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Inhalation Uptake of Low Level Elemental Mercury Vapor and Its Tissue Distribution in Rats

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Although elemental mercury vapor presents less concern than alkyl mercurials found in food, it is the major component of mercury found in the atmosphere. Furthermore, if usage of coal is increased to meet the energy demand, then atmospheric levels of mercury are expected to rise. Current atmospheric concentrations of mercury vapor over select urban areas of the United States range from 0.5-50 ng m^{-3} with a mean of 7 ng m^{-3}. Higher levels may be found near chlor-alkali plants, thermometer factories, and coal-powered plants and heavy industries.

Studies of the inhalation uptake of elemental mercury vapor by the mouse (BERLIN and JOHANSSON 1966, BERLIN 1966, MAGOS 1967), guinea pig (NORDBERG and SERENIUS 1969), rat (ASHE et al. 1969), rabbit (BERLIN et al. 1969), monkey (BERLIN et al. 1969) and man (HURSH et al. 1976, TEISINGER and FISEROVA-BERGEROVA 1965) have been reported. Mercury concentration in brain tissue following inhalation of elemental mercury is significantly higher than those from intravenous injection or oral administration of either organic or ionic mercurials (BERLIN 1966, MAGOS 1967, NORDBERG and SERENIUS 1969). Although elemental mercury is rapidly oxidized in the blood to the less diffusable mercuric ion, the transient occurrence of elemental mercury in the blood stream and the increased levels detected in the central nervous system are likely a result of its rapid diffusion into target tissues (MAGOS 1967, TEISINGER and FISEROVA-BERGEROVA 1965).

Mercury vapor concentrations used in all the research cited above were several orders of magnitude greater than those commonly detected in the environment. This study reports the inhalation uptake and consequent tissue distribution of radioactive elemental mercury vapor in rats over a concentration range of 15-916 ng m^{-3}, with particular emphasis on measurement below 50 ng m^{-3}, in an effort to determine if the tissue distribution of mercury after a low level exposure is similar to those reported using higher concentrations.

MATERIALS AND METHODS

The generating system of radioactive elemental mercury vapor and the regulation of mercury vapor were described previously

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(BROWNE and FANG 1978, FANG 1978). Briefly, a flow of mercury-free air from an aquarium pump, at a flow-rate of 600 mL min^{-1}, was split so that a stream of air at 100 mL min^{-1} was passed over a thermo-regulated mercury generator which contained approximately 96 mg mercury-203 (metal, with an initial specific activity of 0.0517 mCi/mg). This air containing mercury-203 vapor flowed to a mixing flask equipped with a magnetic stirrer and reunited with the other air stream of 500 mL min^{-1} in order to give an initial step of control of mercury vapor concentration. If a slightly higher or lower mercury vapor concentration was needed, a slight change in the air flow ratio between the air entering the generator and the air used for mixing would generally achieve the goal. From this mixing flask, the mercury vapor concentration in the air can be determined by passing the air (100 mL min^{-1}) through a Hopcalite trap for a given time, measuring the radioactivity of the trap, and comparing to a ^{203}Hg standard of the same specific activity. The remainder of air passed through an all glass metabolic chamber, at a flow rate of 500 mL min^{-1}, in which two adult rats were exposed continuously for one to three days. Generally the air entered the chamber from an inlet at the apex and left the chamber from an air outlet near the bottom to avoid stratification. The mercury vapor which was not taken up by the rats after passing through the chamber was collected on a series of Hopcalite traps, which were measured at the end of each exposure experiment. The concentration of mercury vapor for the exposure study can be further regulated by adjusting the temperature of the water bath. Prior to exposing any rats, the system was found to equilibrate within a 2 h period, i.e. the concentration at the inlet was essentially equal to that at the outlet (±10%). Concentrations from 15-200 ng Hg m^{-3} were attainable by varying the water bath temperature from 25 to 45°C, higher concentrations were produced by vibrating the generator assembly a bit more forcefully than the normal vibration conducted through the tubing from the aquarium pump.

Fourteen pairs of female Wistar rats, mean age three months and mass 209±9 g, were exposed to air laden with 15-916 ng m^{-3} for up to three days to determine the tissue distribution of ^{203}Hg as a function of time and concentration. Each rat was sacrificied within an hour of termination. Selected tissues were collected and assayed for ^{203}Hg using a Packard Auto-gamma Spectrometer. Each sample was counted for one hour which yielded a relative standard error of less than 10% for all data reported with the exception of a few of the blood, brain and liver samples from the lowest concentration and the shortest exposure. Although the miniscule amounts of mercury distributed in these tissues under some conditions which resulted in higher error, the trends remained clearly discernable.

RESULTS AND DISCUSSION

Table 1 shows the results of tissue mercury levels from the time course experiment of rats exposed to air containing 21±5 or

41±4 ng m^{-3}. Mercury concentration expressed as ng Hg per gram fresh tissue with the exception of blood is increased with the increase of the exposure time. The proportionality constant is relatively large for the kidney, comparatively small for the other tissues. Practically no increase is observed in the blood. Because the lung is the site of initial uptake, the mercury level is comparatively higher than other internal organs with the exception of kidney. However, its rate of accumulation is similar to that of other tissues. The linear regressions fit most of the data with the exception of the lung at 41 ng m^{-3}.

TABLE 1. Inhalation Uptake of Elemental ^{203}Hg Vapor by Adult Rats in Relation to the Tissue of Exposure

Tissue	^{203}Hg Conc ngm^{-3}	^{203}Hg Concentration, ng/g fresh tissue 1	2	3	Linear Regression y=a+bx	correlation coefficient r^2
Kidney	21	0.18±.04[a]	0.40,0.38[b]	0.88±0.18	=-0.21+0.35x	0.96
	41	0.36,0.38	0.94,0.94	1.8,1.8	=-0.39+0.72x	0.99
Lung	21	0.24±.06	0.24,0.28	0.30±0.10	= 0.21+0.03x	0.96
	41	0.46,0.53	0.62,0.70	0.58,0.53	= 0.51+0.03x	0.13
Heart	21	0.04±.02	0.07,0.07	0.10±0.03	= 0.01+0.03x	1.00
	41	0.05,0.09	0.14,0.14	0.23,0.16	= 0.01+0.06x	1.00
Liver	21	0.02±0.01	0.03,0.03	0.03±0.02	= 0.02+0.01x	0.75
	41	0.04,0.02	0.04,0.06	0.09,0.07	=0.003+0.03x	0.99
Brain	21	0.02±0.004	0.01,0.02	0.04±0.01	= 0.01+0.01x	0.57
	41	0.04,0.03	0.06,0.06	0.07,0.09	= 0.01+0.02x	1.00
Blood	21	0.01±0.004	0.01,0.01	0.01±.001	= 0.01	
	41	0.03,0.01	0.03,0.02	0.02,0.02	= 0.02	

[a] Mean ± standard deviation (4 rats)

[b] Individual value (2 rats)

Table 2 shows the tissue mercury burden of fourteen pairs of rats exposed to air containing elemental mercury vapor ranging from 15 to 916 ng m^{-3} for 1 to 3 days. The results were calculated on a ng Hg per gram fresh tissue per day basis to illustrate the effect of increasing concentration of mercury vapor on tissue uptake. Excellent fit with an increasing linear function is found for each tissue. Correlation coefficients as calculated are greater than 0.9 with the exception of lung, which was 0.72. Among six tissues the kidney has the highest mercury concentration, which was approximately three times than that in the lung, nine times than that in the heart, 20 times

TABLE 2. Inhalation Uptake of Elemental Mercury-203 Vapor by Adult Rats in Relation to Vapor Concentration

Initial ^{203}Hg Vapor Concen. ngm^{-3}	Exposure time (day)	^{203}Hg Concentration, ng Hg/g fresh tissue/day					
		kidney	lung	heart	liver	brain	blood
15	3	0.20	0.06	0.02	0.01	0.01	0.003
18	3	0.26	0.09	0.03	0.01	0.01	0.003
20	2	0.20	0.13	0.03	0.02	0.01	0.005
27	1	0.23	0.32	0.06	0.03	0.03	0.01
37	3	0.53	0.17	0.06	0.02	0.02	0.01
41	2	0.47	0.34	0.07	0.03	0.03	0.02
45	1	0.41	0.54	0.08	0.03	0.04	0.02
149	2	2.21	1.41	0.29	0.11	0.13	0.05
157	2	2.31	1.31	0.30	0.11	0.13	0.05
187	3	2.91	0.82	0.27	0.15	0.12	0.05
371	3	6.51	1.50	0.40	0.19	0.24	0.05
468	3	5.81	3.00	0.81	0.44	0.34	0.10
916	3	20.0	2.40	1.00	0.59	0.63	0.18
Linear regression,	y=a+bx	a=-0.627 b= 0.021	a=0.355 b=0.003	a=0.045 b=0.0012	a=0.0065 b=0.0007	a=0.0044 b=0.0007	a=0.0072 b=0.0002
Correlation Coefficient, r^2		0.96	0.72	0.93	0.95	1.00	0.95

TABLE 3. Comparison of Ratio of Tissue Mercury Burdens from Inhalation Uptake between High and Low Vapor Concentration

References	Vapor Concentration	Exposure time hr.	Sacrificed after exposure day	Lung / Kidney	Heart / Kidney	Liver / Kidney	Brain / Kidney	Blood / Kidney
This study	15-916 ngm^{-3}	24	0(6)[a]	1.35±0.15	0.23±0.07	0.097±0.033	0.095±0.017	0.046±0.018
		48	0(8)	0.64±0.08	0.15±0.02	0.058±0.012	0.054±0.013	0.024±0.004
		72	0(14)	0.31±0.12	0.10±0.03	0.047±0.016	0.042±0.010	0.013±0.004
BERLIN et al. (1969)	1.0mgm^{-3}	4	0(2)	0.62	0.13	0.066	0.067	0.055
			1(2)	0.13	0.06	0.033	0.029	0.011
			4(2)	0.05	0.01	0.015	0.032	0.002
			8(2)	0.03	0.01	0.015	0.027	0.001
			16(2)	0.03	0.01	0.013	0.077	0.002
HAYES & ROTHSTEIN (1962)	1.4mgm^{-3}	5	0(3)	1.46		0.080		0.052
ASHE et al (1953)	0.1mgm^{-3}	5-72 wk	0(23)			0.048±0.044		

[a] Denotes the number of rats.

than that in the liver or brain and 60 times than that in the blood. Despite the disparities in experimental conditions, the relative ratios of tissue mercury burden obtained from exposure to low mercury levels are reasonably in good agreement with the literature reports which were conducted at much higher concentrations (Table 3). Therefore, the distribution pattern is relatively unaffected by the air concentration. The time of exposure, however, appears to affect this ratio more significantly. The ratio appears to decrease curvilinearly with the increasing time of exposure. This is probably due to a difference in their biological half-life and the time required to reach their maximal concentration. The same conclusion can be reached from the result of BERLIN et al. (1969) that the tissue/kidney ratio decreased to a minimum as the time after exposure increased. This result further suggests that the transient appearance of elemental mercury in the circulation system and its rate of transport to the central nervous system are independent to the concentration of mercury vapor in the air or in the blood.

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