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PROGRESS REPORT FOR THE MONTH OF JUNE 1945

CONTRACT # W-7405-eng-48-A

Joseph G. Hamilton, M. D.

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For the Atomic Energy Commission
THE REDMON
for the
Chief, Declassification Branch

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June 14, 1945

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PART I

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SUMMARY

THIS DOCUMENT CONSISTS OF 11 PAGES
NO. 1 OF 9 SERIES B

A. METABOLIC STUDIES OF FISSION PRODUCTS

The soil and plant studies have been concluded for the present and a final report is being prepared. The long term aerosol studies are being continued. A special series of smoke studies appear in a separate report. A method for the isolation of Pa^{233} free from fission products, uranium, and thorium is being developed.

B. METABOLIC STUDIES OF PRODUCT

The retention of Plutonium by the lungs of rats exposed to the inhalation of PUO_2 smokes was found to be approximately 5% of the originally inhaled activity, 256 days after exposure. The rate of elimination of the retained activity in the lungs at the end of this 8½ months interval was approximately 0.5% per day. The behavior of both Plutonium and fission products following inhalation of PUO_2 smoke containing fission product was found to be very similar 64 days after exposure.

A patient suffering from carcinoma of the stomach, received, by intravenous injection, approximately 5 μgms of plutonium as $PUO_2(NO_3)_2$, enriched with Pu^{238} so that the activity was equivalent to 50 μgms of Pu^{239}. Four days later, as a result of surgery, specimens of bone, spleen, tumor, omentum, and skin were obtained. The distribution pattern of these tissues were very similiar to that observed in rats. The highest degree of deposition within the bone was present in the trabecular portion of the marrow. The rate of urine elimination was low falling below 0.1 percent per day at the end of 16 days.

A new method for the relatively rapid analysis of large specimens of urine and feces has been developed, whereby it would be possible to detect 5×10^{-6} μgms of plutonium in each days output of urine or feces. A detailed description of this method is being forwarded to the appropriate parties in all operating areas.

C. 60" CYCLOTRON ACTIVITIES, BERKELEY, CALIFORNIA

The Cyclotron operated extremely well during the month of June 1945. For approximately 80 percent of the time, the instrument was in effective operation. Bombardments for the month included 791.6 microampere hours of alpha particles on Uranium metal, 70.8 microampere hours on U^{238} and 51.8 microampere hours on U^{235}. All three bombardments were for Dr. Glenn T. Seaborg at the Metallurgical Project in Chicago.

Bombardments planned for the next two months include deuteron bombardments of Thorium and Uranium for the production of U^{233} and Pu^{239} respectively, deuteron bombardment of U^{238} and U^{235}, deuteron bombardment of Manganese and alpha particle bombardment of Chromium for the production of Fe^{55} and Fe^{59}. Attempts are being made to develop a new type ion source and to evaluate the possibility of the production of 100 MEV Beryllium ions and 125 MEV Carbon ions.

D. The estimated expense for June 1945 is $5,950.00 as compared to $6,105.00 for May. Personnel increased from 19 to 21.

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PART II

SECTION A.

TECHNICAL PROGRESS REPORT ON THE METABOLIC STUDIES OF PRODUCT [redacted]

1. Radioautographic Studies

Additional bone radioautographs, including samples from a rib of a human subject, are in various states of preparation. A large series of specimens from animals subjected to the decalcification-calcification cycle of treatment will soon be available for radioautographic study.

2. Tracer Studies

The two animals exposed to PuO_2 smoke were sacrificed 256 days later and the results obtained with these two animals appear below. More animals exposed both to PuO_2 smokes and $PuO_2(NO_3)_2$ aerosols are being carried along. Since with only two animals, these results can only be considered qualitative in character.

TABLE I

The Percent Distribution of Plutonium in Two Rat 256 Days After Inhalation of PuO_2 Smoke.

Tissue	Rat #1	Rat #2	Average
Lungs	6.18	3.38	4.78
Liver	.014	.042	.028
Kidney	.0015	.0005	.001
Spleen	.0023	.0039	.0031
G. I.	.022	.0070	.015
Head	<.05	<.05	<.05
Skeleton	.16	<.23	<.20
Balance	.032	.014	.023
Urine	2.34	2.42	2.38
Feces	91.2	93.8	92.5

In Table II there is presented the rate of excretion per day of the activity remaining in the animals at the indicated time intervals.

TABLE II

(see following page)

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The Percent Excretion of Retained Plutonium From the Rats at the Indicated Time Intervals.

Day	Total Excretion Per Day*	Lung Activity*	Percent Excreted Per Day
8 (4-16)	139.9	2604	5.25%
16 (8-24)	59.5	1896	3.14%
32 (24-40)	11.9	1531	.78%
64 (40-80)	10.77	1244	.87%
96 (72-112)	7.53	918	.82%
128 (103-144)	7.20	737	.98%
192 (144-224)	2.47	446	.55%
256 (200-256)	1.29	362	.36%

*Indicated as the average number of counts per second for the two animals.

The three most significant facts to be noted in this experiment are as follows: First, a very significant amount of the originally inhaled PUO_2 is retained by the lungs after eight and one-half months in the rat. Second, there is only a very slight degree of absorption from the lungs, with deposition in other tissues. Third, a very significant rate of loss of material from the lungs continued at a diminishing rate for the 256 day interval. More precise evaluation of the values for lung retention and rates of excretion at this prolonged interval will be available later. However, I doubt if the present figures for the rat will have to be revised at that time by more than a factor of two.

The results are now available from a group of three rats sacrificed 64 days following exposure to PUO_2 smoke prepared from neutron irradiated plutonium metal and the salient facts are summarized in the following table.

TABLE III

The distribution of Plutonium and Long-lived Fission Products in the Same Rats 64 Days after Exposure to PUO_2 Smoke Prepared from Neutron Irradiated Plutonium Metal.

Tissue	Plutonium	Fission Products
Lungs	8.38%	9.51%
Liver	< .01%	.028%
Kidney	< .01%	.033%
G. I. Tract	.09%	.088%
Spleen	< .01%	.014%
Head	< .20%	.20%
Skeleton	< .50%	.27%
Balance	< .20%	.12%
Urine	[illegible]	3.09%
Feces	[illegible]	[illegible]

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It is interesting to compare these results with the corresponding data for the 0, 4, and 16 day intervals which appear in the April 1945 Monthly Report. One inconsistency appears in the relatively lower skelton values at the 64 day interval for fission product deposition. Otherwise the pattern is consistent and the distribution of the two types of active material remained quite similar. The rates of excretion (chiefly lung activity) per day were .29% for plutonium and 1.90% for fission products of the corresponding material remaining in the body at the end of the 64 day interval. The plutonium excretion rate, at the same interval, was greater in the other experiments noted above. Those figures in Table III indicate the similarity between the two types of active material but certain qualitative differences, such as the greater degree of absorption through the lungs, and more rapid excretion of the fission products are evident.

Longer term animals exposed to this type of PuO_2 smoke are on hand and will be sacrificed at the appropriate intervals.

May 14, 1945, a human subject, suffering from a carcinoma of the stomach received approximately 5 μgm of plutonium as $PuO_2(NO_3)_2$ by intravenous injection in a solution of isotonic NaCL at Ph_4. This sample of plutonium contained sufficient Pu^{238} to increase the specific activity of the injected material to the equivalent of 50 μgms of Pu^{239}. Four days later, the patient was operated upon and specimens of rib, spleen, tumor, omentum, subcutaneous tissue, and skin were obtained. At the same time, a sample of blood was also secured. Unfortunately, the surgeon failed to secure a specimen of liver. The patient is a 50 year old male, weighs 58.1 kilograms, and is in good general physical condition, aside from the tumor. All excreta has been collected at daily intervals since the time of injection of the plutonium.

The content of plutonium in the different tissues in terms of percent of the administered dose is given in the following table together with the excretion per day. Due to the surgical procedure, the patient was on a very restricted diet with the result that for the first two and one-half weeks, little fecal elimination took place. The per organ content of skeleton and blood were taken on the basis of these structures, representing 15% and 10% respectively of the patients's weight. The sample of rib was carefully slit open, the marrow removed by gentle washing with normal saline and then the trabecular bone and endosteum were scraped away from the cortex. The periosteum was likewise removed from the cortical bone and all four components assayed for their plutonium content.

The relatively high content of plutonium in the separated trabecular material from the specimen of rib, which also contained the endosteal tissue, is correlated with the radioautographic studies in animals. It will be recalled that bone radioautographs showed the bulk of the plutonium to be concentrated in the endosteal region and about the trabecular bone. The relatively low values for cortical bone and periosteum likewise follow the pattern indicated by the animal studies. However, the high plutonium content of the marrow in man was surprising since no indication of this fact was evident from our animal studies. The possibility of entrapment of plutonium in the colloidal state by the phagocytic cells in the marrow is ruled out in our opinion for two reasons. First, animal studies done concurrently by intravenous injection of aliquots from the same solution of plutonium given

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To the patient showed no excessively high concentration in either the liver or the spleen. The material is colloidal in character, very high uptake values for these two organs have been consistently observed. Second, the plutonium content of the spleen of the patient was quite low. The possibility of leaching of the plutonium from the endosteum, when the marrow was washed out from the bone, is very unlikely due to the fact that under the far more rigorous conditions surrounding decalcification of bone with dilute acid, very little leaching takes place. We have not received radioautographs from rats receiving plutonium by intravenous injection and further more, all bone radioautographs available at present from Berkeley have been from animals that had received the material two months or longer before they were sacrificed. During this interval, the plutonium may have migrated from the marrow to the trabecular bone and the endosteum. Because of these two gaps in the picture we cannot state that under the conditions of this human study, the same type of marrow concentration does not exist in the rat. We are now going to secure bone radioautographs from rats under comparable conditions in an attempt to settle this point.

TABLE IV

The Distribution of Approximatley 5 μgms of Plutonium in a Human Patient, 4 Days Following the Intravenous Administration of the Material as $PuO_2(NO_3)_2$. The Excretion Data for the First 19 Days Following Administration is Included:

	% per Organ	% per Gram
Cortex		.0072
Marrow		.019
Spicules		.032
Periosteum		.0043
Whole Bone	37.2	.010
Spleen	.22	.0019
Tumor		.0011
Omentum		.00043
Skin		.00048
Subcutaneous Tissue		.00037
Blood	7.49	.0013
Plasma		.0023
RBC		.00028

Excretion Data

	1	2	3	4	5	6	7	8	9	10	11
Urine	.43	.5	.12	.031	.037	.014	.014	.016	.069	.026	.036
Feces				.31					.0092		

	12	13	14	15	16	17	18	19
Urine	.029	.017	.017	.013	.016	.0056	.010	.0062
Feces							.017	.010

The human excreti[redacted] the rate of urinary elimination is almost the same [redacted]

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of plutonium, see Table V. [redacted]

TABLE V

A comparison of the Rates of Excretion of Plutonium in the Rat and Man Following the Intravenous Administration of $PuO_2(NO_3)_2$

Day	RAT % Dose per day		MAN % Dose per Day	
	Urine	Feces	Urine	Feces
0 - 1	.32%	1.39%	.48%	
1 - 2	.15%	2.83%	.15%	.076%
2 - 3	.061%	1.54%	.12%	
3 - 4	.033%	1.92%	.031%	
5 - 8	.023%	1.35%	.020%	
9 - 16	.031%	———	.028%	.0026%*

* Also includes feces through 19 days.

The fecal excretion in the patient was far less but perhaps is related to his operation and subsequent lack of fecal output. More specimens will have to be accumulated before any conclusive opinion can be reached in regard to the rate of fecal excretion of plutonium by this patient.

It is planned to continue the daily collections of both urine and feces from this patient for an indefinite period. In addition, there is enough PU^{238} for another human study when a suitable patient is available. It should be pointed out that we feel the use of Pu^{238} as a tracer for a limited number of selected patients is desirable since it is possible to use from 1 to 5 μ gms of plutonium, which is the range of dosage in man that is of greatest interest, due to the high specific activity of this material.

Mr. Scott has recently developed a method for the reasonably rapid and quantitative extraction of plutonium from 24 hour collections of both urine and feces. The material is ashed and then the plutonium extracted from the ash by means of Hexone. From 75% to 90% recovery has been consistantly obtained. The entire procedure of ashing, extraction, and counting can be done with an average expenditure of 2 hours per sample, providing adequate facilities for ashing are available. This method is readily adapted to handling up to ten days accumulation of urine. The final precipitate is mounted on platinum dishes 5 centimeters in diameter to reduce self-absorption but even under these conditions our background of the counter is approximately one count per minute. On the basis of using 10 day urine samples, it should be possible to detect a daily excretion of 2 x 10^{-6} μ gms per day. Difficulty of securing alpha particle free reagents, particularly zirconium and lanthanum, presents a serious problem and must be kept in mind. Mackay's Lanthanum and Zirconium are particularly bad in this respect. The alpha activity from these

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reagents follow very closely the chemistry of plutonium in this type of separation.

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Our work with plutonium has been greatly facilitated by the extensive cooperation given to us by the different members of Doctor Latimer's group and in particular, by Doctor Connick who supervised the preparation of the sample of Pu^{238} and assisted Mr. Scott in developing his method for assaying large samples of urine and feces.

3. Decontamination Studies

Preliminary results indicate that the technique of overlayering the endosteal region of the bone by the decalcification-calcification cycle, described in an earlier report may be successful. Additional data to either substantiate or deny this most hopeful procedure will shortly be available.

4. Soil Studies

Experiments were conducted to determine the degree of fixation of product in its three valence states, on clay. For preliminary experiments, a hydrogen clay (Death Valley Bentonite) was suspended in distilled water at Ph 4.5. Although product in the +3 and +4 states tends to precipitate at the hydrogen ion concentrations used, it is believed that the data nonethe less show pronounced adsorption of these states on the clay. The percentage adsorption of the three valence states on hydrogen clay suspensions of various strengths is given in the following table:

Percent Conc. of Clay	Percent Fixation of +3	Percent Fixation of +4	Percent Fixation of +6
.01	94.2	66.0	18.6
.05	98.5	94.5	68.0
.10	98.7	——	95.0
.50	99.0	——	99.1
1.00	99.3	——	99.4

Additional experiments are being carried out to determine the fixation of product on clay under conditions of greater acidity and electrolyte concentration. It is of interest to note that a pronounced difference in the behavior of +3 and +6 plutonium exists in the higher dilutions of clay which then vanishes at the higher clay concentrations. The lower afinity of clay for +6 plutonium is probably due to the fact that +6 plutonium exists in solution as the plutonyl (PUO_2^{++}) ion while in the +3 state, it exists as Pu^{+++}. The affinity of clay for cations is proportional to the number of positive charges carried by the ions in solution.

Experiments are in progress to ascertain the availability of the three valence states of product to plants.

5. Projected Studies

The tracer, soil, plant, smoke, radioautographic and human studies are to be continued for the next two months.

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Section C:

60" CYCLOTRON ACTIVITIES, BERKELEY, CALIFORNIA - JUNE 1945

The 60" Cyclotron operated extremely well during the month of June 1945. For approximately 80 percent of the time, the instrument was in effective operation which is as high an efficiency as has ever been obtained for an interval of one month. Of the time off for various repairs, adjustments, maintenance, etcetera, approximately 60 hours were lost as a result of several grid filament shorts and replacement of a cracked anode stand-off insulator in the south oscillator tube.

Efficiency from the point of view of average beam currents obtained per hour was also gratifyingly high. During the entire month, we operated exclusively on alpha particles. A total of 913.7 microampere hours of bombardment was accomplished at an average rate of 1.65 microampere hours per hour. At times, steady beam currents up to 4 microampere hours at roughly 140KV input were obtained and on one accasion, we obtained for a brief interval, a steady 5 microampere current of 44 MEV alpha particles. Some time was spent during the month, with the assistance of Mr. John Moore, in attempting to develop a "P.I.G." type ion source. The device was built and tried and while the results were encouraging, further work is yet to be done before its applicability to use in the cyclotron as an ion source can be adequately evaluated. This type of ion source, if successful, would do away with the use of the heated Tungsten filament as part of the ion source system. The filament type of ion source has several serious disadvantages, two of the most troublesome ones being first, on the average, one hour per day is lost in changing the filaments and making the necessary adjustments and, second, the efficiency of the cyclotron varies considerably with the age of the filament when alpha particles are being used.

Some trouble with arcing from surges in the main oscillator rectifier continued, which is not only troublesome from the operational point of view but also significantly shortens the life of the rectifier tubes which is a significant factor of expense. This arcing condition was almost completely eliminated by placing a 70 ohm resistance in series with the output of the rectifier. Approximately 4 to 6 KV is dissipated in this resister but the greater stability of operation and anticipated longer life of the rectifier tubes appears to far outweigh the trifling loss of power.

Bombardments for the month included 791.6 microampere hours of alpha particles on Uranium metal, 70.8 microampere hours on U^{238}, and 51.8 microampere hours on U^{235}. All three bombardments were for Dr. Glenn T. Seaborg at the Metallurgical Project in Chicago. The U^{235} bombardment was done on a new type of target which makes it possible to effectively use the most intense portion of the beam on a specially designed mounting whose area is approximately 10 percent of the regular type targets. This arrangement is obviously extremely desirable whenever rare materials are to be bombarded in the cyclotron such as Th^{230}, Pa^{231}, U^{233}, U^{234}, U^{235}, Np^{237}, and Pu^{239}.

Bombardments planned for the next two months include from two to three weeks of deuteron bombardment of Thorium for the production of U^{232}

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for use by Colonel Stafford L. Warren and his associates; ten days to two weeks of deutron bombardment of Uranium for the production of Pu^{238} for Dr. Robert S. Stone and his associates of the Health Division of the Metallurgical Project at Chicago; deuteron bombardments for several days each of U^{238}, U^{235}, and Thorium, for Dr. Glenn T. Seaborg and his group at the Metallurgical Project at Chicago; several days of deutron bombardment of Manganese and several days of Alpha particle bombardment of Chromium for the production of Fe^{55} and Fe^{59} for the Chemistry Section of the Clinton Laboratories.

When time is available, effort will be directed towards further development of the new type "P.I.G." ion source and to evaluating the possibility of the production of 100 MEV Beryllium ions and 125 MEV Carbon ions.

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PART III

PRIVACY ACT MATERIAL REMOVED

Re: W-7405-eng-48
Report on NDP-48A

This project completed the year 1944-1945 with an estimated balance of approximately $27,000 on hand at June 30, 1945. Expense during June was just under $6,000, estimated as follows:

Payroll	$ 3,800.00
Overhead	[redacted]
Expense and Equipment	1,200.00
Total	[redacted]

Following is a budget estimate for July and August, 1945:

Payroll	$ 8,000.00
Overhead	[redacted]
Expense and Equipment	8,000.00
Total	[redacted]

Personnel on this project at June 30, 1945, included:

Executive	1
Physiologist P-3	2
Lab. Technicians	7
Jr. Lab. Technicians	5
Clerk	1
Secretary	1
Biochemist P-3	1
Biologist P-3	1
Chemist P-3	1
" P-4	1
Total	21

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ESTIMATED STATUS OF NDL-48A
ON JUNE 30,1945

PRIVACY ACT MATERIAL REMOVED

Payroll:

Appropriation		$ 99,000.00	
Payroll to May 31	$ 86,500.00		
June Payroll	3,800.00		
		90,300.00	
Balance			$ 8,700.00

Overhead:

Appropriation		24,750.00	
Overhead to May 31	[redacted]		
June overhead	[redacted]		
		22,575.00	
Balance.			[redacted]

Expense and Equipment:

Appropriation		76,450.00	
Expense to May 31	58,730.00		
June expense	1,200.00		
		59,930.00	
Balance			16,520.00
TOTAL BALANCE			$ 27,395.00

Total Appropriation	$ 200,200.00
Total Expense	172,805.00
Total Balance	$ 27,395.00

Kenneth Priestley
Business Manager
Radiation Laboratory

KP:ml
cc: Dr. J. G. Hamilton (2)

APPROVED

Edgar J. Murphy
EDGAR J. MURPHY
MAJOR, C. E.

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