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Determination of Human Body Burden Baseline Data of Platinum through Autopsy Tissue Analysis

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Results of analysis for platinum in 97 autopsy sets are presented. Analysis was performed by a specially developed emission spectrochemical method. Almost half of the individuals studied were found to have detectable platinum in one or more tissue samples. Platinum was found to be deposited in 13 of 21 tissue types investigated. Surprisingly high values were observed in subcutaneous fat, previously not considered to be a target site for platinum deposition. These data will serve as a human tissue platinum burden baseline in EPA's Catalyst Research Program.

Introduction

This report presents baseline data on various human tissue burdens of platinum. The work was done as part of the Environmental Protection Agency's catalyst research program, which includes some 18 tasks on health effects of the noble metals platinum and palladium. The impetus for the program was Title II provisions of the Clean Air Act of 1970, as amended, which requires reduction of CO, HC, and NO_x emissions from light-duty motor vehicles. The automobile industry's response was the introduction of noble metal catalysts to reduce the regulated emissions. In California all American-made 1975 model automobiles would be equipped with noble metal catalytic converters; in the other 49 states, some 70% would be so equipped. The number of catalyst-equipped vehicles was estimated to increase rapidly over the next ten years, replacing the pre-1975 noncatalyst vehicle population at a rate of about 10%/yr (*1*). Since the employment of the noble metal catalytic converter represented introduction of a new environmental contaminant, it was imperative that a rather broad

Table 1. Areas of study of noble metal health effects in EPA catalyst research program.

Emission characterization (Exhaust)
Measurement methodology development
Exhaust
Ambient air, water, soil
Animal and human tissue, feces, urine
Standard reference material development
Bioenvironmental impact
Methylation chemistry
Population exposure studies
Toxicology
Carcinogenicity
Mutagenicity
Cytogenicity
Inhalation toxicology
Sensitization (allergic response)
Irritation
Immunology
Body burden tissue analysis
Health effects assessment

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integrated information base be developed very quickly. A listing of areas of study undertaken by EPA is presented in Table 1.

Objective

Determination of human tissue burdens of platinum prior to widespread use of the catalytic converter emerged as a key task among the program's areas of study. Future evaluations of noble metal health effects would depend in part upon the ability of researchers to compare baseline (precatalyst) burdens with later human burdens.

Approach

During the winter of 1974-75, autopsy specimens were gathered through the Environmental Protection Agency's Community Health Environmental Surveillance System (CHESS) (2). Up to 21 tissue samples were taken from each of 97 autopsied individuals, of whom 95 had resided in southern California (Los Angeles area).

Tissue sample types analyzed (total 21) were prostate or uterus, thyroid, kidney, brain, gonad, adrenals, pancreas, heart (left ventricle), lung, liver, aorta (descending), muscle (psoas), subcutaneous fat, vertebrae (lumbar), fifth rib, femur, scalp hair, axillary hair, pubic hair, clavicle, and spleen.

Samples were frozen and shipped as soon as possible to Stewart Laboratories for analysis. The method for analysis had been developed by Stewart Laboratories and utilized an emission spectrochemical method for the determination of trace quantities of platinum, lead, and manganese in biological tissue. The analytical technique employed in the study—an emission spectrochemical method utilizing total energy burns in an argon-oxygen atmosphere—has been described previously (3). Although the method does not possess sufficient sensitivity to afford a total evaluation of residual baseline platinum concentrations in autopsy tissues, a detection limit of 10 parts per billion (ppb) can be obtained for a 1-g wet tissue sample. The analytical technique represents a method whose applicability is not dependent on the effectiveness of the sample preparation procedure to prepare a solution which is totally applicable to the potential complexities of platinum compounds which may be present. Total platinum in the sample is analyzed regardless of its chemical state since the method is limited only by its inherent sensitivity. As in all autopsy sample studies, sample size varied greatly.

In addition to the tissue analyses, the following data were available through the CHESS study for 92 of the 97 autopsy sets studied: age, race, sex, occupation, and cause of death. Clinical summaries, where available, were studied; there were no indications that platinum tumor suppressant therapy might have been a source of platinum exposure. Similarly, occupational information available did not indicate opportunity for occupational exposure to platinum.

Results

Of a total of 1313 samples obtained from the 97 individuals and analyzed for platinum, 62 contained detectable platinum concentrations. Of the 97 autopsied individuals, 45 had detectable concentrations of platinum in one or more tissue samples. Thus, though platinum was detected in only 5%of the samples analyzed, 46% of the individuals had detectable platinum in at least one type of tissue (see Table 2). The range of platinum concentrations detected was 0.003 to 1.46 μg/g (wet tissue); the mean value of detected platinum was 0.16 μg/g, and the median value of detected platinum was 0.067 μg/g.

Table 2. Individuals with detectable platinum concentrations.

	Number	%
Individuals in study	97	100
Individuals with Pt in one or more detected tissue	45	46
Individuals with Pt in one tissue	(27)	(28)
Individuals with Pt in two tissues	(18)	(18)
Individuals without detected Pt	52	54

The individual's age, sex, occupation, or major disease process cited as cause of death did not appear to be significant to platinum tissue burden. Age and sex characteristics of those individuals in whom platinum was detected in the tissues are presented in Table 3.

Table 3. Age and sex characterization of individuals showing detectable platinum concentrations.

	Average age, yr	Male		Female		Unknown	
		No.	%	No.	%	No.	%
Total individuals in study	61.5	39	40	52	54	6	6
Individuals with detected Pt	60.5	17	38	26	58	2	4
Individuals with Pt detected in two tissue samples	57.3	7	38	11	62	0	0

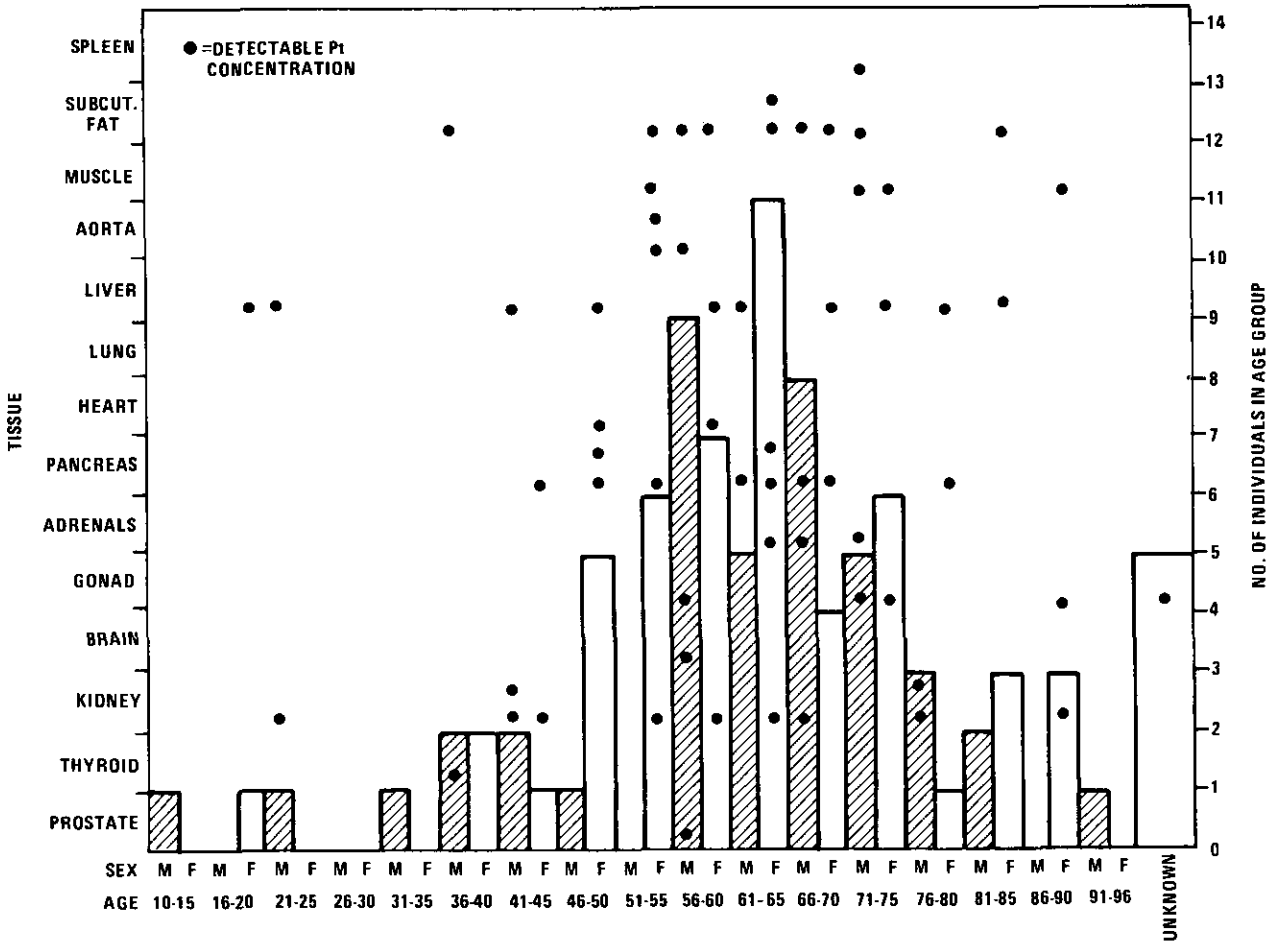

FIGURE 1. Distribution of Pt detected in tissue by age group (15-90) and sex. The points (•) denote detectible Pt concentration.

The apparent "target" sites for platinum deposition in the individuals studied, i.e. tissues in which the highest concentrations of platinum were found were, in descending order: subcutaneous fat, kidney, pancreas, and liver (Table 4).

Tissue deposition of detected platinum concentrations were plotted according to age and sex. Distribution profile followed the age and sex profile of the group fairly closely, so that there appears to be no particular age or sex bias for platinum concentration (Fig. 1).

Discussion

Two rather surprising observations were noted as a result of the autopsy data. First, platinum was present in detectable levels in one or more tissues in almost half of the individuals studied. It was thought that platinum would be an entirely new environmental contaminant, exposure to which had previously been occupational (mining, refining) only (*1*). Second, subcutaneous fat as a "target" site for platinum deposition was unexpected. Previous work with animals identified kidney, liver, and spleen as chief deposition sites for platinum (*4,5*). Perhaps level of exposure is important. The presence of platinum in subcutaneous fat raises the question of transport, since most platinum compounds are lipid-insoluble. Conversion to lipid-soluble compounds through methylation of platinum compounds is one possible explanation of potential significance.

Recent work by Taylor (*6*) has shown that at least two platinum compounds, platinic sulfate and potassium hexachloroplatinate, can be methylated via the same methylcobalamin ($Me\text{-}B_{12}$) reaction as involved in methylation of mercury.

Table 4. Distribution of tissue samples showing platinum.

Tissue sample type	No. samples analyzed	No. samples showing Pt (>detection limit)	% of samples in which Pt detected
Subcutaneous fat [a]	74	10	13.51
Kidney	91	11	12.09
Pancreas	84	10	11.90
Liver	90	10	11.11
Brain	9	1	11.11
Gonad	53	5	9.43
Adrenals	60	3	5.00
Muscle (psoas)	97	4	4.12
Aorta (descending)	92	3	3.26
Heart (left ventricle)	82	2	2.44
Spleen	52	1	2.00
Prostate or uterus	63	1	1.59
Thyroid	73	1	1.37
Lung	95	0	0
Vertebrae (lumbar)	94	0	0
Fifth rib	97	0	0
Femur	57	0	0
Clavicle	30	0	0
Scalp hair	9	0	0
Pubic hair	1	0	0
Total	1313	62	5.0

[a] To determine whether this surprisingly high number of elevated levels might be the result of larger samples supplied in one batch (single hospital source), the average subcutaneous fat sample weight (μg of wet tissue) was computed for each batch. The batch in which seven of the ten levels were found averaged 20.78 μg per fat sample; the average weights for the other four batches were 20.97, 14.44, 19.80, and 32.81 μg, respectively. Size of sample available for analysis may therefore be discounted as a factor.

Whether or not this reaction takes place in the normal environment or in the human body has not been established. Since it has been established that methylation can occur under laboratory conditions, EPA is planning a research program to determine biological activity of the methylated platinum product of this methylcobalamin reaction.

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