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I THE METABOLIC PROPERTIES OF PLUTONIUM AND ALLIED MATERIALS

J. G. Hamilton

Project 48A-I

Radioautographic Studies

Bone radioautographic studies using europium show this element, 16 days after intraperitoneal injection, to be deposited in a manner very similar to that of cerium, i.e., spotty deposition in cortical bone, and surface deposition on the shaft and trabeculae.

Cadmium radioautographs of liver showed a more or less homogeneous distribution throughout this tissue.

A group of short term strontium experiments have been completed using phosphorus deficient and control rats. Strontium uptake in the femur was studied at intervals of 0.5, 1, 4, 12, 24, 48 and 72 hours after administration. A considerable amount of strontium was taken up at the 0.5 hour interval and it appeared to be primarily on the surface of the bone in both the control and phosphorus deficient animals. At the later time intervals, in the phosphorus deficient rats, strontium appeared where calcium was present, i.e., strontium was present throughout the cortical bone, and below the epiphysis in the region of calcified trabeculae. The control rats showed the presence of the element primarily on the shaft surfaces with small amounts in the bone. It was also present below the epiphysis in the region of trabecular bone. Because of the relatively poor resolution obtainable with strontium, it is sometimes difficult to determine whether or not deposition is on the surface or throughout the bone. At 48 hours, strontium in the control series appeared to be more heavily deposited in the endosteal area than at earlier and later time intervals. Further experiments will be set up to check the possibility of this effect.

Preliminary results have been obtained on a series of experiments using the costochondral junction of the rat. In this location, cartilage, calcified cartilage, perichondrium, periosteum, endosteum, and bone are present in a small tissue section. At 72 hours, phosphorus deficient rats showed strontium deposition in calcified cartilage, compact bone, trabecular bone, but was absent from osteoid tissue. In the control series, the small size of the sections of bone coupled with the poor resolution obtainable with strontium precluded the determination of whether the material was on the surface or through the bone. Strontium was present in calcified cartilage in the control series. Experiments are continuing to determine the distribution of strontium at the costrochondral junction, with particular emphasis on the uptake by calcified cartilage at very short time intervals after administration of the strontium.

A series of experiments using the costrochondral junction have been set up using element 61.

Radioautographic experiments to study the uptake by callus have been commenced. Studies of callus formation on the injured tibia are under way with element 61.

An experiment using tin has been set up for the purpose of studying the distribution of this element in bone.

Tracer Studies

Yttrium (Y^{91}). Studies in rats with Y^{91} have been completed up to 32 days after intramuscular injection. Although the material administered was carrier-free it was absorbed from the injection site with difficulty since 52 percent, 38 percent, 33 percent and 27 percent remained at 1, 4, 16, and 32 days after administration respectively. The metabolism of the material absorbed from the injection site is presented in Table I. The major organ of Y^{91} deposition in the rat was the skeleton. More than 50 percent of the Y^{91} absorbed was found here. The relative percentage in the skeleton with respect to the other tissues was not lowered during the time of these studies. This indicates that Y^{91}, once it is absorbed, remains associated with the skeletal system for a long period of time.

The other major areas of deposition are liver, kidney, and muscle. The concentration of Y^{91} is high in liver and kidney because of their apparent metabolic characteristics related to excretion. This is reflected intthe excretion of Y^{91} which appears in urine and feces. Between 5 percent and 2 percent of the Y^{91} absorbed was found in the muscle system of the body primarily because of its relatively large bulk.

Tin (Sn^{131}). Studies in rats with carrier-free Sn^{131}, following intramuscular administration, have been completed up to 32 days. This was administered to the left hind leg of the rat and was complexed with sodium citrate with a concentration of 1 mg. of citrate per cc. Sn^{131}, administered in this manner, was absorbed relatively rapidly as opposed to data reported earlier with uncomplexed tin. Very little tin remained at the injection site since 11 percent, 7 percent, 5 percent and 3 percent of the dose was found there at 1, 4, 16, and 32 days respectively after intramuscular administration.

After absorption, appreciable amounts of Sn^{131} were detected in the soft tissues at 1 day after administration. These data are summarized in Table II. The organ of greatest deposition was kidney. As the study proceeded, the difference between the Sn^{131} concentration in kidney and the other soft tissues became greater although the liver concentrations of tin were never very great, almost one third of the tin excreted being found in the feces. If the liver is responsible for the elimination of tin via the bile, it appears to be able to handle this material in the carrier-free state with ease. The major portion of the tin administered was excreted by the kidneys and was recovered in the urine.

The major area of tin deposition in the body was the skeleton. Unlike the lanthanide and actinide series of elements, tin is more readily lost from the skeleton. These studies indicate that the removal of one-half of the tin incorporated in the skeleton after intramuscular administration of the citrate complex is probably accomplished in a matter of 3 to 4 months.

Samarium (Sm^{151}). Preliminary studies with carrier-free samarium have been initiated. These studies will be continued as additional material becomes available from Oak Ridge. To date, the deposition of Sm^{151} has been studied in rats at 1 and 4 days after intramuscular administration. Like the other members of the lanthanide series of the rare earths, this material is absorbed from the injection site slowly. Ninety percent remained at the injection site one day after administration and 48 percent at 4 days.

The deposition of Sm^{151} in the tissues of the rat following absorption from the

Table I

DEPOSITION OF YTTRIUM IN THE RAT FOLLOWING INTRAMUSCULAR ADMINISTRATION, USING Y^{91} AS A TRACER. VALUES CORRECTED FOR RECOVERY AND EXPRESSED AS PERCENT OF DOSE.

	1 D		4 D		16 D		32 D	
Tissue	% per organ	% per gram	% per organ	% per gram	% per organ	% per gram	% per organ	% per gram
Heart	.08	.13	.04	.06	.03	.04	.03	.04
Lungs	.36	.23	.29	.16	.15	.07	.16	.09
Spleen	.17	.28	.18	.29	.26	.33	.17	.19
Blood	.38	.04	.15	.02	.04	<.01	.03	<.01
Liver	17.2	2.18	12.1	1.58	4.38	.54	2.83	.30
Kidney	2.82	1.84	.81	.45	1.12	.58	.82	.38
Adrenals	<.02	-	<.02	-	<.01	-	<.01	-
Thyroid	<.02	-	.02	-	<.01	-	<.01	-
Lymph Gl	-	.30	-	.18	-	.10	-	.04
Pancreas	.06	.08	.03	.04	.01	.04	.03	.01
Brain	<.02	<.02	<.02	.02	.01	<.01	.01	<.01
Fat	-	.08		.02	-	<.01	-	<.01
Stomach	.38	.09	.21	.09	.12	.03	.10	.04
Sm Int	1.04	.11	.78	.09	.28	.03	.16	.01
Lg Int	1.89	.23	.73	.09	.25	.03	.17	.01
Skeleton	53.6	3.83	55.6	4.03	55.9	3.79	56.8	3.64
Muscle	5.51	.07	2.60	.03	1.96	.02	2.21	.03
Skin	2.54	.09	1.86	.06	.89	.03	.59	.01
Eyes	<.02	.04	<.02	-	<.01	.01	<.01	.01
Pituitary	<.02	-	<.02	-	<.01	-	<.01	-
Gonads	<.02	.13	.02	-	<.01	.06	<.01	.04
Urine	12.6	-	15.6	-	23.1	-	21.4	-
Feces	1.38	-	9.02	-	11.5	-	14.5	-
	100.0		100.0		100.0		100.0	

Table II

DEPOSITION OF TIN IN THE RAT FOLLOWING INTRAMUSCULAR ADMINISTRATION USING Sn^{131} AS A TRACER. VALUES CORRECTED FOR RECOVERY AS PERCENT OF DOSE.
COMPLEXED WITH CITRATE

	1 Day		4 Days		16 Days		32 Days	
Tissue	% per organ	% per gram	% per organ	% per gram	% per organ	% per gram	% per organ	% per gram
Heart	.05	.05	.01	<.01	.02	.02	.02	.02
Lungs	.30	.13	.14	.07	.11	.05	.10	.04
Spleen	.09	.10	.08	.10	.06	.07	.04	.06
Blood	.39	.02	.03	<.01	.02	<.01	<.01	<.01
Liver	1.03	.10	.98	.14	.57	.06	.43	.04
Kidney	2.22	.92	1.53	.61	.67	.32	.65	.28
Adrenals	<.01	-	<.01	-	<.01	-	<.01	-
Thyroid	<.01	-	<.01	-	<.01	-	<.01	-
Lymph Gland	-	.14	-	.11	-	.06	-	.05
Pancreas	.05	.05	.02	.02	.03	.04	.01	.02
Brain	<.01	<.01	<.01	<.01	<.01	<.01	<.01	<.01
Fat	-	.01	-	<.01	-	.02	-	.01
Stomach	.29	.09	.09	.02	.05	<.01	.03	<.01
Sm Int	.55	.07	.28	.02	.15	.02	.11	<.01
Lg Int	1.11	.14	.20	.01	.25	.03	.06	<.01
Skeleton	31.2	1.50	29.4	1.39	22.0	.98	24.2	1.06
Muscle	5.06	.04	2.70	.02	2.09	.02	1.73	.01
Skin	3.08	.05	3.26	.07	2.09	.05	1.53	.04
Gonads	.07	.03	.06	.01	.04	.01	.05	.02
Pituitary	<.01	-	<.01	-	<.01	-	<.01	-
Eyes	.04	.14	.01	.04	<.01	.02	<.01	.02
Urine	52.8	-	50.4	-	48.9	-	46.9	-
Feces	1.64	-	10.8	-	23.0	-	24.1	-
	100.0		100.0		100.0		100.0	

injection site is presented in Table III. As with the other members of the lanthanide series of rare earths, Sm^{151} is primarily deposited in the skeleton and liver. However, the skeletal deposition observed in these preliminary studies was lower than that observed for the members of the lanthanide series of lower atomic number such as lanthanum, cerium, and praseodymium. Because of this, relatively more of the Sm^{151} is excreted since the concentration of Sm in the soft tissues of the body was low with the exception of liver and kidney. The urinary and fecal routes of excretion for Sm^{151} are equally involved at 4 days after intramuscular administration.

Europium (Eu^{154}). The studies on the metabolism of carrier-free Eu^{154} have been completed up to 64 days after intramuscular administration. Since work on europium with carrier has been recounted in earlier reports, it is possible to compare the metabolic effect of this element in the rat in the carrier and the carrier-free state. The carrier-free Eu^{154} used in these studies was believed to be free of other rare earths after spectrographic analysis. The metabolism of carrier-free Eu^{154} is similar to the other lanthanide rare earths. It is absorbed with difficulty following intramuscular administration, 81 percent, 80 percent, 72 percent, 58 percent, and 49 percent of the injected material remaining in the left leg at 1, 4, 16, 32 and 64 days respectively following injection. The distribution of the Eu^{154} absorbed from the injection site is summarized in Table IV. These studies show that europium is tenaciously held by the skeleton. The distribution of europium in the soft tissues of the body is low for all time periods studied with the exception of liver and kidney. Europium is primarily excreted via the feces (38 percent at 64 days). About 14 percent was recovered in the urine at 64 days after intramuscular administration.

Studies on europium with carrier show little difference in absorption from the injection site, tissue distribution following absorption, or route of excretion when compared to carrier-free europium. The metabolism of europium containing 0.6 micrograms of added carrier 64 days following intramuscular administration is presented in Table V. With the carrier-free europium, 64 days after injection, 49 percent remained at the injection site; with carrier, 31 percent. Carrier-free europium showed a skeletal deposition of 40 percent; carrier, 41 percent. With respect to excretion, 14 percent of the carrier-free Eu^{154} was found in the urine, 38 percent in the feces; with carrier, 16 percent was in urine and 35 percent in feces. It would appear that the addition of 2 micrograms of carrier europium per kilo of body weight does not alter the metabolism of this element in the body.

Table III

DEPOSITION OF SAMARIUM IN THE RAT FOLLOWING INTRAMUSCULAR ADMINISTRATION USING Sm^{151} AS TRACER. VALUES CORRECTED FOR RECOVERY AND EXPRESSED AS PERCENT OF DOSE.

	1 Day		4 Days	
Tissue	% per organ	% per gram	% per organ	% per gram
Heart	.03	.02	<.03	<.03
Lungs	.04	.02	.06	<.03
Spleen	.26	.31	.15	.21
Blood	.16	.01	<.03	<.03
Liver	18.4	1.19	7.08	.50
Kidney	.57	.26	.38	.15
Adrenals	<.01	-	<.03	-
Thyroid	<.01	-	<.03	-
Lymph Gland	-	.02	-	<.03
Pancreas	.02	.03	<.03	<.03
Brain	<.01	<.01	<.03	<.03
Fat	-	<.01	-	<.03
Stomach	.04	.02	.06	<.03
Small Intestine	.36	.04	.29	<.03
Large Intestine	4.52	.36	.94	.09
Skeleton	18.1	.42	19.1	.50
Muscle	.94	<.01	.91	<.03
Skin	.47	<.01	.32	<.03
Gonads	.02	<.01	<.03	<.03
Pituitary	<.01	-	<.03	-
Urine	14.0	-	35.8	-
Feces	42.1	-	34.9	-
	100.0		100.0	

Table IV

DEPOSITION OF EUROPIUM IN THE RAT FOLLOWING INTRAMUSCULAR ADMINISTRATION, USING Eu^{154} AS A TRACER. VALUES CORRECTED FOR RECOVERY AND EXPRESSED AS PERCENT OF DOSE.

	1 Day		4 Days		16 Days		32 Days		64 Days	
Tissue	% per organ	% per gram	% per organ	% per gram	% per organ	% per gram	% per organ	% per gram	% per organ	% per gram
Heart	.09	.09	.10	<.10	.07	.07	.06	.06	.05	.08
Lungs	.18	<.09	.39	.10	.26	.13	.25	.09	.13	.08
Spleen	.27	.37	.20	.39	.26	.39	.19	.22	.10	.15
Blood	.64	<.09	.39	<.10	.07	<.07	<.03	<.03	.05	<.03
Liver	61.2	3.75	48.7	5.31	24.5	4.17	7.09	.71	3.43	.36
Kidney	2.75	.64	1.58	.69	1.04	.65	.83	.37	.61	.28
Adrenals	<.09	-	<.10	-	<.07	-	<.03	-	<.03	-
Thyroid	<.09	-	<.10	-	<.07	-	<.03	-	<.03	-
Lymph Gl.	-		-		-	.20	-	<.03	-	.10
Pancreas	<.09	<.09	<.10	<.10	<.07	-	<.03	.03	<.03	<.03
Brain	<.09	<.09	<.10	<.10	<.07	<.07	<.03	<.03	<.03	<.03
Fat	-	<.09	-	<.10	-	.07	-	<.03	-	<.03
Stomach	.27	.09	.30	.10	.20	.13	.12	.03	.08	<.03
Sm Int	.64	<.09	.89	<.10	.46	.07	.37	.03	.15	<.03
Lg Int	.92	<.09	1.09	.10	1.56	.33	.62	.06	.13	<.03
Skeleton	18.1	.54	25.8	1.28	34.3	1.63	37.3	1.85	40.2	1.82
Muscle	3.21	<.09	2.75	<.10	1.63	<.07	2.28	<.03	1.61	<.03
Skin	3.12	<.09	2.16	<.10	1.30	<.07	1.05	<.03	.67	<.03
Gonads	.09	<.09	<.10	<.10	<.07	.26	<.03	.03	<.03	.03
Eyes	<.09	<.09	<.10	-	<.07	.07	<.03	<.03	<.03	<.03
Pituitary	<.09	-	<.10	-	<.07	-	<.03	-	<.03	-
Urine	6.97	-	6.50	-	15.4	-	14.3	-	14.6	-
Feces	1.47	-	8.95	-	19.0	-	35.5	-	38.2	-
	100.0		100.0		100.0		100.0		100.0	

Table V

DEPOSITION OF EUROPIUM* IN THE RAT 64 DAYS AFTER INTRAMUSCULAR ADMINISTRATION USING Eu^{154} AS TRACER. VALUES CORRECTED FOR RECOVERY AND EXPRESSED AS PERCENT OF DOSE

Tissue	% per organ	% per gram
Heart	.03	.02
Lungs	.07	.03
Spleen	.07	.10
Blood	<.02	<.02
Liver	2.64	.21
Kidney	.47	.17
Adrenals	<.02	-
Thyroid	<.02	-
Lymph Gland	-	.05
Pancreas	<.02	<.02
Brain	<.02	<.02
Fat	-	<.02
Stomach	.07	<.02
Small Intestine	.09	<.02
Large Intestine	.07	<.02
Skeleton	41.3	.93
Muscle	2.28	<.02
Skin	1.52	.02
Eyes	<.02	.02
Pituitary	<.02	-
Gonads	.03	.02
Urine	16.1	-
Feces	35.3	-
	100.0	

*Approximately .6 micrograms of europium was administered with the Eu^{154}.

[redacted]

Endocrine Factors Affecting Bone Growth.

1. Effect of Growth Hormone in Phosphate Deficient Rats.

The growth hormone of the anterior pituitary is an important factor influencing the growth of bone. The effect of this factor was studied in rats in which skeletal growth had been retarded by phosphorus deficiency, and a comparison was made with rats which had been pair-fed the complete diet at a level equivalent to that consumed by the deficient animals. After 24 days on the experimental diets, followed by a control period of 10 days during which the urine was collected and analyzed for N, Ca, and P, the rats were given a daily injection of 1 mg. of pure crystalline growth hormone for 10 days. After 8 days treatment with growth hormone, certain of the rats were given an injection of a tracer dose of radio-strontium and the amount deposited in the skeleton was determined. Tibias were taken for histological study.

At present, analyses of the data are incomplete. A full report will be submitted later.

2. Effect of Estrin Therapy on the Deposition of Radio-strontium.

Administration of estrogens results in a marked deposition of new bone in pigeons and fowl, and to a much lesser extent in mice and rats. The effect of daily injection of 1000 units of estradiol benzoate into young female rats is being investigated. After 2 weeks of such treatment, the animals received a tracer dose of radio-strontium by intraperitoneal injection. They were sacrificed 3 days later. Blood, muscle, skeletal tissues, and excreta are being analyzed to determine the effect of estrin on the bone deposition and excretion of radio-strontium. A full report will be submitted later when analyses have been completed.

A Study of the Kinetics of Excretion and Bone Deposition of Radio-phosphorus. A study is being made of the rate of bone deposition and excretion of radio-phosphorus during the critical first few hours following injection of P^{32} phosphate.

A Study of the Structure of Compact Bone with the Electron Microscope. The development of the electron microscope has made it possible to visualize structures far below the range of ordinary light microscopy. It has been widely used in many fields in which a high degree of resolution is desired (e.g., study of bacteria and virus).

The following is a preliminary report on a study of the minute structure of compact bone with the electron microscope. Such bone contains about 45 percent mineral bone salt, 30 percent organic matrix, and the balance water and miscellaneous constituents. With the ordinary microscope it has been impossible to detect any structural relationship between matrix and bone salt. With the electron microscope, however, a hundredfold increase in resolution was obtained which revealed a definite pattern in the samples of compact bone which were studied.

Methods.

Samples of compact bone were obtained from fresh undecalcified rat femur. In order to obtain clear electron micrographs, it was necessary to obtain sections less than 1 micron thick. Microtomy, manual sectioning and crushing all proved unsatisfactory. Sections were finally obtained by chipping the bone at an angle, and selecting pieces under the high power of an ordinary light microscope. The chips were compared with materials of known thickness and only those with a thickness of less than 1 micron were used. These chips were somewhat smaller than a red blood cell. They were picked off with a fine moist needle, and set directly upon the prepared wire mesh screens. Electron micrographs were made with an R.C.A. electron microscope, Type B, set at a magnification of 8000 times. The plates or negatives were enlarged 3-1/2 times and prints were made. A number of chips were obtained which were sufficiently thin to show structural detail.

Fig. 1 is a typical electron micrograph of compact bone. A definite honeycomb pattern may be seen, with light polygonal areas surrounded by dark rods of denser material. Dimensions were measured with a micrometer eyepiece on a light microscope, and the actual distances were calculated from the degree of magnification (28,000x). The light spaces have an average diameter of approximately 545 ± 70Å, while the average width of the dark rods was about 116 ± 16Å. Since the dimensions of apatite are: $a = 9.36A^{o}$, $c_{o} = 6.85A^{o}$(1) the dark rods may represent aggregates of 12-16 apatite crystals. Their smaller area may be accounted for by the greater density of apatite. The light spaces may represent organic material. The greater part of the organic matrix is presumably composed of collagen (2) and the width of such collagen fibers has been reported to be around 500Å (3). It will be noted that these light spaces are rather uniform in size, and do not appear to be elongated in any one direction.

These findings suggest a definite organizational pattern between the organic matrix and mineral salt in compact bone. It would be of interest to compare the pattern in normal bone with that in osteodystrophies and abnormal calcifications.

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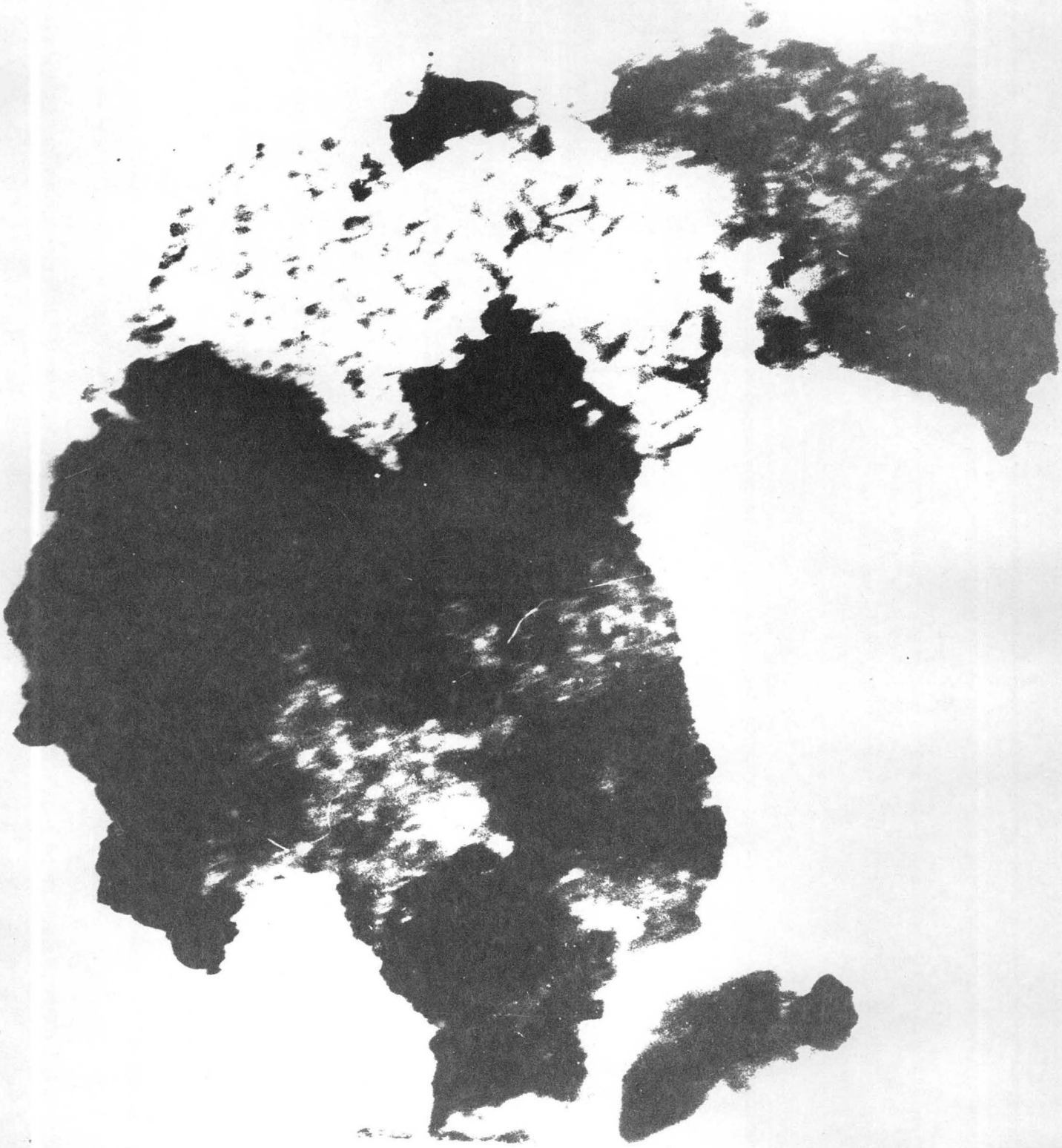

FIG. I.
ELECTRON MICROGRAPH OF COMPACT BONE FROM RAT FEMUR × 28,000

OZ-314

Radiochemical Isolation

Preparations of isotonic saline solutions of At^{211} are now being made at millicurie levels. Yields of At^{211} from alphas on bismuth are ~.5 millicurie per microampere hour. Sufficient aluminum foil is used to degrade the beam energy to the point where the proportion of At^{210} formed is insignificant. A high vacuum system has been set up for the separation of astatine from bismuth using the distillation procedure of Segrè and Leininger. Using a modification of their techniques, it has been found possible to prepare isotonic solutions by simply removing astatine from the surface of the glass U-tube collector by the use of ~60λ of concentrated hydrochloric acid. This solution is then neutralized with sodium hydroxide and diluted to the required volume for injection.

Approximately two millicuries of Cu^{64} and 10 millicuries of Ga^{67} were isolated carrier-free from deuteron bombarded zinc. Solvent extraction methods were used; gallium was removed from a hydrochloric acid solution with ether; copper was removed using a dithizone-chloroform technique.

Several samples of Cb^{95}, at the millicurie level, were separated from Oak Ridge Cb-Zr mixtures. An improved separation method, which is essentially a modification of electrical transference methods, has been developed. This method has also been used successfully in separating milligram amounts of copper from radio-arsenic, tungsten from radio-tantalum, and manganese from radio-columbium.

An Oak Ridge shipment of Sm^{151} was characterized by column separation with added samarium carrier. The activity peak corresponded to the carrier peak as determined by spectrographic analysis. Approximately 120 microcuries of carrier-free tin were separated from a cadmium target. The tin was retained in solution in the presence of 1 mg. of citric acid per ml. of solution. About 2 microcuries of Ta^{182} were separated carrier-free from an alpha bombarded hafnium oxide target.

II BIOLOGICAL STUDIES OF RADIATION EFFECTS

J. H. Lawrence - in charge

Project 48A-II

The Genetic Effects of Low Intensity Irradiation

Delta E. Uphoff and Curt Stern

It has been shown by Spencer and Stern (1948) that irradiation by x-rays at high intensity induces mutations in sperm of Drosophila melanogaster at dosages as low as 50 r and 25 r, and that the proportionality between r-dose and mutation frequency is maintained down to these low dosages. Earlier workers had established independence of induced mutation frequency from the intensity of irradiation at high and medium dosages. In contrast to these findings, Caspari and Stern (1948) obtained no significant difference in mutation rates between controls and experimentals, which had been subjected to a dose of 52.5 r in gamma-rays administered continuously for 21 days at a rate of 2.5 r per day.

This unexpected result required further tests. After consideration of various factors the following were regarded as possible causes for the apparent inactivity of irradiation in the experiment by Caspari and Stern: (1) low sensitivity to irradiation of aged sperm, (2) dependence of induced mutation frequency at low dosages on a time factor, and (3) errors of sampling which might have obscured a true difference between control and experimental rates. The first possibility was studied by administering 50 r in gamma rays continuously over 24 hours to sperm which had been aged previously for 20 days in the spermathecae of females (Uphoff and Stern 1947). In this experiment the intensity of irradiation was raised several times over that used by Raychaudhuri (1944) who had found typical intensity independence of mutation rates. Any deviation from the effect of irradiation expected for 50 r at medium intensity would thus be due to a specific sensitivity or insensitivity of the aged sperm. The second possibility, interference by a time factor, was tested by increasing the intensity of irradiation, and the total dosage, by a factor of 2, that is, by administering 100 r instead of about 50 r through continuous gamma-irradiation over 21 days. The third possibility, chance, was checked by a repetition of the original experiment, that is, by giving once more 52.5 r in gamma rays over 21 days. Parallel with each experiment the spontaneous mutation rate was determined in a set of controls.

The data, together with the earlier ones by Spencer and Stern, and Caspari and Stern are summarized in Table I. It is seen that all three new tests gave an increased frequency of mutations in the treated sperm as opposed to the controls. The experimental rate observed by Caspari and Stern is statistically in good agreement with later determinations. The control rate of 0.2489 percent found by Caspari and Stern is higher than anyone of the later control rates. By itself a rate of 0.2489 percent for sperm aged over 21 days as compared to 0.0974 percent for not aged sperm (Table I, line 1) seemed in line with the degree of increase expected, according to the experience of other workers, after 21 days of aging. The new data on the control mutation rate in aged sperm suggest considerable variation of age accumulation of

Table I

Mutation Rates for Sex-linked Lethals in Sperm of

Drosophila Melanogaster, After Different Types of Treatment

Treatment	No. of Controls	No. of Experimentals	Mutation rate percent Controls	Mutation rate percent Experimentals	Diff.
50 r, 2.3-5 minutes exposure not aged (Spencer and Stern)	73,901	31,560	0.0974	0.2440	0.1466
52.5 r*, 21 days exposure aged (Caspari and Stern**)	56,252	51,963	0.2489	0.2848	0.0359
50 r*, 24 hours exposure after 20 days aging	44,601	46,232	0.1682	0.2834	0.1152
100 r, 21 days exposure, aged	22,958	31,562	0.2352	0.4658	0.2306
52.5 r*, 21 days exposure, aged	36,184	29,424	0.1765	0.2542	0.0777

* Geometric errors in the administration of the radiation are larger than the difference between the values of 52.5 and 50 r.

** The mutation rates obtained by Caspari and Stern have been adjusted to the slightly different scoring of lethals used in the investigations reported in this paper.

mutations in the Canton Special stock on which all tests were carried out.

A comparison of the differences in mutation frequencies between experimentals and controls in the chronic experiments (lines 2-5) with the difference in the acute experiment (line 1) should take into account the fact that the difference in the latter experiment is somewhat larger than expected on the basis of all of Spencer and Stern's data. The maximum likelihood calculation yields about 0.002 percent induced mutation per r which corresponds to an expected difference for the acute 50 r experiment of only 0.1000 percent. Viewing all experiments together it appears that irradiation at low dosages, administered at low intensity induces mutations in Drosophila sperm. A more detailed account of the work will be presented later.

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Sensitivity of Bacteria to Ultraviolet Radiation

Robert Weatherwax and R. Lowry Dobson

Investigation of the effects of radiation upon strain B of Escherichia coli and upon its radiation-resistant mutant, B/r, (Witkin 1947) is in progress. A number of observations offer new material for interpretation of the effects of ultraviolet radiation and for explanation of the nature of the mutation to radiation resistance. Many of the irradiation experiments have been accompanied by cytological examination of the cells involved in an attempt to correlate changes in radiation resistance with possible changes in the number, size, or arrangement of the chromatinic structures believed to represent the bacterial nucleus.

The sensitive strain of bacteria, B, responds to sub-lethal doses of ultraviolet light by forming extremely long filaments on the surface of an agar plate. In such filaments as many as 15 or 20 distinct nuclear structures may be demonstrated by appropriate techniques (Robinow 1945). Survival curves of the populations of such filaments remain exponential in shape but show at least an eight-fold increase in sensitivity to the lethal effect. In nutrient broth the young cells show a similar increase in sensitivity during the first two hours of growth, with the cells becoming at least five times more sensitive than those of the 24 hour old inoculum used to start the fresh culture (Fig. 1). In broth cultures the cells become only slightly elongated during the first few divisions and the average number of nuclei per cell appears to be four as compared with the single nuclear body in the old cells.

A rigid correlation of radiation sensitivity with the number of nuclear structures present has not yet been attempted but it appears that an increase in the number of these bodies, representing possibly an increase in the size of the target area, is associated with the increase in radiation sensitivity, although it is difficult to see why a hit in only one of these apparently identical structures should suffice to kill the cell. At least two other factors however may also influence the slope of the survival curve. One is the presence of a shielding material of some sort about the sensitive area, and the other is the innate susceptibility of the ultimate target to a chemical change when a hit is produced within it. Changes in these factors during growth of the cell may also be involved in the change in radiation sensitivity.

The radiation-resistant mutant, B/r, has been studied in somewhat less detail; but it has been shown definitely that as this organism emerges from the lag phase of growth in a fresh broth medium the resistance to radiation does not decrease, but on the contrary increases to a slight extent (Fig. 2). It is difficult to assign a factor expressing the increase in resistance because of the sigmoid shape of the curve. Experiments to date, however, indicate that the increase in resistance is due to an increase in the number of hits required and not to the accumulation of protective substances about the sensitive area of the cell. The cytological changes in B/r during this growth period are the same as those seen in B: the cell enlarges slightly and the number of nuclei increases from 1 to 4.

In connection with the mutation to radiation resistance it appears that good fitting of the theoretical curves with experimental curves obtained with B/r is achieved when the assumption is made that the change to radiation resistance, i.e., to

a multiple-hit type of inactivation, involves a change not only in the number of hits required but also in the probability that a given hit will contribute its effect. If, for example, the exponential curve obtained with the sensitive organism, B, is accepted as a basic one-hit curve, then the sigmoid curve obtained experimentally with B/r can be closely duplicated in theory by assuming a change to a four-hit type of curve which is further modified in shape and in the slope of the straight-line portion by assuming the probability that a given hit will contribute its effect is reduced by a factor of 1/2.

Experiments of the sort that have been done in the past with bacteria in obtaining evidence for or against the theory of direct action of the radiation seem to be in order with the new mutant strain, and some things have been done along this line. It has been shown that identical survival curves result for B/r when suspensions containing from 10^4 to 10^8 cells per ml are irradiated. In addition experiments in which the dose of irradiation was fractionated or spread out over some period of time have not indicated any recovery phenomenon.

Studies similar to those outlined above are being carried out with ionizing radiation, and further experiments are in progress in an attempt to elucidate the nature of cellular radio sensitivity and radio resistance.

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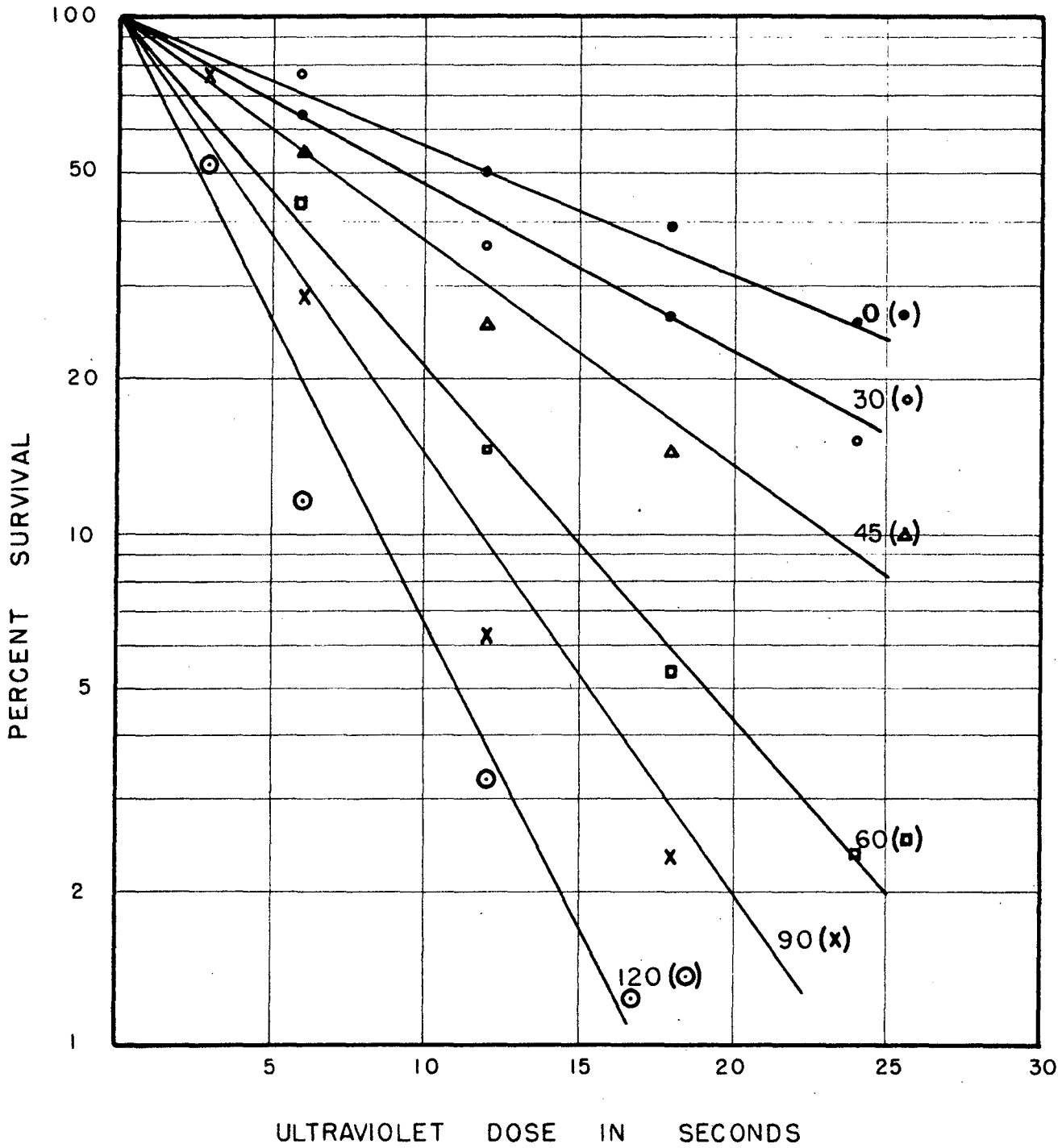
100
50
20
10
5
2
1
PERCENT SURVIVAL
5
10
15
20
25
30
ULTRAVIOLET DOSE IN SECONDS
0 (•)
30 (○)
45 (△)
60 (□)
90 (x)
120 (⊙)

FIG. 1

13355-1

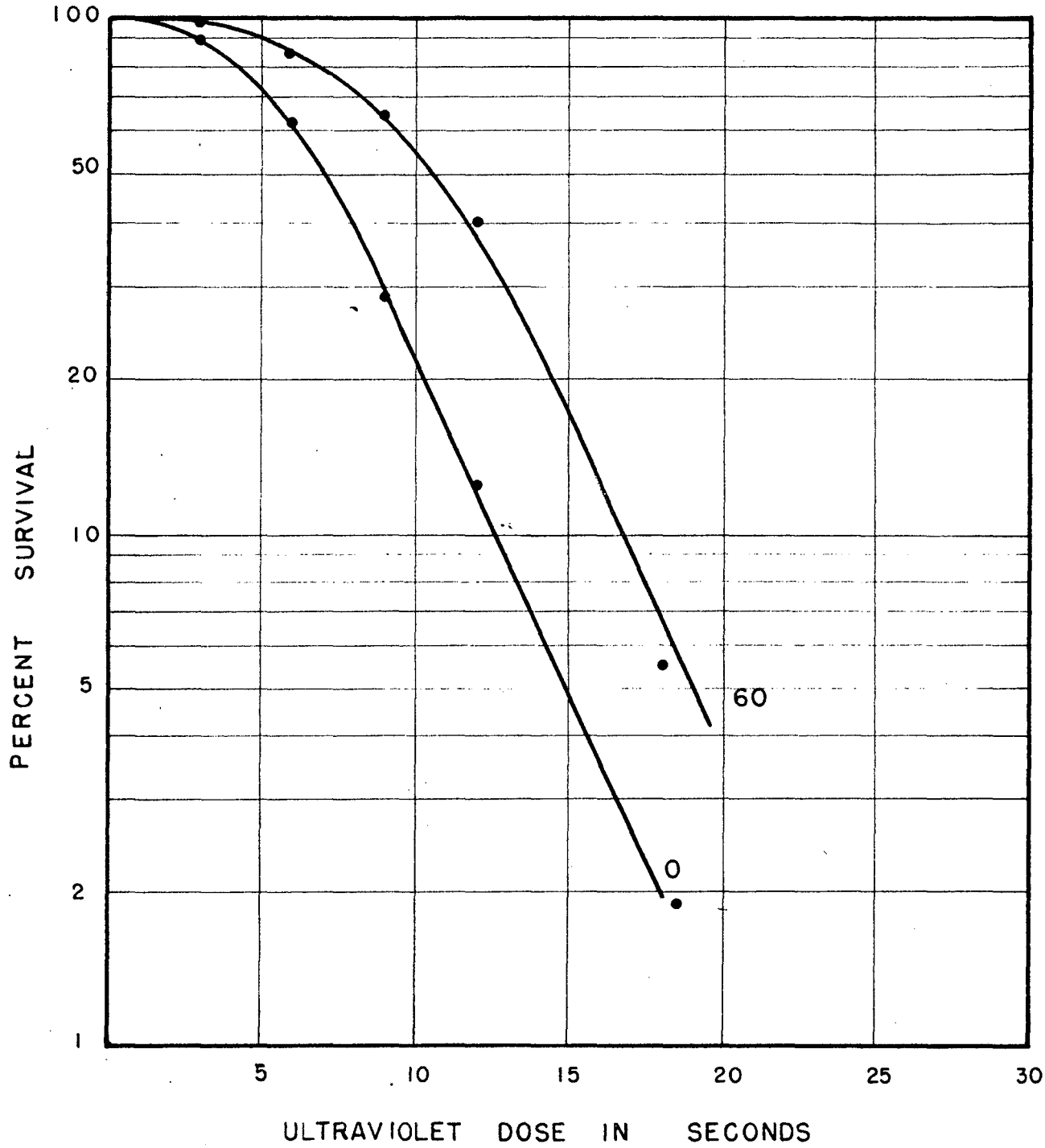
100
50
20
10
5
2
1
PERCENT SURVIVAL
5
10
15
20
25
30
ULTRAVIOLET DOSE IN SECONDS
60
0

FIG. 2

13356-1

The Effects of a Single Whole-Body Exposure to 190 Mev Deuterons on the Blood and Tissues of the White Mouse

Paul Rosahn

With the availability of 190 Mev deuterons from the 184 inch cyclotron, several investigators in this laboratory became interested in the possibility of depositing depth doses in selected organs in animals and humans using the properties of the Bragg ionization curve (1, 2). Qualitatively one expects to find the same type of histological effects with high energy protons or deuterons as with x-rays. Fast neutrons, acting chiefly through proton recoils, show very similar histological changes to those produced by x-rays, as the studies of Lawrence and Tennant (3) first demonstrated. It still seemed worthwhile to initiate a preliminary study of the nature of histological effects caused by high energy deuterons in order to proceed to the quantitative aspects of the problem, that is to the study of the effectiveness of different portions of the Bragg curve. The studies here described were pursued in June, 1948, and they form a part of more extensive work on whole body irradiation of white mice and of mouse tumors. The data presented below are confined to a limited investigation of tissue and blood changes occurring in the white mouse after a single whole body exposure to the deuteron beam. To compare these observations with others reported with the use of x-rays and neutrons there are several original papers and reviews available (see for example 3-7).

Material and Methods. White mice of the strong A strain were employed. They were housed and maintained under uniform and standard conditions. From a pool of approximately 100 such mice, 20 were selected by random choice for preliminary blood studies which were completed during the 72 hours prior to exposure of the experimental group to the deuteron beam. These blood studies included enumeration of erythrocytes, leukocytes and platelets, and differential counts on smears stained by Wright's method. The calculated mean values were employed to establish the normal base lines shown in the text-figures.

On June 13, 1948 the entire population of 100 mice was transported to the Radiation Laboratory where three groups were selected at random for bombardment. Group 1 comprised 13 mice. They received the smallest exposure to the deuteron beam, equivalent to 460 r.e.p. Group 2 consisted of 12 mice which received an intermediate dose, equivalent to 905 r.e.p. Group 3, totaling 15 mice, were bombarded with the equivalent of 1800 r.e.p. All mice, the treated and the untreated, were then returned to their laboratory of origin.

The body weights of all treated mice were recorded at frequent intervals for comparison with pre-treatment values. Systematic examinations of the blood were carried out on the first, third, fifth, tenth and eighteenth day after treatment. At these time intervals two mice were selected at random from the survivors of each of the three groups, and two untreated mice were similarly selected from the control pool. Complete blood studies were conducted on these animals, after which they were sacrificed for tissue examination. Since the experimental groups were continually depleted by sacrifice and spontaneous death, observations to the 18th day were possible only on Group 1. Group 2 had no survivors beyond the 10th day, and Group 3 none beyond the 4th day.

Mice that died spontaneously during the course of the experiment were autopsied and used for tissue studies. Other mice, obviously moribund, were sacrificed terminally for similar studies. The following tissues were saved for histologic study: brain, spinal cord, vertebra, sternum, liver, spleen, lymph nodes, skin, thymus, intestine, stomach, gonads, heart, lung. These organs were fixed in 10 percent formalin or Bouin's solution, and stained with hematoxylin and Eosin. It was possible to prepare satisfactory bone marrow sections from the sternum without preliminary decalcification. Continual reference to control tissues was made throughout the histologic studies.

In the test-figures the abscissa denotes time, which is drawn on a logarithmic scale. Each point in the blood cytology curves represents an average of two observations, indicated as a percentage deviation from the pretreatment normal control value. In Group 1 there was one survivor at 23 days. The observations on this animal were combined with the 18 day value.

Results

1. Survival Time. Table I shows duration of life after bombardment. Estimation of survival time was slightly complicated by the fact that animals were killed from each group for tissue studies, but in spite of this it is evident that survival was closely related to total dosage. Of 5 animals in Group 1 surviving the 5th day, none died spontaneously thereafter, in contrast to 4 spontaneous deaths among the 5 animals in group 2 that were alive on the 5th day after treatment. Three mice from Group 1 survived the 10th day, while all the animals in Group 2 were dead at this time. Group 3, receiving the highest dose, had no survivors after the 4th day.

2. Body Weight. Figure 1 depicts the change in body weight following bombardment. The average pretreatment weights of the control group was 28.1 gms., of Group 1, 27.7 gms., of Group 2, 30.2 gms., and of Group 3, 30.7 gms. There are no significant differences among any of these values. All groups showed weight loss following exposure to the deuteron beam, in direct relation to dosage. Group 1 which received the smallest exposure had the smallest initial average weight loss with a return to normal on the 18th day. Group 3, exposed to the heaviest dose, had the greatest average weight loss at four days when its last surviving member died.

3. Gross Findings at Autopsy. Animals reacted to the toxic effects of the beam by losing weight, developing ruffled fur, becoming listless, and finally exhibiting diarrhea. At autopsy after spontaneous death there was generalized pallor of tissues, particularly of the liver, and watery yellow material in the stomach and intestinal tract. The spleen became markedly atrophic, and lymph nodes and thymus were so strikingly reduced in size that they were sometimes difficult to locate. Animals in Group 1 surviving the 10th day showed no significant gross tissue changes.

4. Hematological Alterations. These are summarized in text-figures 2 - 6 inclusive.

a. Red blood cells. Employing the normal pretreatment average count as a base line, an early slight increase was noted in all groups. Following this initial rise, there was no significant deviation in the average red cell count of any of the three treatment groups during the two and a half week observation period. (Fig. 2)

TABLE I

NUMBER OF MICE SURVIVING STATED PERIOD FOLLOWING BOMBARDMENT

Days After Bombardment	Group I		Group II		Group III	
	Dead	Surviving	Dead	Surviving	Dead	Surviving
1	2 (S)	11	2 (S)	10	2 (S)	13
2	0	11	0	10	0	13
3	2 (S)	9	2 (S)	8	2 (S)	11
4	0	9	1 (D)	7	11 (D)	0
5	2 (S), 2 (D)	5	2 (S)	5		
6	0	5	0	5		
7	0	5	0	5		
8	0	5	2 (D)	3		
9	0	5	2 (D)	1		
10	2 (S)	3	1 (S)	0		
11	0	3				
18	2 (S)	1				
19	0	1				
23	1 (S)	0				

S - sacrificed for blood and tissue studies.

D - died or moribund and sacrificed.

b. Platelets. A precipitous drop in the platelet count was observed in all three groups as can be seen in Figure 3. This was most marked on the third to the fifth day following exposure, and was roughly parallel to the amount of exposure. The depletion of platelets continued in Group 2 to the 10th day. Group 1, however, showed some indication of a rise in the platelet count after the fifth day, but the total number of platelets had not reached a normal level by the 18th day, the last day on which observations were available.

c. White blood cells. Since the great majority of white cells in the peripheral blood of the mouse are lymphocytes, fluctuations in the total white cell count largely reflect changes in the lymphocyte levels. Within 24 hours after bombardment, all three groups showed a striking depletion of the total white cells in the peripheral blood, to about 20 percent of the normal value as shown in Fig. 4. In Group 2 the total white count continued to fall to the 10th post-treatment day, and Group 3 likewise showed a continued drop to the 4th post-treatment day. These were the last days on which observations were available on these two groups. Group 1 with the longest survival period showed a continued fall in the total white count on the 3rd day, after which there was a slow rise to 75 percent of the normal value on the 18th day.

d. Neutrophiles. Within 24 hours after treatment, the total neutrophile count of all three groups sharply fell. (Fig. 5) This fall continued in Group 2 till the 10th post-treatment day, when the lowest point was reached, 12 percent of the normal value. On the 5th day the average neutrophile count in Group 1 was at its lowest level, 15 percent of normal, but thereafter the neutrophile count of this group rose sharply, so that on the 18th day it was higher than normal.

e. Lymphocytes. A prompt and sharp fall in the total lymphocytes occurred in all three groups as indicated in Fig. 6. The first observation after treatment, at 24 hours, showed lymphocyte levels of 10 to 15 percent of normal. The total lymphocyte count in Group 1 was about 15 percent of normal on the 10th day, but the next observation on the 18th day revealed a marked rise to a level approximating normal. In Group 2, however, the total lymphocytes continued to fall to the 10th day when they were less than 5 percent of normal. In Group 3 the total white cell count was so low after 24 hours that differential counts could not be conducted and the lymphocyte level could, therefore, not be determined.

5. Tissue Alteration. Histological sections were prepared from many of the tissues heretofore mentioned, but especial attention was directed at the bone marrow, lymph nodes, and spleen (Fig. I - XI).

a. Bone Marrow. Within 24 hours following exposure there was a noticeable depletion in all the cellular elements comprising the bone marrow with the possible exception of megakaryocytes. (Fig. II) These changes occurred in all three groups, but were most marked in Group 3. At three days marked hypoplasia of the bone marrow was noted in a majority of animals, (Fig. III) in some cases large lakes of red blood cells replacing the young forms usually present. Here and there islands of distorted cells and scattered megakaryocytes could still be seen. At five days the maximum degree of aplasia occurred in both Groups 1 and 2, nearly all blast forms having been obliterated. Thereafter, Group 1 animals showed rapid regeneration (Fig. IV) so that by the 10th day they had bone marrow of normal cellularity, with

distinct hyperplasia of the marrow on the 18th day. In Group 2, however, there was only slight evidence of regeneration on the 10th day, the last day on which observations are available. In general terms the period of hypoplasia and aplasia lasted for about 10 days.

b. Lymph nodes. At 24 hours after irradiation, animals in all three groups showed evidence of lymph node damage. This was characterized by foci of nuclear pyknosis and fragmentation in both the primary and secondary nodules. (Fig. V) Lymphocytes were usually reduced in the secondary nodules where there was evidence of active phagocytosis in the many macrophages which had replaced them. (Fig. VII) Necrosis and macrophages were also present in the medullary cords. In some of the smaller nodes the primary and secondary nodules had completely disappeared. There was distinct loss of cellurity in animals receiving higher doses, with interstitial edema, marked vascular congestion and fibrous proliferation a prominent feature. Reparative processes were evident at three and five days, with clearance of the cellular debris and cell regeneration as indicated by active mitoses. (Fig. VIII) At 18 days the reparative activity was practically complete, the nodes in Group 1 at this time showing definite secondary nodules, dense masses of lymphocytes in the primary nodules, and fully differentiated medullary cords. In summary, exposure to the deuteron beam caused early and marked cellular necrosis in lymph nodes, with loss of cellularity, followed by active macrophagic removal of necrotic debris and ultimate restoration of the anatomic configuration.

c. Spleen. The changes noted in splenic tissue were on the whole similar to those observed in lymph nodes except that they appeared to be of longer duration, with recovery taking place less rapidly. Early cellular necrosis in both the red and white pulp was accompanied by a macrophage response with clearing of the necrotic debris. (Fig. X) There was distinct loss of cellularity at one and three days with reduction in volume of both the splenic follicles and the red pulp. The latter was markedly congested and contained many extravasated red cells (Fig XI) while the former had lost its outer sharp boundary of lymphocytes. Megakaryocytes also participated in this reduction, paralleling the decreased cellurity of the surrounding tissue. A considerable amount of hemosiderin was present in all parts of the spleen as early as 24 hours after exposure, and continuing in Group 1 to the 18th day. Repair proceeded slowly with restoration of the volume and cellularity of the splenic follicles and red pulp. Occasional foci of extra-medullary hematopoiesis were noted.

Discussion. The experiments here reported were undertaken preliminary to an investigation of the effect of the deuteron beam on transplantable malignant tumors. Necessary limitations on the use of the cyclotron for biological studies made it impossible to accumulate data sufficiently numerous for evaluation by statistical methods. However the changes observed so closely paralleled known effects of Roentgen radiation that the need for precise statistical analysis was largely obviated.

Previous workers have emphasized that radiant energy in any form exerts no discernible morphologic effect on circulating blood cells, and this has been found to be true also with respect to the deuteron beam. The toxic effects of radiant energy are localized on the immature cell forms at their site of origin in bone marrow or lymphoid tissue. The resulting structural alterations in these tissues are readily apparent on histologic examination, and the concomitant numerical change in the circulating cells of the peripheral blood is dramatically demonstrated by total and differential counts.

It was anticipated that the changes produced by the deuteron beam on the peripheral blood and hemopoietic organs of the white mouse would closely parallel the alterations known to occur following x-radiation. The experimental findings confirm this expectation. At all levels of exposure there was a prompt fall in the total white count, in the total number of neutrophiles, and in the total lymphocyte count, and a slightly delayed reduction in the platelet count. Bone marrow became hypoplastic, lymph nodes showed atrophy and loss of lymphocytes, spleens showed cellular depletion, focal necrosis and hemosiderin deposits. In animals that survived the two and a half week observation period there was gradual restitution to normal peripheral blood values, and a restoration of the hemopoietic tissues to morphologic normality. The changes were quantitatively proportional to the roentgen equivalent doses, animals receiving the highest dosage responding most severely. The degree of reaction, both in the peripheral blood and in the tissues, was essentially similar to the reaction reported by others following exposure to equivalent levels of x-radiation.

Summary.

1. White mice were exposed to a single whole body irradiation by the deuteron beam of the 184 inch cyclotron in doses equivalent to 460 r.e.p., 905 r.e.p. and 1800 r.e.p.

2. Studies of the peripheral blood showed a prompt and significant reduction in the total white count, and in the absolute number of neutrophiles and lymphocytes. A slightly delayed but marked reduction in platelets also occurred. Surviving animals which received the smallest exposure showed a return of these blood elements to normal levels by the 18th day.

3. Following exposure to the deuteron beam, severe aplasia was noted in bone marrow. Lymph nodes and spleen showed focal cellular necrosis, macrophage proliferation and loss of cellular constituents.

4. The blood and tissue changes after whole body exposure to the deuteron beam were proportional to the roentgen equivalent doses, and similar to the changes known to occur following x-radiation.

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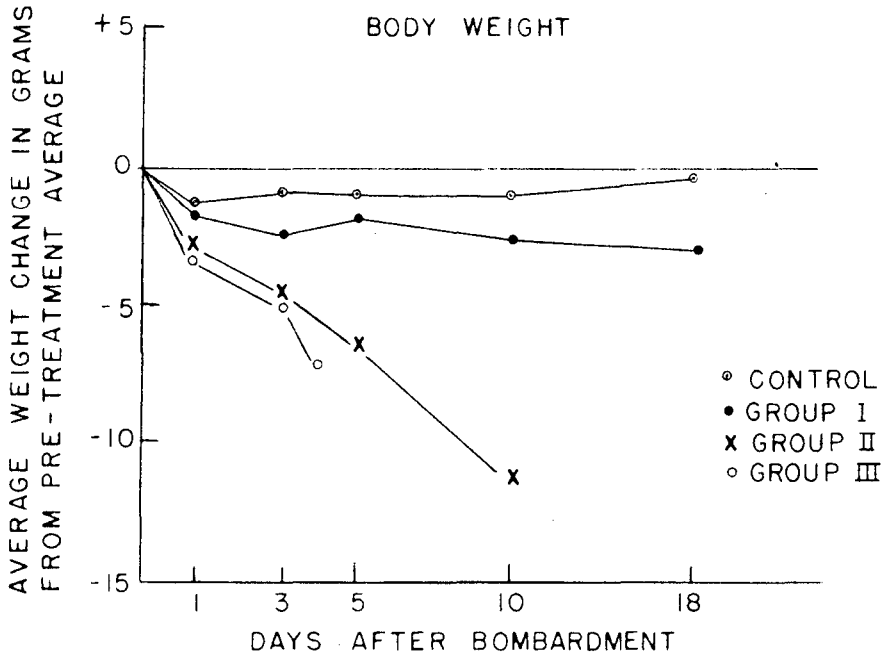

BODY WEIGHT
AVERAGE WEIGHT CHANGE IN GRAMS FROM PRE-TREATMENT AVERAGE
+5
0
-5
-10
-15
1
3
5
10
18
DAYS AFTER BOMBARDMENT
CONTROL
GROUP I
GROUP II
GROUP III

FIG. 1

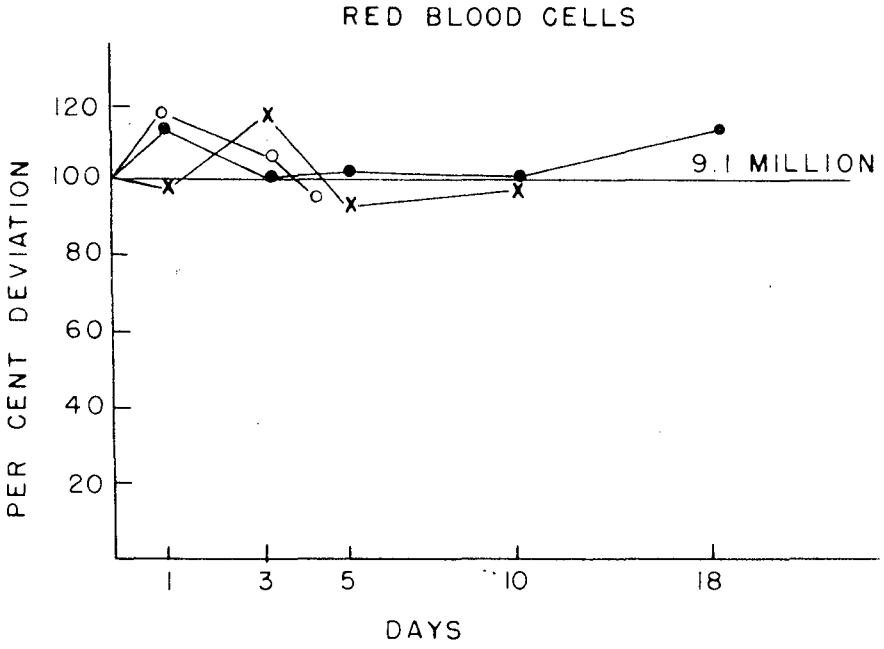

RED BLOOD CELLS
PER CENT DEVIATION
120
100
80
60
40
20
9.1 MILLION
1
3
5
10
18
DAYS

FIG. 2

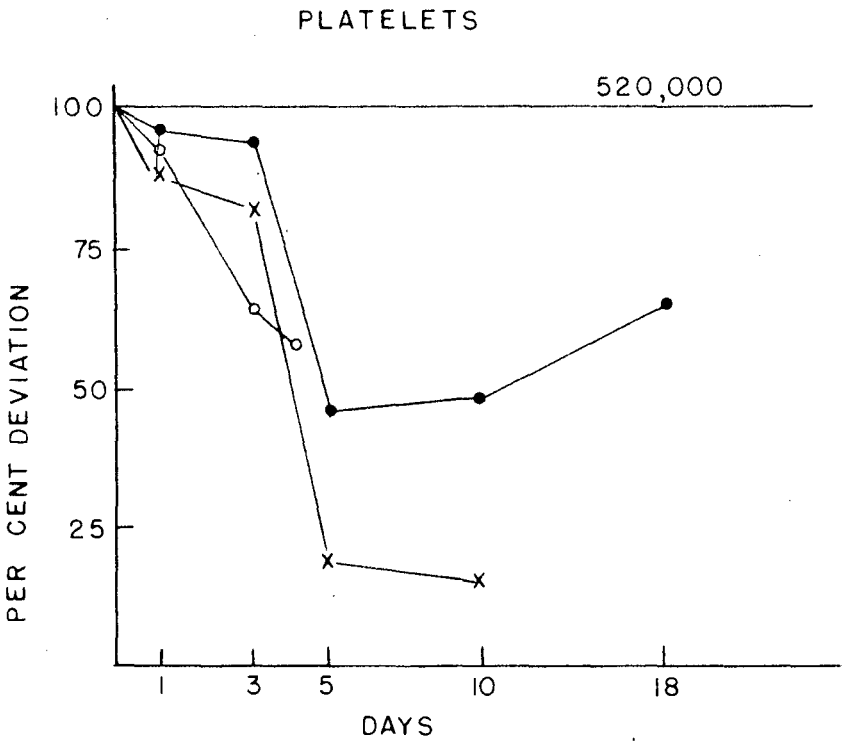

PLATELETS
520,000
100
75
50
25
PER CENT DEVIATION
1
3
5
10
18
DAYS

FIG. 3

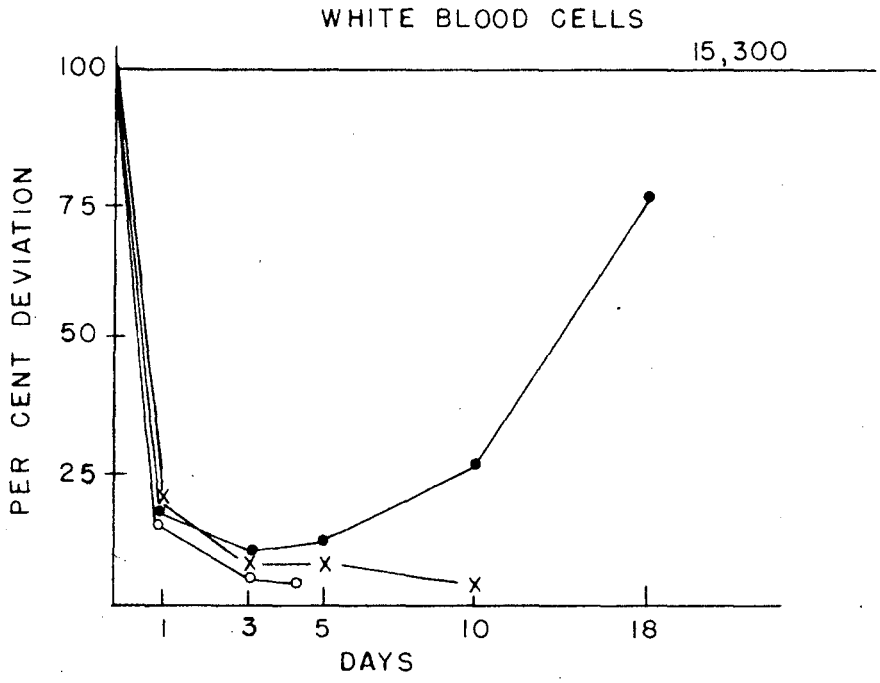

WHITE BLOOD CELLS
15,300
100
75
50
25
PER CENT DEVIATION
1
3
5
10
18
DAYS

FIG. 4

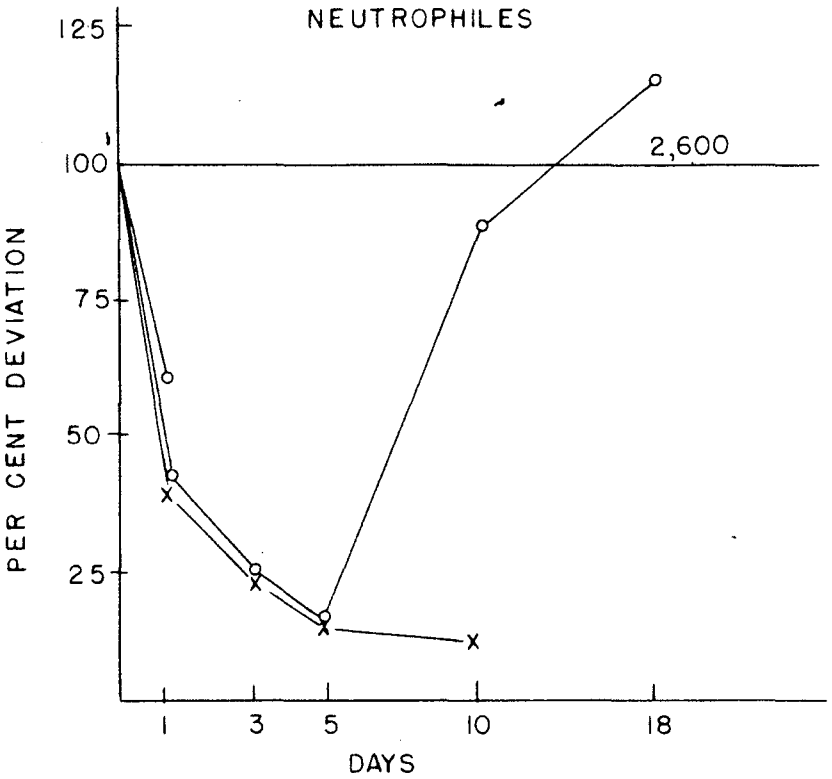

NEUTROPHILES
125
100
75
50
25
PER CENT DEVIATION
2,600
1
3
5
10
18
DAYS

FIG. 5

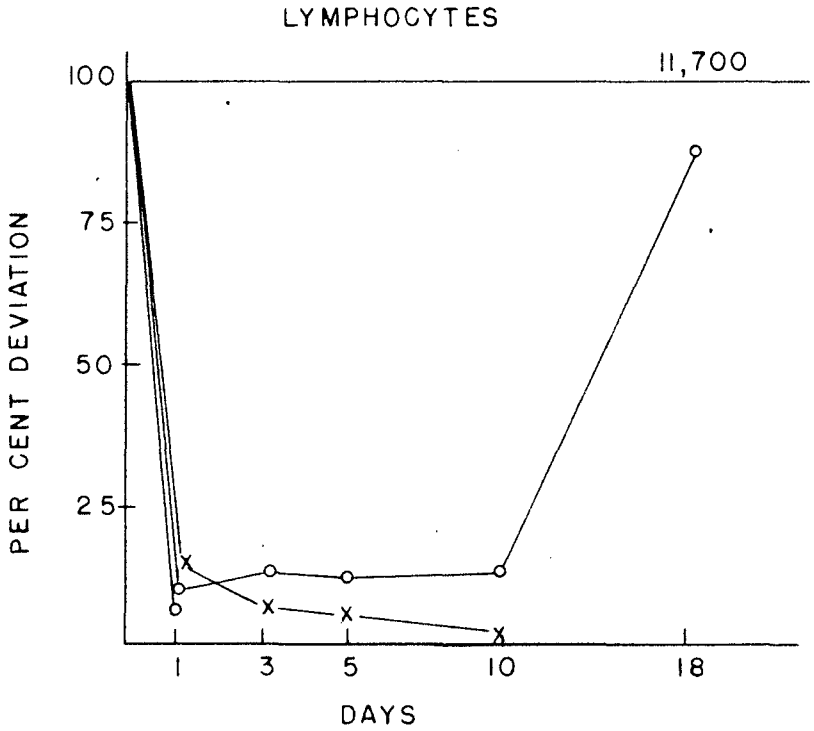

LYMPHOCYTES
100
75
50
25
PER CENT DEVIATION
11,700
1
3
5
10
18
DAYS

FIG. 6

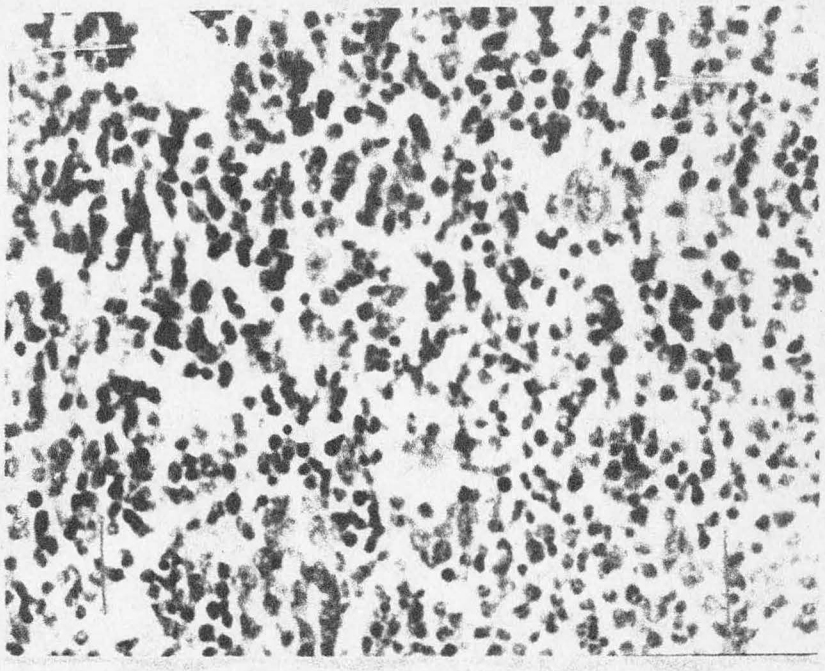


FIG. I - Normal Bone Marrow (X550).

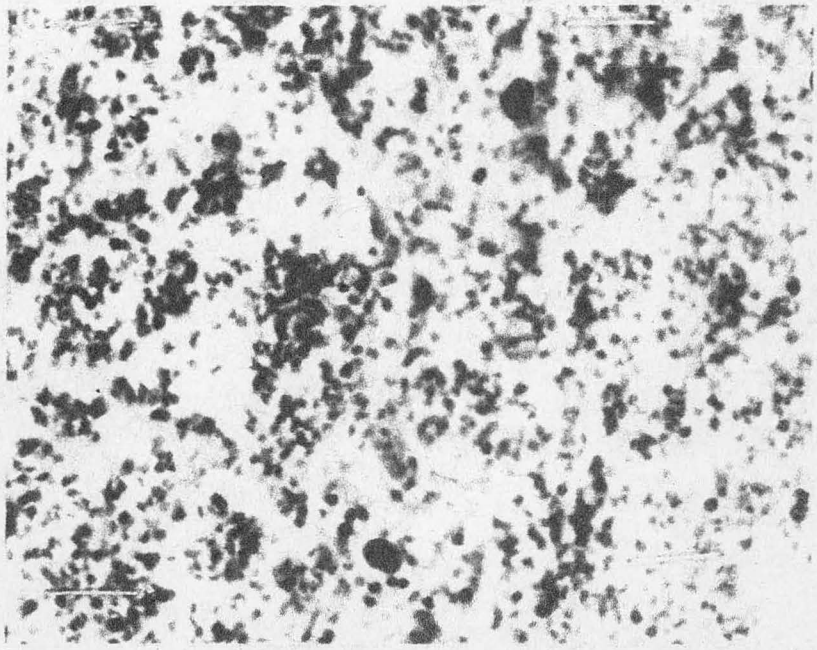


FIG. II - Bone Marrow Shows a Noticeable Depletion of Cellular Elements (X550).

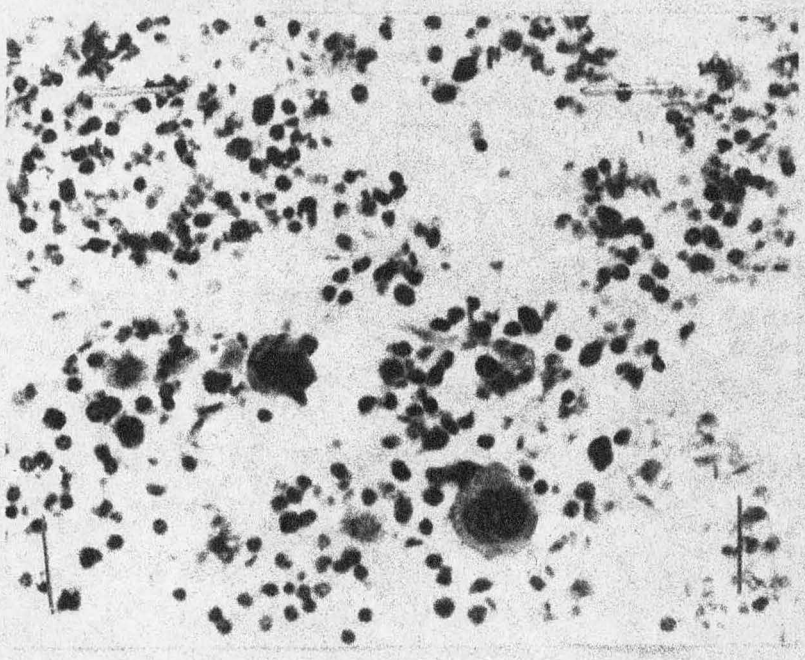


FIG. III - Bone Marrow Shows Depletion of Cellular Elements with Scattered Megakaryotes (X550).

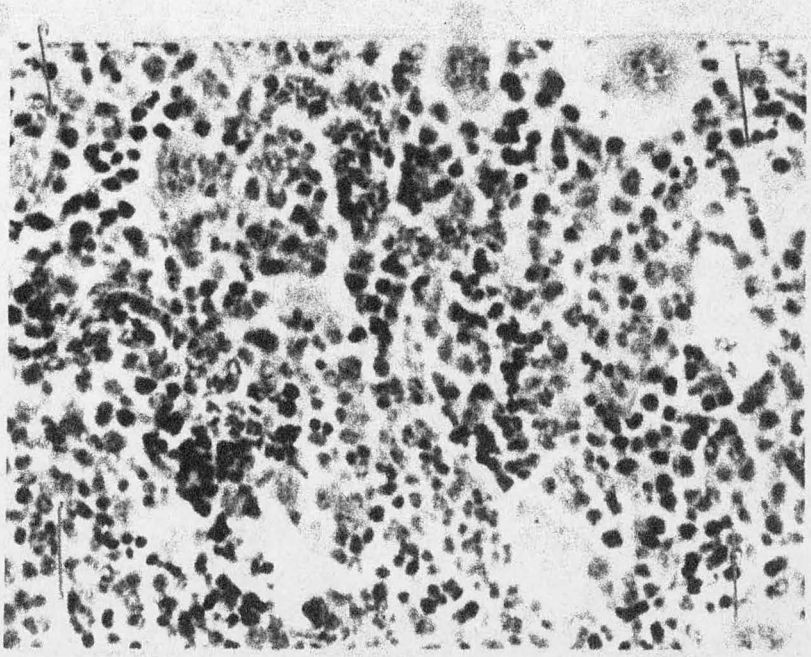


FIG. IV - Regeneration of Bone Marrow 10 Days After Bombardment (X550)

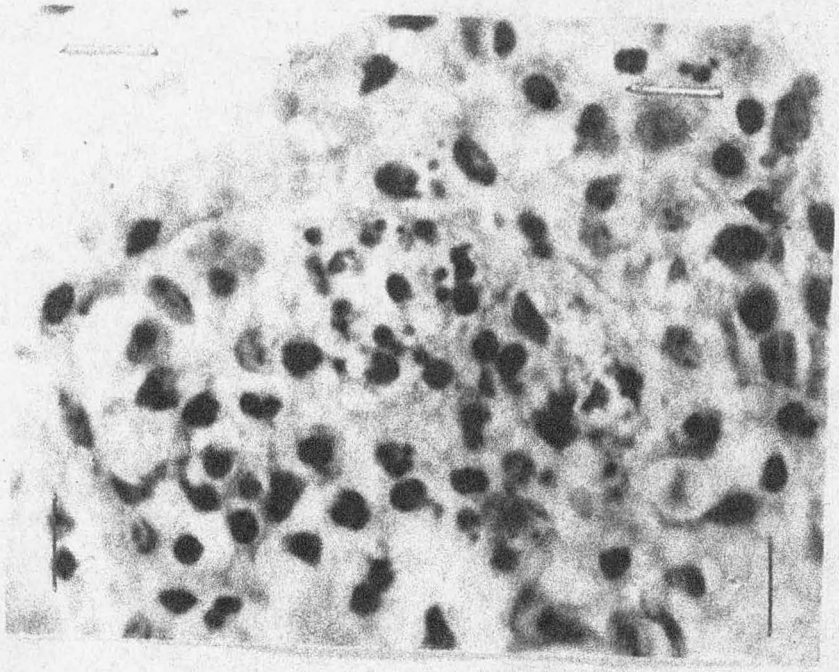


FIG. V - Lymphnode 24 Hrs. After Bombardment Shows Nuclear Pyknosis and Fragmentation (X1200).

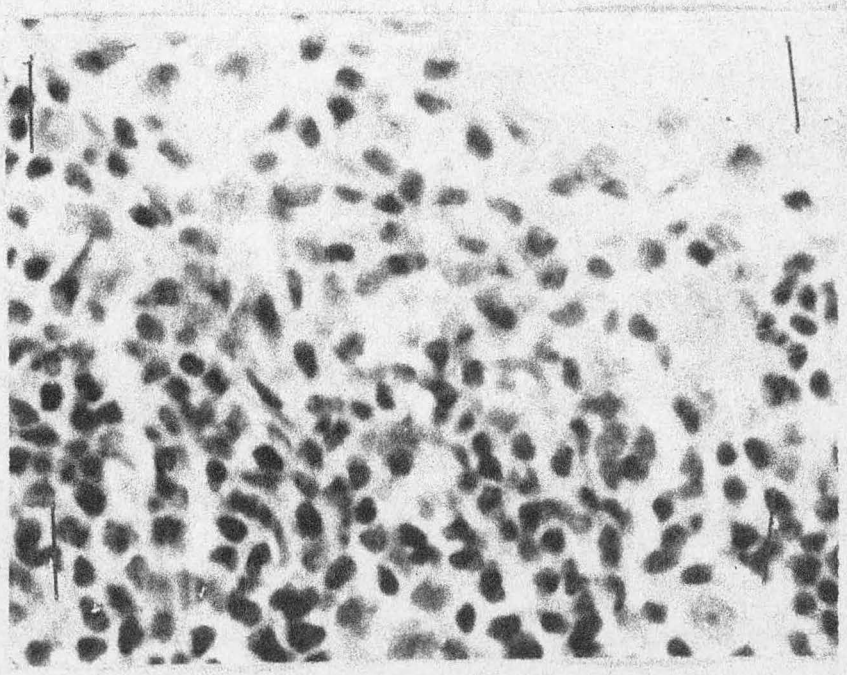


FIG. VI - Normal Lymphnode (X1200).

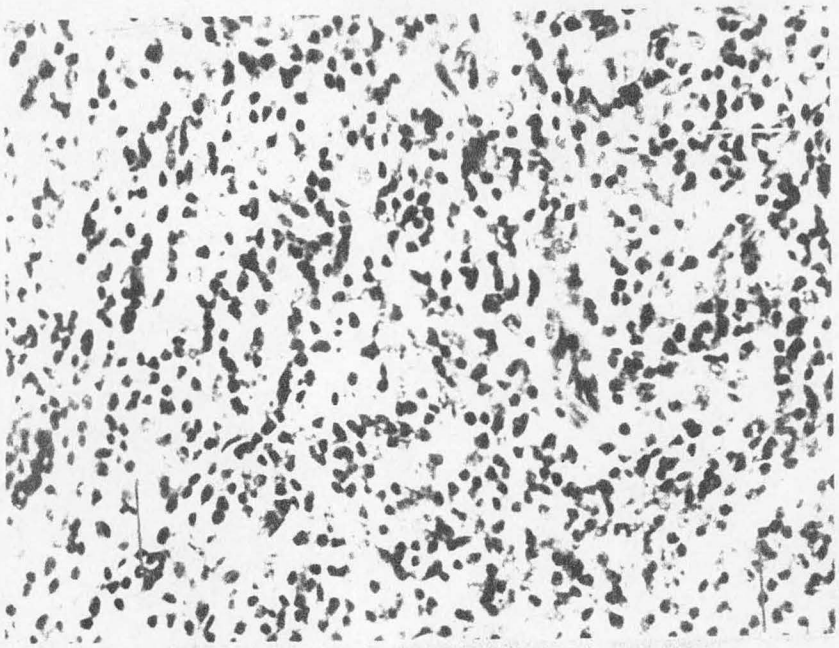


FIG. VII - In the Lymphnode the Lymphocytes Were Reduced and there was Evidence of Phogocytoses by Macrophages (X550).

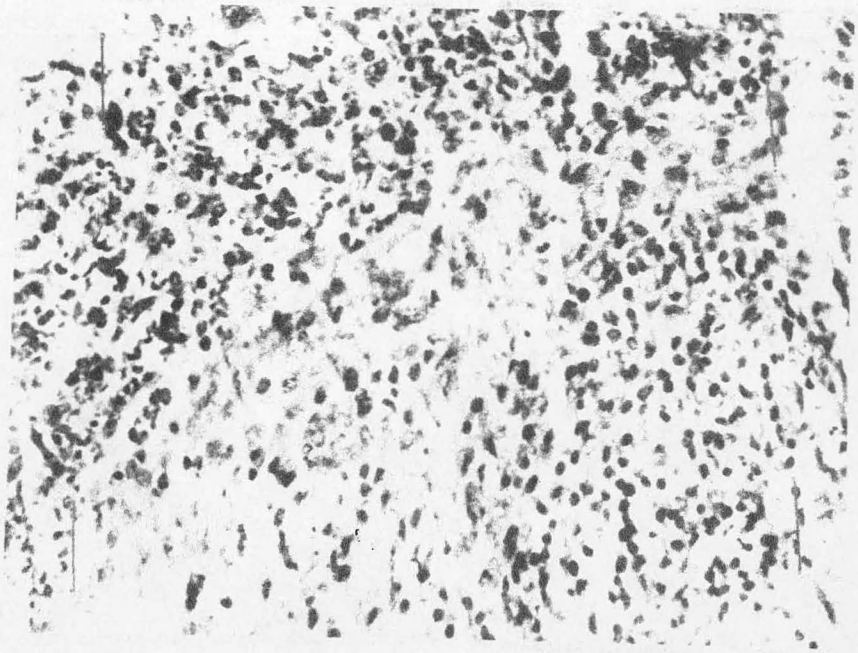


FIG. VIII - Regenerative Processes in the Lymphnode With the Clearance of Some of the Cellular Debri (X550).

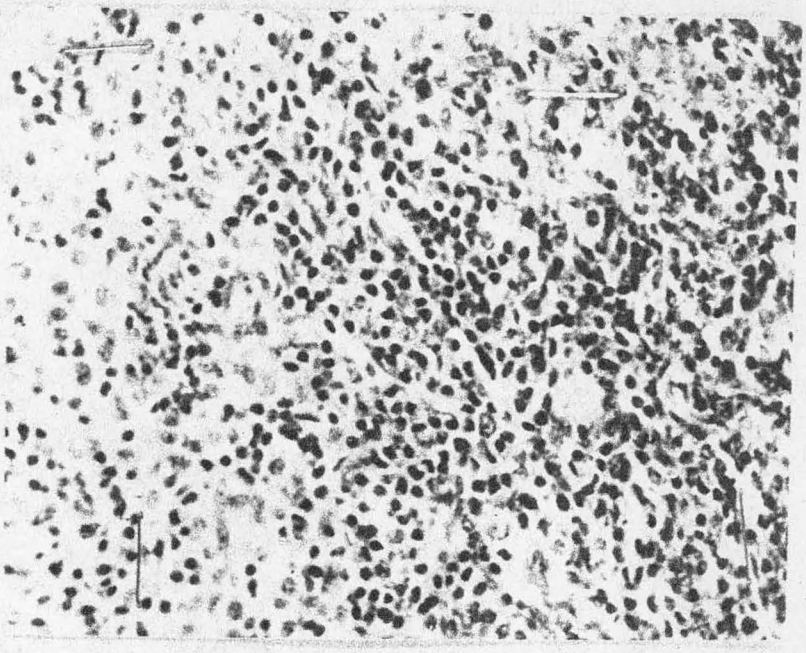


FIG. IX - Normal Spleen (X550).

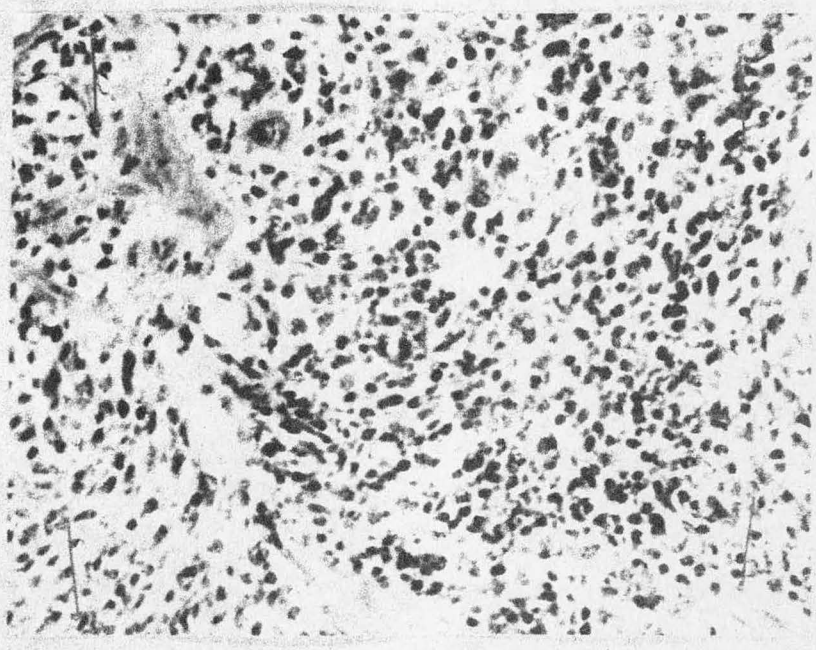


FIG. X - Spleen with Early Cellular Necrosis in the Red and White Pulp (X550).

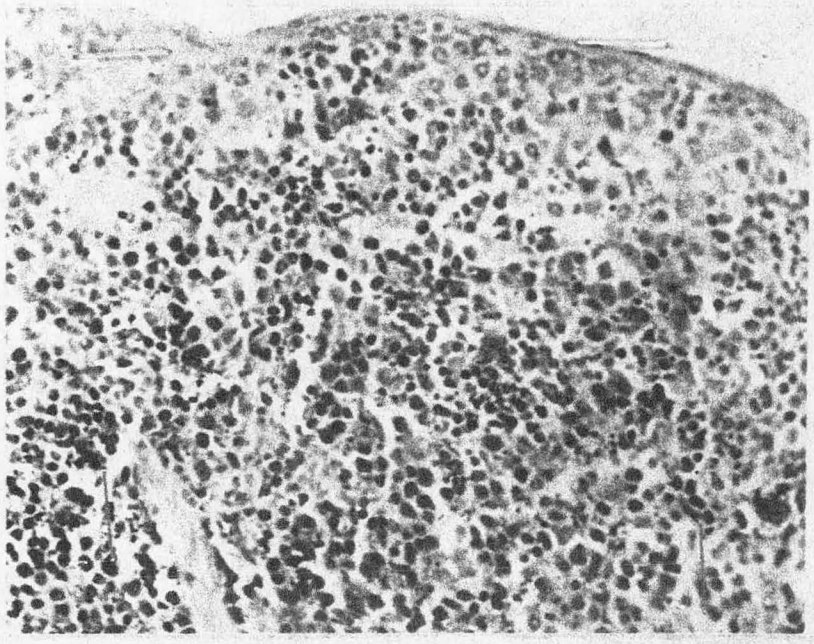


FIG. XI - Congestion and Extravasation of Red Blood Cells in the Pulp and with Cellular Necrosis (X550).

III BIOLOGICAL EFFECTS OF RADIATION FROM EXTERNAL AND INTERNAL SOURCES

Robert S. Stone - in charge

Project 48C

University of California Medical School

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

Earl R. Miller, M.D.

An attempt was made to gather data on the accuracy of the determination of the amount of I^{131} in the thyroid gland of patients by the method of comparing the gamma ray output of a known standard of radioiodine sealed in a rubber capped 33 cc serum bottle with the gamma ray output from the thyroid of a patient. Patients who were to undergo surgery were given a test dose of radio-active iodine a few days before surgery. An in vivo measurement was made immediately before operation. The patient then went to surgery and the tissue removed was immediately weighed. The amount of tissue remaining in the neck after surgery was estimated by the surgeons. The activity of the tissues removed at operation was measured to determine the amount of I^{131} in it, again by comparison with that of the known standard of I^{131}. In each case it was assumed that there was a grossly homogeneous distribution of iodine between that which was removed at surgery and that which remained in the neck after surgery.

The amount of activity found by the postoperative measurements is expressed as a percent of that found by the pre-operative in vivo measurements.

I^{131} in Thyroids

Postoperative Determination as a Percent of Preoperative Determination

Disease	No. of Pts.	Average %	Range % Min.	Range % Max.
Carcinoma	8	94.4	48.6	149.3
Graves	5	69.9	14.1	103.2
Nodular	6	88.2	43.6	115.4
Thyroiditis	9	101.7	80	116.3

The closest agreement of measurement was obtained by this method in the patients with thyroiditis. In these there was a grossly homogeneous distribution of the iodine even though microscopically the distribution was quite inhomogeneous. In the thyroids of patients with Graves disease the distribution of iodine was also found to be grossly homogeneous but the pre and postoperative measurements on the patients with this disease were not nearly so close. In the thyroids of patients with carcinomata and non-toxic nodular goiters, the inhomogeneity is so great that it was to be expected that the results would be far from perfect.

This method is being tried to check the accuracy of the measurements that are taken on patients in vivo. It would appear that much more accuracy is necessary than has been achieved thus far. The sources of error lie, in the preoperative estimation of the amount of iodine in the thyroid due to the varying amount of tissue overlying the thyroid, the effect of size of thyroid upon the accuracy of the determination and other factors, in the loss of iodine through trauma in surgery, in the inaccuracy of the estimation of the residual thyroid postoperatively and in the lack of homogeneous distribution of the iodine. Further work is necessary on patients in whom a relatively homogeneous distribution of iodine can be expected. These will include particularly patients with Graves disease and thyroiditis. We are reporting these results because they are what we have obtained. We believe that greater correlation should be achieved and that this method is worth pursuing in order to give a check of the accuracy of the methods of measurement.

Studies with a Freon filled ionization chamber as an instrument for determining uptake in the thyroid have been pursued for three months and the results compared with the determinations by Geiger counter measurements. Reliable results have not yet been achieved. Study of this method will be continued.

IV HEALTH CHEMISTRY AND PHYSICS

Health Chemistry

N. B. Garden

Monitoring. As of the end of the year many procedures have assumed a routine form and the duties of the monitoring group have become quite well defined. Since the equipment and processes for working with radioactive chemicals is now taking some semblance of standardization, the monitoring duties also are becoming standarized. These have been rather carefully tabulated in detail and from this similar procedures are being set up in the University of California under the supervision of the monitoring section. This is assumed to be a temporary arrangement but furnishes an excellent opportunity of instituting cooperative measures for radioactive protection in Berkeley, since there will always be overlapping of areas and problems between the University and the Radiation Laboratory.

The previously agreed-to provision of having no radioactive materials in Lewis Hall was broken because the x-ray diffraction equipment was moved into the building and makes it highly desirable to take occasional active samples there for analysis. Special precautionary measures have been set up and it is believed no contamination can occur if these are followed.

The monitoring of cyclotron targets and the ensuing protective measures are becoming more difficult as the experiments have been concentrating on short-lived radioactive isotopes. To deal with these no cooling-off period can be permitted and the targets are extremely active.

Transportation, Disposal, Storage and Salvage. The work with the short-lived isotopes has made the transportation problem particularly difficult, as time must be saved at every point. A "jiffy" probe was developed and the truck delivery speeded to the limit. A pneumatic tube connection between the 184 inch cyclotron and Building 5 has been investigated and seems entirely practical. For additional speed in processing targets an equipped gloved box has been mounted on a dolly and can be placed adjacent to the point where the target can be introduced immediately at the conclusion of a bombardment.

Little decontamination work has been carried on as no enclosed space is available and the inclement weather prevents continued work outside which was done during the summer.

Research and Development. The three larger problems on hand were completed during this quarter--the gloved box for Dr. Gofman, the interceptor for highly active bombardments in the cyclotron, and the controlled atmosphere arc stand for Dr. Conway's spectrum analysis of radioisotopes.

Additional progress has been made in improving manipulators, developing a lead glass window of 4" thickness without laminations, shielding syringes, and filter designs.

During this quarter considerable time was devoted to showing visitors the installations and special equipment. These visitors numbered more than 70.

It is clear that in all regularly inhabited areas the radiation level is below tolerance by at least an order of magnitude, even if one adopts .010 r/day as a conservative tolerance figure. It is also evident that the first thing to do in improving further the shielding is to increase the thickness of the concrete roof. Roof slabs are now at hand to provide a 4 ft. roof rather than the present 2 ft. of concrete. The vertical walls are 10 ft. thick.

At the very end of the period of this quarterly report the cyclotron was brought into operation on 350 mev protons. Preliminary surveys show greater variation in radiation intensities than with deuterons as might be expected from the higher energy of the primary neutrons. The 4 ft. roof has markedly decreased the proportion of radiation due to diffusion through the roof and subsequent downward scattering.

Slow Neutron Survey of Crocker Laboratory: A slow neutron survey of the 60 inch cyclotron building was performed under conditions of (1) 2 microampere alpha beam on Ag target (2) 11 microampere deuteron beam on Na target. Maps of flux densities were prepared. In the case of the alpha beam the largest flux found was 520 per cm^2 per sec just outside the east door of the shielding. In the case of the deuteron beam it could not be read at this position with this instrument, showing that it was much more than 1000 per cm^2 per sec.

In the inhabited areas all fluxes were well below tolerance, ranging up to a few hundred for the deuteron beam, and up to 60 for the alpha beam.

Statistical Summary of Monitoring Program.

A. Survey Instruments Maintained.

1.	B-V Ionization chambers	28
2.	Victoreen 263 meters	19
3.	I.D.L. portable survey meters	6
4.	Cutie Pies	2
5.	Recording V-intensity meters	10
6.	Victoreen Proteximeters	3
7.	Fast neutron prop. etc.	1
8.	Balanced chamber slow neutron survey inst.	1
9.	Special tissue-wall (approx.) survey inst.	1

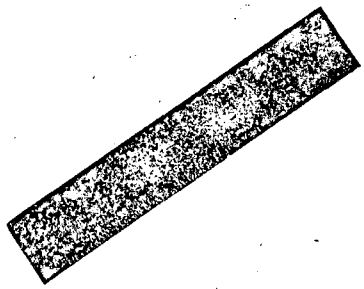
B. Personnel meters in use

1.	Number of people covered with film badges	872
2.	Total man days coverage with pocket chambers	1,953
3.	Total man days coverage with pocket dosimeters	3,513
4.	Total man days coverage with pocket chambers, s.n.	1,869

C. Cases of above weekly tolerance dosage

1.	184 inch area	6*
2.	Linear accelerator area	0
3.	60 inch area	0

* These people are chemists and received their exposures working on radioactive samples. The exposures are respectively as follows:

1.6 x weekly tolerance dose
1.65 x weekly tolerance dose
3.85 x weekly tolerance dose
1.8 x weekly tolerance dose
1.07 x weekly tolerance dose
7.3 x weekly tolerance dose

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Information Division