inflammatory changes in their lungs (focal accumulations of macrophages within the alveoli) and kidneys (scattered areas of thyroidization, with interstitial fibrosis and sclerosis of some glomeruli).

DISCUSSION

Probably the most striking finding in our study, when its results are compared with those reported by Schroeder and Vinton (1962), Schroeder (1964), and Schroeder *et al.* (1966), is that we have not seen the generalized thickening of the renal arterioles and arteries, with proliferation of medial smooth muscle, of subintimal fibroblasts, and of endothelial cells, described by Schroeder *et al.* (1965) and by Kanisawa and Schroeder (1969). Indeed, no lesions were found in our rats that can be related specifically to the concentration of cadmium in the diets supplied to the animals.

There were no consistent effects on growth and mortality among either male or female rats attributable to increases in the concentration of cadmium in the diet by 25 and 56% (Fig. 1 and Table 2). There is an indication in Table 1 that the larger addition of cadmium to the diet decreased fertility. The findings that the proportions of defective pregnancies per female (the sum of pseudopregnancies, stillbirths, and abortions) and of deformities among the pups did not increase in parallel with the concentration of cadmium in the diet suggest that the low reproductive success among the rats fed the diet with the highest concentration of cadmium was due to a failure of fertilization rather than to an effect of the metal on the embryos and fetuses. Because both the male and the female rats were fed the same diets, there is no way of deciding whether the low reproductive success of these rats pertains to the males, to the females, or to both. The most probable situation seems to be that the effect is due primarily to damage to the reproductive apparatus of the males, a number of investigators (Parizek and Zahor, 1956; Parizek, 1960; Kar and Das, 1960; Chiquoine and Suntzeff, 1965; Cameron and Foster, 1963; Mason *et al.*, 1964; Gerrits, 1967; Pate *et al.*, 1970; Nordberg, 1971, 1975; Richardson *et al.*, 1974; Suter, 1975; White *et al.*, 1978) having found that the testes and accessory male sexual organs are especially sensitive to the toxic activity of this metal.

The failure of our diets to produce any significant elevation of the systolic blood pressure in the rats is related probably to their failure to induce significant pathemas in the vasculatures of the heart, the lungs, and the kidneys. The diet that contained the highest concentration of cadmium used in our study is calculated to have supplied to the rats a daily dose of about 7 μg/kg of the metal. This probably is much less than was taken by the rats used by Schroeder and his associates (Schroeder and Vinton, 1962; Schroeder, 1964; Schroeder *et al.*, 1965, 1966; Kanisawa and Schroeder, 1969), who supplied to their animals water containing 5 μg/ml cadmium and a diet containing 20 μg/kg of that metal. Ohanian *et al.* (1978) reported that their rats of the S strain (develop hypertension when fed a diet containing 4% of sodium chloride) underwent cardiac hypertrophy with a daily intake of cadmium of about 80 μg/kg and developed hypertension and vascular pathemas with daily intakes of 80–400 μg/kg.

In addition, the concentration of zinc in our diets probably minimized the toxicity of the cadmium in the diets. The ratio of the concentration of zinc to that of cadmium in our diets fell between 775 and 1212 whereas Parizek *et al.* (1969) and Parzyck *et al.* (1978) found that much lower ratios, of the order of 1–20, reduced markedly adult and fetal mortalities and fetal malformation due to single injections of salts of cadmium.

We believe that our experiment suggests that a person eating a mixed diet has little to fear from a modest increase in the daily intake of cadmium from either the diet or the atmosphere. The average mixed diet in the United States supplies daily 10–15 mg of zinc (Burton, 1976). This amount of zinc would allow an individual to absorb daily about 600 μg/kg cadmium without incurring damage to health, if the ratios found to be effective in the rat apply also to man. Oysters, herrings, oatmeal, liver, and wheat bran are foods that contain especially large concentrations of zinc and that, except for the fact that the organisms from which these foods are derived may concentrate cadmium also from their environments, should be protective components in the diets of people who are exposed, occupationally or otherwise, to cadmium.

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