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REPORT OF HEALTH DIVISION

for

MONTH OF MAY 1945

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ABSTRACTS

CLINICAL MEDICINE AND MEDICAL RESEARCH

During the month of April 16 to May 15, 1945, 243 physical examinations were done; 55 were academic and 188 were non-academic personnel. 67 pre-employment physical examinations were done; 3 persons were rejected because of findings on clinical or laboratory examinations. During this same period 4077 clinical laboratory examinations were made. This included laboratory work on 46 new personnel, 200 controls, and 634 in the work hazard group. Abnormalities considered on the basis of the white blood count alone showed individuals with abnormalities in these groups of 15%, 28% and 17% respectively.

Evidence is presented indicating that acute radiation anemia is due chiefly to a hemolytic reaction and not merely to an inhibition of the erythropoietic system. Several hundred per cent increases in fecal urobilinogen excretion were found during the 4th to 16th day following 200 to 300 r single dose total body x-ray in four dogs.

During this same period the blood hemoglobin falls most rapidly and a green pigment (undoubtedly biliverdin, which is derived from hemoglobin) appears in the urine.

BIOLOGICAL RESEARCH SECTION

The fate of Ru inhaled as an aerosol (in the +3 or +4 valence state) has been compared with that of Ru inhaled as RuO_4 vapor. The "vapor" Ru leaves the lung rapidly at first (T 1/2=1 day) and then quite slowly. The "aerosol" Ru does not show these two phases but leaves with an initial T 1/2 of 7 days. There is relatively little tendency for the absorbed Ru to deposit and it is excreted almost as fast as it is absorbed. Urine and feces activities are of the same order of magnitude.

Rats were exposed by inhalation 4 1/2 months ago to a cerium aerosol (50 µc average per animal). During the first 2 months, 9 out of 21 rats became very ill (weight loss and respiratory involvement) and were sacrificed. At least 6 of these were moribund. The remaining 12 animals after 4 1/2 months seem as health as the controls. Thus this dose (33 µ c per gram of lung or average of 0.25 µ c per gram body weight) would seem to constitute an LD 30.

A study of the comparative toxicity of Sr^{89} via intraperitoneal injection in the rabbit, rat, and mouse gave the following results:

1. The L. D. 50 at 30 days for rabbits and rats was about 5 millicuries administered per kilogram and for the mice was greater than 8 millicuries administered per kilogram of body weight. When

compared on the basis of retained strontium, however, the L.D. 50 was 1, 3, and greater than 2.6 millicuries per kilo in the rabbit, rat, and mouse respectively. From our data, it is not clear whether the higher toxicity of Sr in the rabbit is due to body size or species difference.

2. The rabbits and rats at death usually had hemorrhages at one or more places on the body although the actual loss of blood did not appear to be great enough to be the sole cause of death.

3. Retention of strontium at death or sacrifice amounted to about 65% of the injected dose in the rat, 32% in the mouse, and 20% in the rabbit.

4. In all 3 species the strontium was almost entirely in the skeleton.

5. The relative concentration of strontium was about the same in 8 different bones, irrespective of species.

Rats which have received insoluble ratio-yttrium by stomach tube at 200 μ c daily for 4 1/2 months show no ill effects of the treatment.

There was slight damage to lymphocytes in the mesenteric node, appendix and spleen of rabbits following 25 of x-radiation. There was questionable damage after 12r, and no detectable damage after 6r.

Hybrid guinea pigs were exposed to 8.8 r of gamma rays per 8 hours per day at the N.C.I. A maximum total dose of 715r±10% was delivered to the experimental animals. A significant reduction in the mean lymphocytes per mm^3 was apparent after a total accumulated dose of 130r while other constituents were relatively unaffected until more than twice this dose had been accumulated.

Two dogs received 300r of x-radiation. One died 18 days later while the other is alive after 35 days. Clinical symptons were as reported previously for other dogs. New observations include the following: sedimentation rates increased by as much as 70 times, non-protein nitrogen, creatine and creatinine in plasma diminished, renal clearance of phenol red increased and a green pigment, probably biliverdin, appeared in the urine.

MEDICAL AND INDUSTRIAL HAZARDS SECTION

The betatron installation at the University of Illinois was surveyed and found to have numerous above tolerance areas. Recommendations for the safeguarding of potentially exposed personnel were made. A hot run in Room 6, New Chemistry, was completed with some low over-exposure to hands. However, considering the amount of activity handled and the necessarily temporary character of the shielding, the over-exposures were not exceptional.

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Armory courtyard surveys have demonstrated a diffuse contamination. Study of the operation of the furnace in this courtyard indicates that the conversion of uranium shavings to uranium oxide is probably responsible.

4537 pocket meters were read during the month. 0.7% were above the permissible level of 100 mr for any one day. The decontamination squad has passed to the jurisdiction of the adminstrative offices of the Metallurgical Laboratory.

RADIATION LABORATORY

The uptake of carrier-free radio-tellurium by barley plants from a culture solution showed 0.2% was in the tops and 30% in the roots. In plants Te is absorbed less readily than Sr and more readily than Y, Ce, Zr and Cb. 35 microcuries of U^{232} was made by the 60" Cyclotron and has now been isolated. The blocking action of repeated doses of inert iodine in reducing the uptake of carrier free I^{131} by the thyroids of rats has been found to be discouragingly poor. The inhalation of Uranium free fission product aerosols produced by volatilization of their chlorides in a carbon arc showed high lung retention with a significant degree of deposition in the skeleton.

UNIVERSITY OF CALIFORNIA

In the period of March the twenty-seventh to April the fifteenth nine patients have been studied who were previously treated with 200 K.V. and 1000 K.V. x-rays. No new patients were treated. The blood studies were charted and the findings evaluated.

NATIONAL CANCER INSTITUTE

LAF_1 mice of original experiment. Total chronic doses at present: (4.4 r, 2.2 r, 1.1 r, and 0.11 r per 8 hours per day) 3,500 r, 1,750 r, 875 r and 91 r. The blood picture of the surviving animals is confusing due to changes resulting from kidney lesions, chronic eczema and especially tumor formation, the latter predominating in the experimental animals. The incidence of malignant lymphomas is still decreasing. Ovarian tumors are found in 100% of all animals which come to autopsy with the exception of the controls, the animals exposed chronically only on the 0.11 r level, the animals exposed to an acute exposure of 12.5 r only, at the age of 5 months and, perhaps, those which were exposed chronically on the 0.11 r level and received, in addition the acute exposure of 12.5 r

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Hybrid guinea pigs of original experiment. Total doses and exposure levels are the same as for mice of the original experiment. The blood picture of the control animals, of those exposed on the 0.11 r and 1.1 r level and of those given a limited exposure of 300 r or 600 r respectively on the 8.8 r level at the age of 8 to 9 months and 8 to 10 months respectively is more or less normal. Some of the animals of the 2.2 r level (approximately 50%) show lowered red and platelet count. All surviving animals of the 4.4 r level show a lowering of all counts. One came to autopsy with a red count of 900,000.

Inbred guinea pigs of family 2 exposed to 8.8 r per 8 hours per day. All counts are considered lowered: R.B.C. 1 to 3 million, platelets 10,000 to 20,000 and W.B.C. 1,000 to 3,000 with relative lymphocytosis. All animals with the exception of one male were removed from the field when the red count dropped below 2.5 million. There was no recovery in those animals (5) in which the red count had dropped below 1.5 million; they died within one week after removal from the field, the red count remaining stationary or dropping slightly.

A quantitative morphologic analysis of testes of mice exposed on the 8.8 r level to a total dose of 300 r showed that there is no increase of interstitial tissue associated with atrophy of spermatogonic elements following irradiation.

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CLINICAL MEDICINE AND MEDICAL RESEARCH

L. O. Jacobson, Section Chief

Employees Health Service - J. Garrott Allen

April 16, 1945 to May 15, 1945

A. Total physical examinations		243
a) recheck physicals	142	
b) pre-employment physicals	67	
c) transfers	12	
d) terminal examinations	22	
e) academic	55	
f) Non academic	188	
B. Rejected	3	
C. Routine Office Calls		615
a) first industrials	40	
b) return industrials	50	
c) blood abnormalities	14	
d) personal calls	511	
D. Refers to Billings	46	
a) industrials	6	
b) substantiating diagnosis	6	
c) personal		
E. Total number of visits of personnel to Drexel House		858

Clinical Laboratory Examinations - E. K. Marks

A resume of the clinical laboratory examinations during April 11 to May 10, 1945 is as follows:

Number of Laboratory Procedures performed			Number of abnormal findings
Hemoglobins	620		122
Red counts	522		105
White counts	799	below 5000	49
		above 10000	47
Differentials	799		408
Platelets	137	below 175000	20
		below 150000	2
Urines	515		240
Retics	44		0
Wassermans	162		0
Misc.	20		0
Sedimentation rates	221		0
Hematocrits	200		0
Stipplings			0
Immature cells			30

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Number of individuals examined		Number with clinical laboratory abnormalties *
New Personnel	46	7 or 15%
Controls	200	58 or 29%
Work Hazardous group	634	113 or 17%

* Includes only individuals with a WBC below 5000, reversal of Neutrophile-Lymphocyte-ratio, immature cells and lymphocytes below 1500

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H I Clinical Medicine and Medical Research

L.O. Jacobson, Section Chief
S. Schwartz, Group Leader

Inhibition of erythropoiesis is generally considered responsible for both the acute and chronic anemias produced by either external or internal radiation.

The following theoretical and experimental considerations, however, indicate that the acute anemia appearing within the first month is due chiefly to a hemolytic reaction.

1. Most authorities believe that the average life of a red blood cell is roughly 100 days. Even assuming 100 per cent inhibition of erythropoiesis, this mechanism could, therefore, result in a red cell count fall of only about one per cent daily. Both here and elsewhere declines of up to 50 per cent or more have been reported in dogs during about the 5th to 15th days following large dose total body x-ray. This is about five times as rapid a fall as can be accounted for by the inhibition of erythropoiesis alone.

2. Last month we reported the excretion of a green urine by four dogs receiving total body x-ray and by two of three dogs who received product. The same pigment has been found in the urine of a dog who received a lethal dose of radioactive strontium, and of two more dogs given total body x-ray.

This pigment is almost certainly biliverdin, a derivative of the heme portion of hemoglobin. The appearance of this compound in the urine probably indicates the presence of increased bile pigment formation, either with or without an injury of the intrahepatic biliary tract. (It might be noted that these pigments are excreted in the urine much more readily by dogs than by humans.)

3. The rate of hemoglobin destruction has recently been studied by means of the fecal urobilinogen excretion in four dogs treated with a single dose of 200 to 300 r of total body x-ray. Watson's method of urobilinogen estimation was employed, using ten gram samples from combined consecutive four day stool collections.

The data are presented in Table I in terms of mg. of urobilinogen excreted per day.

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	TREATED DOGS				CONTROL DOGS	
	Dog #24 (250r)	#36 (200r)	#43 (300r)	#44 (300r)	#26	#40
Control Periods						
1.	11.5	0.6	3.4	1.5	6.5	2.3
2.		2.0	9.9	13.8	8.9	2.8
3.			4.7	12.2	6.9	3.1
4.			6.3	21.1	6.0	2.2
5.					5.3	3.8
6.					6.0	5.4
7.						0.9
8.						1.9
Post X-ray						
1-4 days	4.7	9.9	3.1	27.9		
4-8 "	2.3	23.3	32.8	23.5		
8-12 "	17.5	13.4	17.1	30.5		
12-16 "	23.1	30.9	3.0			
16-20 "	8.4	20.4	5.1	Exitus		
20-24 "	2.1	2.1	15.7			
24-28 "			11.1			

Table I: Fecal Urobilinogen Excretion (mg/day) in Dogs Following Total Body X-ray.

The 25 control determinations listed average 6.0 mg/day. The rise in urobilinogen excretion occurs expecially during the 4 to 16 day post-radiation period. The 11 determinations during this 12 day period average 19.7 mg/day. This is the period of most rapid fall in red blood cell count. It is also the period during which the green pigment occurs in the urine.

It should be noted that fecal urobilinogen studies in dogs do not give as complete a picture of hemoglobin metabolism as might be desired, because of the following factors:

1. The frequent occurence of constipation may make the data difficult to interpret. (Thus dog #44 had a fecal urobilinogen concentration before death of 170 mg per 100 grams, an extremely high value. Howevere, for five days he excreted an average of only five grams feces daily (control average almost 200 grams daily), so that the per diem excretion for the period was normal!).

2. It is possible that the bile pigment may not be completely reduced to urobilinogen in the intestinal tract. Thus, dog 37, given radioactive

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strontium had no increase in fecal urobilinogen, but did have a large amount of green pigment (biliverdin ?) in the feces. This is the only time we have noted this phenomenon.

3. Because it is best to do determinations on combined samples collected over a period of several days, the number of analyses done in necessarily limited.

4. There is a time lag of a few days between the time of blood destruction and the excretion of the urobilinogen in the feces.

To obviate these difficulties a series of studies are being planned with Dr. Allen using dogs with external biliary fistulae. Careful daily analyses of the bilirubin and biliverdin excretion, as well as of the urine and bile porphyrin excretion should clarify the picture considerably.

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H-II BIOLOGICAL RESEARCH SECTION

K. S. Cole, Section Chief
C. L. Prosser, Associate Section Chief
A. M. Brues, Assistant Section Chief

000 MUH 2002 Pneumonia Epidemic among Experimental Animals.

During the past month an emergency of major importance occurred in the animal farm.

It has been noted for some months that the rats in one of the rooms have shown a high incidence of pneumonia. This is a broncho-pneumonia of unknown cause which appears to have an immediate mortality of 10 - 20% and which is complicated in some cases by pneumococcus pneumonia; it appears in most cases to result in chronic lung disease with abscess formation. About one month ago, it became clear that this condition had spread to several of the animal rooms and that morbidity was increasing so that it was necessary to take drastic measures. During the past two weeks, it has also become clear that mice are succumbing to the same disease. We have, therefore, been making attempts to ascertain the nature of this disease and have been trying the effects of various therapeutic agents including sulfonamides and penicillin. In addition to this, 1500 infected rats have been sacrificed, and a considerable number of the tested experimental animals have been placed in one room in which is a vaporizer using triethylene glycol. At present our first object is to prevent the extension of this disease.

244 MUH 2111 Inhalation of Ruthenium - I. Wender, M. Dailey

Last month we reported exposing a group of rats to an aerosol of 330 day Ru. Although it is difficult ever to be sure of the valence state of a given sample of Ru, it is probable that the material used here was +3 or +4 or a mixture of both. It was hoped to compare the fate of this material with that of Ru inhaled as the vapor, Ru O_4.

As a result of having available only minute amounts of Ru, the data obtained in those experiments are subject to considerable error. Aside from the lungs, the activity in other tissues was so low as to make accurate analysis impossible. Some facts stand out, however. In both experiments the Ru showed little tendency to deposit anywhere in the body but was excretion almost as fast as it was absorbed from the lungs. Fecal excretion was greater than urinary excretion with Ru +4 vapor whereas urinary excretion exceeded fecal excretion with the aerosol. Our meager data seem most compatible with the assumption however, that with both forms of Ru, the absorbed activity is rapidly excreted, with urine and feces being of the same order of magnitude.

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The evidence seems definite, that RuO_4 is absorbed from the lung more rapidly at first, but whether this is a function of valence state or physical state is not known. The data in Figure 1 indicates that "aerosol" Ru leaves the lung with a 7 day initial half-time while "vapor" Ru leaves with a 1 day initial half-time.

244 MLH 2134 Inhalation of 300 day Ce - R. Abrams

On Dec. 21, 1944 we exposed a group of rats to an atmosphere containing 300 day Ce from a DC carbon arc. (See previous reports for details). At this time, 4½ months later, it is perhaps worth while to summarize the status of the exposed animals (which had received an a average dose of 50 µc per animal). Of 21 rats, 9 became very ill (loss of 30 to 40% body weight and extensive respiratory involvement) within the first 2 months. At least 6 of these 9 were what we call moribund. All were sacrificed before death to obtain tissues for histological workup. In the past 2½ months all of the 12 surviving animals have been gaining weight and appear perfectly healthy. They are being maintained on the assumption that late neoplastic changes may occur. Thus we seem justified in calling this dose (33 µc per gm lung or average of 0.25 µc/gm body weight) an LD 30 or perhaps an SD (sick dose) 50.

244 MLH 2135 Inhalation of 57-day Y - R. Abrams, H. Seibert

Over 7 months ago a group of rats were exposed to an aerosol of 57-day Yttrium put up by atomizing an aqueous solution. Each rat received an initial lung dose of 26 µc. As a result of rapid elimination, these rats received a total lung dose of only some 1500 reentgens. Now after 7 months there is still no evidence of damage to these rats.

During the past month, another attempt was made to produce acute damage with Y. This time 400 mC of Y were evaporated on 4 carbon electrodes The rats were anesthetized and cannulated--the open ends of the cannulas being inserted thru rubber grommets in-to a 1.3 liter brass chamber. The active electrode was inserted through the top of the chamber. After filling the chamber with O_2, the arc was struck (250 volts, 4 amps) for 30 sec, and the animals allowed to breathe for 5 minutes. Then a fresh electrode was inserted, the chamber refilled with O_2, and the procedure repeated. The experimental set-up is shown in Figure 2.

Analytical data on the dose received are not yet available. During the 13 days since exposure 5 out of 21 experimental rats have died and all of 14 controls are still alive.

246 MLH 2211A. Comparative Toxicity of Radio-strontium in the Rabbit, Rat, and Mouse - David Anthony & R. D. Finkle

An experiment was designed to give information about the effect of body size on the toxicity of Sr^{89}. An earlier experiment had indicated that both rats and rabbits have a mid-lethal dose somewhat below 5 mc per

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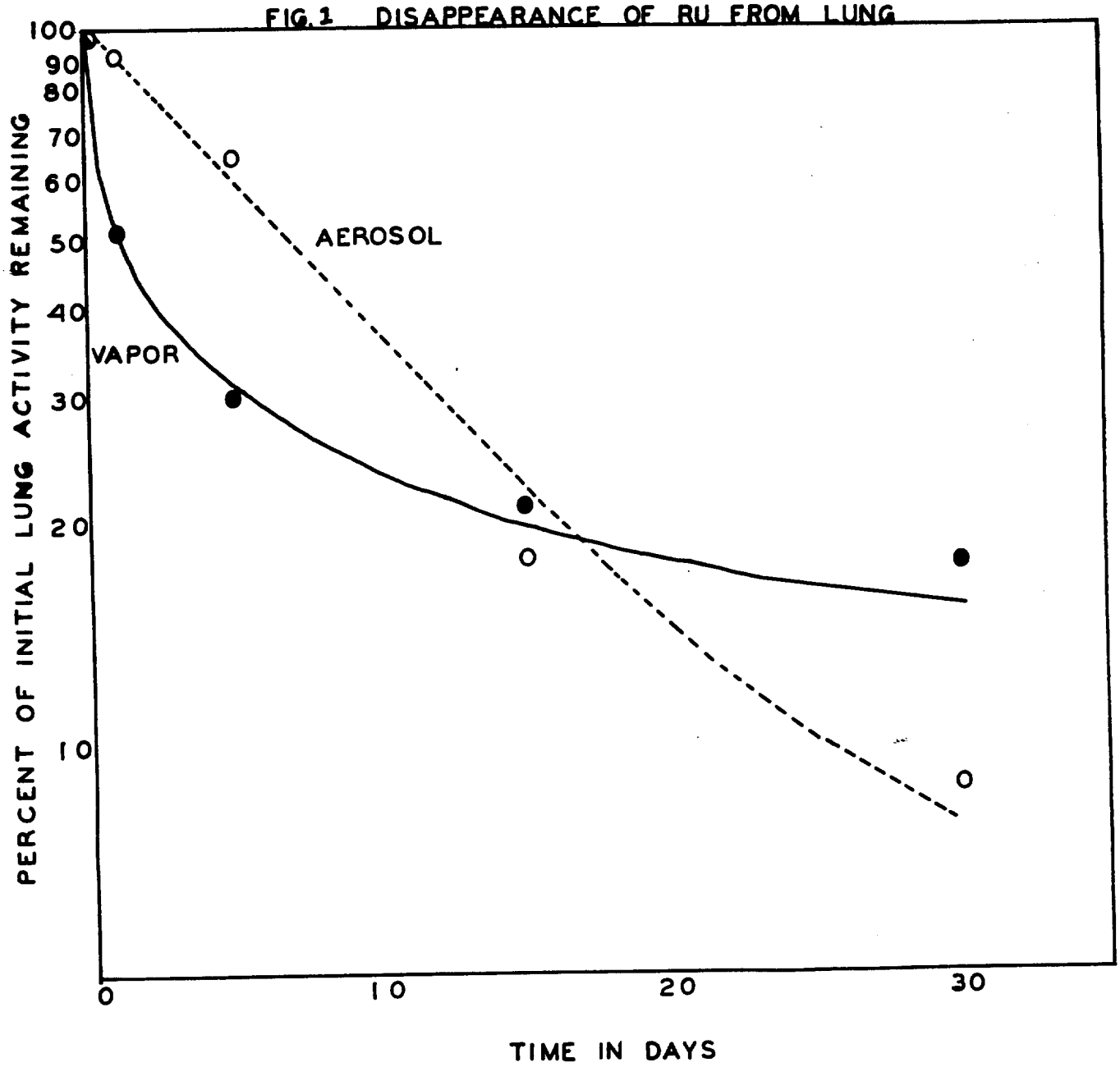
FIG. 1 DISAPPEARANCE OF RU FROM LUNG



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kilogram of body weight. The retention of strontium by the skeletons [illegible] was considerably less (about half) than the retention in rats. The experiment was incomplete in several respects: The mice used developed many bad infections of the feet and legs and hence were unreliable; the number of rabbits on each level was too small to yield conclusive data on either toxicity or rate of excretion.

The animals in this current experiment were given single doses of strontium via intraperitoneal injections on 2/27/45. The dose levels in all three species were the same: 0,2,3,5, and 8 mc per kilogram. There were 6-10 rabbits, 6 rats, and 12 mice (brown and white ABC) at each dose level. All of the animals were males.

The data on the distribution of strontium in rats are presented in Table 1. The ten rats studied for gross distribution retained 64 ± 9% of the injected dose in the carcass, 2.1 ± 0.9% in the femur, and 0.6% or less in the entire viscera. These analyses were made on animals dying in the period 7-17 days following injection. The gross distribution of Sr was determined in 4 rabbits which died between the 8th and 12th day after injection (table 2); their carcasses contained 19 ± 5% of the injected dose, the femurs, 2.3 ± 0.5%, and the viscera contained 0.9 to 1.6%. Data on 15 mice (table 3) showed that the total retention of strontium in this species was about 32% of the injected dose.

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Table 1

Distribution of Sr in Rats

Rat No.	μc/Kilo dose Level	Time of Death in Days	Femur	Carcass	Viscera
			%Of Inj. Dose		
6902	8	9	3.0	73.1	0.3
6901		10	2.7	61.5	0.5
6903		10	2.5	72.5	0.3
6886		12	2.5	61.5	0.1
6894		12	2.5	58.6	0.3
6899	5	7	1.2	57.5	0.3
6869		12	1.3	70.5	0.2
6882		12	2.7	68.0	0.5
6895	2	16	2.6	59.3	0.6
6887		17	2.5	56.8	0.3

[redacted]

Table 2

Distribution of Sr in the Rabbit

Rabbit No.	mc/Kilo Dose Level	Time of Death in Days	Femur	Carcass % of Inj. Dose	Viscera
2178	8	8		20.5	.9
2146		9			
2130		10	.76 .84		
2139		12	1.4	22.4	1.1
2167		12	.97 .91	13.7	1.0
2162		11	1.5 1.5		
2110	3	13	1.3		

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Table 3

Retention of Sr^{89} in the Mouse Femur and Carcass

Mouse Number	Dose/Kilo	Femur-% Retention	Carcass-% Retention
17417	2	1.1	32.0
17418	2	1.3	27.0
17416	2	1.2	
	Ave: 2mC Group	1.2	30
17422	3	1.5	
17455	3	1.0	
	Ave: 3mC Group	1.2	
17469	5	.9	32.0
17472	5	1.4	35.0
17473	5	.9	25.0
17470	5	1.7	34.3
	Ave: 5mC Group	1.2	32
17460	8		30.7
17462	8	1.5	30.0
17464	8	1.6	36.6
17468	8		36.0*
17459	8		38.2*
17465	8	1.8	33.3
17457	8		31.0*
17458	8		29.3*
17461	8	0.8	19.6
	Ave: 8mC Group	1.4	32.5*

*Carcass includes both femurs.

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The distribution of Sr^{89} within the skeleton has been determined on 3 rabbits, 3 rats, and 5 mice to date. There appears to be no species difference in this distribution and there is little consistant difference from bone to bone within a species. With the concentration of strontium in the femur taken as 100 (table 4) the average concentration for each bone studied (with the exception of the sternum) fell in the range of 95 - 16. The sternum was undoubtedly lower because of the inclusion of considerable amounts of non-bony, cartilagenous material. The vertebral segments contained some muscle and connective tissue that could not be removed. It is interesting to note that the variation from bone to bone in an individual animal is usually about 2 to 3.5-fold while in any given bone the concentration also varies from one animal to another by about 2 to 3.5 fold. In general, it can be said that the average concentration of strontium does not vary consistently from bone to bone in any of the three species studied.

Excreta were collected at 3, 7, 14, and 21 days on the 5 mc rabbits, and on the 3 and 5 mc rats and mice. The feces and urine of the rabbits and rats were collected separately from individual animals while mixed excreta collections were made from groups of 6 mice. The overall excretion of 4 of the 6 rabbits studied (table 5) ran from 33-64% of the injected dose, that of the rats (table 6) amounted to 25-35% and of the mice (table 7) about 40%. The amount of Sr excreted by the rabbit, as recorded in our data, is low by an unknown amount, probably about 5%, since the urine collected during the first 18 hours was discarded thru a misunderstanding.

A disturbing feature of the mouse data was the apparent 72% overall recovery of the injected strontium. The 28% not located by our analyses was probably; (1) excreted after the excretion collections were discontinued (14th day) and (2) excreted but then stuck on the cages where it was never collected. Evidence for the former was given by the external counts on ten mice. These counts were taken first shortly after excretion collections were suspended, and then again 6½ weeks later. All ten of the mice lost strontium and the average loss was 11 percent. The second source of loss was probably even more important since it was found that cages which had been used for this experiment had as much as 45 uc of hydrochloric acid-soluble strontium adhering to them even though they had been repeatedly steam-sterilized and washed with soap and water.

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Table 4

Bone Distribution

Animal Number	Dose/Kilo	Two pair ribs	Humorous	Femurs	Vertebral Column: Thoracic	Vertebral Column: Lumbar	Vertebral Column: Sacral	Sternum	Skull	Scapula
(All values are relative concentrations with the femur taken as 100.)										
Rabbits										
2158	2mC	80	112		100	72	82	35	109	112
2163	5mC	89	103	100	59	84	80	31	111	162
2156	2mC	150	98	100		85			144	115
Rats										
6885	2mC	112	122			55	68	27	84	190
6868	5mC	90	51	100	56	44	49	28	54	87
6888	8mC	64	123	100					81	103
Mice										
17416	2mC*	96	100		41	43	85	58	50	56
17470	5mC	75	90	100	87	95	82		87	
17457	8mC*	43	133		122	115	97	79	98	114
17465	8mC	43	103	100	76	99	86	54	73	63
17458	8mC*	65	154		99	110	104		67	103
Average:		82	108	100	79	80	79	45	87	111
Range:		43-150	51-154	100	41-122		43-115	49-104	27-79	50-144 56-190

*Since no femurs were available, relative conc. figures for these animals are based on the average concentration in all bones = 100.

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Table 5

Excretion of Sr^{89} by Rabbits

Rabbit No.	Dose/Kilo	0 to 3 Days		3 to 7 Days		7 to 14 Days		Total		
		Urine	Feces	Urine	Feces	Urine	Feces	Urine	Feces	Total
(All values below are in percent of injected dose.)										
2155	5mC	1.18†	26.5	1.58	.9	1.33		4.0	27.4	32.9*
2162		4.82†	17.9	.79	1.4	.52		6.1	19.3	49.4*
2163		1.75†	20.2	6.35	1.3	3.46	.26	11.6	21.8	39.7*
2169		.52†	93.1	.78	13.7	2.51	0	3.9	106.8	122.8*
2170		4.40†	20.	2.91	.9	1.5	.4	9.4	21.3	63.6*
2174		1.22†	76.6	.59	5.7	2.53	1.7	4.4	84.0	89.1*

† All 0-3 day urine samples are low by an unknown amount due to accidental loss of that collected in first 18 hours.

* This total is greater than the sum of urine and feces. The difference is due to Sr recovered when cages were washed down with dilute HCl at end of experiment.

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[redacted]

Table 6

Excretion of Sr^{89} by Rats

Rat No.	Dose/Kilo	0 to 3 Days		3 to 7 Dasy		7 to 14 days		14 to 21 days		Total	
		Urine	Feces	Urine	Feces	Urine	Feces	Urine	Feces	Urine	Feces
(All values below are in percent of injected dose)											
6883	3mC	9.2	18.8	2.0	3.2	.8	2.5			12.0	24.5
6904		4.7	16.3	1.9	2.9	1.1	2.5	.87		8.6	21.6
6881		4.0	15.9	2.0	2.6	.9	3.3	1.3		8.2	21.8
6877		4.3	19.9	3.1	3.0	1.3	3.8			8.7	26.7
6893		6.3	14.7	2.0	3.1	1.9	4.3	.99		11.1	22.1
6866		4.1	16.2	2.3	2.9	1.7	2.9	1.37		9.5	23.0
6869	5mC	3.2	20.4	1.2	0.3	.5				4.9	20.7
6891		0.9	87.3	0.2	1.6	.1	0		.13	1.2	89.0
6868		7.7	21.3	2.1	2.7	1.3	1.9	.87		12.0	25.9
6899		4.4	23.4	1.7	2.9	0				6.1	26.3
6889		1.8	88.1	0.1	0.2	.1	.14	0		2.0	88.4
6882		7.6	13.5	2.7	4.4	1.1				11.4	17.9

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Table 7

Excretion of Sr^{89} by Mice

Mouse No.	Dose, Kilo	0 to 3 Days Urine & Feces	3 to 7 Days Urine & Feces	7 to 14 Days Urine & Feces	Total Urine & Feces
17420 to 17425	3mC	32.3	4.5	4.1	41
17451 to 17456	3mC	35.2	3.7	3.0	39
17426 to 17431	5mC	31.2	4.2	3.2	39
17469 to 17474	5mC	34.2	4.5	3.6	42

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The effect of radiostrontium on the growth rate was marked by a sharp species difference (Table 8). The rabbits that survived to 35 days regardless of their original dose, grew at about the same average rate. In fact, rabbits that died from the effects of the strontium did not show a greatly decreased rate of growth even a few days before death. In the rats and especially in the mice, however, even the lowest dose of strontium significantly lowered the average rate of growth. As the dose increased, there was a stepwise decrease in growth rate. Those rats and mice that died from the effects of the strontium showed a sharp loss in weight before death.

The survival data (Table9) indicate an acute (30 day) L.D. 50 for radio-strontium in rabbits and rats of about 5 mc/kilo with all deaths occuring between the 7th and 17th day. This is in close agreement with previous experiments. The mice, however, were much more resistant to the strontium than they were in previous experiments. Whereas, an L.D. 50 of about 6 mc/kilo (within 2 to 3 weeks) had been noted in two earlier experiments, in this series the L.D. 50 for the same time period appeared to be greater than 8 mc/kilo. In the period from 5 to 8 weeks, however, all of the eight mice allowed to remain in the 8 mc group lost weight rapidly and died.

The probable explanation of this low toxicity of strontium in these mice, lies in the much lower retention of strontium than seen previously. An analysis of 44 carcasses from mice in previous experiments revealed an average retention of 45% of the injected dose (range 33 to 68%) while a similar analysis on 15 carcasses from this experiment showed only 31% retention (range 20-38%). Since the L.D.50 of 6 mc/kilo was established on these mice showing a total retention of 47% in the carcass plus femur, it could be said that 2.8 mc/kilo of retained strontium represented the L.D.50. The 32% total retention as measured in this experiment would amount to a retention of 2.6 mc/kilo even in the highest (8 mc/kilo) level of this experiment. Therefore, the mortality data, for this experiment is not greatly out of line with that from previous studies.

[redacted]

[redacted]

Table 3

The Effect of Injected of Sr^{89} on Growth

Dose Level mC/Kilo	No. of Animals at time of Inj.	Ave. Weight at time of Inj.	No. of Animals at 35 Days	Ave. Weight at 35 Days	% Change in Wt. 0-35 Day
		Rabbits			
0	10	2210	10	2650	+ 20
2	6	2110	3	2590	+ 23
3	10	2190	9	2700	+ 23
5	6	2120	3	2540	+ 20
8	6	2070	1	2490	+ 23
		Rats			
0	6	174	6	278	+ 60
2		168	3	237	+ 41
3		166	6	233	+ 40
5		163	2	252	+ 55*
8		165	1	147	- 11
		Mice			
0	12	20.6	12	26.9	+ 31
2	13	18.0	12	22.5	+ 25
3	12	20.1	12	22.7	+ 13
5	12	20.1	11	20.1	0
8	12	19.9	9	15.7	- 21

* Excretion data shows these two rats to have been gut-injected. Thus they did not really receive the dose indicated.

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Table 9

Essential & Mortality Data-60 Days

Dose mc/ kilogram	No. Animals	No. Dead in 30 days	Time of Death in Days	No Sacrificed	Time of Sacrifice in Days
			Rats		
8	6	5	9, 10, 10, 12,12	1	48
5		3	7, 12, 12	1	34
3		0		0	
2		2	16, 17	1	24
0		0		0	
			Rabbits		
8	6	5	8,9,10,11,12	1	48
5	6	2	11,11	1	32
3	10	1	14	0	
2	6	0	55	3	24, [illegible] 38
0	10	0			
			Mice		
8	12	0	35,35,45,50,56 56,59,59	4	34,36, 38,5[illegible]
5		0		4	32,4[illegible] 49,4[illegible]
3		0		2	50,5[illegible]
2		0		3	25,4[illegible] 49
0		0		0	

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After death, or following sacrifice when in a moribund condition, autopsies were performed on 10 rats and 8 rabbits. The gross pathological findings and the number of animals in which they occured are given in table 10.

It can be seen that the gross pathological picture in general was one of widespread hemorrhage. In only two or three cases, however, did it seem as though the amount of blood lost was sufficient to be a major cause of death. The peritonitis noted in two rabbits was of a gas-gangrene type and was probably a result of the local irradiation following the injection. In these rabbits there was severe involvement of the cecum, appendix, and terminal ileum with extensive hemorrhage and necrosis. Numerous gas pockets in the ventral abdominal wall were also observed.

When all the data are considered, this experiment gives no clear indication of the relation between body size and toxicity of retained radio-strontium. The mice which retaine about 2.6 millicuries of Sr per kilogram of body weight (32% retention of an 8 mc/kilo dose) were still somewhat below the L.D. 50 level. The retained strontium in the rat at the L.D. 50 amounted to about 3 mC/kilo (65% of 5 mC/kilo) while the rabbit retained about 1 millicurie per kilogram (20% of 5 mC/kilo) at the L.D. 50 level. Whether the greater toxicity of Sr^{89} in the rabbit was due to its size (and attending negligible "radiation leakage") or was a result of a species difference in radio sensitivity is not apparent from this experiment.

Table 10

Gross Pathology of 10 rats

	Number showing symptoms
Hemorrhagic mesenteric lymph nodes	7
Hemorrhagic testes	6
Subcutaneous peticheal hemorrhages	5
Hemorrhage into lumen of intestine	4
Hemorrhage of knee joint	4
Hemorrhage of stomach mucosa	3
Hemorrhage of epicardium	3
Free blood in stomach	2
Edema of face	2
Hemorrhage of kidney cortex	1

Gross Pathology of 8 rabbits

Hemorrhage in wall of cecum, appendix, colon	5
Yellow, spotted liver	4
Hemorrhagic mesenteric lymph nodes	3
Hemorrhagic mucosa of stomach	3
Hemorrhages and degenerative changes in kidney	2
Gangrenous peritonitis of cecum, appendix, and terminal ileum	2
Hemopericardium	1
Hemorrhagic thymus	1
Free blood in stomach	1
Extreme hemorrhage of ureters & exterior surface of urinary bladder	1

1119005

246 MLH 2726 B INGESTION OF RADIO-YTTRIUM - W. Grundhauser

The feeding experiment described in previous reports are being continued. Rats have now been maintained on 200 microcuries of yttrium daily over a four month period without any evidence of pathologic changes. A number of the animals which received six microcuries daily have been sacrificed in order to determine how much material has been absorbed. The results show that one week after feeding, the bodies of animals which received six microcuries daily contained less than 1/100,000 of the total dose which was given.

246 MLH 2721 A CHRONIC TOXICITY OF RADIO-STRONTIUM - M. Finkel

Litters of young have been delivered by several rats and mice which received strontrium and product at various times. Preliminary analyses of the offspring indicate that some of those materials may be transferred to the embryo during gestation, but that the concentrations in the young are in general considerable smaller than in the mother.

142 MLH 2411 THE EFFECT OF GAMMA RAYS ON THE PERIPHERAL BLOOD OF THE GUINEA PIG - L. O. Jacobson
G. Sacher
E. Simmons

Guinea pigs were treated with daily exposures to external gamma rays at N.C.I. The procedure used in this experiment has been described in a previous report, CH 2588 pages 3 through 7. Briefly, a one gram radium bomb is mounted in a brass cylinder filled with lead in the center of a large room. The brass cylinder is supported from the ceiling by a cable which is connected to a motor-driven drum in an adjoining room. A shelf is arranged in a circular manner about the radium bomb at a distance which gives 8.8r (± 10%) in 8 hours in the middle of the cages placed on the shelf. Eight hour exposures were given daily and the bomb lowered into a brass tube 21 feet below the level of the floor during the remaining 16 hours daily. When the bomb is at the bottom of the tube the radiation intensity is negligible in the room.

An equal number of male and female guinea pigs (hybrid NCI stock, four months of age were given 8.8r per 8 hour day by this experimental setup. A comparable number of controls were studied simultaneously. Three complete blood counts were made on the experimental animals and controls at intervals of 2 days prior to the beginning of exposure and again on the day of initial exposure. Complete blood counts were made every 2 days for the first week and at weekly intervals thereafter until a significant reduction in the leucocytes per mm^3 or erythrocytes per mm^3 or both was apparent. Clinical observation and weights were followed as well.

In addition to the above studies, the experiment was designed so as to correlate as closely as possible the peripheral blood findings of the experimental animals exposed to varying amounts of gamma radiation with the histological findings of the hemopoietic organs. To accomplish this, careful and complete blood counts were made of each animal at the intervals previously described.

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*Complete blood counts included Hb in grams per 100cc blood, erythrocytes, platelets and leucocytes per mm^3, reticulocyte percent and differential percent (300 cells counted).

Two experimentals and two controls were then sacrificed after receiving approximately 100r, 200r, 300r, 400r, and 675r. The remaining 10 controls and 10 experimental animals were sacrificed after the latter received approximately 715r. The groups were sacrificed in this manner because a previous experiment at NCI (see CH 2588) had indicated that after a total dose of 700r to 800r delivered at 8.8r/ 8 hour/ day, about 50% of the animals showed hematological effects while the balance were comparable to the controls. Sacrificing in this critical period would then provide a cross section of animals including those which showed no hematological effects (and presumably only subtle or no histological changes in the haemopoietic tissues) and those having a marked anemia, leucopenia and thrombocytopenia, with marked pathological changes, in the hemopoietic tissues. This, in fact, was the case and herewith a summary of the haematological findings is given. The histological study and correlation with the peripheral blood study will be given at a later date.

Clinically, the experimental animals were comparable to the controls from the standpoint of appearance, general activity and food intake until the onset of severe anemia. This occurred in a more or less dramatic manner, but was generally pressaged by a drop of moderate degree in the various constituents of the peripheral blood (Hb, RBC, platelets, leucocytes). A ruffled coat, refusal to eat, cold nose, inactivity and rapid weight loss which occurred abruptly was invariably associated with a severe anemia (less than 2 million RBC per mm^3), leucopenia, reduced hemoglobin and thrombocytopenia. Careful inspection of those animals usually revealed hemorrhagic manifestations. Postmortem examination or autopsy after sacrifice revealed that the degree of hemorrhage which occurred into the gastrointestinal tract, viscera, skin, etc. was usually sufficient to account for the rapid onset of the severe anemia which had occurred, and undoubtedly resulted from the thrombocytopenia. On the other hand, mild anemia which occurred in some animals, i.e. reductions of the order of one to two million per mm^3 in the red cell count and corresponding reduction of hemoglobin could not be accounted for by hemmorrhage seen in the tissues at

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autopsy or by microscopic evidence when such animals were examined histologically. It must be assumed, therefore, that this anemia resulted from the effect of radiation on red cell production and hemolysis as a result of radiation.

INDIVIDUAL CLINICAL RECORDS

Individual data sheets on one of the experimental animals which received 686r and of a control animal are included for comparison (tables 11 and 12);;mean blood units are given in figures 3,4,5,6,7 and 8. These data and other individual data records bring out several important considerations:

1. The onset of significant change in the haematological status of the exposed animal given in tables cannot be differentiated unequivocally from that of the control until the former has received approximately 405r. However, the "mean" data of the exposed group as compared with the normals (figures 3-8) indicate that statistically significant differences between the blood picture of the exposed and control groups are apparent after less than 130r.

2. The differential blood picture in terms of percent of each constituent is not remarkably altered until terminally, when a relative lymphocytosis is the rule. The absolute number of lymphocytes as well as the number of other constituents has, as is indicated by figure 3, been markedly reduced by this stage.

3. The reticulocyte percentage is essentially unaltered in all of the exposed animals and controls. In view of the fact that the reticulocyte percentage is ordinarily considered a relatively sensitive indication of radiation exposure (R. S. Stone et al -- unpublished data) and usually falls concommitantly with the leucocyte count after acute moderate doses of Xray (200r total body to rabbits or with the use of P^{32} therapeutically), it is not entirely clear why such is not the case in this experiment. The facts will await careful histological study of these animals, but obviously red cell production is proceeding at a rate more or less comparable to normal or one cannot use the reticulocyte percentage of the peripheral blood as a criterion thereof.

MEAN BLOOD VALUES

Arithmetic mean levels and standard deviations were computed for hemoglobin, red count, white count, heterophils, lymphocytes, platelets, and percent reticulocytes. In addition to this treatment, geometric means were computed for heterophils, lymphocytes and platelets. The reasons for computing geometric means have been given in earlier reports. In brief, we may say that the geometric mean is more representative of the reponse of a typical animal than is the arithmetic mean, where

variables having relatively large dispersions are involved.

Graphs are presented for hemoglobin, red count, heterophils, lymphocytes, platelets, and reticulocytes. Hemoglobin and red count are plotted on the usual arithmetic grid. Heterophils, lymphocytes and platelets are plotted on a semi-log grid. This is done because it has been shown that for these variables the response as plotted on a semi-log grid is roughly proportional to the size of dose. Also, the responses on a log scale may be resolved into one or more straight line portions. The slope of these straight line portions can be interpreted directly as representing a uniform rate of change of the variable, in terms of per-cent change per day. Finally, on a semi-log scale, the correlated variations due to environmental influences are independent of level. Advantage is taken of this fact in plotting corrected response curves, in which the variations in control level are removed from the controls (resulting in a straight line) and from the experimental group to treatment alone. The quantitative estimates of rates of change given below are made possible by the smoothing effect of this correction.

The geometric means of lymphocytes (fig. 3, corrected) drop to 50% of pre-exposure levels in about 15 days, at a constant rate of 5% per day. Thereafter there is a uniform slow decline of 0.5% per day.

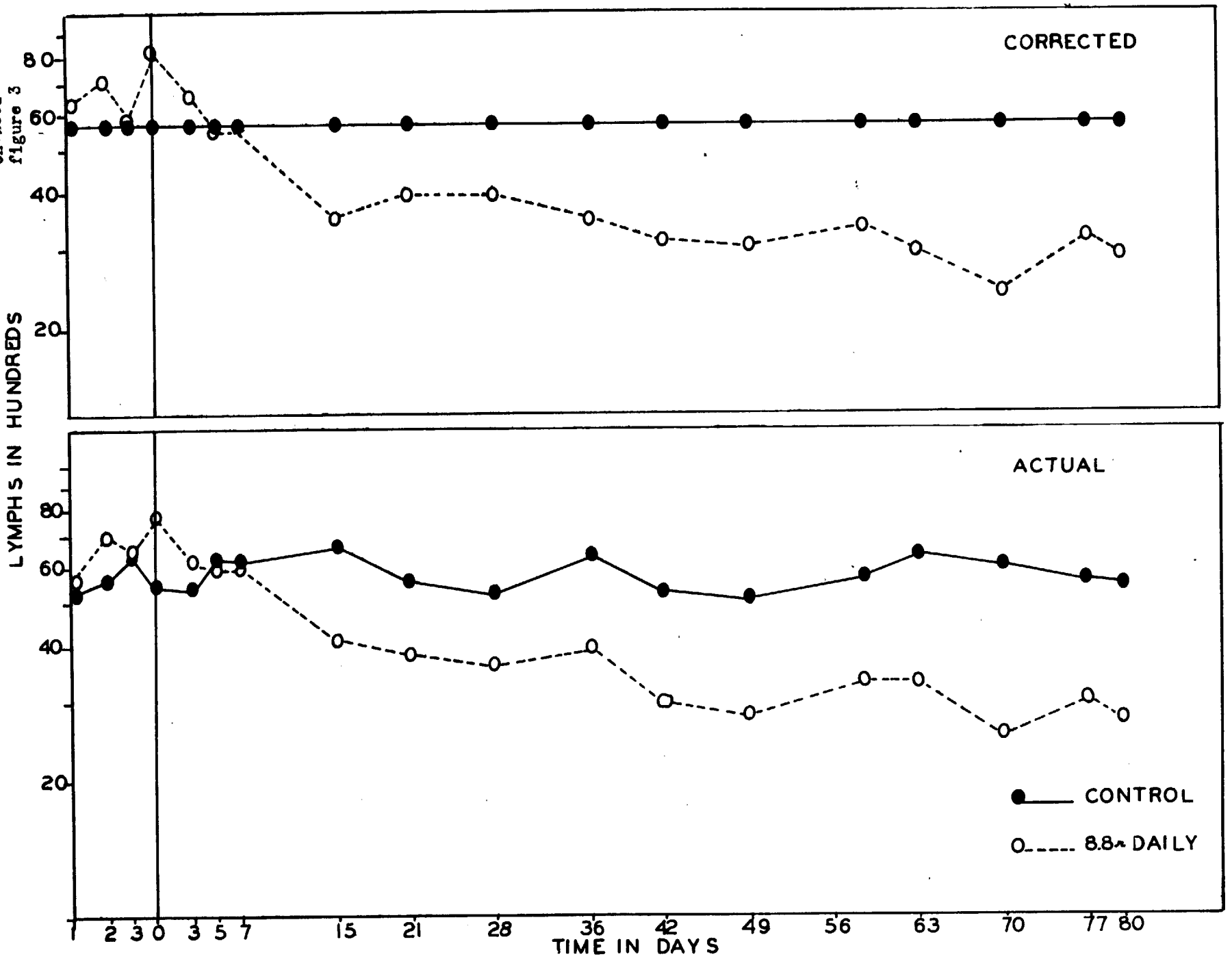
The geometric mean of heterophils (fig. 4, corrected) remain at or slightly above pre-treatment levels for about 10 days, then drop abruptly to about 60% of pre-treatment levels where they remain, with possibly a slow decline, until the 60th day. The effect on the heterophils is roughly of the same magnitude as the effect on the lymphocytes, but because of the greater relative variability of the heterophils, the effect is not as noticeable. The lack of response of the heterophils for the first 10 or 15 days should be interpreted with caution. A short period of rise or slow decline might be expected in multiple exposure experiments, by extension of the finding of an early rise preceding the decline in single dose experiments. The white count (fig. 5) is a composite of the heterophil and lymphocyte responses.

In the platelets (fig. 6) there is no change in the geometric mean values during the first week of treatment. From the first week to the 60th day there is a uniform decline of about 1.5% per day. After the 60th day there is a precipitous drop, which is still accelerating at the last measurement. On an arithmetic scale the platelet picture is one of a linear decline for the last 40 days, but the logarithmic picture corresponds better to the clinical and pathological picture of sudden hemorrhagic demise.

The red count (fig.7) and hemoglobin (fig.8) show no deviations from control behavior until the 63rd day, at which time they drop to a significantly lower level, which they maintain for the remainder of period measured.

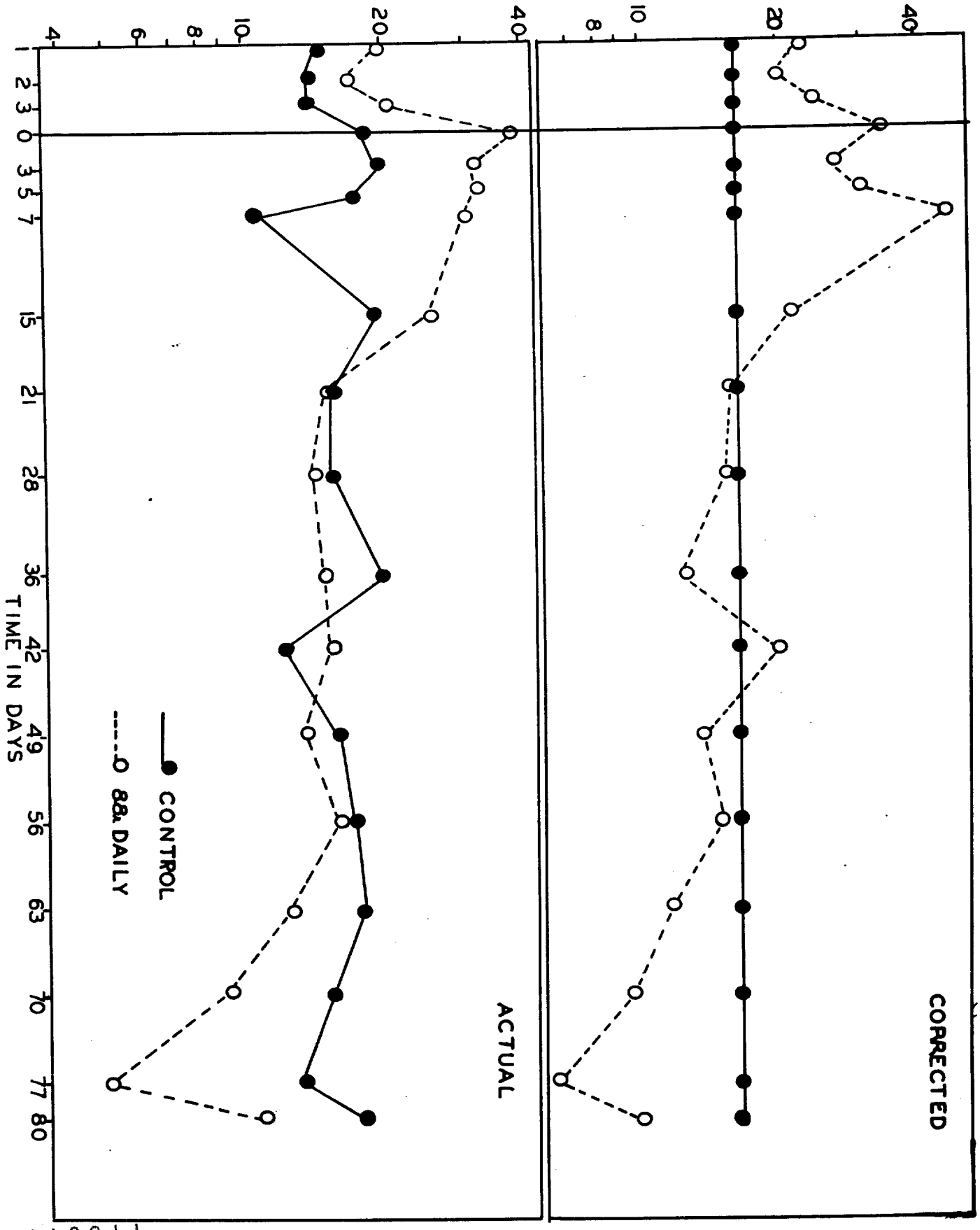
1119009

CB-2991
figure 3



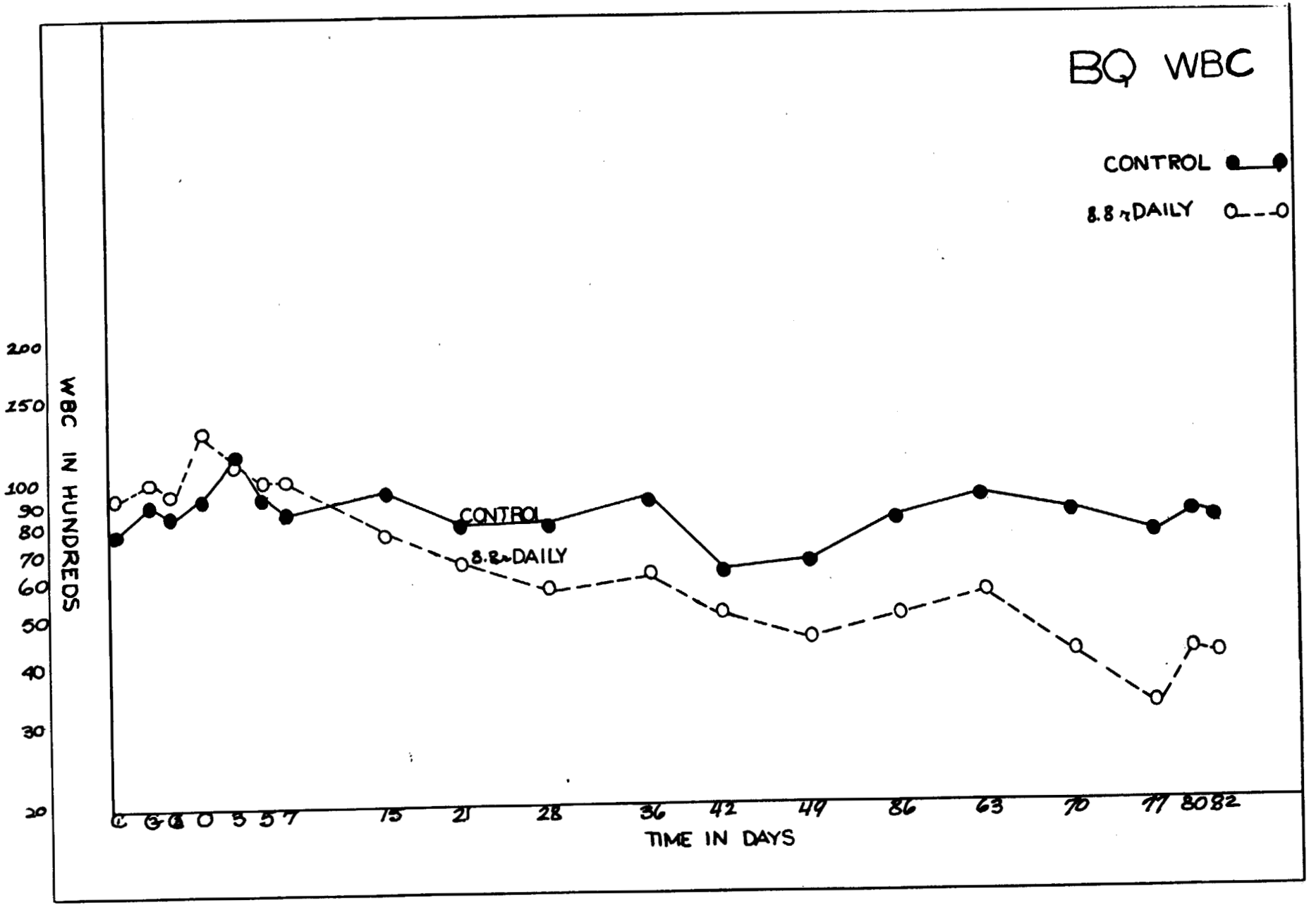
0106111

CH-2991
Figure 4



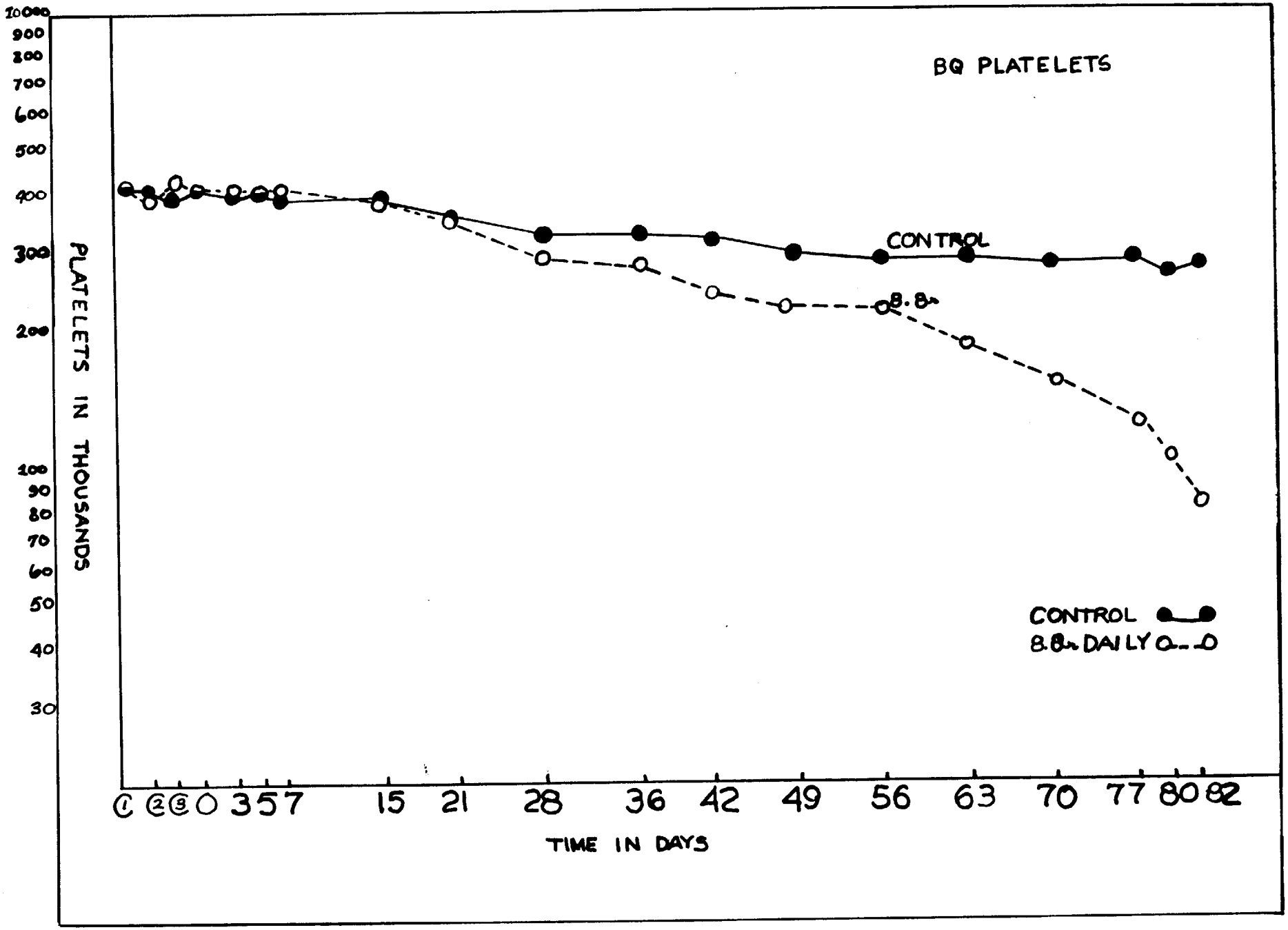
119011

CH-2991
Figure 5



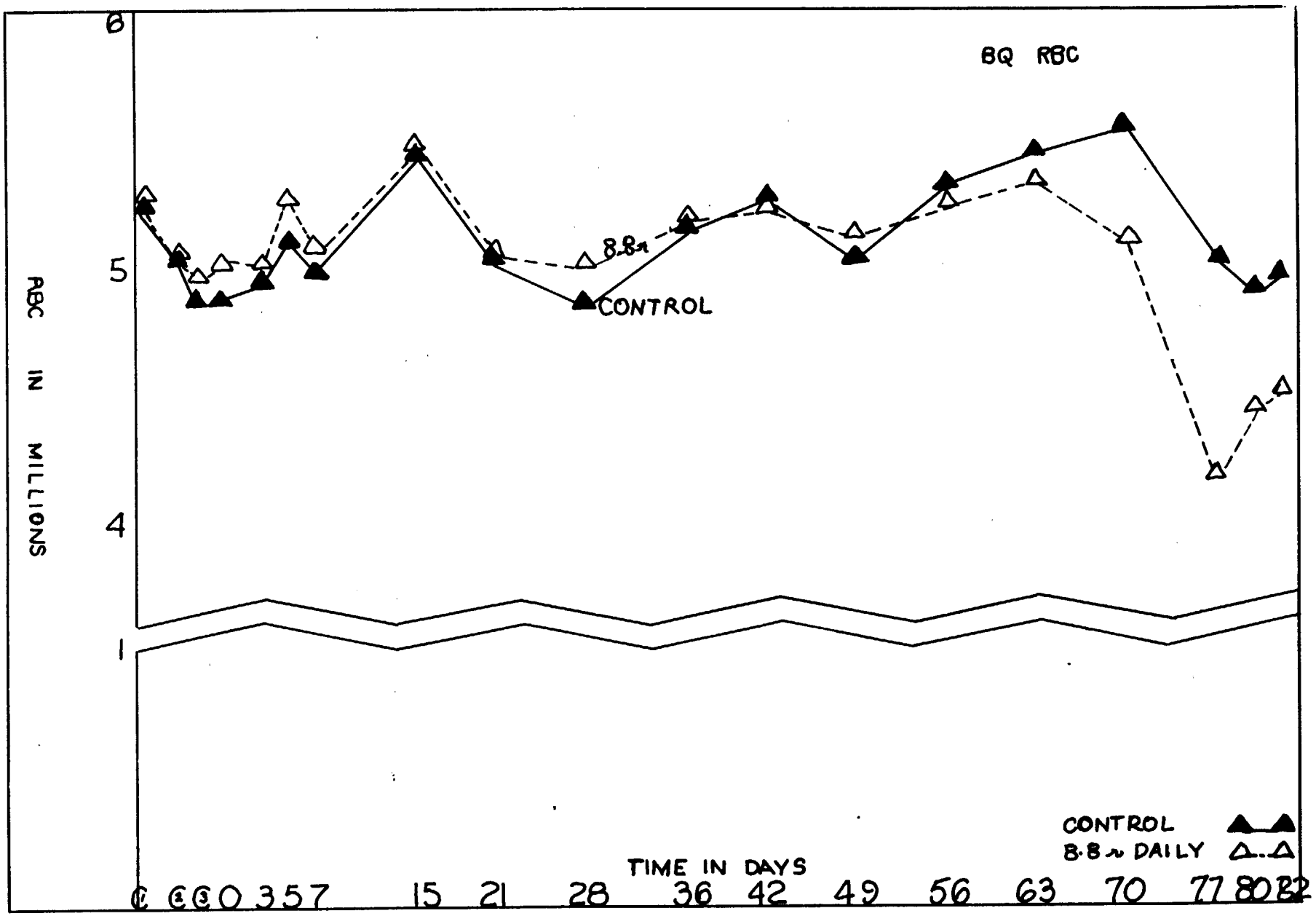
1119012

CH-2991
Figure 6

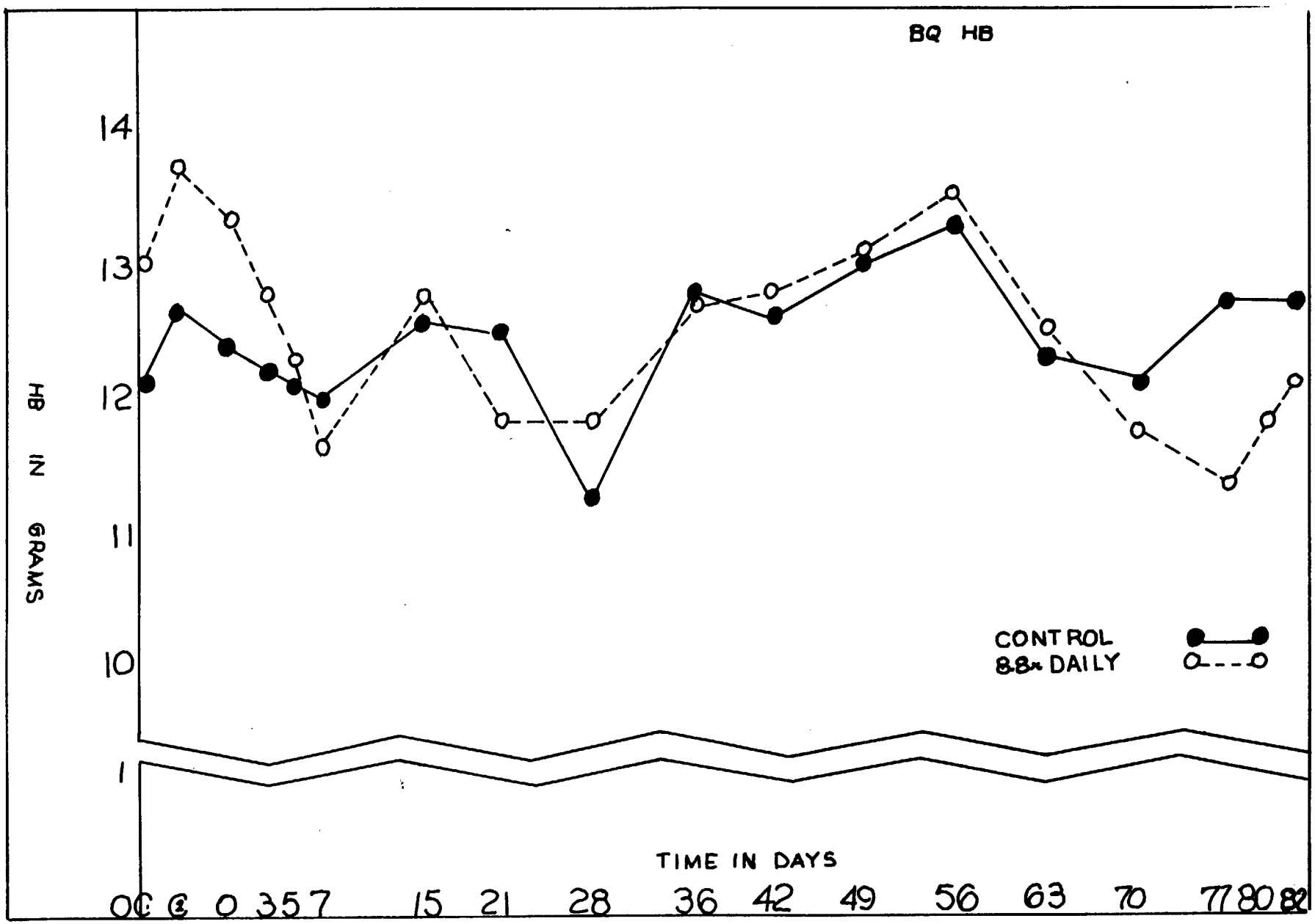


1119013

CH-2991
Figure 7



CH-2991
Figure 8



1119015

142 MLH 3510 HISTOLOGICAL EFFECTS OF SINGLE EXPOSURES TO X-RAYS

The spleen, lymph node, appendix and thymus of rabbits were examined at 1, 3, and 8 hours after exposure to single doses of x-ray at 25r, 12r, and 6r.

The rabbits were not in good health; revealing in both treated and untreated animals an extensive parasitic invasion of the appendix, and chronic involutionary changes in the thymus and in the lymph nodes. But at 25r, in the spleen and lymph node, definite damage was discernible above the background of chronic change. The damage, most obvious at 8 hours, consisted principally of dead small and medium lymphocytes in the lymphocytopoietic nodules. At 3 hours, after 12 r, there was also an increase in nuclear debris in these locations; it is probable that this debris resulted from the radiation. With 6r there was no difference between the treated and untreated rabbits.

142 MLH 2310,2410,2611 EFFECTS OF SINGLE DOSES OF X-RADIATION ON DOGS -

E. E. Painter
M. Swift
O. France

During the past month two dogs were given a single dose of 300r total body x-radiation, primarily to study blood chemistry and secondarily to obtain additional survival data. Two dogs which had been given this dose previously had died, one at 15 and one at 17 days after treatment. One of the animals treated this month (#43) is still alive 34 days after irradiation the other (#44) died on the 18th day.

Clinical data on both treated dogs are given in table 12. The hematological data show that both the white and red cell counts and hematocrits decreased steadily but that in the survivor some recovery in white count and hematocrit was evident by three weeks.

The surviving dog (#43) showed a maximum loss in weight of 11.6 percent on the 22nd day and since then has been slowly gaining. Clinically the period from the 15th to 22nd day was characterised in this dog by a 1.5°C increase in rectal temperature, 10 percent increase in heart rate, excessive salivation, hemorrhagic spots on the skin and lethargy. The urine became slightly green during the critical 10-30 day period and urine output decreased 50 percent. Food and water intake decreased by 75 percent during this period. All of these symptoms have now disappeared.

1119016

Table 12

Dog	Days after Irradiation	W. B. C.	R. B. C.	Hct.	Sedimentation Rate M M (30 min.-60 min	Clotting Time (minutes
	Control	12,400	5,870,000	45.0	2 - 6	3.0
43 (alive on 33rd day)	2	3,550	5,650,000	41.2	4 - 12	3.0
	6	1,600	4,720,000	33.0	45 - 11	2.5
	10	850	4,260,000	31.0	20 - 38	4.5
300r	14	200	3,110,000	22.0	69 - 72	3.5
	19	400	2,930,000	18.0	74.5 - 76.5	8.5
	23	650	2,630,000		65 - 71	6.0
	26	1,800	3,090,000	21.0	64.5 - 71.0	5.0
	28					
	30				48.5 - 68.5	
	33	6,050	3,360,000	22	41,5 - 63.0	
	Control	11,450	7,410,000	48.0	0.5 - 1.0	3.25
44 (died on 18th day)	2	3,600	6,270,000	42.0	0.5 - 1.0	3.5
	6	1,800	5,900,000	39.0	1 - 2	3.5
	10	450	5,320,000	33.5	13.0 - 29.0	5.25
300r	14	100	3,640,000	27.5	59.5 - 65.0	7.25
	15					
	17			20.3	68.0* - 74.0	

* Normal red cells in plasma of x-rayed dog.

1190117

The dog that died (#44) lost 24.6 percent of his body weight. One week preceding death and continuing until death, food intake decreased almost 100 percent, water intake 85 percent and urine output 45 percent. The urine became increasingly green and dark in color during this period. Spectrometric measurements made by Dr. Schwartz showed the green pigment to have a maximum absorption at 640 mμ, the same peak as biliverdin. The blood plasma appeared normal in color on the 15th day but a sample taken on the 17th day, less than 24 hours before death was a bright yellow green. Other late symptoms were in 2.1°C rise in rectal temperature, 100 percent increase in heart rate, excessive salivation, development of hemorrhagic and edematous areas on the skin and mucous membranes and lethargy.

Table 12 shows that clotting time and sedimentation rate increased before the dog showed gross symptoms. The sedimentation rate (mm at 60 min.) increased by 13 times in dog #43 and by 74 times in dog #44. Using normal red cells in the plasma of the irradiated animals and cells of the latter in normal plasma it has been found that the factors responsible for the increase in sedimentation rate resides in the plasma alone. Curves were obtained of sedimentation rate versus hematocrit with added plasma and with serum. These curves show that part of the increase in sedimentation rate can be accounted for by the decrease in hematocrit. The curves for the treated dogs are steeper than for controls and the difference between the plasma and serum curves is greater: hence a second part of the increased sedimentation rate may be due to an increase in fibrinogen. The serum curves for treated dogs lie above those for controls, hence some unknown additional factor must be present in the serum.

The plasma clearance of phenol red was determined on these animals. The one that died showed no change on 7th day after irradiation, but showed a 75% increase in clearance on 13th day. The animal which survived showed no change on 7th day, 110% increase on 13th day and a return to normal clearance on 33rd day. This apparently indicates an increased blood flow through the kidneys for both animals showed a marked increase in the output of phenol red in the urine in the first 15 minutes.

Table 13 shows that there were slight initial decreases followed by increases in plasma and serum protein. The non-protein nitrogen decreased significantly as did plasma creatine and creatinine. Histamine showed a slight increase, more in the dog which died than in the survivor. In fact plasma taken two days before death showed a concentration of histamine 10 times greater than before treatment.

Observations on pigment excretion and on plasma protein distribution are being presented by Dr. Schwartz and Dr Barron.

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Table 13

Dog	Days after irradiation	Plasma Proteins gms/100cc	Serum Proteins gms/100cc	N. P. N mgm %	Urea mgm %	Creati-nine mgm%	Creatine mgm %	Histamine /cc
43	Control	5.63	5.30	26.2		1.17	0.90	0.031
	Control	----	-----	----		----	----	0.019
	1 - 2 hours	----	-----	----		----	----	0.017
	6 days	4.78	-----	----		----	----	0.036
	9 days	----	-----	20.0		0.925	0.785	-----
	10 days	5.30	-----	----		-----	-----	0.012
	14 days	6.35	5.47	----		-----	-----	0.019
	16 days	----	----	16.5		0.925	0.673	-----
	19 days	----	----	----		-----	-----	0.018
	28 days	6.00	5.47					
	30 days	5.81	5.53					
44	Control	6.0	5.47	31.0	----	-----	-----	0.023
	Control	----	----	30.2	20.0	1.32	1.02	0.014
	1 - 2 hours	----	----	----	----	-----	-----	0.012
	6 days	5.3	----	----	----	-----	-----	0.024
	8 days	----	----	20.5	----	1.20	0.69	-----
	10 days	5.63	----	----	----	-----	-----	0.012
	14 days	7.0	5.82	----	----	-----	-----	0.18
	15 days	----	6.58	----	----	-----	-----	-----
	17 days	8.05	----	17.0	12.0	0.94	0.78	-----

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Animal Guinea Pig Animal No. 70 Sex F 8.82/ day

(hybrid) (age 4 months)

Date	H.B	R.B.C.	Platlets	W.B.C.	Neutrophils	Lymphocytes	Monocytes	Eosinophils	Basophils	Blasts	Reticulocytes
8-18-44	10.2	5.23	(500,000)	11,300	15	81	3	1			(1.0%)
8-21-44	12.0	4.66	(405,000)	6,850	20	76	1	2	1		(0.9%)
8-23-44		4.69	(427,900)	7,900	16	82	1	1			(0.9%)
8-25-44	11.5	5.02	(456,500)	16,600	28	70	1		1		(1.1%)
8-28-44	11.0	5.16	(422,700)	13,750	44	51	1	4			(1.1%)
8-30-44	11.6	5.36	(399,700)	12,550	36	59	2	2	1		(1.6%)
9-1-44	12.8	5.18	(377,600)	12,250	44	51	4	1			(1.5%)
9-9-44	14.0	5.66	(367,400)	7,450	39	58	2	1			(1.3%)
9-15-44	12.0	4.99	(314,800)	8,300	50	48	1	1			(1.5%)
9-22-44	11.5	4.88	(280,500)	5,350	44	54	1	1			(1.1%)
9-30-44	12.5	5.02	(251,900)	3,650	21	76	2	1			(1.0%)
10-6-44	13.2	5 57	(232,100)	5,950	51	46	2	1			(1.2%)
10-13-44	13.4	5.09	(225,500)	2,900	51	47		2			(1.0%)
10-20-44	14.4	4.90	(191,300)	4,200	53	43	3	1			(0.9%)
10-27-44	13.2	5.23	(152,500)	3,450	50	48	1	1			(1.0%)
11-3-44	12.0	4.78	(122,500)	2,050	28	70	1	1			(0.7%)
11-10-44	5.0	1.15	(75,600)	1,000	3	96	1			(100 cells)	(0.8%)
11-11-44	3.6	1.08	(66,000)	1,400	19	78	2	1	(100 cells)		(1.2%)

Born beginning of April 1944

Rate of administration of dose: 8.8r per 8 hours per day
(X-ray, 0.5mm Pt, from 11:55 PM to 7:55 AM)

In field from August 25 to Nov. 11, 1944 = 78 d.

Table dose 6.86r

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Table 11

Blood Data on two Animals

Animal Guinea Pig (hybrid) Animal No. 17 Sex F Control

(Age 4 months)

Date	Hb	R.B.C.	Platlets	W.B.C.	Neutrophils	Lymphocytes	Monocytes	Eosinophils	Basophils	Reticulocytes
8-18-44	10.7	4.85	(320,100)	5200	8	90	1	1		(1.0%)
8-21-44	12.0	5.19	(340,000)	5350	27	71	1	1		(1.1%)
8-23-44		4.85	(300,700)	5800	25	73	1	1		(1.3%)
8-25-44	13.0	5.01	(300,000)	6300	9	88	1	1	1	(1.4%)
8-28-44	13.0	5.28	(285,200)	6250	9	90		1		(1.5%)
8-30-44	12.1	5.30	(340,600)	6300	9	89	1	1		(1.1%)
9-1-44	12.7	4.90	(352,000)	4550	12	86	1	1		(0.9%)
9-9-44	13.4	5.62	(303,600)	6550	9	90	1			(0.8%)
9-15-44	11.5	5.56	(281,600)	8000	20	78	1	1		(1.1%)
9-22-44	12.1	4.36	(234,300)	5150	24	73	1	2		(1.0%)
9-30-44	14.0	5.20	(301,400)	7450	16	80	2	1	1	(0.9%)
10-6-44	13.0	5.20	(306,100)	5550	20	77	2	1		(1.2%)
10-13-44	13.6	4.92	(286,200)		13	84	1	1	1	(1.0%)
10-20-44	14.7	5.20	(266,600)	6250	12	87	1			(1.1%)
10-27-44	13.7	5.50	(299,600)	6200	16	83		1		(1.1%)
11-3-44	13.4	5.92	(264,100)	7050	21	76	2	1		(1.3%)
11-10-44	13.0	5.59	(283,800)	5750	14	84	1	1		(1.0%)
11-13-44	12.8	5.30	(246,500)	3550	22	75	2		1	(1.3%)
11-15-44	13.4	5.30	(224,500)	4400	6	92		1	1	(1.1%)

Born beginning of April 1944

Control to H_{59} to H_{64}

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Medical Hazards Section - Section III

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

000 MLH 3250 Special Hazards Survey of Sub-Contractors and Associated Projects

During the month the betatron installation at the University of Illinois was inspected by members of the Health-Physics group. In many areas radiation levels far in excess of tolerance were noted. For the most part the work areas for the individuals running the machine were below tolerance. Areas which exceeded tolerance included regions in which persons not familar with the installation may be working. Because of this fact recommendations were made to responsible persons at this University for increased shielding or for an adequate system of warning individuals away from such areas while the machine is running.

241 MLH 3310 Building and Equipment Surveys for Beta Radiation - Rose, Wallace

241 MLH 3320 Building and Equipment Surveys for Gamma Radiation - Rose, Wallace

New Chemistry. The extent and amount of beta and gamma active materials being handled in the filtered air section of New Chemistry has increased during the recent past. For the most part the shielding, though temporary, has been adequate. Designs are being completed for a permanent hot lab which can handle up to 30 curies of 1.0MEV gamma activity.

As an example of the sort of activity being handled, a recent extraction of an isotope of uranium in room 6 can be cited. C2 slugs whose total activity ran into several hundred curies were processed during a period of several weeks. The shielding installed was adequate for the job. Certain areas adjacent to the chemical equipment had greater than tolerance levels. However, the personnel were aware of the fact and governed themselves accordingly.

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On the 14th of April a spill occurred in the dissolving cave due to the breaking of a dissolving flask. The active solution spilled into a steel tray at the bottom of the installation. During the removal of the spilled solution, measurements of several hundred mr/hr were obtained from the temporary equipment used during the operation.

While the personnel involved were careful to conduct themselves in accordance with safe practice for handling active materials, the incident serves to emphasize the need for adequate facilities for handling very active materials. One cannot expect to handle high activities over long periods of time with makeshift equipment without getting into serious difficulty at one time or another.

Site B. Air samples for uranium were taken near the vertical cutamatic machine during the past month. Values well in excess of the tolerance amounts were obtained. As a result of the finding recommendations were made for more adequate ventilation.

Routine surveys for beta and gamma contamination continue to show the presence of uranium rather diffusely throughout the building. The most active areas are in room 103.

Site B. Annex. No marked changes had been noted in this area during the past month. Rooms 160 and 161 routinely show numerous areas with above permissible levels of activity. For the most part, however, the levels noted do not exceed tolerance. Each week approximately 20 air samples for beta and gamma contamination are taken in these areas. No reading in excess of permissible levels has been found.

Armory. A complete survey of all the rooms in the Armory was done on April 26, 1945. No areas of unknown activity were found on the survey.

The south courtyard of the Armory was surveyed during the month. Beta and gamma activity can be found almost everywhere in this area. The readings noted range from 0.2 to 200 mr/hr. The higher readings were due to the presence of pellets used by the shot-gun crew which had, through error, somehow found their way into the Armory courtyard. These have been removed.

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As a result of the above survey it was felt that the furnace in this courtyard used to convert uranium shavings to uranium oxide might be responsible for the diffuse, low-grade activity. Consequently, a series of air samples were taken during the operation of this furnace. The highest reading obtained was 9500 micrograms of tuballoy per cubic meter of air. The air sampler was located 4 feet from the container into which the oxide is dumped after being heated in the furnace. No precautions were taken to prevent the escape of oxide into the air. Following this reading, taken during average working conditions, a cover was placed over the container to prevent the escape of the oxide into the air. The reading then obtained was 460 micrograms of uranium per cubic meter of air. It would appear then, that the prior practice of placing the oxide from the furnace into the container without control of the escape of the material into the air may be in large part responsible for the overall low-grade contamination of the Armory courtyard.

Psychology Building. The machine shop here was formerly used by the Metallurgical Laboratory. During the past month this area was surveyed for the first time. A rather diffuse contamination with uranium dust was found. Arrangements were made for the decontamination squad to clean up this area.

241 MLH 3359 Personnel Monitoring of Beta Radiation - Rose, Wallace

241 MLH 3360 Personnel Monitoring of Gamma Radiation - Rose, Wallace

Badge meters. 2783 films were developed during the past month. Two total body overexposures to gamma radiation were noted. One of these occurred in New Chemistry and one at the Argonne. The over exposure in New Chemistry occurred during the work-up of 02 metal in room 6 discussed above.

During the "hot run" in room 6, wrist and fingertip films were worn by the workers. The highest exposure for the entire run totaled 3.77 r to the left wrist of one of the workers. This reading was accumulated during a two week period. Considering the amount of activity handled and the temporary nature of the installation, it is the opinion of this section that the fact that the exposure was

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not higher is a tribute to the thought and care given to the execution of this job.

Pocket meter readings. 4537 pocket meters were read during the month ending 5/10/45. 32 readings or 0.7% were above the permissible level of 100 mr for any one day. Of these 20 are, in the opinion of the section, probably valid readings. 50% of the readings are on Argonne personnel.

The breakdown by sites for the number of readings done during the past two months is as follows:

	March	April
New Chemistry	799	732
West Stands	466	360
Site B	1608	1430
Kelhart-Ryerson	184	323
Argonne	1613	1692
Total	4670	4537

Hand counts for beta and gamma contamination. 1586 counts were scheduled. 7[illegible]% or 1093 were done. 1.2% of the counts were above the permissible level.

Survey of clothing beta and gamma contamination has continued. Eight garments were found to have above the permissible level of contamination. These were sent to Clinton for Laundering.

000 MLH 3300 Decontamination Squad

The activities of this group have diminished somewhat during the past month. This, in part, has been due to difficulty experienced in obtaining permission for the group to work in off-project University areas. During the past month direction of this group has passed to the administration of the Metallurgical Laboratory, therefore their activities will not be discussed under a project assignment number in the future.

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CONTRACT # W-7405-eng-48-A

Joseph G. Hamilton, M.D.

SECTION B. TECHNICAL PROGRESS REPORT ON THE METABOLIC STUDIES OF FISSION PRODUCT

1. Soil Studies

A determination of the uptake of radio-tellurium by barley plants from culture solution was completed. At the end of three weeks 0.2% of the added Te* was found in the tops and 30% was found on the roots In its behavior in plants, Te is absorbed less readily than Sr and more readily than the rare earths.

A series of experiments have been completed regarding the decontamination of active soil by leaching with electrolytes. Samples of W topsoil were activated with the following radio-elements: Sr, Y, Zr + Cb, Te, Ce, and a fission mixture from W-6 waste solution. In each case, 4 gms, of soil was leached with 400 cc. of solution. The percentage losses in activity are given in the following table:

TABLE I

Element Fixed on Soil	Treatment H_2O	0.1n HCl	1N NaCl	1N $CaCl_2$
Sr	22.9	98.4	97.5	94.3
Y	1.4	70.8	17.1	21.2
Zr + Cb	15.8	3.8	0.0	12.0
Te	21.5	31.6	5.1	1.3
Ce	23.8	71.0	15.2	22.1
W - 6 mixture	11.9	22.3	9.3	3.7

The losses due to the leaching with water may have been the result of the dispersion and washing out of small soil particles.

Additional investigations regarding the migration of radio-elements in soil have been completed. At the end of 52 days, Y* had migrated less than 0.5 cms. in a moist W topsoil. Under the same conditions and for the same period, Ce* had migrated 3 cms.

U^{232} has been isolated by means of the hydroxylamine method (CC1065) from a thorium target which had received 2,000 μ a hr. 20 MEV of deuterons in the Berkeley Cyclotron. The yield of U^{232} was approximately 35 micro-curies. The fraction containing Pa* has been set aside for its

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isolation. The yield per μ a hr. is 20 times greater at the present operating conditions of the Cyclotron as compared to the previous operating energy of approximately 14 MEV for deuterons.

2. Tracer Studies

Three groups of two rats per group were put on an iodine pre-treatment regime prior to receiving carrier-free radio-iodine. The rats received by I.M. injection the inert iodine at weekly intervals for four weeks and one week after the last dose of inert iodine the radio-iodine was administered by I.M. injection. The dosage levels of the inert iodine were 1 mgm., 10 mgm., and 100 mgm. per kilo of body weight per week. The following table summarizes the results:

TABLE I

The percent uptake of I^{131} by the thyroid gland of the rat four days after the administration of carrier-free I^{131} following the administration of 1, 10, and 100 mgm. of inert iodine per kilo of body weight, at weekly intervals for four weeks.

Control	1 mgm. I^{127} kg.	10 mgm. I^{127} kg.	100 mgm I^{127} kg.
6.52%	5.13%	6.40%	3.00%

It was not expected that the blocking effect of the inert iodine would be so insignificant. In fact, at only the 100 mgm. level of iodine pre-treatment, was there any positive effect. This does not fall in line with some rather incomplete human data. However, these experiments are to be checked using more animals, before any human studies are to be undertaken.

3. Smoke Studies

A series of smoke studies using uranium-free fission products without inert carrier have been initiated. The experiments have been completed for the 0, 4, and 16 day time intervals after exposure and the most important data is summarized in the following table.

TABLE I

The distribution of uranium-free fission products in the rat following the inhalation of an active smoke produced by volatilization of the chlorides of the carrier-free fission products in a carbon arc.

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	0 Time	4 Days	16 Days
Lungs	46.7	49.5	25.4
Liver	.14	1.20	1.62
Kidney	.14	.30	.31
G.I.Tract	6.16	2.56	.60
Head	41.8	2.98	.5
Skeleton	.88	7.44	6.29
Urine		.24	4.77
Feces		30.3	58.3

The smokes used for these experiments were produced by evaporating a solution of long-lived fission products, which were free from Uranium and contained no inert carrier, onto 1 mm. carbon rods and then producing an electric arc with these carbons. The method of exposure of the rats was the same as was used with the UO_2 smokes. The significant observations to be made from this series of experiments are as follows: First, some activity migrates from the lungs to the skeleton during the first four days after exposure. A portion of the activity in the skeleton probably was due to strontium and barium absorbed from the G.I. tract. This fraction of the activity in the skeleton is estimated to be roughly half of the total amount on the basis of known values for the amount of activity absorbed by way of the digestive tract following the oral administration of a mixture of the long lived fission products. It will be recalled that the inhalation of UO_2 smokes containing long-lived fission products was followed by a very trivial deposition of activity in the skeleton. Second, the proportion of activity deposited in the head was lower and higher in the lungs than was observed in the corresponding UO_2 fission product smoke studies.

The explanation for these results lies in the probable fact that some of the fission product mixture was volatilized as the chlorides and that the particle size of the remainder, which was driven off as oxides, was extremely small.

Longer term studies using these uranium-free fission product smokes are in progress. It is planned to conclude the fission product inhalation studies using aerosols of a soluble form of the mixture by the spray technique which has been described in another section. This will cover four general types of conditions under which fission products might be expected to be present in the air. These four types of fission product aerosols are: UO_2 smokes, active recoils, smokes from intense heating of uranium-free fission products, and suspensions of a soluble form of the mixture. Many other possible types of aerosols could be encountered but it is our opinion that the group of conditions listed above will be helpful in evaluating the problems that would arise as the result of any major accident.

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In addition, this type of information should prove to be of use for evaluating the hazards arising from the usual laboratory routines employed with these substances where the possibility of their escape into the air may exist.

4. Projected Studies for the Next Two Months

The tracer and smoke studies are to be continued. The soil experiments will be concluded June 30, 1945 and a terminal report presented. Tracer studies with photoactinium are to be initiated now that a source of Pa^{233} is available.

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Contract # W 7405 eng 48 c

B.V.A. Low-Beer

This report refers to previously treated patients.

[redacted]

200 K.V.
1000 K.V.
3000 K.V.
3000 K.V.
200 K.V.
200 K.V.
1000 K.V.
200 K.V.

[redacted] Male: The blood counts on this patient have been followed since 27-43. His chart shows that there was a decrease of the RBC five weeks after inauguration of treatment. The Hgb showed a very slight (?) decrease at that period. During the whole period there was a consistent relatively high WBC with moderate lymphocytosis; during a period of regional treatment, (following the total body treatments) the lymphocyte count decreased but returned again to the moderately high pre-irradiation level. The segmentation of the PMN was not significant.

[redacted] Female: The review of the blood counts of this patient who was treated on the 1000 K.V. up to a total of 302 r (skin) in November, 1944, shows a slight decrease of red cell count two weeks after treatment without change in the Hgb. Subsequently the red cell count returned to normal. The WBC did not show any considerable change during the period of observation except on November thirtieth when it came down to 3,700 however without change in the differential count. No monocytosis developed. At the time of the decrease of RBC there was moderate microcytosis, anisocytosis and poikylocytosis.

[redacted] Female: This patient was treated on the 1000 K.V. up to a total of 283 r (skin) between Oct. 23, and Nov. 10, 1944. She developed a marked microcytic anemia about four months after onset of treatment which is now improving. There was only a very slight insignificant drop in Hgb. The WBC remained within the limits of normal variations. Similarly, there has been no significant change in the differential count, including the nuclear pattern of the PMN. Microcytosis and smudge cells were seen in the count taken 4-4-45.

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[redacted], Male: This patient started his treatment on April 14, 1943 and finished April 29, 1943. Thus the observation period is now twenty-three months. The changes in RBC, and total WBC, were insignificant. However, the patient developed a definite but moderate monocytosis. Variations in the monocytes can be seen during this observation period. The two recent blood counts, 2-27-45 and 4-9-45, show a red blood cell count, and particularly a Hgb contnet which exceeds the previous findings. The patient appears clinically slightly plethoric. The differential count has fluctuated, but the significance of this is questionable.

[redacted], Male: This patient was treated 5-12-43 to 5-28-43 up to a total of 299 r (skin) with 200 K.V. x-rays. There has been no sign of change in RBC nor in WBC except for flucuations which may be considered within physiological limits. Moderate monocytosis developed in this patient, which in the recent eight months shows a return to normal limits. The nuclear pattern of the PMN has been followed only for the last four months and does not reveal anything significant.

[redacted], Female: This patient was treated from 11-1-44 to 11-24-44 on the 1000 K.V. up to a total of 300 r (skin). No changes in RBC of any significance developed, nor any changes in Hgb. The WBC remained within the limits of normal variations. The differential count has not shown anything significant.

[redacted], Female: This patient was treated from 11-2-44 to 11-22-44 on the 1000 K.V. up to a total of 292 r (skin). She showed a moderate decrease of RBC and Hgb about two months after conclusion of the treatment. This has returned to a level of normal variations. The differential count does not show anything which could be considered significant except for a slight shift toward the left in the nuclear pattern of PMN. This, however, should be followed further.

[redacted], Female: This patient was treated from 5-4-43 to 5-20-43, twenty three months observation time up to a total of 370 r (skin), .685 HVL. During the observation period no significant changes occured in RBC. There was however, a slight decrease of Hgb about five months after conclusion of treatment. The WBC has not shown any significant changes. The differential count indicates some monocytosis at the end of the treatment, but it returned to limits of normal variations. The nuclear pattern of the PMN has been followed only since November 1944 and there is no left shift of any significance.

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N.C.I.

I. Continuous exposure for 8 hours daily
Surviving original mice and guinea pigs (daily doses 4.4r, 2.2r, 1.1r and 0.11r)

Approximate total doses: 3500 r, 1750 r, 875 r, and 91 r. (Additional acute exposures not added).

Rabbits (daily doses 8.8r, 4.4 r, 2.2 r, 1.1 r and 0.11 r).
Approximate total doses: 5800 r, 2900 r, 1450 r and 725 r and 72 r.
(Additional acute exposures not added).

Term experiments

Mice: (daily doses 8.8 r, 4.4 r and 1.1r).
16 and 14 months: total doses: 1300 r, 650 r and 160 r.
12 and 10 months: total doses: 900 r, 450 r and 100 r
8 and 6 months: total doses: 360 r, 180 r and 45 r.
4 and 2 months: total doses: 20 r, 10 r and 2.5 r.

Inbred guinea pigs of family 2 (daily dose 8.8 r) total dose: 1000 r.
During the month 8 mice of the original experiment died and 16 were killed because they were in a moribund condition or had tumor formation. The animals which died were distributed among the different groups as follows: one control female, one male and 2 females of the 0.11 r level (the females having received an acute exposure of 50 r in addition at the age of 5 months), one male of the 1.1 r level, one female of the 2.2 r level, one male of the 4.4 r level and one female, exposedon the 8.8 r level for one month at an age of 3 to 4 months. The cause of death of all these animals was obscure. No malignant lymphomas were observed. Most of the males showed polycystic kidneys, all females, with the exception of the control animal had bilateral ovarian tumors.

The animals which were killed were divided among the different groups as follows: one control male with malignant lymphoma,
one male of the 0.11 r group (cystic kidneys), 2 females of the 0.11 r group, one of which had received an acute exposure of 12.5 r at the age of 5 months. In both there was no gross sign of ovarian tumors. One had a malignant lymphoma,
two males of the 1.1 r group both of which had hepatomas and 3 females of the same groupl two had gross ovarian tumors and one in addition a hepatoma and subcutaneous tumor,
one male of the 2.2 r group (polycystic kidneys) and 3 females, all of which had ovarian tumors and malignant lymphomas grossly,
one female mouse of the 4.4 r group with bilateral ovarian tumor,
one male and one female exposed on the 8.8 r level for 2 months at the age of 5 to 7 months. The female had a bilateral ovarian tumor.

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The death or moribund condition of the males at present seems to be due primarily to diseased kidneys, which in turn may be due in part to the chronic dermatitis predominant in the males. The case of death or moribund condition in the females, apart from those that have malignant lymphoma, is obscure. It may occasionally be due to hemorrhage from the ovarian tumors but it does not seem to be due to the tumor itself, as they are often small and as they do not metastasize. It may also be due to hepatomas or or subcutaneous tumors; however, these tumors usually do not reach dimensions which are lethal.

Ovarian tumors are found in all animals now which have been exposed to an acute exposure of 50 r early in life, in those that have been given in addition the chronic exposure of 0.11 r, in all animals of the higher levels and in those which have been given term exposures of 300 r or 600 r respectively on the 8.8 r level.

One of the guinea pigs of the original experiment exposed on the 4.4 r level (total dose approximately 3300 r) was killed and autopsied on account of aplastic anemia (R.B.C. 0.9×10^6), it showed at autopsy the typical picture of patchy ecchymoses of the small intestine. All rabbits are alive.

Four of the guinea pigs of family 2, exposed on the 8.8 r level died of anemia and 2 were killed to study testicular damage (see hematology).

II. Breeding experiments
Nothing new to report.

III. Hematology
The blood picture of the surviving control and experimental LAF_1 mice is the same as that previously reported. Due to the fact that chronic exposure is complicated by tumor formation which is considerably more prevalent among the experimental animals and kidney disease changes in blood counts in the experimental animals (lowering of the red and platelet count) are difficult to interpret. It is felt, however, as previously expressed, that the blood picture of the experimental animals shows little if any effect of radiation damage. This is supported by the histologic findings of normal bone marrow and changes in the lymph nodes which are independent of total dose. The blood picture of the surviving control and experimental guinea pigs is unchanged from that reported last month . The control animals, the acute exposure animals, the 0.11 r and 1.1 r animals and the animals exposed on the 8.8 r level for one or 2 months respectively have more or less identical blood pictures. Some of the animals of the 2.2 r group show lowered red and platelet counts. All animals of the 4.4 r group have all counts lowered in varying degrees. The total dose of this group is at present 3500 r, 5 are still alive.

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In surviving animals of family 2 exposed to 8.8 r per 8 hours per day (total dose approximately 1,000r) all counts are drastically lowered: R.B.C. <3 million, platelet count 10,000 to 20,000 and total white count below 3,000 with a relative lymphocytosis. With the exception of one (R.B.C. - 3 million) all were removed from the field when the R.B.C. reached 2.5 million and below to study recovery from anemia. There is no recovery from anemia when the R.B.C. is equal or smaller than 1.5 million (platelets 10,000 to 20,000, W.B.C. 1,000 to 2,000 with relative lymphocytosis). The animals die within one week after removal from the field. In none was the death caused by intraabdominal hemorrhage, autopsies showed only ecchymoses of various organs especially the upper small intestine.

The blood picture of the experimental rabbits is, as previously reported mainly characterized by a reversal of the differential count, the degree of reversal depending upon total dose.

IV. Pathology

Mice: Tissues have become available for histologic study on the following mice: Six on the 4.4 r per 8 hours per day level (total dose 3,100 to 3,350 r); three on the 2.2 r per 8 hours per day level (total dose 1,500 to 1,600 r); nine on the 1.1 r per 8 hours per day level (total dose 770 to 820 r); and three on the 0.11 r per 8 hours per day level (total dose 80 to 86 r). In addition to the chronically exposed animals are two mice that had been given limited chronic exposure on the 8.8 r per 8 hours per day level (total dose 300 r or 600 r respectively given at the age of 5 to 6 or 5 to 7 months respectively).

All females exposed on the 4.4 r, 2.2 r and 1.1 r levels and the one female that had been given limited chronic exposure on the 8.8 r per 8 hours per day level (total dose approximately 300 r) have ovarian tumors.

Recognizable damage to spermatogenic elements of the testes continue to be apparent only on the 8.8 r and the 4.4 r levels.

Several additional malignant lymphomas have appeared and their occurence in relation to total dose is in keeping with the general remarks regarding the occurrence of these tumors made in the last report.

A quantitative morphologic analysis of testes of mice exposed on the 8.8 r per 8 hours per day level (total dose approximately 300 r) is nearing completion. There is much confusion in the literature on the question as to whether there is an increase of interstitial tissue associated with atrophy of spermatogenic elements following irradiation. The conclusions reached by others have been that interstitial tissue is definitely increased, or appears increased or is unchanged in quantity. With excessive damage of spermatogenic elements examination of a section of a testis without making measurements reveals an apparent increase of interstitial tissue, at least, realtive to the content of spermatogenic elements. Our measurements have shown that there is no absolute increase of quantity of interstitial tissue, and that, in fact, there is a slight decrease. Details of the experimental procedures, methods of measurements and tabulated figures will be presented in the next report.

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Guinea pigs: No tissues have become available for histologic study since the last report.

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