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Radiation and the Lymphatic System

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Radiation and the Lymphatic System

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Studies of Plutonium in Human Tracheobronchial Lymph Nodes

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ABSTRACT

Since 1959, tissues from 70 occupationally exposed former employees of the Los Alamos Scientific Laboratory have been examined following autopsy. Exposure in most cases was to inhaled plutonium oxide aerosols. Chemical analyses of selected tissues were performed to determine the amount of plutonium retained in the body at the time of death. On the basis of the measured tissue concentrations of plutonium, extrapolations of total-body burdens were made. Thirty-three of the measured cases had plutonium depositions in the tracheobronchial lymph nodes ranging from 0.1 to 4000 dpm per gram of tissue (0.05 to 1800 pCi/g). The duration of exposures ranged from 4 to 30 years. Microscopic examination of representative sections of these lymph nodes revealed no abnormalities other than those which were directly attributable to the basic disease that caused the demise of the various persons in this study. The size distribution of plutonium particles in nodes from one individual was determined by exposing tissue sections to nuclear track film. The estimated mass median diameter of the particles was 0.3 μm, and the distribution had a geometric standard deviation of 1.6. It is estimated that 95% of the individual particles had corresponding plutonium concentrations between 0.001 and 0.22 pCi.

A great deal of interest and concern has been generated regarding the effects on the human body of internally deposited alpha-emitting radioisotopes. Although animal data are abundant, the collection of human data has been rather meager and the extrapolation from animals to humans always results in some doubt as to its reliability. Tissues from 70 former employees of the Los Alamos Scientific Laboratory (LASL) who had potential occupational exposures to plutonium were removed for analysis after death. Histologic studies were made on most of these tissues, and radiometric analyses were performed on the same tissues to determine the amount of plutonium, if any, retained at the time of death. From these data whole-body contents of plutonium were extrapolated and compared with in vivo estimates based on data from both urine analysis and lung counting techniques.[1] This kind of comparison is part of the ongoing program at LASL to improve the urine bioassay calculations on laboratory personnel currently working in the plutonium laboratories. Thirty-three of the cases analyzed chemically had tracheobronchial lymph node depositions of plutonium ranging from 0.1 to as high as 4000 dpm per gram of tissue (0.05 to 1800 pCi/g). This paper reports the plutonium concentrations and pathological data on those cases for which the tracheobronchial lymph nodes were examined at autopsy. In case 7-138, in which the highest concentration of plutonium (1800 pCi/g) was observed, attempts were made to estimate the size range of the plutonium particulates dispersed throughout the node.

METHODS

The whole lung and associated tracheobronchial lymph nodes, the liver, the kidneys, and a bone specimen (usually a vertebral wedge) were routinely taken at autopsy for radiometric analyses. Small samples were removed from these tissues and processed with other tissues of specific interest to the pathologist as part of the autopsy protocol. Histological slides of tracheobronchial lymph nodes were available for study in 14 of the previously mentioned cases.

The tissues were weighed and muffled, and the inorganic residue was wet-ashed in nitric acid. The resulting salts were treated with hydrofluoric acid to solubilize any remaining plutonium ceramics and, after removal of the excess fluorides, the salts were dissolved in nitric acid. Initially, an internal tracer of ^{236}Pu (which more recently has been replaced by ^{242}Pu) was used to determine the chemical yield of the $^{239-240}$Pu and ^{238}Pu. The plutonium was isolated by anion exchange and electrodeposited onto stainless steel disks. Alpha-pulse-height spectrometry was used to measure the 4.9- to 5.7-MeV plutonium alpha energies.

In a few cases of suspected high levels of activity in the lymph nodes, the specimen was counted with a thin CsI–NaI X-ray detector for both the 17-keV X ray emitted in the plutonium decay and the 17- and 60-keV X rays associated with ^{241}Am. This method has the advantage of being nondestructive and was used to obtain the relative activities in each of the 12 lymph nodes obtained from case 7-138, an occupationally exposed worker with an

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estimated body burden of 33 nCi of ^{239}Pu on the basis of urine assay[2] (see Table 1). Two of the nodes containing the highest alpha activity were selected for autoradiography. The Formalin-fixed nodes were embedded in paraffin and cut into 6, 12, and 18 μm thick sections, which were then mounted on standard microscope slides and stained. The slides were dipped into nuclear track photographic emulsion, and the film was allowed to expose for 1 week under standard nuclear track activity (NTA) conditions. The slides were then developed and examined for the presence of alpha tracks. A typical star pattern resulting from this method of recording the presence of alpha-active particulates is illustrated in Fig. 1. By counting the number of tracks in the emulsion associated with each star and by knowing the exposure time, we can calculate[3] the size of each alpha-emitting particle from the formula

$$d = \left(\frac{KC}{t}\right)^{1/3}$$

where C = number of tracks in the emulsion from particles of diameter d microns, assuming 50% geometry
t = autoradiograph exposure time
K = constant = 6.32×10^{-12} $[M/(\rho\lambda f)]$ = 2.76 for $^{239}PuO_2$
and with M = molecular weight of compound = 271 for $^{239}PuO_2$
ρ = density of compound = 11.46 g/cm³
λ = decay constant of the alpha emitter
f = number of radioactive atoms per molecule of compound

The alpha tracks were assumed to originate from $^{239}PuO_2$ particles. A seven-day exposure and a three-track star permit the detection of a plutonium particle 0.09 μm in diameter (0.0002 pCi plutonium). The tissue sections used in this study were also examined histologically for evidence of abnormalities resulting from the alpha radiation.

RESULTS

Alpha-Radiation Effects on Tracheobronchial Lymph Nodes

Selected information on one biopsy and 13 autopsied cases in which the tracheobronchial lymph nodes were examined both histologically and chemically is sommarized in Table 2. For the autopsied cases the years since the first potential exposure are represented as the time from the date of hiring at Los Alamos Scientific Laboratory to death. It was assumed that the exposure incidents were inhalation exposures which occurred during the early years of the laboratory operation (1945 to 1955) before improved industrial hygiene and health physics requirements reduced significantly the air levels of plutonium in the laboratories and the workers were provided with more efficient personal respiratory protection.

Microscopic examination of the stained thin sections of lymph node revealed no abnormalities other than those

TABLE 1 Concentration of Plutonium and Americium in the Tracheobronchial Lymph Nodes of a Plutonium Worker

Node No.	Weight, mg	Estimated isotope concentration* pCi/node ^{239}Pu	^{241}Am	pCi/gram of tissue ^{239}Pu	^{241}Am	Pu/Am
[illegible]	589	274	29	465	149	[illegible]
[illegible]	131	26	4	198	30	6.5
[illegible]	159	ND†	ND†	ND†	ND†	
[illegible]	275	74	10	269	36	7.4
[illegible]	448	151	28	337	52	5.4
[illegible]	625	659	77	1054	123	8.5
[illegible]	500	483	44	966	38	11.0
[illegible]	108	119	3	1102	28	[illegible]‡
[illegible]	114	39	7	342	61	5.6
[illegible]	180	182	12	1011	67	15.1
[illegible]	181	327	26	1806	144	12.5
[illegible]	433	401	39	926	90	10.3
			Mean	770	80	9.2
			±1 S.D.	493	43	3.1

*Based on 17 and 60-keV X irradiation measurements.
†ND, not detectable.
‡Not included in calculated mean of data.

which would be expected from the individual disease processes that caused the demise of the various individuals followed in this study. Many of the nodes appeared to contain normal activity, such as hyperplasia in pneumonia and tumor metastasis in cancer. The pulmonary nodes of persons who died from trauma were pathologically unremarkable.

Particle Size Distribution of $^{239}PuO_2$ in Lymph Nodes

Because of the relatively high levels of deposition observed in the lymph nodes of case 7-138 (a metal fabrication technician employed 26 years at LASL), it was deemed feasible to attempt measurement of the alpha-emitting particle size distribution by using the autoradiographic techniques developed by Leary.[3] Table 3 lists the calculated relationships between the number of alpha tracks radiating outward from a particle to the $^{239}PuO_2$ particle diameter and the amount of ^{239}Pu present (in femtocuries per particle). These data are corrected for the mean contribution of ^{241}Am that was suspected in the nodes. Table 4 gives the frequency distribution of $^{239}PuO_2$ particle sizes as determined by manual counting of the alpha tracks associated with 1215 stars observed in lymph node 6. These data were assumed to be log normally distributed, and the log probability of these data is plotted in Fig. 2. Because the distribution of count diameters is a log normal function, a mass–diameter plot can be calculated from these data by using the Hatch–Choate equations.[4] The alpha-emission rate is directly proportional to the mass of $^{239}PuO_2$ present in the particles, and therefore the mass–diameter plot also represents the

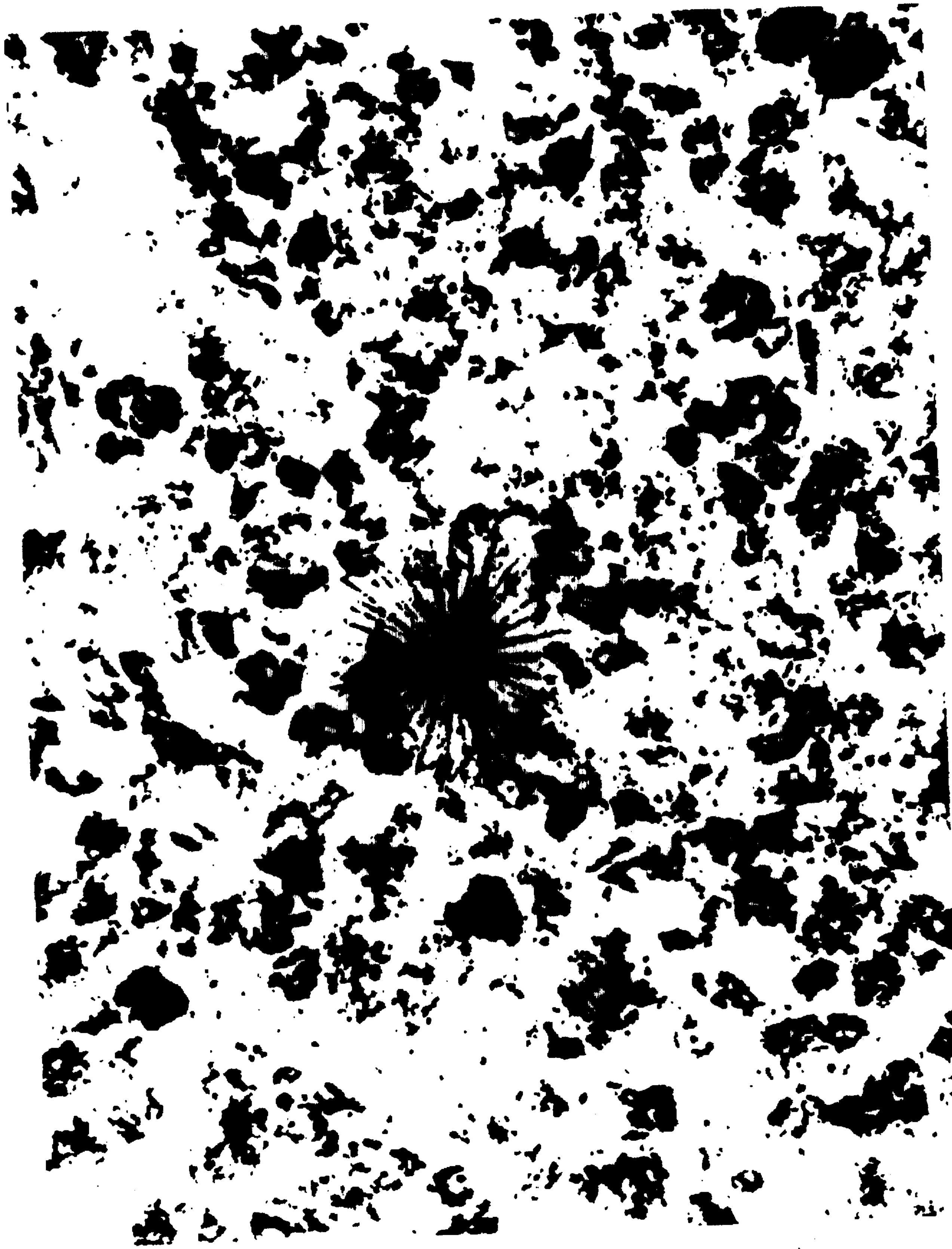

FIG. 1 Tracheobronchial lymph node tissue section showing alpha tracks radiating out from an alpha-active particle in a typical star pattern.

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TABLE 2 Concentration of ^{239}Pu in Tracheobronchial Lymph Nodes of Occupationally Exposed Workers

Case No.	Occupation	Cause of Death	Year of death	Age at death	Years since first exposure*	Alpha activity in TBLN,† pCi/g
7-138	Metals fabrication technician	Crushed chest	[illegible]	47	26	[illegible]
3-138	Chemist‡					[illegible]
2-[illegible]4	Health physics monitor	Cancer, lung	[illegible]	58	32	20
3-3[illegible]4	Chemical technician	Stroke	[illegible]	49	21	6.3
7-[illegible]	Pipefitter	Cancer, lung	[illegible]	58	23	1.8
7-004	Accountant	Carcinoma, colon	[illegible]	76	24	0.24
[illegible]	Plumber	Cardiac	[illegible]	51	8	0.23
[illegible]-024	Physicist	Heart attack	[illegible]	43	5	0.22
7-076	Maintenance mechanic	Ruptured aorta	[illegible]	72	24	0.18
8-142	Engineer	Cardiac arrest	[illegible]	48	14	[illegible]
5-016	Machinist	Heart attack	[illegible]	62	26	0.10
5-198	Technician	Pneumonia	[illegible]58	69	26	0.09
3-086	Technician	Diabetes	[illegible]75	34	15	0.05
7-028	Design engineer	Heart disease	[illegible]	60	28	0.05

*Years from time of hiring to death.
†TBLN, tracheobronchial lymph node.
‡Biopsy tissue was taken from this employee in 1973, at which time he was [illegible] years old; 27 years had elapsed since his first exposure to plutonium.

TABLE 3 Alpha Tracks Associated with $^{239}PuO_2$ Particle Diameter and Concentration in Particle

Number of tracks	Plutonium particle diameter, μm	Plutonium concentration per particle, fCi
5	0.11	0.4
10	0.14	0.9
20	0.18	1.8
30	0.20	2.7
40	0.22	3.6
50	0.24	4.5
100	0.30	8.9
200	0.38	17.9
500	0.52	44.7
1000	0.65	89.4

TABLE 4 Frequency Distribution of Plutonium Particles 0.06 nCi from Scars Observed in Tracheobronchial Lymph Node No. 6, Case No. 7-138

Plutonium particle diameter, μm	Frequency	Cumulative frequency, %
0.11	92	7.5
0.14	142	19.2
0.18	146	31.2
0.20	147	43.1
0.22	125	53.6
0.24	206	70.5
0.30	199	86.9
0.38	92	94.5
0.52	52	98.8
0.65	15	100.0

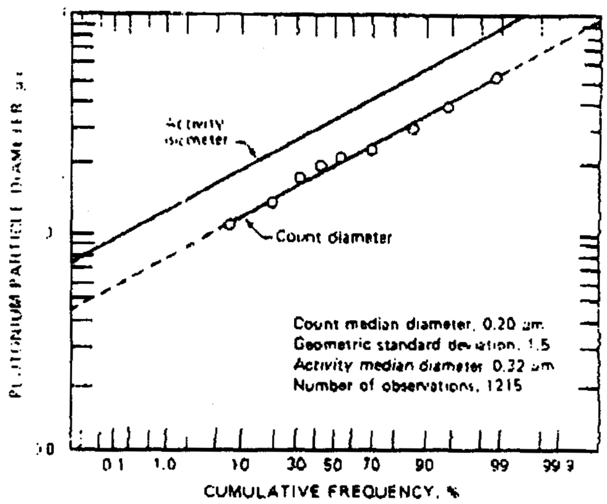

FIG. 2 Log-normal cumulative frequency plot of $^{239}PuO_2$ particles in tracheobronchial lymph node.

distribution of particles by activity. The frequency of the various size $^{239}PuO_2$ particles in this lymph node is projected from the least-squares fit to the midpoints of the frequency distribution of particle sizes in Fig. 2 is given in Table 5. Data on size distribution of plutonium particles in nodes 8 and 12 gave similar results.

The size frequency distribution of plutonium particles in the tracheobronchial lymph nodes of case 7-138 appeared to be similar to the size distribution of plutonium aerosols sampled and measured during plutonium [illegible]

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TABLE 5 Frequency of $^{239}PuO_2$ Particles in Tracheobronchial Lymph Node No. 6, Case 7-138

Diameter, μm	Midpoint	Fraction: Cumulative	Fraction: Incremental	Activity: pCi/particle	Activity: pCi/node	Particles per node
	0.1		0.12	0.0003	79	2.6×10^5
0.2		0.12				
	0.3		0.58	0.009	382	4.2×10^4
0.4		0.70				
	0.5		0.23	0.04	151	3.7×10^3
0.6		0.93				
	0.7		0.056	[illegible]	37	3.4×10^2
0.8		0.986				
	0.9		[illegible]	0.24	[illegible]	2.9×10^1
1.0		0.997				
	1.1		0.002	0.43	1	2.3×10^0
1.2		0.999				
					Total	3.1×10^5

ation and reduction operations in the facility in which this employee had worked[5,6] (see Table 6). From the tabulation of plutonium-aerosol sizes and the estimated plutonium activity in the entire node (659 pCi), the number of plutonium particles of various diameters were calculated (Table 5). The parameters associated with the logarithmic normal distribution indicate that 95% of the alpha-active particles in this lymph node have corresponding plutonium activities between 0.001 and 0.22 pCi.

TABLE 6 Average Particle-Count Median and Mass Median Diameter Measured in LASL Metal Preparation and Metal Fabrication Areas

Operation in area	Count median diameter, μm	Geometric standard deviation (σ_g)	Mass median diameter, μm
Fluorination of nitrate	0.26	1.5	0.45
Reduction to metal	0.17	1.6	0.32
Lathe operation	0.19	1.4	0.28

SUMMARY

Microscopic examination of lymph node tissue from occupationally exposed workers has revealed no abnormalities other than those directly attributable to the basic disease that caused the death of the various persons in this study.

The distribution of $^{239}PuO_2$ particles in one tracheobronchial lymph node was determined to have a mass median diameter of 0.3 μm, with a geometric standard deviation of 1.6. Ninety-five percent of the particles in the node were estimated to have a ^{239}Pu concentration less than 0.22 pCi.

Studies on the distribution and effects of plutonium particulates in lymphatic tissue are continuing.

ACKNOWLEDGMENTS

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