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March 22, 1954

Dr. W. H. Sweet
Massachusetts General Hospital
Boston 14, Massachusetts

Subject: First Results of Uranium Distribution and Excretion Study

Dear Doctor Sweet:

Following our discussion with you and others in the Atomic Energy Commission and at the Oak Ridge National Laboratory, we agreed to provide analytical services in exchange for additional data, not directly concerned with the therapeutic application of uranium to the treatment of brain tumors. This experiment, as you well know, provides a wonderful opportunity to secure "human data" for the analysis and interpretation of industrial uranium exposures. We have completed the analysis and assembly of the data taken from patient number 68927. The purpose of this letter is to inform you of our general observations concerning the results obtained on this subject.

It might be of interest to restate what we believe to be the objectives of our cooperative effort. These objectives are:

1. Concentration of uranium in normal fluids and tissues and in tumor after intravenous administration.

2. Concentration of uranium in blood with respect to time after injection.

3. Distribution of uranium within major organs and bone.

4. Build-up and disappearance of uranium in urine and feces.

5. Evaluation of urine excretion curves in terms of our method of analysis.

MEDICINE, HEALTH & S operate Br

On November 11, 1953, patient number 68927 received, by intravenous administration, 12.9 milliliters of sterile isotonic solution containing 1.60 milligrams of uranium 233 and 3.90 milligrams of uranium 238. This is a

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dose equivalent to .30 microcuries per kilogram of body weight.

Urine Excretion - (Table I.) The elimination pattern is as expected, i.e., large quantities of uranium appear in the urine immediately following injection, followed by a gradual decrease in rate of excretion; there are the usual fluctuations in individual samples; and a large percentage of the injected dose is eliminated in the urine.

Biopsy Samples - (Table II.)

Bone - This tissue shows a significant uptake of uranium at one hour post injection and remains fairly constant throughout the remainder of the study. The variations in the sample concentrations indicate that the techniques of sampling may have resulted in contamination of the small samples because of the existing high activity level in the blood. However, the amount of the injected dose found in the bone (14 percent) agrees well with previous experimental findings.

Muscle - The muscle data similarly indicates the possibility of contamination, with added factor of vascularity in this tissue to further this possibility. The samples taken from 8 hours to 32 hours post injection show little uranium depositing in the tissue.

Cerebrospinal Fluid - The lumbar fluid shows a slight concentration of uranium at one hour with subsequent samples showing comparable amounts. The ventricular fluid exhibits little uptake of uranium for the first 16 hours post injection. However, at this latter time an elevated value appears which is higher than previous values by a factor of approximately 10. This observation is again evident at 32 hours post injection. The significance of these elevated values is unknown to us. In comparing lumbar fluid with ventricular fluid it is evident that the former exceeds the latter consistently, with the exception of the ventricular samples at 16 and 32 hours post injection. Here again the explanation is not obvious to us.

Blood - The activity in the blood at one hour after injection is not indicative of the rapid decrease that is expected to occur during the first 60 minutes. Considering the injected dose and assuming a total volume of blood for the standard man of 5.5 liters, it is seen that the blood concentration has decreased by an approximate factor of 10. Following the rapid decrease, the blood concentration is observed to deminish slowly for the duration of the study.

Autopsy Samples - (Table III) The kidney, as expected, contained the highest concentration of uranium per unit weight. The next three sites in order of decreasing content per unit weight are pancreas, brain and bone. In summary the data are presented in the following table.

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Distribution of Injected Dose at 57 Hrs Post Injection

Site	Percent of Injected Dose
Bone	13.6
Kidney	11.2
Soft Tissue (other than kidney)	13.3
Urine	54.3
Total	92.4

The results obtained in the first experiment are generally incomplete and inconclusive due to the brief duration of the study. Furthermore, there are discrepancies in duplicate samples which appear to have been caused by cross contamination. We have discussed with you the inadequacies of our experimental technique and it is expected that the changes we have inaugurated will lead to more precise results.

Sincerely yours,

John C. Gallimore, Jr.

John C. Gallimore, Jr.
Associate Health Physicist

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Approved by:

Edw. G. Struxness

Edw. G. Struxness, Superintendent
Health Physics Department
Y-12 Plant

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TABLE I

SAMPLE	SAMPLE NUMBER	VOLUME (ml)	POST INJECTION TIME (hours)	ALIQUOT ACTIVITY (counts/minute)	URINE CONCENTRATION (counts/minute/hour)
Urine	1	65	1.1	14182	1,350,667
	2	30	2.2	12392	686,326
	3	20	3.0	10677	640,620
	4	20	4.2	8576	563,901
	5	28	5.1	7468	733,563
	6	24	6.0	5431	571,684
	7	16	7.0	75	492,351
	8	20	8.0	5806	413,018
	9	23	9.1	8301	333,782
	10	26	10.0		294,828
	11	36	11.0	13607	255,874
	12a**	20	12.0	11760	196,000
	12b	25	12.0	8847	237,822
	13	29	13.0	10205	210,939
	14	8	14.0	2219	38,259
	15	25	15.0	12995	294,259
	16	9	16.0	4753	68,549
	17	12	17.0	5873	69,920
	18	19	18.0	9917	132,810
	19	21	19.1	9711	88,276
	20	30	20.0	7015	213,986
	21	3	21.0	1832	2,187
	22	2	22.0	1407	7,155
	23	2 drops	23.0	246	1,210
	24	10	24.0	2946	3,019

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TABLE I (cont.)

SAMPLE	SAMPLE NUMBER	VOLUME (ml)	POST INJECTION TIME(hours)	ALIQUOT ACTIVITY (counts/minute)	URINE CONCENTRATION (counts/minute/hour)
Urine	25	35	25.0	11,528	10,410
	26	650	33.0	6,550	89,000
	27	70	42.0	7,511	39,533
	28	1020	54.0	7,985	24,258
	29	112	57.0	1,196	2,296

TABLE II

BIOPSY SAMPLES

SAMPLE	SAMPLE NUMBER	WET WEIGHT (grams)	POST INJECTION TIME (hours)	ALIQUOT ACTIVITY (counts/minute)	TISSUE CONCENTRATI (counts/minute/gra
Bone[X]	1	0.1339	1.1	15	109
	2	0.1824	2.1	18	99
	3	0.1804	4.3	53	293
	4	0.1396	8.4	28	203
	5	0.1536	12.4	16	103
	6	0.1502	16.6	25	167
	7	0.1581	20.6	35	223
	8	0.4771	32.0	42	87
	9	0.0432	43.8	8	188
Muscle[*]	1	0.1687	1.3	25	146
	2	0.0698	2.3	25	354
	3	0.2768	4.3	31	113
	4	0.4440	8.1	14	30
	5	0.3475	12.5	10	30
	6	0.1686	32.3	4	22

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TABLE II(cont.)

AMPLE TYPE	SAMPLE NUMBER	VOLUME (ml)	POST INJECTION TIME (hours)	ALIQUOT ACTIVITY (counts/minute)	TISSUE CONCENTRATI (counts/minute/hour
SF lumbar)*	0	1.0		24	24
	2	2.1	1.0	29	14
	4	1.7	2.1	28	16
	6	2.0	4.4	63	31
	8	2.0	8.0	55	27
	10	1.0	12.0	12	12
	12	0.9	16.4	29	32
	14	1.0	24.1	14	14
CSF (Ventricular)*	1	1.0		8	8
	3	2.6	1.0	18	7
	5	3.7	2.1	21	6
	7	2.0	4.5	14	7
	9	2.0	8.0	13	7
	11	1.0	12.0	5	5
	13	2.0	16.4	116	58
	15	2.0	24.1	7	4
	17	1.0	33.0	44	44
Blood[X]	0	10.0		60	6
	1	10.0	0.9	396	396
	2	10.0	2.0	436	218
	3	10.0	3.0	630	315
	4	10.0	4.3	414	207
**	6	10.0	6.1	379	126
**	7	10.0	7.0	385	128
**	8	4.1	8.2	170	139
	9	8.0	10.0	620	78

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TABLE II(cont.)

SAMPLE TYPE	SAMPLE NUMBER	VOLUME (ml)	POST INJECTION TIME (hours)	ALIQUOT ACTIVITY (counts/minute)	TISSUE CONCENTRATION (counts/minute/hour)
Blood (continued)	10	4.2	10.2	409	97
	11	8.0	11.1	694	89
	14	10.0	14.1	327	33
	15	5.0	15.4	539	108
	16	8.0	16.1	691	86
	17	2.5	17.1	116	46
	18	1.5	18.3	60	40
	19	8.0	19.5	418	56
	20	5.0	20.2	289	58
	21	6.0	21.5	239	40
	22	10.0	32.5	262	26
	23	6.4	43.0	194	30
	24	8.0	54.1	573	72
	Unknown	9.0		624	71
	Unknown	10.0		1098	110
	Unknown	10.0		560	56

TABLE III

AUTOPSY SPECIMENS

SAMPLE TYPE	SAMPLE NUMBER	WET WEIGHT (grams)	TISSUE CONCENTRATION (counts/minute/gram)
Liver		3.1	142.0
Muscle	1	3.4	2.3
	2	2.0	8.6
Bladder	1	1.6	31.0
	2	1.6	28.0
Heart	1	0.7	28.2
	2	0.6	25.4
Lung	1	0.9	64.0
	2	1.4	13.2
Stomach	1	1.3	61.3
	2	1.8	26.0
Kidney	1	17.3	7032.0
	2	15.0	6187.0
	3	18.3	7525.0
	4	24.3	7620.0
	5	17.0	6665.3
	6	24.0	7451.0
	7	25.1	7121.4
Necrotic Lung	1	0.4	316.3
	2	0.4	334.3
Left Kidney	1	2.0	8840.4
	2	3.4	9246.2
Small Intestine	1	1.3	25.2
	2	1.4	33.2
Pancreas	1	0.9	414.9
	2	0.02	2216.1

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TABLE III (cont.)

AUTOPSY SPECIMENS

TYPE	SAMPLE NUMBER	WET WEIGHT (grams)	TISSUE CONCENTRATION (counts/minute/gram)
orta*	1	0.3	121.0
	2	0.9	72.0
Skin*		0.5	40.8
Gall Bladder*		2.0	64.7
Subcutaneous Fat*		1.0	8.6
Right Adrenal Gland*	1	0.38	54.2
	2	0.3	247.5
Left Parietal Lobe*	1	1.1	17.0
	2	1.1	751.0
Left Frontal Lobe	1	0.1	2305.3
	2	0.95	506.3
e from Tumor*	1	0.21	393.4
	2	0.22	604.4
	3	1.8	190.0
	4	1.9	166.4
Spleen[X]	1	0.77	204.0
	2	0.64	266.0
Skull[X]		1.1	99.0
Thoracic Vertebra[X]	1	0.99	623.8
	2	0.92	719.0
Rib[X]	1	1.17	283.0
	2	2.17	208.0

TABLE III (cont.)

SAMPLE TYPE	SAMPLE NUMBER	ASH WEIGHT (grams)	TISSUE CONCENTRATION (counts/minute/gram)
Feces	1a	0.80	1552.0
	1b	1.14	327.0
	1c	0.70	348.3
	1d	0.83	321.0

The following table lists the limit of error (95%) associated with the above results.

Designation	Limits of Range	Average Recovery
*	± 6.6	
**	± 4.7	92.4%
None	± 3.8	
X	± 14.6	87.4%

Patient B-1 Injected Dose (diluted to 2000 ml)

Dummy #1 (sent 12.9 ml)	Dummy #2 (sent 12.65 ml)
Average c/m/ml= 8419	Average c/m/ml = 8431

Injected 12.9 ml of solution having 24/39 X 0.2 mgm of U 233 and 13/39 X 0.9 mgm of U 238

$$\text{Injected Dose} = \frac{8390 \times 2 \times 10^3}{0.92} = 18.217 \times 10^6 \text{ counts/minute (5.50 mgm).}$$

Hospital Number - 68927
Age - 26
Sex - Male
Weight - 55.9 Kilograms

	NOV. 9, '53 Day 0-2	NOV. 10, '53 Day 0-1	NOV. 11, '53 Day 0	NOV. 12, '53 Day 1	NOV. 13, '53 Day 2
Time	400 800 1200 1600 2000	400 800 1200 1600 2000	400 800 1200 1600 2000	400 800 1200 1600 2000	400 800 1200 1600 2000 2300
Electrolytes			URANIUM IV		EXPIRATION
Na (meq/L)		143.0		135.0	135.0
K (meq/L)		3.5		3.0	3.4
Cl (meq/L)		111.0		107.0	89.0
PO_4 (meq/L)		3.0		3.7	3.6
Alk. Phos'tase (units %)		4.0		5.5	4.4
Ca (meq/L)		8.86		8.0	8.0
NPN (mg %)		52.0		41.0	52.0
Mg (meq/L)		2.0		1.7	
BUN (mg %)		44.0		26.0	38.0
CO_2 (meq/L)		24.0		21.0	21.0
pH		7.36		7.38	7.34
TP (Gm %)		7.2		5.9	5.7
A/G		0.7		0.84	0.9
alb. (Gm %)		2.7		2.7	2.7
glb. (Gm %)		3.8		3.2	3.0
amylase (units %)		47.0		15.0	
Liver Function					
BSP (%)	32				6
Ceph. Floc.	3+ 24° 3+ 48°			2+ 24° 3+ 48°	
Thymol Floc.				8.5	
Cholesterol (mg %)	288			194	
Chol. Esters (mg %)	149			153	
Van den Berg (mg %)	0.6			4.4	6.8
Prothrombin	15 sec (N=14)75%				17 sec (N=14)55%

	NOV. 9, '53 Day 0-2	NOV. 10, '53 Day 0-1	NOV. 11, '53 Day 0	NOV. 12, '53 Day 1	NOV. 13, '53 Day 2
Time	400 800 1200 1600 2000	400 800 1200 1600 2000	400 800 1200 1600 2000	400 800 1200 1600 2000	400 800 1200 1600 2000 2300
CSF - Lumbar					
Glucose (mg %)			109	111	
Protein (mg %)			11	48	
Cl (meq/L)				123	
CSF - Ventric.					
Glucose (mg %)			91	101	
Protein (mg %)			66	10	
Cl (meq/L)					
IV Glu. Tol.					
Control (mg %)	105				
30 "	238				
60 "	157				
90 "	129				
150"	121				
Clearances					
Inulin (cc/min)		59			64.7
Tm. Pah. (mg/min)		79.8			67.4

URANIUM IV

EXPIRATION

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	NOV. 9, '53 Day 0-2	NOV. 10, '53 Day 0-1	NOV. 11, '53 Day 0	NOV. 12, '53 Day 1	NOV. 13, '53 Day 2
Time	400 800 1200 1600 2000	400 800 1200 1600 2000	400 800 1200 1600 2000	400 800 1200 1600 2000	400 800 1200 1600 2000 2300
Hematology			URANIUM IV		EXPIRATION
WBC (mm^3)		20,650		20,300	
RBC (mm^3)		3.50		3.17	
Hgb		13.5		11.0	
Diff.		P=95 L=5		P=97 E=1 L=2	
Sed. Rate					
Plat.				Normal	
Retic.					
EKG	sinus tachycardia 125 Normal vertical heart			NSR 100 No Change	
Urine					
Glucose (mg/cc)		5.4		0	
Protein (%)		0.01	0.05 0.09	0.06	0.02
Cl^- (meq/L)		5		5	
Phosphatase (units %)		2		3	12
Catalase (cc_{O_2})		0.054	0.563	0.814 0.841	0.629
Acetone		0	0	0	0
Micro.					
WBC/HPF		8-12		10-15	1-2
RBC/HPF		1-2		1-2	Occ.
Epi. Cells		Occ.		Occ.	0
Eryst.		0		0	Amph. Phos.
Casts		Occ. Hyalin Granular		Occ. Cell Cast	Occ. Granular
Bilirubin				4+	4+

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