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Special Review of
Declassified Reports

Authorized by USDOE JK Bratton

Unclassified TWX P182206Z May 79

REPORT PROPERLY DECLASSIFIED

JU Green — AUG 21 1979

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I THE METABOLIC PROPERTIES OF VARIOUS MATERIALS

Joseph G. Hamilton, M.D.

Project 48A

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TRACER STUDIES

Kenneth G. Scott

Metabolism of Fission Products.

Preliminary studies have been continued on the metabolism of fission products which were available at and obtained from Oak Ridge. These studies were conducted on rats after the fission products were made physiologically compatible. They were administered to rats by intravenous injection and by intragastric administration. Time studies at 1 and 16 days were conducted after intravenous injection. These data are presented in Table I. It can be seen from examination of this Table that the distribution in the tissues of the rats was similar to that which was obtained from earlier studies of fission products; for example, a large percentage of the material administered was recovered from the skeleton and from the liver, with relatively small amounts of excreted in the urine and feces.

Animals which were sacrificed 8 days after intragastric administration showed a relatively small percentage of the material given was absorbed. Therefore, at 8 days, of the material which was given, less than 0.01 percent was found in any gram of wet weight tissue, with the exception of the skeleton, which showed 0.02 percent of the dose per gram. These data are summarized in Table II.

Because of the uncertain age of the fission products as supplied by Oak Ridge and the lack of information as to the actual elements present in the mixture, it was decided that this type of material would not be suitable for chronic contamination studies in monkeys. The fission products had a half-life of approximately 43 days when they were received from Oak Ridge. As is characteristic with this material, this became longer and was approximately 73 days when the tissues were taken from the animals and counted. See Fig. 1 for decay curve. A mass absorption curve, which is characteristic of this material, is shown in Fig. 2.

Cyclotron Produced Fission Products.

One uranium target has been bombarded in the 60-inch cyclotron and subsequent to this the uranium was separated radiochemically and the resulting material administered to 4 rhesus monkeys and 12 rats as an intramuscular injection. Unfortunately, this material proved to be toxic, due to impurities in the uranium, and contained in milligrams the following elements per 100 ml of solution: copper 300, vanadium 30, iron 30, chromium 30, and uranium 15.

The fission product mixture was 32 days old when it was administered to the monkeys and the rats. The combined half-lives was 9 days at the start of the measurements 25 days after the bombardment. Thirty-five days later the short-lived components had decayed away and resulted in a combined half-life of 30 days.

* Previous Quarterly Report UCRL-1694

This material, because of the difficulty of chemically separating such a large amount of uranium from the fission products and plutonium present is also not suitable. It is hoped that more suitable material may be obtained in the future so that these studies can be continued.

Preliminary studies have been done on the rhesus monkeys with respect to their blood constituents, since these are one of the routine tests which will be employed in the chronic fission products and plutonium intoxication studies after these studies have been set up. A more suitable supply of fission products is forthcoming for these studies from fission products which are to be made available from Dr. Seaborg's group.

Versene Pu Complexing Studies.

Studies upon the effect of calcium EDTA have been continued in order to obtain more information upon the ability of this material to increase the excretion rate of plutonium by rats. In one experiment 4 groups of animals were employed, 3 animals per group. Two groups of these animals were fed CaEDTA in their diet in a concentration of 3.5 percent; this feeding was started 24 hours prior to Pu administration. During the time the plutonium was injected they were given in addition 2 milligrams of CaEDTA intravenously along with the Pu^{238}, which was administered in the +6 state and was complexed with 0.1 m sodium citrate. One group of these animals was sacrificed at 1 day after plutonium administration and the other at 15 days. The control animals were also sacrificed at the same time periods. One day after Versene administration a slightly larger excretion of plutonium occurred in the animals fed and treated with CaEDTA. This increase, however, amounted to only 3.37 percent of the total amount given and was found in the urine, whereas the control animals excreted 0.89 percent. The distribution in the tissues was very similar in both the Versene-treated animals and in the control animals. It was concluded that this method of administration was not particularly efficient in increasing the elimination of plutonium from the body after its intravenous injection or that feeding in the diet was practical in enhancing Pu excretion. These data are summarized in Table III.

Animals killed 15 days after plutonium administration, which had received in addition Versene in their diet as well as that given along with the plutonium did show a fivefold increase in excretion in the urine during the time period studied. This increase in excretion, however, did not reflect any reduction of plutonium in the skeleton and appears to have come from soft tissue deposits. These data are summarized in Table IV.

Additional studies were conducted in larger groups of animals. In this case 10 control animals were given plutonium intravenously in the +6 state complexed with sodium citrate, and the distribution in this group of animals was compared to that obtained in rats which were fed 3.5 percent CaEDTA in their diet 5 days before the plutonium was injected. In addition the animals were given 186 milligrams of CaEDTA intraperitoneally at the same time they were given the plutonium intravenously. In these studies presented in Table V it can be seen that this amount of Versene given intraperiotneally increased the plutonium excretion rate in the urine approximately tenfold during the first day. From the second to the fifteenth day the excretion rate, although higher than the controls, dropped to a lower lever which is not particularly significant in removing large amounts of plutonium from the body. These data agree with earlier studies made in this

laboratory in which animals were fed Versene in their diet for 8 months and showed only a slight reduction in plutonium as compared to the untreated animals with respect to the concentration in the skeleton. These and earlier studies suggest, then, that the oral administration of CaEDTA is not a particularly efficient way of reducing the plutonium content of the tissues and that relatively large amounts of Versene must be given parenterally during the time the plutonium is in a relatively labile state in the body with respect to the blood levels and excretion levels. As can be seen from an examination of Table V, animals treated with large amounts of Versene given intraperitoneally showed a reduction of the plutonium found in the skeleton, this being lower than the controls by a factor of almost 2. Over the entire time period studied the Versene treated animals excreted about 62 percent of the plutonium administered, this being considerably higher than the controls, which was 26 percent.

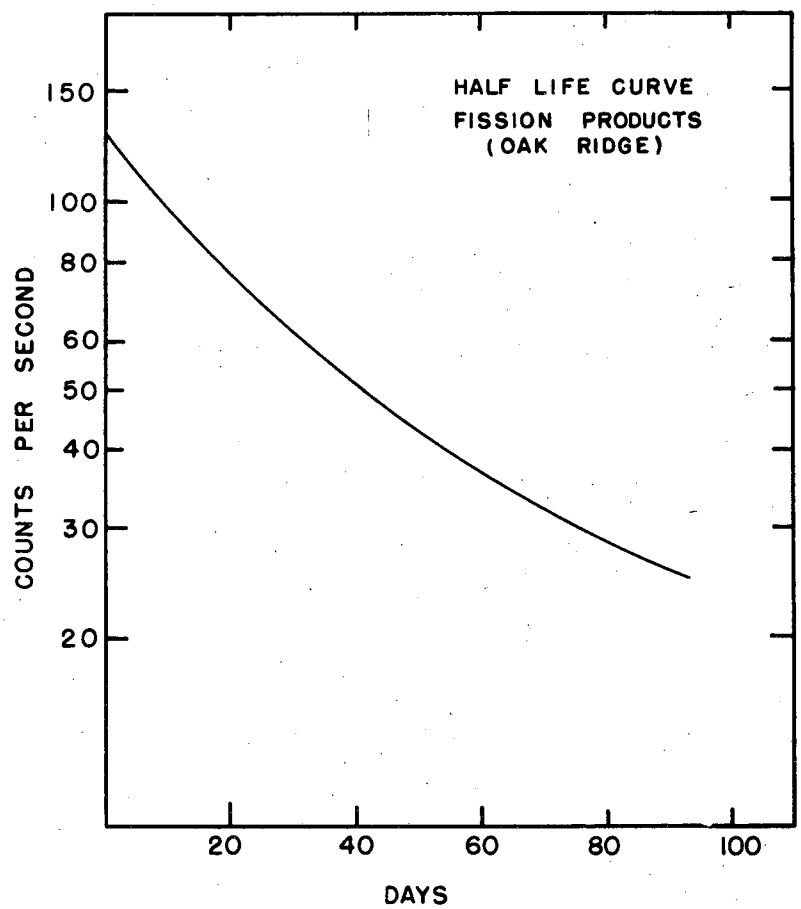
HALF LIFE CURVE
FISSION PRODUCTS
(OAK RIDGE)
COUNTS PER SECOND
150
100
80
60
50
40
30
20
20
40
60
80
100
DAYS

FIG. 1

MU 3782

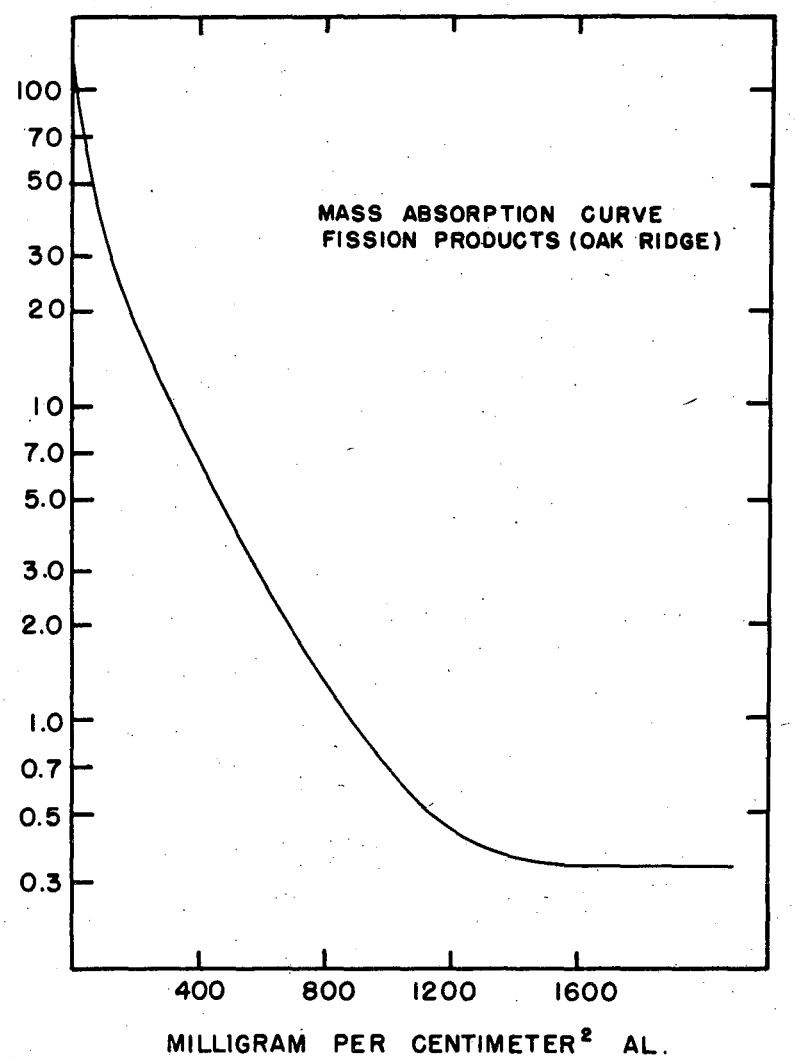
MASS ABSORPTION CURVE
FISSION PRODUCTS (OAK RIDGE)
100
70
50
30
20
10
7.0
5.0
3.0
2.0
1.0
0.7
0.5
0.3
400
800
1200
1600
MILLIGRAM PER CENTIMETER² AL.

FIG. 2

MU 3783

TABLE I

THE DEPOSITION OF FISSION PRODUCTS (OAK RIDGE) IN THE RAT 1 AND 16 DAYS AFTER INTRAVENOUS INJECTION. VALUES ARE CORRECTED FOR RECOVERY AND ARE EXPRESSED IN PERCENT OF DOSE. EACH RAT RECEIVED 10.0 MICROCURIES OF FISSION PRODUCTS.

	1 Day		16 Days	
Tissue	% per organ	% per gram	% per organ	% per gram
Heart	.13	.15	.05	.06
Lung	.25	.18	.17	.10
Spleen	.15	.15	.17	.14
Blood	1.72	.12	.06	<.01
Liver	32.8	3.72	13.2	1.30
Kidney	1.54	.91	.77	.41
Stomach	.18	.17	.08	.06
St. Cont.	.04	-	.01	-
Sm. Int.	.39	.10	.19	.04
S.I. Cont.	.46	-	.06	-
Lg. Int.	.30	.13	.11	.05
L.I. Cont.	1.46	-	.30	-
Pancreas	.08	.06	.07	.05
Skeleton	34.6	1.90	31.8	1.64
Muscle	3.32	.04	2.13	.02
Skin	2.95	.07	1.21	.04
Fat	-	.04	-	.02
Brain	.02	.01	.01	.01
Eyes	.01	.05	.01	.02
Pituit.	<.01	-	<.01	-
Gonads	.02	.12	.01	-
Thyroid	<.01	-	<.01	-
Adrenal	<.01	-	<.01	-
Lym. Gl.	-	.11	-	.11
Urine	11.8	-	16.1	-
Feces	4.53	-	31.3	-

TABLE II

THE DEPOSITION OF FISSION PRODUCTS (OAK RIDGE) IN THE RAT 8 DAYS AFTER ORAL ADMINISTRATION. VALUES ARE CORRECTED FOR RECOVERY AND ARE EXPRESSED IN PERCENT OF DOSE. EACH RAT RECEIVED 100 MICROCURIES.

Tissue	% per organ	%per gram
Heart	<.01	-
Lung	<.01	-
Spleen	<.01	-
Blood	<.01	-
Liver	.02	<.01
Kidney	.01	<.01
Stomach	<.01	-
Sm. Int.	.01	<.01
Lg. Int.	.02	<.01
Pancreas	<.01	-
Skeleton	1.08	.02
Muscle	.50	<.01
Skin	.05	<.01
Fat	-	<.01
Brain	<.01	-
Eyes	<.01	-
Pituit.	<.01	-
Gonads	<.01	-
Thyroid	<.01	-
Adrenal	<.01	-
Lym. Gl.	<.01	-
Urine	1.84	-
Feces	96.5	-

TABLE III

THE EFFECT OF CALCIUM EDTA (ETHYLENEDIAMINE TETRACETIC ACID) ON THE DISTRIBUTION IN THE RAT OF Pu^{238} 1 DAY AFTER INTRAVENOUS ADMINISTRATION OF Pu^{238}. VALUES ARE CORRECTED FOR RECOVERY AND ARE EXPRESSED IN PERCENT OF DOSE. EACH ANIMAL RECEIVED 0.18 MICROCURIES OF Pu^{238} AS PuO_2^{++} IN A SOLUTION CONTAINING 0.1 MOLE SODIUM CITRATE AND 0.01 MOLE SODIUM BROMATE. EACH RAT RECEIVED 2 MILLIGRAMS CaEDTA INTRAVENOUSLY SIMULTANEOUSLY WITH Pu^{238} INJECTION AS WELL AS 3.5 PERCENT CaEDTA IN THEIR DIET STARTING 24 HOURS PRIOR TO THE INJECTION.

	CaEDTA				CONTROL			
Tissue	% per organ	% dev.	% per organ	% dev.	% per organ	% dev.	% per organ	% dev.
Spleen	.65	39.6	.48	28.8	.43	32.7	.38	43.3
Blood	13.2	12.2	.81	9.89	15.7	10.1	.94	23.1
Liver	14.9	17.4	1.36	23.8	11.05	10.3	.94	23.2
Kidney	1.04	13.3	.52	14.4	1.20	19.9	.58	23.8
G.I.	4.21	10.1	-	-	3.56	7.08	-	-
Skeleton	47.1	5.79	3.01	10.0	47.8	3.80	2.99	5.66
Muscle	5.70	23.6	.05	5.85	7.23	10.0	.06	16.4
Skin	7.37	33.3	.14	18.6	9.88	22.3	.19	10.8
Urine	3.37	-	-	-	.89	-	-	-
Feces	2.36	-	-	-	2.23	-	-	-

TABLE IV

THE EFFECT OF CALCIUM EDTA (ETHYLENEDIAMINE TETRACETIC ACID) ON THE DISTRIBUTION IN THE RAT OF Pu^{238} 15 DAYS AFTER INTRAVENOUS ADMINISTRATION OF Pu^{238}. VALUES ARE CORRECTED FOR RECOVERY AND ARE EXPRESSED IN PERCENT OF DOSE. EACH ANIMAL RECEIVED 0.18 MICROCURIES OF Pu^{238} AS PuO_2^{++} IN A SOLUTION CONTAINING 0.1 MOLE SODIUM CITRATE AND 0.01 MOLE SODIUM BROMATE. EACH RAT RECEIVED 2 MILLIGRAMS Ca EDTA INTRAVENOUSLY SIMULTANEOUSLY WITH P^{238} INJECTION AS WELL AS 3.5 PERCENT Ca EDTA IN THEIR DIET STARTING 24 HOURS PRIOR TO THE INJECTION.

	Ca EDTA				CONTROL			
Tissue	% per organ	% dev.	% per organ	% dev.	% per organ	% dev.	% per organ	% dev.
Spleen	.73	37.4	.58	35.5	.55	49.3	.39	55.4
Blood	.45	8.68	.02	3.65	.45	7.84	.02	10.5
Liver	5.72	24.6	.44	23.2	7.73	9.84	.57	26.2
Kidney	.56	24.8	.27	30.0	.57	41.1	.27	50.0
G.I.	.79	28.8	-	-	.76	1.29	-	-
Skeleton	59.1	4.03	3.76	5.71	64.6	4.26	3.78	16.1
Muscle	1.12	18.9	.01	17.5	2.48	25.4	.01	34.4
Skin	2.11	40.7	.05	18.2	1.09	18.2	.01	28.0
Urine	10.5	-	-	-	1.90	-	-	-
Feces	17.6	-	-	-	16.0	-	-	-

TABLE V

THE EFFECT OF CALCIUM EDTA (ETHYLENEDIAMINE TETRACETIC ACID) ON THE DISTRIBUTION IN THE RAT OF Pu^{238} 15 DAYS AFTER INTRAVENOUS ADMINISTRATION OF Pu^{238}. VALUES ARE CORRECTED FOR RECOVERY AND ARE EXPRESSED IN PERCENT OF DOSE. EACH RAT RECEIVED 0.09 MICROCURIES OF Pu^{238} AS PuO_2^{++} IN A SOLUTION CONTAINING 0.1 MOLE SODIUM BROMATE. EACH RAT RECEIVED 186 MILLIGRAMS Ca EDTA INTRAPERITONEALLY SIMULTANEOUSLY WITH Pu^{238} INJECTION AS WELL AS 3.5 PERCENT Ca EDTA IN THEIR DIET STARTING 5 DAYS BEFORE INJECTION AND CONTINUING DURING STUDIED PERIOD. THE DATA PRESENTED ARE THE AVERAGE VALUES OBTAINED FROM 10 ANIMALS IN EACH GROUP, AND ARE GIVEN AS THE PERCENT OF THE DOSE FOUND IN THE WHOLE ORGAN AND PER GRAM OF TISSUE WET WEIGHT.

	Ca EDTA				CONTROL			
Tissue	% per organ	% dev.	% per gram	% dev.	% per organ	% dev.	% per gram	% dev.
Spleen	.36	68.8	.29	84.6	.61	31.5	.77	23.5
Blood	.28	56.0	.018	51.9	.41	47.2	.025	43.6
Liver	3.60	31.9	.39	25.7	8.75	19.2	.88	14.1
Kidney	.49	48.9	.27	50.0	1.36	28.9	.75	27.0
G. I.	.31	42.9	-	-	.88	24.7	-	-
Skeleton	30.57	8.10	2.02	11.6	55.6	17.1	3.64	17.0
Muscle	.70	39.7	.007	41.7	1.41	36.4	.011	39.0
Balance	.90	29.6	-	-	2.69	20.1	-	-
Skin	.51	37.0	.011	26.0	1.47	21.5	.032	20.0
Urine	50.61	-	-	-	6.10	-	-	-
Feces	11.64	-	-	-	20.7	-	-	-

	Ca EDTA		CONTROL	
Excretion days	Urine	Feces	Urine	Feces
1	44.92	1.49	4.56	3.62
2	1.42	2.53	.38	2.32
3	1.03	.69	.21	1.44
4	.70	.95	.18	1.18
5	.48	.75	.17	1.29
6	.36	.69	.10	1.30
7	.30	.67	.10	1.41
8	.27	.59	.07	1.63
9	.21	.46	.07	1.05
10	.22	.62	.06	1.30
11-15	.83	2.22	.24	4.32

RADIOCHEMISTRY

W. M. Garrison and J. Gile Melchert

Separation of Mixed Fission Products from Uranium.

A 20 mil thick uranium foil was bombarded in the 60-inch cyclotron using 19 Mev deuterons for a total of 320 microampere hours. The uranium was separated from the mixed fission products, of the bombardment by an ether extraction method.

Thirty grams of the active uranium were dissolved in concentrated HNO_3. The clear uranyl nitrate solution was evaporated until its boiling point reached 118°C., diluted with water, and re-evaporated to the composition $UO_2(NO_3)_2 \cdot 6H_2O$. Upon cooling and with stirring, the solution solidified to a mass of yellow crystals which, when covered with 1-1/2 times their weight of ethyl ether, dissolved without difficulty. The resulting solution separated into two layers. The aqueous layer was transferred to a beaker and the ether phase washed several times with a small amount of water to remove any fission products remaining in the ether phase.

All the aqueous solutions were combined and a small amount of ether added to extract and reduce the amount of uranium, and to insure complete separation of the original two phases.

The resulting aqueous solution was re-evaporated to crystals of $UO_2(NO_3)_2 \cdot 6H_2O$ and the ether extraction was carried out again. This was done five or six times with continual reductions in volume until no uranium appeared in the solution. The solution was evaporated to dryness on $NaNO_3$ and the dry crystals dissolved in 0.5 N HCl. A small amount of residue appeared which was centrifuged down but which did not carry any activity. The solution was again taken to dryness to remove any nitrates present and redissolved in 2 ml 0.5 N HCl. The HCl solution was diluted to 100 ml, neutralized to pH 4, and submitted for injection.

RADIATION CHEMISTRY

Radiation Induced Effects on Organic Substances in Aqueous Solution

Warren M. Garrison, H. R. Haymond,
J. Gile Melchert, D. C. Morrison, and B. Weeks

Studies of the products resulting from irradiation of aqueous solutions of acetic acid have been continued as part of the general program on radiation induced effects on organic substances in aqueous solution. The general method for these studies is as follows: An aqueous solution of acetic acid, usually containing some $CH_3C^{14}OOH$, is irradiated in an all-glass target assembly with helium ions in the 60-inch cyclotron. After irradiation the acetic acid and the volatile products of irradiation are removed by distillation *in vacuo*. The dry non-volatile products are stored in a freezer between irradiation and analysis to avoid bacterial action. The non-volatile products are separated by a method of partition chromatography on a silicic acid column. In this method, which has been described in detail previously, the products are eluted from the column with a solvent whose composition is gradually changed from pure chloroform to pure butanol. The solvent is forced through the column at approximately 2.5 ml per minute under a pressure of one-half to one atmosphere. The apparatus used for the irradiations also has been described previously.[1] A description of a calorimetric method for determination of the energy of the cyclotron ions is given in a later section of this report.

An elution curve for an irradiation at the level of 4.46×10^{21} ev/ml was given in a previous report.[1] Figures 1, 2 and 3 are elution curves for irradiations of 0.25 M acetic acid, containing $CH_3C^{14}OOH$, at levels of 1.44×10^{20} ev/ml, 5.83×10^{20} ev/ml, and 1.99×10^{21} ev/ml respectively. The eluant in every case was collected in 10 ml samples.

Six non-volatile products have been detected by the partition chromatography method. In the eluant from the column these products usually reach maximum concentrations at 440 ml, 550 ml, 650 ml, 740 ml, 850 ml, and 950 ml. All of these are known to be acids.[1]

Several methods are being used to identify the products. The simplest of these is to run a sample of the product through a silicic acid gel column with a known amount of an acid which is known to elute near the same point and which might be expected as a product of the irradiation. If the irradiated solution contained some $CH_3C^{14}OOH$ the product is active and the titre and activity curves can be compared. Exact correspondence of the curves is a good indication of identical substances. The method can also lead to disqualification of suspected products if the titre and activity peaks do not correspond. In this manner the product corresponding to the peak at 440 ml has been identified as succinic acid.[1] In addition, enough of this product has been produced recently to obtain a melting point (182-184° C. after two recrystallizations from ether) and a mixed melting point with known succinic acid (182-184° C.), which confirm the identity.

[1] UCRL-1694, Medical and Health Physics Quarterly Report, Oct.-Dec., 1951.

The advantage of tagging some of the target acetic acid with C^{14} is clearly shown by our experience in identifying the product which elutes at 650 ml. After an early irradiation of unlabelled acetic acid the product from the 650 ml peak was tentatively identified as glycolic acid.[1] The identification was based on a co-chromatograph with known glycolic acid in which only one broad titre peak was detected in the eluant. A later irradiation of labelled acetic acid provided some labelled product which was run through a silicic acid gel column with known glycolic acid. The titre and activity curves in this case did not exactly correspond (Fig. 4). Another portion of the active product was run through a column with known tricarballylic acid. The correspondence of titre and activity peaks in this case is shown in Fig. 5. In Figs. 4 through 8 the points on the titre curve are shown by crosses and the points on the activity curve by circles.

In attempts to identify some of the products of irradiation, some interesting information on operation of the silicic acid gel column has been obtained. For example, the product which elutes at 850 ml is not malic acid, although it reaches a maximum concentration in the eluant near malic acid, as shown in Fig. 6. Similarly, the product which elutes at 950 ml does not correspond exactly to citric acid when both are run through a silicic acid get column (Fig. 7) and the product eluting at 550 ml does not correspond exactly to malonic acid (Fig. 8). Butane tetracarboxylic acid reaches a maximum concentration near 850 ml but this acid has not yet been run with the active product which comes off the column at this point. Other acids which have been run on the silicic acid gel column with the location of their maximum concentrations are as follows: Pyruvic (290 ml), glyoxylic (450 ml), oxalic (1080 ml), oxalacetic (570 ml), aconitic (500 ml), fumaric (330 ml), and methyl succinic (330 ml).

Yield data for six of the non-volatile products from helium ion irradiation of acetic acid are given for three irradiation levels in Table I. Irradiation data for each of these three experiments are given in Table II. Several other irradiations have been made, the data from which are incomplete and are not included in Table I. These include one at a reduced concentration of acetic acid, two at lower irradiation levels, and one with hydrogen peroxide in the initial aqueous solution of acetic acid. A run has been made with the centrifugal pump target assembly in which 400 ml of 0.25 M acetic acid (not labelled) was irradiated at a level of 4.8×10^{21} ev/ml. Analysis of the products of this run is not complete, but it is believed that milliequavalent amounts of the principal products were produced and that some may be identified by common semi-microchemical procedures.

Several additional helium ion irradiations of hydrogen saturated aqueous solutions of formic acid containing some $HC^{14}OOH$ have been made. Two-dimensional paper chromatography, with water saturated phenol used in the first direction and n-butanol (52 percent) - acetic acid (13 percent) - water (35 percent) used in the second, has been employed for detection and identification of the irradiation products. It was previously noted that over 90 percent of the non-volatile products from these irradiations is oxalic acid and that glycolic acid is possibly one of the other products. No further evidence has been obtained to substantiate the presence of glycolic acid. The non-volatile products from one helium ion irradiation of C^{14}

labelled formic acid were run through a silicic acid gel column in the same manner described for the acetic acid irradiations. The level of irradiation was 2.6×10^{20} ev/ml. The only detectable radioactive peak was oxalic acid, which was eluted at 1080 ml. It is probable that other peaks will be detected when the experiment is repeated with a higher $HC^{14}OOH$ content. An aqueous solution of ammonium formate, approximately 0.005 M, 8.5 ml at pH 7, which contained 250 microcurie of $HC^{14}OOH$, was irradiated with helium ions at a level of 2.32×10^{20} ev/ml. After irradiation the target solution was distilled *in vacuo* at room temperature. The residue was dissolved in dilute HCl and again distilled. To eliminate any remaining HCl the residue from the second distillation was dissolved in water and again distilled. The residue from the third distillation was chromatographed by the two-dimensional method mentioned above. Small amounts of glycine and phenylalanine were employed as internal standards from the chromatogram. The amino acids were detected by ninhydrin spraying. The amino acid spots could be compared with the active spots detected by radioautographs of the chromatogram. The principal product of this irradiation was oxalic acid. The presence of glycine was doubtful. Only four radioactive spots other than oxalic acid appeared on the chromatogram.

TABLE I

YIELD DATA

Peak Sample No.	Identity	Conc. at end of irradiation in units of 10^{-4} meq/ml A (5.91×10^{20} ev/ml)	B (19.9×10^{20} ev/ml)	C (44.6×10^{20} ev/ml)
44	Succinic Acid	12.8	43.7	58.9
55	-		7.0	16.9
65	(Tricarballylic Acid)	2.84*	15.1	27.7
74	-		5.6	17.2
85	-		12.7	30.0
95	-	1.75	13.5	48.3

*In experiment A this peak actually occurred at 690 ml and it has not yet been established that this product is the same as that which occurs at 650 ml in the other experiments.

TABLE II

IRRADIATION DATA

Experiment	Ml 0.25 M HA_c	μc $CH_3C^{14}OOH$	Helium Ion Energy-Mev	Helium Ion Current-μa	Total μah	ev/ml
A	11.7	291	34.3	0.1	0.018	5.91×10^{20}
B	76	282	33.8	1.0	0.400	19.9×10^{20}
C	84	168	33.8	1.0	0.990	44.6×10^{20}

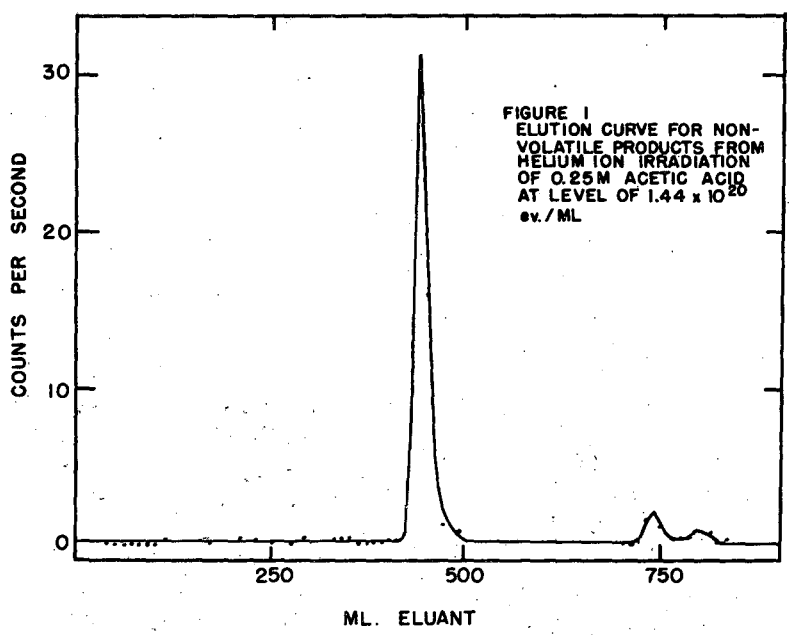

FIGURE 1
ELUTION CURVE FOR NON-VOLATILE PRODUCTS FROM HELIUM ION IRRADIATION OF 0.25 M ACETIC ACID AT LEVEL OF 1.44×10^{20} ev./ML

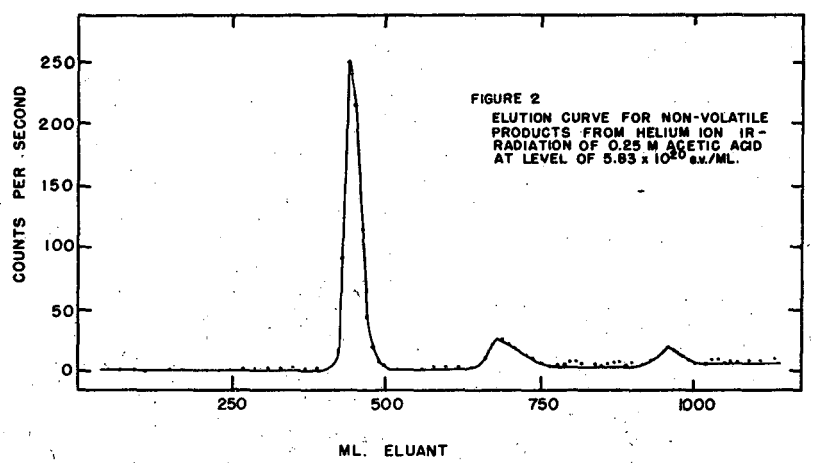

FIGURE 2
ELUTION CURVE FOR NON-VOLATILE PRODUCTS FROM HELIUM ION IRRADIATION OF 0.25 M ACETIC ACID AT LEVEL OF 5.83×10^{20} e.v./ML.

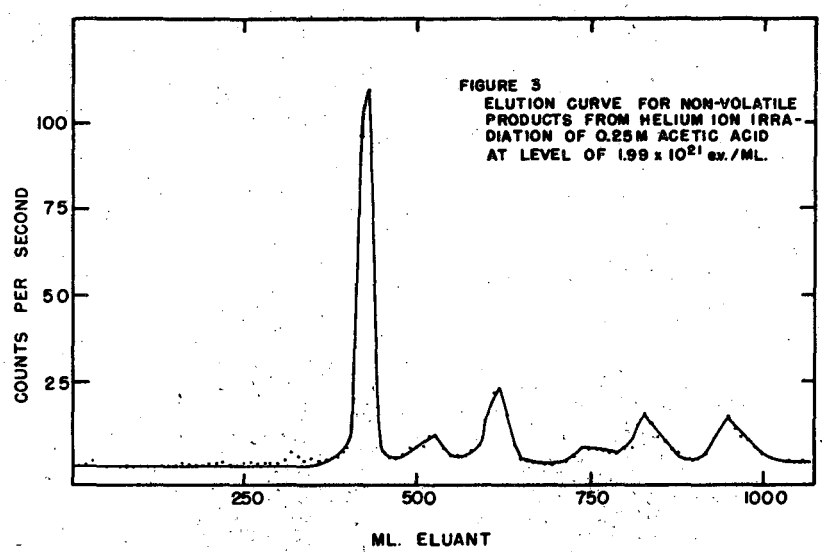

FIGURE 3
ELUTION CURVE FOR NON-VOLATILE PRODUCTS FROM HELIUM ION IRRADIATION OF 0.25M ACETIC ACID AT LEVEL OF 1.99×10^{21} ev./ML.

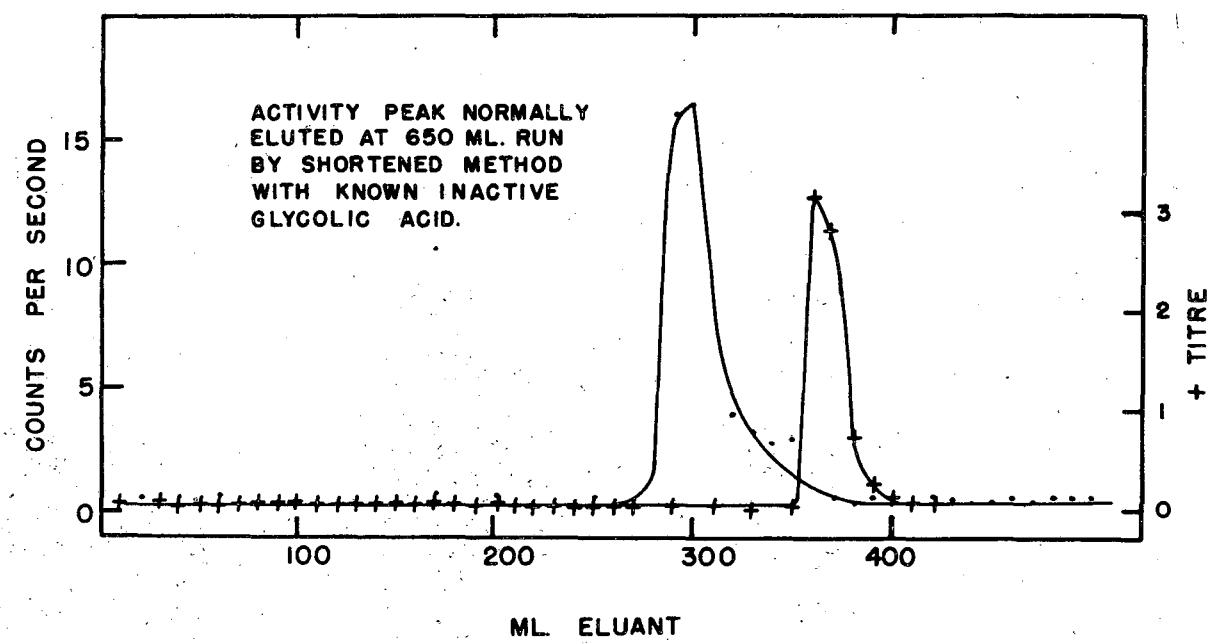
ACTIVITY PEAK NORMALLY
ELUTED AT 650 ML. RUN
BY SHORTENED METHOD
WITH KNOWN INACTIVE
GLYCOLIC ACID.
COUNTS PER SECOND
15
10
5
0
100
200
300
400
3
2
1
0
+ TITRE
ML. ELUANT

FIG. 4

MU 3784

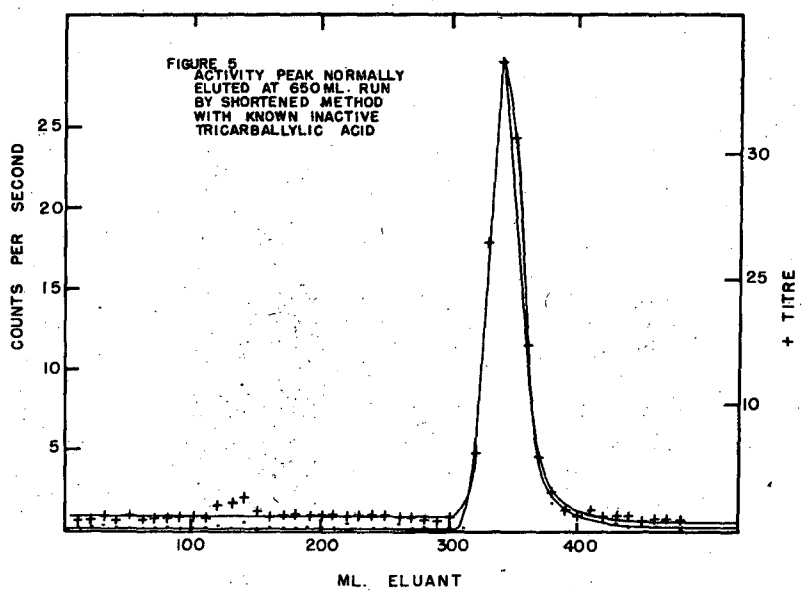

FIGURE 5
ACTIVITY PEAK NORMALLY ELUTED AT 650 ML. RUN BY SHORTENED METHOD WITH KNOWN INACTIVE TRICARBALLYLIC ACID

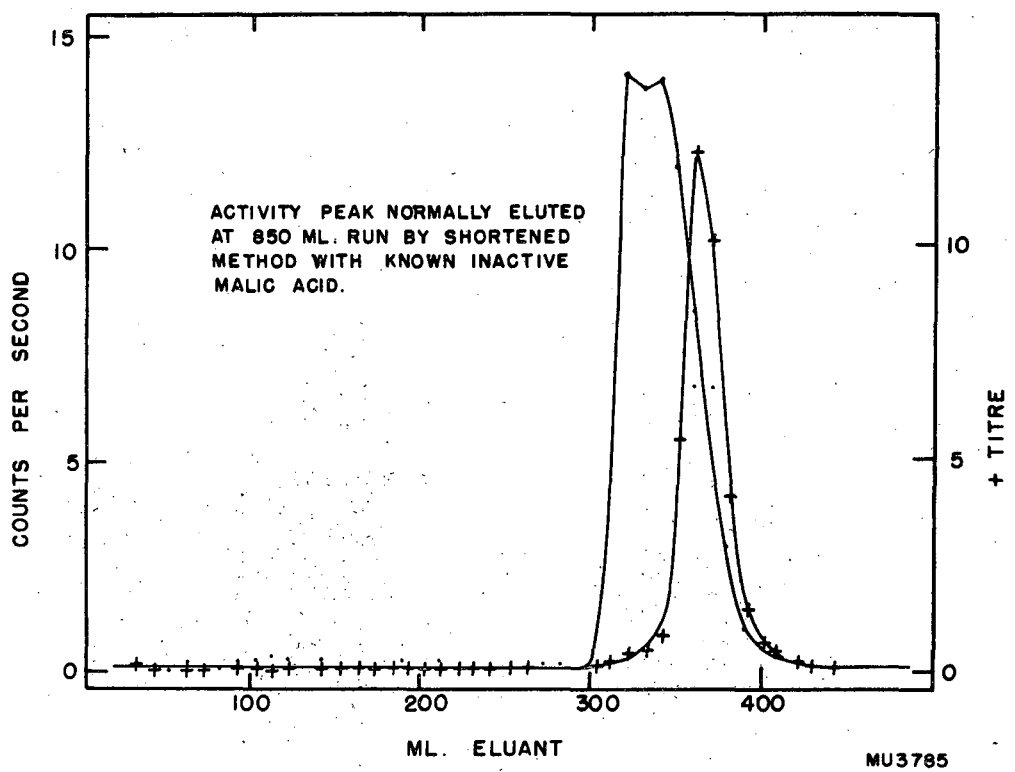
ACTIVITY PEAK NORMALLY ELUTED AT 850 ML. RUN BY SHORTENED METHOD WITH KNOWN INACTIVE MALIC ACID.
COUNTS PER SECOND
+ TITRE
ML. ELUANT
15
10
5
0
100
200
300
400
MU3785

FIG. 6

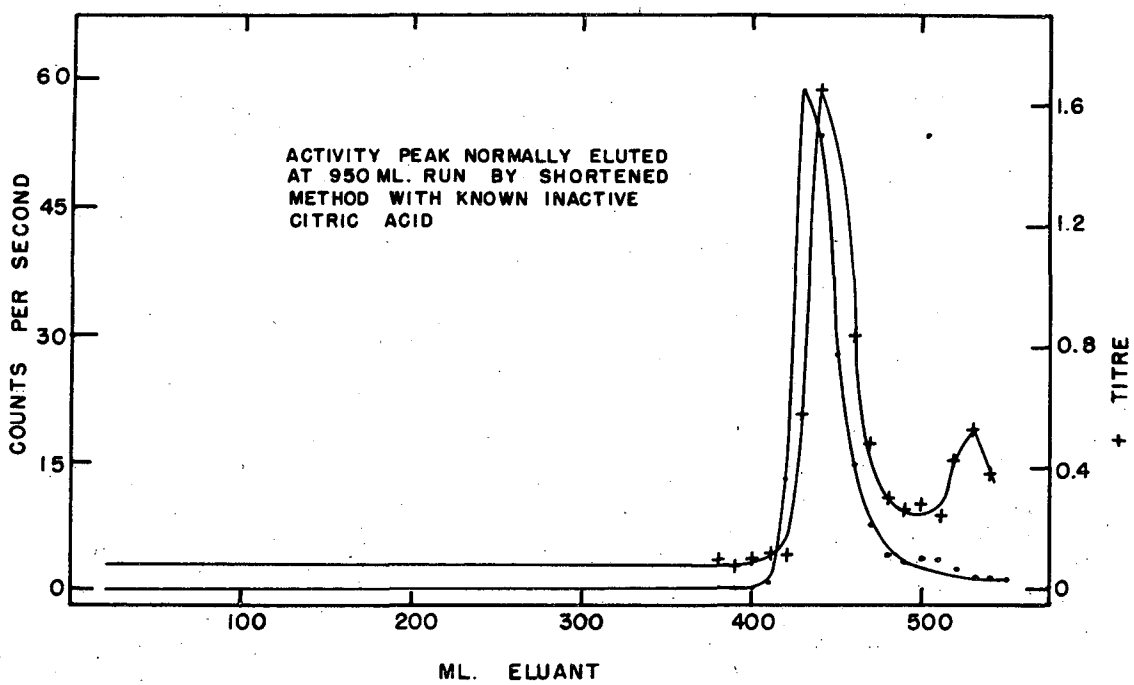
ACTIVITY PEAK NORMALLY ELUTED AT 950 ML. RUN BY SHORTENED METHOD WITH KNOWN INACTIVE CITRIC ACID
COUNTS PER SECOND
60
45
30
15
0
100
200
300
400
500
ML. ELUANT
1.6
1.2
0.8
0.4
0
+ TITRE

FIG. 7

MU 3786

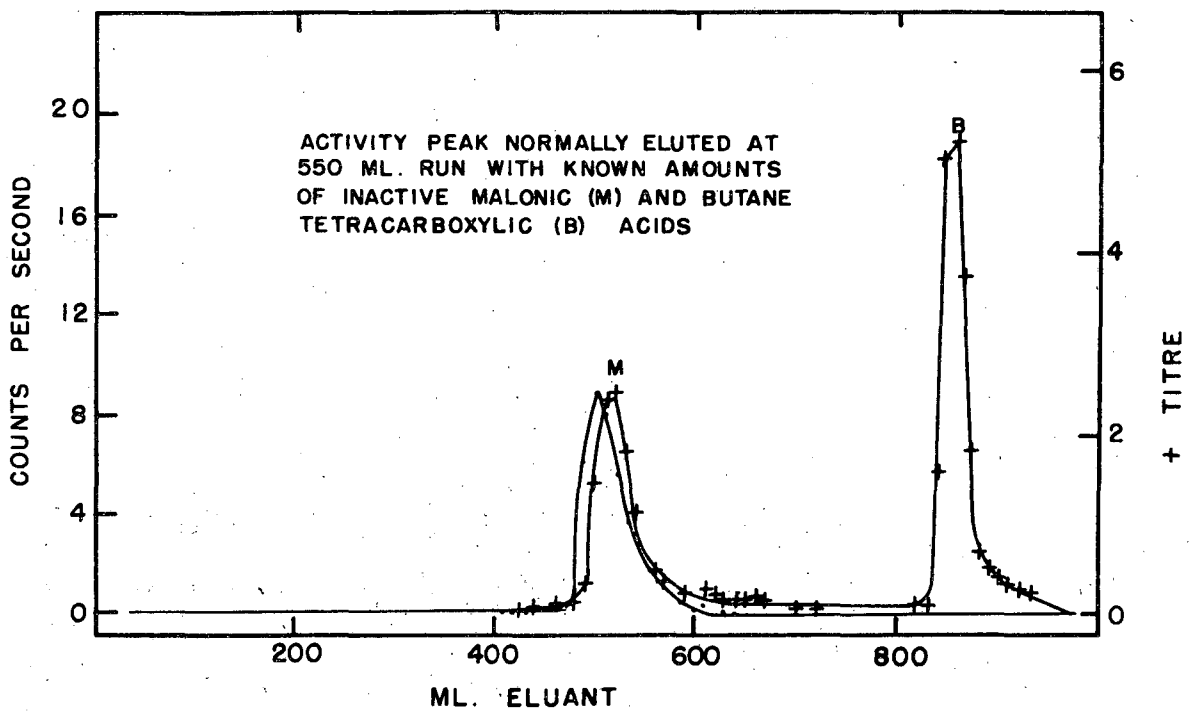
ACTIVITY PEAK NORMALLY ELUTED AT
550 ML. RUN WITH KNOWN AMOUNTS
OF INACTIVE MALONIC (M) AND BUTANE
TETRACARBOXYLIC (B) ACIDS
M
B
COUNTS PER SECOND
+ TITRE
ML. ELUANT
0
4
8
12
16
20
0
2
4
6
200
400
600
800

FIG. 8

MU3787

Calorimetric Determination of the Cyclotron Helium Ion Beam Energy

Warren M. Garrison and Boyd Weeks

In order to determine the ion-pair yield for the $Fe^{++} \rightarrow Fe^{+++}$ reaction and hence be able to use it as a standard for compairson with other radiation-induced reactions, it is necessary to know the over-all energy input of the cyclotron beam incident on the $FeSO_4$ solution. To know this it is necessary to know the time integral of the ion current and the average energy per ion in the beam. The cyclotron is already equipped with two separate beam current integrating circuits* each having at present a maximum error of 1 percent. With modified equipment now under construction the maximum error will be reduced to 0.3 percent. A reliable average energy per He ion in the beam was not available to us for the following reasons: (a) The actual distribution of particle energy about an average value is dependent to an unknown extent on the segment of the beam employed for the bombardment and this, of course, is dependent on the geometry of the assembly used. Previous measurements of the beam energy, by other groups from the Radiation Laboratory, employed unspecified and narrowly collimated segments of the beam at greater distances from the target snout than our $FeSO_4$ target assembly[2] and presumably, therefore, used more nearly mono energetic beams than we did. (b) All previous determinations of beam energy were made by measuring range in aluminum, the thickness of aluminum necessary to absorb half the incident particles being taken as the range and the energy then computed on theoretical grounds.[3,4] It was felt that this criterion for the range was somewhat arbitrary in view of the recognized spread of energy when a large segment of the beam is employed and a different sort of energy measurement was thought advisable if only as a check on the available value for the He ion beam energy. (c) To obtain a value for the beam energy incident on the $FeSO_4$ solution it was necessary to calculate from theoretical range-energy data the energy degradation in the dural and platinum windows.

It was therefore decided to build a calorimeter that would provide an absolute measurement of average particle energy regardless of extent of energy spread and would employ geometry essentially identical to the $FeSO_4$ target assembly. In this way by suitable design and use of the calorimeter, the total energy actually dissipated in the $FeSO_4$ solution could be measured to a precision limited only by our ability to measure the integrated beam current.

The calorimeter as finally used consisted of a solid copper sphere 2 in. in diameter in a highly evacuated glass vessel (corresponding to the rotary pump chamber of the $FeSO_4$ assembly). The beam passed through a 0.001 in. platinum

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* These integrating devices were designed and constructed by Kenneth Jenkins of the 60-inch Cyclotron group. His advice in all the electrical aspects of the calorimeter design and use was also most helpful.

2 For a complete description of this assembly see UCRL-1437, Medical and Health Physics Quarterly Report, April-June 1951.

3 W. A. Aron, B. G. Hoffman, F. C. Williams, "Range-Energy Curves," AECU-663 (or UCRL-121) 1949.

4 B. Rossi, B. Jones, "Range-Energy for Alphas," Crocker Laboratory 60-49 (unpublished) 1948.

window in the glass vessel (corresponding to the Pt window in the $FeSO_4$ assembly) and struck the copper sphere at the bottom of a milled slot. The walls of the slot trapped any secondary electrons that may have been emitted at the site of beam incidence since the cyclotron's magnetic field causes them to move in sharply curving paths. Imbedded in dental amalgam, for good thermal contact, in a hole drilled in the sphere was a W.E. Thermistor type 14B to monitor thermal changes in the sphere. The Thermistor is a sensitive resistance thermometer with a resistance-temperature characteristic shown in Fig. 9. With a good Wheatstone bridge 0.01°C. temperature change is easily detected.

Also imbedded in dental amalgam in a hole drilled through the center of the sphere was a small electric heating element made from a 5 watt Sprague Koolohm 1500-Ω wire-wound resistor with all the outside insulation stripped off. Excellent thermal contact with the copper sphere was accomplished by the dental amalgam imbedding material and a thin coat of Sauereisen (a porcelain-like insulating material) painted on the bare wires of the heater element. As much as 20 watts of electrical power could be dissipated in this heater (imbedded in the sphere) without a temperature-induced change in current (at constant voltage) exceeding 0.2 percent of the total current. This heating element was used to calibrate the thermal behavior of the Cu ball as follows:

Current was supplied to this heating element from a voltage-regulated power supply. The voltage at the heater terminals was measured by a Leeds and Northrup portable potentiometer across the low-resistance leg of a voltage divider. The elements of this voltage divider were precision wire-wound resistors especially calibrated by the meter shop of the Radiation Laboratory with a maximum error of ~0.1 percent of the determined values. The current to the heater was also measured by a Leeds and Northrup potentiometer across a shunt resistance measured to the same precision as the voltage divider resistances. In use power was supplied to the heater at about 17 watts (the expected hour of a 1 μa He ion beam) and the voltage maintained constant by the power supply. The average current for a run was within 0.2 percent of any instantaneous current value over the temperature ranges used and could easily be estimated from 3 or 4 readings taken over a 5 minute run. An electric stop clock was controlled by a gang switch which also shifted the applied voltage from the heater element to a 1500-Ω dummy load and vice versa. The integrated electrical energy (voltage x current x time) supplied to the heater could then be correlated to associated change in resistance of the Thermistor. The resistance-power relationship for the calorimeter assembly was thus calibrated as shown in Fig. 10. The entire set-up is as shown in Fig. 11.

To make the actual determination of cyclotron beam energy, a series of runs was made with the cyclotron and heater separately such that approximately the same resistance change was produced in each case. An accurate plot of the resistance-power characteristic for the assembly was then used to adjust the resistance interval to exactly the same value for each run (3645-Ω initial to 1649-Ω final ≅ 10°C. initial to 30° C. final). These "end corrections" for unavoidable under-or over-shooting the desired initial and final resistances (temperatures) amounted to ~1 or 2 percent of the total heat input. Corrections for heat transfer between the calorimeter and the exterior, made by taking warming and cooling rates at the initial and final temperatures respectively for each run, amounted to ~ 0.5 percent of the total heat input. Possible effects of radiation, stray rf fields, mechanical vibration in the magnetic field, etc. were found to

to be negligible and were included in the initial and final warming and cooling rate determinations since these were made with the calorimeter in place with the cyclotron beam on but with the shutter (6, Fig. 11) closed.

In this way it was found that a change in resistance of the thermistor from 3645 Ω ($\sim$10°C.) to 1649 Ω ($\sim$30°C.) correspond to 134.4 watt-minutes (maximum error $\sim$0.2 percent) electrical work input into the heater element or 7.83 μ ampere-minutes (maximum error $\sim$ 1 percent) cyclotron He ion beam incident on the copper sphere. The average energy per He ion striking the copper sphere is then given by:

$$\frac{\text{watt-minutes heater input}}{\text{1/2 integrated beam current}} = \frac{134.3}{1/2 \times 7.83} = 34.3 \text{ Mev}$$

1/2 the integrated beam current = the ion current since each He ion is doubly charged. Thus, since the geometry of the calorimeter was kept similar to that of the $FeSO_4$ target assembly the average energy per He ion incident upon the contained solution is 34.3 Mev.

Using theoretical considerations[2,3] the energy degradation caused by the platinum and aluminum windows and the air space in between (Fig. 11) was calculated to be 6.1 Mev for He ions of 34.3 Mev emergent energy which yields a value of 40.4 Mev for the "naked" cyclotron He ion beam before its penetration of any matter. As a comparison, the best determination[5] of beam energy by absorption in aluminum was carried out for a very narrowly collimated and sharply mono energetic deuteron beam at a distance of > 20 feet from the cyclotron's target snout. The energy, thus determined, was found to be 20.1 $\pm$ 0.1 Mev.

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[5] J. Hadley -- Current unpublished work for UCRL using 60-inch cyclotron

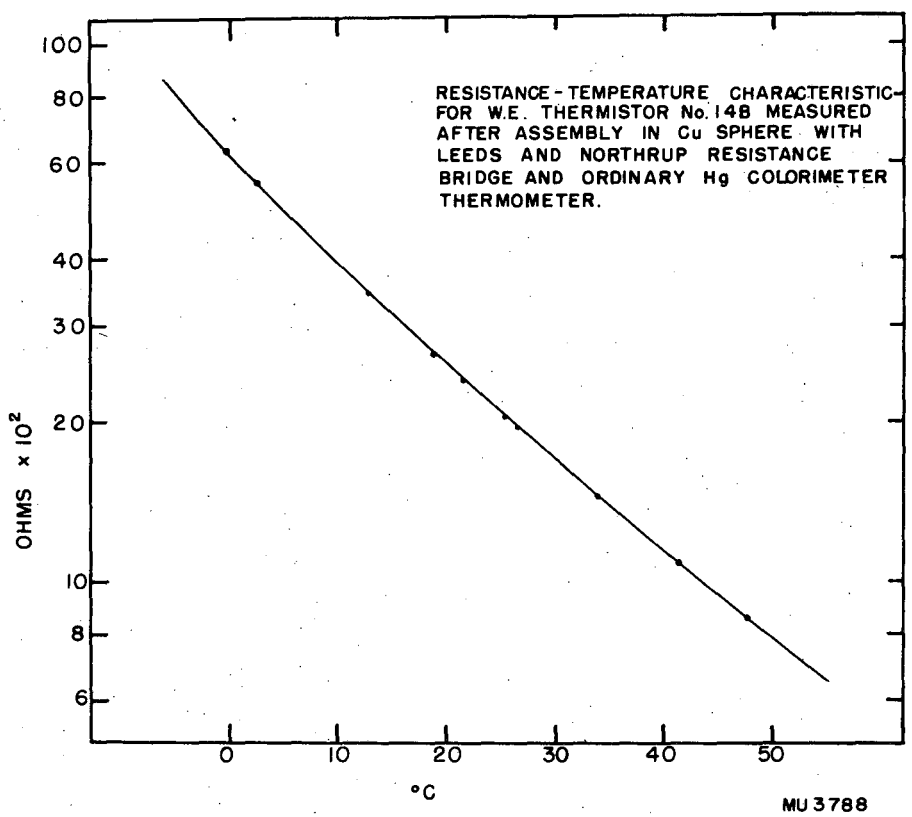
RESISTANCE - TEMPERATURE CHARACTERISTIC FOR W.E. THERMISTOR No. 148 MEASURED AFTER ASSEMBLY IN Cu SPHERE WITH LEEDS AND NORTHRUP RESISTANCE BRIDGE AND ORDINARY Hg COLORIMETER THERMOMETER.
OHMS x 10²
100
80
60
40
30
20
10
8
6
0
10
20
30
40
50
°C
MU 3788

FIG. 9

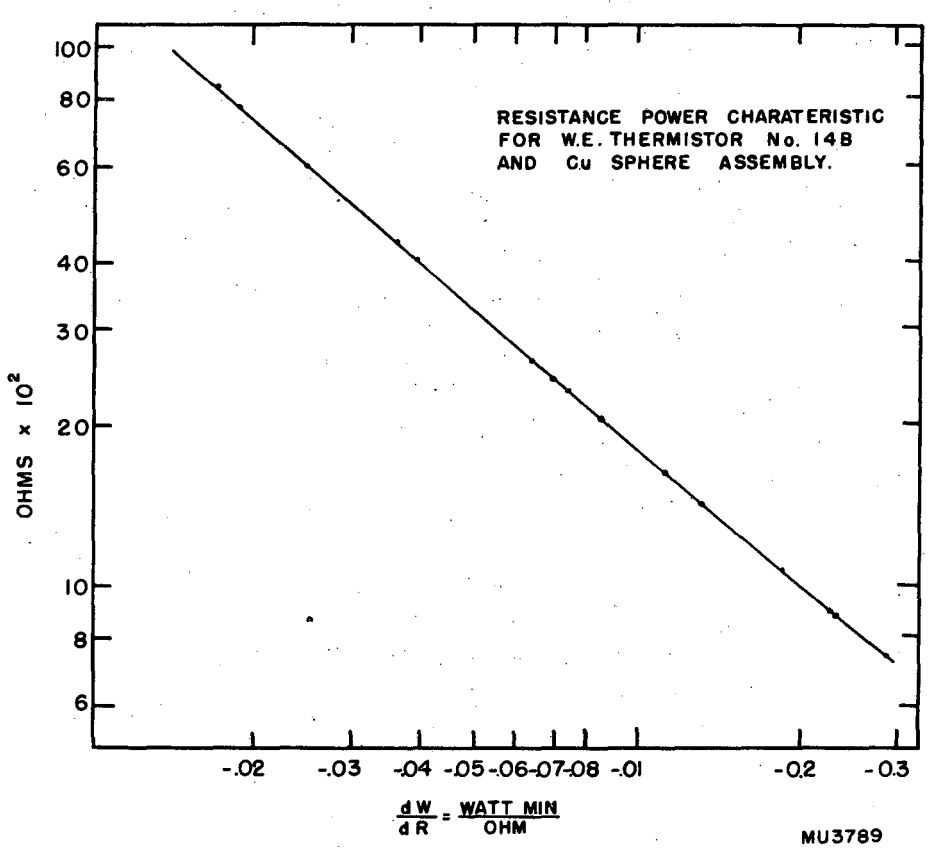
RESISTANCE POWER CHARATERISTIC
FOR W.E. THERMISTOR No. 14B
AND Cu SPHERE ASSEMBLY.
OHMS x 10²
100
80
60
40
30
20
10
8
6
-.02
-.03
-.04
-.05
-.06
-.07
-.08
-.01
-0.2
-0.3
dW/dR = WATT MIN/OHM
MU3789

FIG. 10

Legend for Fig. 11

Diagrammatic arrangement of calorimeter assembly:

(1) Standard target face plate for sealing assembly to cyclotron vacuum.

(2) Aperture (1/8 in. x 5/8 in.) delimiting beam to calorimeter.

(3)-(5) 0.001 in. Al window and assembly.

(6) Shutter (in closed position).

(7) Calorimeter supporting frame.

(8) 0.001 in. platinum window.

(9) Calorimeter vessel (connected to cyclotron vacuum chamber by a short jumper).

(10) Cu calorimeter unit.

R_1	100.3 Ω	Voltage divider
R_2	250 800 Ω	
R_3	0.496 Ω	series shunt
R_4	1500 Ω	dummy load

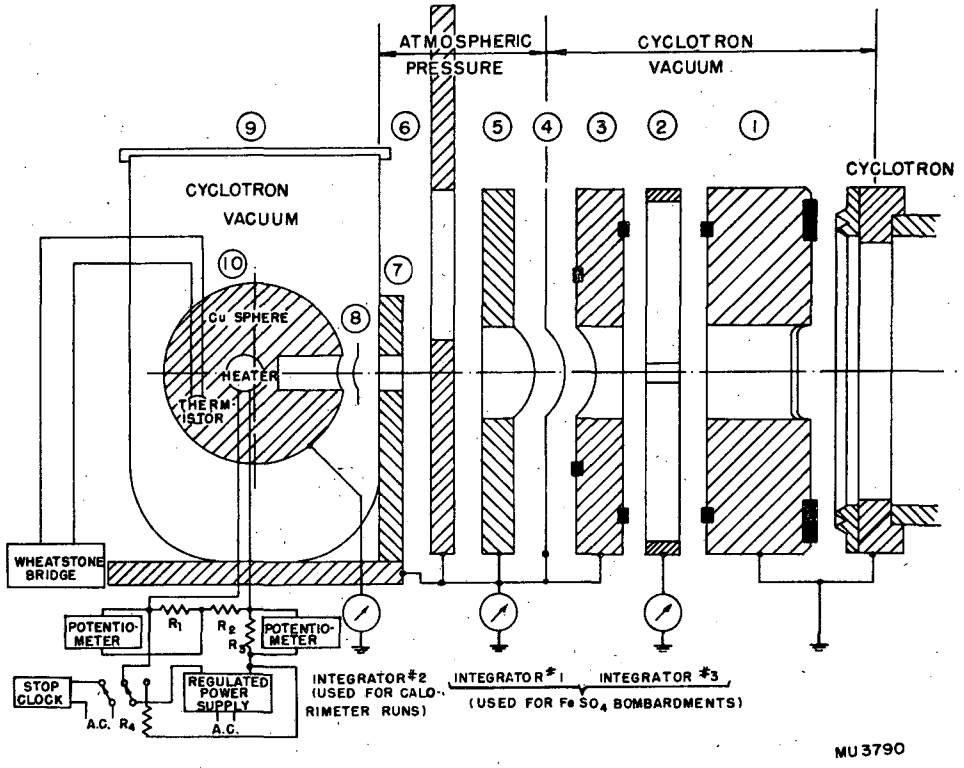
ATMOSPHERIC PRESSURE
CYCLOTRON VACUUM
CYCLOTRON
CYCLOTRON VACUUM
Cu SPHERE
HEATER
THERMISTOR
WHEATSTONE BRIDGE
POTENTIOMETER
POTENTIOMETER
STOP CLOCK
REGULATED POWER SUPPLY
A.C.
A.C.
INTEGRATOR #2 (USED FOR CALORIMETER RUNS)
INTEGRATOR #1
INTEGRATOR #3
(USED FOR FeSO4 BOMBARDMENTS)
MU 3790

Fig. 11

RADIOAUTOGRAPHY

Radioautographic Studies of the Pulmonary Deposition of Plutonium Aerosols

C. W. Asling, and Gretchen Thilo

The main features of the present experiment have been reported by Scott et al.[1] In the study rats were made to inhale a smoke for 30 to 60 seconds, the vapor being generated by burning in an electric arc graphite rods impregnated with plutonium (either metallic or as the nitrate). The fate of this inhaled plutonium (as $Pu\ O_2$) was followed by examination of the excreta over a 64-day period and by radio-analysis of lungs, bone, and head of rats sacrificed at selected intervals during this period (10 minutes, 1 day, 4, 16, and 64 days after inhalation). The lungs were also examined by radioautography, chiefly by the contact-film technique. By this method it was possible to account for the chief features in the movement of the inhaled material. (A study having some comparable features should also be mentioned here.[2] As a part of this study monkeys were exposed to a Cr_2PO_4 fog for 40 minutes to establish by subsequent radio-analysis and radioautography the pulmonary mechanics of the vapor.)

In the quarterly report immediately preceding the current presentation, it was contended that improved radioautographic techniques justified a re-evaluation of the tissue localization of the plutonium-bearing carbon. The method of preparing NTA stripping-film radioautographs of lung sections was described, and a preliminary survey of the series of lungs was made.

In this report, a further study of the material, advantage has been taken of an additional technique improvement. Under some circumstances it appeared that it would be advantageous to the minute study of lung macrophages, both fixed and free, if radioautographic tracks could be slightly separated from the level of the tissue section, thus avoiding the obscuring of cellular detail. Accordingly, additional autographs were prepared as described below, including a relatively recent development in the technique of tissue radioautography.

In 1950 Dr. R. H. Herz of Research Laboratories, Kodak Limited, England, published a paper on a new technique for tissue autography.[3] This method entailed using a special type of film first produced by Kodak Limited. It is similar to stripping film but consists of elumsion and an inert layer of gelatin,

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[1] K. G. Scott, Dorothy Axelrod, Josephine Crowley, and J. G. Hamilton. Deposition and fate of plutonium, uranium and their fission products inhaled as aerosols by rats and man. Arch. Path, 48, 31-54 (1949).

[2] Personnel of Naval Laboratory Research Unit No. 1 and W. R. Lyons. The inhalatory route for prophylaxis and treatment of experimental influenza. I. The distribution of inhaled material. Am. J. Med. Sci., 203, 40-60 (1944).

[3] R. H. Herz, Autoradiography. Medical Radiography and Photography 26, No. 2, 46-51 and 84 (1950).

whereas the former has an impervious support to the emulsion. The entire preparation is 10 micra thick - 5 micra of emulsion and 5 micra of gelatin. Eastman Kodak Company in this country has recently produced this film on an experimental basis and furnished this laboratory with a sample for experimentation. This preparation was used with the plutonium lung sections with a fair amount of success. The film is supplied in a roll 5 feet in length and 35 mm wide without sprocket perforation. It was used in the following manner

The lung sections were cut and mounted on microscope slides. The paraffin was removed in xylol and the slides dipped in 1 percent collodion. The slides were then soaked for approximately 15 minutes in a dilute solution of detergent and water, to wet the surface of the section thoroughly and get rid of any clinging air bubbles.

In the dark room under an AO safelight the slides were places in a large glass dish of distilled water, section side up. The film was unrolled and cut in pieces one inch in width, one piece for each slide. With a pair of forceps the emulsion was gently stripped off the heavy support. It was placed emulsion side down on the surface of the water and allowed to remain for a minute or two. This procedure caused the gelatin to swell and stretch in all directions, increasing its size by approximately one-third, i.e., a piece of gelatin measuring 35 mm x 1 inch would increase in size to approximately 47 mm x 1-1/3 inches. The slide was then brought up under the gelatin, the excess gelatin wrapped itself around under the slide. The preparation was then dried in a stream of cool air, with the result that the stretched gelatin dries down very closely against the section and seals itself against the glass slide. The slides were then placed in a light-tight box and left for the proper exposure period. At time of development the slides were placed in absolute alcohol, 70 percent alcohol, and water to hydrate the tissue underlying the gelatin. The emulsion and gelatin backing are completely permeable to all solutions.

The emulsion was developed in D-19 for 3-1/2 to 4 minutes at 68° F., washed in water, cleared in hypo, and washed in running tap water for 30 minutes.

It was found that the wet gelatin was thin enough to permit the staining of the tissue underneath. The preparations were stained in modified Harris hematoxylin as for the stripping film. After bluing in tap water, the slides were placed in eosin (0.25 percent in 70 percent alcohol) for 3 minutes. They were then carefully washed in 80 percent alcohol to remove as much stain as possible from the emulsion without also removing it from the tissue. This step was followed by two washings in 95 percent alcohol and two in absolute alcohol. Because of the hardening effect of absolute alcohol on gelatin, the clearing and mounting were carried out in the following easy stages:

	Solution	Time
1.	100% alcohol - 3 parts xylol - 1 part	2 minutes
2.	100% alcohol - 1 part xylol - 1 part	2 minutes
3.	100% alcohol - 1 part xylol - 3 parts	2 minutes
4.	xylol	2 minutes

The slides were then mounted in water thin clarite dissolved in xylol and allowed to dry for 48 hours. It was found that if the steps of this procedure were carried through too quickly, that is, from absolute alcohol directly into xylol, and then clarite, the gelatine would separate away from the tissue. Even with the above procedure this separation occurred in about one-third of the preparations.

In the experiment there were thus available two types of stripping-film autographs, each representing several radioautographic exposure periods. The number of animals studied at each interval was as follows:

Post-inhalation Interval	10 min	1 day	4 days	16 days	64 days
Number of Animals	2	2	4	3	3

The following discussion presents, chiefly by photomicrographs, a description of the various features which appear to characterize the lungs of these animals.

Some remarks concerning photography are pertinent here. First, the heavy staining (usually with eosin) of the stripping film emulsion which overlies the tissue section renders difficult the obtaining of adequately contrasting photomicrographs. In many preparations the gray background appearance is due to this non-specific stain. Second, the various radioautographic exposure periods have specific advantages. Low-power photomicrographs, where a general impression of distribution is sought, were best made from the longer exposures (20 days). When more detail was sought in the higher magnifications, heavy bursts from long radioautographic exposures would obscure underlying structures, and the shorter exposures (10 and even 5 days) were preferred. To maintain comparability of the various specimens, the lowest magnifications all represent 20-day radioautographic exposures, and all higher magnifications were based on 5-day exposures (exception: Figs. 2 and 3, 10-day exposures).

When rats were sacrificed 10 minutes after exposure the greatest part of the activity was found on the free margin of the bronchial and bronchiolar epithelium. The heavy concentrations of these sites are seen in Fig. 1. Fig. 2 illustrates this at higher magnification, and shows that the terminal and respiratory bronchioles bear heavy deposits. Even at this interval, however, the lung tissue proper contains a distinguishable deposit. It is noteworthy that this deposit is not evenly dispersed, but shows regional concentrations. It would be profitable to explore, by thick sections or serial reconstruction, whether the variations in deposition are on a lobular basis; i.e., whether one pulmonary lobule may receive and an adjacent one escape the exposure through some functional sphincter-like control. The susceptibility of tissue prominences to a marked concentration is seen at the bifurcation of bronchioles (Fig. 2) and, at the alveolar level, in the margins of the ostia of individual alveoli (arrows in Fig. 3). The surface position of radiating particles is also seen in Fig. 3.

One day following the exposure, the bronchioles are seen to be virtually empty of material. This is in accord with the marked elimination via the feces during the first day, reported earlier.[1] Doubtless material trapped in mucus has been moved up the trachea by ciliary action and subsequently swallowed. The

material is still unevenly dispersed throughout the lung tissue (Figs. 4 and 5). A few "hot spots" of concentration persist on the bronchial epithelial surfaces. These may represent macrophages which have concentrated some of the plutonium-bearing smoke particles. One such macrophage may be seen in Fig. 6, free in the lumen of a respiratory bronchiole. In Fig. 7 it is evident that considerable concentrations are found in alveolar walls, possibly in fixed macrophages, though some material is still free in the alveolar space (center of photomicrograph).

By the fourth post-inhalation day dispersal is slightly more uniform, the areas showing minimal concentration being sparse (Fig. 8). At higher magnification (Fig. 9) the bronchioles continue to show no activity, and the concentrations are chiefly in alveolar walls, as was noted after the one-day interval. The appearance under high magnification so closely resembled that seen in Fig. 7 that it is not illustrated.

Sixteen days after exposure the uniformity of distribution is marked (Fig. 10). As heretofore, occasional macrophages are seen in bronchioles (arrow, Fig. 10). Higher magnification (Fig. 11) is much like that seen earlier (for example, Fig. 9). Close inspection may demonstrate the very large number of single tracks which were found throughout the lung. Fig. 12 is chiefly of interest in suggesting a possible mechanism for redistribution of the material. At the arrow tip a disintegrating macrophage is seen. (Nuclear fragments could be found at a deeper level in the cell, not in focus here). It will be noted that the tracks do not converge at any point, but that each appears to have a different origin. It is possible that in the disintegration of the cell its cytoplasm, falling apart, results in a spreading of the particles which had been concentrated. Further disintegration might allow these particles to be freed - either for phagocytosis by adjacent cells or to float in the air diffusion currents to other alveoli. Whatever the fate, it would appear likely that some of the material can be re-cycled by disintegration of phagocytes.

One of the familiar fates of smoke particles is to be carried by macrophages to lymphatic tissue. Fig. 13 shows peribronchial lymphatic tissue from the same specimen. Fig. 14 at higher magnification, shows the multiplicity of macrophages (indicated by arrows) bearing radioactive material which have localized in this region.

Sixty-four days after inhalation, the dispersion is still rather uniform (Fig. 15). It is noteworthy that rather more of the material is near the pleural surface of the lung than at the earlier intervals. The study of the principles underlying this centrifugal movement might throw additional light on the mottling of the lung surface characteristic in anthracosis. The higher magnifications (Figs. 16 and 17) are much like those seen after sixteen days, (Figs. 11 and 13), save for an apparently sparser distribution.

An attempt has been made in Figs. 18 and 19 to illustrate a point of special interest. As stated in the earlier report,[1] the particles in the smoke were estimated to have average dimensions of 0.63 micra, and not to exceed 1 micron. At best such sizes are at the limit of microscopic visibility. It was occasionally possible to find black (carbon?) particles in macrophages, in accord with the well-known function of these cells to concentrate particulate matter which eventually coalesces to masses of visible size. More frequently, however, particles were not

visible by conventional microscopy in cells which obviously were the source of radiation as evinced by the convergence of alpha-tracks on restricted points in their cytoplasm. However, dark-field examination often disclosed minute particles in the cytoplasm of such cells. In Fig 18 a macrophage is seen, the arrow ending near its cytoplasm. Fig. 19, shows the same region. Several granules, one very bright, are disclosed in its cytoplasm by dark-field illumination. The photomicrograph is a double exposure since, after registering the granules, the focus was changed to record the alpha tracks in the silver radioautographic emulsion overlying the section. (The lens necessary for this magnification is very short focus and has a consequently shallow depth.) The site of the cell nucleus showed no granules by dark-field, though some lay very close to the nuclear membrane.

Although this study cannot yet be regarded as definite, it has served to suggest the chief features in the minute mechanics of the lung which account for the fate of inhaled particulate matter. It is believed that this technique should allow experiments to be devised which would markedly expand our knowledge of pulmonary histophysiology and histopathology. It should be particularly applicable to public health studies on smokes and industrial vapors, to experimental studies on such problems as anthracosis, and to basic investigations on the micromechanics of pulmonary ventilation. Modification to include inhalation of bacteria and viruses tagged by radioisotopes might be valuable in studies on infectious diseases and immunology.

Legends for Illustrations

Photomicrographs and stripping-film radioautographs of rat lungs after exposure to a smoke containing plutonium.

Fig. 1 Spec. 8096, immediately after inhalation. Radioautographic (R-A) exposure time 20 days. Mag. 42.5 x.

Fig. 2 Same animal. R-A exposure 10 days. Magn. 110 x.

Fig. 3 Same slide as Fig. 2. Magn. 380 x. Arrows indicate projection formed by alveolar ostia; note concentration at such sites.

Fig. 4 Spec. 8103, one day after inhalation. R-A exposure 20 days. Magn. 42.5 x.

Fig. 5 Same animal. R-A exposure 5 days. Magn. 110 x.

Fig. 6 Same slide as Fig. 5. Magn. 380 x. Arrow indicates macrophage in respiratory bronchiole.

Fig. 7 Slide and magnification as in Fig. 6, illustrating lung tissue proper.

Fig. 8 Spec. 8100, 4 days after inhalation. R-A exposure 20 days. Magn. 42.5 x.

Fig. 9 Same animal. R-A exposure 5 days. Magn. 110 x.

Fig. 10 Spec. 8093, 16 days after inhalation. R-A exposure 20 days. Magn. 42.5 x. Arrow indicates burst from macrophage in bronchiole.

Fig. 11 Same animal. R-A exposure 5 days. Magn. 110 x.

Fig. 12 Same slide. Magn. 380 x. Arrow indicates disintegrating macrophage. Note beginning dispersal of sources of radioactivity.

Fig. 13 Same slide. Peribronchial lymphatic tissue. Magn. 110 x.

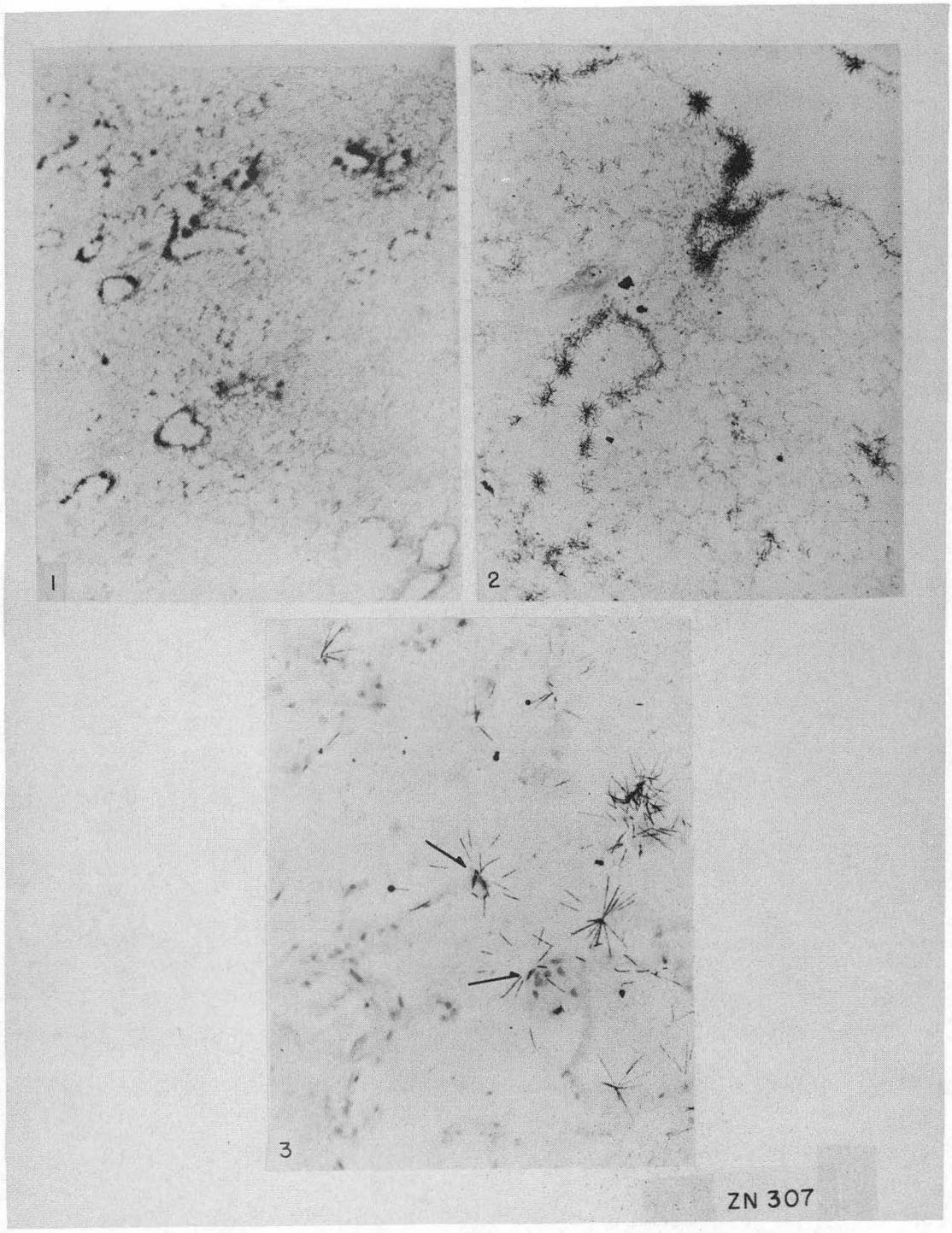
Fig. 14 Higher magnification (380 x) of tissue shown in Fig. 12. Arrows indicate macrophages which are source of radioactivity.

Fig. 15 Spec. 8101, 64 days after inhalation. R-A exposure 20 days. Magn. 42.5 x.

Fig. 16 Same animal. R-A exposure 5 days. Magn. 110 x.

Fig. 17 Same slide, magn. 380 x.

Figs. 18 and 19 Same slide. Magn. approximately 2000 x. Upper picture by conventional illumination; arrow indicates cytoplasm of macrophage in alveolus of lung. Nucleus shows few if any granules visible. Lower picture is same cell, by dark-field illumination. Granules visible in cytoplasm at arrow; nucleus not visible. The photomicrograph shows also (by double exposure) the alpha tracks present in the radioautographic emulsion, which was at a higher focal level in the slide.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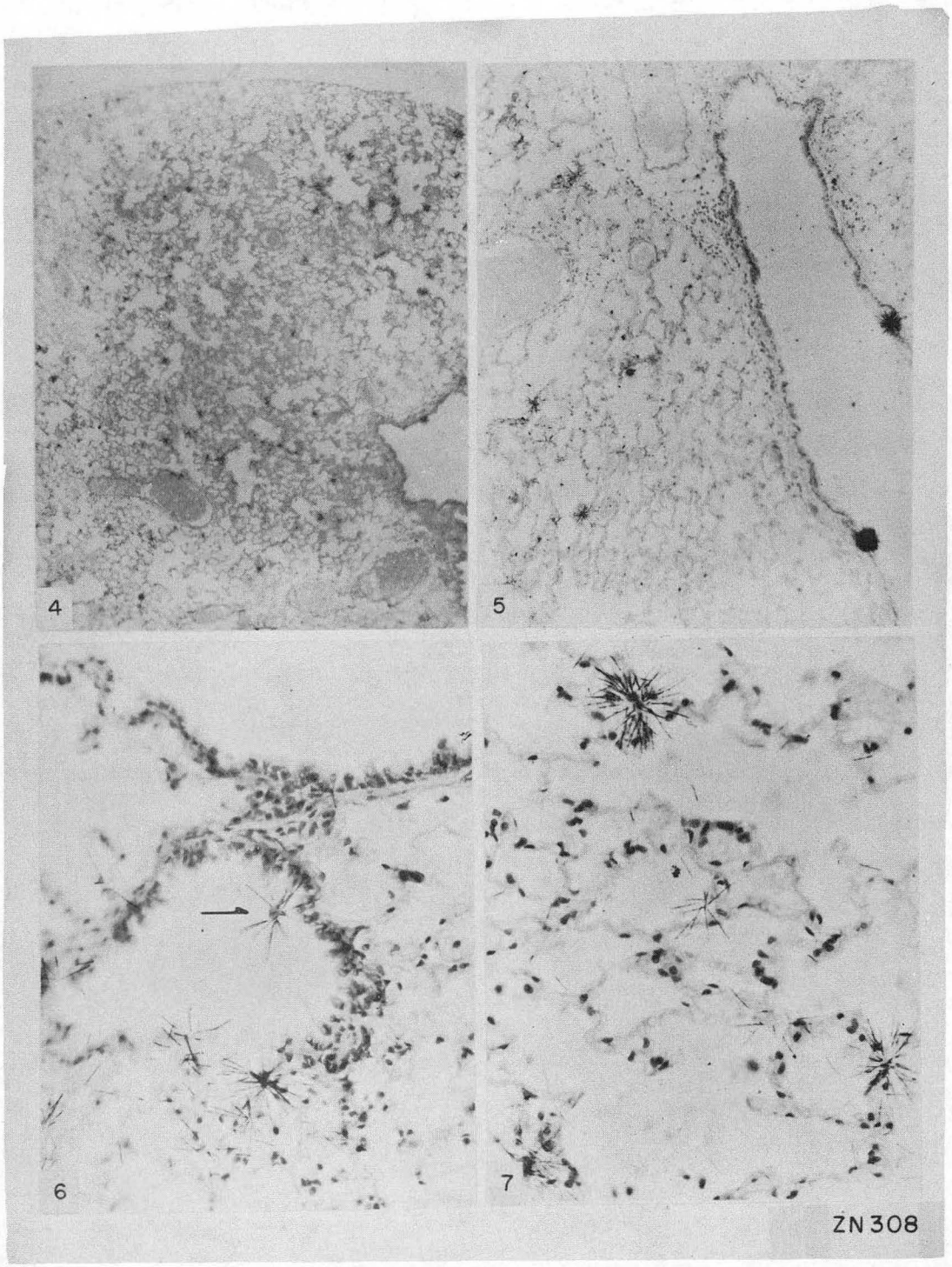
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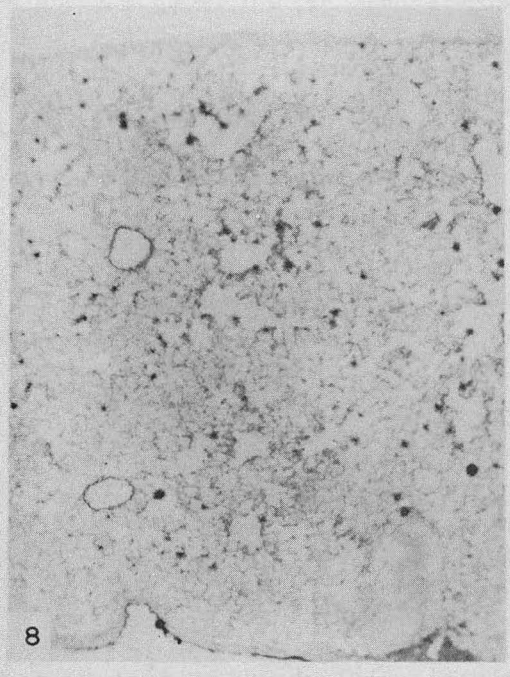

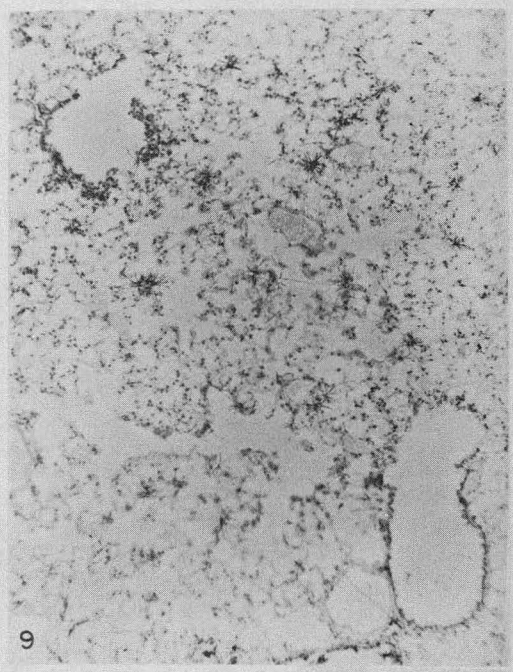

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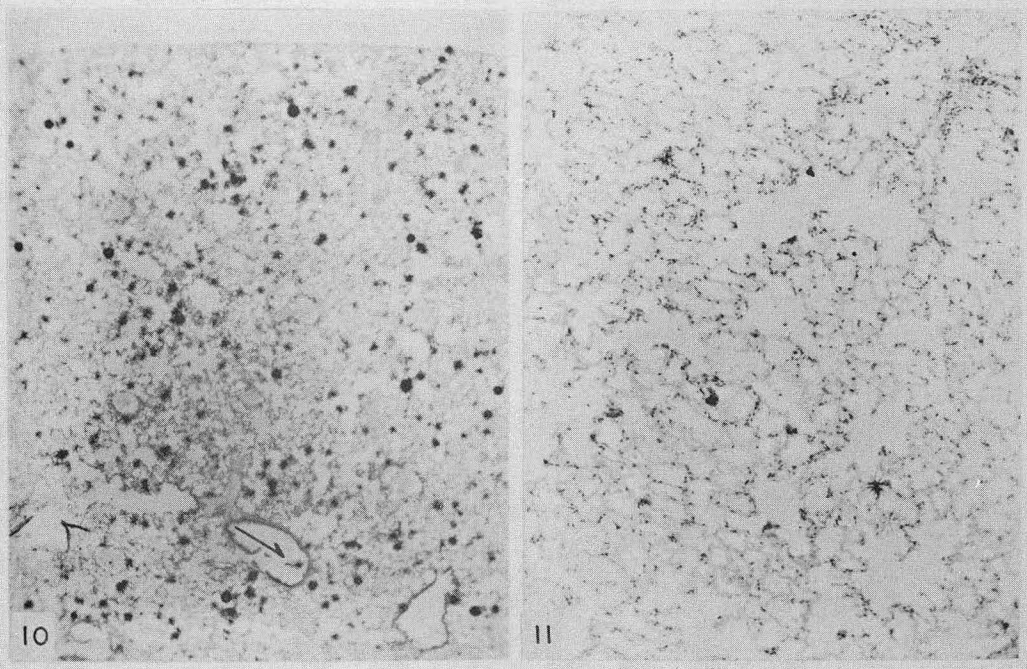

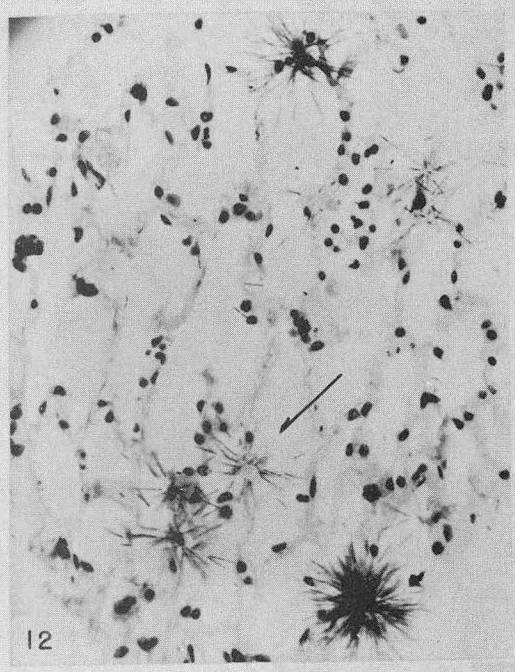

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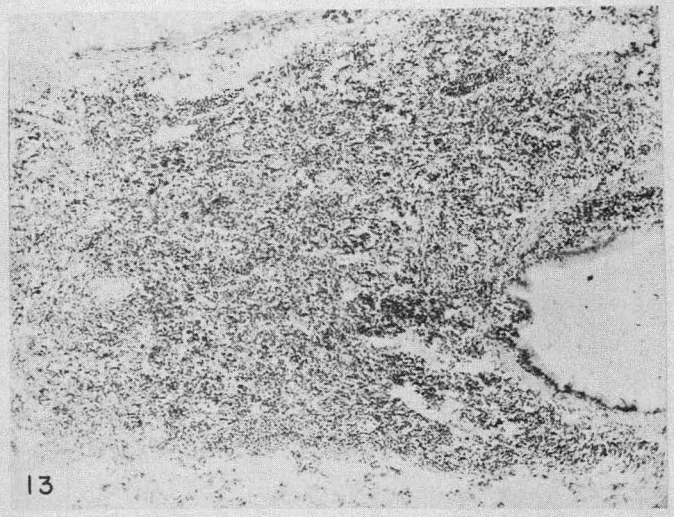

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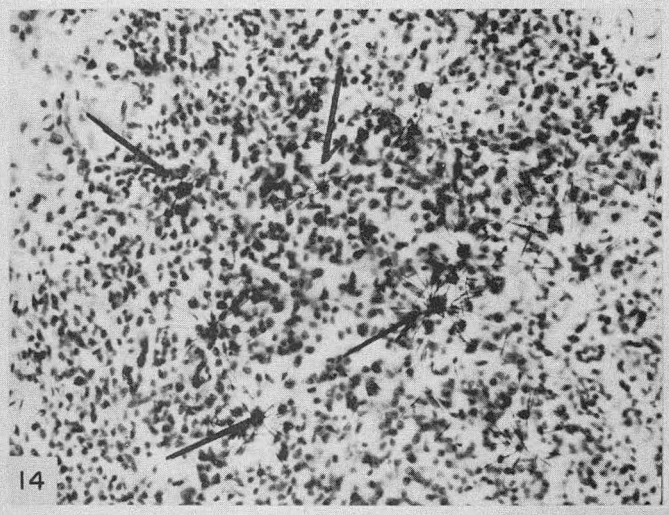

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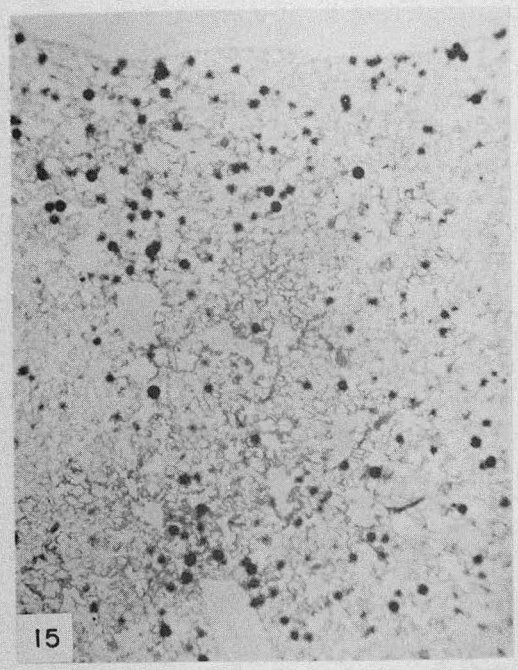

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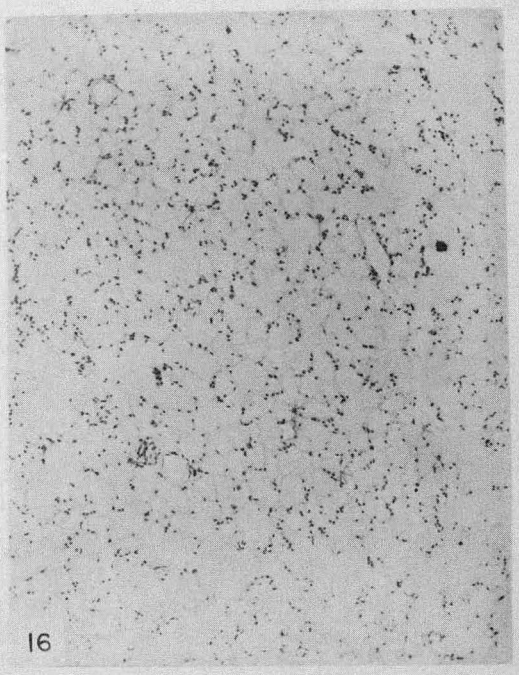

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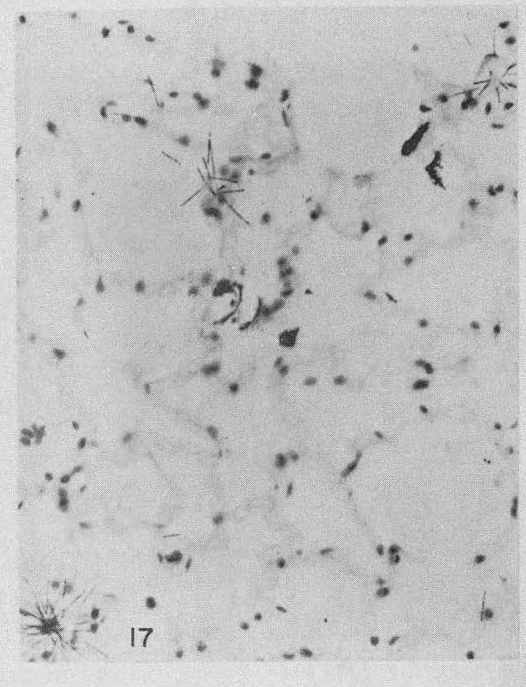

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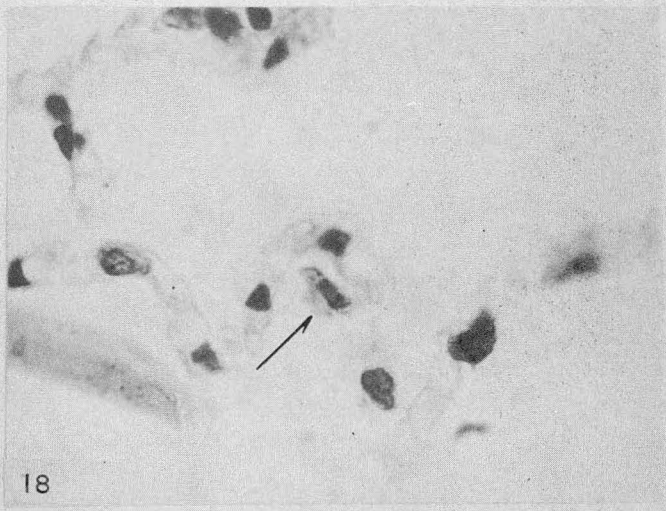

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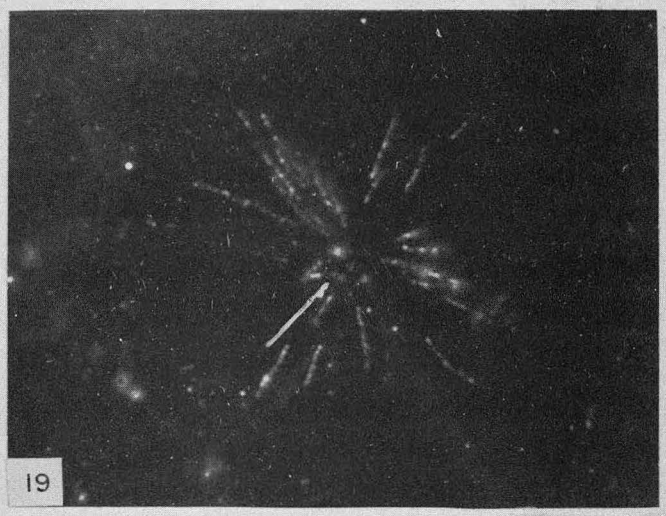

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(2) Submitted for publication and accepted:

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Morrison, D. C.: Grignard Preparation of Fluorene-2-Carboxylic Acid. (Journal of the American Chemical Society).

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(3) Publications in progress:

Hamilton, J. G.: Astatine Data.

II BIOLOGICAL STUDIES OF RADIATION EFFECTS

J. H. Lawrence - in charge
Project 48A-1

THE METABOLISM OF GLYCINE-2-C^{14} IN MAN: III CUMULATIVE DOSIMETRY AND URINARY EXCRETION OF C^{14}

Nathaniel I. Berlin, Bert M. Tolbert, and Helen C. Lee

In previous communications it was reported that following the intravenous administration of 100 microcuries of carbon-14 as methylene labeled glycine (8.0 mgm) 86 percent of the injected dose was excreted via the lungs as $C^{14}O_2$,[1] and that autopsy data showed there was present a component of elimination of carbon-14 from the tissues having an average half-time of 50 days.[2] The present communication is to report the urinary excretion of carbon-14 in patients given 100 microcuries of carbon-14 methylene labeled glycine and to consider the radiation dosage received by these patients.

Methods

Five patients were given 100 microcuries of glycine-2-C^{14} (8.0 mgm) intravenously; the time and volume of each spontaneous urinary voiding was noted for the first 10 days; thereafter an aliquot of a spontaneous morning voiding was collected once per week. An aliquot (5 or 10 ml) was dried *in vacuo*, then combusted to carbon dioxide with a chromic-sulfuric acid mixture.[3] The carbon dioxide was converted to barium carbonate, the specific activity of which was measured in a proportional counter if greater than 10 dis/min/mg $BaCO_3$; if less, the sample was reconverted to carbon dioxide and introduced into a 100 cc ionization chamber operating at atmospheric pressure; a vibrating reed electrometer and recording potentiometer were used to measure the rate of voltage change in the ionization chamber.[4,5]

Results

Figure 1 shows the specific activity of the urinary carbon-14 in patient EP and is typical of the data obtained. Table I summarizes the data for the 5 patients. Figure 2 shows the cumulative urinary carbon-14 excretion in patient EP and is calculated by graphical integration of the data presented in Fig. 1. The amount of total carbon excreted per day was calculated from the amount produced during the first 10 days.

DISCUSSION

Excretion Rates

The data indicate that these patients excrete in the urine on the average 11.8 percent of the carbon-14 administered and that the excretion may be described in terms of three rate components having average half-times of 0.26, 2.5 and 53 days. The urinary carbon-14 radioactivity was followed until it could no longer be measured satisfactorily. Almost complete excretion of carbon-14 via this

route would require approximately 200-250 days, i.e., five times the half-time of the slowest known component. It should be noted in Fig. 1 that during the period from 60 to 85 days the specific activity of the urinary carbon-14 showed a definite increase, occurring at the same time that this patient (with chronic myelogenous leukemia) destroyed the majority of the red cells which had carbon-14 incorporated in their hemoglobin. This probably represents the excretion in the urine of some of the end products of hemoglobin catabolism. It is of interest to note that after four days the specific activity of the urinary carbon gradually becomes much greater than the breath carbon. This would indicate a certain independence of the sources of the carbon in these two end products.

As has been pointed out with respect to the breath excretion, the biochemical significance of each of these components is not evident. The 53 day urine component is mirrored in the 50 day tissue component both with regard to half-time and to quantity. Thus this 53 day urinary component probably represents the major route of excretion of the 50 day tissue component.

This data now makes possible almost complete accountability for the injected carbon-14: 86 percent is excreted via the lungs; 12 percent via the urine and 2 percent is retained for a longer period of time, but must be excreted. No appreciable amount of activity (1 percent) is eliminated in the feces.

The carbon-14 in any given compound will be present largely as the result of synthesis at the time when the precursors have a high specific activity since exchange of carbon atoms in a carbon skeleton is usually not possible without extensive changes to the molecule. Only compounds that are being synthesized will contain carbon-14 and as most compounds are in a steady state there must be a corresponding catabolism and replacement of the carbon-14 by carbon-12 since in the intervening time the precursor specific activity will decrease. It is, however, possible that units such as amino acids can exchange in peptides and perhaps in more complicated proteins. Should such an exchange occur, it would continue and again the carbon-14 must gradually approach natural concentration.[6,7] The autopsy data indicate that the rate of elimination of this small fraction (approximately 2 percent of the dose) must have a half-time of several hundred days or more. Furthermore, there may be more than one of these very slow components. The route of excretion for this last 1-2 percent will be difficult to determine and will probably involve special preparation of the samples and measuring instruments of great sensitivity.

Calculation of Radiation Dose

If it is assumed that this radioactive carbon is uniformly distributed throughout the body, it is possible to make some calculations of the radiation dose delivered to the tissues. At zero time the dose rate will be:

$$\text{mrep/day} = \frac{(N)\,(\bar{E}\beta)\quad(\text{erg/ev})}{(\text{ergs/gm/rep})\;(\text{wt, gms})}$$

N = No. of β^-/day

$\bar{E}\beta$ = 50,000 ev (average energy of C^{14} βs)

wt = 70 Kg

ergs/gm/mrep = $\frac{83}{1,000}$

mrep/day/100 microcuries C^{14} = 4.36

TABLE I

The Percent of the Administered Dose Excreted and Half-time for each of the Three Rate Processes

Patient	$T_1(1/2)$ (days)	%	$T_2(1/2)$ (days)	%	$T_3(1/2)$ (days)	%	$BaCO_3$ excreted/day	Total % excreted
EP	0.10	0.9	1.4	0.9	48	5.7	90.6	7.5
LY	0.37	3.7	2.4	1.5	45	9.0	140.0	14.2
WF	0.17	8.5	1.4	3.3	44	0.6	304.7 (diabetic)	12.4
MM	0.45	5.5	5.0	2.7	84	3.5	82.2	11.7
ESP	0.30	5.7	2.3	1.3	43	6.4	100.9	13.4

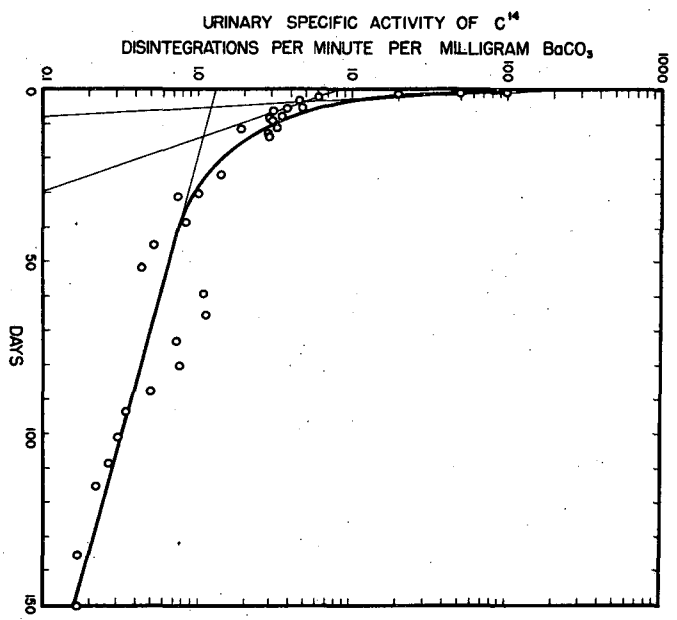

Fig. 1

The specific activity of the urinary carbon in patient E.P. (in dis/min/mgm $BaCO_3$).

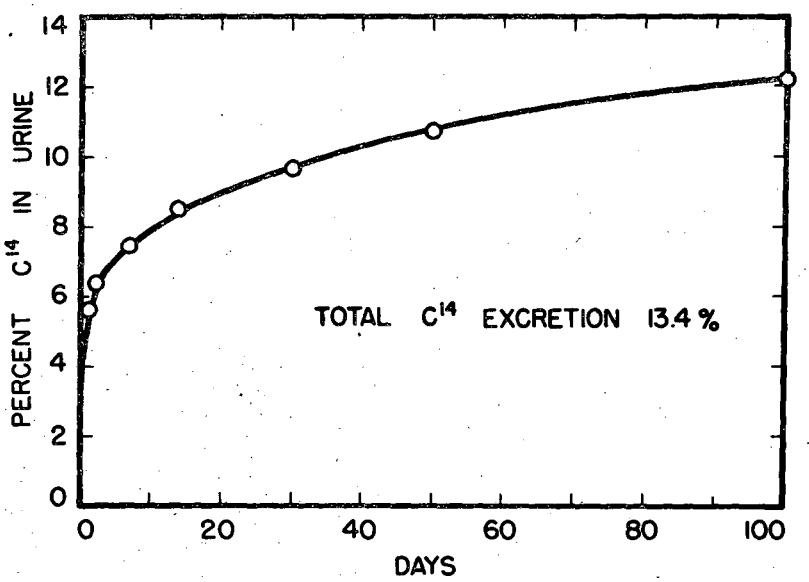

Fig. 2

The cumulative urinary carbon-14 excretion in patient E.P.

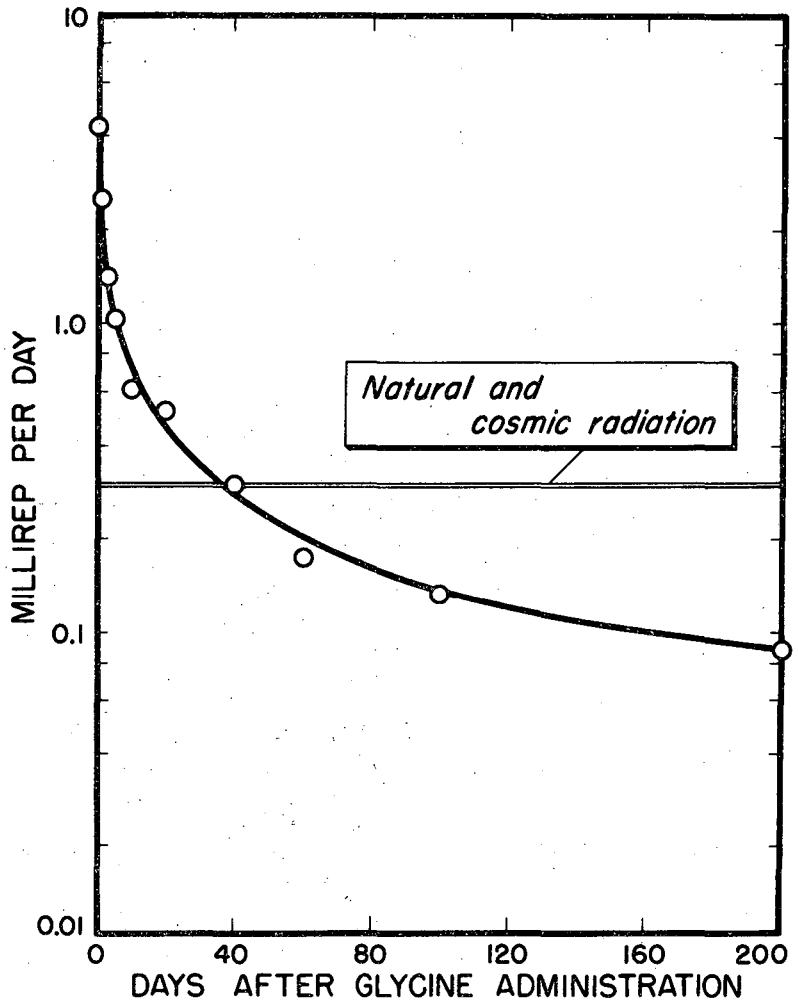

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Fig. 3

The daily radiation dosage rate due to carbon-14. The radiation dosage rate from the naturally occurring radioactive isotopes and cosmic radiation is indicated as being 0.3 mrep/day.

In a similar manner the dose rate at various times may be calculated from the retention of carbon-14. These data are given in Table II and Figure 3. In this figure the "normal" radiation dose is indicated by a horizontal line and is about one-third due to potassium[42] and rubidium[87 8] one-third to cosmic radiation,[9] and one-third from the earth's surface.[10] Following the administration of 100 microcuries of carbon-14 the mean radiation dose falls by 40 days to 0.3 mr/day which is an average "normal" dosage rate.

The data listed in Table II were integrated graphically and the cumulative radiation dose determined (see Table III).

The present continuous tolerance dose for gamma radiation in man has been set at 300 mrep/week by the International Committee on Radiobiology Protection meeting of July, 1950.[11*] There is also general agreement that it is justifiable to integrate radiation doses over a three-month (13 week) period. This tolerance dose would be 3.9 rep. From the data (Table III) it is seen that 2.76 millicuries of glycine-2-C^{14} would be necessary to give an integrated dose of 300 mrep in the first week and 10.6 millicuries would be necessary to give an integrated dose of 3.9 rep in three months.

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* Since this is in terms of mrep, one can utilize this value as a tolerance dose limit for the β radiation of C^{14}.

TABLE II

Cumulative Elimination of 100 microcuries Carbon-14

Injected as Glycine-2-C^{14}

Time	Microcuries Carbon-14 eliminated			Mrep/day
	Breath	Urine	Total	of remaining C^{14}*
0	0	0	0	4.36
1 hr.			4.8	4.15
2 hr.			10.2	3.91
4 hr.			18.7	3.54
8 hr.			27.0	3.18
12 hr.			32.2	2.95
1 day	40	2	42	2.53
3 days	62	6	68	1.40
5 days	70	6.5	76.5	1.03
10 days	78	8	86	0.61
20 days	80	8	88	0.52
40 days	84	9	93	0.31
60 days	86	10	96	0.175
100 days	86	11	97	0.131
200 days	86	12	98	0.087

TABLE III

Cumulative Carbon-14 Radiation Dosage for a 70 Kg Man Given 100 microcuries Glycine-2-C^{14} Assuming Uniform Distribution

Time Interval	Dose, Mrep
0 - 1 day	3.18
0 - 7 days	11.0
0 - 3 months (13 weeks)	36.9
0 - 6 months (26 weeks)	45.2

These figures are for external gamma radiation. It must be remembered that all the calculations have been made on the assumption of uniform distribution of radioactivity. This is not the true situation and in recommending safe doses for the use of glycine-2-C^{14} in patients or normal people some factor must be included for this non-uniform distribution. This lack of uniformity may be greatest during the first few days following the injection of the carbon-14. However, in Table III it is seen that the cumulative dose during this period is only about 10 - 20 percent of the first Quarter's total figure, so it is not as critical as inhomogeneities occurring after the first four to five days. The autopsy data and mice data[12] indicate that the upper maximum variation from the average tissue activity in this later period is not more than a factor of 2-3 so that a factor of five for inhomogeneity would probably be a reasonable value. On this basis one could then administer 2 mc of carbon-14 as glycine-2-C^{14} to a man and not exceed the quarterly tolerance of "safe" dose in any organ. These figures for the cumulative tolerance for a week or for a quarterly period are predicted upon the assumption that the dosage rate following administration of glycine-2-C^{14} constantly decreases so that integration of the dose received for a period of time longer than one week would tend to allow the utilization of a larger quantity initially. Assuming that 100 mr per day is the maximum daily tolerance dose, one could then administer 2.2 millicuries of carbon-14 and glycine-2-C^{14} to man and both not exceed the daily dose for any day and not exceed the weekly cumulative and the quarterly cumulative dose provided there were uniform distribution. Utilizing a factor of 5 for inhomogeneity during the first day or week one could administer 460 microcuries to man and probably not exceed the maximum tissue dosage rate per day, week or quarter in any tissue at any time.

Whether the calculation of safe tracer doses rests upon a maximum dosage rate per day, week or quarter will have to be determined in the future. Certainly, at present, the use of 100 microcuries of C^{14} as glycine-2-C^{14} has been sufficient to carry out these studies and yet not exceed the safe tracer dose as calculated by any of these three indices.

SUMMARY

1. The urinary excretion of carbon-14 following the intravenous administration of 100 microcuries of carbon-14 as glycine-2-C^{14} may be described in terms of 3 rate components having half-times of 1/4, 2-1/2, and 53 days and amounts of 11.8 percent of the dose. The 53 day component probably represents the route of excretion of the 50-day tissue component.

2. Complete accountability for the injected carbon-14 is now possible permitting calculation of the dosage rate. For 100 microcuries glycine-2-C^{14} given to a 70 kg man the cumulative doses are: 0 - 1 days, 3.08 mrep; 0 - 7 days, 11.0 rep; 0 - 3 mo., 36.9 rep. Internal radiation levels from the carbon-14 fall to natural radiation levels in 40 days.

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PROTECTION AFTER IRRADIATION BY A TISSUE EXTRACT THAT STIMULATES TISSUE PROLIFERATION

Lola S. Kelly and Hardin B. Jones

In a study of formation of tissue desoxypentose nucleic acid (DNA) two general relationships have been noted: 1) that irradiation can depress the DNA formation in tissues; this effect can be an indirect effect of radiation easily observed in unirradiated tissues of an irradiated animal and hence is mediated by some humeral mechanism[1,2,3] and 2) that the presence of growing tissue (tumor or embryo) within an animal can stimulate the formation of DNA in other tissues of the host animal.[4,5,6,7] This was interpreted as evidence of the release of a humeral agent by the rapidly dividing tissue which increases the rate of cell division in the normal tissues of the host. The radiation depression of DNA formation is approximately 0.3 percent per r of whole body radiation; this depression by irradiation is approximately the same as depressing effect of radiation on the formation of red and white blood cells.[3] Small tumors and embryos can increase DNA formation in normal tissues of the host by a factor of 2 to 6 times.[4,5,6,7] Relative DNA formation rate has been used as a probable indicator of tissue cell division; only recently, however, have we measured mitotic indices in livers of A strain mice bearing a transplanted mammary carcinoma and have found a marked increase in mitotic rate compared to livers of normal controls and thus substantiate the association of increased DNA turnover and tissue mitosis.

Current studies now demonstrate that the DNA turnover can also be increased, at least in livers and spleens of normal mice, by repeated injection of various fractions of homologous tissue mashes and extracts of tissue mashes. Earlier experiments with single injection of tissue mash preparations gave negative results. Heparin had preliminary been reported to stimulate DNA turnover, but this effect was later traced to the probable stimulus to proliferation of the bone marrow caused by the bleeding at injection sites when animals were kept heparinized. Slightly less heparin gave no effect in animals that did not lose blood.

The following information constitutes evidence that substances capable of stimulating DNA formation can be obtained from mashes and extracts of rapidly growing tissues and that these substances may offer some protection after exposure to radiation.

Table I summarizes the DNA specific activities (in counts per mgm DNA phosphorus divided by the number of counts of P^{32} injected per mouse normalized for the mouse weight) obtained with various tissue mashes and fractions. The procedures used for the DNA isolation and specific activity measurements have been described.[2,4,5] The tissue mashes (experiments 1 - 5) were made by blending the tissue for 15 minutes with approximately one volume of physiological saline in a Waring Blendor which was refrigerated by an ice jacket. They were then centrifuged 10 minutes in an international clinical centrifuge to remove large particles and the supernate was either refrigerated or frozen until it was injected. Each mouse received 8 daily intraperitoneal injections, the last being given just before the $Na_2HP^{32}O_4$ injection for the DNA specific activity measurement. In most of the experiments the controls received the same volume of physiological saline daily. Table I lists the total weight of tissue from which the

mash injected per mouse was obtained.

Experiments 6, 7, and 8, Table I, represent various attempts at liver fractionation. In #6 liver tissue was homogenized in a Potter Elvejhem homogenizer with 4 volumes of physiological saline and then centrifuged 4 minutes at 14,000 x g to separate nuclei and cytoplasm. The nuclear fraction was not washed so that it still contained some cytoplasmic contamination. Owing to the large volume obtained the cytoplasm from only 0.5 gm of liver could be injected per mouse (total for 8 injections) whereas the nuclei from 1 gm of liver were injected.

In Experiment #7 the general procedure of Roberts and White[8] was followed for the fractionation. They found a substance in thymus which had growth promoting properties for lymphoid tissue. The water homogenate of liver was centrifuged at 15,000 RPM for 1 hour in a high speed attachment for the model PRI Internation Refrigerated Centrifuge. This extract was assumed to be cell free. A portion of the extract was precipitated with ethyl alcohol in the cold and the precipitate resuspended in saline for the injections. This precipitate was rich in nucleoprotein (0.25 mgm nucleic acid phosphorus injected per mouse). This agrees with Roberts and White who found nucleoprotein or nucleic acid to be a major component of their active fraction by electrophoretic analysis.

In Experiment 8 a crude nucleoprotein fraction was tested for activity. It was prepared by grinding livers and spleens in a Waring Blender and then extracting with 4 volumes of 0.5 M NaCl for several hours. After centrifuging, the supernate was precipitated by the slow addition of ethyl alcohol in the cold to a final concentration of 40 percent. The precipitate was re-extracted with 0.5 M NaCl and after centrifuging off all insoluble material the supernate was again precipitated with alcohol. This precipitate was suspended in saline before injection. The nucleic acid in this fraction was a mixture of DNA and PNA. The nucleic acid phosphorus injected per animal was approximately 0.25 mgm which is the same order of magnitude as the nucleic acid content of the various tissue mashes that have been tested. These results suggest that nucleoprotein or its breakdown products may be the active principle in the tissue mashes. More specific fractionations of tissues are planned in the near future.

A satisfactory explanation for these experiments is that rapidly dividing cells release some active substance into the circulation which stimulates other cells to divide and that this same substance or a similar one exists in tissue mashes. There is a possibility that the spleen protection effect in irradiated animals and the protective effect of embryo mash injections observed by Jacobson, et al.[9] is based on the same mechanism possibly repeated administration of the extract can approximate the longer action of the functioning surviving tissues of Jacobson. If the active ingredient helps to relieve the severe depression in the rate of cell division in irradiated animals it may aid in recovery from irradiation injury. Table II lists a series of preliminary experiments testing this hypothesis. A strain mice were irradiated with x-rays (215 KV, 15 m.a.; 1.5 mm Cu + 1 mm Al filters) and then divided into 2 groups. Twenty-four control mice received no further treatment, while 24 mice were given one or several injections of embryo mash prepared as described above. At various time intervals after irradiation the mice were given a tracer dose of $Na_2HP^{32}O_4$, killed 4 hours later and the DNA specific activities determined in the usual manner. As is shown in Table II the specific activities of liver DNA are higher in all the groups which received embryo mash compared to the controls while the spleen DNA values do not show a difference until the 7th day post irradiation group. Experiments are in progress now to determine if tissues

such as bone marrow and lymph nodes which show severe irradiation damage are also helped towards recovery by embryo mash or other tissue mash injections.

Preliminary experiments suggest that the DNA turnover is also increased by the repeated injection of bacteria.

A preliminary test has been made of the irradiation protection capacity of the proliferation promoting extracts of tissues. Twenty-four mice were irradiated with 800 r and were given the extract from 0.7 gm of embryo divided in 10 equal doses (2 injections per day for 2 days post irradiation and 1 injection daily for 6 days). Twenty-four comparable irradiated mice, paired at random, were given injections of saline. The extract was made by grinding embryo in a Waring Blender at (0-4°C) for 15 minutes; extracting the mash for 18 hours in one volume of isotonic saline; and collecting the extract, as a supernate after centrifuging the tissue blend for one hour at 15,000 RPM in a high speed refrigerated centrifuge. A significant differential of protection has been maintained between the mice receiving embryo extract and those receiving saline see Table III.

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TABLE I

DNA Specific Activities*

			No. mice	Livers x 10^4 Treated	Livers x 10^4 Controls	Spleens x 10^3 Treated	Spleens x 10^3 Controls
1.	Embryo mash	.4 gm	30	4.82±.32		6.93±.36	
	Saline controls		20		1.55±.1		
2.	Tumor mash	.6 gm	30	2.77±.18		8.22±.25	
	Saline controls		18		1.59±.15		5.84±.29
3.	Spleen mash	.25 gm	11	3.05±.24		10.6±.6	
	Saline controls		18		1.61±.25		4.92±.12
4.	Liver mash	.35 gm	30	2.98±.16		5.85±.41	
	Saline controls		18		1.43±.2		5.29±.28
5.	Liver mash	.65 gm	18	2.95±.16		8.4±.11	
	Liver Fractions						
6.	Nuclei	1.0 gm	20	2.79±.15		6.84±.24	
	Cytoplasm (cell free)	.5 gm	20	2.83±.25		6.75±.16	
	Saline controls		18		1.49±.15		5.88±.19
7.	Water extract (cell free) high speed cent.		20	2.90±.23			
	C_2H_5OH ppt. (cell free) from above		20	2.78±.14			
	Saline controls		20		1.43±.09		4.76±.20
8.	Crude Nucleoprotein (cell free)		20	2.84±.2		6.49±.17	
	Saline controls		20		1.44±.19		4.43±.37

* In counts/mgm DNAP/cts. injected per mouse normalized to 25 gm wt. 4 hours after i.p. injection of $Na_2HP^{32}O_4$.

TABLE II

DNA Specific Activities after Irradiation*

			Livers x 10^4		Spleens x 10^3	
Dose	Time after irrad.	No. of injections	Embryo mash	Controls	Embryo mash	Controls
1040 r	12 hours	1	.29**	.19**	.43**	.41**
700	3 days	5	.82±.06	.61±.08	1.66±.33	1.96±.22
700	7 days	8	2.08±.09	1.25±.12	3.21±.15	1.98±.2

* Each value represents the average from 24 mice.

** Value is for one pooled sample from 24 mice.

TABLE III

	Post irradiation day	Control saline injected		Embryo extract injected		Probability of no significant observation
		Living	Dead	Living	Dead	
Injection Period	0-5	24	0	24	0	
	6	23	1	24	0	
	7	20	4	24	0	
	8	18	6	24	0	p = .02
	9	18	6	24	0	p = .02
	10	15	9	24	1	p = .01
	11	12	12	23	1	p = .01
	12	8	16	22	2	p = .01
	13	7	17	19	5	p = .01
	14	6	18	15	9	p = .02
	15	5	19	13	11	p = .03
	16	5	19	12	12	p = .06
	17	5	19	12	12	p = .06
	18	5	19	12	12	p = .06

III HEALTH CHEMISTRY AND PHYSICS

HEALTH CHEMISTRY

N. B. Garden

Equipment Development Group.

The main effort during this period has been spent on producing equipment and developing techniques, first, for processing two irradiated samples of transuranic materials to be received in May from the Chalk River reactor, and, second, for processing plutonium cows for the extraction of americium. The cow equipment is being assembled and will be ready in the middle of April, when chemists from the Argonne National Laboratories will arrive to do part of the chemistry, in collaboration with the Radiation Laboratory chemists and members of Health Chemistry; the first phase of the work will be done on a 24-hour basis for several days.

The processing of the Canadian samples will involve extensive equipment, including the six-inch straight-type lead cave, currently improved by the addition of ball-socket manipulators (employing uranium balls) and a lead glass window in the wall of the cave, plus the usual use of the two-inch lead shields, equipped with ball-socket manipulators and other remote control features. The setup for the straight-type cave has been greatly simplified in comparison with previous similar samples, and the work is expected to be done with considerably more speed and efficiency.

Among the items completed by the Equipment Development group are (1) a special double-envelope-type target holder for use with milligram amounts of plutonium in the 60-inch cyclotron; (2) an all-metal box for chemistry processing in an inert atmosphere; (3) equipment for magnetic susceptibility experiments with transuranic materials; (4) additional columns and slug-handling equipment to be used in the pile-bombarded animal ash work.

This group, in conjunction with the Chemistry Department, is giving preliminary consideration to the equipment necessary in forthcoming irradiation programs at the Arco pile. This consideration is with respect to target construction and handling and processing equipment.

Monitoring Group.

A new animal house has been included in the areas covered by the monitoring group, where meters and other monitoring supplies have been established. For purposes of education and indoctrination of new graduate students, new monitors and chemists, a typical gloved box for use with alpha emitters has been set up in Health Chemistry quarters; this box is to be used for illustration and for practice with inactive materials. Three new alpha foot counters have been acquired--for the animal house, the decontamination house and a chemistry building. Five new monitors have been added to the group during this period, including an off-shift man for the increasing amount of work during these times; this man will also be available for experimental projects for the monitoring group.

Activity Handling Group.

Subsequent to the detection of a daughter of radon (with a 38-minute half-life) in the Central Storage Facilities (pit room), the contents of the pit (standard storage containers in tubing) have been removed. While the pit is empty, the concrete walls will be waterproofed. This is necessary in view of a seepage which occurred during the past winter, attributable to the exceptionally heavy rains. No presence of moisture has previously been observed during the five-year existence of the pit. New cabinets and shelves have been made for storage of alpha-emitting samples in this area, and new cow-stall arrangements are being made.

All Radiation Laboratory drums containing active waste are now painted with a yellow stripe before disposal at sea to differentiate them from drums from the Naval Radiological Laboratory and from the Livermore operations that are handled at the same dumping from the Navy barge used for this purpose.

The new decontamination chamber is reaching completion. This improved setup is based on a design made following use of a pilot model for a year. Its features include a revolving table within the chamber, with suitable entry and exit interchange compartments for the material before and after decontamination; troughs and baths of various shapes and volumes, lined with polyethylene for longer life and periodic relining; a metering compartment for testing the decontaminated items, etc. Row of gloved ports line all walls; all activity-exposed surfaces are to be lined.

In view of the large quantity of active material to be handled during phases of processing of the cows described in the Equipment Development section, a medical ward has been set aside as a precautionary measure in the University's Cowell Hospital. It is equipped to handle personnel involved if an accident should occur.

With the current accumulation of large quantities of uranium and thorium chips and shavings from machining and other processes, a space for drums containing this material has been allocated. Inspection of the protective oil content is made routinely. A small fire occurred in one of the barrels during the early stage of this accumulation which furnished an opportunity to study methods of control. It was concluded that such fires would be controlled best with sand. It was also found that the barrels must be loosely covered to prevent formation of gaseous pressures.

This group, having the Central Storage Facilities close at hand, has been filling an increasing number of requests for specific types of radioactive sources of designated strengths, shapes and emitters.

Airborne Activity Control Group.

Process flow and equipment design in connection with the plutonium cow project described above were discussed. This has resulted in a definite construction program to be completed by the middle of April.

Recommendations, following consultation and investigation, have been made regarding several problems. (1) Mercury emergencies have been considered in

collaboration with California Research and Development and the Engineering Section. A new detector has been developed by the Electronics Production group. With advice from this group it was field-tested and found most satisfactory. Considerable off-project interest has been shown in this device. (2) The ventilation of the animal house has been studied because a major design defect was revealed. (3) Further work is being done on design of the new chemistry building.

A second emergency portable air cleaner, of the 600 CFM size, was ordered because of the increased need following successful application of the original model. Other equipment developed includes a small portable air cleaner (45 CFM) for use in the 60-inch cyclotron in cleaning dee interiors and associated equipment. Six additional air samplers have been ordered to meet partially an increased demand for information on airborne contaminants.

Berkeley Box Group.

With the continuing rise in the activity levels of samples processed in the Berkeley Gloved Boxes, increased diligence and consideration in gloved box assembly and fabrication have been mandatory. There is also a noticeable trend during the last few months toward the use of the gloved boxes without gloves: examples are cases where either very low level activity or none at all is involved, or in operations with foul or irritating gases or dusts. Use of gloved boxes as sterile enclosures, with ultraviolet lamps, is fairly common.

Five methods of lengthening the life of the Berkeley Boxes have been employed. (1) Unnecessary metal has been eliminated from the interior of the box; these parts are replaced with plastic proto types. (2) Increasing amounts of interior coverings such as plastic tape and plastic films are being used. (3) Incoming air is being filtered. (4) Fume hoods with the box are being used to remove corrosive and/or contaminating gases and vapors. (5) Directional control of inside air is being accomplished with a rotary air valve.

Recent improvements of the equipment within the gloved box are found in a water tap which may be placed at any desired location and a low-set induction heater coil.

General.

Requests for information on Health Chemistry equipment, procedures, prints, etc., continue to be received, and requests for equipment itself have been received and fulfilled when feasible or desirable. Present and potential industrial users of radioactive materials, other atomic sites and Civil Defense groups comprise the bulk of the questioners.

HEALTH PHYSICS

B. J. Moyer

Preparation of Article on Neutron Survey Methods

During this past quarter an article has been written which is to appear in one of the technical journals* dealing with the subject of neutron survey methods. This article attempts to review the leading techniques used in various laboratories of the country in the evaluation of neutron radiation levels. The separate methods involved for slow neutrons, fast neutrons, and high energy neutrons are discussed. In particular, the methods in use at the Radiation Laboratory in the fields of fast neutrons and high energy neutrons developed by the accelerators are given in considerable detail, since this is the first occasion of their publication in the open literature.

Service to Classified Projects

A large number of instances could be reported, if it were useful to do so, in which the Health Physics Department has been called upon by the various classified projects to assist in the evaluation of x-ray and neutron fields associated with the project's work. Included also in activities of this kind are a number of instances of consultation and calculations on problems of shielding and health protection.

Beginning Studies on Neutron Spectrum in the Cyclotron Shielding.

The evaluation of the biological hazard associated with a field of neutron radiation is greatly facilitated by a knowledge of the relative numbers of the neutrons in the different energy ranges. In particular, it is desirable to delineate the character of the equilibrium secondary neutron radiation which accompanies the primary high energy neutron flux in its progress through the shielding.

In an attempt to investigate this equilibrium neutron flux a number of threshold detectors are being employed which make use of n, 2n reactions leading to positron emitters. The attempt is made to count the annihilation radiation from the various threshold detector samples with a geometric and conversion efficiency which is essentially identical for all samples. Under such circumstances the relative counting rates will reflect accurately the relative disintegration rates; and assuming knowledge concerning the activity production cross sections, the neutron flux associated with the various threshold energies may be relatively ascertained. Work is at present being carried on with carbon, copper, and silver detector samples.

* UCRL-1635, to be published in Nucleonics.

Visual Display Radiation Level Indicators

A visual display radiation level indicator has been built by Mr. George Schrader of the counting equipment department. It consists of a thin-walled aluminum ionization chamber, an electrometer circuit, the output of which energizes a series of relays which operate 110v 60 watt lamps behind glass plates on which are printed the appropriate radiation levels. For example, when the unit is in operation near an accelerator the lowest glass plate is always illuminated, displaying the symbol 30 mr/hr. If, however, the radiation level suddenly increases to 400 mr/hr all the glass panels up to and including 300 mr/hr are illuminated. Five levels of radiation are displayed at present, 100 mr, 300 mr, 1 r, 3 r, 10 r. The sensitivity can be modified to include radiation rates from 10 mr to 10 r. The display box itself may be separated from the electrometer and ionization chamber by any convenient length of cable.

An additional unit is under construction.

Statistical Summary of Monitoring Program

Survey instruments maintained:

1.	B-γ Ionization Chamber	38
2.	Victoreen 263 Meter	19
3.	I.D.L. Portable Survey Instruments	20
4.	Cutie Pies	3
5.	Recording γ-Intensity Meters	17
6.	Victoreen Proteximeter	3
7.	Fast Neutron Proportional Counters	5
8.	Slow Neutron Proportional Counters	15
9.	Balanced Chamber (Slow Neutron Survey Instrument)	2
10.	Fast Neutron Proportional Counter (Portable)	2
11.	Balanced Chamber (Fast Neutron Survey Instrument)	1
12.	Special Tissue Wall Survey Instrument	1

Personnel meters in use:

1.	Total Personnel Covered with Film Badges	1,900
2.	Total Man Days Coverage with Pocket Chamber	1,035
3.	Total Man Days Coverage with Pocket Dosemeters	3,563
4.	Total Man Days Coverage with Pocket Chambers (SNi)	2,614

Cases of weekly exposure above 0.3r:

Weekly film Exposure Above	184" Area	60" Area	Lin.Acc.	Chem.	Other	Total
.3	0	17	7	16	17	57
.5	0	4	1	6	9	20
1.0	0	0	1	1	4	6
1.5	0	0	0	1	1	2
2.0	0	0	0	0	1	1
2.5	0	0	0	0	0	0

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