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HEALTH DIVISION
R.S. Stone, Director

REPORT OF CONFERENCE ON PLUTONIUM - MAY 14th and 15th

edited by
J.J. Nickson

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UNCLASSIFIED

I Summary of Requests for Information Desired Concerning Plutonium

Drs. L. H. Hemplemann, S. T. Cantril, J. E. Wirth, J. J. Nickson and Mr. S. G. English wrote the letters on which this section is based. Immediate problems of importance about which further information is needed are emphasized.

I Diagnosis and Estimation of the Amount of Plutonium in the Human Body

A. Detection of amounts in the body in excess of the permissible level

1. Development of a satisfactory means of assay of urine and feces

   a. Need more information on elimination rate as a function of time
   b. Need more information on elimination rate as a function of route of intake

2. Determination of percentage of plutonium excreted daily by humans

3. Can blood samples be utilized for this purpose?

B. Detection of plutonium in the lung

1. Development of a satisfactory means of estimation of the amount of plutonium in the lung

2. Compounds of interest are +3, +4, nitrate in aqueous solution, +6 nitrate in ether solution, tetrafluoride, +4 oxide, +4 oxalate, +4 peroxide as slurry

C. Development of a method for detection and quantitation of plutonium in wounds

II Absorption

A. Skin

1. Need more information on absorption rate on various plutonium compounds through the intact skin

2. Is absorption influenced by use of potassium permanganate solution followed by sodium hypo-sulphide solution on the skin?

B. Gastro-Intestinal tract

1. Need more information on absorption rates of various plutonium compounds. Specific information is desired about those compounds mentioned under "diagnosis".

2. Can the elimination of plutonium be used in the event of gross intake to detect the amount that will be fixed in the bone?

C. Wounds

1. The rate of diffusion of plutonium from the wound area

2. The effect of different plutonium compounds on the rate of diffusion

3. How is the distribution pattern altered by having different sorts of wounds, e. g. puncture wounds as opposed to lacerations?

D. Lung

1. How much of the amount breathed is retained in the human lung?

2. How much material is absorbed from the lung to the blood and then to the skeleton?

III Permissible levels of Plutonium

A. In the lung

B. In the bone

C. What is the minimum amount necessary to produce damage in the body?

D. Are the alpha rays from plutonium capable of producing damage to the skin?

IV Metabolism

A. Distribution pattern as a function of rate of intake

B. Distribution pattern as a function of diet

C. What is the rate of elimination of plutonium from bone?

D. Are the differing diets in the different laboratories effecting the results of animal experiments?

V Pathology

A. What is the nature of liver damage after intravenous administration of plutonium?

B. What is the nature of liver damage after sub-lethal doses given through other routes of entry?

C. Does pre-existing kidney damage diminish the elimination of plutonium from the body? Should persons with kidney damage be excluded from working with plutonium?

VI Therapy

A. Development of methods of increasing elimination from the body

1. Effect of diet

2. Effect of injection of complexing or other agents

B. Methods of covering up material deposited in bone

C. Development of methods of therapy for plutonium in wounds (specific mention is made of those compounds mentioned under "diagnosis")

1. The effect of suction

2. The effect of increased venous flow

D. Formulation of a recommended procedure for treatment in case of a known over-dosage by inhalation, by mouth, or by wound

E. How much time can lapse before treatment must be instituted?

VII Protection

A. Is inactive dust in a work area an additional hazard in that it increases the probability of breathing plutonium?

B. Improvement of existing means of the physical protection of personnel from ingestion, inhalation or direct innoculation of plutonium

C. Development of a method for the rapid determination of the quantity of plutonium in the atmosphere

D. Development of a continuous monitoring device for atmospheric or dust borne plutonium which is effective in concentrations just above or at tolerance levels

E. Analysis of masks and respirators for percentage efficiency in filtering out various chemical forms of plutonium. Special mention was made of +4 and +6 nitrate, +3 and +6 sulphate, +3 and +4 chloride, +4, +5 and +6 carbonate.

F. Do various chemical structures play some part in the efficiency of respirators or is particle size the important factor?

VIII Plutonium-radium Ratios

A. What ratio for acute effects?

B. What ratio for chronic effects?

Table XIII

Effect of Method of Collecting
Sample on Counts Found in the Urine

Person	c/m and Place of Collection of Sample	
	At Home*	In Hospital**
D. W.	10.1	2.2
W. A. B.	41.6	4.3
W. B. G.	16.1	3.4
W. G. T.	2.8	0.1
J. P.	17.8	—
D. D.	30.6	2.2
Average:	20.0	2.2

* Samples collected at home were two overnight voidings collected by the individual after thorough bathing and washing of hands.

** Samples collected in hospital were 24-hour samples collected under the rigorous hospital plan after a two day leave from the Site.

Table XIV

Recovery of Known Amounts of Pu
From Regular and Mock Urine Samples

No. of Detns.	Nature of Samples	Amt. of Spike c/m	Recovery %	Spread %
24	Blanks (reg. urine)	0.	(ave. 0.5 c/m)	(0-1.2 c/m)
4	mock urine sol.	29.2	94	88-100%
11	" " "	10.0	93	85-101%
12	reg. urine	10.0	88	73-104%
3	reg. urine	4.5	95	81-105%

VII Excretion Studies

Wright Langham

The primary interest of our health department is the immediate development of a method of monitoring personnel for internal body contamination with plutonium. The obvious purpose of a monitoring plan is to enable us to retire individuals from further contact with the material before they have absorbed harmful amounts. The execution of such a plan depends on the establishment of a number of factors among which are the following:

1) The development of a method of determining exceedingly small amounts of plutonium in some body fluid or excrement;

2) The establishment of the relationship between the body fluid or excrement and the amount of plutonium contained in the human body;

3) The development of a sampling system which excludes the possibility of external contamination of the sample.

This report summarizes our attempts to establish some of the above factors. The urine has been chosen as the source of the sample for study.

Method of Sampling and Analysis:

Because of the extreme difficulty of detecting small amounts of internal contamination with plutonium, and because of the great possibility of external contamination of the sample, the practice has been to collect 24-hour samples under very rigorous conditions. The subject is directed to stay away from work and preferably away from the Site for a 48-hour period preceding the period of collection of the sample to be analyzed. All persons are asked to wear freshly laundered clothing during this preliminary period and to bathe and wash their hands frequently.

The subject is asked to report to the hospital at eight o'clock in the morning at the close of the 48-hour preliminary period. He is given hospital clothing and after taking a shower, is admitted to a special room provided for collecting the 24-hour urine sample. He is asked to remain in this room for the entire 24-hour period. It is requested that the subject restrict his fluid intake to one cup or glass of fluid per meal to avoid an abnormally large sample.

A hand counter is available in the room and a note is made as to whether or not the individual has a hand count. The subject is instructed to wash his hands each time before he voids and to wear white cotton gloves during voiding, thus preventing epithelial scales of the hands from falling into the flask and contaminating the sample. The voidings are collected in a 2 liter erlenmeyer flask which is placed at such a height that it is not necessary for the person to touch the flask or the funnel while urinating. When the collection is completed, the subject dresses and

leaves the hospital leaving his specimen where it was collected. The sample is picked up and delivered to the laboratory by a member of the group doing the analyses.

Rigid adherence to the procedure described above should permit the collection of a 24-hour urine sample as nearly free from external contamination as possible.

The effectiveness of the above method is indicated by the data in Table XIII which gives a comparison of the analyses of samples consisting of two overnight specimens collected in the individuals' homes with 24-hour samples collected from the same individuals by the above hospital method. The average counts per minute obtained in the samples collected at home was 20 as compared to 2.2 counts per minute per sample when collected under hospital conditions. The most probable explanation of this great difference is that external contamination was avoided in the latter case.

The samples collected in the hospital are analyzed by the following method: The entire 24-hour specimen is evaporated almost to dryness and the residue wetashed using one addition of conc. HCl and repeated additions of conc. HNO_3 and 30% H_2O_2. The ashing is continued until a white solid almost completely free of organic matter is all that remains. The residue is taken up in 2 N HCl and a complete hydroxide precipitation carried out. The hydroxide precipitate is dissolved in 2 N HCl, the solution is adjusted to a pH = 0.3-0.5 and the Pu, plus 1 mg. of ferric iron as a carrier, is extracted into chloroform using cupferron. The chloroform is evaporated off and the cupferron residue digested off with nitric and perchloric acids. The Pu is then carried out of the perchloric acid solution with lanthanum fluoride. The lanthanum fluoride precipitate is transferred to a platinum disc and counted for 30 minutes in an alpha counter.

The data reported in Table XIV give some idea as to the performance of this method when applied to spiked urine samples and to mock urine ash solutions. Blank determinations were made on 24 samples of urine from persons never having worked with Pu. These samples ranged in size from 800 to 1200 ml. The average of all blank determinations was 0.5 c/m per sample with a spread of 0-1.2 c/m.

Results of Personnel Monitoring:

Thirty-six members of the staff were chosen for the first test of the above monitoring method. These people were chosen to represent high, moderate, and low or no exposure groups. The number in each group was too few to give any definite significance to the classification. The results are indicative, however, and are summarized in Table XV. It may be significant that all individuals showing a positive count in the urine had had one or more high nose counts on record since joining the project. A high nose count is recorded against an individual when a moist filter-paper swab inserted into the nostril and rotated shows 50 c/m or greater when counted in an alpha counter.

Urinary Excretion of Plutonium by the Human:

If urinary excretion values are to be used to establish the actual amount of internal body contamination it is essential to know the relation

between the amount of Pu in the human system and that excreted in the urine per 24 hours. On April 10, 1945, an attempt was made to establish this relationship by injecting a human subject intravenously with 4.7$ of +4 Pu which was complexed with sodium citrate(0.3% solution) and adjusted to a pH of 6.0.

The subject was an elderly male whose age and general health was such that there is little or no possibility that the injection can have any effect on the normal course of his life. The patient might not have been an ideal subject in that his kidney function may not have been completely normal at the time of injection as indicated by slight albuminuria and a low urine specific gravity.

The +4 citrate complex was used in order to produce the maximum deposition in the bone. This presumably would produce an excretion rate comparable to that of a worker having absorbed the material at a slow rate thereby depositing a maximum amount in the bone where it is probably the most damaging.

The results obtained for the first 18 days after injection are presented graphically in Figure 1 by blocking in the per cent of the total injected dose excreted per day.

These data show the excretion during the first day was surprisingly low and that the leveling off of the excretion rate was much slower than with rats. The most probable explanation of these observations is that they represent some metabolic abnormality of the subject. It is possible, however, that the stability of the +4 citrate complex is a factor. A blood sample taken 4 hours after the injection showed that about 50 per cent of the injected dose was still in the circulating blood. The calculation, however, was based on the assumption that there had been a complete mixing of the material throughout the total blood volume.

A rather favorable excretion rate is indicated by the observation that the leveling off point seems to be about 0.02 per cent instead of 0.01 per cent as observed for rats.

The Effect of Size of Dose on Urinary Excretion of 49:

A number of fundamental assumptions must be made in regard to the metabolism of Pu if a limited amount of human tracer data are to form the basis of a method of diagnosing internal body contamination. (1) It is necessary to assume that, once absorbed, all valence states and all compounds of Pu are metabolized by the animal organism in essentially the same way. (2) It is necessary to assume that Pu is metabolized in the same way regardless of the route of absorption or administration. (3) It is also necessary to assume that the fraction deposited and therefore the fraction excreted is independent of the size of the dose administered or absorbed.

Hamilton (CN-2383) has reported a limited amount of information in support of the validity of the first two assumptions. The following experiment was performed to test the validity of the third

Five groups of mature male rats were injected with 0.032γ (2250 c/m), 1.1γ, 5.3γ, 15.0γ, and 52.0γ of Pu respectively. The material was administered as the citrate complex in a solution 0.5 per cent with respect to sodium citrate. The pH of the solution was 6.0. The urine and feces were collected daily for five days from each group and analyzed for Pu. The results of the urine analyses are given in Table XVI. These data show rather conclusively that the per cent of the total injected dose excreted in the urine of the rat under the above conditions is independent of the size of the dose administered.

Table XV

Results of Monitoring Site Personnel

Classification	No. of Persons	ive. c/m/24 hr. urine sample*
Highly exposed	5	2.2
Moderately exposed	23	0.4
Low or no exposure	8	0.2
Those having high nose counts** recorded	14	1.2
Those having no high nose counts recorded	22	0.2

* 0.5 c/m was subtracted from each value as a blank.

** A high nose count is recorded against an individual when a moist filter-paper swab inserted into the nostril and rotated shows a count of 50 c/m or greater when counted in an alpha counter.

Table XVI

Effect of Dosage on Per Cent Excretion of Pu (+4) Citrate in the Urine of the Rat

Period after Inj. - Days:	% of Inj. Dose Excreted per Day Dosage γ				
	0.032	1.1	5.3	15	52
1st	0.72	0.71	0.73	0.57	0.77
2nd	0.27	0.22	0.31	0.20	0.26
3rd	0.22	0.12	0.18	0.16	0.19
4th	0.15	0.11	0.13	0.13	0.17
5th	0.14	—	—	0.12	—