Environmental Health Perspectives
Vol. 12, pp. 35–39, 1975

Whole Body Retention in Rats of Different ^{191}Pt Compounds Following Inhalation Exposure

by W. Moore, Jr.,* M. Malanchuk,* W. Crocker,* D. Hysell,* A. Cohen,* and J. F. Stara*

The whole body retention, excretion, lung clearance, distribution, and concentration of ^{191}Pt in other tissues was determined in rats following a single inhalation exposure to different chemical forms of ^{191}Pt. The chemical forms of ^{191}Pt used in study were $^{191}PtCl_4$, $^{191}Pt(SO_4)_2$, ^{191}PtO, and ^{191}Pt metal. Immediately after exposure most of the ^{191}Pt was found in the gastrointestinal and respiratory tract. Movement of the ^{191}Pt through the gastrointestinal tract was rapid, most of the ^{191}Pt being eliminated within 24 hr after exposure. Lung clearance was much slower, with a clearance half-time of about 8 days. In addition to the lungs, kidney and bone contained the highest concentrations of ^{191}Pt.

Introduction

Automotive manufacturers have incorporated into the exhaust train a noble metal oxidation catalyst which reduces the concentrations of carbon monoxide (CO) and total hydrocarbons (THC) in the exhaust. The substrate material used in the catalyst is coated with a small amount of platinum (Pt) and palladium (Pd) (approximately 1 g Pt and 0.5 g Pd). It is not unreasonable to assume that some of the catalytic material will be emitted into the atmosphere, and recent studies at this laboratory have identified the presence of noble metals in the exhaust. The chemical form of the Pt and Pd emitted in the exhaust has not been determined. We have given first consideration to the study of Pt compounds because of the larger quantity of this metal used in the catalyst (*1*).

The toxicity of Pt is variable, depending on its chemical form. Investigators have described the toxicity of the soluble Pt salts following industrial exposure and use the term platinosis in referring to the respiratory and/or cutaneous reactions (*2–4*). The threshold limit value for industrial exposure to the soluble Pt salts is 2 $\mu g/m^3$ as Pt (*5*). With the emission of Pt in automobile exhaust, the lungs could serve as the major portal of entry for human exposure. Because of the paucity of available information, this study was undertaken to provide data on whole body retention, tissue distribution and excretion of different chemical forms of Pt following inhalation exposure. Major emphasis was placed on the fate of PtO and Pt metal because it was believed that these chemical forms might be formed preferentially in the high temperature of the exhaust.

*U.S. Environmental Protection Agency, National Environmental Research Center, Environmental Toxicology Research Laboratory, Cincinnati, Ohio 45268.

Methods

Animals

Eighty-seven outbred albino rats (Charles River CD1 strain) weighting 100–120 g were used for exposure to each ^{191}Pt compound. The animals were maintained on a commercial diet (Purina Lab Chow) and tap water *ad libitum*.

Aerosol Exposure

The animal exposure chamber was constructed according to the design of Raabe et al. (*6*). The

design allows for the simultaneous exposure of the nose only; each of the 87 rats breathes its own portion of the same aerosol during the exposure period.

A Retec X 70/N nebulizer was operated at 15 psig pressure to produce the aerosol of aqueous droplets. The 2 l./min (STP) of air flowing into the nebulizer was diluted by 7 l./min of dry air at the entrance into the drying tube. Thermo-Systems, Inc. Model 301Z Aerosol Neutralizer served the dual function of neutralizing the particle electrostatic charge as well as providing the capacity for removing the water from the aqueous droplets by the addition of heat. A heating tape of 300-W capacity controlled by a rheostat was wrapped around the Neutralizer, and the temperature within the Neutralizer was elevated 20–25°C as an aid in drying the particulate. The aerosol was further diluted at the entrance to the trapezoidal plenum so that the total air flow through the exposure chamber was 80 l./min. Samples were taken during each exposure for analysis.

$^{191}PtCl_4$ Particulate: The nebulizing solution for the $^{191}PtCl_4$ particulate consisted of 5.8 ml of $^{191, 193m}Pt^{+4}$ in 1*M* HCl assaying 7 mCi in the form of ^{191} Pt and 4.2 ml of stable $PtCl_4$ in aqueous solution, giving a final concentration of 2.2 mg/ml. Based on this concentration and a mean droplet diameter of 6–8 μm generated by the nebulizer, the aerodynamic size diameter was calculated to be nearly 1.0 μm. The measured particulate load was 5.0 mg/m^3 over the 48-min exposure period.

$^{191}Pt(SO_4)_2$ Particulate: The nebulizing solution contained 5 ml of $^{191, 193m}Pt(SO_4)_2$ in 0.5*M* H_2SO_4 assaying 10 mCi in the form of ^{191}Pt and 5 ml of $Pt(SO_4)_2$ dissolved in deionized water. There was no evidence of precipitation of the solids in the combined solution which contained 1.5 mg/ml. A particulate load of 5–7 mg/m^3 was generated with an aerodynamic size diameter of nearly 1.0 μm.

PtO_2 Particulate: For the PtO_2 exposure, a 5.0 ml supply of $^{191, 193}Pt(SO_4)_2$ containing 8 mCi of ^{191}Pt in 0.3*M* H_2SO_4 was mixed with 5 ml of stable $Pt(SO_4)_2$ in a slightly acidified aqueous solution to provide a final 10 ml volume of approximately 1.5 mg/ml. Following passage of the aerosol through the drying tube, the dry particles of the solute were then passed through a Lindberg furnace tube (600°C) to decompose the $Pt(SO_4)_2$ into PtO_2 and SO_2. The SO_2 and the H_2SO_4 vapor formed by volatilization of the original acidified solution were largely removed by reaction with the $CaCO_3$ in an absorption tube, so that only the PtO_2 remained in the aerosol stream entering the exposure chamber. The final concentration of PtO_2 was 7–8 mg/m^3.

Pt Metal Particulate: For the Pt metal exposure, a 10.0 ml supply of $^{191,193m}PtCl_4$, assaying 6.85 mCi for ^{191}Pt in 0.5*M* HCl was used. To it was added 21.9 mg of stable $PtCl_4$ to provide a final concentration of 2.2 mg/ml. The $PtCl_4$ aerosol was decomposed in the furnace to Pt metal particles and chlorine gas. The chlorine and the HCl vapor volatilized from the original acidified solution were absorbed by activated char surrounding the tubular space in the absorption tube section. Air flows were similar to those used in the other exposures and calculated to give a final concentration of 7–8 mg Pt metal/m^3 in the exposure chamber atmosphere.

Radioactive Counting

Following exposure, the rats were washed to minimize radioactive contamination of the skin and hair. Whole body counts were then made on all animals used in the retention studies. The animals were counted daily for the first few days and then every other day for the duration of the experiment. The rats were housed in metabolism cages, and 24-hr urine and feces samples were collected for counting. A 200-channel gamma spectrometer with a 5-in. NaI (TC) crystal was used for whole body counts. Some of the animals were sacrificed and dissected so that the lung, gastrointestinal tract (contents not removed), kidney, bone, and liver burdens of ^{191}Pt could be determined by tissue counting. Tissue, urine, and feces samples were counted in a refrigerated well-type scintillation spectrometer.

The radioactive platinum solution consisted of a mixture of ^{191,193}Pt, at least 50% being ^{191}Pt. Only the ^{191}Pt was counted, and all values were corrected for decay (^{191} Pt has a half-life of 3 days).

Results

There was considerable individual variation in the amount of radioactivity present in some of the animals immediately after exposure. Although differences in the total volume of air breathed by individual animals may have been partly responsible, the major reason for the variation was attributed to the rat removing its nose from the exposure port and trying to turn in the cylinder.

Whole body retention curves for ^{191}Pt as a function of the type of compound and time following inhalation exposure are presented graphically in Figures 1 and 2. The retention curves showed an initial rapid clearance of ^{191}Pt from the body

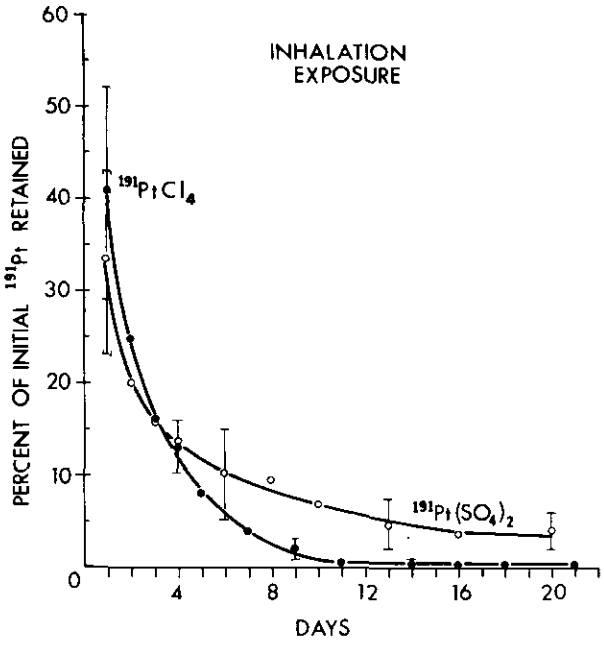

FIGURE 1. Whole body retention in adult rats of ^{191}Pt following inhalation exposure to $^{191}Pt\ Cl_4$ and $^{191}Pt(SO_4)_2$.

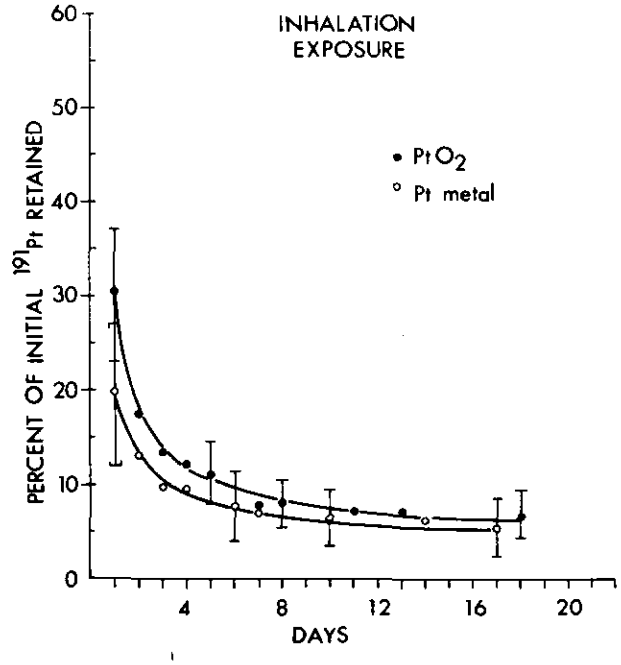

FIGURE 2. Whole body retention in adult rats of ^{191}Pt following inhalation exposure to $^{191}PtO_2$ and ^{191}Pt metal.

followed by a slower clearance phase during the remainder of the post-exposure period. No significant difference in whole body retention of ^{191}Pt was apparent following inhalation exposure to the different chemical forms; however, clearance of $^{191}PtCl_4$ seemed to be more rapid.

Excretion

Radioactive counts of 24-hr urine and feces samples from rats following inhalation exposure to the different ^{191}Pt compounds indicated that most of the ^{191}Pt was eliminated in the feces, and only a small amount was excreted in the urine (Figs. 3 and 4). These values support the whole body data that showed that only a small amount of ^{191}Pt was retained by the animals. Most of the ^{191}Pt was rapidly cleared from the lungs (probably by mucociliary action), swallowed, and excreted via the feces. The presence of ^{191}Pt in the urine indicated the absorption of a small fraction of the ^{191}Pt, although it was impossible to determine the relative contributions of lung and of gastrointestinal absorption to the total body burden.

Tissue Clearance

Eight animals were sacrificed at each time interval so that lung and other organ burdens of ^{191}Pt

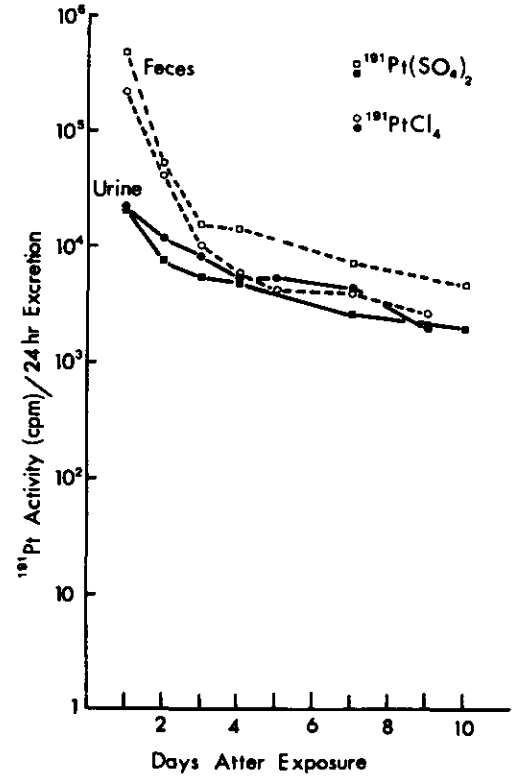

FIGURE 3. Excretion of ^{191}Pt following inhalation exposure to $PtCl_4$ and $^{191}Pt(SO_4)_2$.

could be determined by tissue counting. The clearance curves for different organs following exposure to ^{191}Pt metal and ^{191}PtO are presented in

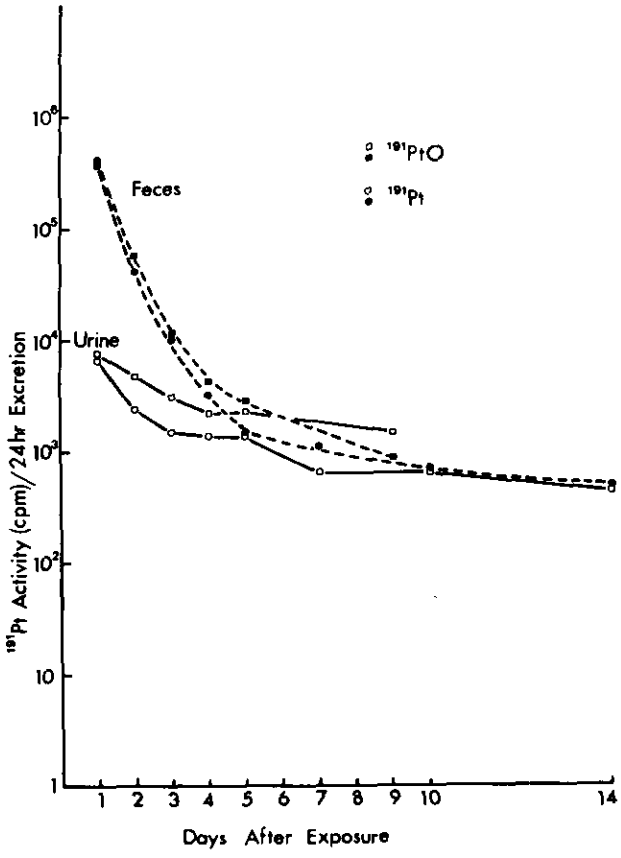

FIGURE 4. Excretion of ^{191}Pt following inhalation exposure to ^{191}PtO and ^{191}Pt metal.

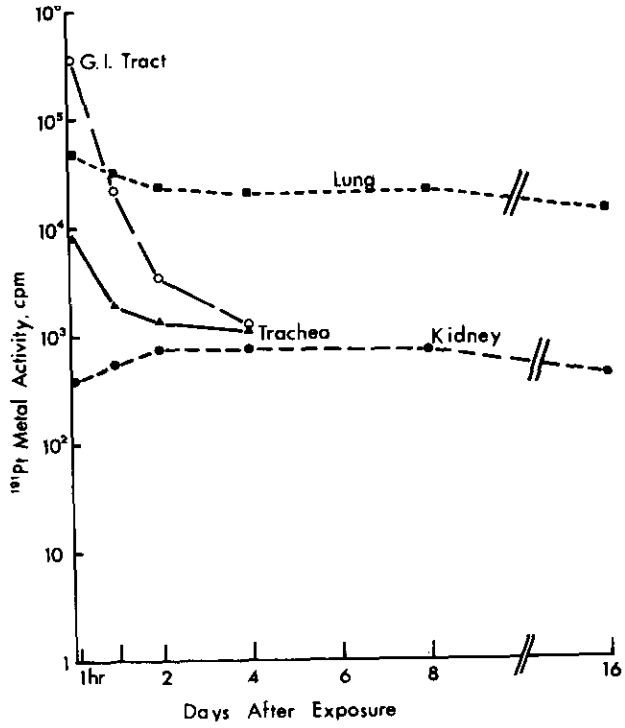

FIGURE 5. Clearance of ^{191}Pt from different organs following inhalation exposure to ^{191}Pt metal.

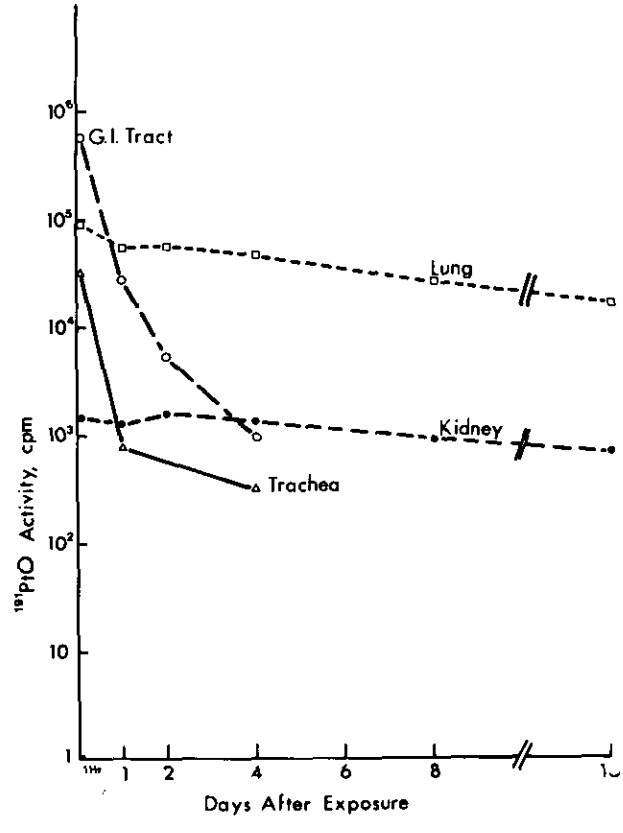

FIGURE 6. Clearance of ^{191}Pt from different organs following inhalation exposure to ^{191}PtO.

Figures 5 and 6. Immediately after exposure most of the radioactivity was found in the gastrointestinal and respiratory tract. Movement of the ^{191}Pt through the gastrointestinal tract was rapid, most of the ^{191}Pt being eliminated within 24 hr after exposure. Removal of the deposited ^{191}Pt from the lungs was much slower.

The initial lung burdens for ^{191}Pt metal had a coefficient of variation of about 34% and a range of about a factor of 2.6. The initial lung burdens for ^{191}Pt metal represented about 14% of the initial body burdens. For the ^{191}PtO exposure, the initial lung burdens had a coefficient of variation of 30% and a range of about 3. The initial lung burdens for ^{191}PtO were about 16% of the initial body burdens. This spread was consistent with the reported variability in rodent inhalation exposures (6, 7). The percentage of the initial lung burden retained for the duration of the study is given in Table 1. The data indicate that $Pt(SO_4)_2$ may be more rapidly mobilized from the lung.

The clearance of ^{191}Pt from the lungs may be divided into an initial rapid decrease of activity

Table 1. Percentage of initial lung burden retained with time in the lungs.

Time, days	Portion of Pt burden retained, %		
	Pt metal	PtO	$Pt(SO_4)_2$
1	63.0	57.2	73.7
2	49.5	60.9	43.4
4	41.3	49.0	20.4
8	42.9	28.6	—
16	28.0	17.9	4.4

over the first 24 hr followed by a slower clearance phase during the rest of the post-exposure period. For the slow phase, the clearance half-time was about 8 days.

The distribution and concentration of ^{191}Pt in other tissues following exposure to ^{191}Pt metal are given in Table 2. In addition to the lung and trachea, the kidney and bone contained the highest amount of ^{191}Pt. The relative large amount of ^{191}Pt found in the kidney and bone suggests that these

Table 2. Radioactive ^{191}Pt in selected tissues following inhalation exposure to Pt metal.

Tissues	Mean counts per gram			
	1 day after exposure	2 days after exposure	4 days after exposure	8 days after exposure
Blood	61	43	30	12
Trachea	1909	2510	738	343
Lung	45,462	28,784	28,280	23,543
Liver	52	46	37	17
Kidney	750	1002	906	823
Bone	281	258	231	156
Brain	5	3	1	0
Muscle	22	10	28	0
Spleen	39	73	23	5
Heart	37	58	23	5

organs accumulate this element. The low radioactive count for the brain suggested the possibility that the circulating ^{191}Pt may be complexed to large molecules that do not cross the blood brain barrier.

Discussion

Clinical platinosis has been found in individuals working with the complex platinum salts (sodium, potassium, or ammonium tetrachlorplatinate or hexachloroplatinate) encountered in refining and analysis of the metal. The majority of individuals working in atmospheres containing these salts develop respiratory symptoms or skin lesions or both only after occupational exposure periods of months or years. Only one case of dermatitis has been reported from metallic platinum (*8*). Evidence indicates that the clinical syndrome of platinosis in man is the result of hypersensitivity to platinum salts. The platinum salts apparently act as a hapten and combine with an endogenous protein to form an allergenic hapten–protein complex (*9*).

The results from this study indicate that all the chemical forms tested [$PtCl_4$, $Pt(SO_4)_2$, PtO, Pt] were absorbed from the lungs and entered various body pools. Also a comparison of absorption following inhalation and oral exposure indicate that the respiratory route is a more effective portal of entry for Pt (*10*). It is reasonable to assume that these forms of Pt are also absorbed following inhalation exposure in humans. The question remains why metallic and other simple salts of Pt have not been reported as being effective agents in producing platinosis. Platinosis is a rare disease outside platinum refineries; however, if platinum increases as an atmospheric pollutant, one might anticipate concomitant increase in allergic reactions.

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