UCRL 414
~~Copy~~ 90/A

UNIVERSITY OF CALIFORNIA

Radiation Laboratory

TWO-WEEK LOAN COPY

This is a Library Circulating Copy which may be borrowed for two weeks. For a personal retention copy, call Tech. Info. Division, Ext. 5545

BERKELEY, CALIFORNIA

UCRL-414 c.2

Special Review of
Declassified Reports

Authorized by USDOE JK Bratton

Unclassified TWX P182206Z May 79

REPORT PROPERLY DECLASSIFIED

M. B. Stuart 8-20-79

Authorized Derivative Classifier Date

DISCLAIMER

This document was prepared as an account of work sponsored by the United States Government. While this document is believed to contain correct information, neither the United States Government nor any agency thereof, nor the Regents of the University of California, nor any of their employees, makes any warranty, express or implied, or assumes any legal responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference herein to any specific commercial product, process, or service by its trade name, trademark, manufacturer, or otherwise, does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof, or the Regents of the University of California. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof or the Regents of the University of California.

UNIVERSITY OF CALIFORNIA
Radiation Laboratory

Cover Sheet
Do not remove

INDEX NO. UCRL 414
This document contains 42 pages
This is copy 90 of 101 Series A

DECLASSIFIED

Issued to Info Div.

[redacted]
Classification

Each person who receives this document must sign the cover sheet in the space below

Route to	Noted by	Date	Route to	Noted by	Date
R Ball	RWBall	OCT 3 - 1949			
W Barkas	WWB	June 22, 1950			
Bio Med Lib.		OCT 8 1966			
		APR 17			
Bio Med - Livermore					

DECLASSIFIED

UCRL 414

Health and Biology

DECLASSIFIED

CLASSIFICATION CANCELLED - CHANGED TO ~~CONFIDENTIAL~~
ON 12-9-57 BY R K Waberling
(SIGNATURE OF PERSON AUTHORIZING CHANGE)

UNIVERSITY OF CALIFORNIA

Radiation Laboratory

Contract No. W-7405-eng-48

Special Review of Declassified Reports
Authorized by USDOE JK Bratton
Unclassified TWX P182206Z May 79

REPORT PROPERLY DECLASSIFIED

Authorized Derivative Classifier — Date 8-20-79

By — Date 1-22-80

MEDICAL AND HEALTH DIVISIONS

QUARTERLY REPORT

April, May, June 1949

August 10, 1949

Berkeley, California

DECLASSIFIED

STANDARD DISTRIBUTION: Series A	Copy Numbers
Argonne National Laboratory	1-8
Armed Forces Special Weapons Project	9
Atomic Energy Commission, Washington	10-11
Battelle Memorial Institute	12
Brookhaven National Laboratory	13-16
Bureau of Medicine and Surgery	17
Carbide and Carbon Chemicals Corp. (K-25 Plant)	18-21
Carbide and Carbon Chemicals Corp. (Y-12 Plant)	22-25
Chicago Operations Office	26
Columbia University (Dunning)	27
Columbia University (Failla)	28
General Electric Company, Richland	29-34
Hanford Operations Office	35
Iowa State College	36
Kellex Corp.	37-38
Knolls Atomic Power Laboratory	39-40
Los Alamos	41-43
Massachusetts Institute of Technology (Kaufmann)	44
Mound Laboratory	45-47
National Advisory Committee for Aeronautics	48
National Bureau of Standards	49
Naval Radiological Defense Laboratory	50
NEPA Project	51
New Brunswick Laboratory	52
New York Operations Office	53-55
North American Aviation Company	56
Oak Ridge National Laboratory	57-68
Patent Branch, Washington	69
Public Health Service	70
Sandia Laboratory	71
Sylvania Electric Products, Inc.	72
Technical Information Branch, ORE	73-87
UCLA Medical Research Laboratory (Warren)	88
University of California Radiation Laboratory	89-93
University of Rochester	94-95
University of Washington	96
Western Reserve University	97-100
Westinghouse Electric Corporation	101

INFORMATION DIVISION
Radiation Laboratory
Univ. of California
Berkeley, California

DECLASSIFIED

TABLE OF CONTENTS

		Page
I	THE METABOLIC PROPERTIES OF PLUTONIUM AND ALLIED MATERIALS	
	Radioautographic Studies	4
	Tracer Studies	4
	Decontamination and Bone Metabolism Studies	14
	Radiochemistry	22
II	BIOLOGICAL STUDIES OF RADIATION EFFECTS	
	Effects of Total Body X-Irradiation on Blood Coagulation in the Rabbit (Preliminary Study)	25
	The Elimination of C^{14} Administered as $BaCO_3$	33
III	BIOLOGICAL EFFECTS OF RADIATION FROM EXTERNAL AND INTERNAL SOURCES	
	Hematological Effects of Total Body Irradiation	35
	Metabolism and Effects of Radio-Iodine (I^{131})	36
IV	HEALTH CHEMISTRY AND PHYSICS	
	Health Chemistry	38
	Health Physics	39

DECLASSIFIED

I THE METABOLIC PROPERTIES OF PLUTONIUM AND ALLIED MATERIALS

J. G. Hamilton

Project 48 A-I

Radioautographic Studies

In the praseodymium studies, very low activity was present in the bone tissues and the autographs were not very satisfactory. The Pr autographs appear to resemble the earlier findings, which demonstrated a deposition of Pr similar to the lanthanide rare earths, such as cerium, element 61, etc.

Preliminary studies with plutonium at one day after administration, indicated that this element was not laid down in the region of the perichondrium-calcified cartilage junction, as was found with strontium and element 61. Later studies, in which alpha tract autographs were made (instead of density autographs) showed that plutonium was deposited in this area, but to a very slight degree. When the first autographs were set up for three times the original exposure time, there was a faint blackening in this area. Further experiments are in progress at the one hour interval, to correlate the plutonium findings with those of strontium and element 61.

A great deal of time has been spent on working out methods to use in applying the use of NTB plates to the study of bone tissue. The problem of emulsion staining, of mounting the tissue with the least amount of distortion, etc., continue to be major problems.

Tracer Studies

Selenium 75. Selenium 75 prepared by cyclotron bombardment has been given to rats by intramuscular injection. These animals were sacrificed 1 and 4 days after the carrier-free selenium was administered. This material is very readily absorbed from the injection site. All but 2.5 percent of the Se^{75} administered was absorbed into the body one day after injection, and 1.4 percent four days after administration. Of the material absorbed, the major part was excreted in the urine one day after injection with measurable amounts of selenium still present in the blood, liver, kidney, muscle and skeleton. The excretion continued which is primarily urinary so that at four days after injection, blood, liver, kidney, were slightly lower, skeleton was markedly lower. These preliminary data suggest that carrier-free selenium is not retained by the body for any long period of time. The data are summarized in Table I.

Europium 155. Studies involving Eu^{155} have been completed. The data presented here are from animals kept for 8 months following intramuscular administration of carrier-free europium 155. The data are not markedly different from the results

TABLE I

DEPOSITION OF CARRIER-FREE Se^{75} IN THE RAT AFTER INTRAMUSCULAR ADMINISTRATION. VALUES ARE GIVEN AS PERCENT OF ABSORBED DOSE AND CORRECTED FOR RECOVERY

	1 Day		4 Days	
	% per organ	% per gram	% per organ	% per gram
Heart	.32	.33	.20	.21
Lung	.73	.58	.44	.21
Spleen	.34	.51	.27	.24
Blood	6.08	.53	3.99	.25
Liver	7.29	1.07	6.22	.61
Kidney	3.80	2.37	2.65	1.11
Pancreas	.22	.32	Not taken	
Stomach	.49	.37	.27	.18
Stom. Cont.	2.10	1.00	2.01	.02
Sm. Int.	2.73	.65	.99	.25
Sm. Int. Cont.	.53	1.08	.55	.14
Lg. Int.	.94	.71	.42	.16
Lg. Int. Cont.	2.07	3.54	.24	.07
Skeleton	8.14	.31	1.68	.06
Muscle	9.57	.11	9.18	.08
Skin	5.33	.17	3.37	.09
Testes	.80	.31	.77	.23
Urine	40.0	-	61.3	-
Feces	9.85	-	7.51	-
Expired air	.74	-	Not accounted for	

already reported with Eu^{154} containing carrier. The deposition is that of a typical lanthanide rare earth. Eight months after administration, 30 percent of the absorbed activity was found in the skeleton. Concentration in the soft tissues of the body was low and approximately 70 percent of the material absorbed from the injection site was excreted in the urine and feces. An average of 21.8 percent remained at the injection site eight months after intramuscular administration. The data suggest that one europium is deposited in the skeleton, it will remain there for a very long period of time. The data are summarized in Table II.

Neptunium 237. Studies involving the intramuscular administration of Np^{237} have been completed for 1 and 16 days after intramuscular administration. Due to the fact that the neptunium is alpha emitter, the samples were counted after its separation from the residue of animal ash using the lanthanum fluoride procedure. Np was administered intramuscularly complexed with 0.1 M sodium citrate. The Np^{237} was given as a citrate complex and was presumably Np^{IV}. Such complexing facilitated absorption from the injection site. One day after administration, 13.6 percent of the injected material remained in the left leg. Further absorption up to 16 days was not significant since there remained 12.2 percent of the Np^{237} in the left leg 16 days after injection. After absorption, the major areas of deposition of Np^{237} in the body were skeleton, liver and kidney. An appreciable fraction of Np was found in the urine at 1 day and 16 days after administration being 29 percent and 38 percent respectively. At 16 days after intramuscular administration of Np^{237}, skeletal deposition was continued. A slight reduction in the soft tissue concentration was observed. These data are summarized in Table III.

Several years ago a very limited series of tracer studies was done with the 2.2 day Np^{239} using rats as the experimental animals. Three time intervals were chosen, 1, 4 and 8 days. The 8-day period was never considered too reliable in view of the degree of radiation decay that had taken place by the time this time interval had elapsed and the tissues assayed. A comparison of the 4-day point using Np^{238} without either carrier or the presence of any elements possessing chemical similarity, such as uranium, to the present studies at 4 days using of the order of 0.25 milligram of Np^{237} shows a fairly close degree of similarity.

The data obtained from the Np^{237} tracer studies presents several points of considerable interest. A comparison of these data with the corresponding tracer studies for the other members of the actinide series suggest that Np is handled rather differently from any of the others. The retention by the liver is far lower than is observed in actinium, americium or cerium, the values being more comparable with that noted with thorium, protoactinium, uranium and plutonium. The retention by the skeleton was observed to be higher than for actinium, americium and cerium, about equivalent as was found with thorium and protoactinium and lower than observed with plutonium. Excretion occurred quite rapidly during the first four days of the experiment and the chief channel of elimination was the kidney, and in this respect Np metabolically resembles uranium which is the only member of the series to demonstrate a high degree of urinary excretion. It has been frequently emphasized that the predominantly tri-valent members of the group, actinium, americium and cerium are metabolically almost indistinguishable from one another. Likewise, thorium and plutonium act in a very similar manner in the body with protoactinium demonstrating metabolic characteristics of a somewhat similar character to thorium and plutonium. All of this comes to the point

TABLE II

DEPOSITION OF CARRIER-FREE Eu^{155} IN RATS 8 MONTHS AFTER INTRAMUSCULAR ADMINISTRATION. VALUES ARE GIVEN AS PERCENT OF ABSORBED MATERIAL CORRECTED FOR RECOVERY

	% per organ	% per gram
Heart	.04	.03
Lungs	.10	.03
Spleen	.07	.13
Blood	<.01	<.01
Liver	1.16	.10
Kidney	.32	.13
Adrenals	<.01	-
Thyroid	<.01	-
Lymph Gl.	-	.04
Pancreas	<.01	<.01
Brain	<.01	<.01
Fat	-	<.01
Stomach	.04	.008
Sm. Int.	.06	.004
Lg. Int.	.04	.004
Skeleton	36.0	1.68
Muscle	.92	.007
Skin	.56	.01
Eyes	<.01	.01
Pituitary	<.01	-
Gonads	<.01	.03
Urine	14.8	-
Feces	45.9	-

TABLE III

DEPOSITION OF Np^{237} IN RATS COMPLEXED WITH CITRATE FOLLOWING INTRAMUSCULAR ADMINISTRATION. VALUES ARE GIVEN AS PERCENT OF ABSORBED DOSE, CORRECTED FOR RECOVERY

	1 Day		15 Days	
	% per organ	% per gram	% per organ	% per gram
Heart	.03	.04	.01	.02
Lungs	.17	.09	.07	.05
Spleen	.13	.19	.15	.17
Blood	.45	.04	.06	.005
Liver	8.49	1.01	2.90	.31
Kidney	2.55	1.40	1.00	.50
Adrenals	<.01	-	.02	-
Thyroid	<.01	-	<.01	-
Lymph Gl.	-	.04	-	.02
Pancreas	<.01	.03	<.01	<.01
Brain	<.01	<.01	<.01	<.01
Fat	-	.01	-	<.01
Stomach	.17	.06	.01	.003
Sm. Int.	.49	.06	.10	.008
Lg. Int.	2.03	.23	.16	.01
Skeleton	44.3	2.62	44.5	2.03
Muscle	3.21	.04	2.27	.02
Skin	1.14	.04	.38	.01
Pituitary	<.01	-	<.01	
Eyes	<.01		<.01	<.01
Gonads	<.01	.01	<.01	.01
Urine	29.8	-	38.6	-
Feces	7.06	-	9.80	-

that the three trivalent members of the group are very much alike. Thorium and plutonium are presumed to be so similar on the presumption that plutonium exists in the body in the plus 4 state. Metabolic studies done with uranium here and elsewhere suggest that this element is metabolized as the UO_2^{++} ion or some complex associated with hexavalent uranium. In the case of Np, it may be that part is metabolized in one valence state and part in another. While much of the foregoing is purely speculatory, it is of obvious interest to attempt to correlate the chemical and metabolic interests and these other radio-elements.

Praseodymium 143. The metabolism of carrier-free Pr^{143} has been studied in the rat 1, 4, 15 and 32 days after intramuscular administration. This has been compared to similar studies involving Pr^{143} to which 0.5 milligram of inactive isotopic Pr carrier was added. In addition to this, the fate of Pr^{143} administered intragastrically and intravenously has been studied in rats. Pr^{143} given intramuscularly as the carrier-free radio-element, is not readily absorbed from the injection site. For example, 48.9 percent, 43.0 percent, 22.8 percent, 16.1 percent remained in the left leg at 1, 4, 15 and 32 days after intramuscular injection. When this is compared with the same radioactive solution of Pr^{143} to which 2 milligrams of sodium citrate were included with each injection, it can be seen that citrate complexing of Pr^{143} facilitates absorption from the injection site. 8.3 percent, 5.5 percent, 5.5 percent, and 2.5 percent of the administered Pr^{143} remained at the injection site at 1, 4, 15 and 32 days after the administration of complexed Pr^{143}. These data are summarized in Tables IV and V. The addition of 0.5 milligram of Pr carrier to Pr^{143} greatly retarded absorption of material from the injection site. 94 percent, 94 percent, 99 percent and 86.4 percent of the administered Pr^{143} remained at the injection site on 1, 4, 15 and 32 days after intramuscular administration. After absorption of carrier-free Pr^{143}, the major organs of deposition at the early time periods were liver, kidney and skeleton. Pr^{143} was released from the liver, and slowly liberated into the gastro-intestinal tract and appeared in the feces at later time periods. Therefore, in a period of 32 days the Pr^{143} accumulated by the liver was eliminated by the body to an extent of 80 percent of the total deposited at 1 day after Pr^{143} administration. A gradual loss of Pr^{143} from the other soft tissues occurred as well. The skeletal deposition was of a more permanent nature, the data suggesting that little or none of the Pr^{143} deposition in the skeleton was eliminated during the time periods studied. Citrate complexing of Pr^{143} gave no essential difference in body deposition after absorption from the injection site. These data have been summarized in Table V. The addition of carrier Pr so influenced the absorption of Pr^{143} that the tissues of the animal other than the injection site were difficult to count because of the low amount of radioactivity involved. The data suggest, however, that the addition of massive amounts of Pr carrier reduces the skeletal deposition of the absorbed Pr to a marked extent. These data are summarized in Table VI.

Pr^{143} is not absorbed after intragastric administration. Less than .01 percent of the administered Pr^{143} was found in any of the tissues of the rat which were measured, this value representing the sensitivity of the method used rather than the frank demonstration of Pr^{143} in the tissues investigated. Pr^{143} was administered to animals by intravenous injection as the carrier-free material and as the carrier-free material complexed with citrate. Citrate complexing did not alter the region of deposition in the body. Comparative data are summarized in Table VII.

TABLE IV

DEPOSITION OF CARRIER-FREE Pr^{143} IN RATS FOLLOWING INTRAMUSCULAR ADMINISTRATION. VALUES ARE GIVEN IN PERCENT OF ABSORBED DOSE, CORRECTED FOR RECOVERY

	Time After Injection									
	1 Day		4 Days(1)		4 Days(2)		15 Days		32 Days	
	% per organ	% per gram	% per organ	% per gram	% per organ	% per gram	% per organ	% per gram	% per organ	% per gram
Heart	.17	.13	.11	.08	.11	.11	.05	.05	.05	.04
Lungs	.44	.12	.30	.09	.24	.11	.26	.08	.16	.05
Spleen	.08	.10	.14	.11	.23	.21	.09	.08	.12	.11
Blood	.48	.02	.08	<.02	.09	<.02	.01	<.01	.02	<.01
Liver	53.6	4.42	51.5	3.88	43.0	3.43	19.5	1.30	10.2	.69
Kidney	9.57	3.34	2.12	.71	2.83	1.31	1.87	.62	.90	.29
Adrenals	<.02	-	<.02	-	<.02	-	<.01	-	<.01	-
Thyroid	<.02	-	<.02	-	<.02	-	<.01	-	<.01	-
Lymph Gl.	-	.15	-	.12	-	.17	-	.08	-	.04
Pancreas	.04	.06	.03	.05	.08	.08	.01	.03	.01	.02
Brain	<.02	<.02	<.02	<.02	<.02	<.02	<.01	<.01	<.01	<.01
Fat	-	<.02	-	<.02	-	<.02	-	<.01	-	<.01
Stomach	.54	.19	.42	.12	.34	.06	.20	.05	.18	.03
Sm. Int.	.69	.06	.77	.06	.66	.06	.81	.05	.23	.01
Lg. Int.	3.25	.35	1.95	.18	.68	.06	.45	.04	.24	.02
Skeleton	20.8	.75	24.8	.80	33.4	1.65	24.2	1.03	25.6	1.14
Muscle	3.57	.02	2.34	<.02	2.91	.02	2.31	.01	1.40	<.01
Skin	3.13	.04	2.54	.03	1.95	.06	1.99	.04	.66	.01
Eyes	.02	.06	.02	.05	.02	.08	.01	.05	.01	.03
Pituitary	<.02	-	<.02	-	<.02	-	<.01	-	<.01	-
Gonads	.12	.02	.17	.05	.11	.04	.08	.03	.09	.02
Urine	2.90	-	6.89	-	5.29	-	7.22	-	9.47	-
Feces	.61	-	5.85	-	8.12	-	40.9	-	50.7	-

TABLE V

DEPOSITION OF Pr^{143} COMPLEXED WITH CITRATE* IN RATS FOLLOWING INTRAMUSCULAR ADMINISTRATION. VALUES ARE GIVEN AS PERCENT OF ABSORBED DOSE CORRECTED FOR RECOVERY

	Time After Injection							
	1 Day		4 Days		15 Days		32 Days	
	% per organ	% per gram	% per organ	% per gram	% per organ	% per gram	% per organ	% per gram
Heart	.12	.09	.07	.07	.05	.04	.03	.03
Lungs	.19	.06	.18	.07	.11	.05	.09	.03
Spleen	.14	.12	.10	.10	.13	.12	.09	.10
Blood	.14	<.01	.18	<.01	.01	<.01	<.01	<.01
Liver	58.9	4.73	49.3	4.78	19.1	1.58	6.47	.46
Kidney	4.62	1.53	3.25	1.15	1.11	.45	.60	.21
Adrenals	<.01	-	.01	-	<.01	-	<.01	-
Thyroid	<.01	-	<.01	-	<.01	-	<.01	-
Lymph Gl.	-	.09	-	.12	-	.07	-	.09
Pancreas	.03	.03	.03	.02	.01	.02	.01	.02
Brain	<.01	<.01	<.01	<.01	.01	<.01	<.01	<.01
Fat	-	<.01	-	<.01	-	<.01	-	<.01
Stomach	.24	.10	.29	.12	.25	.07	.10	.02
Sm. Int.	.52	.05	.52	.06	.49	.03	.15	.01
Lg. Int.	.67	.10	.23	.03	.55	.06	.18	.01
Skeleton	23.0	.73	27.2	1.00	33.9	1.57	23.4	.94
Muscle	2.44	.01	1.70	.01	1.53	.01	1.90	.01
Skin	2.66	.05	2.42	.05	1.25	.03	.94	.01
Eyes	.01	.03	.01	.06	<.01	.03	<.01	.02
Pituitary	<.01	-	<.01	-	<.01	-	<.01	-
Gonads	.10	.03	.08	.03	.15	.05	.09	.03
Urine	5.89	-	6.68	-	7.36	-	6.61	-
Feces	.34	-	7.73	-	34.0	-	59.3	-

* 2 mg. citrate as sodium salt administered to each animal.

TABLE VI

DEPOSITION OF Pr^{143} PLUS Pr CARRIER* IN RATS FOLLOWING INTRAMUSCULAR ADMINISTRATION. VALUES ARE GIVEN AS PERCENT OF ABSORBED DOSE CORRECTED FOR RECOVERY

	Time After Injection							
	1 Day		4 Days		15 Days		32 Days	
	% per organ	% per gram	% per organ	% per gram	% per organ	% per gram	% per organ	% per gram
Heart	<.33	<.33	<.17	<.17	<.22	<.22	<.12	<.12
Lungs	<.33	<.33	<.17	<.17	.44	.22	<.12	<.12
Spleen	<.33	<.33	<.17	<.17	.22	.22	<.12	<.12
Blood	<.33	<.33	<.17	<.17	<.22	<.22	.12	<.12
Liver	12.3	.99	5.99	.68	8.00	.67	1.30	<.12
Kidney	<.33	<.33	.17	<.17	.22	<.22	<.12	<.12
Adrenals	<.33	-	<.17	-	<.22	-	<.12	-
Thyroid	<.33	-	<.17	-	<.22	-	<.12	-
Lymph Gl.	-	<.33	-	<.17	-	.44	-	.24
Pancreas	<.33	<.33	<.17	<.17	<.22	<.22	<.12	<.12
Brain	<.33	<.33	<.17	<.17	<.22	<.22	<.12	<.12
Fat	-	<.33	-	<.17	-	<.22	-	<.12
Stomach	.99	<.33	<.17	<.17	<.22	<.22	<.12	<.12
Sm. Int.	4.30	.33	.34	<.17	<.22	<.22	<.12	<.12
Lg. Int.	58.6	7.28	1.88	.34	<.22	<.22	<.12	<.12
Skeleton	9.60	.33	6.85	.34	6.89	<.22	2.01	<.12
Muscle	1.66	<.33	.34	<.17	1.56	<.22	.83	<.12
Skin	6.63	<.33	.34	<.17	.44	<.22	.24	<.12
Eyes	<.33	<.33	<.17	<.17	<.22	<.22	<.12	<.12
Pituitary	<.33	-	<.17	-	<.22	-	<.12	-
Gonads	<.33	<.33	<.17	<.17	.22	<.22	<.12	<.12
Excretions	5.96		84.1		82.2		95.5	

* 0.5 mg. Pr carrier administered to each animal.

TABLE VII

DEPOSITION OF CARRIER-FREE Pr^{143} IN RATS AT 4 DAYS FOLLOWING INTRAVENOUS INJECTION. VALUES ARE GIVEN AS PERCENT OF ABSORBED DOSE CORRECTED FOR RECOVERY

	Pr^{143} injected in carrier-free state uncomplexed.		Pr^{143} injected in carrier-free state complexed with citrates.	
	% per organ	% per gram	% per organ	% per gram
Heart	.06	.07	.03	.05
Lungs	.40	.33	.23	.15
Spleen	.33	.54	.50	.66
Blood	.02	<.01	<.01	<.01
Liver	52.9	6.48	59.6	7.83
Kidney	1.07	.65	.52	.36
Adrenals	<.01	-	<.01	-
Thyroid	<.01	-	<.01	-
Lymph Gl.	-	.07	-	.21
Pancreas	.03	.03	<.01	.02
Brain	<.01	<.01	<.01	<.01
Fat	-	<.01	-	<.01
Stomach	.19	.10	.45	.16
Sm. Int.	.70	.07	.37	.04
Lg. Int.	.82	.17	.95	.20
Skeleton	19.0	1.40	18.6	1.34
Muscle	1.08	.01	1.28	.01
Balance	5.56		1.06	
Skin	5.29	.17	.66	.03
Eyes	<.01	.03	<.01	.01
Pituitary	<.01	-	<.01	.01
Gonads	<.01	.05	<.01	
Urine	2.54	-	8.59	-
Feces	9.97	-	7.06	-

In addition to this, some short-term intravenous studies using carrier-free Pr^{143} were done. Deposition observed 4 days after administration is approximately the same as that observed at 1 hour after intravenous administration, but more than 3 minutes is needed for the high liver and skeletal accumulation to occur, since animals sacrificed at 65, 105, 120 and 170 seconds showed the Pr^{143} to be primarily in the circulating blood stream.

Decontamination and Bone Metabolism Studies

Decontamination Studies. Effect of Zirconium Citrate and Sodium Citrate on Decontamination of Y^{90} and Zr^{95}. Administration of massive doses of zirconium citrate appears to provide one of the best means for decontamination of plutonium, radioyttrium, and certain other metallic fission products[1]. It has been suggested that this effect may be due to ionic exchange with the metallic ions in the bone and tissues, or may be due to a "carrier" effect of the massive concentrations of zirconium used.

In the following experiment, this phenomenon was investigated further using radioyttrium as the element for "decontamination", and radiozirconium to tag the therapeutic dose of zirconium citrate. A comparison was made with rats to which equivalent amounts of sodium citrate and carrier-free radiozirconium were administered.

Procedure: The radioyttrium used was Y^{90} (62 hour half life) separated chemically from Sr^{90}. It contained a very small amount of carrier yttrium (45 micrograms). The Zr^{95} (65 day half life) was chemically separated from a Zr^{95}, Cb^{95} mixture (fission) in carrier -free state. To avoid contamination with the daughter Cb^{95}, it was freshly separated before use.

Normal adult female rats weighing approximately 225 grams were used for the experiment, and they were maintained on the regular stock colony diet. The first group (5 rats) received 40 microcuries of Y^{90} and 5 microcuries of Zr^{95} in 1.6 ml. of 10 percent sodium citrate solution at pH 6. The two radioisotopes were distinguished in the same animal by differences in half life.

The second group (4 rats) received an intraperitoneal injection of 1.6 cc of a solution containing 40 mg. Zr as citrate "tagged" with 5 microcuries of Zr^{95}, while the third group (5 rats) received a similar injection with a solution containing 40 mg. Zr as citrate and 40 microcuries of Y^{90} (45 micrograms Y). The animals were placed in individual metabolism cages, and urine and feces were collected separately. They were sacrificed after 3 days, and femur, liver, kidneys, urine, feces and residual carcass were analyzed for Y^{90} or Zr^{95}. The results of the experiment are given in Table VIII.

Results: Simultaneous administration of a massive dose of zirconium citrate resulted in a tremendous increase in the urinary excretion of both Y^{90} and Zr^{95} and a marked (12 fold) reduction in the amount of these elements retained in femur, liver and kidney, as compared to the distribution when an equivalent amount of

---

(1) J. Schubert, J. Lab. & Clin. Med., 34; 313 (1949)

TABLE VIII

COMPARISON OF THE EFFECT OF SODIUM CITRATE AND ZIRCONIUM CITRATE ON THE DISTRIBUTION AND EXCRETION OF Y^{90} and Zr^{95}

(Values are expressed as percent of the administered dose ± the standard deviation)

Group	Element	Urine	Feces	Femur	Liver	Kidneys	Carcass
Control (no treatment)	Y^{90}	9.7±0.8	9.5±0.9	2.9±0.1	10.1±1.3	2.3±0.2	62.8±4.4
I. Sodium citrate (1.6 cc 10% sodium citrate)	Y^{90}	16.4±5.7	7.3±4.4	2.4±0.4	5.1±2.0	3.4±0.6	65.4±8.6
Sodium citrate (1.6 cc 10% sodium citrate)	Zr^{95}	4.3±1.5	6.5±1.5	2.4±0.4	6.2±1.3	4.8±0.7	75.8±5.9
II. Zirconium citrate (40 mg Zr as citrate)	Zr^{95}	86.6±25.7	6.5±4.8	0.2±0.08	0.3±0.1	0.3±0.1	6.1±1.4
Zirconium citrate (40 mg Zr as citrate)	Y^{90}	91.3±8.6	6.0±4.1	0.2±0.1	0.4±0.2	0.1±0.06	2.0±0.8

sodium citrate was administered. The general distribution of the two isotopes was very similar in both cases, and the evidence suggests that the action of zirconium citrate may be a "carrier" effect of the massive dose of zirconium administered.

Bone Metabolism Studies. High Initial Uptake and Rapid Release of Radiostrontium from the Skeleton of Rachitic Rats. Low phosphorus rickets has a profound effect on the skeleton because of the inhibition of bone salt deposition associated with the low plasma phosphate level. Jones[2] showed that there was a high uptake of radiostrontium in the bones of rachitic rats at 1 hour, while Chace[3] found very little radiostrontium left in the skeleton after four days. On the other hand, when radiostrontium is administered to young normal rats of the same age, a large proportion of the dose is promptly deposited in the skeleton, and remains fixed there.

Because of its possible value in radiostrontium decontamination, and the interest in the fundamental process of bone salt deposition, this phenomenon was investigated in the following experiment.

Procedure: A group of 12 female rats were weaned at 21 days of age, and reared on a purified phosphorous deficient diet for 7 weeks. At this time, all rats showed signs of severe low phosphorous rickets. A group of 10 female rats, weaned at the same time, were pair fed the control (phosphorous supplemented) diet for the same period. Each rat was then injected intraperitoneally with 0.5 cc of a solution containing 5 microcuries of $Sr^{89,90}$ (carrier-free) in isotonic saline. They were placed in individual metabolism cages, and urine and feces were collected separately. One half of each group were sacrificed 1 hour after injection - the balance 72 hours after injection. Femur, tibia, 2 incisors, molar teeth, urine and feces were taken for determination of radiostrontium content. The residual carcass was also ashed and assayed. These were dry ashed, dissolved in 2N HCl, and aliquots were evaporated and analyzed for radiostrontium with a G.M. Counter.

Results: The results are shown in Table IX. Both the rachitic and control animals show a high and almost equivalent uptake in the skeleton. The values for femur and tibia indicate a skeletal uptake equivalent to 60-70 percent of the administered dose. However, while the radiostrontium in the bones of the control animals is slightly higher after 72 hours, there is a tremendous decrease in the radiostrontium in the rachitic bone after this time interval. This loss was associated with a much greater urinary excretion of radiostrontium in the deficient animals, both after one hour and after 72 hours.

---

(2) D. C. Jones and D. H. Copp, AECD - (1948)

(3) M. J. Chace, M.A. Thesis, U. of Calif., (1946)

TABLE IX

UPTAKE AND DISTRIBUTION OF RADIOACTIVE STRONTIUM
IN YOUNG RACHITIC AND YOUNG PAIR FED CONTROL RATS

% Dose

Deficient	No. rats	Carcass	Femur	Tibia	Incisor	Molar	Urine	Feces
1 hr.	6	81.5±2.5	2.5±0.2	2.7±0.2	1.4±0.2	0.7±0.2	8.2	0.06
72 hrs.	6	16.3±4.1	0.65±0.1	0.6±0.1	1.3±0.2	0.9±0.1	81.3	3.65
PF Controls								
1 hr.	5	86.1±4.8	2.8±0.2	2.6±0.1	1.6±0.2	1.2±0.2	0.3	0
72 hrs.	5	68.5±2.1	3.1±0.2	2.7±0.1	3.3±0.3	1.3±0.2	13.5	8.7

Figures are given as the average of 5 or 6 rats plus or minus the standard error of the mean.

The uptake of radiostrontium in the incisors was approximately the same in both groups of animals at one hour, but there was a considerable net increase in the control group after 72 hours. No such gain was observed in the rachitic group. In the molar teeth there was little difference in the amount of radiostrontium present after the two time intervals, or between the two groups. These differences in behavior may be associated with the stable nature of the molars, and the continued growth of the incisors.

Discussion: The most striking effect observed was the high initial uptake of radiostrontium in the rachitic rats which was comparable to that of control rats, and the subsequent loss of much of this radiostrontium by 72 hours. This would suggest that the initial uptake was in some highly labile form distinct from the general bone salt and from which the radiostrontium was readily released. The initial uptake of radiostrontium by the control rats was just as great but this material appeared to become fixed as no loss was observed at 72 hours. It would appear probable that the initial failure of the radiostrontium in the rachitic rats to become fixed is associated with the lack of bone mineralization in these animals. The site of the initial labile radiostrontium deposition is open to question, but because of the large amount present and its relation to bone formation, the osteoid is a definite possibility.

Although the blood level of radiostrontium in the rachitic and control animals was comparable, the urinary excretion was 6 to 25 times greater in the rachitic animals suggesting that renal excretion is also directly affected.

In the case of the molar teeth very little if any growth is taking place and the uptake of radiostrontium in this organ is probably chiefly an adsorption-exchange phenomenon and therefore is little affected by the rachitic condition.

In the case of the incisor teeth new dental growth at the base would account for the continued uptake of radiostrontium in the control animals. In the rachitic animals, this continued uptake does not occur.

The potential decontamination value of a low phosphorous regimen is being further investigated.

Bone Metabolism Studies. Effect of Pure Pituitary Growth Hormone in Severe Low Phosphorous Rickets. Administration of the growth hormone of the anterior pituitary gland results in general body growth associated with nitrogren retention, increase in soft tissue mass, and longitudinal growth of the bones. Day and McCollum[4] have suggested that when the diet is very deficient in phosphorous, essential phosphorous for growth of soft tissues is supplied by resorption of bone salt. In such case, it might be expected that the increase in soft tissue induced by growth hormone administration would further increase the severity of the low phosphorous rickets. In the following experiment, this was investigated using rats reared on the severe phosphorous deficient diet previously described, and purified growth hormone prepared by C. H. Li[5].

---

(4) Day, H. D. and McCollum, E. V., J. Biol. Chem., 130: 269 (193).
(5) Li, C. H., Evans, H. M., and Simpson, M. E., Science, 108: 624 (1948).

Procedure: Female rats were weaned at 21 days, and reared on the phosphorous deficient diet (0.005 percent P). A similar group were pair-fed the phosphate supplemented control diet (0.40 percent P). After 4 weeks on these diets, 10 rats from each group were placed in individual metabolism cages. 5 rats in each group were given 1.0 mg. pure crystalline growth hormone daily in two divided doses, by intraperitoneal injection. The remainder served as uninjected controls. Urine was collected daily in 2 cc of 6N sulfuric acid, and was analyzed for nitrogen by the microkjeldahl method. At the end of 10 days, the animals were sacrificed, tissues were analyzed, and tibias were taken for histology. 48 hours prior to sacrificing, the animals were given 5 microcuries of radiostrontium ($Sr^{89,90}$) - carrier-free in isotonic saline. A tibia and scapula were taken from each animal and analyzed for radiostrontium.

Results:

a) Growth: The growth of the untreated phosphorous deficient and pair fed control rats appeared to be comparable to that reported earlier. However, the growth hormone treated rats showed a definite increase in weight, which was approximately 6 grams for the deficient rats and 14 grams for the pair fed controls as compared to their untreated fellows.

b) Nitrogen Retention: This weight gain was associated with a retention of nitrogen, as may be seen in Table X. The urinary excretion of nitrogen was averaged for each rat the ten day pre-injection period, for the 9 day injection period, and for the 4-5 day post-injection period. These values were in turn averaged, and are given in the table - the standard error. The decreased urinary excretion indicates positive nitrogen retention, which was somewhat greater in the deficient animals than in the pair fed controls. Following growth hormone injection, the nitrogen excretion promptly returned to the pre-injection level or slightly higher.

c) Histology: A tibia was taken for histology from 4 treated and 4 untreated rats in both deficient and control groups. A line test was performed on the opposite tibia by the method of Von Kossa. The split tibias were immersed in a 2 percent solution of silver nitrate for 2-1/2 minutes, and then exposed to light until the silver-deposited in the bone salt was reduced and blackened. The widths of the epiphyseal disks were measured with an optical micrometer, and the average values are shown in Table XI. Both treated and untreated phosphorous deficient animals showed the broad, irregular epiphyseal disk characteristic of rickets, but in the group receiving growth hormone, the disk was much broader.

Histological sections of tibia show this effect very clearly. The epiphyseal disc of the rachitic animals treated with growth hormone was almost twice as broad as in the untreated group. In both cases, there were large amounts of osteoid in region of the metaphysis, while the shaft consisted of a thin shell of calcified bone. Histologically, the growth hormone appears to have caused growth of epiphyseal cartilage and increased severity of the rickets.

d) Effect of Deposition of Radiostrontium in Bone: Severe rickets is associated with a marked decrease in the deposition of radiostrontium in the skeleton. 4 rats from each group were injected with 5 microcuries of carrier-free radiostrontium ($Sr^{89,90}$) intraperitoneally 48 hours before the animals were sacrificed. The femur (long bone) and scapula (flat bone) were taken as typical bones for analysis.

TABLE X

THE EFFECT OF 1 MG PER DAY INJECTION OF G.H. ON THE URINARY EXCRETION OF DEFICIENT AND P.F. CONTROL RATS

(mg N per 24 hours)

Nitrogen	Pre-inj. Control	Inject. Period	Post-inj. control	Mean Change from 1st Control
Deficient	82.1±4.7	68.1±4.2	97.0±9.7	- 14.0
P.F. Control	87.3±3.8	78.2±5.3	106.0±5.5	- 9.1

TABLE XI

WIDTH OF THE EPIPHESEAL DISK OF THE TIBIA OF G.H. TREATED AND UNTREATED DEFICIENT AND CONTROL RATS.

Deficient	(No. of Rats)	Width in Micron.
Treated	3	758±95
Untreated	4	472±87
Control, P.F.		
Treated	4	182±11
Untreated	4	160± 6

Figures are given as the average of 3 or 4 rats plus or minus the standard error of the mean.

The results are shown in Table XII. The skeletal radiostrontium was computed from previously established ratios of femur/skeleton.

The radiostrontium in bones of the rachitic animals was low, and was further reduced in the group treated with growth hormone. This suggests increased severity of the rickets associated with growth hormone treatment.

The control group retained a large part of the dose of radiostrontium in the skeleton, and there was no apparent effect of the growth hormone treatment.

Experiments in Progress.

1. Effect of zirconium citrate therapy on decontamination of radiocolumbium.
2. Stimulation of new bone formation in pigeons with estrogenic hormone, and the effect on the deposition of radiostrontium.
3. Development of a method for assay of Ca^{45}.
4. Effect of purified growth hormone on rachitic and control rats, as studied by histology, radioautographs, and by the effect on the metabolism of Ca^{45} and P^{32}.
5. Kinetics of uptake of radiostrontium in bone, and the mechanism of bone salt deposition.

Radiochemistry

Carrier-free Mn^{54} has been isolated from a spectrographically pure iron target. The iron was dissolved in 6N HCl and extracted with ether. The aqueous phase contained Mn^{54} and $Co^{56,57}$. These activities were separated by treating the solution with Br_2 and NH_4OH after the addition of 10 mg. of Fe^{+++}. The $Fe(OH)_3$ precipitate carried all of the Mn^{54} and approximately 1 percent of the cobalt activity. The precipitation was repeated twice with cobalt hold-back and twice more without added cobalt. The $Fe(OH)_3$ precipitate plus Mn^{54} activity was dissolved in 6N HCl and the iron was extracted with ether. The aqueous phase was evaporated to dryness on NaCl. Approximately 10^4 C/S of 310-day Mn^{54} were obtained. Mass absorption data and half-life measurements agree with published values.

The cobalt fraction containing approximately 2 mc of $Co^{56,57}$ is being separated from traces of cadmium presumably introduced from the solder used to hold the iron target onto the target plate.

110 μc of Zn^{65} were separated from a copper target. The target was dissolved in HNO_3 and taken to dryness. The $Cu(NO_3)_2$ plus activity was dissolved in 6N HCl and the copper was precipitated as CuS. The Zn^{65} remained in the supernatant. Traces of CuS were removed by dithizone extraction using a previously reported method.

Ta^{182} was isolated, carrier-free, from alpha bombarded HfO_2. The HfO_2 was dissolved in HF and taken up in 10N HNO_3. After removing HF by heating, the Ta^{182} was carried on MnO_2, precipitated from $KMnO_4$. The tantalum activity was separated from MnO_2 by the transference technique previously reported for the separation of carrier-free Cb^{45} from MnO_2.

TABLE XII

EFFECT OF GROWTH HORMONE ON THE UPTAKE OF RADIOSTRONTIUM BY BONE

		Percent of Administered Dose of Radiostrontium		
Group	No. of Rats	Femur	Scapula	Skeleton*
Low Phosphorous Rickets				
Untreated	4	0.69±0.18	0.20±0.06	17±4
GH treated	3	0.36±0.06	0.10±0.01	9±2
Controls (Pair Fed)				
Untreated	4	3.30±0.05	0.9 ±0.04	73±1
GH treated	4	3.48±0.09	1.2 ±0.07	77±2

*Skeletal value computed from previously established femur/skeleton ratio.

Additional data were obtained on the distribution of At^{211} in the rat. The results agree with the previously reported values.

Na^{22} is being separated from a magnesium target. The activity does not carry on a precipitate of $Mg(NH_4)_2(CO_3)_2$ used to remove magnesium from solution. Repeated precipitation are required for complete removal of magnesium.

Chemical activation of Br^{80} by isomeric transition has been studied in NaBr-protein systems. Separations of the 4.4 hr. and 18 min. activities were obtained. The results appear to be pH dependent.

The complexing of carrier-free Cb^{95} by organic substances of biological significance is being studied. The removal of Cb^{95} from a pyrex surface is being used to evaluate the complexing agents. Rate and equilibrium data will be obtained.

Several separate reports on the preparation of carrier-free radioisotopes have been written for publication.

II BIOLOGICAL STUDIES OF RADIATION EFFECTS

J. H. Lawrence - in charge

Project 48A-II

Effects of Total Body X-Irradiation on Blood Coagulation in the Rabbit (Preliminary Study)

Robert L. Rosenthal and Agnes L. Benedek

Introduction

Hemorrhage has long been recognized as a serious and important consequence following the exposure of man and other species to ionizing radiation. Because of a lack of knowledge concerning its exact mechanism, no effective method has been available either for the treatment or prevention of this hemorrhagic disease.

The thrombocytopenia produced by radiation has generally been considered the most important causative factor in the bleeding. Allen[1], Jacobson and associates have recently reported finding in the blood of irradiated dogs[1] and rabbits[2] an anticoagulant, similar to heparin. This was demonstrated by a prolonged clotting time which could be restored to normal upon the addition of heparin antagonists such as toluidine blue or protamine. They believe that this heparinemia is the most important factor in the hemorrhage following X-irradiation and thus that the platelet changes are of secondary importance. Field and Rekers[3] in the dog; Kohn, Robinett and Cupp[4] in the rat; Holden, Cole, Portmann and Storaasli[5] in the dog; and Rosenthal[6] in the mouse could not demonstrate a heparinemia follow-in X-irradiation.

This is a preliminary study upon the blood coagulation and hematological responses of rabbits to single doses of total body X-irradiation (200 to 1000 r). The prognostic significance of a serum opalescence, appearing in these rabbits 24 hours after radiation, was presented in a previous report[7].

Materials and Methods

Animals. Twenty healthy, adult rabbits, chiefly of the New Zealand white strain, maintained on a standard laboratory diet, were used.

Procedure of X-Irradiation. The rabbits were given over the whole body 200 kilovolt X-rays in a single dose. The dosage was measured in air by a Victoreen ionization chamber situated at a point corresponding to the lower portion of the animal. One mm. aluminum and 1/4 mm. copper filters were used. The distance from the filter to the top of the animal was about 10 inches. The dose rate averaged between 40 to 50 r per minute. Animals were given the following doses:

200 r	1 rabbit
400 r	3 rabbits (2 rabbits given 400 r 28 days after first dose)
800 r	8 rabbits
1000 r	10 rabbits

Hematological Studies. Red and white cell counts, differential counts and platelet counts were performed on blood obtained from an ear vein, according to routine laboratory procedure. For the platelet counts, Rees-Eckers diluting fluid and the red cell pipette were used. The absolute values for the heterophils and lymphocytes were calculated from the white cell count and differential.

Coagulation Studies Upon Whole Blood. These tests were done upon blood obtained by cardiac puncture performed on the animals lightly anaesthetized by intraperitoneal nembutal (1 to 1.5 grains). Five cc. of blood were sufficient for all coagulation tests. These were performed in a constant-temperature water bath set at 37 degrees centigrade.

Clotting Time. (Modification of the Lee-White technique.) One-half cc. of blood was placed in each of 2 dry Pyrex tubes, 10 mm. in diameter. The first tube was examined at half-minute intervals until a solid clot formed, at which time the second tube was examined. As there was no significant difference between the trend of clotting times of either tube, only the results for the first tube are reported.

Clot Retraction Rate. This measure was obtained from electric resistance measurements of blood as it clots. This technique has been described in previous publications[8,9,10]. The clot retraction rate, expressed in ohm-cm. per minute, represents the rate of increase of the electric resistance of clotting blood. It provides a quantitative measure of the speed and degree of clot retraction.

Initial Blood Resistance. This is a measure of the specific electric resistance of blood before it clots. This measurement is chiefly a function of the red cell volume and, accordingly, bears a high correlation to the hematocrit or packed red cell volume.

Clot Retraction by Inspection. The tubes used for the clotting time and electric resistance measurements were examined for the presence of clot retraction at 1, 4 and 24 hours. Clot retraction was recorded as present, fair, poor or none.

Coagulation Studies upon Oxalated Plasma. 2.25 cc. of cardiac blood were mixed with 0.25 cc. of .1 M sodium oxalate and centrifuged for 15 minutes at medium speed in a clinical centrifuge. The plasma was removed and was used for various tests; namely, the recalcified plasma clotting time, toluidine blue titration and heparin clotting time. Clotting times were performed upon a basic system composed of 0.1 cc of plasma to which 0.1 cc of .025 M calcium chloride was added. Tubes were then examined at 15 second intervals for the presence of a firm clot.

Recalcified Plasma Clotting Time. Clotting times were obtained after the addition of none, .05 cc. and .1 cc. of isotonic sodium chloride to the plasma in the basic

system described above. These tests served also as controls for the tests described below.

Toluidine Blue Titration Test. Clotting times were obtained after recalcification of plasma to which were added each of the following amounts of toluidine blue* in .05 cc of saline: .0015, .0031, .0062, .0125, .025 and .05 mg.

Heparin Clotting Time. Clotting times were obtained after recalcification of plasma to which was added .001 mg. of heparin in .1 cc. of saline.

Experimental Procedure

The hematological studies and coagulation measurements on whole blood were performed on all animals before X-irradiation and at various intervals for a period of 30 days after irradiation. Coagulation tests on recalcified plasma were performed upon rabbits #1 to #9. In addition, all animals were followed with respect to weight changes and clinical evidence of bleeding. Post mortems, consisting of the gross examination of tissues, with emphasis upon evidence of hemorrhage, were performed upon most of the animals.

Results

Table I summarizes the results pertaining to coagulation and hemorrhage.

The red cells consistently showed an increase at 4 hours after radiation and a slight decrease until 18 days at which time there was a gradual return to normal. The lymphocytes showed a maximum reduction of 85 percent of the pre-irradiation level at 24 hours, followed by a gradual increase. At 28 days, there was a depression of 66 percent. The heterophils showed a rise to twice the pre-irradiation level at 24 hours. At 3 days, there was a decrease of 72 percent. Recovery towards the control values was almost complete at 28 days. The initial electric resistance of blood showed a fall of 10 percent at 24 hours. Its change thereafter was similar to that of the red cell count.

The clotting time showed no significant prolongation at any time. Pre-irradiating clotting times ranged from 3 to 15.5 minutes, while the highest post-irradiating clotting time was 16.5 minutes. The platelets began to decrease 24 hours after radiation and showed a maximal average depression of 42 percent between 8 and 11 days. Thereafter, a gradual increase occurred but at 28 days the platelet counts were slightly below the pre-irradiation levels. The clot retraction rate showed a marked decrease from an average of 7 ohm-cm. per minute to 3.9 ohm-cm. per minute after 24 hours. The pattern of change over 28 days was similar to that for the platelets, except greater in magnitude. The maximum depression at 8 to 10 days averaged 73 percent. Estimation by inspection gave little indication of these variations in degree of clot retraction.

---

* Toluidine blue O, made by National Aniline Division, Allied Chemical and Dye Corp., New York, N. Y. Total dye content 69 percent.

TABLE I

EFFECT OF TOTAL BODY X-IRRADIATION ON COAGULATION TESTS AND APPEARANCE OF HEMORRHAGE IN RABBITS

Rabbit	X-ray dose	Day died after radiation	Cause of death +	Evidence of hemorrhage		Clotting time of blood (Min.)			Platelet Count			Clot retraction rate			Toluidine blue titration test for heparinemia
				Clinical	Post-mortem (gross)	Before x-ray	Highest value	after X-ray	Before X-ray	Lowest value	after X-ray	Before X-ray	Lowest Value	after X-ray	
	r					Minutes		Day	x10^3		Day	Ohm-cm./min.		Day	
2	200	-*	-	None	-	3	10	3,20	350	220	9,16	7.6	2.7	27	Neg
1	400	-*	-	None	-	3	9	16	360	140	16	7.0	2.3	20	Neg
1	400	34	Sac	None	None	7	9.5	9	320	190	16	7.0	1.0	20	Neg
2	400	34	Sac	None	None	2.5	13	1	290	170	9	2.7	2.2	9	Neg
3	800	32	Sac	None	None	15	12.5	7	460	180	9	8.2	0.7	9	-
7	800	5	Rad	None	Slight	7.5	10	1	660	440	4 hr	3.3	-	-	Neg
8	800	2	Rad	None	None	9.5	16.5	1	440	280	1	3.3	(3.7)	(1)	Neg
10	800	16	Oth	None	Slight	9	16.5	1	550	290	8,11	9.5	2.9	11	-
11	800	31	Sac	None	-	5.5	14	1	320	270	3	12.4	2.0	8	-
12	800	9	Oth	None	Slight	8	14	9	440	280	9	8.7	1.4	9	-
13	800	31	Sac	None	-	10.5	12	9	390	280	17	9.4	1.8	3	-
5	1000	5	Rad	Sl.	Slight	4	11	1	550	300	4 hr	5.2	4.4	3	Neg
9	1000	30	Sac	None	-	8	10.5	4	490	250	8	6.5	1.6	8	Neg
14	1000	10	Oth	None	Mod.	-	7	3	340	190	7	-	1.4	7	-
15	1000	1	Rad	None	None	3	8.5	1	310	390	1	-	(3.1)	(1)	-
16	1000	35	Sac	None	-	3.5	13	3	290	210	10	3.2	1.2	10	-
17	1000	1	Rad	None	None	4.5	-	-	310	250	4 hr	7.1	-	-	-
18	1000	1	Sac	None	None	15.5	9.5	1	280	290	4 hr	-	-	-	-
19	1000	1/6	Rad	None	None	7.5	-	-	300	-	-	-	-	-	-

*400 r given on 28th day after first irradiation.

+Sac-sacrificed; Rad-radiation (cause unknown); oth-#10 and #12 died shortly after the administration of nembutal; #14 died 1/2 hour after cardiac puncture, marked hemopericardium present.

Coagulation tests performed upon plasma showed a consistent increase of almost twice the pre-irradiation value at 6 to 10 days after radiation with a subsequent return to normal.

The heparin clotting time increased up to 2-1/2 times at 4 to 16 days after exposure. The different amounts of added saline produced slight but inconsistent variations in the clotting time. The toluidine test was negative at all times for the presence in the blood of excessive or neutralizable heparin. A suspicious lowering by 15 to 45 seconds of the control clotting time for the smallest toluidine blue concentration (.000 5 mg.) 8 or 9 days following radiation in some of the animals could not be considered significant.

The anticoagulant effect of toluidine blue showed marked increases following radiation. This effect was most marked 4 to 10 days after radiation, especially for the highest toluidine blue concentration.

No clinical evidence of bleeding was apparent except for one animal, as shown in Table I. This animal showed a bloody discharge from the nostrils shortly before death. At post mortem, gross examination revealed some evidence of bleeding in 5 of 13 rabbits. This usually consisted of blood and blood clots in the thorax and pericardial sac which can be attributed to the cardiac puncture. None of the 6 rabbits which presumably died as a direct effect of the radiation showed any unusual hemorrhage or clotting reaction.

A slight elevation of the erythrocyte count was noted immediately after irradiation. This effect was gone by 12 hours. In a series of 17 rabbits the elevation at 4 hours proved to be statistically significant by using the Student t test:

Before x-ray	red cell count	6.24 million
4 hours after 400 to 1000 r x-ray	red cell count	6.77 million

The difference is significant at the 1 percent level.

This series is too small to evaluate the dose-effect relationship in this study. In general, it appeared that the hematological and coagulation alterations were more marked in the animals receiving the higher dosages and that these animals showed the maximum coagulation depression sooner after the radiation.

Discussion

The changes in the red cell, heterophil and lymphocyte counts are in agreement with those reported by Jacobson and associates[11]. These changes serve as an index confirming that the animals received and reacted to the approximate amount of X-irradiation given.

The alterations in the platelet count, clot retraction rate, plasma clotting time, heparin clotting time and toluidine blue titration test indicate a definite

impairment of coagulation following all the doses of radiation (200 to 1000 r). This impairment could be detected 24 hours after radiation, was most severe between 6 to 10 days, and had almost disappeared by 28 days. The depression in platelet count and function can account to a large extent for the changes in the various coagulation tests. The clot retraction rate, which provides a sensitive measure of this phenomenon, shows a high correlation with the platelet count[9,10]. The recalcified plasma clotting time has been shown to vary inversely with the reduction of the number of platelets by increased amounts of centrifugation[12,13,14]. As indicated by Jacques and associates[15], a thromboplastin factor independent of the platelets also may be involved in this reaction. A review of the literature and other experiments in this laboratory indicate some relation between the increased effect of heparin upon the clotting time and a thrombocytopenia[9,10].

The increased clotting sensitivity to toluidine blue following x-irradiation has not previously been reported. Since the mechanism of the anticoagulant action of toluidine blue is not known, the significance of this finding can only be surmised. This effect appears to be related in part to the platelets. It is most marked at the period of greatest platelet reduction and is accentuated by centrifugation of the plasma.

No significant prolongation in the clotting time of blood occurred at any time. This finding and the results of the toluidine blue titration test do not indicate the presence of free or excess heparin in the blood (heparinemia) following x-irradiation, as has been reported by Allen and Jacobson[1,2]. Other investigators have been unable to demonstrate a heparinemia in the dog, rat and mouse[3,4,5,6]. It is possible that there is a species difference in tendency towards a heparinemia response to x-irradiation as appears to be the case in anaphylactic and peptone shock[9].

A species difference also exists in the extent of the hemorrhagic syndrome following x-irradiation. Hemorrhage was inconspicuous in the rabbit in this study, while it is generally prominent in the dog, guinea pig and possibly man. The rat and mouse resemble the rabbit in this respect. The explanation for these differences is not known but it may be related to species differences in heparin physiology and properties which were revealed by a critical review of the literature[9].

Evaluation for the various species of the relative importance of each of the main coagulative and hemostatic factors in the hemorrhagic syndrome following x-ray is essential in order to understand, treat and prevent it. These factors appear to be: platelet function, capillary wall integrity and anticoagulants in the blood as in heparinemia.

Summary

1. Following exposure to single doses of total body x-irradiation ranging from 200 to 1000 r, rabbits show a coagulation impairment characterized by a thrombocytopenia, diminished clot retraction, increased clotting time of recalcified plasma, and increased clotting times after the addition of either heparin or toluidine blue. These changes can be attributed chiefly to the diminished platelet count and function.

2. No free or excess heparin could be demonstrated in the blood following radiation, as evidenced by the lack of significant prolongation of clotting time and the negative toluidine blue titration test.

3. The rabbit, in contrast to the dog and guinea pig, shows an inconspicuous hemorrhagic response following x-ray exposure. The importance of species differences in the clotting and hemostatic mechanism and its response to x-irradiation and other agents is suggested.

Bibligraphy

1. Allen, J. G., Sanderson, M., Milham, M., Kirschon, A., and Jacobson, L. O.: Heparinemia (?). J. Exp. Med., 87: 71, 1948.

2. Jacobson, L. O., Marks, E. K., Gaston, E., Allen, J. G., and Block, M. H.: The Effect of Nitrogen Mustard and X-Irradiation on Blood Coagulation. J. Lab. and Clin. Med. 33: 1566, 1948.

3. Field, J., and Rekers, P.: Ionizing Irradiation Disease and a Study of the Protective Nature of Flavonones. Manhattan District Declassified Document No. 1672, 1948, P. 25.

4. Kohn, H. I., Robinett, P. W., and Cupp, M. N.: The Effect of Rutin Upon the Response of the Rat to Total Body X-Irradiation. Atomic Energy Commission Declassified Document No. 2176, 1948.

5. Holden, W. D., Cole, J. W., Portmann, A. F., and Storaasli, J. P.: Hypothromboplastinemia Following Total Body Irradiation. Proc. Soc. Exp. Biol. Med. 70: 553, 1949.

6. Rosenthal, R. L.: Studies on the Effect of Total Body X-Irradiation on Mast Cells and Coagulation in the Mouse. In preparation.

7. Rosenthal, R. L.: Opalescence of Serum after Total Body X-Irradiation as a Prognostic Sign of Death. Science. 110: 43, 1949.

8. Rosenthal, R. L., and Tobias, C. W.: Measurement of the Electric Resistance of Human Blood; Use in Coagulation Studies and Cell Volume Determinations. J. Lab. and Clin. Med. 33: 1110, 1948.

9. Rosenthal, R. L.: Blood Coagulation in Polycythemia and Leukemia; Relation of Heparin and Platelets; Quantitative Measure of Clot Retraction and Heparin Clotting Time. University of California Radiation Laboratory Report No. 332, 1949, p. 25.

10. Rosenthal, R. L.: Blood Coagulation in Leukemia and Polycythemia; Value of the Clot Retraction Rate and Heparin Clotting Time. To be published.

11. Jacobson, L. O., Marks, E. K., and Lorenz, E.: The Hematological Effects of Ionizing Radiations. Radiology. 52: 371, 1949.

12. Mosen, R.: Die Herstellung wagbarer Mengen von Blutplattchen. Arch. f. Anat. u. Physiol., Physiologische Abtheilung., 1893, pp. 352-370.

13. Lee, R. I., and Vincent, B.: The Coagulation of Normal Human Blood; and Experimental Study. Arch. Int. Med. 13: 398, 1914.

14. Nygaard, K. K.: Hemorrhagic Diseases, C. V. Mosby Co., St. Louis, 1941, p. 96

15. Jacques, L. B., Fidlar, E., Feldsted, E. T., and MacDonald, M. A.: Silicones and Blood Coagulation. Can. M. A. J. 55: 26, 1946.

The Elimination of C^{14} Administered as $BaCO_3$

Hardin B. Jones

Laboratory dusts and glassware splinters are significant laboratory hazards to personnel in studies involving the use of C^{14}. Quantative studies of dust inhalation, fixation and exchange are difficult to make and for this reason the two following aqueous colloidal suspensions of $BaCO_3$* were used in intravenous and interstitial administration.

Barium Carbonate Exchange in Lung Tissue of Mice - J. Govaerts**

Barium Carbonate (C^{14} labeled) suspensions were prepared and injected intravenously into mice. Immediately after injection most of the material was contained in the lungs; practically no C^{14} was found in the other soft tissues. The $BaCO_3$ so fixed principally in the pulmonary tissue exchanged rapidly with bicarbonate so that 85 percent was eliminated as CO_2 in 12 hours. This elimination was characterized as a two process exponential function in which 60 percent and 40 percent of the administered $BaCO_3$ were eliminated at half-times of 1 hour and 9 hours respectively:

$$\text{Percent Eliminated}_t = 60\ \%\ (1-e^{-.69t}) + 40\ \%\ (1-E^{-.077t})$$

The 15 percent which still remains in the tissues at 12 hours is apparently still exchanging at the instantaneous rate, k = 0.077, of 7.7 percent per hours, within the limit of experimental measurement. It is estimated that if <u>any</u> of the administered $BaCO_3$ remains in the tissues in a non-exchangeable form, it must be of the order of 1 percent of the amount injected.

The above study establishes the rapidity of exchange of $BaCO_3$ in contact with tissue. There is, however, reason to believe that the situation in the lung of an inhaled dust particle may differ in site and mechanism of exchange from the intravenously deposited particles. A final experiment was made in which a single mouse insufflated a drop of the $BaCO_3$ suspension placed in the nose while in the anesthesized state. The precise amount reaching the lungs is doubtfully recorded (due to contact with the nasal pharynx, splattering, and possible swallowing.) However, 70 percent of the amount (probably as much as was in physiological contact with the mouse) delivered to the nose had been recovered in the expired CO_2 from the mouse by 7 hours, indicating an even more rapid exchange than that of the $BaCO_3$ administered intravenously.

---

* This $BaCO_3$ was prepared in the usual manner of precipitation, drying and heating laboratory samples of C^{14}. The heating process particularly produces a change in the $BaCO_3$ such that its exchange with atmospheric CO_2 is significantly reduced, a fact that should make it a more significant hazard in personnel contamination.

**While on leave from the Laboratory of Radioactivity and Nuclear Physics, University of Liege, Liege, Belgium.

It is implied that Barium Carbonate ingested, injected, or inhaled is rapidly exchanged with bicarbonate and eliminated from the body. In the mouse these dilute suspensions so introduced are accountably eliminated at the rate of approximately 7 percent per hour or faster.

The Elimination of Barium Carbonate Paste From Tissue Wounds - Robert Delcourt*

After traumatic introduction of about 3 milligrams (0.5 microcuries of C^{14}) as $BaCO_3$ in the muscles of adult mice, approximately 80 percent remains at the site from 2 days to 33 days. Five to seven percent is eliminated through the lungs as CO_2 during the first 24 hours and 3 to 5 percent may be eliminated by other pathways. These data concern only compact $BaCO_3$ and the amount of elimination is increased 3 to 4 times when the $BaCO_3$ is introduced in fine powder allowing a much larger surface to be reached by the tissue fluids. The exchange of these relatively large masses of $BaCO_3$ is greatly slowed as they contract and become encased in a connective tissue sac.

---

* A Fullbright Foundation Fellow while on leave from Institute for Nuclear Research, University of Brussels.

III BIOLOGICAL EFFECTS OF RADIATION FROM EXTERNAL AND INTERNAL SOURCES

Robert S. Stone - in charge

Project 48C

University of California Medical School

Hematological Effects of Total Body Irradiation

B. V. A. Low-Beer

There are no significant changes to report at this time.

Metabolism and Effects of Radio-Iodine (I^{131})

Earl R. Miller

Ionization Chamber Studies. Several hundred measurements have been made of the gamma rays emission from the necks of patients who were given I^{131} using both a Geiger Counter and a freon filled ionization chamber. The chamber used was 2 inches in diameter and 10 inches long, and the ionization current was amplified and read on a microameter. The sensitivity of this combination was so low that the chamber had to be placed in contact with the neck of the patients receiving only test doses. The results showed that if the Geiger Counter measurements are taken as standard, the ionization chamber measurements are not reliable. The ratios of the gamma ray output as measured by the two methods varied from about .7 to 1.3 in the same patient when the measurements were taken at various times. No correlation was found in the early or the late measurements. The lack of correlation probably depends on the fact that slight differences in the distance between the chamber and the thyroid makes a significant difference in the readings. For the present, work with this ionization chamber has been discontinued.

A second freon filled ionization chamber has been obtained that is larger and has greater sensitivity. It is now being calibrated. It is hoped that it will be usable as a clinical instrument of great stability and simplicity.

The accurate determination of the size of the thyroid is of paramount importance in determining the radiation dose to the thyroid when a subject has been given I^{131}. Some idea of the size of the thyroid might be obtained if one measurement could be made under conditions such that the results were independant of the size of the thyroid and another measurement could be made under conditions such that the results were highly dependent upon the size of the thyroid. It is hoped that a comparison of the measurements made with the ionization chamber in contact with the neck with those made with the Geiger Counter at a great distance from the neck will accomplish this. Further studies along this line will be made.

Carcinoma of the Thyroid. Up to the present time, 56 patients having carcinoma of the thyroid have been studied. The studies have included at least the following: a test dose of I^{131}; a biopsy 48 hours later; and a determination of the amount of I^{131} in the tumor tissue by Geiger Counter and radioautography. The radioiodine was sufficiently concentrated in the thyroid of only two of the patients to make a therapeutic attempt with the I^{131} reasonable. One of these is being treated now. Studies of blood changes and blood chemistry are in progress. The second patient has no symptoms and is not being treated even though he has widespread metastases.

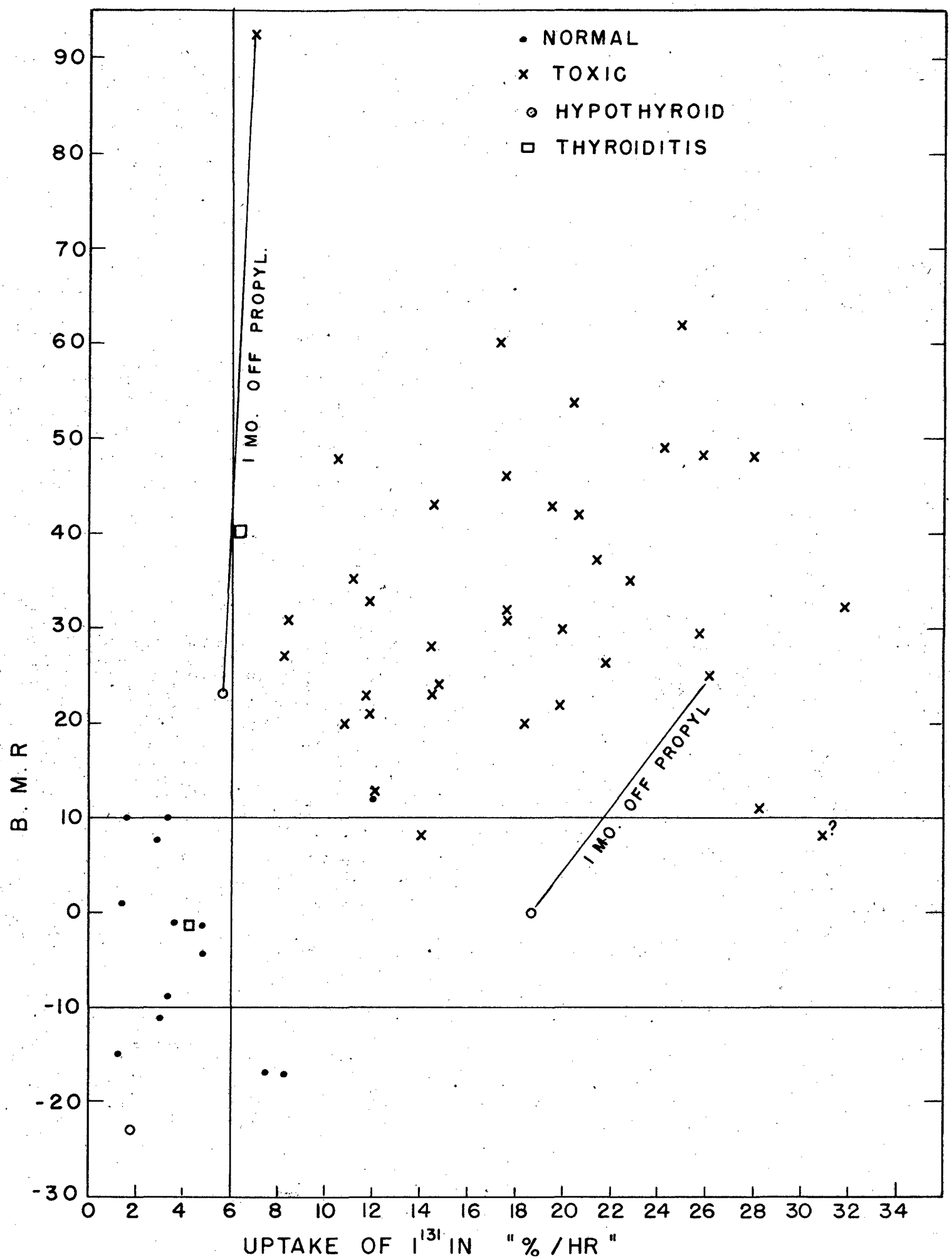
Total thyroidectomy, destruction of the thyroid by I^{131}, administration of thyroid stimulating hormone, and diet low in iodine have been tried to determine whether or not these measures would affect the uptake of I^{131} in tumors that initially did not concentrate I^{131}. So far none of these measures has had any effect. Thiouracil derivatives are to be tried next in high doses - (up to 1-1/2 gms/day for months).

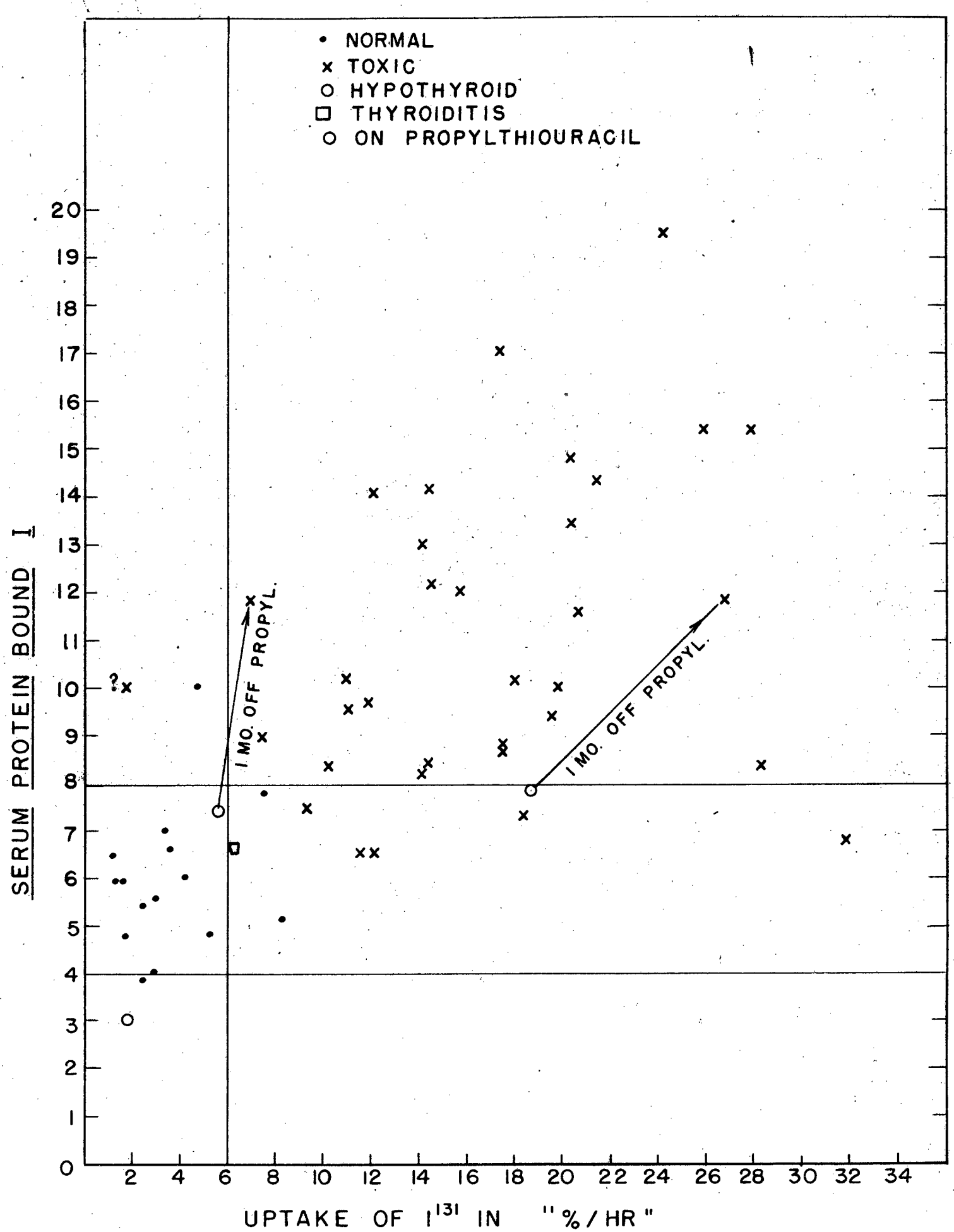
Studies on Patients with Normal Thyroid Function. A group of patients with various mental diseases was studied clinically and shown by clinical observation and laboratory results to be within normal limits as regards thyroid function. These patients were given I^{131} and uptake curves were made on them. The psychiatrists had hoped that this test might show significant variations from the normal in the different diseases. No such differences were found. This study by Dr. Karl M. Bowman, Dr. Earl R. Miller, Dr. Morris Dailey, Dr. Alexander Simon, Dr. Berdeen Frankel and Miss Genevieve Lowe, technician, permits us to observe the variations in the uptake curves in a group of normals. The results are to be published in the Journal of the American Psychiatric Association.

Uptake of I^{131} in the Thyroid Correlated with Clinical Evidence of Thyroid Toxicity. One hundred thyrotoxic patients have been studied with I^{131}. The disease in these patients varied from mild to severe. Attempts were made to correlate the various phases of concentration of I^{131} in the thyroid with clinical evidence of toxicity by means of graphs. The curve has a sharp rise, a maximum, and a fall-off portion. The "percent per hour" uptake of I^{131} in the early part of the study is determined usually at three hours after the dose has been given. The "percent per hour" is the percent of the total dose concentrated in the thyroid divided by the time. The three hour time was chosen because data was available and because this time is long enough so that small variations in absorption time will not play too significant a role. In the group in which data has been studied, it appears that there is excellent correlation between the "percent per hour" uptake in the early part of the absorption curve and the clinical evidence of toxicity. The results show that normal individuals will usually take up between one and six "percent per hour" while those with definite evidence of toxicity will usually take up over nine "percent per hour". (See graphs)

There is a fair correlation between the clinical evidence of toxicity and the maximum uptake and there seems to be no correlation between the so-called biological half life and the toxicity.

Further Studies. We plan to continue the studies on patients who have been given tracer, test or therapeutic doses of I^{131} for Graves disease, carcinoma of the thyroid and for study of other conditions. The ionization chamber studies will be pursued. Variations in the uptake curves will be studied in patients who have been given various drugs which affect the thyroid. An attempt will be made to set up chemical studies of the protein bound fraction of iodine in the serum using I^{131} as a tracer in normals and in patients with thyroid disease.


NORMAL
TOXIC
HYPOTHYROID
THYROIDITIS
1 MO. OFF PROPYL.
1 MO. OFF PROPYL
B. M. R
UPTAKE OF I131 IN "% / HR"
90
80
70
60
50
40
30
20
10
0
-10
-20
-30
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34


• NORMAL
× TOXIC
○ HYPOTHYROID
□ THYROIDITIS
○ ON PROPYLTHIOURACIL
SERUM PROTEIN BOUND I
UPTAKE OF I131 IN "%/HR"
1 MO. OFF PROPYL.
1 MO. OFF PROPYL.
?
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
2
4
6
8
10
12
14
16
18
20
22
24
26
28
30
32
34

13942-1

IV HEALTH CHEMISTRY AND PHYSICS

Health Chemisty

N. B. Garden

Monitoring. The monitoring personnel of the Health Chemistry group have made progress in their program for increased use of protective equipment, such as tongs, pipette manipulators and shields, especially by chemists working with radioisotopes. Likewise the chemists have found favorable the use of finger films available for checking radiation on the hands. There is continuous evidence that for successful and safe radiochemistry it is necessary that the chemist and health chemist must work in close cooperation. The chemist, must be persuaded and educated to be aware of the benefits derived from the use of already existing devices and he must aid the health chemist by making known his needs for new types of equipment.

Transportation, Decontamination, Disposal and Storage. Continuing developments in the handling of cyclotron bombardment targets has taken place; installation of a pneumatic tube for quick transfer of targets from the cyclotron to the chemistry laboratories, especially for short-lived targets, has begun. This device will be an asset to the chemist from a scientific standpoint and will reduce radiation hazards to the handlers.

Research and Development.

Unique remote control devices for use with both a straight-type lead wall cave and a one inch portable lead shield surrounding a Berkeley box processed the samples successfully from both a scientific and a health standpoint. New general equipment developed also includes a universal pipettor for microchemistry, a remote stirring device for use in an yttrium-processing box, long tongs for handling radioactive foils, a nitric acid mist separator for use with filtering systems on gloved and manipulator boxes, a hood for electrodeposition involving radioactive material, modified high-capacity blowers for use with alpha-enclosing gloved boxes, and a modified gloved port for the Berkeley gloved box with added safety factors and increased ease of changing gloves.

Health Physics

B. J. Moyer

Radiation Field of 184-inch Cyclotron. Measurements of the penetration in the concrete shielding of the radiation developed by the 184-inch cyclotron when producing 340 Mev protons have shown that the primary neutrons in the forward direction from the target are attenuated with a half-value thickness of 18 inches. The attenuation of the equilibrium radiation in other azimuths from the proton beam direction shows 11 inch to 13 inch half-value thickness.

These results indicate that in any azimuth very high energy neutrons are penetrating the shielding, and it is necessary to estimate the flux density of such particles outside the shielding. Further point is given to such measurements by the fact that these neutrons are sufficiently energetic to produce stars, and the biological damage produced by the intensely concentrated ionization of the star fragments is not experimentally known.

Purely on the basis of considerations of energy dissipation within the body tissue, one can calculate from tissue composition and recently measured cross sections that the tolerance flux density of high energy neutrons in the region of 100-200 Mev would be about 100 $cm^{-2}sec^{-1}$. But this does not take account of the unknown rem/rep ratio for the star fragments and recoil nuclei. If this ratio is even no larger than 10 the tolerance flux density is 10 $cm^{-2}sec^{-1}$, which is quite low indeed.

Experimental measurements to estimate the existing flux density have been made with a Bi fission chamber, whose threshold energy for neutrons detected is about 50 Mev. This was roughly calibrated by counting in the fast neutron beam flux from the target at 0° where the flux density is approximately known.

The measurements indicate a flux ranging from 0.5 to 2 neutrons/cm^2sec over 50 Mev, depending upon azimuth with respect to the 0.5 microampere proton beam.

Because of anticipated higher beams, and in view of the unknown rem/rep ratio, it has been decided to add yet five more feet of concrete in certain azimuths around the cyclotron.

Radiation Field of the Linear Accelerator. This accelerator has only recently (as of July 1) resumed operation after an extensive rearrangement of shielding and facilities to create safer and more convenient working conditions.

Complete measurements of its radiation are not yet in hand. It seems clear, however, that the neutron intensities outside the target-end shielding enclosure are at present yet too high at maximum beam. Simple additions to the shielding, and closure of some remaining apertures should reduce this intensity satisfactorily.

Radiation Field of Synchrotron. In order to obtain an approximate measure of energy absorption by a human body in the synchrotron radiation field, a phantom with a variable-size ionization chamber is under construction.

Statistical Summary of Monitoring Program. Survey Instruments maintained:

1. B-V ionization chambers	28
2. Victoreen 263 portable survey meters	19
3. I.D.L. portable survey meters	18
4. Cutie pies	2
5. Recording γ-intensity meters	10
6. Victoreen proteximeters	3
7. Fast neutron proportional counter	1
8. Slow neutron proportional counter	1
9. Balanced chamber (slow neutron survey instrument)	1
10. Special tissue wall survey instrument	1

Personal meters in use:

1. Number of people wearing film badges	1,250
2. Total man days coverage with pocket chambers	1,481
3. Total man days coverage with pocket dosimeters	3,042
4. Total man days coverage with pocket chambers, s.n.	2,915

Cases of weekly exposure above .3 r

Weekly Film Exposures Above	184 inch Area	60 inch Area	Linear Accelerator	Synchrotron	Chemistry	Total
0.3 r	6	9	5	-	19	39
0.5 r	2	1	1	-	6	10
1.0 r	-	-	-	-	2	2
1.5 r	-	-	-	-	1(2.7r)	1

LMB/8-15-49
Information Division

DECLASSIFIED

[redacted]