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DOCUMENT NO. 701880
BNWL-SA-918 (918)

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TITLE

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TISSUE SAMPLING FOR PLUTONIUM THROUGH AN AUTOPSY PROGRAM [a]

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September 30, 1966

Paper for oral presentation and publication in the proceedings of the Twelfth Annual Bioassay and Analytical Chemistry Meeting to be held at Gatlinburg, Tennessee October 13-14, 1966.

(a) This paper is based on work performed under United States Atomic Energy Commission Contract AT(45-1)-1830.

TISSUE SAMPLING FOR PLUTONIUM THROUGH AN AUTOPSY PROGRAM

There are three generally recognized methods available for the assessment of organ or whole body doses due to the intake and deposition of radionuclides:

a) Measurement of the environment

b) Measurement of the excreta

c) Direct measurement of the exposed worker.

Environmental programs provide useful data for assessing dose to workers in a gross manner, but because the quantity of radioactivity taken into the body is not accurately known, they do not lend themselves to precise interpretations. Nevertheless, environmental data such as aerosol concentrations, particle size distributions, duration of exposure and chemical form of the contaminant are of prime importance as supportive information for other modes of dose assessment.

Measurement of radioactivity in excreta is another method of indirect assessment. Here again, the results may be imprecise because of biological variability, inadequate sampling techniques and lack of models responsive to the exposure conditions experienced by the worker.

Direct measurements of the exposed worker, of which the autopsy program can become a component part, provide the best available method for assessing organ retention and dose. "In vivo" measurements, however, have two serious limitations. They are restricted to external counting techniques and the assessment of individual organ doses can be masked or impossible to determine as

in the case of trying to determine separately the contributions from the lungs and the pulmonary lymph nodes. Information obtained from autopsy samples can help considerably in future assessments made of the retention characteristics and doses to specific organs by the "in vivo" external measurement techniques.

When in the early 1940's, employees at the Hanford Atomic Energy Plant in Richland, Washington began to work with plutonium isotopes in various chemical forms, surveillance programs were initiated to determine the air concentration of plutonium, detect and control environmental contamination and estimate the internal deposition in the plant employees. The chief mechanism used to estimate the body burden of plutonium was the evaluation of bioassay data. It was recognized that the sole mathematical model developed for this type of evaluation was predicated on the results obtained from the administration of only one chemical form and by one method of administration.[1] Necessarily the extrapolation of the interpretations for application to various other chemical forms or to other methods of administration would be of questionable validity.

Through the cooperation of the local pathologist and personnel of the medical department, a modest autopsy program was started in 1949 to obtain various tissue samples from both former employees and residents. By analyzing the samples and segregating the results between those who formerly worked with plutonium and those who did not, we had a mechanism for determining the extent of deposition attributable to occupational exposures and relating this to the theoretical models that had been used earlier to estimate the depositions.

Considering the length of time that the program has been established, the total number of 286 cases seems somewhat small. This is still a rather large number, however, considering the sensitive nature of the program and the informal arrangements necessarily used to keep the program supported. Of the total, 242 represent non-occupationally exposed personnel and 44 represent personnel potentially occupationally exposed to plutonium at Hanford.

The types of samples collected have varied according to particular interests prevalent at the time the samples were taken, but in all cases lung, liver and bone samples were obtained although occasionally some of these results were lost. The routine collection of pulmonary lymph nodes was initiated in 1960 when studies commenced to assess the extent of plutonium depositions in these samples, especially following chronic occupational exposure to low activity aerosols. Also collected, but on an intermittent basis, and analyzed for Pu were blood, pancreas, prostate and seminal vesicle samples. The specific location for tissue sampling was not specified to the pathologist, and as a result, tissues were taken from the most convenient or randomly selected areas of the designated organ.

The sample weights varied considerably; for instance, the lung samples varied from 10-300 grams, the liver samples from 15-300 grams, and bone samples, which were taken from the rib, varied from 4-25 grams. The weights of the lymph nodes, although referred to in some of the data, has little meaning inasmuch as the nodes were not stripped clean of associated tissue.

The chemical procedures used in analyzing the tissue were the standard

procedures used for the separation of Pu in excreta, and the detection of the residual Pu was by counting tracks in NTA film exposed to the deposition of Pu on stainless steel discs. In recent years, sensitivity of about 0.05 dpm was obtained using this procedure. However, only average or expected yields from the chemical procedures could be used because the film detection technique is unsatisfactory for the discrimination of various isotopes of plutonium.

The pathologist when submitting tissue samples avoided, where possible, samples evidencing gross abnormalities although it was not always possible to do so. In each case the coroner's statement of death was obtained and included with the data so that these irregularities may be considered. For instance, resulting data on lung depositions may not be considered normal in the case of pulmonary emphysema or carcinoma.

The radiochemical analyses of tissues from former Hanford plutonium workers, presented in Table I, show that for a number of the former long-term Hanford workers, small but measurable internal depositions of plutonium were found. For these individuals some 523 urine samples were analyzed for plutonium during the course of their work with this material. A positive bioassay result, i.e. samples with activity greater than 0.05 dpm, was obtained for only one employee where three positive urine samples appeared following the accidental inhalation of plutonium oxide dust. The results were evaluated as having indicated no significant deposition; less than 1% of the maximum permissible body burden of 0.04 μCi with bone as a reference, had occurred. The data presented in Table I are interesting in that they demonstrate the presence of small body depositions of plutonium in plutonium workers whose depositions are below detection with present bioassay surveillance techniques. The data are, however, disappointing in that the sensitivity was insufficient to obtain statistically

Table I
DATA FROM AUTOPSY

Case Number	Work Exposure in Plutonium Facility (years)	Date of Last Exposure	Dates of Known Incidents	Coroner's Statement of Death	Date of Death	AUTOPSY RESULTS							
						LUNG		LIVER		BONE		LYMPH NODES	
						Weight grams	Activity 10^{-3}d/m/g	Weight grams	Activity 10^{-3}d/m/g	Weight grams	Activity 10^{-3}d/m/g	Weight grams	Activity 10^{-3}d/m/g
1	2	1949	0	Calculus & Peritonitis	1949	13.3	<25	15.2	<22	7	<47	—	—
2	4	1950	0	Tuberculosis & Pericarditis	1950	24.8	<13	36.8	13	---	—	—	—
3	2	1951	0	Carcinoma Kidney	1952	---	< det.	—	< det.	---	< det.	—	—
10	10+	1955	9-11-52 4-14-53	Carcinoma Colon	1955	40	< 1.3	32.7	10	7.2	< 7	—	—
11	1.5	1955	0	Blast Injuries	1955	71.5	< 0.7	24.5	< 2	9	< 6	—	—
12	4.5	1955	0	Polyserositis	1955	33	< 1.5	21.5	< 2.5	8.5	< 6	—	—
13	7.5	1956	2-5-53	Pulmonary Emphasema	1956	48	24	27.5	76	12	< 4	—	—
14	1	1955	0	Bronchogenic Carcinoma	1956	30.8	< 1.6	25.8	< 2	8.4	< 6	—	—
4	4	1952	0	Coronary Arteriosclerosis	1952	---	< det.	—	< det.	---	< det.	—	—
5	1	1952	0	Peritonitis	1952	---	< det.	30	10	—	< det.	—	—
7	1.5	1953	0	Myocardial Infarct	1953	42	69	30	130	—	< det.	—	—
6	5	1953	0	Carcinoma Kidney	1953	42	7.1	30	7.0	—	< det.	—	—
8	1.5	1950	0	Malignant Melanoma	1953	---	< det.	—	< det.	---	< det.	—	—
9	5	1954	0	Ruptured Aneurysm of Aorta	1954	26	< 2	29	6.8	8	< 6	—	—

Table I (continued)

Case Number	Work Exposure in Plutonium Facility (years)	Date of Last Exposure	Dates of Known Incidents	Coroner's Statement of Death	Date of Death	AUTOPSY RESULTS							
						LUNG		LIVER		BONE		LYMPH NODES	
						Weight grams	Activity 10^{-3}d/m/g	Weight grams	Activity 10^{-3}d/m/g	Weight grams	Activity 10^{-3}d/m/g	Weight grams	Activity 10^{-3}d/m/g
15	9	1956	0	Subaracnoid Hemorrage	1956	50.8	1.3	27	9.5	5.5	< 9	---	---
16	1.5	1957	1-15-52	Rheumatic Heart	1957	34	0.9	24	2.2	6.5	3.7	---	---
17	8	1954	0	Carcinoma Rectum	1958	23	< 1.1	27	< 1	6.5	< 4	---	---
19	2	1953	0	Cerebral Hemorrage	1958	33	< 0.8	33	< 0.8	5	< 5	---	---
18	2	1958	4-29-55	Hodgkin's Disease	1958	43	1.4	27	2.6	---	---	---	---
20	2	1955	0	Laennec Cirrhosis-Liver	1958	35	< 0.7	26	1.2	12	8.1	---	---
21	8	1958	0	Laennec Cirrhosis-Liver	1958	30	< 0.9	23	< 1.1	6	< 4	---	---
23	1	1960	0	Subdural Hemorrage	1960	20	< 1.3	38	< 0.8	4	< 6	0.2	<130
24	2.5	1960	10-30-59	Bronchogenic Carcinoma	1960	41	< 0.8	20	4.4	6	< 4	0.6	< 40
25	10+	1960	0	Myocardial Infarct	1960	27	< 0.9	26	3.1	5	< 5	0.8	< 30
26	4	1961	0	Fibrosarcoma	1961	39	0.9	26	< 0.1	8	< 3	1.2	< 20
27	0.5	1961	0	Myocardial Infarct	1961	39	1.7	22	11	3.2	< 8	1.4	20
28	7	1953	0	Laennec Cirrhosis-Liver	1961	26	< 1	19	< 1.3	4.3	< 6	1.4	< 20
29	10+	1961	0	Cerebellar Hemorrage	1961	49	< 0.5	27	1.2	4.3	< 6	7.0	< 4
30	3	1962	0	Myocardial Infarct	1962	40	< 0.6	29	< 0.9	4	< 6	7	< 4
32	1.5	1962	0	Bronchogenic Carcinoma	1962	55	< 0.5	20	< 1.3	5	2.4	4	< 6

Table I (continued)

Case Number	Work Exposure in Plutonium Facility (years)	Date of Last Exposure	Dates of Known Incidents	Coroner's Statement of Death	Date of Death	AUTOPSY RESULTS							
						LUNG		LIVER		BONE		LYMPH NODES	
						Weight grams	Activity 10^{-3}d/m/g	Weight grams	Activity 10^{-3}d/m/g	Weight grams	Activity 10^{-3}d/m/g	Weight grams	Activity 10^{-3}d/m/g
31	10-	1962	10-14-57 12- 6-58	Skin Burns	1962	47	76	26	18	5	< 5	5	130
37	3.5	1956	0	Bronchogenic Carcinoma	1963	67	2.4	28	6	6.5	< 4	3.9	< 6
40	4	1962	0	Myocardial Infarct	1963	67	0.7	94	< 0.3	6.4	< 4	3.6	< 6
39	9	1963	0	Carcinoma Colon	1963	33	2.1	25	< 1	3.7	< 6	3.5	< 6
34	3	1963	0	Myocardial Infarct	1963	49	0.9	24	1.7	6.1	< 4	5.6	< 5
38	7	1963	0	Coronary Arteriosclerosis	1963	70	1.0	56	< 0.5	3.8	< 6	13	< 2
36	1	1963	0	Cerebral Hemorrage	1963	43	0.7	32	< 0.8	5	< 5	3	14
33	6	1962	1953 to 1961	Myocardial Infarct	1962	32	55	28	18	3.7	< 6	3.5	18
35	4	1962	0	Pulmonary Emphysema	1963	46	1.3	30	17	5	< 5	4	< 6
41	3	1963	0	Carcinoma Stomach	1963	90	0.9	35	1.0	8	< 3	4	< 6
22	13	1958	0	Myocardial Infarct	1958	54	20	27	17	6	< 4	—	—
42	8	1957	2-16-48	Ruptured Aortic Aneuryism	1964	280	0.8	277	0.6	7.2	< 4	6.5	< 4
43	3	1964	0	Emphysema	1964	271	0.4	120	7.5	23	< 1	8	< 3
44	1	1964	0	Carcinoma Lung	1964	148	1.6	87	0.7	12	< 2	---	---

good results for bone and the lymph nodes. Another disappointing feature is the absence of more positive urinalysis data with which some of the current ideas of retention versus excretion could be tested.

A review of the data shows that the largest deposition of 130×10^{-3} d/m/g occurred in an employee who was not involved in any known accidents. Assuming standard man parameters, this concentration implies 0.1nC in the liver. Since 15% of the plutonium in the blood reaches the liver, again using ICRP parameters, a blood content of 0.7 nC is indicated. Depending on the time of sampling after intake such a deposition, if occurring all at once, and if excreted according to the Langham model, would be detectable according to present practice for about 9 months after intake. The worker in question was sampled mostly on a quarterly basis but at no time did urinalysis yield positive results. Recent experiments with inhalation of plutonium oxides by dogs conducted by Drs. Bair and Park[2] at Battelle Northwest indicates that the excretion rate as a percentage of body burden may be considerably smaller than that given by the Langham model and depending on the state of the plutonium inhaled may preclude detection by urinalysis of the autopsy results reported here.

Bearing in mind the limitations of the program, particularly in extrapolating sample activity to the total activity for the organ concerned, the data indicate that the lung and the liver, for the majority of cases, are the favorite sites for deposition. There are 29 cases where either the lung or the liver is positive and in 19 of these 29 cases the liver contained a higher concentration of Pu than did the lung. The fact that the lymph nodes do not seem to contain high concentrations of Pu can be related to both the uncertainty of the sample size and to the uncertainty as to whether or not the lymph nodes

that were obtained represented those having the highest concentration. It is of interest, however, that the bone depositions do not show the order of activity expected. The tabulations of the ICRP[3] suggest that when inhalation is the route of intake, one might expect five times the amount in bone as that in liver. However, the data of Bair, et al,[4] suggest for the acute cases, beagles sacrificed soon after intake, that about the same amount of plutonium oxide will be seen in the skeleton as in the liver. Park has reported about four times the amount of Pu oxide in the liver as that in the bone for dogs sacrificed at 900 days after intake. Langham[5] reports about the same in the skeleton as in the liver for a radiation worker exposed occupationally to both oxide and nitrate for 12 years prior to a radiation accident at Los Alamos. The autopsy results show that qualitatively, in 10 cases out of 23, the amount of Pu in the liver is at least three times that in the bone, assuming that Pu is uniformly distributed through the mass of the organ (standard man parameters).

Langham, et al[1] reported the results of measurements of plutonium concentration in tissues obtained at autopsy from nine chronically exposed workers at Los Alamos. Their measurements show qualitatively that the relative tissue concentrations are, in decreasing order, respiratory lymph nodes >lungs >liver >bone. In only one instance, that of case 31, does the present data clearly follow the suggested pattern.

For comparison, data from the literature regarding plutonium distribution in the human body and in dogs are presented in Table II. The frequency of cases as a function of amount of depositions and work experience are presented for the individuals listed in Table I together with non-occupational cases in Table III.

TABLE II

PLUTONIUM DISTRIBUTION DATA OBTAINED AT AUTOPSY FOR HUMANS AND BEAGLE DOGS EXPRESSED AS PERCENTAGE OF THE BODY BURDEN AT DEATH OR AS PERCENTAGE OF THE INTAKE FOR THE DOGS[5]

	Langhams's[a] Patient	Radiation[b] Worker	Beagle Dogs[c]	
			Pu Citrate Injection	PuO Inhalation
Reference	Langham et al[1]	Langham[5]	Stover et al[6]	Park et al[7]
Skeleton	66	36	58	0.4
Liver	23	49	11	1.7
Lungs		10		25.0
Respiratory Lymph Nodes		3		14.0
Spleen	0.4	0.3		

(a) Autopsy data obtained five months after injection of Plutonium Citrate.

(b) Occupationally exposed to plutonium for 12 years prior to a radiation accident at Los Alamos.

(c) Distribution data at death, 900 days after intake expressed as a percentage of initial intake.

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TABLE III

DISTRIBUTION OF DEPOSITIONS BY WORK EXPERIENCE

Category	Number of Cases	Percentage of Cases					
		Lung			Liver		
		Units of x 10^{-3} d/m/g			Units of x 10^{-3} d/m/g		
		<1	1-5	>5	<1	1-5	>5
Work in Pu Facility	44	68	18	14	48	18	34
Non-Radiation Workers	77	83	17	0	82	17	1
Environmental Residents	165	85	15	0	90	10	0

The distinct break between the number of cases at a certain burden level for the plutonium worker and the non-plutonium worker and the environmental resident suggest that the latter two belong to the same class as having received plutonium predominantly as worldwide fallout from weapons testing.

The frequency of occurrence of measurable organ depositions as a function of time working with plutonium is presented in Table IV.

TABLE IV

DISTRIBUTION OF DEPOSITIONS AS A FUNCTION OF LENGTH OF EXPOSURE

Years of Exposure	Number of Cases	Percentage of Cases			
		Lung		Liver	
		Units of x 10^{-2} d/m/g		Units of x 10^{-2} d/m/g	
		≤ 1	> 1	≤ 1	> 1
< 5	30	97	3	83	17
>	14	72	28	65	35

Qualitatively it can be concluded from that table that there is a greater likelihood of a larger deposition with increase in exposure time. Still unknown is whether this is caused by longer exposure to a chronic low-level concentration of plutonium or expresses the increasing likelihood of involvement with a minor or unnoticed accident with increasing time or association with the element.

As the program has evolved, both correctible and uncorrectible deficiencies have appeared and should be noted. The per cent of yield of the chemical procedures needs to be known more precisely for each individual sample. Recent animal data indicate variabilities as high as a factor of 3 between identical samples processed using NTA film analysis technique. It is now possible to tag the samples with Plutonium-236 and use alpha spectrometry instead of NTA film, thus the per cent of yield for each sample will be known. The large variations in the total weight of the lung, particularly as associated with the cause of death, prevented extrapolation from a sample weight to an estimate of the activity in the total lung. To standardize the results, the entire left lung, including the hilar lymph node section, is now being used for analysis. The liver samples are now taken in sizes that weigh at least 200 grams. There has been much discussion concerning the selection of the bone sample. Various authorities indicate that the bone deposition for Pu seems highest in various locations such as the rib, sternum, vertegrae, femur and etc. Other factors additionally enter into the selection of this sample such as convenience for the coroner or the pathologist to obtain the desired samples either due to location or because of interference with further processing of the cadaver by the undertakers. After much deliberation, the sternum has been selected for future collection and analysis. The stripping of the tracheobronchial lymph nodes is not being routinely undertaken due to the difficulty of locating them. They will only be taken when clearly abnormal situations exist which make them readily observable or they appear to the

pathologist to be of particular interest.

Autopsy programs, like other measurement programs, require precisely specified and controlled-imput from other sources in order to secure the maximum information. The most difficult and least precise information is the occupational exposure history on the employee. Typical of required data are: length and type of exposures, details on known radiation incidents, aerosol concentrations, particle size distributions and chemical forms and results of surveillance programs such as whole body counting and bioassay evaluation.

In conclusion, an autopsy program can become a useful adjunct to the three different measurement techniques used to assess organ doses due to internally deposited radionuclides. The importance of this program increases as the number of potential exposures to new and larger quantities of contaminants increases. Additionally, as the age of the nuclear industry increases, so does the age of the occupational worker who has perhaps already received prolonged low-level exposures. Difficulties and the sensitive nature that such programs can portray vary according to State law, company policies and perhaps the extent of personal association between the pathologist and the investigator. In spite of the problems associated with a program of this type, it is a highly recommended source of information which can be developed into larger programs through the increased participation of hospital, other medical personnel, and other sites without adverse publicity. It certainly gives irrefutable information as to the concentrations and locations of the depositions of contaminates in man as a result of environmental pollution.

(1) Langham, W. H. et al, Los Alamos Scientific Laboratory Report LA-1151 (1950)

(2) Bair, W. J. and Park, J. K., "Comparative Disposition of Four Types of Plutonium Dioxides Inhalaed by Dogs", 1966

(3) Recommendation of the International Commission on Radiological Protection, ICRP Publication 2

(4) Bair, W. J., in: Inhaled Particles and Vapours, Pergamon Press, London (1961) 192-207

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(6) Stover, B. J., Atherton, D. R., Bruenger, F. W., and Buster, D. S., Health Phys. 8 (1962) 589-597

(7) Park, J. F. and Clarke, W. J., HW 76000 (1963) 118-125