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NO. 1 OF 8 SERIES B

715876

PROGRESS REPORT FOR MONTH OF SEPTEMBER 1945

CONTRACT #W-7405-eng-48A

Joseph G. Hamilton, M.D.

September 14, 1945

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PART I

SUMMARY

A. Metabolic Studies of Plutonium and Allied Materials

Results of the decontamination studies have shown further evidence that the decalcification-recalcification cycle in rats results, in some instances, in the burying of plutonium within the mineral structure of the bone and thus reducing the surface Alpha activity of the endosteal layer by as much as 100 fold. The evidence for this most encouraging phenomena has been obtained by both the direct measurements of the changes in the surface radioactivity of the skeleton as well as the radioautographic technique. A repetition of the oral studies of Plutonium in rats, using much larger doses of this element as $PuO_2(NO_3)2$ has shown that absorption by the gastro-intestinal tract does take place to a very limited degree. The absorption averaged .0006% of the administered dose with almost all of the Plutonium being deposited in the skeleton. The tracer studies with Pa^{233} have been initiated. Radioautographic, smoke, tracer, decontamination, and human studies are to be continued. Tracer studies with 95^{241} and Th^{234} are to be initiated.

B. 60" Cyclotron Activities, Berkeley, California

A serious delay of operations on the 60" Cyclotron was occasioned by excessive R.F. heating in the region of the west D house and the west dee stem liner. These areas were repaired in such a manner so that it is unlikely that we will have future difficulties in this region. The water cooling of the cyclotron was increased and water cooled plate transmission lines were installed.

Bombardments for the month included deuteron bombardment of Thorium for Colonel Warren at Oak Ridge, deuteron bombardment of U^{238} and Ionium, the alpha particle bombardment of Thorium and U^{233} for Doctor Seaborg at Chicago, the deuteron bombardment of Lithium for Doctor Daniels at Chicago, the deuteron bombardment of Strontium for Doctor Whitaker at Oak Ridge, and the deuteron bombardment of Yttrium for the Biological Group at Berkeley.

C. The estimated expense for September 1945 is $6,200.00 as compared to $_,725.00 for August. Personnel remained at 22.

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PART II

SECTION A.

TECHNICAL PROGRESS REPORT ON THE METABOLIC PROPERTIES OF PLUTONIUM AND ALLIED MATERIALS

1. Radioautographic Studies

During the past month, all of the radioautographic work has been devoted to preparation of pictures from samples supplied by Doctor Copp and his group in the Decontamination Section. The radioautographic results during this interval will be discussed under that section.

2. Tracer Studies

The excretory data presented below under Table I, presents the information from the 86th to 99th day inclusive, on the human subject who received Pu^{238} several months ago. More samples are now in process of assay together with the fecal material.

TABLE I

The Daily Rates of Excretion of Pu in a Human Subject Following the Administration of 5μgrams by Intravenous Injection (88th to 99th Day)

Day	Activity in % of Dose	Weight in Grams	Sample Vol. in Ml.
88	.0037	5.5	1200
89	.0071	4.15	1000
90	.00765	11.0	500
91	.0088	4.8	400
92	.00705	7.0	1300
93	.00598	4.3	550
94	.00705	1.8	1700
95	.0052	4.5	500
96	.00419	4.5	1600
97	.0057	13.0	750
98	.0053	9.0	1100
99	.00695	8.2	1100

It can be seen that no striking decrease in the average elimination rate has taken place during this interval as compared to the earlier periods.

A series of oral experiments in rats, using approximately 45μgrams of $PuO_2(NO_3)_2$ per animal was done in order to more accurately determine the minimum uptake value by way of the gastro-intestinal tract.

The entire skeleton was assayed for each animal by the T.T.A. method in order to determine as accurately as possible, the presence of any absorbed Plutonium. In the four animals studied, the average uptake was .0006% of the administered dose and the range fell between .0004% and .0007%. It appears that this uptake is real and not due to any contamination. In view of the extremely minute absorption, which would require the ingestion of approximately 200 milligrams of Plutonium in order to have 1 gamma gram absorbed, it would appear that for all intents and purposes the absorption of Plutonium as Plutonyl Nitrate by way of the digestive tract can be considered negligible. It is highly unlikely that other inorganic compounds of Plutonium in either the +6 or the other valence states would be absorbed more readily than the nitrate. Likewise it is not probable that there should be any significant variation between rats and other animals, including man. However, at some future date, it would appear desirable to check this point at a time when less urgent work is at hand.

The long-term smoke and spray studies are being continued.

3. Decontamination Studies

During the past month, more animals have been made available that were subjected to the decalcification-recalcification cycle following the administration of Plutonium by intramuscular injection. Examination of the endosteal and periosteal surface activities in those animals, who showed adequate recalcification, revealed that the surface activity was strikingly diminished. The Procedure employed was as follows: a 5 to 8 millimeter bone disc is removed by trephine, dried at air temperature, and the endosteal and periosteal activities determined by counting the surface Alpha activity on both sides. The disc was then assayed for its total Plutonium content. It has been found in normal animals that, on the average, the number of Alpha particles counted from the endosteal surface was approximately 30% of the total number of counts secured from the assay and the activity of the periosteal surface was usually quite low. After adequate recalcification frequently the endosteal surface activity fall to less than 1% of the total activity of the bone disc. This appears as quite convincing presumptive evidence of the phenomena of overlayering of the Plutonium by the calcium salts of the newly deposited bone. Radioautographs taken of these bones showed definitely two striking results. First, the very heavy deposition of Plutonium about the region of the cancellous bone was significantly diminished, and secondly, a considerable amount of the Plutonium was buried within the shaft of the bone, in some cases 100 microns below the endosteal surface. This has been seen in at least a half dozen instances. It should be noted that this apparent overlayering observed both in the bone disc experiments and the limited number of bone radioautographs on hand at the moment, only occurs when adequate recalcification takes place after the decalcification cycle. For some reason, not yet apparent, recalcification does not take place adequately in all animals. However, we are inclined to look upon this fact without too much concern since the important aim has been to explore whether it is possible to overlay the endosteal deposition of Plutonium by new bone and it now appears that this is possible.

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Quite a few additional radioautographs are now in process of preparation and new groups of animals are being subjected to the decalcification-recalcification cycle. In addition to the rat studies described above, some radioautographs are now in process of preparation taken from pigeons which had been subjected to a decalcification-recalcification cycle. The purpose of using these birds has been because of the fact that in the female, the cycle can be completed with greater rapidity than with rats. It is planned that for the November meeting, Doctor Copp will present in person a complete picture of his work which certainly now appears to hold very definite promise. It should be kept in mind that if confirmation of this effect continues in additional experiments, the application of the method from rat to man should not be as difficult as it might appear. This is because the relative dimensions of bone thickness in man is so many times greater than in the case of a small animal, such as the rat, that one would expect a less rigorous decalcification procedure should be necessary for human subjects.

In addition to the continuation of the type of studies indicated above, which have employed adult female rats that have reached full growth, similar experiments will be initiated with younger animals and the fracture studies are to be repeated using radio-Yttrium and radio-Strontium, as well as Plutonium in order to compare the type of distribution of these three substances.

4. Protoactinium Studies

Approximately 3 millicuries of Pa^{233} were isolated by Doctors Overstreet and Jacobson and a large series of rats were given this material by intramuscular injection. The animals from the earlier intervals have been sacrificed and the tissues are now being assayed.

5. Radio-Chemical Isolation

Protoactinium was isolated from a Thorium metal target which had received approximately 318 micro-ampere hours of 22 MEV deuterons on July 30th to August 3rd, 1945. The Pa^{233} was separated from the Thorium and Fission Products by a method suggested by G. T. Seaborg which involved the carrying down of the radio-element on MnO_2 in acid solution and its subsequent extraction with di-isopropylketone.

It was found that the extraction could be considerably improved by making the solution to be extracted, one molal in zirconyl nitrate. The addition of zirconyl nitrate is particularly important where even a trace of fluoride is present.

The yield of Pa^{233} was found to be 2.78 millicuries on September 6, 1945.

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6. Projected Studies for the Next Two Months

Tracer, smoke, radioautographs and human studies will be continued for the next two months. In addition, the next human subject that is available is to be given, along with the Pu^{238}, small quantities of radio-Yttrium, radio-Strontium and radio-Cerium. This procedure has in mind two purposes. First, the opportunity will be presented to compare in man the behavior of these three representative long-lived Fission Products with their metabolic properties in the rat, and second, a comparison can be made of the differences in their behavior from that of Plutonium. The second factor may shed additional light on the mechanisms for the accumulation of Plutonium in the skeleton. A sample of 95^{241} is to be made available to us by Doctor Seaborg and his group for a limited series of tracer experiments in rats. Tracer studies with Th^{234} (UX_1) will also be started. Here again, two purposes will be served by these studies. First, quite appreciable quantities of 95^{241} appears in high level pile operations and thus may be a health hazard in the future; and second, a comparison of the behavior of these two radio-elements with that of Plutonium can be expected to be at least helpful in correlating the chemical and biological properties of these three radio-elements.

PART II

Section B

60" CYCLOTRON ACTIVITIES, BERKELEY CALIFORNIA, SEPTEMBER 1945

During the first half of September, the 60" Cyclotron operated quite satisfactorily. At the end of this interval it was necessary to remove the dees since serious radio-frequency heating appeared at the juncture of the west U house to the dee where both are joined to the dee stem liner. It will be recalled that this point has given trouble in the past. To correct this difficulty and forestall any future repetition, much heavier supports were installed to permit a more firm union between the end of the stem liner at the U house. At the same time, a new water cooled plate transmission was put in place. This takes the place of the temporary and somewhat inadequate cooling which had been installed several months earlier. Also, the water cooling for the cyclotron was increased by approximately 30 percent by altering the arrangement of the two water circulators. The previous arrangement, which had been the one originally installed when the instrument was first built, was laid out in such a manner that most of the water circulated through the cyclotron was handled by one of the pumps and the second pump was used primarily to re-circulate water within the tower itself for better cooling of the water, particularly during warm weather. After a careful study of the problem, we felt that it would be possible to use both pumps for circulating water through the cyclotron and so during this shut-down interval, the cooling system was rearranged so that one pump circulates water through the west side and the other through the east side of the instrument. As soon as all of these jobs had been satisfactorily completed and the instrument was put back into adequate operating condition, it was found that the water cooling of the cyclotron was much better with the new arrangement. The west U house gave no signs of further overheating and the plate transmission line ran at a satisfactory temperature. However, no sooner had steady and reasonably effective operational conditions been achieved than a new difficulty developed in the melting through of the terminal end of the dee stem liners from the clamp which joins it with the U house. This was due to the fact that the stems which are constructed out of 30 mil copper, are somewhat light for the R.F. current carried and, moreover, they are cooled by water lines that are attached inside the liners by means of soft solder. Presumably the adequate repair of the west U house connection permitted more current to flow down the dee stem with the result that the next weakest link parted. This, of course, not only necessitated the removal of the dees but also disassembly of the dee stem tanks due to the fact that the point where the dee stem liner had burned through was some 8 inches beyond the point where the U house joins to the stem and was otherwise inaccessible. This failure was repaired by replacing the terminal 4 feet of the stem with a 3/16 inch liner into which the water tubes were attached with hard solder. This section represents the portion of the stem liner which is the smallest in diameter and hence carries the greatest current density. At this time, the east dee stem was carefully inspected for any possible evidence of overheating and none was found. It was felt inadvisable to alter the east dee stem liner at this time since it dissipates only approximately one-half the power of that of the west dee stem liner. At some later date, it is planned to replace both the dee stem and dee stem tank liners with much heavier copper to which

all of the water lines are bonded by means of hard solder. It will be recalled that during the past five months, most of our difficulties have been with R.F. heating in the region of the liners, the ion source, and the deflector. The first two items are the only complete holdovers from the overhaul period and the deflector, while new, insofar as its physical structure is concerned, is still of the same design as the original installation. As has been indicated in earlier reports, a new removable type of ion source has been designed and is to be soon built. This arrangement will permit the removal of ion sources without letting the cyclotron down to air. It is now planned to replace the present dee stem and dee stem tank liners. The third situation can only be adequately met by re-design of the deflector dee so that it will not be necessary to use such excessively high voltage which is a serious source of annoyance and loss of time.

This major repair on the west dee stem liner was completed by September 30, 1945, and the cyclotron was being pumped down preparatory to being put into operation.

Bombardments for the month included the deuteron bombardment of Thorium to prepare U^{232} for Colonel Warren and his associates at the University of Rochester at Rochester, New York. This concluded the Thorium bombardment for this purpose and Doctor Louis Jacobson was sent to the Clinton Laboratories to separate the U^{232} from the Thorium target. This was necessary due to the very intense induced radioactivity in the Thorium disc, chiefly from fission and Protoactinium 233, and adequate facilities were not available here. A total of approximately 200 microcuries of Uranium was obtained from this bombardment. A significant proportion estimated to be of the order of 25 per cent, of this alpha particle activity was due to the new isotope of Uranium, U^{230}, recently observed by Doctor Seaborg and his associates at Chicago, from deuteron bombarded Thorium. This new isotope of Uranium is produced by the Beta decay of Pa^{230} which in turn is formed by the d-4n reaction on Thorium. The threshold of the reaction is approximately 18 to 20 MEV inasmuch as this new isotope is found only within the first .001 of an inch of the target surface. U^{230} decays by alpha emission to Thorium 226 and has a half-life of approximately three weeks. The total yield of U^{232} of deuterons on Thorium at our present measured energy of 22 MEV for deuterons, is up by approximately a factor of 40 from our earlier energy level of about 14 MEV.

A sample of Strontium was bombarded with deuterons for the production of Y^{86} for use by Doctor Waldo Cohn at Clinton Laboratories. Lithium was bombarded with deuterons to produce Be^{7} for Doctor Daniels at Chicago which is to be used by his group for the study of the errosion of Beryllium under intense neutron irradiation for developmental work for high powered Beryllium moderated piles. A sample of Ionium was bombarded with deuterons for Doctor Seaborg and his associates at Chicago, for the further identification of U^{230}. This isotope of Uranium was found together with a new isotope of Protoactinium (Pa^{229}) which is produced by the d-3n reaction and decays by alpha emission with a half-life of from three to four days. The deuteron bombardment of U^{238} in the form of the metal as well as the alpha particle bombardment of both Thorium and U^{233} were also undertaken for Doctor Seaborg. The last two bombardments have not as yet been completed. A sample of Yttrium was bombarded with deuterons for the production of Zr^{89} for the study of the inhalation of radioactive smokes in human subjects and is being done under Project 48-A at Berkeley.

SECTION C.

Distribution of Effort for the Month of September 1945

Problem No.	Title	Approx. No. Employees per problem	% Effort September	% of Effort Distribution Estimate for October	November
1.	Writing Project Record	2	10%	10%	10%
2.	Evaluation of Metabolic Properties of Plutonium and Allied Materials in Plants, Animals, and Man	7	50%	50%	50%
3.	Decontamination Studies	7	40%	40%	40%
		16	100%	100%	100%

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October 8, 1945

PART III

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

Project 48A expense in September, 1945, is estimated as follows:

Payroll	$ 3,200
[redacted]	[redacted]
Expense & Equipment	2,200
Total	[redacted]

Following is a budget estimate for the months of October and November 1945:

Payroll	$ 8,000
Overhead	[redacted]
Expense & Equipment	4,000
Total	[redacted]

The payroll included the following at September 30, 1945:

Executive	1
Laboratory Technicians	6
Jr. Lab. Technicians	3
Sr. Lab. Technicians	1
Secretary	1
Clerk	1
Physiologist, P-3	1
" P-4	1
Biochemist, P-1	2
" P-3	1
" P-4	1
Biologist, P-2	1
Chemist, P-4	2
Total	22

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October 8, 1945

ESTIMATED STATUS OF NDP-48A
ON SEPTEMBER 30, 1945

Payroll:

Appropriation		$ 139,000.00
Payroll to August 31	$ 98,500.00	
September payroll	3,200.00	
		101,700.00
Balance		$ 37,300.00

Overhead:

Appropriation		34,750.00
Overhead to August 31	[redacted]	
September overhead		[redacted]
Balance		[redacted]

Expense and Equipment:

Appropriation		126,450.00
Expense to August 31	62,830.00	
September expense	2,200.00	
		65,030.00
Balance		61,420.00
TOTAL BALANCE		$108,045.00

Total appropriation	$ 300,200.00
Total expense	192,155.00
Total balance	$ 108,045.00

/s/ Kenneth Priestley
Business Manager
Radiation Laboratory

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

APPROVED
Edgar J. Murphy
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