BNWL-1221
UC-48, Biology
and Medicine

PLUTONIUM INHALATION STUDIES

(A series of lectures given in Japan in 1969 at
the invitation of the Japanese Atomic Energy Commission)

by

W. J. Bair

Biology Department
Environmental and Life Sciences Division

February 1970

BATTELLE MEMORIAL INSTITUTE
PACIFIC NORTHWEST LABORATORIES
RICHLAND, WASHINGTON 99352

LECTURE 4

THE DISPOSITION OF INHALED PLUTONIUM

PART III. PULMONARY RETENTION OF ^{238}Pu MICROSPHERES*

Previous discussions have been concerned with plutonium compounds dispersed in air as particles in the so-called respirable size range. However, there is poor understanding of what constitutes the respirable size range. No one is prepared to state categorically that a 15-μm plutonium particle is respirable or not. In fact, there has been little work done to determine the maximum size particle that can be inhaled and deposited in the lung.

Because of the expanding peaceful uses of plutonium, there is increasing probability that large as well as small size particles will be accidentally dispersed into the environment. Because large particles can constitute significant radiation sources, there is a need to know whether large plutonium particles can be deposited in the lung and their retention times. Therefore, we initiated a program to investigate this problem. Preliminary results are available.

The purpose of this study was to obtain experimental data relating to the possible inhalation, deposition, and retention of $^{238}PuO_2$ microspheres that might be dispersed in air as a result of their use in space systems for auxiliary power. These data are required for assessment of radiation safety problems.

The objectives of these experiments were to determine whether 50-μm $^{238}PuO_2$ particles could be inhaled and deposited in the respiratory tract, how long large ^{238}Pu particles would be retained if the particles were deposited in the lungs, and the biological effects that might develop.

---

* *Principal Investigators: P. J. Dionne, J. F. Park, B. O. Stuart, D. H. Willard, W. J. Bair*

A series of five experiments was performed. This is shown in Table 4.1. First, 22 dogs were exposed to air in which 50-μm $^{238}PuO_2$ particles were dispersed. Second, single or several 50-μm particles were placed in the lungs of six dogs. Third, 120-μm particles were given 22 dogs by intubation under sodium pentothal anesthesia. Fourth, two dogs were given 120-μm particles by intravenous injection. In the final experiment, six dogs were exposed to aerosols of ^{238}Pu dust prepared by crushing the $^{238}PuO_2$ microspheres. This discussion will be concerned only with deposition and retention of large particles.

TABLE 4.1. Experimental Plan for Studies of $^{238}PuO_2$ Microspheres in the Lungs of Dogs

Material	Method of Administration	Particle Size, μm	Number of Dogs
Microspheres	Inhalation	50	22
Microspheres	Intubation	50	6
Microspheres	Intubation	120	22
Microspheres	Intravenous	120	2
Crushed Microspheres	Inhalation		6

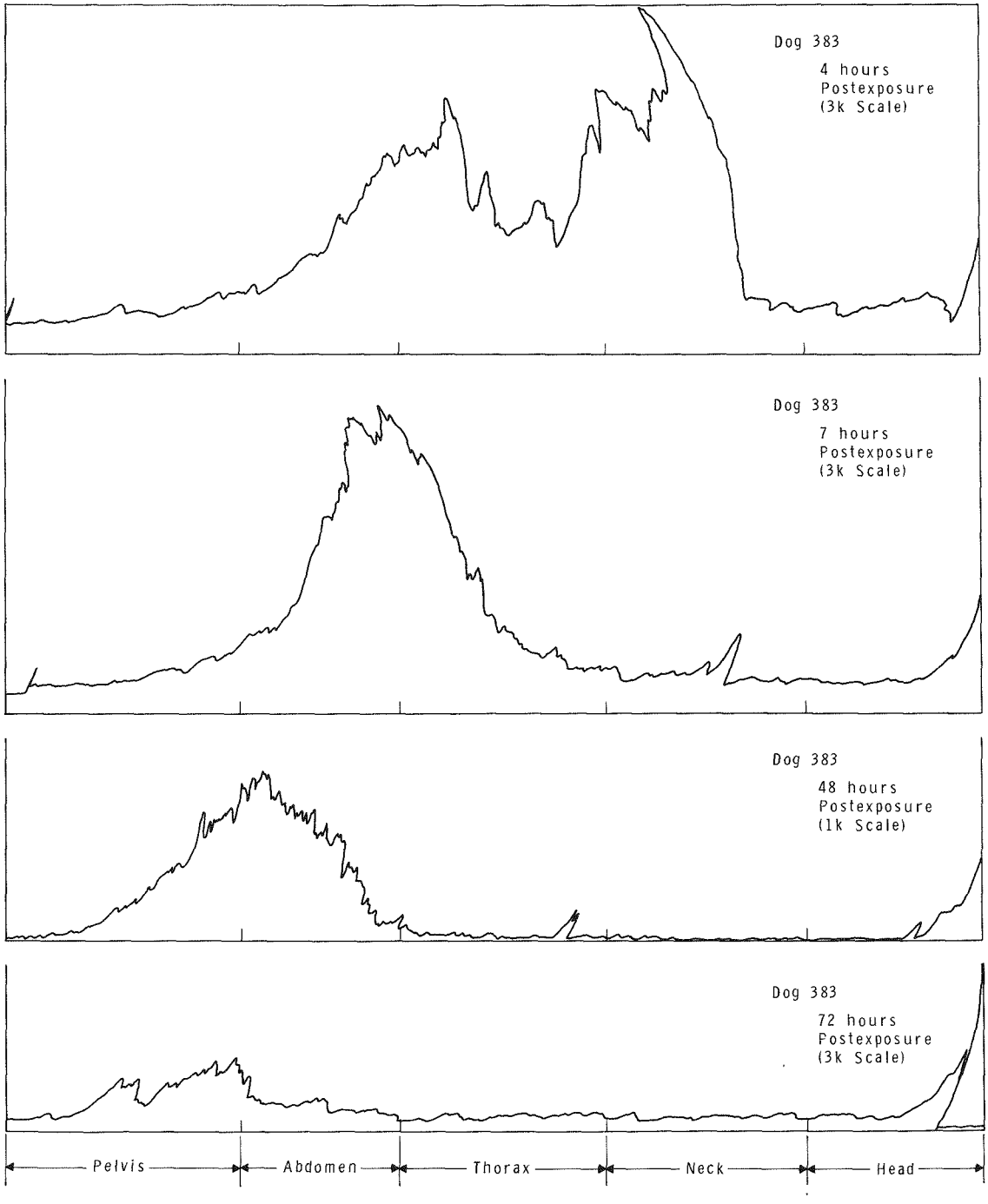
In all of these experiments, whole body longitudinal scanning techniques were used to follow the course of the particles in the dogs.

Dogs were exposed for 10 minutes to 50-μm particles dispersed in air. Because of the density of the particles and the heterogenous dispersion of particles in the chamber it was not possible to obtain a value for aerosol concentration with which to relate deposition in the dogs. Approximately 12 to 85 mCi or 4,000 to 29,000 particles were passed through the chamber. Amounts deposited in the dogs were estimated from whole body counts as 10 to 900 μCi.

Figure 4.1 is an example of scans from a dog which inhaled 50-μm particles. A significant fraction of the plutonium deposited was deposited in the nasal pharynx region. Subsequent scans show the passage of the plutonium through the animal. Comparison of the animal scans with a scan of a dog phantom with ^{238}Pu particles in the lung region indicate that either no $^{238}PuO_2$ particles were deposited in the lung or if they were, they were cleared very rapidly. Complete elimination of the ^{238}Pu particles occurred in all dogs by 16 days after exposure. One dog was killed 20 minutes postexposure and analysis showed 83% in stomach and 17% in the tongue. Another dog sacrificed 2-1/2 minutes postexposure revealed 9.7% in the oral cavity, 80.4% in the stomach, 4.4% in the esophagus, 3.2% in the nasal cavity, 0.8% in the trachea, and approximately 1.3% in the head and pelt of the head.

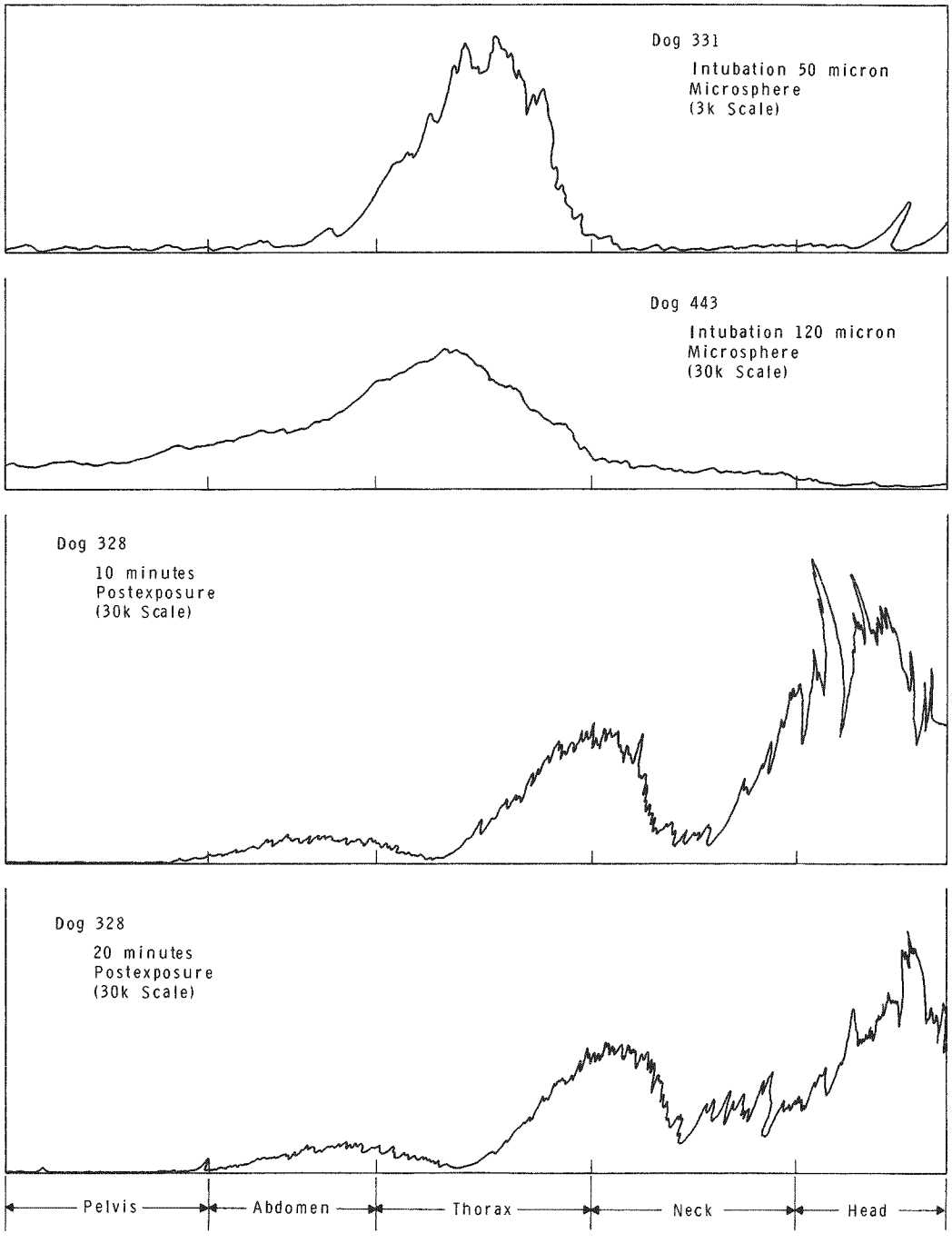
In the next experiments, one or several 50-μm particles were placed in lungs of six anesthetized dogs by means of a bronchoscope. Figure 4.2 shows typical scans. Most particles were cleared after 2 to 8 days, although several were retained for 2 months or longer. One remained for 3 months and another has been retained for more than 6 months.

In another group of dogs, 300-to 120-μm particles were placed in the lungs by intubation. Figure 4.3 shows the passage of a 120-μm particle through the dog. The particle cleared the lung within 45 minutes. Retention data are summarized in Table 4.2. In all but five dogs, the 120-μm particles were cleared within 10 days. One dog retained the particle 2 months, another 3 months, and two dogs have retained the particles more than 6 months. One dog has retained a 120-μm particle and another dog a 300-μm particle for nearly 3 years.



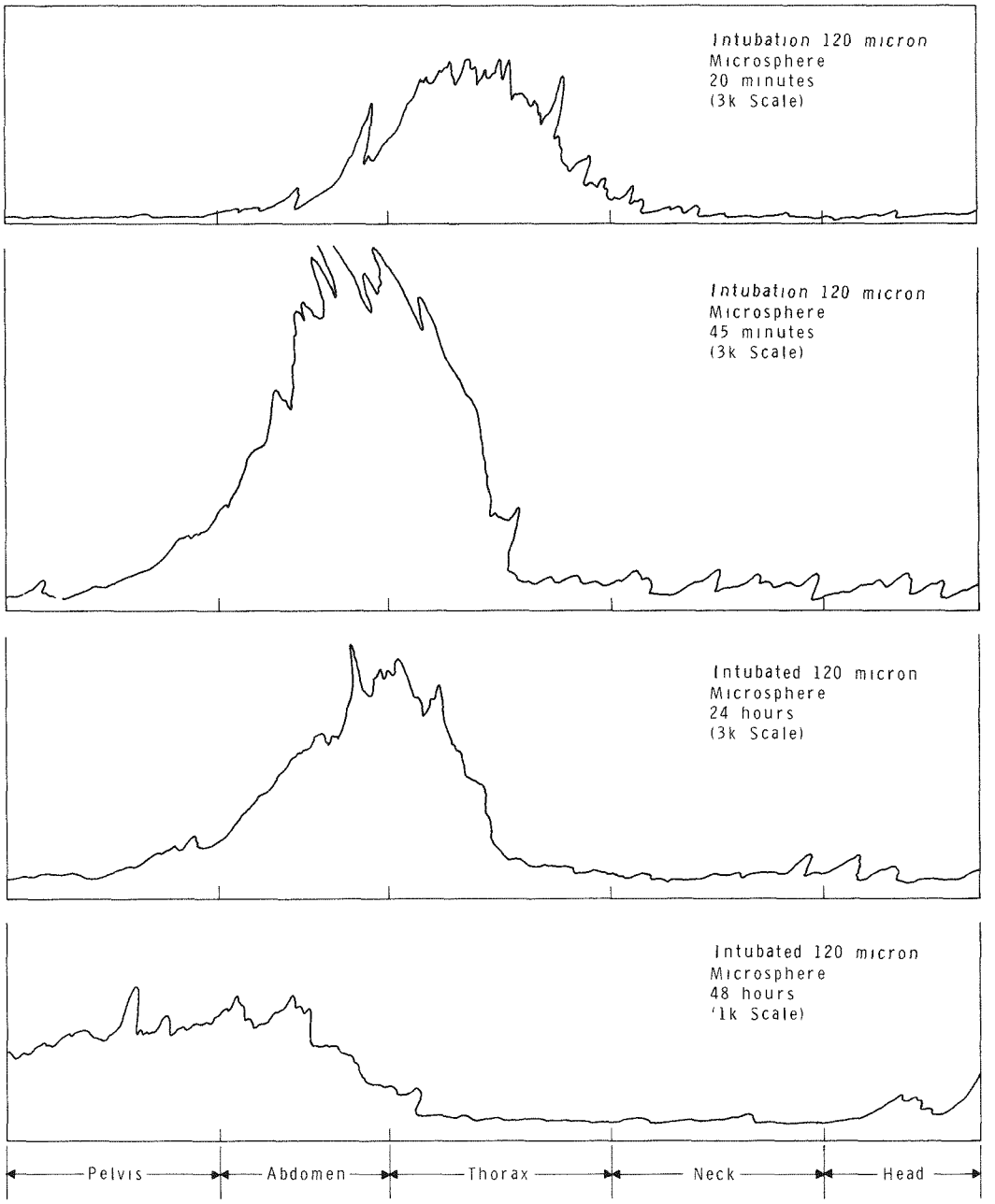
Neg 0672096-5

FIGURE 4.1. Longitudinal Scans of Dog After Inhaling 50 Micron Microspheres



Neg 0672096-4

FIGURE 4.2. Longitudinal Scans of Dogs



Neg 0672096-6

FIGURE 4.3. Longitudinal Scans of Dog After Intubation of 120 Micron Microsphere

TABLE 4.2. Lung Retention of $^{238}PuO_2$ Microspheres

Dog No.	Particle Size, μm	Number of Particles	Retention Time: Days 1 2 3 4 5 6 7 8 9 10	Months 2 3 4 5 6	Years >1
365		1	1		
360		1	1		
365	~300	1	1		
360		1	1		
365		1			1*
346		1	1		
331		1			1*
346		1		1	
368		1		1	
417		3	2 1		
430		3	1 2		
431		8	2 2 1 2	1	
432		1		1*	
443	120	4	2 2		
444		1	2		
454		1	1		
346		1	1		
346		3	1 1 1		
454		2	1 1		
439		2	1 1		
417		2	1 1		
443		2	2		
444		1	1		
368		4	1	2	1*
439		5	3	2	
444		3	1 2		
417	50	3	1 1 1		
346		3	2 1		
443		1		1	

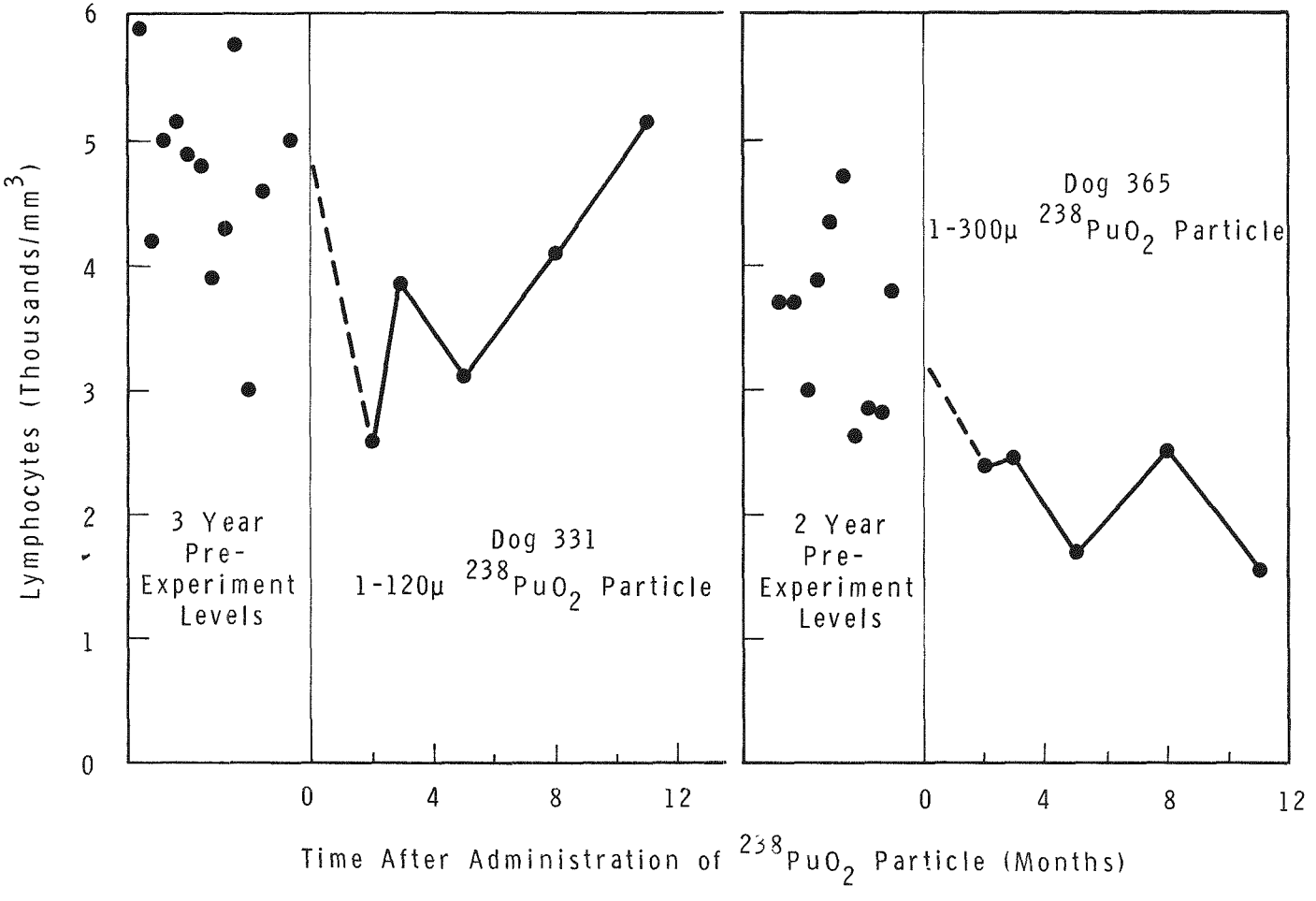
* *Particle is still in the lung*

The dogs which retained the particles more than 2 weeks were examined regularly for clinical symptoms of radiation injury. Chest radiographs have shown no areas of pathology. In our other plutonium inhalation studies, the earliest and most consistent effect observed has been a chronic lymphopenia. Lymphocyte counts for two dogs which have retained single particles for more than a year are shown in Figure 4.4. In both cases a reduction of circulating lymphocytes appeared to occur after administration of the particle. However, the lymphocyte level returned to the dog's normal range after 8 months. The lymphocyte level continues to decrease in the dog with the 300-μm particle. In experiments with inhaled ^{239}Pu, we have observed chronic lymphopenia occurring in dogs with lung burdens of 0.5 μCi. The dog with a 120-μm particle has a lung burden of nearly 100 μCi ^{238}Pu, yet it does not show a chronic lymphopenia. Therefore, as far as lymphopenia is concerned, a single Pu particle in the lung is considerably less effective than smaller quantities of plutonium dispersed throughout the lung.

Some interesting autoradiographs have been obtained from our ^{238}Pu experiments. Figure 4.5 shows several normal size alpha stars. In addition there are three giant stars. Figure 4.6 shows a giant star with tracks emanating from only part of the particle. Figure 4.7 shows additional giant stars. Another unusual phenomenon is shown in Figure 4.8. Rays tend to emanate in three directions. These strange alpha tracks are more commonly seen in ^{238}Pu autoradiographs than in ^{239}Pu autoradiographs.

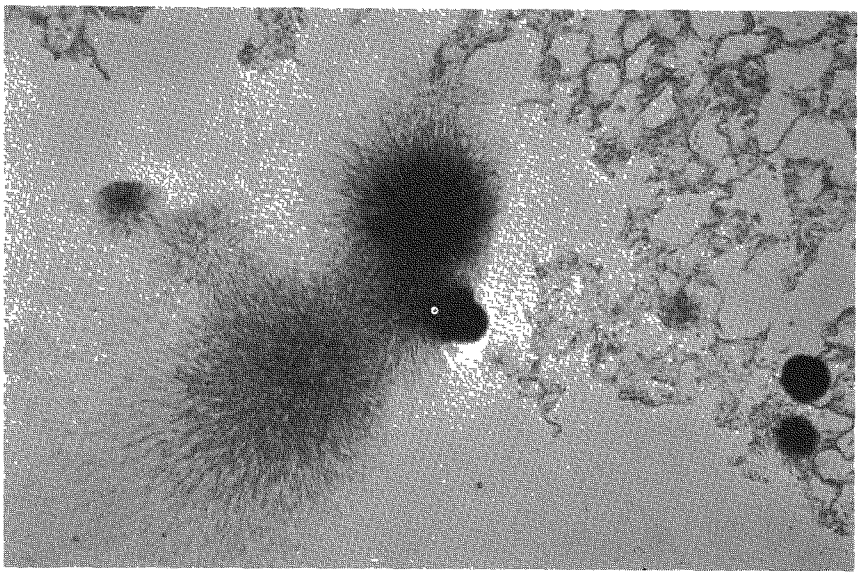
In summary:

- The $^{238}PuO_2$ particles as large as 50 μm dispersed in air were inhaled by beagle dogs. However, the particles were deposited in the nasal pharynx region of the respiratory



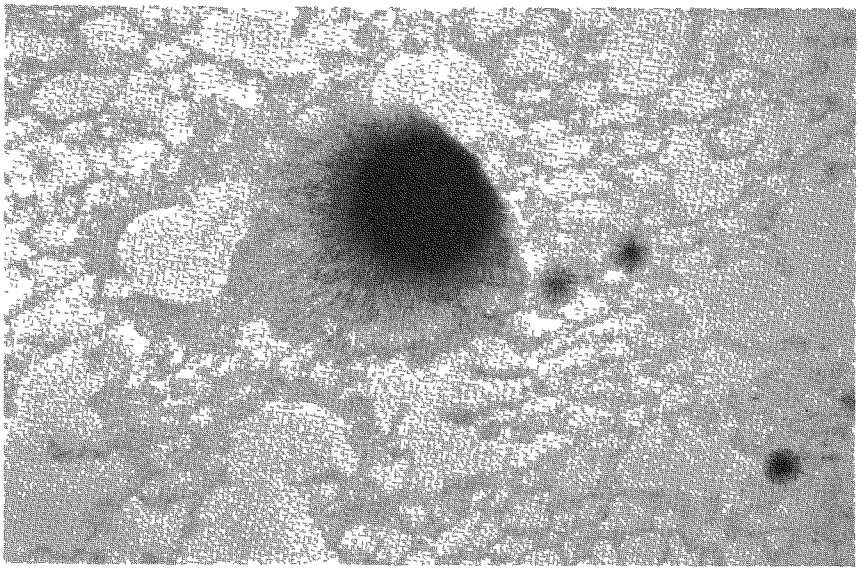
Neg 0672096-8

FIGURE 4.4. Effect of Single $^{238}PuO_2$ Particles in Lungs on Circulating Lymphocyte Levels in Dogs



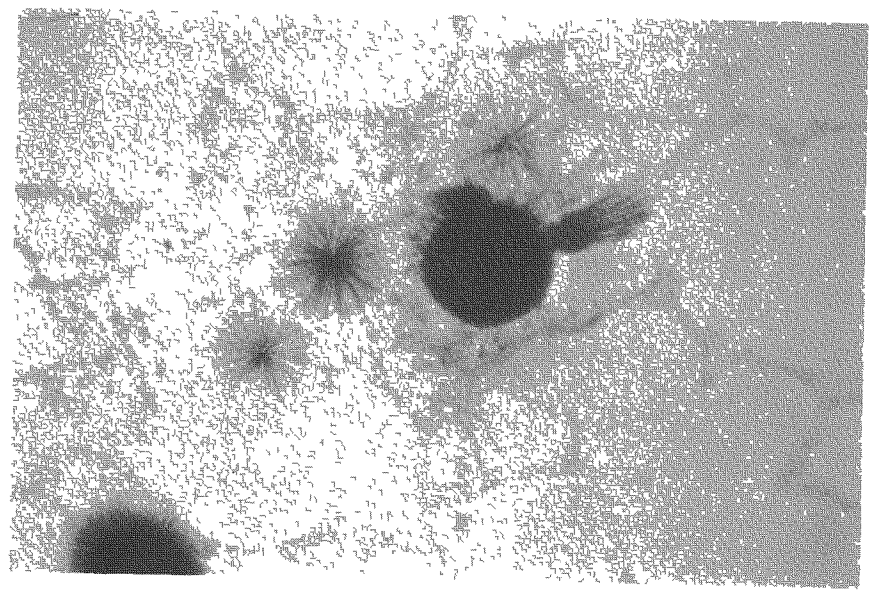
Neg 0693716-4

FIGURE 4.5. Autoradiograph of Lung Section from Dog Given $^{238}PuO_2$ (Typical "alpha stars")



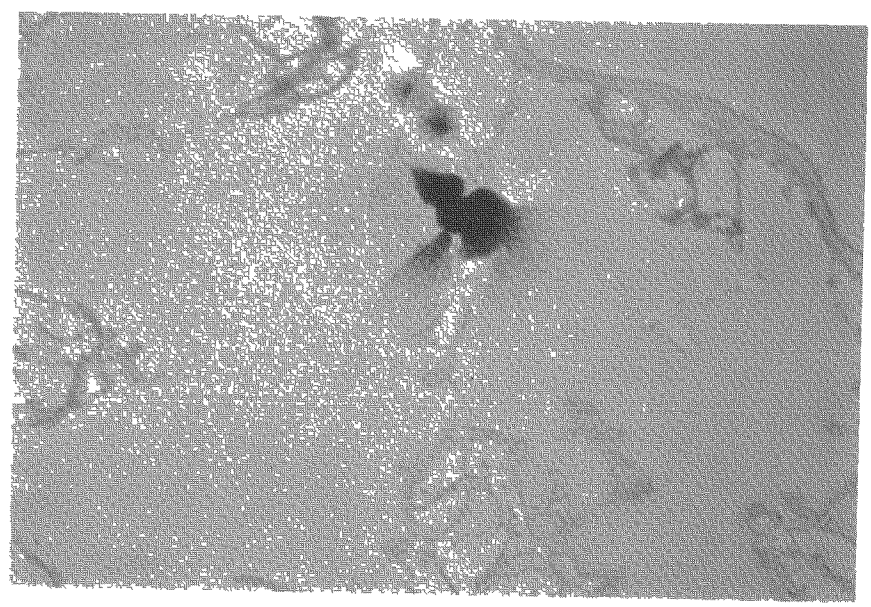
Neg 0693716-2

FIGURE 4.6. Autoradiograph of Lung Section from Dog Given $^{238}PuO_2$ (Giant alpha star with tracks emanating from only part of the particle)



Neg 0693716-1

FIGURE 4.7. Autoradiograph of Lung Section from Dog Given $^{238}PuO_2$ (Giant alpha stars)



Neg 0693716-3

FIGURE 4.8. Autoradiograph of Lung Section from Dog Given $^{238}PuO_2$ (Alpha star with tracks emanating in three directions)

tract and excreted in the feces over a period of a few days. Apparently no particles were deposited in the lower respiratory tract, or if they were, clearance was rapid and complete.

- In 30 dogs, 50-, 120-, and 300-μm $^{238}PuO_2$ deposited in the lungs by intubation were cleared within 10 days. However, nine dogs retained particles for several months, up to a year in two cases. No biological effects have been seen except for a possible lymphopenia in one which has retained a 300-μm particle for over a year.