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REPORT FOR MONTH ENDING OCTOBER 23, 1943

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Human Subjects Project

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REPORT FOR MONTH ENDING OCTOBER 23, 1943

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A. BIOLOGICAL RESEARCH SECTION

K. S. Cole, Section Chief

Report for four weeks ending October 23, 1943

Abstract

The Biological Research Section is continuing to build up background on the effects of radiations and to develop procedures for chemical separations and for animal experiments against the day when F.P. are available in quantity. A report is presented on the present status of the blood changes following x-ray and n exposures. Experiments on the diffusion of Xe from X_3O_8 indicate that the release during bombardment at Clinton should be more than 25 percent of the requirements.

1. Xenon Research - R. Abrams

Animal exposures. An exposure of a guinea pig to Xe^{127} which previously had been reported as in progress has been terminated. The animal was kept for 43 days in an Xe atmosphere. The Xe concentration was 280 μ C/li at the beginning and decayed down to 81.2 μC/li at the end. Thus the bottle half-life was 24 days as compared to the normal decay of 34 days.

The β radiation dose to the walls of one of the large bronchi was calculated using the following expression (after Failla):

$$\text{Dose} = \frac{3.7 \times 10^{10} \times 86400}{1.6 \times 10^{12}} \quad \frac{CE}{\lambda W} \quad \left(\frac{V}{ARD} + \frac{V_L}{M_L} + F\right) \quad (1 - e^{-\lambda t}) \text{ roentgens}$$

C = Xenon concentration (curies/cc). E = Average beta energy = 0.24 x 10^6 x 0.3 ev. λ = Decay const. (days) = $\frac{.693}{24}$. W = Energy required to produce 1 ion pt. = 33 ev. V = Volume of bronchus (cc). A = Surface area of bronchus (cm^2). R = Range of beta in tissue (cm). D = Density of tissue (gm/cm^3). V_L = Total air volume of lungs (cm^3). M_L = Total weight of lung (gm). F = Distribution coefficient for Xe between air and tissue. t = Time of exposure (days).

This gives total dose of 290 r. The dose rate ranged from 12.7 r/day at the beginning to 2.8 r/day at the end. Grossly, the animal was normal at the end of the experiment. It had gained 96 gm in weight and its blood picture was normal. As yet no report is available on the microscopic observation of the lungs.

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Chamber development. The work begun last month on the design and construction of 1 cu. ft. and 6 cu. ft. exposure chambers has been continued. Except for pump design which has not been frozen, all the equipment is in the process of being assembled or built. Some time has been spent on the development of a flow meter involving the cooling effect of a stream of air on a hot filament. The work will be described in detail after assembly is complete and preliminary tests have been run. It is expected that the chambers will be in operating order before active material becomes available from X.

Adsorption. This work has been cut short this month as a result of a shortage of active Xe as well as lack of manpower. An experimental line has been set up so that with the Xe that has become available from the exposure experiment adsorption experiments can be continued with active carbon and started with silica gel.

A small portable adsorption train consisting of an empty trap followed by a carbon trap (both in CO_2 - ether) has been tested and found adequate for recovering Xe from exposure chambers.

Production. Some time has been spent in carrying out experiments on the diffusion of Xe out of X_3O_8. This is being done to determine whether or not it will be feasible to prepare Xe at Clinton by packing X_3O_8 into the pile and passing air thru to wash out the Xe.

Our experimental set-up was as indicated in Fig. 1a. 20 gm of X_3O_8 which had received a neutron bombardment at the cyclotron (100 μA hours with good geometry) was placed in tube A which was then evacuated down to an air pressure of 10 cm Hg. The temperature was controlled by furnace, B. Periodically the gas in A was pulled into the Toepler pump C and transferred to the thin mica window gas holder D. This was then counted with an end-on mica window counter tube.

At the end of the experiment, the Xe remaining in the X_3O_8 was released by dissolving in nitric acid. The apparatus is shown in Fig. 1-b. The X_3O_8 is placed in flask A which is then evacuated. 50 cc conc. HNO_3 is added thru funnel B. The mixture is boiled until solution is complete, and the gases evolved are collected in tube C over 10% KOH. Finally, water is poured in thru B to displace all the gas into C. The mica window gas holder, D, is evacuated, and the gas from C allowed to enter. Total gas volume is recorded as well as the volume of the gas holder, D. Our most representative data are shown in Fig. 2. This was obtained on a sample of X_3O_8 which was old enough so that gases other than Xe^{133} had completely decayed (including I^{133}). The curves indicate that an initial instantaneous evolution occurs followed by a very slow evolution. The instantaneous evolution is an exponential function of temperature and may be described by the empirical equation:

$$\alpha = 10.49 \times 10^{.00253T}$$

α = fraction of Xe which diffuses out instantaneously

T = temperature in °C.

The obvious interpretation is that the Xe in the surface layers diffuses out rapidly while that deep within the particle of oxide comes out at a slow rate. For the case of a continuous bombardment one can say that the amount diffusing out instantaneously is α times the rate of formation. Then for equilibrium,

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$$P = \frac{\alpha\lambda + \beta}{1 - \alpha} Q$$

P = Release of Xe from X_3O_8 $\left(\frac{\text{curies}}{\text{Kw. Kg. day}}\right)$. Q = Xe present in the X_3O_8 at equilibrium $\left(\frac{\text{curies}}{\text{Kw. Kg.}}\right)$. α = fraction of Xe which diffuses out instantaneously. λ = Decay constant. β = Fraction of total Xe which diffuses out of X_3O_8 per day.

At 485° C. α = .017, β = .005 day^{-1}, λ = .13 day^{-1}, Q = 10^{-3} curies/Kw-Kg. at X

For a column of X_3O_8, 10 cm in diameter and 4 meters long, one finds 132 kg. X (assuming density = 5 gm/cm^3). Then for X at 1000 Kw. one finds

$$P = .0077\ (10^{-3})\ (132)\ (10^3) = 1.0\ \frac{\text{curie}}{\text{day}}$$

Experiments are in progress to further verify the present results, to check the diffusion of I^{135}, and to seek methods of increasing the yield which is at present too low to be safe - by about a factor of four.

2. Dust Exposure - W. Lohr

Two experiments with radioactive dust have been carried out during the past month. In one, X_3O_8 containing F.P. was used. The dust content of the air was roughly 0.25 mg./li. The animals are being sacrificed periodically to check lung retention as well as to look for kidney damage due to X poisoning. A second dusting was carried out with LaF_3 containing F.P. This is a test run to determine the chemical toxicity of the fluoride as well as solubility in body fluids. These will be discussed in detail when completed.

Microscopic equipment has been obtained, and some time has been spent in developing dust counting and size-estimation technics.

3. Physiological and Anatomical Data on Laboratory Animals - E. Painter

The data in Table I have been collected with three purposes in mind: (1) to obtain information necessary for the design of exposure chambers; (2) to be able to calculate gas and dust dosages; and (3) to test lung sensitivity as a function of geometry so that animal experiments may be extrapolated to man. The table is preliminary and will be enlarged. Letters in the table refer to following references:

(L) Loosli, Robertson, and Puck, J. Infec. Dis. 72, 142 (1943)
(B) Bancroft, J. Hyg. 31, 1 (1931)
(D_1) Donaldson, "The Rat", (1924)
(A_1) Adolph, "Physiological Regulations" (1943)
(D_2) Dickson, Univ. Toronto Collect. 1924 - Effect of Insulin on Respiratory Exchange
(A_2) Aeby, "Der Bronchialbaum der Säugethiere und des Menschen" (1880)
(W) Went and Drinker, Am. J. Physiol. 88, 468 (1929)

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TABLE I

Animal	Mouse (15 gm)	Rat (20 gm)	Guinea Pig (350 gm)	Rabbit (3.0 Kg)
Daily Water Intake (cm^3)	6	30	50	300
Daily urine output (cm^3)	4	20 (D_1)	35	250
Daily Ammonia production (gm)		0.01 (D_1)		0.07
Blood Volume (Per cent body weight)		6.0 (D_1)	6.5 (W)	5.5 (A_1)
Lung Weight (Per cent body weight)		0.6 (D_1)	0.9	
Lung Volume (cm^3)			10	
Ventilation (cm^3/min.)	20 (L) (B)	300 (B)	310 (B)	1600 (B_2)
Respiratory Rate/min.	200-300	80-90	90-120	40
Tidal Air (cm^3)	0.06-0.1	3.9	3.5	37.5
Trachea-Length (cm)		3.02	5.08	
Trachea-Diameter (upper) (cm)		.115-.082	.234	
Trachea-Diameter (lower) (cm)		.107-.097	.195	
Right Bronchus-Length (cm)	.556	.72	.357	.6 (A_2)
Right Bronchus-Diameter (upper) (cm)	.048		.12 - .08	.8 - .72
Right Bronchus-Diameter (lower) (cm)				
Left Bronchus-Length (cm)		.675	.278	.798 (A_2)
Left Bronchus-Diam. (upper) (cm)		.074-.055	.156 - .12	.70
Left Bronchus-Diam. (lower) (cm)				

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4. Comparative Effects of Fast Neutrons and X-rays - C. W. Hagen, Jr.

Rabbits. A number of animals have been irradiated in an effort to establish the x-ray survival curve for rabbits. Since added data have caused a shift in the survival curve since the last report, a copy of this curve is appended, Fig. 3. The 50% dose appears to be near 825 r, as measured in air at the position of the center of the animal. Determination of correction factors for the actual dose at different portions of the rabbits body have been limited to development of technique.

Three rabbits have been exposed to neutron doses higher than have been previously obtained. Two that received 129 n died within 12 days, while one that received 138 n has survived for 28 days. An estimate, based on complete survival at 105 n and fractional survival at 130 n, places the x/n ratio between 5.5 and 7.

A group of twelve animals have been irradiated at 300 r to extend our information on blood changes after x-irradiation. Similar groups will be irradiated at lower dose levels. Comparisons of x-ray and neutron effects on while blood cell, neutrophile, and lymphocyte counts have been extended in collaboration with Dr. Jacobson.

The radiobiology and hematology groups have cooperated in an effort to determine the blood changes occurring within the first 48 hours after x-irradiation. The first of a series of experiments designed to test these effects is nearing completion.

Rabbits have been irradiated for Mr. Murray and Dr. Bloom, at 400 r and at 800 r. These are to be killed at intervals for histological study. This is a pilot experiment designed to determine the relative severity and the time of appearance of injury to selected tissues at various x-ray dose levels.

Mice. Bar Harbor mice have been received in limited numbers during the past month and larger shipments are promised. Since the demand has greatly exceeded the supply, mice have not been used extensively for general irradiation.

5. X-ray Studies on Various Animals - C. W. Hagen, Jr.

Rats. A considerable number of rats have now been treated and it is possible to draw a tentative x-ray survival curve on the basis of survival for fifteen days, Fig. 4. This period is not long enough to provide an accurate measure of the mortality at the lower dose levels, so the 50% dose will probably be somewhat lower than is shown on the curve, or between 600 r and 700 r.

Guinea Pigs. About 100 guinea pigs have been irradiated with variable results. The survival data for animals treated over 25 days ago are as follows:

Dose (r)	Number of Guinea Pigs	Number of Survivors
200	20	10
300	24	11
400	24	7
500	14	6
600	6	2

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These data indicate a rather flat survival curve or a plateau over the dose range tested. Guinea pigs have been treated in lots of four or six. The results for any particular lot may vary considerably from any other lot at the same dose level. At 300 r, for example, results varied from 100% mortality to 100% survival. This variability is not obviously correlated with sex of the animals, data of receipt, or date of treatment. One factor contributing to the peculiar shape of the curve may be the length of time that guinea pigs will survive before succumbing to the treatment. The longest survival at present is twenty-nine days after 200 r.

Chicks. Chicks have been irradiated with 800 r and 1200 r of x-rays for histological and hematological study. The birds not used in this study were exposed to 800 r for data on the lethal dose. Of twelve birds treated, two have survived for twenty-six days.

Salamanders. Work with Amphiuma has been discontinued in favor of a form that is more easily handled and more readily available. The first shipment of the common newt (Triturus viridescens) has just been received and has not yet been treated.

6. Radiobiology of Goldfish - C. W. Hagen, Jr.

Lethal Action of Graded Single X-ray Doses. To more rigidly define the x-ray survival curve, lots of 15 goldfish each have been given doses of 0, 400, 700, and 1050 r. It is too early to report the results of this experiment.

Action of Divided Doses of X-rays. Lots of 15 goldfish each (the 50 r group consisted of 20 fish) have been given daily of 0, 12.5, 25, 50, and 100 r. These fish have received forty doses between September 6 and October 18. The experiment is not complete, and the handling incident to the treatment has resulted in rather high loss of the controls. Sharp changes in slope of the survival curves are observed and probably indicate the point at which the treatments became effective.

Effects of Low Intensity Gamma Irradiation. Groups of ten fish each have been exposed to 0, 10, and 23.5 r/day of gamma rays as measured with a Victoreen r-meter immersed in Gooch tubing in the culture water.

In this experiment a test-tube containing a mixture of long-life F.P. (residue of an extraction of a S.L. run) was shielded with 1/8" of lead and inserted into a small Florence flask. A cylinder of galvanized iron wire mesh with ca. 6" diameter was fixed in position around the flask. The whole was immersed in water in a five gallon battery jar. Fish were confined within the wire mesh and held at a more or less uniform distance from the active mixture by the walls of the flask. The three jars so prepared differed only in the amount of active material used.

No deaths were recorded in the experimental jars for fifty-three days. At the end of this period the culture water had become cloudy and within ten days, six of the fish exposed to the stronger source and three of the controls had died. The water was changed at this time and no more fish have been lost in the strong source or in the control. After 68 days the water in the jar containing the weak source again became turbid and nine of the ten fish were lost within 8 days.

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The deaths in this series are not considered due to irradiation for several reasons.

(1.) All deaths in experimental jars occurred during a period in which the water had obviously become fouled.

(2.) Some of the dead fish exhibited an emaciated appearance characteristic of certain bacterial diseases of fish and not generally associated with x-irradiation.

(3.) The loss of fish exposed to the strong source stopped shortly after change of the culture water.

(4.) Four of the ten fish exposed to the stronger source have survived eighty-one days of treatment, while only one of the ten fish exposed to the weaker source has survived for the same period.

(5.) When only one of the three jars fouled, deaths occurred only in the fouled jar, in spite of the fact that it contained the weaker source.

Chemical Toxicity of Anticipated F.P. Carriers. An experiment designed to test the toxicity of UNH is in progress. In this experiment, seven fish were placed in two liters of the solutions indicated below. Each concentration except the lowest was duplicated. Concentrations of 10^{-3}, 10^{-4}, and 10^{-5} parts by weight of UNH killed all of the exposed fish within twenty-four hours. Concentrations of 10^{-6}, 10^{-7}, and 10^{-8} have not differed from the controls.

7. Comparative Effects of Fast Neutrons and X-rays on Blood. L. O. Jacobson and R. E. Zirkle

Rabbits. In cooperation with Dr. Zirkle's program of determining x/n lethal ratios, blood studies were simultaneously made in an attempt to determine the relative effectiveness of these two radiations upon certain cellular constituents of the peripheral blood. The following constituents of the blood have been studied:

Hemoglobin
Erythroctyes
Total leucocytes
Platelets
Reticulocytes
Differential blood picture (Wrights stain - 300 to 500 cells)

Although definite change is noted in all of these with the doses of x-ray and fast neutrons employed, only the data on total leucocyte count, total lymphocytes, and total polymorphonuclear cells is presented graphically in this preliminary report. Further, the data on certain doses of x-ray and fast neutrons only are presented because they represent the dosages where statistically significant numbers of animals have been studied.

Graph II, Parts 1, 2, 3, represents data on the effect of fast neutrons on the total leucocytes per mm^3 as well as certain constituents of the leucocyte picture.

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Graph I, Parts, 1, 2, 3, represents a similar study with varying doses of x-ray.

Graphs IV, Parts 1, 2, 3, represents x/n ratios for the total leukocytes per mm^3, absolute polys, and absolute lymphocytes at an arbitrarily chosen hour (80 hours) after the various irradiations.

Graph III, Parts 1, 2, 3, represents a study of the total WBC/mm^3, absolute polys, and absolute lymphocytes expressed in terms of percent of the controls at intervals of 1 to 4 hours for a period of 48 hours after 500 Roentgens of total body irradiations.

Graph II, Part 1 - Total Leukocytes-Fast Neutrons: Except with a dose of 26 n, a slight drop in the total leukocyte count has occurred at 3 hours; at 24 hours a further slight decrease is apparent except with higher doses of 105 n and 90 n. At 48 hours the total leukocyte count has fallen precipitously with all doses, and it reaches the lowest point at 72 hours. Thereafter a very slow increase occurs up until 250 hours and then a more rapid increase in the direction of normal. The degree of depression varies inversely with the dose (See also Graph IV, Part 1).

Graph II, Part 2 - Absolute Polymorphonuclear Heterophiles: At 3 hours the total polymorphonuclear heterophiles have risen considerably; with doses of 105 n and 90 n they have risen even higher at 24 hours, and at 48 hours all have returned to the normal range. At 80 hours, in general, the largest degree of depression is apparent, and thereafter there is a gradual return to normal in 450 hours. The degree of depression does not vary inversely with the dose as shown on Graph II, Part 1, for total leukocytes and Graph I, Part 3, for total lymphocytes, nor are the levels of depression as significantly separated. (See Graph IV, Part 2).

Graph II, Part 3 - Absolute Lymphocytes-Neutrons: An immediate precipitous fall in the total lymphocytes occurs within the largest degree of depression at 24 hours for the two lowest doses and at 48 hours for the three highest doses. Except with the lowest dose (26 n), a relatively constant level of depression continues thereafter for 200 hours. At 450 hours a steady tendency in the direction of normalcy is apparent, and a significant separation in level of depression is still apparent. Again the degree of depression varies inversely with the dose. (See Graph IV, Part 3).

Graph I, Parts 1, 2, and 3, showing the effect of x-rays on the total leukocytes, absolute lymphocytes, and polymorphonuclear cells respectively, are essentially similar in pattern to the graphs showing the effect of neutrons on the blood constituents. The degree of depression of these cellular elements with doses of 500, 600 and 700 Roentgens is comparable.

Graph IV, Parts 1, 2, and 3: In the September, 1943 monthly report, Dr. Zirkle compared the blood changes after exposure to x-rays and fast neutrons by plotting survival curves based on arbitrary definitions of a survivor according to the degree of depression of the leukocytes per mm^3; absolute lymphocytes per mm^3, and absolute polymorphonuclear heterophiles per mm^3. Using these criteria, respective x/n ratios of 8.3, 8.1, 7.1 were obtained.

Although the final x/n lethal ratio on rabbits has not been completely and finally established, a conservative estimate has been placed at 6 to 7. Using this estimate of the x/n lethal ratio, Graph IV, Parts 1, 2, and 3, was drawn plotting in the leukocyte level per mm^3 at an arbitrarily chosen hour

(30 hours) after irradiation. From Graph IV, Part 1, an x/n ratio on the effect on total leukocytes at a level of 2200 cells equals ca.9.3. Graph IV, Part the x/n ratio for the absolute polys at 550 cells equals 9.2; at 1150 cells it equals 21. Graph III, Part 3, the x/n ratio for the absolute lymphocytes at 800 cells equals ca. 8.5.

The data in Graphs I and II indicated that very significant changes in the first 48 hours occurred in the total leukocytes/mm^3 as well as in constituents making up the majority of these cells. The three counts usually made during this period (3 hrs., 24 hrs., and 48 hrs.) were obviously inadequate and consequently an experiment was devised to study in more detail the events occurring in the blood during this period.

Graph III, Parts 1, 2, and 3, represents the data on the total leukocytes per mm^3, absolute lymphocytes, and polys respectively in terms of percent of control after an initial dose of 500 r. Blood counts are represented at zero hour (immediately following completion of irradiation) at intervals of one hour for the first 4 hours and every 4 hours thereafter for a period of 48 hours. These data agree essentially with those represented in the Graphs I and II (x-rays and fast neutrons respectively) except that a peak in the WBC/mm^3, previously unknown, appears as early as 8 hours and is even greater than that which has been seen at 24 hours. This increase is seen to result from the increase in the circulating polymorphs. The two components (Parts 2 and 3) are much simpler than the composite WBC curve.

8. Histopathology - R. Murray and M. Block

Work on the comparison of histopathologic effects of gamma and neutrons continues on animals dying in Dr. Zirkle's lethal series. In addition, gamma irradiated animals have been sacrificed at short intervals to sample the early stages. No comparable material with neutron exposure is yet available.

From the still patchy examination of material, one interesting observation has been the relative resistance of the reticular cells in apparent contradiction to the usually observed decrease in sensitivity with increased differentiation of cells. The reticular cells are at least as undifferentiated as the lymphocytes which latter are among the most sensitive of cells. One mouse was examined that had been exposed to the pile to several times the median lethal dose of neutrons and probably a comparable dose of gamma as well. In the spleen and bone marrow of this animal, reticular cells survived where all other cellular elements were destroyed.

The fundamental experiments on the nature of the hemopoietic changes are continuing. The amphiuma has been replaced by the common newt because of the difficulty of procuring the former in adequate quantities. A second series of chicks was irradiated at a higher dose (1200 r) but all the animals died in the first 24 hours, of unknown causes. It was noted in some of the chickens surviving the 800 r exposure for several weeks that there was a marked retardation of comb growth in the experimentals as compared to the controls. This apparent effect on the endocrine system will be investigated further.

9. Separation of Carrier-free F.P. R. D. Finkle

The separation of F.P. from UNH sample S-17-T is nearly complete. The residue from ether extractions had specific activity of 40 mC/gm which is too low for radio-toxicity studies. By following a scheme depending upon the

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repeated reworking of precipitates for adsorbed activities a specific activity of 240 mC/gm was obtained. The total activity of 5 to 10 mC expected from this sample will probably be used for radio-chemical analysis. Further investigation is necessary to develop a satisfactory separation of the rare earths from the dissolved constituents of stainless steel.

The HF sample has been evaporated, nitrated and extracted but this process must be repeated too often to be practical. As an alternative, the HF is driven off by digestion with H_2SO_4, the activity carried down by $PbSO_4$ and separated from it with H_2S. This process will give primarily Sr with a "decontamination factor" of over 200. The filtrate after Pb contains most of the gamma activity which will be used for external exposures.

The LaF_3 sample from S 17 does not have the large amount of Ce which was present in earlier samples and is being held to work up for Ce activity.

10. Miscellaneous

Radio-autographs - G. Svihla

Density-exposure curves of sixteen different film samples exposed to beta-radiation have been determined. With the aid of these curves four films have been selected for radioautographic studies, Agfa non screen x-ray films (very fast, contrasty, large grain), Dupont Xtra fast (fast, medium grain), Eastman Single Coated (medium speed, medium grain and single coated), and Dupont Industrial 509-109 (slow, long gradation, very fine grain).

The resolving powers of these films are being investigated by means of model cells and tissues composed of small spheres of lucite coated with active Sr which are moulded into discs by heat and pressure.

Graininess and resolution have been examined in enlargements from radioautographs of the model tissues.

Methods for removing background fog and for removing one of the two coats of x-ray emulsions have been obtained.

The collodion photographic process of ninety years ago is being investigated for possible use in connection with direct radioautographs in celloiden embedded material.

Catalase - C. L. Prosser

Determinations of catalase activity were made with diluted whole blood from rabbits before and at intervals of hours, then days, after x-radiation. Each of 4 rabbits receiving 800 r showed a decrease in catalase activity of about 50%. In one receiving 1200 r the catalase was reduced somewhat more. Recovery after 800 r occurred after 2-3 days except for one rabbit which lost weight and retained a low catalase activity; after three weeks this rabbit began gaining weight and its catalase activity increased. Under condition of the experiment 1 cc. of normal blood destroys 4.4×10^{-2} mols of H_2O_2/min. On the basis of Fricke's determinations, the production of 8.2×10^{-13} mols of H_2O_2/cc r it was calculated that if blood catalase were not depressed and radiation occurred at a 1 r level there would be at equilibrium $.36 \times 10^{-12}$ mols of H_2O_2/cc. Unless catalase is nearly completely inactivated it is unlikely that peroxide from radiation or from respiration could reach a toxic level in blood.

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Absorption of F.P. by Fish - C. L. Prosser

Fish are known to selectively absorb certain salts from water and it is possible that they may be useful as detectors for very low levels of activity in water. Preliminary exposures of goldfish to Sr^{89} indicate an ability to concentrate this element 10-25 times in 2-4 days.

Training Program

The series of lectures on radiobiology has continued throughout the present month. With few exceptions, lectures have been presented five times a week. W. E. Cohn presented aspects of his work in three lectures. R. E. Zirkle concluded his series on October 9th. R. Abrams then gave a series of four lectures on radiobiology of the lungs. The program is expected to conclude after another week with lectures by Murray, Block and Jacobson.

Test runs have been made on the Chicago cyclotron to determine the yields of Sr, Y and Br in anticipation of tracer and toxic experiments.

Three tracer exposures of mice to Na and Br have been made with low specific activity samples. The results were erratic and unsatisfactory.

No further work on electrically conducting plastic has been done except to mould samples for instrument development by the physics division.

11. Program for the Coming Month.

1. Haematology and histopathology of x and n exposures will be continued to lower dose levels.

2. X and n lethal exposures will be continued.

3. Animal and fish experiments with F.P. and other isotopes will be made as material is available.

4. Dust development and exposures will continue.

5. Lower dose exposure in CP2 will be made if possible.

6 Development and construction of gas exposure chambers will be continued.

7. Investigation on production and recovery of Xe will continue.

8. A "scout" experiment will be made on the relation of nicotinic acid and radiation injury.

9. Fundamental Histopathology will continue.

10. Radio-autographic work will continue.

1118604

Fig. 1a

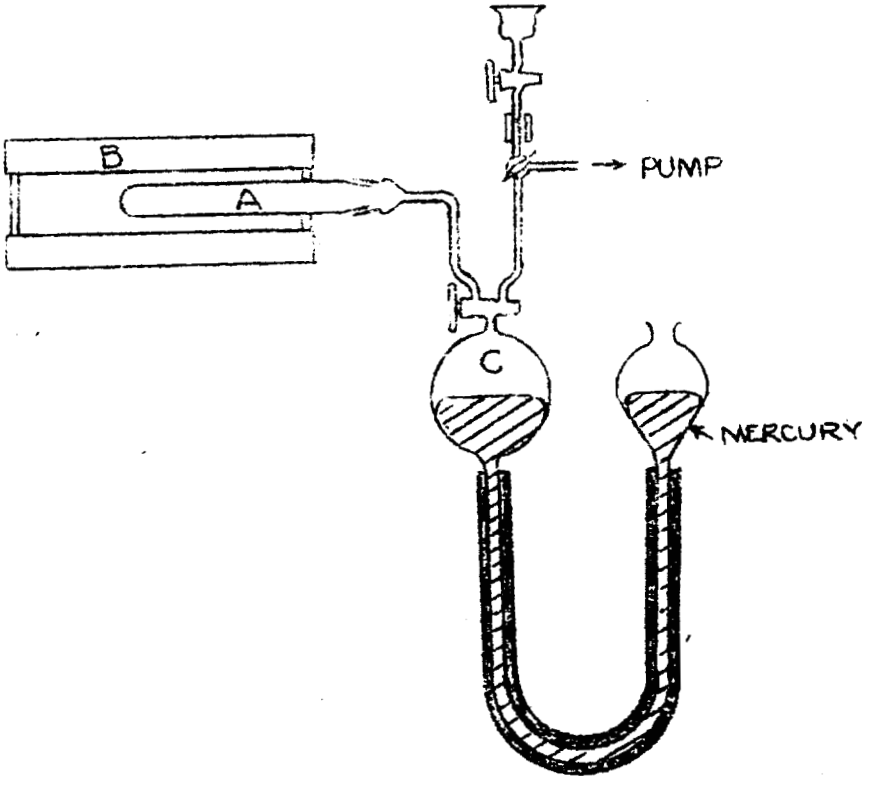
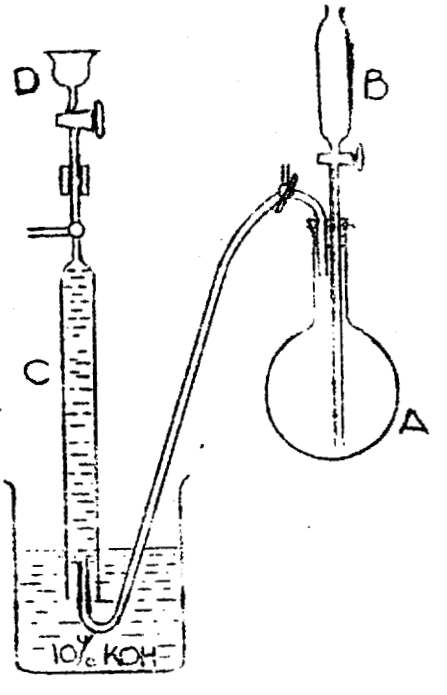


Fig 1b



1118605

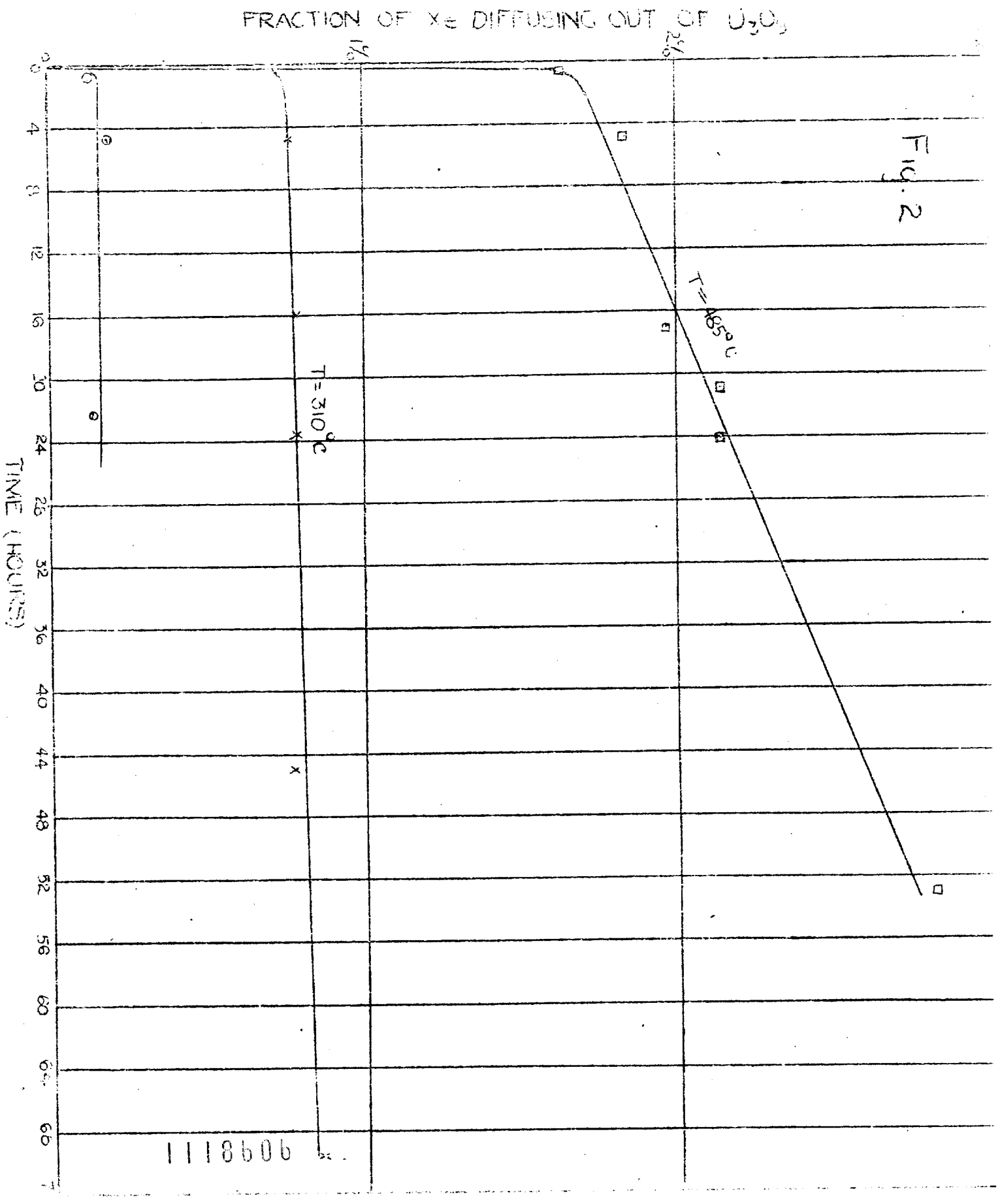
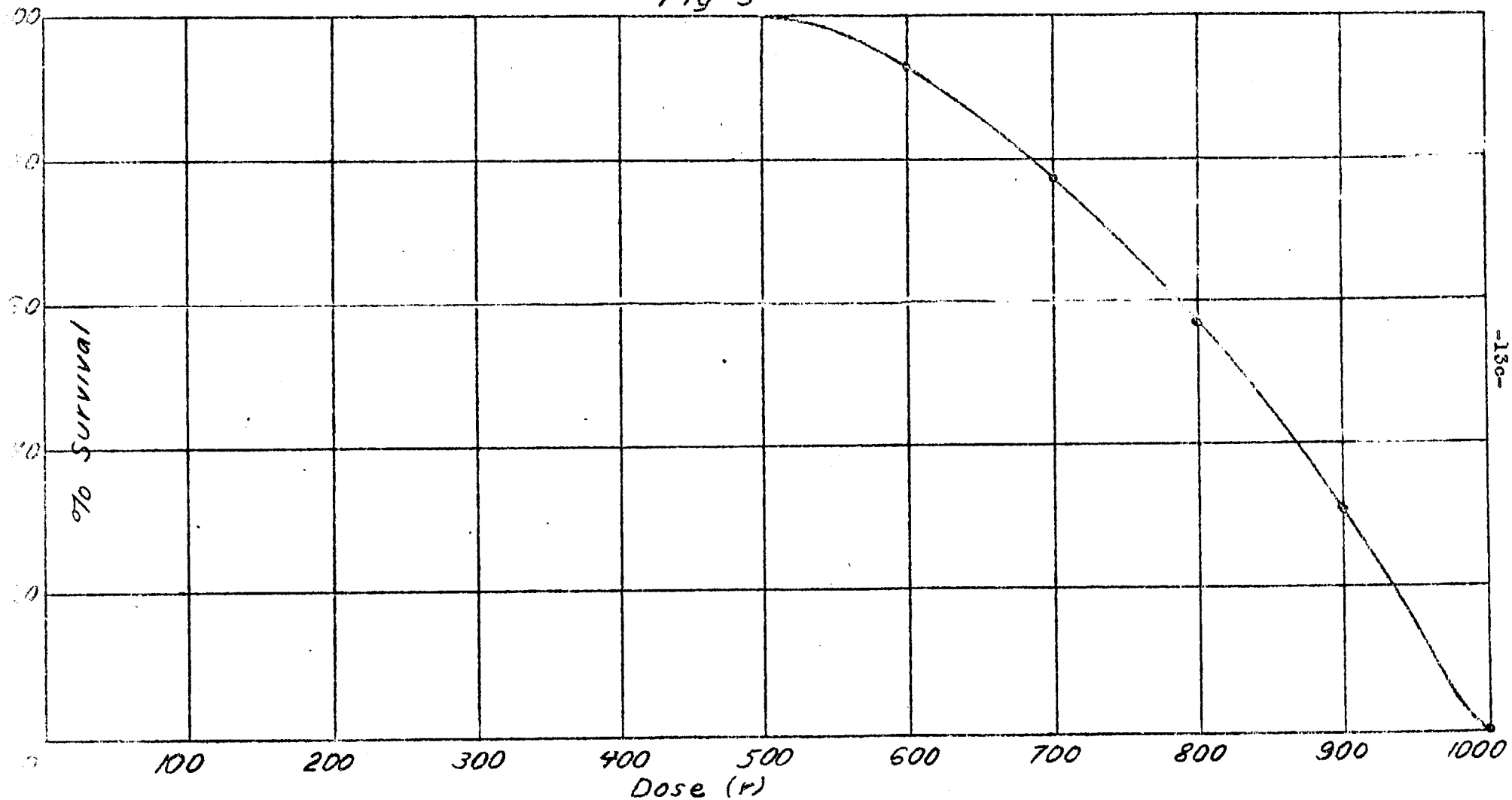


FIG. 2

1118606

1098111

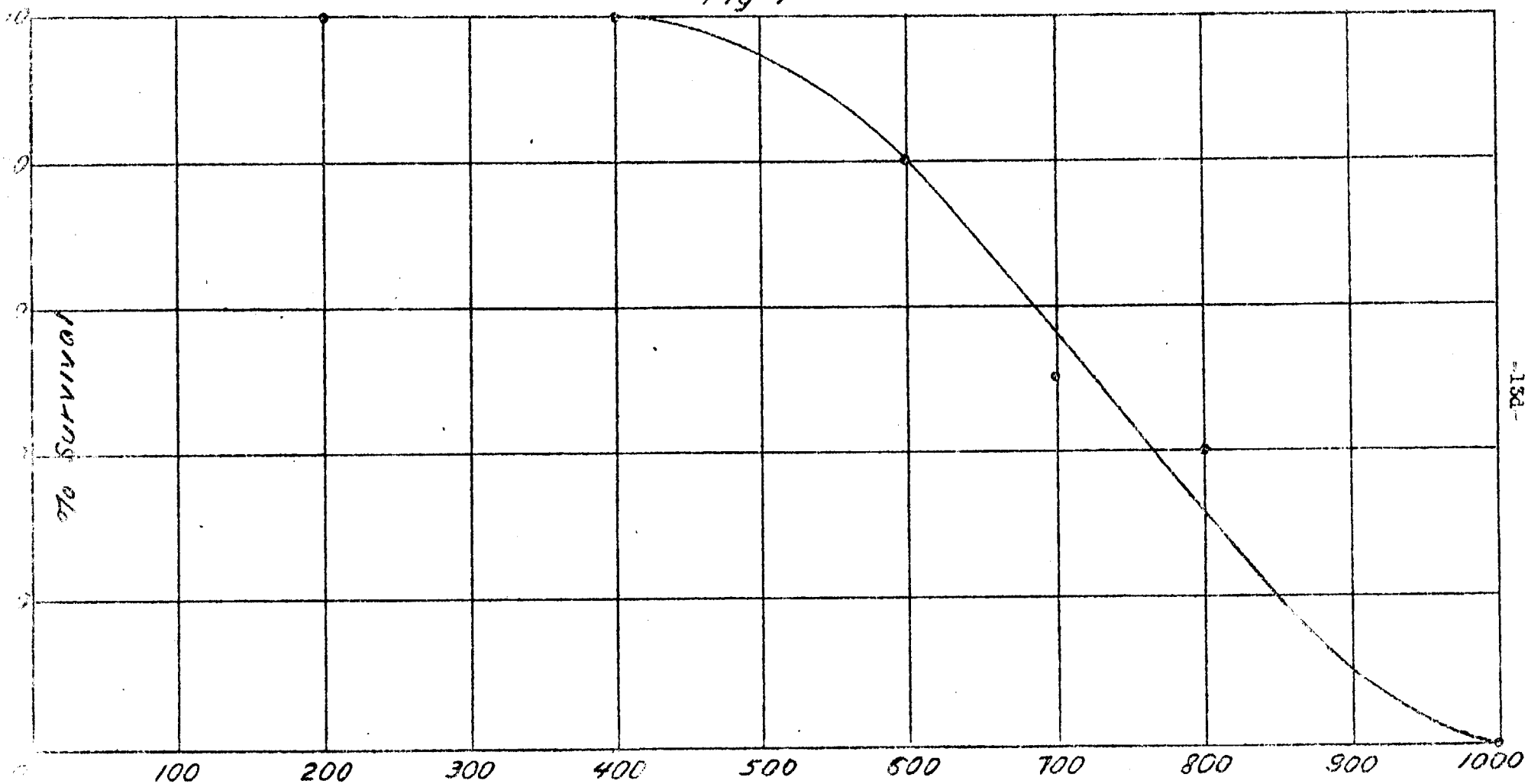
Fig 3



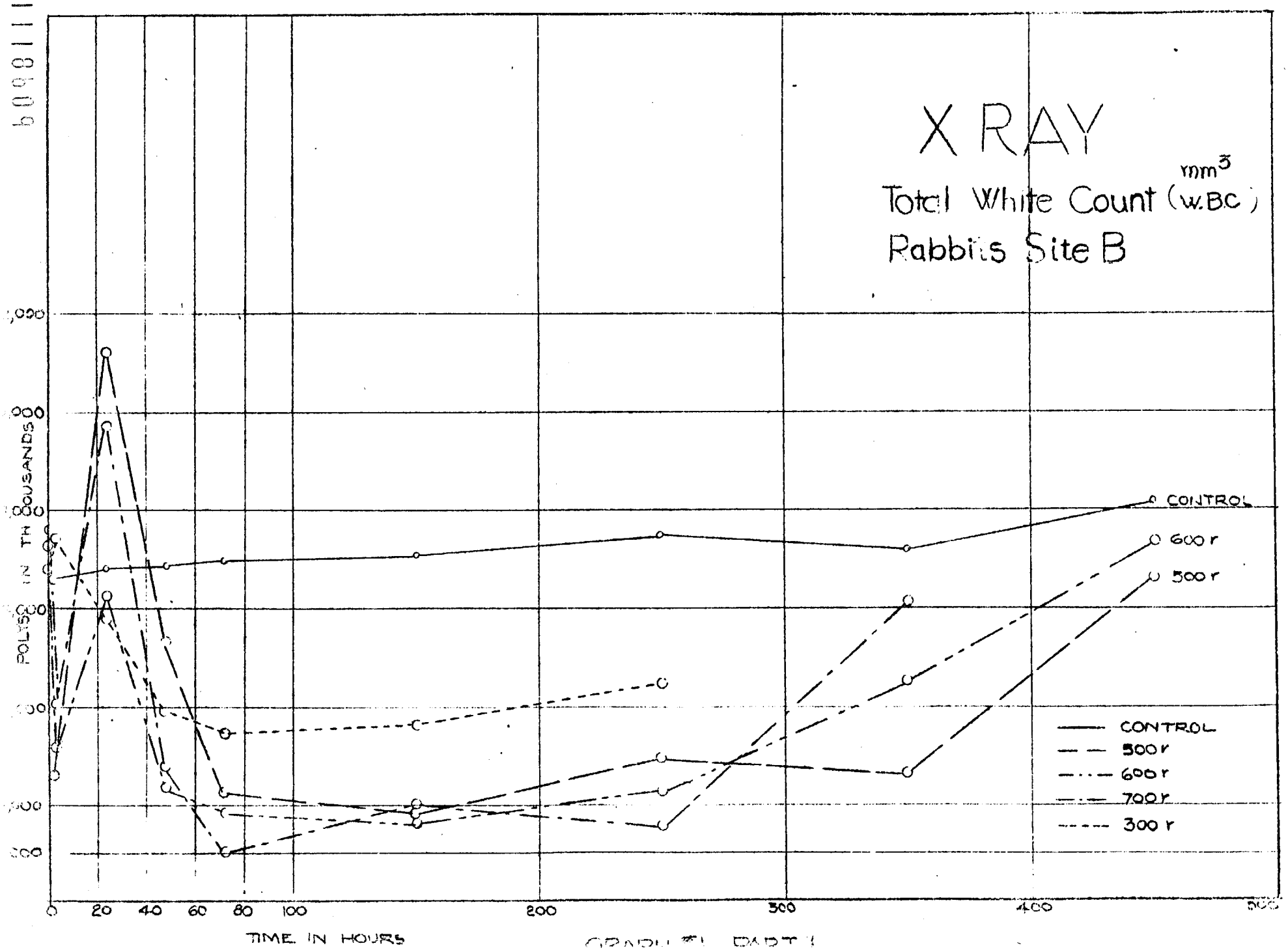
Rabbits ——— X-ray Survival

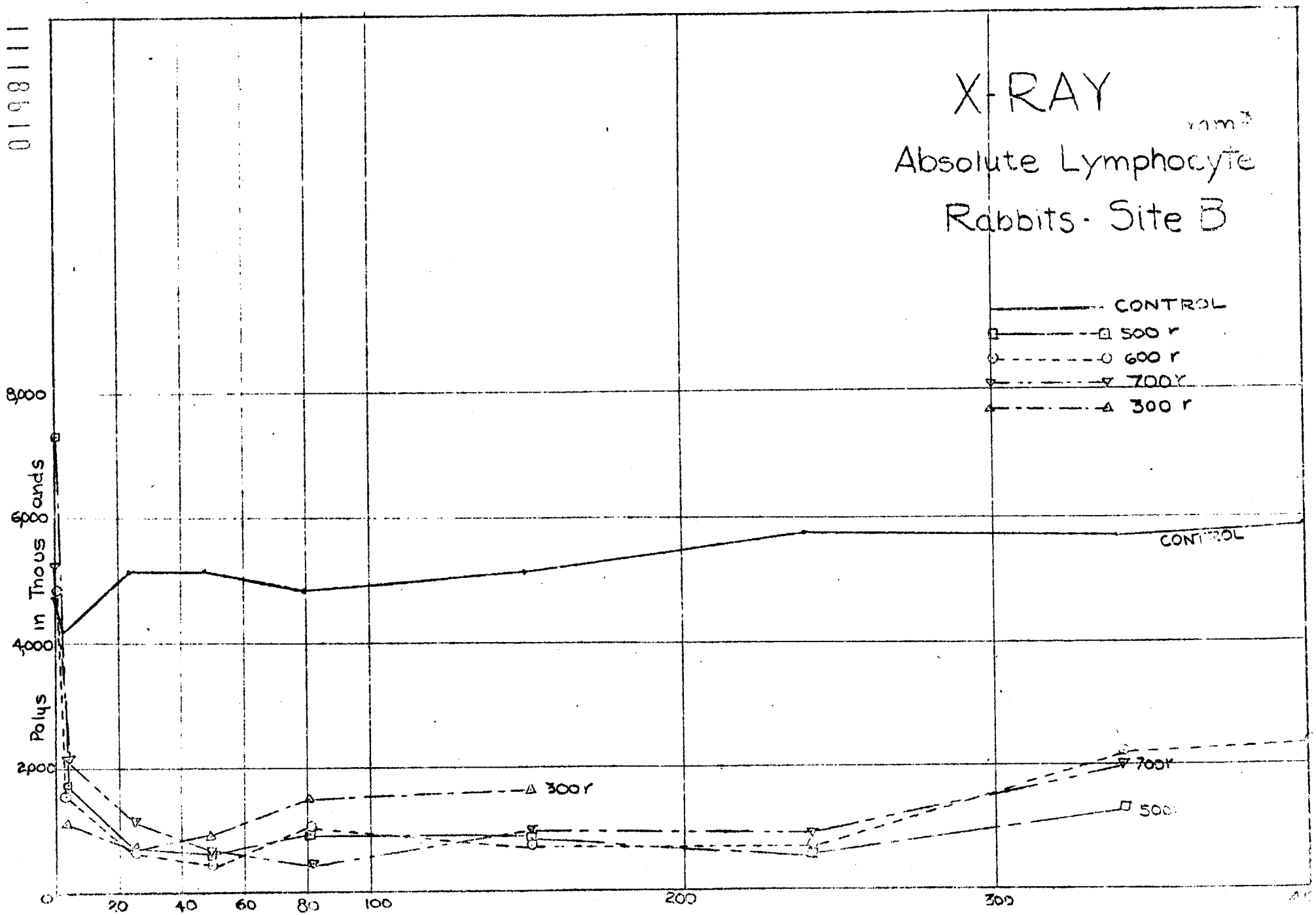
1118608

Fig 4



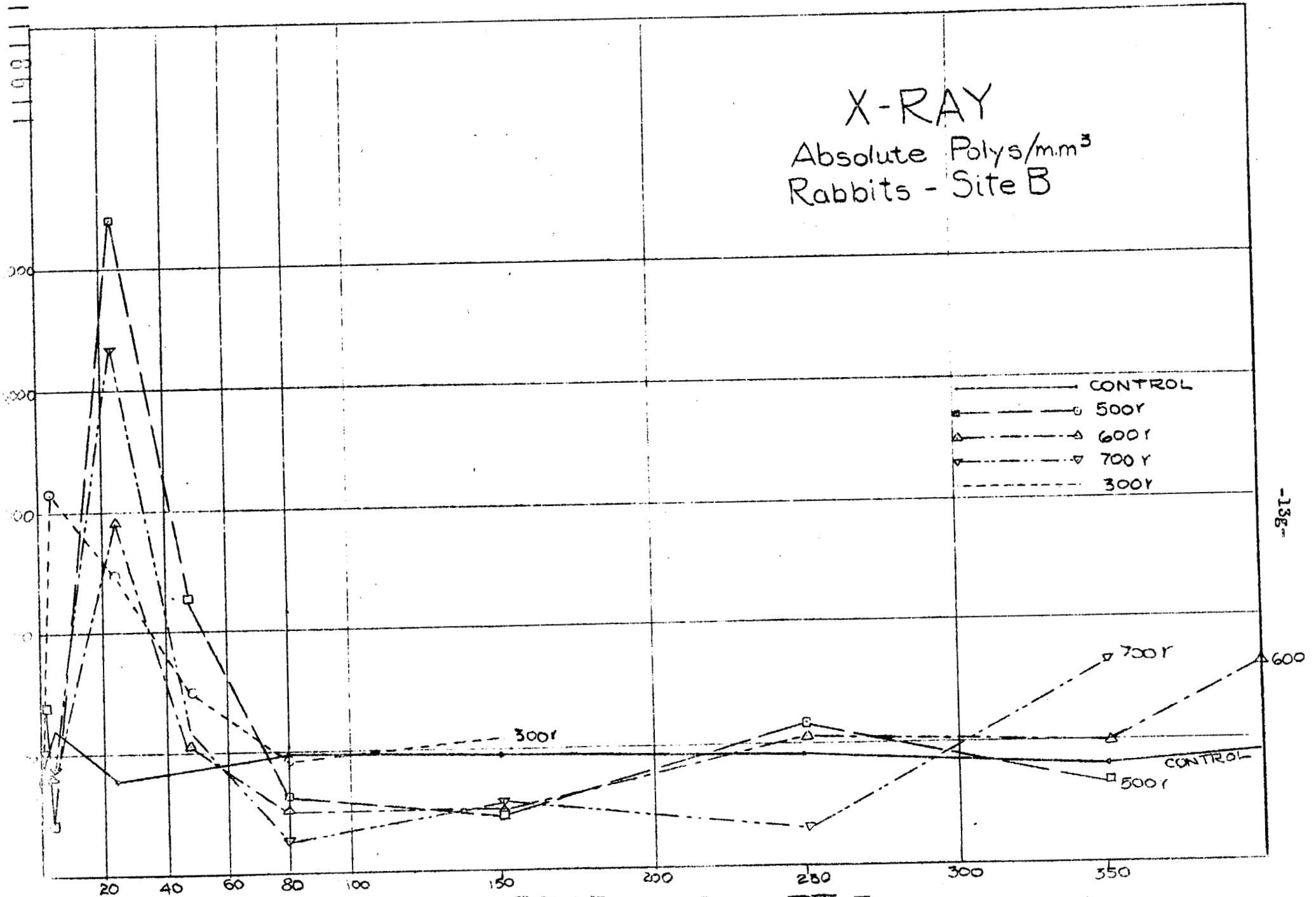
Rats — X-ray Survival


X RAY
Total White Count (W.B.C.) mm3
Rabbits Site B
CONTROL
600 r
500 r
CONTROL
500 r
600 r
700 r
300 r
POLYSO IN THOUSANDS
TIME IN HOURS
0
20
40
60
80
100
200
300
400
500

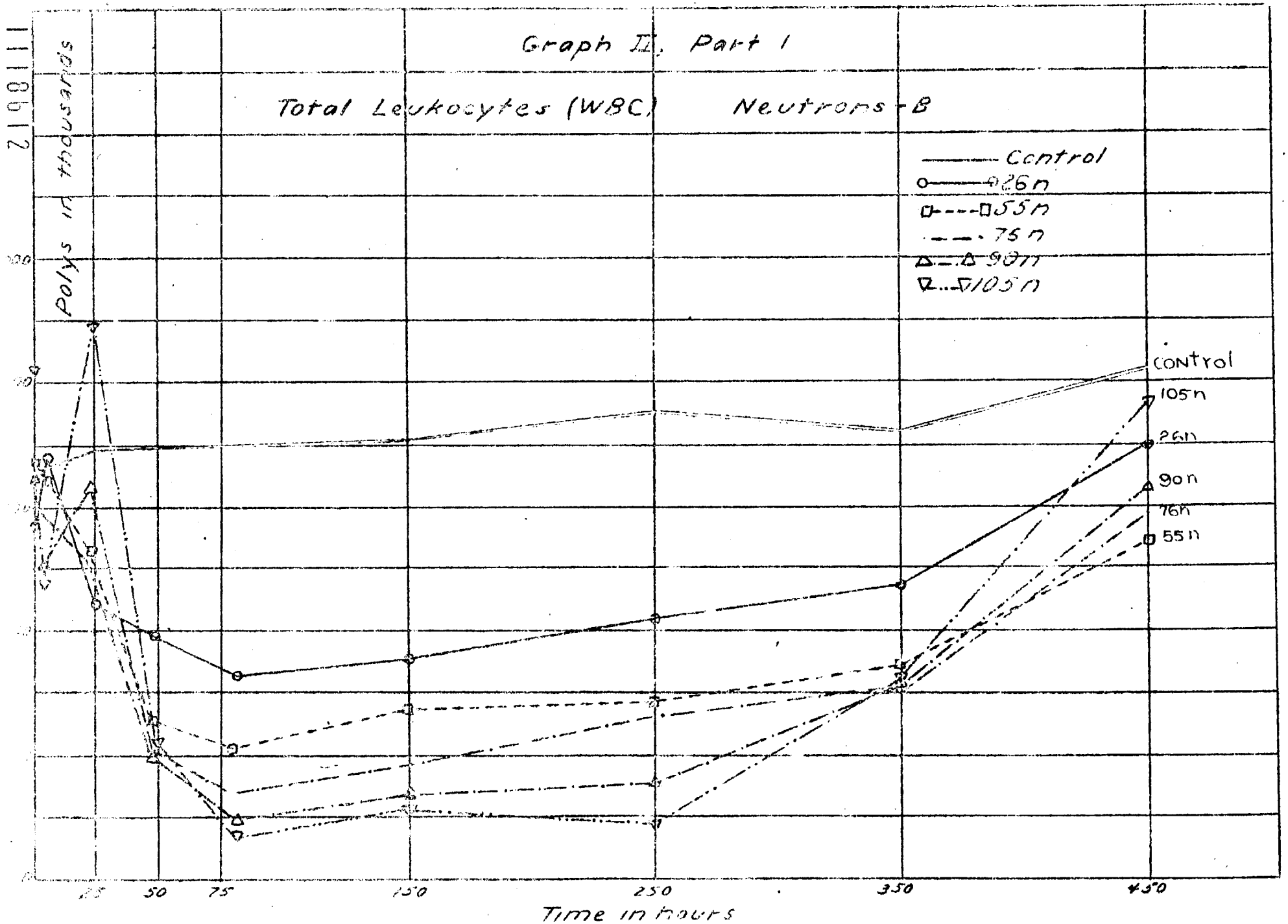


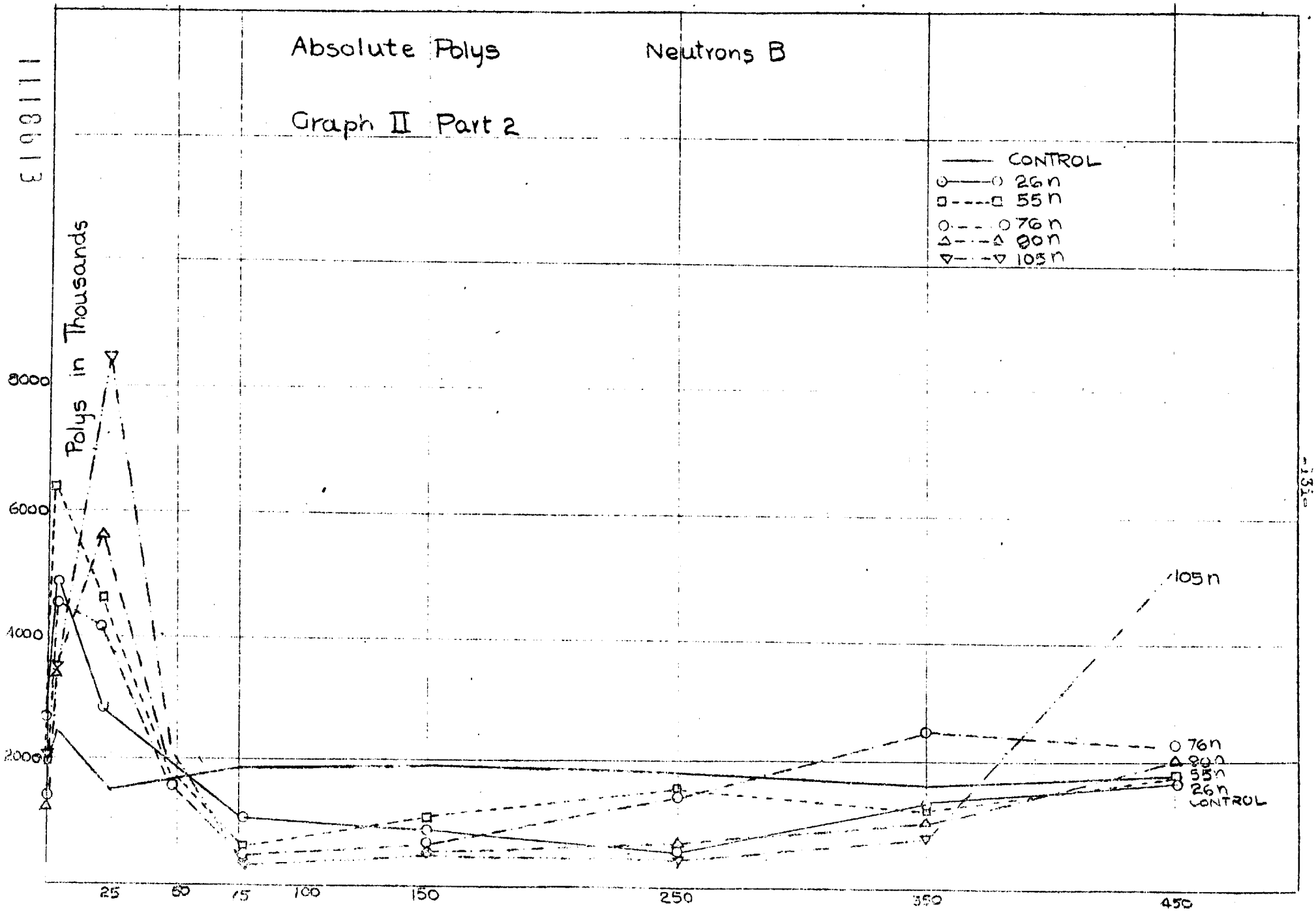
GRAPH. NO. 1 PT. 2

0198111

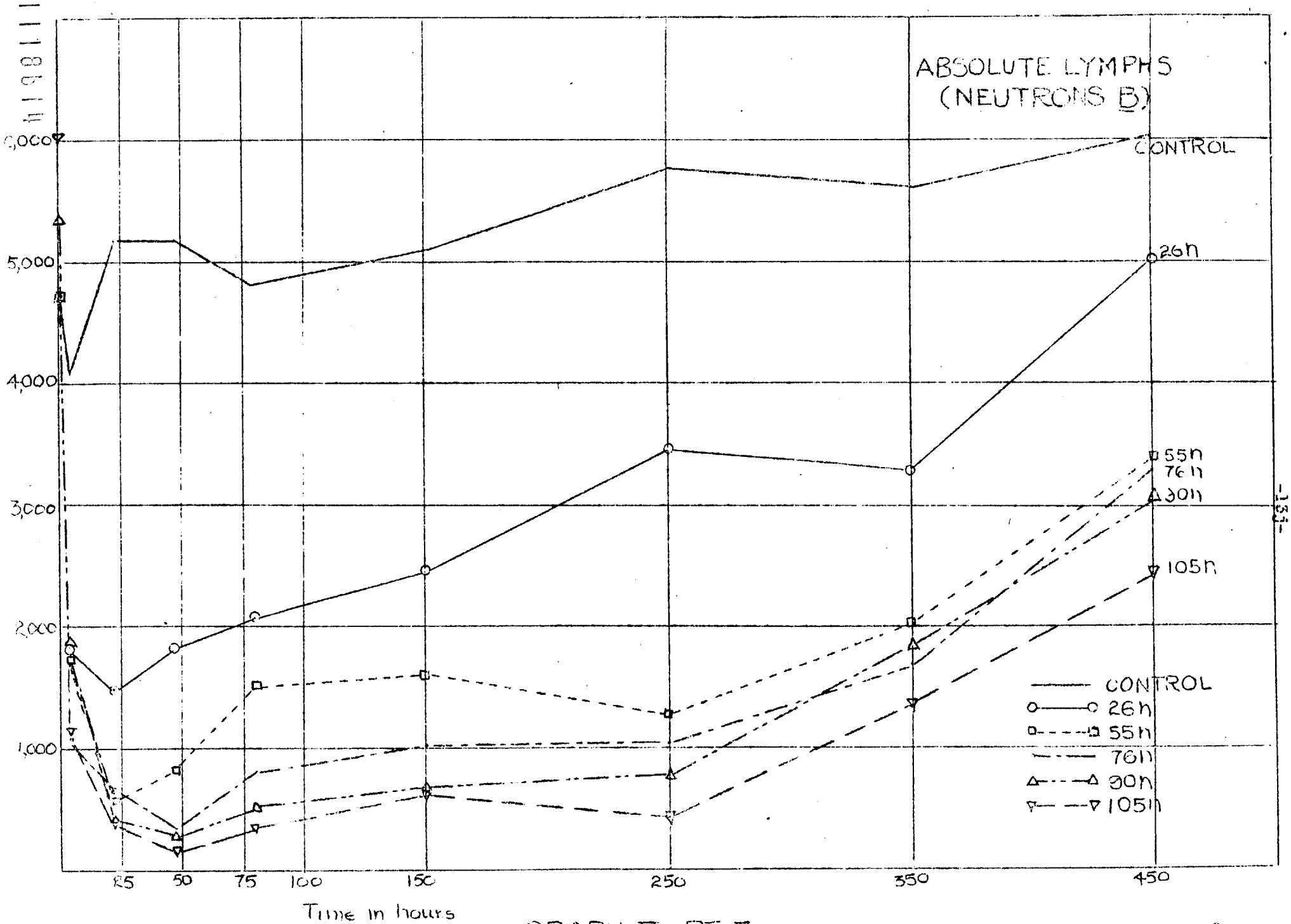


GRAPH NO. 1 PT. 3

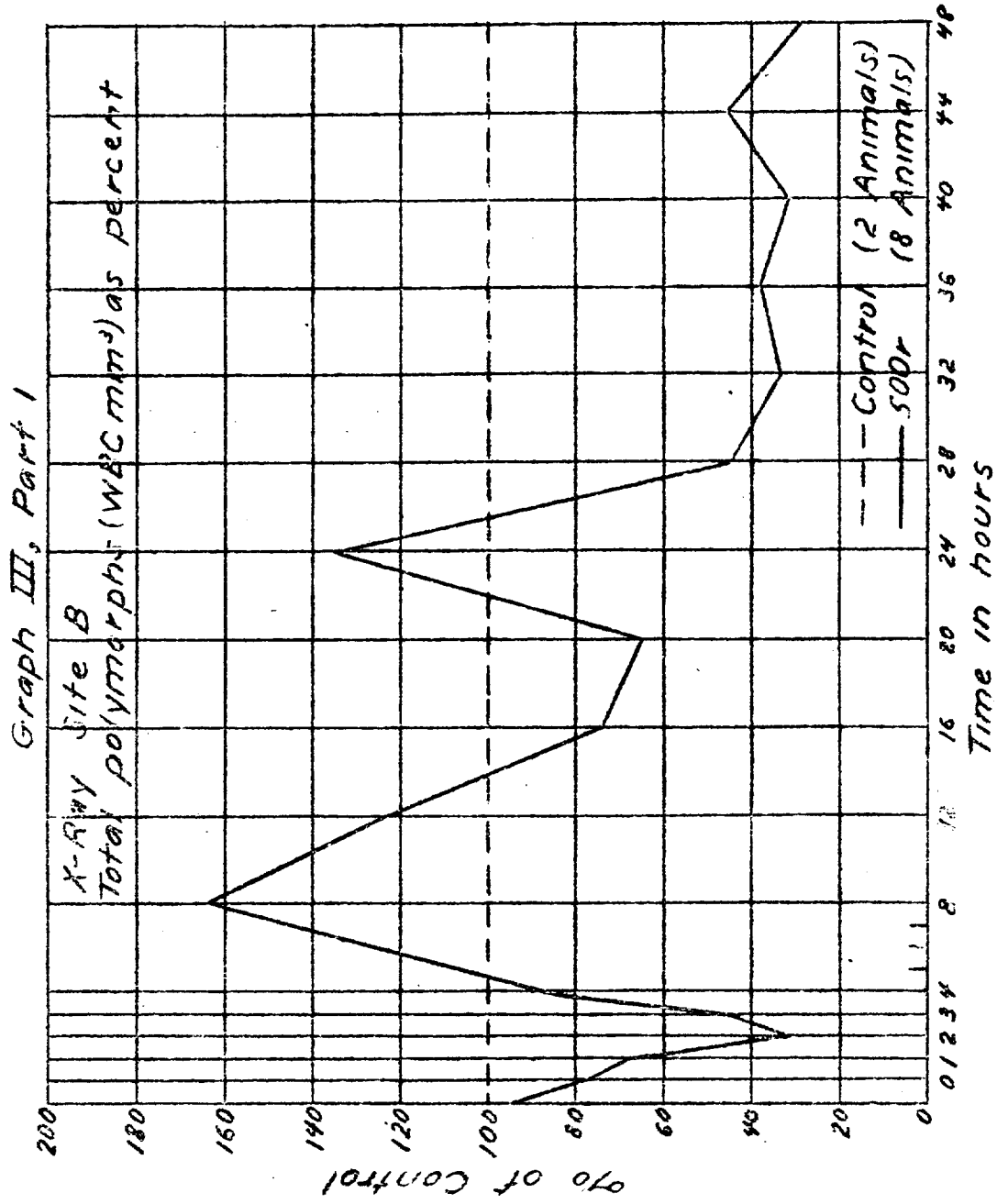

Graph II, Part 1
Total Leukocytes (WBC) Neutrons - B
Control
26 n
55 n
75 n
90 n
105 n
Polys in thousands
Time in hours
25
50
75
150
250
350
450
control
105 n
26 n
90 n
76 n
55 n


Absolute Polys
Neutrons B
Graph II Part 2
CONTROL
26n
55n
76n
80n
105n
Polys in Thousands
8000
6000
4000
2000
25
50
75
100
150
250
350
450
105n
76n
80n
55n
26n
CONTROL

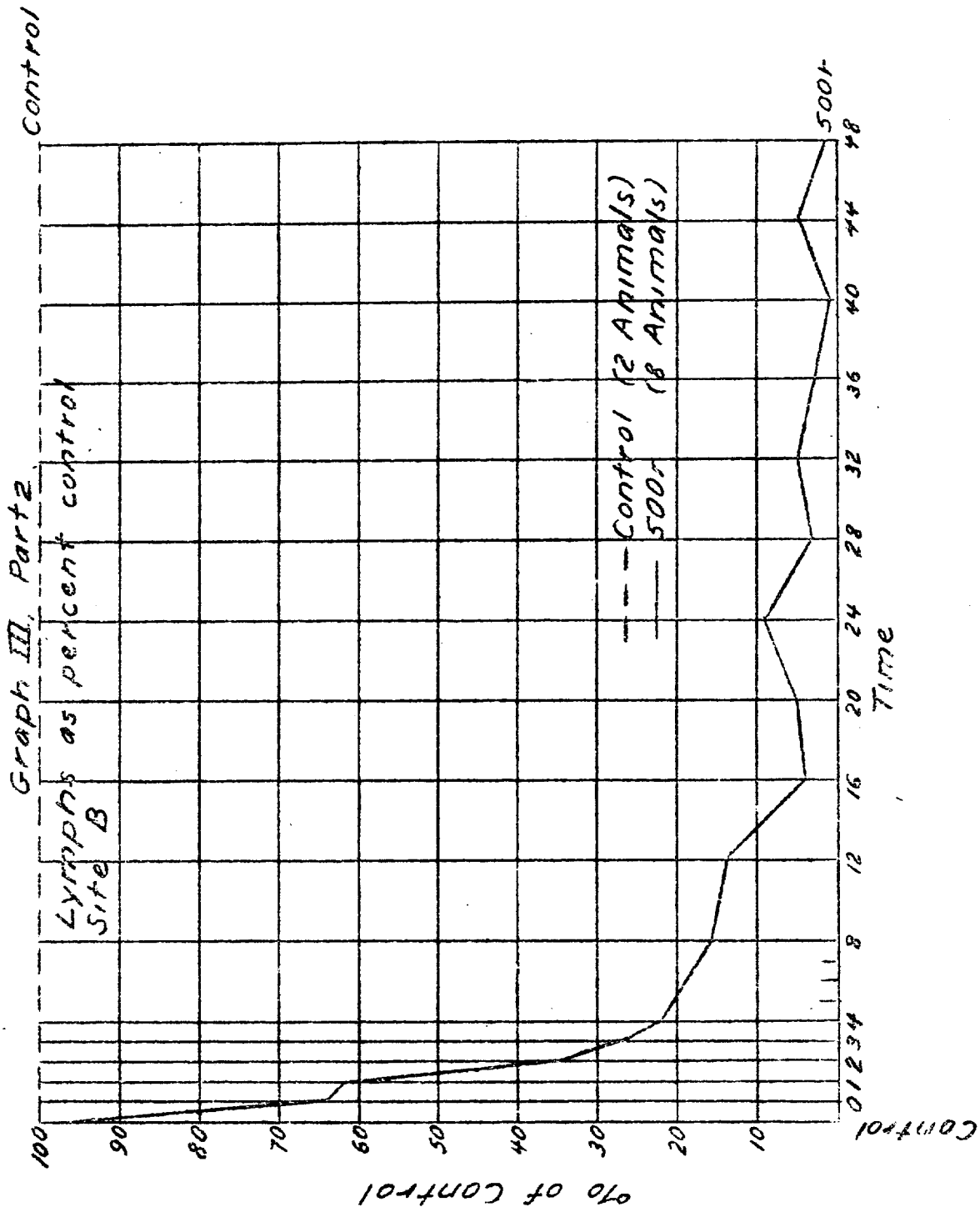
116613


ABSOLUTE LYMPHS
(NEUTRONS B)
6,000
5,000
4,000
3,000
2,000
1,000
25
50
75
100
150
250
350
450
Time in hours
CONTROL
26h
55h
76h
90h
105h
CONTROL
26h
55h
76h
90h
105h

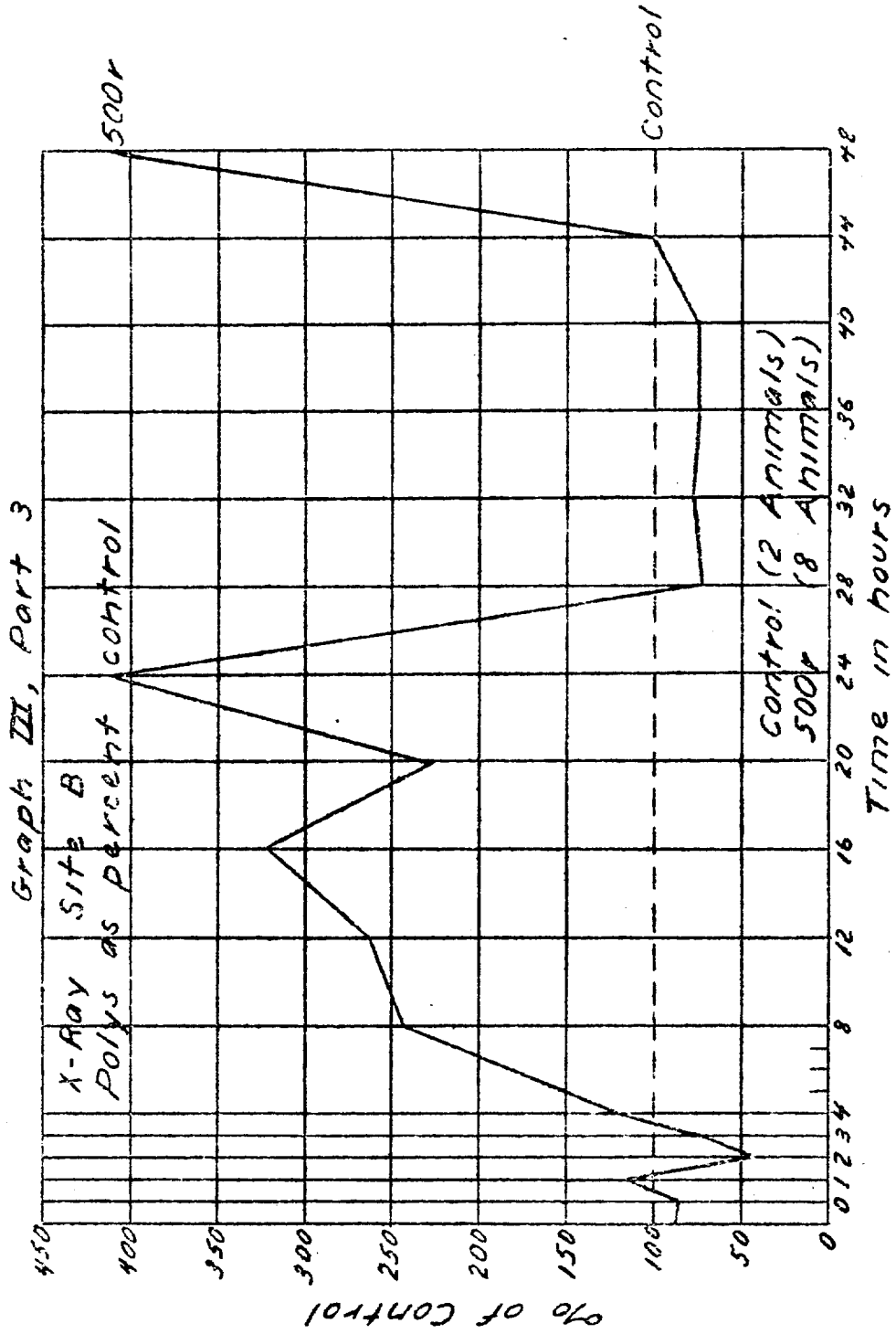
GRAPH II, PT. 3


Graph III, Part 1
X-Ray Site B
Total polymorphs (W&C mm³) as percent
% of Control
200
180
160
140
120
100
80
60
40
20
0
0 1 2 3 4
8
16
20
24
28
32
36
40
44
48
Time in hours
Control (2 Animals)
500r (18 Animals)

1118615

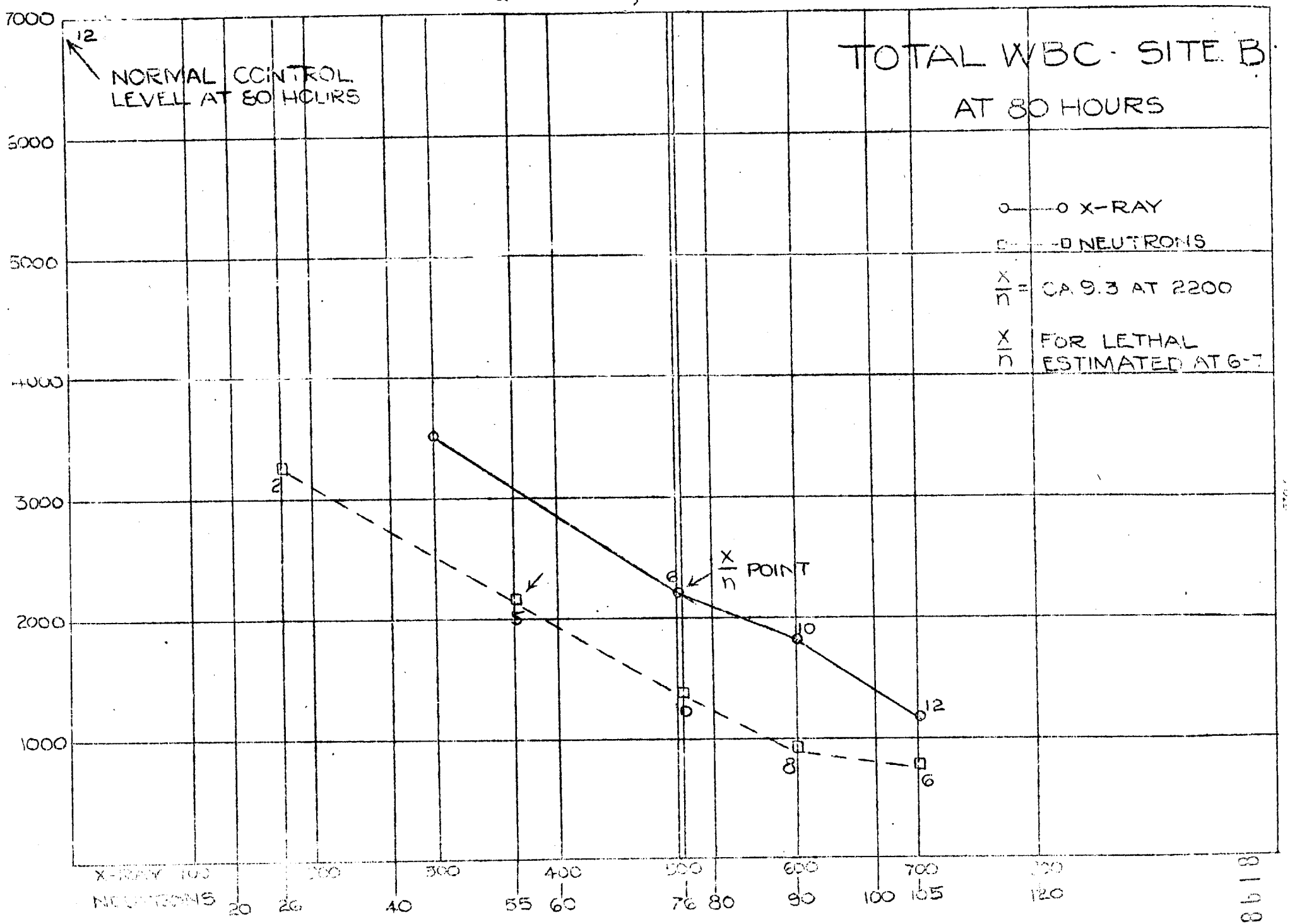

Graph III, Part 2
Lymphs as percent control
Site B
Control
500r
Control (2 Animals)
500r (8 Animals)
% of Control
100
90
80
70
60
50
40
30
20
10
Control
0 1 2 3 4
8
12
16
20
24
28
32
36
40
44
48
Time

1118616

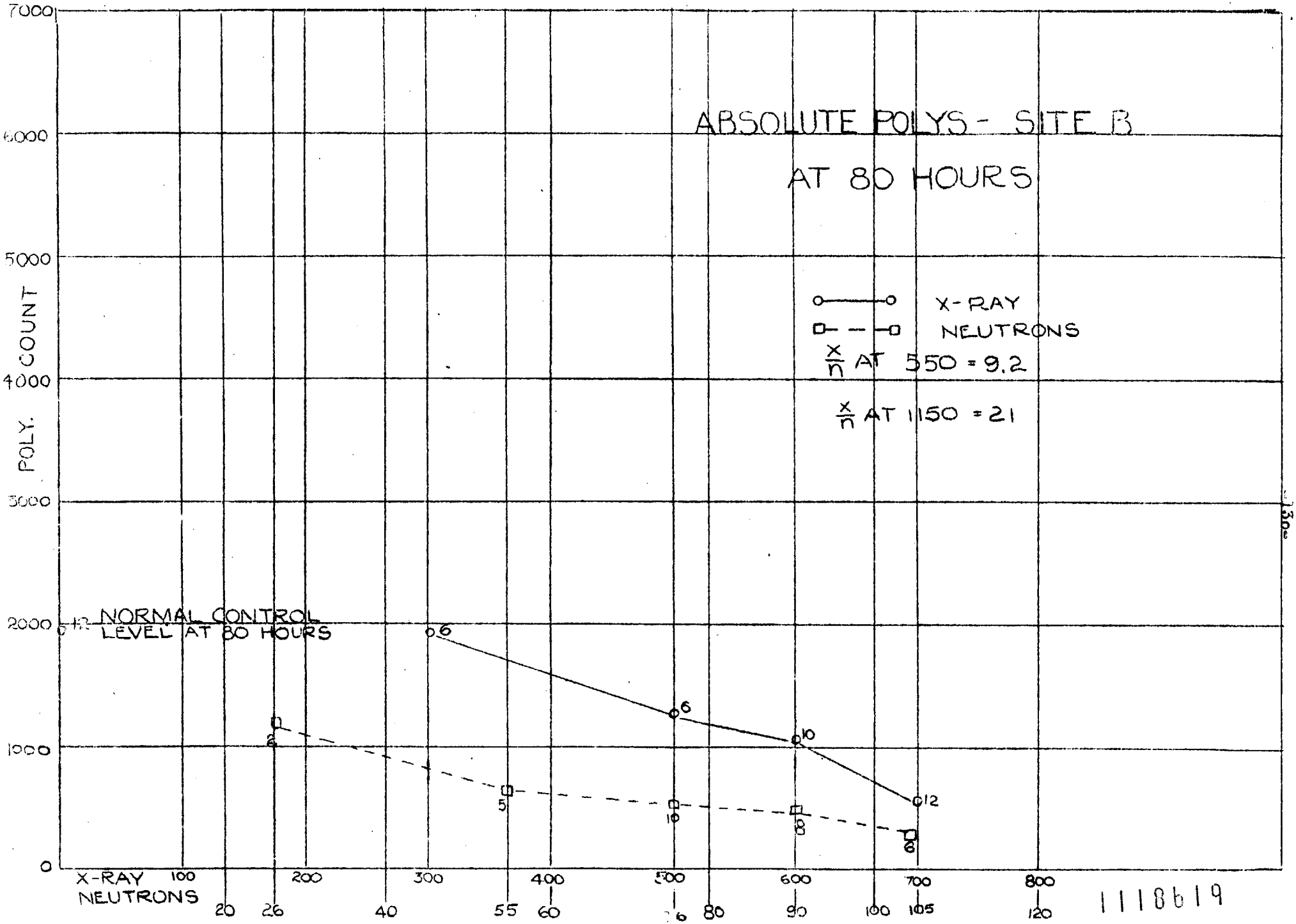

Graph III, Part 3
X-Ray Site B
Polys as percent control
500r
Control
Control (12 Animals)
500r (8 Animals)
Time in hours
% of Control
0
50
100
150
200
250
300
350
400
450
0 1 2 3 4 8 12 16 20 24 28 32 36 40 44 48

1198111

GRAPH IV, PART I

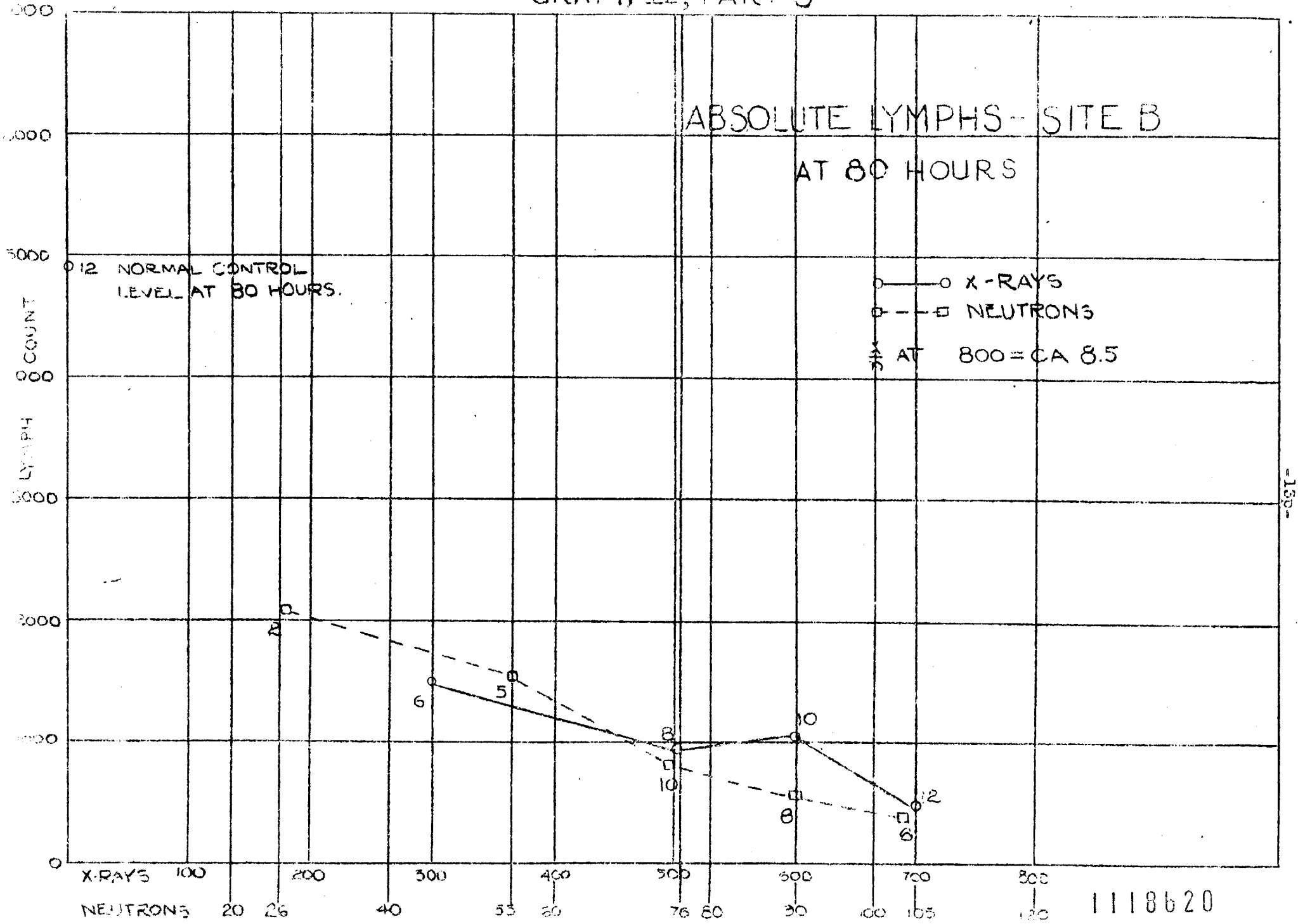


GRAPH V, PART 2



1118619

GRAPH IV, PART 3



1118620

B. CLINICAL MEDICINE AND MEDICAL RESEARCH

C. J. Watson, M.D., Associate Director

Abstract

Industrial surveys at two plants were carried out by Dr. Norwood.

A survey of the tuballoy dust hazard at site "B" is in progress; the amount of dust and particle size is being studied.

A preliminary report on the toxicology of TO_2 and $TO_2(NO_3)_2$ in mice is presented. Except for a possibly significant depression in the weight curve of mice ingesting 2.0 mg and 20 mg daily the general health of these animals remained unimpaired for a year. In the analysis of extraparenteral organs (bone, liver, kidney, etc.) no T was detected in animals ingesting the oxide. T was detected in the bones and kidneys and questionably in the liver of mice ingesting 2.0 and 20 mg daily of the nitrate. Application of an other solution of the nitrate to the skin of mice equivalent to 2 mg/day gained weight and appeared healthy. T was found in the kidney and bone and questionably identified in the liver of these animals.

No physical or laboratory changes have been noted in personnel due to hazardous materials.

The program to be undertaken in pigment metabolism is outlined.

1. Clinical Medicine - J. J. Nickson and M. Nickson

The necessary pre-employment examinations were performed during this period.

Industrial Surveys: Dr. Norwood visited two plants. At one, monthly physical examination revealed no abnormality which was felt to be due to exposure to special materials. At the other, blood counts were taken by one of Dr. Jacobson's technicians. No significant abnormalities were noted.

Metallurgical Laboratory Surveys:

Site B: The installation of grinders in Room 109 was checked with the electrostatic precipitator. The amounts of tuballoy dust collected exceeded 150 micrograms per cubic meter of air in but one instance.

At the suggestion of Dr. K. S. Cole, particle size determination was run by Dr. Abrams on a specimen collected during the dry machining of a tuballoy bar. A total of 3.25×10^8 particles were found with most of the particles being between 2-3μ in their largest diameter. Other particle size determinations will be obtained in the future.

New Chemistry;

A proposal for a means of detecting the approximate amounts of radioactive material on the hands of persons working with active substances was

1118621

given to Dr. Franck for consideration.

2. Toxicology - A. Tannenbaum and H. Silverstone

In October, 1942, experiments concerning the toxicology of a) ingested TO_2 and $TO_2(NO_3)_2$, and b) an ether solution of $TO_2(NO_3)_2$ applied to the skin, were initiated. Mice of both sexes were used as the experimental animals. (In a preliminary experiment the toxicity of $TO_2(NO_3)_2$ administered parenterally to mice was found to be of the order reported for other species.

Both TO_2 and $TO_2(NO_3)_2.6H_2O$ were fed to different groups in amounts ranging from .0005 to 0.5% of the diet (from .02 to 20 mg. per day for the male mice that consumed about 4 gm. of food per day. 20 mg. per day for a mouse is estimated to be the equivalent of one pound per week for a 70 kilo. man). The experiments were continued for almost one year during which time the weights of the animals were recorded and their general condition observed. Near the termination of the experiments (when an electroscopic method of analysis became available) animals were sacrificed for determination of the T content of their organs.

No deaths occurred due to T poisoning (a few animals died but these occurred in all groups and were caused by fighting, breast tumors, etc.). The weight curves did not show any depression from normal in any of the groups receiving the oxide, or 0.2 mg. or less of the nitrate per day. A small and possibly significant growth rate depression was observed in the two groups receiving 2 and 20 mg. respectively, of the nitrate per day. It must be emphasized however that these animals were in excellent health and, on the average, increased in weight during the entire course of the experiment. In analyzing for the T content of the organs, none was detected in the extra-parenteral organs of the mice receiving the oxide, or 0.2 mg. or less of the nitrate per day. In the bones and kidneys of the mice receiving 2 and 20 mg. of the nitrate T was found, while a questionable quantity (certainly less than 0.5 μg. per liver) was found in the liver None could be demonstrated in the other organs examined (lungs, heart, spleen).

In experiments on the application of an ether solution of the nitrate to the skin the mice received the equivalent of approximately 2 mg. per day. Since the number of animals in the groups were small no conclusions could be reached regarding the effect on growth rate other than that the effect was not of large magnitude. Again, as in the feeding experiments, the mice increased in weight and appeared healthy; no deaths due to T poisoning occurred. As in the series ingesting the nitrate, T was found in kidney and bone, and questionably identified (less than 0.5 μg.) in the liver.

A full report of these experiments is in preparation.

From these experiments it is concluded that the nitrate (water soluble) is more readily absorbed from the gastro-intestinal tract than is the oxide (water insoluble). The low toxicity of the oxide and nitrate observed in these experiments (as compared to that of parenterally administered nitrate)

1118622

is probably due to the fact that absorption through the gastro-intestinal tract or thru intact skin is of very low order.

Experiments on the toxicology of other compounds of T have been initiated. They include studies of TF_4, TF_6, TCL_4, and T_3O_8.

3. Haematology - L. O. Jacobson and E. Marks.

The work of examining blood and urine on new personnel, repeat examinations on control individuals (those not exposed to radiation), and personnel working with hazardous or potentially hazardous material has continued. No individuals have been encountered during this month whose blood indicates undue exposure to radiation. A careful check has continued on those individuals who were previously found to have a change in the blood, presumably due to radiation exposure.

A reorganization in the procedure of notifying personnel of appointments for laboratory precedures is under way. Instead of a verbal appointment via the telephone, which has been our policy in the past, appointments will be made by means of a letter. If the appointment is not filled, a second appointment letter will be sent to the individual and a copy to his section chief. In the event the individual still fails to report, a letter will then be sent to the Personnel Director for whatever further action is necessary. Copies of all letters will be filed in the individual's chart. The purpose of this new scheme is to indicate officially and permanently that our responsibility to the individual and the University has been fulfilled.

Plans are now under way to take blood counts, etc., on personnel in the building in which they work. This is already under way at Site B and Argonne, and is currently proposed for New Chemistry and Eckhart.

4. Pigment Metabolism - S. Schwartz

The effort during October has been largely concerned with organization of the laboratory and training of new personnel. Preliminary pigment studies on the urine of dogs who have received parenteral tuballoy compounds has begun. The program to be undertaken, and which in general will be actively begun during November, is as follows:

I. Study of T_3O_8 or TO_2NO_3 toxicity in dogs with particular reference to determining means of detecting incipient damage

A. Acute experiments (parenteral, oral and cutaneous, in that order) Four dogs to receive daily per kilo amounts equivalent to those already shown to be lethal for smaller animals. A larger series may be required depending upon uniformity of findings.

B. Chronic experiments. (Route of administration to be determined on basis of results of acute experiments)
Three groups of 4 dogs each; animals of each group to receive, respectively, 60%, 40% and 20%, of the per diem lethal dose, as established in the acute experiments.

1118623

C. Procedures (8 day baseline in all experiments). Frequency indicated is for the acute experiments only; to be determined for the chronic.

1) Hematology

a. Hemoglobin, leukocyte count, differential daily
b. RBC count, retic. count, platelet count, every other day.
c. Hematocrit, MCD (halometer) every 4th day.

2) Pigment metabolism and liver function.

a. Serum bilirubin every 3rd day.
b. Feces urobilinogen - continuous 4 day collections. Per diem to be determined on each.
c. Urine urobilinogen daily - both quantitative and semi-quantitative (comparator block) if possible.
d. Urine PDP every other day Qualitative only
e. Urine urorosein every other day semi-quantitative
f. Urine indican every other day qualitative
g. Urine indirubin every other day qualitative
h. Urine coproporphyrin total and isomers, if possible daily
i. Urine porphobilinogen qualitative every other day
j. Erythrocyte protoporphyrin every 3rd day
k. Serum or plasma porphyrin (qualitative) every 6th day
l. Cephalin-cholesterol flocculation and semi-quantitative formal-gel test every 3rd day
m. Bromsulph. 5 mg. per kilo 30' on 1st and 8th days of control period and at weekly intervals during experiment
n. Blood volume on last (8th) day of control period and at weekly or 10 day intervals during experiment

3) Toxicology

a. Weight curve
b. Appetite--food and water intake
c. General appearance and behaviour. Tongue, hair, nails.
d. Study of U-content of organs, at autopsy

4) Pathology

a. Autopsy - gross and microscopic.

II. Study of total body radiation effects in humans

Patients to be hospitalized.
Procedures and frequently to be approximately as noted under Study I.
Daily 24 hour urine uric acid and total N.P.N. on weighed diet.

III. Study of total body radiation in rabbits and dogs. Wherever possible, experiments will be carried on in collaboration with group at Site B.

1118624

a. Acute experiments - Sufficient per diem r to cause death in from 2 - 4 weeks.

b. Chronic experiments. Groups of animals, procedures and frequency to be approximately as noted in Study I. In the rabbit experiments procedures a, b, c, k, m, and n will be entirely omitted, while j and l will be done every 4th or 5th day, rather than every 3rd. In addition, the 24 hour urinary purine bases and N.P.N. will be determined daily.

Certain aspects of the above are to be carried on in cooperation with Dr. Watson by other members of the Clinical Section:

Haemotological aspects - Dr. Jacobson

Pigment metabolism and liver function tests - Dr. Schwartz; Cephalin-cholesterol; formol gel, etc., Drs. J. J. Nickson and M. Nickson

Toxicology - Drs. Tannenbaum and J. J. Nickson

Autopsy and Pathology - Drs. Bloom and Jacobson

5. Work For the Coming Month

The pre-employment examinations and re-examinations will be continued as well as the haematological and urine studies. Further examinations of material from mice exposed to tuballoy compounds will be continued. The study of pigment metabolism of the rabbit and the dog after administration of T_3O_8 and TO_2NO_3 will be actively begun as well as similar studies of animals and humans after total body irradiation.

1118b25

C RADIATION MEASUREMENT SECTION

E. O. Wollan, Consulting Section Chief

Report by L. A. Pardue, Group Leader

Abstract

The addition of a laboratory technician to the group [illegible] radiation measurements has made it possible to [illegible] the work somewhat. Pocket chamber and film [illegible] records are used to locate places needing surveys which are made promptly. Weekly reports on exposures received by project workers are made to the medical group. The badge for the new film meter has been ordered. While awaiting delivery, film tests are being made to find out the best films for various uses.

* * * * *

Mrs. Mary Nachtrieb joined the group on October 6, 1943. She will do most of the pocket chamber and film meter work. The group now has only four members and its work for the Health Division will consist mainly of measurements of and protection from radiations. The research work of this group is being carried on in Dr. Wollan's section of the General Physics Division.

The pocket chamber situation seems now to be on a fairly sound basis. Of course a more severe test will come in more humid weather. Mr. Lester has done a good job organizing the work and Mrs. Nachtrieb is learning rapidly to carry it on. 164 chambers are now in service at New Chemistry, Site B, West Stands, Eckhart, and Kent Laboratories. Readings are made daily and permanent records are kept. 259 chambers have been purchased which originally had a leakage less than 10 milliroentgens per day. There is one discouraging feature. 14 of the reserve supply of 90 now have a leakage rate of more than 10 milliroentgens per day - 4 more than 200 milliroentgens per day. This slow deterioration can in time impair the supply to a point where it will be inadequate. The calibration while not bad leaves something to be desired. A test of 10 chambers with small leakage showed they were on the average 20 per cent low when exposed to gamma-rays from Radium in equilibrium.

Film meters continue to give significant protection. Mr. Goldstein has turned over to Mrs. Nachtrieb a going system which will be improved considerably when the new badge and film become available in a few weeks. Better control of development conditions would now be possible if the new General Electric Impermo thermostatically controlled tank had not arrived in a damaged condition. This may mean a delay of from four to six weeks.

1118626

Further tests have been made on DuPont film NS2-506 which behaved somewhat erratically in previous tests. This was done at the suggestion of Dr. Stone who thought this film might be useful up to 5r in contrast with SB1-502 which is reasonably linear to 2r and had been selected tentatively. Both films have desirable features and may be used. Figure I shows the results of the recent tests on NS2-506. The circles and crosses signify separate runs. Conditions will be more favorable for smooth and reproducible curves when the film is obtained in light tight packages of the right size. Now it has to be cut from large sheets and put in home-made packages. Many tests have been made of the wave-length dependence of DuPont films. Figures II and III are typical of the results. The data was taken at Site B. The exposures for many more studies have been made at the Chicago Tumor Institute where the machine goes up to 400 KV. It is expected that the data when completed will settle the matter on films. Figure II indicates that SB1-502, with a 1 mm Ag filter, could be used on wave lengths from 70 KV to 2 MEV with an uncertainty of about 25 per cent. Figure III shows the wave length dependence from 50 KV to gamma-ray wave lengths with the same filter. Cadmium will probably be used because of its availability.

Weekly reports are now given to Dr. Nickson of people receiving .6r or more for the week. In the last report the agreement between chambers and films was surprisingly good - better than 1 per cent. One cannot avoid admitting that this was somewhat fortuitous. The chamber readings are gone over daily and the badge readings weekly. Surveys are made immediately at places where tolerance conditions are approached. Surveys have been made at the Cyclotron, Ingleside, Site B, West Stands and Eckhart. The Cyclotron and the Vandergraff are the most critical places. As a rule reasonable precaution is taken. Also a survey of the Cyclotron Laboratory has been made at the University of Michigan. The exposure rates during 1μa operation - large for this machine - ranged from .00065r/hr. to .16r/hr. Workers should have no difficulty avoiding overexposure. A complete report of the survey has been given to the people concerned.

The Radium sources have been unusually "active" this month. Approximately one-third of them have changed hands one or more times.

Two developments in Dr. Wollan's section are of interest. O. G. Landsverk has constructed a compact electroscope of the Lauritsen type with a built-in timing mechanism which would be very serviceable for quick detection of radiation. H. W. Vandersall has well underway a chamber for Victoreen condenser r-meters which should increase the accuracy of determining the values of neutron exposures. The chamber now in use has a bakelite wall with a graphite coating. This latter feature makes it difficult to determine the effect of the wall. The new chamber will have conducting walls of known composition, e.g. C. H.

1118627

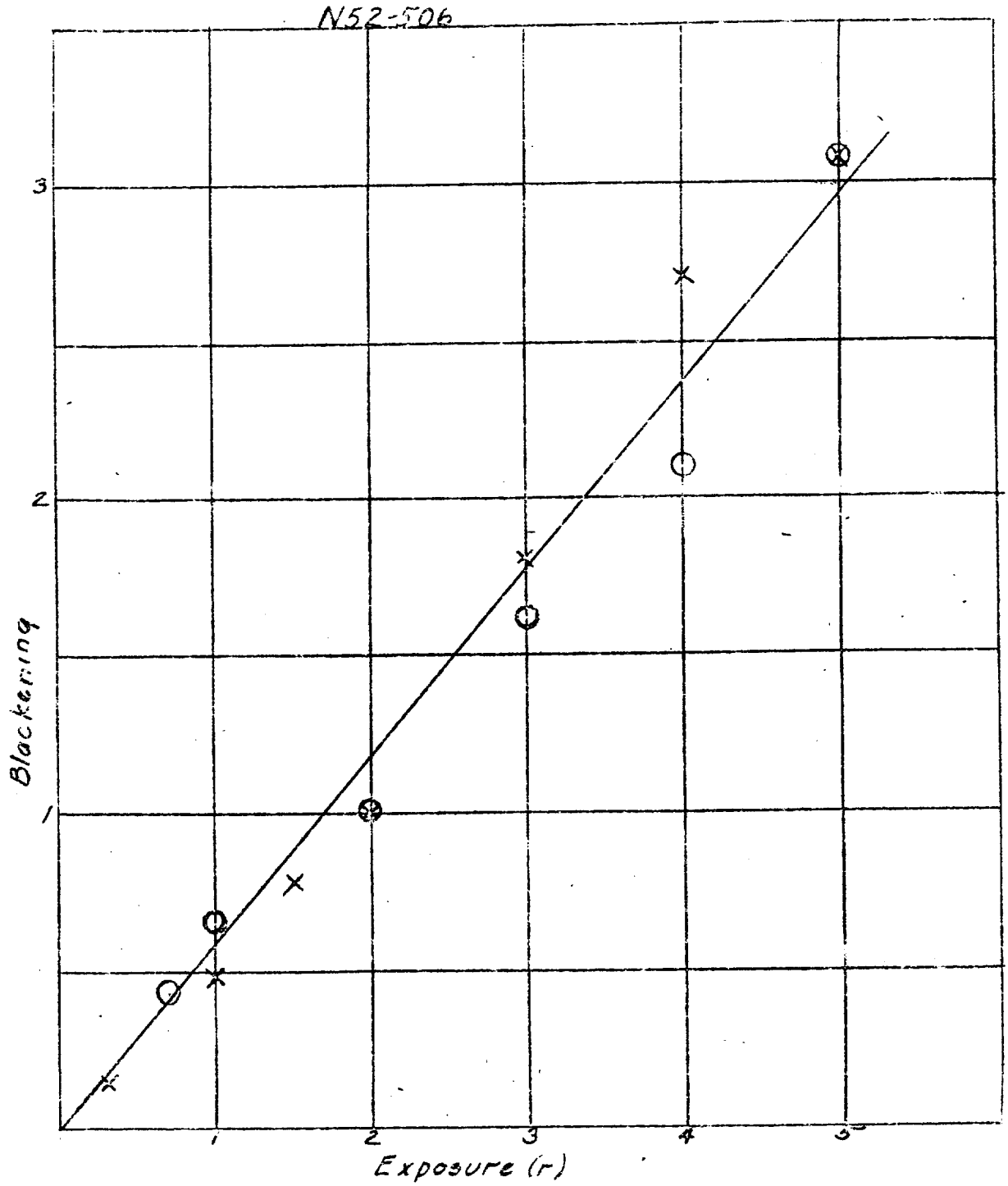


FIGURE I

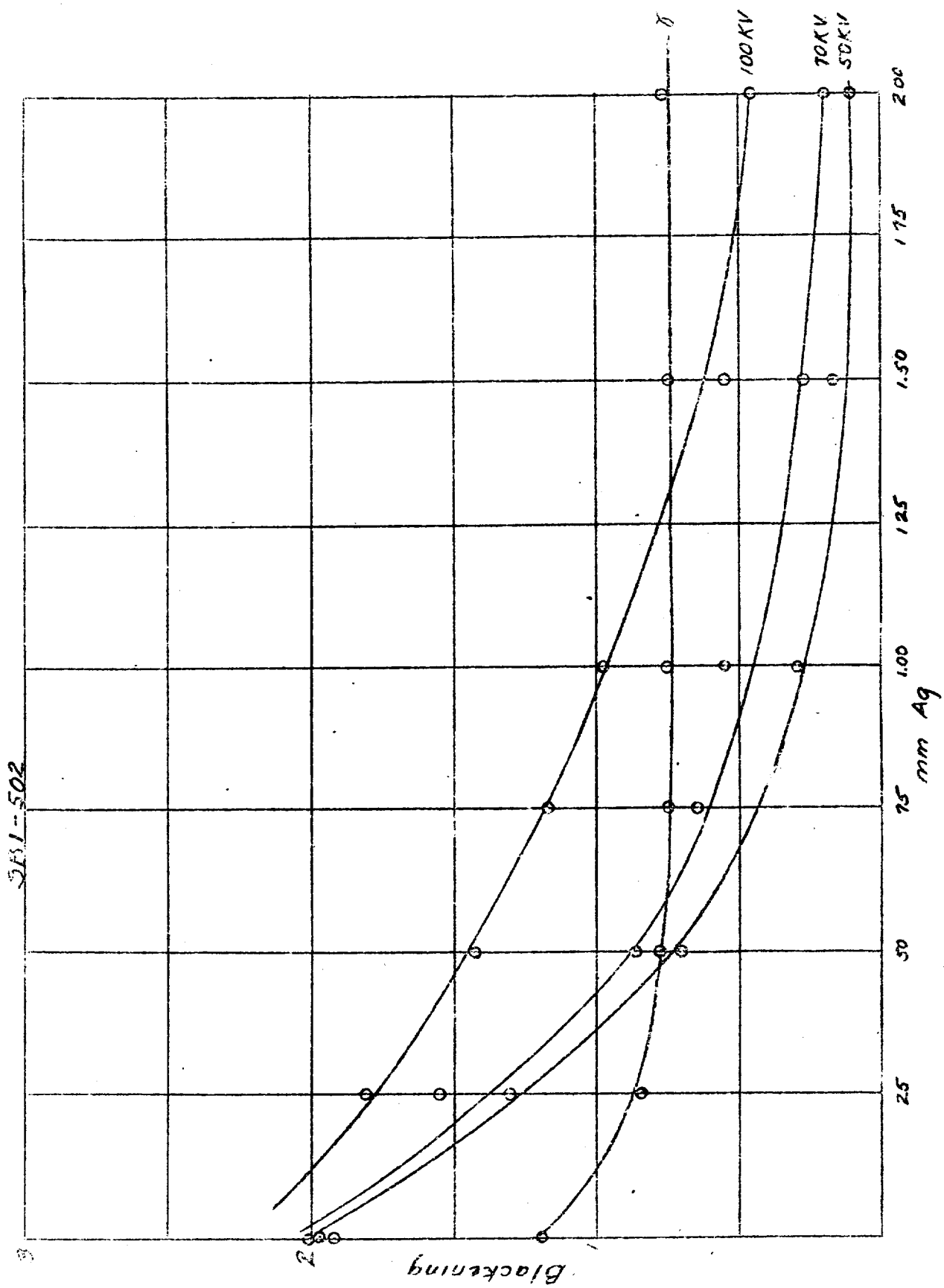


FIGURE II

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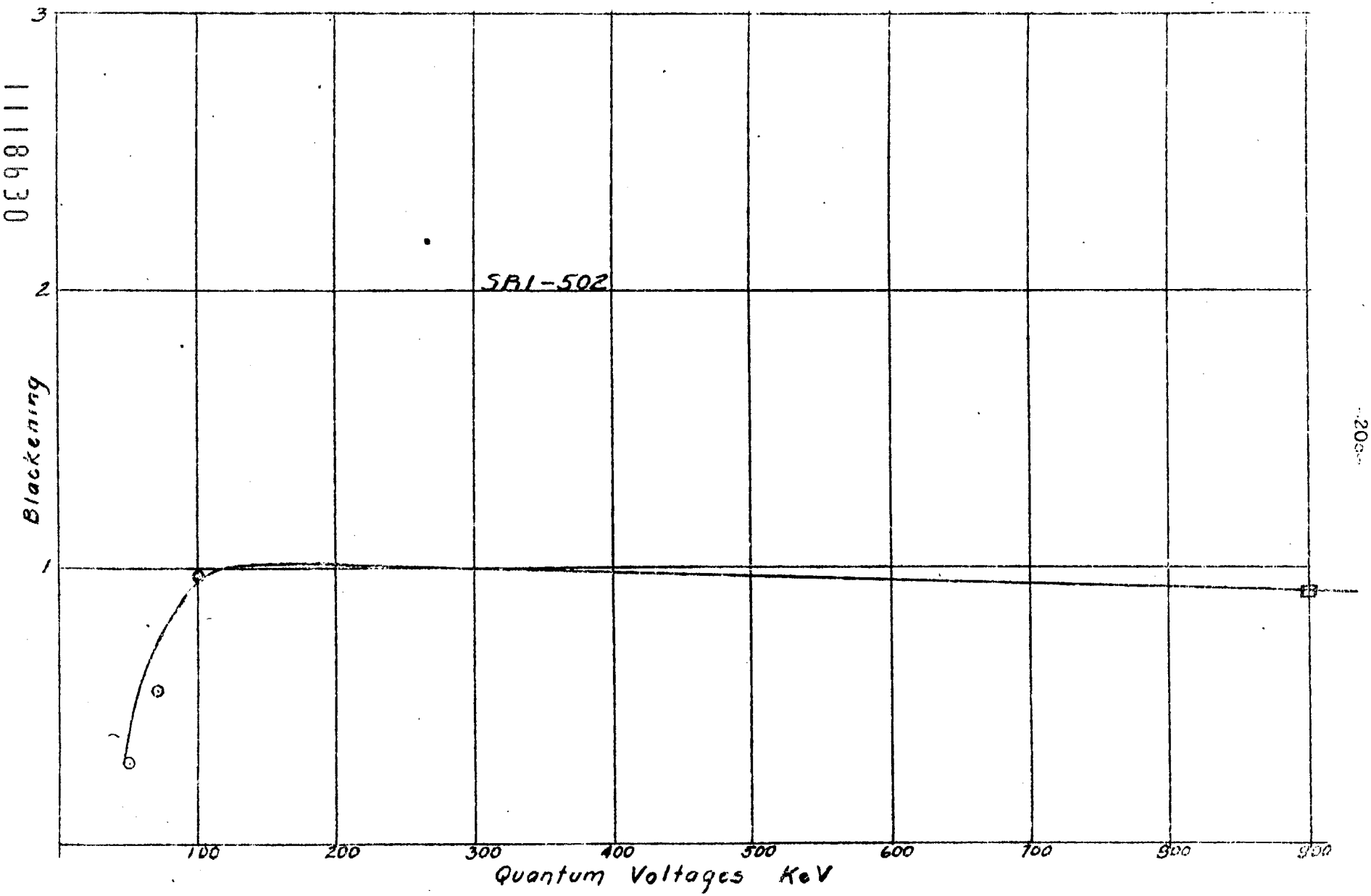

FIGURE III

1118630

D. METEOROLOGY SECTION

P. E. Church, Section Chief

1. Site W

The work on observing the wind pattern vertically and horizontally at Site W is still being carried forward. In addition, the crew has been observing and recording the river stage and river temperatures daily. Still further, they have been supplying weather information of various sorts that have been requested by the proper authorities there.

Owing to the large amount of data now being received from Site W, it was necessary to employ another meteorologist to evaluate the data. That part of the program is being carried forward here at the University.

Before the end of this month, three new techniques for observing certain weather data will be attained.

2. Site X

A portion of the meteorological equipment to be established at Site X is in operation.

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E. CLINTON LABORATORIES

I. MEDICAL DIVISION

S. T. Cantril, M.D. - Director

1. Personnel

Since the report of October 1, 1943, personnel added to the Medical Staff are:

R. S. Stone, M.D. - Associate Director, Clinton Laboratories
Miss Nina Melgui - Medical Technician
Miss June Hoback - Laboratory Helper

2. Building

The Medical wing of Building 719 is now completed with the exception of telephone installations, which are now beginning to appear and will be of considerable aid. The Clinical Laboratory is now in use.

When Construction Medical Department completes its activities, the x-ray equipment will be moved to Operations Medical Department for emergency use.

3. Medical Activities

(a) Pre-employment physical examinations.
As of September 25, 1943, 289 employees had been examined according to the program as outlined in the previous monthly report. Since the above date additional examinations, as of October 18, 1943, have been:

New employees	94
Transfers	92
Total examined to date (289 - 186)	475
Total plant personnel as of Oct. 18, 1943	595

(b) Typhoid and Smallpox innoculations:*

Transfers innoculated and/or vaccinated in Chicago	103
New employees or other transfers innoculated and/or vaccinated	145
Employees not requiring innoculation and/or vaccination by reason of previous sufficiently recent protection	26
Total personnel protected	274
Personnel unprotected to date	321

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*To date we have encountered only one severe local reaction from smallpox vaccination which has subsided satisfactorily under treatment.

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(c) Dispensary

Carring for minor injuries and ailments, assisting in innoculations and vaccinations and caring for equipment occupies the full time of two nurses at the present time. The third nurse has been employed for training and a fourth will be employed shortly so that 24 hour first aid service will be available. In the meantime, Construction Medical Department is giving first aid to Operations personnel on the night shifts.

(d) Hematology

Initial complete blood counts done on new employees and transfers are complete to date. Monthly counts have begun on operations groups working for sufficient time. We have encountered two instances of low white blood count.

1. 4400 - Chemist transferred from Chicago and who was engaged in work on active samples while there. This is now rectified.

2. 4100 - Normal differential and red blood count. Maintenance helper newly employed. In all other respects the man is healthy, and we have accepted him for employment with periodic (monthly) blood counts to follow.

Four instances of mild secondary anemia have been encountered on new personnel. These are receiving iron therapy. The cause in most cases has been nutritional.

Platelet counts have been started routinely on the men in:

1. No. 26 - Mr. Perlman's Section - Chemistry
2. 16 - Mr. Coryell's Section - Chemistry
3. 6 - Mr. Shapiro's Section - Chemistry
4. 4 - Mr. Parker's Section - Health Physics
5. 5 - Mr. Cohn's Group - Biochemistry
6. 4 - Mr. Zirkle's Group - Biology
7. 10 - Mr. Newson's Section - Physics
8. 14 - Mr. Sinclair's Section 100 area operations
9. - Controls

4. Special Hazard Activities

(a) Considerable time has been spent in cooperation with the Sub-Committee on Activity Hazards in preparing a policy for adoption by the Central Safety Committee. When adopted these procedures will form part of the Safety Manual for Operations.

(b) Cooperation has also been given to the Sub-Committee on Injury Procedure in classifying and recommending for adoption by the Central Safety Committee, the possible injuries or time loss due to special hazards.

(c) Since the arrival of Mr. Parker's Section surveying and meter distribution have been taken over by them, as contained in Mr. Parker's report.

The hand monitoring program is reported by Mr. Parker and initial results summarized. It would seem that this program may become quite extensive as operations progress if surveys continue to show contamination significantly above background. We are still of the opinion that the possibility of damage to skin of hands is one of the most important and incidious hazards to be closely watched.

5. Work for the Coming Month

(a) Continuance of pre-employment examinations, first aid supervision, etc.
(b) Continued survelliance of special hazards in conjunction with Mr. Parker's Section.
(c) After all Chicago personnel have been transferred, it will be of interest to compare the blood counts of this group (though relatively small) with blood counts of personnel from other areas and occupations.
(d) Periodic re-examinations will begin as operations progress.

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CLINTON LABORATORIES

II. HEALTH PHYSICS

H. M. Parker, Section Chief

This report covers the period from October 5th to October 20th. A large fraction of the time of the section has been spent in searching for equipment and in assembling such as could be found.

1. Fast Neutron Meter

K. Z. Morgan has reassembled the meter and has made some changes in the method of filling the chambers so that it can be done under water. With Chang filled with methane at 165 lbs/sq. in. and Eng filled with argon at 114 lbs./sq. in. the system is balanced and saturation for gamma rays is reached at 550 volts. A mixed source has not yet been available for the neutron saturation curve.

2. Pocket Chambers

Three technicians have been trained to use the minometers. The principal hold-up is still the availability of chambers. As far as possible two chambers have been used on each man with notable reduction in the number of meaningless records.

Caps have been ordered to fit over the present chamber numbers. In this way the visible number will be the same as a man's badge number. In the measuring room the caps can be changed around so that the same chamber is not repeatedly given to one man.

3. Survey Work

The only meters available are five Lauritsen type meters from Hansen Company and four assembled here for temporary use by W. P. Overbeck. These have been calibrated with gamma radiation.

4. Integrons

Five integrons are available. Two have been calibrated with gamma radiation, using a 25 mg. source at 1 meter.

	Calculated mr/hr.	Observed mr/hr	Set at
#235-3	21.1	19.5 - 28.0	21.7 mr/hr.
236-6	21.1	19.5 - 27.5	21.7 mr/hr.

The meters were set slightly higher than the calculated setting to allow for possible scatter in the tests.

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The wide range of calibration adjustment means that the control must be securely locked at the proper position or that frequent checks will be required. The automatic 8-hour recharge gave some trouble, which the instrument shop has corrected.

5. Water Sampling

Water sampling of beta and gamma radiation will be carried out by F. B. Vaughan's section with our cooperation. Provisionally solutions of T-nitrate have been prepared of standard B-activity, measured by thin wall chambers. These can be used in the counter for testing contamination due to hard beta rays. Other standards will be made later for soft radiation. Gamma ray emmitters can be calibrated either with T-nitrate solutions or with radium. Again there may be an error at the present time for soft radiation

More refined methods of calibration can be introduced later. For the present, if any tested water indicates high activity by counter methods, it would be checked by ion chambers.

6. Hand Contamination

A program of testing hands for possible beta-contamination on a weekly basis has been initiated. No attempt has yet been made to express the results in terms of r/hr. because this will depend on the area of skin contaminated. Equipment is being built to readily determine this area. For the present, the results are quoted either as counts per minute or as number of times background. The background is currently 20 c/m. A count of 500 c/m is considered bad. The estimated count corresponding to 100 milliroentgens per day is 100 c/m/cm^2 skin, or about 2500 c/m to 5000 c/m from a uniformly contaminated hand in the present counter.

The first 100 men gave the following results:

Counts per min.	No. of times background	% occurrence
100	5	17
200	10	12
500	25	9
2000	100	2

7. Work for Coming Month

Setup of pocket meter organization and surveys incidental to start up will probably occupy most of the time. Hand tests and water tests will be extended. The fast neutron measurements will be made.

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CLINTON LABORATORIES

III. BIOLOGICAL SECTION

H. J. Curtis - Section Chief

During the month six members of the Chicago group were transferred to Clinton Laboratories. The main building was turned over from Construction on October 8th. The animal farm is functioning and laboratory work has been started. It is expected that most of the experiments will be ready for the start of operations.

1. Gamma, fast n and slow n effect on Rabbits and Mice: R. F. Zirkle, John Raper, G. E. Stapleton

The preparations for the work on the effects of external radiations is now fairly complete. A phantom is being constructed to hold 75 mice, the atomic composition of which is approximately the same as that of tissue, so that statistically significant numbers of animals can be run in a relatively short time in a small space. Special cages, constructed of plastic impregnated with boron carbide, are being constructed to absorb slow neutrons, so it will be possible to distinguish between the effect of gamma rays, slow neutrons and fast neutrons.

2. Biological Monitoring: H. J. Curtis, M. Day, L. B. Morris.

The equipment for monitoring the pile stack gases is now complete and ready for testing, which should be complete by the time of start up. The cages for the out-door monitoring are now being tested in Chicago.

3. Xe Exposure: H. J. Curtis, F. E. Painter.

The problem of finding a suitable method for the manufacture of Xe is still far from solved. The method involving the dissolving of very fresh metal, extracting the gas, holding the solution for 40 days and returning to the plant is probably satisfactory, but very expensive. The method involving passing air through oxide in the pile produces only relatively small amounts. A combination method is being considered which would use the oxide method to maintain the tolerance experiments and the dissolver to run the lethal experiments. The advantage would be that the dissolver would run only occasionally, and the produce discarded, in which case HCl could be used as the solvent. This would enormously simplify the construction and operation of the factory. Plans are progressing for an addition to the Xe laboratory, which has been necessitated by the increased numbers of animals required for exposure.

4. F.P. Extraction:

The extraction of F. P. in pure form has turned out to be a much harder job than was anticipated. Since the work in Chicago has shown that it will not be possible to use wastes from the extraction plant, it will be necessary to build a small extraction and separation plant to do this. Very meagre facilities for hot work have been provided in the present Chemistry Laboratory, so a new building is required. Some of the chemistry group are also interested in such a laboratory, so it is a cooperative effort. Consider-

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able time has been spent on the design of this laboratory, and on the design of methods for performing the various manipulations by remote control. In addition, work is in progress to determine better separation methods. For this purpose, 10 lbs. of nitrate from the recent St. Louis bombardment has been received and is being processed to give tracer amounts of material. In the meantime, space has been made available in the Chemistry Building so that operations can be made behind temporary lead walls on amounts up to 1/2 curie of activity. These facilities will be used until the new building is complete.

5. Work for the Coming Month

In the coming month it is expected that the plant will start and the biology program can start. Rabbit and mouse exposures will be the first to start. The equipment in the pile stack building will be tested and put in service. Animals will be placed around the grounds and buildings for monitoring. The separation work will continue, and it is hoped that the building plans can be turned over to the design department very soon, which will allow more effort to be put on the actual separation.

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I. N. C. I. - R. R. Spencer, Director

BIOLOGICAL ACTION OF GAMMA AND X RADIATIONS

E. Lorenz, W. E. Heston, M. K. Deringer,
M. B. Shimkin and A. Eschenbrenner

Abstract

The blood picture of mice having received approximately 1600 r up to the present at the rate of 8 r per 8 hours per day shows a decrease in RBC and WBC. All other experimental mice exposed for the same length of time but at lower rates (4 r, 2 r, 1 r, 0.1 r, per 8 hours per day) show an essentially normal blood picture.

The blood picture of guinea pigs having received 1600 r up to the present at the rate of 8 r per 8 hours per day shows considerable decrease in all counts with a terminal relative lymphocytosis and aplastic anemia. Four of the original 18 guinea pigs are still alive. Additional acute exposures given to some of these guinea pigs of 12.5 or 50.0 r respectively (administered in 5 hours) are of no influence upon the terminal picture. Guinea pigs having received 800 r up to the present at the rate of 4 r per 8 hours per day show a decrease in red and total white count. Guinea pigs on the other levels show an essentially normal picture.

Male mice exposed to 1600, 1000, 800, and 600 r on the 8 r per 8 hour per day level 50% of which were autopsied and 50% of which were bred after exposure showed testicular damage increasing with dose. In spite of this they produced so far normal litters (experiment not completed for 1600 r).

Male mice exposed to 1000, 800, and 600 r on the 4 r per 24 hour per day level showed no testicular damage and produced normal litters. These two experiments indicate the importance of the rate of administration of the dose.

Female mice exposed on different levels (8 r, and 4 r per 8 hours per day and 8 r, 4 r, 2 r, and 1 r per 24 hours per day) to doses ranging from 600 to 100 r gave birth to normal litters and their ovaries showed no striking differences from normal ovaries. (Experiments partly incomplete as to litter size and histological studies of ovaries).

1. Continuous exposure for 8 hours daily.

Daily doses 8 r, 4 r, 2 r, 1 r, and 0.1 r.

The experiments are progressing according to schedule. The general blood picture of the experimental animals shows no appreciable changes from that reported last month. One guinea pig of the 8 r level had to be killed as it showed a rapid drop in red count and hemoglobin. Grossly intussusception was found in addition to the changes observed generally in this group of guinea

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pigs and described previously. One guinea pig died and showed at autopsy hemorrhage into the abdominal cavity.

Some of the rabbits of all levels as well as control rabbits received the additional acute exposure to x-rays of 12.5 or 50.0 r respectively. No striking effects of these additional exposures upon the blood picture were observed.

All animals show normal appetite and weight.

The breeding experiments gave the following results:

Males - 8 r level

Total dose 1600 r Number of males - 16 8 mated, 8 autopsied	Females to which irradiated males were mated immediately after irradiation are not pregnant at 2 weeks after mating.
Total dose 1000 r Number of males - 16 8 mated, 8 autopsied	Males were mated two months after removal from field. Average litter size - 8.4. (Incomplete)
Total dose 800 r Number of males - 16 8 mated, 8 autopsied	Males were mated two months after removal from field. Average litter size - 8.6.
Total dose 600 r Number of males - 16 8 mated, 8 autopsied	Males were mated on removal from field. Average litter size 7.5. Four of males remated one month later. Average litter size - 9.1.

Histological findings:

Males which had received 1000 r and were autopsied one month after being removed from the field showed testicular damage. Many of the seminiferous tubules were necrotic, some nearly void of spermatogenic cells. In spite of this damage the mated males produced normal litters. Few normal appearing sperms were present in the epididymis and immature spermatogenic cells were numerous. Males which had received 800 r and autopsied one and one-half months after being removed from the field were within the limits of the controls. However, males receiving 600 r and autopsied at one month after removal from the field showed a few immature spermatogenic cells in the epididymis. This difference between the 600 r and 800 r groups was possibly due to more recovery in the 800 r group.

Breeding results: Females - 4 r level

Total dose 500 r Number of females - 16 Mated 28 days after removal	Average litter size 6.5 (Incomplete) Controls - Average litter size 8.6

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Total dose 400 r Number of females - 16 Mated 28 days after removal	Average litter size 7.6. Half of females remated. Average litter size 7.7 (Incomplete). Controls - average litter size 8.6.
Total dose 300 r Number of females - 16 Mated 28 days after removal	Average litter size 9.3. Two females remated. Average litter size 8.0 Controls - Average litter size 8.7.

8 r level

Total dose 500 r Number of females - 16 Mated 28 days after removal	Average litter size 5.8 (Incomplete) Controls - Average litter size 8.4.

2. Continuous exposure for 24 hours daily:

Daily doses 8 r, 4 r, 2 r, 1 r, and 0.5 r.

Breeding results: Males - 4 r level

Total dose 1000 r Total number - 16 8 mated, 8 autopsied	Average litter size 9.0. Four remated. Average litter size 10.1
Total dose 800 r Total number - 16 8 mated, 8 autopsied	Average litter size 7.3.
Total dose 600 r Total number - 16 8 mated, 8 autopsied	Average litter size 7.4.

Histological findings:

Slides of the testes and epididymes of males receiving 1000 r, 800 r, and 600 r and autopsied at time of removal from the field were within the limits of the controls.

Breeding results - Females

In addition to data presented in previous reports the following can be added:

8 r level

Total dose 600 r Total number - 16 Mated 28 days after removal.	Average litter size 7.5. Controls 8.6.

2 r level

Total dose 400 r Total number - 16 Mated 28 days after removal	Average litter size 5.7. Controls 6.1.

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Histological findings:

Ovary slides have been observed of females of the following groups which were autopsied at time litters were weaned:

8 r level - Total dose 300 r, 400 r, and 500 r.
4 r level - Total dose 100 r, 200 r, 300 r, and 400 r.
2 r level - Total dose 100 r, and 200 r.
1 r level - Total dose 100 r, and 200 r.

No striking differences have been observed between these ovaries and those of the controls.

3. Continuous exposure for 8 hours daily plus daily acute exposure of 5 r given in one hour:

These experiments are being continued. The blood picture is still normal, having received a total daily acute exposure of approximately 750 r. Two were killed accidentally and autopsied, grossly the organs and tissues appeared normal. Three female mice of one of the control experiments, removed after a total exposure of 300 r and mated immediately to normal males gave an average litter size of 7.7. Three more mice, removed after a total exposure of 400 r were mated to normal males immediately after exposure. Two so far have shown vaginal plugs and one of the mice is pregnant.

4. Pathology:

Nothing new to report.

5. Hematology:

The present status of the animals exposed to higher doses is as follows:

Group	Daily dose 8 hrs. exp. r	Total dose to date, r (approx.)	RBC No. x 10^6	WBC No.	PMN Percent	Platelets No. x 10^3
			Guinea Pigs			
A	---	---	5.35	9,100	23.9	575
F	2	400	5.26	6,750	27.4	---
G	4	800	4.88	5,050	30.4	580
H	8	1600	3.71	4,000	19.0	179
			Mice			
A	---	---	10.59	4,760	20.0	1,183
G	4	800	9.55	4,350	19.1	---
H	8	1600	8.80	3,090	22.8	936

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The differences in R.B.C. and W.B.C. of untreated mice and mice exposed to 8 r per day are significant ($P < 0.01$). Tests of significance were not done on the guinea pigs, but it is obvious that the red count and white count decrease with increased dosage, but that the neutrophils and platelets fall rather sharply with 8 r. Some of the guinea pigs of the highest dose group had red counts of 1 to 2 million, almost no neutrophils (1-4 percent) and less than 100,000 platelets a few days before being sacrificed.

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Associated Projects

II. Radiation Laboratory, U. of C.

J. G. Hamilton & Associates

Technical Progress Report on the Metabolic Studies of Fission Products

1. Yttrium (Y^{86})

Intramuscular studies at one, four, and sixteen days indicated that next to bone; kidney, liver and spleen were the most active. Their Y^{86} content ranged from ½ that of bone at one day to from 1/16th to 1/30th at sixteen days. The excretion pattern for the intramuscular groups was comparable to the corresponding intraperitoneal experiments. Two series of lung studies have now been completed through thirty-two days and the degree of pulmonary retention varied considerably between the two series at corresponding intervals. Further studies will be necessary for significantly quantitative results.

2. Radio-Autographic Studies

Bone radio-autographs of Y^{86} have been made and the preliminary results suggest a very similar behavior to that of Strontium in that deposition at four days is primarily in the periosteal layer and epiphiseal regions. Lung radio-autographs of Y^{86}, Ru^{105}, Cb^{93}, Cs^{135}, and Pr^{143} are being prepared.

3. Columbium (Cb^{93})

A new sample containing 250 microcuries of Cb^{93} free from carrier and with less than 3% of radioactive impurities has been prepared. A large series of intramuscular, oral, and intrapulmonary studies are now under way with this preparation.

4. Cesium (Cs^{135})

Forty microcuries of Cs^{135} free from carrier and containing less than 5% of radioactive impurities has been isolated. Tracer studies which include a large series of intramuscular, oral and intrapulmonary studies is now under way. Preliminary results indicate the metabolic behavior of cesium resembles that of Potassium in that the Cs^{135} was rather evenly distributed throughout the tissues with no striking selective localization.

5. Barium (Ba^{140})

The $PbSO_4$ procedure for isolation of Ba^{140} free from carrier and Sr^{89} proved to be unsuccessful. Ba^{140} and Sr^{89} without carrier were isolated together and the mixture turned over to Professor Chaikoff and his associates. They have initiated a large series of oral and intramuscular tracer studies extending to thirty-two days to supplement the earlier Ba^{133} experiments which could only be carried out for eight days. They have developed with the assistance of Drs. Overstreet and Jacobson a satisfactory method for isolating from the tissues the Ba^{140} free from Sr^{89}.

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6. Xenon (Xe^{127})

Tracer studies with four animals with Xe^{127} have been done to check the preliminary experiments done last fall and were found to be in substantial agreement.

7. Praeseodymium (Pr^{143})

A sample of Pr^{143} free from inert rare earth carriers and containing less than .5% of radioactive impurities has been prepared. Radio-Cerium free from all other radioactive contaminents was isolated with 5 mgm of Cerium carrier from a deuteron bombarded Uranium target and the Pr^{143} allowed to grow from the Ce^{143}. The Pr^{143} was then separated without carrier by the iodate method.

A large group of intramuscular, oral, and intrapulmonary experiments have been initiated and preliminary results indicate that the metabolic pattern of Pr^{143} is quite similar to that of La^{140}. In both the intramuscular and pulmonary experiments with Pr^{143} at one and four days the uptake by the liver was approximately equal to that of bone, and from 70% to 80% of the absorbed Pr^{143} was accumulated in these two organs. This tendency was not present with Y^{86} but did occur with La^{140}.

8. Chemical Preparations

From the neutron bombarded sixty pounds of $UO_2(NO_3)_2 \cdot 6H_2O$ we have already prepared carrier free purified Cb^{93}, Ru^{105}, and Cs^{135}. Samples of carrier free purified Zr^{93} and Ce^{140} are to be prepared shortly. The presence of several hundred milligrams of Calcium in the sixty pounds of nitrate made it undesirable to use the carrier free Sr^{89} for tracer studies.

9. Decontamination Studies

Further experiments are now in progress to study the inhibition of absorption by agents such as sodium phosphate, sodium bi-carbonate, columbium oxide, and tricalcium phosphate following the oral administration of Sr^{85} without carrier. The effect of high and low calcium diets prior to the administration of Strontium orally is now being investigated. The leaching effect of large and frequent doses of inert Strontium is being studied in animals which have previously received Sr^{89} by intraperitoneal injection.

10. Emanation Studies

The measurements of the tissues from the last emanation experiment have been completed. This last experiment was highly successful in that, for the first time, reasonably accurate assays were possible on most of the tissues. The source was a deuteron bombarded Uranium plate and the emanation was removed by a stream of helium flowing at such a rate that the mean time between the formation of a fission particle and its transportation to the animals was approximately 20 seconds. The mean time that such a particle remained in the chamber enclosing the animals was approximately 100 seconds. During the four hour exposure each of the three animals acquired by inhalation approximately 10% of the total number of radioactive atoms present in their environment.

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One animal was sacrificed immediately and the tissues assayed within 40 minutes and again eleven days later. Initially, on a per gram basis, the order of activity was: Trachea, lung, kidney, fat, and finally bone. After eleven days the order of activity was upper respiratory tract (est.) trachea, bone, and finally lungs. The other two animals were sacrificed four days after the exposure. The tissues were measured eleven days after the exposure and 93.3% of the activity in the animals was found in the skeleton. The thyroid was the next most active tissue and had 1/10th the activity of bone per gram. Lung was next with 1/30th of the activity per gram of bone.

The small total uptake by the thyroid in terms of actual counts suggests that very little iodine was present in the emanation and that most of the activity arose from Krypton and Xenon and their active deposits. The activity of the inhaled gas mixture at the time of exposure was estimated to be approximately $5X10^{-3}C\ L^{-1}$. A more precise value will be available when assays of the active deposit has been completed. The lungs were estimated to have received roughly 100 r during the four hours. Lung sections showed no observed radiation damage.

11. Projected Studies for the Next Two Months

Tracer studies are to be continued with Krypton, Yttrium, Columbium, Cerium, Barium and Praeseodymium. Experiments will be started with Tellurium. Tracer studies with Mo, 43, Rh, Sb and Pa^{233} will be initiated if the possible hazards from these radio elements make such investigations desirable.

Intramuscular tracer studies, to supplant the less accurate corresponding intraperitoneal experiments, will be done with Cerium. The Zirconium (Zr^{89}) tracer studies which cover a period of time up to sixteen days will be extended with Zr^{93}. Emanation experiments, radio-autographic and decontamination studies are to be continued.

It is anticipated that by January 1, 1944 we shall have a complete quantitative survey of the metabolic picture of each of the long lived fission products which together comprised over 99.9% of the total energy dissapation of the fission products remaining in a pile operated for thirty days and followed by twenty-five days cooling.

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