



Section - L. A. Parure, Acting  
Section Chief

- Pack of X-rays
- File folders
- Books, Monitoring
- Vials, Both
- Lead, Leadon
- Aluminum Foil
- Microscope Calibration
- Books, Statistics
- Books, Curves

Section - K. S. Cole, Section Chief

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- Production
- Production of vapors
- Production and exposure
- Toxicity of mixed fission products in rats
- Toxicity of mixed fission products in mice
- Toxicology - 100 r X-ray
- Toxicology - 100 r X-ray
- Radio-biogenesis
- Protective action of nicotinamide
- Food intake and weight changes
- Effects of radiation on circulatory system
- Accumulation and distribution of Sr<sup>89</sup> and of Ba<sup>140</sup> - La<sup>140</sup> in goldfish
- Tracheal metastasis

Microbiology Section - P. E. Church - Section Chief

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- Books
- Reference
- Books

Associated Projects

1. California Project - J. C. Hamilton and Associates  
Biological Progress report on the metabolic studies of fission products

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2. National - R. E. Spencer, Chief  
Biological Action of Gamma and X-Radiation - E. Lorenz,  
W. E. Boston, A. B. Eschenbrenner and M. K. Deringer

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A. SUMMARY OF OVER-ALL PROJECT HEALTH ACTIVITIES

Robert S. Stone, M. A.  
Associate Project Director for Health

Personnel Studies

Six applicants of Chicago and eleven at Clinton were rejected on medical grounds.

The hands of some workers in Chicago, Clinton, Berkeley and Los Alamos have been examined and no changes definitely due to radiations have been found.

Blood studies have uncovered two individuals at Chicago whose counts might be due to over-exposure to radiation. Two individuals at Berkeley who have had persistent low white blood levels have had some over-exposures. Two workers at Clinton have shown a lowering of count with no over-exposure.

A dispensary service for the Metallurgical Laboratories' employees has not yet been fully established because of our inability to produce a doctor. It is expected that one will arrive during March. The Clinton Laboratory dispensary service continues to operate satisfactorily. Two sub-major injuries were cared for: 2 RT burns, 2 finger fractures.

Radiation Hazards

Pocket Ionization Chambers continue to yield valuable information. The chambers in use are not perfect (what instruments are!) but they are sufficiently accurate in a high percent of instances. We ask the cooperation of all offices in investigating high readings since this is the best way of checking them. Under usual conditions low readings are accurate.

Hand and glove contamination studies are well under way at Clinton and are getting started at Berkeley. They have shown many instances of serious contamination that has been radically reduced by proper washing. No satisfactory substitute for soap and water has been found.

Tongue contamination from pipetting an active solution of radon-zirconium has occurred at Clinton. If mouth suction for pipettes continues to be used someone will experience a severe case of radioactive poisoning.

Contamination with product and methods of preventing same are receiving a great deal of attention. Studies of various places in the product laboratory and Room 1 of the separation plant show contamination of desk tops, jacks of centrifuges, gloves, handles of equipment.

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air, etc. A rugged type of portable  $\alpha$ -ray detector is needed for all places when product is used. The Health Division, Chemical Division and Instrument Groups both at Clinton and Chicago are cooperating in developing such instruments. The most important procedure now is for the personnel to protect themselves by extreme precautions including masks when work is not done under a hood.

"Vinylon" has been found by the Chicago group to be an acid resistant cloth that can be decontaminated easily and hence may prove useful for coats and towels.

#### Clinical Biochemical Studies

Liver function tests (colloidal gold, cephalin-cholesterol, and formol-gel) have shown some positive reactions in personnel exposed to radiation and toxicological hazards, but the tests have not yet been tried widely enough to gauge their significance.

Pigment metabolism studies show that (a) project workers exposed to lead or radiation tend to have definite increase in red blood cell protoporphyrin, (b) no essential change in urine coproporphyrin, (c) 17 out of 43 project workers showed positive urine uroporphyrin tests compared to 1 of 12 controls.

Kidney function tests by urine sulfur excretion methods have been negative so far as personnel are concerned but positive for rabbits receiving relatively large injections of tubanyl nitrate.

Initial studies of blood proteins by the electrophoretic method indicate some changes possibly due to radiations.

#### Biological Research

The use of heated  $T_2O_8$  to produce Xe <sup>133</sup> has been set aside to further test  $T(OH)_4$  at pile operating temperatures.

Inhalation experiments are still in the "study of method" stage.

5 mC ( $25 \times 10^{-6} \text{C/gm}$ ) of mixed f-products by stomach tube killed rats; apparently by damage to stomach and intestines because very little was absorbed. 0.64 mC did not kill them.

Ba<sup>140</sup> - La<sup>140</sup> in equilibrium, given to mice by intraperitoneal injection kill the animals with amounts of the order of 17  $\mu\text{C/gm}$ . The retained activity is mostly in the bones. Lymphocytes are affected early, polymorphs later. On the other hand, the bone marrow destruction was most complete and occurred very early.

Total body radiation with external  $\beta$  rays has its earliest effect on eyes of rabbits. 600 r seems to be the minimal effective dose.

Stable cerium and barium are toxic to goldfish in concentrations of 10 ppm (by weight) and non lethal in 30 days at concentrations of 1 ppm.

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$Sr^{89}$  and  $Ba^{140} - La^{140}$  are taken up rapidly by goldfish initially. The high point is not reached, because for several weeks the fish continue to take up more even though the water concentration is decreasing. The skin and scales contain the greatest concentrations of both (40 - 75%). For strontium the skeleton contains the highest concentration and for barium-lanthanum the organs and muscles. The feces become highly contaminated apparently by adsorption, reaching 1000 times the water concentration.

Bar Harbor mice have a 50% lethal dose of 117 n of pile (Clinton) neutrons and about 800 r of pile (Clinton) gamma rays. Exposure to mixed neutron and gamma ray radiations in the pile give confusing results since one experiment showed only partial additivity and the other showed more than total additivity.

A method of preparing a good fixed source of beta rays for testing external effects of these has been devised. Red phosphorus powder mixed with lucite (100 to 120) can be made into sheets and exposed in the pile. A satisfactory yield of  $P^{32}$  results.

It has been found that the fission recoil apparatus delivers not only gaseous parents of fission products but also normally solid fission products which have no gaseous point, such as tellurium.

"Pure" fission products are now being separated at Clinton and used there and in Chicago for biological studies: 40 mC of Sr, 18 mC of Sr plus Ba; considerable "super-juice" (mixed fission products free from tuballoy).

The rabbits in pile stack gases are receiving about 0.6 r/day of external beta rays plus an unknown amount of unknown elements into the body.

University of California Radiation Laboratory

Final reports on the metabolic studies of columbium, cesium, barium, praseodimium and emanation studies have been completed and will appear as CH reports in the next month.

Attempts at removing Yttrium and Cerium from the body have so far been unsuccessful.

30% of the fission activity in powdered tuballoy was found to be volatilized by using a carbon arc. When this smoke was inhaled the various fission products were found to behave in the same manner as when injected separately into the lungs in solution.

Product studies: - Oral absorption of all valence states is less than 0.05%; lung retention high; absorbed material predominately in skeleton; excretion very small in urine and feces.

Health Physics and Radiation Measurements

Pocket meter service is expanding both at Clinton and in Chicago.

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The percent of off-scale readings for February at Clinton was 2.7 for single meters and 0.1 for double meters. The statistically probable percent of "double events" is 0.07. Thus with two meters per individual good accuracy is possible. By the use of single meters plus cooperation on the part of the group leaders, etc. in checking man's action a fair record of each individual's exposure is possible.

Parker's section has found that at 35% humidity there is no leakage of pocket chambers, with or without dessicator but that at 75% humidity there is trouble without dessicator.

Projection minometers have been found to have the following defects: (1) charging voltage changes with time, (2) the charging button sticks too frequently, (3) repair and replacements of rectifier circuit is unsatisfactory.

Both at Clinton and Chicago it has been found that Lauritsen electroscopes require a complete calibration chart for all intensities if they are to be interpreted accurately. Moreover, the calibration for  $\gamma$  rays does not correspond with that for beta rays.

Methods of surveying for  $\alpha$  rays are receiving a great deal of attention. In addition to  $\alpha$  ray counter the Clinton group have developed an electroscope (modified Lauritsen) to test table tops, etc. At Chicago Dersham electrometers and Wollan-Landsverk electroscopes are being tried out.

Atmospheric surveys at Clinton have shown no appreciable activity to date.

Surveys of activities of all kinds have been routinely conducted throughout the Clinton and Metallurgical laboratories, including the Argonne gas

At Clinton it has been found that in tanks of "average" chemical solutions 100 curies of 2 MEV beta activity the gamma radiation by Bremsstrahlung is the same as from 1 curie of 2 MEV gamma activity. This must be taken into consideration in shipments of large quantities of beta emitters.

N. C. I.

Breeding experiments are showing possible irradiation effects in reduced litter sizes. The effects are more severe with more intense radiation. With 8 r per 8 hours the same effect is found from 500 r total as from 800 r when given at the rate of 8 r per 24 hours. Male mice receiving 1600 r at 8 r per 8 hours do not mate for a period of approximately two months, but subsequently matings result in a normal litter size production. Female mice receiving 300 r as a single acute whole body exposure remain fertile for not more than two months but then become sterile with apparently no recovery. Mice exposed to doses of 4 r and less per 8 hours still show normal blood pictures while those

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getting 8 r show definite decreases. Mice getting 4 r in one hour out of each 24 show a normal blood picture. One animal in the group developed a leukemia. Rabbits getting 8 r per 8 hours and having received approximately 2000 r still have normal blood findings. At least the abstract of the N.C.I. report should be read as it is too complicated to synopsise.

Memorial Hospital

Two patients are under observation, getting 10 r per 24 hours.

U. of C. Hospital

In addition to the previous patients treated on the 100 and 200 KV machines, some further patients are being given total body radiation on the 1000 KV apparatus.

Meteorology

The Meteorological work is continuing at Site W. Arrangements are being made to study dilution from the stack by means of SO<sub>2</sub>. Further observation has shown that the most dangerous time so far as concentration is concerned is in the early morning, just as the cloud inversion is breaking up, the vertical circulation starts. It has been found that the up and down drafts bring the smoke to the surface in dense columns within the 200 W area itself.

Note:

For Clinton Laboratories Health Report see CH-1470 (A-2060).

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B. 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 Period Covering January 15 - February 29, 1944

A. Clinical Section - J. J. Nickson, M.D. and M. J. Nickson, M.D.

1. Pre-Employment Examinations

During the period January 15 - February 15, 1944, 189 examinations were done. Thirty-nine of these were on academic personnel, 130 on non-academic personnel. Six applicants were rejected.

2. Health Surveys off the Project

From February 1 - 2, a radium dial painting plant was visited. The trip was planned to obtain background for the planning of New Chemistry alterations. On February 3, a metal machining plant was inspected. Details of this report will be found in the Clinical Section of the Clinton report.

On February 21, the St. Louis Cyclotron was visited. The main purpose of this trip was to discuss the possible effects of radiation with the cyclotron crew. Inspection of the men's hands revealed no detectable change.

3. Liaison Committee Meetings

No attempt will be made to discuss the Committee reports in detail. Those interested will find the minutes on file in the Library.

Dr. Pardue made 24 surveys at the request of the Committee. In two instances, the surveyor felt that over-exposure was probable.

Dr. Schwartz was asked to survey 23 individuals by the Committee. His findings will be found in his section of this report.

Three product accidents were discussed in the minutes. During the month, Mr. Pyle joined the Committee. He will be responsible for disposal of waste active materials, discussed below.

Dr. M. Nickson reported on the literature of the toxicity of Biphenyl and acenaphthene at the request of the Technical group.

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## Trichlorethylene Hazard

Site B, room 135, has a Blakeslee degreaser which operates with trichlorethylene. The usual tolerance figure given is 200 parts per million in air. On February 17, 1944, Mr. Goldberg of the Illinois Department of Public Health determined the amounts of trichlorethylene in air at various times during the operation of the degreaser. The highest value obtained was 138 p.p.m.

MUC-EG-392 gives the details of this survey.

## Radiation Over-Exposure Records

During the past month, a new system of checking the persons having chamber readings of greater than 100 milliroentgens was instituted. A letter is sent to the exposed individuals' group leader requesting information concerning: (1) the person's activities on the day of over-exposure, (2) knowledge of accident to the chamber, and (3) group leader's evaluation of the correctness of the reading. A monthly summary of this information will be presented in future reports.

## Acid Resistant Cloth for Protective Clothing

During the month, the idea of obtaining an acid resistant cloth which could be decontaminated by rinsing in strong acid solutions was developed. A search, aided by Mr. Kimpton's Office, showed that Vinyon, a polymerized vinyl acetate, was the most likely available woven material. Decontamination tests with both product and fission products were carried out by this group and Dr. Pardue's group. Details of the tests are found in Dr. Pardue's report. In brief, the tests indicated that all of the samples could be decontaminated with ease.

Because of the expense involved (\$16.00 per coat, estimate) and because of uncertainties as to the material's resistance to ordinary wear, a "scout" order of but 100 coats and 50 towels was placed. Vinyon 26 was selected. It would seem that Clinton and Hanford might be able to use this or a similar material to good advantage.

If subsequent experience indicates that widespread use of such coats would be desirable, a larger order can be considered.

## Tuballoy Dust Survey

During the month, a non-academic employee was added to the personnel of the Clinical Group. It is planned to expand the monitoring of amounts of Tuballoy dust in air. For the most part, the monitoring locations will be in Site B. Mr. Tourek will spend one-half of his time on this work.

## Finger Printing Study

Mr. Tourek will devote one-half of his time taking Finger Prints. The impressions will be sent to Dr. Roger A. Harvey for interpretation.

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Projected Work for Month

1. Continuance of pre-employment exams.
2. Continuance of Metallurgy Laboratory surveys.
3. Continuance of Product Hazard surveys.
4. Expansion of Finger Print program.
5. Expansion of Tuballoy dust surveys.

B. Hematology - L. O. Jacobson and E. Marks

The clinical hematology group examined 1107 individuals during the period 1/15/44 to 2/15/44. The following table gives an analysis of the laboratory examinations made:

No. of Exams.	Hgb.	RBC	WBC	Differentials	Platelets	Urines	Retics.	Wass.
	685	600	970	970	135	700	50	200

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Two individuals showed blood abnormalities possibly due to over-exposure to radiation. The first occurred in a person working with a gram Ra-Be source. Since this work has stopped, his white blood cell count which had fallen has risen in the direction of normalcy. The second person was overexposed to a Rn source. There was a small drop in the total leucocytes and a marked change in the P/L ratio. This has slowly corrected itself.

C. Electrophoretic Studies of Proteins - E. S. Guzman Barron and John Muntz

There is evidence, from the published literature, that serum proteins change in distribution as a consequence of X-ray treatment. It is our purpose to follow these changes by electrophoretic analysis of the proteins both in patients receiving X-ray therapy and in animals treated with X-rays. We are well aware that in patients it will sometimes be impossible to obtain the control analysis. However, data for electrophoretic distribution of serum proteins obtained by a number of investigators agree so closely that the normal values of this laboratory can be used as control values.

One patient, J. M., has been studied on different occasions after he received X-ray therapy. Unfortunately we do not have the serum electrophoretic pattern before radiation started. On Nov. 26 and 27 the patient received two X-ray applications of 100 r each; on Dec. 16, 17, 18 and 20 he received 75 r each day; on the 25th he received a blood transfusion. The serum proteins were determined electrophoretically on seven different occasions from Dec. 15 to Dec. 27 (Table I). On Dec. 15, 18 days after X-ray therapy the distribution of serum proteins was about normal. On Dec. 16, the day after application of 75 r, there was a profound modification in the distribution of serum proteins, characterized by a decrease of albumin and an increase of globulin. Whether this was due to the action of X-rays or not cannot

be decided until more observations are made. This pattern was maintained with some modifications; the last sample of blood, taken 7 days after radiations stopped there was still some decrease in albumin and increase in  $\gamma$  globulin. Two patterns accompany this report: one, of J. M. on Dec. 24; the other from a normal serum. The distribution of serum proteins of another patient (J. G.) is being studied. Unfortunately this is a patient with carcinoma of the stomach where there is ordinarily an increased  $\gamma$  globulin.

The effect of radiation on the distribution of serum proteins cannot be reasonably determined unless we find an animal having a constant electrophoretic pattern. The dog had to be discarded because the serum has four to five globulins which seem to change from one to the other. We are now studying for this purpose the electrophoretic patterns of the serum proteins of the rabbit, the rat, and the goat. Rabbit sera was analyzed at the following ionic strengths: 0.05, 0.06, 0.075, 0.1 and 0.15. In general, only three components were observed regardless of the serum concentration. Furthermore there was no constancy in the mobility of the protein components. Goat serum was analyzed at ionic strength 0.075. Four components were observed which separated from each other to allow their measurement. The mobilities of the protein fractions resembled those of human serum. Rat serum was analyzed at ionic strength 0.075. Further work will be done with this animal. It is our opinion that work on the effect of radiation on blood proteins must be concentrated to studies on the goat and the rat.

Table I

Distribution of serum proteins of J. M. from electrophoretic analysis.

Date	Total protein %	Alb.	Glob.	Percent B. glob.	$\gamma$ glob.
12-15-43	6.97	63.0	5.7	11.5	19.9
Radiation 75 r 12-16-43	5.74	47.9	5.4	16.4	30.2
Radiation 75 r 12-17-43	6.85	57.5	1.5	10.7	30.2
Radiation 75 r 12-18-43	5.46	64.1	2.7	7.5	25.5
Radiation 75 r Dec. 20 12-22-43	6.12	49.4	5.6	14.9	31.2
12-24-43	5.55	50.2	5.8	12.3	31.7
12-27-43	6.53	57.1	7.4	10.7	24.8
Normal values	7.00-7.60	62.5-65.5	6.2-7.9	12.6-15.2	13.1-15.7

Electrophoretic patterns of Blood Serum

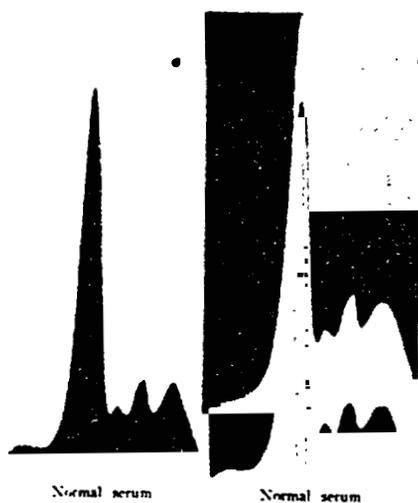
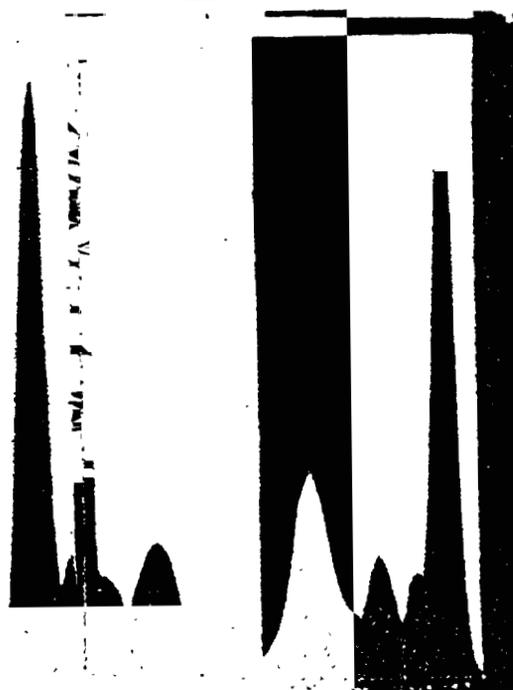


FIG. 1. NORMAL SERUM



Patient J. M. Dec. 24, 1943

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D. Toxicology Group: Albert Tannenbaum, H. Silverstone

The chronic feeding experiments on the toxicity of various T compounds are being continued, and are now in their fifth month. The toxicity of single subcutaneous injections of T compounds is being studied, including the effect of second injections. A program of inhalation studies is being investigated.

E. Report of Biochemical Group: S. Schwartz

The study of numerous tests which aim at the early detection of exposure to and toxicity from radiation and metal has continued along the general lines previously outlined. The results of these studies to date are summarized below.

In these studies the control series consists of 14 medical students, several non-exposed members of the project staff, and a few newly employed project members. It is recognized that some of the latter, at least, may not have been perfectly "normal." The exact number of controls for each test are shown on the appropriate figure.

The project members investigated have been those believed most likely to yield positive results. For radiation effects the groups of Mr. Cunningham and Sugarman in New Chemistry were studied. The group in Room 109, Site B, was studied because of considerable tuballoy dust exposure. In addition, several individuals were investigated because of exposure to lead or various chemicals.

I. Liver function studies.

A. Serum proteins - (with L. Schneider and J. J. and M. Nickson)  
Three tests have been studied to gain insight into both qualitative and quantitative protein changes in project personnel, namely, colloidal gold, cephalin-cholesterol, and formol gel. The first two of these tests, at least, have been shown to be commonly positive in liver disease as a consequence, chiefly, of altered serum globulin.

1. Colloidal gold test.

The method used is that described by S. Gray (to whom we are indebted for aid in preparing our solutions). Three serial dilutions of serum are used, with results expressed in terms of 0 - 5 depending on the color change and amount of precipitation present. Normally all of the tubes will read 2 or 3. A weakly positive test is indicated by a reading of 4 or 5 in the first tube. With increasing liver dysfunction the second and third tubes read 4 and 5 also.

In none of the control series was a positive test obtained. On the other hand, 12 of 42 project members

studied had at least a weakly positive test. This is illustrated in Fig. 1 where the number in each group is plotted against the sum of the 3 tubes. With this scheme only 8 are seen to fall outside the normal range. It might be pointed out here that only 3 of this group had a positive cephalin-cholesterol test, (2 plus or more).

## 2. Cephalin-cholesterol

The method of Hanger has been modified to include 8 tubes with serial dilutions containing from 0.2 to 0.0001 cc. of serum. Results are read in terms of 0 - 4 plus depending upon the amount of flocculation and clearing present. A 2 plus or greater reading in the first tube is believed indicative of liver dysfunction.

Although to date the first tube only appears to be significant we are for the time being plotting our data in terms of the sum of the first 3 tubes.

In none of the normal controls studied has a 2 plus or more test been encountered. In 8 project members 2 plus to 4 plus flocculation has occurred. The test was repeated at a later date in 2 of these 8 with positive results again. It might be pointed out that only 2 of these 8 had a positive colloidal gold reaction, indicating again a different mechanism for the two tests.

Strongly positive tests (3 - 4 plus) were obtained from the sera of two individuals exposed to considerable tuballoy dust in Room 109, Site B. A 4 plus reaction was also obtained on one individual exposed to lead. The data is illustrated in Fig. 2.

## 3. Formol gel

The emptying time of serum from a modified white blood cell pipette is measured before and about 6 hours after the addition of a drop of formaldehyde. The ratios of these two times is dependent upon the globulin content of the serum. As shown in Fig. 3, the ratio in project members has been found to vary widely from about 1.0 - 1.7. Four have been over 2. Our normal control series is still too small to permit any conclusions to be drawn.

Protein studies in dogs and rabbits exposed to either radiation or metal have yielded no worthwhile information. Both species normally have a 3 - 4 plus cephalin cholesterol test. In acute experiments in rabbits no change has been noted in the colloidal gold test. Isolated observations indicate a marked increase in sedimentation rate following tuballoy injection. This point is being studied further at the present time.

## II. Pigment Metabolism Studies (with E. Katz, F. Felter and M. Mandel)

### A. Red blood cell protoporphyrin

The most marked increases in red cell protoporphyrin have been encountered in workers exposed to lead. Thus 2 of 4 workers in the foundry Room 42 in Ryerson had levels of above 65 gamma per cent, (normal level 15-30 gamma per cent). Other high values have been encountered in personnel receiving relatively large radiation exposure of chronic type. In general it can be said that, compared with medical students, exposed project members have relatively high red cell protoporphyrin levels. This is illustrated in Fig. 4.

It might be noted that only one of the control group had a value above 33 gamma per cent, and his protoporphyrin level was up to 65 gamma per cent. A repeat determination 4 days later showed a fall to 41 gamma per cent. While the explanation for this increase is uncertain, it might be noted that he had had an acute bronchitis 4 days earlier for which he had taken 8 grams sulfathiazole. It is believed that this is sufficient to exclude him as a control.

B. Urine coproporphyrin

Project members with a few exceptions, appear to have a relatively normal urine coproporphyrin excretion. At the present time this is being quantitated from an aliquot of a 3 hour afternoon specimen. Most of the studies done to date are on 24 hour collections.

In Fig. 5 the data is given in terms of coproporphyrin concentration in the urine. The highest concentration (19.5 gamma per cent) was found in the urine of Mr. Y., exposed to considerable trichlorethylene fumes at Site B.

Coproporphyrin studies on rabbits receiving subcutaneous injections of tuballoy nitrate are illustrated in Fig. 6. These graphs might more properly be included in the section on kidney function, since the damaged kidney will not excrete coproporphyrin. This undoubtedly is the explanation for the marked fall observed, despite any tendency which might have been present to cause an increased excretion because of tuballoy toxicity. Experiments are now in progress to determine whether doses of 0.25 mg/Kg or less will cause an increased coproporphyrin excretion which will not be inhibited by kidney insufficiency.

C. Urorosein

Urorosein is a red compound formed in strong acid solution from oxidized indolacetic acid. Its exact clinical significance is unknown but it often appears to be associated with dietary deficiency. The urorosein test is performed by extracting a 100 cc aliquot of urine with ether following acidification with 15 cc glacial acetic acid. The ether is first extracted repeatedly with 10% HCl to remove the porphyrin, and then with 25% HCl to remove the urorosein. A positive test is indicated by a red color with absorption maximum at 543 mμ. Using the Evelyn photoelectric colorimeter maximum absorption is obtained using the 520 mμ filter. Because the 25% HCl extract contains numerous pigments in addition to urorosein, we have been measuring its absorption in the Evelyn colorimeter using various filters.

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Urine sulfur has been quantitated using the nephelometric method of Freon and Crutchfield. Blood sulfur has been quantitated by a modification of the method of Denis, using 20 - 30 mesh barium chloride rather than 10% barium chloride to precipitate the sulfur.

- a. A study of 3 rabbits who received 4 mg/Kg tuballoy nitrate.

All died from 12 - 15 days following oliguria or anuria of several days duration. The number of sulfur determinations done following the injections was very small but indicated a marked drop in sulfur excretion. Thus average control levels of 100 - 150 mg per cent fell to 2 - 36 mg per cent before death.

Since the blood sulfur method was not available at the outset, control determinations on the injected animals were not obtained. However, postinjection levels on the injected rabbits and on 3 control animals reveal a marked increase in blood sulfur as demonstrated in Fig. 7.

- b. A study of 3 rabbits who received 1.5 mg/Kg tuballoy nitrate by subcutaneous injection.

As shown in Fig. 8 all 3 rabbits had a marked fall in urine sulfur concentration. The sulfur level of I-14 and I-16 rose shortly to normal and these animals have shown apparent complete recovery. Sulfate excretion of I-15 remained low. He died 17 days after the injection.

Attention is called again to the reduction in urine coproporphyrin; following tuballoy injection. (See Fig. 6)

#### IV. Phosphorus studies - (with L. DeGrazia and A. Edwards)

Abels et al have reported a marked increase in the organic acid soluble phosphorus of white blood cells following total body radiation of as little as 3 r to leukemic patients. They were, however, unable to adapt their method to the small number of white cells in normal blood.

A simple procedure has been worked out for quantitating several phosphorus fractions in the white cells of less than 1 cc normal blood. Both human and animal studies are in progress and will be reported next month.

#### V. Individual scoring.

In the table which follows, the results of our studies of representative members of 4 groups of exposed and non-exposed individuals are summarized in terms of 0-4 + reactions. The following significance may be attached to each of these figures:

0 = Definitely normal range

1+ = Borderline values

2+ through 4+ = Increasingly positive reactions

In order to arrive at a composite value which will roughly represent the individual's reactions to the various tests used, the following method of scoring has been devised:

Cephalin cholesterol 1 - 4+ with increasing flocculation as described by Hanger.

Colloidal gold: Sum of 3 tubes.

- 0 = 5 - 8
- 1+ = 9 - 10
- 2+ = 11
- 3+ = 12 - 13
- 4+ = 14 - 15

RBC protoporphyrin in gamma per 100 c.c. erythrocytes

- 0 = < 30
- 1+ = 30 - 40
- 2+ = 40 - 50
- 3+ = 50 - 70
- 4+ = > 70

Urorosein and associated pigments

Evelyn reading at 400 mμ and 520 mμ

400 mμ	520 mμ
0 = 100 - 60	0 = 100 - 75
1+ = 60 - 50	1+ = 75 - 60
2+ = 50 - 30	2+ = 60 - 40
3+ = 30 - 20	3+ = 40 - 25
4+ = 20 - 0	4+ = 25 - 0

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Urine coproporphyrin in gamma per 100 c.c. urine.

- 0 = < 8
- 1+ = 8 - 10
- 2+ = 10 - 13
- 3+ = 13 - 18
- 4+ = > 18

## Group I. Controls. Normal medical students

ect	Cephalin- chlesterol*	Colloidal gold*	R.B.C. proto- porphyrin	Urine copro- porphyrin*	Spectroscopy "urorosein" fraction		Abs. 510 m $\mu$	Score
					400 m $\mu$	520 m $\mu$		
1.	0	0	1	0	0	0	0	1
2.	1	0	0	0	0	0	0	1
3.	0	0	0	0	0	0	0	0
4.	0	0	0	0	0	0	0	0
5.	0	0	0	0	0	0	+++	1
6.*	0	0	3	1	1	0	0	5
7.	1	1	0	0	0	0	0	2
8.	0	1	0	0	0	0	0	1
9.	1	1	1	0	0	0	0	3
10.	1	0	0	0	0	0	0	1

## Group II. Controls. Project members with what is believed to be relative by slight exposure.

1.	1+	0	0	0	0	0	0	1
2.	0	0	1+	0	0	0	0	1
3.	0	0	0	0	0	0	0	0
4.	0	0	1+	0	0	0	0	1
5.	0	0	0	0	0	0	0	0

Group III. Predominant exposure: T-dust and chemicals. (Site B)  
Project members.

1.	1+	2+	1+	3+	2+	2+	+	12
2.	4+	1+	1+	2+	2+	3+	+	14
3.	1+	2+	2+	0	1+	1+	+	8
4.	3+	1+	0	0	0	0	+	5
5.	1+	0	0	4+	3+	4+	+	13

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Group IV. Project members. Predominant exposure:  
radiation and chemicals. (New Chem.)

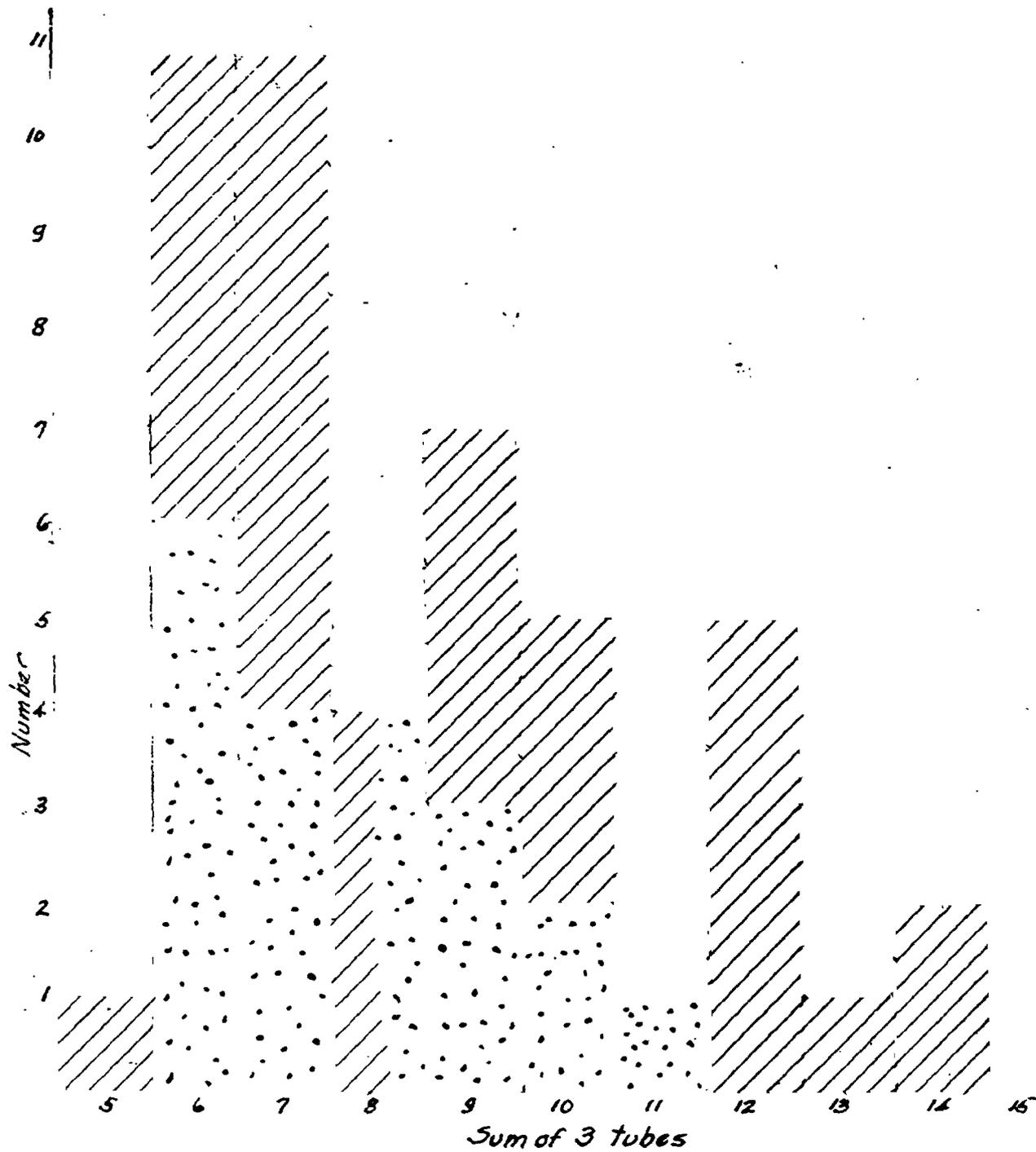
ject	Cephalin cholesterol*	Colloidal gold*	R.B.C. proto- porphyrin	Urine copro- porphyrin*	Spectroscopy "urorosein"		Abs. 510 m	Score
					400 m	520 m		
1.	1+	3+	2+	2+	1+	1+	0	10
2.	1+	1+	0	1+	2+	2+	0	7
3.	1+	0	2+	1+	3+	3+	0	10
4.	0	3+	3+	0	0	0	0	6
5.	4+	4+	-	1+	4+	3+	0	16

6 grams sulfathiazole 4 days previously  
weak absorption only after standing 48 hours

Summary

A high incidence of project members exposed to relatively large amounts of radiation, tuballoy, or chemicals have been found to have positive reactions to several different tests. These indicate an effect of some kind on the liver, kidney, or hematopoetic systems. In general, a "positive reactor" will be positive for several different tests. Data is as yet insufficient to ascertain the seriousness of these positive results, though it should be emphasized that most of the deviations from normal are only moderate.

**FIGURE 1**  
**Colloidal Gold Test**  
*(Human Studies)*



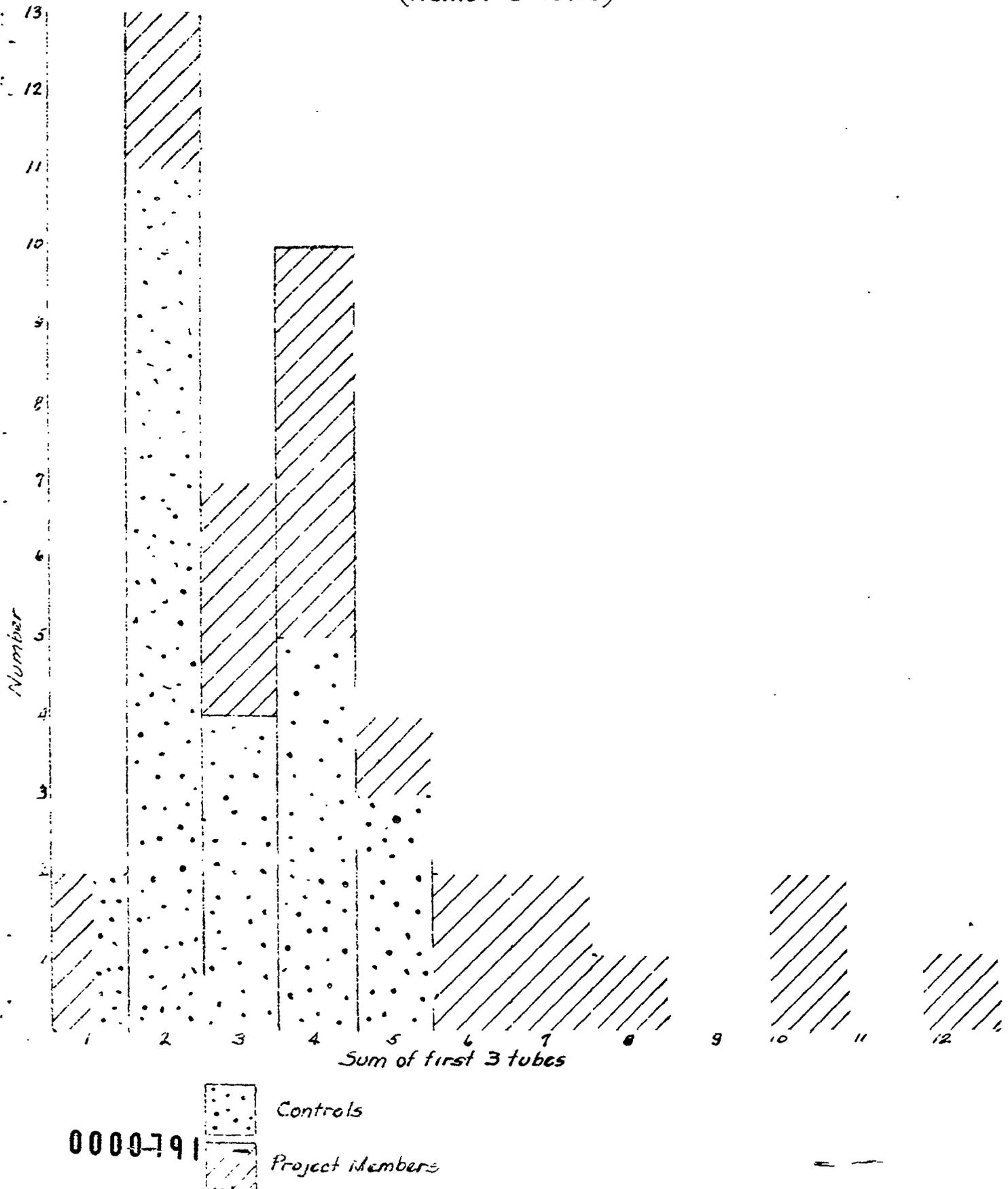
 Controls

 Project Members

0000790

FIGURE 2

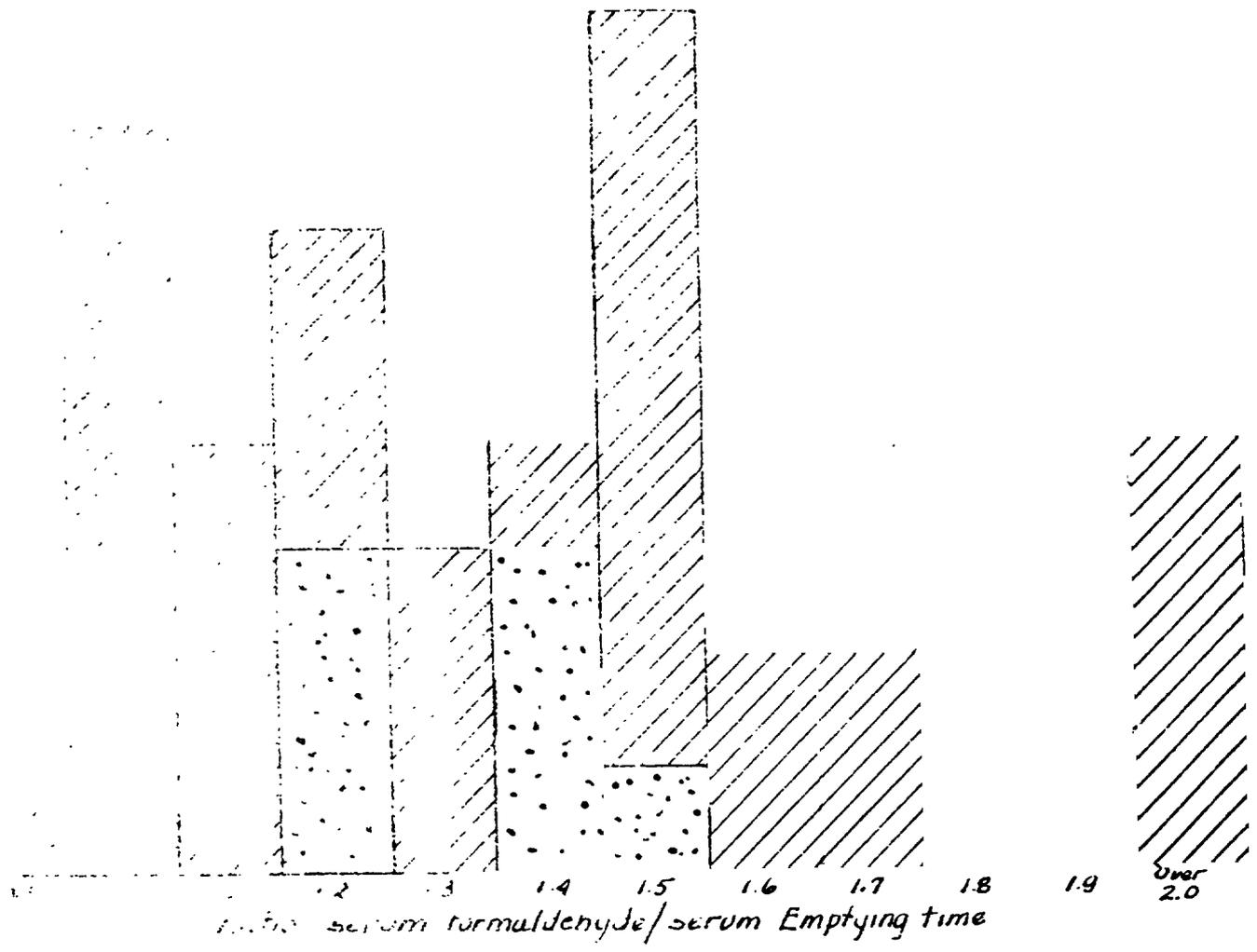
Cephslin Cholesterol Test  
(Human Studies)



0000-791

FIGURE 3

*Formol Gel Test  
(Human Studies)*



 Controls  
 Project members

FIGURE 4

Red Blood Cell Protoporphyrin  
(Human Studies)

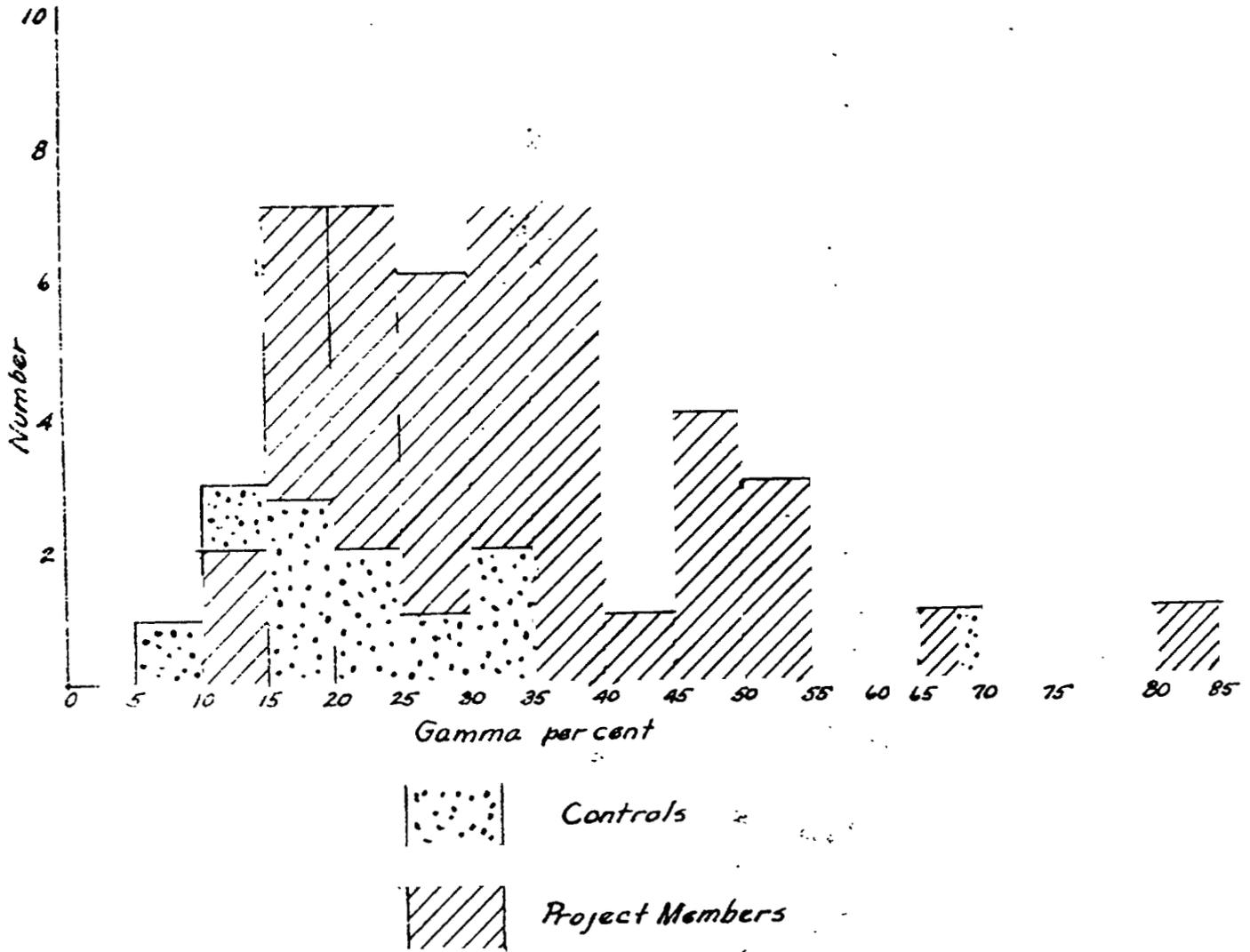
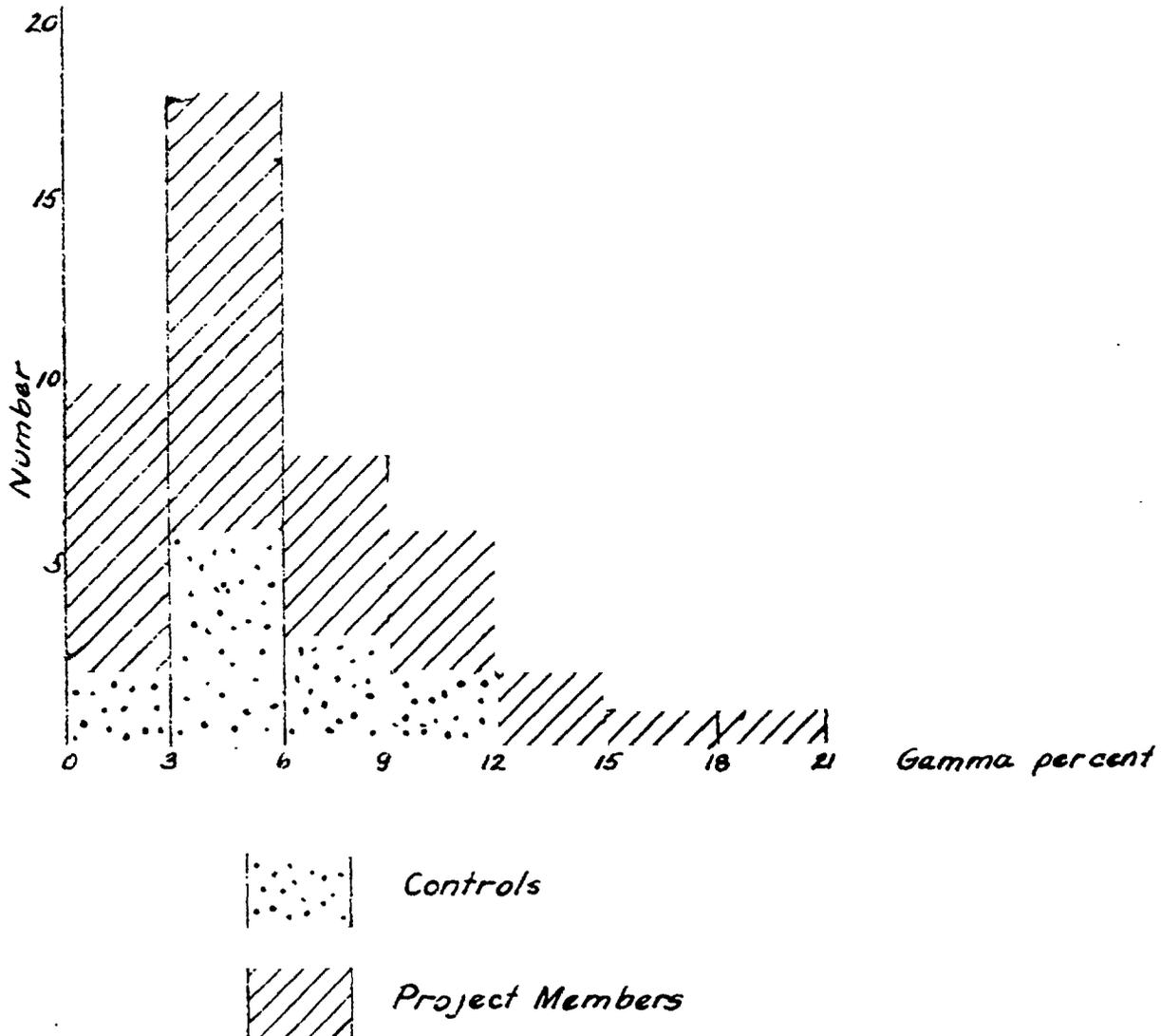


FIGURE 5

Urine Coproporphyrin Concentration  
(Human Studies)



F. 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

ABSTRACTA. Breeding Experiments

The data presented in this report tend to substantiate the following tentative conclusions.

1. The first indication of a possible irradiation effect, namely, reduced litter size, is noted in the following groups of females - those receiving 800 r on the 8r/day level, those receiving 500 r on the 8r/8 hour level, and those receiving 700 r at the rate of 5 r/1 hour.

2. The rate of administration appears to have an effect on the production of reduced litter size. The first indication of reduced litter size in the females on the 8r/day level was in those receiving 800 r while on the 8r/8 hour level, reduction was apparent in those receiving 500 r.

3. Results obtained to date from subsequent matings have not given any indication that following irradiation there is a reduction in the period of fertility in animals which produced normal-sized first litters.

4. A dose of 1600 r administered at the rate of 8r/8 hour is sufficient to prevent mating of male LAF<sub>1</sub> mice for a period of approximately two months following irradiation. Recovery follows with subsequent matings which result in normal litter size production.

5. It now appears that a single acute whole body exposure with a total dose of 300 r is sufficient to prevent reproduction in LAF<sub>1</sub> female mice after an initial fertile period of not more than two months. This is in line with earlier studies on the effect of irradiation on fertility in mice.

6. In former work the initial indication of chromosomal changes (mutations) produced by irradiation in mice has been reduced litter size. It should be emphasized that in these experiments in all cases when the males mated normal sized litters were produced. Furthermore, any reduction in litter size from the irradiated females was associated with a reduction in follicle number when the ovaries were sectioned one month after the birth of the litter. Thus, as yet, there is no tangible evidence of chromosomal changes. It is recognized, however, that these tests could not be expected to reveal slight increases in mutation rate.

B. Histology of Genital Organs of the Animals of the Breeding Experiment

The histologic findings of the genital organs of the animals of the breeding experiments have been in line with the breeding results.

The only change noted in the males on the 4 r per 8 hours per day level was a slight decrease in the size of the testes and a slight reduction in sperm content of the epididymis although one group received a total dose of as much as 1000 r. At a total dose of 1000 r on the 8 r per 8 hours per day level the males showed changes in spermatogenesis which indicates an influence of rate of administration of dose when compared to the results of the 4 r level, the effect of the latter being less severe. Spermatogenesis was almost completely absent in males after a total dose of 1600 r given at 8 r per 8 hours per day, but nearly complete recovery had occurred by 3 1/2 months after the animals were removed from the field.

Males were exposed continuously on the 4 r per day level to total doses ranging up to 1000 r. The only change noted was a slight reduction in size of the testes of the animals receiving the total dose of 1000 r.

Females exposed on the 8 r per 8 hour per day level to a total dose of 500 r showed histologic changes of the ovaries. There was a decrease in number of follicles, especially the more mature ones, and an increase in luteal and luteal-like tissue. There was also marked invagination of the germinal epithelium. They were still having estrous cycles. Females exposed on the 4 r per 8 hour per day level received total doses of 300 r, 400 r and 500 r. Those receiving 500 r showed a slight decrease in size of the ovaries but aside from that, no changes were found that could definitely be attributed to the irradiation. When compared to the results of the 8 r level this again emphasizes the importance of the rate of administration of dose.

Females were exposed continuously on the 8 r per day level to total doses of 300 r, 400 r, 500 r, 600 r and 800 r. Those receiving 800 r showed ovarian changes. The ovaries were reduced in size, being composed, chiefly of luteal and luteal-like tissue. There were but few follicles, the more mature ones being extremely rare. The germinal epithelium showed extensive invaginations. However, the vaginal epithelium indicated normal estrous cycles.

Slight change was seen in the 600 r group and those receiving 500 r and less showed no change. Those receiving 500 r on the 8 r per 8 hour per day level showed some change indicating that the effect is more severe when the 8 r is given in 8 hours each day than when given in 24 hours.

Females were exposed on the 4 r per day level to total doses up to 500 r on the 2 r per day level up to 400 r on the 1 r per day level up to 300 r and on the 0.5 r level up to 100 r. The only changes noted on these levels were probably old age effects.

### C. Hematology

The blood picture of mice having received approximately 2800 r up to the present at the rate of 8 r per 8 hours per day is essentially unchanged from that given in previous reports (decrease of W.B.C., some animals having a W.B.C. of 800-1000, and slight decrease in R.B.C. and platelets in some animals). All other mice exposed for the same length of time at lower rates (4 r, 2 r, 1 r, 0.1 r per 8 hours per day) show a normal blood picture in comparison to that of the controls. All animals receiving either a daily acute exposure of 5 r given in 1 hour or this daily exposure in addition to a chronic exposure of 0.1 r per day (total dose 1350 r) show a normal blood picture although they all have chronic pneumonia and the majority died from this disease. One animal of the 8 r per 8 hour group had to be killed on account of leukemia (terminal W.B.C. 54000). So far, altogether 4 animals of this group developed leukemia (3 had lymphosarcoma, see previous report).

The blood picture of the guinea pigs exposed since March 1941, is as follows: 8 r per 8 hour group (2 out of 18 alive, total dose approximately 2800 r). Slightly lowered W.B.C., lowered R.B.C. and platelet count. 4 r per 8 hour group. Lowered W.B.C. and platelet count. R.B.C. either normal or only slightly lowered. Animals of the 2 r, 1 r and 0.1 r per 8 hour groups show a normal blood picture. Inbred guinea pigs (male) on 8 r per 8 hour level: (approx. dose 900 r) Lowered W.B.C. and platelet count. R.B.C. normal. Hybrid guinea pigs (2nd series) 8 r per 8 hour level (approx. dose 650 r) lowered W.B.C. R.B.C. and reticulocyte count normal.

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One animal of the 4 r per 8 hour group was killed and autopsied due to anemia. (approx. dose 1200 r).

One animal of the 8 r per 8 hour group (2nd series) died of internal hemorrhage (approx. dose 650 r).

The blood picture of the rabbits is essentially normal. The 8 r per 8 hour group having received so far approximately 2000 r.

#### D. Pathology

Two male guinea pigs that had received less total amount of radiation (approx. 500 r) on the 8 r per 8 hour level than any previously observed had marked atrophy of spermatogenic elements but with a few mature spermatazoa in the epididymis. In one male guinea pig that had received a total of approximately 32r on the 0.1 r per 8 hour level all tissues appeared normal.

Two male mice that had received a total of approximately 2600 r on the 8 r per 8 hour level had extreme testicular atrophy yet with spermatogenic elements persisting in a few places. One of these animals had leukemia.

In one female mouse that received a total of approximately 1200 r at the 5 r per 1 hour level no follicles were present in the ovaries.

BIOLOGICAL ACTION OF GAMMA AND X RADIATIONI. Continuous Exposure for 8 Hours Daily

Approximate doses up to date (mice and guinea pigs 1st series) 2300 r, 1400 r, 700 r, 350 r and 40 r (acute exposures of 12.5 or 50 r respectively not added). Approximate doses up to date (rabbits) 2000 r, 1000 r, 500 r, 225 r and 23 r (acute exposures of 12.5 r or 50 r resp. not added). Approximate doses up to date of male inbred guinea pigs (family 2) exposed on 8 r per 8 hour level 900 r. Approximate dose up to date of female inbred guinea pigs (family 2) - exposed since February 3, 1944 - 230 r. Approximate dose up to date of hybrid guinea pigs (2nd series) exposed on the 8 r per 8 hour level 650 r.

The experiments are progressing according to schedule. Two mice of the 8 r per 8 hour level were killed and autopsied after having received approximately 2500 r. One showed grossly markedly enlarged lymph nodes. Testes were extremely small in both animals. Another mouse of the same level died. The autopsy showed grossly normal organs with the exception of extremely small testes. The cause of death was not apparent. One control female mouse and one female mouse on the 1 r per 8 hour level (total dose approx. 230 r) were killed and autopsied on account of mammary carcinoma. They showed grossly normal organs.

Two male guinea pigs (2nd series) on the 8 r per 8 hour level were killed and autopsied after having received approximately 500 r to obtain information as to early damage to the testes. Grossly the testes were somewhat small, all other organs appeared normal (see V). In the first experiment on this level it was found that a total dose of approximately 1000 r showed considerable atrophy of the testes with almost complete absence of spermatogenesis. Another male guinea pig of this series died after having received an approximate dose of 650 r the cause of death was a massive intra-abdominal hemorrhage. It is interesting to note that the first guinea pig of the 1st series had to be killed on account of anemia after having received approximately the same dose. One control guinea pig and one guinea pig of the 0.1 r per 8 hour level had to be killed on account of intercurrent disease.

Three male and three female guinea pigs each of the 2 r and 1 r per 8 hour level which had received an additional acute exposure of 50 r two months after the start of the experiment, were given another acute exposure of 50 r during the month. So far, no change in above picture has been observed.

RESULTS OF BREEDING EXPERIMENTS

This report contains only additional results since the report of January 1944.

Males 8 r Level

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

First litter born 2 and 1/2 mo. after irradiated males were mated. Average litter size 8.3. 4 remated one month later. Av. litter size 10.2 (Inc.)

Total dose 1000 r  
Number of males 16  
8 mated, 8 autopsied

Males were mated 2 months after removal from field. Average litter size 8.2 4 remated 1 1/2 mo. later. Average litter size 8.1. 4 again remated 1 1/2 mo. later. Average litter size 9.3 (Inc) 4 remated 1 1/2 mo. later. Av. litter size 8.3 (Inc.)

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 1 1/2 mo. later. Average litter size 10.0. 4 remated again 1 1/2 months later. Average litter size 10.0 (Inc.) 4 remated 1 1/2 mo. later. Av. litter size 10.0 (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 1 1/2 mo. later. Average litter size 9.1. 4 again remated 1 1/2 months later. Average litter size 8.7. Remated for the third time 1 1/2 mo. later. Average litter size 9.3.

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. 4 remated 1 1/2 mo. later. Av. litter size 9.6 (Inc.)

Total dose 800 r  
Number of males 16  
8 mated, 8 autopsied

Males mated on removal from field. Average litter size 8.3. 4 remated 1 1/2 months later. Average litter size 9.4. 4 remated 1 1/2 mo. later. Av. litter size 8.7 (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 re-  
mated 1 1/2 months later. Average  
litter size 9.0. 4 remated 1 1/2  
mo. later. Av. litter size 8.1 (Inc)

Females 8 r Level

Total dose 500 r  
Number of females 16  
Mated 28 days after  
removal

Average litter size 5.8. 8 remated.  
Average litter size 5.5 (Inc).  
Controls - 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  
again. Average litter size 5.0 (Inc)  
Controls - average litter size 8.6

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 4.4.  
8 again remated. Av. litter size  
4.6 (Inc) Controls - average litter  
size 8.6. (Control for 1st mating)

Total dose 300 r  
Number of females 16  
Mated 28 days after re-  
moval

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. 2 remated for 4th time.  
Average litter size 9.0. Controls -  
Average litter size 8.7.

Histological Findings on Reproductive Organs

Males 8 r Level

Total dose 1600 r -

8 males autopsied at time of removal from field.

The testes are greatly decreased in size. There is a decrease in tubular area and a relative increase in interstitial tissue. All tubules show destruction of the spermatogenic cells. In some a ring of Sertoli cells is all that is present; in others a few spermatogonia and primary spermatocytes also are found, but more mature spermatogenic cells are extremely rare. There are no spermatozoa in the epididymis.

2 males autopsied after 1st mating (Approx. 3 1/2 months after time of removal from the field).

These animals show almost complete recovery. Normal spermatogenesis is found in most of the tubules and the sperm content of the epididymis is comparable to that of the controls. The interstitial tissue of the testes appears as that of the controls. This supports the previous opinion that the increase in interstitial tissue of the males autopsied at the time of removal is a relative increase only. Normal females mated to these males had litters approximately 2 1/2 months after the males were removed from the field.

Total dose 1000 r -

8 males autopsied one month after time of removal from field.

The testes were decreased in size. Some of the tubules show only early spermatogenic cells; others show progressively later stages with a few showing spermatozoa. There are but few spermatozoa in the epididymis, and immature forms (spermatids and spermatocytes) are found there.

4 males autopsied after 1st mating (4 months after removal from field).

The testes and sperm content of the epididymes of these males were within the limits of the controls. Normal females mated to these males 2 months after the males were removed from the field gave birth to normal sized litters.

Total dose 800 r -

8 males autopsied 1 1/2 months after time of removal from field.

Histology of testes and spermatozoa content of epididymis were within the limits of the controls.

4 males autopsied 3 1/2 months after time of removal (after 1st mating).

Same as those autopsied at 1 1/2 months. Normal females mated to these males 2 months after the males were removed from the field gave birth to normal sized litters.

Total dose 600 r -

8 males autopsied one month after time of removal from field.

The testes were slightly decreased in size. While most of the tubules show approximately normal spermatogenesis

some have only early stages and still more have but few spermatids and spermatozoa. The number of spermatozoa in the epididymis is reduced and immature forms are present. The testes of the 800 r group described above were in better condition than the testes of this 600 r group. This is probably because of more recovery in the 800 r group as the time was extended 15 days for the 800 r group.

3 males autopsied after 1st mating (1 to 2 mo. after removal from the field).

The testes and spermatozoa content of the epididymis show more recovery than the above group autopsied one month after removal, and were within the limits of the controls except for possible decrease in size. Females mated to these males immediately after the males were removed from the field gave birth to normal sized litters. Additional groups are being exposed on this level to total doses of 1000 r, 800 r, and 600 r to get the histologic picture of the testes at the time of removal from the field.

#### Males 4 r Level

Total dose 1000 r -

8 males autopsied at time of removal from field.

Testes are slightly reduced in size. Tubules show normal spermatogenesis with a possible reduction in mature sperm number. The sperm content of the epididymis is slightly reduced.

Total dose 800 r -

8 males autopsied at time of removal from field.

Except for a possible slight decrease in size of the testes, the picture for these animals is within the limits of the controls.

4 males autopsied after 1st mating (1 1/2 months after time of removal).

Histology of testes and sperm content of the epididymis of these males are within the limits of the controls. Normal females mated to these males at time of removal from field gave birth to normal sized litters.

Total dose 600 r -

8 males autopsied at time of removal from field.

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Although there was slight decrease in size of the testes, spermatogenesis and sperm content of the epididymis were within the limits of the controls except for one male. This male had a right inguinal hernia accompanied by extreme atrophy of the right testis with absence of tubules.

4 males autopsied after 1st mating ( 1 1/2 months after removal from the field).

Histology of the testes and sperm content of the epididymis of these males were within the limits of the controls. Females mated to these males at the time the males were removed from the field gave birth to normal sized litters.

Females 8 r Level

Total dose 500 r -

5 females autopsied after weaning 1st litter (3 to 4 months after removal from field).

Ovaries are slightly decreased in size. There appears to be a reduction in the number of the more mature follicles and an increase in luteal and luteal-like tissue. This increase may be only relative. Invaginations of the germinal epithelium appear to be more extensive than in the control ovaries.

The vaginal epithelium indicates normal estrous cycles.

These females showed reduced litter size when mated 28 days after removal from field.

Females 4 r Level

Total dose 500 r -

8 females autopsied after weaning 1st litter.

Two of these females showed an endometritis with an attempt to resorb a retained foetus. Of the other six the ovaries were slightly decreased in size but otherwise they were within the limits of the controls.

Vaginal epithelium indicated normal estrous cycles.

These six females gave birth to normal sized litters.

Total dose 400 r -

7 females autopsied after weaning 1st litter.

Ovaries were within the limits of the controls except for one female whose ovaries were slightly decreased in size. This female had had a litter of six stillborn.

Vaginal epithelium of all these females indicated normal estrous cycles.

With the one exception these females gave birth to normal litters.

Total dose 300 r -

14 females autopsied after weaning 1st litter.

Appearance of ovaries within limits of controls. Vaginal epithelium indicates normal estrus cycles.

These females gave birth to normal litters.

## II. Continuous Exposure for 24 Hours Daily

### Results of Breeding Experiments

#### Females 8 r Level

Total dose 800 r	Average litter size 2.6
Total number females 15	(Inc.) Eight animals have had
15 mated 28 days after removal.	litters to date. Average
	litter size controls - 8.5

16 LAF<sub>1</sub> female mice have been exposed on the 8 r 1 day level and will receive a total dose of 700 r.

#### 4 r Level

16 LAF<sub>1</sub> female mice have been exposed on the 4 r 1 day level; 8 will receive a total dose of 800 r and 8 will receive a total dose of 700 r.

#### Females 2 r Level

Total dose 500 r	Average litter size 3.7
Total number females 16	(Inc) Ten animals have had
Mated 4 days after removal from field.	litters to date

## Females 0.5 r Level

Total dose 100 r	Average litter size 4.2
Total number females 15	Average litter size -
All mated 28 days after removal	Control 6.0

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

16 females entered 4 r/day field at 3 months of age and received a total dose of 400 r. Eight were mated at removal, average litter size 7.4. Eight were mated 28 days after removal. Average litter size 6.4 (Inc.)

16 females entered 4 r/day field at 4 months of age and received a total dose of 400 r. 8 were mated at removal. Average litter size 6.1. 8 were mated 28 days after removal. Average litter size 4.1 (Inc.)

16 females entered 4 r/day field at 5 months of age and received a total dose of 400 r. 8 were mated at removal. Average litter size 7.2 (Inc). 8 were mated 28 days after removal. Average litter size 6.0 (Inc.).

## Histological Findings on Reproductive Organs

## Males 4 r Level

Total dose 1000 r -

7 males autopsied at time of removal from field.

Except for a possible reduction in size the testes of these males are within the limits of the controls, and the sperm content of the epididymis is comparable to that of the controls.

3 males autopsied after 1st mating (1 mo. post irradiation)

Histology of testes and sperm content of epididymis within limits of controls. Normal females mated to these males gave birth to normal litters.

4 males autopsied after 2nd mating (3 mo. post irradiation)

Histology of testes and sperm content of epididymis within limits of controls. Normal females mated to these males gave birth to normal litters.

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Total dose 800 r -

8 males autopsied at time of removal from field.

Histology of testes and sperm content of epididymis within limits of controls.

7 males autopsied after 1st mating (28 days post irradiation).

Histology of testes and sperm content of epididymis within limits of controls. Normal females mated to these males had normal litters.

Total dose 600 r-

8 males autopsied at time of removal from field.

Histology of testes and sperm content of epididymis within limits of controls.

7 males autopsied after 1st mating (28 days post irradiation)

Histology of testes and sperm content of epididymis within limits of controls. Normal females mated to these males had normal litters.

#### Females 8 r Level

Total dose 800 r -

2 females autopsied after weaning 1st litter (2 to 2 1/2 months post irradiation).

The ovaries of these females are reduced in size. The organ is primarily composed of luteal and luteal-like tissue. Developing follicles are few in number the more mature ones being extremely rare. There are numerous anovular rings some of which have hyaline centers - the remnants of the zona pelucida. The germinal epithelium shows extensive invaginations.

The vaginal epithelium of one female was cornified, the other was classified as metestrus - 2.

These females had had litters reduced in size.

Total dose 600 r -

14 females autopsied after weaning 1st litter.

The ovaries of 12 of these females were within the limits of the controls. Of 2 females the

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ovaries were more like those of the 800 r group described above. These two females had litters of 3 each while the others had litters of normal size.

The vaginal epithelium of all indicated normal estrous cycles.

Total dose 100 r -

15 females autopsied after weaning 1st litter.

Appearance of ovaries and vaginal epithelium within the limits of controls. Reared litters of normal size.

Total dose 400 r -

15 females autopsied after weaning 1st litter.

Appearance of ovaries and vaginal epithelium within the limits of controls. Reared litters of normal size.

Total dose 300 r -

15 females autopsied after weaning 1st litter.

Appearance of ovaries and vaginal epithelium within the limits of controls. Reared litters of normal size.

Females 4 r Level

Total doses, 100 r, 200 r, 300 r, 400 r and 500 r.

15 females for each total dose autopsied after weaning 1st litter.

The histology of the ovaries of all was within the limits of the controls. In all the vaginal epithelium indicated normal estrous cycles. Females of all groups had normal litters.

Females 2 r Level

Total doses, 100 r, 200 r, 300 r and 400 r.

15 females for each dose autopsied after weaning 1st litter.

The ovaries of all were within the limits of the controls and in all the vaginal epithelium

indicated normal estrous cycles. All groups had normal litters.

#### Females 1 r Level

Total dose 100 r - 11 females.

10 females autopsied after 1st litters.

The histologic pictures of the ovaries of these females were within the limits of the controls. In three females the vaginal epithelium was not typical of a normal estrous cycle but this was the following abnormal parturition. These 10 females had litters of reduced size as did the control females of comparable age.

One female of this group which did not have a litter and was autopsied 6 months post irradiation had ovaries which were reduced in size. There were no follicles, the organ being composed chiefly of luteal-like tissue. The vaginal epithelium showed deep cleft-like invaginations. These changes, however, may be old age effects only, a point which will be checked further.

Total doses 100 r and 200 r.

15 females each, autopsied after 1st litters.

The histologic pictures of the ovaries of these females were within the limits of the controls, and the vaginal epithelium in each case indicated a normal estrous cycle, except for one animal with endometritis resulting from an attempt to resorb a foetus. The litter size for these groups was comparable to that of the controls.

#### Females 0.5 r Level

Total dose 100 r -

11 females autopsied after 1st litter.

The histologic pictures of the ovaries of these females were within the limits of the controls. In three females the vaginal epithelium was not typical of any phase of a normal estrous cycle, but this was probably an old age effect.

III. Continuous Exposure for 8 Hours Daily Plus Daily Acute Exposure of 5 r Given in One Hour

Approximate dose up to date: 1350 r. All animals of the control group, receiving the 5 r daily exposure only died of pneumonia. Only 3 animals of the experimental group receiving beside the daily exposure the chronic exposure of 0.1 r in 8 hours daily are alive. The remainder died of pneumonia. As these 3 animals also have pneumonia, it is planned to kill them within the next few days. All animals that came to autopsy showed - as for the more or less severe autolysis made possible to ascertain - grossly normal organs and small ovaries. A complete report of this experiment will be made after all histological sections are available for examination.

Results of breeding experiments (acute daily exposure only):

Total dose 300 r                      Average litter size 7.6. Re-  
Number of females 3                  mated average litter size 9.3.  
All mated immediately              Remated again - average litter  
after receiving total dose          size 11.3. Remated again.  
of 300 r                              Average litter size 8.0 (Inc)

Total dose 400 r                      Average litter size 8.0. Re-  
Number of females 3                  mated - average litter size 7.6.  
All mated immediately              Remated again. Average litter  
after receiving total dose          size 7.0 (Inc)  
of 400 r.

Total dose 700 r                      1 female had a litter of 1 - a  
Number of females 3                  Stillbirth. 2nd female had a  
All mated immediately              litter of 2 - both Stillborn.  
after receiving total dose  
of 700 r.

IV. Single Acute Whole Body Exposure - Total Dose 300 r -

Number of females - 7                  Average litter size 6.3.  
All mated immediately              All animals remated. After having  
after irradiation                      been remated from one to two  
months, none of these females has  
become pregnant.

V. Pathology

Mice

One male mouse that was killed due to poor general condition after receiving a total of approximately 700 r on the 2 r per 8 hour level showed no changes attributable to radiation. Its poor condition was due to chronic urinary obstruction of non-infectious origin.

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Of four female mice receiving approximately 1300 r on the 5 r per 1 hour level the gross findings in three are given elsewhere in this report, tissues being too autolyzed for histologic examination. One mouse exposed on this level for a total of approximately 1200 r was examined histologically and the findings were similar to those observed in the mice on the 8 r per 8 hour or the 4 r per 8 hour level that had received a total of approximately 1000 r. The ovaries were small, devoid of follicles and there were invaginations of the germinal epithelium. Lymph nodes contained giant follicles and there was no bone marrow atrophy.

Two male mice on the 8 r per 8 hour level that had received a total of approximately 2600 r showed extreme atrophy of the tubules of the testes yet with a small amount of spermatogenic elements remaining in places. No mature spermatozoa were present. One of these mice had lymphatic leukemia with extensive infiltrations of almost all organs.

#### Guinea Pigs

Two male guinea pigs (series 2) that were killed after exposure for two months for a total of approximately 500 r on the 8 r per 8 hour level showed marked tubular atrophy in the testes although some mature spermatozoa were present in the epididymis. The atrophy of spermatogenic cells was of about the same order as was noted in another animal (series 1) observed after three months on the same level (total of approximately 750 r), but the tubules had not shrunken in diameter to as great a degree. In the two guinea pigs receiving a total of 500 r there was no apparent atrophy of the bone marrow in contrast with the impression of slight atrophy existing in the guinea pig that received a total of 750 r.

One male guinea pig was examined after receiving a total of approximately 32 r (20 r chronic and 12.5 r acute exposure) on the 0.1 r per 8 hour level. All tissues appeared normal.

#### VI. Hematology

There is little change in the blood picture since the last report. All mice exposed on the 4 r, 2 r, 1 r and 0.1 r per 8 hour level still show an essentially normal blood picture as compared to that of the controls. The total white count of the animals on the 8 r per 8 hour level is persistently considerably lower than that of the controls. Some of the animals (females) show a total white count of 1000. The average total white

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few animals show also a slight decrease in Red count, hemoglobin and platelets with the majority of these animals showing these counts normal. One male mouse of this level developed leukemia after an exposure of approximately 2500 r. Its total white count rose from 3000 to 54000 in 4 weeks with 5% polys and 94% lymphs. It also showed anemia. This is the fourth animal of this group developing leukemia.

The blood picture of the guinea pigs on the 2 r, 1 r and 0.1 r level is normal in comparison to that of the controls. Reticulocyte counts on the normal guinea pigs gave values between 0.3 % and 1 %, the majority having 0.6 % to 0.7 %. The total white count of the guinea pigs on the 4r per 8 hour level is lower than normal, the platelet's count is also lower while only a few animals show a decrease in red count and hemoglobin. One animal of this group (female) was killed and autopsied during the month after having received a dose of approximately 1200 r. Its red count was 1.6 and platelet count 100,000. The 2 (out of 18) animals surviving on the 8 r per 8 hour level have received so far approximately 2800 r; this is on an average approximately twice the dose at which the other 16 animals had to be killed. The total white count is only slightly lowered, with a somewhat more pronounced lowering of red count and platelets. There has been no change in the counts of these animals for the past three months, they behave in every way like normal animals.

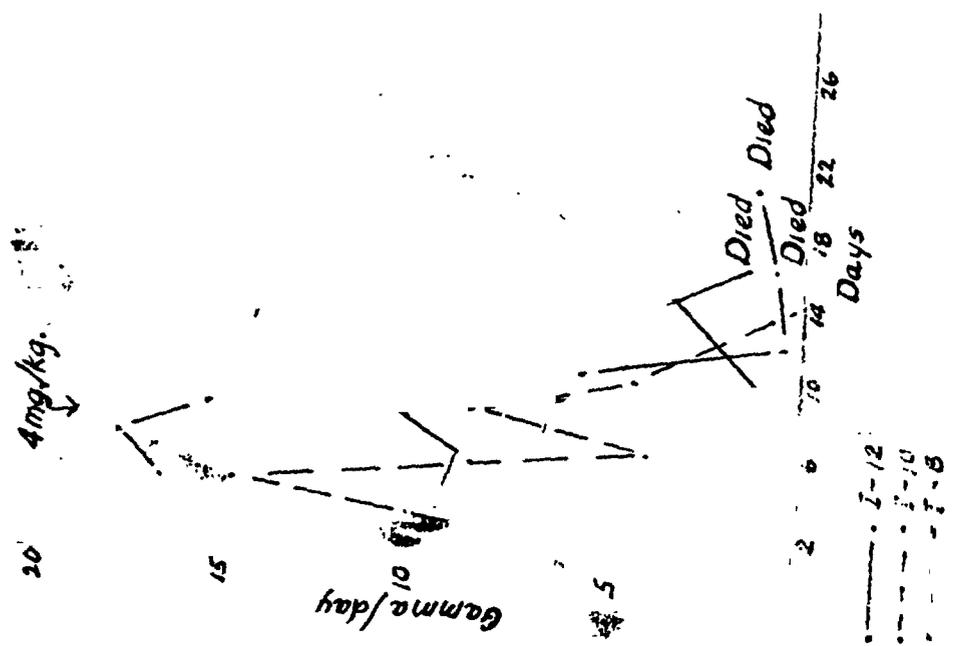
The blood picture of the male inbred guinea pigs on the 8 r per 8 hour level (dose approximately 900 r) shows a lowered total white count (between 2500 and 5000) and a lowered platelet count (200,000). The blood picture of the female inbred guinea pigs is normal (approximate dose 230 r). The blood picture of the 2nd series of hybrid guinea pigs on the 8 r per 8 hour level (approximate dose 650 r) shows a lowered total white count (2000-5000) the red count is normal, likewise reticulocyte count is normal. The red count of the guinea pig which died of internal hemorrhage was normal. Platelet count was not taken; it is assumed that the hemorrhage was due to a low platelet content.

The blood picture of the rabbits is normal. Those on the 8 r per 8 hour level which showed a lowered total white count in previous months, show now a fluctuating essentially normal white count.

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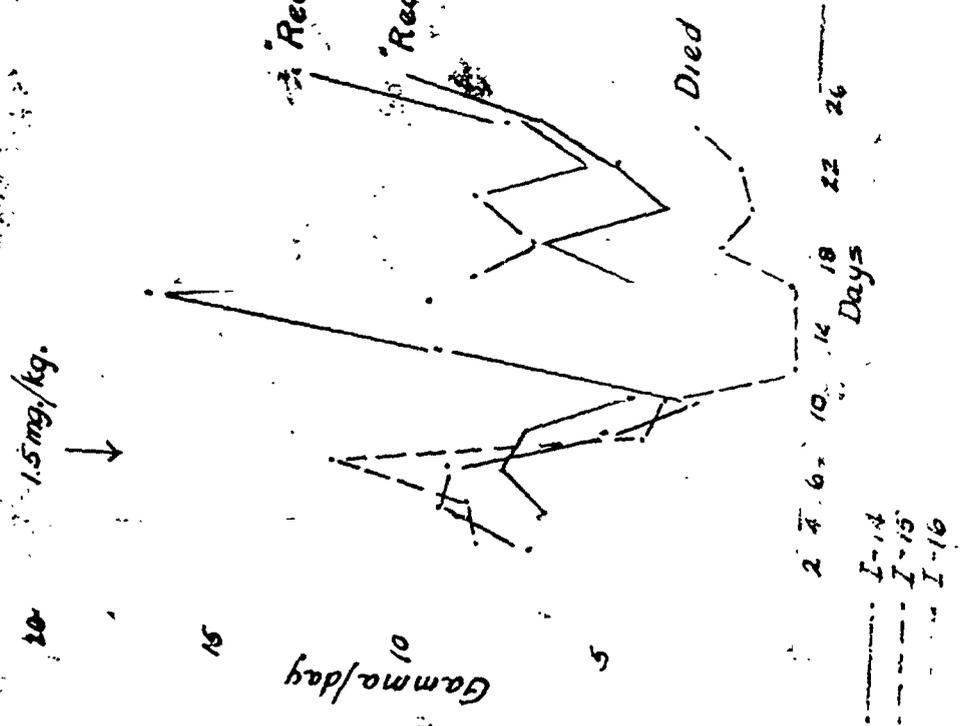
FIGURE 6.

a.



b.

1.5mg/kg.



Urine Cuprenone Excretion in Rabbits Following Subcutaneous Injection of Relatively Large Doses of methyl Nitrate

## F. ASSOCIATED PROJECTS

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

#### Abstract

Tracer studies with Columbium (with the exception of the 64 day lung experiments which must be repeated) have been completed, and are presented in a final report. Tracer studies with Zirconium have been completed on rats receiving this element by intramuscular and intrapulmonary administration, and the complete report has been prepared for the emanation studies. Radio-autographic studies with Yttrium, Zirconium, Columbium, and Cerium are being continued, and decontamination studies with Cerium and Yttrium are also being continued. A small series of smoke experiments using powdered Uranium metal containing the long-lived fission products together with appropriate amounts of ammonium perchlorate, ammonium chloride, and hexachlorethane have been initiated. It was established that almost 100% of the total activity present in the metal was distributed in the smoke. Tracer studies with product have now been initiated and will be continued.

\* \* \*

#### A. Technical progress report on the metabolic studies of fission products

##### 1. Radio-autographic studies

Lung radio-autographs with  $Y^{86}$ ,  $Zr^{93}$ ,  $Cb^{93}$ , and  $Ce^{140}$  are being continued. Bone radio-autographs for the long lived fission products which show selective deposition in the skeleton are now being made.

##### 2. Columbium ( $Cb^{93}$ )

The tracer studies, with the exception of the 64 day lung experiments which must be repeated, have been completed and are presented in the final report.

##### 3. Zirconium ( $Zr^{93}$ )

The assays of the distribution of this element following intramuscular and intrapulmonary administration have been completed. Unfortunately, it will be necessary to repeat the 64 day I.M. studies due to the accidental loss of two of the animals. The outstanding character of carrier-free Zr following I.M. administration is that the unabsorbed portion remaining at the site of injection ranges from 90% at one day, to 70% at 64 days. The skeleton is the chief depot of retention for the absorbed portion and also has the highest activity per gram of wet weight. The next most active tissue is kidney, which averages approximately one-third the activity per gram of bone. This ratio apparently persists throughout the entire 64 days. The pulmonary retention of radio-Zr is extremely high. It ranges from 75% to 90% during the first four days to 70% at 64 days, of the retained activity. The corresponding per gram values are 60% during the first four days and 45% at the 64 day interval.

#### 4. Decontamination Studies (Dr. Greenberg and Dr. Copp)

Decontamination studies with Ce and Y following intramuscular administration revealed that the addition of inert carrier, and the use of various agents employed in the Sr experiments produced no significant evaluation in the rates of elimination.

#### 5. Emanation Studies

The complete report has been prepared for the animal studies. Likewise, the determination of the half-lives of the noble gaseous ancestors of the long life fission products has been reported. The apparent half-lives are as follows: Sr<sup>89</sup>, approximately 33 seconds; Y<sup>92</sup>, 5.7 seconds; Zr. fraction, 3.1 seconds; Ba<sup>140</sup>, 9.8 seconds; Ce<sup>141</sup>, 1.7 seconds; and Pr<sup>143</sup>, less than 0.2 second. These values are subject to some error due to weak activities available. The Zr fraction apparently did not contain Zr<sup>93</sup> and possibly the activity may have been due to the 20 day Zr.

#### 6. Radio-active Smokes and dusts

A small series of smoke experiments using powdered U metal containing the long lived fission products together with appropriate amounts of ammonium perchlorate, ammonium chloride, and hexachlorethane have been initiated. It was established that almost 100% of the total activity present in the metal was distributed in the smoke. A group of rats were exposed to this material. The animals were sacrificed in three groups, one group immediately after exposure, the second group at four days and the third group at 16 days. The animals sacrificed immediately after were found to have 86% of the total activity retained and deposited in the lungs. The corresponding lung deposition at four and sixteen days was found to be 36% and 45% respectively. With both these groups, most of the absorbed activity was deposited in the skeleton. Recently, a new and more representative method for the production of radio-active smokes from U has been developed. Powdered U metal containing the long lived fission products is packed within a core of a carbon rod. The carbon rod is then used with a second rod to produce an electric arc. The procedure has been found not only to produce a very finely divided U smoke but also approximately 35% of the fission activity in the U can be volatilized. Animals have been exposed to this smoke and the assays of the distribution of the inhaled activity are now being made.

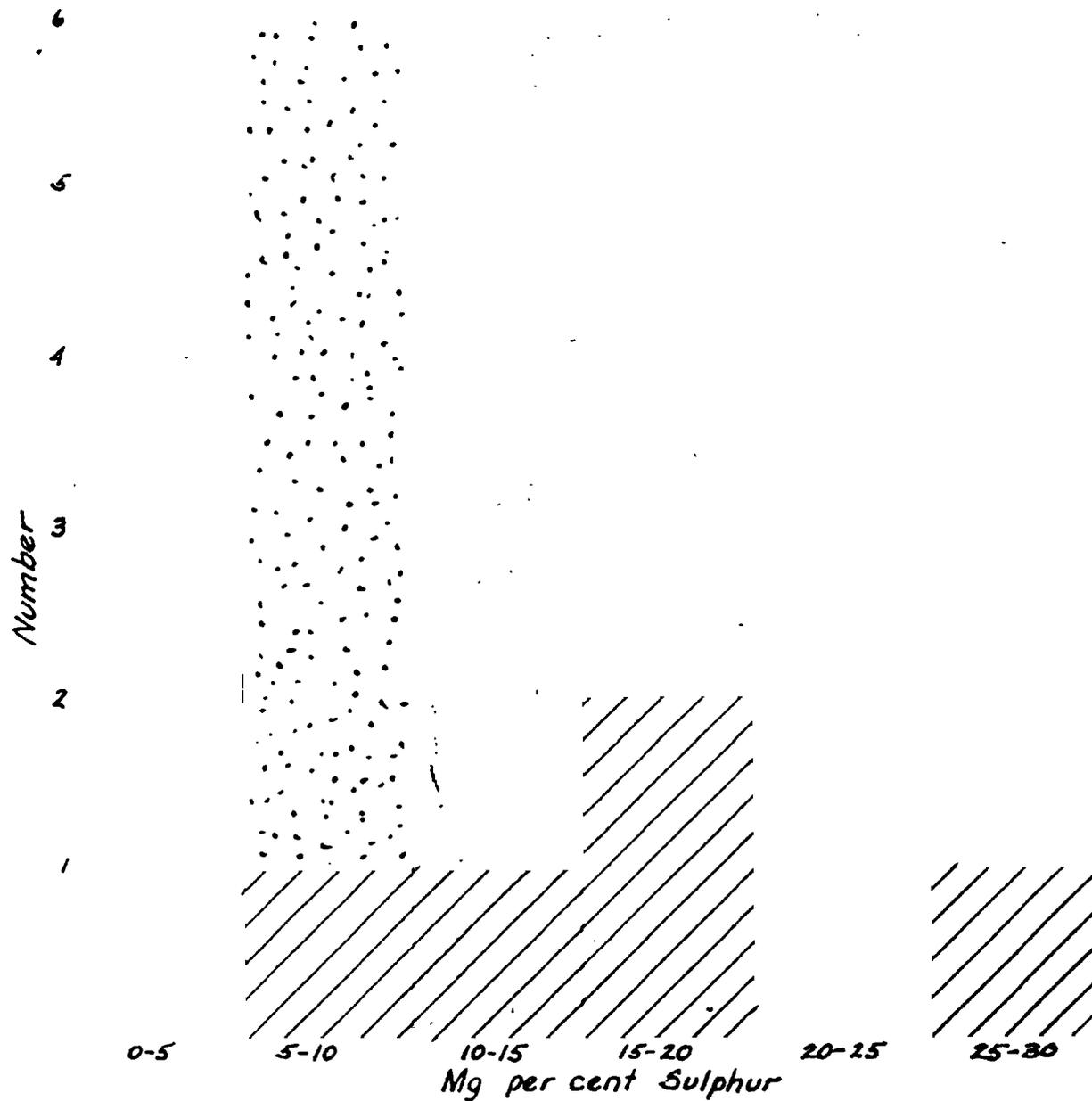
#### 7. Product

Eleven milligrams of product as the tetrachloride was received February 8, 1944. A portion of the sample was converted to the plus 3 and plus 6 forms with the aid of members of Professor Latimer's group and preliminary experiments initiated to determine the metabolic behaviour of the 3 valence states following I.M. and oral administration. Each animal received approximately 15 micrograms. The animals are to be sacrificed at four and sixteen day intervals. Preliminary results reveal the following points: (1) In the plus four state it is not absorbed from the digestive tract in rats to any significant degree. (2) The initial experiment sets an upper level of 0.3% for oral absorption for plus 4. (3) The initial I.M. studies with plus 4 indicate that at four days, less than 5% of the injected dose is absorbed from the site of injection. Apparently the skeleton is the chief organ of deposition. (5) These very preliminary results suggest a considerable metabolic resemblance of plus 4 product to Zirconium.

8. Projected Studies for the Next Two Months

Tracer studies are to be continued with product and Cesium. Tellurium studies will be initiated shortly since we now have available a considerable quantity of radio-tellurium. Radioautographic studies and the decontamination program are to be continued.

# Serum Sulfur in Rabbits



 Controls

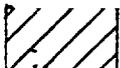
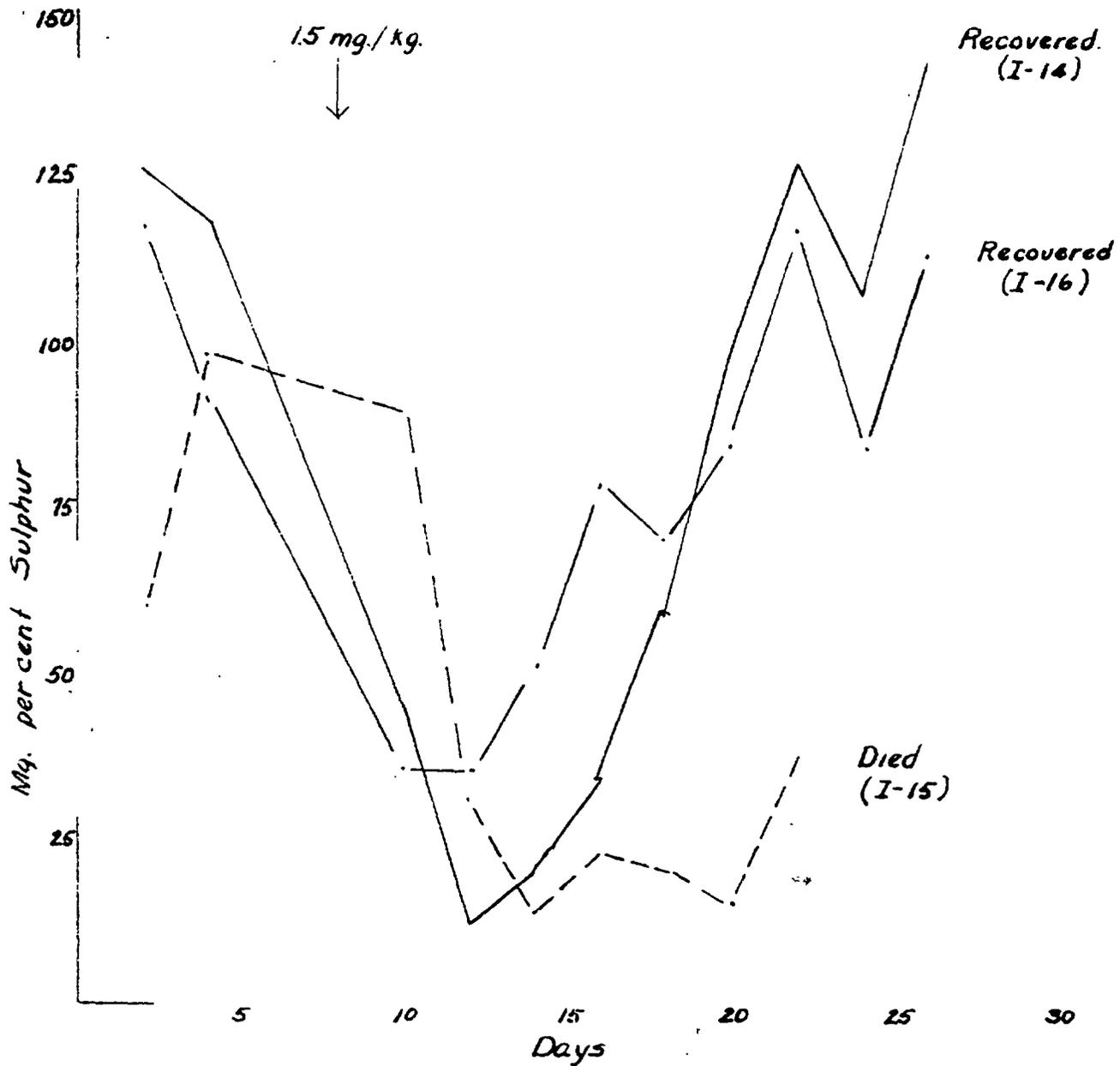
 Injected Rabbits  
(4mg/kg.)

FIGURE 8



Urine Sulphur Concentration in Three Rabbits  
Following Subcutaneous Injection of 1.5mg/kg. Tuballoy Nitrate

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### C. RADIATION MEASUREMENT SECTION

L. A. Parque, Acting Section Chief

E. O. Wollan, Consulting Section Chief

#### Personnel

Mr. C. L. Wesenberg joined the group on February 4, 1944 as a research assistant. He will help with instrument maintenance and calibration and radiation surveys. Mr. J. S. Blair came into the group on February 21, 1944 as a research assistant. He will be half-time in the Radiation Measurement Group and has been assigned to work with Landsverk on a cooperative program on radiation measuring instruments of the two groups.

#### Pocket Meters

The pocket chamber service continues to expand. All of our chambers are in use, are read daily and all readings above 90 mr per day are reported to the Clinical Section each day. The 250 chambers on order should give an adequate supply when they are obtained. Unfortunately, the acquisition time is very indefinite because of the slowness of delivery and uncertainty of the percentage (approximately 60 %), of each shipment that probably will be acceptable. Obviously it will be a great while before all of these chambers will be available for use if 40 % of each lot received must be returned.

#### Film Meter

Considerable progress was made during the month in the direction of the new film meter. The 400 badges were finally delivered. By expending several man hours they have been assembled and are ready for use as soon as the film can be obtained. Du Pont representatives, recently contacted, say our order should be filled very soon now. A special report on film metering is in the final stages of preparation.

#### Laundry Monitoring

A thin glass walled Geiger counter and rate meter is being installed at the Armory for monitoring all outgoing laundry suspected of contamination. Setting a good tolerance count will be difficult but it seems not too difficult to set a safe value. A count of 1000/min. has been chosen tentatively.

## Vinyon Cloth

Tests have been made on decontaminating samples of Vinyon cloth which are acid resistant. It was hoped a laundering process could be found which would adequately remove activity. The samples were contaminated by dipping in an acid solution of fission products, then blotted and allowed to dry partially. Counts were made. They were then scrubbed under warm water for one minute, then counted again. Finally they were washed in aqua regia for five minutes and scrubbed under warm running water.

The following table summarizes the results:

Vinyon on Sample	<u>1</u>	<u>6</u>	<u>11</u>	<u>15</u>	<u>26</u>	<u>23</u>
Contamination Count	6000	13000	10600	10200	13400	6600
After washing in water	566	97	1891	885	365	556
After washing in acid and water	228	75	750	254	156	211

(The samples seemed unaffected by the acids.)

## Lead-Leather Gloves

An experiment was made to test the protective value of some lead-leather gloves in the handling of x-metal. Out of 48 pairs, 12 pairs were taken at random. The fractional transmission of betas from x-metal was measured at three different places on each glove. The following results were obtained:

Glove Pr. No.	Fractional Transmission						Max. r/8 Hr.
	<u>R<sub>1</sub></u>	<u>R<sub>2</sub></u>	<u>R<sub>3</sub></u>	<u>L<sub>1</sub></u>	<u>L<sub>2</sub></u>	<u>L<sub>3</sub></u>	
1	.070	.082	.087	.090	.132	.118	.275
2	.081	.093	.089	.133	.126	.115	.276
3	.062	.118	.089	.085	.085	.059	.245
4	.109	.133	.129	.092	.116	.063	.276
5	.062	.086	.067	.131	.140	.112	.292
6	.06	.055	.131	.061	.065	.090	.272
7	.058	.081	.065	.096	.082	.058	.200
8	.114	.166	.168	.066	.082	.083	.350
9	.061	.100	.090	.062	.074	.042	.208
10	.072	.096	.081	.077	.089	.089	.200
11	.066	.093	.143	.073	.101	.040	.210
12	.091	.104	.083	.100	.131	.067	.273

## α-ray Measurements

Two Bershem electrometers have been equipped for ionization measurements by the Clinical section. A critical examination of the lowest alpha emission rate that can be measured is being made and a comparison is being made

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with the general film alpha electroscope constructed by Landsverk. Present results are very preliminary.

A portable battery operated counting rate meter has been constructed by Lester following Hinch's design which has already been very useful in survey work.

### Lauritsen Electroscope Calibration

A program of calibration of survey instruments was begun during the month. Usually in the past Lauritsen electroscopes have been calibrated by exposing them to a known dose and then by following one of two equivalent procedures: (1) a 45° line was drawn through the above determined point on logarithmic paper; (2) k was determined from the above data in  $D = \frac{k}{T}$ .

The calibration is considerably in error at large doses and is reasonable over a rather limited range. In order to be able to use the instruments at high rates they are being calibrated over a wide range of intensities and a curve is supplied with each one. Fig. 1 shows the results for one of the electroscopes.

In this work since we have only one standard source we sought the arrangement in a laboratory room which gives the longest reading at a given distance from the source, care being taken that none of the direct beam was cut out. After many trials it was found best to suspend the source from the ceiling and place the meter on a small tripod. Obviously this gave the least amount of scatter. Incidentally, readings were taken out of doors and there was no observable difference at a given distance if the source and meter were as much as four feet from the walls when measurements were taken indoors. This curve shows that Lauritsen's have a rather bad intensity dependence. Incidentally the electroscope recently built by Landsverk and Wollan has a better characteristic at our regard as the table below shows:

<u>Landsverk-Wollan</u>		<u>Lauritsen</u>	
Distance from 53.16 mg Source	$D^2/t$	Distance from 53.16 mg Source	$D^2/t$
2 m	56	2 m	32
1.5 m	54	1.5 m	30
1 m	53	1 m	28
.75 m	50	.45 m	23
.30 m	49	.30 m	18.5
		.2 m	17

## Argonne Pile Gas

Measurements were made on the activity of the pile gas at the Argonne. Cells approximately 2 in. square and 0.5 in. deep, having tops of .125 in. brass perforated with 0.125 in. holes and covered with thin aluminum (approximately 10 mg/cm<sup>2</sup>), were filled with the gas after evacuation. These cells were placed under a standard thin-walled glass counter and approximately 0.25 in. from it. This arrangement did not give particularly good geometry but the thickness of the tops did give some collimation. The decay curve was followed for 45 minutes during which time the count fell to 10% of the original. This curve could be expressed as the sum of two exponentials corresponding to half lives of 3.3 min. and 33 min. respectively. The decay has been followed for longer times at the Argonne but was not repeated in these experiments since our main interest was in absorption measurements to be made during the first 20 min. of decay. Within the accuracy of the experiments the range was found to be 1.4 gm/cm<sup>2</sup> and the absorption coefficient in Al, 10 cm<sup>-1</sup>. This corresponds to a maximum energy of about 3 MEV. From this one would infer an average energy somewhat less than 1.5 MEV. On the basis of Failla's calculations (CH-1347) which were used in setting the tolerance limit of  $3 \times 10^{-10}$  C, this limit could be as much as 25% high.

However, when one<sup>CC</sup> considers the rapidity of decay at the time the present monitoring measurements are made, this excess is more offset. So there is no evidence in these experiments to cause doubt of the validity of the present tolerance count which is 15000 counts/min. in the counter now in use. Incidentally, Kyslender has plotted counting rate vs. Lauritsen readings taken at the same times and places as the gas samples and found surprisingly that the result was a straight line. An even more curious coincidence was the fact that the same fraction of tolerance was found for breathing and for external radiation.

## Product Monitoring

As is coming to be rather generally recognized, one of the major hazards is from ingestion and inhalation of an  $\alpha$ -raying body. Since there is no way to monitor the amount of intake, the problem seems to be one of preventing such intake. This means good housekeeping to prevent ingestion and inhalation. However, it is not unreasonable to set a tolerance concentration in the air which could be monitored. In the absence of knowledge of the physiology involved, information can be drawn from experience with Radium and Radon in setting the safe concentration.

## Radiation Surveys:

As usual considerable time was spent on radiation surveys. While no part of the laboratory area was missed, room by room surveys were made at New Chemistry and at Site B. Also counting of contamination on hands was continued at New Chemistry. It is hoped to extend this service to other areas.

### Work for coming month:

Routine measurements.

Surveys.

Extension of hand counting service.

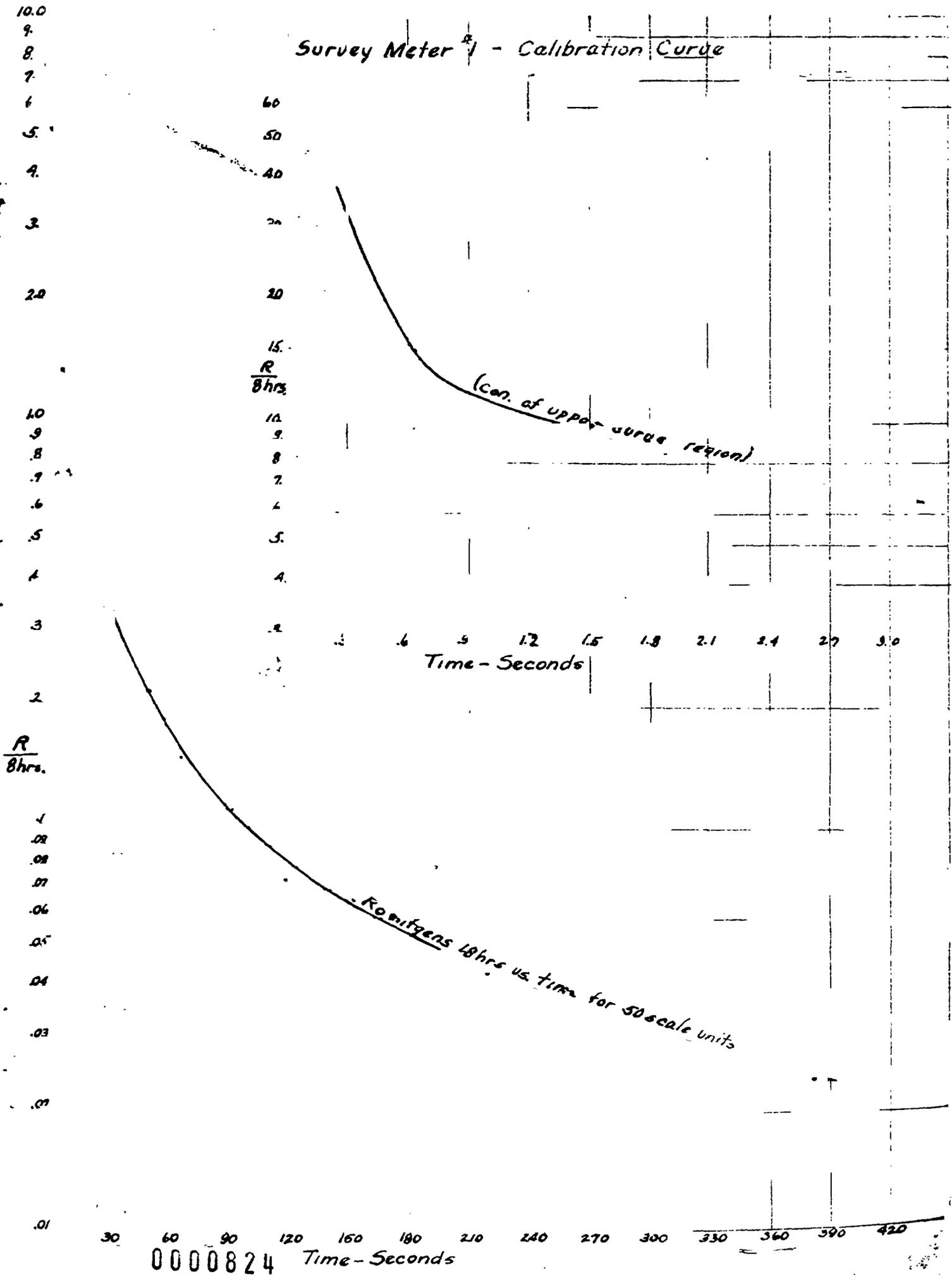
Establishment of full-time surveying service at  
New Chemistry.

Instrument Development.

Instrument calibration.

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# Survey Meter #1 - Calibration Curve



0000824 Time-Seconds

D. BIOLOGICAL RESEARCH SECTION

K. S. Cole, Section Chief

Report for Month Ending February 29, 1944

$Xe^{133}$  production

A crack was found in the quartz tube leading from the pilot  $U_3O_8$  xenon generator in the Clinton pile. This probably explains the low yields obtained in the test runs even at  $1050^{\circ}C$ . The design of a more rugged apparatus of this type is being considered.

It has not been possible to maintain more than a 25 per cent yield of xenon from  $U(OH)_4$  at graphite temperature because of instability of the pure material under operating conditions. A pilot unit of 500 gm. is being placed in the Clinton pile for test.

Lung absorption of vapors

A satisfactory process for the production of  $I^{131}$  vapor has not been found as yet. Methods for analysis of the iodine content of tissues are being tested. No further work has been done on  $RuO_4$ .

Aerosol production and exposure

The reciprocating bellows dust injector used for  $U_3O_8$  has been tested with  $SrCO_3$  dust of  $1.9 \mu$  average particle size. In 3 hours, 2.5 gm. of a 10 gm. charge was injected at a uniform rate.

Preliminary tests have been made on an injector in which air is blown through a porous plate below the dust charge. In 30 minutes 0.5 gm. of a 3 gm.  $CaCO_3$  charge was injected at a uniform rate.

A right angle jet atomizer did not produce satisfactory liquid aerosols with water or glycerol, but propylene and triethylene glycols were very satisfactory. A  $Sr^{89}$  tracer exposure of mice to  $SrCl_2$  in triethylene glycol is in progress.

Toxicity of mixed fission products in rats.

Mixed fission products were given to rats by stomach tube. By the 24th day, all animals receiving  $25 \times 10^{-6}$  C/gm or higher had died. None receiving  $6.4 \times 10^{-6}$  C/gm or less had died. Absorption through the gut is very low; the carcass of a rat which died in four days contained only 2% of the administered activity. Damage to the G.I. tract was severe and was probably a major contributor to death.

$Ba^{140}$  -  $La^{140}$  in mice

(1) Toxicity.

Barium<sup>140</sup> - Lanthanum<sup>140</sup> in equilibrium was injected intraperitoneally into mice at six different concentrations. Over 30% of the injected dose was excreted within the first 24 hours; the total excretion in 25 days is

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below 50%. The bones contain about half of the administered dose, the content in the "soft tissues" is very small. Mortalities at 60 days are:  $50 \times 10^{-6}$  C/gm - 100%,  $17 \times 10^{-6}$  C/gm - 86%,  $5.5 \times 10^{-6}$  C/gm - 50%,  $1.9 \times 10^{-6}$  C/gm - 0%,  $0.6 \times 10^{-6}$  C/gm - 86%,  $0.2 \times 10^{-6}$  C/gm - 7.1%, control 7.1%. Initial weight losses were observed at doses of  $5.5 \times 10^{-6}$  C/gm and higher.

#### X-ray survival

Preliminary mouse survival curves for single doses indicate a significant difference between the sensitivities of male and female Carworth mice. The median lethal dose for females is near 500 r, while the same point for males is 300 r. Black Bar Harbor females resemble Carworth females, with a median lethal dose at 500 r.

Results of paired doses on rabbits indicate a residual effect after a mean interval of 130 days equal to 10 - 30% of the initial effect.

Preliminary results of paired doses administered to rats indicate fairly rapid recovery during the first two weeks.

Rats receiving daily doses of 25 r and 12.5 r have accumulated 2050 r and 1025 r respectively without mortality.

Groups of fruit flies which receive in daily doses a total of  $\frac{1}{2}$  to  $1\frac{1}{2}$  times the midlethal massive dose over a period equal to the average life duration of the control groups are showing a marked prolongation of life. Higher daily doses cause a sharp reduction of average life duration. All massive doses so far administered have shortened average duration.

#### Fast n survival

Preliminary results of rabbit exposures to fast neutrons indicate a survival curve which lies between 125 n and 180 n, with a midpoint near 150 n.

#### External beta radiation

External beta radiations to eyes at about 200 r/hr have caused slight clouding of the cornea of dark-eyed rabbits after 600 r; an inflammation of the lids, nictitating membrane, and cornea of an albino rabbit after 800 r; and inhibition of hair development in a young rat after 400 to 600 r. Doses are approximate.

#### Stable isotope toxicity

Cerium is toxic to goldfish in concentrations of  $10^{-5}$  parts by weight and higher. Concentrations of  $10^{-6}$  and less are nonlethal in 30 days. Solutions were in synthetic pond water.

Barium is toxic to goldfish in concentrations of  $10^{-5}$  parts by weight and higher. Concentrations of  $10^{-6}$  and less are non-lethal in 30 days. Solutions were in distilled water.

## (2) Hematology

Intraperitoneal injection of  $17 \times 10^{-6}$  C/gm of  $Ba^{140}$  to mice causes a sharp fall in lymphocytes, a less rapid fall in granulocytes, both continuous until death. With  $1.9 \times 10^{-6}$  C/gm the lymphocytes fall less rapidly and recover by 25 days to normal levels; the heterophils fall slowly and remain depressed at 25 days. There is a questionable gradual rise in lymphocytes and gradual fall in heterophils with  $0.2 \times 10^{-6}$  C/gm.

## (3) Histopathology

In the mice injected with  $Ba^{140}$  -  $La^{140}$  the spleen and lymph node showed no degeneration at 4 days (first interval) even with  $17 \times 10^{-6}$  C/gm. There was a slight but definite increased lymphopoiesis at this and the  $1.9 \times 10^{-6}$  C/gm levels and possibly even at the  $0.2 \times 10^{-6}$  C/gm level. The bone marrow showed virtually complete destruction of hemopoietic elements with  $17 \times 10^{-6}$  C/gm at the 4 day interval. With  $1.9 \times 10^{-6}$  C/gm the destruction was much less at 4 days, and most marked in the region of bone growth (the metaphysis). In this latter region destruction of hemopoiesis with  $1.9 \times 10^{-6}$  C/gm at 11 days was comparable to the  $17 \times 10^{-6}$  C/gm. There was no detectable change with  $0.2 \times 10^{-6}$  C/gm at 4 days (i.e. maximal). The kidney showed no change.

Earlier stages at these levels must be studied to explain the apparent discrepancy between the spleen and lymph node findings and the definite fall in peripheral blood lymphocytes. The bone marrow picture is quite consistent with the observed fall in the blood polymorph (heterophile) counts.

### Hematology - 100 r X-ray

Rabbits receiving 100 r X-ray show a depression in lymphocytes less marked than with higher doses, but maximal at 3 hours and maintained through 48 hours. This depression is not reflected in the total leukocyte curve because of slight but significant rises in the heterophils at 4 and 12 hours.

### Histopathology - 400 r X-ray

The 400 r X-ray rabbits showed changes qualitatively similar to the 800 r series. Again the lymphatic tissue was hardest hit. The lymph nodes in particular. The bone marrow suffered damage to both the granulocyte and erythrocyte series but the latter appeared to recover more rapidly. Epithelial findings in the gut were a repetition of 300 r changes. In no case was the damage nearly as extensive with 400 r. Onset of damage was as early as with 800 r but recovery was evident almost immediately and in all tissues reached a stage by 3 - 5 days comparable to that shown at 14 days with 800 r. Liver, heart, lung, adrenal, kidney, pancreas and the reproductive organs showed no significant changes, or none which should be relied on from the small series investigated.

### Radio-autography

Radio-autographs of lungs of Uranium and Lanthanum dusted mice and of bone and soft tissues of strontium injected chickens were obtained. Minute spicules of bone show clearly and activity is marked in periosteum and endosteum.

Ilford Q III and Eastman III O 1. plates and sensitive plates are being tested as a possible material for radiography of fish or invertebrates.

The distribution of radiation from deposited active isotopes is being studied by measuring the density of photographic films exposed in contact with thick sections of imbedded tissues.

#### Protective action of nicotinamide

Six groups of 10 mice each were given 100 r daily and the various groups injected with .1 mg thiamin chloride, .2 mg riboflavin, 1.0 mg. nicotinamide, .05 mg. pyridoxine, .1 mg diphosphopyridine nucleotide and .2 cc Ringer solution. Survival curves for animals receiving pyridoxine, thiamine, Ringer and riboflavin are very close to each other, the mid-lethal point for the Ringer injections being at an accumulated dose of 1140 r. The mid-lethal for those receiving nicotinamide is 1230 r and for those receiving diphosphopyridine nucleotide is 1350 r. These results support the hypothesis presented previously that radiation prevents the synthesis of diphosphopyridine nucleotide.

#### Food intake and weight changes

Eight rabbits were given a single dose of X-ray of 800 r, four were given 400 r and seven were kept as controls. Weights and food intake were followed for several weeks. Controls show two patterns: (1) a relatively constant weight with constant food intake, (2) an increasing weight with constant food intake. Irradiated animals fall into four different patterns: (1) an initial temporary fall in food intake, a constant or increasing weight (2) immediate cessation of eating, fall in weight and early death (3) initial steep fall in food intake, gradual fall in weight, recovery in food intake followed after several days by recovery in weight, (4) sharp fall in food intake followed by recovery in food intake but continued weight loss. The weight loss is definitely greater than can be accounted for by failure to eat, or failure in intestinal absorption, hence tissue breakdown is occurring.

#### Effects of radiation on circulatory system

An experiment on the physiological effects of irradiation on dogs is being planned in collaboration with Dr. Schwartz. Techniques for measurement of acetone bodies, total protein in blood and measurement of blood volume and circulation time have been perfected and are now ready to be used.

#### Accumulation and distribution of $Sr^{89}$ and of $Ba^{140} - La^{140}$ in goldfish

Complete curves are now available for uptake of  $Sr^{89}$  and  $Ba^{140} - La^{140}$  over a period of more than a month in skeleton, skin and scales, gills, feces, muscles and other soft parts. Uptake of  $Ba - La$  reaches a peak at 5 - 10 days; uptake of strontium at 3 - 5 days. Over a period of several weeks the amount of active material slowly increases in spite of decay in the external medium. High concentrations of calcium or inactive strontium diminish the uptake of  $Sr^{89}$ . At equilibrium the distribution of strontium in the fish is: skeleton 10 - 30%, skin and scales 50 - 75%, gills 5 - 15%, organs and muscles 3 - 10%, feces 5 - 35%. For  $Ba - La$  the distribution of beta activity is: skeleton 5 - 15%, skin and scales 40 - 70%, gills 10 - 20 %, organs and muscles 10 - 20%,

feces  $40 \times 10^6$ . Feces are very high (1000 times concentration) but this is due to adsorption rather than excretion since inactive feces suspended in the water take up nearly as much as those from the intestine. Injected strontium shows the same distribution as that taken up from the water except for absence of activity in the feces. When transferred to fresh water lacking active salts, the activity of the feces is lost within a few hours; thereafter activity is lost from the fish very slowly except by decay. Decay curves for fish from Ba - La show that the activity in feces is due almost entirely to lanthanum, that in the skeleton and scales to barium. Tank water loses activity initially due to adsorption on the glass and due to uptake by fish and feces; after about a week the water approaches the decay curve.

#### Tissue metabolism

Respiration and glycolysis of strips taken at six levels of the small intestine of rats were measured. The  $QO_2$  in normal rat intestines is between 8 and 9. Four hours after 900 r of X-irradiation the  $QO_2$  dropped to 5; at 24 and 48 hours it rose to the normal level and dropped again at 72 hours. Glycolysis was unaffected. Phosphorylation in the intestine was examined by measuring the increase in organic P after feeding fructose. In normal rats the Organic P content of the mucosa increased from 43 to 83 % of the total P after ingestion of 4 cc of 2.5% fructose. Four and 24 hours after irradiation (500 r total body) the organic P after fructose was 57 and 59%, but at 72 hours it was 75% of the total P. Urea synthesis by liver slices was depressed at 4 and 24 hours after irradiation, was normal at 48 hours, depressed at 72 and 96 hours and normal at 120 hours.

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E. METEOROLOGY SECTION

P. E. Church - Section Chief

Abstract

Aside from preliminary analysis of lapse rate data and consultation at Site X and the initial arrangements made at the Metallurgical Laboratory for using SO<sub>2</sub> at the 200 area at Site W to determine dilution rates, nearly all manpower and work again was concentrated at Site W.

Smoke runs made up the auxiliary 200 ft. stack during the early morning hours have shown quite conclusively that as long as an inversion lasts the smoke will stay in a thin layer, which spreads widely, at the level where the smoke reaches the same density as the air. Downward dilution is slow. Upward dilution appears to be nearly nil in an inversion for there is a definite top.

When, in the morning, the inversion is obliterated up to the smoke level then vertical circulation produces excellent mixing from the ground to the height that the dry adiabat extends. This vertical mixing occurs in alternate up and down drafts and brings dense smoke to the ground near the stack.

\* \* \*

Site X

Mr. Bentley was to be at Site X for consultation during the last two weeks of February and will likely remain there for the first week of March. During that time he will make a preliminary analysis of the data on lapse rates as obtained from the recording thermocouples which are placed at 50 foot intervals up a 200 foot stack.

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Arrangements were completed for the installation of unit to vaporize liquid SO<sub>2</sub> so that the gas could be introduced at the base of the auxiliary stack in the 200 area at Site W. This unit is now nearly completed. The SO<sub>2</sub> concentration will be measured downstream in the smoke trail to determine the amount of dilution that is occurring under different weather conditions.

Remodelling of a meteorograph that was in use in the field during the month of January was completed before my return to Site W in mid-February.

Analysis of some of the data taken during the month of January at Site W was carried on until interrupted by the trip to Site X by Mr. Bentley and my return to Site W. From airplane observations the area covered by the output from the auxiliary stack was made for most of the January runs and some volumes through which the smoke was distributed were computed.

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## Site W

On my return to Site W a trip was made to Trail, B.C. accompanied by Messrs. Newton, Gosline, and O'Connor, the latter being a chemist from Du Pont's Technical Department. All arrangements for this trip were made from the U. S. Engineer's Office at W. The problems of smoke dispersion of the smelter at Trail were gone over quite carefully with the men there. Their problem was one quite different from the one at Site W; only in a few instances did some phases of both places have common ground. Some equipment was obtained on a loan from them. Mr. O'Connor and Mr. Brugmann made a trip to Salt Lake City to borrow more SO<sub>2</sub> analysis equipment.

During the month of January, between the 17th and the 31st, 8 runs from the auxiliary stack were made and each run was sustained with a map of the area covered as viewed from the airplane and each run had further information of lapse rates at various intervals prior to and during the smoke runs, wind velocity gradients (vertical) from pilot balloon observations, wind direction and temperatures. All these runs were made in the early morning at a time when the stability in the inversion was greatest.

During February, 16 runs have been made prior to the 26th. These have been supported by maps of 12 runs and photographs for 6 runs. Lapse rates, wind velocity gradients, and temperatures have also been taken. Again all runs have been made between 0500 o'clock and 0800 to 1000 depending upon the time that a plane was available.

From the January and February runs certain features stand out quite clearly:

(1) There is an inversion (ground type) present nearly every night. The only exceptions are the windy nights of which there have been but two during February. The temperature difference between the surface and the lid of the ground inversion has averaged a little more than 8°F. for the February runs, the least being 2° and the most being 14°. The lid of the inversion over the 200 W area is between 750 and 1000 feet above the surface. Above that, at the general crest of the Rattlesnake Mountains, there is another inversion most of the time, but not always. The most persistent feature of the vertical temperature distribution is a night time inversion.

(2) Between the hours of 0200 and 0300 the pilot balloon observations show an average velocity of 3.5 ft/sec. at the surface, 12.5 ft/sec. 400 feet up, and 16.2 ft/sec. 1000 ft. up. Pilot balloon observations cannot be made at the time the smoke run is in progress, but there seems to be an increase in the velocity at the 200 foot level shortly after daybreak.

(3) Nearly nine-tenths of the smoke runs have shown a wind direction between WNW and NNW during the early morning hours.

(4) The early morning smoke runs, which invariably have started while a ground inversion of greater height than that to which our smoke is sent, show that the smoke rises but little, probably owing to the higher temperature and the stack velocity, reaches very quickly the same density as that of the

air and remains at that level. The stream of smoke widens to about 50-75 ft. in the first mile, a veritable thin ribbon. Beyond that lateral spreading is quite considerable. The top remains at a constant altitude above the ground, some 200 to 400 ft. up. Under the average inversion, no smoke reaches the ground less than 2 miles from the stack and on most of the runs the first that can be visually detected as reaching the ground is from 5 to 10 miles from the source.

(5) Several runs have continued until after the time the ground inversion has become erased by increase of temperature at the surface during the morning. As soon as heating starts vertical mixing occurs to distribute the accumulated surface heat. When the vertical circulation has reached an altitude to which the smoke is sent, then the columnar structure of vertical up and down drafts becomes apparent and smoke reaches the surface in dense columns within the 200 W area itself. Most of the columns that come to the surface strike the ground between 1000 and 1500 feet from stack. The change from level laminar flow within the inversion to vertical up and down columns is rapid, the character changing within 10 to 15 minutes. The thickness through which the mixing occurs is that layer in which the dry adiabatic lapse rate is present. Vertical mixing is excellent under this condition with a nearly homogeneous thin screen of smoke existing within two miles from the stack. Dangerous concentrations may exist within the first mile, however. For this reason mainly, a known amount of  $SO_2$  is to be sent up the stack, samples to be taken and analyzed within the 200 W area to determine how much dilution has occurred by the time the effluent from the stack reaches the ground.

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