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STUDIES ON THE INHALATION OF FISSIONABLE MATERIALS AND FISSION PRODUCTS AND THEIR SUBSEQUENT FATE IN RATS AND MAN

K. G. Scott, Dorothy Axelrod, Josephine Crowley,
H. C. Lenz, Jr., and J. G. Hamilton

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Human Subjects Project

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STUDIES ON THE INHALATION OF FISSIONABLE MATERIALS AND FISSION PRODUCTS AND THEIR SUBSEQUENT FATE IN RATS AND MAN

K. G. Scott, H. C. Lanz, Dorothy Axelrod,
Josephine Crowley, and J. G. Hamilton

ABSTRACT

The purpose of these experiments was to ascertain the possible hazard resulting from inhalation of fissionable materials and fission products. Aerosols of plutonium, uranium plus fission products, protoactinium, and short-lived fission products obtained from the cyclotron and the Clinton Pile were administered to rats. A Zr^{89} aerosol was administered to one human subject and to rats. Aerosols of the above elements were almost totally retained by the head and lungs immediately after exposure. After four days the lungs contained the largest percentage of these elements. The elements deposited in the head were quickly eliminated via the gastro-intestinal tract. The same avenue of elimination was used by the lungs, but at a slower rate. The small percentage absorbed into the body was primarily deposited in the skeleton after conditions of equilibrium had been established. Radioautographic studies indicate that the site of deposition in the lungs of these materials is in the bronchial passages and the alveolar structures. They are rapidly removed from the bronchial tree, presumably by ciliary action and are very slowly released from the alveoli. No accumulation of any of the radioelements was observed in either blood vessels or lymph nodes.

Introduction: The studies presented here were undertaken to determine the distribution and fate of fissionable materials and their products in rats and in man. The work in particular deals with the metabolism of plutonium, uranium, protoactinium, and the products of nuclear fission when these elements are introduced into the lungs of rats. The elements mentioned were studied as finely divided smoke particles, produced by high temperatures, or as the finely divided nitrates of plutonium.

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General Techniques: The methods described below were used in all experiments which were designed to deposit activity in lungs of animals. With the exception of the one human study, young rats weighing between 200 and 300 grams were used in all experiments. These rats were prepared for exposure by an intraperitoneal injection of sodium pentobarbital. The dose was 40 mg. per kgm. of body weight for male rats, 30 mg. per kgm. for female rats. After the drug had taken effect, the long whiskers on the rats' noses were closely clipped. The lips were fastened together with a three-cornered stitch between the lower lip and the two halves of the upper lip. Then, glass nosepieces were cemented in place with celloidin. The mouth was also sealed at this time with celloidin to prevent any passage of air between the lips. The above procedure completely sealed off the openings of the mouth and directed the rats' respiration through a single channel. The completed preparation is illustrated in Figure 1. The animals thus prepared were then attached to the exposure chambers, which were the same as or similar to the chamber shown in Figure 2.

After exposure to aerosols containing the above mentioned elements, the rats were kept in metabolism cages so that fecal and urinary excretions could be collected separately. The animals were killed at varying times after exposure and their tissues, urine, and feces were assayed for the element being studied.

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The method of assay varied with the type of radiation produced by the element under study. The assay was accomplished as follows:

1. The animals were killed with chloroform.
2. The tissues of interest were removed by dissection and weighed.
3. Tissues were then wet or dry ashed.
4. In the case of plutonium, the animal ash was separated from the element by chemical means. These analyses were carried out by performing lanthanum fluoride precipitations of the animal ash in acid solution, or by extracting the plutonium from solutions of animal ash with thiophenyltrifluoroacetone. The exact details are given in the report covering the fate of plutonium when injected intravenously into rats and human beings. The amount of plutonium present in the samples was determined by counting its alpha emission in a linear amplifier.
5. In the case of beta and gamma emittors, the activity of the animal ash was counted directly with a Geiger-Muller counter or a Lauritzen electroscope. Corrections were then made for the absorption of activity by the animal ash present in the samples.

1119210

Figure 1

This illustration shows a rat which has been prepared for aerosol exposure, with nosepiece in place and mouth sealed with celloidin.

1119211

FIGURE I

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Figure 2

The complete aerosol exposure system is herein illustrated. The anesthetized rat is breathing oxygen, at a rate illustrated by the flow meter, along with the active aerosol produced in the electric arc.

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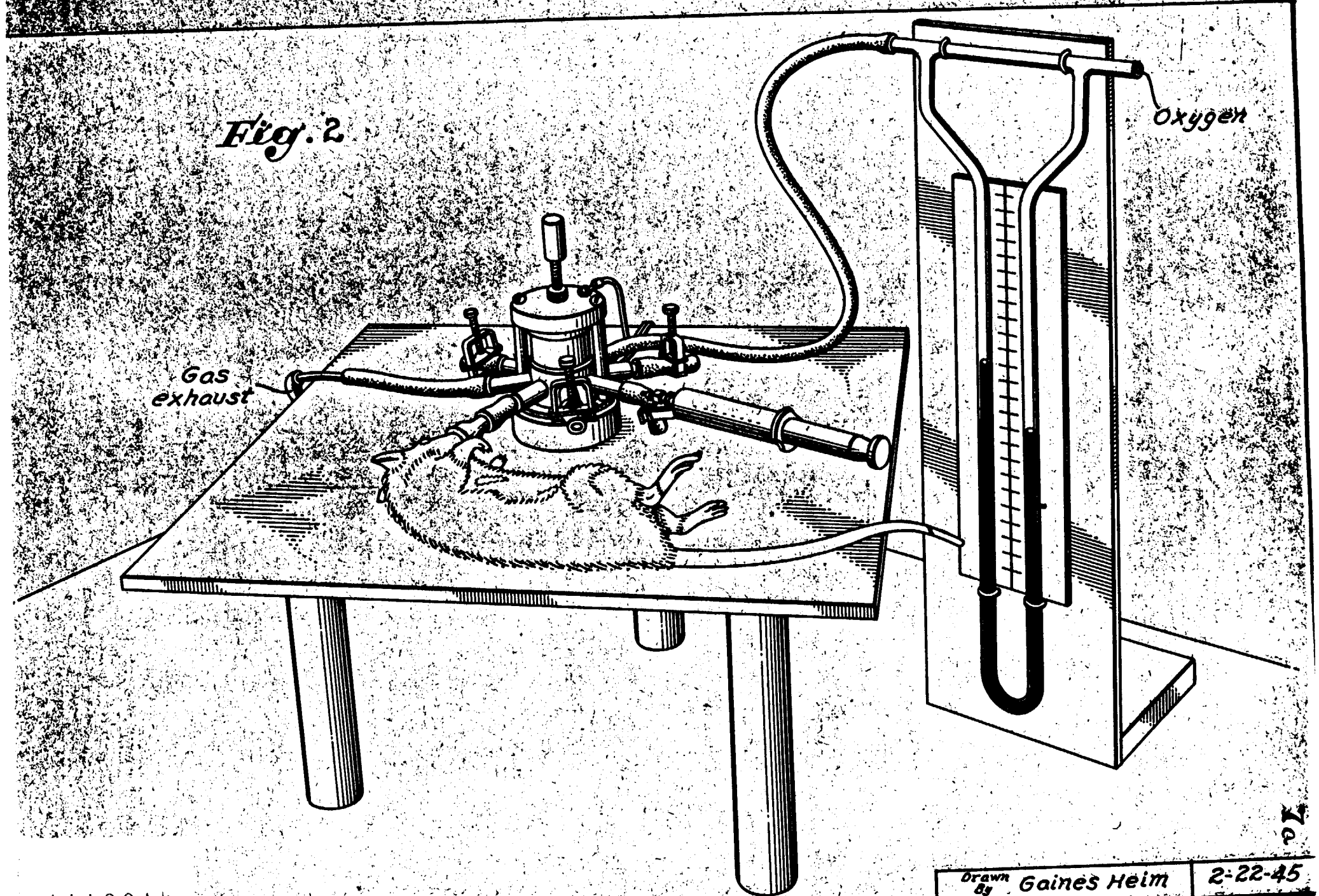

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CHAPTER I

PLUTONIUM STUDIES

1. Intrapulmonary Deposition of Plutonium as $PuO_2(NO_3)_2$

a. Element and Method:

A method for the introduction of small particles of plutonium nitrate into the lungs of rats was developed after considerable experimentation. Particles of plutonium nitrate 0.34 to 0.20 microns in diameter were produced when $PuO_2(NO_3)_2$ was dissolved in ethyl ether, carbonated with dry CO_2 gas at 760 pounds pressure per square inch, and forced through a gold jet at the above mentioned pressure into an exposure chamber. The exposure chamber was warmed to 110° F. with a heat lamp. The orifice of the gold jet was about 0.001 inches in diameter. When the ether-plutonium-CO_2 mixture was ejected from a jet of this size, all of the ether droplets evaporated immediately upon entering the exposure chamber. The dissolved CO_2 caused the small ether droplets formed by the jet to decrease their size further because of the effervescence of the CO_2 at the reduced pressure of the exposure chamber. Rats were connected to the exposure chamber shown in Figure 3, after having been prepared for exposure as described in the Introduction and General Techniques.

b. Equipment:

The quipment used in these experiments is shown in detail in Figure 3.

c. Yield:

Three to four per cent of the total amount of plutonium dissolved in the ether and later introduced into the exposure chamber

1119215

Figure 3

Figure 3 is a diagramatic sketch of the equipment used to produce aerosols of $PuO_2(NO_3)_2$. The plutonium dissolved in ether with CO_2 in the lower chamber is forced through the gold jet at 760 pounds pressure into the upper exposure chamber. As the ether evaporates in the warm chamber, the $PuO_2(NO_3)_2$ aerosol is suspended. Its droplet size is further reduced by the extreme effervescence of the CO_2 in the ether at atmospheric pressure.

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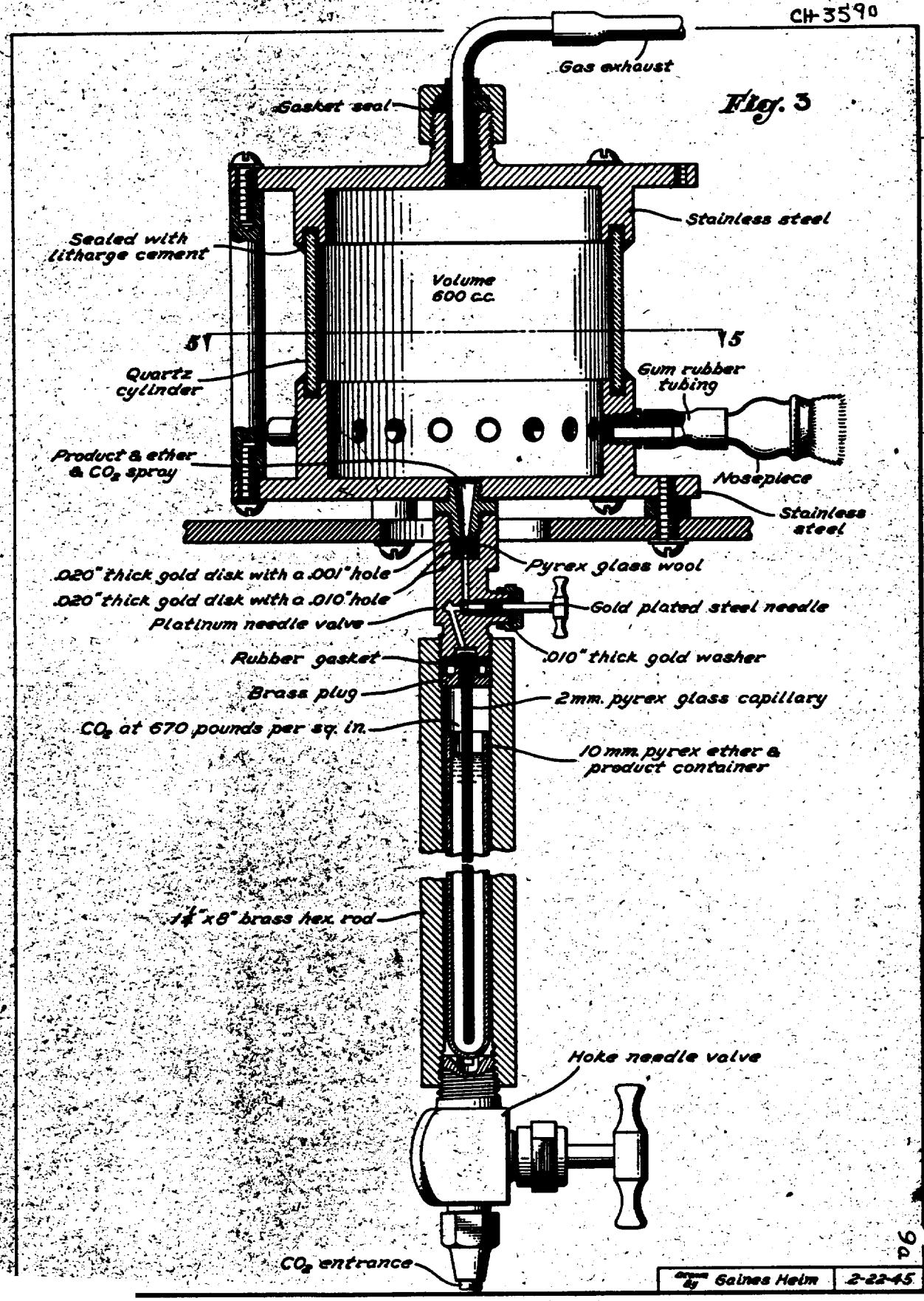

Fig. 3

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was deposited in the rats. This was sufficient activity to follow the fate of plutonium in rats for long periods of time.

d. Size of Particles:

Particles of plutonium produced with the above described ether spray were trapped on amyl acetate films and were later viewed with an electron microscope in order to determine particle size. The size was determined by placing electron microscope screens in a glass tube which was connected on one end to the exposure chamber and on the other end to a one milliliter syringe which was made to correspond to the respiratory rate and volume of the tidal air in rats. The type of particles produced are shown in Figure 4, which is representative of several sets of electron microscope screens which were exposed. Particles ranged in size from 0.6 to 0.01 microns. The average particle was 0.25 microns in diameter. It can be seen from the picture that the particles were very compact and round as contrasted to the chain-like appearance of the particles produced by burning plutonium or uranium (see Chapter II, Section 1d, 2d, and Figures 13, 16, 17, and 18). The electron microscope screens were counted for plutonium activity and were found to contain 8×10^{-4} micrograms of plutonium per square mm. of microscope film.

e. Results:

The fate of plutonium nitrate when administered to rats by the method described in Section 1a is summarized in Table I. Plutonium assays on rat tissues and excreta were performed. The

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Figure 4

Electron microscope pictures of plutonium aerosols as $PuO_2(NO_3)_2$, particle size averaging 0.28 microns, X 8000.

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FIGURE 4

1119220

TABLE I

Distribution of Plutonium in Rats When Inhaled as $P_uO_2(NO_3)_2$ Spray

	0 Time 6 Animals		1 Day 3 Animals		40 Days 6 Animals		16 Days 2 Animals		64 Days 1 Animal	
	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram
LUNGS	48.8	25.8	39.2	18.0	28.5	17.0	20.9	12.8	8.95	4.47
LIVER	0.62	0.05	.99	.07	.87	.07	.38	.03	.55	.04
KIDNEY	0.17	0.06	.11	.05	.10	.03	.13	.04	.09	.03
SPLEEN	0.02	.03	.04	.06	.03	.04	.07	.08	.08	.12
[illegible]	4.75	.20	8.00	.33	10.9	.41	6.75	.29	11.8	.44
BALANCE 1	4.21	.03	3.18	.02	3.64	.02	.83	.01	.52	<.01
G.I.	5.00	.50	13.4	.51	1.16	.04	.63	.02	.30	<.01
HEAD	37.1	1.51	4.35	.21	1.25	.05	.84	.04	.13	<.01
SKIN	1.95	.03	1.16	.02	.43	<.01	.40	<.01	.38	<.01

Daily Rate of Excretion in Per Cent

	1 Day	4 Days	16 Days	64 Days
FECES	23.2	2.82	.82	.25
URINE	.58	.04	.009	.006

1 Balance is primarily composed of muscle, but also includes any tissue residues and fat not listed in table.

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data is presented as the retention and/or excretion of plutonium in per cent of the dose for the following time periods after inhalation:

(1) Immediately after exposure, which is entitled zero time in the tables.

(2) At one day after exposure.

(3) At four days after exposure.

(4) At sixty-four days after exposure.

It can be seen by an examination of Table I that at zero time, the major part of the plutonium was deposited in lungs and the respiratory passages in the head. In addition, a proportion of the plutonium in the lungs was rapidly absorbed into the blood stream. The major part of the plutonium in the blood was withdrawn from the blood stream by the skeleton. Measurable amounts of activity were found in liver, kidney, spleen, and muscle.

One day after plutonium administration, absorption of activity from the lungs into the blood stream continued to occur but at a decreasing rate. The major part of the activity earlier deposited in the head appeared in the first day's feces collection and in the gastro-intestinal tract. In general, concentrations of plutonium in liver, kidney, and spleen approached their maximum values at this time period.

Four days after administration, the head was practically clear of plutonium. There appeared to be continued excretion of plutonium from the lungs via the bronchial tree. The data suggests that any additional passage of plutonium through the lung capillaries did not occur in large amounts.

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By the sixteenth day, the lungs had lost over 50% of the plutonium which they contained at the beginning of the experiment. The major part of this appeared to have been eliminated via the trachea and appeared in the feces. The data also suggests that the deposition of plutonium in the animal proper had reached a quasi-equilibrium among the various tissues. The only additional change noticed at sixty-four days was the continued lung elimination which at sixty-four days had removed five-sixths of the original plutonium deposited at zero time. Figure 5 represents rate of elimination of plutonium from the lungs.

The values for lung elimination of radio-elements given in Figure 5 and other lung excretion charts pertain to the activity deposited in the lung only, and not to the activity in the whole animal.

After exposure, lungs could conceivably eliminate activity via the bronchial tree or by absorption of the radio-elements into the blood stream. Since absorption is a small factor with the elements studied herein, the main avenue of lung elimination is via the bronchial tree. From the bronchial tree, the elements are swept into the gastro-intestinal tract, and, since little absorption occurs, are eliminated from the body.

During aerosol administration to lungs, large amounts of activity are deposited in the naso-pharyngeal region as well. This activity is completely swept into the gastro-intestinal tract presumably by ciliary action in the first four days after inhalation. For this reason, studies of fecal excretion will not

1119223

Figure 5

Figure 5 illustrates the elimination of plutonium from the lungs when administered as an aerosol of $PuO_2(NO_3)_2$ in ether. These values were calculated as described in Chapter I under results. It can be seen that approximately four-fifths of the plutonium is eliminated sixty-four days after administration of the aerosol.

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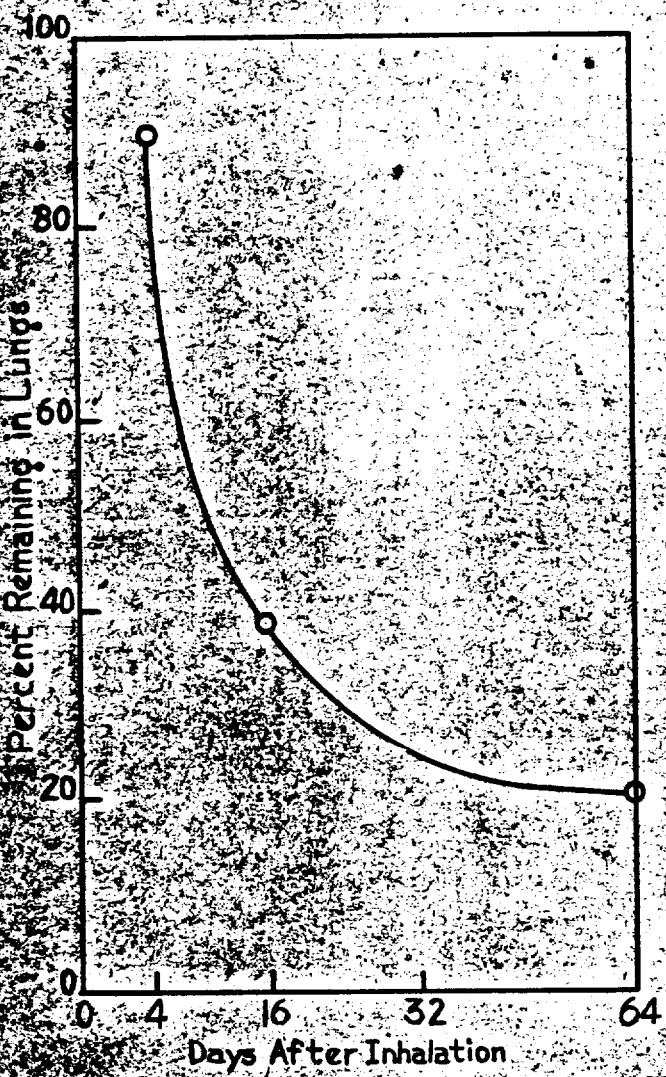
Figure 5

Lung Elimination of Plutonium Administered as $PuO_2(NO_3)_2$ in Ether Spray



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serve as an index of the lung elimination during this time interval, although radio-autographic studies show that the major portion of activity trapped in the bronchial tree is eliminated during this time.

For the above reasons, the value used for lung elimination four days after aerosol administration was calculated as follows: For example, when several groups of animals were exposed at one time, some of them were always sacrificed immediately after exposure. The total amount of the activity in the lungs of the zero time animals was considered to be the initial dose. If this value is one thousand counts per second and the four day animals had eight hundred counts per second remaining in their lungs, the four day animals were considered to have 80% of the initial dose still remaining in their lungs. The calculation of lung elimination figures after four days was more direct since the per cent remaining in the lungs was merely the percentage of the activity found in the lung, plus that occurring in the feces.

The data in Table I for three rats, suggests, therefore, that plutonium administered via the lungs was deposited primarily in the lungs and skeleton, with measurable amounts in liver, kidney, and spleen, and very small amounts in muscle and skin after conditions of equilibrium had been reached.

2. Intrapulmonary Deposition of Plutonium as PuO_2

a. Element and the Methods:

Additional aerosols of plutonium, these being plutonium oxide, were administered to rats. Small particles of plutonium

111922b

oxide were produced (1) by burning with an electric arc the chlorides or nitrates of plutonium which had previously been evaporated upon carbon electrodes from an aqueous solution, and (2) by burning metallic plutonium imbedded in carbon electrodes with an electric arc. The electrodes used with plutonium metal had been prepared for the experiment by drilling holes 0.01 inches in diameter, and 0.25 inches in depth, on the ends, and then imbedding 200 to 300 micrograms of plutonium in the holes. Rats were prepared in the same manner as in Section 1, and were allowed to breathe the gas containing the plutonium particles during the period of burning. This was done in an atmosphere of pure oxygen in order to avoid the production of undesirable amounts of carbon monoxide.

b. Equipment:

The details of the equipment used are to be found in figures 6, 7, and 8. It can be seen from an examination of these figures that two sizes of exposure chamber were employed. These were similar with the exception of volume: 65cc. in Figures 6 and 7, and 600 cc. in Figure 8.

c. Yield:

The yield of plutonium oxide to the rats, when administered by the above method, varied between 2% and 13% and was not related to the size of the exposure chamber, but more apparently was related to the respiratory rate of the rats during the few minutes of exposure time. The average yield for twelve exposures was 5.4%.

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Figures 6 and 7

Figures 6 and 7 show the details of the exposure chamber used to produce aerosols by burning the radio-element deposited on graphite electrodes in an electric arc. This was done in an atmosphere of pure oxygen in order to prevent the formation of poisonous amounts of carbon monoxide.

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Fig. 6.

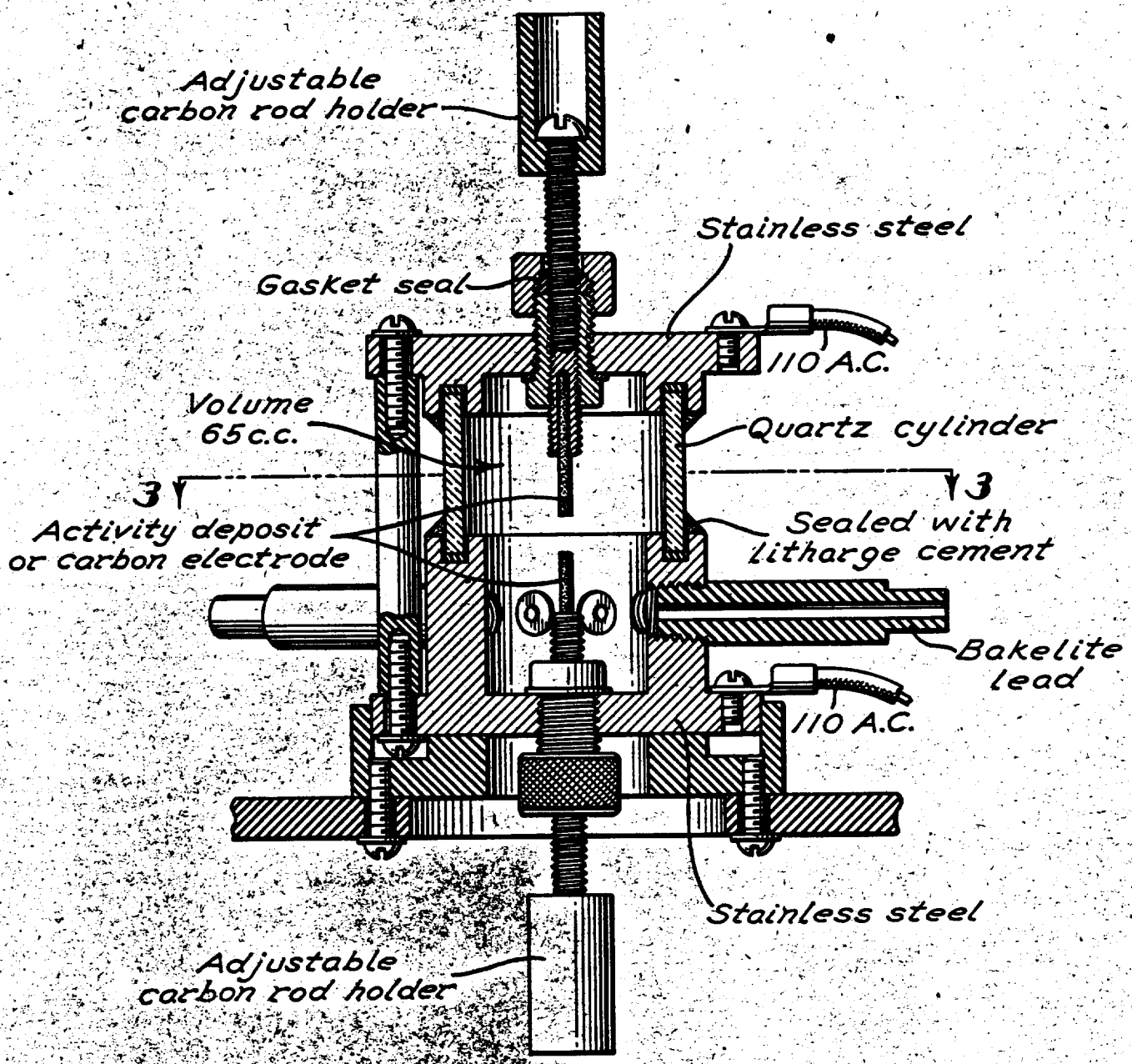

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Fig. 7.

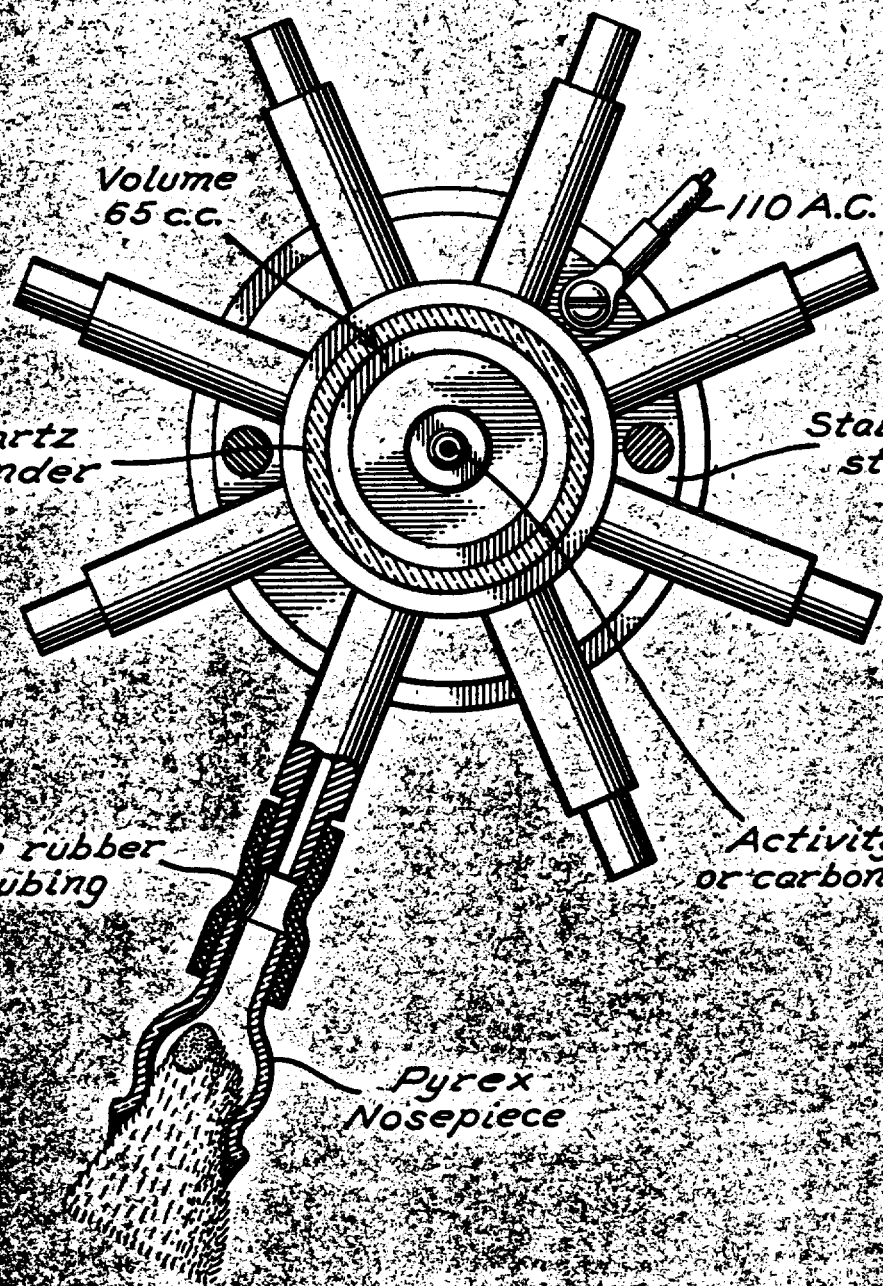

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Figure 8

Figure 8 depicts the larger type of aerosol producer. This accommodates a larger number of rats than the type shown in Figures 6 and 7.

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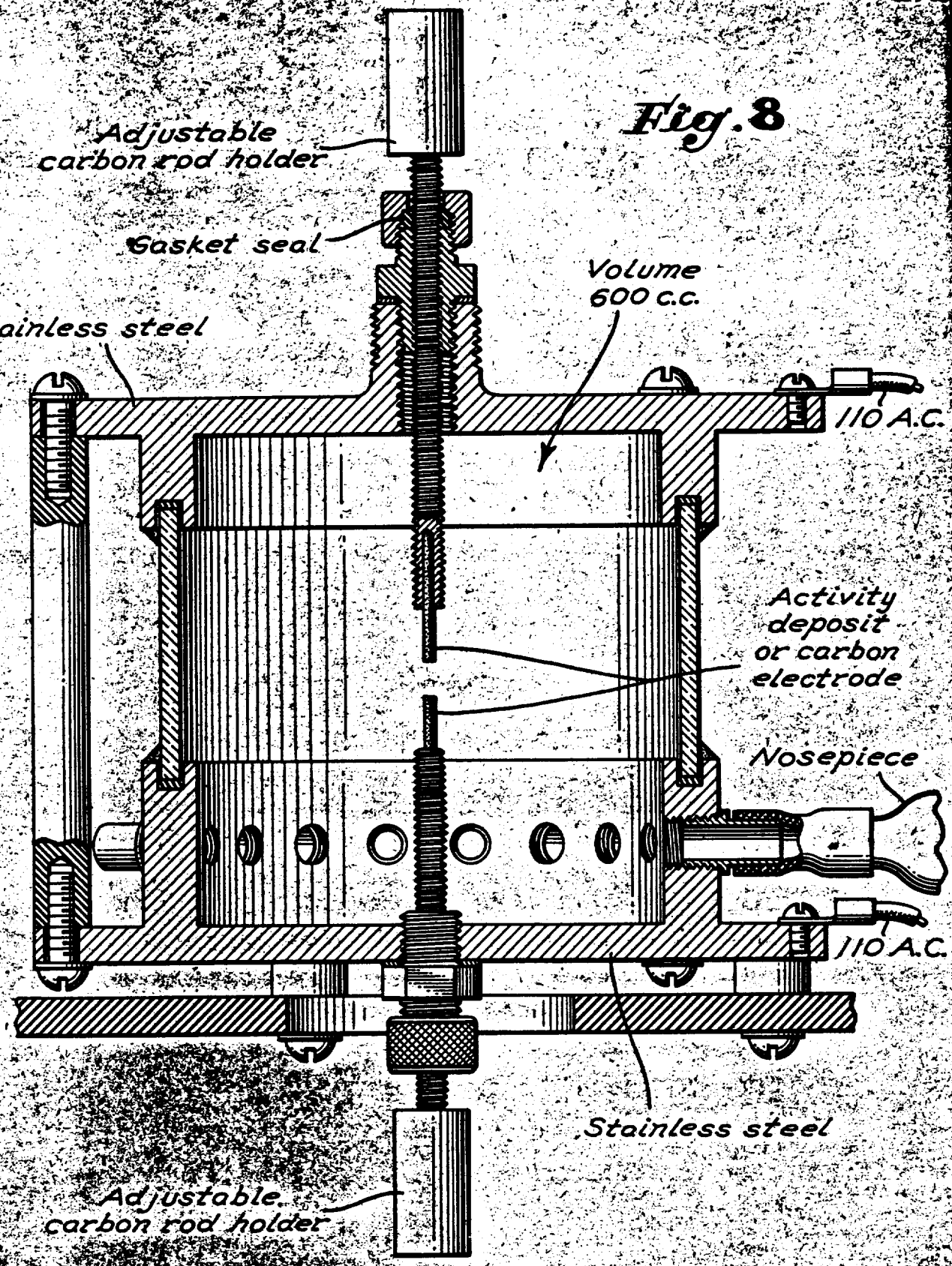

Fig. 8

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d. Size of Particles:

Aerosols produced for these studies were not collected on electron microscope screens for determining particle size. These aerosols were, however, produced under the same conditions as the aerosols of plutonium plus fission products which were collected on screens during burning and were measured. Figure 13 shows these particles which varied in size between 0.06 and 38 microns in diameter. The average size was 0.49 microns in diameter.

e. Results:

Sixty-three rats were exposed to plutonium oxide smokes as described above and sacrificed at periods from zero time, one day, four days, sixteen days, sixty-four days and two hundred fifty-six days. The plutonium content of their tissues and excreta was determined with the following results: (See Tables II and III). Immediately after exposure (at zero time) most of the plutonium was deposited in the head and lungs. Measurable amounts of plutonium were detected in skeleton, and in the soft tissues at zero time.

At one day after plutonium administration, the loss of plutonium from the head was the major change. The plutonium lost from the head was found mainly in the feces and in the gastro-intestinal tract. This elimination continued, so that at four days, the respiratory passages of the head were practically free from plutonium, and any further fecal excretion appeared to come from the lungs via the bronchial tree.

Sixteen days after plutonium administration, equilibrium appeared to have been reached with respect to the absorbed plu-

1119233

TABLE II

Distribution of Plutonium in Rats When Inhaled as PuO_2 Aerosol

Prepared by Burning the Chlorides and Nitrates of Plutonium in Carbon

	0 Time 7 Animals		4 Days 5 Animals		16 Days 12 Animals		16 Days 4 Animals	
	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram
LUNGS	37.5	16.3	42.1	31.8	19.7	12.2	11.4	5.2
LIVER	.27	.03	.07	.01	.11	.01	.03	.01*
KIDNEY	Not Taken		.01	.01*	.01*	.01*	.01	.01*
SKELETON	1.13	.04	.42	.02	.38	.02	.38	.02
BALANCE [1]	2.30	.01	1.38	.01	.35	.01*	.01	.01*
G.I.	.71	.03	2.50	.20	.60	.03	.08	.01*
HEAD	5.82	2.80	3.19	.13	.30	.02	.13	.01

Daily Rate of Excretion in Per Cent

	1 Day	4 Days	16 Days	64 Days
FECES	20.7	6.7	1.4	.02
URINE	2.5	.12	.04	<.001

1. Balance is primarily composed of muscle, but also includes any tissue residues and fat not listed in table.

* Value measured was less than 0.01% of the total activity in animal.

1119234

TABLE III

Distribution of Plutonium in Rats When Inhaled as PuO_2 Aerosol

Prepared by Burning Plutonium Metal with Carbon

	0 Time 8 Animals		1 Day 7 Animals		4 Days 4 Animals		16 Days 7 Animals		64 Days 5 Animals		256 Days 2 Animals	
	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram
LUNGS	34.2	20.8	35.5	16.3	27.7	18.4	29.3	14.7	12.2	7.3	4.8	1.6
LIVER	.04	.01*	.07	.01*	.02	.01*	.05	.01*	.03	.01*	.03	.01*
KIDNEY	.01*	.01*	.01*	.01*	.01*	.01*	.01*	.01*	.01*	.01*	.01*	.01*
SPLEEN	Not Taken		--	--	--	--	--	--	--	--	.01*	.01*
SKELETON	1.17	.10	3.40	.29	.92	.06	.75	.04	1.5	.08	.15	.01*
BALANCE [1]	1.53	.01	2.57	.03	.68	.01*	.54	.01*	.20	.01*	.02	.01*
G.I.	2.07	.09	23.5	1.1	1.17	.06	.46	.01	.16	.01*	.02	.01*
HEAD	59.3	3.93	13.3	.72	.24	.02	.24	.02	.52	.04	.01*	.01*
SKIN							.10	.01*	.03	.01*	.01*	<.001

Daily Rate of Excretion in Per Cent

	1 Day	4 Days	16 Days	64 Days	256 Days
URINE	3.3	.13	.05	.01*	.01*
FECES	25.2	6.3	.99	.24	.01*

1. Balance is primarily composed of muscle, but also includes any tissue residues and fat not listed in table.

* Value measured was less than 0.01% of the total activity in animal.

1119235

TABLE IV

Distribution of Plutonium in Rats When Inhaled as PuO_2 Aerosol

Prepared by Burning Plutonium Plus Fission Products on Carbon

	0 Hours 4 Animals		4 Days 3 Animals		16 Days 3 Animals		64 Days 3 Animals		128 Days 2 Animals	
	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram
LUNGS	40.5	9.60	61.2	15.3	16.4	4.67	8.38	1.69	15.3	8.51
LIVER	.07	*	0.22	.02	.04	*	*	*	*	*
KIDNEY	.04	.01	.15	.05	.04	.01	*	*	*	*
SPLEEN	.04	.05	.13	.15	.02	.02	*	*	*	.01
SKELETON	2.12	.07	1.8	.07	2.0	.07	*	*	.01	*
BALANCE [1]	4.4	.01	1.4	*	.35	*	*	*	.04	*
G.I.	21.0	3.78	6.04	.24	.54	.02	.09	*	.03	*
HEAD	35.6	1.2	2.4	.08	.30	.01	.18	*	.08	*
SKIN					.08	*	*	*	*	*

Daily Rate of Excretion in Per Cent

	1 Day	4 Days	16 Days	64 Days	128 Day	256 Day
URINE	1.55	.27	.02	*	*	*
FECES	17.7	.26	.28	.18	.05	

1. Balance is primarily composed of muscle, but also includes any tissue residues and fat not listed in table.

* Value measured was less than 0.01% of the total activity in animal.

1119236

tonium in the soft tissues and in the skeleton. Skeleton contains the greatest concentration of plutonium, whereas liver, kidney, and spleen contained relatively more plutonium than the soft tissues of the head, the balance, and the skin.

At sixty-four days, one-half of the plutonium remaining in the lungs at sixteen days had been excreted. This excretion continued at decreasing rates. However, it was still a measurable value at two hundred fifty-six days, at which time the lungs contained approximately one-ninth of the plutonium originally deposited in them. Figures 9 and 10 demonstrate the rate of elimination of this plutonium from the lungs.

3. Quantitative Studies on the Fraction of Inhaled Plutonium Oxide Retained by Rats

a. and b. Element, Method, and Equipment:

A series of experiments was undertaken in an attempt to ascertain what proportion of inhaled PuO_2 smoke was retained in rats. A valve system (diagrammed in Figure 11) had been developed which made it possible to determine on a quantitative basis the proportion of inhaled plutonium which was retained. The capillaries in the valve were filled with mineral oil, and the nose piece was attached to the animal in the usual manner as described in the Introduction and the General Techniques. The exhaust (exhalation) outlet side of the system had a small glass-wool plug inserted to entrap the exhaled activity. In addition, this outlet was connected to a large flask to catch any plutonium that might not have been adsorbed on the glass-wool.

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Figure 9

Figure 9 represents plutonium elimination by the lungs of rats after exposure to aerosols produced by burning plutonium chlorides or nitrates in an electric arc. It can be seen that approximately four-fifths of the administered dose has been eliminated after sixty-four days.

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Figure 9

Lung Elimination of Plutonium following Inhalation of Plutonium Oxide Prepared by Burning the Chlorides and Nitrates of Plutonium

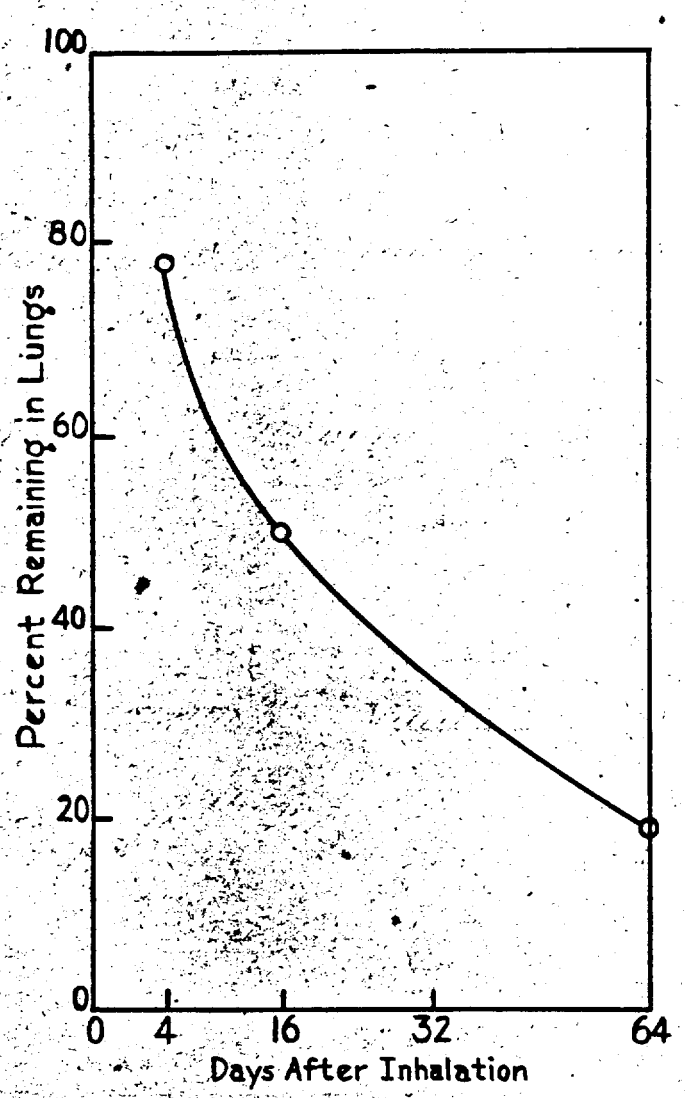

Figure 10

Figure 10 represents the rate of plutonium elimination from the lungs after the administration of plutonium oxide aerosols produced by burning metallic plutonium imbedded in carbon electrodes with an electric arc. As in Figure 9, Figure 10 shows that about four-fifths of the plutonium is eliminated in sixty-four days. About nine-tenths is eliminated in 256 days after aerosol administration.

1119240

Figure 10

Lung Elimination of Plutonium Following Inhalation of Plutonium Oxide Prepared by Burning Metallic Plutonium

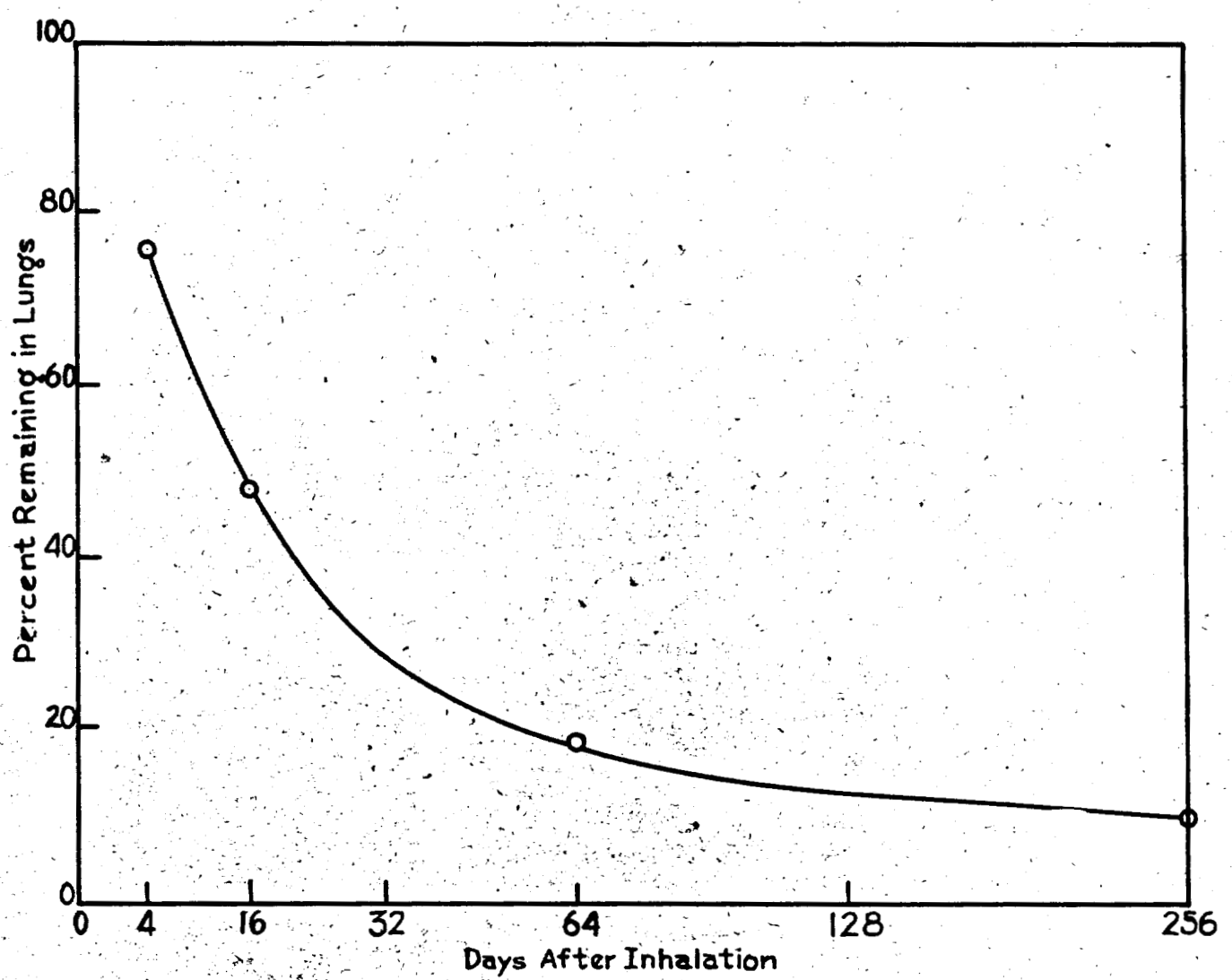

Figure 11

Figure 11 illustrates the construction and operation of the one way trap used to determine the amount of aerosol retained by the rat in one inspiration and expiration. The aerosol enters through opening 1 and is pulled through oil trap 2 into space 3 which is connected to the rat's nose. Upon exhalation, trap 2 prevents the escape of the aerosol in that direction so that the expired aerosol leaves the system via oil trap 4 which leads to exit 5. The aerosol is caught in the glass-wool filter at 6.

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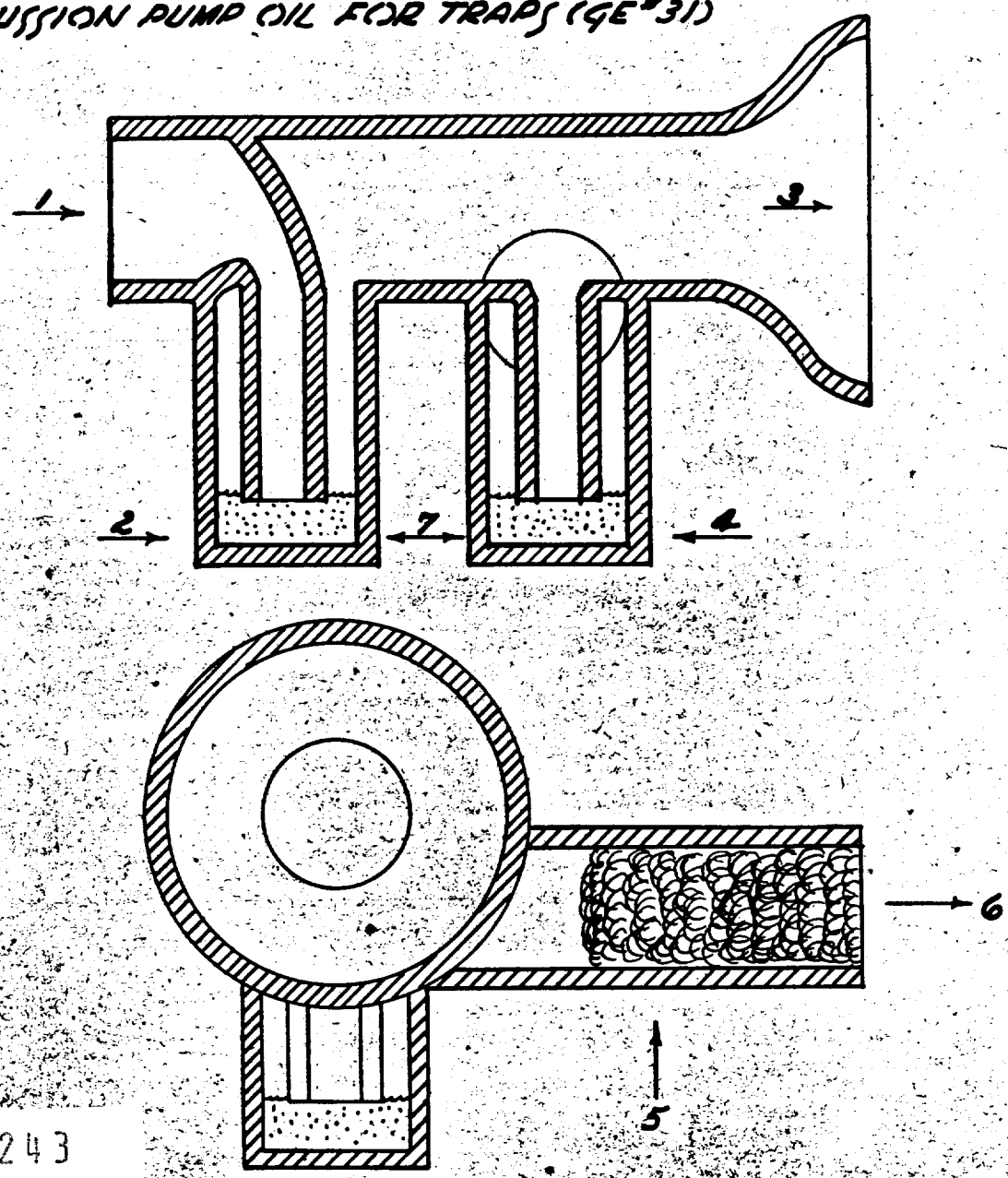
ONE WAY VALVE FOR RAT RESPIRATION STUDIES

FOUR TIMES ACTUAL SIZE

1. SMOKE ENTRANCE
2. INLET TRAP
3. RAT NOSE CONNECTOR
4. OUTLET TRAP
5. OUTLET TUBE. LOCATION OF E.M. SCREENS
6. GLASS WOOL FILTER (PYREX)
7. DIFFUSSION PUMP OIL FOR TRAPS (GE #31)



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c. Size of Particles:

Photomicrographs taken with the aid of the electron microscope of the PuO_2 smoke in the exhaled air (see Figure 11 for position of collecting screens) revealed particle sizes ranging from 0.1 to 1.0 micron in diameter. Figure 12 shows particle size.

d. Results:

The plutonium in this portion of the exhaust system together with the small quantity in the nose piece, exhaust valve, and the short length of tubing connecting the two valves was considered to represent the exhaled PuO_2 smoke. The plutonium in the animal plus that which was exhaled, as noted above, was considered to represent the total amount inhaled. On this basis, with a group of four animals exposed to PuO_2 smoke produced by burning plutonium metal in a carbon arc, the following values were observed:

The Distribution of PuO_2 Smoke in the Rat Immediately After Exposure on the Basis of the Amount of Plutonium Inhaled

	Rat #1	Rat #2	Rat #3	Rat #4
Lungs	12.7%	23.2%	29.0%	9.32%
Head	50.7%	53.8%	58.6%	57.2%
Exhaled	36.6%		12.4%	33.5%
Total Retained by the animal	63.4%		87.6%	66.5%

It can be seen from these results that in the rat approximately 75% of the inhaled PuO_2 smoke was retained in the animal. Also, it must be kept in mind that all of the material in the upper respiratory tract (head) was rapidly removed by ciliary action, then

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Figure 12

Figure 12 is an electron microscope picture of plutonium oxide aerosols exhaled by rats (X 8000).

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FIGURE 12

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swallowed and eliminated by way of the digestive tract without having been absorbed. The volume of the dead space between the intake valve and the nose of the rat was approximately 0.2 cc. This was of the order of 20% of the volume of air moved through the system with each respiration. Hence, the factor of error introduced by re-breathing did not appear to be significant.

1119247

CHAPTER II

STUDIES ON FISSION PRODUCTS

1. Aerosols of Plutonium Plus Fission Products

a. Element and the Method:

Carbon rods containing imbedded Plutonium metal were bombarded with slow neutrons in the heavy water pile at Argonne for a period approximating one month. The fission products thus formed were then dispersed as aerosols along with the plutonium in an electric arc and administered to rats by the methods described in Chapter I, Section 2a. The fission products were approximately four months old when these studies were initiated.

b. Equipment:

The equipment used was the same as that employed for the plutonium oxide smokes, as described in Chapter I, Section 2b. (See Figures 6, 7, and 8.) The fission products which were available in this mixture were mainly the long-life elements resulting from plutonium fission.

c. Yield:

The yield of both plutonium and fission products in the rat was high enough to follow animals for one hundred twenty-eight days. The yields were similar to those in the plutonium oxide experiments of Chapter I, Section 2.

d. Size of Particles:

The particles resulting from the combustion of these carbon-plutonium rods were trapped upon amyl acetate films and

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electron microscope pictures were taken of them. Of several screens studied, it was found that the range in particle size varied between 0.06 and 38 microns in diameter. The average particle size was 0.49 microns in diameter. In addition, the screens were checked for radio-activity and were found to contain 1.5×10^{-4} micrograms of plutonium per square millimeter of electron microscope screen, and 1.6×10^{-6} microcuries of activity from fission products per square millimeter. The type of particle observed when aerosols of plutonium are made by this method is shown in Figure 13.

e. Results:

The data obtained on the pulmonary administration of plutonium produced by burning the metal with carbon electrodes is summarized in Table IV. The results were similar in most respects to the data obtained by burning plutonium metal, as described in Chapter 1, with the exception of lower skeletal deposition at sixty-four and one hundred twenty-eight days. The rate of lung elimination is represented in Figure 14.

A comparison of the distribution of fission products in rats after pulmonary administration of aerosols containing plutonium plus fission products is summarized on Table V. It can be seen from an examination of Table V that the major portion of the fission products was deposited in lung and head at zero time. Measurable amounts of activity were also found in the skeleton, the liver, the kidney, and the spleen.

The fission products deposited in the head were cleared out during the first four days after aerosol administration, and appeared in the excreta.

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Figure 13

Figure 13 depicts plutonium aerosols as PuO_2 produced by burning plutonium metal with graphite electrodes in an electric arc.(x3000)

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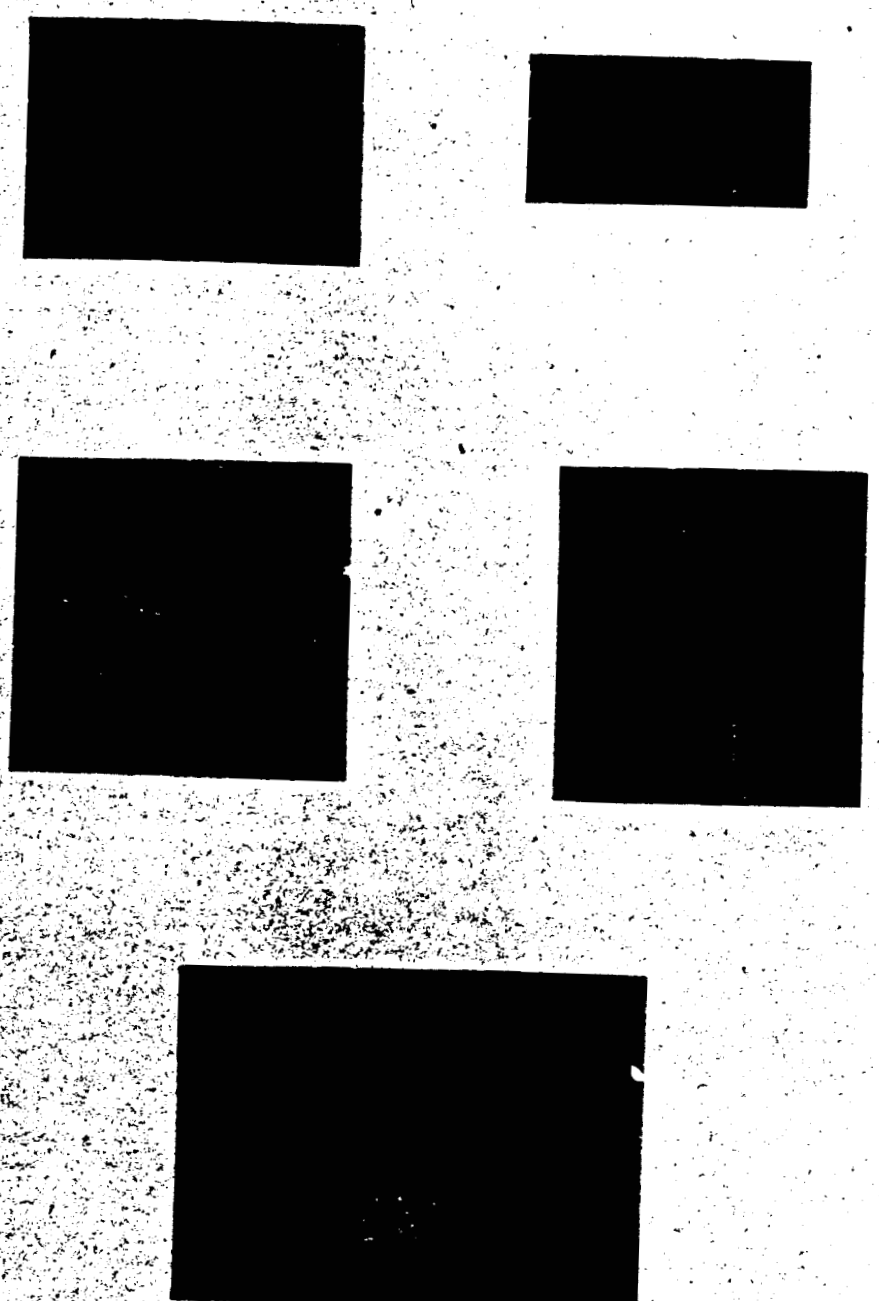

FIGURE 13

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Figure 14

Figure 14 represents the rate of plutonium elimination from the lungs of rats following administration of aerosols of plutonium with its fission products. It can be seen that about two-thirds of the plutonium has been eliminated one hundred twenty-eight days after exposure.

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Figure 14

Lung Elimination of Plutonium Prepared by Burning Plutonium and its Fission Products

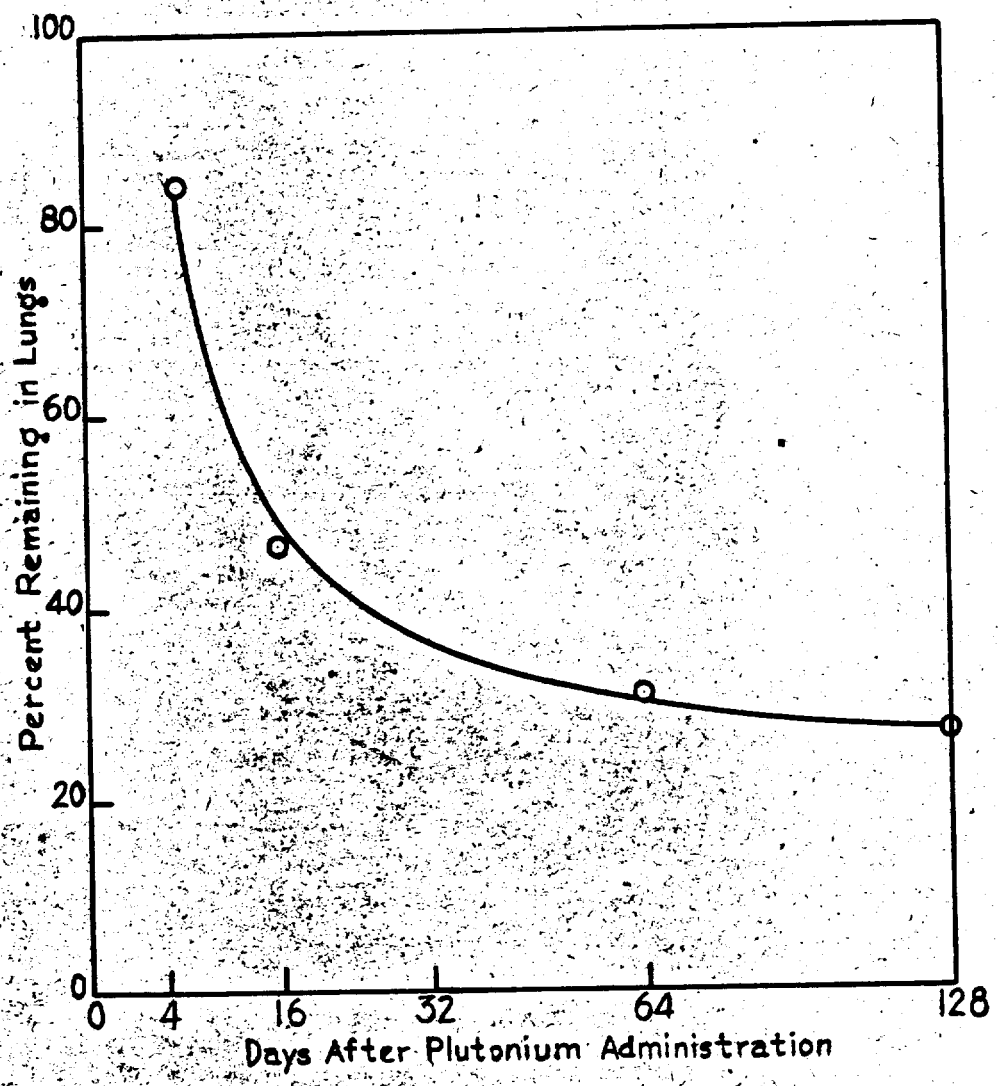

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TABLE V

Distribution of Fission Product Aerosols When Inhaled by Rats

Prepared by Burning Plutonium Plus Its Fission Products on Carbon

	0 Hours 4 Animals		4 Days 3 Animals		16 Days 3 Animals		64 Days 3 Animals		128 Days 2 Animals		256 Days 3 Animals	
	% per Organ[1]	% per Gram[1]	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram
LUNGS	43.0	10.6	56.2	14.5	17.0	4.83	8.84	2.12	8.82	4.90	2.3	.27
LIVER	.37	.03	.20	.05	.04	*	.03	*	.04	*	.08	*
KIDNEY	.26	.54	.19	.05	.04	.01	.02	*	.03	*	.03	*
SPLEEN	.02	.03	.05	.05	.02	.02	.01	.02	.02	.03	.01	.02
SKELETON	2.7	.10	6.9	.26	2.10	.08	.26	*	.42	.02	.17	*
BALANCE[2]	1.9	.01	2.0	.01	.36	*	.13	*	.23	*	.10	*
G.I.	18.4	.69	5.3	.15	.55	.02	.09	.01	.09	*	.03	*
HEAD*[3]	40.1	1.25	2.4	.08	.29	.01	.14	*	.30	*	.05	*
SKIN	Not included due to Surface Contamination				.08	*	.06	*	.06	*	.02	*

Daily Rate of Excretion in Per Cent

	1 Day	4 Days	16 Days	32 Days	64 Days	128 Days	256 Days
URINE	2.56	0.18	0.07	.04	.01	.02	.02
FECES	20.4	3.58	.84	.34	.18	.07	.02

1. Wet weights of tissues.
2. Balance is primarily composed of muscle, but also includes any tissue residues and fat not listed in table.
3. Activity excluding that deposited in bone.

* Value measured was less than .01% of the total activity in animal.

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The fission products deposited in the lungs were not rapidly removed but appeared to be excreted slowly via the bronchial tree, so that at sixteen days, approximately two-thirds of the activity had been eliminated. Relatively little of these elements was absorbed via either the lung capillaries or the gastro-intestinal tract, as deposition values of skeleton, liver, and kidney did not increase as the experiment progressed, but tended to decrease.

Lung elimination of fission products continued for the duration of the experiment which, in this case, was two hundred fifty-six days. At this point, but one-twentieth of the fission products originally deposited remained in the lungs. (See Figure 15.)

2. Aerosols of Fission Products from Uranium Metals

a. The Element and the Method:

Uranium wire containing fission products was used for aerosol studies after it had been exposed to slow neutrons in the Clinton Pile. At the beginning of the animal exposures, the uranium contained 6.8 microcuries of fission product activity per milligram of uranium. These fission products were approximately two months old when these studies were initiated. The wire was 0.020 inches in diameter and the total weight of uranium burned in each experiment was 0.048 grams. It was found that uranium was extremely pyroforic in an atmosphere of pure oxygen. When an electric arc was struck between two carbon electrodes (110 A.C., 440 ohms resistance) in which lengths of uranium wire had been inserted, the uranium burned completely and rapidly.

1119255

Figure 15

Figure 15 demonstrates lung administration of fission products of plutonium following administration of aerosols of the oxide of plutonium plus its fission products. Comparison of figures 14 and 15 shows that the persistence time of the fission-products fraction in the lungs is less than the persistence time of the plutonium fraction of the aerosol.

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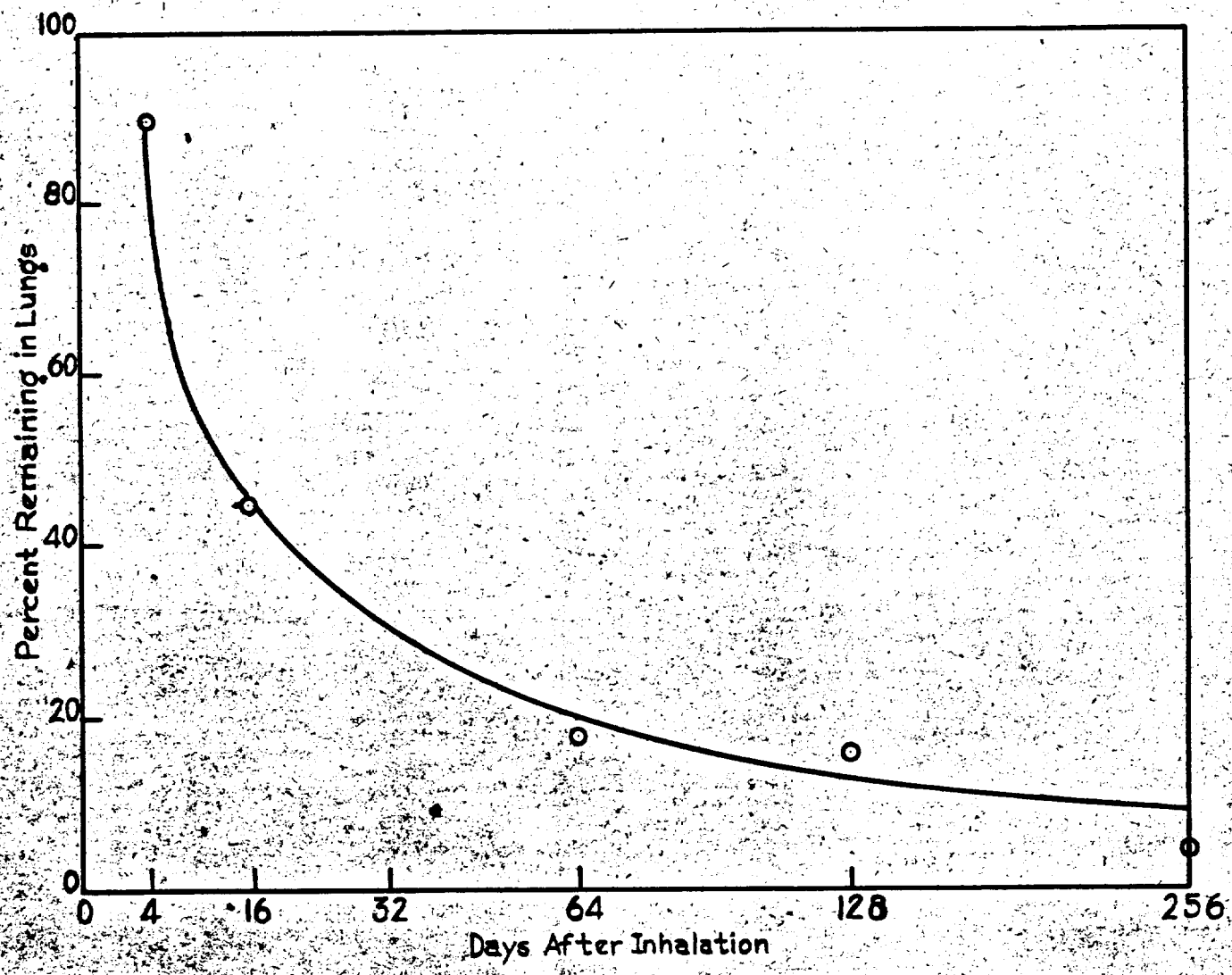
Figure 15

Lung Elimination of Fission Products Prepared by Burning Plutonium plus its Fission Products



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b. Equipment:

All of the exposures were carried out in the chamber described in Figure 8. The other details of the experiment were exactly the same as those described in Chapter I, Section 2b.

c. Yield:

In three separate exposures 13.8%, 13.1% and 14.6% of the total fission products activity were deposited in the rats.

d. Size of Particles:

Uranium fission product aerosols were collected upon electron microscope films; (See Figures 16, 17, and 18). Very diffuse, chain-like structures were formed when the uranium was burned, making it rather difficult to determine the exact particle size. Estimations of particle size varied between 0.06 and 9.4 microns, the average size being 0.97 microns.

e. Results:

Animal studies of uranium-fission products aerosols were carried out for sixty-four days and the average values are summarized on Table VI. It can be seen that these relatively larger particles, as compared to PuO_2 smokes, were trapped primarily in the respiratory passages of the head of rats, resulting in a relatively low lung deposition at zero time. In addition to lung and head deposition, small amounts of activity from fission products were found in the skeleton and in the soft tissues of the rats.

One day after exposure, the head was practically free of fission products. Further absorption of fission products appeared to have taken place, since the total percentage of fission products in the body was greater at one day than at zero time.

1119258

Figure 16

Figure 16 illustrates aerosols produced by burning uranium wire containing fission products. The fission products were produced by exposing the uranium wire to slow neutrons in the Clinton Pile. Lengths of the uranium wire plus its fission products were inserted in two carbon electrodes. An electric arc was struck between the electrodes to produce the aerosol. (X 40,000).

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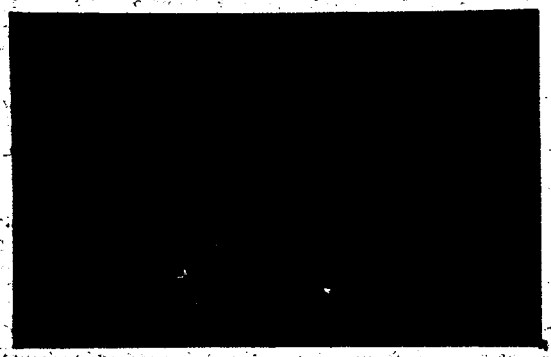

FIGURE 16

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Figure 17

Figure 17 depicts aerosols prepared by burning uranium metal plus fission products in graphite electrodes in an atmosphere of oxygen. (X 8000).

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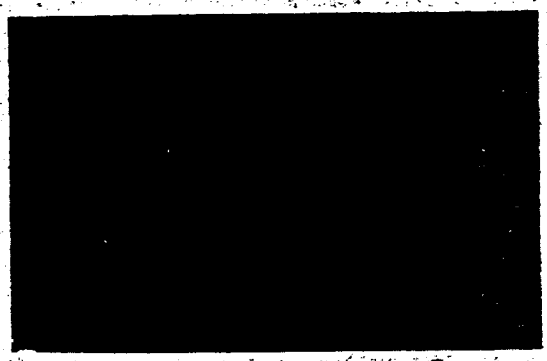

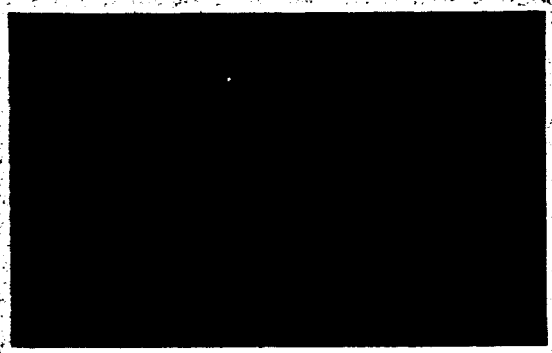

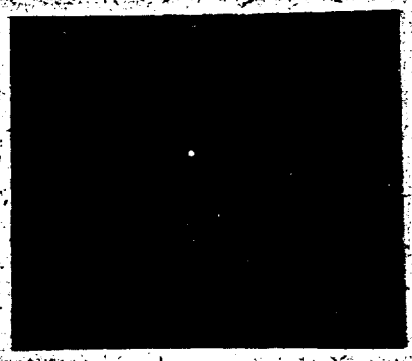

FIGURE 17

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Fig. 14

Figure 14 represents samples of uranium [illegible] in burning metal and fission products with graphite as [illegible]

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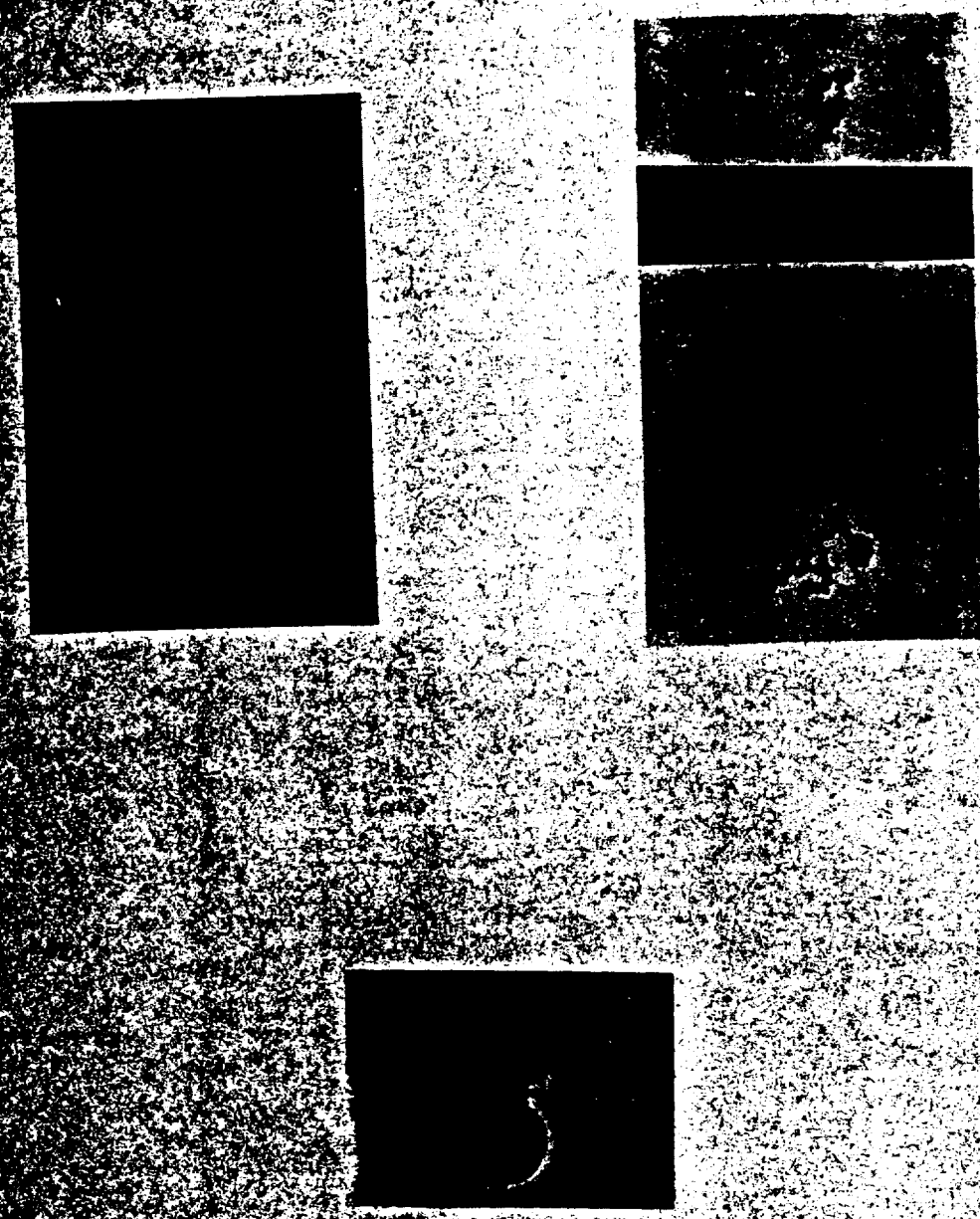

FIGURE 18

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By the fourth day, over 90% of the fission products deposited in the rats had been eliminated, primarily via the gastro-intestinal tract. The maximum values for skeletal deposition were obtained at this time.

Fission products deposited in the lungs were eliminated via the bronchioles and trachea, so at sixteen days after exposure almost half of the fission products had been disposed of and were found in the feces. The fission products remaining in the body at sixteen days were less than those found at four days.

This suggests that the body is capable of excreting some portion of the fission products rather rapidly. Sixty-four days after fission products administration, the lungs had lost two-thirds of their activity either by capillary absorption or by excretion via the bronchial tree. (See Figure 19). In addition, considerable excretion of fission products from the body was observed. Skeletal deposition was approximately one-half of what it had been at four days. Loss of fission products by soft tissues at sixty-four days proved to be even greater than that from skeleton. (See Table VI.)

3. Carrier-free Fission Products

a. and b. Element, Method, and Equipment:

Aerosols containing carrier-free fission products were prepared by burning them on carbon in an electric arc and were deposited in rats using the technique described in Chapter I, Section 2a. The carrier-free fission products represented the long-lived fraction of elements resulting from uranium fission in the pile at Clinton Laboratory six months prior to this study. This material was obtained

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TABLE VI

Distribution of Fission Product Aerosols in Rats

Prepared by Burning Uranium Plus Fission Products in an Electric Arc

	0 Time 7 Animals		1 Day 4 Animals		4 Days 5 Animals		16 Days 5 Animals		64 Days 7 Animals	
	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram
LUNGS	11.61	6.53	9.76	6.40	5.23	2.87	7.31	3.61	4.27	2.48
LIVER	.10	.01	.08	.01	.06	.01	.07	*	.02	*
KIDNEY	.05	.03	.03	.02	.02	.01	.02	*	*	*
SPLEEN	Not	Taken	--	--	--	--	--	--	--	--
SKELETON	.43	.03	1.44	.11	1.93	.08	1.34	.07	.93	.04
MUSCLE	1.40	.01	2.46	.01	.67	*	.47	*	.19	*
G.I.	1.05	.01	33.94	1.52	1.14	.05	.15	*	.04	*
HEAD	82.3	3.97	6.59	.43	*	*	.05	*	.08	*
SKIN							[illegible]	*	.02	*

Daily Rate of Excretion in Per Cent

	1 Day	4 Days	16 Days	64 Days
URINE	3.58	.31	0.07	*
FECES	30.3	3.3	.46	.07

* Value measured was less than .01% of the total activity in animal.

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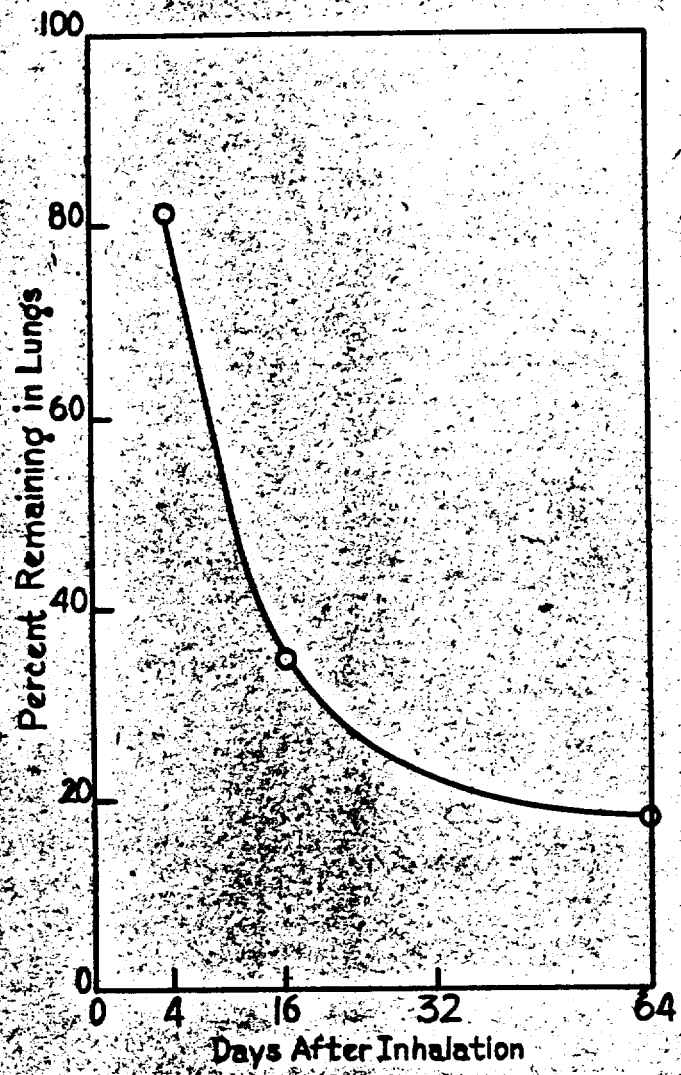
Figure 19

Figure 19 represents the elimination of fission products from the lungs of rats for a period of time four to sixty-four days after inhalation. The per cent remaining at four days is 82% of the initial dose. The initial dose is the amount of fission products found in the lungs of rats sacrificed immediately after inhalation. After sixty-four days, approximately four-fifths of the total fission products inhaled has left the lungs, and is found primarily in the excreta.

1119267

Figure 19

Lung Elimination of Fission Products
After Inhalation of Aerosols of
Uranium Oxide plus Fission Products



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from Clinton in diluted acid and was free from uranium and inert carriers. It was evaporated upon carbon electrodes by the use of an infra-red lamp. The electrodes were subsequently burned in an electric arc in the exposure chamber to produce the aerosols.

c. Size of Particles:

Electron microscope pictures of the carrier-free fission product aerosol showed that the particles produced were from five to one-tenth microns in diameter with an average size of .63 microns. (See Figure 20). These particles were primarily carbon. There was no obvious relation between the apparent number of particles and the particle activity when the electron microscope screens were assayed for fission product activity. Since the fission products themselves were not intimately bound up with the carbon originally as was the case with fission product plus plutonium and uranium, it seems very unlikely that they were transferred to the rats solely on the carbon particles. It is suggested, then, that a part of the fission products retained by the rats were of a particle size smaller than the range of the electron microscope.

d. Results:

Two groups of animals were exposed to fission product aerosols prepared in the above manner. The results are summarized in Table VII. It can be seen from an examination of the zero time exposures that there was great variation in relative percentages of fission products deposited in lungs versus the head. In the first exposure, 22% of the activity was found in the lungs and 50%

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Figure 20

Aerosols of carrier-free fission products evaporated on graphite rods and burned in an electric arc. (X 8000).

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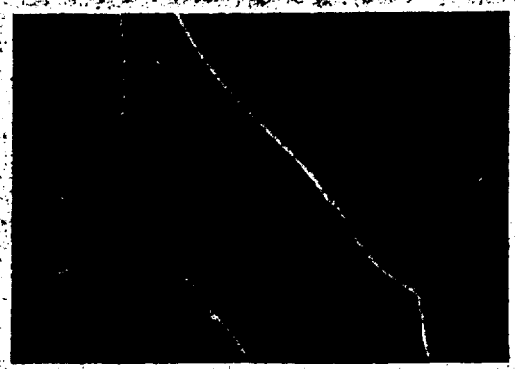

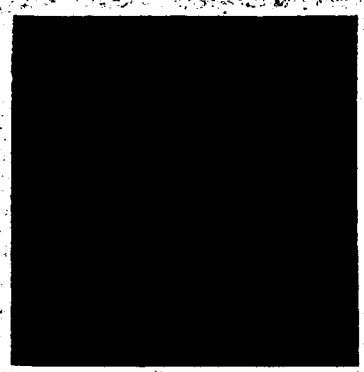

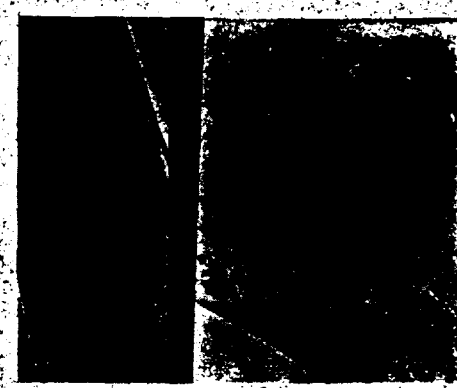

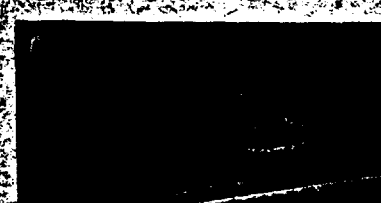

FIGURE 20

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in the head. (See Table VII, Animal Group A). In the second exposure, 65% was found in the lungs and but 15% in the head. (See Table VII, Animal Group B). Such a difference in the location of fission product retention makes consideration of the trends of movement of fission products at later dates difficult. Thus, it can be seen that at four days the animals taken from Group A contained 14% of the total fission products in their lungs, whereas at sixteen days animals taken from Group B contained 25%. If the early deposition in the head is discarded, the lung values obtained from the two different exposures are more comparable.

In general, however, about 10% of the fission product aerosols prepared in the above mentioned manner found their way into the body tissues quite readily. It can be seen that there were measurable amounts in all of the tissues at zero time. The retention of fission products by skeleton increased during the entire sixty-four days of the experiment.

Liver and kidney took up increasing amounts of fission products for the first sixteen days after exposure to fission product aerosols. The primary avenue of elimination of fission products in these studies was via the feces. The feces contained at least ten times as much fission products as was found in the urine, from the sixteenth day to the sixty-fourth day of the experiment. The data also shows that lungs were again able to eliminate the major portion of the fission products deposited in them originally by excretion via the bronchial tree and by entrance of the activity into the blood stream

1119272

TABLE VII

Distribution of Carrier-Free Fission Product Aerosols in Rats

When Burned on Carbon Electrodes

	0 Time[1] 3 Animals		0 Time[2] 2 Animals		4 Days[1] 3 Animals		16 Days[2] 2 Animals		64 Days[2] 2 Animals	
	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram
LUNGS	22.44	13.44	65.4	36.3	14.4	8.18	25.4	12.7	5.68	294
LIVER	.10	*	.13	.01	.30	.02	1.62	.12	.46	.03
KIDNEY	.11	.04	.11	.04	.09	.03	.30	.17	.29	.07
SPLEEN			.12	.17	.01	.02	.02	.02	.02	.02
SKELETON	1.77	.08	1.55	.06	2.3	.10	6.44	.27	6.71	.24
MUSCLE	4.26	.03	1.06	*	.93	*	.82	*	.50	*
G.I.	3.77	.15	12.9	.43	.81	.02	.60	.02	.20	*
HEAD	50.8	2.38	15.4	.70	.61	.04	*	*	*	*
SKIN	17.3	.34	3.38	.06	4.63	.09	.27	*	.37	*

Daily Rate of Excretion in Per Cent

	1 Day	4 Days	16 Days	64 Days
FECES	29.3	3.30	0.73	.20
URINE	1.12	0.60	.07	*

1 Exposure #1

2 Exposure #2

* Value measured was less than 0.01% of the total activity in animal.

1119273

through the capillary walls. Figure 21 presents rate of fission product elimination from the lungs.

4. A Preliminary Study of the Fate of Short-Lived Fission Products

A preliminary study of the fate of short-lived fission products had been conducted before the Clinton Pile was placed in operation. The purpose of this series of somewhat laborious and elaborate experiments was to evaluate the possible hazards arising from the inhalation of the short-lived, noble gas ancestors of the long-lived fission products and the subsequent deposition of the long-lived active deposits in the lungs and other tissues of the body. It was not within the scope of this work to consider in detail the various situations which might arise during operation of a pile and result in the release of the short-lived radioactive isotopes of krypton and xenon. However, it is apparent that such a possibility exists, in particular with an air-cooled pile. The possibility exists that in addition to krypton and xenon, bromine and iodine might also act as gaseous components in view of their volatility. However, the well known high degree of chemical reactivity of both of these elements in the monoatomic state tends to cause their deposition upon the first surface encountered. This phenomenon has been observed in the experiments to be described and will be discussed later. The known long-lived fission products which have noble gas ancestors are Sr^{89}, Sr^{90}, Y, Zr^{93}, Cs^{135}, Ba^{140}, Ce^{141}, Ce^{140}, Pr^{143}. It is these fission products with which the experiments of this report are concerned.

This particular problem had been first considered several months before the operation of the pile at X. This made it necessary to

1119274

Figure 21

Figure 21 represents the lung elimination of carrier-free fission products which were also free of uranium or plutonium. About nine-tenths of the initial dose is eliminated sixty-four days after administration.

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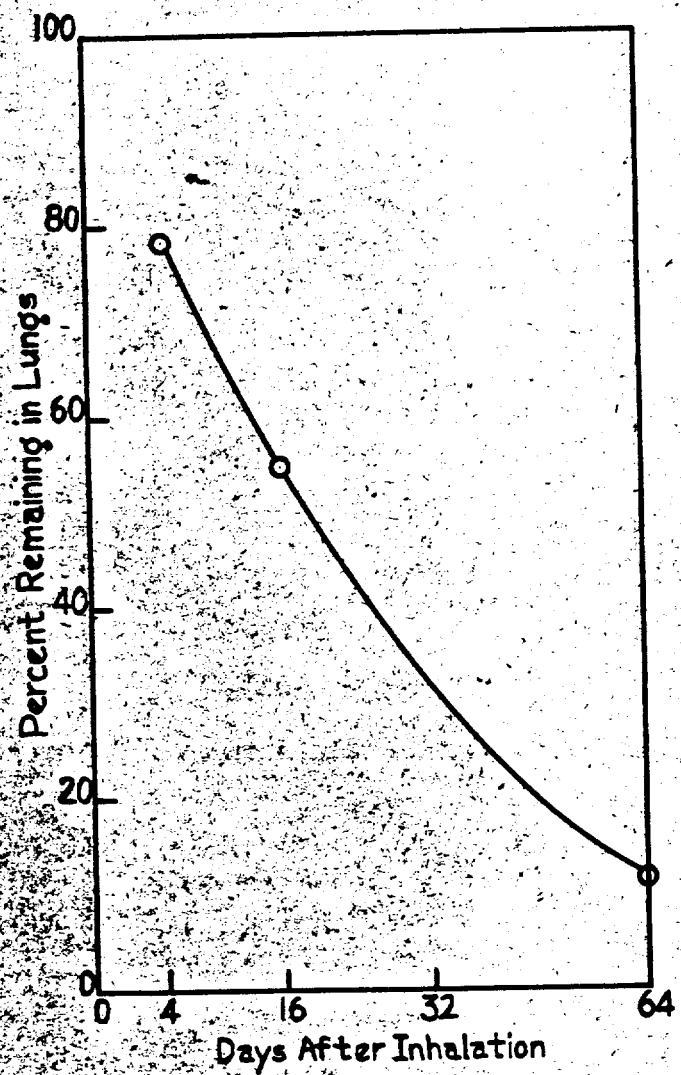
Figure 21

Lung Elimination of Carrier-Free Fission Products



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employ the 60-inch cyclotron for the production of the radioactive amanation. The plan of the experimental approach was to expose rats to the inhalation of the short-lived gaseous fission products and then to determine, both immediately afterwards and several days later, the distribution of retained activities in the various tissues. This scheme, while simple in theory, was found to be most difficult to execute. The requirements of such experiments, were of such a nature as to almost make it impossible to obtain any useful results. In the first place, most of the half-lives of the gaseous ancestors of the long-lived fission products are very short. At the time most of the experiments were done only one of these half-lives was known with any reasonably accuracy (Kr^{89}, half-life 180 seconds) and the others were either indicated as less than 30 seconds or very short. This consideration, therefore, made it necessary to devise an emanation generator which would permit the removal of the radioactive recoils from the source and their transfer, within a few seconds, to a chamber containing the animals. This, of course, required that the dimensions of the source be as small as possible. Such a requirement of size did not lend itself readily to using the neutrons from the cyclotron, which are predominately of high energy (16-20 Mev), with a maximum density of approximately 3×10^{11} $cm.^{-2}$ seconds $^{-1}$, and a total of 10^{12} seconds $^{-1}$ from a Be target, when bombarded with 200 microamperes of 16 Mev deuterons. The alternative solution was to bombard a uranium plate directly with the beam of 16 Mev deuterons in a small bell-jar and to sweep out the recoils with a stream of

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gas. This was the arrangement employed and the emanation generator is shown in Figure 23. This system was relatively unsatisfactory since the yields of fission activities were low. However, it appeared to be the most practical approach, when these experiments were done, and a series of animal exposures were made with this device.

a. Method:

The emanation generator and exposure chamber containing three rats were set up as indicated in Figures 23 and 24. The exhaust gases from the exposure chamber were collected in the two large bottles. This was done in order to determine the total quantity of long-lived fission products arising from the gaseous emanation that was delivered to the exposure chamber. In one of the experiments (#3), an assay of the collected long-lived fission products was made and is shown in Table VIII. In the first four experiments, helium was used to sweep out the recoils from the emanation generator. The rate of oxygen flow into the exposure chamber ranged from 45-50 milliliters cm^{-1} and averaged 45 milliliters $min.^{-1}$. Because of its greater density, argon was employed in the last experiment in place of helium in an attempt to improve the efficiency of the emanation generator by collecting more of the recoils. The rate of flow of argon for this experiment was 35 milliliters $min.^{-1}$. The rate of flow of oxygen was the same for both the helium and argon experiments. The deuteron bombardment of the U plate in the emanation generator varies from 100 microampere hours to 500

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Figure 22

Figure 22 represents the target chamber used for the production of Fission Product recoils administered to the rats pictured in Figure 23. In addition, a detailed view is given of the wire used to collect for assay the fission products produced by the generator.

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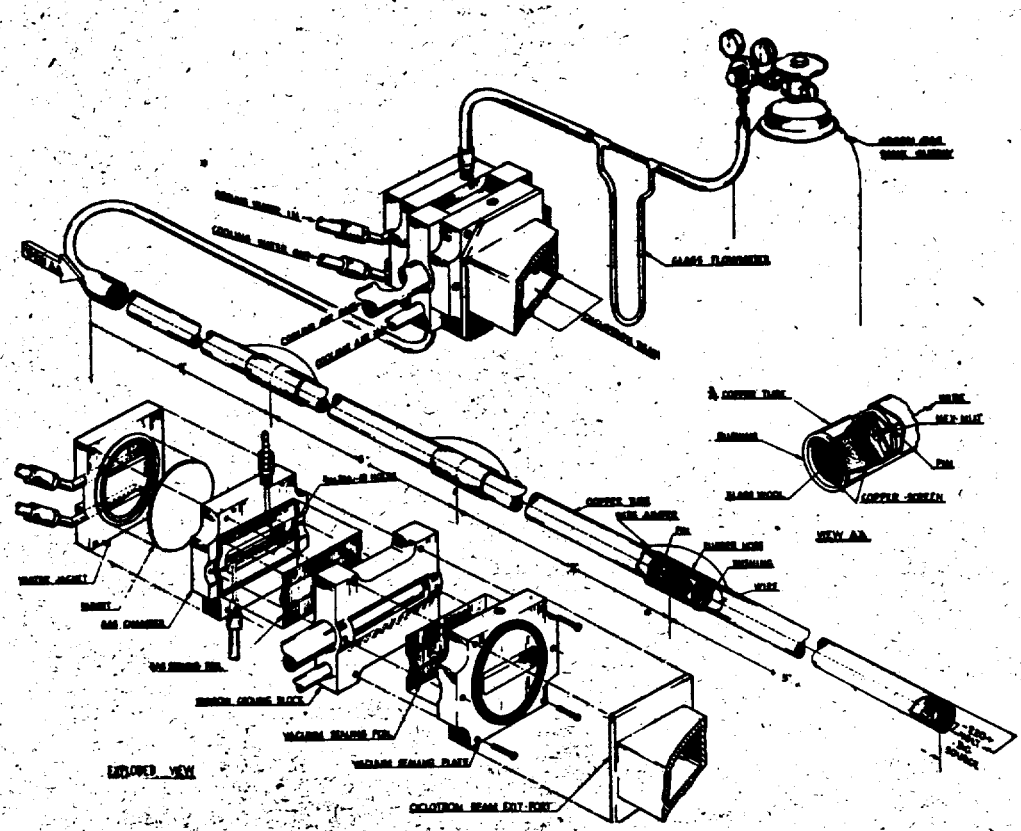
GLASS FLOWMETER
COPPER TUBE
NUT
HEX NUT
PIN
GLASS WOOL
COPPER SCREEN
VIEW AA
COPPER TUBE
PIN
RUBBER HOSE
WIRING
WIRE
WATER JACKET
GASKET
GAS CHAMBER
VACUUM SEALING PIN
VACUUM SEALING PLATE
CYCLOTRON BEAM EXIT PORT
EXPLODED VIEW

FIGURE 22

Figure 23

General view of arrangement for animal exposures to short-lived emanations from uranium fission. The emanation generator is connected to the animal exposure chambers by a copper tube with a 1 mm. bore. The bottles for collecting the exhaust gases are also shown. The lines for the helium and oxygen may be seen.

1119281

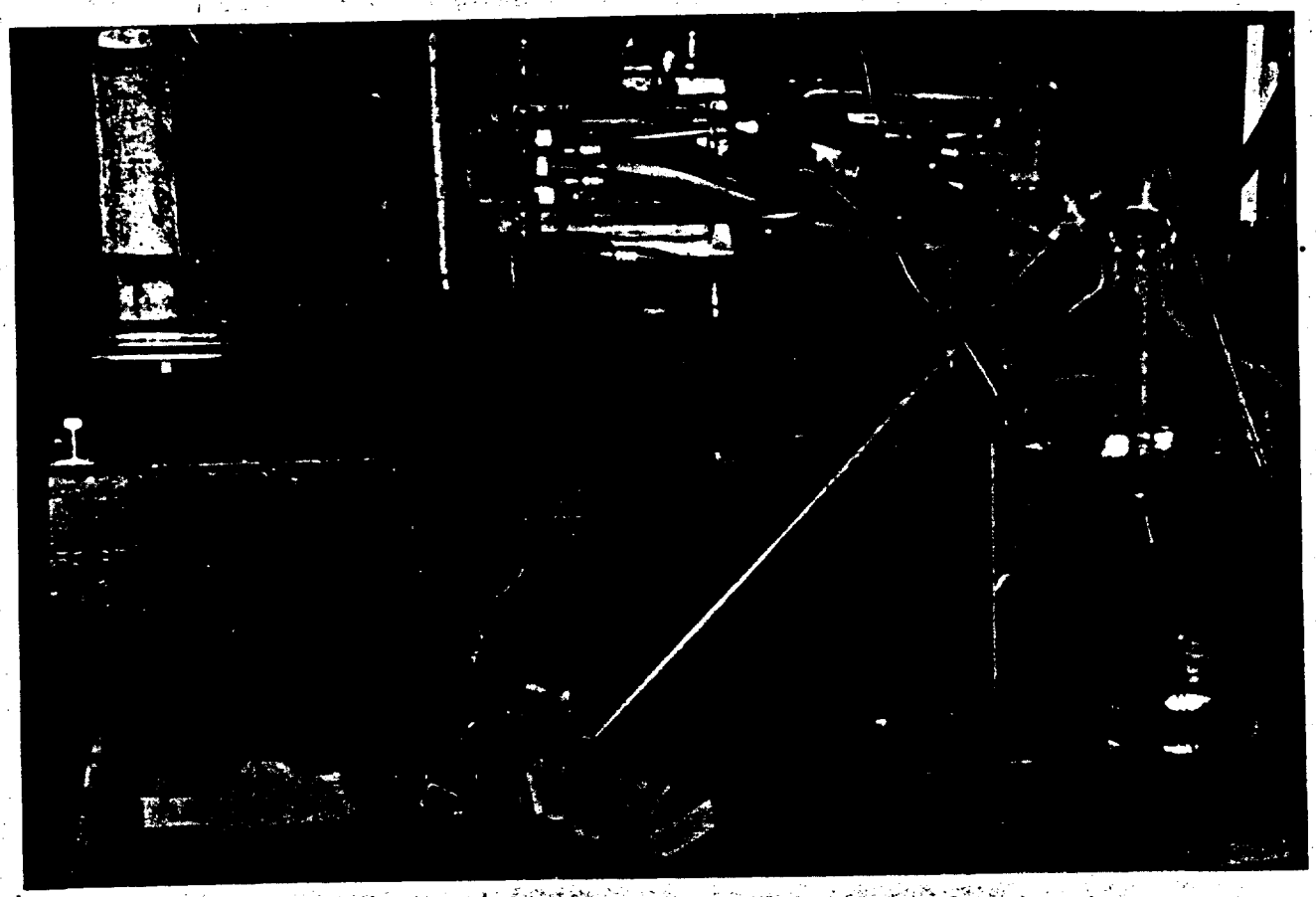

FIGURE 23

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Figure 24

Close up view of exposure chamber containing three rats. The "T" connection conducted the oxygen and helium, the latter gas containing the emanation. The short tube with a pinch clamp was designed for the removal of gas samples and was rarely used. The third tube carried the exhaust gases to the two collection bottles. The volume of the system from which the rats breathed was 180 cc.

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FIGURE 24

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TABLE VIII

ASSAY OF EXHAUST FROM EMANATION EXPERIMENT #3	
Bombardment Sept. 20, 1943 500 Microampere Hours	
GAS FLOW O_2 = 49 cc/Min.	He = 35 cc/Min.
Assay (corrected to 0 time and 0 Thickness)	
Strontium	1010 cts/sec
Barium	3620 cts/sec
Cerium	73.5 cts/sec
Zirconium	39.0 cts/sec
Yttrium	89.5 cts/sec

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microampere hours. The time of exposure varied from two to six hours. The gamma-ray exposure of the animals from the cyclotron ranged from 20r to 100r.

In the second, third, and fourth experiments, some of the animals were sacrificed immediately at the termination of the exposure and the active tissues measured within two hours. No corrections for self-absorption by the samples could be conveniently applied. However, most of the samples fell within a range of two to four grams in weight, and the energies of the beta rays of the fission products present at this time interval were quite penetrating. The errors introduced were probably not in excess of ten to thirty per cent. Corrections for decay during the interval required to measure the samples averaged less than fifteen per cent and were omitted. These tissues, after completion of their immediate measurements, were added and again measured a week to ten days later for their content of the long-lived fission products. To these series of determinations, appropriate corrections for self-absorption were applied.

The remaining animals were kept for four days before they were sacrificed. The collection of excreta, ashing, and measurement of all samples were conducted in the same manner as has been described in earlier reports. The fission products collected from the walls of the exposure chamber and the exhaust were employed for determination of the necessary self-absorption correction to be applied to the ashed specimens.

b. Results:

The results of these experiments are shown in Tables IX to XIX, and the assay of the collected residual activity from the expo-

1119286

sure chamber and its exhaust for the third experiment is shown in Table VIII. Due to the high degree of activity noted on the skins of the animals, a partially successful attempt to reduce this effect was accomplished in the last experiment by wrapping the animals in cellophane during the exposure period. Tables X, XIII, and XVII, which present the data from the animals whose tissues were measured within two hours after removal from the exposure chamber, reveal that fairly uniform distribution took place for most of the tissues. The most notable exception to this general pattern was observed with the lungs which showed the highest deposition per gram. This general pattern was duplicated in the measurements taken of these samples at a much later interval after all of the short-lived fission products had decayed (Tables XI, XIV, XVIII). The distribution percentages are expressed in terms of retained activity and excludes both skin and the gastro-intestinal tract. These tissues and the excreted activity are omitted since during exposure a considerable portion of the active deposit settled out on the hair and was subsequently licked off by the animals and swallowed. Considerable variation was noted between the different experiments but several consistent trends may be observed. First, from fifty-five per cent to ninety-five per cent of the retained activity was retained by the skeleton. The only soft tissue, aside from the thyroid, showing a consistently high uptake was lung. The remainder revealed a per gram specific activity which ranged from one-twentieth to one-hundredth of that of the skeleton. Although these soft tissues showed a small uptake, it was detectable with an average accuracy of approximately twenty-five per cent.

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c. Discussion:

The high degree of deposition of activity in the skeleton compared to the relatively low activities in the soft tissues indicated that most of the retained activity (excluding skin and the gastro-intestinal tract) was due to strontium and barium. This inference was substantiated both by the assay of the exhaust (See Table VIII) and the experiment described in the following section. The amounts of activities swallowed and subsequently excreted were not of sufficient magnitude to account for the observed activities in the skeletons of the animals at the four-day periods. It must be kept in mind that the oral absorption of strontium and barium (the principle components observed in these experiments) in rats is from eight per cent to fifteen per cent. The relative amounts of retained activities of the animals at the four-day intervals in these experiments ranged from twenty per cent to eighty per cent and averaged approximately forty per cent. The levels of the small amounts of activities in the soft tissues (excluding skin and gastro-intestinal tract) were too high to be due to strontium and barium and were thought to be small amounts of the rare earths and Zr. This inference was also substantiated by the assay shown in Table VIII and the experiment described in the next section.

The small amount of activity per organ observed for the thyroid indicates that most of the iodine produced in the generator was retained there or was filtered out by the filter in the tube connecting the emanation generator to the exposure chamber.

The practical results of these experiments suggest that the danger of a high degree of pulmonary activity from deposited long-lived fission

1119288

TABLE IX

EMANATION EXPERIMENT #1

THREE ANIMALS EXPOSED FOR 100 MICROAMPERE HOURS 6-4-43

SACRIFICED FOUR DAYS AFTER EXPOSURE

AND TISSUES MEASURED TWELVE DAYS AFTER EXPOSURE

GAS FLOW Helium 35cc Min^{-1} Oxygen 45cc Min^{-1}				
	Measured Activities		Distribution Less Skin and Excreta	
	% Per Organ	% per gram	% per Organ	% per gram
Liver	.42	.02	.64	.03
Kidney	.07	.04	[illegible]	.06
Skin[1]	(86.5)			
Bone[2]	47.6	2.65	73.0	4.1
Balance[3]	17.0	.17	26.0	.26
Thyroid	.15	1.80	.23	2.8
Total Retained Less Skin	65.3			
Urine	6.5			
Feces	145.0			

1. Animals skinned, measured value for entire skin is not included in distribution calculation.
2. Measured value for entire skeleton.
3. Measured value for remaining carcass less skin and skeleton but including blood and muscle.

1119289

TABLE X

EMANATION EXPERIMENT #2

THREE ANIMALS EXPOSED 7-10-43 FOR 111.6 MICROAMPERE HOURS

ONE ANIMAL IMMEDIATELY SACRIFICED AND TISSUES MEASURED WITHIN TWO HOURS

AFTER EXPOSURE TO EMANATION. G. I. TRACT AND SKIN OMITTED FROM MEASUREMENTS

GAS FLOW				
Helium 38cc Min^{-1}			Oxygen 49cc Min^{-1}	
	Measured Values		Distribution	
	Count Per Organ	Count per Gram	% Per Organ	% Per Gram
Heart	3.5	3.5	1.0	1.0
Liver	16.6	1.5	4.7	.43
Kidney	7.0	3.2	2.0	.91
Testes	3.8	1.2	1.1	.34
Spleen	4.8	3.5	1.4	1.0
Muscle[1]	81.(est)	.9	23.(est)	.26
Bone[2]	50.(est)	2.5	14.3(est)	.71
Brain	1.4	.8	.4	.23
Lungs	12.0	4.3	3.4	1.2
Fat	2.1	.8		.23
Blood[3]	170.(est)	11.3	48.3(est)	3.23
Total	352.2			

1. Muscle estimated on basis of 45% of body weight.
2. Bone estimated on basis of 20 grams.
3. Blood estimated on basis of 8% of body weight.

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TABLE XI

EMANATION EXPERIMENT #2

SAMPLES FROM SAME ANIMAL ASHED AND MEASURED TWENTY-THREE DAYS LATER

	Measured Values		Distribution Less Skin and G.I. Tract	
	Count per Organ	Count per Gram	% per Organ	% per Gram
Heart	.1	.1	.7	.7
Liver	.48	.04	3.5	.29
Kidney	.1	.04	.7	.3
Testes	.1	.03	.7	.2
Spleen	.1	.1	.7	.7
Muscle[1]	1.95 (est)	.02	14.3 (est)	.15
Skin[2]	35.8	.85		
G.I. Tract[3]	2.6	.1		
Bone[4]	6.42	.15	46.8	1.1
Brain	.1	.06	.7	.4
Fat		.04		.3
Blood[5]	.48 (est)	.03	3.5 (est)	.22
Lungs	.95	.33	6.8	2.4
Balance[6]	5.75	.06	42.1	.4
Total Retained less Skin and G. I. Tract	13.68			

1. Estimated on basis of 45% of body weight.
2. Animal skinned, measured value for entire skin.
3. G. I. tract removed and measured as a unit.
4. Measured value for entire skeleton.
5. Blood estimated on basis of 8% of total body weight.
6. Measured value for remaining carcass less skin and skeleton but including blood and muscle.

1119291

TABLE XII

EMANATION EXPERIMENT #2

REMAINING TWO ANIMALS SACRIFICED FOUR DAYS AFTER EXPOSURE,

AND SAMPLES MEASURED TWENTY-THREE DAYS AFTER EXPOSURE

	Measured Activities		Distribution Less Skin G. I. Tract and Excreta	
	Count per Organ	Count per Gram	% per Organ	% per Gram
Heart	.05	.05	.5	.5
Liver	.20	.02	2.0	.2
Kidney	.05	.02	.5	.2
Testes	.05	.02	.5	.2
Spleen				
Muscle[1]	1.0(est)	.01	10.(est)	.1
Skin[2]	5.8	.14		
G. I. Tract[3]	.48	.024		
Bone[4]	5.48	.20	54.8	2.0
Lungs	.24	.13	2.4	1.3
Fat		.1		1.0
Blood[5]	.3(est)	.02	3(est)	.2
Thyroid	.05	1.0	.5	10.0
Balance[6]	4.04	.04	40.4	.4
Total Retained less Skin and G. I. Tract	10.0			
Urine	.86			
Feces	15.0			

1. Estimated on basis of 45% of body weight.
2. Animal skinned, measured value for entire skin.
3. G. I. tract removed and measured as a unit.
4. Measured value for entire skeleton.
5. Blood estimated on basis of 8% of total body weight.
6. Measured value for remaining carcass less skin and skeleton but including blood and muscle.

1119292

TABLE XIII

EMANATION EXPERIMENT #3

ONE ANIMAL EXPOSED 9-20-43 FOR 250 MICROAMPERE HOURS

ANIMAL IMMEDIATELY SACRIFICED AND TISSUES MEASURED WITHIN TWO HOURS AFTER EXPOSURE TO EMANATION. G. I. TRACT AND SKIN OMITTED FROM MEASUREMENTS

GAS FLOW Helium 38cc Min^{-1} Oxygen 49cc Min^{-1}				
	Measured Values		Distribution	
	Counts per Organ	Counts per Gram	% per Organ	% per Gram
Heart	10.5	8.48	.78	.63
Liver	62.8	7.81	4.64	.58
Kidney	58.1	32.2	4.31	2.38
Testes	8.12	3.46	.60	.26
Spleen	7.51	9.38	.56	.70
Muscle[1]	443.0 (est)	4.28	32.8 (est)	.32
Bone[2]	330.0 (est)	15.5	24.6 (est)	1.23
Brain	9.02	6.33	.68	.47
Lungs	120.0	79.7	8.88	5.90
Fat	67.2	30.1		2.23
Blood[3]	154.0 (est)	8.32	11.4 (est)	.62
Thyroid	1.0	20.0	.1	1.5
Trachea	85.8	187.0	6.34	13.8
Total	1354.0			

1. Muscle estimated on basis of 45% of body weight.
2. Bone estimated on basis of 20 grams.
3. Blood estimated on basis of 8% of body weight.

1119293

TABLE XIV

EMANATION EXPERIMENT #3

SAMPLES FROM SAME ANIMAL ASHED AND MEASURED ELEVEN DAYS LATER

	Measured Values		Distribution Less Skin and G. I. Tract	
	Counts per Organ	Counts per Gram	% per Organ	% per Gram
Heart	.25	.21	.31	.27
Liver	2.07	.26	2.53	.32
Kidney	.45	.25	.55	.31
Testes	.1	.05	.1	.05
Spleen	.1	.1	.1	.1
Muscle[1]	15.4(est)	.17	18.9(est)	.2
Skin[2]	197.0	4.68		
G.I. Tract[3]	26.4	1.23		
Bone[4]	34.7	1.62	42.4	1.98
Brain	.59	.42	.73	.51
Fat	.1	.05	.1	.05
Blood[5]	2.28	.12	2.78	.15
Lungs	2.34	1.53	2.87	1.90
Trachea	2.09	4.57	2.57	5.61
Thyroid	.1	2.0	.1	2.5
Balance[6]	39.2	.4	48.1	.5
Total Retained less Skin and G. I. Tract	81.76			

1. Estimated on basis of 45% of body weight.
2. Animal skinned, measured value for entire skin.
3. G. I. tract removed and measured as a unit.
4. Measured value for entire skeleton.
5. Blood estimated on basis of 8% of total body weight.
6. Measured value for remaining carcass less skin and skeleton but including blood and muscle.

1119294

TABLE XV

EMANATION EXPERIMENT #3

TWO MORE ANIMALS EXPOSED FOR 500 MICROAMPERE HOURS

SACRIFICED FOUR DAYS LATER AND TISSUES MEASURED ELEVEN DAYS AFTER EXPOSURE

	Measured Activities		Distribution Less Skin and G. I. Tract	
	Counts Per Organ	Counts Per Gram	% per Organ	% per Gram
Heart	.15	.15	.02	.02
Liver	.63	.06	.097	.009
Kidney	.54	.26	.083	.04
Testes	.19	.06	.029	.009
Spleen	.25	.60	.038	.092
Muscle[1]	6.6	.09	1.0	.014
Skin[2]	253.0	6.0		
G. I. Tract[3]	24.3	1.2		
Bone[4]	608.2	14.1	93.6	2.15
Brain	.1	.07	.15	.1
Lungs	.92	.54	.14	.083
Fat		.1		.15
Blood[5]	1.2(est)	.07	.18(est)	.01
Trachea	.1	1.0	.15	1.5
Thyroid	.07	3.5	.01	.54
Balance[6]	38.6	.43	5.93	.068
Total Retained Less Skin and G. I. Tract	650.0			
Urine	21.4			
Feces	393.1			
Dose per Animal	1794.0			

1. Estimated on basis of 45% of body weight.
2. Animal skinned, measured value for entire skin.
3. G. I. tract removed and measured as a unit.
4. Measured value for entire skeleton.
5. Blood estimated on basis of 8% of total body weight.
6. Measured value for remaining carcass less skin and skeleton but including blood and muscle.

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TABLE XVI

EMANATION EXPERIMENT #4

TWO ANIMALS EXPOSED 11-12-43 FOR 500 MICROAMPERE HOURS

ANIMALS SACRIFICED FOUR DAYS LATER AND TISSUES MEASURED THIRTEEN DAYS AFTER EXPOSURE

	GAS FLOW Helium 95cc Min^{-1} Oxygen 45cc Min^{-1}			
	Measured Activities		Distribution Less Skin and Excreta	
	Counts per Organ	Counts per Gram	% per Organ	% per Gram
Heart	.05	.06	.03	.04
Liver	.33	.046	.21	.029
Kidney	.12	.056	.075	.035
Testes	.05	.02	.03	.02
Spleen	.05	.05	.03	.03
Muscle[1]	6.44	.066	4.0	.04
Skin[2]	118.5	3.63		
G. I. Tract[3]	13.6	.39		
Bone[4]	128.8	6.00	79.7	3.75
Lungs	.17	.14	.10	.09
Blood[5]	.50 (est)	.03	.31 (est)	.02
Balance[6]	31.4	.34	19.5	.21
Brain	.07	.045	.04	.03
Total Retained Less Skin and G. I. Tract	160.9			
Urine	43.20			
Feces	594.6			
Dose per Animal	2160.0			

1. Estimated on basis of 45% of body weight.
2. Animal skinned, measured value for entire skin.
3. G. I. tract removed and measured as a unit.
4. Measured value for entire skeleton.
5. Blood estimated on basis of 8% of total body weight.
6. Measured value for remaining carcass less skin and skeleton but including blood and muscle.

1119296

TABLE XVII

EMANATION EXPERIMENT #5

TWO ANIMALS EXPOSED 12-15-43 FOR 100 MICROAMPERE HOURS

ANIMALS IMMEDIATELY SACRIFICED AND TISSUES MEASURED WITHIN TWO HOURS AFTER EXPOSURE TO EMANATION. G. I. TRACT AND SKIN OMITTED FROM MEASUREMENTS - ANIMALS WRAPPED IN CELLOPHANE TO REDUCE ACTIVE DEPOSIT ON SKIN

GAS FLOW				
Argon 38cc Min^{-1} Oxygen 49cc Min^{-1}				
	Measured Values		Distribution	
	Counts per Organ	Counts per Gram	% per Organ	% per Gram
Heart	4.8	9.0	.44	.82
Liver	34.9	4.33	3.17	.40
Kidney	19.1	14.4	1.74	1.31
Spleen	3.22	8.67	.29	.79
Muscle[1]	500. (est)	7.89	45.5	.72
Bone[2]	270. (est)	18.2	24.6	1.66
Brain	1.72	2.96	.16	.27
Lungs	105.0	69.3	9.57	6.30
Fat	35.0	24.9		2.27
Blood[3]	123. (est)	11.0	11.2 (est)	1.0
Thyroid	2.0	40.0	.18	3.64
Total	1099.0			

1. Muscle estimated on basis of 45% of body weight.
2. Bone estimated on basis of 20 grams.
3. Blood estimated on basis of 8% of body weight.

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TABLE XVIII

EMANATION EXPERIMENT #5

SAMPLES FROM SAME ANIMALS ASHED AND MEASURED EIGHT DAYS LATER

	Measured Values		Distribution Less Skin and G. I. Tract	
	Counts per Organ	Counts per Gram	% per Organ	% per Gram
Heart	.1	.2	.30	.60
Liver	1.78	.16	5.25	.47
Kidney	.35	.25	1.05	.74
Spleen	.1	.3	.3	.9
Muscle[1]	5.1 (est)	.08	15.0 (est)	[illegible]
Skin[2]	12.5	.41		
G.I. Tract[3]	6.85	.52		
Bone[4]	22.0	.59	65.2	1.74
Brain	.19	.32	.56	.95
Lungs	3.47	2.28	10.2	6.74
Fat	.21	.69		2.03
Blood[5]	1.5 (est)	.1	5. (est)	.3
Thyroid	.14	2.7	.41	8.0
Balance[6]	5.7	.06	16.8	.18
Total Retained less Skin and G.I. Tract	33.8			

1. Estimated on basis of 45% of body weight.
2. Animal skinned, measured value for entire skin.
3. G. I. Tract removed and measured as a unit.
4. Measured value for entire skeleton.
5. Blood estimated on basis of 8% of total body weight.
6. Measured value for remaining carcass less skin and skeleton but including blood and muscle.

1119298

TABLE XIX

EMANATION EXPERIMENT #5

TWO MORE ANIMALS EXPOSED FOR 200 MICROAMPERE HOURS

SACRIFICED FOUR DAYS LATER AND TISSUES MEASURED EIGHT DAYS AFTER EXPOSURE

ANIMALS WRAPPED IN CELLOPHANE TO REDUCE ACTIVE DEPOSIT ON SKIN

	Measured Activities		Distribution Less Skin and G. I. Tract	
	Counts per Organ	Counts per Gram	% per Organ	% per Gram
Heart	.1	.1	.15	.15
Liver	1.28	.14	1.91	.21
Kidney	.31	.16	.46	.24
Spleen	.29	.47	.43	.70
Muscle[1]	3.1(est)	.04	4.6	.06
Skin[2]	27.4	.67		
G.I. Tract[3]	2.05	.07		
Bone[4]	59.6	3.35	89.2	5.01
Lung	1.20	.77	1.79	1.15
Trachea	.1	.4	.15	.6
Thyroid	.1	1.0	.15	1.5
Balance[5]	4.25	.05	6.33	.07
Total Retained Less Skin and G. I. Tract	66.9			
Urine	13.2			
Feces	100.6			
Dose Per Animal	729.0			

1. Estimated on basis of 45% of body weight.
2. Animal skinned, measured value for entire skin.
3. G. I. Tract removed and measured as a unit.
4. Measured value for entire skeleton.
5. Measured value for remaining carcass less skin and skeleton but including blood and muscle.

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products is not great when the gases leak from the pile at rates of the order of ten feet per second or more and thus result in the release of significant amounts of the gaseous parents of the rare earths and zirconium.

5. Short-lived Fission Products from the Clinton Pile*

a. and b. The Elements, the Method, and the Equipment:

A study was made of the fate in rats of short-lived fission products produced by the Clinton Pile. The exposures were conducted between November 7, and December 10, 1944. The rats were exposed to fission products from the pile for periods of time approximating two hours. The fission products were produced by the action of slow neutrons on uranium foil which was located in the fission recoil apparatus of the pile. The recoils from the above mentioned uranium fission were caught in the air circulating in the recoil apparatus and were transferred to the rats. This air was kept at humidity of 60% and a temperature of 75°F. The air and the fission products were brought through a one and one-half inch pipe with twelve outlets fitted for rat exposure. This part of the system at which the rats were exposed was run at a slight negative pressure. The average time which elapsed between the departure of the fission products from the recoil apparatus and the arrival of the fission products at the site of exposure was three seconds in the first group of experiments and twelve seconds in the second group of experiments. This difference in hold-up time

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*These studies were made possible through the cooperation of Dr. F. J. Curtis, Dr. Walter Cohn, and Dr. Miles Leverett.

1119300

resulted in a variation in the relative percentage of short-lived fission products, administered to the rats. Details of the operation pile fission recoil apparatus are summarized in the following list:

Expt. No.	Pile Power	Activity of Gas	Holdup Time	Pressures of Rat Manifold	
				Inlet Pressure	Outlet Pressure
1 & 2	4,200 Kv.	18 /cc.	3 sec.	-2 cm. of water	-3 cm. of water
3 & 4	4,100 Kv.	15 /cc.	12 sec.	-1 cm. of water	-1 cm. of water

Schematic diagrams of the fission recoil apparatus are shown in Figures 25 to 28.

Fission products from the circulating air in the fission recoil apparatus were trapped on glass wool. A subsequent analysis at a later date showed the following elements to be present, with their relative percentages of Beta emission listed as follows:

	Per Cent of Total Beta Emission*
Strontium	4.4
Columbium	6.9
Zirconium	9.5
Ruthenium	4.4
Cerium	28.3
Yttrium	41.6
Barium	2.4
Cesium	0.0
Tellurium	1.9

The analysis given above was performed when the fission products collected were approximately four months old.

*We are indebted to Doctor N. V. Eume for the above analyses of the fission products from the pile.

Figures 25 - 28

Figures 25 to 28 illustrate by a schematic diagram how fission products were administered to rats. The fission products which recoil from the uranium foil in the pile are brought to the rats by the circulation of air in the system shown. The average age of the fission products delivered to the rats can be varied. Automatic recording and control of the temperature and humidity of the air is accomplished. The activity of the fission products is continuously recorded by the ionization chamber.

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Fig. 25.

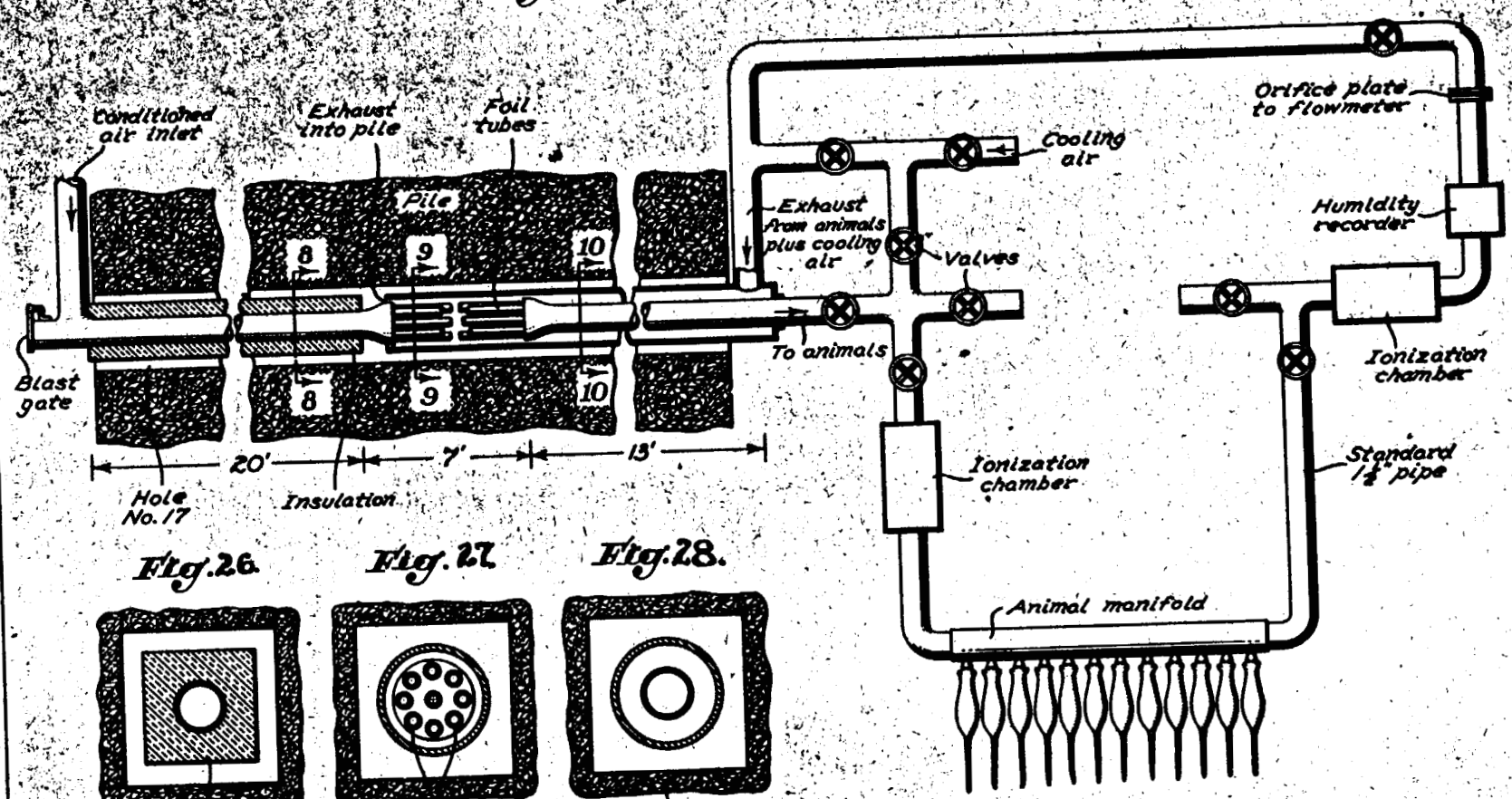

Fig. 26.

Fig. 27.

Fig. 28.

Schematic Diagram of F.R.A. and Apparatus

Drawn by Gaines Helm 2-22-45

1119303

c. Results:

Tables XX, XXI, and XXII summarize the data from the experiments at Clinton. Fission products were detected in all of the tissues from the rats killed at zero time. No essential difference in deposition of activity at zero time was observed between the three-second and the twelve-second holdup times. At the cessation of exposure a major portion of the fission products found in the animals was contained in the lungs. Large amounts of fission products were also deposited in the head and skeleton. Liver and kidney contained the largest amounts of fission products of the soft tissues with the exception of thyroid, which absorbed extremely large amounts of what was apparently radioactive iodine.

One day after exposure, the lungs had lost approximately one-half of the activity measured at zero time. Skeleton, liver, and thyroid contained an even greater percentage of the activity at one day than at zero time. The rather high activities originally observed in muscle had apparently been lost to other tissues or had been eliminated from the body since these values were lower at one day than at zero time. The values obtained on excretion of fission products by the four groups of rats after exposure to emanations from the pile are presented in Table XXII. One day after exposure, one-fifth of the activity was excreted in the feces and one-tenth in the urine. In general, at four days, the activity values for the lung, head, liver, kidney, and thryroid were lower than at one day. Skeleton apparently had reached equilibrium by four days. The lungs continued to eliminate fission products so that at four days less than one-half of the

1119304

products originally present in them remained. The activity deposited in the head had been reduced to a much lower level at this time period. The activity from iodine detected in the thyroid at four days was less than the values obtained for one day. This is presumably explained by the decay of iodine which has a shorter half-life than the half-lives of the combined fission products. There was continued fecal and urinary excretion at four days but at a reduced rate. The activity in the feces was primarily due to fission products excreted from the lungs via the bronchial tree.

Nine-tenths of the original activity deposited in the lungs was either absorbed or was eliminated sixteen days after fission products had been administered to rats. (See Figures 29 and 30). Since the values for the other tissues in the body at this time period were essentially the same or lower than those obtained at four days, fission products lost from the lungs appeared in the feces. This value approached one per cent per day, sixteen days after exposure. The value for urine was 0.1%.

Because of the relatively short half-life of many of the fission products used in this study, the longest time period used in these experiments was thirty-three days after exposure.

Of the activity remaining in the animals at thirty-three days, the largest percentage of the fission products was held by the skeleton. The activity found in the lungs did not seem to be essentially different in percentage from the values observed at sixteen days. On a per gram basis, liver and kidney contained but 0.1 of the activity deposited in the skeleton. Values obtained for thyroid were comparable

1119305

to liver and kidney. On a per gram basis, muscle and skin contained but 0.1 of the activity value detected in liver and kidney.

1119306

TABLE XX

Distribution in Rats of Short-lived Fission Products from the Clinton Pile

	GAS HOLDUP TIME = 3 SEC.							
	Exposure 1 0 Time 3 Animals		Exposure 1 1 Day 3 Animals		Exposure 1 4 Days 3 Animals		Exposure 2 16 Days 3 Animals	
	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram
LUNGS	39.2	20.75	15.62	7.85	11.74	8.32	4.47	3.46
LIVER	4.61	.49	6.61	.82	4.20	.56	1.55	.17
KIDNEY	1.16	.61	.57	.28	.36	.21	0.11	.07
G. I.	6.61	.40	7.76	.42	1.52	.09	1.04	.04
SKELETON	20.4	.98	27.00	1.51	22.9	1.16	22.9	1.26
MUSCLE	8.57	.15	2.94	.03	1.86	.03	2.11	.02
HEAD	24.0	1.54	1.00	.07	2.01	.13	.85	.06
SKIN	6.61	0.24	1.84	.07	.73	.03	0.40	.02
THYROID	0.41	20.7	3.01	150.0	1.90	95.0	.07	3.40
HEART	0.20	0.20	*	*	>0.001	0.001	*	*
SPLEEN	0.18	0.23	.06	.07	0.04	.05		
BLOOD			.40	.13	.33	0.09		
FAT	0.05	0.05	<0.001	<0.001	<0.001	<0.001		
TUMOR								

* Value measured was less than 0.01% of the total activity in animal.

1119307

TABLE XXI

Distribution in Rats of Short-lived Fission Products from the Clinton Pile

	GAS HOLDUP TIME = 12 SEC.									
	Exposure 3 1 Day 3 Animals		Exposure 3 4 Days 3 Animals		Exposure 3 16 Days 3 Animals		Exposure 4 0 Time 3 Animals		Exposure 4 33 Days 4 Animals	
	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram
LUNGS	24.10	15.53	16.00	9.42	2.94	2.09	43.8	28.3	4.25	2.73
LIVER	7.67	.96	5.00	.52	1.33	.16	4.73	.61	1.45	.15
KIDNEY	.59	.34	.34	.17	.16	.08	.53	.31	0.28	.14
G. I.	7.32	0.48	1.89	0.07	.33	0.02	3.85	0.19	0.21	.02
SKELETON	17.73	1.02	25.93	1.36	23.0	1.10	20.0	1.16	24.2	1.21
MUSCLE	3.25	.04	2.35	.03	1.67	.02	5.81	.07	1.21	0.01
HEAD	3.98	0.26	2.06	0.12	.67	0.04	18.4	1.23	0.61	0.04
SKIN	1.21	0.05	.56	0.02	.26	*	2.57	0.10	0.20	*
THYROID	4.75	23[illegible].0	3.47	173.5	0.10	5.13	1.42	71.2	.29	14.4
HEART	.04	0.04	*	*	0.08	0.08	.09	.07		
SPLEEN	.06	0.09	0.17	0.20			.05	0.07		
BLOOD										
FAT	.02	0.02					0.04	0.03		
TUMOR									0.47	0.07

* Value measured was less than 0.01% of the total activity in animal.

1119308

TABLE XXII

Daily Rate of Excretion in Per Cent of Short-lived Fission Products from the Clinton Pile

	GAS HOLDUP TIME = 3 SEC.					
	Exposure 1 1 Day		Exposure 1 4 Days		Exposure 2 16 Days	
	Feces	Urine	Feces	Urine	Feces	Urine
1st Day	21.00	11.66	14.72	8.78	10.51	4.07
4th Day			5.44	.38	2.97	0.35
16th Day					1.04	.10
33rd Day						

	GAS HOLDUP TIME = 12 SEC.							
	Exposure 3 1 Day		Exposure 3 4 Days		Exposure 3 16 Days		Exposure 4 33 Days	
	Feces	Urine	Feces	Urine	Feces	Urine	Feces	Urine
1st Day	16.24	10.00	18.50	7.80	19.75	3.03	5.22	3.09
4th Day			5.22	1.00	2.90	0.67	1.89	0.23
16th Day					.79	.09	1.64	.20
33rd Day							0.92	.16

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Figure 29

The lung excretion of fission products produced from uranium foil in the pile and breathed by rats is shown in Figure 29. In this case the holdup time is three seconds. It can be seen from the data that about 95% of the total activity deposited in the lungs at zero time has been eliminated sixty-four days after administration.

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Figure 29

Lung Elimination of Short-Lived Fission Products from Clinton Pile. Three Second Hold-Up Time

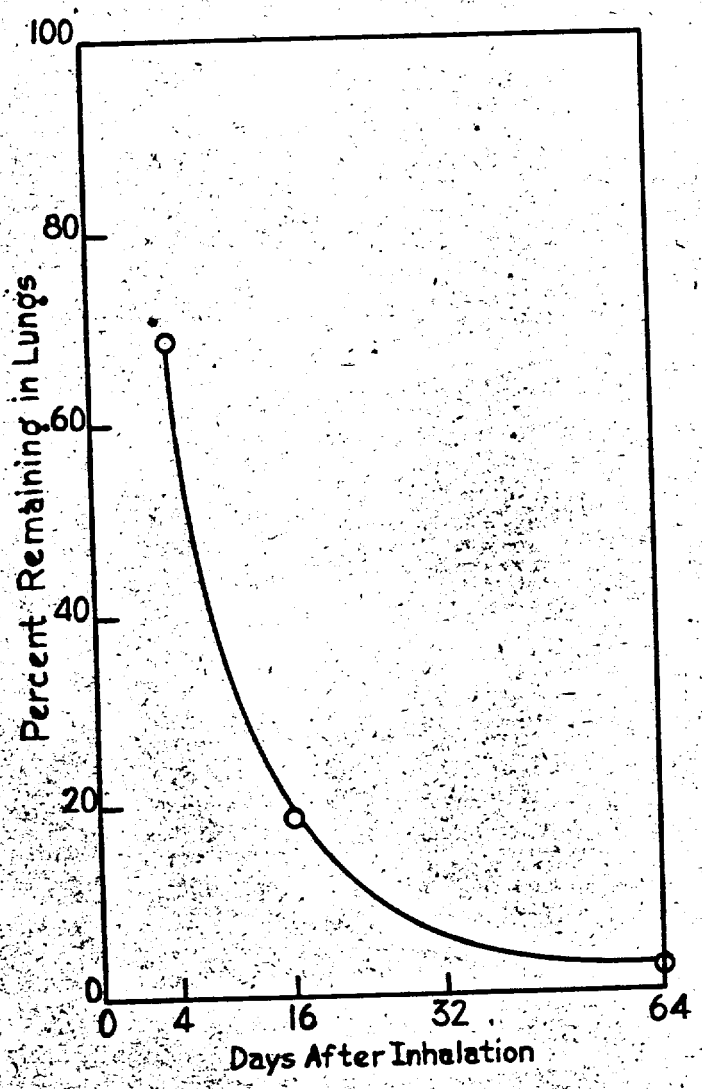

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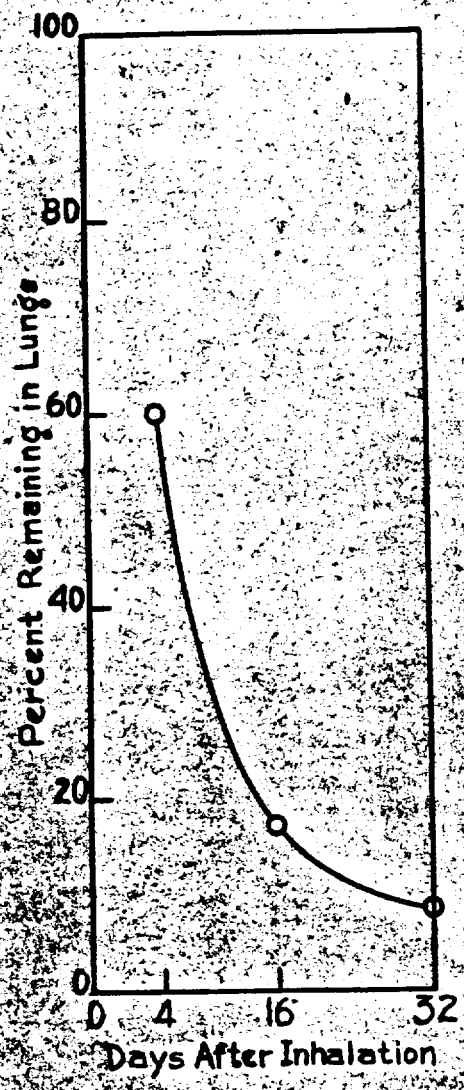
Figure 30

The lung excretion of fission products produced from uranium foil in the pile and breathed by rats is shown in Figure 30. The average age of the recoil fission products was twelve seconds in these experiments. About nine-tenths of the activity had left the lungs sixty-four days after administration of fission products.

1119312

Figure 30

Lung Elimination of Short-Lived Fission Products from Clinton Pile. Twelve Second Hold-Up Time



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CHAPTER III

STUDIES ON THE FATE OF PROTOACTINIUM WHICH WAS DEPOSITED IN LUNGS OF RATS

1.& 2. The Element, the Method, and the Equipment:

In order to study the metabolism of protoactinium, Pa^{233}, without carrier, was introduced into the lungs of rats as an aerosol in argon. The aerosol was obtained by creating electric discharges between two electrodes which had protoactinium deposited upon their surfaces. The electrodes used were concave gold buttons, one centimeter in diameter, on which carrier-free protoactinium in solution had been evaporated with the aid of a heat lamp. The electrodes were then installed in the large size exposure chamber in place of the carbon electrodes used in preceding experiments. The protoactinium was then dispersed in an atmosphere of argon by passing 15,000 volts between the two electrodes which were placed five to eight mm. apart. A 0.01 microfarad condensor was connected across the high voltage line, which aided in causing the electric discharge. It was found that rats could breathe argon without oxygen during the time of protoactinium inhalation without injury to them. Oxygen was avoided in the exposure chamber because of the production of undesirable amounts of ozone.

3. Yield

The yield of activity obtained was proportional to the time the arc was allowed to operate. Thirty seconds of electric arc was

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sufficient to deposit adequate activity in the rats for studies up to sixty-four days.

4. Results

Table XXIII presents the results of the administration of protoactinium to eleven rats, which were sacrificed at times ranging from zero time to sixty-four days after the exposure to activity. At zero time, protoactinium was deposited in approximately equal amounts in the lungs and head, each of which contained about forty per cent of the total activity. Muscle, skeleton, and liver contained sufficiently high concentrations of protoactinium to indicate a fairly rapid absorption of the element from the lungs. A certain amount of skin contamination occurred, presumably from contact with the large amounts of activity found around the nostrils during dissection of the animals. The activity found on skin should probably be considered as part of the protoactinium deposited in the head.

Further evidence of lung absorption is supplied by data taken five days after protoactinium exposure. The retention values of protoactinium by the skeleton had increased by a factor of ten during this time. The protoactinium level of balance remained as high as it was at one day. Most of the protoactinium deposited in the head had been excreted in the feces. The lungs remained the primary depository of protoactinium at five days after intrapulmonary administration. Data obtained on rats sixteen days after protoactinium administration was similar to that of five days, no large translocation of protoactinium being observed between these two time periods.

1119315

TABLE XXIII

Distribution in Rats of Carrier-Free Protoactinium Inhaled as Aerosol

Dispersed by Electric Arc

	0 Time 2 Animals		5 Days 3 Animals		16 Days 3 Animals		64 Days 3 Animals	
	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram	% per Organ	% per Gram
LUNGS	42.55	10.55	46.00	15.70	39.03	13.01	6.85	1.16
LIVER	.20	.02	.29	.03	.14	.01	.17	.01
KIDNEY	.03	.01	.20	.08	.22	.07	.08	.03
SPLEEN	Not Taken		--	--	--	--	--	--
SKELETON	.31	.01	3.19	.11	.91	.03	1.14	.06
BALANCE [1]	2.06	*	2.78	.02	1.99	.01	3.00	.02
G. I.	6.10	.16	1.74	.05	.70	.03	.41	.01
HEAD	39.05	1.09	.81	.03	.42	.02	.42	.01
SKIN	9.68	.13	.48	*	.58	.01	.58	.01

Daily Rate of Excretion in Per Cent

	1 Day	4 Days	16 Days	64 Days
Urine	.59	.24	.20	.26
Feces	23.42	2.06	.53	.47

1. Balance is primarily composed of muscle, but also includes any tissue residues and fat not listed in table.

* Value measured was less than .01% of the total activity in animal

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Some lung elimination via the bronchiole tree was observed as well as loss from the body via the urine. This lung elimination continued during the course of the experiment. (See Figure 31). At sixty-four days, only one-eighth of the protoactinium originally in the lungs remained. The levels of protoactinium found in the urine were half as high as those of feces. This suggests that protoactinium was readily lost from the body through kidney function. It will be further noted that the balance continued to contain more activity than skeleton. Since these tissues are very active metabolically and enjoy a large blood circulation, this situation probably facilitates loss of protoactinium from the body.

1119317

Figure 31

Figure 31 shows the elimination of protoactinium from the lungs of rats after exposure to an aerosol of protoactinium produced by a 15,000V A.C. electric discharge in argon. Protoactinium can be quite readily removed from the lungs. More than four-fifths of the material has been eliminated sixty-four days after administration of the aerosol.

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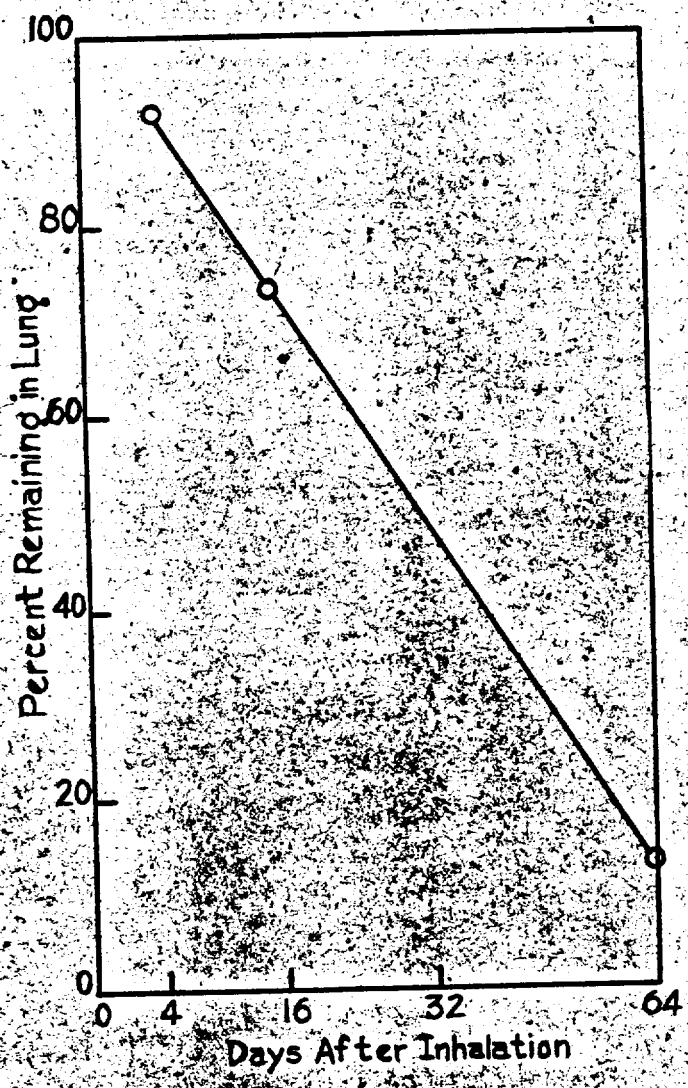
Figure 31

Lung Elimination of Proactinium



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CHAPTER IV

RETENTION OF INHALED ZIRCONIUM AEROSOLS IN MAN AND RATS

1. Element

A single inhalation experiment was done on one of us [redacted] using the eighty-one hour Zr^{89}. This material had been produced from the d - 2n reaction on yttrium by the 60" Cyclotron. It had been prepared in the carrier-free state and free from other radioactive contaminants. No detectable amounts of long-lived activity are produced in this type of preparation of Zr^{89}.

2. Method of Producing Smoke

This material was suspended as an aerosol in argon using the electrical discharge equipment described in Chapter III. The chamber in which the Zr^{89} smoke was produced was the large size. This is shown in Figure 6, Chapter I. It had a volume of six hundred cubic centimeters. A series of preliminary runs were made so that a predetermined amount of Zr^{89} could be suspended as an aerosol avoiding the danger of volatilizing excessive amounts of this substance. The final arrangement was such that thirty seconds of electrical discharge produced an aerosol which contained approximately one microcurie of Zr^{89}. Before the actual experiment was undertaken, a series of determinations for the rate of settling of the aerosol within the cylinder were made, so that the necessary correction factor could be applied for the few seconds required for the active material to be transferred from the exposure chamber to the lungs of the subject.

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3. Human Study

While the aerosol was being inhaled through a short rubber tube placed in the left nostril, one hundred cubic centimeters of argon containing the Zr^{89} aerosol was withdrawn for assay. The inhaled gas was exhaled through the mouth into a glass wool filter, and several additional breaths of inactive air were taken which were also exhaled through this filter.

4. Equipment for Rats

A similar experiment was done on rats using the traps described in Chapter I, Section 3, so that the data obtained on both rats and a human being could be correlated.

5. Results

The results obtained from the human study are tabulated in Table XXIV and the results obtained from the rats on Table XXV.

It can be seen from these results that in the case of the human, the amount of Zr^{89} retained at the end of three days was approximately three times the amount found in rats at the same time interval. This difference would appear to be represented to a large degree by the fact that in the case of man, very little Zr^{89} was exhaled and only thirty-two per cent of the total of inhaled Zr^{89} was excreted. The amount excreted in the human experiment was approximately three-fifths of that observed in the rats. From this human experiment, it would appear that from two to three times the pulmonary retention takes place in man as compared with the rat. This hypothesis assumes that the upper respiratory tract and bronchial tree of both animals were almost completely cleared out of activity by the end of the

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third day. It is known from radioautographic studies in rats that this is the case, and the very rapid decrease in excretory rate in man after the third day suggests that this assumption is valid for the human. The amounts of Zr^{89} absorbed through the lungs and deposited in the skeleton at the three-day interval in the rats was small and it is assumed a comparable effect took place in the human study.

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TABLE XXIV

A HUMAN INHALATION STUDY WITH CARRIER-FREE Zr^{89} AS A SMOKE

(Total Activity Inhaled = 2,430 c/s)

Fecal Excretion			
Time		c/s	% Excreted
1st Day	12 hours	171	7.1
	25 hours	426	17.5
	45 hours	134	5.5
2nd Day	49 hours	40	1.6
	59 hours	3.7	0.15
3rd Day	71 hours	2.3	0.10
	Total Excreted	777.0	32.0
	Total Activity Exhaled	53.0	2.20
	Estimated Activity Retained	1600.0	66.70

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TABLE XXV

PARALLEL INHALATION STUDIES WITH CARRIER-FREE Zr^{89} IN THE RAT

Zero Time

Tissue	Animal A	Animal B	Average	Animal A	Animal B	Average
Lungs	28.1	21.0	24.6	11.3	26.4	18.9
Liver	.1	.1	.1	.30	.62	.46
G. I. Tract	.31	.1	.16	2.14	2.05	2.20
Skeleton	.1	.1	.1	4.80	1.89	3 35
Head	39.7	42.1	40.9	2.51	2.46	2.49
Urine						
0-1 Day				.31	.23	.27
1-2 Days				.73	.54	.64
2-3 Days				.68	.50	.59
Total				1.72	1.27	1.50
Feces						
0-1 Day				9.62	7.41	8.50
1-2 Days				3.34	25.6	29.5
2-3 Days				14.2	10.9	12.5
Total				57.2	43.9	50.6
Activity Exhaled		30 5	28.8			

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CHAPTER V

RADIO-AUTOGRAPHIC STUDIES OF THE DISTRIBUTION OF INHALED FISSIONABLE MATERIALS AND FISSION PRODUCTS IN RAT LUNGS

1. Histological and Radio-autographical Methods

After intervals, as stated in the text, following the inhalation of the aerosol being studied, the rats were killed with chloroform. The lung tissues were fixed, while intact in the animals, by the injection of 80% alcohol (pH approx. 8.0) into them through the trachea. (Zenker-formol could not be used as a fixative because it was found to cause the fogging of the X-ray film; formalin could not be used because it leached plutonium from the tissues.) The lungs were then dissected out, and after overnight fixation the tissues were dehydrated in dioxane and embedded in paraffin. Sections ten micra in thickness were cut and mounted on microscope slides. The paraffin was removed by washing the slides in xylol. The slides were dipped into very thin celloidin and set on edge to dry, the latter material serving to afford them a thin, protective covering.

Each slide was covered with a piece of Eastman or Agfa no-screen X-ray film, carefully wrapped in blackpaper to exclude light, and placed under a lead weight to hold the film in close contact with the sections. (To check the possibility of the weight of the lead blocks causing a blackening of film, inactive tissue sections were set up in the method described above; no film darkening was observed.) With alpha particles, at least one

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count per second per square centimeter was required to strike the film to obtain sufficient blackening in ten days. After sufficient time had elapsed for getting an adequate blackening of the film, the films were removed and developed, and the slides were stained with hematoxylin and eosin. Each stained slide and its radio-autograph was examined microscopically, and the regions of darkening were compared with the corresponding histological structure. The areas of darkening on the film correspond to the regions in the sections where the administered material was accumulated. Representative slides and their corresponding autographs were selected to be photomicrographed and are presented here.

2. Results

a. The Distribution of Plutonium as $PuO_2(NO_3)_2$ in Lung Tissue. (Pu^{+6})

Small particles of plutonium were produced by dissolving $PuO_2(NO_3)_2$ in ethyl ether and ejecting it as a spray. (See page 8 for detailed method). Lung radio-autographs of rats sacrificed immediately after inhalation of this material showed a concentration of plutonium on the surface of bronchi, small, terminal and respiratory bronchioles, alveolar ducts, and a random distribution throughout the alveolar structure. (Figure 32.) The total plutonium content of this lung approximated three micrograms at this time. Sixteen days after exposure, the amount of plutonium present was considerably less and was cleared off of the surface of the structures noted at zero time, i.e., small bronchi, small and terminal bronchioles, alveolar ducts; the remaining activity in the lung tissue was scattered through the lung and was apparently in the alveoli. (Figure 33.)

1119326

Figure 32

Deposition of Plutonium as $PuO_2(NO_3)_2$ in Ether Spray. Zero time. Lung. (X 10). Note deposition of plutonium on the surface of a bronchus (largest structure in lung section), absence of plutonium in blood vessels located above and below latter structure, surface concentration on small, terminal, and respiratory bronchioles, and alveolar ducts.

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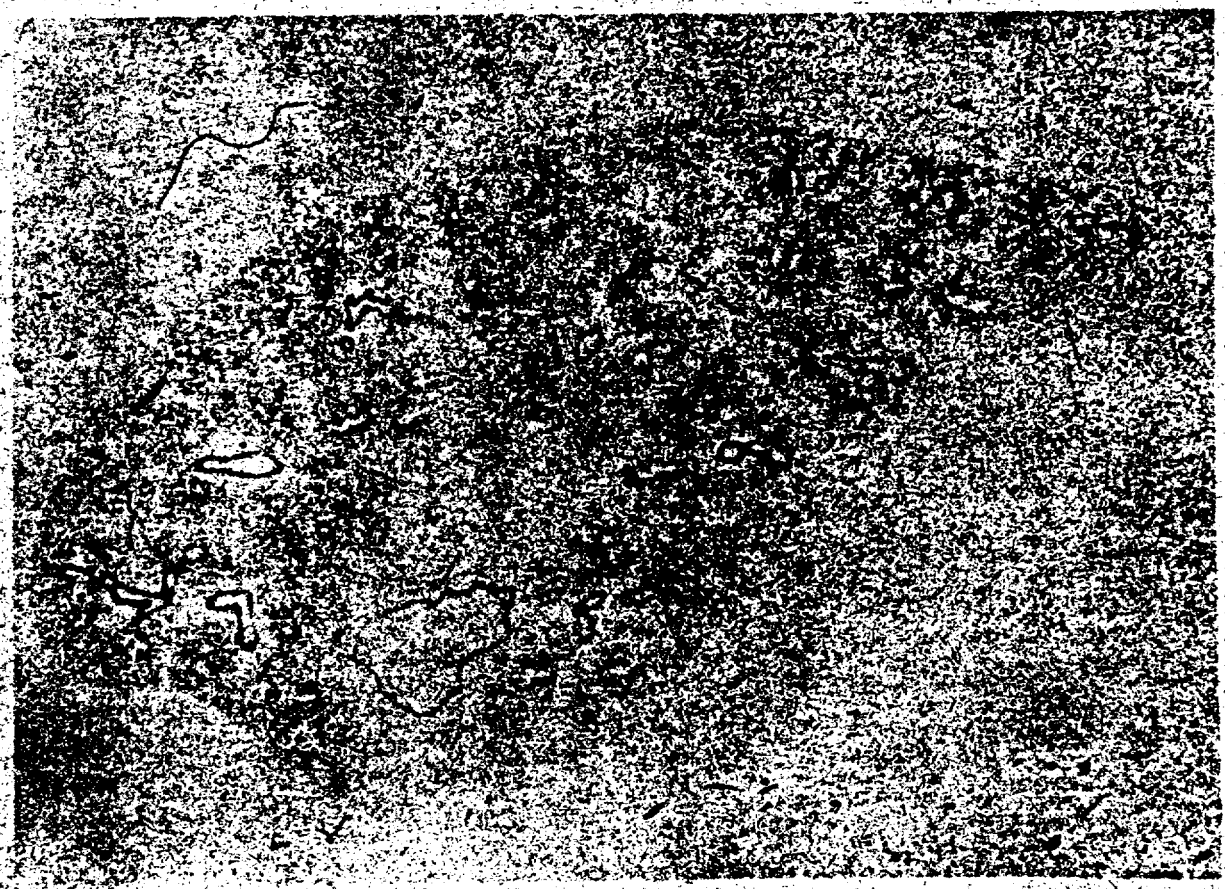

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Figure 32

Figure 33

Deposition of plutonium as $PuO_2(NO_3)_2$ in [illegible] after inhalation. (Dang. J 9). Plutonium is considerably [illegible] out of lung with new assumed data of [illegible].

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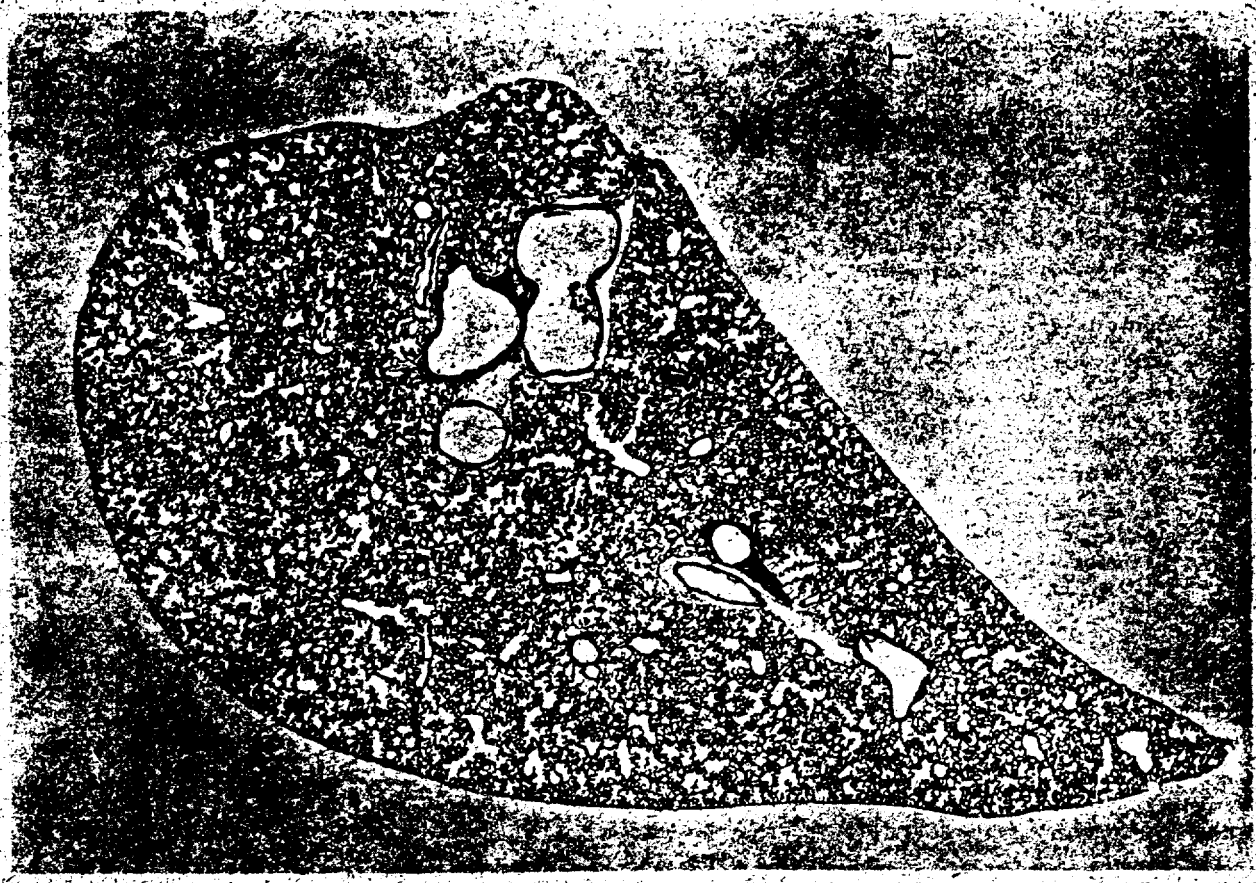

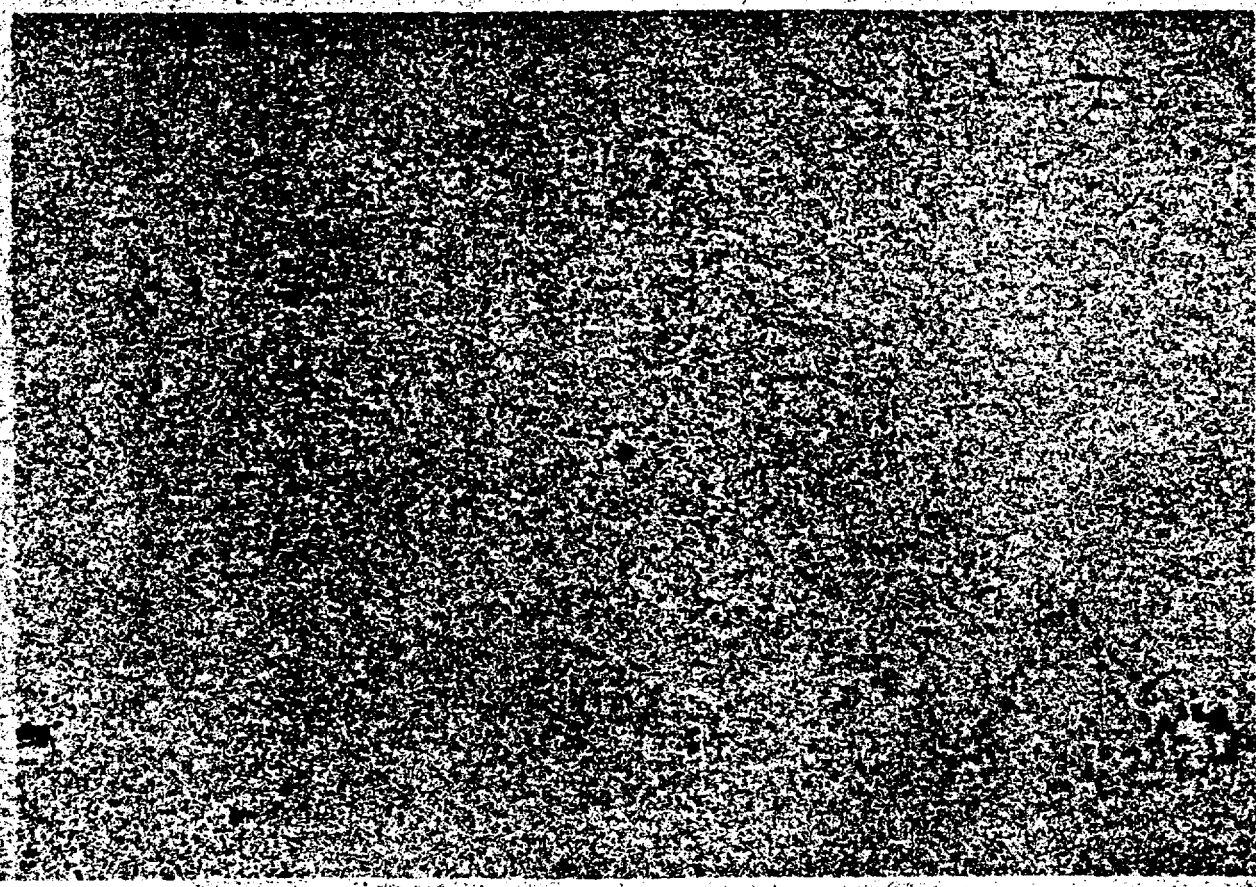

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Figure 33

b. The Distribution of Plutonium as PuO_2 in Lung Tissue. (Pu^{+4})

(1) Plutonium oxide was produced by the intense heating of the nitrates and chlorides of plutonium by means of an electric arc. (See page 17). Immediately after inhalation, the lungs showed a concentration of plutonium on the walls of small bronchi, small and terminal bronchioles, alveolar ducts, and a random distribution in alveoli. (Figure 34). At sixteen days (Figure 35), this surface concentration of plutonium disappeared, leaving spots of activity quite uniformily arranged throughout the lung tissue. Sixty-four days after exposure (Figure 36), the plutonium remained in a spotty distribution pattern throughout the lung.

(2) Plutonium oxide was produced by burning plutonium metal by means of an electric arc. (See page17). The results of this and the previous experiment were identical. At zero time, most of the plutonium was concentrated on the walls of bronchi, small and terminal bronchioles, and on alveolar-duct walls (Figures 37, 38). After one day, the plutonium was cleared off of these surfaces and was distributed in a random, spotted pattern throughout the lung. (Figure 39). At 4, 16, and 64 days, the plutonium was still spotty, with a small degree of clearing out of the material. (Figures 40, 41, 42).

c. The Distribution of Aerosols of Fission Products Obtained From Burning Uranium Oxide Plus Fission Products

Uranium wires containing fission products were burned in an electric arc, resulting in the production of uranium oxide plus fission product aerosols. (See page 36). It must be noted that

Figure 34

Deposition of Plutonium as PuO_2 - obtained from burning nitrates and chlorides of Plutonium. Zero time. Lung (X 9). Note deposition of plutonium primarily on surface of bronchial tree, with absence of radio-activity in blood vessels.

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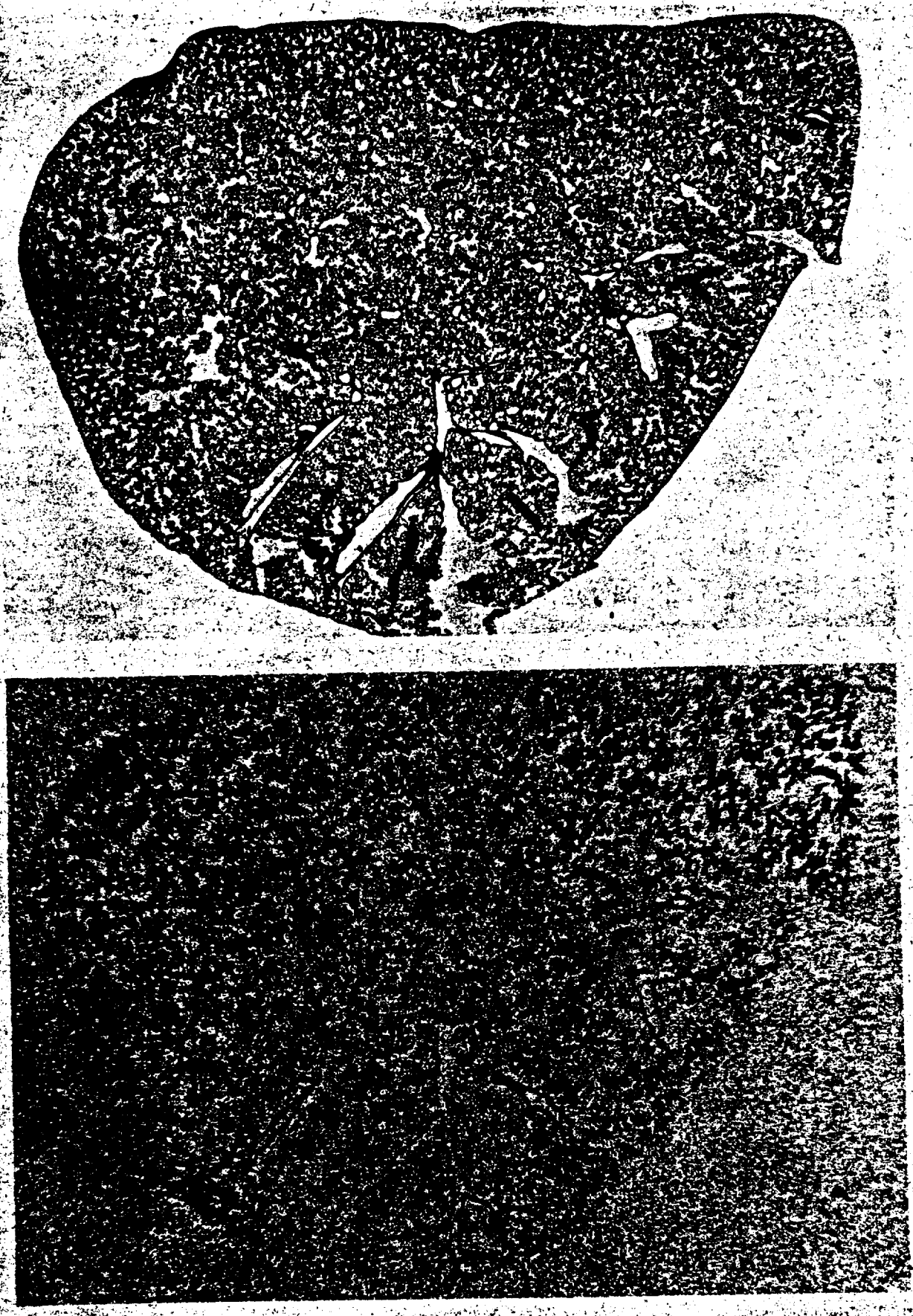

1119333

Figure 34

Figure 35

Deposition of Plutonium as PuO_2 from burning nitrates and chlorides of plutonium. 16 days after inhalation. Lung. (X 14). Plutonium cleared off surface of bronchial tree, with scattered spots of activity throughout alveolar structure of lung section.

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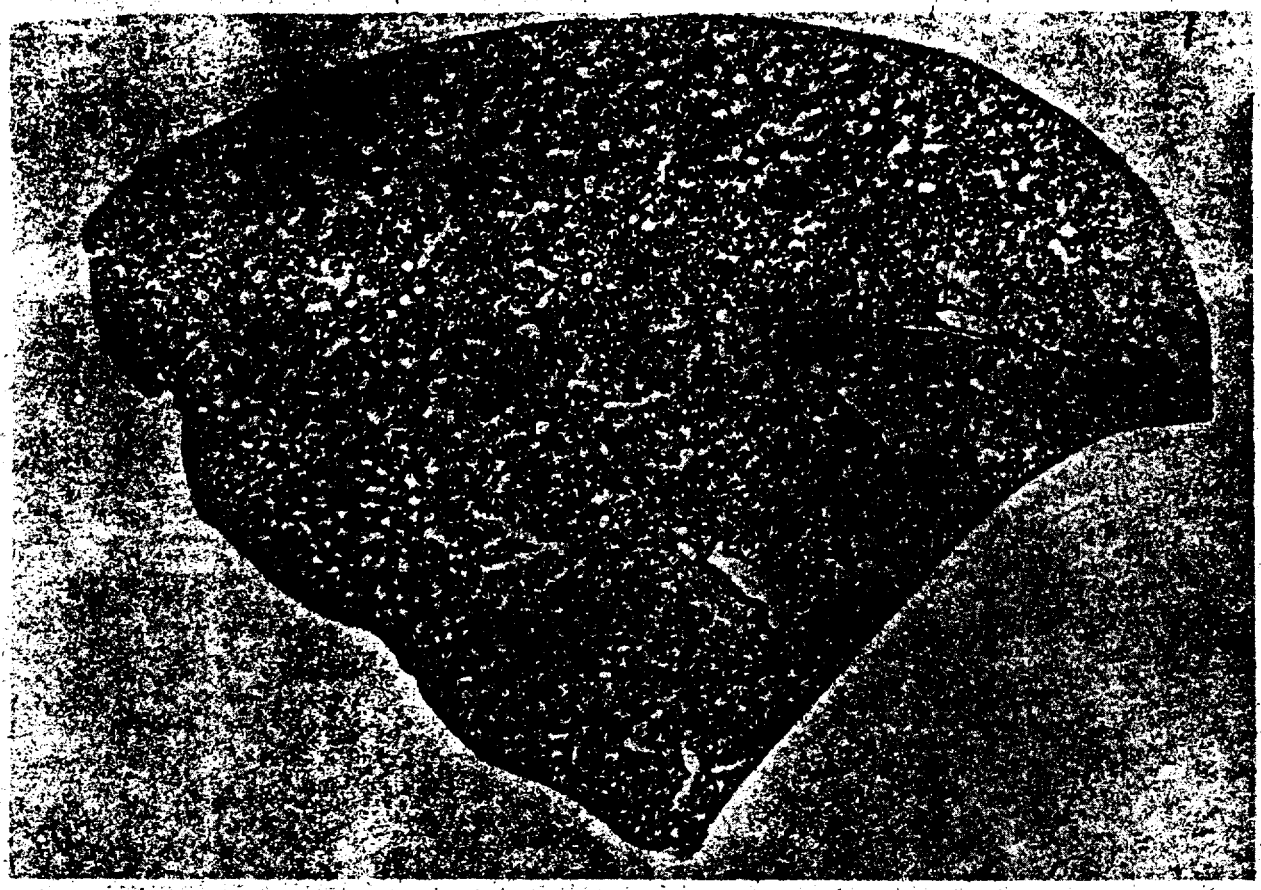
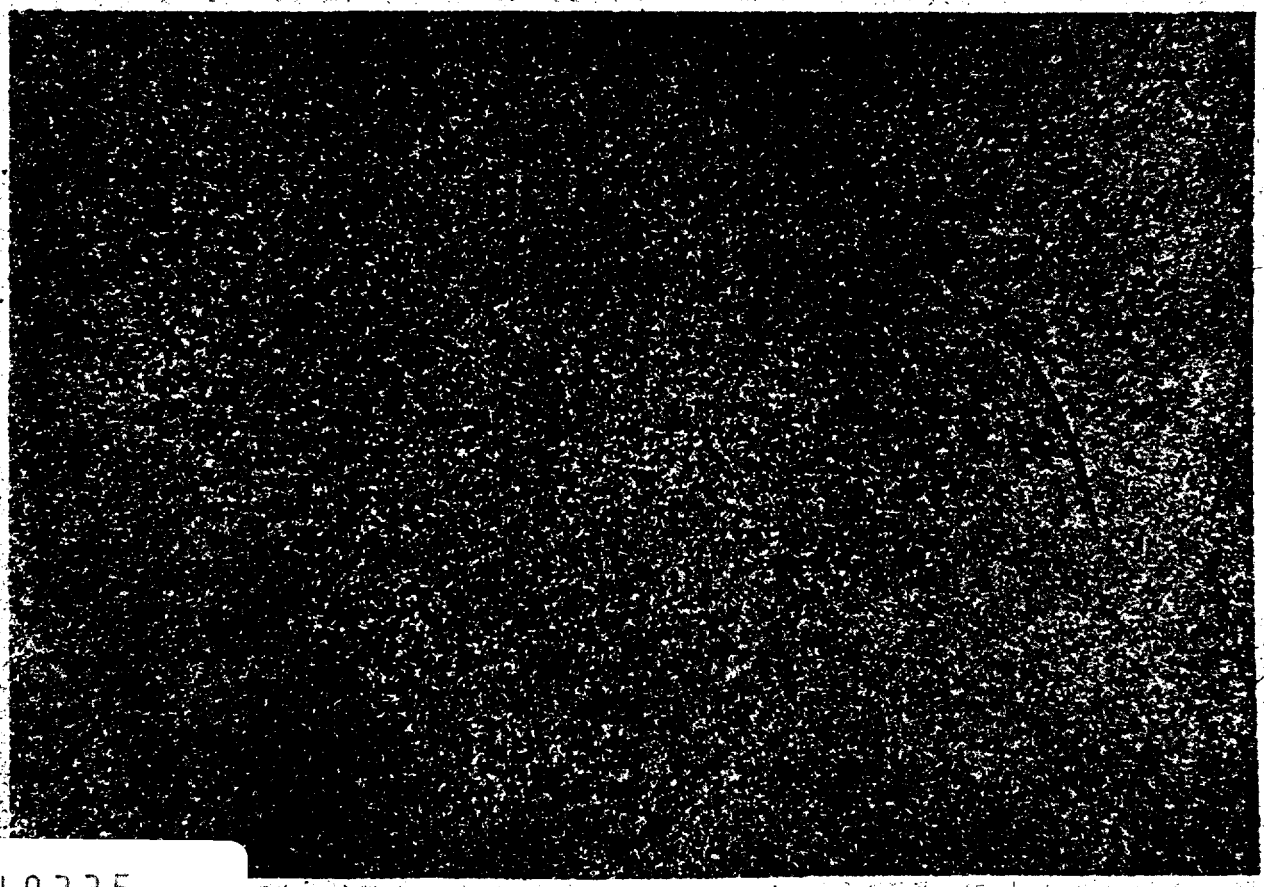




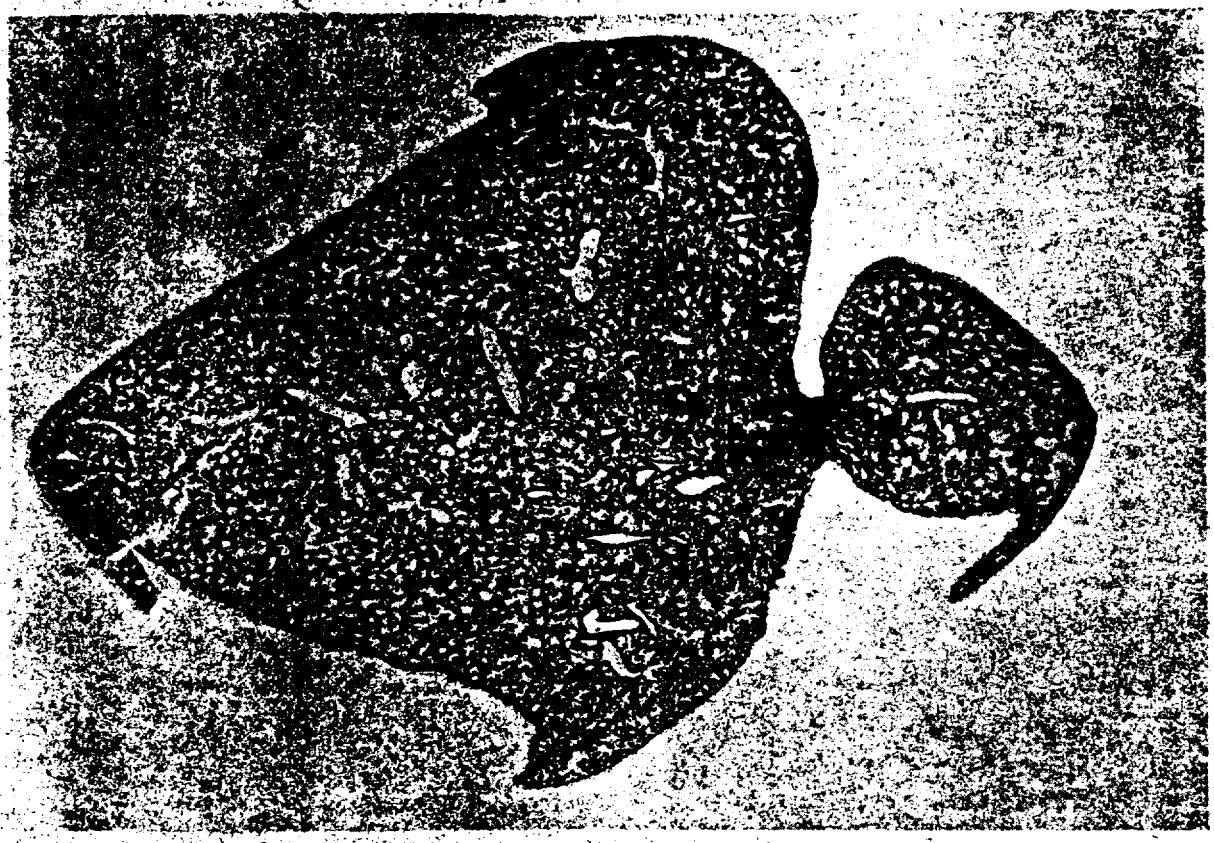
1119335

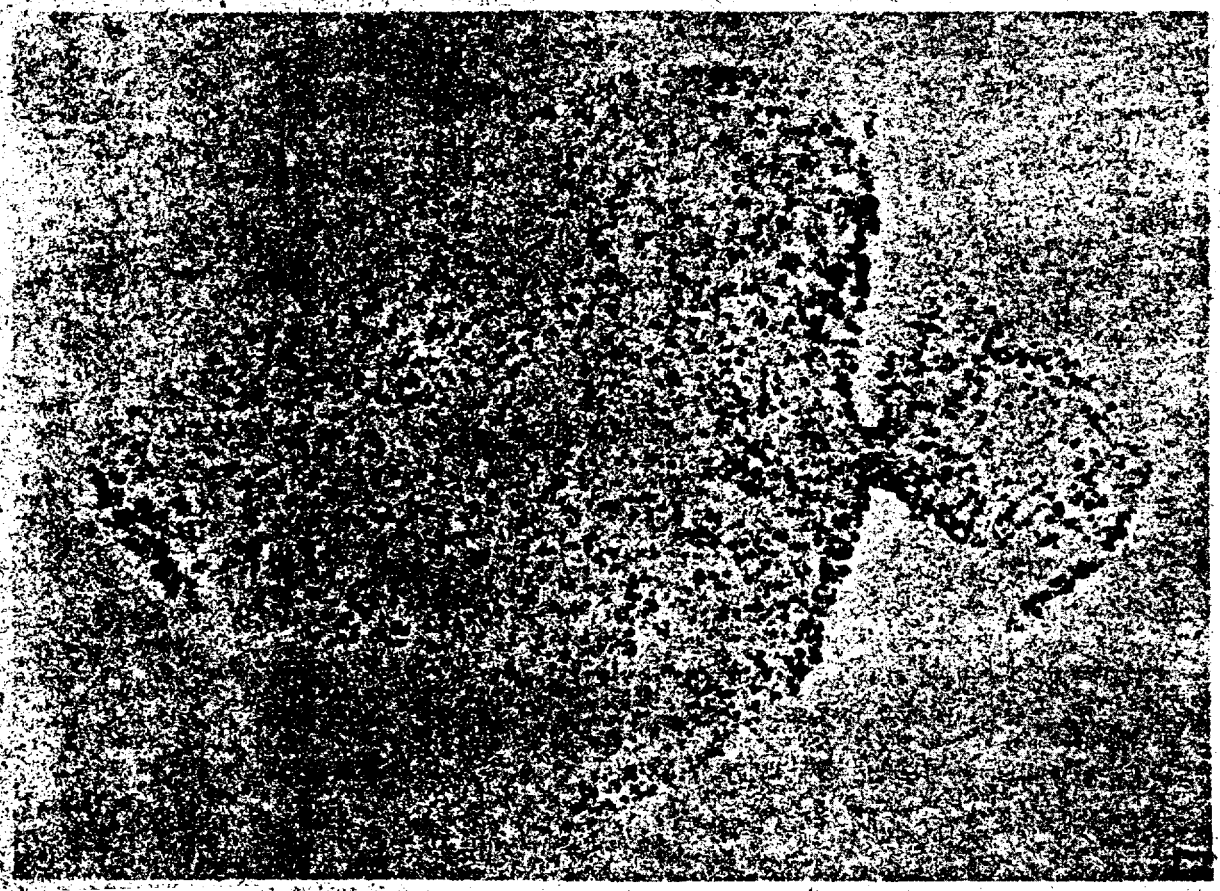
Figure 35

Figure 36

Deposition of plutonium as PuO_2 from burning nitrates and chlorides of plutonium. 64 days after inhalation. Lung. (X 10). After 64 days, considerable plutonium remaining in spotty pattern throughout lung.

1119336





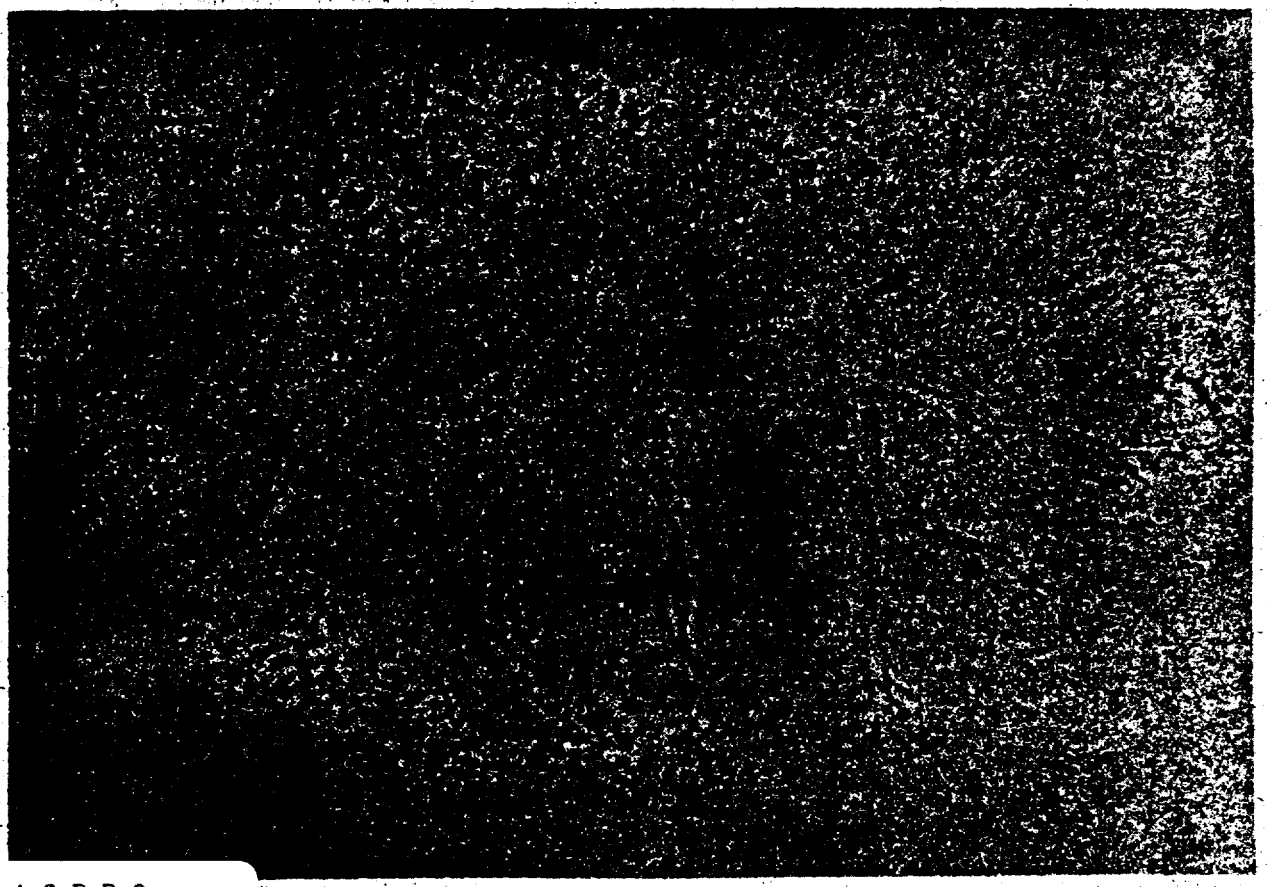
1119337

Figure 36

Figure 37

Deposition of Plutonium as PuO_2 (from burning Pu metal). Zero time. Lung. (X 10). Note deposition of plutonium on bronchial tree surface with scattered activity throughout the rest of the lung.

1119338



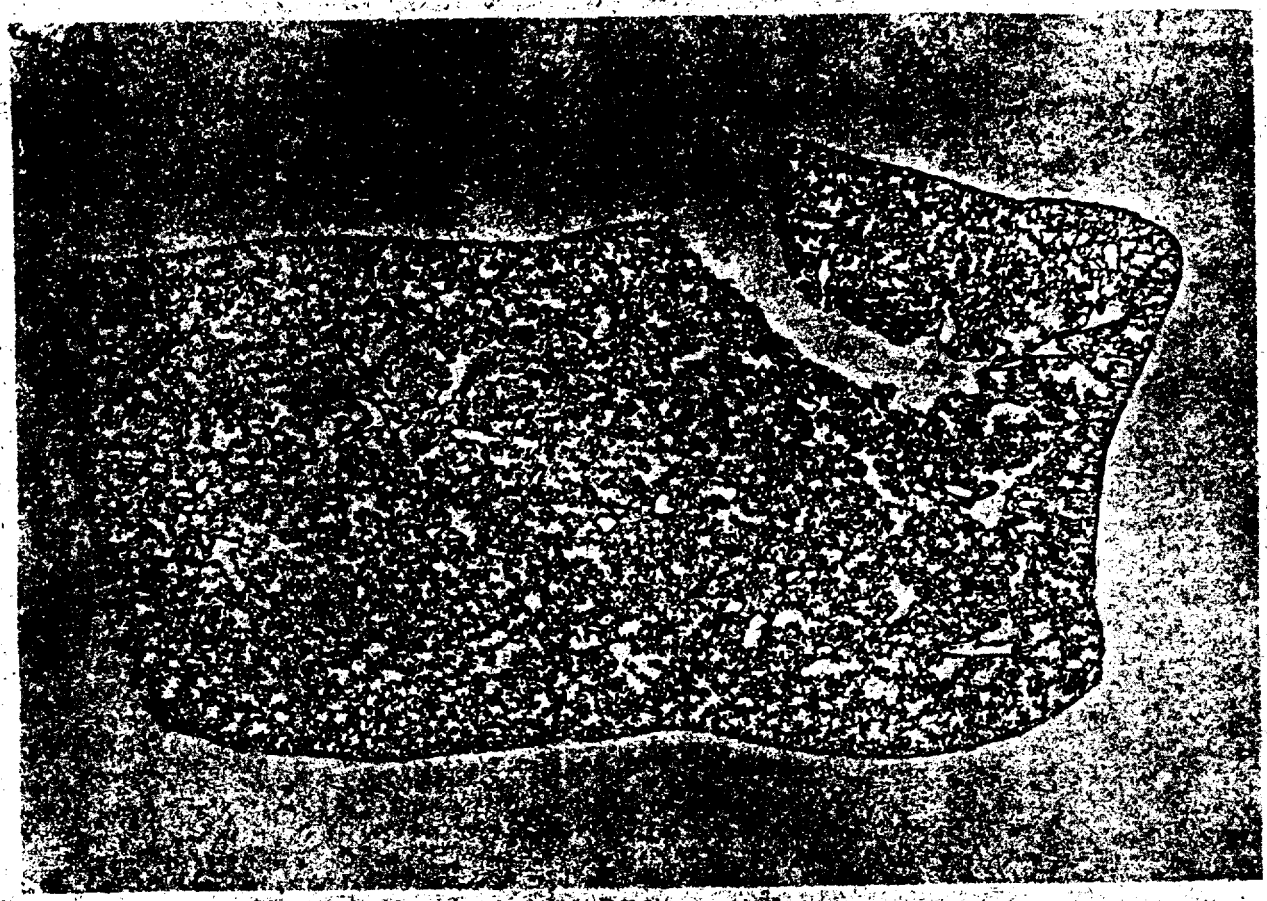
1119339

Figure 37

Figure 38

Deposition of Plutonium as PuO_2 (from burning Pu metal). Zero time. Lung. (X 10). Note deposition of plutonium on bronchial tree surface with scattered activity throughout the rest of the lung.

1119340



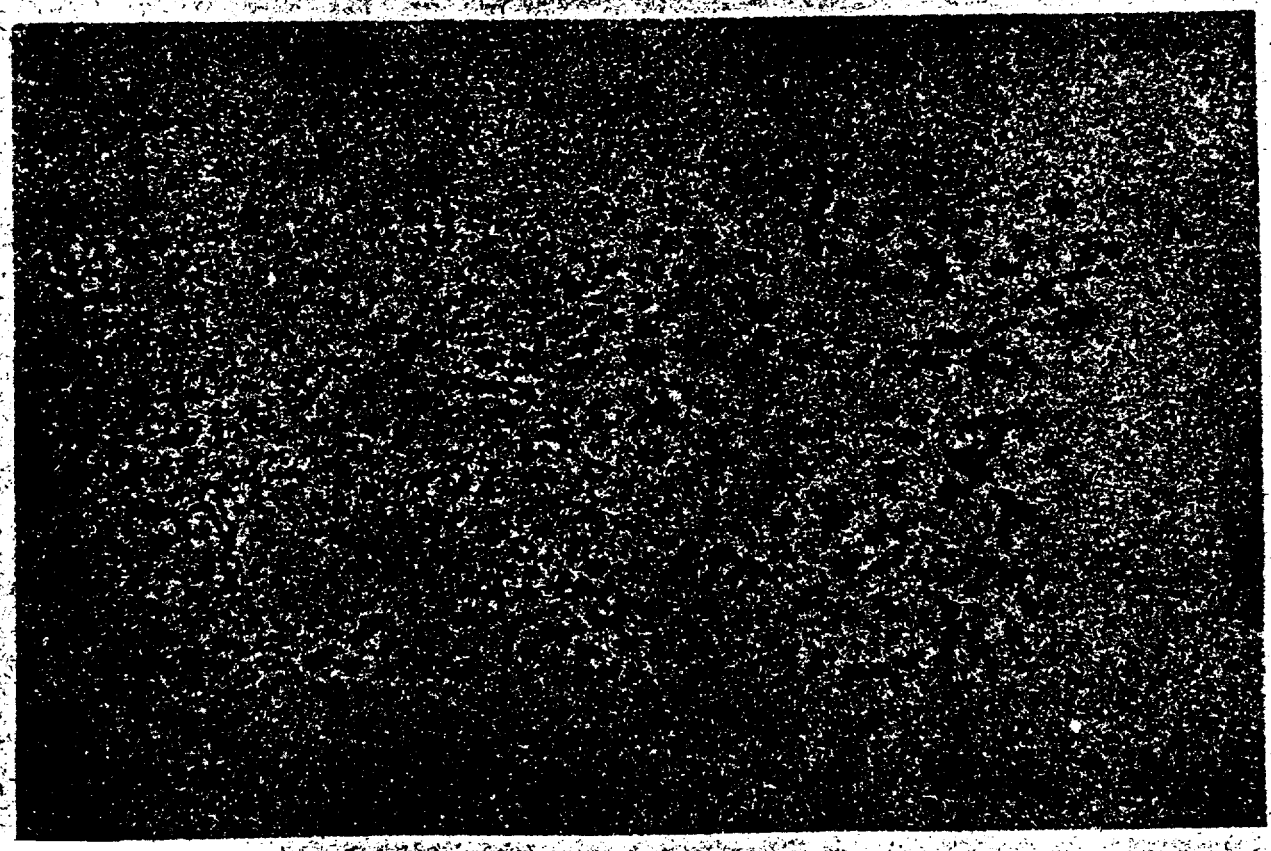


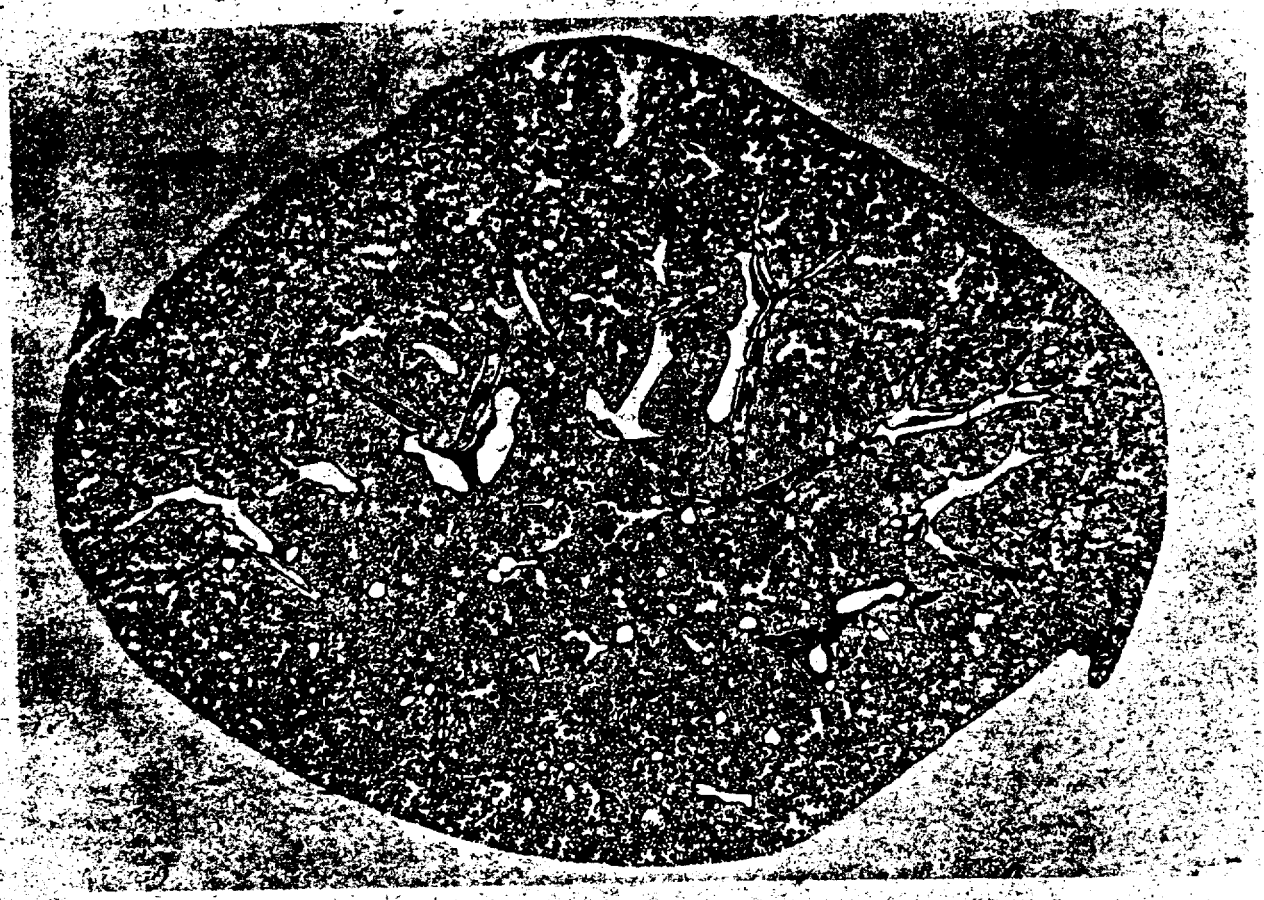
Figure 38

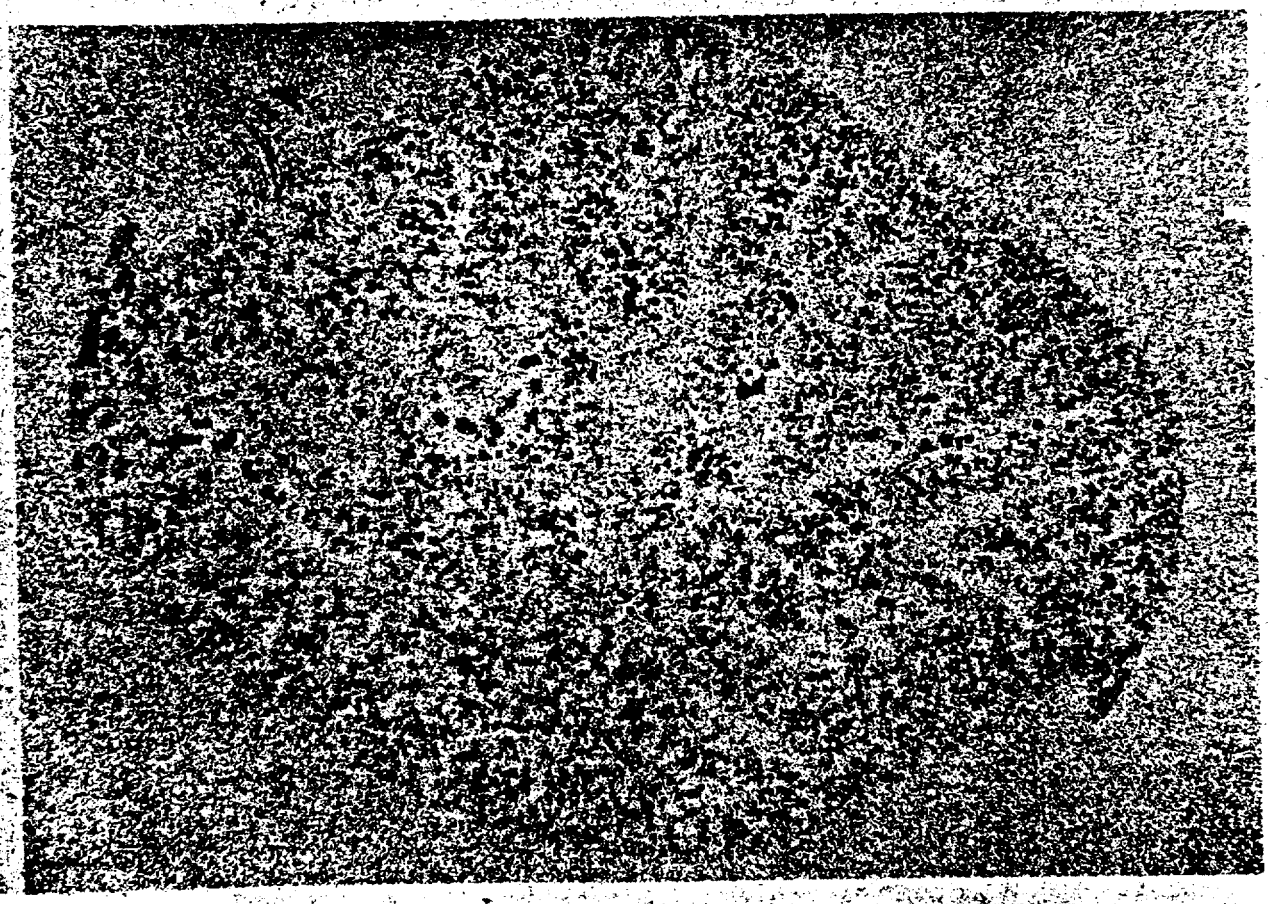
1119341

Figure 39

Deposition of plutonium as PuO_2, from burning Pu metal. One day after inhalation. Lung. (x 11). No plutonium remains on bronchial tree surfaces, as at zero time; radio-activity is arranged in spots throughout all of alveolar structure.

1119342





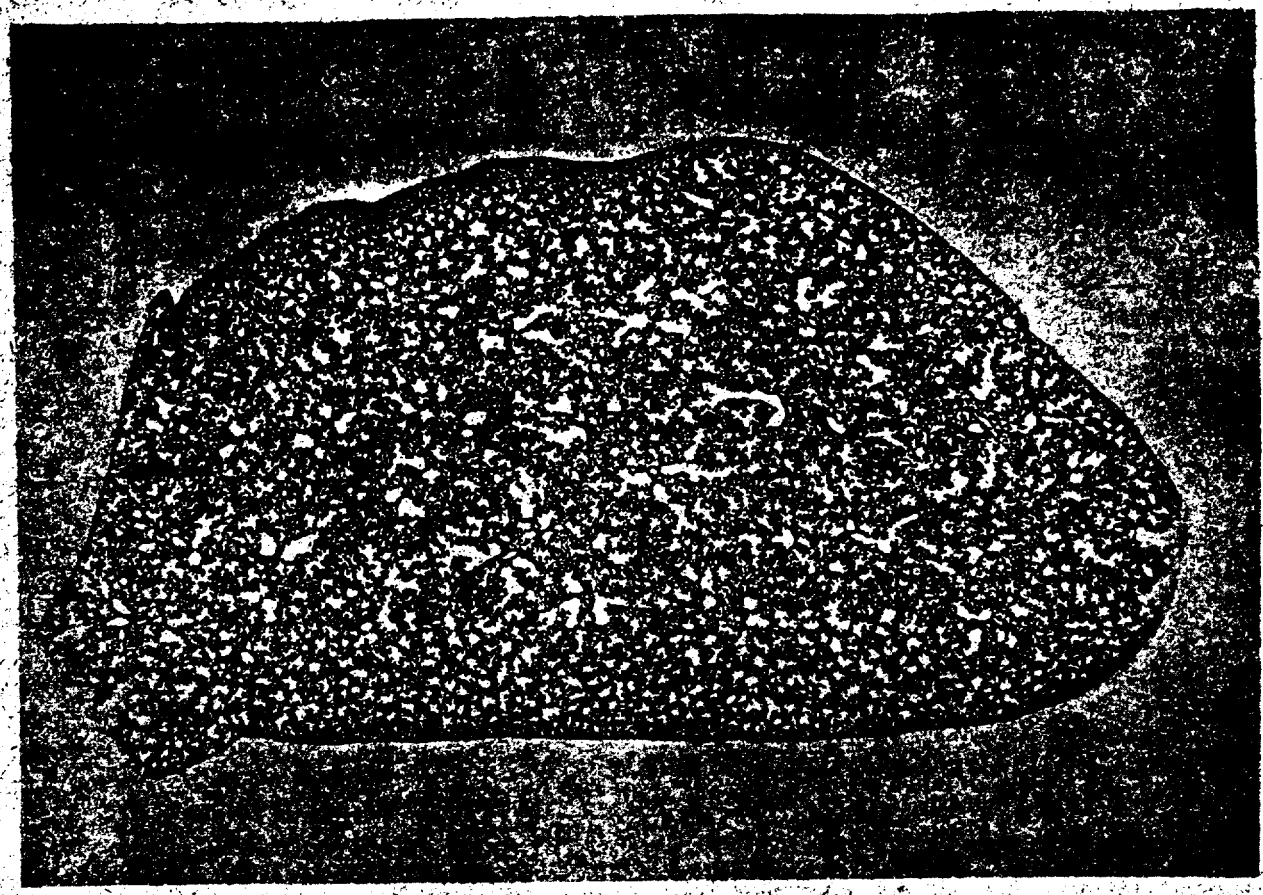
1119343

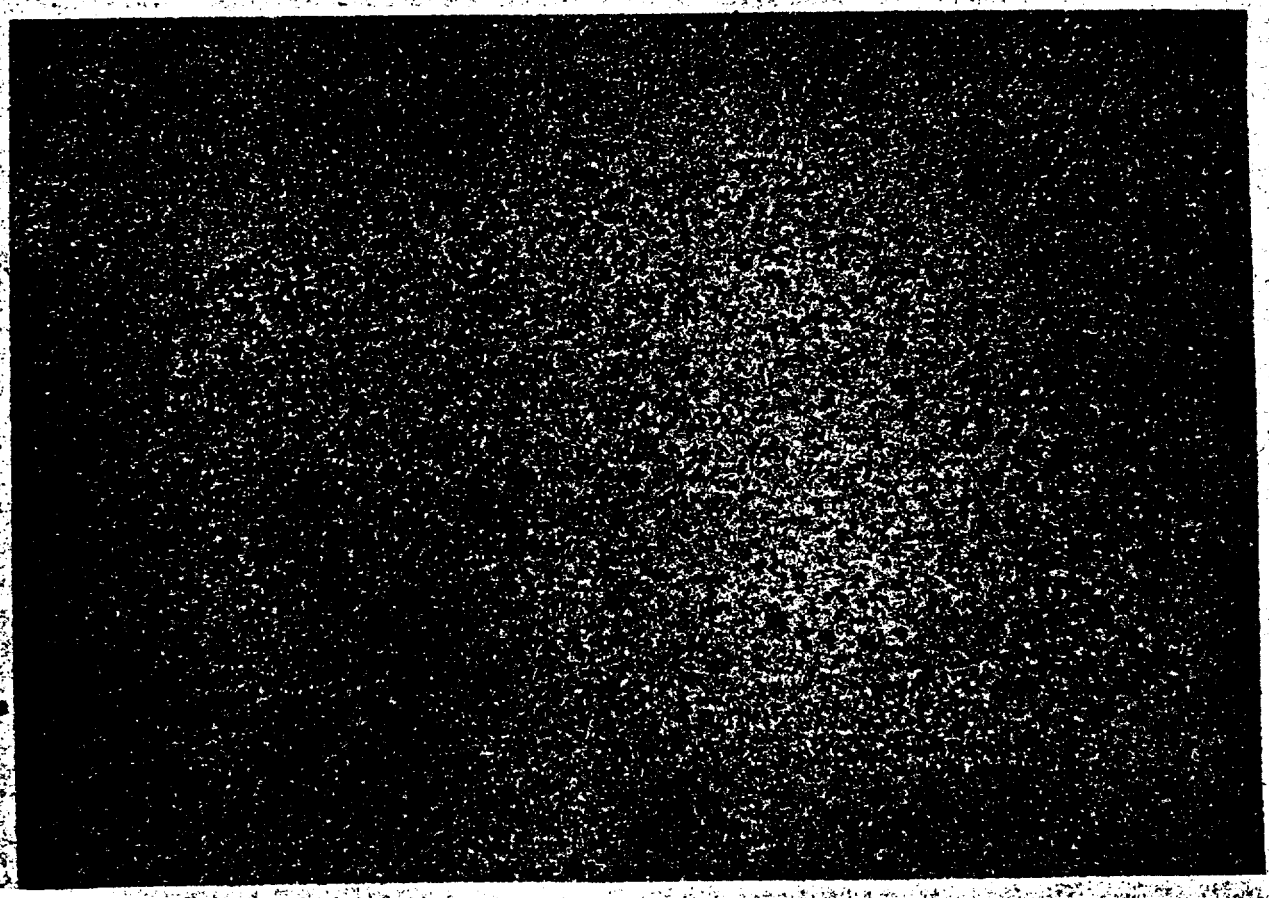
Figure 39

Figure 40

Deposition of plutonium as PuO_2 from burning Pu metal. Four days after inhalation. Lung. (x10). Radio-activity is arranged in spots throughout all of alveolar structure

1119344





1119345

Figure 40

Figure 41

Deposition of plutonium as PuO_2 from burning Pu metal. Sixteen days after inhalation. Lung. (x10). Radioactivity is arranged in spots throughout all of alveolar structure.

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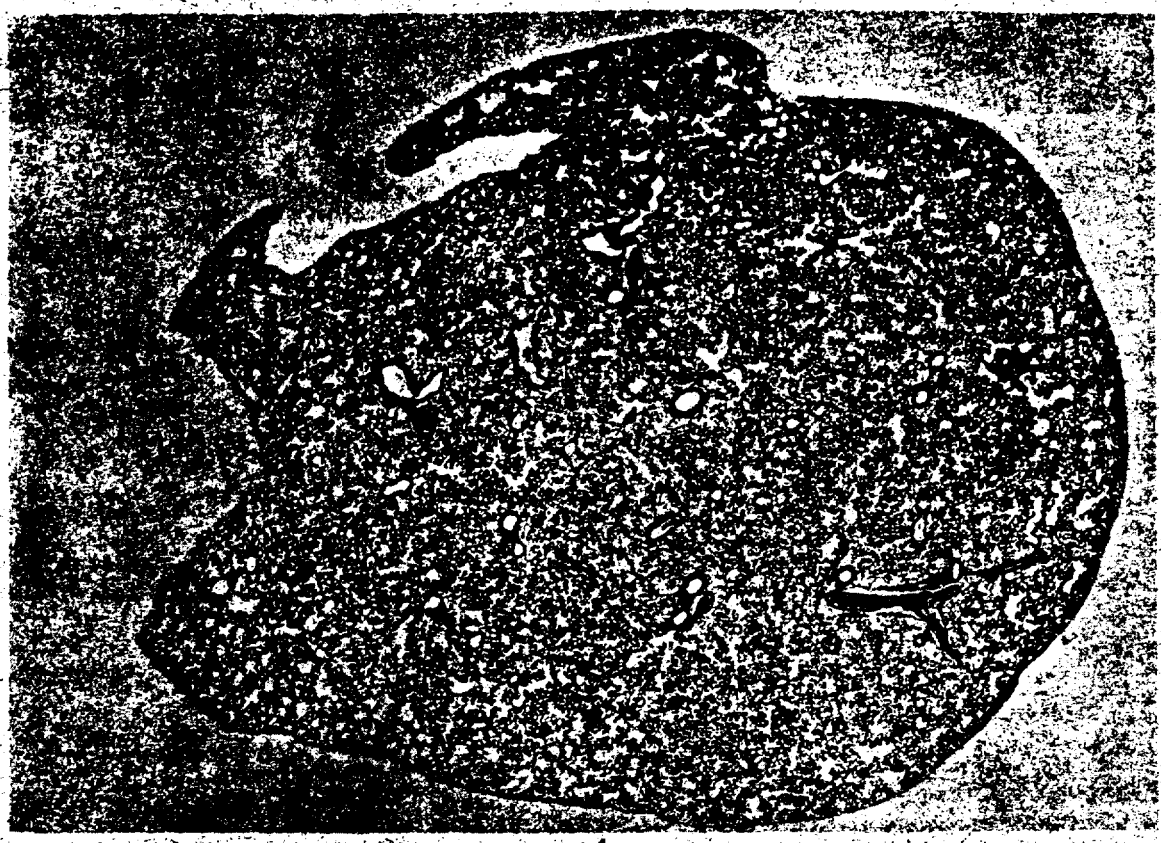


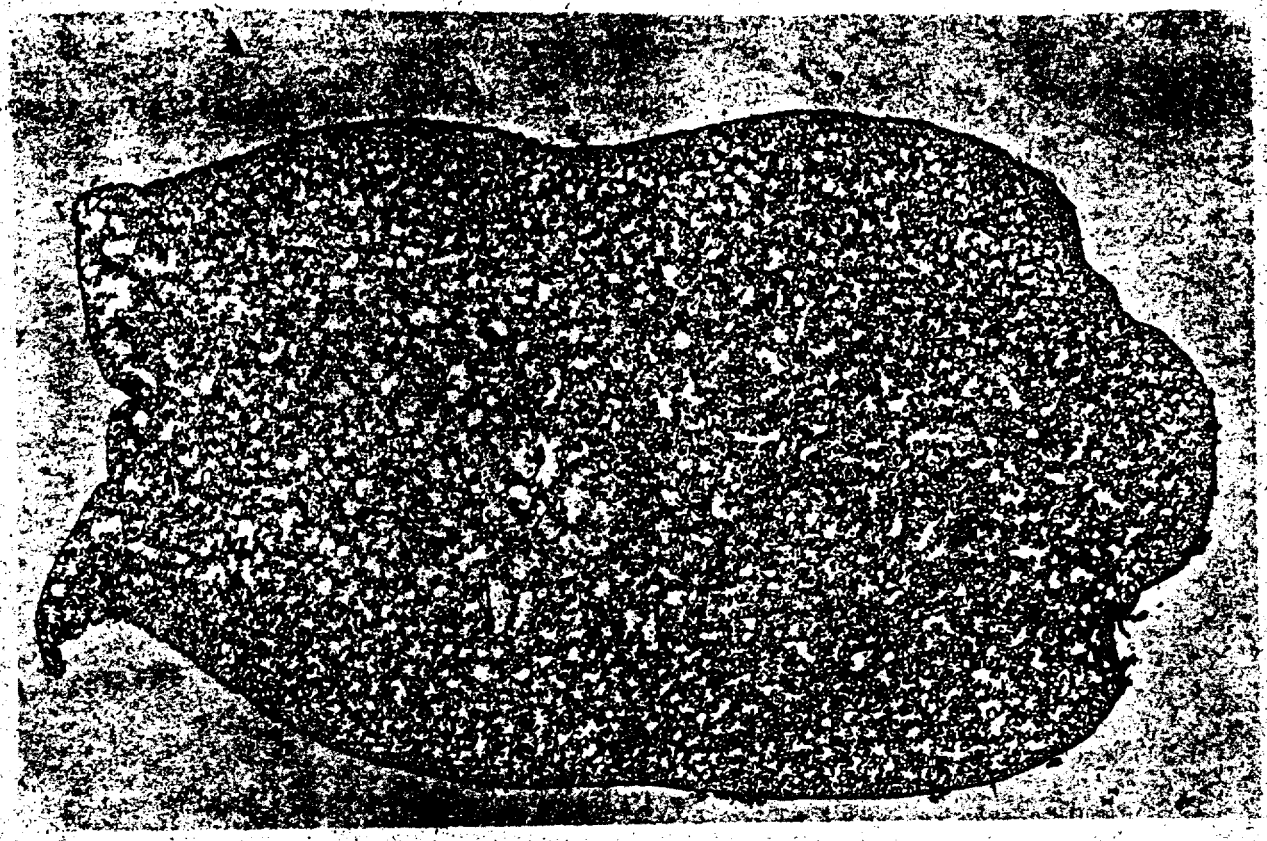
1119347

Figure 41

Figure 42

Deposition of Plutonium as PuO_2 from burning Pu metal. Sixty-four days after inhalation. Lung. (x 12). A considerable amount of plutonium still remains in the lung in a spotty distribution pattern.

1119348



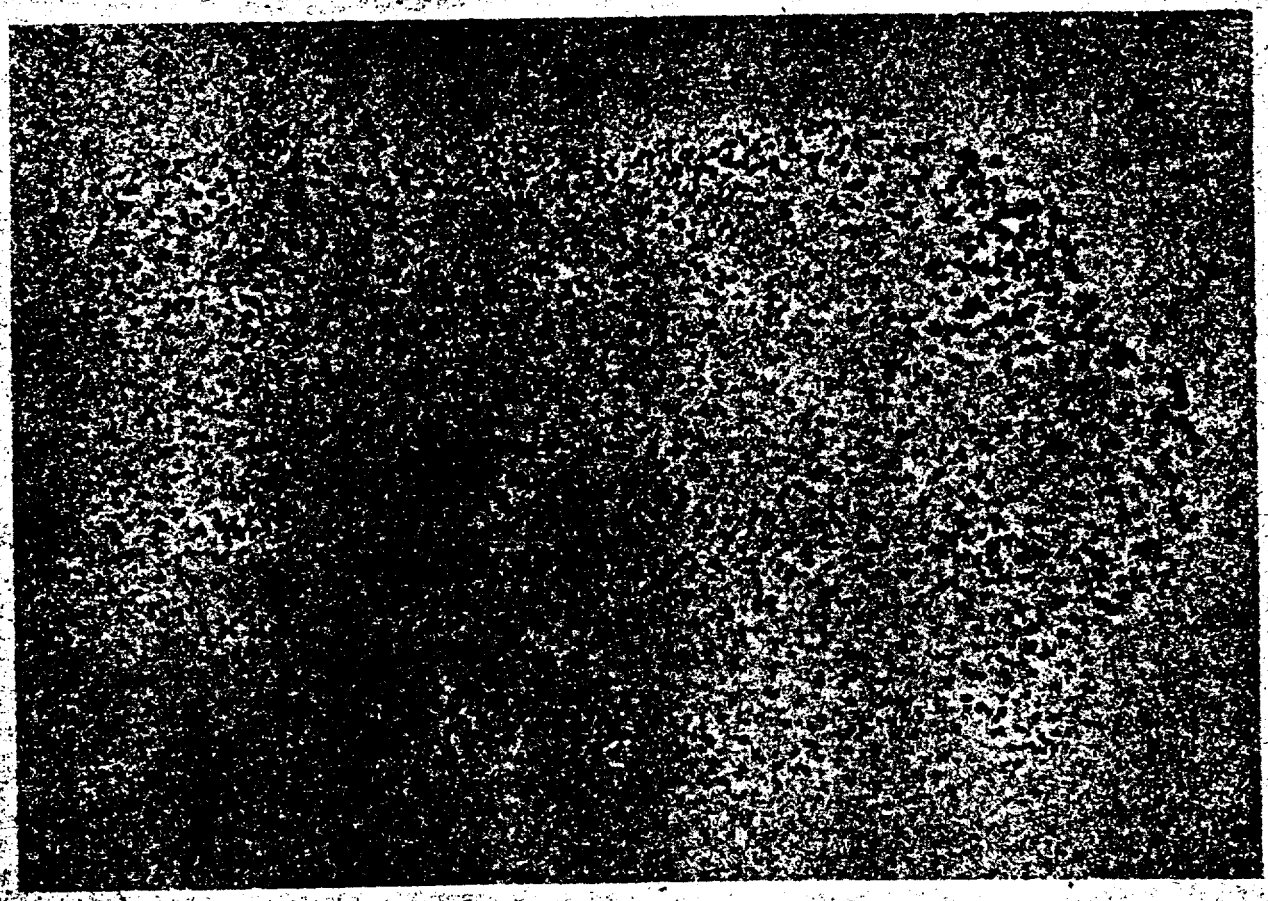


Figure 42

1119349

the radioautographs are from the fission product activity, uranium being of extremely long half-life. At zero time, the material was diffusely distributed, with some concentration on bronchiolar walls. (Figures 43, 44). After one day, the latter surface concentration was no longer noted, the activity arranged diffusely throughout the lung. (Figure 45). After four and sixteen days (Figures 46, 47) there was a random distribution similar to that noted after one day. At sixty-four days, the material was fairly uniformily distributed throughout the tissue in about half of the sections (Figure 48), and in the other half there was peripheral concentration (Figure 49).

d. <u>The Distribution of Short-Lived Fission Products from the Clinton Pile in Lung</u>. (See page71 for description of method.)

At zero time, the fission products were unevenly distributed in the lung tissue, with some of the bronchial passages being outlined with activity. (Figure 50). At one day the fission product distribution was fairly uniform throughout the lung tissue. (Figure 51). It was not possible to get autographs from the longer recovery period animals due to the low activities remaining in the lung tissues at those times. It will be noted from the autographs that the particle size of the fission products in this experiment were much smaller than those in the experiment described above under c. As was pointed out in the metabolic studies, the smaller sized fission products were removed from the lung faster than the larger particles (Section c); presumably the small particles passed across lung capillary walls and entered the general circulation.

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Figure 43

Fission products from burning uranium and fission products. Zero time. Lung. (X 10). Fission products deposited throughout the lung with some concentration on bronchiolar walls.

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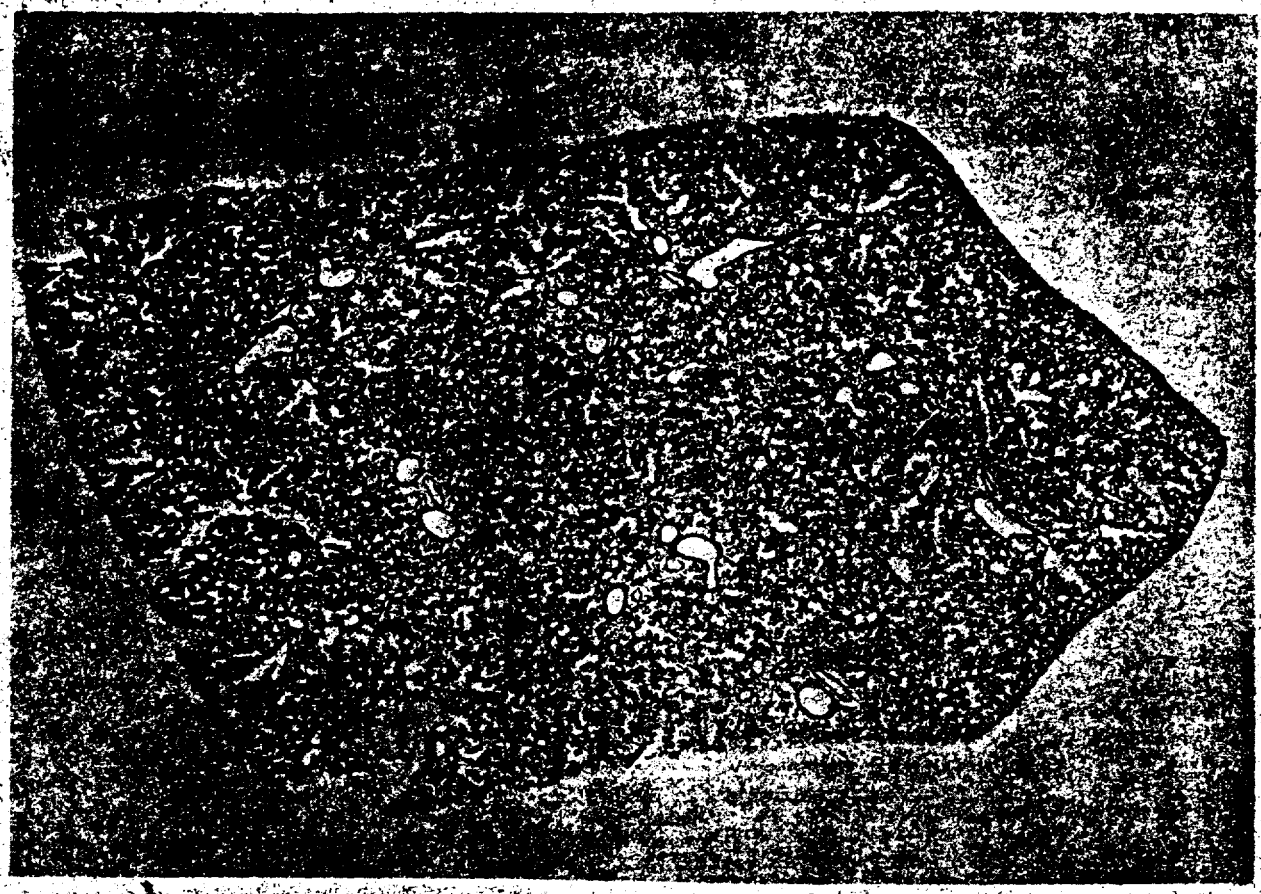
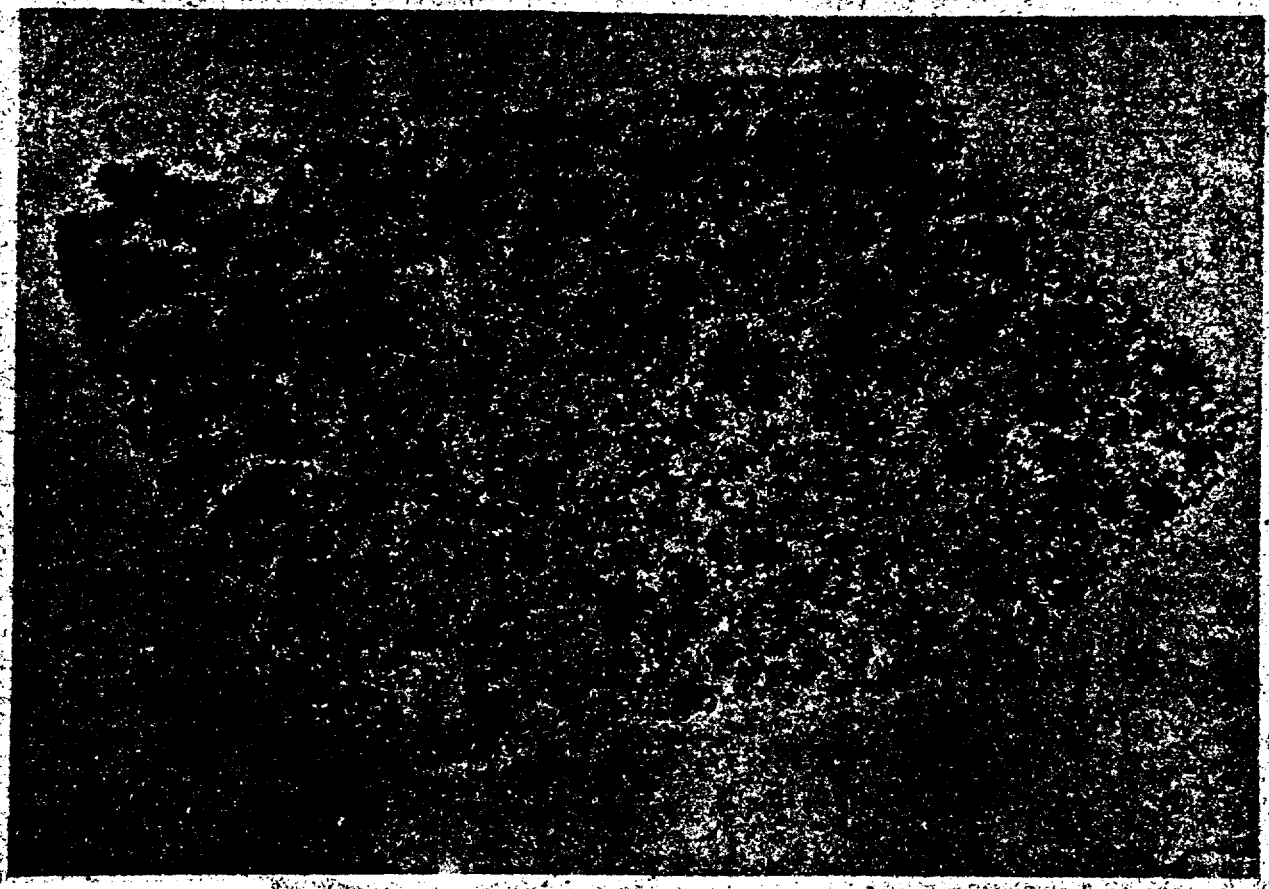




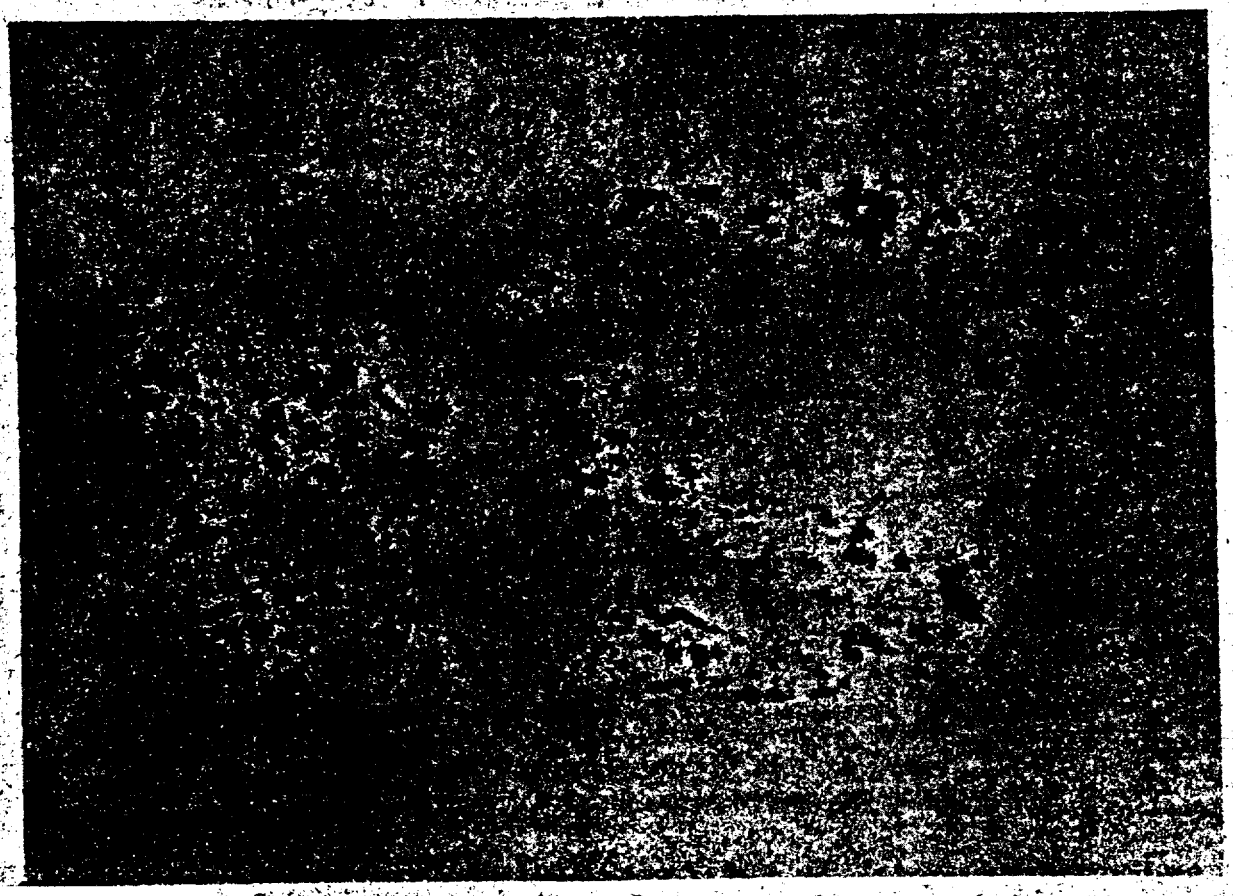
1119352

Figure 43

Figure 44

Fission products from burning uranium and fission products. Zero time. Lung. (x 9). Note absence of radio-activity from lymphoid tissue and blood vessels.

1119353



1119354

Figure 44

Figure 45

Fission Products from burning uranium and fission products. One day after inhalation. Lung. (x 12). Fission products are distributed throughout the lung.

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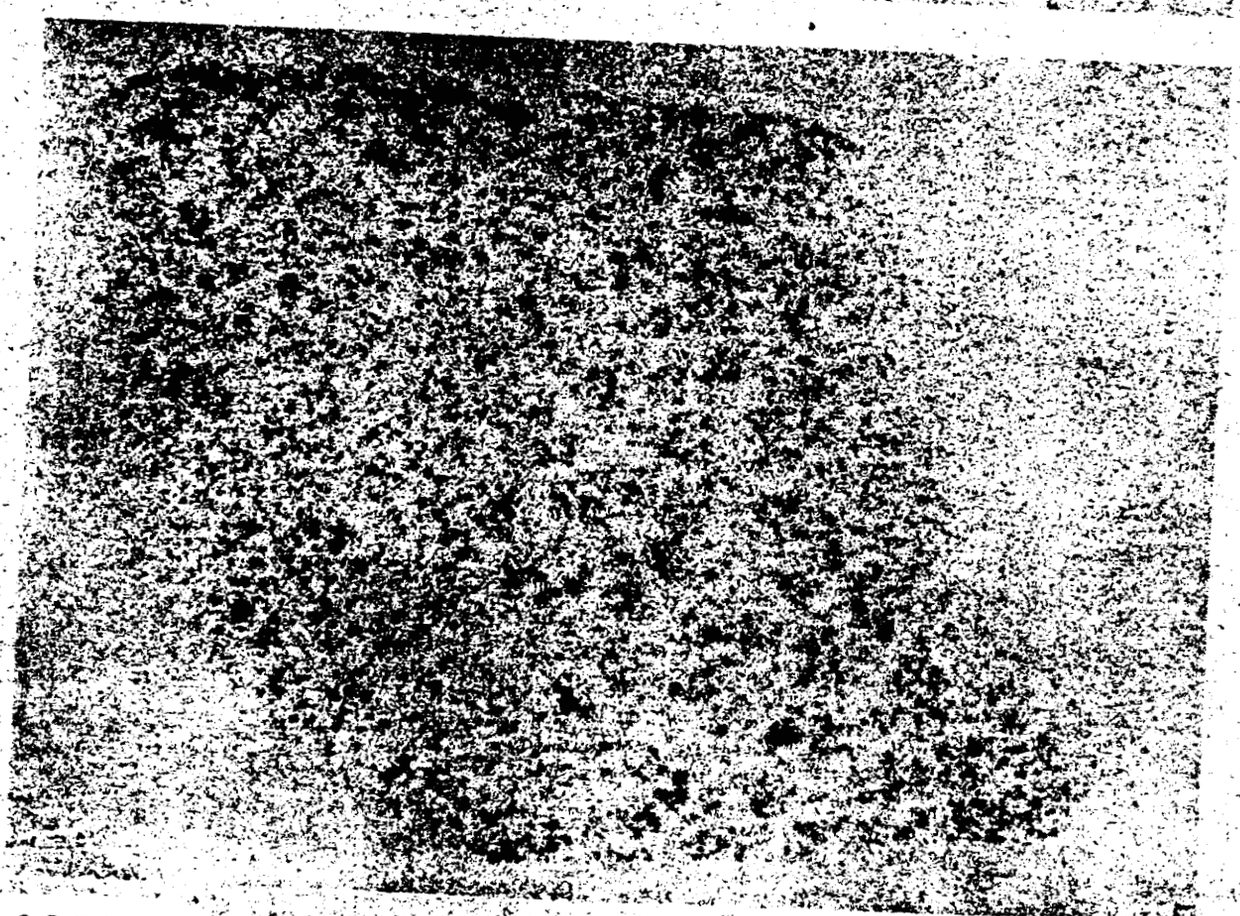
CH-5570 10/10



1119356

Figure 45

Figure 46

Fission products from burning uranium and fission products. Four days after inhalation. Lungs. (x 8). Fission products distributed throughout the lung.

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1119358

Figure 47

Fission products from burning uranium and fission products. Sixteen days after inhalation. Lung. (x 11). Fission products are distributed throughout the lung.

1119359

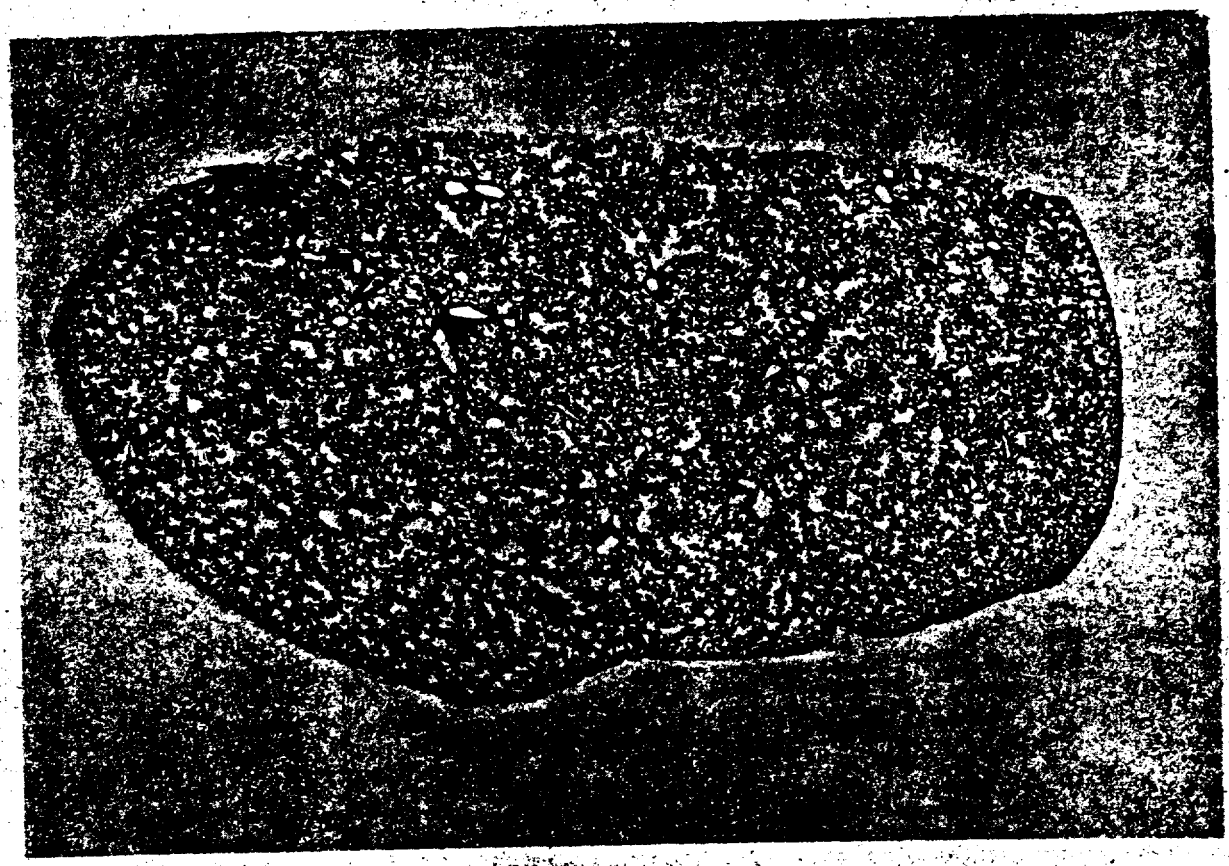

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Figure 47

Figure 48

Fission products from burning uranium and fission products. Sixty-four days after inhalation. Lung. (x 9). Fission products are distributed throughout the lung.

1119361

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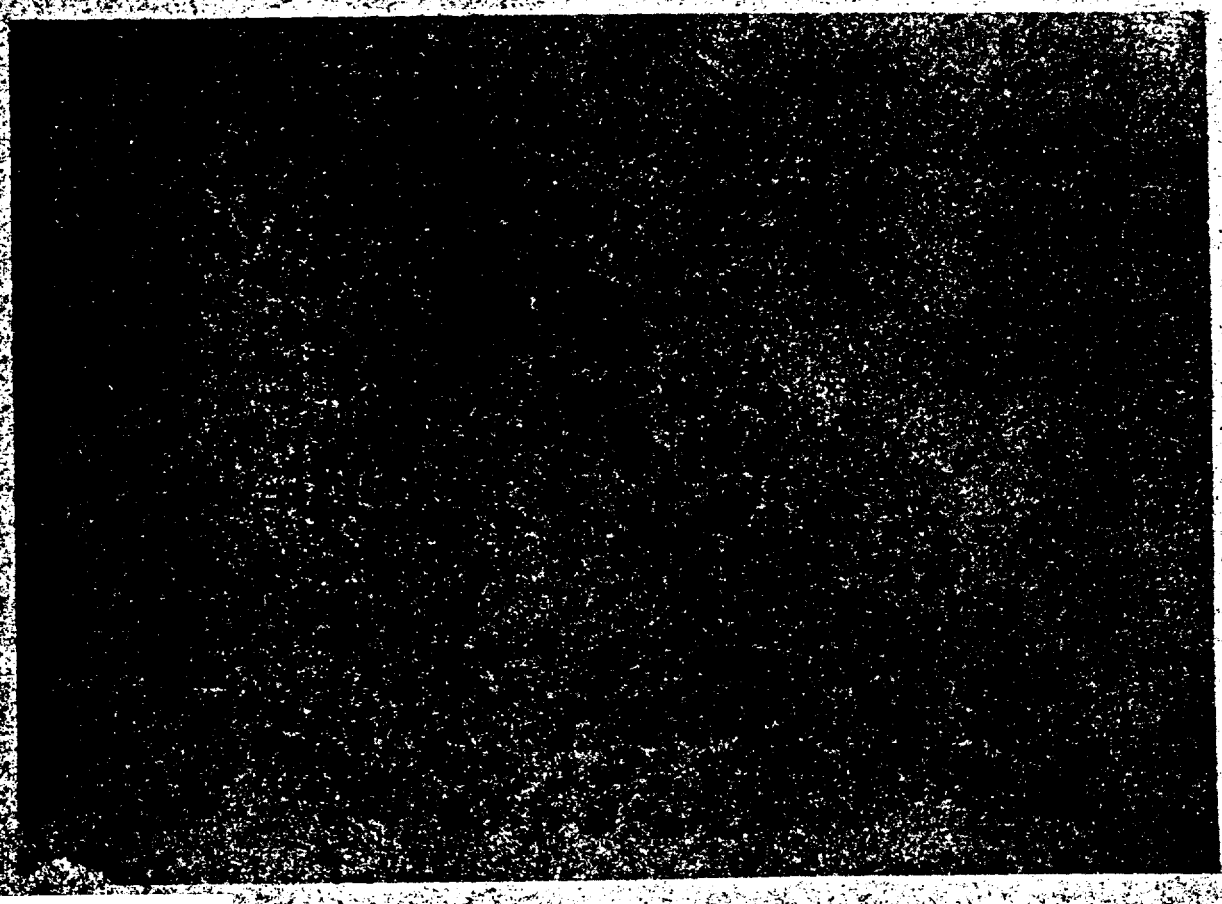

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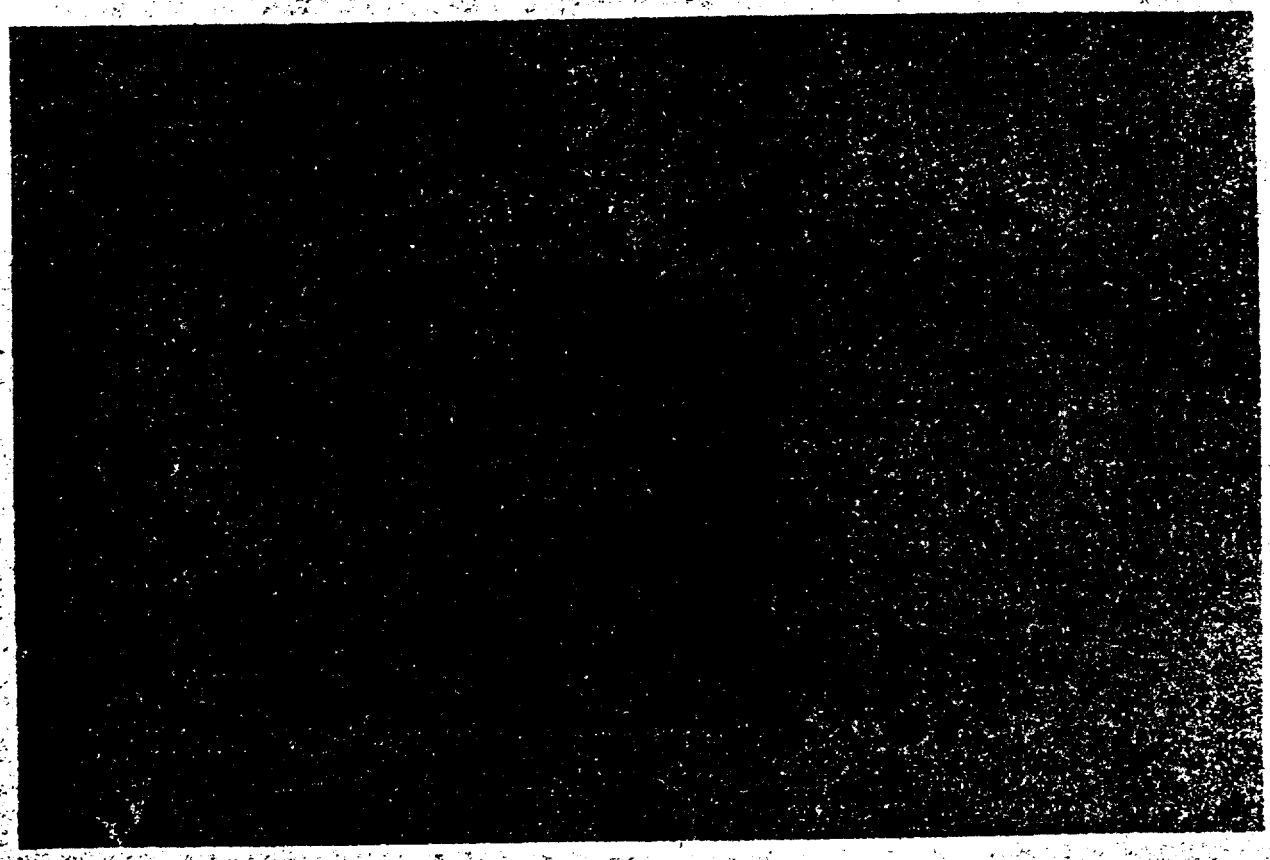
Figure 48

Figure 49

Fission products from burning uranium and fission products. Sixty-four days after inhalation. Lung. (x 9). Peripheral accumulation of fission products.

1119363



1119364

Figure 49

Figure 50

Fission Products from Clinton Pile. Zero time. Lung. (X 14). Note uneven distribution of fission products, with the surfaces of a few of the bronchiolar passages outlined with radio-activity.

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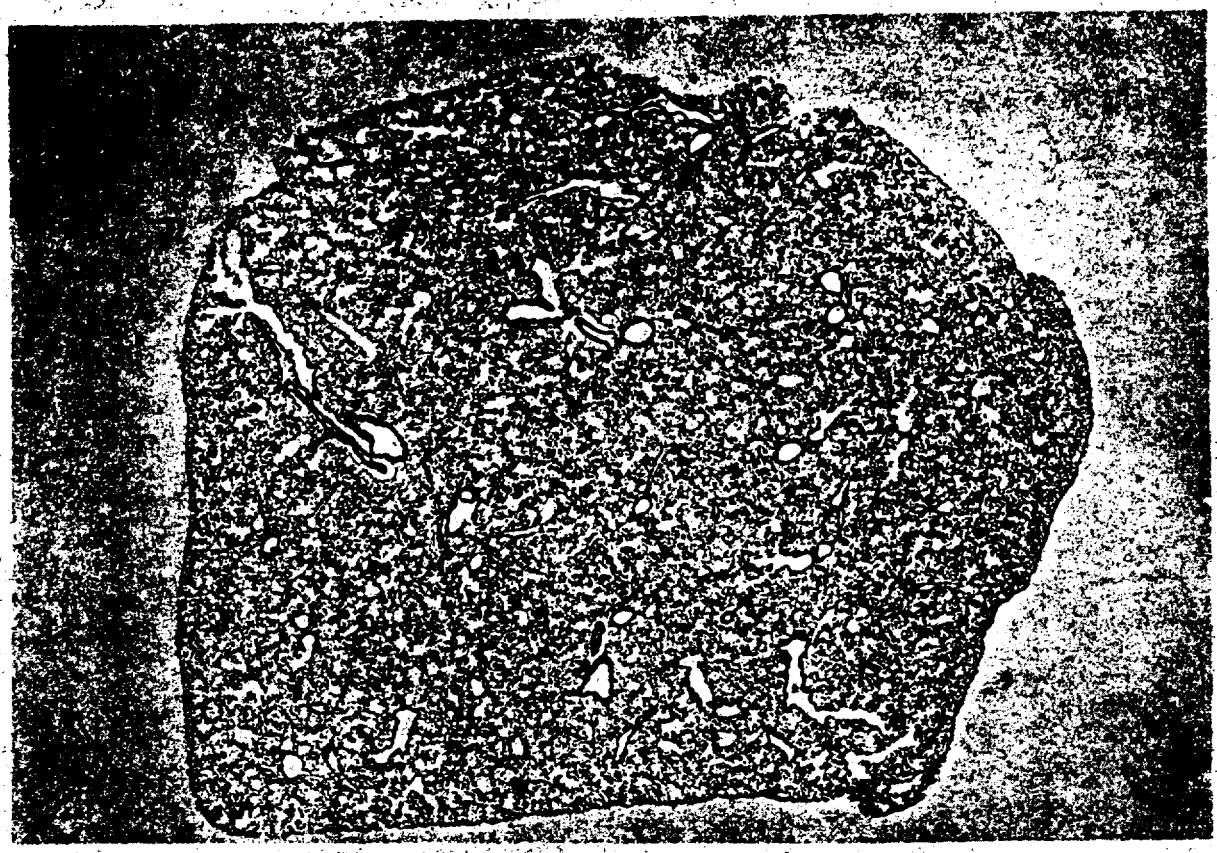

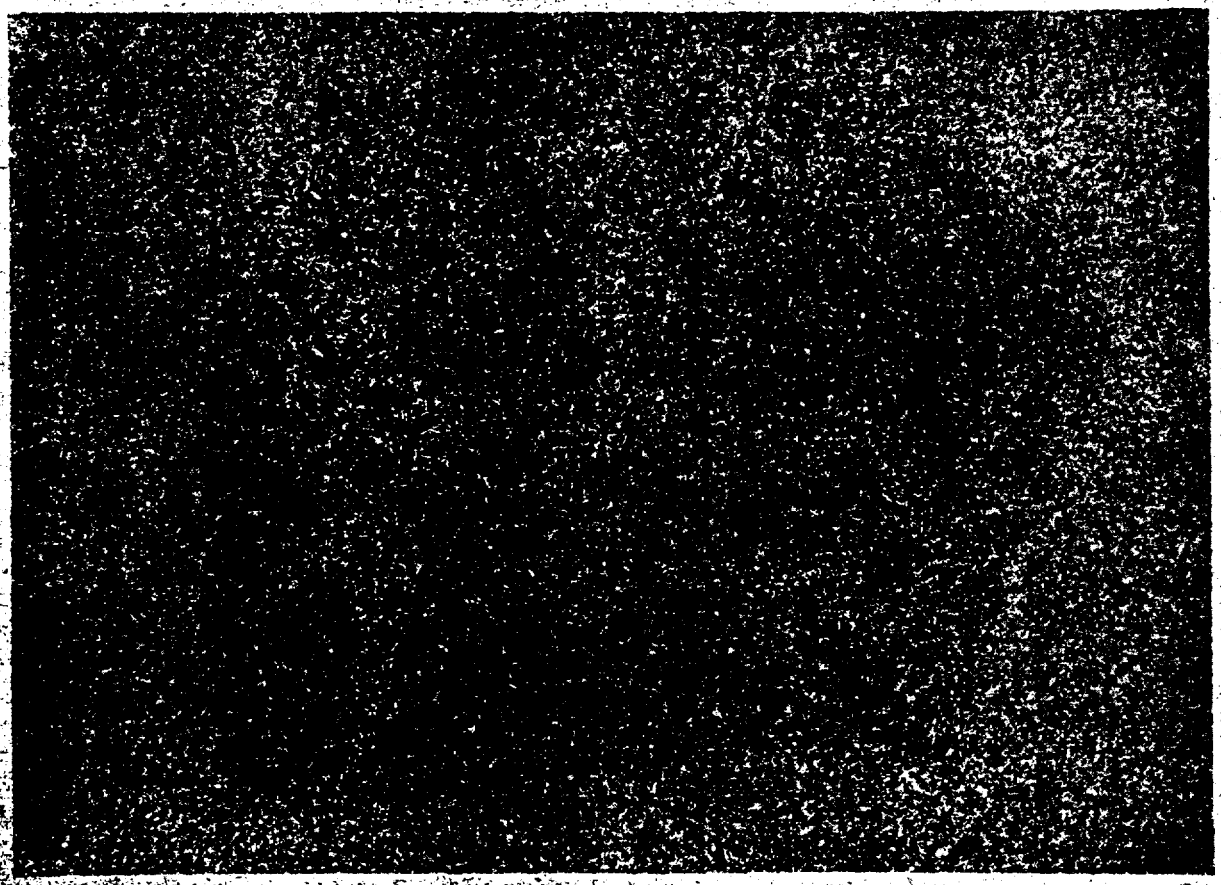

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Figure 50

Figure 51

Fission Products from the Clinton Pile. One day after inhalation. (x 10). Note the even distribution of fission product activity throughout the lung tissue. Note difference in size of particles as compared with plutonium and aerosols of fission products.

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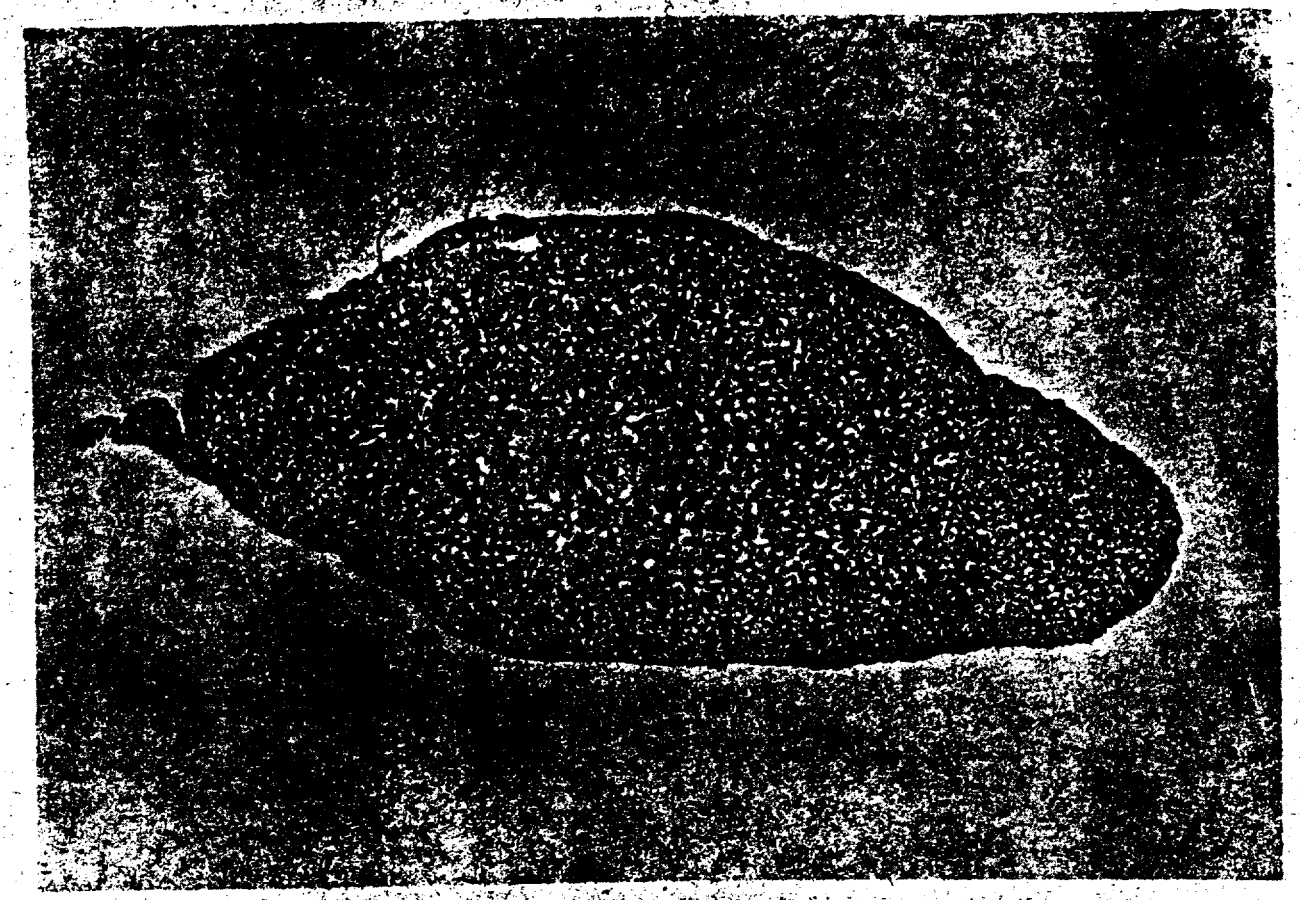
CH-3590

115a



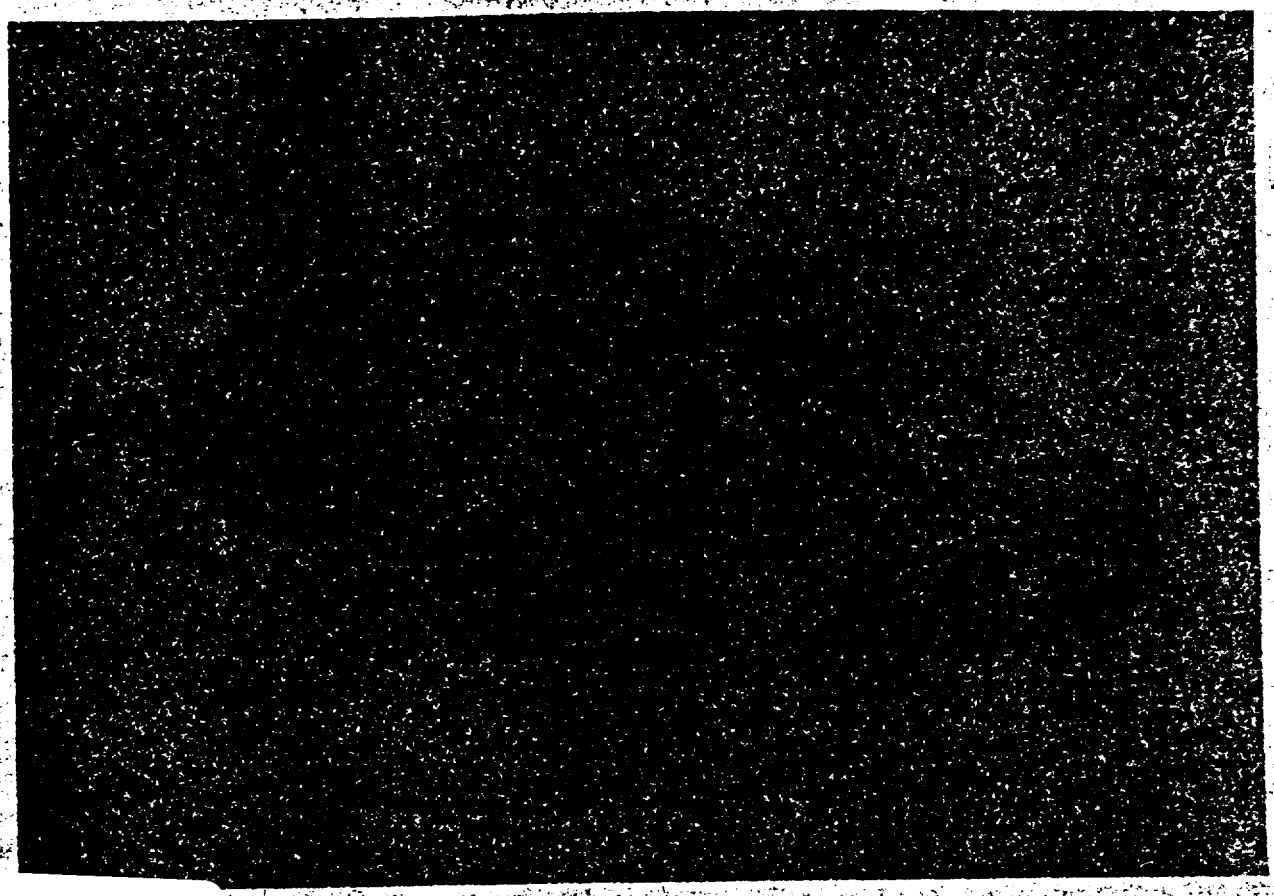


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Figure 51

Discussion:

The foregoing studies demonstrate that, upon inhalation, aerosols produced by any of the methods used in these investigations are primarily trapped in the head and lungs. The radio-elements used in these studies which are deposited in the respiratory passages of the head are rapidly eliminated via the gastro-intestinal tract, so that these passages are relatively free from contamination four days after exposure. The time for half-elimination of activity from the upper respiratory tract was less than twenty-four hours. The above mentioned elements, when inhaled, persist in the lungs for longer periods of time, but a definite excretion via the bronchial tree was observed in all of the elements studied for the duration of intervals up to 256 days.

The rate of elimination of these aerosols appears to be somewhat proportional to the particle size. A comparison of the groups shows that plutonium inhaled in the form of the oxide, which had an average particle size of 0.49 microns, was eliminated more rapidly than particles of $PuO_2(NO_3)_2$, which were of smaller particle size, the average size of the latter being 0.25 microns. It will be noted further that a greater proportion of these relatively larger particles was deposited in the respiratory passages of the head rather than in the lungs. This was demonstrated when uranium plus fission products was inhaled. These particles had an average size of 0.97 microns. Furthermore, it appears that the passage of the elements in question through the capillary

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walls of the lungs is related to particle size. A comparison of aerosols of uranium plus fission products (whose particles averaged 0.97 microns) with carrier-free fission products aerosols (whose particles were much smaller than the above) demonstrated a much greater absorption of the latter.

When plutonium was inhaled in the plus six valence state, as the soluble compound $PuO_2(NO_3)_2$ in an ether spray, a greater percentage of plutonium was absorbed into the body via the capillaries of the lungs, than when plutonium was inhaled in the plus four valence state as an insoluble compound (PuO_2).

Radio-autographic studies of lung tissue showed that upon inhalation of the different aerosols the site of deposition of the radio-element was the epithelium of the bronchial tree, with a spotty distribution throughout the rest of the lung. There was a rapid removal of the radio-elements from the bronchial and alveolar duct surfaces as compared with their slow disappearance from the remainder of the lung, the latter localization being primarily in the alveoli. There was no concentration of the radio-elements in either lymph nodes or blood vessels.

The lung autographs from inhalation experiments with (1) plutonium oxide, PuO_2, obtained from burning the plutonium metal, (2) plutonium oxide, PuO_2, obtained from burning the nitrates and chlorides of plutonium , and (3) fission products produced by burning uranium metal containing fission products were strikingly similar.

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Plutonium oxide, PuO_2, is very insoluble in tissue fluids, and one would, thus, expect it to be retained in lung for a long time, i.e., slowly absorbed from lung tissue. In the case of fission products, the radio-elements which were retained in the lung were undoubtedly the rare earths, zirconium, and columbium, (rather than the more soluble radio-elements such as barium, strontium, cesium, iodine, and tellurium), and these, too, due to their insolubility, one would expect to be held in the lung for a long time. From observation of the radio-autographs, this appears to hold true in both cases. Plutonium as $PuO_2(NO_3)_2$ is much more soluble than plutonium as PuO_2, and the former should disappear from the lung at a much more rapid rate than the oxide, which is apparently what occurs in the autographs. Furthermore, the metabolic studies showed that relatively little PuO_2 is absorbed into the blood stream, while considerable $PuO_2(NO_3)_2$ was absorbed, which again would account for the more rapid disappearance in the autographs of the soluble $PuO_2(NO_3)_2$ as compared with PuO_2.

The autographs of plutonium from the insoluble oxide and the soluble nitrate, and those from the fission products produced by burning uranium wire plus fission products differed from those autographs of the fission products from the Clinton pile; the latter were recoils from the neutron fission of uranium, and were, therefore, of much smaller size than the above mentioned plutonium and fission product aerosols. This difference in size is obvious in the autographs. It is conceivable that their small size would allow their passage across capillary walls to enter the general circulation, thus clearing the lungs at a much faster rate. This would account for the fact that autographs of longer recovery periods were

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impossible to obtain due to the small amount of radio-activity present at those times. Moreover, since these fission products are the short-lived precursors of the long-lived fission products, (the radio-activity from the latter elements giving the autograph), and are soluble, they would travel quite some distance before decaying to their insoluble long-lived ancestors. The latter effect could account for the quite uniform distribution of the radio-activity throughout the lung.

1119372

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