COPY

INTRA-LABORATORY CORRESPONDENCE

OAK RIDGE NATIONAL LABORATORY

September 3, 1968

707719

To : W. H. Jordan

From : K. Z. Morgan

Subject: Proposed Study of Distribution and Excretion of Enriched Uranium Administered to Man

Enclosed herewith is a copy of a proposal for a cooperative project with Argonne Cancer Research Hospital on the distribution and excretion of enriched uranium administered to man.

This project was suggested by Dr. C. L. Dunham several years ago. He encouraged Dr. R. J. Hasterlik to cooperate with us in this work, and it is now coming to fruition.

It probably will not be necessary for the Laboratory to furnish funds to ACRH. However, some additional technicians will be required to perform routine analysis of biopsy and autopsy samples.

Original Signed By
K. Z. MORGAN
K. Z. Morgan

Enclosure

cc: B. R. Bernard
W. S. Snyder

KZM:SRB:ss

REPOSITORY OAK RIDGE/ENERGY SYSTEMS/ ORNL (X-10)
COLLECTION OFFICE OF RADIATION PROTECTION
BOX No. K. Z. MORGAN'S FILES (PAST DIV. DIR OF HEALTH PHYSICS
FOLDER BLD 4500 S., WING 4 ATTIC

A-00125

Human Subjects Project

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INTRA-LABORATORY CORRESPONDENCE AUG 28 1963

OAK RIDGE NATIONAL LABORATORY

August 28, 1963

To : K. Z. Morgan
W. S. Snyder
E. G. Struxness

From : S. R. Bernard

Subject: A Proposal for a Cooperative Study with Argonne Cancer Research Hospital of the Distribution and Excretion of Enriched Uranium Administered to Man

Attached hereto is a copy of a proposal for our cooperative project with Dr. R. J. Hasterlik. If this meets with your approval, I need to send ~ 10 copies to Dr. Hasterlik so that he may apply to the ACRH Clinic's Radioisotope Committee for permission to carry out this study.

SRB

S. R. Bernard

Attachment

SRB:ss

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UCN-430

COPY

PROPOSAL FOR A COOPERATIVE STUDY WITH ARGONNE CANCER RESEARCH HOSPITAL OF THE DISTRIBUTION AND EXCRETION OF ENRICHED URANIUM ADMINISTERED TO MAN

Purpose

Human data are needed on the distribution and excretion or uranium following administration of low levels of uranium for estimation of the maximum permissible concentration (MPC) values for chronic exposure of industrial employees to low levels of uranium. The need for human data arises from the following considerations:

1. In previous studies, reported in detail by Bernard and Struxness and Bernard and performed in cooperation with the Massachusetts General Hospital, 11 terminal brain-tumor patients were administered relatively high doses of uranium (60 to ~ 1000 μgm of U/Kgm of body weight). This study had a triple purpose, viz., that of obtaining human data with which to estimate parameters of uptake and elimination of uranium by various organs and tissues of man, to estimate the possibilities of employing enriched uranium in neutron-capture therapy, and to estimate the toxicity of uranium in man. In this study it was found, at autopsy, that there were two chief organs for storage of uranium--the skeleton and kidneys--both of which contained almost identical amounts of uranium and had a biological half-life of ~ 300 days. These results were different from the ones found in experiments performed at the University of Rochester on small animals. Here it was found that skeleton was the chief

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organ for retention of uranium, but the kidney was not of equal importance for long-term storage of uranium. The biological half-life for uranium in the skeleton of a small animal is ~ 300 days, the same as was observed in the brain-tumor patients, but the half-life in kidneys of small experimental animals is only ~ 6 days, a factor of 50 less than that observed in the brain-tumor patients.

2. When the parameters for uptake and elimination obtained from the studies on these terminal patients are employed in estimation of an $(MPC)_a$ for industrial exposure to soluble uranium (40 hours per week), the value obtained by Bernard is ~ 10 μgm U-nat/M^3 of air. This is ~ 1/5 of the level of 50 μgm/M^3 based on small-animal experimental data and recommended by leading investigators of the toxicity of uranium.

3. The following questions arise: Is the retention of uranium in man's kidneys more prolonged than that observed in small animals, i.e., is this a species difference? Is the 300-day kidney half-life value observed on bed-ridden brain-tumor patients applicable to normal man? Also, since the injection levels in the terminal patients produced nephrotoxic effects, might it be that the renal clearance was slowed? At present the answers to these questions are not known because of a lack of adequate data.

4. Some studies carried out by Muir and Fish on small animals suggest that when nephrotoxic doses of uranium are administered, the retention

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in the kidney is increased and prolonged. In other studies employing dogs, no significant perturbation of retention in kidneys was observed.

5. The Committees on Internal Dose of the ICRP and NCRP have an express interest in this study. Dr. Morgan has stated that errors are made in estimating MPC's with parameters from small-animal experimental data, but probably even greater errors are made in using data from experiments in which large masses or doses of radionuclides are employed. In metabolic studies it is possible that an increased deposition and prolonged retention result when the metabolism is perturbed from its normal physiological state by the large dose or mass of the radionuclide.

Thus, there is a need to carry out a study of the distribution in and excretion of uranium by humans administered low doses of uranium. Dr. R. J. Hasterlik of ACRH has expressed an interest in this study and will cooperate with the ORNL Health Physics Division in obtaining data to provide some answers to these questions. In preliminary talks he has stated that low doses of uranium could be administered to hospital patients, and studies of the retention of uranium in the body and kidney could be made using his whole body counter. Also, samples of urine, feces, and blood would be obtained from the patients, and at death attempts would be made to obtain autopsy tissues which would be shipped to ORNL for radiochemical analysis.

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It is clear that the data obtained will not provide us with a completely unambiguous answer to the question as to the applicability of the data to normal man since the study employs hospitalized patients generally suffering from cancer. However, it is expected that some of these patients will be ambulatory and, except for the cancer, may be considered as reasonably normal so far as metabolism is concerned. A better estimate of the degree of approach to normal metabolism may be possible after the clinical course of the patient is known and the results of the study are analyzed. When these studies are completed, it may be anticipated that from the experience gained some further studies on human volunteers can be carried out.

The information to be obtained in this program will consist of the following:

1. An estimate of the following parameters required in the ICRP-NCRP model for estimation of $(MPC)_w$:
   a. f_w, the fraction of an ingested dose going from the gut to the critical organ (kidney or skeleton);
   b. f_2', the fraction going from the blood to the critical organ;
   c. f_1, the fraction of ingested uranium absorbed into the blood stream;
   d. T_b, the biological half-life of uranium in the critical organ;
   e. f_2, the fraction of the total body burden that is present in the critical organ.

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2. Both urinary and fecal excretion data after a single injection and after and during multiple injection and continual ingestion. This is important in interpreting data on excretion of uranium by employees in order to estimate their body burdens.
3. Kidney and body burden measurements on the whole body counter which would be a check on the excretion data and also enable one to follow the retention in time.
4. Blood disappearance measurements.

The following procedure will be employed: Four groups of patients will be used. Each group will be administered product-level or more enhanced enriched uranium (U^{235}). This isotope of uranium is used because it has a relatively abundant (85%) 186-Kev photopeak γ-ray in its decay scheme and because of its availability. Patients in group I will receive single intravenous injections of uranyl nitrate in doses ranging from 1 to 10 μgm/kgm buffered with sodium acetate. This is the type of solution used in the Boston studies. Urine specimens and samples of blood will be collected from each patient. Whole body and kidney counts will be made immediately after injection and each day or once a week thereafter for as long as they can be counted. The frequency of collection of samples is indicated in Appendix I. The patients in group II will receive multiple injections of 1.5 mgm/wk per week of uranyl nitrate buffered with sodium acetate at the rate of one injection per week for a total period of 10 weeks. Body and kidney counts will be made three times a week during the injection period as well as after

1026203

injection stops. Twenty-four-hour feces and urine samples should be collected each day for the entire period or as long during this period as significant data are obtained. Periodic samples may be taken thereafter as indicated by the trend of the data. Blood samples will be taken at least 3 or 4 times per week. If signs of kidney damage begin to develop, the injection should be stopped.

Group III patients will ingest 150 mgm/wk of uranyl nitrate solution in water or juice each week for a period of 10 weeks. The same sampling and counting frequency employed for group II patients will be used on this group but with one exception. The patients will be counted routinely just before ingestion of the uranium dose, and some counting studies will be carried out at early times following ingestion to obtain information on calibration and the passage of the material through the GI tract. Daily urine and feces samples will be collected as above. Blood samples will be taken 2 or 3 times per week during the period of administration.

Group IV patients will ingest 150 mgms of an insoluble oxide (U_3O_8 or UO_2 placed in water, juice, or a gelatin capsule) at the rate of one ingestion per week for 10 weeks. The same sampling schedule used for group III patients will be employed for this group of patients.

The burdens of uranium in skeleton, kidneys, and whole body and the radiation dose received by these organs in a 5-year period have been extimated, and these calculations follow:

1026204

Body and Organ Burden Estimates

In arriving at suitable levels to be injected into or ingested by patients, the data on toxicity of uranium obtained by other investigators have been used for guidance. For guidance in the single injection studies, the data on the sixth patient in the series injected by Bassett et al. suggested that the tolerance had been reached since there was a slight rise in urinary catalase and protein. The patient received two injections, each 3.1 mgm of uranium, the second given 17 days after the first. Luessenhop et al. state that the minimal injected dose necessary to produce catalaseuria and albuminuria is ~ 0.1 mgm per Kgm of body weight for hexavalent uranium. Thus, the single injection dose level of 1 to 10 μgm/Kgm in the study proposed here is below these levels at which albuminuria and catalaseuria should be produced.

An estimate of body, kidney, and skeletal burdens of patients receiving the single injections can be made with the ICRP-NCRP model and parameter values, and these will be compared with estimates based on acute data. Let q denote the μc (or μgm) of uranium in the whole body, f_2 the fraction of the body burden that is present in the critical organ, f_2' the fraction going from the G.I. tract to the critical organ, λ_b the biological elimination constant, and λ_r the radiological decay constant. In the case of a single injection of I μgms of material, the organ burden or body burden should follow

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the equation

$$qf_2 = f_2' \, I \, e^{-\lambda t} \tag{1}$$

where $\lambda = \lambda_b + \lambda_r$ ($\lambda_r \sim 0$ for uranium isotopes in enriched uranium).

Table I presents the values of the parameters to be employed in estimating organ burdens. When 700 μgm are injected into the patient, the amount in the kidneys is

$$qf_2 = 0.11\ (700)\ e^{-0.7t/15}$$

while the amount in the skeleton is

$$qf_2 = 0.11\ (700)\ e^{-0.7t/300}$$

and the amount in the total body is

$$qf_2 = 700\ e^{-0.7t/100}.$$

Table I. Parameter Values Used in Estimating Body and Organ Burdens*

Organ	f_w	$\frac{0.693}{\lambda_b}$ (= T_b) days	f_2'	f_2
Kidneys	0.0011	15	0.11	0.065
Bone	0.0011	300	0.11	0.85
Whole Body	0.01	100	1	1

*ICRP Handbook values

The peak burden in kidneys of 77 μgms should be established instantaneously according to the model, but most probably there will be some time lag and the peak will occur at a later time. Note that the maximum concentration

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in kidneys should not exceed 77/300 μgm/gm = 0.26 μgms/gm assuming the kidneys weigh 300 grams. This concentration value is a factor of 10 below the level for chronic exposure recommended by Neuman and by Bernard.

Bernard, in interpreting the Boston patient data, noted that the power function $0.2\ It^{-1/2}$ $t \geq 1$ day fitted the skeleton and kidney data. If this function applies, then at 1 day after injection, the amount present in kidneys should be 140 μgms. At 100 days, the amount should decrease to ~ 14 μgms. We note that if the power function will apply to the data, then the maximum concentration of 140/300 μgms/gm will still not exceed the recommended chronic level in the kidney. We also mention that the latest ICRP report (Publication 6), following some recommendations of Eve, suggests that the single inhalation intake into the lungs be limited to 2.5 mgms. Assuming, as is done in the ICRP report, 1/4 of this is absorbed into the blood stream (as is commonly the case for soluble compounds that are inhaled), then ~ 625 μgms are taken into the blood. It also recommends that no more than 150 mgms of Uranium averaged over a two-day period be ingested. The same reference assumes 1% is absorbed into blood, and thus 1.5 mgms would enter the blood stream in the two-day period. Except for the period of time over which the material enters the blood stream (~ 1 day for inhaled uranium and 2 days for ingested uranium), it would appear that an injection of 700 μgms is a "safe" or nontoxic level of injection.

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These levels in kidneys may prove to be difficult to count if the calibration data obtained by Bernard apply to the ACRH whole body counter. In Bernard's study a 4"x4", thallium-activated, NaI, side-shielded crystal gave a net count rate of ~ 20 c/m per mgm of U^{235} in the kidneys. The background count rate over the kidney is ~ 50 c/m. With these data it can be shown that the counting time, t_c, to obtain ± 100% limit of error on the counts, is inversely proportional to the square of the mass of uranium (mgms) in kidney. Thus for 140 μgms in kidneys, t_c ~ 51 minutes, while at 100 days t_c ~ 5000 minutes. This indicates that if these calibration figures apply, then only the initial deposition can be established on the whole body counter. At autopsy the content of the kidneys can be estimated by radiochemical or other methods of quantitative analysis.

In order to establish the multiple injection and ingestion level, the recommendations of the ICRP are employed together with the data of Butterworth cited by Eve. In Butterworth's study a human volunteer ingested 0.47 gm of uranium in 200 cc of water. He experienced rather violent vomiting, diarrhea, and slight albuminuria. Thus 0.47 gm is too much. Therefore, the ICRP report recommendation listed above will be employed. Also, the ICRP report recommends that in one quarter the total intake by ingestion should not be greater than ~ 3.5 gms of U^{235}. If 1% is absorbed into the blood stream, then 35 mgms enter the blood. However, they further state as discussed above that no more than 150 mgms

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averaged over a two-day period should be ingested. Thus in the multiple ingestion studies the patient takes 150 mgms per week for 10 weeks and his total intake is 1.5 gms. This is a factor of 23 less than the permissible quarterly intake and is below the limit recommended for limiting acute exposure.

To estimate the body and organ burdens for the case of multiple injections, we let t be an integral number of weeks during which an injection is made and t' a fraction of a week $(0 \leq t' \leq 1)$. In the general case let τ be the number of weeks after the last injection so that the total lapsed time is $t + t' + \tau$. Thus a common formula can be used for times before the end of the injection period or for times following that period. In case a time following the last injection is under consideration, $t' = 0$ and τ need not be an integer. Then

$$qf_2 = f_2' \, I \sum_{i=0}^{t} e^{-\lambda(i+t'+\tau)} = f_2' \, I \, e^{-\lambda(\tau+t')}\left(\frac{1 - e^{-\lambda(t+1)}}{1 - e^{-\lambda}}\right). \qquad (2)$$

The amount in kidneys is

$$qf_2 = 0.11 \, I \, e^{-\frac{4.9}{15}(t'+\tau)}\left(\frac{1 - e^{-\frac{4.9}{15}(t+1)}}{1 - e^{-\frac{4.9}{15}}}\right) \qquad (3)$$

while that in the skeleton is

$$qf_2 = 0.11 \, I \, e^{-\frac{4.9}{300}(t'+\tau)}\left(\frac{1 - e^{-\frac{4.9}{300}(t+1)}}{1 - e^{-4.9/300}}\right) \qquad (4)$$

and that in total body is

$$qf_2 = I\ e^{-\frac{4.9}{100}(t'-\tau)}\left(\frac{1 - e^{-\frac{4.9}{100}(t+1)}}{1 - e^{-4.9/100}}\right). \qquad (5)$$

We insert $I = 1.5$ mgms/week into (3), (4), and (5) and plot these equations, and they appear in Fig. 1. From these graphs, the peak burdens are obtained. These appear in Table II. As can be noted, the kidney burden should not exceed 0.57 mgms, and the peak concentration in kidneys will be just slightly less than 2 μgms U/Kgm. We also mention that this should be fairly easy to count on the whole body counter if t_c (mgms U in body)$^{-2}$, as is the case with the ORNL whole body counter, because at this peak level $t_c \sim 3$ minutes for ± 100% limit of error, and thus a 10-minute count should give a good estimate of the kidney burden.

Table II. Peak Body and Organ Burdens for Patients Ingesting 150 mgms/wk or Injected with 1.5 mgms/wk for 11 Weeks

Organ	Peak Burden (mgms)
Kidneys	0.57
Skeleton	1.65
Whole Body	13

Estimate of Radiation Doses and Dose Rates

In order to estimate the radiation doses and dose rates to organs and tissues, we need the exact assay of product-level material. This is classified. The mean specific activity of the enriched uranium is not classified. We derive our equations so that the mean specific activity can be employed in the calculations.

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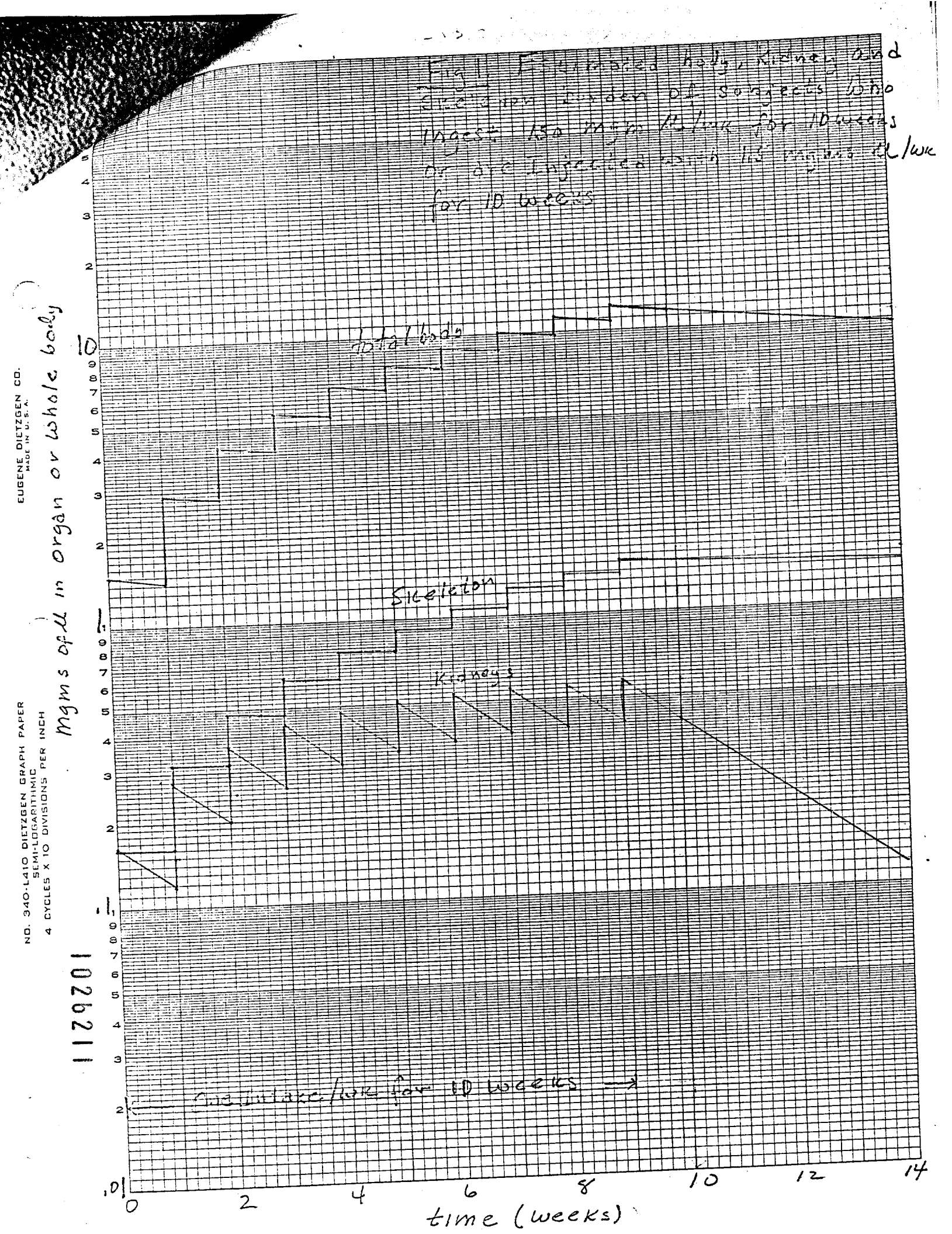
Fig 1 Estimated body, kidney and skeleton burden of subjects who ingest 150 mgm μ/wk for 10 weeks or are injected with 1.5 mgms μ/wk for 10 weeks
total body
Skeleton
Kidneys
Mgms of μ in organ or whole body
time (weeks)
0
2
4
6
8
10
12
14
.01
1
10
EUGENE DIETZGEN CO.
MADE IN U.S.A.
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SEMI-LOGARITHMIC
4 CYCLES X 10 DIVISIONS PER INCH
1026211

Let qf_2 denote the mass of uranium put into the body, ρ_i the fractional amount of qf_2 that consists of the $i^{\underline{th}}$ isotope, and S_i the specific activity of the $i^{\underline{th}}$ isotope in $\mu c/\mu gm$. Then $(qf_2)\rho_i S_i$ is the μc of $i^{\underline{th}}$ isotope injected or ingested. The dose rate R_i in rem/wk from deposition in an organ of mass M is

$$R_i = \frac{(qf_2)\ \rho_i S_i\ \epsilon_i}{2.8 \times 10^{-3}\ M}\ \text{rem/wk}$$

where ϵ_i is the effective energy of the $i^{\underline{th}}$ isotope. The total dose rate is

$$R' = \sum R_i = \frac{(qf_2)}{2.8 \times 10^{-3}\ M} \sum \rho_i S_i\ \epsilon_i \quad \text{rem/wk.}$$

In general for the isotopes of uranium the ϵ_i does not differ much and thus can be replaced by an average value $\bar{\epsilon}$. Thus,

$$R' = \frac{(qf_2)\ \bar{\epsilon}}{2.8 \times 10^{-3}\ M} \sum \rho_i S_i \quad \text{rem/wk.}$$

In this equation the value $\sum \rho_i S_i$ is the mean specific activity of the enriched uranium and it is $\sim 6.5 \times 10^{-5}$. Thus we may write for the dose rate from the mixture

$$R' = 2.32 \times 10^{-2}\ \frac{(qf_2)\ \bar{\epsilon}}{M}\ \text{rem/wk.} \tag{6}$$

Single Injection Doses

From equation (1) we obtain the expression for qf_2 when I is in μgms, and this with (6) gives

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$$R' = 2.32 \times 10^{-2} \frac{f_2' I \bar{\epsilon}}{M} e^{-\lambda t} \text{ rem/wk.} \tag{7}$$

The average values of ϵ for kidneys, bone, and total body appear in Table III.

Table III. Values of ϵ for Organs from ICRP Handbook

Isotope	ϵ (Mev/disintegration)		
	Kidney	Bone	Total Body
U^{234}	49	240	49
U^{235}	46	230	46
U^{236}	47	230	47
U^{238}	43	220	43
Avg	~ 45	~ 230	~ 45

To estimate the integral dose D we divide (7) by 7 days/wk and integrate from 0 to 5 x 365 days (the estimated life span of the patients) to obtain

$$D = \int_0^{1825} R' \, dt = 3.3 \times 10^{-3} \frac{f_2' I \bar{\epsilon}}{M\lambda} (1 - e^{-1825\lambda}) \text{ rem.} \tag{8}$$

Multiple Injections

To estimate the peak dose rates to organs, we let $(qf_2)_{max}$ denote the peak organ burden in μgms from Table II and insert this into (6) and find

$$R' = 2.32 \times 10^{-2} \bar{\epsilon} \frac{(qf_2)_{max}}{M} \text{ rem/wk.} \tag{9}$$

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To estimate the total dose D, all we have to do is multiply equation (8) by 10 since the patient receives 10 injections, and we obtain

$$D = 10 \int_0^{1825} R' \, dt = 3.3 \times 10^{-2} \frac{f_2' \, I \, \epsilon}{M\lambda} (1 - e^{-1825\lambda}) \text{ rem.} \qquad (10)$$

Multiple Ingestions

The peak dose rates and total doses to the organs and whole body are estimated to be the same as in the multiple injection case. The dose rate and dose to G.I. tract from ingestion must be estimated also. To do this we employ equation (6) where now we let (qf_2) denote the amount ingested into the G.I. tract. This ingested amount is assumed to reside in a portion of mass M grams. Also, we assume only 1/2 of the effective energy is dissipated in tissue. From the ICRP report we find the average effective energy $\bar{\epsilon}$ is ~ 0.5 Mev. Substituting for ϵ and using the factor of 1/2, the equation for dose rate for R' is obtained.

$$R' = 8 \times 10^{-4} \frac{(qf_2)}{M} \text{ rem/day.}$$

Now let T denote the residence time in the region of the G.I. tract being considered. In the ICRP model, four regions are considered--stomach, small intestine, upper large intestine, and lower large intestine, and the residence times for these sections are 1/24, 4/24, 8/24, and 18/24 days, respectively. Then

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$$R'T = 8 \times 10^{-4} \frac{(qf_2)\ T}{M} \text{ rem/wk} \tag{11}$$

is delivered to the portion of the G.I. tract from an intake of (qf_2) units per week.

The total dose D from 10 weeks intake is just

$$D = 10\ R'T = \frac{8 \times 10^{-3}\ (qf_2)\ T}{M} \text{ rems.} \tag{12}$$

The appropriate values for M, (qf_2), and other parameters have been inserted into the above equations, and the estimated peak dose rates and doses appear in Table IV. An estimate of quarterly doses has been

Table IV. Estimates of Doses and Dose Rates to Various Organs and Tissues from Intake of Enriched U

Mode and Amount of Intake	Organ	Peak Dose Rates (rem/wk)	Total Dose (5 years) (rem)
Single Injection 10 μgm/Kgm	Kidney	0.264	0.8
	Bone	0.059	3.6
	Total Body	0.010	0.2
Multiple Injection 1.5 mgm/wk for 10 weeks	Kidney	2	18
	Bone	1.3	77
	Total Body	0.2	4
		(rem/day)	
Multiple Ingestion 0.15 gm/wk for 10 weeks	Stomach	0.48	0.2
	Small Intestine	0.11	0.2
	Upper Large Intestine	0.89	0.3
	Lower Large Intestine	0.8	6

made too, and these appear in Table V, together with the permissible occupational quarterly doses.

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Table V. Quarterly Doses to Organs from Intake of Multiple Injections Compared with Permissible Occupational Doses

Organ	Rem Dose to Organ 1st Quarter	Rem Dose to Organ 2nd Quarter	Permissible Occupational Quarterly Dose (rem)
Kidneys	16	1.6	$15/4 \cong 4$
Skeleton	10	13	$30/4 = 7.5$
Whole Body	1.5	1.4	$5/4 = 1.25$

In Table IV it is noted that the total bone dose is highest, ~ 77 rem over a period of 5 years, when patients receive multiple injection treatments of enriched uranium. In Table V it is noted that the quarterly dose to kidneys during the first quarter would exceed the permissible occupational dose by a factor of 4. The use of more enhanced uranium (> 99% U^{235}) would reduce this dose and dose rate, and it might be possible to employ the super-enriched uranium (> 99% U^{235}) in this study of multiple injections. The value of $\sum \rho_i S_i$ for this material is 4.6×10^{-6}. The doses and dose rates could be scaled down by a factor of 14 if the super-enriched uranium is employed in the multiple injection study.

It should be noted that these estimates of dose and dose rate employ data obtained from both small-animal and human experiments. The study proposed here is to be initiated with the single injection program. When data are made available in this phase of the program, then the estimates of dose and dose rate can be refined with the more adequate human data.

1026216

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APPENDIX I

PRELIMINARY URANIUM EXPERIMENT

DAY 0 - 2

7 AM 1. ~~pt. fasting since midnight~~

2. pt. weighed

3. catheterize and pass gastric tube if necessary

4. start vital signs t.i.d.

5. blood sample taken for prothrombin time, cephalin floc., thymol floc., cholesterol and esters, and Van den Berg tests

8 AM 1. start urine collection

2. start IV glucose tolerance test

3. start 2 hour tube feedings after glucose tol. test completed

4. EKG

5. start collection of control feces specimens

2 PM 1. control inulin and PAH clearance tests

DAY 0 - 1

7 AM 1. blood sample for Na, K, NPN, Cl, pH, Ca, BUN, PO_4, CO_2, TP, A/G, alk. phosphatase, and serum amylase (hereafter these tests will be referred to as electrolytes)

2. blood for RBC, WBC, diff., sed rate, platellets, and reticulocytes (hereafter these tests will be referred as hemotology)

3. ~~CSF, lumber and/or ventricular for cells, Cl, protein, colloidal gold, and uranium control. (hereafter these will be referred to as CSF tests)~~

8 AM 1. 24 hour urine sample for vol., s.g., pH, microscopic, quant. protein, quant. sugar, catalase, Cl, phosphatase, citric acid, acetone (hereafter these tests will be referred to as urine tests)

9 AM 1. BSP test

DAY 0

8 AM 1. blood for electrolytes, hemotology, and uranium control

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2. 24 hour urine sample for urine tests and uranium control

3. start collection of feces for uranium

4. start collection of hourly urine, CSF, and blood for uranium level (5 cc blood specimens will be drawn for first 12 hours and thereafter 10 cc specimens)

5. start 0.050 mgm of uranium as nitrate per kilo body weight IV in saline to run in in 1 hour.

8 PM 1. specimens for urine tests, CSF tests, hematology, electrolytes

2. blood for liver function tests

3. inulin and PAH clearances

DAY 1

8 AM 1. start 12 hour specimens of urine, blood, ~~CSF for uranium levels~~

2. blood for electrolytes, hematology, liver function

3. 12 hour composit urine for urine tests

4. start IV glucose tol. test

9 AM 1. EKG

2 PM 1. BSP test

8PM 1. 12 hour urine for urine tests

DAY 2

8 AM 1. start 24 hour specimens of urine, blood, ~~CSF~~ for uranium levels

2. 12 hour urine for urine tests

3. blood for hematology, electrolytes

4. CSF for CSF tests

5. inulin and PAH clearances

DAY 3

8 AM 1. 24 hour urine for urine tests

2. blood for hematology, electrolytes, and liver function tests

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3. glucose tol. test

2 PM 1. BSP test

DAY 4

8 AM 1. blood for hematology and electrolytes

2. 24 hour urine for urine tests

3. inulin and PAH clearances

4. EKG

DAY 5 same as day 3

DAY 6 same as day 4

The experiment to be carried as long as possible and further tests to be done will be determined by results of previous tests. Fecal and 24 hour urine and blood specimens will be taken as long as it is possible.

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