

728601

REPOSITORY

DOE-OHRE

COLLECTION

PLUTONIUM INJECTION

BOX NO.

3

FOLDER

40-005

8005590

delete

8005591

Chi-II (1)
(WX-300)

Name

Hospital No

377135

Path 6670

Date of birth

Date of injection

Dec. 27, 1945

²³⁹Pu(VI) citrate

Age at injection

55

Date of death

Jan 13, 1946

Age at death

Time after injection - 19 days

Death certificate no

delete

0005593

2

40-005 (in 1)

Sister - ?

La Grange, Ill

8005594

delete

0005595

CENTER FOR HUMAN RADIOBIOLOGY

✓ (3)

40-005 RI

D-46

B 89

CHR Exams

Death Certificate

1946 Autopsy

Medical Reports from Physicians and Hospitals

Correspondence

___ ANL

___ MIT

___ NJRRP

0005596

make some
deletions
that open
patients
in file in Box 1

0005597

4

IN THIS FORM (except signature)
IN TYPEWRITER OR LEGIBLE PRINTING

1. PLACE OF DEATH.

City of COOK

Registration No. 3104

Dist. No.

CHICAGO

Village

Township

Primary

Dist. No.

3104

and the three terms not applicable—Do not enter "R. R." "R. F. D." or other P. O. address

not and

number, No.

St. 5TH Ward A.M. BILLINGS Hospital

LENGTH OF TIME AT PLACE WHERE DEATH OCCURRED? 0 yrs. 1 mo. 10 da.

PLACE OF RESIDENCE: STATE ILLINOIS County COOK Township LYONS Road Dist. 1
(Usual place of abode—Do not enter "R. R." "R. F. D." or other P. O. address)
City or Village LA GRANGE Street and Number

18. LIST NO.

520

3. PRINT FULL NAME

10. If veteran,

3 (a) Social Security

name was NONE

No. UNKNOWN

Sex FEMALE

E. Color or

race WHITE

8 (a) Single, widowed, married, divorced SINGLE

11. Name of husband or wife

8 (c) Age of husband or wife if

alive — years

Birth date of deceased

1

25

1889

(Month)

(Day)

(Year)

AGE: Years

Months

Days

If less than one day

56

11

18

hr. min.

Birthplace

CINCINNATI

OHIO

(City, town, or county) (State or foreign country)

Usual occupation

TEACHER

Industry or business

DAYTON BOARD OF EDUCATION

12. Name

CINCINNATI

OHIO

(City, town, or county) (State or foreign country)

13. Birthplace

CINCINNATI

OHIO

(City, town, or county) (State or foreign country)

14. Maiden name

MADISON

INDIANA

(City, town, or county) (State or foreign country)

15. Birthplace

MADISON

INDIANA

(City, town, or county) (State or foreign country)

INFORMANT

(Signature)

Signature with pen and ink

P. O. Address

1111

Wheaton

(Township, Road Dist., Village or City)

County

COOK

State

ILL.

Address

1111

Wheaton

(Township, Road Dist., Village or City)

License No.

1111

Wheaton

(Township, Road Dist., Village or City)

(personal signature with pen and

(Signature)

License No.

1111

(from name, if any)

1111

Wheaton

(Township, Road Dist., Village or City)

MEDICAL CERTIFICATE OF DEATH

20. Date of death: Month JANUARY day 13
year 1946 hour 1 minute 30 PM

21. I hereby certify that I attended the deceased from
12/13 to 1/13 1946

that I last saw him alive on 1/13 1946

and that death occurred on the date and hour stated above.

Immediate cause of death

METASTATIC CARCINOMA OF

ABERRANT BREAST TISSUE

Associated diseases

5 NO.

Other conditions

(Include pregnancy within 3 months of death)

Was an operation performed? YES Date of 12/20/46

(For what disease or injury? C.A. OF ABERRANT BREAST

Was there an autopsy? YES

Findings: METASTATIC C.A. OF BREAST - LIVER,

MESENTERY + BOWELS.

22. If a communicable disease; where contracted?

NONE

Was disease in any way related to occupation of deceased? No

If so, specify how:

(Signed) Norman B. McCullough M.D.

Address Norman B. 950 E 57th St. Chicago, Ill.

Date 1-14-46 1946 Telephone 6811

"N. B.—State the disease causing death. All cases of death from "violence, casualty, or any undue means" must be referred to the coroner. See Section 10 Coroner's Act.

23. Filed 1-14-46 1946 Registrar.

P. O. Address 145 JAN 17 PM 10 06 Ill.

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J.J. Hickman, Section Chief
J.E. Rose, Associate Section Chief

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REPORT FOR MONTH OF JANUARY 1946

- 1. R.S.S.
- 2. R.S.S. (Z)
- 3. L.O.J.
- 4. J.E.H.
- 5. K.Z.H.
- 6. H.J.C.

- 7. L.H.H.
- 8. J.C.H.
- 9. A.H.D.
- 10. S.L.H.
- 11. K.S.C.
- 12. S.T.C.

- 13. J.E.R.
- 14. E.R.R.
- 15. R.E.Z.
- 16. G.F.
- 17. J.J.N. (2)
- 18. Chl. Tech. File
- 19. Chl. Con. File

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Name	Date	Name	Date
<i>W.C. ...</i>	<i>2-1-46</i>		

8005600

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11 January 1946

To: Dr. J. J. Nickson
From: E. R. Russell
In Re: Abstract of Work for the Month Ending
January 11, 1946

for Plutonium Activity

I. Routine Urine Survey - 249-MLH-3501

A. Urine Specimens Received

Chicago 80
Other 10

B. Backlog of Specimens

Chicago 51
Other 28

C. Specimens Analysed

Chicago 69
Other 38

CLASSIFICATION CANCELLED
DATE JAN 11 1967
For the Atomic Energy Commission
RAYMOND A. CARPENTER
for the
Chief, Declassification Branch

Of the Chicago specimens analysed, 7.3% showed a body content of plutonium greater than 0.1 ug, 32% showed negative counts (maximum being less than 0.1 count per minute) and the remainder showed less than 0.1 ug retained in the body.

The laboratory which was designed to be dust-free in order to avoid outside contamination has not met the specifications. However, control urines have been run quite frequently and none have shown counts in excess of 0.1 count per minute per 1000 ml sample.

Special Urines: Two humans were injected with 94.91 ug of plutonium on December 27, 1945. The composition of the injected solution and the volume injected is given in Table I. The urinary plutonium excretion for the male subject is given in Table II and for the female in Table III.

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unauthorized person is prohibited by law.

Table I
Composition of Solution

Plutonium Concentration.	.21.57 ug/ml
Volume injected (each)	.4.4 ml
pH	.6.5
Sodium citrate	.0.01 M
Isotonic Saline	

Table II

D
Daily Plutonium Urinary Excretion (Male)
MX-200

Chicago Case #3 RER
12/19/72

Days after Injection	24-hour Volume	Specific Gravity	% of injected dose excreted
1	1130 ml	1.014	0.857
2	1425 ml	1.013	0.182
3	940 ml	1.012	0.063
4	1400 ml	1.012	0.077
5	1160 ml	1.012	0.026
6	1270 ml	1.014	0.0256
7	1290 ml	1.012	0.0234
8	9940 ml	1.012	0.0227
9	550 ml	1.012	0.0082
10	535 ml	1.012	0.0097
11	650 ml	1.010	0.0097
12	640 ml	1.010	
13	640 ml	1.010	

Observation techniques. A report summarizing the results obtained in preliminary studies of the colloidal behavior of PuO₂ in dilute aqueous solution has been submitted. The results of these studies are summarized in the following table. It is seen that the colloidal behavior of PuO₂ is strongly dependent on the extent of the acid concentration. At a pH of 7.5 and in the presence of varying amounts of citric acid, it is found that:

(a) As little as 0.001 M citric acid completely inhibits the colloidal behavior of PuO₂.

(b) A similar inhibition of the colloidal behavior of PuO₂ occurs at 0.005 M citric acid. It is probable, but not yet confirmed, that this is due to the formation of a positively charged Pu colloid by the reaction of PuO₂ with citric acid. Migration experiments are planned to check this idea on the Pu colloid and compare with the results obtained with the PuO₂ colloid.

Table III

Daily Plutonium Urinary Excretion
(Female-WX-300)

Chicago Case #2

Days after Injection	24-hour volume	Specific gravity	% of Injected dose excreted
1	1660 ml	1.012	0.152
2	1725	1.010	0.167
3	1750	1.012	0.067
4	1150	1.012	0.033
5	2020	1.010	0.042
6	1300	1.010	0.042
7	1190	1.010	0.0243
8	1500	1.010	0.0254
9	1400	1.010	0.019
10	1280	1.010	0.030
11	1120	1.010	0.019
12	940	1.010	0.014
13	875	1.010	
14	630	1.010	
15	830	1.010	

Plutonium Therapy: Studies are being completed on the effect of pH and citric acid concentration on the diffusibility of Pu(IV) through cellophane membranes using low pressure ultrafiltration techniques. A report summarizing the results obtained in preliminary studies of Pu therapy is being prepared.

Results of ultrafiltration to date show that a pH of about 2.5 immediately precedes a steep drop in the extent of Pu(IV) which is diffusible, thus indicating, it is presumed, the onset of definite colloidal. At a pH of 7.3 and in the presence of varying amounts of citric acid, it is found that:

(a) As little as 0.0001 M citric acid appreciably increases the diffusibility of Pu.

(b) A minimum in the diffusability of Pu occurs at .005-.006M citric acid. This phenomenon, if confirmable, may be related to the neutralization of a positively charged Pu colloid by the negatively charged citrate ion. Migration experiments are planned to study the sign on the Pu colloid and complex directly.

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see p. 10

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MUC-ERR-209

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DCU-A30887

Date: June 11, 1946

Subject: Distribution and Excretion of Plutonium

Chapter VII. Volume 20 A, PPR

By: E. R. Russell and J. J. Nickson, M.D.

To: _____

Before reading this document, sign and date below:

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<i>Kisela</i>	<i>7/15/46</i>		
<i>R. M. Zogaria</i>	<i>7/22/46</i>		

Kisela

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5-15-56 TID-1116
Authority of: USAEC
5-27-63 T. H. Sloan

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8005604

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Acknowledgement

It has been difficult to give credit to specific individuals for their contributions which are included in this chapter. Some of the work was done at other sites and privately communicated to us.

Specifically, we are indebted to Dr. Wright Langham and associates for information concerning the cupferron-chloroform procedure, to Dr. K. G. Scott and his associates for the information on the hexone and T.T.A. extraction procedures and to Dr. M. D. Taylor, Mr. E. E. Motta, Mr. D. Revinson, Mr. Harold Delaney, Miss J. A. Jackson, Miss Cordelia Brown, and Miss Wilana Monroe, all of our group, for testing and working out most of the procedures.

J. J. Nickson, M.D.
E. R. Russell

Table of Contents

1. Introduction	1
2. Estimation of Plutonium in the Body	4
2.1 Methods of Urine Analysis	
The adsorption procedure	5
Solvent extraction procedures	6
The cupferron-chloroform method	7
The T.T.A. procedure	7
Precipitation methods of analysis	9
The bismuth phosphate-lanthanum fluoride procedure. .10	
2.2 Methods of Fecal Analysis	
Wet ashing.	.14
Dry ashing	.14
Method for ashing feces for plutonium analysis	.15
2.3 Methods for the Analysis of Tissues	.16
3. Results of the Routine Urine Surveys	.19
3.1 Chicago.	.19
3.2 Clinton Laboratories	.22
4. Experimental Studies	
4.1 Results of Human Excretion Studies	
Urinary excretion of plutonium	.26
Fecal excretion of plutonium	.27
Distribution of plutonium in the body	.28
5. Summary and Suggestions	.31

1. Introduction

Following the discovery of plutonium, the determination of its half life as 24,300 years, and the fact that the material is alpha active, it became obvious that elaborate precautions were necessary if the worker was to be protected from harm. Experience in the radium industry had indicated clearly that very small amounts of the radium element deposited in the body were capable of producing serious illness or death. As a result of these considerations, the conditions under which plutonium is handled in the laboratory have been ringed about with elaborate protective regulations and devices.

In addition, however, it seemed highly desirable, if not essential, to know as precisely as possible the amount of plutonium in the individual worker. Animal experimentation indicated that the plutonium content of the urine and feces would be a useful guide to the total amount of plutonium in the body. It was decided to use urine for the routine determination⁽³⁾ primarily because of the greater ease in handling urine samples. As will be discussed below, it appears that in humans the amount of plutonium excreted per day is greater in the urine than in the feces.

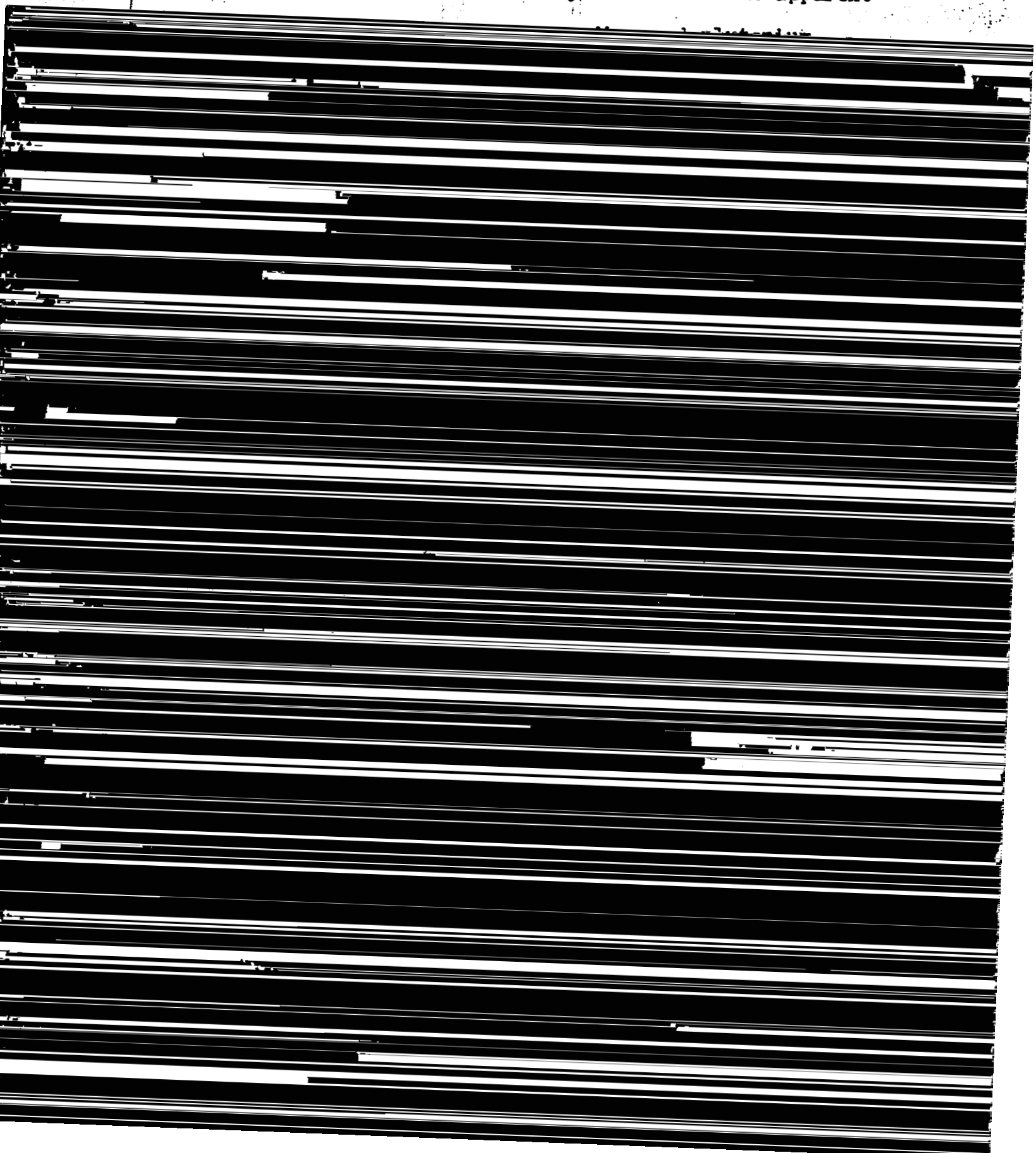
Initially, a tentative maximum permissible body content of plutonium was established on an arbitrary basis. From purely physical considerations it seemed that plutonium,

weight for weight, should be approximately one-fiftieth as toxic as radium. Since the tolerance amount of radium is generally accepted as 0.1 microgram in the body, the plutonium tolerance value was initially set at 5.0 micrograms in the body.

In order that one might estimate the plutonium content of the body through analysis of the urine, it was necessary first to establish the excretion rate. Preliminary experiments⁽¹⁾ with rabbits indicated that after the first two or three weeks of plutonium intake, approximately 0.01% of that retained in the body is excreted in a 24-hour urine specimen. Many excretion experiments with other animals and man have shown that this is nearly the correct value for the sub-acute excretion rate. Recent work discussed elsewhere indicates that this figure may be greater than the true excretion rate of plutonium which has been in the body for a year or more. It is possible that the figure of 0.01% may have to be reduced in the future.

If 5 micrograms is to be the body threshold, and 0.01% excretion is assumed, then analytical procedures capable of detecting 28 alpha counts per minute (plutonium) in a 24-hour urine specimen, or 2 counts per minute in a 100 ml specimen should be adequate. An adsorption procedure, described later, was designed specifically to assay 100 ml specimens. Any specimen showing less than 2 alpha counts per minute was not considered significant. This procedure

served its purpose well. However, when it became apparent



urine be carried out under "sterile" conditions.

It is the purpose of this chapter to present a detailed description of the methods used in the detection of plutonium in humans and to briefly discuss the results. In closing, suggestions are given for the establishment and operation of a laboratory for the detection of plutonium in individuals working with or in areas contaminated by the element.

2. Estimation of Plutonium in the Body

2.1 Methods of Urine Analysis: A survey of the analytical methods for plutonium used by the chemistry division revealed that with certain modifications some of these might be used to assay urine. A direct lanthanum fluoride precipitation from a small volume of acidified urine is adequate for many purposes. Where the volume is large and the concentration of plutonium is exceedingly small, such a method is not applicable as too large a quantity of lanthanum is required. In addition, certain salts in the urine may cause difficulty.

In the development of analytical methods applicable to urine analysis the time element as well as manpower requirements to assay a given number of samples were considered. It was felt that an adsorption procedure would offer the greatest possibility of routinely assaying daily the largest number of specimens with a minimum of personnel. As was

It was previously mentioned that plutonium is eliminated from the body in the urine at a fairly constant rate--the rate being approximately 0.01% per day. This figure was proposed on the basis of some very preliminary excretion studies on rabbits⁽¹⁾. Subsequent experiments on mice, rats, and dogs showed that the excretion rate may vary by a factor of five in the different species⁽¹¹⁾. It was felt necessary to establish independently the excretion rate of humans.

The fecal plutonium excretion, however, varied as much as a thousand fold from species to species. This made it difficult to assign any rate for human fecal plutonium excretion.

4.1. Results of Human Excretion Studies:

Urinary excretion of plutonium. Three experiments were begun within a few weeks (one at Chicago) in which plutonium was injected into a human and the plutonium excretion followed daily. During the first 15 days of the experiments there was less than 10% difference between the daily urinary plutonium excretion of the individual studied by Dr. W. Langham and associates at Los Alamos and the individual studied by Dr. J. J. Nickson, E. R. Russell and associates at Chicago. The individual studied by Dr. J. G. Hamilton at Berkeley showed a slightly lower excretion but not by a factor of 2. Following the initial period where a rapid decrease in the excretion rate is observed, there was a slight divergence in the results obtained from the three subjects. The individual

studied at Los Alamos showed an average daily excretion of slightly less than 0.02%, the one at Chicago slightly above 0.012% and the individual at Berkeley slightly less than 0.006%. These values persisted over a 100-day period. Since these experiments were completed, two additional studies have been made at Chicago. The excretion rate of one of these individuals after the first two weeks has remained between 0.010 and 0.015% per day. The other individual was not available for further study after the 16th day.

In view of the fact that the majority of the urinary plutonium excretion studies on humans have indicated that a sub-acute excretion rate of 0.01% per day is very nearly correct, this value appears to be at this time a reasonable one to use in determining the concentration of plutonium in the body of workers. It may be pointed out that the urinary plutonium excretion of dogs⁽¹³⁾ parallels that of man.

Fecal excretion of plutonium. In addition to following the urinary excretion of plutonium of the above individuals, the plutonium content of the daily fecal specimens was also determined. It has been predicted by several workers on the basis of animal excretion studies, that the plutonium fecal excretion rate would be greater than the urinary excretion rate. It therefore appeared that stool determinations would be easier to interpret. All of the human studies that have been made have failed to confirm this thesis. Plutonium in

a 24-hour fecal specimen is from 2 to 4 times less than that in a corresponding 24-hour urine specimen.

The average daily fecal plutonium excretion for the four cases studied is 0.003% ranging from 0.001% to 0.006% of that contained in the body. From the difficulties encountered in detecting 2×10^{-5} micrograms of plutonium, it would appear that surveys of personnel through fecal analysis would be difficult.

4.2 Distribution of Plutonium in the Body: The development and understanding of any satisfactory means of plutonium therapy is dependent upon a knowledge of the distribution of the element in the organism. Since nearly 90% of the plutonium finding its way in the body is retained there for many years it is vitally important that we seek some means of increasing the excretion rate. The first step in devising means of therapy is to learn in what organs the plutonium is concentrated.

There have been many experiments involving animals in which plutonium was injected and at some later date its distribution determined. The majority of these tests have shown that the liver, spleen, bone marrow, and lymph nodes are the principle sites of deposition. The same general distribution has been found for the one fairly normal human which was studied. The distribution data is given in Table I. In addition the distribution of plutonium in a female containing

approximately 90 micrograms was determined (see Table II.) This individual had many abnormally functioning organs and therefore the distribution may not be representative. It is interesting to note that even under these conditions the marrow and bone are among the principle sites of deposition.

Table I

Chicago Case 1:

RER 12/19/72

Distribution of Plutonium in a 68-year, White Male
(155 days after injection of 6.5 ug of plutonium as the citrate)

Tissue	Grams of tissue analysed	Cts/gram of tissue	*Relative Affinity for Plutonium
Marrow (rib)	0.8292	70.9	10.13
Liver	34.11	59.8	8.54
Sternum	5.38	20.6	2.94
Periosteum	0.1215	20.0	2.86
Spleen	32.12	11.1	1.59
Tumor (lung)	2.03	7.4	1.06
Cancer Tissue	2.87	7.2	1.03
Rib (cortex)	1.0125	7.0	1.00
L.Nodes. (aorta)	0.63	6.7	0.96
Lung	15.39	2.6	0.37
Testicle (glandular)	4.3425	2.3	0.33
Kidney	27.35	1.7	0.24
Heart	4.9435	1.2	0.17
Diaphragm	35.73	1.0	0.14
Abdominal Fat	17.05	0.2	0.03
Bile	8 cc	?	---

* = cts/gram found ÷ cts/gram assuming equal distribution throughout the body.

Chicago Case 2:

REF 12/14/

Table II

Distribution of Plutonium in a 54-year, White Female
 (16 days after injection of 94.91 μ g of plutonium citrate)

Tissue	Grams of tissue Analysed	cts/gram of tissue	*Relative Affinity for Plutonium
Marrow (rib	0.2065	1399	8.49
Rib (cortex)	0.430	1299	7.88
Callus and bone	0.1933	828	5.02
Callus (bone free)	0.262	534	3.17
Kidney	6.00	360	2.13
Thyroid	2.64	226	1.37
Contents (lower bowel)	10.05	183	1.11
Liver	8.70	162	1.00
Pancreas	6.045	148	0.90
Periosteum (rib)	0.461	123	0.75
Lung	14.40	107	0.65
Fat	5.850	96	0.58
Spleen	10.850	94	0.57
Tumor (liver)	1.97	71	0.43
Heart	0.40	70	0.42
Ovary (l.)	1.975	63	0.38
L. Node (abd.)	1.53	48	0.29
Intestines (small)	3.40	45	0.27
Intestines (large)	6.87	43	0.26
Muscle (striated)	15.32	40	0.24
Blood (heart clot)	1.835	22	0.13

* = cts/gram found + cts/gram assuming equal distribution
 throughout the body.



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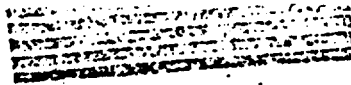


Table of Contents

I. Introduction	1
II. The History of the Disease	2
III. The Pathology of the Disease	3
IV. The Clinical Features of the Disease	4
V. The Diagnosis of the Disease	5
VI. The Treatment of the Disease	6
VII. The Prognosis of the Disease	7
VIII. The Prevention of the Disease	8
IX. The Epidemiology of the Disease	9
X. The Social and Economic Impact of the Disease	10
XI. The Role of the Patient in the Management of the Disease	11
XII. The Role of the Family in the Management of the Disease	12
XIII. The Role of the Community in the Management of the Disease	13
XIV. The Role of the Government in the Management of the Disease	14
XV. The Role of the International Community in the Management of the Disease	15
XVI. The Role of the Media in the Management of the Disease	16
XVII. The Role of the Religious Community in the Management of the Disease	17
XVIII. The Role of the Arts in the Management of the Disease	18
XIX. The Role of the Sports in the Management of the Disease	19
XX. The Role of the Education in the Management of the Disease	20
XXI. The Role of the Science in the Management of the Disease	21
XXII. The Role of the Technology in the Management of the Disease	22
XXIII. The Role of the Law in the Management of the Disease	23
XXIV. The Role of the Ethics in the Management of the Disease	24
XXV. The Role of the Philosophy in the Management of the Disease	25
XXVI. The Role of the Literature in the Management of the Disease	26
XXVII. The Role of the Music in the Management of the Disease	27
XXVIII. The Role of the Dance in the Management of the Disease	28
XXIX. The Role of the Visual Arts in the Management of the Disease	29
XXX. The Role of the Performing Arts in the Management of the Disease	30

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Chicago Case #1
RER 12/19/72



...the ...

Chicago Case #2
RER 12/19/72

Case No. 2

A fifty-five year old white female was admitted to the Billings Hospital in December, 1945 for diagnosis and treatment. Six months previously (June, 1945), she had noted generalized lymphadenopathy. Two months later (August, 1945), pain, aggravated on motion, developed in the trunk. On admission to the Billings Hospital in December, 1945 the essential physical findings were the presence of bilateral non-tender, moderately enlarged lymph nodes in the cervical, axillary, and inguinal regions and generalized tenderness to pressure over the ribs. X-ray examination of the chest, pelvis, skull, and spine revealed many small, rounded areas of decreased density scattered throughout the bones examined. In addition, partial collapse and wedging of the last thoracic and first and second lumbar vertebrae with some associated calcification was noted.

Laboratory examinations were essentially negative except for a moderate hypochromic anemia and leukocytosis. Wasserman and Kahn were negative. Study of sections of the tumor excised from the skull and left axilla revealed carcinoma-like tissue. It was felt that the carcinoma probably originated in the left breast.

The patient's general condition was poor at the time of admission and deteriorated steadily throughout the period of hospitalization. On December 27, 1945 at 9:03 AM, 25.5 micrograms of ^{239}Pu plutonium citrate were injected intravenously. The salt was contained in 4.4 cc of an isotonic saline solution 0.02 M in citrate at pH 6.5. The clinical course was not visibly altered following the injection. The patient expired on January 13, 1946.

The major autopsy findings were: (1) an adenocarcinoma probably arising in atypical ductal breast tissue with metastases to the liver, mesentery of the small intestine, lumbar vertebrae, ribs, skull and pelvis. Numerous healing pathological fractures of the ribs were found. (2) A lymphoblastoma involving the axillary, cervical, postbronchial, periaortic, and pelvic lymph nodes. Thus the patient had two co-existing presumably independent tumors, an unusual finding. The weight at autopsy was recorded as 35 pounds (38.6 kg.).

Histologically, the bone marrow in all places examined was almost entirely replaced by tumor. The spleen showed a marked atypical metaplasia. The kidneys showed dilated tubules filled with hyaline casts. The tubular epithelium showed evidence of degeneration and repair. Comparison of the biopsy sections with the post-mortem sections shows no evident difference in the character of the tumor following the injection of plutonium. The cells characteristic of lymphoblastoma are also present in the biopsy sections.

II. EXPERIMENTAL

The animal used in Case I was one week long and was used primarily to determine approximate daily urinary output available for analytical purposes. No control period was somewhat shorter and was used for the same purpose.

Each time the specimens were collected in the usual animals and the urine, after being transferred in the case of the urine, to a gallon bottle 3.0 M of concentrated hydrochloric acid had been added. The addition of the acid was to prevent the likelihood of absorption of plutonium by the container. The urine was transferred to "acid-washed" containers.

(10)

In Case II because of the condition of the patient, adequate separation of the urine and fecal specimens was not always possible. As a result adequate fecal excretion data could not be obtained.

Hematological studies made at frequent intervals in both cases included: hemoglobin in grams per ml; erythrocytes, leucocytes, platelets per cubic mm; reticulocytes in per cent; leucocyte differential; sedimentation rate (Westergren); and hematocrit reading. Liver function tests were performed in Case II by S. Schwartz using the cephalin flocculation and thymol turbidity tests and bilirubin determinations. .

Pathology: The autopsies were performed by members of the Pathology Department of the School of Medicine of the University of Chicago. The specimens were placed in 95 per cent alcohol as experience elsewhere had shown that the usual ten per cent formalin preservative tends to leach plutonium out of the specimen. Insofar as possible the specimens were placed in individual containers.

RESULTS

Case I

Excretion of Plutonium in the Urine: For forty-eight hours following intravenous injection of the plutonium solution, each specimen of urine was collected and analyzed separately. The first voiding was approximately six hours after the injection. The results of the analyses are given in Tables I, II and III and Figure 1. It is interesting to note that there is very little difference in the percent of the plutonium excreted in the third through the twelfth specimens though the unit concentration of plutonium in the urine varies widely. After forty-eight hours, the specimens voided in each 12 hour period were pooled for analysis, followed by pooling of specimens for each twenty-four hour period for the duration of the experiment. The results are given in Tables III and IV. The twenty-four urine volumes ranged from 1500 ml to 3600 ml. There was little correlation between urinary volume and quantity of plutonium excreted.

The urinary excretion of plutonium in the first 24 hour period is very nearly 11 per cent of the total excreted in the urine throughout the entire period of observation, and is 36 per cent of the total excreted in both urine and feces. The rapidity with which the rate of excretion diminishes is remarkable. Within 48 hours, the excretion level had fallen to approximately one-hundredth of that noted during the first six hours. In approximately two weeks the excretion rate had fallen to approximately 0.004 times the initial rate.

Table I.

Percent of Plutonium Excreted in Urine in the First 33 Hours.
(Individual Specimens)

Specimen No.	Volume of Specimen (cc)	c/n per 100 ml urine	% of injected plutonium excreted
1 (6 hours)	152	6550	2.23
2	218	255	0.175
3	325	45	0.023
4	245	65	0.026
5	434	37	0.035
6 (24 hours)	182	78	0.032
7	103	123	0.033
8	122	137	0.042
9	73	95	0.020
10	97	92	0.020
11	148	67	0.024
12 (48 hours)	160	100	0.024

Table II.

Percent of Plutonium Excreted - 2nd to 6th Day.
12 Hour Urinary Output Analyzed

Days after Injection	Volume of Specimen (cc)	c/n per 100 ml urine	% of Injected Plutonium Excreted
2.4	253	77	0.045
3	415	41	0.137
3.5	630	54	0.035
4	540	39	0.043
4.5	515	19	0.032
5	430	29	0.030
5.5	660	15	0.032
6	485	13	0.027
6.5	603	10.5	0.024
7	380	11	0.0314
7.5	920	6.5	0.023
8	695	5	0.0095

Table III.

Percent of Plutonium Excreted - 9th to 155th Day.

Days after Injection	Volume of Specimen (cc)	c/a per 100 ml urine	% of Injected Plutonium Excreted
9	2570	5	0.037
10	3250	4.7	0.034
11	3275	6.6	0.037
12	2320	5.2	0.047
13	1490	5.4	0.036
14	2635	5.7	0.034
15	2133	4.7	0.036
16	2520	2.1	0.012
17	2650	4.5	0.030
18	2920	4.6	0.036
19	2560	2.1	0.015
20	3060	5.6	0.030
21-30 avg.	2723	3.2	0.015
31-40 avg.	3018	1.9	0.012
41-50 avg.	3246	2.2	0.017
51-60 avg.	3520	3.3	0.021
61-70 avg.	2505	2.9	0.015
101-125 avg.	2125	1.7	0.011
126-152 avg.	---	2.0	0.010
129-155 avg.	---	1.7	0.008

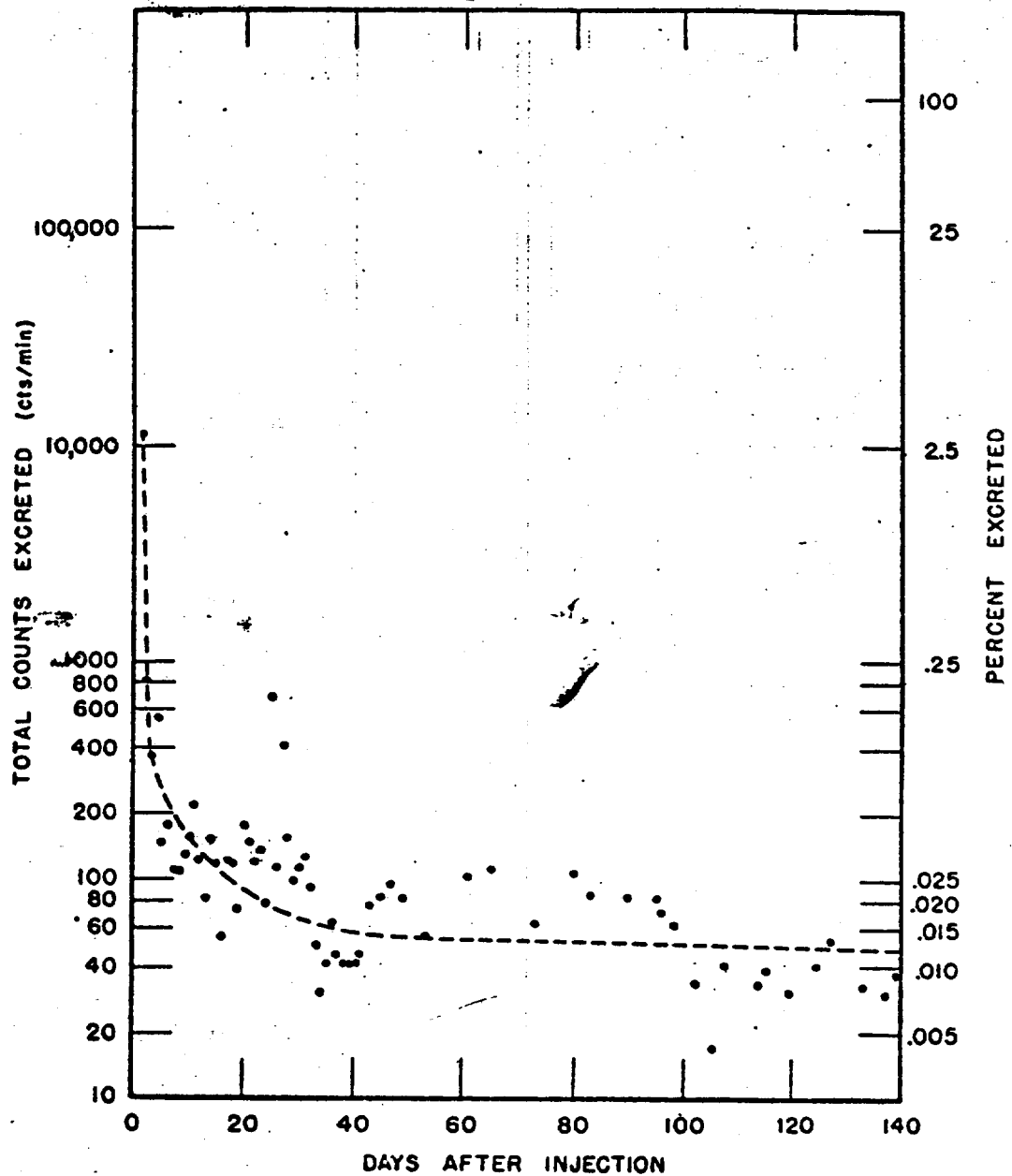


Figure I

Primary excretion of plutonium in a sixty-eight year old white male following the injection of 6.50 micrograms of plutonium citrate.

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Fecal Plutonium Excretion. During the first four days after injection seven individual fecal specimens were collected and analyzed for plutonium. Following this period the samples were collected at 24 hour intervals for several months and then 24 hour specimens were taken every four days until death. The results are given in Tables IV and V and Figure II.

Table IV.

Fecal Plutonium Excretion
Individual Fecal Specimens Collected in First 96 Hours.

Sample No.	Time of Collection after Injection	Weight of Specimens (gms)	c/m per gm of feces	% of Injected Plutonium Excreted
1	6 hours	13.0	26.0	0.076
2	26 hours	159.5	3.7	0.157
3	40 hours	45.5	16.2	0.162
4	51 hours	106.9	11.2	0.270
5	not recorded	141.5	6.2	0.195
6	not recorded	313.7	3.7	0.284
7	96 hours	76.2	9.1	0.154

Table V.

Fecal Plutonium Excretion
Daily Specimens from the 5th to the 133th Day

Days after Injection	Weight of Specimen (gms.)	c/m per gram feces	% of Injected Plutonium Excreted
5	49.5	19.3	0.214
6	57.0	8.7	0.109
7	54.2	6.3	0.076
8	64.4	7.3	0.105
10	273.3	3.2	0.200
11	129.9	2.8	0.062
12	144.7	1.2	0.040
13	70.1	2.8	0.044
14	166.7	1.0	0.042
15	122.7	1.1	0.059
16	222.1	0.6	0.021
17	120.9	0.9	0.037
18	130.0	0.53	0.035
19	112.4	0.59	0.034
20	115.5	0.29	0.033
21	123.0	0.18	0.023
22	143.6	0.21	0.024
23	23.2	0.16	0.022

CH-3607

131

Total excretion of plutonium for 133 days is estimated as 8.18 percent of the injected dose. The urinary excretion is estimated as 5.24 percent of the injected dose, the fecal excretion as 2.90 percent of the injected dose. The average excretion figures are multiplied by the appropriate factor in arriving at the above estimates, since average figures only are given throughout much of the period of study.

Clinical Studies of Peripheral Blood. No changes were observed in the hematological constituents of the peripheral blood which could be attributed to the action of the isotopes administered. These data are recorded in Table VI and in Figures III, IV and V.

Table VI.

Blood Findings - Case I

Age	Hgb. %	Hct. ml.	Hematocrit cc/100 cc	Red blood cells $\times 10^6$	Platelets/ $\times 10^3$	PLM %	PLM Absolute	Lymphocytes %	Lymphocytes Absolute	Monocytes %	Eosinophils %	Basophils %	Sed Rate 60 (unadjusted) (Westergren)
4-23-45	10.6	2.97	34	1.0	499,400	77	7233	17	1593	4	1	1	103
4-24-45	9.7	3.64	35	1.4	531,000	77	8045	15	1550	9	1	1	106
4-25-45	10.9	3.55	35	1.6	332,200	69	5741	37	2403	7	2	1	100
4-26-45	Intravenous injection of 6.50			1.5	480,700	79	10191	15	1935	4	1	1	113
4-27-45	10.5	3.61	34.5	1.5		81	7057	15	1455	4	1	1	115
4-28-45	10.5	3.71		1.5		64	4255	21	1396	8	2	1	
4-29-45	10.3	3.90	31	1.2	298,100	66	4323	23	1675	11	9	1	
5-1-45	10.0	3.52		1.5	292,000	63	4221	20	1377	5	6	1	
5-2-45	9.5	3.66		1.7	290,200	63	2959	24	1500	3	9	1	
5-3-45	9.5	3.12	32	3.8	435,700	70	5250	20	1395	6	6	1	
5-4-45	9.7	3.72		2.5		75	4632	24	1704	7	2	1	
5-5-45	10.4	3.77		1.5	350,900	70	5160	23	1870	5	9	1	
5-6-45	9.7	3.79		3.0	274,800	70	5633	15	1300	4	9	1	
5-7-45	9.8	3.30		3.0		70	5355	17	1152	6	11	1	60
5-8-45	9.2	3.53	30	3.0	246,200	64	4026	14	1020	5	9	1	33
5-9-45	9.3	3.53		2.1		60	4000	25	1715	5	7	1	109
5-10-45	9.1	3.20	29	2.0	261,000	62	4037	28	2105	3	12	1	94
5-11-45	9.0	3.52	31	1.5	317,000	61	3355	35	2375	7	9	1	103
5-12-45	9.5	3.24	31	1.6	246,500	55	4012	26	2030	4	12	1	99
5-13-45	9.2	3.50	28.5	2.0	326,400	62	4495	29	1319	5	9	1	70
5-14-45	8.5	3.09	28	3.3	323,600	62	8120	13	1530	6	12	1	24
5-15-45	10.0	3.79	34	1.9	141,000	62	4643	30	2837	4	2	1	33
5-16-45	9.5	3.34	31.5	1.7	203,600	65	6337	30	1583	3	1	1	85
5-17-45	10.1	3.70	32	1.0	272,800	72	5254	30	2316	5	2	1	89
5-18-45	9.8	3.60	33	1.0	202,700	55	3655	33	2215	5	1	1	120
5-19-45	9.7	3.57	33	1.6	228,700	69	4653	23					
5-20-45	10.0	4.07	33	1.1									

151

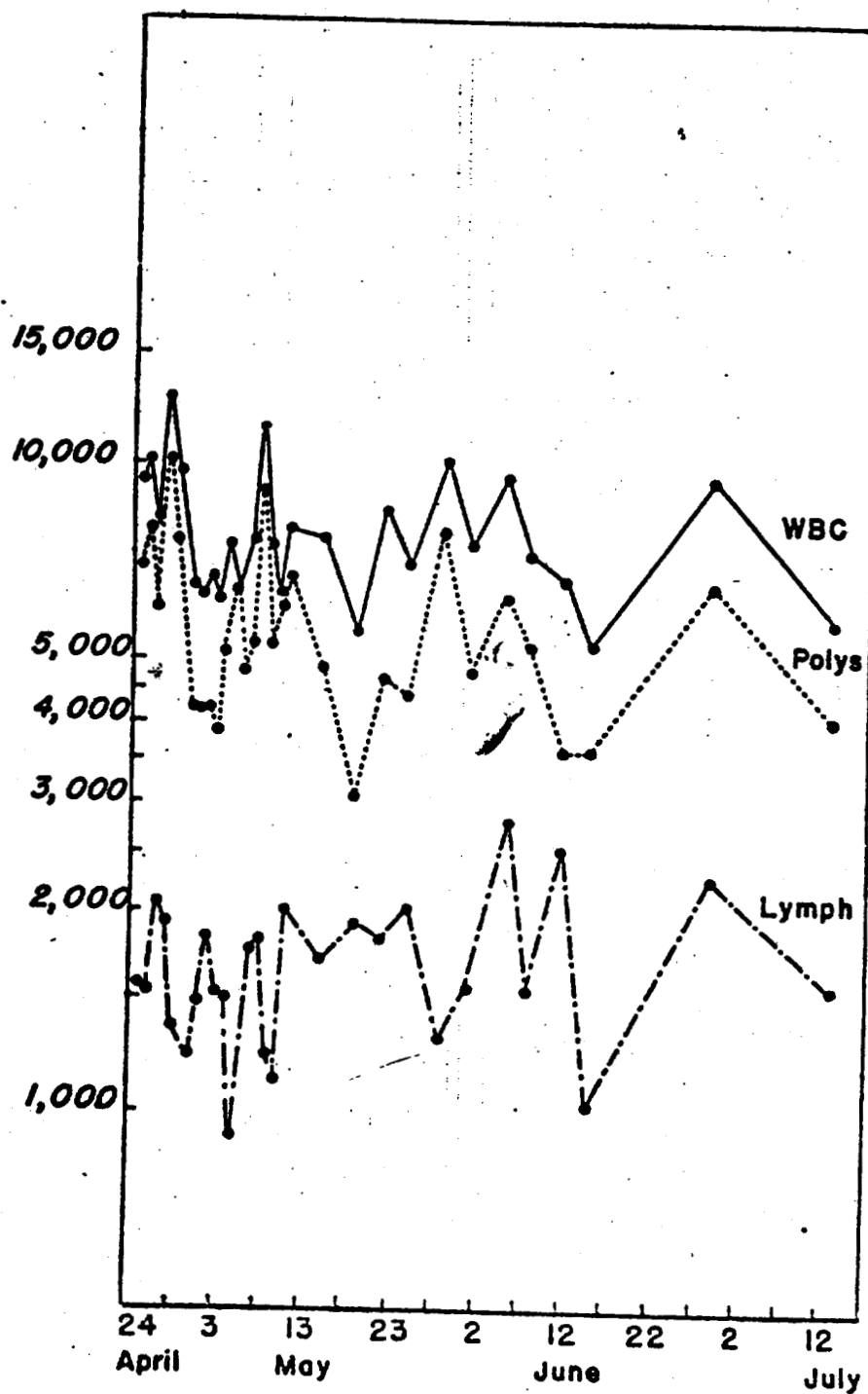


Figure III

Total white blood cell, polymorphonuclear cell, and lymph cell counts per cubic millimeter, in Case I.

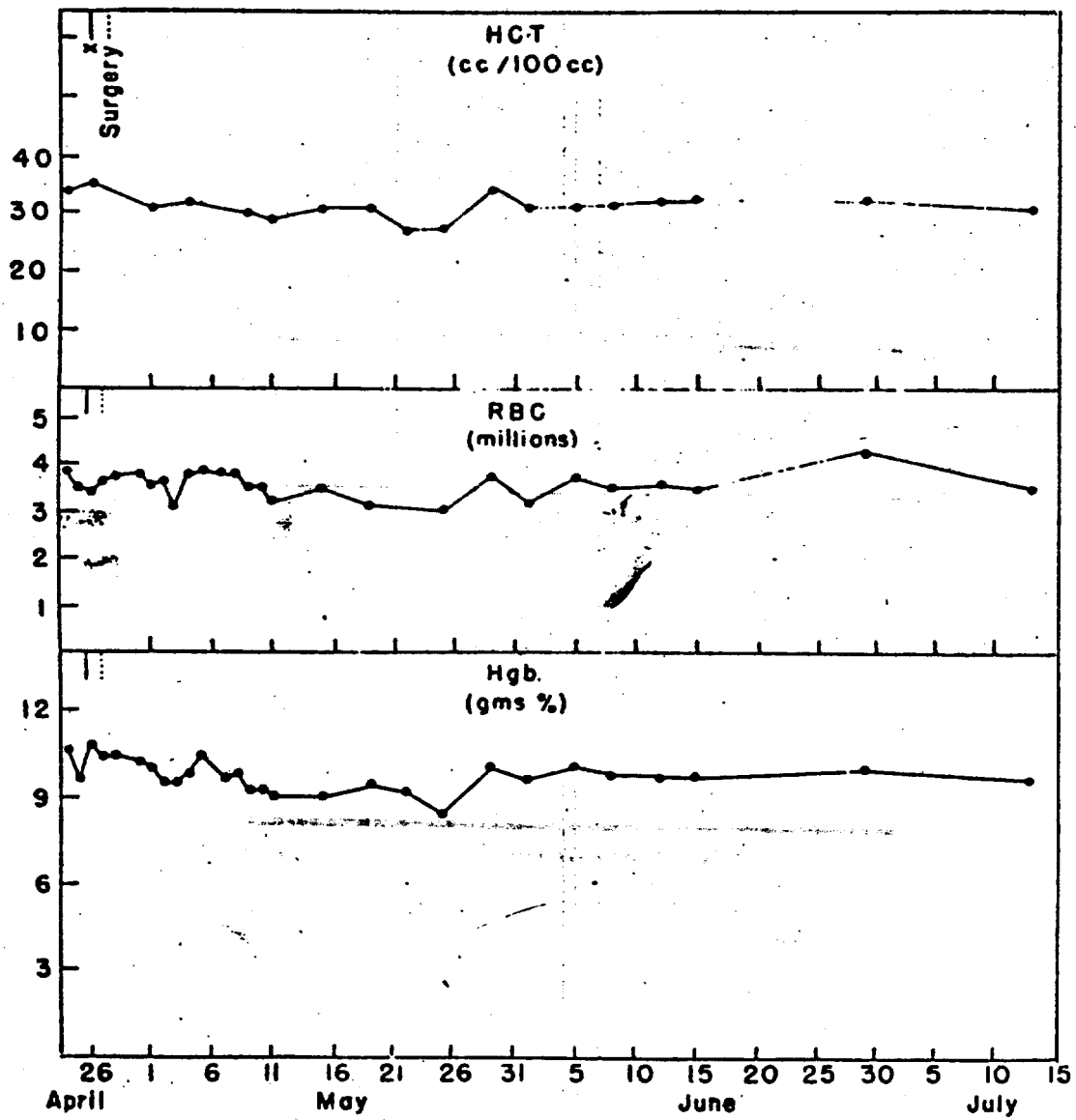
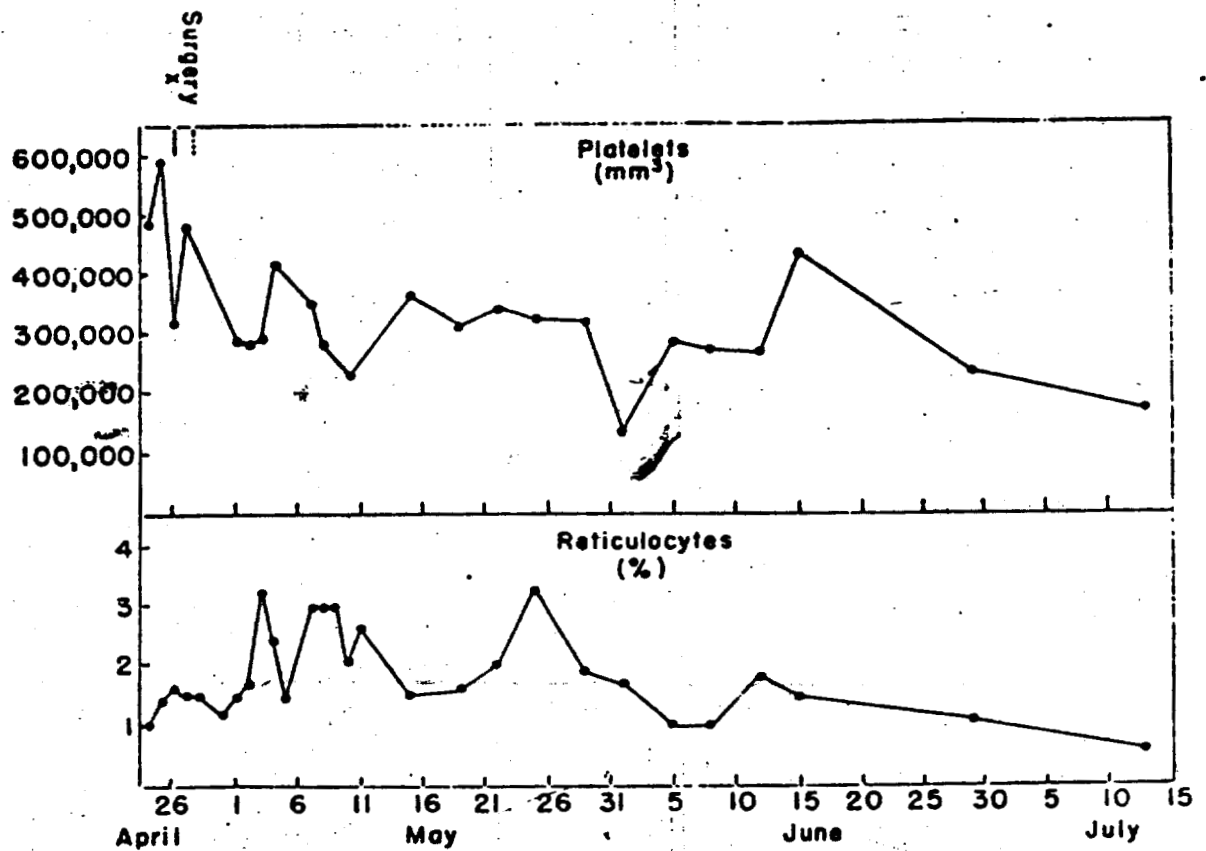


Figure IV

Hematocrit reading, red blood cell count, hemoglobin determination in Case I. The collection was given on April 26, 1945.

Figure V

Platelet and reticulocyte counts in Case I.



19

Post Mortem Findings. The patient died 155 days after the injection of plutonium. The analytical data is recorded in Table VII. The specimen of marrow and spicules showed the greatest activity per gram of tissue. The plutonium content per gram of liver was nearly as great. The activity of the cortex of the rib was one-tenth that of the bone marrow. No activity could be detected in the sample of bile analyzed. The effects of plutonium on normal and tumor tissue was looked for in the post mortem material by H. Lisco. He found no changes which he felt could be attributed to the action of the plutonium.

Table VII.

Distribution of plutonium in tissues of Case I, 155 days after the injection of 6.5 microgram of plutonium.

Tissue	Weights of Organs (gms)	Gms of Tissue Analyzed	Observed Counts per/min.	Cts/gm of Tissue per/min.	ug/gm of Tissue ($\times 10^{-3}$)	Relative Affinity for Plutonium*
Marrow + Spicules	2050	0.8292	58.8	70.9	1.043	10.13
Liver		34.11	2040.0	59.8	0.837	8.54
Sternum		4.38	111.1 ¹	20.6	0.303	2.94
Parosteum (rib)		0.1215	2.12	20.0	0.299	2.86
Spleen	260	32.12	37.9	11.1	0.164	1.59
Lung Tumor		2.03	14.8	7.4	0.109	1.03
Cancer Tissue		2.87	20.9	7.2	0.103	1.03
Rib (cortex)		1.0125	6.06 ¹	7.0	0.103	1.00
L. Nodes (aortic)	1950	0.63	4.17	6.7	0.099	0.93
Lungs		15.39	40.7	2.6	0.038	0.37
Testicle (gl. portion)		4.3425	10.0	2.3	0.034	0.32
Kidneys		27.35	53.3	1.7	0.025	0.24
Heart	340	4.9435	6.0	1.2	0.018	0.17
Diaphragm		35.73	33.3	1.0	0.015	0.14
Fat (abd.)		17.05	3.6	0.2	0.003	0.03
Bile		8 cc	2.6	?	0.000	---

* Counts per gram/counts per gram assuming uniform distribution of plutonium.
¹ 90% correction factor applied to observed counts to give actual counts/gm.

(11)

Case II.

Excretion Studies. The urinary excretion data is listed in Table VIII and plotted in Figure VI. Unfortunately no comparison of fecal and urinary excretion can be made in this case. The collection of separate urine and stool samples was impossible. In fact the graph of urine excretion in Figure VI might with greater truth be called the graph of total product excretion.

The 24 hour excretion rate was 0.152 percent of the amount injected. This represents an excretion of 0.144 micrograms of the 94.9 micrograms injected. Following the initial 24 hour period the excretion rate was comparable to that in the other cases studied. The total known excretion was 0.684 percent of the amount injected, or 0.649 micrograms.

Table VIII.

Daily Plutonium Urinary Excretion, Case II.

Days after Injection	24-hour Volume	Alpha Counts/min/100 cc.	% of Injected Dose Excreted
1	1660 ml	594	0.152
2	1725	622	0.167
3	1750	250	0.067
4	1150	186	0.033
5	2020	134	0.042
6	1300	207	0.042
7	1190	132	0.0243
8	1500	110	0.0244
9	1400	89	0.019
10	1280	154	0.030
11	1120	103	0.019
12	940	100	0.014
13	875	251	0.034
14	630	99	0.009
15	830	124	0.016
16	150	164	0.004

Studies of the Peripheral Blood: No alterations in the hematological constituents of the peripheral blood occurred following the administration of 97.2 micrograms of plutonium which could be attributed to the presence of the element. The interpretation of changes in the thymol turbidity and cephalin flocculation tests, and the amount of bilirubin in the blood serum was not possible because of the terminal state of the subject. These data are presented in Table IX and in Figure VII.

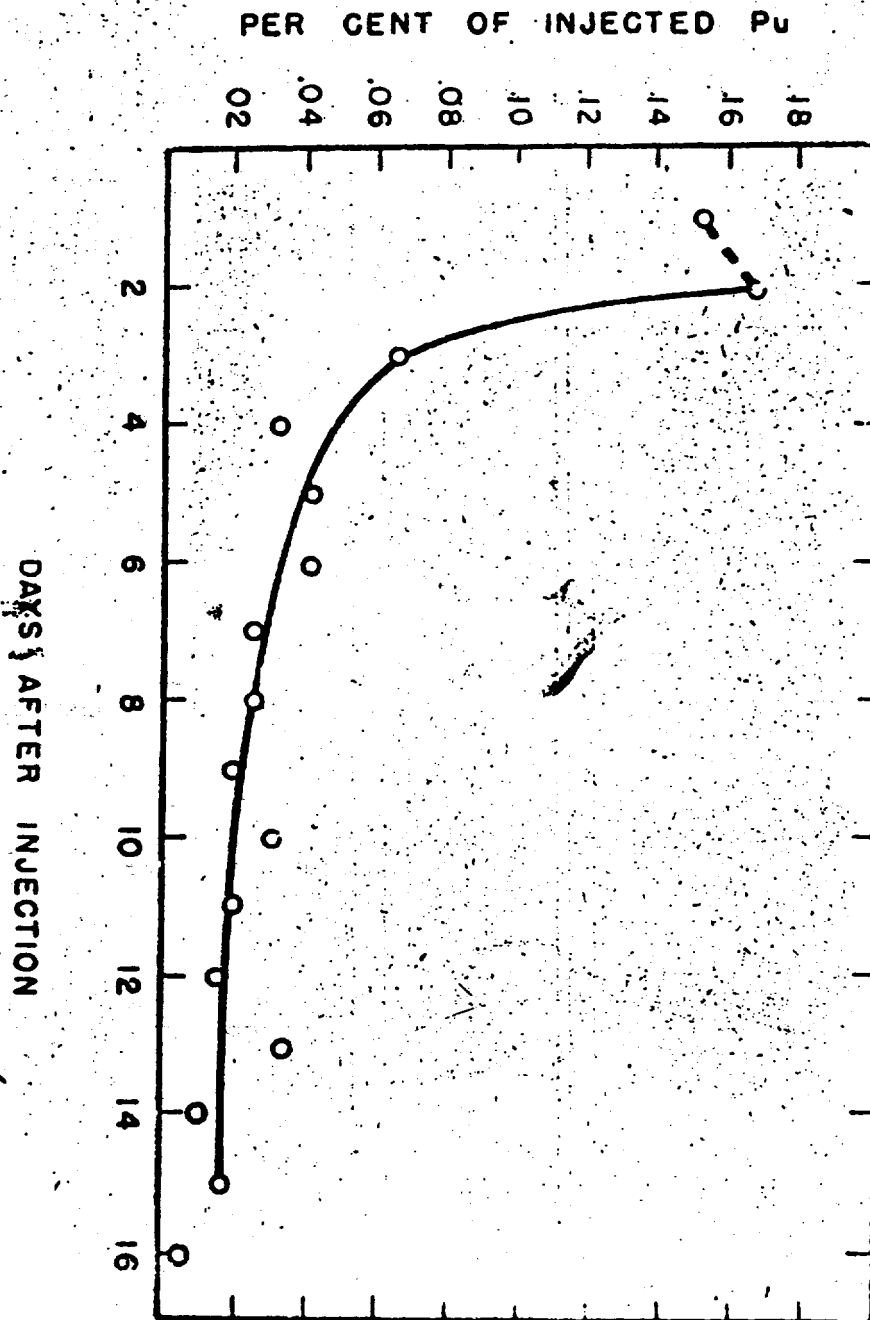


Figure VI

Excretion of plutonium in the urine following the injection of 94.9 micrograms of plutonium citrate.

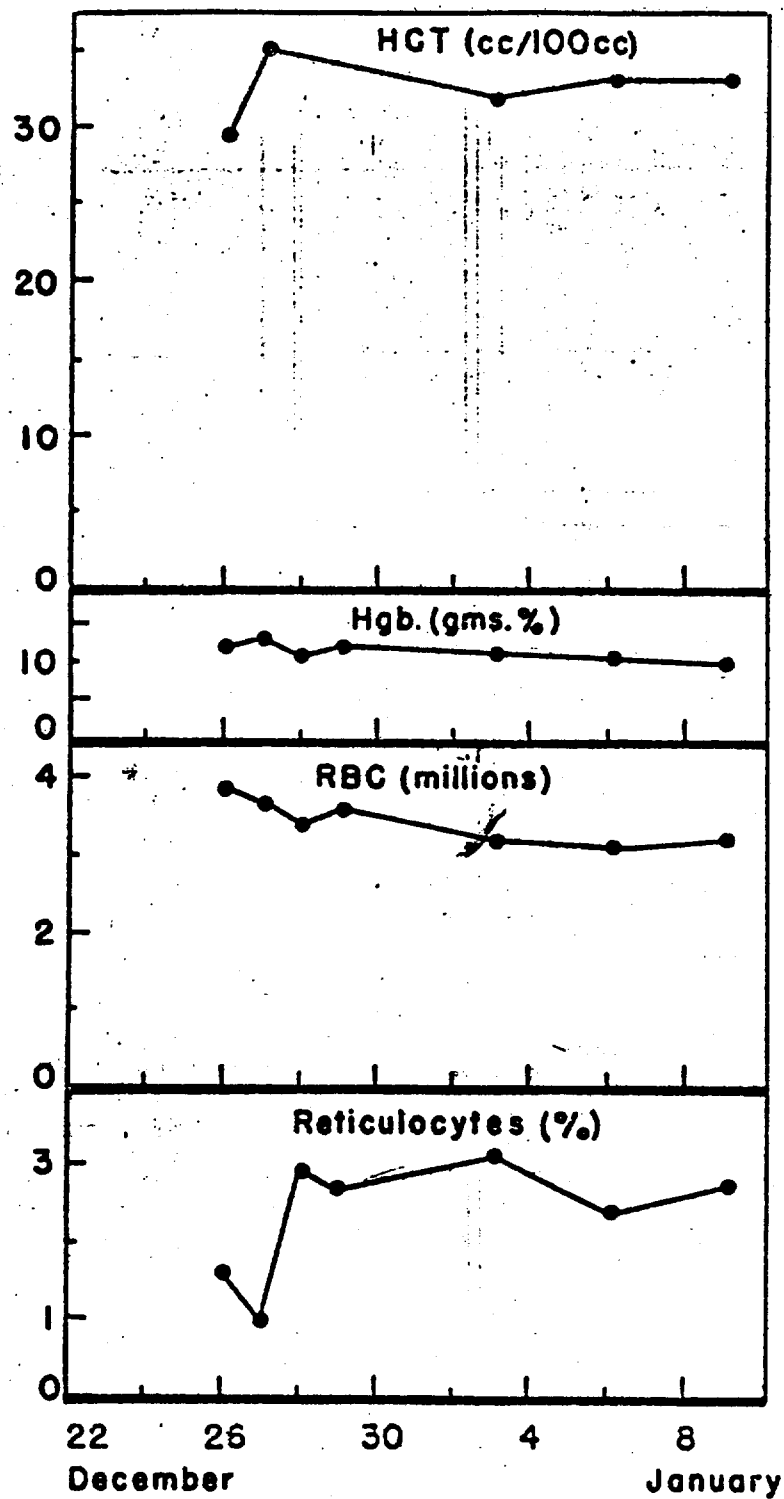


Figure VII

Hematocrit, hemoglobin, red blood cell and reticulocyte findings in Case II.

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Table IX

Blood Findings in Case II

Date	12/26/45	12/27/45*	12/28/45	12/29/45	1/2/46	1/5/46	1/8/46	1/12/46
Hb	12.1	12.9	11.8 gm	11.8 gm	11.1	11.0	10.5	11.0
REC	3.96	3.72	3.47	3.65	3.37	3.25	3.32	3.36
Hematocrit	29	35			32	33	33	33
WBC	17,250	20,950	16,550	18,300	17,900	18,950	20,500	20,950
Reticulocytes	1.6%	1.0	2.9%	2.7%	3.2	2.4	2.8	1.9
Sed Rate	115	101			59		58	57
Neutrophils, %	83	75	77	71	81	82	80	85
Neutrophils, No.	14,276	15,675	12,705	12,993	14,489	15,498	16,400	17,765
Eosinophils, %	5	2	4	3	2	1	2	12
Basophiles, %	12	15	11	15	10	13	13	12
Lymphocytes, %	2,064	3,135	1,815	2,745	1,790	2,457	2,665	2,508
Lymphocytes, No.	3	8	7	10	7	4	5	3
Monocytes, %				1%				
Stabs					2			
Neutamyelocytes, %					sl.	sl.	sl.	sl.
Polychromasia	sl.	sl.	sl.	sl.	sl.	sl.	sl.	sl.
Hypochromasia	sl.	sl.	sl.	sl.	sl.	sl.	sl.	sl.
Anisocytosis	x							x
Normoblasts								
Polys. toxic								
Cephalin								
Flocculation								
Serum								
Bilirubin								
15 min.								
Total								
Tu/mol								
Turbidity								

* Injection of plutonium on this day following the withdrawal of blood for study.

Distribution of Plutonium in the Tissues. The Plutonium content of the tissues analyzed is listed in Table X. The marrow and rib specimens showed the highest specific activity, as would be expected from the animal work. The plutonium content per gram of liver tissue was roughly one-tenth that of the bone marrow. The specific activities per gram of muscle and fat were respectively one-twentieth and one-thirty-fifth that of the bone marrow. H. Lisco reviewed the histological material for evidence of changes similar to that attributed to plutonium in the experimental animals. No such change was observed. It should be pointed out that the amounts per gram of body weight were greater in the animals in which changes were seen.

Table X.

Plutonium Distribution in Tissue 16 Days after Injection.

Tissue	Weight of Organ (gms)	Weight of Sample (gms)	Total Counts ¹ in Sample	Counts ¹ /gm of Tissue	Micrograms Plutonium/gram of tissue ($\times 10^{-3}$)	Relative Affinity for Plutonium ²
Marrow (Rib)		0.2065	289	1399	20	5.49
Rib (Cortex)		0.430	558	1299	18.6	7.83
Callus and Bone		0.1933	160	828	11.2	5.02
Callus (bone free)		0.262	140	534	7.7	3.17
Kidney	190	6.00	2162	360	5.1	2.18
Thyroid		2.64	597	226	3.2	1.37
Contents (lower bowel)		10.05	1833	183	2.6	1.11
Liver	1110	8.70	1405	162	2.3	1.00
Pancreas	60	6.045	893	148	2.1	0.90
Periosteum		0.461	57	123	1.7	0.75
Lung	490	14.40	1533	107	1.5	0.65
Fat, Mesenteric		5.850	560	96	1.2	0.53
Spleen	85	10.850	1021	94	1.2	0.57
Tumor (Liver)		1.970	140	71	1.0	0.43
Heart	250	9.40	660	70	1.0	0.42
Ovary, L.		1.975	122	63	0.90	0.38
Lymph Node (abd.)		1.53	73	48	0.70	0.29
Intestines (small)		3.40	151	45	0.64	0.27
Intestines (large)		6.87	291	43	0.60	0.26
Muscle (Str.)		15.32	613	40	0.57	0.24
Blood (Heart Clot)		1.835	40	22	0.31	0.13

1 - Alpha counts per minute from plutonium.

2 - Counts/gram found divided by counts/gram assuming equal distribution of the plutonium.

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DISCUSSION

It must be emphasized that the data discussed above, while obtained on humans, may not be applicable to the population with which we are mostly concerned. The majority of occupationally exposed persons are in the 20-40 year age group and are in good general health. The persons discussed above both had carcinomas, one of which had widespread metastases. In case #2, the injection was made but seventeen days before death and the terminal state may have influenced the metabolic behavior of the element. In case #1 no gross evidence of other than local disease, except for the metastasis to the lung, was noted at the time of injection. Thus, barring alterations due to age, the early distribution of the plutonium was presumably a "physiological" one. However, it must be pointed out that we have no information on the early distribution pattern of the plutonium in this case. The data given in Table VII represents the distribution of the injectate 155 days later, after profound metabolic disturbances, causing his death, had occurred. It is impossible to say what influence this may have had in altering the early distribution pattern.

As is well-known, the biological behavior of a given agent varies greatly from one species of mammal to another. Hence, experience with humans injected with plutonium was vital to any interpretation of the data obtained from animals. The rate of plutonium excretion in rats⁽²⁾, mice⁽²⁾, rabbits⁽³⁾ and dogs⁽⁴⁾ varies widely. The route of excretion varies from species to species^(2,4). Since our estimate of the body content, and hence ultimately of the desirability of removing a given worker from his job, depended upon the excretion rate of plutonium in the human, it became necessary to determine that rate directly in the species concerned. Knowledge of the distribution of the element as well as its rate and route of elimination from the human body provided information which could be correlated with the more extensive experimental investigation in animals and provided information which made possible the estimation of the amount of plutonium already deposited in the workers by the determination of the daily plutonium excretion rate of the individual concerned.

Clinical Picture. Insofar as can be determined the clinical course in neither of the two cases was influenced by the injection of plutonium. In Case #1, the concentration of that material was 0.085 micrograms per kilogram of body weight immediately following the injection. In the second case the concentration of plutonium was 2.46 micrograms per kilogram of body weight.

That the amount of plutonium injected in these subjects produced no appreciable clinical effect is likely in view of the fact that the amount of plutonium necessary to produce damage is far greater. Table XI lists some of the experimental values⁽²⁾.

Table XI.

Comparison of Dose Levels of ²³⁹Pu in Animals and Their Effects.

	ug/kg	Effects	Time
Rats	700 - 1000	LD 50% in	30 Days
Rats	200 - 600	LD 50% in	150 Days
Rats	10	None	420 Days

It will be seen that the level of 10 micrograms per kilogram is approximately 1/7 times the dosage level in Case I and 4 times the dosage level in Case II.

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Hematological Studies. No hematological changes of the peripheral blood were observed in either subject. In view of the very slow excretion rate and long half-life of deposited plutonium it might be assumed however that a condition comparable to that described by Hartland(5), Castle(8) and Bomford and Rhoads(9) in individuals with chronic radium poisoning (severe anemia, leukopenia and thrombocytopenia with or without bone sarcoma) might well develop in either case were it possible to observe subjects over extended periods of time. The difficulty which arises in attempting to extrapolate from the radium damage data on the human to the expected effect of plutonium is, among other things, due to the difference in the excretion pattern and the impossibility of estimating what the ingested dose might have been in the individuals who have succumbed to radium poisoning. While bone sarcomas have been reported in individuals with a total of 0.5 μ g of radium in the body at death, little information is available as to the amount which was in the body initially and this initial dose may be the critical amount.

Case I

Excretion Studies. The fact that the rate of excretion of plutonium apparently had not reached a constant even 100 days after injection deserves emphasis. The rate of fall is slight but definite. This point deserves emphasis as it may indicate that the excretion rate 1000 days after exposure may be even less than the average of 0.012 per cent found after 150 days in this case. Evidence for continued diminution in the excretion rate of plutonium 238 (isotope of plutonium 239) is found in the patient studied by the University of California group which is described in the biology volumes of this report. In this patient, 158 days after injection, the daily excretion rate is approximately 0.0015 per cent of the injected dose(6), a figure definitely lower than our figure of 0.012 per cent one hundred and fifty days after injection.

Should the lower figure prove to be the more correct, one the difficulty of detecting tolerance concentrations of plutonium by means of the urinary excretion of that element is materially increased.

It is interesting to note the totals of urinary and fecal excretion for the time periods of 0-24 hours, 2-10 days, and 11-100 days. Table XII gives these data for Case I in terms of per cent of the injected dose:

Table XII

Summary of Plutonium Excretion for Indicated Time Periods, Case I

Time	Urine	Stool	Total
0-24 hours	2.53%	0.233%	2.764%
2-10 days	0.638%	1.748%	2.386%
11-100 days	1.902%	0.767%	2.669%

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It is apparent that the total excretion is roughly equal for each of the various periods. One might speculate that the next order of magnitude, that is 101-1000 days, might also show a total plutonium excretion of approximately 2.5 percent. If this percentage excretion for the 101-1000th days period is subsequently borne out by experimental observation, it would paint a rather discouraging picture from the point of view of the normal excretion rate for plutonium.

The fecal excretion pattern is similar to that described for the excretion in the urine. No sharp early peak in the excretion rate is noted however. On the other hand, the rapidity with which the rate falls is not so marked. Indeed, the total plutonium excreted from the second to the tenth day is greater in the feces. However, as pointed out above, the fecal excretion after the twentieth day is distinctly less than the urinary excretion.

It will be noted that throughout this paper the excretory rate is given as "percent per day of the injected dose". It would be more accurate to speak of the percent per day of the amount in the body. Because of the low rate of excretion of plutonium the correction factor is small and it is felt that the small inaccuracy introduced by this practice is justifiable, particularly in preliminary studies.

Distribution of plutonium in the Body. It may be useful to compare the relative concentrations of plutonium in the various organs in the two cases. It is recognized that such comparisons cannot be pushed too far because of the many uncontrolled variables.

For ease of comparison, the values from Case I in Table XIII are adjusted to an injection amount of 94.91 micrograms, the amount injected in Case II, assuming the same distribution would occur with the larger dose.

In both cases the bone marrow shows the greatest concentration of plutonium per gram of tissue. On the basis of animal experimentation it is felt that the plutonium probably initially localizes in the osteoblastic and collagenous tissue surrounding the spicules, forming the endosteum. Since the proportion of this tissue is greatest in the marrow specimen, it shows the highest activity. It is of interest also to note the much higher proportional activity of the bone cortex in Case II, where the cortex shows almost as much activity as the marrow. The decalcification of the bones noted in this case would result in a greater proportion of plutonium-containing tissue than found in the comparable specimens in Case I, where the calcium content of the bones was apparently normal. The specimen of callus from the rib in Case II did not show as high concentration as the cortex or marrow specimens do. Since the callus represents a healing pathologic fracture, it is entirely possible that the uptake of plutonium was abnormally low.

Table XIII

Comparison of the concentration of plutonium per gram of tissue. For ease of comparison the values from Case I are adjusted to an injection amount of 94.91 micrograms, the amount injected in Case II.

Tissue	Case I Gm Pu/gm tissue ($\times 10^{-3}$)	Case II Gm Pu/gm tissue ($\times 10^{-3}$)
Bone Marrow + Spicules	15.2	20.0
Bone Cortex	1.50	18.6
Kidney	0.36	5.1
Liver	12.8	2.3
Lung	0.55	1.7
Fat	.04	1.5
Spleen	2.39	1.2
Tumor	1.59	1.0
Heart	0.26	1.0
Ovary		0.90
Testicle	0.50	
L. Nodules	1.44	0.70
Muscle, striated	0.22	0.57

The amounts in the livers are of considerable interest. The reasons for the wide discrepancy shown are not known at the present time. In Case I the liver content at death, some 150 days after injection, constituted approximately one-third of the injected amount. This value is far higher than the data from experimental animals would lead one to anticipate(2). It is true that early values comparable to the one listed here may be found in the experimental animal. Almost uniformly, however, the initial high value has dropped by a factor of five or ten by the hundredth day(2). Why, in this instance, the liver should have retained plutonium so tenaciously is not understood. Indeed, it must be admitted that we cannot rule out the possibility that the amount in the liver was at one time lower than the final value. Liver biopsies would be extremely useful in following the plutonium content of that organ over a wide time range.

In Case II the content of plutonium in the liver was approximately one-sixth of the amount noted in Case I and constituted approximately one percent of the amount injected. This figure is, if anything, somewhat lower than one would expect the concentration in the liver to be on the 16th day after injection, judging again from the results of animal experiments.(2)

The concentration of plutonium in the spleen in Case I, which showed some congestion but no other evidence of pathologic change, was distinctly greater than the concentration in the spleen in Case II where a marked myeloid metaplasia was observed. The relative concentration of plutonium in the spleen observed in these two cases given here are distinctly less than those observed in experimental animals, particularly in dogs(4). In most instances the plutonium concentration in the spleen compares favorably with that of the bone marrow. Certainly the difference noted between the results in the two human cases are far less than the difference between species(2,4). Again no explanation for this fact can be given at this time.

KW

It is interesting to note that in both cases the primary tumors, two carcinomas and a lymphosarcoma, did not concentrate plutonium to a significant degree. While it is impossible to generalize from two cases, it seems unlikely that plutonium will be of any value in the treatment of carcinomas in humans. As a general principle any radioactive agent injected for therapeutic purposes must concentrate to a greater degree in the tumor than elsewhere.

There is a marked difference in the concentration of plutonium in the kidneys of the two cases. The higher value is found in Case II. Two factors may reasonably be expected to operate in the direction of producing a higher concentration of plutonium in this case. First, and probably more important, is the fact that the death occurred shortly after the injection. The data obtained from animal experiments indicates that the kidney concentration is higher shortly after injection⁽²⁾. In both cases evidence of degenerative changes in the tubules of the kidneys was noted in the tissue sections. In addition, in Case I changes suggestive of a pyelonephritic lesion were noted. It is possible that the urinary excretion data will be found subsequently to be too low because of the presence of disease in the



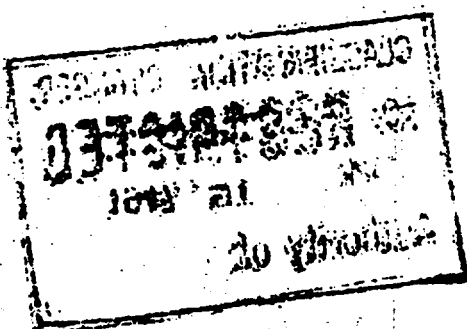
cases reported elsewhere) the following tentative conclusions may be drawn. It must be recognized clearly that these are not in the true sense of the word conclusions but are only working hypotheses that must be confirmed and elaborated upon by subsequent investigations.

- (1) The urinary rate of excretion of plutonium in humans is exceedingly low. The best evidence available at this time would indicate that the "chronic" (150th day) excretion rate does not exceed 0.01 percent per day of the amount fixed in the body.
- (2) The fecal rate of excretion of plutonium fixed in the body is lower than the urinary rate by a factor of approximately three. What evidence we have would indicate that the rate of fecal excretion does not exceed 0.003 percent per day of the amount in the body.
- (3) The highest concentration of the plutonium fixed in the body is found in the bone marrow. The liver concentration has varied so widely in the two cases here reported that it is impossible to predict on a reasoned basis what the general picture might be.
- (4) The concentration of plutonium in the neoplastic tissue of these cases was not high.

(54)

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**THE DISTRIBUTION AND EXCRETION OF PLUTONIUM
IN TWO HUMAN SUBJECTS**

E. R. RUSSELL AND J. J. HIGSON, H.D.

Assisted by

W. Harrou, R. Lesko, L. J. Jacobson

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Report Received: August 29, 1946
Figures Received: September 13, 1946
Issued: October 2, 1946

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14 bone specimens
Radius head
patella
rib whole
vertebra
sternum

Fig. = 00905

X7000 = 52.4

Declassified as part of

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CDC Document No. 701330

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Date 5/17/91 BA 64-179

TABLE 3

DISTRIBUTION OF PLUTONIUM IN HUMAN TISSUES FOLLOWING
INTRAVENOUS INJECTION OF PLUTONIUM SALTS

Tissue (2)	151 456 Subject (3) and % of Injected Dose/g of Tissue									Rel. Pu Affinity (3)	Org. Wt./g (4)	Calc. %/Organ
	Hp-5	Hp-9	Hp-11	Chi. I	Chi. II	Hp-12	Cal. I	Avg. %/g				
Bone Marrow	--	--	.0096	.0153	.0210	--	.0290	.0187	13.3		3,000	(56.1)(6)
Radius (Frag. head)	--	--	--	--	--	.0187	--	--	--		--	--
Liver	.0320	.0144	.0053	.0139	.0024	--	--	.0136	9.7		1,700	23.1
Rib (Cortex)	--	--	--	.0015	.0196	--	.0170	.0127	9.1		--	--
Patella	--	--	--	--	--	.0109	--	--	--		--	--
Vertebra	.0071	.0080	.0070	--	--	--	--	.0073	5.2		--	--
Sternum	.0070	--	.0100	.0044	--	--	--	.0071	5.1		7,000	65.7(5)
Rib (Whole)	.0050	.0038	.0063	--	--	--	--	.0052	3.7		--	--
Periosteum (Rib)	--	--	--	.0043	.0019	--	.0048	.0037	2.6		--	--
Spleen	.0007	.0015	.0048	.0024	.0014	--	.0019	.0021	1.5		200	0.4
Kidney	.0002	.0002	.0015	.0004	.0054	--	--	.0015	1.0		300	0.4
Thyroid	.0001	--	.0009	--	.0034	--	--	.0014	1.0		30	--
Adrenal	.0004	--	.0022	--	--	--	--	.0013	1.0		14	--
Lung	.0005	--	.0016	.0005	.0016	--	--	.0011	0.8		950	1.0
Pancreas	.0002	.0002	--	--	.0022	--	--	.0009	0.6		65	--
Gonads	.0003	--	.0012	.0005	.0009	--	--	.0007	0.5		--	--
Lymph Node	--	--	--	.0014	.0001	--	--	.0007	0.5		700	0.5
Teeth (Av. of 7)	--	--	--	--	--	.0003	--	--	--		--	--
Heart	.0000	.0000	--	.0003	.0011	--	--	.0003	0.2		350	0.1
Large Intestine	.0002	--	.0004	--	.0001	--	--	.0002	0.1		2,300	0.5
Small Intestine	.0001	--	.0005	--	.0001	--	--	.0002	0.1		--	--
Muscle and Skin	.0000	--	.0002	.0002	.0001	--	--	.0001	0.1		38,500	3.9
Blood	--	--	--	--	--	--	--	--	--		5,400	0.2(8)
Balance	--	--	--	--	--	--	--	.0001(7)	--		9,600	0.9
Total	--	--	--	--	--	--	--	--	--		70,000	96.7

- (1) The various subjects received the following doses of plutonium: Hp-5 = 5 μ g; Hp-9 = 6.3 μ g; Hp-11 = 6.5 μ g; Chi. I = 6.5 μ g; Chi. II = 94.9 μ g; Hp-12 = 4.7 μ g; Cal. I = 103 μ g.
- (2) Tissues were obtained at the following times after injection: Hp-5 151 days; Hp-9 456 days; Hp-11 5 days; Chi. I 155 days; Chi. II 16 days; Hp-12 5 days; Cal. I 4 days.
- (3) Calculated by dividing %/g of tissue by %/g of body weight if a unit dose of Pu was equally distr. in a 70 Kg. man.
- (4) Hermann Lisco, Memorandum to AEC, July 21, 1947, Project Standard Man.
- (5) Assumption made that vertebra, sternum and whole rib represent average bone of skeletal system.
- (6) Bone marrow not included in total recovery because bone samples were not freed of marrow before analysis.
- (7) Balance assumed to have same Pu content as muscle.
- (8) Value for blood taken at 30 day point, Fig. 3.

Table 1. (1) (2)

Material balances of soft tissues and ex. retina. Six persons injected i. v. with Pu(IV) citrate, Pu(VI) nitrate, Pu(VI) nitrate, or Pu(VI) citrate

[illegible]

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(mid-range 42.5)

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APPENDIX 5

Reconstruction of whole rib from divided samples. Original data were consulted and computational and typographic errors corrected.

<u>Case No.</u>	<u>Sample</u>	<u>Pu conc</u> <u>(%/g)</u>	<u>Sample</u> <u>weight</u> <u>(g)</u>	<u>% dose</u> <u>in</u> <u>sample</u>
<u>Chi-1</u>	Sternum	0.0047	4.38	
	Rib, cortex	0.0016	1.0125	0.0016
	Periosteum	0.0046	0.1215	0.00056
	Marrow & spicules ^a	0.0160	<u>0.8292</u>	<u>0.0133</u>
	Whole rib (calculated)	0.0079	1.963	0.0155
<u>Chi-2</u>	Rib, cortex	0.0210	0.43	0.0090
	Marrow	0.0196	<u>0.2065</u>	<u>0.0040</u>
	Whole rib (calculated)	0.020	0.6365	0.0013
<u>Cal-1</u>	Rib, cortex	0.0072	9.0	0.065
	Periosteum	0.0048	0.445	0.00216
	Trabeculae	0.0319	0.84	0.0269
	Marrow	0.0190	-	<u>0.019</u>
	Whole rib (calculated)	0.0081	140 ^b	0.113

^a Origin of marrow sample noted as rib in Russell, Nickson (Ref. 47).

^b Whole rib sample weighed before division into four separate samples.

Footnotes to Table I

- a Body weight estimated to be the mean weight of six male cases whose body weights were recorded.
- b Measured tissue weight.
- c Pu concentrations in muscle and skin (when not measured) were estimated to be the average of other measured soft tissues such as heart, pancreas, etc.
- d Pu concentration of residual soft tissue was estimated to be one-half the concentration in skin and muscle.
- e Measured totals are used when available. Excretion between the cessation of collections and deaths of HP-5 and HP-9 was estimated from extrapolation of the last available measurements and the slopes of the U and F curves of persons followed for longer times. Excreta from HP-11 were estimated to be the mean for all the other Pu(IV) citrate-injected cases.
- f Includes 7.95%, the average Pu content of blood of the two sickest persons (HP-4 and HP-10), from whom blood samples were obtained at this time.
- g Pu of Pu recalculated from original data.
- h Includes 3.25% estimated from the tissues of Chi-2, and HP-11.
- i Chi-2 was emaciated; her skeleton was assumed to be the average reported by Mechanik⁶⁶ for slightly built females. Chi-1 had lost 15 lb during his illness; his skeletal weight was calculated from his body weight in good health, 64.8 kg.

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TABLE 6

INDIVIDUAL URINARY EXCRETION VALUES OF PLUTONIUM FOLLOWING INTRAVENOUS ADMINISTRATION
TO HUMAN SUBJECTS (EXPRESSED AS PER CENT OF DOSE EXCRETED PER DAY)

DAYS POST INJECTION	PER CENT OF INJECTED DOSE EXCRETED PER DAY													
	Hp-1	Hp-2	Hp-3	Hp-4	Hp-5	Hp-6	Hp-7	Hp-8	Hp-9	Hp-10	Hp-12	Chl-1 ⁽¹⁾	Chl-2 ⁽²⁾	Chl-3 ⁽³⁾
1	.181	.472	.569	.440	.293	-	.217	.377	.160	.414	.101	.057	2.531	.480
2	.146	.294	.269	.236	.163	.213	.212	.232	.035	.330	.103	.182	.153	.150
3	.114	.174	.112	.221	.077	.127	.137	.123	.069	.218	.088	.033	.184	.120
4	.091	.123	.107	.132	.052	.111	.098	.140	.066	.170	.078	.077	.133	.031
5	.062	.118	.078	.116	.030	.076	.069	.033	.047	.039	.063	.028	.032	.037
6	.083	.081	.043	.119	.020	.057	.059	.078	.052	.060	.044	.0256	.029	.042
7	.032	.062	.043	.077	.033	.044	.045	.056	.050	.079	.039	.0231	.024	.024
8	.055	.043	.049	.031	.023	.043	.037	.057	.032	.065	.060	.0227	.023	.016
9	.051	.046	.022	.035	.027	.032	.033	.047	.032	.051	.043	-	.027	.069
10	.045	.038	.027	.081	.022	.031	.023	.050	.035	.044	.033	.0032	.034	.026
11	.040	.048	.027	.075	.021	-	.018	.044	.026	.041	.038	.0097	.047	.036
12	.038	.039	.015	.072	.026	.024	.019	.023	.030	.038	.027	.0093	.047	.029
13	.034	.045	.020	.067	.023	.023	.019	.037	.027	.029	.030	.0236	.018	-
14	.035	.036	.020	.058	.019	.020	.013	.035	.030	.029	.039	.007	.034	.009
15	.034	.039	.028	.050	.015	.022	.012	.035	.030	.025	.029	.0059	.023	.013
16	.026	.024	.024	.033	.020	.017	.012	.035	.043	.021	.023	.0109	.012	.016
17	.027	.027	.021	.032	.020	.013	.011	.032	.033	.023	.029	-	.023	.0056
18	.028	.020	.017	.037	.020	.015	.011	.029	.027	.021	.026	-	.023	.016
19	.025	.019	.018	.032	.018	.015	.010	.031	.029	.017	.029	.0022	.015	.066
20	.017	.021	.012	.025	.021	.013	.003	.032	.029	.018	.032	.0093	.033	.0043
21	.017	.017	.018	.029	.020	.012	.010	.029	.032	.022	.025	.0078	.032	.0017
22	.018	.015	.014	.035	.013	.012	.013	.021	.032	.016	.025	.0145	.027	.0059
23	.025	.018	.014	.014	-	-	.008	.021	.032	.019	.039	.0151	.029	.0091
24	.021	.014	-	-	-	-	.008	.025	.032	.016	.023	.0129	.020	.0076
25	.013	.014	-	.011	-	-	.003	.023	.029	.016	.021	.0128	.148	.011
26	-	.017	-	.011	-	-	.007	.022	.032	.016	.023	.0175	.024	.0022
27	-	.008	-	.008	-	-	.003	.028	.032	.014	.017	.0151	.043	.0041
28	-	.009	-	-	-	-	.008	.023	.024	.013	.024	.0197	.034	.0074
29	-	.009	-	-	-	-	.003	.019	.025	.014	.023	.0138	.022	.0043
30	-	.008	-	-	-	-	.006	.021	.024	.014	.021	.0151	.024	.0069
31	-	.007	-	-	-	-	.005	.017	.023	-	.021	.010	.027	.0077
32	-	.007	-	-	-	-	.007	.018	.024	-	.012	.010	.020	.0063
33	-	.009	-	-	-	-	.006	.015	.022	-	.037	.017	.011	.0073
34	-	.009	-	-	-	-	.003	.015	.020	-	.020	.0139	.003	.0084
35	-	-	-	-	-	-	.008	-	.02	-	.026	.0127	.009	.0069
36	-	-	-	-	-	-	.008	.019	.022	-	.018	.0165	.015	.0079
37	-	-	-	-	-	-	.005	.011	-	-	.025	.0111	.011	.0063
38	-	-	-	-	-	-	.016	-	-	-	.018	.0174	.009	.0065
39	-	-	-	-	-	-	.012	-	-	-	.021	.0112	.009	.0034
40	-	-	-	-	-	-	.017	-	-	-	.019	.0072	.009	.0072
41	-	-	-	-	-	-	.019	-	-	-	.013	.0092	.011	.0030
42	-	-	-	-	-	-	.014	-	-	-	.013	.0127	-	.0031
43	-	-	-	-	-	-	.016	-	-	-	.015	.0095	.017	.0076
44	-	-	-	-	-	-	.014	-	-	-	.015	.0091	-	.0055
45	-	-	-	-	-	-	.013	-	-	-	.017	.013	.018	.0063
46	-	-	-	-	-	-	.015	-	-	-	-	.012	-	.0072
47	-	-	-	-	-	-	.014	-	-	-	.015	-	.020	.0059
48	-	-	-	-	-	-	.014	-	-	-	.017	.0064	-	.0059
49	-	-	-	-	-	-	.016	-	-	-	.015	.0063	-	.0083
50	-	-	-	-	-	-	.014	-	-	-	-	.0054	.018	.0078
51	-	-	-	-	-	-	.013	-	-	-	-	.007	-	.0022
52	-	-	-	-	-	-	-	-	-	-	.035	.0073	-	.0093
53	-	-	-	-	-	-	.013	-	-	-	.019	.0023	-	.0074
54	-	-	-	-	-	-	.013	-	-	-	.019	-	-	.0077
55	-	-	-	-	-	-	.015	-	-	-	.043	.0073	.014	.0066
56	-	-	-	-	-	-	.013	-	-	-	.030	.003	-	.0054
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59	-	-	-	-	-	-	.012	-	-	-	-	.011	-	.0063
60	-	-	-	-	-	-	.011	-	-	-	-	.0033	.022	.0067
61	-	-	-	-	-	-	.012	-	-	-	-	.0033	-	.0033
62	-	-	-	-	-	-	.010	-	-	-	-	.0030	-	.0033
63	-	-	-	-	-	-	.010	-	-	-	-	.0034	-	.0031
64	-	-	-	-	-	-	.012	-	-	-	-	.0071	-	.0032
65	-	-	-	-	-	-	.011	-	-	-	-	.0099	.024	.0032
66	-	-	-	-	-	-	-	-	-	-	-	.014	-	.0037
67	-	-	-	-	-	-	-	-	-	-	-	.014	-	.0031
68	-	-	-	-	-	-	-	-	-	-	-	.011	-	.0031
69	-	-	-	-	-	-	-	-	-	-	-	.011	-	.0031
70	-	-	-	-	-	-	-	-	-	-	-	.011	-	.0031
71	-	-	-	-	-	-	-	-	-	-	-	.0066	-	.0031
72	-	-	-	-	-	-	-	-	-	-	-	.0033	.014	.0032
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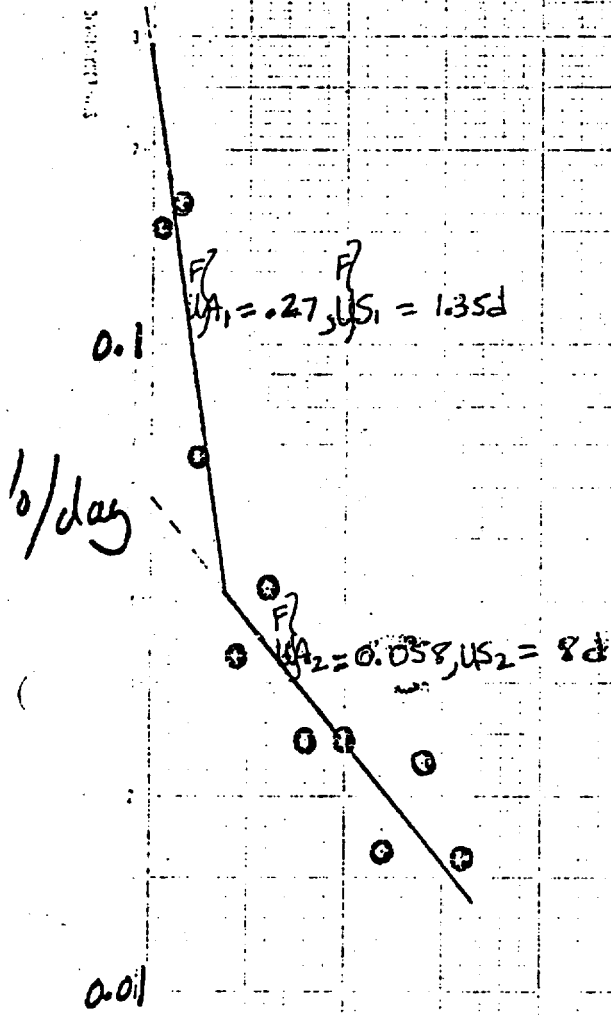
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CENTER FOR HUMAN RADIOBIOLOGY

Argonne National Laboratory • Massachusetts Institute of Technology • New Jersey Field Station • Southwest Field Station

TO: M. M. Shanahan MIT Radioactivity Center
FROM: A. F. Stehney RER Division
SUBJECT: Exhumation of CHR cases with prefix number 40.

Enclosed are folders containing copies of all CHR information on ten radioactivity patients in the "40" series. These are all the cases in this series for which we now have death certificates.

Please take the necessary steps to locate relatives and obtain permissions to exhume any or all of these ten persons. It should be noted that we want to examine the remains in order to determine the microscopic distribution of residual radioactivity from past medical treatment.

Date

A. F. Stehney, Deputy Director
Center for Human Radiobiology

Today, I received from A. F. Stehney copies of folders for the following ten CHR cases:

40-001	40-005	40-008	40-011	40-015
40-004	40-007	40-010	40-013	40-017

Date

M. M. Shanahan, Deputy Director
MIT Radioactivity Center

dk

cc: R. D. Evans
R. E. Rowland
CHR Records Room

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mache"

← Delete
"Una
mache"

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"Arthur
Hubbard"

Orig.: Purch. Dept.
cc: R. E. Rowland
A. F. Stehney

2 copies
Una Macke

(19)

CENTER FOR HUMAN RADIOBIOLOGY

January 2, 1973

Mr. Leo A. Ozier
Chief, Office of Vital Records and
Deputy State Registrar
Springfield, Illinois 62706

Dear Mr. Ozier:

We would like very much to have you search the death records of Illinois for the two names below. We do not have the residential addresses, but hope that you can locate the records from the information we do have.

Una Macke (Female)
Date of Birth: about 1891
Date of Death: 13 January 1966
(Place of Death: Billings Memorial Hospital, Chicago)
(Occupation: High School Teacher)

Arthur Hubbard
Date of Birth: about 1877
Date of Death: 3 October 1966
(Place of Death: Billings Memorial Hospital, Chicago)
(Occupation: Machinist)

Again, I am asking that the scientific search fee of \$1.00 per name be sent in advance. Please send the results of your search to my personal attention, at the address at the bottom of the page.

Many thanks for your continuing cooperation.

Very truly yours,

Harvey A. Schultz
Curator of Records
Center for Human Radiobiology

at

8005655

Chicago Case #2

R&R 12/10/72

Case #2

A fifty-five year old white female was admitted to the Billings Hospital in December, 1945 for diagnosis and treatment. Six months previously (June, 1945), she had noted generalized lymphadenopathy. Two months later (August, 1945), pain, aggravated on motion, developed in the trunk. On admission to the Billings Hospital in December, 1945 the essential physical findings were the presence of bilateral non-tender, moderately enlarged lymph nodes in the cervical, axillary, and inguinal regions and generalized tenderness to pressure over the ribs. Examination of the chest, pelvis, skull, and spine revealed many small, roundish areas of decreased density scattered throughout the bones examined. In addition, partial collapse and wedging of the last thoracic and first and second lumbar vertebrae with some associated calcification was noted.

Laboratory examinations were essentially negative except for a moderate hypochromic anemia and leukocytosis. Wasserman and Kahn were negative. Study of sections of the tumor excised from the skull and left axilla revealed carcinoma-tous tissue. It was felt that the carcinoma probably originated in the left breast.

The patient's general condition was poor at the time of admission and deteriorated steadily throughout the period of hospitalization. On December 27, 1945 at 9:00 AM, 0.01 micrograms of ^{239}Pu plutonium citrate were injected intravenously. The salt was contained in 4.0 cc of an isotonic saline solution 0.01 M in citrate at pH 6.5. The clinical course was not visibly altered following the injection. The patient expired on January 13, 1946.

The major autopsy findings were: (1) an adenocarcinoma probably arising in ectopic left axillary breast tissue with metastases to the liver, mesentery of the small intestine, lumbar vertebrae, ribs, skull and pelvis. Numerous healing pathological fractures of the ribs were found. (2) A lymphoblastoma involving the axillary, inguinal, peribronchial, periaortic, and pelvic lymph nodes. Thus the patient had two co-existing presumably independent tumors, an unusual finding. The weight at autopsy was recorded as 85 pounds (38.6 kg.).

Histologically, the bone marrow in all places examined was almost entirely replaced by tumor. The spleen showed a marked myeloid metaplasia. The kidneys showed many dilated tubules filled with hyaline casts. The tubular epithelium showed evidence of degeneration and repair. Comparison of the biopsy sections with the post-mortem sections shows no evident difference in the character of the tumor following the injection of plutonium. The cells characteristic of lymphoblastoma are also present in the biopsy sections.

II. METHODS

Control period in Case I was one week long and was used primarily to determine approximate daily urinary output available for analytical purposes. In Case II the control period was somewhat shorter and was used for the same purpose.

In cases the specimens were collected in the usual animals and the urine, after being transferred in the case of the urine, to a gallon bottle to which a concentrated hydrochloric acid had been added. The addition of the acid was to prevent the likelihood of absorption of plutonium by the container. The urine was then transferred to "radiochemical" analytical containers.



...of necessity seemed to come down to phlebotomy and since
...to be very tedious it was designedly directed to have
...of determining whether or not a given person had any phlebotomy in
...It was equally desirable to be able to estimate as accurately as possible
...was deposited in any person. Animal experiments were used to procure
...as possible. Some human studies were made to see how to apply
...data to the human problem. Hence, two people were selected whose
...was such that they could not be endangered by injections of
...phlebotomy

L. CASE HISTORY

Chicago Case #1
RGR 12/29/22

Case #1

A forty-eight year old white male was admitted to the Billings Hospital in April, 1945 for surgical treatment of a recurrent epithelioma of the buccal mucosa. Prior to admission to the Billings Hospital in March, 1945 the abnormal findings on physical examination were limited to the findings in the face and neck. The anterior portion of the maxilla and contiguous area of the sub-maxillary gland area, a large infected ulcerating area approximately seven centimeters in diameter. The anterior portion of the maxilla was exposed in the depth of the ulcer. The margins of both the buccal mucosa and the cutaneous portions of the ulcer were defined and hard. There was exposed in the central portion of the ulcer a cutaneous surface.

Examination of the chest revealed a tubercular lesion in the left lung. The laboratory examinations were essentially negative except for a mild leukocytosis. The Wassermann and Kahn were negative. Studies of the sputum from the patient were negative for diagnosis of epithelioma carcinoma. Radical head surgery was performed on April 11, 1945 and April 25, 1945. On April 25, 1945 at 9:17 AM the patient was given an intravenous injection of 0.5 cc of 1% solution of 26 phlebotomy as a citrate salt in 0.9 per cent salt solution at a rate of 1 cc. The volume of the injection was 0.05 cc. The patient remained in bed until August, 1945 when he complained of pain in the chest. There was no evidence of extension of the pulmonary metastases was found. He expired on October 1, 1945.

Autopsy findings were weight, 186 pounds (76.4 kg.). An extensive ulcer of the buccal mucosa of the epithelioma carcinoma of the mouth was found. There was a large, carcinomatous invasion of the structures of the sub-maxillary gland area. Bilateral pulmonary metastases were present. Arteries of the lungs showed thromboses, cavitation and abscess formation, some of which were large. There was evidence of metastatic carcinoma in the lower lobe of the left lung. There was noted on gross examination of the lungs, metastatic carcinoma. There was noted in mild focal interstitial pneumonia, probably a post-operative reaction. The only moderately calcified metastatic carcinoma was noted in the right lung, and a few smaller and calcified metastatic carcinoma were noted.