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A. H. Compton - Project Director
R. S. Stone, M.D. - Associate Project Director for Health

* * *

METALLURGICAL LABORATORY

S. K. Allison - Laboratory Director

* * *

HEALTH DIVISION

R. S. Stone, M.D. - Director
C. J. Watson, M.D. - Associate Director

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* * *

NATIONAL CANCER INSTITUTE

R. R. Spencer, Chief

REPORT FOR MONTH ENDING JANUARY 22, 1944

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ABSTRACTS

A. Biological Research

A significant decrease of lymphocytes is found in rabbits after a 50 r single dose of x-ray. A significant retardation of growth is observed in rabbits after a single 100 r irradiation. The completion of the histological examination of rabbits after 800 r emphasized the damage to lymphoidal tissues. Nearly 60 percent of injected $Ba^{140}La^{140}$ has been accumulated by the skeleton at one week and remains unchanged at three weeks. Considerable activity is found in other organs. The lethal level of these isotopes is about 3 mC/Kilo for mice. The oxide Xe generator has been installed in the Clinton pile for test.

B. Radiation Measurement Section

The general reliability of pocket meters is discussed. Counting of contaminated hands is now an established routine. The method is used also on gloves. Dr. G. Failla, consultant, came to the laboratory. Consideration was given particularly to the air in the pile building at the Argonne. A hydrogen filled survey meter has been tried out at the Argonne pile. The need for recalibration of instruments under more favorable circumstances is pointed out.

C. Meteorology Section

Dr. Church reports further studies on meteorological conditions at Site W.

D. Clinical Medicine and Medical Research

The effect of x-rays on the SH- group of proteins was studied with denatured egg albumin and native myosin. The former exhibited a reduction of SH- groups equivalent to 14% after 3000 r. The presence of catalase had no effect on the destruction of SH- groups by x-rays, nor did x-ray have any effect on the activity of catalase. X-rays produced an increase in the SH-groups of native myosin thought to be due to a partial denaturization of the protein. Further studies will be carried out using careful temperature control. Electrophoretic analysis of the serum proteins after x-rays in one human patient indicated an increase in the γ globulin. 154 pre-employment physical examinations were performed. 800 individuals had a total of 3067 clinical laboratory examinations. A summary is included. Five individuals were thought to have abnormal blood counts on the basis of radiation or tuballoy. Four of these were in Mr. Cunningham's group. Fifteen special irradiation exposure surveys were made during the month. Fifteen persons were referred to special clinics for study. Resurveys of Site B (room 108 and 130) were done and recommendations reiterated. Recommendations for improved ventilation in Ryerson 59 were made because of the lead hazard. Gross contamination of laboratory table tops with radioactive materials was found in Room 10, New Chemistry. Proper recommendations have been made. Personnel in New Chemistry are placed on weekly schedule of hand counts. The pigment metabolism and liver function studies on experimental animals as well as Metallurgical personnel is continuing. The toxicity studies with tuballoy are progressing.

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E. Associated Projects

California Project

Tracer studies with Cesium and Barium have been completed and the detailed report concerning these two long-lived fission products will follow shortly. Tracer work with Yttrium, Columbium, Zirconium, and Cerium are being continued, and will be initiated with Tellurium following the isolation of Te^{121} free from carrier. Radio-Autographic, emanation, and decontamination studies are being continued. A series of experiments on radioactive dusts and smokes has been initiated and preliminary experiments with a zinc chloride smoke containing the unseparated fission products revealed the metabolic behavior of this smoke following inhalation in rats to be similar to that noted following the direct administration into the lungs of Uranium free solutions containing the unseparated fission products. Studies with Uranium smokes are now under way. The purpose of this work is, of course, to evaluate the possible hazard arising from a serious disaster to an operating plant.

N. C. I.

The blood picture of mice having received approximately 2500 r up to the present at the rate of 8 r per 8 hours per day is essentially the same as that reported last month (slight decrease in RBC, WBC and platelets.) All other experimental animals exposed for the same length of time but at lower rates (4r, 2r, 1r and 0.1r per 8 hours per day) show a normal blood picture as compared with that of the controls. Four animals of the 8 r per 8 hours group were autopsied during the month due to moribund condition. 3 showed malignant lymphomas and one reticuloendotheliosis (dose approximately 2300-2500r). One animal of the 2r per 8 hour group was autopsied during the month due to moribund condition. It showed grossly enlarged spleen and lymph nodes (dose approximately 600 r).

The blood picture of the guinea pigs exposed since March, 1943, is essentially the same as that reported last month: Decrease in hemoglobin, red count, platelets and white count in the animals of the 8r per 8 hour level and 4r per 8 hour level. All other experimental animals on the 2r, 1r and 0.1r per 8 hour level and those on the 8r per 8 hour level exposed since October or November respectively show an essentially normal blood picture.

The blood picture of the rabbits is normal with the exception of the animals on the 8r per 8 hour level which show a lowered total white count:

The breeding experiments give the following additional results (see abstract of last report): Male mice exposed to 1600r on the 8r per 8 hour level were sterile for 2 and ½ months; after that time they mated successfully (average litter size 8.6 incomplete). Males exposed to lower doses (800 r and 600 r on the 8 r per 8 hour level and 1000r, 800r and 600r on the 4r per 8 hour level) gave normal litter sizes

Female mice exposed to 500r on the 8 r per 8 hour level gave slightly decreased litter size in 1st and second breeding. Female mice exposed to 800r

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on the 8r per 24 hour level gave an average litter size of 2.5 (incomplete). Two out of 3 female mice exposed to 5r per 1 hour daily and exposed to 700r are sterile so far. The third gave birth to 1 stillborn. Female mice exposed to a single whole body exposure of 300r (in 10 min.) showed a slightly decreased litter size and are being remated.

Three mice on the 8r per 8 hour level that received a total of about 2350r had malignant lymphomas, apparently arising in the thymus, with local extension and distant metastases including the bone marrow. In the males there was extreme testicular atrophy yet with a few spermatagonia remaining and in the females no follicles were seen in the ovaries. Since lymphomas are frequently observed in old mice the results are only suggestive that the lesions have been induced by radiation.

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A. BIOLOGICAL RESEARCH SECTION

K. S. Cole, Section Chief

I. Biological effects of external radiation.

A. Animal weight and survival

1. X-ray - C. W. Hagen

a. Single doses

The survival curve for rats is now based on approximately fifty animals at the critical points. Survivors have been kept for approximately three months. The mean lethal dose for the whole population is near 650 r. On the curve appended, (fig. 1), points show percent survival of each sex at each dose level. With all doses except 500 r, males are considerably less resistant than females. It is apparent that for further work, sexes must be equally mixed, or separate curves must be run for each sex.

Three rats were given 24,000 r in an attempt to determine the dose required to kill under the beam. Treatment was halted because the machine was needed. The rats died three days after treatment.

Data on rabbit weights have been compiled and plotted. They are reproduced in part in fig. 2. The points are based on weights obtained from all animals treated at each level. Curves based only on survivors are not significantly different. Change in slope of the growth curves is consistent with the severity of the initial dose. The two minima in the 800 r curve correspond to periods during which animals die, although these minima are shown in the weight curve based only on survivors.

b. Paired doses

Rats have been given single initial doses of 200, 300 and 400 r followed after 7 days by second doses of 400 to 700 r. Results are not

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yet sufficiently complete to report.

c. Daily doses

Daily exposures of rats at several levels have been continued. There have been no deaths in the 25 r and 12.5 groups after sixty treatments. Figure 3 presents the relation between daily dose and the accumulated dose for 50 percent survival. A minimum exists at 100 r. Below this value a recovery factor increases the total dose; above it the time for the injury to reach a lethal level increases the observed total dose.

Drosophila. Treatments with daily doses of 10,000 r and 20,000 r are being continued.

2. Fast neutrons - C. W. Hagen and R. D. Finkle

a. Single doses

Rabbit exposures to single high doses of neutrons at the Chicago cyclotron are being continued to give survival data.

Three animals exposed to 180 n were placed in metabolism cages two and one-half hours after the mid point of the exposure. No gamma radiation could be detected with a Lauritson electroscope placed close to the animals. The urine was collected, evaporated and the beta measured. Measurements on two samples gave a half life of 17.5 hours. From this figure and the relatively high concentration of Na in urine it is assumed that the principal activity is Na^{24}. The average activity of urine collected over a 22-hour period, corrected to the mid point of the exposure, was approximately $3 \cdot 10^{-9}$ curie/cm^3 of urine. Taking one Victoreen n as equivalent to 10^9 fast neutrons/cm^2 and the Na concentration as 0.15% the apparent cross-section is 10^{-24} cm^2. This high value as compared to $0.4 \cdot 10^{-24}$ cm^2 for the slow neutron cross-section suggests that activity may be induced in elements other than Na,

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and that no higher activity of Na will be found for a slow neutron exposure.

Under optimum conditions a count of ten times background can be obtained for 10^{-9} curie. This amount of activity in a 300 cm^3 sample of urine corresponds to an exposure of 0.2 n which is considerably above the tolerance specified.

3. External β radiation - C. W. Hagen

There have been persistent reports of eye irritation which appeared to be correlated with exposure to β radiation. A preliminary experiment is being set up to test the effect of β radiation on the rabbit eye. An approximation to a point source was prepared by evaporating 0.4 cc of a solution of Sr^{89} in a 1/8 inch depression at the tip of an iron rod. The material at the tip is covered with a thin sheet of mica. The intensity of radiation at one cm. was approximately 200 r per hour. Rabbits, held in a special restraining box, have been exposed for 1½- and 3-hour periods. There has been no clouding of the cornea and no apparent irritation of the eye.

B. Hematology - L. O. Jacobson

1. X-ray, single dose

Graphs (figs. 4 and 5) of the peripheral blood changes of the rabbit after a single dose of 50 r are presented. Previously reported curves for higher dosage are included for comparison. It will be noted that the lymphocytes are definitely depressed within 3 hours but return to normal by 300 hours. The heterophiles are not affected appreciably.

Several facts which are mentioned in the histological report on the 800 r series in the rabbit are particularly interesting because they coincide with findings observed in the peripheral blood. 1) An invasion of various tissues and especially the lymph node and spleen with heterophiles beginning as early as ½ hour and perhaps reaching its maximum at about

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3 hours in the node and 8 hours in the spleen. 2) The lymphopenia in the peripheral blood within 3 hours coincides with the marked destruction of these cells in the nodes and reduction in their transport from the nodes. The eventual return of lymphocytes in the peripheral blood coincides with the gradual resumption of formation and transport in the nodes. 3) The degenerative nuclear changes in the lymphocytes which are described histologically are seen within the first 24 hours in the peripheral blood. 4) The heterophile rise in the peripheral blood is coincident with a loss of mature forms from the bone marrow.

C. Histopathology - R. Murray

1. X-ray, single dose

The work of the past month has been primarily concerned with completion of the study of rabbits given 800 r whole body irradiation by 200 K.V. X-ray. The histopathology of bone marrow, appendix and duodenum was presented in CH 1162.

All time intervals are measured from the midpoint of irradiation. The animals were sacrificed by a blow on the head, fixed in Zenker-formol solution, sectioned in nitrocellulose and stained with hematoxylin-eosin-Azure II.

Adrenal

There are minute highly questionable changes in the nuclei of the chromaffin cells and the zona glomerulosa of the gland. The changes in fat content of the cortical cells and the chromaffin granules of the chromaffin cells are so variable in control and experimental that they are useless to determine X-ray damage in this dosage range.

Testis and Epididymis

This material is quite incomplete since ½ the animals were females.

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We have 24 hours, 72 hours and 5 day stages. At 24 hours the sperm are gone and the spermatagonia are decreased but mitoses are still present in the spermatocytes. By 5 days there are definite signs of regeneration evidenced by what are probably atypical sperm and what certainly are atypical spermatids. The connective tissue cells and fibers are swollen, the nuclei are hyperchromatic and slightly lobed at 24 hours but gradually return to normal.

Beginning at 24 hours and continuing through 5 days the cytoplasm of the interstitial cells becomes darker and the cytoplasmic edge becomes sharply marked. These cells are supposedly the source of the male hormone, testosterone, but we are unable to correlate this cytological change with changes in the secondary sex characters in these rabbits. In chickens 800 r irradiation decreases the growth of the comb in males, a delicate test for activity of the male hormones.

There are slight, but definite changes in the epididymis epithelium. The chromatin loses its fine speckled appearance. In the head of the epididymis small basophil droplets and sometimes little cysts appear in the cytoplasm of some of the cells.

Ovary and Oviduct

The cells most affected are the ova and the follicular cells. Beginning at ½ hour an increasing amount of degeneration of follicular cells, primarily of the larger follicles, occurs. Even before obvious degeneration is seen in a cell the chromatin becomes larger and heavier. In the later stages the follicular cell degeneration becomes more intensive and then includes those cells in the smaller follicles. At 48 hours, the last stage studied, the follicular cells are being replaced by a mucoid acidophil secretion. Beginning at 8 hours the chromatin of the ova is seen

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to clump about the nucleolus and this progresses till at 48 hours many ova are obviously dying. Coincidental with the changes in follicular epithelium the heterophils migrate into the follicles and then begin to degenerate by 16 hours.

In the oviduct at ½ hour there is a discharge by the secretory granules which increases greatly at 3 hours and at 16 hours the secretion is almost completely discharged. There are slight nuclear changes in the epithelial cells which resemble those in the epididymis.

Kidney

The changes are restricted to fine cytological changes in the nuclei of the epithelial cells of the tubules and ducts. The nuclei are more vesicular; the chromatin masses sharper and the nucleoli rounder. These changes are apparent at ½ hour, increase at about 8 - 16 hours and then decrease gradually. In some animals the tubular cells are most affected in others the greatest change is in the excretory epithelium.

Heart

No significant changes.

Stomach

At one-half hour from midpoint of irradiation there is complete absence of mitotic activity which is normally found at the bases of the gastric pits. Many of the cells in this region become large, pale and vacuous beginning at the one-half hour stage. At 16 hours mitoses are again seen, becoming very numerous, but many are abnormal. The vacuous cells increase in number, size and lobation. Many are definitely premitotic and mitotic stages. The principal result of the mitotic activity appears to be a marked increase in large bosophile mucous neck cells which are normally very inconspicuous. At 5 days, but more marked at 9 days, there

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is a deepening of the pits and glands and a decrease in the acid and particularly the zymogen cells of the glands. At 14 days the glands are very deep but the cells are more normal in appearance and mitoses of normal number and appearance.

The zymogenic (or pepsin secreting) cells lose their granules by three hours and undergo scattered cytoplasmic and less occasional nuclear degeneration from 8 - 14 hours. Secretory activity is returning at 9 - 14 days. Isolated parietal (or acid secreting) cells undergo degeneration from 8 - 24 hours. At the height of the resurgent mitotic activity (24 hours) occasionally mitoses are seen in parietal cells.

There is some suggestion that increased mucuous is being produced throughout the series but this point requires special stains for verification.

Pancreas

There is an increase in the occurrence of the degenerate acinar (exocrine) cells, especially at 72 hours, but there are occasional cells in the controls also. The islet (endocrine) cells show no change except a questionable increase in chromaphile substance.

Liver

There are no consistent changes in the epithelial cells of the liver, either nuclear or cytoplasmic. The lymphocytes in the C.T. are dead by 6 hours and heterophils appear here at 3 hours and degenerate by 18 hours. There are also many degenerate heterophils, in the sinuses. There is no marked phagocytic activity by the sinus macrophages but remains of dead cells, mostly heterophils, and eventually green pigment appears in their cytoplasm. There are no changes in the bile duct epithelial cells.

Skin

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The most marked changes occur from three to 16 hours after irradi-

ation. There is an increase in heterophils in the connective tissue starting at 3 hours and continuing up to 16 hours. At 8 and 16 hours many of them degenerate. The fibroblasts and macrophages become vesicu ated and greatly increased in size.

Lymph follicles that may be present in the connective tissue of the dermis also show degeneration with phagocytic polyblasts appearing at 16 hours.

The surface epithelium seems relatively unaffected. Some cells show slight vacuolation, and lobing especially at 16 hours. Mitosis occurs much less frequently at 5 and 8 hours than in the controls.

Hair follicles show some radiation changes. Mitosis are probably entirely absent at 5 and 8 hours, returning at 16 hours.

The underlying striated muscle shows no significant variation from the controls.

Spleen

At the earliest stage, before much definite damage is seen, the great majority of medium lymphocytes show a definite, though subtle change in the pattern of nuclear chromatin. The particles are heavier, more rounded, less numerous; they have more tendency to precipitate along the nuclear membrane. These cells resemble the lymphocytes of the guinea pig.

At 5 hours all these cells are dead. The areas of their destruction are flooded with granulocytes. Mitotic activity is absent but lymphocytes both large and medium begin to develop from the reticular cells. Many of these new cells in turn degenerate. The death of free cells leaves a prominent cellular reticulum with much intercellular substance. There is at all times a small number of surviving small lymphocytes. The reticular cells at 8 and 16 hours occasionally show nuclear

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changes similar to those seen in the lymphocytes but they apparently recover by 24 hours. The formation of lymphocytes continues sporadically until at 14 days reconstitution of the white pulp is beginning and is nearly complete at one month.

Lymph Node

By one-half hour mitoses are nearly absent and the majority of small and medium lymphocytes have the "clumped" appearance previously described for the lymphocytes of the spleen. Death of small and medium lymphocytes by darkening, vacuolization, and fragmentation, begins at one-half hour. Phagocytosis of the cellular debris begins at once. Most of the reticular cells and many of the free cells become intensely phagocytic so that by 16 hours most of the debris is in macrophages and the amount in the node is much decreased. Heterophils are prominent at 3 hours in the areas of great destruction, and are seen again at 24 hours, at this time largely in the sinuses. They degenerate and are taken up by the macrophage.

The great loss of cells causes a shrinking of the node, and leaves wide open, practically cell-free lymphatic sinuses and a prominent cellular reticulum.

During this period (5 - 24 hours) many hemocytoblasts develop from the reticulum and undergo a transformation similar to the polyblastic formation of macrophages from small lymphocytes in inflammation. Most of these macrophages are formed too late to take part in the cleaning up of debris.

This series is lacking in stages from 24 hours to 5 days. By this latter stage formation of lymphocytes and their transportation from the node has resumed. However, most of these lymphocytes at this and subsequent stages up to 14 days transform into plasma cells. There is no re-

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constitution of lymph follicles within the term (14 days) of this experiment but other animals at one month show almost complete reconstitution of the node.

Thymus

The lymphocytes (or thymocytes) are very rapidly destroyed in the cortex beginning probably as early as ½ hour. The reticulum, whether epithelial or of connective tissue, is immediately and intensely phagocytic of the cellular debris, and does not look damaged at any stage. Destruction of cells is not complete until 16 hours and even here many lymphocytes survive in the medulla. There is new formation of lymphocytes, large and medium, from the reticulum beginning at 8 hours and continuing to at least 14 days. Mitotic proliferation of lymphocytes ceases at ½ hour and does not resume until the 48-hour stage.

There apparently is no mitotic proliferation of the reticulum at any stage. It becomes prominent from 24 - 48 as the cellular debris is destroyed by the phagocytes. There is a contraction of the lobules and connective tissue proliforation around them with a resulting sheet of epithelium surrounding a core of Hassels bodies, lymphocytes and a denser epithelium. The lymphocytes are multiplying rapidly from 5 days on and being transported from the thymus in the lymph vessels, but reconstitution of the dense lymphatic mass of the cortex is only beginning at 14 days.

Lung

The lymphatic tissue undergoes degeneration similar to the nodes as described previously. An invasion of the connective tissue around the bronchi, and of the capillary network with heterophiles is quite marked at 8 hours. At 16 hours many eosinophiles are seen in the connective tissue. There are no gross changes in the epithelium. Minute changes could not be evaluated because of poor fixation.

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D. Enzyme Studies

1. Respiration and glycolysis of appendix and marrow - E. S. G. Barron and C. L. Prosser

Rabbit appendices were slit longitudinally, the mucosa scraped off and the pieces sliced horizontally to remove the muscular layer. The remaining lymphoid tissue was cut with a razor into slices .1 - .4 mm. thick. Pieces of red marrow from femurs and tibiae of rabbits were similarly sliced. Respiration (Q_{O_2} = cmm^3 O_2/gm. dry wt./hr. in O_2) and anaerobic glycolysis ($Q_{CO_2}^{N_2}$ = mm^3 CO_2/gm. dry wt./hr. in N_2) were measured with a Warburg apparatus.

The following average values were obtained.

	Q_{O_2}	$Q_{CO_2}^{N_2}$		Q_{O_2}	$Q_{CO_2}^{N_2}$
appendix			marrow		
normal	7.75	4.52	normal	1.205	0.238
800 r 5 hrs.	4.67	5.55	800 r 5 hrs.	1.26	0.752
" 8 days	3.31	9.6	" 8 days	0.45	0.71

These preliminary results indicate that radiation of 800 r causes a decline in respiration of lymphoid tissue within five hours and a decline in respiration of bone marrow which appears later. These differences between appendix and marrow agree with the time relations of histological changes. Glycolysis increases in the appendix, particularly at the 8-day level. Glycolysis also increases in the marrow.

2. Protection of mice by enzyme precursors - C. L. Prosser

Seven groups of ten male mice each were injected for eight days with vitamin B components in Ringer solution as follows: group (1) .2 mg. thiamin chloride, (2) .1 mg. thiamin chloride, (3) .5 mg. riboflavin, (4) .2 mg. riboflavin, (5) .1 mg. pyridoxine, (6) 1 cc Ringer,

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(7) uninjected. On the eighth day they were given X-irradiation of 700 r. Weights were taken daily during the pre- and post-irradiation periods.

All of the groups maintained a fairly constant or slightly increasing weight prior to irradiation. Immediately after irradiation a fall in weight occurred and continued until death. The slopes of all the weight curves are essentially similar. The survival curves overlap, the survival time for 50 percent being longest in those with .2 mg. riboflavin and those uninjected controls. It is concluded that thiamin, riboflavin, and pyridoxine in the concentrations used do not protect against loss of weight or against the lethal action of large single doses of X-irradiation.

II. Biological effects of radioactive isotopes.

A. Inhalation - R. Abrams

1. Xenon preparation

Thermal diffusion of Xe from U_3O_8 at elevated temperatures. In previous reports data was presented on the diffusion of Xe^{133} out of finely ground U_3O_8 which had been bombarded with slow neutrons at the cyclotron. It was necessary to make certain extrapolations from the results there obtained to a steady state where Xe is being formed and being removed continuously.

We have constructed a small scale apparatus based on our preliminary data. It is shown in Fig. 6. Five hundred fifty gm. of micronized U_3O_8 were placed in a quartz tube 40 cm. long and 2.5 cm. in diameter. The tube is drawn down to 1.2 cm. at either end. The section containing the oxide is surrounded by a nichrome heater (nichrome wire wrapped in asbestos). A Pt - .9 Pt, .1 Rh-thermocouple in a small quartz tube is buried in the oxide. The entire quartz tube is placed inside a 2½" aluminum tube, and surrounded by silica gel which serves as a thermal insulator. The aluminum

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tube is made in two sections, one of 5 ft. and the other 8 ft. The quartz tube ends in a graded seal to a pyrex ball joint. Several pieces of 2 mm. pyrex capillary, connected by ball joints, lead to the open end of the tube. The ball joints tend to ease any strains that might develop. An iron-constantan thermocouple is welded to the aluminum tube. The tube is placed in the pile on V-shaped graphite stringers so that the quartz part extends into the pile while the rest of the tube is in the concrete shield. In operation, a water siphon is used to pull air through the U_3O_8 into a 700 cc. glass holdup tube inside a heavy lead shield. Since the gas space in the U_3O_8 tube is only 180 cc. this transfers all the active gas to the holdup tube. It is allowed to stand here for 24 hours until the short-lived materials decay. Then it is pulled through a cold trap (-80°) to remove water and a charcoal trap (-80° C) where the Xe is adsorbed. A third cold trap on the far side of the charcoal serves to prevent entrance of water vapor from the siphon.

To date only one preliminary run has been made at 700° C. after the tube had been in the pile for 3500 K.W. days after the tube had been in the pile for 3500 K.W. days. Twenty mC of Xe^{133} were obtained. Experiments are under way to obtain quantitative information on feasible yields which do not involve undue amounts of shielding for the apparatus.

O. Hahn and others have done considerable work on emanating sources for radon and thoron. Radium or thorium are co-precipitated with a gelatinous substance of very large internal surface and after very careful drying Rn is liberated to the gas phase as fast as it forms.

By analogy, it seemed worthwhile to try to make a uranium preparation with an open, gel structure on the assumption that upon neutron bombardment the gaseous fission products would go into the gas phase at a rapid rate and at low temperatures.

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The only U compound which a priori seemed to have the desired gelatinous properties was $U(OH)_4$. We prepared this from $U\ Cl_4$ as follows: 6 gm. of $U\ Cl_4$ were dissolved in 100 cc. of distilled water. To this was added 100 cc. of 2.5% NH_4OH, slowly, with stirring, at room temperature. The gelatinous green precipitate was allowed to settle and then washed with water on the centrifuge until all trace of Cl^- were removed. It was finally washed 4 times with absolute ethyl alcohol followed by 3 washings with ether. Ether was removed by evacuation. If care was taken to exclude O_2 from all washing solutions, one obtained a black (partially oxidized) powder which when exposed to air oxidized very rapidly becoming extremely hot.

To test emanating power we placed both oxidized and unoxidized samples in quartz tubes and bombarded with neutrons at the cyclotron. Samples were taken from the gas phase after short-lived elements decayed and then the solid was dissolved in nitric acid and the residual gas collected. Results are as follows:

	Unoxidized	Oxidized
Xe in gas	439 c/sec	68
Xe in solid	37 c/sec	59
Emanating Power	92%	53%

Even the oxidized preparation is much more satisfactory than U_3O_8.

Further work is being done on methods of preparation, effect of aging at pile temperature on emanating power, and other possible compounds that might suffice.

At present we have 60 gm. of a partially oxidized preparation. It is planned to place this in a small Al tube in the pile at X to observe how the yields of Xe vary with aging and how they compared with the thermally hot U_3O_8.

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2. Dust

Work has been mainly developmental. A bellows type dust injector is being tested with various dry dusts. It will be described in detail when calibrations have been completed. Methods of covering the skin of animals are being studied to prevent external deposition of dust. Exposures of mice to U_3O_8 dust are being continued. Preliminary work is being done with inert Sr CO_3 since this seems a good form of 55-day Sr to use as a dust. The Sr is expected to be available from X within the coming month.

3. Ru, I_2

Work of last month continued. Nothing new. A sample of 8.0 day iodine has been obtained by placing Te in the pile at X. This is being used in attempts to prepare carrier-free I_2 gas.

B. Injection and Immersion

1. Ba^{140} plus La^{140}

a. Mouse survival and distribution - R. D. Finkle

The first shipments of radioactive substance from Clinton included 50 mC of Barium in 30 cc. The method of preparation required that one milligram of inert Ba be added. The daughter activity, Lanthanum, was present in an equal quantity and in a "carrier-free" state.

The solutions were made isotonic with NaCl and were injected intraperitoneally into mice. The amounts of Ba plus La injected into each of 7 animals, the mortality, the bone contents and weight changes are tabulated below.

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TABLE I

Group	μC Injected	mC/Kilo of Body Wgt.	Mortality	μC deposited / gm. of Bone (Wet Wt.)	% of Injected Material deposited in skeleton (calculated)	Weight Changes
I	1000	50	7 in 7 days	520 (Femur) 446 (Tibia)	62% 54%	18% in 5 days
II	333	17	5 " 22 "	192 (Femur)	69%	The animals in all groups continued to gain weight until shortly before death. 24 - 48 hrs. before death they lost body weight very rapidly - 10 - 20% per day.
III	111	5.5	4 " 22 "	55 "	57%	
IV	37	1.7	0 " 22 "	19 "	62%	
V	12	0.55	5 " 22 "	5.0 "	50%	
VI	4.0	0.18	1 " 22 "	1.8 "	54%	
VII (Control)	None (0.03 mgm of inert Ba and 0.003 mgm of inert La, I.P.)	None	0 " 22 "	-		Plus 15% in 22 days

A second set of experiments with mice covered the range from 25 to 2.5 mC/kilo of body weight and gave the following mortality:

mC/kilo	2.5	3.75	5.5	12.5	17	25
% mortality	0	43	71	86	100	100
Time, day	13	13	13	13	12	10

The distribution and excretion data are not yet complete.

From the data in hand at the present time we would judge that the 50% survival dose of Ba^{140} and La^{140} is 2 - 4 mC/Kilo of body weight in mice. Analyses of the femurs and tibiae show that over half of the injected activity is still in the bones after death. The results of an experiment in progress on rats show that the 50% survival dose of Ba^{140} and La^{140} is below 4 mC/Kilo of body weight.

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Tissues from Barium-injected mice gave autographs showing localization in a variety of tissues. The amount deposited was roughly proportional to the amount injected. The greatest amount was in bone, particularly at the epiphyses. Next to bone the most active tissues were spleen, liver and kidney. Traces of activity were observed in stomach, intestine, heart, pancreas, and lymph nodes. No activity was noted in lung or muscle. In the spleen of a mouse receiving .333 mC the red pulp took up active material so that the follicles were clearly outlined. The kidneys show more activity in the cortex than in the medulla.

b. Accumulation in goldfish - C. L. Prosser

Seven goldfish were put into each of four beakers each containing two liters of Ba^{140} in equilibrium with La^{140} made up in synthetic pond water. One fish was removed from each for radio-autographs. The composition of the solutions and the accumulation of activity are given in Table II.

The data in Table II indicate a somewhat slower uptake of Ba^{140}-La^{140} than was found for Sr^{89}. Except for the eight-day sample, uptake from high Ca water was less than from water with low calcium. Presence of small amounts of inactive carrier seem not to affect the uptake.

Data on body distribution will be presented next month. Radioautographs of two of the fish were of interest in that one had half the tail injured while in the other, part of the tail had been cut off and had regenerated. Both the injured and regenerating parts of the tails showed much greater activity than the normal parts of the fin.

2. Sr^{89}: Accumulation in goldfish - C. L. Prosser

Carrier-free strontium^{89} as strontium chloride was added to synthetic pond water. Eighteen liters of solution contained fifteen fish. Initial activities of the tanks were: (1) 413 μC/cc, (2) 144 μC/cc (3) 56.6 μC/cc (4) control. Six fish from each jar were sacrificed at intervals during

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TABLE II

Day	Pond water with 5 mg $Ca\ Cl_2$/l 5 μC of Ba^{140}/l			Pond water with 5 mg $Ca\ Cl_2$ .1 mg $Ba\ Cl_2$ .01 mg $La\ Cl_3$ 5 μ C Ba^{140}/l			Pond water with 5 mg $Ca\ Cl_2$ .1 mg $Ba\ Cl_2$ .01 mg $La\ Cl_3$ 50 μ C Ba^{140}/l			Pond water with 100 mg $Ca\ Cl_2$ 60 μ C Ba^{140}/l		
	Water μC/cc	Fish Activity μC/gm	Conc.	Water μC/cc	Fish μc/gm	Conc.	Water μC/cc	Fish μC/gm	Conc.	Water μc/cc	Fish μC/gm	Conc.
0	.005			.005			.049			.068		
1	.005	.02	4.0X	.0004	.0156	3.9X	.04	.636	15.7X	.045	.554	12.3X
2	.005	.03	6 X	.004	.112	28 X	.033	.344	10.4X	.037	.214	5.8X
4	.0043	.0535	12.5X	.0037	.121	33 X	.039	.831	23 X	.037	.161	4.35X
5	.004	.0514	12.7X	.0036	.142	39.4X	.036	.461	12.8X	.037	.184	4.9X
6	.0038			.0035			.0293			.030		
7	.003			.0025			.028			.031		
8	.003	.090	30 X	.0025	.120	48X	.026	1.2	46.1X	.035	3.74	107X
11				.0016	.177	110X	.019	3.06	180 X	.019	.422	22.2X

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25 days. Within one day the fish took up active strontium to 4.4 - 6.5 times the concentration in the external medium. During twenty-five days the strontium content of the fish fluctuated around the initial value. In the fish in the highest level tank there was a decline in total amount of Sr^{89} while in the others the amount of strontium remained fairly constant. The concentration of activity did not go above ten times that of the medium. These results agree with the figures reported previously (CH-1162) for the uptake of Sr^{89} with carrier from pond water high in calcium.

When the radiation received is calculated on the basis of total wet weight, the fish in the highest level tank were receiving at the end of the first day β radiation of about 79 r for 24 hours and after 25 days 52 r/day giving a total of approximately 1600 r. Those in the second tank received an average of 20.6 r/day and those in the third 5.8 r/day. In 25 days two fish have died in tank (1), two in tank (2), none in tank (3) and one in the control tank.

3. Na^{24}: Histopathology of spleen - R. Murray

In the normal spleens of the mice of our stock, extensive extramedullary myelopoiesis and erythropoiesis is always found. Death of the small lymphocytes begins at 4 hours after injection of 1.5 mC and grows progressively to a maximum at 13½ hours and then the rate of damage decreases. The extramedullary myelopoiesis disappears completely, the erythroblasts having died off completely by 13½ hours and the myelocytes almost completely by 20 hours. The rate of formation and death of megakaryocytes is greatly increased all through the experiment. During the middle stages, just after the height of necrosis, many atypical, bizarre variations of all of the normal cell types are found. In the last half of the experimental period, tremendous numbers of plasma cells are found so that perhaps all free cells except for the

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megakaryocytes ultimately become plasma cells. By five days there is a definite trend towards repopulation of the free cells but plasma cells still are in abnormally high percentage. Beginning with the first stage ($\frac{1}{2}$ hour) mitoses practically cease although they may be found in small numbers at all stages. This indicates a heteroplastic formation of most of the free cells; i.e. transformation from reticular cells.

Other organs are yet to be examined and will be reported later.

III. Plans for coming month

A few single dose exposures to X-ray will be made to complete weight, food intake and survival curves. Paired and daily doses of X-ray will be continued with rats, rabbits and Drosophila. Fast n exposures will be continued.

Histopathological studies of rabbits given single doses of 400 r and 100 r will continue. A similar survey of rats and mice is being made.

Changes in the blood picture of rabbits given 25 r will be examined. Several clinically useful drugs will be tested for their effect on blood damage in irradiated animals.

Alterations in metabolism of tissues from irradiated animals will be studied and purified enzyme systems will be irradiated.

Xenon^{133} should be available from the model generator at X and animal exposures will be started.

Active strontium carbonate dusts will be available for inhalation experiments and it may be possible to start tracer experiments on ruthenium oxide and iodide.

The metabolism, distribution and biological effects of mixed fission products will be started and work on Sr^{89} and Ba^{140} - La^{140} will be continued. Radioautographic and histopathological work on preliminary Sr^{89} and Ba^{140} experiments should be complete.

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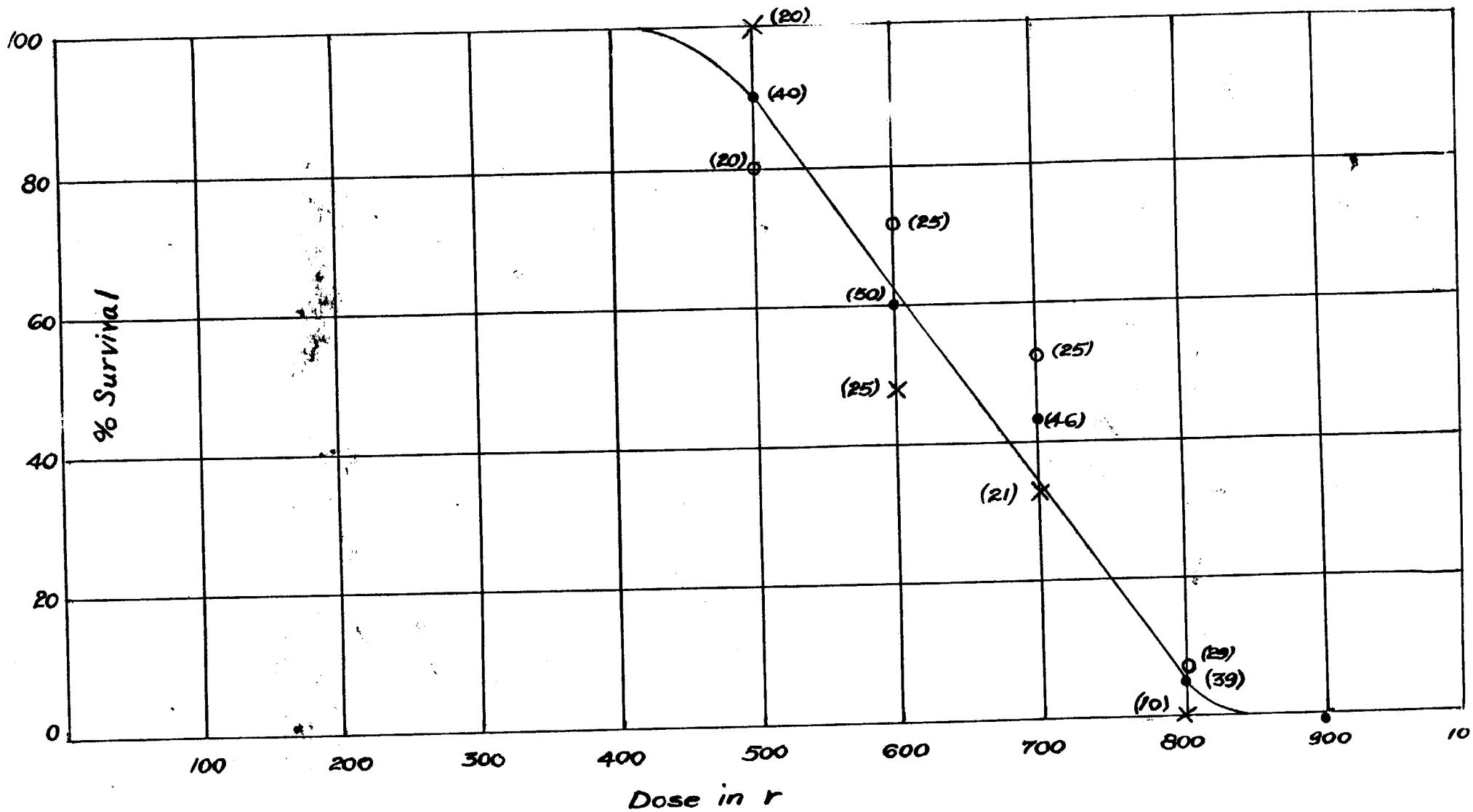
Figure 1.



Rat - X-Ray Survival

Figures in parentheses indicate number of animals at each point.

• = total animals
x = males only
o = females only

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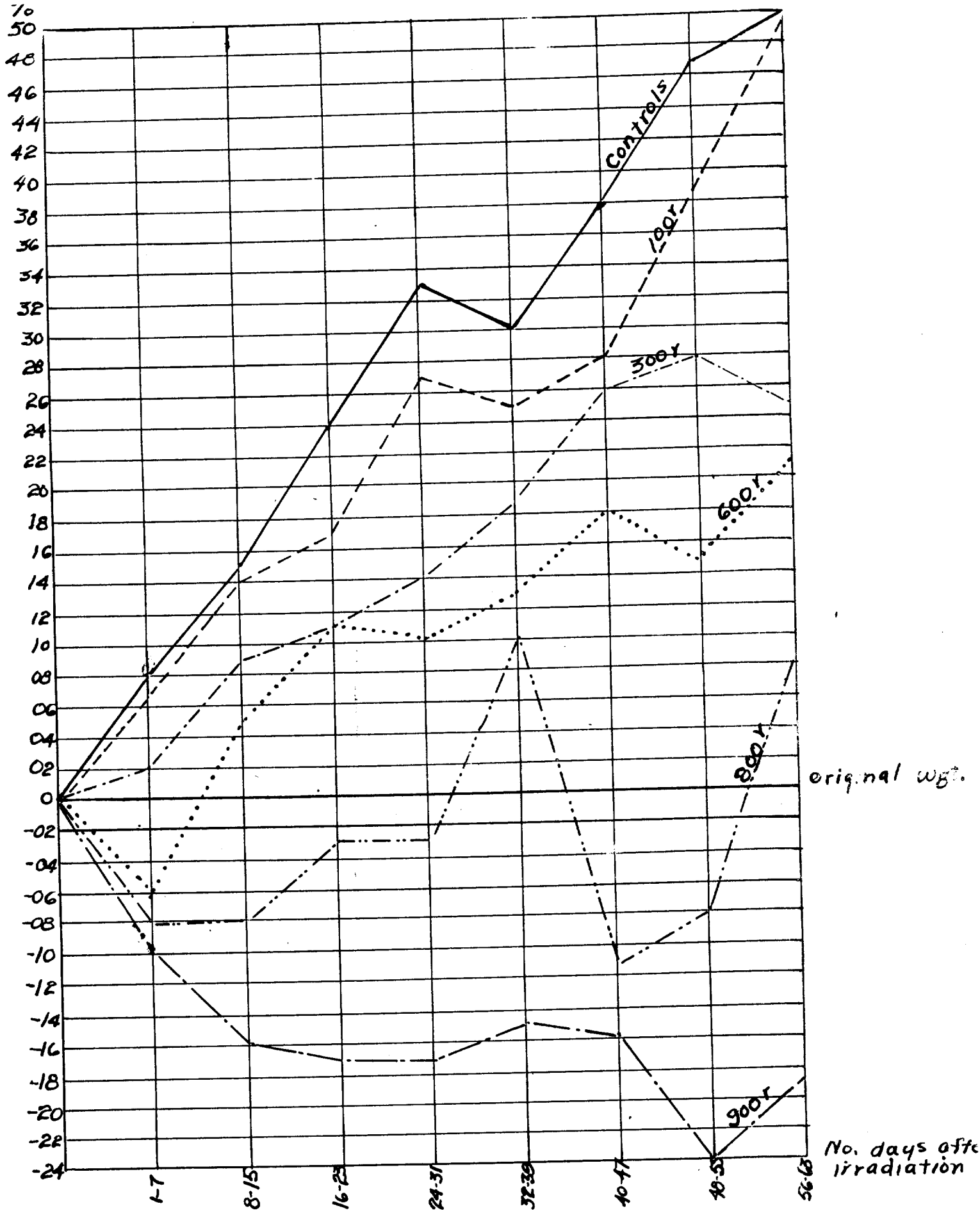

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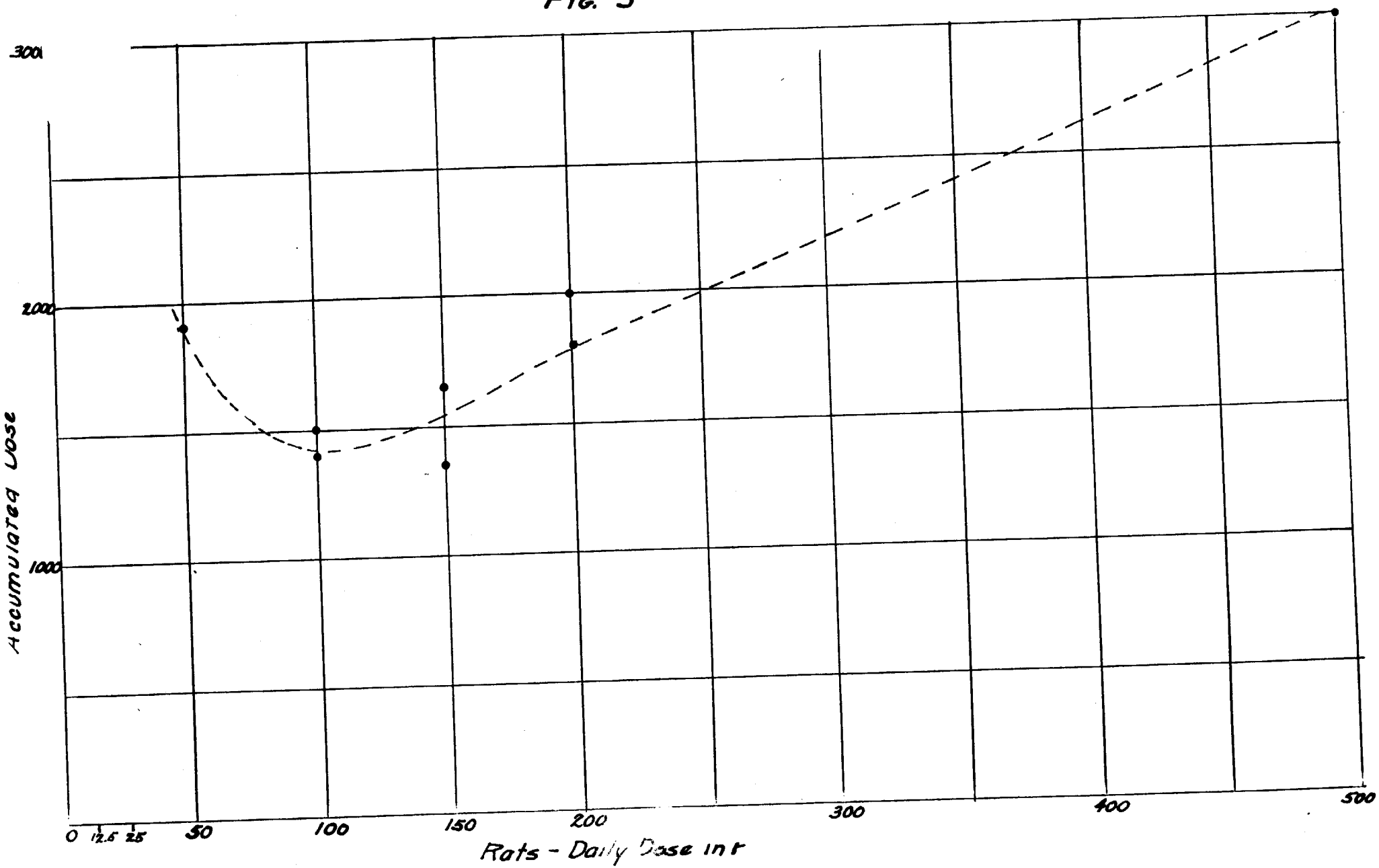
RABBIT WEIGHT CHART

E9L8111

FIG. 3



Accumulated dose in R for 50% mortality in lots of ten rats.

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FIG 4

RABBITS TOTAL NEUTROPHILES - X-RAY

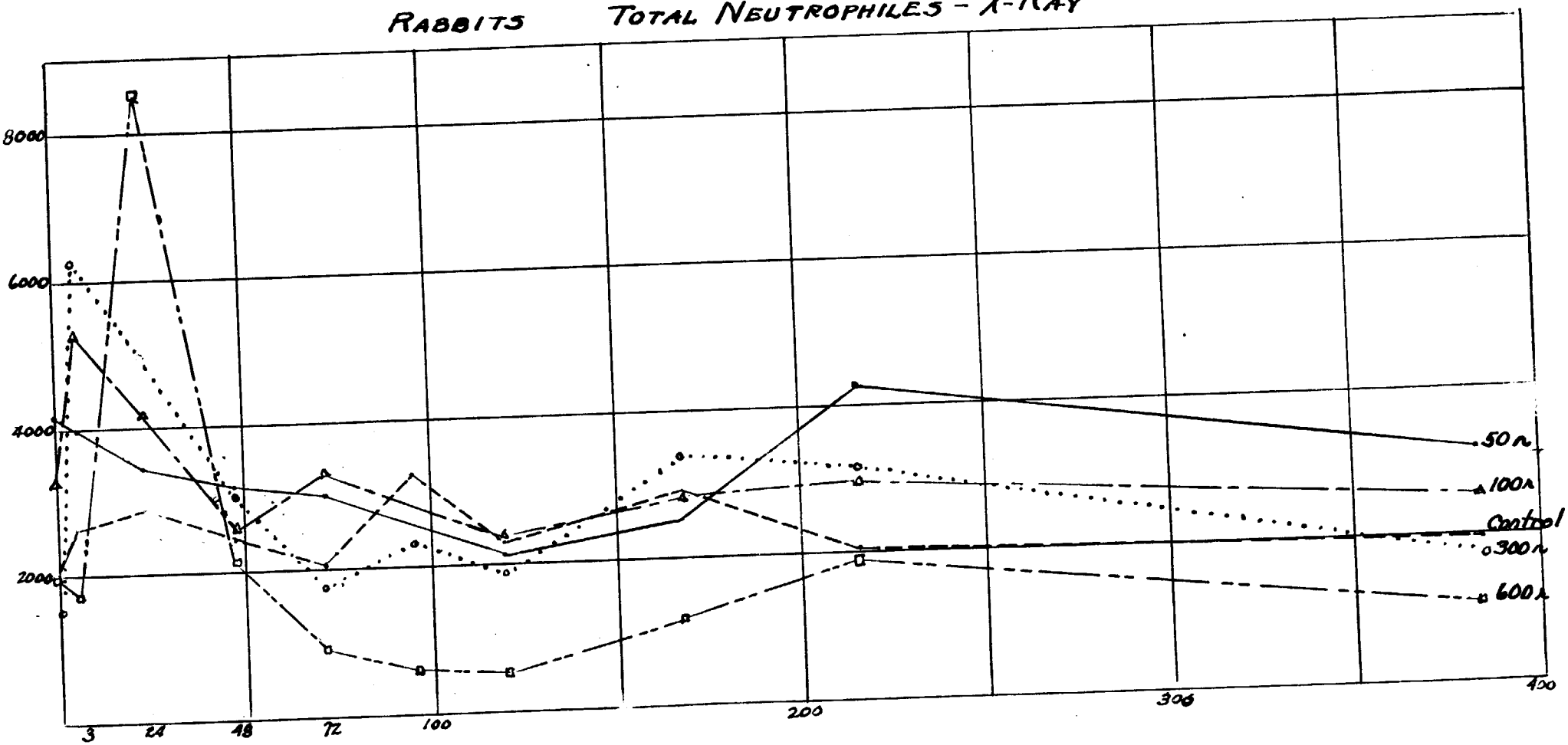


Figure 5

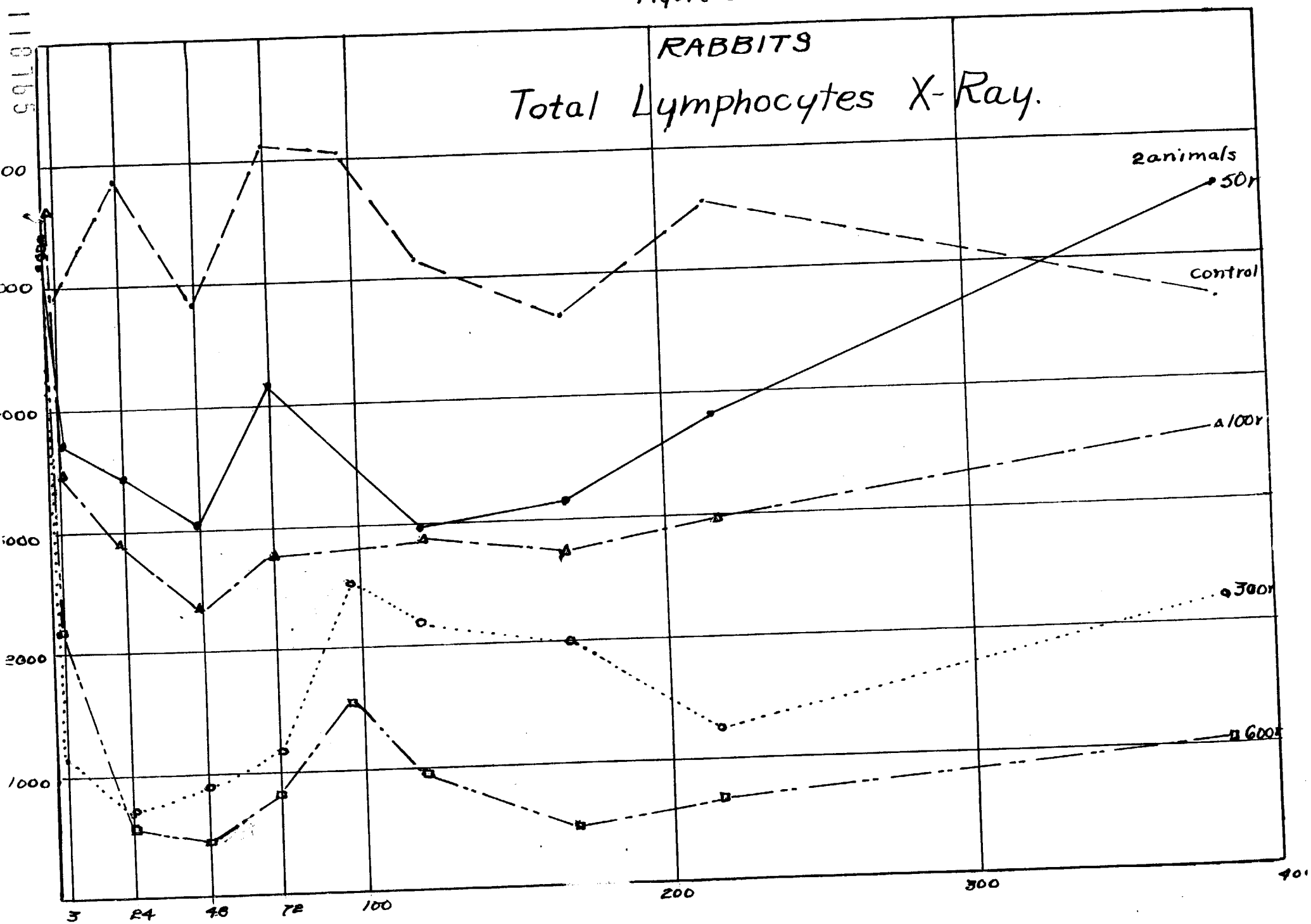
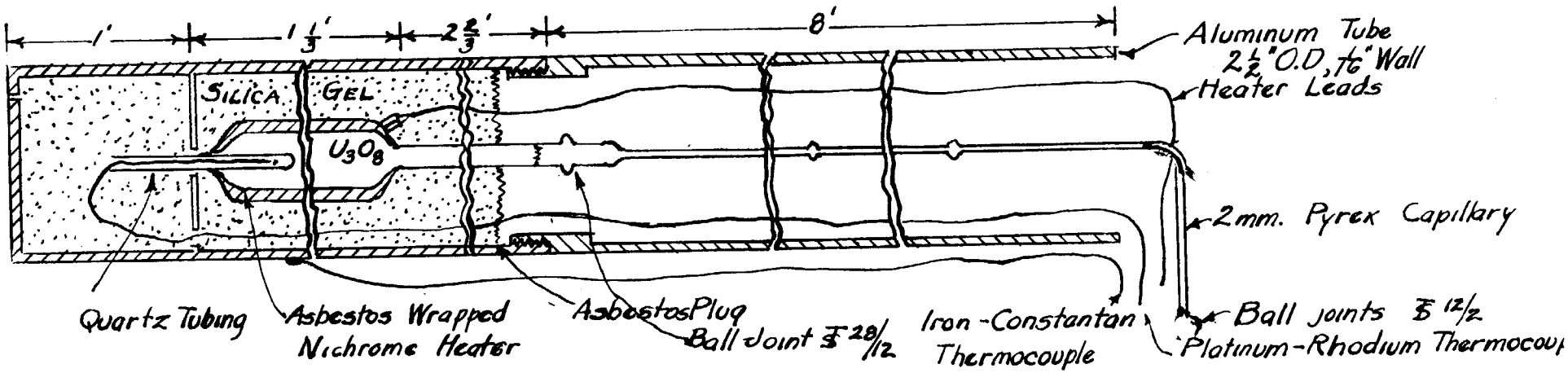

RABBITS
Total Lymphocytes X-Ray.
2 animals
50r
Control
100r
300r
600r
1000
2000
3
24
48
72
100
200
300

Fig. 6



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B. RADIATION MEASUREMENT SECTION

E. O. Wollan, Consulting Section Chief

Report by L. A. Pardue, Group Leader

Miss Virginia Brantner has taken Mrs. Mary Nachtrieb's place as a technician in the group. Mrs. Nachtrieb is leaving to join her husband who has been transferred to another of the sites within the project.

Daily readings of pocket chambers and weekly readings of film meters have continued with the exception of one week when film was not available. Some mention might be made about a change of attitude towards pocket chambers which one finds occasionally. At first they were not too reliable because of leakage. Frequently they were off scale, indicating large exposure without reason. That fault has disappeared almost entirely and workers now are asking why they do not get larger readings. As an example of the reliability of the insulators, a chamber was sent with the driver of a truck to California. It read 38 mr when it was returned two weeks later. Further evidence of their reliability is found in the fact that only 384 off-scale readings have been made in the total of 12,800 readings to date. Thus, leakage is not now a serious fault of the chambers. To determine how accurately they indicate the exposure to which they are subjected, 22 chambers were exposed to 100 mr using a standard radium source. The average reading was 82.5 mr. The consistency was better as only one read over 100 mr. The mean residual was 8 mr. The calibration is thus about 20% low and chambers are reliable to within 10%. One point deserves considerable emphasis. The radiation dose due to gamma rays can be determined with reasonable accuracy at the location of the meter. Body extremities, e.g. hands, in certain types of work may receive many times the meter reading.

A one-tenth installment of the order for new film badges is promised for delivery by January 20. Cadmium for filters, on order for about the same length of time, is likewise promised for early delivery and has been so for

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some time. Assembly will start just as soon as the parts become available.

Measurements on contaminated hands are being done regularly and under more favorable circumstances in a special room in New Chemistry. So far the readings have not been very disturbing, however one count was over ten times background, indicating approximately tolerance contamination for a uniformly covered hand. Four pairs of gloves used at the Argonne have been measured. The worst pair gave these counts:

Background	Right Inside	Right Outside	Left Inside	Left Outside	
90	8752	914	3296	766	Gloves
90	104	104	164	164	Linings

The counter has been used to measure the contamination of clothing before and after laundering.

A Lindemann electrometer and ionization chamber are being set up to test people whose breath is presumed to be alpha contaminated. It will be useful in other types of measurements; e.g. studies of hydrogen filled chambers as neutron meters.

Dr. G. Failla came to the laboratory as a consultant during the month. In particular, consideration was given to the air in the pile building at the Argonne. It was concluded that careful observations are being made there and reasonable precautions are being taken. Tolerance has been set at 3×10^{-10} curies/cc. In the present counter this corresponds to approximately 15,000 counts/min. Measurements are being undertaken to determine the energy of the betas.

To determine the daily dose near the Chicago Cyclotron, four pocket chambers were placed on different sides of the machine and at the approximate distances of 9 feet, 10 feet, 14 feet and 30 feet. Readings were made for six days. The first three were off scale 10 times. The fourth averaged 44 mr/day.

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Tests of the Landsverk-Wollan neutron meter have been made at the Argonne Pile. The meter has a hydrogen filled chamber and a quartz fibre electroscope. Hydrogen has the property that for equal amounts of ionization induced in it by neutrons and gammas, the corresponding flesh ionization would be in the ratio of 1 to 5 which is the frequently accepted ratio of relative biological effects. This gas has the advantage that the scale can be marked off in dose units which may be used for both causes. Readings were made atop the pile and on the loading platform at the middle of the front face.

Top of pile

Power (Watts)	Lauritsen	Neutron meter	Remarks
8×10^{-2}	15 mr/hr	15 mr/hr	Directly over thermal column
10^5	22.5 mr/hr	21.3 mr/hr	Outside room

On Loading Platform
100 K.W.

Distance from Pile Face	Lauritsen	Neutron meter
4'	84.7 mr/hr	143.7 mr/hr
8'	62.9 mr/hr	93.7 mr/hr
12'	41.7 mr/hr	67.5 mr/hr

The readings indicate no measurable amount of fast neutrons on top of the pile. On the loading platform the situation was different. Approximately 50% of the biological dose is the result of them.

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It is desirable that a thorough calibration be made of survey instruments under more favorable circumstances than have been available in the past. It should be done in a large room or perhaps with a directed beam so that the unknown amount of scatter may be reduced to a minimum. The following data taken in one of the small rooms now available suggest the need.

Distance from source	Calculated dose	Measured dose Victoreen meter	Measured dose Lauritsen
200 cm	10.21 mr/hr	13.2 mr/hr	10.5 mr/hr
150 cm	18.4 mr/hr	21.0 mr/hr	17.7 mr/hr
100 cm	41.5 mr/hr	39. mr/hr	36.6 mr/hr
45 cm	204. mr/hr		151. mr/hr
30.5 cm	445 mr/hr		250 mr/hr
20.3 cm	1000 mr/hr		545 mr/hr

Undoubtedly the departures of the Lauritsen readings from the calculated values cannot be explained away as scatter and uncertainty of the "position" of the chamber. The advantages of the instantaneous readings obtainable on the Victoreen instrument suggest its use where a gain in time more than offsets the value of the more reproducible Lauritsen readings.

As usual, a rather extensive program of surveys and routine measurements has consumed much of the time of the group.

Work for the coming Month

1. Continuation of pocket chamber and film meter service
2. Probably assemble new film badges and start using them
3. Surveys
4. Routine measurements
5. Calibration of instruments
6. Measurements at the Argonne on air in pile room

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C. METEOROLOGY SECTION

P. E. Church, Section Chief

All work thus far during January has been at Site W, where all the men in the section are located at present. The first two weeks of the month were spent in observing the various changes in the lapse rates during the daylight hours in the 200 W area, and in getting ready to operate the auxiliary stack in the same area. On January 17, the auxiliary stack went into operation.

Until the auxiliary stack became available, all smoke runs were made during the daylight hours with the generators at the ground. About 25 operations were completed during November, December and early January. Except for two runs made during the early morning hours, the resulting drift of the smoke showed much the same profile pattern; to wit, vertically ascending and descending columns; the ascending ones reaching to or a little above the base of the inversion. No smoke runs were made during those days when ground fog was present.

Airplane flights were usually made at the conclusion of each smoke run, at approximately 1400 o'clock. Almost invariably an inversion was present, the lid of which was between 2000 and 3000 feet above the ground surface. This level coincides with the top of the surrounding mountains and indicates the presence of a stagnant air mass in the valley with overlying warm air as perhaps the normal pattern. The smoke would reach that altitude only a mile or two downwind from the generator and would spread out to a width of 5 to 10 miles some 10 miles down from the smoke generator when seen from above in the plane. Nearly all of the runs were made under a northwest surface wind. Some smoke reached Richland and some went up the Yakima Valley via the Benton City gap. Dilution of the smoke appeared to be such that there was a nearly uniform

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distribution of particles when viewed from above.

Realizing that the above conditions probably represent the optimum that can be expected during the season most favorable to building and maintenance of inversions (cold surface with snow intermittently remaining on the ground, minimum insolation, and overrunning warm air) it was decided to attempt to compute dilution under the least favorable conditions, i.e., at night and until the sun was up at least two hours. The stack was ready for operation on the 17th and the first smoke from the stack began that night. The site had been swept clean of the inversion by a strong southeast wind that day but by night it was calm at the surface. Free and captive balloon ascents, the latter with a meteorograph, showed a ground inversion from 200 to 400 feet thick with calm air below. Above that a moderate wind was present. By daylight the smoke from 2 hours generation had spread widely but remained in a layer less than 100 feet thick. No smoke came to the ground except where the overhead wind reached the surface. Smoke runs of 18-19th and 19th-20th showed much the same condition; i.e., no smoke reaching the ground and a moderate wind only a few hundred feet up, and the smoke being concentrated within a narrow layer. On the morning of the 20th it was calm at the surface but a northwest wind of 15-20 mph was blowing at the top of the stack. Lateral spreading was very little, the smoke trail being 25-50 feet wide 1 mile downwind. A flat core, recognizable 15 miles downwind from the generator, appeared to be not more than 500 feet wide, though quite thin, 200 to 300 feet above the surface and was moving at least 20 mph. The observer in the plane, however, reported that the smoke spread laterally as a fairly dense curtain, to a width of more than [illegible] miles.

Two shifts are maintained by the schedule now followed. The first starts at 1730 and lasts till about 0230, the second from about 0130 to about 1030. No observations are made during the day. Because of the marked increase

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of velocity of wind found at a small increase of altitude above the ground during a low ground inversion, ascents of slowly rising balloons observed by two theodolites are made three or four times each night and also a like number of meteorograph ascents. Once or twice during the late hours, from 2200 to 0200 o'clock, the generator may be run for half an hour or so depending on wind direction and velocity. Again depending on these two elements, the generator is started from two to four hours before sunrise. A roving observer follows the trail of smoke to note what areas it occupies, the visual character of it, density, thickness, etc. from the ground. Another observer goes up in the plane as soon as one is available, obtains the lapse rate up to 4000 feet and maps the outline and density of the trail.

At the date of writing this report only three runs have been made from the stack and the different character of the smoke trail from that when the generators were at the ground does not permit any definite conclusions to be reached as yet. Runs from ground plus the three from the stack allow the following tentative conclusions:

1. Smoke and haze is limited on the top by inversions.
2. Vertical mixing during a clear or partly cloudy day reaches an altitude in January which is approximately one-half mile above the ground.
3. No conclusions can yet be ventured as to the ratio of lateral spreading under varying degrees of stability, but spreading seems to be considerable under any condition.
4. Under stagnant conditions a northwest wind appears to be the dominant direction during most hours at 200 W.
5. If the boundaries of the visible smoke are true boundaries, that is no evaporation of smoke particles occurs, the amount of dilution can be easily and quickly computed for the conditions present during the run.

1118713

D. CLINICAL MEDICINE AND MEDICAL RESEARCH

C. J. Watson, M.D. - Associate Director and Section Chief

L. O. Jacobson, M.D. - Acting Section Chief

Report for month ending January 14, 1944

I. The Effect of Radiations on Proteins - E. S. Guzman Barron, John Muntz

A number of papers on the biologic effects of radiations attribute them to peroxides produced during ionization. Proteins possess two kinds of SH- groups: those detected in the native state and those that are detected only after denaturation; denatured proteins on unfolding have all their SH- groups exposed to the action of SH- reagents and complete titration of these groups is thus possible by the use of oxidizing agents of high oxidation-reduction potential. To test the effect of x-rays on the SH-groups of proteins, two systems were selected: denatured egg albumin, a protein of small molecular weight where all the SH- groups have been made easily detectable, and native myosin, a protein of large molecular weight with a large number of SH- groups in the native state and after denaturation.

Crystalline egg albumin denatured with guanidine (2 M) was treated at different concentrations with x-rays, 3000 r, for 18 minutes. The sulfhydro groups were then titrated with $K_3Fe(CN)_6$. As can be seen in Fig. 1, there was a loss of SH- groups equivalent to 14 per cent. To see whether this loss of SH- groups was due to peroxide action, the experiment was repeated in the presence of catalase (crystalline beef catalase). The presence of catalase has no effect at all in the destruction of SH- groups by x-rays. It must be added that x-rays had no effect on the activity of catalase. (Fig. 2).

When native myosin was exposed to the same amount of x-rays (3000 r for 18 minutes) there was an increase of SH-groups instead of loss. This increase can be due only to a partial denaturation of the protein which left

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exposed more SH- groups (Fig. 3). Thus, the possible loss of SH- groups due to irradiation was more than compensated by the number of SH- groups made available for titration through protein denaturation.

There is one objection to these experiments: the temperature of the solutions during radiation was not controlled. The possibility of oxidation by molecular oxygen and increased temperature was not eliminated. The experiments will be repeated at 0°.

However it may be concluded that x-rays can destroy the SH- groups of proteins and produce their denaturation.

The electrophoretic analysis of serum proteins of men and animals submitted to the action of x-rays have been started. We have now the analysis of the blood serum of a man in whom an increase of the γ globulin was found after he had received 350 r, total body radiation.

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FIG. 1

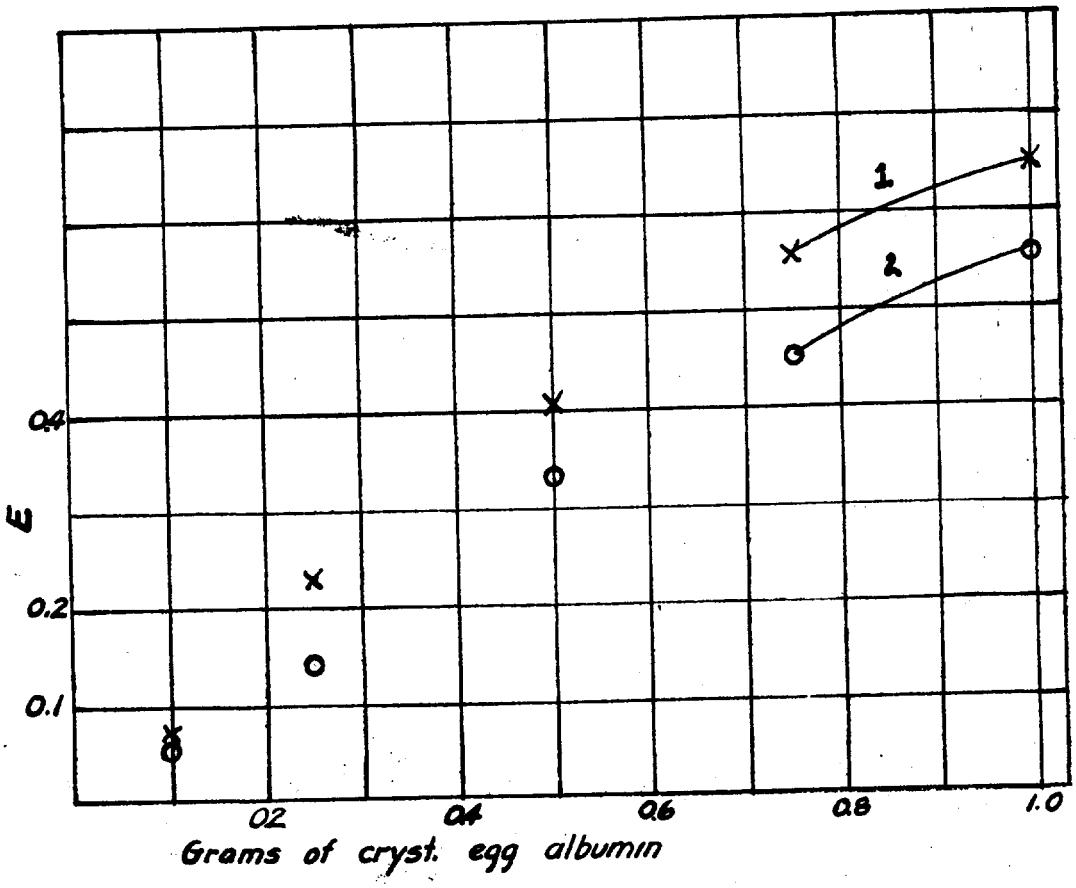

Fig. 1

Effect of x-rays on the SH- groups of denatured egg albumin.

Abscissa, grams of egg albumin

Ordinate, E, extinction coefficient representing SH- groups.

1 - Control; 2 - x-ray treated

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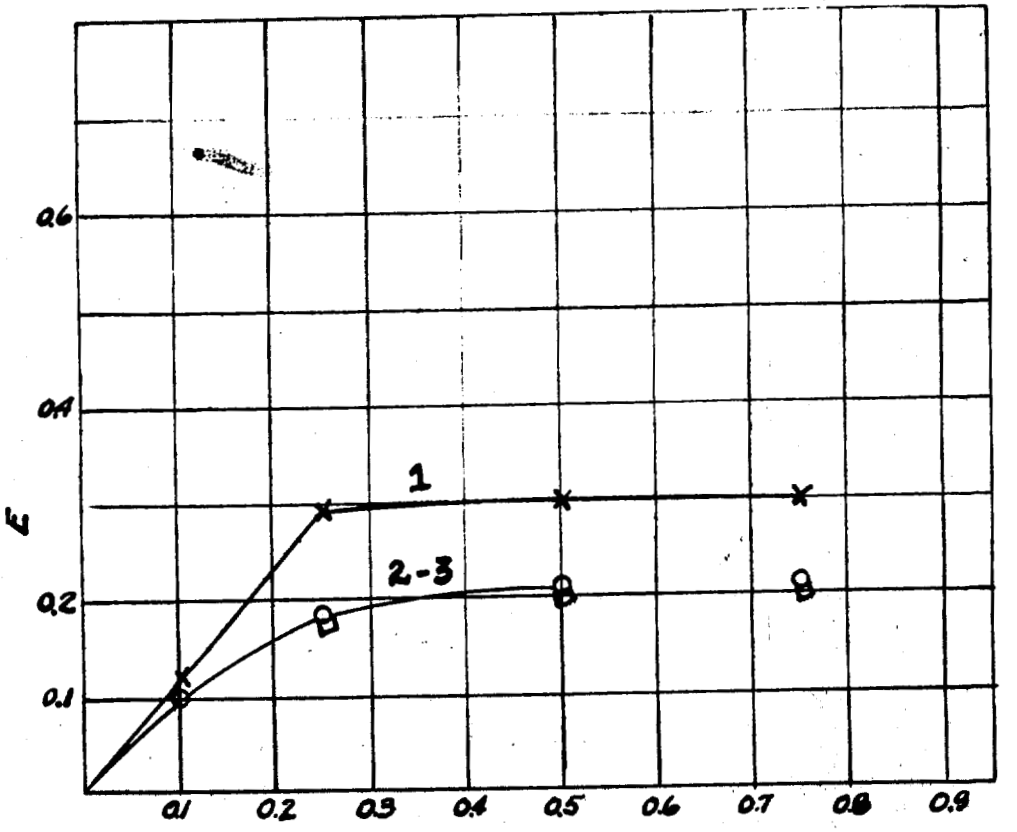
FIG. 2



Effect of x-rays on the SH-groups of denatured egg albumin containing catalase.

1 - control; 2 - x-ray treated; 3 - albumin containing catalase, x-ray treated.

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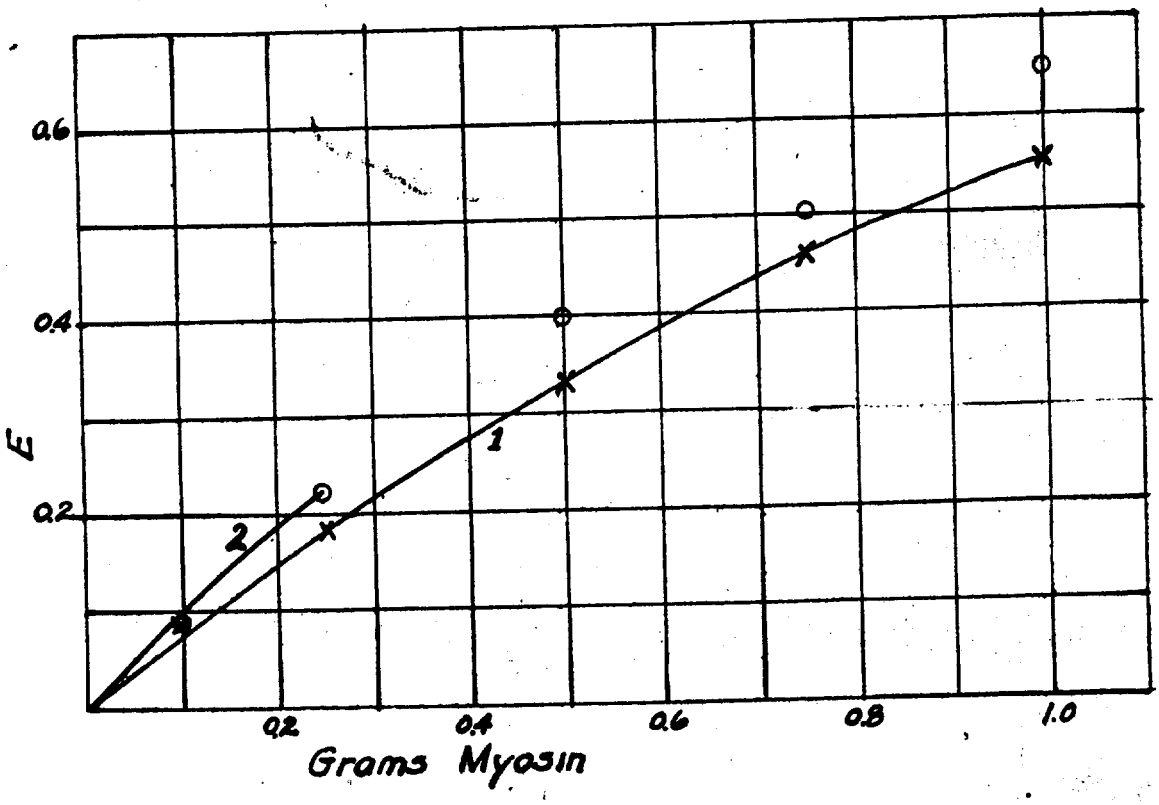
FIG. 3



Effect of x-rays on myosin

Abscissa, myosin in grams

Ordinate, E, extinction coefficient representing SH-groups.

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II. Clinical Section - J. J. Nickson, M.D. and M. H. Nickson, M.D.

Pre-employment examinations. 154 examinations have been done since December 15, 1943. 121 were on non-academic personnel, 33 on academic personnel. 10 persons were rejected on the basis of their pre-employment examinations. One person has been accepted provisionally, pending a statement from the Navy giving the reason for his discharge from that service.

Hematology

The Clinical Hematology Group examined 800 patients during the period 12-15-43 to 1-14-44. The following table gives an analysis of the laboratory examinations done:

	Hgb.	RBC	WBC	Differential	Platelets	Urines	Retics.
No. of exam.	547	474	700	750	146	430	20
Abnormalities							
1. New Personnel 155 persons	7½%	7½%	10½%	18%	-	7½%	0
2. Controls 165 persons	16%	16%	10%	16%	-	16%	0
3. Scientific Personnel (580)	8%	8%	10%	28%	6%	10.%	0

Five blood or urine abnormalities in the opinion of the Health Group were due to exposure to radiation or tuballoy. Four of these occurred in Mr. Cunningham's group. Three of the four individuals showed a lymphocytosis. One showed a lymphopenia. One individual showed a marked drop in the platelet count. One of these occurred in Mr. Sugarman's group. A drop of 1500 cells in the total WBC has occurred in a member of his group who carried ~50 millicuries of radon on his lap for ½ hour. The radon was shielded by 1 inch of lead.

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Activities of Liaison Committee

During the previous month, L. A. Pardue reported 19 persons with badge or meter readings of greater than .6 r for a week. Four of these readings were associated with changes in blood counts which are felt to be due to over exposure. Mr. Pardue's group was requested to make 15 surveys on the work areas of persons with low counts. Radiation conditions were satisfactory in each instance. Other surveys made by Mr. Pardue's group are reported in detail in his section of this report. Dr. Schwartz examined 14 Metallurgical employees. He will report his findings in detail at a later date.

During the month, 15 persons were referred to the Clinics of the Billings or Provident Hospital. One person was relocated on the Project because of a low red blood cell count. It was felt by the Committee that she should have little or no exposure and that her previous work offered opportunities for over exposure.

Metallurgical Laboratory Surveys

The situation in Room 108, Site B has been considerably improved by the installation of suction hoods around the two cut-off machines. The grinders on the same bench have not been provided with hoods as yet. No improvement in the hood installation on the large grinders in the center of the room was noted on 1-14-44.

Site B Machine Shop. The general room ventilation in Room 130 has not been improved as yet. Dry machining of tuballoy has continued. On 11-29-43 its discontinuance was recommended by the Health Group. The undesirability of this practice has been re-emphasized, and assurance has been given that it will be stopped.

Ryerson 59 N. Lead has been handled for some months in this room. It is melted, and then poured into molds. The ventilation has been grossly

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inadequate. Dr. Schwartz' studies on the workers there show changes consistent with the diagnosis of sub-clinical lead poisoning. At our recommendation, the installation of a ventilation system was given the highest priority. The installation was completed 1-14-44. Unfortunately it is not adequate. Revision will be recommended.

Room 10, New Chemistry was surveyed by Mr. Goldstein during the month. His surveys indicated gross contamination of the laboratory desk tops with radioactive materials. Removal and replacement of the contaminated surfaces has been recommended and will be done in the immediate future. Laboratory desk tops which are apt to be contaminated should be covered with a surface impermeable to solutions. Dr. Hogness has suggested the use of glass. Its use gives a non-porous, acid resistant surface. Other suggestions will be welcomed.

It is probable that other laboratory tables will have to be similarly treated.

Hand Contamination

The laboratory personnel of New Chemistry has been placed on a weekly schedule for hand counting. Eventually it is planned to place the program on a daily basis. A program of glove monitoring will be started as soon as space in New Chemistry is made available for the work.

Projected Work

1. Expansion of hand contamination determination
2. Glove monitoring program
3. Centralization of distribution of meters and badges
4. Continuance of pre-employment examinations
5. Extension of finger-print studies.

III. Pigment Metabolism and Liver Function Studies - S. Schwartz

Continuing. No new material to report

IV. Toxicology Group - A. Tannenbaum and H. Silverstone

Continuing. No new material to report

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E. ASSOCIATED PROJECTS

I. California Project - J. G. Hamilton and Associates

A. Technical Progress report on the Metabolic Studies of Fission Products

1. Radio-autographic Studies

Lung radio-autographs with Y^{86}, Cb^{93}, Zr^{93}, and $Ce^{>140}$, are being continued. Bone radio-autographs for the long lived fission products which show selective deposition in the skeleton will be made shortly following the preparation of suitable bone sections which is now under way.

2. Columbium (Cb^{93})

The tissues and excreta for the 32 and 64 day groups of animals are to be assayed shortly.

3. Cesium (Cs^{135})

Tracer studies with this element have been completed and the experimental data will be reported in detail shortly.

4. Zirconium (Zr^{93})

It is anticipated that the assay will be completed shortly and a full report will follow.

5. Decontamination Studies (Dr. Greenberg, and Dr. Copp)

A series of preliminary experiments to determine the quantitative relationship between the calcium content of diet in rats and the oral uptake of Strontium has been completed. The rats were maintained on a synthetic low calcium diet supplemented by varying amounts of calcium carbonate for two weeks prior to oral and intraperitoneal administration of radio-Strontium. The animals were sacrificed at 4 days and the tissues assayed. The oral absorption of animals on low calcium diets was high as has been previously noted, ranging from 60% to 70%. Animals whose calcium intake was comparable to the average adult human diet revealed a radio-Strontium uptake of approximately 58%. This value fell to approximately 7% when the calcium in

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the diet approximated the equivalent of .5% of calcium carbonate for the average human adult which is from 5 to 10 times the usual calcium intake. Some diminution of retention of radio-Strontium following intraperitoneal administration was noted in the animals which had previously received the high calcium diet, but further experiments will be necessary to obtain a significantly quantitative evaluation of this effect. Further studies on the absorption of radio-Strontium from animals on diets containing .1%, .2%, .3%, .4% and .5% calcium carbonate are now under way for the purpose of determining the critical level of calcium in the diet with respect to the absorption and retention of Strontium. Long term studies of the decontamination of Yttrium and Cerium in rats is now under way. The dose of radioactive material is administered by intramuscular injection and the leg amputated two weeks later to avoid delayed absorption of material at the site of injection.

6. Emanation Studies

The active deposits from the last emanation experiments have been assayed and found to contain, approximately three weeks after the time of bombardment, 57.3% Strontium, 35.0% Barium (La free), 6.2% Cerium, Zr+Cb 1.5% (accuracy doubtful in view of week activity of sample), Yttrium and Praeseodymium less than 1%. These results agree closely with the assays done on the active deposits from another experiment. A more precise and quantitative study of the half lives of the noble gas ancestors of the long lived fission products is now under way. The gaseous emanation from a deuteron bombarded plate is passed through a long copper tube containing axially mounted negatively charged wire. The emanation is passed through the tube at a rate of 10 cm a second and at the termination of the bombardment of the wire, whose total length is approximately 500 cm, is divided into sections of appropriate lengths and each section assayed for long lived

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fission products. This work was undertaken for the purpose of proper planning of the exposure of animals to the emanation products arising from the operation of the pile at "X".

7. Tellurium (Te^{121})

Considerable difficulty has been encountered in the isolation of Te^{121} without carrier from deuteron bombarded antimony. We hope to solve this problem within the next few weeks.

8. Radioactive Smokes and Dusts

A series of preliminary experiments with zinc chloride smoke have been initiated. It has been found that it is possible to deposit up to 40% of the unseparated Uranium free fission mixture on a stable zinc chloride smoke. The animals exposed to this smoke were found to have accumulated a large proportion of the inhaled smoke in their lungs followed by the redistribution of a portion of the retained material in other parts of the body. The proportion of the inhaled activity absorbed from the lung and deposited throughout the other tissues resembled quite closely the results obtained following the direct administration of a solution of the Uranium free unseparated fission products directly into the lungs.

9. Projected Studies for the Next Two Months

Tracer studies are to be continued with Yttrium, Columbium, Zirconium and Cerium. Tracer experiments with Tellurium will be initiated as soon as a satisfactory method for isolating Te^{121} free from carrier has been completed. Emanation experiments, Radio-autographic studies, and decontamination studies are to be continued. Experiments with the zinc chloride smokes will be continued and studies with Uranium smokes are to be initiated shortly. Later, similar investigations will be used with smokes with misch metal and appropriate radioactive dusts.

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ASSOCIATED PROJECTS

II. N.C.I. - R. R. Spencer, Chief

BIOLOGICAL ACTION OF GAMMA AND X RADIATION

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

I. Continuous exposure for 8 hours daily.

Approximate doses up to date (mice and guinea pigs) 2500 r, 1250 r, 625 r, 310 r and 36 r (acute exposures of 12.5 r or 50 r respectively not added). Approximate doses up to date (rabbits) 1800 r, 900 r, 450 r, 225 r and 21 r (acute exposures of 12.5 r or 50 r respectively not added). Approximate dose up to date of inbred male guinea pigs (family 2) exposed on 8 r per 8 hour level 620 r. Approximate dose up to date of hybrid guinea pigs exposed on the 8 r per 8 hour level 400 r.

The experiments are progressing according to schedule. Two male and 1 female mouse of the 8 r per 8 hour level had to be killed and autopsied on account of mediastinal tumors and another female of the same level on account of reticuloendotheliosis of liver and spleen; the diagnosis of reticuloendotheliosis was made from observation on microscopic slides of other mice of this laboratory showing the same gross picture. One female mouse of the 2 r per 8 hour level had to be killed and autopsied due to moribund condition. It showed grossly a large spleen and enlarged lymph node. None of the experimental guinea pigs was autopsied during the work.

Results of Breeding Experiments

This report contains only additional results since the report of December, 1943.

Males 8 r level

Total dose 1600 r
Number of males - 16
8 mated, 8 autopsied

First litter born 2 and ½ months after irradiated males were mated.
Average litter size 8.6 (inc)

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Total dose 800 r Number of males - 16 8 mated, 8 autopsied	Males mated 2 months after removal from field. Average litter size 8.6. 4 remated 2 months later. Average litter size 10.0. 4 remated again 2 months later. Average litter size 9.5 (Inc)
Total dose 600 r Number of males - 16 8 mated, 8 autopsied	Males mated on removal from field. Average litter size 7.5. 4 remated 2 months later. Average litter size 9.0. 4 again remated 2 months later. Average litter size 8.7

Males 4 r level

Total dose 1000 r Number of males - 16 8 mated, 8 autopsied	Males mated on removal from field. Average litter size 7.1
Total dose 800 r Number of males - 16 8 mated, 8 autopsied	Males mated on removal from field. Average litter size 8.2. 4 remated 2 months later. Average litter size 7.3 (Inc.)
Total dose 600 r Number of males - 16 8 mated, 8 autopsied	Males mated on removal from field. Average litter size 7.7. 4 remated 2 months later. Average litter size 7.1 (Inc.)

Females 8 r level

Total dose 500 r Number of females - 16 Mated 28 days after removal	Average litter size 5.9. 8 [illegible] Average litter size 5.0. (Inc. co average litter size 8.66)

Females 4 r level

Total dose 500 r Number of females - 16 Mated 28 days after removal	Average litter size 5.9. 8 remated. Average litter size 5.6. 8 remated. Average litter size 5.6 (Inc.) Controls - average litter size 3.6
Total dose 400 r Number of females - 15 7 mated 40 days after removal. 8 mated 34 days after removal.	Average litter size 7.6. 8 remated. Average litter size 6.8. 8 again remated. Average litter size 3.8 (Inc.) Controls - average litter size 8.5
Total dose 300 r Number of females - 16 Mated 28 days after removal	Average litter size 9.3. 2 remated. Average litter size 8.0 2 again remated. Average litter size 10.0. 2 again remated. Average litter size 9.0. Controls - average litter size 8.7

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II. Continuous exposure for 24 hours daily

Results of breeding experiments

Females 8 r level

Total dose 800 r Total number females - 15 15 mated 28 days after removal	Average litter size 2.5 (Inc.) Six animals have had litters to date. Average litter size, controls - 8.5

Nothing further to report on the histological findings of the breeding experiments.

The test for the influence of age gave the following results:

16 females entered 4 r per day field at 3 months of age and received a total dose of 400 r. 8 were mated at removal. Average litter size 6.4 (Inc.) 8 were mated 28 days after removal.

16 females entered 4 r per day field at 4 months of age and received a total dose of 400 r. 8 were mated at removal. Average litter size 7.6 (Inc.). 8 were mated 28 days after removal.

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

Approximate dose up to date: 1200 r. One mouse died of pneumonia and only 5 mice out of the original 9 of each group are alive.

Results of breeding experiments (acute daily exposure only)

Total dose 300 r Number of females - 3. All mated immediately after receiving total dose of 300 r	Average litter size 7.6. Remated - average litter size 9.3. Remated again - average litter size 10.5 (Inc.)
Total dose of 400 r Number of females - 3 All mated immediately after reaching total dose of 400 r	Average litter size 8.0. Remated - average litter size 7.6
Total dose 700 r Number of females - 3 All mated immediately after reaching total dose of 700 r	1 female had a litter of 1 - a stillbirth.

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IV. Single acute whole body exposure, total dose 300 r

Number of females - 7
All mated immediately after irradiation

Average litter size 6.3. 7 were remated.

V. Pathology

Three mice on the 8 r per 8 hour level that received a total of about 2350 r were autopsied because of their moribund condition and all were found to have massive enlargement of the thymus. Microscopically these are all classifiable as malignant lymphomas. There was a variable degree of infiltration of these cells in various organs in different animals but in all considerable replacement of marrow space in the bones was observed.

In two males the testes were extremely atrophied yet with a few spermatagonia in mitosis in some tubules. The interstitial tissue appeared increased but this is considered to be only relative to tubular atrophy.

In one female, serial sections of one ovary are not yet available for study but in one section of the other ovary no follicles were seen. Slight invagination of the surface germinal epithelium was present and seemed increased over that seen in the animals of the same level that were autopsied after receiving a total of approximately 2000 r. Likewise downgrowth of the capsular cells of the adrenal seemed a little more marked but no definite adrenal cortical adenomas were observed.

VI. Hematology

All mice exposed on the 4 r, 2 r, 1r and 0.1 r per 8 hour levels still show an essentially normal blood picture as compared to that of the controls. The animal of the 2 r per 8 hour level which was killed and autopsied during the month and which grossly showed enlargement of spleen and lymph nodes had a hemoglobin and red count of approximately 50% normal, a total white count of 16,000 with 1% neutrophils and 97% lymphocytes. The total white count of the animals on the 8 r per 8 hour level is lower than that of the controls. Red

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count, hemoglobin and platelets are slightly lowered. No essential change in the counts was observed since the last report. The blood count of the animals killed and autopsied in this group (see I) was essentially the same as that of the other animals of the group.*

The blood picture of the guinea pigs of all levels is essentially the same as that reported last month. Two guinea pigs of the 4 r per 8 hour level are showing a consistent decrease (in comparison with the other animals of the group) in the red count, hemoglobin and platelets. They also show a beginning lymphocytosis.

The blood picture of the rabbits is essentially the same as that reported last month.

*With the exception of the animal showing reticuloendotheliosis of liver and spleen (WBC 1550, neutrophils 63%, lymphocytes 34%).

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