Life-term Effects of Mercury, Methyl Mercury, and Nine Other Trace Metals on Mice[1]

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ABSTRACT To evaluate recondite effects of certain trace elements, 1,557 mice were exposed in groups of 36 to 54 of each sex to soluble salts of lead, nickel, vanadium, and titanium, a repetition of previous experiments; to beryllium, barium, and aluminum, to inorganic and methyl mercury; and to boron and tungsten. Exposures were in low doses and for life in an environment controlled as to contaminating trace elements. The diet was low in trace elements, and those studied were added to drinking water. There were three groups of controls. Males given vanadium were somewhat larger than their controls. Methyl mercury at 1 ppm increased body weights of both males and females, whereas at 5 ppm, it decreased growth and was toxic; mercuric chloride had no demonstrable effect. No element was tumorigenic, but aluminum and vanadium had slight effects ($P < 0.05$) in females. Longevity was increased in mice fed nickel and vanadium and in the survivors of those initially fed 5 ppm methyl mercury and later 1 ppm. Mercuric chloride was nontoxic. These studies provide guidelines for the relative toxicities of some common metals when ingested. J. Nutr. *105:* 452–458, 1975.

INDEXING KEY WORDS life-term studies · methyl mercury · beryllium · barium · aluminum · boron · tungsten · titanium · lead · nickel · vanadium · survival

Studies on the recondite toxicities of low doses of various abnormal trace elements in drinking water have been conducted on mice in an environment that excludes metallic contaminants. These effects concerned growth, survival, life-span, and tumors, and involved 21 trace elements (1). Some of these studies were done 10 years or more ago (2–4). We have repeated four of them on lead, nickel, vanadium, and titanium, which were fed to chromium-deficient mice in previous work. In this series the mice were given adequate supplies of chromium. In addition, identical studies were made on two group IIA elements, beryllium and barium, two group IIIA elements, boron and aluminum, a study on tungsten, and three studies on mercury.

These studies will complete our series of 27 elements with mice, of which 4 elements had 2 valence states. Not studied were group IA metals, group IIA metals magnesium, calcium, and strontium, the lanthanides and actinides, technetium, ruthenium, silver, and all metals of the third transitional group except tungsten and mercury, as well as thallium, bismuth, and polonium. These 29 metals and metalloids and 2 nonmetals make up most of those to which industrialized man is exposed.

METHODS

Random-bred white Swiss mice of the Charles River CD strain, numbering 1,557, were born in our laboratories from purchased pregnant females.[3] At the time of weaning, 19 to 20 days of age, groups of 54 of each sex were separated and placed, 6 mice to a cage, as littermates.

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TABLE 1

Weights of mice fed one of four trace metals in drinking water for life (Series 1)

Age	Control-6	Vanadium, 5 ppm	Nickel, 5 ppm	Titanium, 5 ppm	Lead, 5 ppm
days			*g*		
Males					
30	23.1±0.63[1]	25.5±0.45[2]	23.1±0.33	23.5±0.33	25.3±0.89
60	34.5±0.95	38.1±0.90[3]	35.3±0.78	36.7±0.54[4]	34.4±0.67
90	40.2±0.62	42.5±0.85[5]	40.3±0.89	42.3±0.48[3]	41.2±0.63
120	43.2±0.75	43.5±1.18	41.8±1.76	44.7±0.41	43.2±0.92
150	44.6±0.92	46.8±0.98	49.4±1.32[2]	46.0±0.67	45.8±0.87
180	45.6±1.15	49.0±1.32[4]	47.0±0.81	47.5±0.75	46.5±0.94
360	47.4±1.01	49.7±1.81	45.1±1.59	51.0±1.49[4]	48.8±1.39
540	40.6±2.45	45.5±1.89[5]	41.8±0.92	45.1±1.48	44.0±2.24
Females					
30	20.1±0.79	21.3±0.48	19.8±0.73	19.6±0.26	20.2±0.44
60	27.6±0.72	29.0±0.55	27.6±1.06	30.7±0.96[5]	27.1±1.00
90	33.3±0.82	33.8±0.61	31.3±1.11	33.2±0.68	32.6±0.76
120	36.8±1.18	35.9±1.34	37.4±0.86	35.2±0.75	35.8±0.89
150	38.5±1.68	39.6±1.34	37.7±1.12	36.4±0.97	38.4±1.33
180	38.8±1.42	40.3±1.49	37.6±1.05	37.7±1.16	38.3±1.10
360	42.2±1.19	43.4±1.54	41.4±0.98	42.0±0.33	44.5±2.07
540	36.3±1.56	43.2±2.18[3]	42.8±2.05[5]	38.3±1.30	42.7±2.50[5]

There were 54 mice in each group. [1] ± SEM. [2] Differs from controls by Student's *t* test; $P < 0.005$. [3] $P < 0.01$. [4] $P < 0.05$. [5] $P < 0.025$.

Three experiments were run at different times. The first (series 1), on lead, nickel, vanadium, and titanium, with their controls, involved 541 mice. The second (series 2), consisted of aluminum, barium, beryllium, and mercury with 692 mice involved. In the third (series 3), the tested mice received added boron or tungsten. A total of 324 mice was used in this series.

Cages were plastic with stainless steel tops and stacked on wooden racks. The diet was composed of whole untreated Balbo rye flour (60%), powdered skim milk (30%), corn oil (9%), and iodized sodium chloride (1%), with added vitamins and iron (2).[4] The trace mineral contents of the diet have been reported (5). The basal drinking water, doubly deionized and with no detectable cations, contained soluble salts as simple complexes (in ppm): zinc, 50; manganese, 10; copper, 5; chromium, 5; cobalt, 1; and molybdenum, 1. In series 1, the controls were designated 0–6, and they were contemporary with mice fed lead acetate (25 ppm Pb), nickelous acetate (5 ppm Ni), vanadyl sulfate (5 ppm V), and potassium titanium oxalate (5 ppm Ti) in the basal drinking water. In series 2, controls were designated 0–7, and they were contemporary with mice fed aluminum potassium sulfate (5 ppm Al), beryllium sulfate (5 ppm Be), barium acetate (5 ppm Ba), methyl mercury acetate (5 ppm Hg for 70 days and 1 ppm Hg subsequently), and mercuric chloride (5 ppm Hg) in the basal drinking water. In series 3, the controls received plain deionized water without added supplements and were contemporary with mice fed sodium metaborate (5 ppm B), and sodium tungstate (5 ppm W), which also received these metals dissolved in plain water.

Animals dying a natural death were weighed and dissected, gross tumors were detected, and some sections were made of heart, lung, liver, kidney, and spleen for microscopic examination. Tumors were considered malignant when they were multiple, but in our experience most tumors in mice were malignant.

RESULTS

Growth and body weights. Weights of mice are shown in tables 1–4. Those fed vanadium were heavier than their controls at 15 of 16 intervals, and the increase was significant in 6 intervals. No such effect

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[4] To each kilogram of diet was added (in mg): ferrous sulfate, 100; calcium pantothenate, 10; niacin, 50; pyridoxine hydrochloride, 1.0; and vitamin A, 5,000 IU; vitamin D, 1,000 IU.

TABLE 2

Weights of mice fed three trace metals in drinking water for life (Series 2)

Age	Control-7	Aluminum, 5 ppm	Barium, 5 ppm	Beryllium, 5 ppm
days		*g*		
Males				
30	21.7 ±0.33[1]	21.4 ±1.44	20.4 ±0.93	24.4 ±0.80[2]
60	33.0 ±0.33	32.2 ±1.82	33.0 ±0.48	33.2 ±0.53
90	37.7 ±0.53	36.7 ±1.06	35.8 ±1.16	39.4 ±0.61
120	41.5 ±0.53	40.2 ±1.35	40.4 ±0.93	42.5 ±0.75
150	43.0 ±0.64	42.1 ±1.64	42.2 ±1.11	43.3 ±1.04
180	43.5 ±0.95	43.4 ±1.18	43.7 ±1.13	45.5 ±0.98
360	45.2 ±1.59	47.5 ±1.68	46.5 ±1.89	47.4 ±1.18
540	37.7 ±2.12	41.0 ±2.80	37.7 ±1.72	40.8 ±1.74
Females				
30	20.5 ±0.49	18.8 ±0.81	17.8 ±0.41[3]	20.7 ±0.53
60	26.5 ±0.36	25.5 ±0.81	26.5 ±0.41	25.6 ±0.35
90	31.1 ±0.83	30.5 ±0.81	30.1 ±0.18	29.0 ±0.24[4]
120	34.5 ±0.83	34.1 ±1.33	34.6 ±0.67	31.3 ±0.35[5]
150	35.7 ±1.13	36.4 ±1.64	36.0 ±0.45	33.7 ±0.60
180	37.6 ±1.23	38.3 ±1.64	38.0 ±0.15	34.6 ±0.73
360	43.0 ±3.00	44.4 ±3.05	45.3 ±1.15	41.0 ±1.42
540	34.5 ±2.32	35.7 ±2.78	37.6 ±1.41	35.1 ±2.26

There were 54 mice in each group except for the barium group, which had 42 males and 36 females. [1] ± SEM. [2] Significance of difference from controls by Student's *t* test; $P < 0.005$. [3] $P < 0.001$. [4] $P < 0.025$. [5] $P < 0.01$.

occurred with nickel, titanium, or lead. In table 2 the weights of mice fed aluminum, barium, and beryllium are given. Females given beryllium were lighter than their controls at six of eight intervals, and the difference was significant at two intervals. Males tended to be slightly heavier than their controls. Mice fed aluminum and barium were remarkably uniform in respect to weight. In all cases the 540-day weights were less than those at a year of age. This loss of weight also occurred in the controls and in 8 of the 10 groups shown in table 1.

For purposes of clarity, the weights of mice given mercuric chloride as mercury and two concentrations of methyl mercury as mercury are shown in table 3 using the same controls as in table 2. The mice fed mercuric chloride were larger than their controls at 13 of 16 ages and significantly so in females at 2 ages. Mice given 5 ppm Hg as methyl mercury were smaller than their controls at 15 of 16 intervals, of which 12 were significant. There was a high mortality during the first 2 months of administration of this dose, which was reduced to 1 ppm Hg at the age of 90 days. Mortality decreased immediately, and the survivors continued to grow. Methyl mercury at 1 ppm from weaning time produced a significantly increased growth rate in both males and females, resulting in some

TABLE 3

Weights ± SEM of mice fed mercury and methyl mercury in drinking water for life (Series 2)

Age	Control-7	$HgCl_2$, 5 ppm Hg	MeHg, 5 ppm Hg	MeHg, 1 ppm Hg
days		*g*		
Males				
30	21.7 ±0.33	22.4 ±0.95	21.5 ±0.61	22.6 ±0.34[1]
60	33.0 ±0.33	34.0 ±0.62	30.0 ±0.65[1]	35.8 ±0.58[1]
90	37.7 ±0.53	38.7 ±0.68	32.2 ±1.24[1]	40.4 ±0.88[1]
120	41.5 ±0.53	41.4 ±0.80	36.1 ±0.72[1]	44.2 ±1.00[2]
150	43.0 ±0.64	41.0 ±1.09	37.3 ±0.75[1]	45.6 ±1.57[3]
180	43.5 ±0.95	44.7 ±0.93	38.3 ±0.97[1]	47.8 ±1.88[3]
360	45.2 ±1.59	47.3 ±1.43	42.6 ±1.67	50.2 ±2.71
540	37.7 ±2.12	41.2 ±1.08	42.0 ±1.03	42.2 ±2.74
Females				
30	20.5 ±0.49	20.5 ±0.44	18.8 ±0.36[4]	25.6 ±3.09
60	26.5 ±0.36	29.0 ±0.41[1]	22.6 ±0.77[1]	31.8 ±3.90
90	31.4 ±0.83	32.2 ±0.68	25.0 ±0.53[1]	35.4 ±1.70[1]
120	34.5 ±0.83	36.2 ±1.05	27.8 ±0.90[1]	36.7 ±0.72[3]
150	35.7 ±1.13	38.3 ±1.25	28.6 ±0.67[1]	39.4 ±0.88[5]
180	37.6 ±1.23	40.7 ±1.33	29.3 ±0.67[1]	41.5 ±1.01[5]
360	43.0 ±3.00	46.0 ±2.30	33.5 ±1.17[5]	48.4 ±0.81
540	34.5 ±2.32	43.4 ±2.77[5]	32.1 ±1.11	43.8 ±2.16[4]

Mice were weighed in groups of six. There were 54 males and 54 females in each group, except for the 1 ppm methyl mercury groups, which had 30 males and 42 females. At 90 days of age, because of a high mortality in the group given methyl mercury at 5 ppm Hg, the dose was reduced to 1 ppm Hg as methyl mercury. [1] Differs from controls by Student's *t* test; $P < 0.001$. [2] $P < 0.01$. [3] $P < 0.05$. [4] $P < 0.005$. [5] $P < 0.025$.

TABLE 4

Weights of mice fed boron and tungsten in drinking water for life (Series 3)

Age	Control-8	Boron, 5 ppm	Tungsten, 5 ppm
days		*g*	
Males			
30	20.0±0.42[1]	18.1±0.45[2]	20.1±0.59
60	34.6±0.59	35.8±0.56	35.1±0.59
90	38.5±0.65	40.6±0.67[3]	39.6±0.59
120	42.5±0.97	43.6±0.80	42.6±0.69
150	45.8±1.36	46.3±0.95	44.7±0.75
180	49.2±1.64	46.3±0.95	46.3±1.01
360	46.6±2.66	46.0±1.75	48.2±1.32
540	46.8±1.33	47.7±1.21	43.5±1.80
Females			
30	18.3±0.20	17.3±0.33[3]	19.0±0.24
60	26.7±0.37	27.4±0.53	27.2±0.33
90	29.5±0.72	31.2±0.85	30.8±0.92
120	31.8±0.55	31.8±1.25	31.8±0.48
150	34.8±0.54	36.1±1.58	34.6±0.63
180	38.3±0.70	38.0±1.18	37.0±0.75
360	42.9±1.14	43.6±1.46	40.7±1.64
540	42.6±1.32	41.3±1.74	40.0±1.25

There were 54 mice in each group. [1] ± SEM. [2] Significance of difference from controls by Student's *t* test; $P < 0.005$. [3] $P < 0.025$.

TABLE 5

Effects of trace metals on tumors, edema, and blanching of the incisor teeth of mice fed for life (Series 1)

Group	No. autopsied	Mean weight at death[1]	No. with white teeth	Edema	Tumors No.	Multiple	LL[2]	Lung	% of mice with tumors
Males									
Control-6	43	28	12	11	10	2	2	4	23.3
Lead	49	31	14	13	15	9	8	8	30.6
Nickel	37	29	6	13	4	3	0	2	10.8
Vanadium	38	31	6	13	5	8	4	4	13.2
Titanium	45	31	7	15	17	7	9	9	37.8
Females									
Control-6	45	29	9	15	9	9	8	1	20.0
Lead	37	28	11	8	8	7	1	5	21.6
Nickel	44	25	12	13	10	7	12	1	22.7
Vanadium	51	25	6	14	19[3]	15	9	3	37.3
Titanium	36	28	8	11	13	14	13	5	36.1

[1] Individual weights at death varied approximately 35% in the various groups. [2] Lymphoma leukemia. [3] Significance of difference between means by chi-square; $P < 0.05$.

of the largest mice that we have encountered in this study.

In all of the mercury groups and controls, there was a decrease in weight from 1 year to 18 months of age. The mice were weaned and given methyl mercury at 5 ppm Hg when they were 20 days old. They began to die 38 to 40 days later, and 20 of 54 males and 23 of 54 females died when they had taken the methyl mercury for 66 to 70 days. When they were 90 days old (given methyl mercury for 70 days), the dose was reduced to 1 ppm, and mortality ceased within 10 to 15 days.

Two groups of mice were given boron or tungsten in doubly deionized water. There were no significant differences from the controls except for three boron groups, two of which were slightly lighter and the other slightly heavier than the controls

TABLE 6

Effects of trace metals on tumors, edema, and blanching of the incisor teeth of mice fed for life (Series 2)

Group	No. autopsied	Mean weight at death[1]	No. with white teeth	Edema	Tumors No.	Multiple	LL[2]	Lung	% of mice with tumors
Males									
Control-7	38	28	3	0	11	2	3	5	28.9
Aluminum	41	28	11	10	15	9	9	9	36.6
Barium	37	27	5	11	12	6	7	4	32.4
Beryllium	48	30	10	0	17	4	3	7	35.4
Mercury (Cl_2)	48	31	11	14	21	1	5	9	43.8
MeHg (5 ppm)	32	32	3	9	10	2	3	3	31.3
MeHg (1 ppm)	25	20	4	7	9	3	4	4	36.0
Females									
Control-7	47	26	19	3	14	4	3	9	29.8
Aluminum	41	33	5	4	19	12[3]	10[4]	11	46.3
Barium	21	26	7	7	5	4	5	3	23.8
Beryllium	52	25	14	3	20	6	9	5	38.5
Mercury (Cl_2)	41	28	10	4	21	9	11	7	51.2
MeHg (5 ppm)	40	21	2	1	4	0	1	3	10.0
MeHg (1 ppm)	31	30	7	7	12	2	1	3	38.7

[1] Individual weights at death varied approximately 35% in the various groups. [2] Lymphoma leukemia. [3] $P < 0.025$. [4] Significance of difference between means by chi-square; $P < 0.05$.

TABLE 7

Life-spans and longevities of mice fed lead, nickel, vanadium and titanium for life (Series 1)

Group	No. mice	Mean age	50% dead	75% dead	90% dead	Last	Longevity[1]
					days		
Males							
Control-6	54	556	568	654	730	817	763 ± 14.4
Lead	54	534	542	605	689	784	748 ± 11.4
Nickel	54	519	528	635	684	991	831 ± 49.6
Vanadium	54	578	569	634	741	966	880 ± 36.0[2]
Titanium	54	546	536	641	722	866	791 ± 30.8
Females							
Control-6	54	565	547	654	727	861	790 ± 19.7
Lead	54	585	632	701	774	872	804 ± 18.9
Nickel	54	597	577	679	820	904	864 ± 11.4[2]
Vanadium	55	620	615	704	826	1,000	878 ± 30.8[3]
Titanium	55	546	545	660	697	820	760 ± 17.5

[1] Mean age of last surviving 10% ± SEM. [2] Differs from controls by Student's *t* test; $P < 0.005$. [3] $P < 0.025$.

(table 4). Growth weights of the controls were not very different from those of other controls. Dead weights are shown in tables 5 and 6. There are no consistent differences in the controls.

Mortality and survival. The mean survival times and longevities of mice given lead, nickel, vanadium and titanium are given in table 7. Mice fed vanadium had a lower mortality and a higher longevity, as shown by the last surviving 10%, than did any of the other groups. The next longest survivors were in the group fed nickel. In table 8 are given the life-spans and longevities of mice fed aluminum, barium, beryllium, and mercury. The longest living mice were the survivors of those fed 5 ppm Hg as methyl mercury, which was reduced to 1 ppm when they were 90 days of age. The effects of boron and tungsten on the life-span of series 3 rats are given in table 9. In terms of recondite toxicity, mercuric chloride and methyl mercury appeared to have the greatest effect in males, but not in females, although differences in longevity were not statistically significant.

Tumors. The numbers of tumors are shown in tables 5 and 6. No element was significantly tumorigenic, although the fewest tumors occurred in the nickel groups. Leukemia lymphoma was found most frequently in the female aluminum, mercuric chloride, and titanium groups. The incidence of edema was low in the male control-7 and beryllium groups. Blanching of incisor teeth was not confined to any one group.

DISCUSSION

Our first report on mice exposed to trace metals concerned chromium-deficient mice

TABLE 8

Life-spans and longevities of mice fed various trace metals (Series 2)

Group	No. mice	Mean	50% dead	75% dead	90% dead	Last	Longevity[1]
					days		
Males							
Control-7	54	540	602	648	789	1,010	920 ± 28.2
Aluminum	54	568	568	668	819	1,086	936 ± 48.9
Barium	42	548	549	634	709	849	815 ± 28.4[2]
Beryllium	54	574	548	653	792	1,253	903 ± 39.4
Mercury (Mg Cl$_2$)	54	490	540	599	697	858	751 ± 28.7
Methyl mercury (5 ppm)	54		430	660	888	1,138	1,013 ± 47.9[3]
	(33)	(703)	(751)	(826)	(952)		
Methyl mercury (1 ppm)	30	580	616	634	764	801	772 ± 24.3
Females							
Control-7	54	533	539	622	691	1,001	823 ± 60.3
Aluminum	54	533	524	611	702	958	846 ± 44.0
Barium	36	566	580	670	778	852	796 ± 24.7
Beryllium	54	590	596	683	840	1,001	932 ± 28.3
Mercury (Mg Cl$_2$)	54	542	575	632	736	849	983 ± 21.2
Methyl mercury (5 ppm)	55		383	690	934	1,083	1,013 ± 28.3[3]
	(31)	(555)	(679)	(904)	(939)		
Methyl mercury (1 ppm)	44	589	550	709	787	965	854 ± 10.6

[1] Initial dose of 5 ppm Hg reduced at 90 days of age to 1 ppm. Numbers in parentheses are the number of survivors and their data. [1] ± SEM. Longevity is the mean of the last five survivors in each group. [2] Significance of difference between means of controls and treated groups by Student's *t* test; $P < 0.025$. [3] Differs from following group; $P < 0.001$.

fed titanium, nickel, cadmium, and lead for life and indicated that chromium increased growth and survival, and titanium increased growth (3). Males were affected more than females. Since that time (1963), chromium has been accepted as an essential trace metal for animals (6). Therefore, it seemed worthwhile to repeat the experiments on nickel, lead, titanium, and vanadium (reported later) (3, 4) in mice fed chromium to see whether toxic effects of metals were enhanced by chromium deficiency. If these two series with and without chromium, which were done 8 years apart, could be compared, they would show that chromium suppresses toxicity of lead and titanium.

Such a comparison was made. For 50% survival, male titanium controls fed chromium lived 58 days longer than chromium-deficient animals; animals fed lead and chromium lived 79 days longer than their chromium-deficient counterparts; animals fed vanadium lived 69 days longer; and animals fed nickel lived 52 days longer. These increases were quite consistent, although they were not statistically significant. In the females, the reverse held true. Without chromium, the median life-span was greater than with chromium in the controls and all the other metal groups but vanadium.

Since these experiments were begun, vanadium and nickel have been found to resemble essential metals (7, 8). Therefore, it is not surprising that vanadium showed biological effects on weight. We cannot account for the increase in weight associated with the feeding of titanium at 11 intervals (only 3 were significant, however), which was observed previously (2). Evidence of this nature is not sufficient to characterize a trace metal as essential. It is clear that lead in this dosage is not toxic to chromium-fed mice.

Beryllium is a highly toxic metal when inhaled as a dust (9). It also can be toxic by mouth, but in the dosage used in these experiments it was not. Only slight effects on body weight of females were disclosed by this study, and there were no striking effects on life-span and survival. All studies indicate that beryllium is poorly absorbed through the gut, and that ingestion is not a hazard.

TABLE 9

Effects of boron and tungsten on the life-spans of mice fed plain water for life (Series 3)

Group	No. mice	Mean	50% dead	75% dead	90% dead	Last dead	Longevity[1]
					days		
Males							
Control-8	54	480	422	609	705	1,012	939 ± 44.25
Boron	54	560	548	661	827	941	879 ± 20.6
Tungsten	54	570	594	656	726	810	797 ± 7.5[2]
Females							
Control-8	54	650	678	778	853	1,100	922 ± 28.44
Boron	54	660	658	775	896	994	963 ± 37.92
Tungsten	54	654	656	717	767	996	945 ± 22.99

[1] Mean age of last surviving 10% ± SEM. [2] Differs from control female group; $P < 0.001$.

Aluminum is also poorly absorbed (10) and has little toxicity when taken by mouth, but combines with phosphate in the intestine, and in large doses aluminum can produce phosphate deficiency. Aluminum may be involved in the succinic dehydrogenase–cytochrome *c* system in vitro (10). It performs no essential function in mammals as far as is known.

In males longevity was slightly reduced by barium, but weight was not significantly affected. Inhaled barium dusts are only slightly toxic, but soluble barium salts by mouth are highly toxic in large doses (11).

Boron is essential for higher plants, but it apparently has no part in the metabolism of animals. It is toxic given parenterally.

Mercury and methyl mercury behave differently as to relative toxicities. Mercuric ion has a low order of toxicity when given by the oral route, especially in mice and rats. It is a little more toxic than aluminum at 5 ppm in drinking water; longevity tended to decrease in males and increase in females. Mercury, 5 ppm as methyl mercury, however, was highly toxic, although 1 ppm was well tolerated. A curious phenomenon was the enhancement of growth by 1 ppm methyl mercury in both sexes, which occurred at every age. Another unexpected effect was the long lives of the surviving mice given 5 ppm methyl mercury at first, and then 1 ppm. This difference suggested that the weaker animals were eliminated and the strong ones were somehow given an extra life-span. The mice given 5 ppm Hg as methyl mercury for 70 days, and then 1 ppm, lived longer, gained weight faster, and survived significantly longer ($P < 0.001$) than did their littermates given 1 ppm methyl mercury from the time of weaning. These phenomena deserve further study.

The low number of tumors in the mice given methyl mercury is noteworthy.

In a study made by Darrow, Nason, and Schroeder in our laboratory,[5] mice were fed methyl mercury 1 ppm Hg, and mercuric chloride 5 ppm Hg for 286 to 653 days. In the five organs of the controls, mercury varied from 0.013 to 0.034 ppm. In the mercuric chloride-fed mice, the same organs varied from 0.16 to 0.93 ppm, the kidney having the largest amount. In the methyl mercury-fed mice, the organs had 3.8 to 6.2 ppm mercury, showing that methyl mercury is much more firmly bound to mammalian tissues than is inorganic mercury.

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LITERATURE CITED

1. Schroeder, H. A. (1973) Recondite toxicity of trace elements. In: Essays in Toxicology, vol. 4, chap. 3, Academic Press, New York.
2. Schroeder, H. A., Vinton, W. H., Jr. & Balassa, J. J. (1963) Effect of chromium, cadmium and other trace metals on the growth and survival of mice. J. Nutr. *80,* 39–47.
3. Schroeder, H. A., Balassa, J. J. & Vinton, W. H., Jr. (1964) Chromium, lead, cadmium, nickel and titanium in mice: effect on mortality, tumors and tissue levels. J. Nutr. *83,* 239–250.
4. Schroeder, H. A. & Balassa, J. J. (1967) Arsenic, germanium, tin and vanadium in mice: effects on growh, survival and tissue levels. J. Nutr. *92,* 245–252.
5. Schroeder, H. A., Mitchener, M. & Nason, A. P. (1971) Influence of various sugars, chromium and other trace metals on serum cholesterol and glucose of rats. J. Nutr. *101,* 247–257.
6. Mertz, W. (1959) Chromium occurrence and function in biological systems. Physiol. Rev. *49,* 163.
7. Nielsen, F. H. (1973) Essentiality and function of nickel. In: Trace Element Metabolism in Animals, Proc. Second Conference, 18–22 June, Madison, Wis., pp. 381–395.
8. Schwarz, K. & Milne, D. B. (1971) Growth effects of vanadium in the rat. Science, *174,* 426.
9. Hamilton, A. & Hardy, H. L. (1974) Industrial Toxicology, ed. 3, p. 49, Publishing Sciences Group, Inc., Acton, Mass.
10. Underwood, E. J. (1971) Trace Elements in Human and Animal Nutrition, ed. 3, p. 426, Academic Press, New York.
11. Browning, E. (1969) Toxicity of Industrial Metals, ed. 2, p. 64, Butterworth & Co. Ltd., New York.

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[5] Darrow, D. K., Nason, A. P. & Schroeder, H. A. (1973) Mercury accumulation in mice fed alkyl, inorganic or natural mercury from tuna and mako shark. Presented at the third scientific session of the Champlain Section of the Society for Experimental Biology and Medicine, Burlington, Vt.