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718491

THE
UNIVERSITY OF ROCHESTER

ATOMIC ENERGY PROJECT

ROCHESTER, NEW YORK

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UR-174

Health and Biology

THE UNIVERSITY OF ROCHESTER
Atomic Energy Project
P. O. Box 287, Station 3
Rochester 20, New York

Contract W-7401-eng-49

QUARTERLY TECHNICAL REPORT

April 1, 1951 thru June 30, 1951

Submitted by: Henry A. Blair
Director

Date of Report: 7/31/51

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TABLE OF CONTENTS

Page No.

INTRODUCTION AND EXPLANATION OF PROGRAM AND PROBLEM CODES

The scientific work at The University of Rochester Atomic Energy Project has been coded at the program and problem levels. The programs, in general, indicate broad fields of investigative or service activities while the problems indicate divisions of these fields. Although no consistent method of division into problems was possible, an attempt was made to achieve a natural division in the sense that each problem would encompass a subject normally written up and generally considered as a unit. The program on chemical toxicity of uranium for example, has been broken down into problems according to the divisions commonly employed by toxicologists.

It has not been possible to code the problems sufficiently broadly to avoid all overlapping. In cases in which various parts of a given investigation might be coded differently, the whole work was coded according to its principal subject matter as long as the minor subjects were relatively unimportant. Otherwise, the work was divided under appropriate codes.

The problem codes are not related directly to the administrative organization of the Project. Consequently, the smallest administrative unit, the section, may work on more than one of the coded problems. Conversely, more than one section may work on the same coded problem.

It should be noted that the Quarterly Technical Reports of The University of Rochester Atomic Energy Project do not attempt to describe progress in all of the research programs but only in those in which some significant results have been achieved but which are not sufficiently complete to be written up as a final report.

PROGRAM AND PROBLEM CODES

I. X.R. BIOLOGICAL EFFECTS OF EXTERNAL RADIATION (X-RAYS AND γ RAYS)

- X.R.1 Tolerance Studies (dose levels, survival time, gross and histo-pathology)
- X.R.2 Mechanism of Effects (physiological and biochemical)
- X.R.3 Therapy (measures against radiation effects)
- X.R.4 Hematology
- X.R.5 Genetics (histogenetics)
- X.R.6 Embryology
- X.R.7 Bacteriology and Immunology

II. I.R. BIOLOGICAL EFFECTS OF EXTERNAL RADIATION (INFRA-RED & ULTRA-VIOLET)

- I.R.1 Flash Burns

III. R.M. BIOLOGICAL EFFECTS OF RADIOACTIVE MATERIALS (CONTACT, INGESTION, ETC.)

- R.M.1 Polonium
- R.M.2 Radon
- R.M.3 Thoron
- R.M.4 Miscellaneous Project Metals

IV. U. URANIUM

- U.1 Physical and Chemical Properties
- U.2 Toxic Effects (description of acute and chronic toxicity)
- U.3 Toxic Limits (respiratory; oral; skin; eye; parenteral)
- U.4 Fate (distribution and excretion)
- U.5 Mechanism of Toxic Effects
- U.6 Methods of Detection of Poisoning, Prophylaxis, Treatment and Protection

V. Be. BERYLLIUM

Be.1 Physical and Chemical Properties

Be.2 Toxic Effects (description of acute and chronic toxicity)

Be.3 Toxic Limits (respiratory; oral; skin; eye; parenteral)

Be.4 Fate (distribution and excretion)

Be.5 Mechanism of Toxic Effects

Be.6 Methods of Detection of Poisoning, Prophylaxis, Treatment and Protection

VI. Th. THORIUM

Th.1 Physical and Chemical Properties

Th.2 Toxic Effects (description of acute and chronic toxicity)

Th.3 Toxic Limits (respiratory; oral; skin; eye; parenteral)

Th.4 Fate (distribution and excretion)

Th.5 Mechanism of Toxic Effects

Th.6 Methods of Detection of Poisoning, Prophylaxis, Treatment and Protection

VII. F. FLUORIDE

F.1 Physical and Chemical Properties

F.2 Toxic Effects (description of acute and chronic toxicity)

F.3 Toxic Limits (respiratory; oral; skin; eye; parenteral)

F.4 Fate (distribution and excretion)

F.5 Mechanism of Toxic Effect

F.6 Methods of Detection of Poisoning, Prophylaxis, Treatment and Protection

VIII. Zr. ZIRCONIUM

Zr.1 Physical and Chemical Properties

Zr.2 Toxic Effects (description of acute and chronic toxicity)

Zr. ZIRCONIUM (cont.)

Zr.3 Toxic Limits (respiratory; oral; skin; eye; parenteral)

Zr.4 Fate (distribution and excretion)

Zr.5 Mechanism of Toxic Effect

Zr.6 Methods of Detection of Poisoning, Prophylaxis, Treatment and Protection

IX. S.M. SPECIAL MATERIALS

S.M.1 Physical and Chemical Properties

S.M.2 Toxic Effects (description of acute and chronic toxicity)

S.M.3 Toxic Limits (respiratory; oral; skin; eye; parenteral)

S.M.4 Fate (distribution and excretion)

S.M.5 Mechanism of Toxic Effect

S.M.6 Methods of Detection of Poisoning, Prophylaxis, Treatment and Protection

X. I.S. ISOTOPES

I.S.1 Tracer Chemistry

I.S.2 Radioautography

I.S.3 Therapy

I.S.4 Diagnosis

XI. O.S. OUTSIDE SERVICES

XII. P.H. PROJECT HEALTH

XIII. H.P. HEALTH PHYSICS

H.P.1 Research and Development

H.P.2 Service

XIV. C.S. CLINICAL SERVICE

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330	Radiation Tolerance	George Casarett
331	Radiation Physiology	John B. Hursh
340	Radiation Chemistry	Kurt Salomon
350	Spectroscopy	Luville T. Steadman
360	Radiation Mechanics	Michael Watson
370	Radiation Toxicology	J. Newell Stannard

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Section Code	Section	Administrative Head
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440	Radioactive Inhalation	William F. Neuman Aser Rothstein
450	Pathology	James K. Scott
460	Physiology	Aser Rothstein

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520	Medical Physics	Herbert Mermagen
530	Hematology	Marylou Ingram
531	Project Medical Service	Marylou Ingram

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820	Flash Burn	Harry D. Kingsley
840	Zirconium	Herbert E. Stokinger
850	Therapy	Frank W. Furth

Program Code: X.R. BIOLOGICAL EFFECTS OF EXTERNAL RADIATION(X-RAYS AND γ RAYS)

Problem Code: X.R.3 Therapy (measures against radiation effects)

Section Code: 516

Author: T. R. Noonan

Effect of Diet on Radiation

Background: Cornatzer and co-workers have reported (1) that survival of mice injected intraperitoneally with a mid-lethal dose of radioactive phosphorus (P^{32}) was adversely affected by feeding a diet high in fat and protein. It seemed of value to investigate whether variations in the diet would affect the survival of animals following a single exposure to whole body x-irradiation. Information on the effect of diet after irradiation is lacking and such data are needed in order to guide treatment of humans following acute over-exposure.

Methods: Albino rats from the University of Rochester colony were used. Prior to irradiation, the animals were numbered, housed two in a cage, and fed a diet consisting of Purina Fox Chow ad libitum. The rats were exposed, sixteen at a time, in a segmentally divided cage, each rat being placed in a separate compartment. Radiation was given with a Picker Industrial X-Ray machine, operated at 250 KVP. The total exposure was 625 roentgens (measured in air on the floor of the exposure cage), delivered at a rate of 17.8 roentgens per minute. Following irradiation, the animals were randomly divided into three groups as shown in Table I.

TABLE I

Group	Number of Animals	Diet Post-Radiation
A	32	High fat, high protein
B	32	Low fat, low protein
C	16	Regular (Purina Fox Chow)

The special diets were prepared by mixing the list of components in the proportions shown in Table II.

TABLE II

High Fat, High Protein		Low Fat, Low Protein
25%	Casein	10%
2	Cod liver oil	1
30	Crisco	4
19	Dextrin	40
18	Sucrose	39
2	Alphacel	2
4	Salt mixture with vitamins	4
5.36 Cal./gm.		4.01 Cal./gm.

The regular diet consisted of Purina Fox Chow. The animals, two to a cage, were allowed water ad libitum and provided with 15 grams of food per rat per day. Food consumption was measured roughly by weighing the uneaten food and at least the major portion of the spilled food. Because of food spillage, the values for food eaten tend to be high, particularly during the first few days after irradiation. The animals were weighed twice weekly.

Results: The mortality after thirty days was 34.4% in Group A (high fat, high protein diet), 31.3% in Group B (low fat, low protein diet), and 18.8% in Group C (Purina Fox Chow diet). Statistical analysis by the usual chi-square tests indicated that there is no significant difference between any two of the mortality rates of the three groups. The increased survival of the group fed the regular diet was probably due to random variation in sensitivity to irradiation, since the appropriate statistical test indicates that such a difference in mortality

could arise purely by chance in fifty percent of similarly designed experiments. The difference in mortality between the groups fed high fat-high protein and low fat-low protein diet was too small to have any significance. No differences were noted in the survival times of animals which died, all deaths occurring between the seventh and twenty-sixth days after irradiation.

The mean daily food consumption of the surviving animals following radiation is presented in Graph A. A period of anorexia extending from the 2nd to the 4th or 5th day after exposure was followed by a period, lasting until about the 9th to 12th post-irradiation day, during which food consumption was higher than "normal". (Since the experiment was designed to test the effect of variations in diet after radiation, no measurement was made of food consumption of non-irradiated rats. The food consumption after the twelfth post-irradiation day, however, was relatively constant and probably can be assumed to represent the normal amount of food eaten by rats of this strain and size).

Graph B shows the pattern of weight loss of the surviving animals. The pattern (temporary weight loss followed by return to normal weight) is characteristic of the reaction of this species following exposure to approximately mid-lethal doses of roentgen rays. Non-survivors characteristically stopped eating a day or two before death and showed a weight loss terminally.

The initial and final mean body weights of the survivors on the three regimens are given in Table III.

TABLE III

Diet	Number in Group	Mean Initial Weight (gms.)	Mean Final Weight (gms.)	Weight Gain (gms.)
High fat-high protein	21	178.5	199.3	20.8
Low fat-low protein	22	178.5	189.5	11.0
Regular	13	178.4	191.2	12.8

The gain in weight of surviving animals fed a diet rich in protein and fat is significantly greater than the gain in weight of animals fed the regular or the low fat-low protein diet.

Discussion: The results of this experiment do not agree with the data of Cornatzer et al. It is possible that the rat may differ from the mouse but it is more probable that the discrepancy is due to the difference between the types of irradiation used. From the published results of the experiments with P^{32}, it is not clear whether or not the deleterious effect of the high fat-high protein diet may be due to some alteration in phosphorus metabolism such that the excretion of phosphorus is decreased or the radioactive phosphorus is distributed in greater than normal amounts to the more radio-sensitive tissues of the body.

Although this experiment has yielded only negative results, it is of some value in evaluating the treatment of casualties from an atomic bomb explosion. Since high protein diets are often given to patients with thermal burns, it is of interest to have evidence that such a regimen is not contra-indicated in cases where thermal burns may be complicated by radiation injury.

Summary: The survival of rats following a single exposure to 625 roentgens of whole-body x-irradiation is not significantly altered by feeding diets varying in the relative concentrations of proteins, fats and carbohydrates.

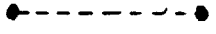
Bibliography

1. Cornatzer, W. E., Harrell, G. T. Jr., Cayer, D., Artom, C., Proc. Soc. Exp. Biol. Med., 73:492 (1950).

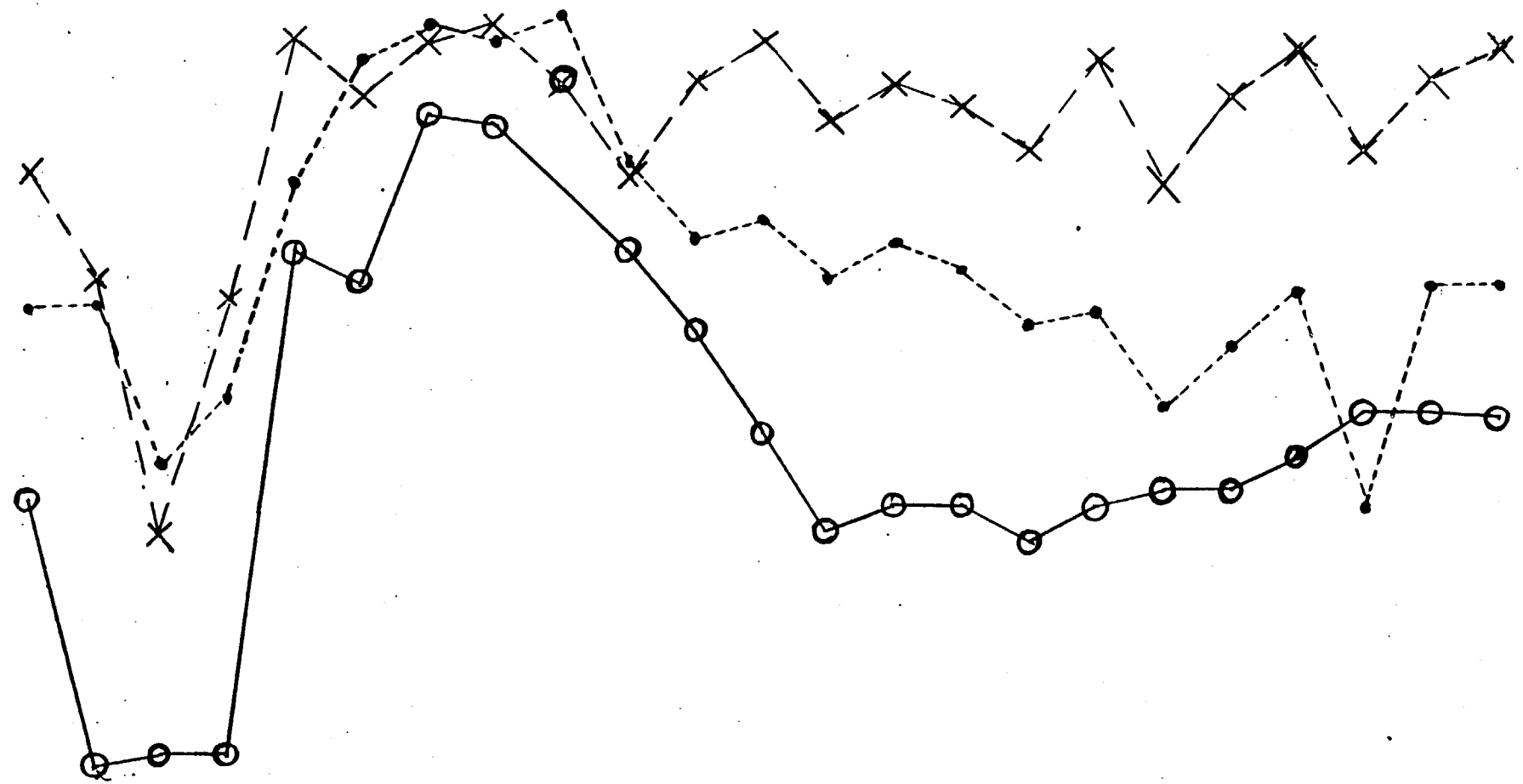
Graph A Daily Food Consumption (in grams)

Regular Diet

High Protein - High Fat Diet



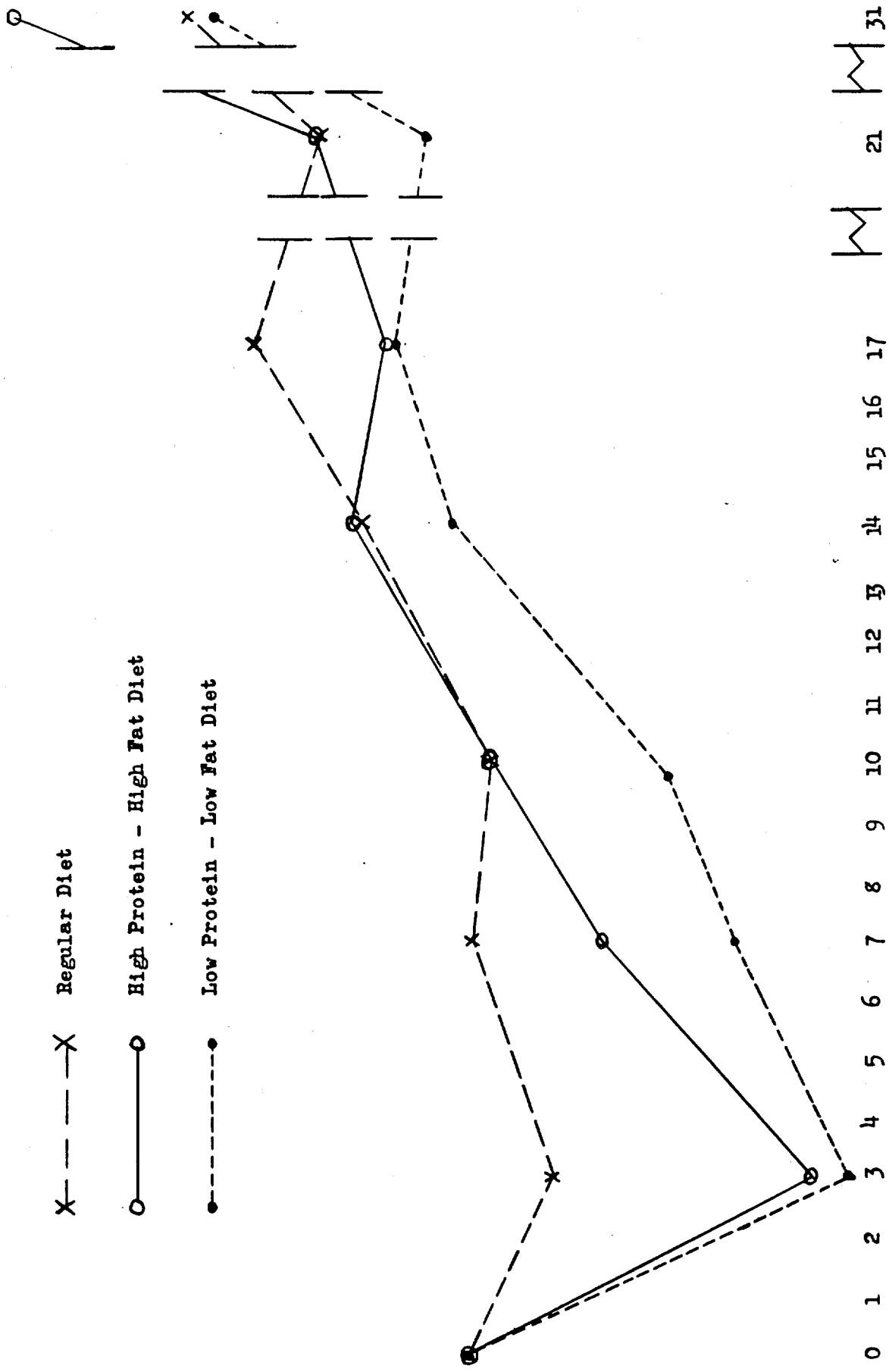
Low Protein - Low Fat Diet



1 2 3 4 5 6 7 8 9 10 11 12 13 17 18 19 20 21 22

Days After Irradiation

Graph B Body Weight (in grams)



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Program Code: X.R. BIOLOGICAL EFFECTS OF EXTERNAL RADIATION (X-RAYS AND Y RAYS)

Problem Code: X.R.3 Therapy (measures against radiation effects)

Section Code: 540

Authors: F. W. Furth, M. P. Coulter, J. Shrier, J. Markham

A Study of the Protective and Therapeutic Effect of Folic Acid and the Citrovorum Factor on the X-Irradiated Rat

Background: In preventing or alleviating the effects of x-irradiation upon the living organism, it would seem most logical to attempt to prevent or correct the alterations in the cyto-chemistry of the cell caused by the ionizing effect of the irradiation. One of the alterations in cellular chemistry which apparently occurs after exposure to ionizing radiation is an interference with nucleic acid metabolism. Studies (1,2,3) on the effect of x-irradiation on desoxypentose nucleic acid in vitro and in vivo have been made and show that x-irradiation causes an apparent depolymerization of nucleic acids and a marked depression in the tissue turnover rate of these substances. Since the nucleic acids are fundamentally concerned with cellular metabolism and multiplication, the demonstration of altered nucleic acid metabolism certainly offers a partial explanation at least of the destructive effect of x-irradiation on living tissue. In general it appears that the rapidly multiplying tissues are most sensitive to the effects of x-rays, the bone marrow being an outstanding example of this.

Aside from x-irradiation there are other methods of interfering with nucleic acid metabolism. One of these methods is by the administration of 4-aminopteroylglutamic acid (aminopterin). In studies on the chick embryo (4) it has been found that aminopterin inhibits the synthesis of thymine and one

or more of the purine desoxyribosides. In other studies (5) it has been demonstrated that large doses of aminopterin will cause profound bone marrow hypoplasia. The administration (6) of aminopterin to the dog causes a syndrome characterized by bleeding tendencies, panhematopenia and intestinal ulceration terminating in death in 80% of the animals. This syndrome is very similar to that occurring in the x-irradiated dog. It has also been shown (4,5) that pteroylglutamic acid (folic acid) and the citrovorum factor (folinic acid) will prevent some of the inhibition of cellular metabolism caused by aminopterin. The citrovorum factor, a chemical derivative of folic acid, is the more potent of the two substances in this respect. Both substances have been shown (7) to produce remissions in nutritional macrocytic anemias in the human.

Since both x-irradiation and aminopterin apparently alter one aspect of cellular chemistry in similar fashion, and since effective antagonists of aminopterin are available it becomes of interest to determine the protective and therapeutic effect of these antagonists on the x-irradiation syndrome.

Methods: A total of 90 adult Wistar-Strain male white rats weighing 170-180 gms. was used in this experiment. The animals were separated into five equal groups containing 18 rats and received the medication as follows.

Group I - 0.1 cc of 0.85% saline intraperitoneally daily starting immediately after irradiation and continuing 28 days.

Group II - Citrovorum factor, 200,000 units in 0.1 cc. of 0.85% saline daily starting 5 days before irradiation and continuing 28 days after irradiation.

Group III - Citrovorum factor 200,000 units in 0.1 cc. of 0.85% saline daily starting immediately after irradiation and continuing 28 days after irradiation.

Group IV - Folic acid 0.1 mg. in 0.1 cc. of 0.85% saline starting 5 days before irradiation and continuing 28 days after irradiation.

Group V - Folic acid 0.1 mg. in 0.1 cc. of 0.85% saline starting immediately after irradiation and continuing 28 days.

The rats were given liberal amounts of water and Fox Chow feed. Erythrocyte and leucocyte counts were done from the tail vein of each rat twice before irradiation. The rats were irradiated in groups of 15 containing 3 rats from each experimental group. A total of 700 r of x-radiation was given from a 250 KV source at 15 ma. and a rate of 16 r/min. with 0.5 mm. copper and a planoconvex aluminum filter.

Results: The results are summarized in the accompanying graphs. Graphs I and II (see page 23) demonstrate that there was no difference in the rate of or final 30 day mortality between the saline control group and the experimental groups. Graphs III, IV (page 24), Graphs V and VI (page 25) demonstrate in a similar fashion the lack of difference between control and experimental groups of the average erythrocyte and leucocyte counts.

Discussion: There are several obvious explanations of the failure of these substances to afford protection against the lethal effects of x-radiation. One of these is dosage. It may be that the dosage of x-radiation may produce such a large amount of ionization with secondary chemical effects per unit of tissue that the alteration of nucleic acid metabolism is so great that the folic acid and citrovorum factor could not correct the defect. Another associated factor is that x-radiation probably causes alteration in more than one of the vital cytochemical processes - processes which could not be affected by folic acid of citrovorum factor. It may also be that aminopterin in disrupting the nucleic acid metabolism may do so at a different point than

x-irradiation does. It may be of interest to test the therapeutic effect of these substances at a dosage level of x-irradiation which is below the maximum bone marrow sensitivity level, and to test the effect of the administration of folic and folinic acid in increased dosages.

Summary: The administration of folic acid (0.1 mg.) and citrovorum factor (200,000) daily before and after irradiation to a group of rats which received 700 r of whole body x-irradiation failed to change the mortality or hematology from those of a similarly irradiated group of control rats.

Bibliography

1. Limperos, G., Mosher, W. A., Am. J. Roentgenol. Radium Therapy, 63, 681-690, (1950)

2. Ibid. 691-700.

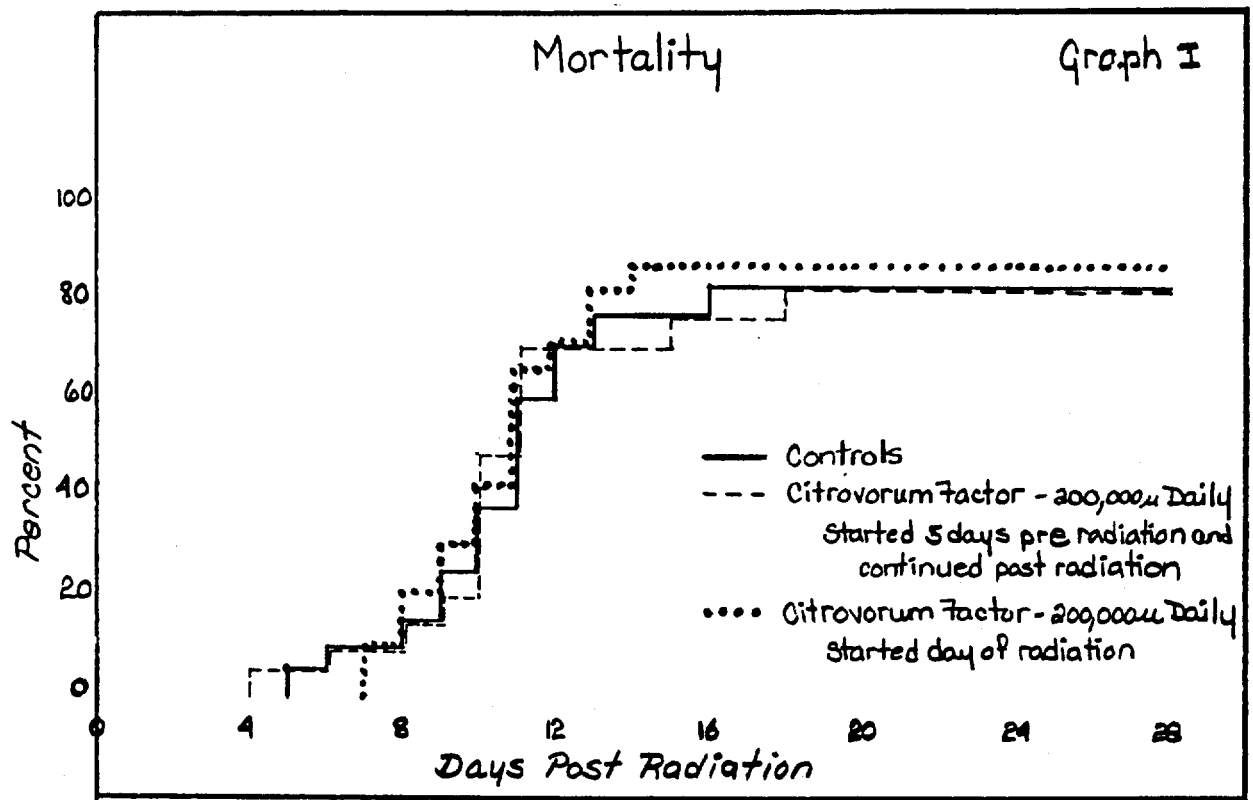
3. Kelly, L. S., Jones, H. B., Proc. Soc. Exp. Biol. Med., 74, 493-497 (1950).

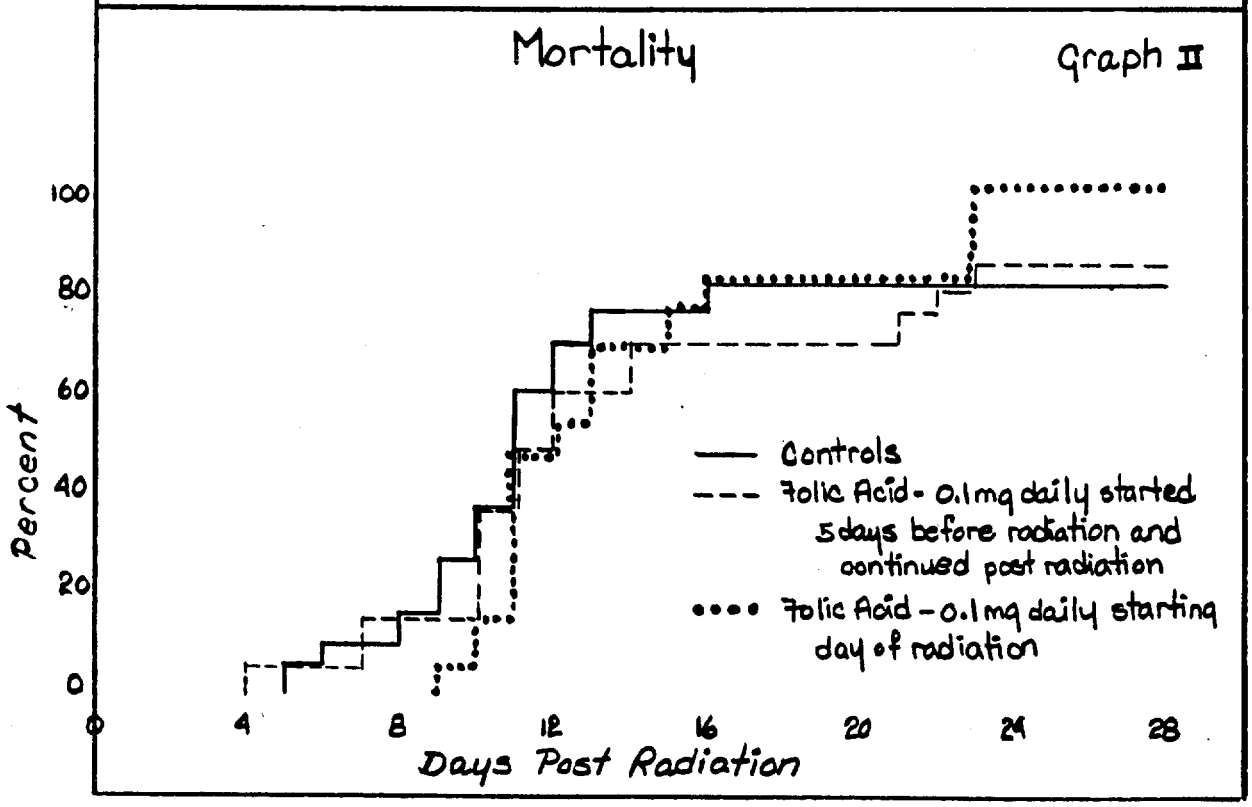
4. Cravens, W. W., Snell, E. E., Proc. Soc. Exp. Biol. and Med., 75, 43-45, (1950).

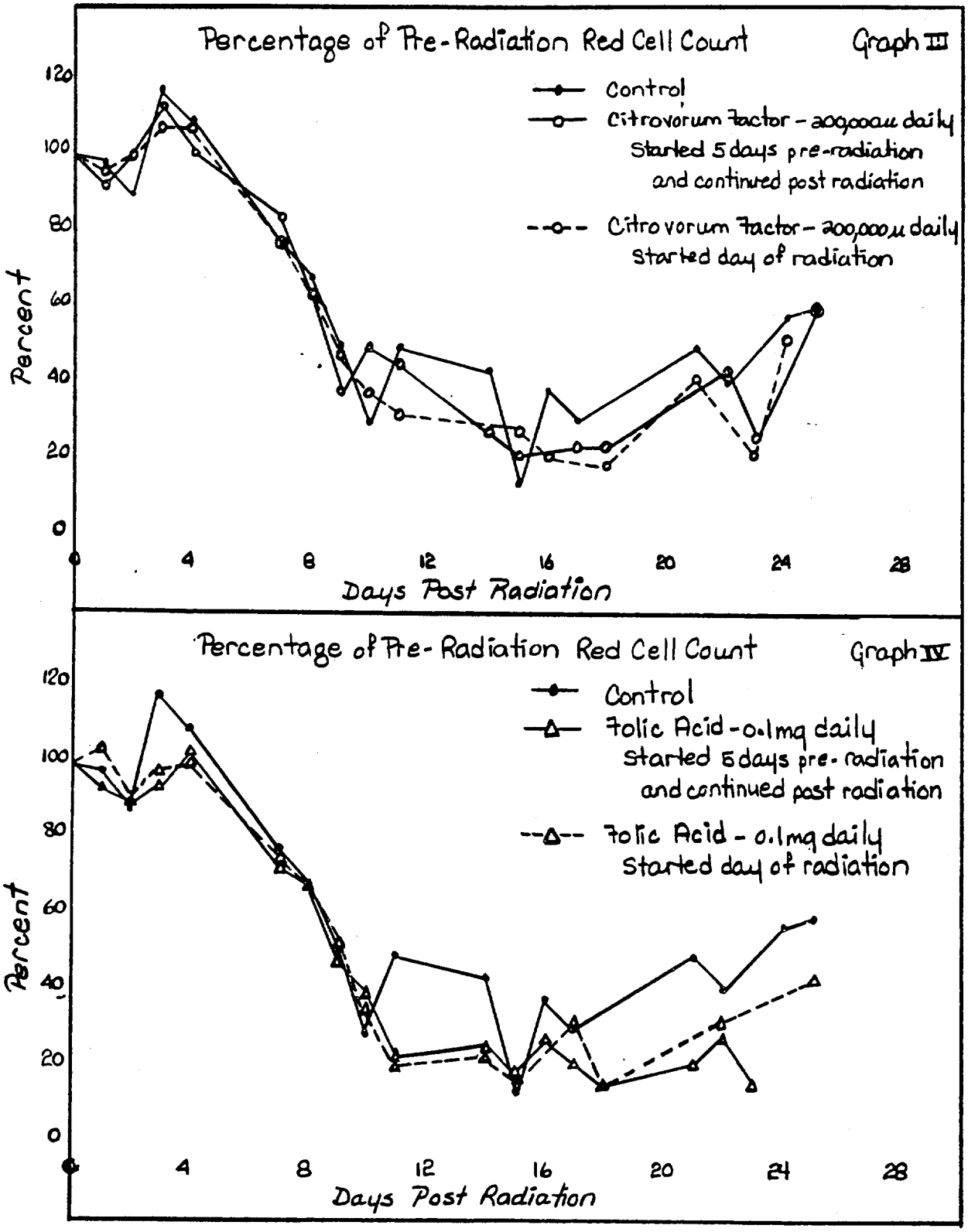
5. Mannich, V., Moore, C. V., Smith, D. E., Elliott, G. V., A.M.A. Arch. Path., 50, 787-799, (1950).

6. Grosman, B. J., Sanderson, M. H., Allen, J. G., Argonne National Laboratories, ANL-4474, 60-68, (1950).

7. Spies, I. D., et al., Southern Med. J., 43, 1076, (1950).


Mortality
Graph I
Percent
100
80
60
40
20
0
4
8
12
16
20
24
28
Days Post Radiation
Controls
Citrovorum Factor - 200,000u Daily Started 5 days pre radiation and continued post radiation
Citrovorum Factor - 200,000u Daily Started day of radiation


Mortality
Graph II
Percent
100
80
60
40
20
0
4
8
12
16
20
24
28
Days Post Radiation
Controls
Folic Acid - 0.1mg daily started 5 days before radiation and continued post radiation
Folic Acid - 0.1mg daily starting day of radiation


Percentage of Pre-Radiation Red Cell Count
Graph III
Control
Citrovorum Factor - 200,000u daily
Started 5 days pre-radiation
and continued post radiation
Citrovorum Factor - 200,000u daily
Started day of radiation
Percent
120
100
80
60
40
20
0
4
8
12
16
20
24
28
Days Post Radiation
Percentage of Pre-Radiation Red Cell Count
Graph IV
Control
Folic Acid - 0.1mg daily
Started 5 days pre-radiation
and continued post radiation
Folic Acid - 0.1mg daily
Started day of radiation
Percent
120
100
80
60
40
20
0
4
8
12
16
20
24
28
Days Post Radiation

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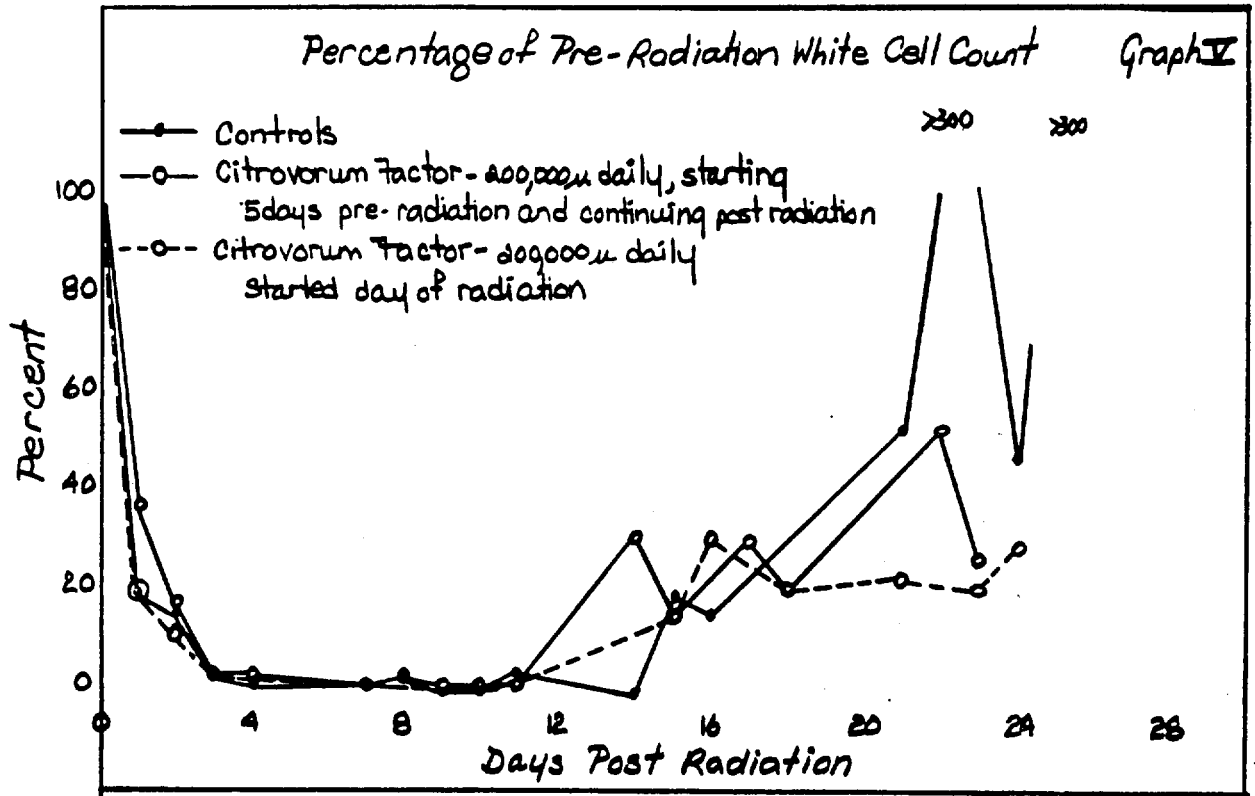
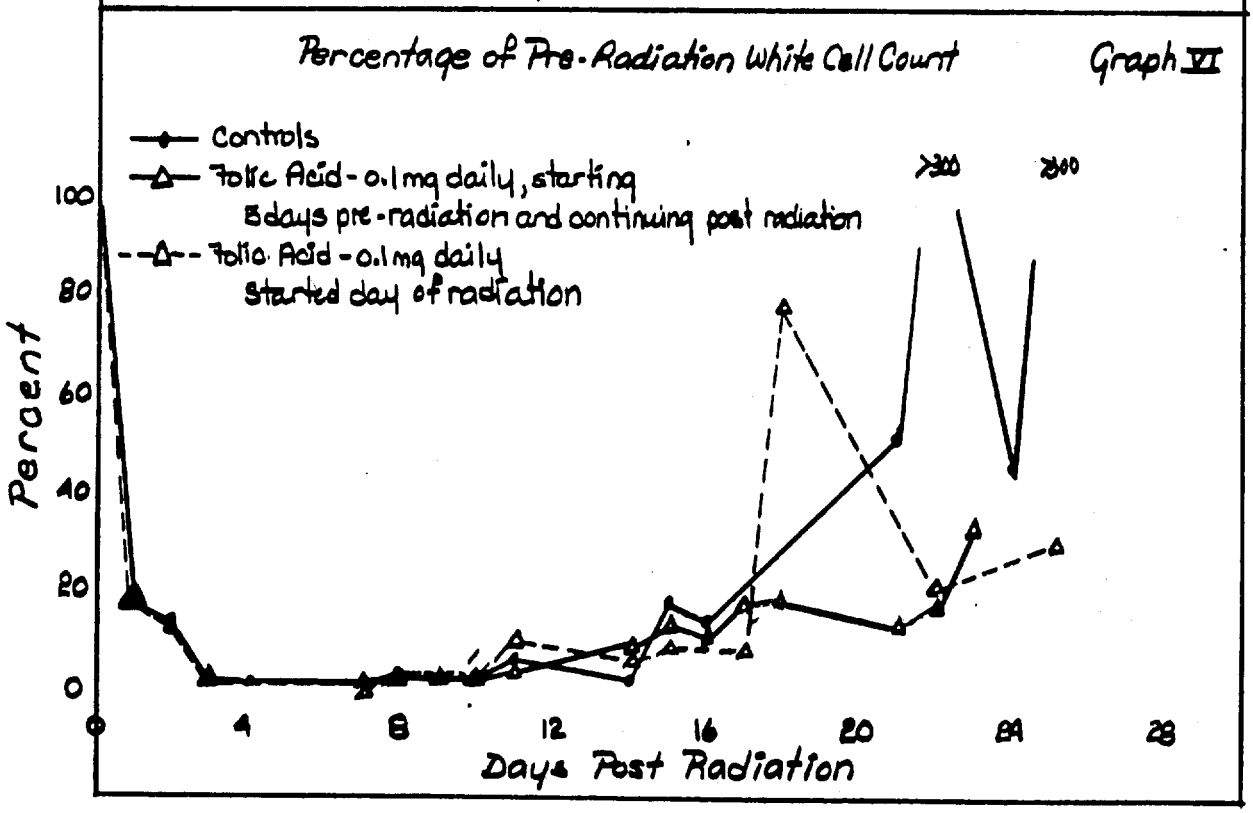




Program Code: X.R. BIOLOGICAL EFFECTS OF EXTERNAL RADIATION (X-RAYS AND γ RAYS)

Problem Code: X.R.3 Therapy (measures against radiation effects)

Section Code: 540

Authors: M. P. Coulter and F. W. Furth

The Effect of Polymyxin on X-Irradiated Rats

Background: Recent reports (1,2) indicate that a high incidence of bacteremia occurs in mice and rats that have received a large dose of whole body x-irradiation during the period of greatest mortality. In one of these studies (2), a strain of Pseudomonas was isolated from 83% of 40 positive blood cultures obtained from x-irradiated (700 r whole body) rats.

Studies on the effect of antibiotics on the radiation syndrome in rats (3) have shown that Aureomycin and Terramycin are effective in decreasing the incidence of diarrhea post-irradiation but probably have no consistent effect on decreasing total mortality. In vitro studies reveal that most strains of Pseudomonas are quite resistant to Aureomycin and Terramycin (4,5). Polymyxin appears to be a more effective anti-bacterial agent against this organism (4,5,6). Therefore, this study was designed to determine the effectiveness of Polymyxin alone and in combination with Aureomycin as a therapeutic agent in the radiation syndrome in rats.

Methods: Ninety adult Wistar rats were housed in separate cages and given water ad lib. Thirty of these rats served as controls and received plain Fox Chow feed. Thirty received Polymyxin, 2 mgm./rat/day, admixed with the feed. The remaining 30 rats received feed containing Polymyxin in the above dosage plus Aureomycin, 125 mgm./kg./day. For the first 5 days post-irradiation, when all the rats showed a diminished appetite, feed containing an increased concentration of drugs was given to maintain a uniform

daily dosage. The feed was weighed and 15 grams offered to each rat daily. Left over feed was weighed the following day so that a measure of the amount of feed and drug consumed was obtained. The feed containing the antibiotics was offered to the rats immediately following irradiation. X-irradiation was administered with a Picker 250 KV machine at 15 ma., using a plano-convex aluminum filter with 0.5 mm. of copper. The target skin distance was 40 inches and the total target skin dose was 700 r administered at the rate of 16 r min. The radiation was administered to groups of rats containing equal numbers of experimental and control animals.

The rats were weighed and examined for diarrhea daily.

Results: Graph I shows that during the first 5 days post-irradiation all of the rats showed a loss of weight. There is no difference shown in the rate at which the animals regained weight.

The most marked difference between the control and treated rats was in the incidence of diarrhea. As shown in Graph II, the rats that received Polymyxin alone had a lower incidence of diarrhea than did the controls, and those that received both Polymyxin and Aureomycin showed practically no diarrhea. The lower incidence of diarrhea, as seen in those rats fed Polymyxin alone, is of the same order as obtained in other studies (3) in which rats were fed either Aureomycin or Terramycin alone. The incidence of diarrhea in the rats fed a combination of Polymyxin and Aureomycin is lower than any obtained in other antibiotic studies carried out in this laboratory.

There was no significant difference in the rate of, or total mortality between the groups, as shown in Graph III.

Summary: Ninety rats received 700 r total body x-irradiation. Of these, 30 served as controls, 30 received Polymyxin, orally, post-irradiation and 30 received a combination of Polymyxin and Aureomycin, orally, post-irradiation.

The antibiotic-treated animals had a much lower incidence of diarrhea than did the controls. The combination of the antibiotics was the more effective in reducing the diarrhea.

No significant differences in weight loss or mortality were noted between the 3 groups.

Bibliography

1. Miller, C. P., Hammond, C. W., Tompkins, M., Science, 111, 540, 1950.

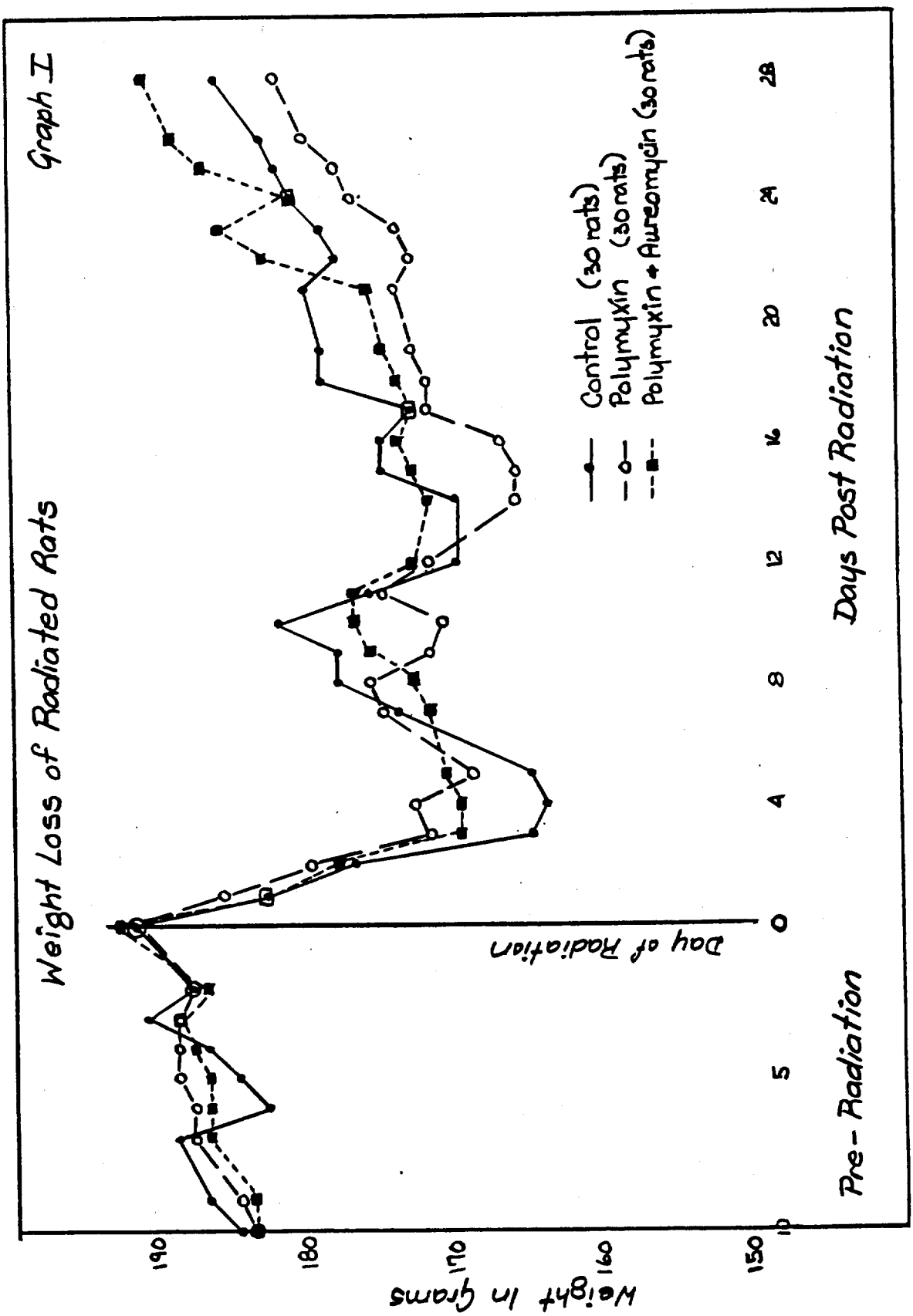
2. Coulter, M. P., Furth, F. W., Howland, J. W. UR-152, Quarterly Technical Report, February 1, 1951.

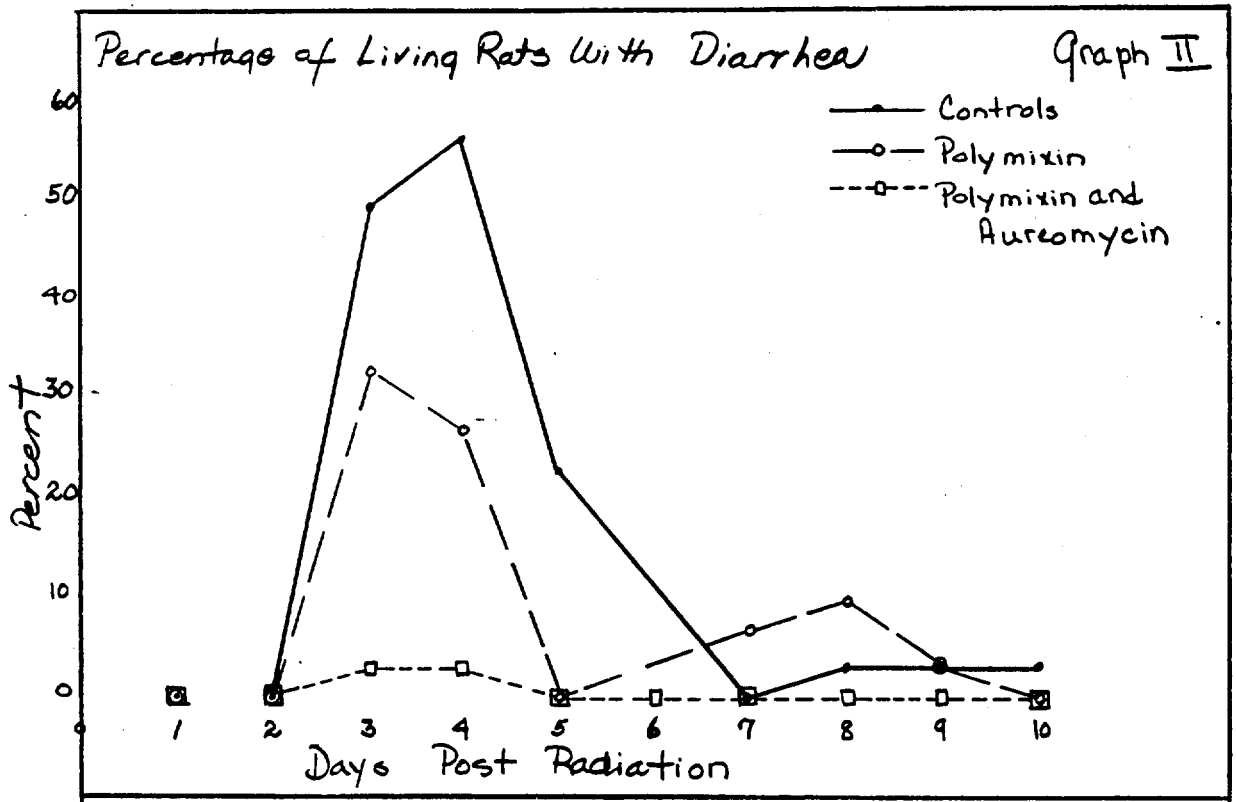
3. Furth, F. W., Coulter, M. P., Howland, J.W., UR-158, February 14, 1951.

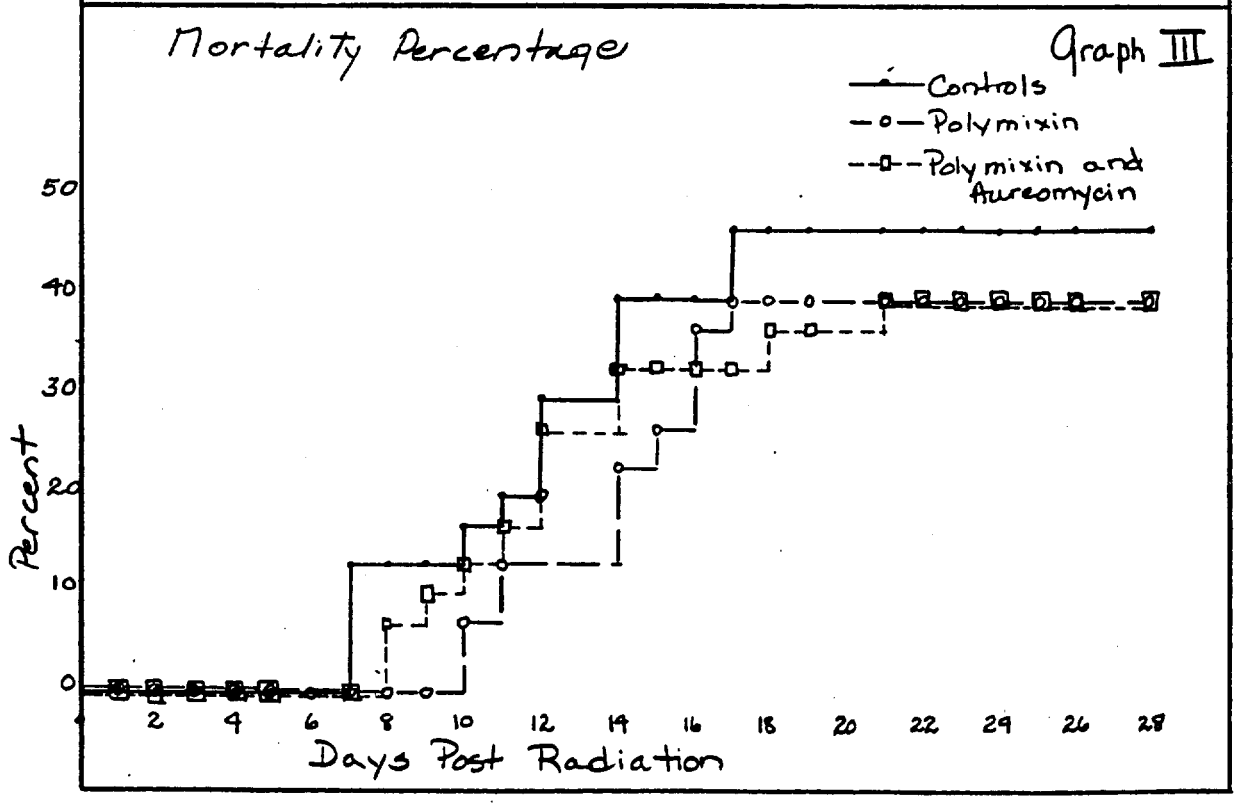
4. Frank, P. F., Wilcox, C., Finland, M., J. Lab. and Clin. Med., 35, 205, 1950.

5. Armstrong, C. W. J., Larner, A. E., J. Lab and Clin. Med., 37, 584, 1951.

6. Stansly, P. G., Am. J. Med., 7, 807, 1949.




Percentage of Living Rats With Diarrhea
Graph II
Controls
Polymixin
Polymixin and Aureomycin
Percent
60
50
40
30
20
10
0
1
2
3
4
5
6
7
8
9
10
Days Post Radiation


Mortality Percentage
Graph III
Controls
Polymixin
Polymixin and Aureomycin
Percent
50
40
30
20
10
0
2
4
6
8
10
12
14
16
18
20
22
24
26
28
Days Post Radiation

Program Code: X.R. BIOLOGICAL EFFECTS OF EXTERNAL RADIATION (X-RAYS AND γ RAYS)

Problem Code: X.R.3 Therapy (measures against radiation effects)

Section Code: 540

Authors: F. W. Furth and M. P. Coulter

The Effect of Aureomycin at Two Dosage Levels on the Acute Radiation Syndrome in the Dog

Background: Previous reports (1,2) from this laboratory indicate that certain broad spectrum antibiotics favorably influence the morbidity and mortality of the acute radiation syndrome in the dog. It was found that Aureomycin was one of the most effective antibiotics in reducing the mortality of the radiation syndrome. However, the dosage (100 mg./kg. of body weight/24 hours) used in these experiments was approximately 2 to 4 times the recommended dosage for humans. Even at this higher dosage there were no toxic effects observed in the dog which were attributable to the Aureomycin. Because toxic symptoms in human might become much more prevalent with this high dosage, it becomes desirable to know the minimal effective dose of the antibiotic. The experiment reported here was designed to determine what effect halving the previously used dosage of Aureomycin would have upon the morbidity and mortality of the acute radiation syndrome in the dog.

Methods: A total of 54 adult healthy mongrel dogs averaging approximately 10 kg. in weight were used in this experiment. All the dogs were housed in individual cages, given water ad libitum, and fed accurate amounts of a soft mash made from Purina Dog Chow, Kibbled Meal. During a two week control period, previous to irradiation, observations of weight and complete blood counts were performed on each dog.

All of the dogs received a total of 450 r of total body irradiation administered at 15 ma by a 250 KV Industrial Picker x-ray Machine at a rate of

7.2 r/min. The beam was filtered with 0.5 mm. of copper, and a plano-convex aluminum filter. The target skin distance was 40 inches.

Immediately after irradiation, 16 of the dogs were started on Aureomycin in a dosage of 50 mg./kg./24 hours, orally, (one 250 mg. capsule every 12 hours), and this medication was continued for 28 days post-irradiation. Fifteen of the dogs were given 100 mg./kg./24 hours, orally, (one 250 mg. capsule every 6 hours), immediately after irradiation and continued at this dosage for 28 days post-irradiation. The remaining 23 dogs received no medication and served as controls. Complete blood counts were done on all dogs at intervals following irradiation.

Results: The results are summarized in Graphs I, II, III, and IV. As shown in Graph I (Page 35), the most marked effect that these antibiotic substances have is on the mortality. With both dosage levels of Aureomycin there is an apparent reduction of mortality from 60% in the control group to 20-25% in the treated groups. The first death in the control group occurred four days before the first death in the treated groups. By the 17th day, post-irradiation, when the first dog in each of the treated groups died, 30% (7) of the control dogs had succumbed. There appears to be no significant difference in the rate of mortality or total 30 day mortality between the two groups of dogs treated with different dosage levels of Aureomycin. No dogs died after 30 days post-irradiation.

As shown in Graphs II, III, and IV, the peripheral blood counts in all groups decreased at essentially the same rate following irradiation, except for some variation in the hematocrit between the control group and treated groups. This difference in hematocrit value, especially during the 12th to 16th day, post-irradiation, may reflect the earlier morbidity with associated bleeding tendency which occurred in the control group.

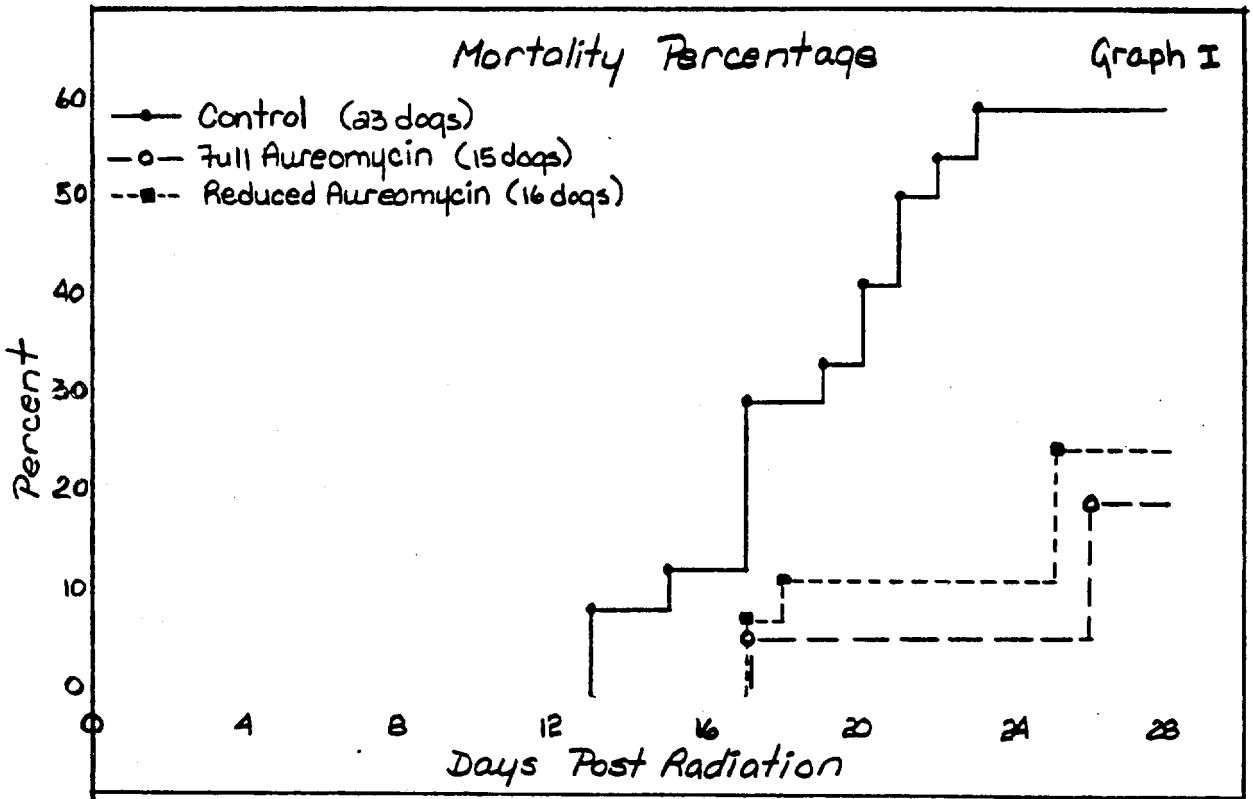
Discussion: During the course of this experiment no detailed studies were undertaken to determine the mode by which the antibiotic reduced the mortality. In the previous experiments (1,2), serial blood cultures and quantitative fecal bacteriologic studies were done on antibiotic treated x-irradiated dogs. The results of these studies, and a discussion of their significance is given in the reports of the experiment. Essentially, it was found that there was an increase in the incidence of positive blood cultures in the control groups, post-irradiation. There was no conclusive evidence that the antibiotics completely suppressed or controlled bacterial infection in the x-irradiated dog. However, it must be emphasized that the methods of study may not have been adequate to demonstrate the actual effect of the antibiotic. Complete autopsy studies on all the dogs which died in this experiment showed no essential difference in the gross pathology between control and treated groups. The most frequent cause of death was a severe hemorrhagic diathesis with hemorrhage in or around various major organs.

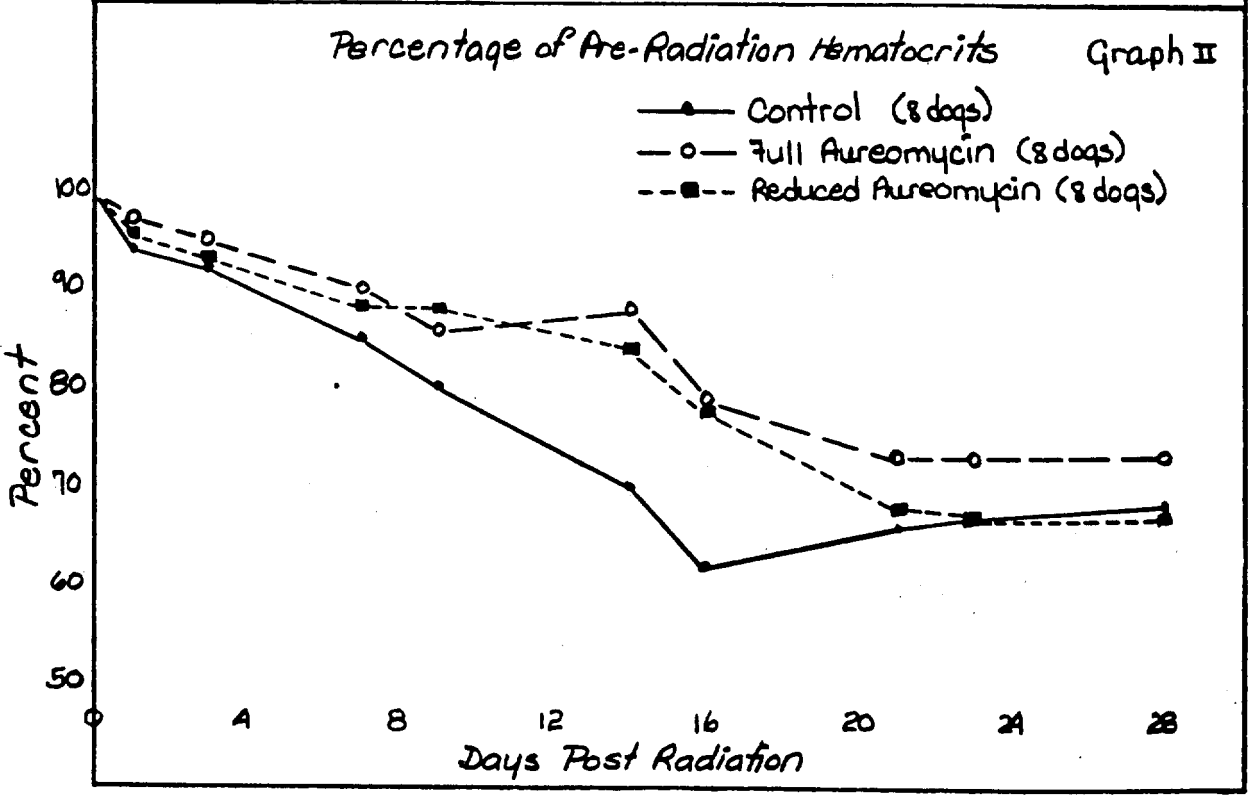
Summary: Fifty-four adult mongrel dogs were exposed to 450 r of whole body x-irradiation. Fifteen of these dogs were started on 100 mg./kg./24 hours in divided doses of Aureomycin, orally, starting immediately after irradiation. Sixteen of the dogs began to receive Aureomycin, orally, in a dosage of 50 mg./kg./24 hours immediately after irradiation. The Aureomycin was continued daily for 28 days after irradiation in both groups. The remaining 23 dogs received no medication and served as controls. The 30 day mortality in the control group was 60%, in the 50 mg./kg. group was 25%, and in the 100 mg./kg. group 20%. No significant difference in leucocyte or platelet count was noted between the groups but the hematocrit in the control group decreased more rapidly.

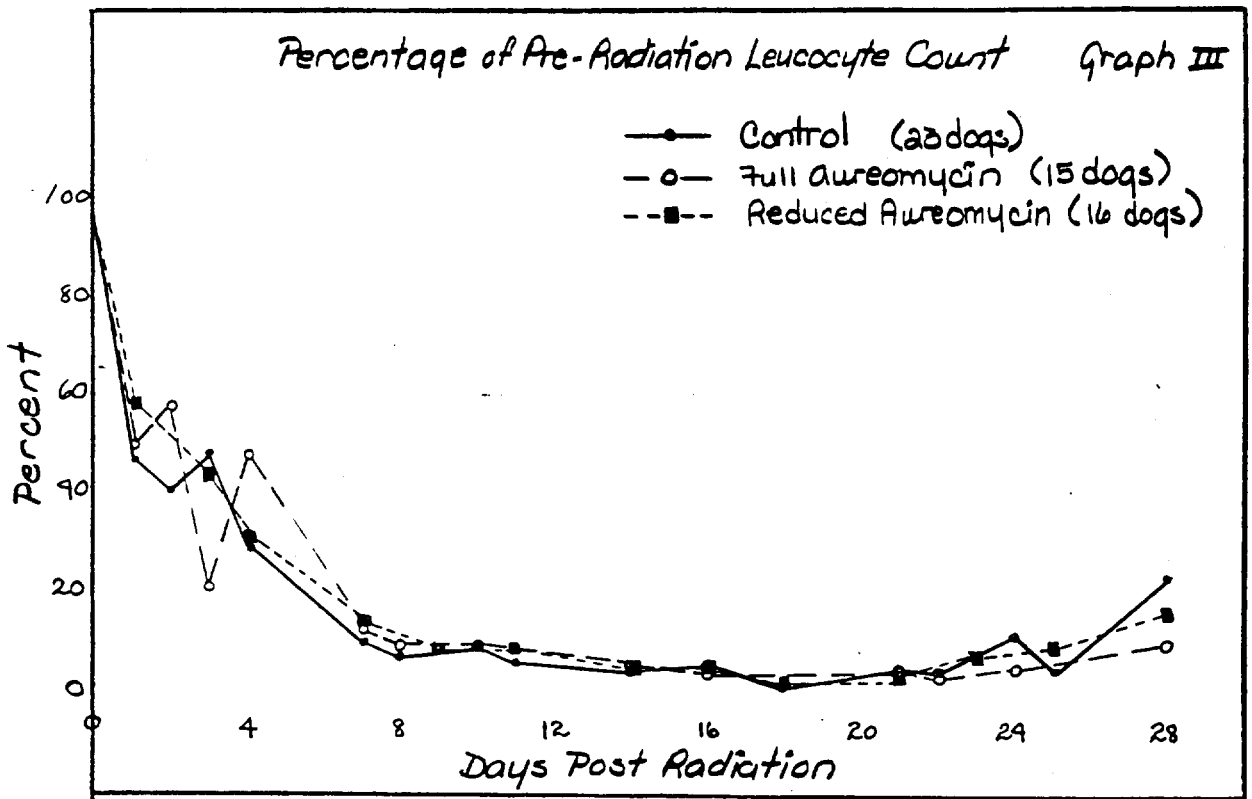
Bibliography

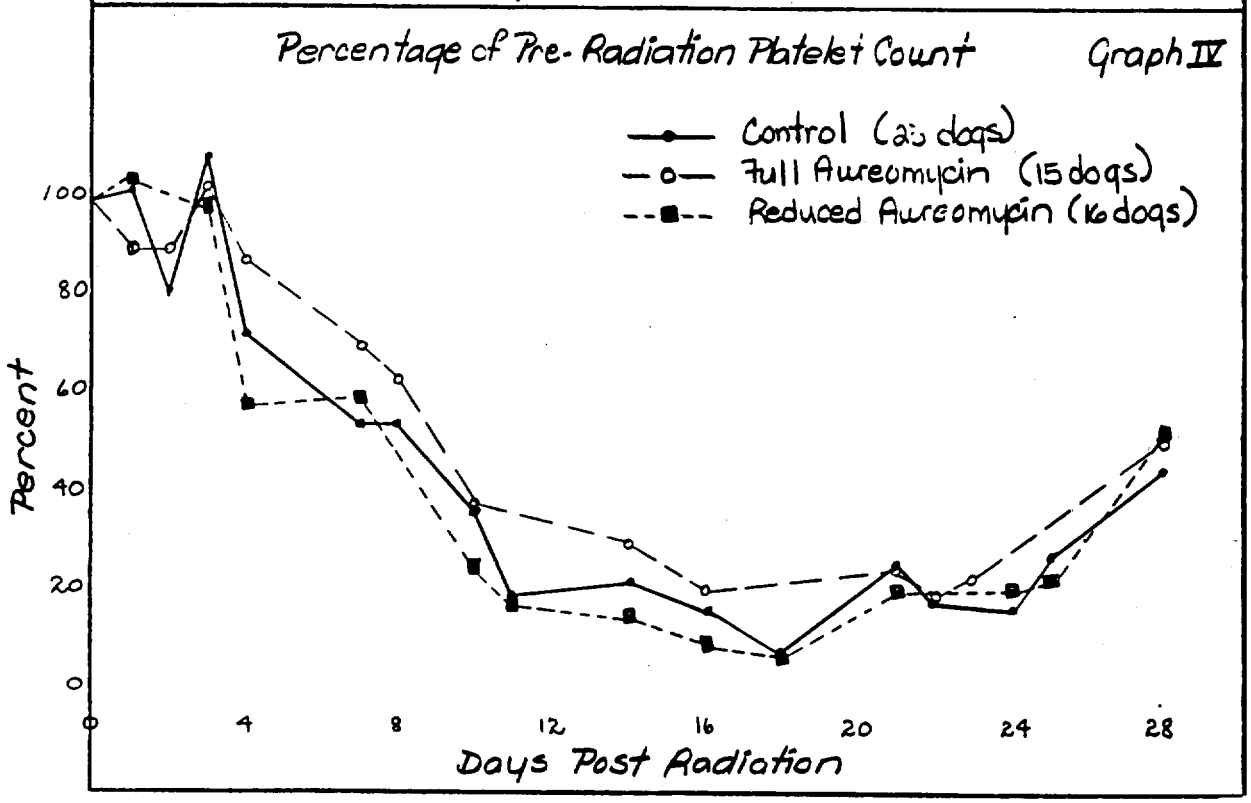
1. Furth, F. W., Coulter, M. P., UR-146.

2. Furth, F. W., Coulter, M.P., Howland, J. W., UR-157.






Percentage of Pre-Radiation Leucocyte Count
Graph III
Control (23 dogs)
Full Aureomycin (15 dogs)
Reduced Aureomycin (16 dogs)
Percent
100
80
60
40
20
0
0
4
8
12
16
20
24
28
Days Post Radiation


Percentage of Pre-Radiation Platelet Count
Graph IV
Control (23 dogs)
Full Aureomycin (15 dogs)
Reduced Aureomycin (16 dogs)
Percent
100
80
60
40
20
0
0
4
8
12
16
20
24
28
Days Post Radiation

Program Code: X.R. BIOLOGICAL EFFECTS OF EXTERNAL RADIATION (X-RAYS AND γ RAYS)

Problem Code: X.R.3 Therapy (measures against radiation effects)

Section Code: 540

Authors: F. W. Furth, J. Shrier, J. Markham, M. Crociata

The Octab Reaction of Dog Serum Following X-Irradiation

Background: Recently, Jacox (1) has described a flocculation test on human sera, employing the quaternary ammonium salt, Octab, which presumably measures one of the components of the globulin fraction. In further studies (2), Jacox and Gale were able to establish a definite correlation between this test and the erythrocyte sedimentation rate in certain disease states. In their studies they found that in rheumatic fever, chorea, and rheumatoid arthritis, the Octab test showed an increased sensitivity over the erythrocyte sedimentation rate as a measure of the activity of the disease process. Correlated electrophoretic studies on serum seem to indicate that this test measures, principally, the alpha prime of globulin.

Previous to the investigation reported here, no studies were reported using this test on dog serum. Since we are studying some of the physiological aspects of x-irradiation, it was of interest to determine the variations in the degree of flocculation of the serum of dogs that had been exposed to a large dose of x-irradiation.

Methods: The serum from a total of 18 dogs was used in this experiment. The blood was drawn from the external jugular vein, allowed to clot, and the serum was drawn off following centrifugation. The serum was diluted 1-200 in 0.08 M sodium chloride solution. This dilution was higher than the 1-100 dilution employed by Jacox, since the dogs had a somewhat greater degree of flocculation. To a 2 ml. aliquot of this diluted serum, 5 ml. of 0.08 M

saline buffered to pH 6.8 with 0.05 M collidine buffer was added. To this solution 1.0 ml. of 0.1% Octab solution is added and mixed. The turbidity of this solution was measured by determining the optical density in a Coleman Senior photoelectric colorimeter. The turbidity unit is then expressed by multiplying the optical density by 1000.

Previous to irradiation, two determinations were made on each of the dogs. Following irradiation, determinations were made twice weekly for four weeks. The dogs were given 450 r of whole body x-irradiation from a 250 KV source filtered with 0.5 mm. of copper and a plano-convex aluminum filter. The irradiation was administered at a rate of 7.0 r/min. The sedimentation rates were done by the Wintrobe method and are expressed in millimeters per hour. The sedimentation rate was corrected for variation in hematocrit, using the standard Wintrobe chart employing 46 as the normal mean line.

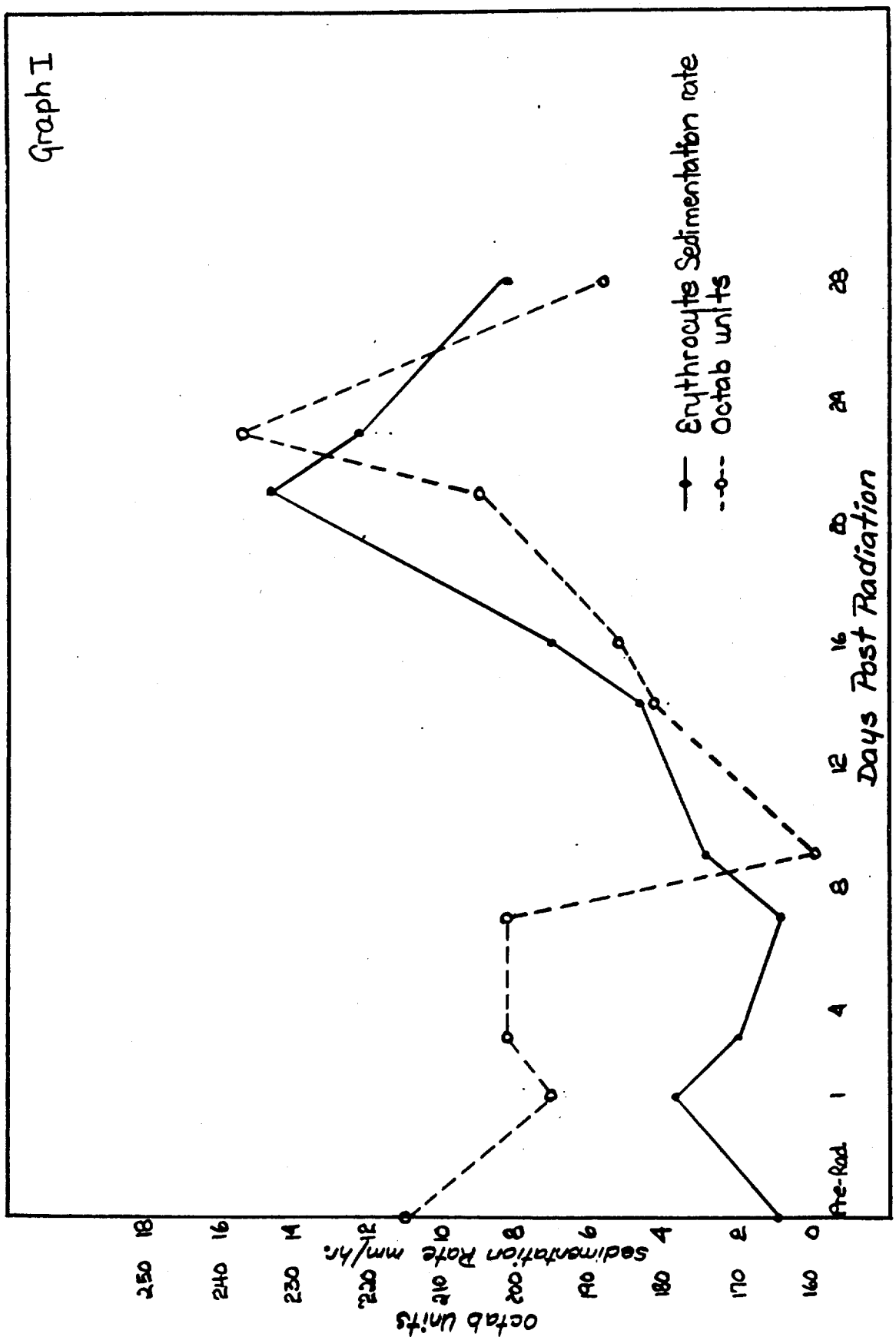
Results: The results are summarized in Graph I (Page 40). The points on this graph represent averages of the results on all 18 dogs on the various days, post-irradiation. The average pre-radiation Octab value was 215 units with a maximum variation of 150 units to 330 units. The average pre-radiation sedimentation rate was 1 mm./hour. Following irradiation, there was a fall in the degree of Octab flocculation to a low point of 160 units on the 10th day. Following this, the Octab flocculation gradually increased to a maximum of 238 units on the 23rd day. The variation on this day was from 170 units to 390 units. There was a decline to a value within normal range by the 28th day. The sedimentation rate did not show any consistent change until an increase began during the 2nd week, post-irradiation. This increase paralleled the increase in Octab flocculation during the 3rd and 4th week, post-irradiation. The maximum variation of the sedimentation rate during this period was 0 to 32 mm./hour. There was little correlation between Octab flocculation and

[redacted]

in this group died on the 21st and 23rd day post-irradiation respectively. Neither the Octab flocculation test nor the sedimentation rate varied significantly from the average in these two dogs, so that no prognostic information in respect to death could be derived from the tests. However, the increases in the values of both tests occurred when the animal appeared sick.

Discussion: This study would indicate that the Octab flocculation test and sedimentation rate are an indication of a morbid state in the dog, produced by exposure to x-irradiation. A correlation between Octab flocculation and sedimentation rate, similar to that reported by Jacox in inflammatory disease, occurred in the irradiated dogs. There did not seem to be any prognostic significance in either test in respect to death.

Summary: The Octab flocculation test described by Jacox, involving the precipitation of a serum globulin fraction by means of quaternary ammonium compound was applied to serum of dogs given whole body x-irradiation. Erythro-


Graph I
Erythrocyte Sedimentation rate
Octab units
Days Post Radiation
Pre-Rad
1
4
8
12
16
20
24
28
Sedimentation Rate mm/hr.
0
2
4
6
8
10
12
14
16
18
Octab units
160
170
180
190
200
210
220
230
240
250

Program Code: X.R. BIOLOGICAL EFFECTS OF EXTERNAL RADIATION (X-RAYS AND γ RAYS)

Problem Code: X.R.3 Therapy (measures against radiation effects)

Section Code: 540

Authors: M. Coulter, F. W. Furth

The Sensitivity to Aureomycin and Terramycin of Bacteria from X-irradiated Dogs

Background: During the past two years, bacteriological studies have been made on groups of dogs which received 450 r whole body x-irradiation. One-half of these dogs served as controls, the remainder received either Aureomycin or Terramycin therapy, post-irradiation. These bacteriological studies included frequent blood cultures and an analysis of the fecal flora. The sensitivity to Aureomycin and Terramycin of the bacteria isolated from the above sources was determined.

Methods: The details of the bacteriological studies and the radiation factors have been presented elsewhere (1,2). The sensitivity to the antibiotics of the various organisms isolated was determined by a tube dilution method, using serial dilutions of the antibiotic with a standard amount of a 24 hour thioglycollate broth culture of the organisms. The end points were read after 18 hour cultures at 37° C. The end point is defined in terms of the antibiotic content of the tube containing the least amount of Aureomycin in which no growth has occurred. These readings, therefore, presumably represent the bacteriocidal level.

No attempt was made to differentiate between serologically distinct strains of E. coli recovered from the feces. It is recognized that the strains recovered from the same dog at various periods were frequently not the same, as evidenced by their varying sensitivity to the antibiotics.

Antibiotic therapy was instituted on the day of radiation immediately following radiation. Each treated dog received 100 mgm./Kgm./24 hours

of the antibiotic, given in divided doses every 6 hours, day and night. Therefore, the first week of antibiotic therapy, as will be referred to later, is also the first week post-irradiation.

Results: In the following data a sensitive (S) organism showed no growth at 6.25 mcgm./cc. or lower; a moderately resistant (MR) organism showed no growth from 7-25 mcgm./cc. and a resistant (R) strain showed no growth from 50-100 mcgm./cc. of antibiotics to Aureomycin and Terramycin.

Table I below. shows the relative sensitivities of the bacteria isolated from blood cultures from control dogs prior to irradiation and from antibiotic treated dogs, post-irradiation.

TABLE I

	No. of Cultures	Aureomycin			Terramycin		
		S	MR	R	S	MR	R
Control Dogs	14	57%	29%	14%	54%	8%	38%
Aureo-Treated Dogs	3	33%	66%				
Terra-Treated Dogs	9	11%	89%		22%		78%

The resistant strains were recovered from blood cultures obtained within one week of the institution of antibiotic therapy, as shown in Table II below. The positive blood cultures listed in the table were obtained from Terramycin treated dogs.

TABLE II

	No. of Positive Cultures	Aureomycin	Terramycin
Control Period	2 (Strep and Alkalegenes)	100% S	100% S
1st Week of Therapy	4 (3 Staph, 1 Strep)	100% MR	100% R
2nd Week of Therapy	2 (1 Staph, 1 Pseudomonas)	100% MR	50% S, 50% R
3rd Week of Therapy	2 (Staph)	100% MR	100% R

Table III below, shows the relative sensitivities of the coliform organisms isolated from the stools of the dogs pre and post-irradiation.

TABLE III

	Aureomycin				Terramycin			
	No. of Cultures	S	MR	R	No. of Cultures	S	MR	R
Control Dogs (Pre-Irradiation)	50	70%	12%	18%	39	54%		46%
Control Dogs (Post-Irradiation)	49	57%	35%	8%	39	33%	18%	49%
Aureomycin-Treated Dogs (Post-Irradiation)	22	36%	59%					
Terramycin-Treated Dogs (Post-Irradiation)	41	12%	2%	85%	41	5%		95%

It is evident that organisms isolated from antibiotic treated dogs were relatively more resistant than those isolated from control dogs. The rate of the development of resistant strains is shown in the following table (Table IV) for Terramycin-treated dogs.

TABLE IV

	Aureomycin		Terramycin	
	S	R	S	R
Control Period	86%	7%	57%	43%
1st Week of Therapy	7%	86%		100%
2nd week of Therapy		100%		100%
3rd Week of Therapy	25%	75%	12%	88%
4th Week of Therapy	33%	66%	17%	83%

As mentioned before, the sensitivity determinations were made on strains of coli isolated at random from the stools at various periods post-irradiation and no serological identification was made, so that various strains from the same dog are being compared. However, it does not seem likely that the differences in sensitivity listed heretofore are dependent upon the coincidence of recovering a sensitive strain at one period and an entirely different resistant strain at another time. There appears to be a definite trend for a higher incidence of resistant bacteria to appear in the antibiotic-treated dogs. The bacteria also show a definite tendency to develop cross resistance, that is, organisms recovered from Terramycin-treated dogs not only develop resistance to Terramycin but also to Aureomycin. This is shown in the following table (Table V), where the sensitivity of the organisms to both Aureomycin and Terramycin was determined.

TABLE V

Control Dog Blood Cultures	54% sensitive to Aureo and Terra
Terramycin-Treated Dogs Blood Cultures	78% resistant to Aureo and Terra
Control Dogs Stools - E. Coli	54% sensitive to Aureo and Terra
Terramycin-Treated Dogs Stools - E. Coli	85% resistant to Aureo and Terra

Summary: The sensitivity to Terramycin and Aureomycin of organisms from x-irradiated dogs has been determined. Sensitivity determinations were made on coliform bacteria isolated from the stools and from bacteria isolated from positive blood cultures. Some of the dogs studied received either Aureomycin or Terramycin daily following x-irradiation. Bacteria isolated from control dog blood cultures are more sensitive to the antibiotics than those recovered from antibiotic-treated dogs. Similarly, the coliform

bacteria from control dog stools are more sensitive than those from the treated dogs. The resistant strains are isolated from the blood cultures and stools one week after the onset of antibiotic therapy. The bacteria show a tendency to develop resistance to both Aureomycin and Terramycin, although the organisms are recovered from a dog that has received only one of the antibiotics.

Bibliography

1. Furth, F. W., Coulter, M. P., Howland, J. W., Bacteriological Studies in the X-Radiated Dog, UR-157.

2. Furth, F. W., Coulter, M.P., Howland, J. W., The Effect of Aureomycin on the Radiation Syndrome in Dogs, UR-146.

Program Code: X.R. BIOLOGICAL EFFECTS OF EXTERNAL RADIATION (X-RAYS AND γ RAYS)

Problem Code: X.R.4 Hematology

Section Code: 530

Authors: M. Ingram, L. Coonan, G. Nielsen, J. Jespersen, D. Piatt, M. Wright.

Bone Marrow Studies on Dogs which Survived Single Whole-Body Exposure to LD_{90-100} Doses of X-Rays.

Background: This study represents a preliminary investigation of the myelograms of dogs which survived single whole-body exposure to an LD_{90-100} dose of X-radiation. The particular dogs on which this report is based had been members of a group of experimental animals under study by Drs. Howland, Furth, Coulter, et al. The dogs were turned over to the Hematology Section for bone marrow studies during the 11th post-radiation week when it was clear that the animals had successfully survived the critical post-irradiation period during which death usually occurs as a result of the acute radiation syndrome or as a result of complications clearly related to that syndrome.

Methods: Bone marrow studies consisted of total nucleated cell counts and determination of the myelograms of bone marrow obtained by aspiration biopsy. These initial studies utilized marrow aspirated from three sites: sternum, vertebrum, and iliac crest. This was done to permit evaluation of the three sites as regards ease of obtaining representative samples on a routine basis, as well as to study the validity of the method of sampling one site only. Briefly, the marrow aspiration technique is as follows:

The site selected for biopsy is clipped with electric hair clippers, cleaned with soap and Zephiran, and draped with a sterile L. P. sheet. The operator scrubs for approximately three minutes, and sterile gloves are worn for the biopsy in most instances. The needles, syringes, mallet, sponges, etc.,

etc. have previously been autoclaved as a pack. Local anesthesia of the biopsy site is accomplished by infiltration with 1% procaine. A 1 inch No. 18 or 17 LNR needle obtained from Paine Drug Company is used for the biopsy except in the case of large dogs when a 2 or 2.5 inch needle is used for the iliac crest biopsy. The needle is inserted until it contacts bone and then tapped sharply with a small metal mallet until the marrow cavity is entered. Marrow is aspirated into a 2 cc. syringe containing powdered heparin. An attempt has been made to keep the volume of the aspirate constant by withdrawing 0.2 cc. of marrow in each instance. A large drop of heparinized marrow is delivered to a glass slide for total nucleated cell counts and the remainder of the marrow is used for coverslip smears which are subsequently stained with Wrights stain diluted 1:1 with absolute methyl alcohol.

Results: Results are presented in Tables I and II (pages 49-51).

Discussion: In general, myelograms of marrow from the three sites studied are similar. The greatest difference among them relates to the total nucleated cell counts. Instances in which the myelogram was not determined were due to poor samples, most commonly the result of extensive dilution of the marrow with blood. In most cases, differential counts were done in areas where intact clumps of marrow were retained with approximately normal architecture on the smear, so that, in general, there is good agreement among the differential counts representing the various sites.

The bone marrow of dogs 11 weeks after an LD_{90-100} dose of X-rays indicates that the myeloid tissue at that time is cellular and active, and that cell types are normal in general. Apparently hematopoiesis has not yet stabilized, however, for two weeks later (13 weeks post-exposure) the picture has changed and both erythroid and myeloid series have shifted to the right relative to

the picture at 11 weeks.

The bone marrow aspiration method described in the present report is well tolerated by the dogs and is readily adaptable to routine serial studies.

More extensive studies of the bone marrow of heavily irradiated dogs are now being carried out and will be reported in subsequent reports.

Summary: Bone marrow studies have been carried out on four dogs 11 and 13 weeks after single whole body exposure to an LD_{90-100} dose of X-rays. The method of aspiration biopsy from sternum, vertebrum and iliac crest is presented briefly. Results are presented in table form.

TABLE 1

BONE MARROW IN DOGS RECOVERING FROM AN LD_{90-100} DOSE OF X-RAYS

Dog No.	Time Post-exp.	Marrow Site	Total Nucleated Cell Count	% Nucleated RBC	Approximate Absolute Nucleated RBC	% Myeloid Series Cells	Approximate Absolute Myeloid Series Cells	Myeloid/Erythroid Ratio
Female 1771*	11 wks.	S	195,000	27.6%	53,820	72.4%	141,180	72.4/27.6 = 2.6
		V	116,250	23.4%	27,202	76.6%	89,047	76.6/23.4 = 3.3
		I	373,750	42.4%	158,470	57.6%	215,280	57.6/42.4 = 1.4
1771	13 wks.	S	47,500 65,000	39.4%	22,162	60.6%	34,087	60.6/39.4 = 1.5
		V	103,750 90,000	37.4%	36,231	62.6%	60,643	62.6/37.4 = 1.7
		I	158,750 210,000	43.8%	80,756	56.2%	103,618	56.2/43.8 = 1.3
Female 1749	11 wks.	S	685,000 687,750	53.3%	363,439	46.6%	317,754	53.3/46.6 = 1.1
		V	95,500 135,000	66.3%	76,411	33.7%	38,839	66.3/33.7 = 2.0
		I	191,250 172,500	55.8%	101,486	44.2%	80,389	55.8/44.2 = 1.3
1749	13 wks.	S	450,000 451,250	45.6%	205,485	54.4%	245,140	54.4/45.6 = 1.9
		V	-------**					
		I	-------**					

* Delivered of 4 pups approximately 8 weeks post-exposure
** Unsatisfactory sample

TABLE 1 (Continued)

Dog No.	Time Post-exp.	Marrow Site	Total Nucleated Cell Count	% Nucleated RBC	Approximate Absolute Nucleated RBC	% Myeloid Series Cells	Approximate Absolute Myeloid Series Cells	Myeloid/Erythroid Ratio
Male 1699	11 wks.	S	340,000 307,500	62.2%	201,373	37.8%	122,378	37.2/62.2 = .06
		V	-------*					
		I	193,750 243,750	61.2%	133,875	38.8%	84,875	38.8/61.2 = .06
1699	13 wks.	S	347,500 306,250	54.6%	178,474	45.4%	148,401	45.4/54.6 = .08
		V	223,750 200,000	47.8%	101,276	52.2%	110,599	52.2/47.8 = 1.1
		I	-------*					
Female 1760	11 wks.	S	962,500 871,250	25.0%	229,219	75.0%	687,656	75.0/25.0 = 3.0
		V	213,750 282,500	31.8%	78,904	68.2%	169,221	68.2/31.8 = 2.1
		I	446,250 386,250	30.2%	125,708	69.8%	290,543	69.8/30.2 = 2.3
1760	13 wks.	S	95,000 80,000	26.0%	22,750	74.0%	64,750	74.0/26.0 = 2.9
		V	336,250 390,000	38.6%	140,166	61.4%	222,959	61.4/38.6 = 1.6
		I	476,000 595,000	34.2%	183,141	65.8%	352,359	65.8/34.2 = 1.9

* Unsatisfactory sample

TABLE 2

THE INCIDENCE OF RELATIVELY YOUNG CELLS IN THE MARROW OF DOGS RECOVERING FROM AN LD_{90-100} DOSE OF X-RAYS

Time Post-Exposure	Dog No.	% of Nucleated RBC which are Polychromatophilic Erythroblasts or Younger	Peripheral Blood RBC/mm^3	% of Myeloid Series Cells which are Stabs or Younger	Peripheral Blood WBC/mm^3
11 wks.	female 1771*	51.17%	5.4m	65.65%	19,850
13 wks.	1771	18.41%	5.9m	40.64%	17,500
11 wks.	female 1749	36.5%	6.9m	76.4%	8,250
13 wks.	1749**	23.5%	8.15m	50.0%	12,700
11 wks.	male 1699	51.23%	4.5m	56.66%	6,500
13 wks.	1699	23.24%	5.2m	50.61%	9,900
11 wks.	female 1760	42.76%	5.7m	85.63%	15,625
13 wks.	1760	28.15%	6.0m	53.06%	19,300

* Delivered of 4 puppies approximately 8 weeks post-exposure
** 13 week figures based on studies of sternal marrow only

Program Code: I.R. BIOLOGICAL EFFECTS OF EXTERNAL RADIATION

Problem Code: I.R.1. (Flash Burns)

Section Code: 620

Authors: John H. Morton, M.D., Harry D. Kingsley, M.D., and Herman E. Pearse, M.D.

Studies on Flash Burns: Threshold Burns

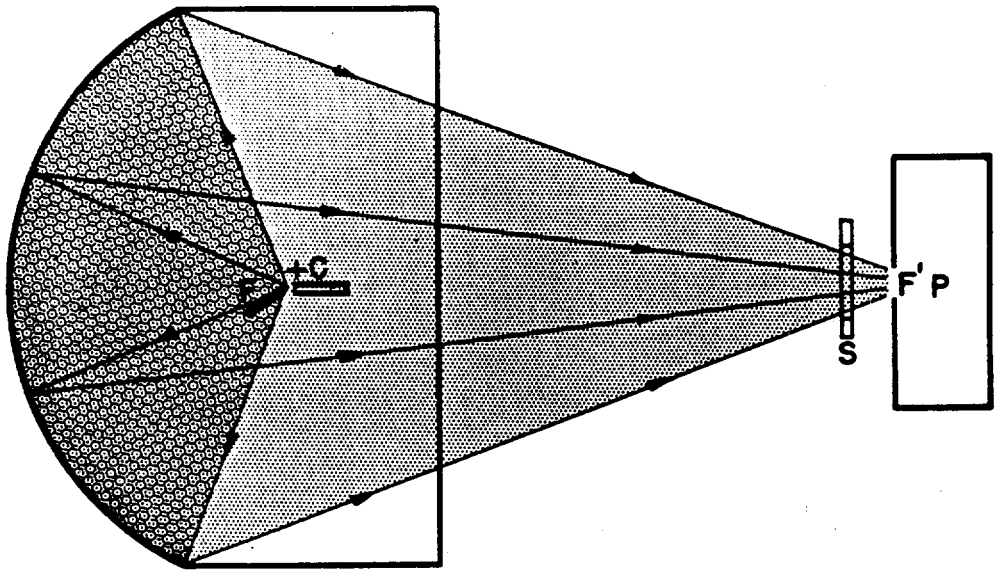
Introduction: Burns produced by a brief exposure to high intensity radiant energy assumed great medical importance during World War II. These "flash burns" were encountered at Pearl Harbor in December 1941 (10) and, to a much greater extent, at Hiroshima and Nagasaki following the atomic bomb explosions in August 1945 (4). The appalling number of burn casualties in the two Japanese cities made a study of flash burns of paramount importance (8,9).

Since 1947, work in this laboratory has been directed towards an understanding of the characteristics of flash burns (7,3). The present experiments were designed to study the burns produced by energy of varying intensity delivered by a high intensity, short duration source. Information of this nature was necessary in order to compare flash burns with conventional burns produced by longer exposures to lower temperatures (5).

Material and Methods: The radiant energy source was a modified 24-inch U. S. Navy carbon arc searchlight. Experimental high intensity carbons manufactured by National Carbon Company were used, the positive carbons being Ultrex #084 and the negative Orotip #537. The arc was operated at 80 volts and 150 amperes D. C. Although spectral analysis of the light source was not carried out, information from the manufacturer indicated that approximately 25% of the radiation emitted was in the ultraviolet, 40% in the visible, and

35% in the infrared. The parabolic reflector of the searchlight was removed and replaced by an ellipsoidal mirror having a primary focus 11 inches and a secondary focus 52.5 inches from the center of the mirror. This mirror was front-surfaced aluminum on glass and was positioned so that the arc crater was at the primary focus. The skin area to be exposed was placed at the secondary focus where the arc crater was magnified about five times in diameter. In the path of the arc beam on the front of the searchlight drum from which the glass face had been removed, an adjustable transite diaphragm was placed. The searchlight was mounted at one end of a lathe bed and a spring-driven sliding shutter in front of the secondary focus at the other. The open period of the shutter could be varied from 0.1 to 1.0 seconds by an electrically-activated timing cam controlling solenoid releases for opening and closing the shutter. Behind the shutter was placed an animal container with a perforated transite shield in one side to expose the test area of skin. The holes in the transite shield were 1.7 cm in diameter and were countersunk from the outside to reduce the penumbra produced by the shield. The entire exposure container could be moved so that the exposed skin could be positioned precisely at the secondary focus. Adjustment of the diaphragm and shutter respectively permitted variation in the intensity of the incident radiant energy and the time of exposure. Figure 1 (Page 54) shows a diagram of the optical system of the apparatus, and Figure 2 (Page 54) is a photograph of the arc and shutter mechanism.

The energy intensity was measured by exposing at the secondary focus a hollow, thin-walled copper sphere calorimeter blackened on the inside and admitting thermal radiation through a circular opening one square centimeter in area (1). The temperature rise of the sphere was a measure of incident energy, and from this data the calories could be calculated. There was found to be an



SCHEME FOR OPTICAL SYSTEM OF 24 INCH SEARCHLIGHT
(ELLIPSOIDAL MIRROR)

Figure 1. F - primary focus of ellipsoidal mirror; F' - secondary focus of ellipsoidal mirror; +C - positive carbon; S - shutter; P - animal container.

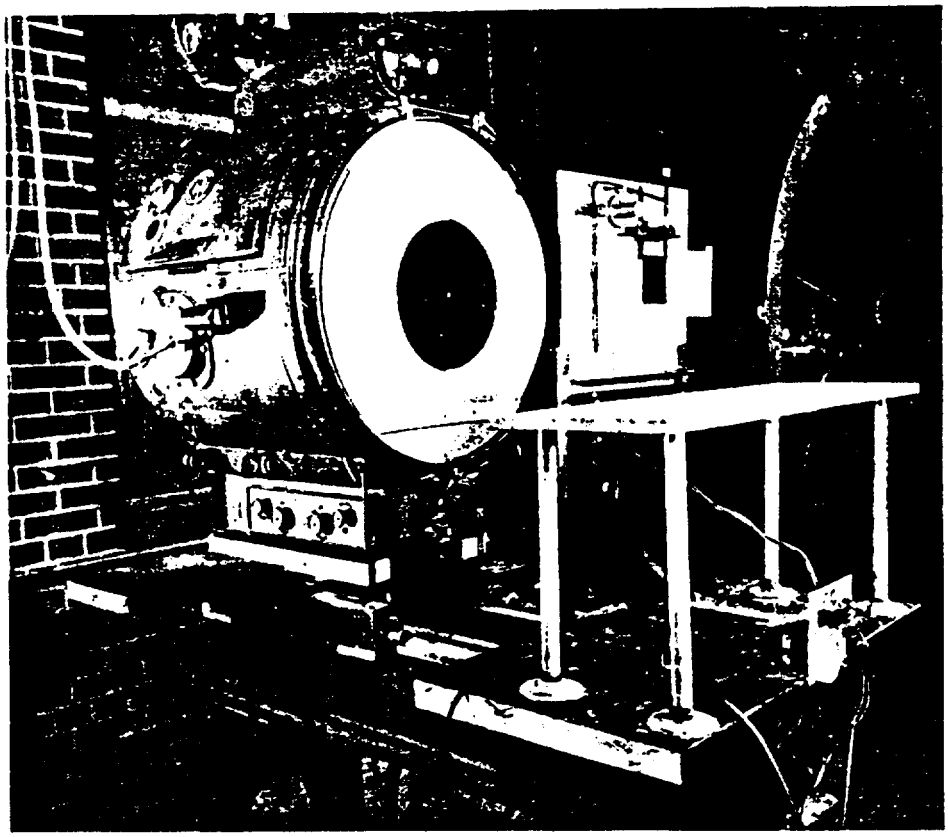


Figure 2. Arc with adjustable diaphragm and shutter mechanism.

inherent variation in the arc energy of about ±10%, but within these limits the energy recorded for a given diaphragm setting was found to be constant. The incident energy was varied from a maximum of 34 cal/cm^2/sec. to a minimum of 1.5 cal/cm^2/sec. by adjusting the diaphragm.

Moritz and Henriques (5) showed that swine possess skin similar in structure and physiological reaction to that of the human. Hence, young Chester White pigs varying in weight from 10 to 27 kg. were selected as experimental animals. Before burning, the pig was anesthetized with Dial in urea-urethane (Ciba) given intraperitoneally in doses of 65 or 70 mg. Dial per kg. body weight (2), and the area to be exposed was clipped closely with animal clippers. The pig was then placed in the animal container and positioned with the skin to be exposed pressed gently against the inside of the perforated transite shield. In each experiment, a series of four to eight burns at different intensity levels was made, the burns being placed on the animal's side between the shoulder and the thigh. In this study, 22 such experiments totalling 146 burns were carried out on 14 animals. A small number of lesions were biopsied immediately or in the first few days after production, but in most cases the progress of the burns was followed by photography and clinical observation until healing occurred. All animals were kept in cages and allowed regular pig rations after recovery from anesthesia which lasted 18 to 24 hours. The burns were left exposed and no treatment was given.

Since physical calculations of atomic explosions indicated that most of the thermal energy was emitted in the first second after the explosion (11), it was decided to keep the time of exposure constant at one second in these experiments. Studies are now in progress on the effect of variation of the time of exposure.

Results: In the analysis of the threshold burns, an arbitrary system for grading the severity of the lesion was adopted. A 4+ burn was one showing some carbonization of the burned coagulum. A 3+ burn was one without carbonization but with coagulation covering the entire exposed surface. A 2+ burn showed patchy or central coagulation with underlying erythema. The 1+ burn was one without coagulation but showing an area of erythema at the end of 24 hours. 0 was used for an exposed area which had no obvious damage at 24 hours.

The 4+ burns showed an immediate area of brown carbonization of varying degree. Around the carbonization was an area of dead white coagulation surrounded by erythema. There was immediate contracture of the carbonized and coagulated area with resultant puckering of the surrounding unburned skin. During the healing phase, the carbonized area formed a firm, depressed eschar which remained intact until it was sloughed. The soft coagulum was occasionally scraped away by the pig to leave an open granulating surface. When the coagulum was undisturbed, its dead white color gradually turned to red brown and a firm encrustation developed. The entire eschar was slowly lifted up as re-epithelialization occurred beneath it and was gradually sloughed after two or three weeks, leaving a well-epithelialized surface which later showed regrowth of hair. Histological examination in the early post-burn period showed damage extending deep into or completely through the dermis of these lesions. Microscopically, there were frequently blebs present within the epidermis. Since these blebs did not contain fluid, they were thought to represent steam blisters formed during the burning.

The 3+ burns showed an immediate coagulation of the superficial tissues in the exposed areas, the opacity of the coagulum varying with the incident energy. Erythema appeared at the periphery of the coagulum in a few seconds

and gradually increased in intensity. The subsequent course of these lesions was much like that of the 4 + burn. An eschar formed over the entire burned area by the end of the first week, and after two or three weeks it separated from the newly epithelialized surface. After hair regrowth had occurred, it was difficult or impossible to distinguish the traumatized area from the surrounding unburned skin. The early histological picture showed injury extending through the epidermis and for varying distances into the dermis.

Severe 2+ burns differed from the 3+ lesions only in that the coagulum was confined to the center of the exposed area rather than covering it completely. In less severe 2+ burns, however, the animal's skin appeared undisturbed immediately after exposure. In 10 to 15 seconds, a general erythema began to develop in and around the exposed area. In two or three minutes, erythema was quite intense and did not blanch on external pressure. Small patches of opaque white coagulation could then be detected on the surface of the erythema. At 24 hours, central or patchy coagulation and persistent erythema were evident. These lesions gradually became darker in color and developed a small eschar towards the end of the first week. In most cases, the areas were completely re-epithelialized and showed no evidence of damage two weeks after burning. Early microscopic examination revealed some areas of trans-epidermal injury, but in other areas the injury was confined to the epidermis.

The 1+ lesions showed a transient blanch with the development of erythema becoming apparent in a varying period up to 20 seconds after exposure. Erythema rapidly became more intense and, after several minutes, assumed a faintly cyanotic hue. At this stage, these areas could not be completely blanched by external pressure. Gradually, edema developed beneath the erythema, but it regressed in a few hours. After a few hours, most of these lesions showed

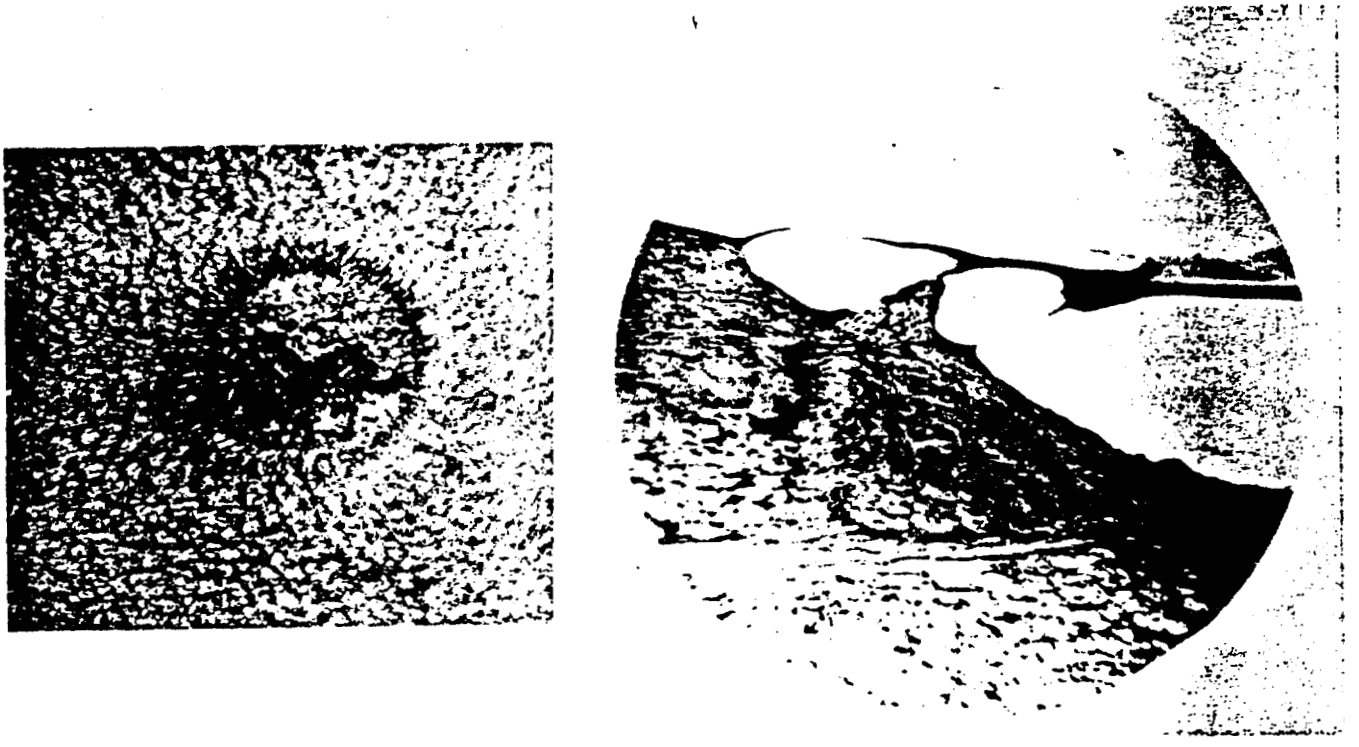


Figure 3. 4 + Burn: Photograph and photomicrograph.
Note unruptured steam bleb and destruction of dermis.

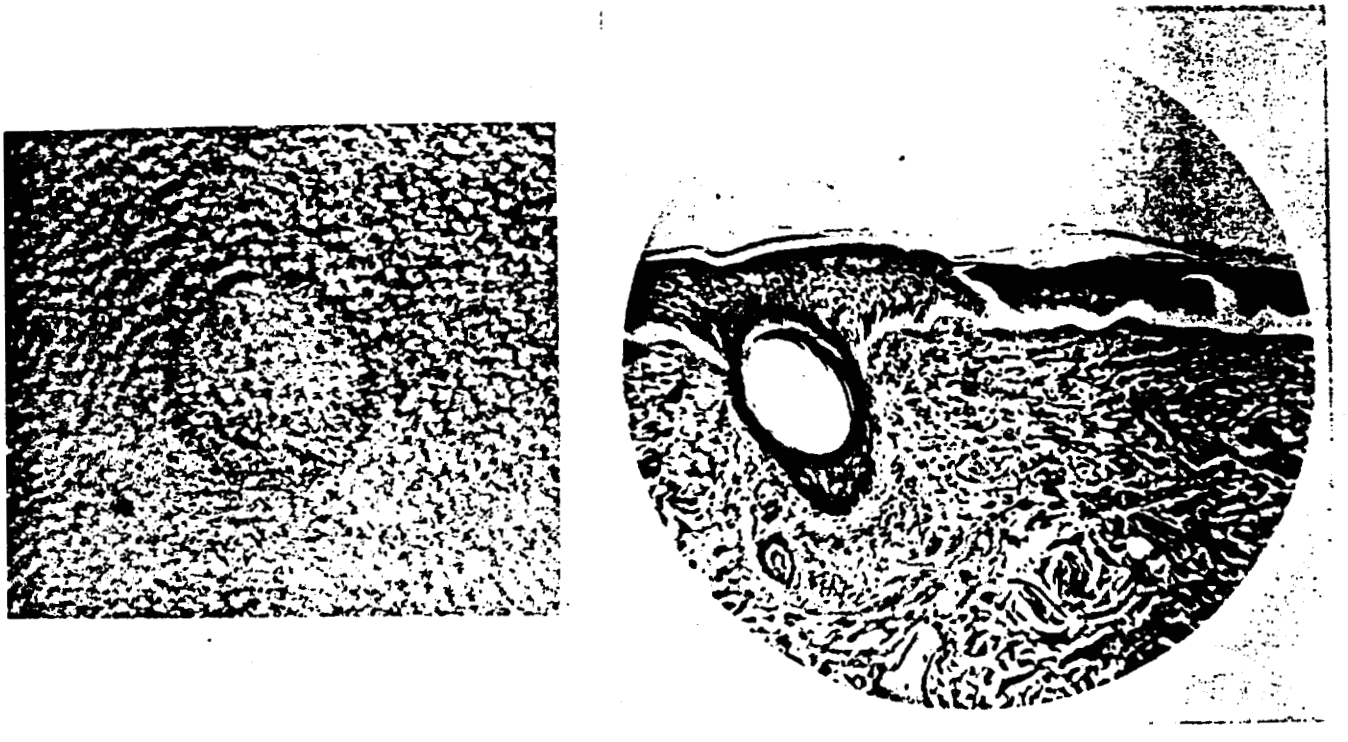


Figure 4. 3+ Burn: Photograph and photomicrograph.
Note total destruction of hair follicle and dermal-epidermal separation.

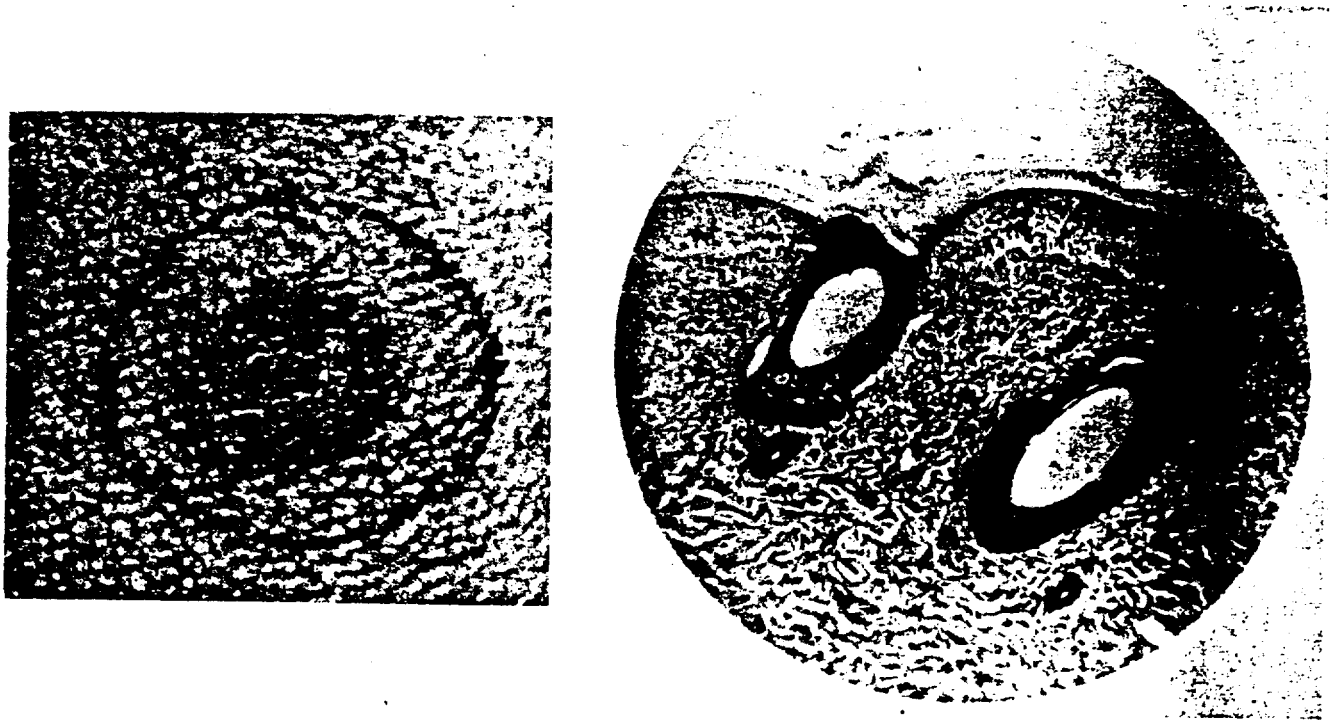


Figure 5. 2+ Burn: Photograph and photomicrograph.
Note demarcation of damage in hair follicles as well as complete destruction of the epidermis.

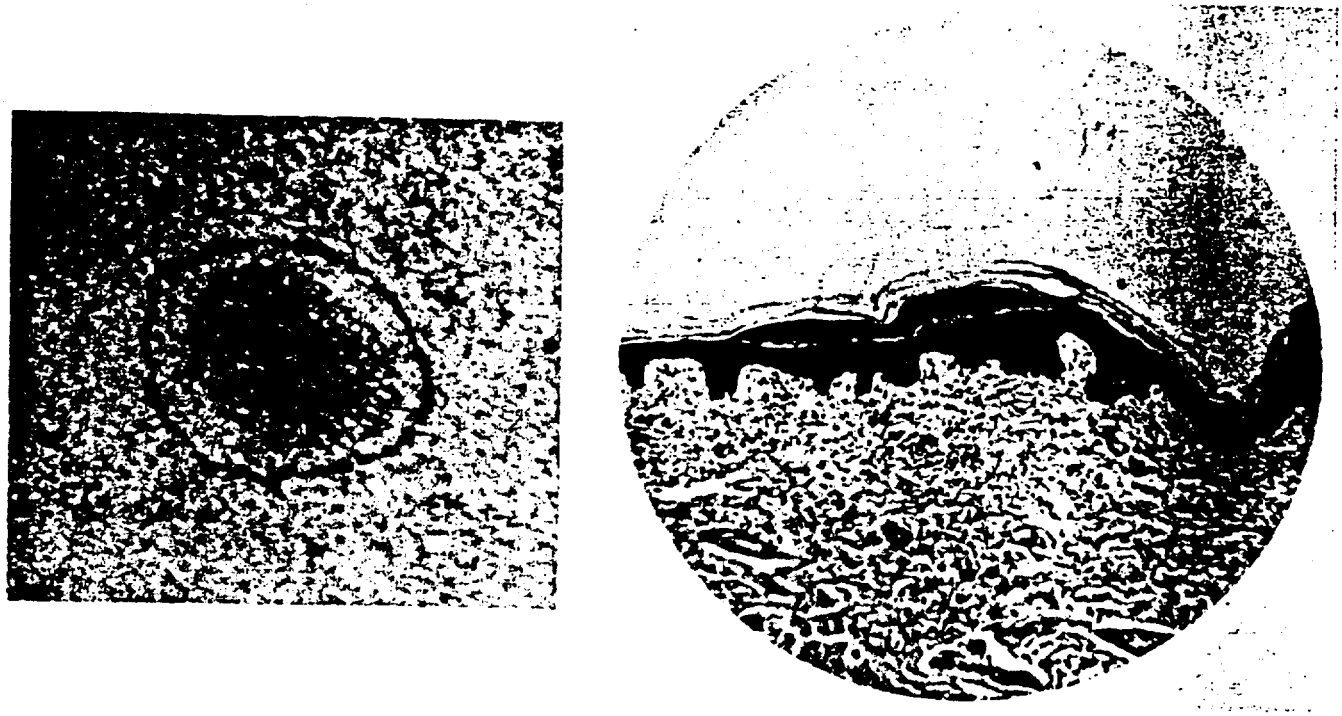


Figure 6. 1+ Burn: Photograph and photomicrograph.
Note level of destruction in superficial epidermis.

Table 1

Threshold Burn Data - Unprotected Skin
One-Second Exposure

Cal/cm^2	Total exposures at given intensity	4+	3+	2+	1+	0
34.0	5	5				
23.5	6	5	1			
22.0	8	7	1			
21.0	8	8				
19.5	8	2	6			
18.0	8		8			
16.5	8		8			
15.5	9	1	8			
14.0	4		4			
12.5	3		3			
11.0	4		4			
10.0	7		7			
8.5	6		5	1		
7.0	11		4	7		
5.5	14			12	2	
4.0	14				14	
3.0	13				9	4
1.5	10				3	7
TOTAL	146					

gradual diminution in the intensity of the erythema and some of them actually disappeared completely only to become apparent again before the end of the first 24 hours. Any lesion showing erythema at 24 hours was considered to represent a burn, and histological study showed damage to the epidermis extending, in some cases, to the basal layer. These lesions appeared erythematous for several days, but by the fourth or fifth day, they became brown in color. At this time, the pigmentation was confined to damaged epidermis which gradually developed a scaly appearance and separated from the underlying undamaged epithelium. Usually by the seventh to ninth day after exposure, all evidence of these burns had disappeared.

When the intensity of the incident energy was lowered further, it was possible to reach a level where the exposed skin showed an early mild erythema which rarely reached the intensity seen with the 1+ burn. This erythema could be blanched by external pressure and disappeared spontaneously in a few minutes or hours after the stimulus was applied. Subsequently, these areas showed no further local change grossly. Histological sections taken immediately after burning and at 24 hours showed no cellular damage. This was termed "0 response" in the classification of the data.

Figures 3-6 (Pages 58-9) show photographs of the gross and microscopic appearance of the various burns at 24 hours.

Using this classification, the burns produced in this study were graded on the day after their production, and the results are shown in Table 1 (Page 60). There was a certain degree of variation in the results which probably represented both biological variation in the animals and slight variation in the intensity of the arc. However, using a one second exposure, the following threshold values were usually found:

1.5	cal/cm^2	- 0 response
3.0	"	- 1+ burn
5.5	"	- 2+ burn
8.5	"	- 3+ burn
21.0	"	- 4+ burn

Discussion: The modification of the carbon arc used in these experiments proved to be a satisfactory instrument for the production of a graded series of high intensity, short duration burns. The results were reasonably consistent and the data provided a satisfactory base line for further work.

Gross examination of the lesions at 24 hours was found to be a reliable means of grading the burns. The results obtained correlated well with the histological picture and their subsequent clinical course. Moritz (6) did not find gross appearance to be a valid criterion for judging the severity of burns produced by exposure to hot water. In his experiments, both the temperature of the water and the duration of application were varied over a wide range. The fact that our studies covered a much narrower range of investigation may explain this difference.

These burns were carried out in white-skinned animals whose skin reflectance to radiant energy was comparatively high. No reflectance measurements were made, but it is probable that less intense incident energy would cause equally severe burns in animals with darker skin. With dark-skinned animals gross evaluation of the lesion by the grading system would be difficult or impossible.

Summary and Conclusions:

1. A modification of the carbon arc as a source for reproducible high intensity, short duration burns was described.

2. A series of small-area burns of graded severity was produced in the anesthetized Chester White pig.

3. The burns were graded from 0 to 4+ according to the criteria described.

4. Using a one second exposure throughout, it was found in most cases that 1.5 cal/cm^2 failed to produce a burn whereas 3 cal/cm^2 produced an erythema which was evident 24 hours after burning, 5.5 cal/cm^2 a burn with patchy coagulation, 8.5 cal/cm^2 a burn with complete surface coagulation, and 21 cal/cm^2 a lesion with superficial carbonization.

5. Histological study demonstrated that burns showing only erythema at 24 hours had injury confined to the epidermis. In burns with surface coagulation or carbonization, injury was trans-epidermal.

Bibliography

1. Blakney, R. M., Davis, T. P., Krolak, L. J., and Pearse, H. E. Development of a Copper Sphere Radiometer. Univ. of Rochester, Atomic Energy Project Report, UR-152, pg 76 (1951)

2. Kingsley, H. D., Hogg, L., Jr., Payne, J. T., and Morton, J. H. Studies in Prolonged Anesthesia in Swine and Dogs. Univ. of Rochester, Atomic Energy Project Report, UR-152, pg 65 (1951)

3. Kingsley, H. D., Hogg, L., Jr., Pearse, H. E., DeLalla, V., Blakney, R. M., and Davis, T. P. Biological Effects of External Radiation. Univ. of Rochester, Atomic Energy Project Report, UR-96, pg 35 (1949)

4. LeRoy, G. V. The Medical Sequelae of the Atomic Bomb Explosion. J. Am. M. Ass., 134:1143 (1947)

5. Moritz, A. R., and Henriques, F. C., Jr. Studies on Thermal Injury. II. The Relative Importance of Time and Surface Temperature in the Causation of Cutaneous Burns. Am. J. Path., 23:695 (1947)

6. Moritz, A. R. Studies on Thermal Injury. III. The Pathology and Pathogenesis of Cutaneous Burns, An Experimental Study. Am. J. Path., 23:915 (1947)

7. Payne, J. T., Hogg, L., Jr., and Pearse, H. E. The Experimental Study of Flash Burns. Univ. of Rochester, Atomic Energy Project Report, UR-79, pg 1 (1949)

8. Pearse, H. E., and Payne, J. T. Mechanical and Thermal Injury from the Atomic Bomb. N. England J. M., 241:647 (1949)

9. Pearse, H. E., Payne, J. T., and Hogg, L., Jr. The Experimental Study of Flash Burns. Ann. Surg., 130:774 (1949)

10. Saxl, N. T. Burns En Masse. U. S. Nav. Med. Bull., 40:570 (1942)

11. The Effects of Atomic Weapons. Secs. 6.6-6.7. Washington: U. S. Govt. Printing Off., (1950)

Program Code: I. R. BIOLOGICAL EFFECTS OF EXTERNAL RADIATION

Problem Code: I.R.1. (Flash Burns)

Section Code: 620

Authors: John H. Morton, M. D., Harry D. Kingsley, M.D., and Herman E. Pearse, M.D.

Studies on Flash Burns: The Protective Effects of Certain Fabrics.

Introduction: Clinical studies of flash burns emphasized that these burns were largely confined to exposed skin areas and that clothing afforded a high degree of protection against burning. In reporting the Pearl Harbor experience, Eckert and Mader (1) wrote: "Only exposed surfaces were burned; even an undershirt or shorts appeared sufficient to protect the areas covered from being burned." Reports from Hiroshima and Nagasaki indicated that, although most flash burns were confined to exposed areas, a few cases were seen in which burning occurred through one or more layers of clothing (5). It was also noted that dark clothing, which had a low radiant energy reflectance, afforded less protection than white clothing. Further clinical observations (4) indicated that clothing wet with perspiration and adherent to the skin might have been responsible for some of the burns on covered areas.

A more precise knowledge of the protection afforded by clothing was desirable. The present experiments were designed to study the skin burns produced by a brief exposure to high intensity radiant energy when the skin was covered by certain fabrics and fabric combinations. The changes in protection produced by dyeing and by moistening some of the fabrics were also tested.

Materials and Methods: This work was carried out using the carbon arc searchlight described in the threshold burn studies previously reported (3).

A similar group of Chester White pigs was used, and their pre-and post-burn treatment was identical in the two studies. In some cases the same animals were used in both experiments.

The fabric or combination to be tested was attached to the inner surface of the perforated transite shield and the animal positioned in gentle apposition to it. All experiments were done with a one second exposure and with variations in the incident energy so that the results would be directly comparable with those in the threshold studies on unprotected skin.

The fabrics studied were herringbone twill cotton, linen, water-repellent sateen, wool serge, silk and two batches of cotton undershirt fabric. Herringbone twill was a rough fabric of greenish-brown color. It had a relatively porous weave and showed moderate transmission of a flashlight beam when the light was held directly against the material. The linen had a rough texture, a slightly irregular surface and a light yellow color. Its weave was quite porous, and a flashlight beam was readily transmitted. Sateen was a greenish-

Light transmission was also measured using an Ansco-Sweet Densitometer. Densitometer readings for the materials were as follows:

	Dry	Wet
Herringbone Twill	2.65	2.72
Linen	0.95	
Sateen	>3.0	* >3.0
Serge	>3.0	>3.0
Silk	0.81	
Undershirt A	0.76	0.73
Undershirt B	0.79	
Undershirt A black	1.42	1.54

These measurements confirmed the visual impression gained with the flashlight beam.

The two undershirt materials were tested in combination with the other fabrics. In the cloth combinations, the two layers were placed together in front of the animal with the undershirt material against the pig's skin. Herringbone twill, sateen and serge were tested in combination with batch A, and silk and linen with batch B. In another study using batch B, the fabrics were reversed and herringbone twill was placed against the animal's skin with the undershirt material outside. Also, a series of experiments was done using two layers of undershirt material, batch B in front of the animal.

Herringbone twill, sateen, serge, batch A of undershirt material and black undershirt material were also tested after being moistened. The fabric was allowed to stand in tap water until thoroughly soaked. It was then removed from the water and any excess moisture removed by gentle blotting with a paper towel. The fabric was then placed in front of the animal and the exposure carried out immediately before further drying could occur. In several experiments normal saline was substituted for tap water without altering the results.

In these studies a series of five to ten burns was produced in each experiment. The total number of burns, experiments and animals used in each group is shown in Table 1 (Page 68).

*Note - 3.0 was the limit of the instrument used.

Table 1

Fabrics and Fabric Combinations Tested

Material	No. of Burns	No. of Experiments	No. of Animals
Herringbone twill	39	6	6
Sateen	47	7	6
Serge	61	9	7
Linen	47	6	4
Silk	47	6	5
Undershirt material, batch A	87	14	10
Undershirt material, batch A black	48	6	5
Undershirt material, batch B	30	4	4
Herringbone twill and undershirt material A	60	8	7
Sateen and undershirt material A	57	8	7
Serge and undershirt material A	63	8	6
Linen and undershirt material B	50	6	6
Silk and undershirt material B	48	6	5
Undershirt material B, two layers	46	6	6
Undershirt material B and herringbone twill	53	6	4
Herringbone twill wet	63	8	8
Sateen wet	62	8	8
Serge wet	58	10	9
Undershirt material A wet	43	6	6
Undershirt material A black wet	48	6	5
Total	1057	Total 144	Total 124

Results: The grading system described in the threshold studies (3) was also used in these experiments. A "0" response indicated no damage on gross examination at 24 hours. Erythema alone at 24 hours was labelled 1+. Burns with central or patchy surface coagulation were called 2+, and burns completely covered with coagulation were labelled 3+. In the threshold studies a 4+ burn showing carbonization was also recognized. In the present studies, however, no attempt was made to distinguish a 4+ from a 3+ lesion. When fabrics were charred through and adherent to the skin, it was difficult or impossible to know if the skin was carbonized. Also, with the darker fabrics dye transfer occurred at the higher intensities, giving a brown color to the coagulum in the absence of carbonization. Consequently, all burns greater than 2+ were termed 3+ in the present study. The grading system was not confirmed by biopsy studies in the burns behind fabrics. However, the clinical course of these lesions was observed and proved to be identical with lesions of similar grade on unprotected skin.

The results of these experiments are tabulated in Tables 2-21 (Pages 71-90). Effects noted on fabrics as well as on the skin are listed. As mentioned above, dye transfer to the animal's skin was regularly noted when the darker fabrics (herringbone twill, sateen, serge, undershirt material dyed black) were exposed to the higher intensities. However, dye transfer did not occur when these same materials were exposed while wet, but cutaneous damage occurred none the less. The results in all experiments were reasonably consistent except those obtained using herringbone twill and sateen with undershirt material. In both instances the amount of protection afforded was less in late experiments than in earlier ones. Apparently the fabrics themselves altered somewhat in the course of several months although there was no obvious change.

Figures 1-3 (Pages 92-3) and Table 22 (Page 91) show the caloric values necessary to produce a burn with surface coagulation and with erythema only at 24 hours when the skin was protected by the various fabrics and fabric combinations. Threshold values for unprotected skin are shown for comparison.

Table 2

Skin Covered by Herringbone Twill

Cal/cm^2	Effect on Fabric		Total exposures at given intensity	GRADE			
	Arc surface	Animal surface		3+	2+	1+	0
34	Flame; hole through cloth	--	3	3			
15.5	Fragile; charred through	--	1	1			
11	Moderate scorch	Slight stain	3	3			
10	Moderate scorch	0 or minimal stain	4	3	1		
8.5	Slight scorch	0	4	3	1		
7	Minimal scorch	0	6	1	4	1	
5.5	0	0	6		2	4	
4	0	0	6			1	5
3	0	0	4				4
1.5	0	0	2				2

Table 3

Skin Covered by Sateen

Cal/cm^2	Effect on Fabric: Arc surface	Animal surface	Total exposures at given intensity	GRADE 3+	2+	1+	0
34	Flame; hole through cloth	—	3	3			
15.5	Fragile; charred through	—	2	2			
11	Moderate scorch	Slight or minimal stain	4	4			
10	Moderate scorch	0 or minimal stain	6	6			
8.5	Slight scorch	0	5	4	1		
7	0 or slight scorch	0	7		6	1	
5.5	0 or slight scorch	0	7		2	4	1
4	0 or minimal scorch	0	7			4	3
3	0	0	4			1	3
1.5	0	0	2				2

Table 4

Skin Covered by Serge

Cal/cm^2	Effect on Fabric: Arc surface	Effect on Fabric: Animal surface	Total exposures at given intensity	GRADE 3+	GRADE 2+	GRADE 1+	GRADE 0
34	Flame; hole through cloth	---	6	6			
15.5	Marked char	0 or slight stain	6	6			
14	Marked char	0	3	3			
12.5	Marked char	0	3	3			
11	Marked char	0	7	4	3		
10	Marked char	0	9	3	5	1	
8.5	Moderate char	0	9		5	4	
7	Slight char	0	6		1	5	
5.5	Slight scorch	0	5			3	2
4	0	0	4			1	3
3	0	0	3				3

Table 5

Skin Covered by Linen

Cal/cm^2	Effect on Fabric: Arc surface	Animal surface	Total exposures at given intensity	GRADE 3+	2+	1+	0
34	Hole through cloth	—	1	1			
14	Moderate scorch	Slight stain	1	1			
12.5	Moderate or slight scorch	Minimal of slight stain	5	5			
11	Slight scorch	Minimal stain or 0	6	4	2		
10	0 or minimal scorch	0	6	1	5		
8.5	0	0	6		6		
7	0	0	6			6	
5.5	0	0	6			5	1
4	0	0	6				6
3	0	0	4				4

Table 6

Skin Covered by Silk

Cal/cm^2	Effect on Fabric		Total exposures at given intensity	GRADE			
	Arc surface	Animal surface		3+	2+	1+	0
34	Flame; hole through cloth	—	1	1			
15.5	Melted with small hole through cloth	—	1	1			
12.5	Slight scorch	Minimal stain	3	3			
11	0 or slight scorch	0 or minimal stain	6	5	1		
10	0 or minimal scorch	0 or minimal stain	6	1	4	1	
8.5	0 or minimal scorch	0	6	1	4	1	
7	0	0	6		2	4	
5.5	0	0	6			5	1
4	0	0	6				6
3	0	0	5				5
1.5	0	0	1				1

Table 7

Skin Covered by Undershirt Material, Batch A

Cal/cm^2	Effect on Fabric		Total exposures at given intensity	GRADE			
	Arc surface	Animal surface		3+	2+	1+	0
34	Flame; hole through cloth	—	4	4			
15.5	Slight scorch	0	3	3			
14	Slight scorch	0	1	1			
12.5	Minimal scorch	0	3	1	2		
11	0	0	11	3	8		
10	0	0	13	2	9	2	
8.5	0	0	13		4	9	
7	0	0	14			13	1
5.5	0	0	13			9	4
4	0	0	9			1	8
3	0	0	3				3

Table 8

Skin Covered by Undershirt Material, Batch A Dyed Black

Cal/cm^2	Effect on Fabric: Arc surface	Animal surface	Total Exposures at given intensity	GRADE 3+	2+	1+	0
11	Flame; hole through cloth	--	6	6			
10	Flame; fragile and charred through with dye removed	--	6	6			
8.5	Flame; fragile and charred through with dye removed	--	6	5	1		
7	Flame; fragile and charred through with dye removed	--	6	2	4		
5.5	Moderate scorch with dye removed	Slight dye removal or 0	6		6		
4	Slight scorch with dye removed	0 or minimal dye removal	6			6	
3	0	0	6			1	5
1.5	0	0	6				6

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Table 9

Skin Covered by Undershirt Material, Batch B

Cal/cm^2	Effect on Fabric		Total exposures at given intensity	GRADE			
	Arc surface	Animal surface		3+	2+	1+	0
14	Minimal scorch or 0	0	3	3			
12.5	0	0	3	3			
11	0	0	4	1	3		
10	0	0	4		3	1	
8.5	0	0	4			4	
7	0	0	4			4	
5.5	0	0	4				4
4	0	0	4				4

Table 10

Skin Covered by Herringbone Twill and Undershirt Material A

Cal/cm^2	Effect on Fabric: Arc surface	Effect on Fabric: Animal surface	Total exposures at given intensity	GRADE 3+	GRADE 2+	GRADE 1+	GRADE 0
34	Flame; charred through	—	4	4			
15.5	Marked char	Moderate stain	3	1	2		
14	Marked scorch	Moderate stain	7	5	2		
12.5	Marked scorch	Moderate stain	9	6	2	1	
11	Moderate scorch	Moderate or slight stain	7	3	3	1	
10	Moderate scorch	Slight stain	8	3	3	1	1
8.5	Slight scorch	Minimal or slight stain	7		4	1	2
7	Slight or minimal scorch	Minimal stain or 0	7			5	2
5.5	Minimal scorch	0	5			3	2
4	0	0	3				3

Table 11

Skin Covered by Sateen and Undershirt Material A

Cal/cm^2	Effect on Fabric		Total exposures at given intensity	GRADE			
	Arc surface	Animal surface		3+	2+	1+	0
34	Flame; hole through cloth	—	4	4			
15.5	Moderate char	Moderate stain	3		3		
14	Marked scorch	Moderate stain	8	5	2	1	
12.5	Moderate scorch	Moderate or slight stain	8	4	2	1	1
11	Moderate or slight scorch	Slight or minimal stain	8	4	1	2	1
10	Slight scorch	Minimal stain	6	4	1	1	
8.5	Slight or minimal scorch	Minimal stain	6		4	1	1
7	Minimal scorch	0	6			5	1
5.5	0	0	5			3	2
4	0	0	3				3

Table 12

Skin Covered by Serge and Undershirt Material A

Cal/cm^2	Effect on Fabric: Arc surface	Effect on Fabric: Animal surface	Total exposures at given intensity	GRADE 3+	GRADE 2+	GRADE 1+	GRADE 0
34	Flame; marked char	Slight or minimal stain	4		4		
15.5	Marked char	Slight or minimal stain	3		2	1	
14	Marked or moderate char	Minimal stain or 0	8	4	2	2	
12.5	Moderate char	0	8	3	2	3	
11	Moderate char	0	8		3	5	
10	Moderate char	0	8		3	5	
8.5	Moderate or slight char	0	10		1	9	
9	Slight char	0	8			4	4
5.5	Minimal scorch	0	5				5
4	0	0	1				1

Table 13

Skin Covered by Linen and Undershirt Material B

Cal/cm^2	Effect on Fabric		Total exposures at given intensity	GRADE			
	Arc surface	Animal surface		3+	2+	1+	0
34	Flame; incomplete hole through cloth	—	2	2			
15.5	Marked scorch	Slight stain	6	5	1		
14	Marked scorch	Minimal stain	6	4	2		
12.5	Moderate scorch	Minimal stain or 0	6	1	5		
11	Slight scorch	0	6		2	4	
10	Minimal scorch or 0	0	7			7	
8.5	0	0	6			1	5
7	0	0	6				6
5.5	0	0	6				6

Table 14

Skin Covered by Silk and Undershirt Material B

Cal/cm^2	Effect on Fabric		Total exposures at given intensity	GRADE			
	Arc surface	Animal surface		3+	2+	1+	0
34	Flame; hole through cloth	—	2	2			
15.5	Silk melted	Moderate or slight stain	6	5	1		
14	Center of silk melted	Slight stain	6	3	3		
12.5	Smaller area of silk melted	Slight stain or 0	6	2	3	1	
11	Slight scorch	0	6		1	5	
10	Minimal scorch	0	6			6	
8.5	0 or minimal scorch	0	6				6
7	0	0	6				6
5.5	0	0	4				4

Table 15

Skin Covered by Two Layers of Undershirt Material B

Cal/cm^2	Effect on Fabric		Total exposures at given intensity	GRADE			
	Arc surface	Animal surface		3+	2+	1+	0
34	Flame; hole through arc layer	Fragile; charred through	6	6			
15.5	Moderate scorch	0 or slight scorch	6	1	5		
14	0 or slight scorch	0	6		3	3	
12	0	0	6			5	1
11	0	0	6			4	2
10	0	0	6			2	4
8.5	0	0	6				6
7	0	0	4				4

Table 16

Skin Covered by Undershirt Material B and Herringbone Twill

Cal/cm^2	Effect on Fabric		Total exposures at given intensity	GRADE			
	Arc surface	Animal surface		3+	2+	1+	0
34	Flame; hole through arc layer	Fragile; charred through	5	5			
15.5	Moderate scorch	0	6	5	1		
14	Slight or minimal scorch	0	6	4	2		
12.5	0 or minimal scorch	0	6		6		
11	0	0	7		3	4	
10	0	0	6		1	5	
8.5	0	0	6			5	1
7	0	0	6			1	5
5.5	0	0	4				4
4	0	0	1				1

Table 17

Skin Covered by Herringbone Twill Wet

Cal/cm^2	Effect on Fabric: Arc surface	Effect on Fabric: Animal surface	Total exposures at given intensity	GRADE 3+	GRADE 2+	GRADE 1+	GRADE 0
11	0	0	8	8			
10	0	0	8	6	2		
8.5	0	0	8	5	1	2	
7	0	0	8	2	4	2	
5.5	0	0	8		2	6	
4	0	0	8		1	7	
3	0	0	8			2	6
1.5	0	0	7				7

Table 18

Skin Covered by Sateen Wet

Cal/cm^2	Effect on Fabric		Total exposures at given intensity	GRADE			
	Arc surface	Animal surface		3+	2+	1+	0
15.5	Moderate scorch	0	1		1		
11	0	0	8	7	1		
10	0	0	8	4	1	3	
8.5	0	0	8	3	2	3	
7	0	0	8		4	4	
5.5	0	0	8		1	7	
4	0	0	8			8	
3	0	0	8			1	7
1.5	0	0	5				5

Table 19

Skin Covered by Serge Wet

Cal/cm^2	Effect on Fabric		Total exposures at given intensity	GRADE			
	Arc surface	Animal surface		3+	2+	1+	0
34	Moderate scorch	0	2	2			
18	0	0	2	2			
16.5	0	0	4	4			
15.5	0	0	8	3	2	3	
14	0	0	1			1	
11	0	0	8			8	
10	0	0	8			5	3
8.5	0	0	8			2	6
7	0	0	8				8
5.5	0	0	6				6
4	0	0	3				3

Table 20

Skin Covered by Undershirt Material A Wet

Cal/cm^2	Effect on Fabric		Total exposures at given intensity	GRADE			
	Arc surface	Animal surface		3+	2+	1+	0
11	0	0	6	6			
10	0	0	6	4	2		
8.5	0	0	6		5	1	
7	0	0	6		1	5	
5.5	0	0	6			6	
4	0	0	6			1	5
3	0	0	6				6
1.5	0	0	1				1

Table 21

Skin Covered by Undershirt Material A Dyed Black, Wet

Cal/cm^2	Effect on Fabric		Total exposures at given intensity				
	Arc surface	Animal surface		3+	2+	1+	0
11	Minimal scorch	0	6	6			
10	0	0	6	6			
8.5	0	0	6	6			
7	0	0	6	4	2		
5.5	0	0	6	1	5		
4	0	0	6		1	5	
3	0	0	6			4	2
1.5	0	0	6				6

Table 22

Threshold Levels and Amount of Protection From Various Fabrics and Fabric Combinations

Fabric	Threshold Cal/cm^2 Needed to Produce: 1+ burn	2+ burn	Calories of Protection Compared to Unprotected Skin 1+ burn	2+ burn
Unprotected skin	3	5.5	--	--
Herringbone twill	5.5	7	2.5	1.5
Sateen	4.5	7	1.5	1.5
Serge	6	9	3	3.5
Linen	5.5	8.5	2.5	3
Silk	5.5	8.5	2.5	3
Undershirt material, batch A	5.5	9.5	2.5	4
Undershirt material, batch A black	4	5.5	1	0
Undershirt material, batch B	7	10	4	4.5
Herringbone twill and undershirt material A	6	8.5	3	3
Sateen and undershirt material A	6	8.5	3	3
Serge and undershirt material A	7.5	11	4.5	5.5
Linen and undershirt material B	10	12	7	6.5
Silk and undershirt material B	10	12.5	7	7
Undershirt material B, two layers	11	14.5	8	9
Undershirt material B and herringbone twill	8.5	11.5	5.5	6
Herringbone twill wet	3.5	7	0.5	1.5
Sateen wet	4	7.5	1	2
Serge wet	9.5	15.5	6.5	10
Undershirt material A, wet	5.5	8.5	2.5	3
Undershirt material A, black wet	3.5	5.5	0.5	0

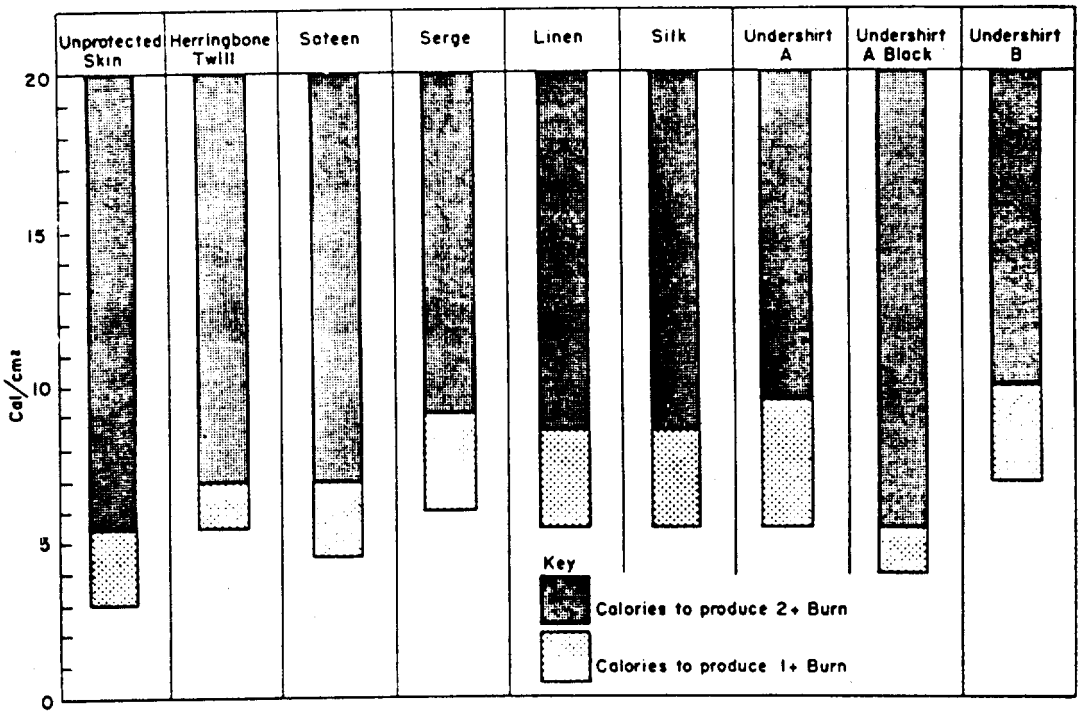


Figure 1. The lower end of the left hand cross hatched block gives the threshold for 1+ burn on unprotected skin. The upper end of this block shows the level at which the burn has increased in severity to 2+. Burns of greater degree lie above the top of the diagram. The other blocks in the figure show the raising of these thresholds by the protective action of the designated materials.

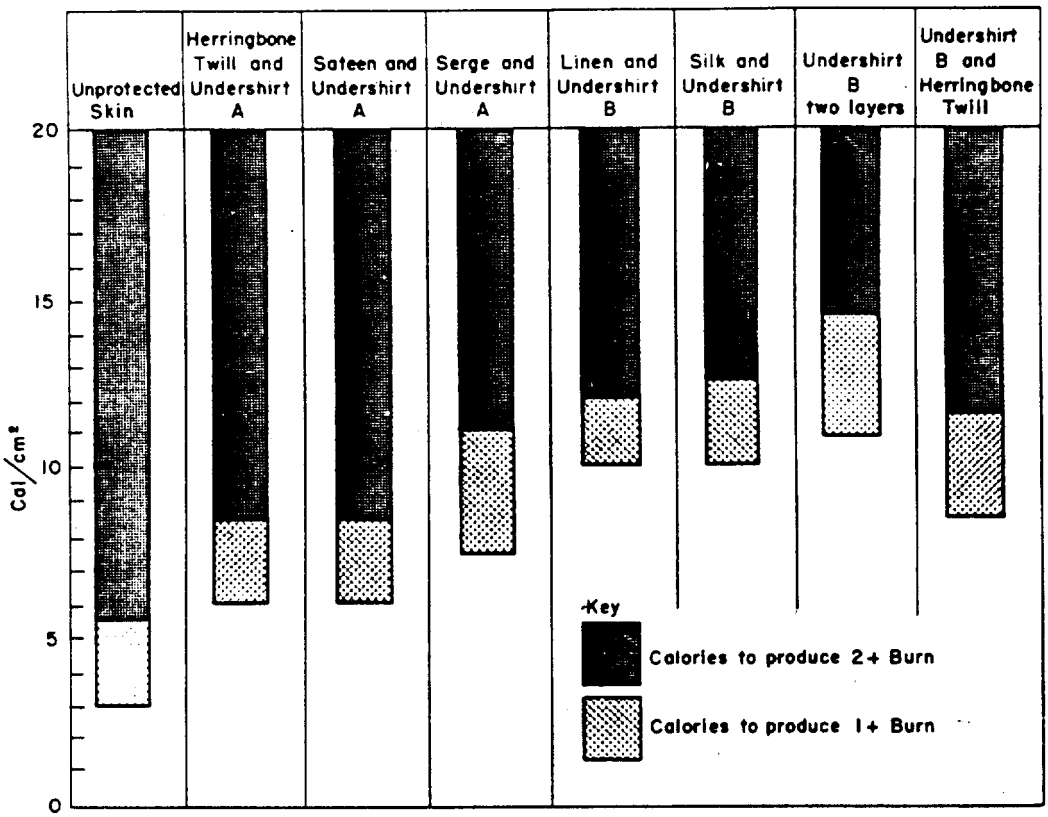


Figure 2. See legend to Figure 1.

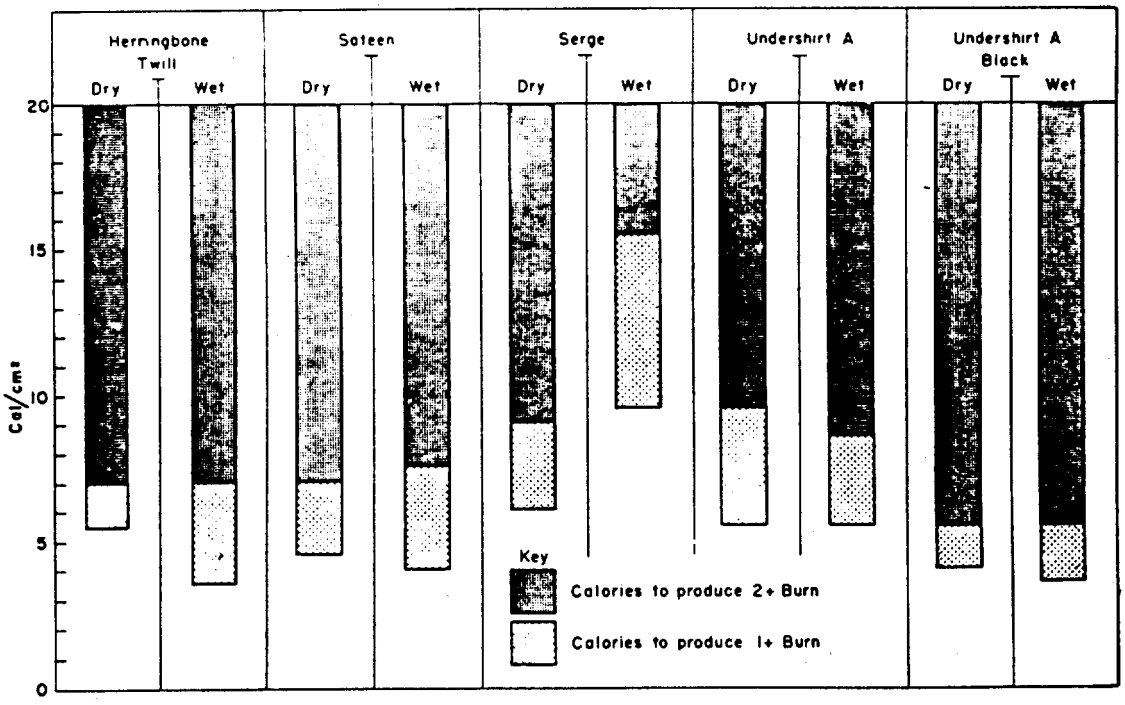


Figure 3. See legend to Figure 1.

Discussion: The caloric values listed in the tables indicate the energy incident on the surface of the fabric. Using these values, a direct comparison can be made between burns behind fabric and burns on unprotected skin. No measurements were made of the calories transmitted through the fabrics to the skin. These figures are of interest and will be measured in future studies.

It was discovered that the effects of the radiant energy on fabrics were not a good indication of what was happening to the skin behind them. In every experiment there were skin burns produced when there was no obvious damage on the surface of the fabric next to the animal's skin. In many cases severe burns with skin coagulation occurred although no damage was visible on either surface of the cloth.

The studies with white and black undershirt material afforded a demonstration of the importance of absorption of radiant energy by dark objects. The white fabric gave about 1.5 cal/cm^2 more protection from erythema and 4 cal/cm^2 from coagulation than did the same cloth dyed black.

During the course of these studies, two lots of undershirt material were used. They were the same material obtained from the same source and the two lots were identical in appearance. However, there was a consistent difference in the degree of protection afforded, batch B giving greater protection than batch A. The reason for this difference was not apparent but was borne out by simultaneous experiments using the two materials on the same animal.

When two layers of cloth were used, the protection afforded (cf Table 22, Page 91) was not necessarily additive. In this respect there was a difference between dark and light fabrics in combination with the undershirt

material. Using linen or silk in combination or two layers of undershirt material, the experimental results were in close agreement with those predicted by adding the amount of protection afforded by each of the two layers. When herringbone twill, sateen or serge was used in front of undershirt material, however, the protection afforded was less than the predicted values in each case. Actually, the combination with either herringbone twill or sateen afforded less protection from coagulation than did a single layer of undershirt material alone. In the reversed experiment, however, when undershirt material was placed in front of herringbone twill, exactly additive protection was found. It would seem that when a dark fabric was exposed to radiant energy, a significant amount of absorption and re-radiation or conduction of heat through the undershirt material to the skin occurred. With the lighter colored fabrics, absorption of energy was less marked and the second layer did afford additive protection.

The studies with wet fabrics showed considerable variation which depended to some extent upon the amount of moisture absorbed by the material. Serge had the greatest water-absorbing capacity of the materials tested and was considerably more protective wet than dry. The other fabrics absorbed a smaller amount of moisture and results differed little between the wet and dry state. Herringbone twill and undershirt material were somewhat less protective wet than dry. Both of these fabrics were darker in color in the wet state and this fact may have been responsible for the decreased protection.

In these experiments all fabrics were positioned in immediate apposition with the animal's skin. It was recognized that such close positioning was a somewhat artificial condition which occurred infrequently with actual clothing. In future studies, the fabrics will be studied when positioned at

varying distances from the animal.

In analyzing the different degrees of protection given by the various fabrics, it seemed that the color was of greater importance than its weave, weight or light transmission. Serge, the heaviest material tested, was the only one of the darker materials affording as much protection from coagulation as the lighter colored fabrics. Sateen, the material with the lowest light transmission, gave very little protection.

Moritz and Henriques (2) concluded from their studies that when animals were exposed to flame temperatures over 1000°C, "the interposition of anything capable of impeding heat transfer to the skin may be sufficient to make the difference between burning and absence thereof". In the present study, all materials afforded some protection to the skin but the degree of protection was not marked in many instances. Apparently thermal radiation is so intense that greater impedence of heat transfer is needed to prevent skin damage.

Summary and Conclusions:

1. Studies of the effects of various fabrics and fabric combinations in protecting the skin of the anesthetized Chester White pig from flash burning were carried out.

2. The effects of changing the color and moistening certain of the fabrics were tested.

3. All fabrics afforded some protection but there was considerable variation in the extent of protection with different materials.

4. It seemed that the color of a fabric was the single most important quality in determining the amount of skin protection. Light-colored fabrics were more protective than darker ones.

5. The effect on the fabric itself was not a good indication of the

changes in the animal's skin. In all experiments, burns occurred when there was no apparent damage to the surface of the material touching the animal.

Bibliography

1. Eckert, G. A., and Mader, J. W. The"Solace" in Action. U. S. Nav. Med. Bull., 40:552 (1942)

2. Moritz, A. R., and Henriques, F. C., Jr. Studies on Thermal Injuries. II. The Relative Importance of Time and Surface Temperature in the Causation of Cutaneous Burns. Am. J. Path., 23:695 (1947)

3. Morton, J. H., Kingsley, H. D., and Pearse, H. E. Studies on Flash Burns: Threshold Burns. Univ. of Rochester, Atomic Energy Project Report, UR-174, pg (1951)

4. Pearse, H. E., and Payne, J. T. Mechanical and Thermal Injury from the Atomic Bomb. N. England J. M., 241:647 (1949)

5. The Effects of Atomic Weapons. Sec. 6.55. Washington: U. S. Govt. Printing Off., (1950)

Program Code: I. R. BIOLOGICAL EFFECTS OF EXTERNAL RADIATION

Problem Code: I.R.1. (Flash Burns)

Section Code: 620

Authors: Daniel B. Williams, Capt., USAF and Charles H. Murden, Lt. Col., USAF

Biochemical Studies on the Flash Burn: A Device for the Removal of Uniform Samples of Skin in the Frozen State.

Introduction: Since 1947 this laboratory was concerned with the characterization of flash burn trauma. Large and small area burns were produced on experimental animals using both high and low temperature sources as previously reported (1,2). All of these burns were evaluated by clinical and histological observations. The systemic effects of large area burns were subsequently investigated by a study of the chemical and physical changes occurring in the blood of experimental animals during the post-burn period (2).

A search of the literature revealed a lack of information concerning the fundamental biochemical changes occuring at the site of the burn lesion itself. Consistent with the development of rational burn therapy, it was important that information of this nature be obtained.

In a study of the biochemistry of the flash burn tissue, the problem was encountered of obtaining proper skin samples for analysis. In this case, the sampling of a heterogeneous portion of a living animal became a problem.

As in most analytical procedures, the technique of sampling had to be carefully developed in order that the analytical results were representative of the system concerned. Consideration of the factors involved indicated that the sampling procedure should satisfy a number of requirements. Comparative samples should be uniform in size and should be taken from corresponding areas of skin. During excision, there should be no transfer of fluid between the

sample and the surrounding tissue. Moreover, the components of the excised section should be unaltered physically or chemically by the sampling process.

With the above considerations in mind, the sampling device described was constructed and tested. It was used successfully for four months and appeared to meet all of the necessary requirements.

Methods and Materials: The sampling device as shown in Figure 1 (Page 100) was essentially a section of high grade carbon steel pipe sharpened on one end to an extremely sharp cutting edge. Serrations filed into the edge of the blade enhanced its cutting action. The brass handle in the opposite end of the device provided additional leverage, thus insuring easier rotation of the cutting edge against the skin surface. The depth of the incision made by the instrument was regulated by the position of the external collar which served as a "stop" against the animal tissue.

Prior to removing the sample of skin, the site of the excision was prepared by clipping the hair as closely as possible. The instrument was placed in position perpendicular to the skin surface making certain that the cutting edge was in firm contact with the skin. By rotating the cylinder under sufficient pressure, the cutting edge made a circular incision to a depth limited by the prior adjustment of the external sleeve.

Simultaneous with the rotation of the instrument, liquid nitrogen (-146°C) was poured into the top of the cutting device. Thus, the sample was frozen as the cutting proceeded. Asbestos gloves were worn by the operator for protection against cold injury. The sample was then excised and stored in the quick-freeze unit.

Upon reaching equilibrium temperature (-4°C), the thickness of the sample was reduced to 3 mm. by means of a simple microtome. The skin section was placed

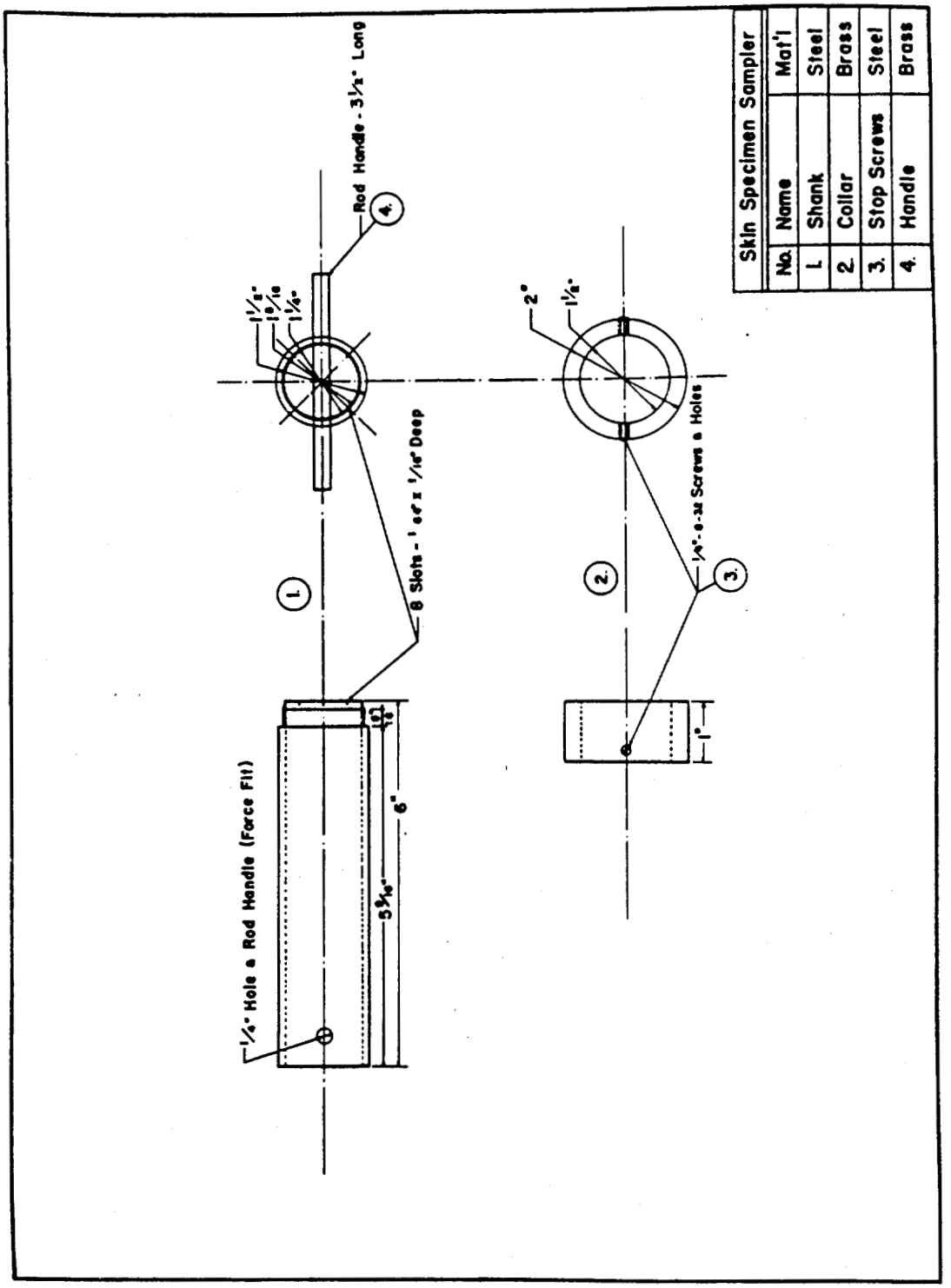


Figure 1.

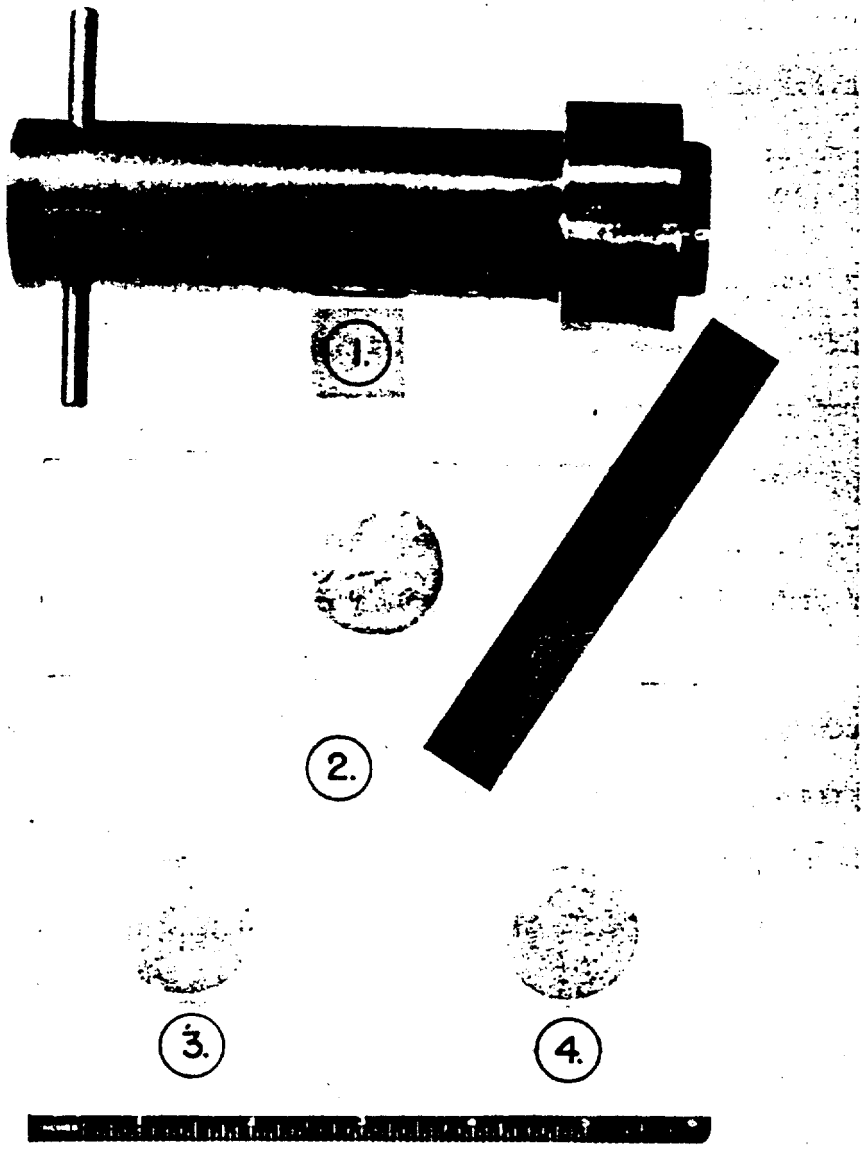
upside down in a plastic receptacle having the same dimensions as the sample except that it was only 3 mm in depth. The excess fatty tissue was removed by means of a long microtome blade using the top edges of the receptacle as a guide. All of the above was performed rapidly in order to avoid thawing of the sample. The sample was then stored in the quick-freeze unit until subsequent preparation for analysis.

The physiological structure and reaction of pig skin was reported by Moritz and Henriques (3) as being similar to that of the human. Consequently, young Chester White pigs averaging about 20 kg. were chosen as experimental animals in the burn study.

Results: Figure 2 (Page 102) shows 1) the sampling device 2) the sample in the tissue-slicing device prior to reducing its thickness to 3 mm and 3 & 4) finished samples of normal and burned pig skin respectively. The average sample weight obtained by this procedure was 2.9 grams ±4%.

Discussion: It was found that approximately 100 ml. of liquid nitrogen was sufficient to freeze a circular section of pig skin measuring about 2 inches in diameter by 0.5 inches in thickness. This included a frozen peripheral area around the excised sample. In actual practice, it was this outer frozen area which made it possible to excise the sample without any fluid exchange between the sample and the surrounding tissue.

Irreversible protein coagulation did not appear to occur during the sampling process. Samples were stored in the deep-freeze unit for several months with no apparent change. There was, however, the possibility that the freezing process during incision was not quick enough to prevent the formation of histamine as occurs in other forms of trauma.



1. Skin Specimen Sampler
2. Normal Skin Sample prior to trimming
3. Finished Normal Skin Sample
4. Finished Burned Skin Sample

Figure 2.

In the application of this skin sampling technique to other experimental animals, both the instrument and procedure necessarily would be modified depending upon the species of animal and the thickness of its skin.

Summary and Conclusions:

1. A device designed and constructed for the removal of uniform samples of animal skin has been described.

2. The procedure used in connection with the sampling device appeared to produce a skin sample in which there was a minimal alteration of its chemical and physical structure.

3. Such a device and procedure is valuable in investigating the chemical constitution of animal skin.

Bibliography

1. Kingsley, H. D., Hogg, L., Jr., Pearse, H. E., DeLalla, V., Blakney, R. M., and Davis, T. P. Biological Effects of External Radiation. University of Rochester Atomic Energy Project Report, UR-96, pg 35 (1949)

2. Payne, J. T., Kingsley, H. D., Morton, J. H., and Pearse, H. E. Comparative Effects of Large Area High and Low Temperature Burns. University of Rochester Atomic Energy Project Report, UR-175 (1951), to be published.

3. Moritz, A. R., and Henriques, F. C., Jr. Studies on Thermal Injury. II. The Relative Importance of Time and Surface Temperature in Causation of Cutaneous Burns. Am. J. Path., 23:695 (1947)

Program Code: Be. (BERYLLIUM)

Problem Code: Be.3 (Toxic Limits)

Section Code: 410

Authors: L. J. Leach, S. Laskin, and K. E. Lauterbach

Experimental Production and Studies of a Beryllium Oxide Fume.

In an attempt to define the etiology of beryllium poisoning, numerous exposures of animals to various compounds of beryllium have been conducted. Among the materials investigated were dusts and mists of the sulfate, the fluoride, and various industrial grades of the oxide. The results from these studies appear to have fairly well defined the acute phase of the disease, and have been described in previous publications and quarterly reports of the Industrial Hygiene Section.

The implication of beryllium oxide, probably of small particle size, in the chronic human exposures (1) has stimulated work in the direction of trying to develope similar symptoms with this material in laboratory animals. The purpose of this report is to present a method for the production of a beryllium oxide fume from metallic beryllium, to discuss an animal exposure unit designed specifically for experimentation with highly toxic dusts and fumes, and to report the results of a preliminary short-term inhalation study with a limited number of animals.

Fume Feed and Exposure Unit: Prior to the present studies, numerous attempts at the continuous production of fumes from beryllium metal or its compounds were unsuccessful because of complex practical or contaminant difficulties. The most successful method found to date simply consists of a beryllium metal arc burning in an oxygen-argon atmosphere. This method

is based on previous work done with uranium metal fumes (2). The apparatus illustrated in Figure 1 (page 112) represents the fume feed in its present stage of development.

The arc is formed between two beryllium metal electrodes held in position by brass supports. An electric motor, with a Graham variable speed transmission, coupled to the upper electrode is used to maintain a proper arc-gap. Power is supplied to the arc by a 220 volt A.C. line passing through a water-cooled resistor. A current of 12 amperes and an arcing distance of 1/4 inch results in a steady arc which can be maintained for several hours with only minor adjustments.

Since it was anticipated that the extremely small particle size of the beryllium fume, and its comparatively large surface area, might enhance the toxicity of the compound, extensive safety precautions were exercised in these studies to protect the personnel. The animals were housed within the exposure unit for the duration of the experiment. A "dry" box was provided for the isolation of the animals during washing and maintainence of the chamber. Figure 2a (page 113) shows the position of the dry box with respect to the exposure chamber. Standard arm-length veterinarian gloves, attached to ports in the chamber door, were used by the operator to shuttle the animals from "dry" box to chamber. Strategically placed water jets in the chamber's 3 inch drain line provided an excellent means for carrying of animal wastes. All other necessary precautions were observed to prevent contamination of the chamber area and personnel.

The inhalation chamber was designed and constructed of plywood with an internal volume of approximately 700 liters. (See Figure 2b, page 114)..

To facilitate streamed-lined air flow, and uniform distribution of contaminant, the chamber was basically cubical in shape, with pyramidal top and bottom. All internal corners were filleted and smooth. A negative pressure of 0.05 inches of water was maintained within the chamber, with an air flow of 6 cubic feet per minute, as measured by a venturi meter.

Operation of the Fume Feed: For operation, the flask was evacuated with a Welch Duoseal pump, flushed with argon and re-evacuated. This process was repeated several times to eliminate traces of moisture and residual air*. The flask was then filled with argon and the arc struck. A continuous flow of 5 liters of argon per minute was established through the flask. To insure controlled oxidation of the material given off by the arc, oxygen at the rate of 150 cc per minute was also metered into the flask.

Physical Properties and Particle Size Data: In order to characterize the fume produced, electron micrographs were made from samples taken by means of a thermal precipitator. The material illustrated in Figure 3 (page 115) was photographed at an initial magnification of 10,100 times. The fume consists of extremely small unit particles approaching the resolution limits of the photograph (0.01 microns). Crystal structure seems to be that of the hexagonal system. The fume exhibits a marked tendency to form irregular branched chains or agglomerates ranging from 0.5 to several microns in length.

A sample was also obtained with an electrostatic precipitator for x-ray diffraction studies and surface area determinations. The diffraction patterns for the sample were obtained with copper radiation, filtered by nickel foil.

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* The elimination of water vapor and residual air prevents the formation of hydroxides, nitrides, carbides, etc. which may be formed under the arcing conditions.

A Straumanis-type powder camera with a diameter of 114.7 mm was used. The sample was mounted in a small, thin-walled cellulose acetate tube. The diffraction pattern of the beryllium fume sample was mostly due to beryllium oxide, although the interplanar spacings correspond to a unit cell which is slightly contracted along the a axis and slightly expanded along the c axis with respect to the pattern in the A.S.T.M. files of powder data. This might be caused by substitution of F, or OH for part of the oxygen.

To verify the presence of fluorine in the beryllium oxide fume, a determination was made by the Willard-Winter distillation and thorium titration procedure, as used in these laboratories. A 10 mg sample contained 0.05% fluorine. Further purity studies by spectrographic analysis are now in progress.

Animal Exposure Study: The above results in producing a beryllium oxide fume were sufficiently encouraging to attempt a pilot animal-exposure study. The purpose of this preliminary study was to demonstrate the significant entrance of beryllium fume into the respiratory system, its distribution within the body, and whether or not acute effects might complicate extended chronic exposures. The exposure consisted of approximately four hours each day, for five days per week. A mean concentration of 0.2 mg Be/m^3 was maintained for 47 hours over a period of three weeks. A typical concentration study for a four hour exposure is shown in Figure 4 (page 116). The mean concentration for this specific exposure day was 0.35 mg Be/m^3, with extreme variations from 0.06 to 0.90 mg Be/m^3.

Six albino rabbits were used for this study. The animals were all young males weighing between four and six pounds. Four controls were also selected on the same weight, sex, and age basis. Three of the exposed

animals were sacrificed five days after termination of exposure. The remaining three were kept for future examination. Initial and terminal weight and hematologic data were obtained on each of the animals. Upon sacrifice, sections of lung, liver, kidney, and pulmonary lymph node were taken for micropathology and spectrographic analysis. Bone sections were also taken for chemical analysis.

Results of Animal Exposure: The animal weight data showed no definite trend. Hematologic data consisted of red blood cell counts, mean corpuscular volume, and hemoglobin content. The only significant finding in this study was a moderate increase in mean corpuscular volume for each of the exposed animals. Concentration of beryllium in the tissues and bone was determined by spectrographic analysis. The results are shown in Table 1.

TABLE 1

BERYLLIUM CONCENTRATION OF TISSUE AND BONE SECTIONS TAKEN FROM THREE RABBITS EXPOSED TO A BERYLLIUM OXIDE FUME

(Micrograms of Beryllium per Gram of Tissue)

Animal Number	Lung	PLN*	Kidney	Liver	Femur
	μg of Beryllium per Gram of Tissue				
007	4.08	0.000	0.001	0.000	0.003
020	2.26	0.000	0.001	0.000	0.003
005	5.00	0.000	0.001	0.000	0.004

The following is a pathology report by Dr. James K. Scott on three rabbits sacrificed after exposure: "Gross findings: Animal No. 5 showed moderate emphysema of the lungs. Rabbit No. 20 showed an abscess

* Pulmonary lymph nodes.

in the left lung with enlarged pulmonary lymph node at the hilum of this lung. No changes were seen grossly in the lungs of rabbit No. 7.

Microscopic findings: The emphysema of animal No. 5 was observed microscopically; it was fairly diffuse but none of the blebs were large. The abscess of rabbit No. 20 was a chronic abscess with central necrosis of pulmonary tissue and exudate. The exudate was composed of polymorphs and monocytes. No change was seen in the lung of animal No. 7. The liver and kidneys were also sectioned and no changes were observed in these organs.

The abscess involving one lobe of rabbit No. 20 was of the structure and inflammatory reaction frequently observed in control rabbits; therefore, without further supportive evidence, it cannot be attributed to inhalation of beryllium fumes. The emphysema observed in rabbit No. 5 could possibly be caused by the fume inhalation; however, its presence in the lung of only one of the three rabbits makes it doubtful. The absence of lesions in the kidney and liver would indicate that the amount of beryllium absorbed was insufficient to produce necrotic changes in the cells of these organs".

Discussion of Results: The distribution studies for the 47 hour animal exposure to a beryllium oxide fume showed reasonable amounts of the material deposited and retained in the lung. Although the increased mean corpuscular volume in all exposed animals indicates a tendency toward minimal acute damage, the pathology findings in these limited experiments are perhaps indicative but cannot be considered as other than questionable trace damage. The findings of a quantity of beryllium deposited in the femur and none in the pulmonary lymph node appears to suggest that removal of the deposited material from the lungs is by solubility rather than phagocytosis. It is of interest to note that in agreement with lack of changes found in

pathological examination of the liver and kidney, no beryllium was found in the liver upon spectrographic analysis, and only trace quantities in the kidneys.

Summary: The implication of beryllium oxides in the chronic human exposures has stimulated studies in these directions. This preliminary report describes a successful method of a continuous production of beryllium oxide fumes from metallic beryllium. Characterization of the fume is made in terms of electronmicrographs, spectrographic, and x-ray diffraction analyses. Utilizing the method as a fume feed specialized small scale animal inhalation exposure equipment was also developed. Preliminary to chronic exposures, a 3-week acute study was made with male albino rabbits at a level of 0.2 mg Be/m^3. Distribution studies showed reasonable amounts of the material deposited and retained in the lung. Small quantities in the femur and only trace quantities in the kidney. No beryllium was found in the liver. Hematologic and pathological data indicate no or trace acute damage at this level of concentration.

Acknowledgment

The authors acknowledge with appreciation the contributions of the following individuals who have assisted in this study.

Robert H. Wilson	Engineering consultation
Dr. L. T. Steadman A. Levi	Spectrographic analysis
Dr. J. K. Scott and staff	Pathology
M. Watson and staff	Electron microscopy
K. Stroud H. Church	Hematology
Dr. F. A. Smith D. A. Gardner	Fluorine analysis
Dr. J. A. Leermakers Dr. Griffith, Eastman Kodak Co.	X-ray diffraction studies

Bibliography

1. Eisenbud, M., and others, J. Indust. Hyg. and Toxicol., 31, 282 (1949)
2. Laskin, S., Leach, L., and Wilson, R. H., UR-116 Quarterly Technical Report, Jan. - March, 1950

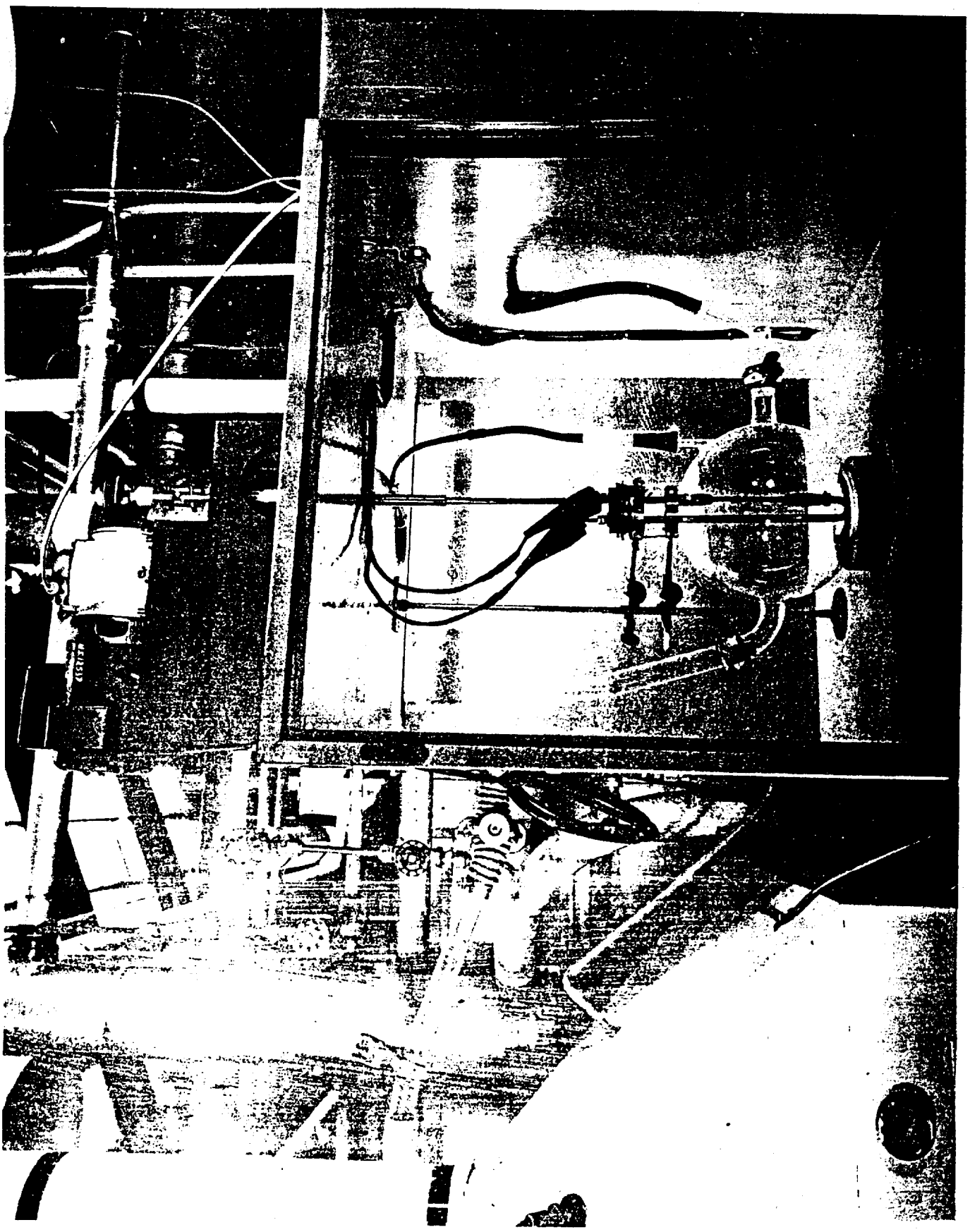


Figure 1. Fume Feed in Present Stage of Development.

1131931

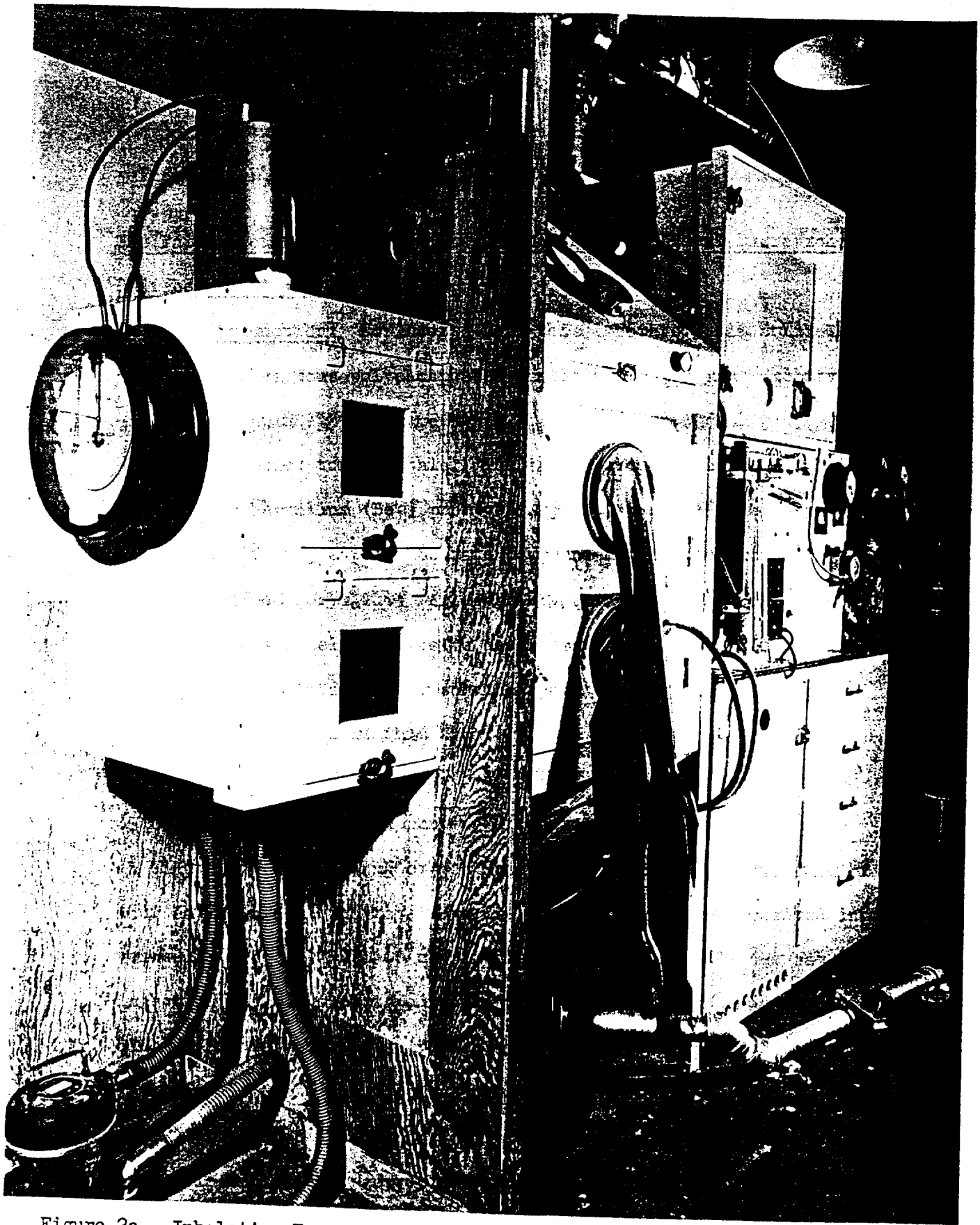


Figure 2a. Inhalation Exposure Unit Showing Application of Dry Box Techniques to Exposure Chamber.

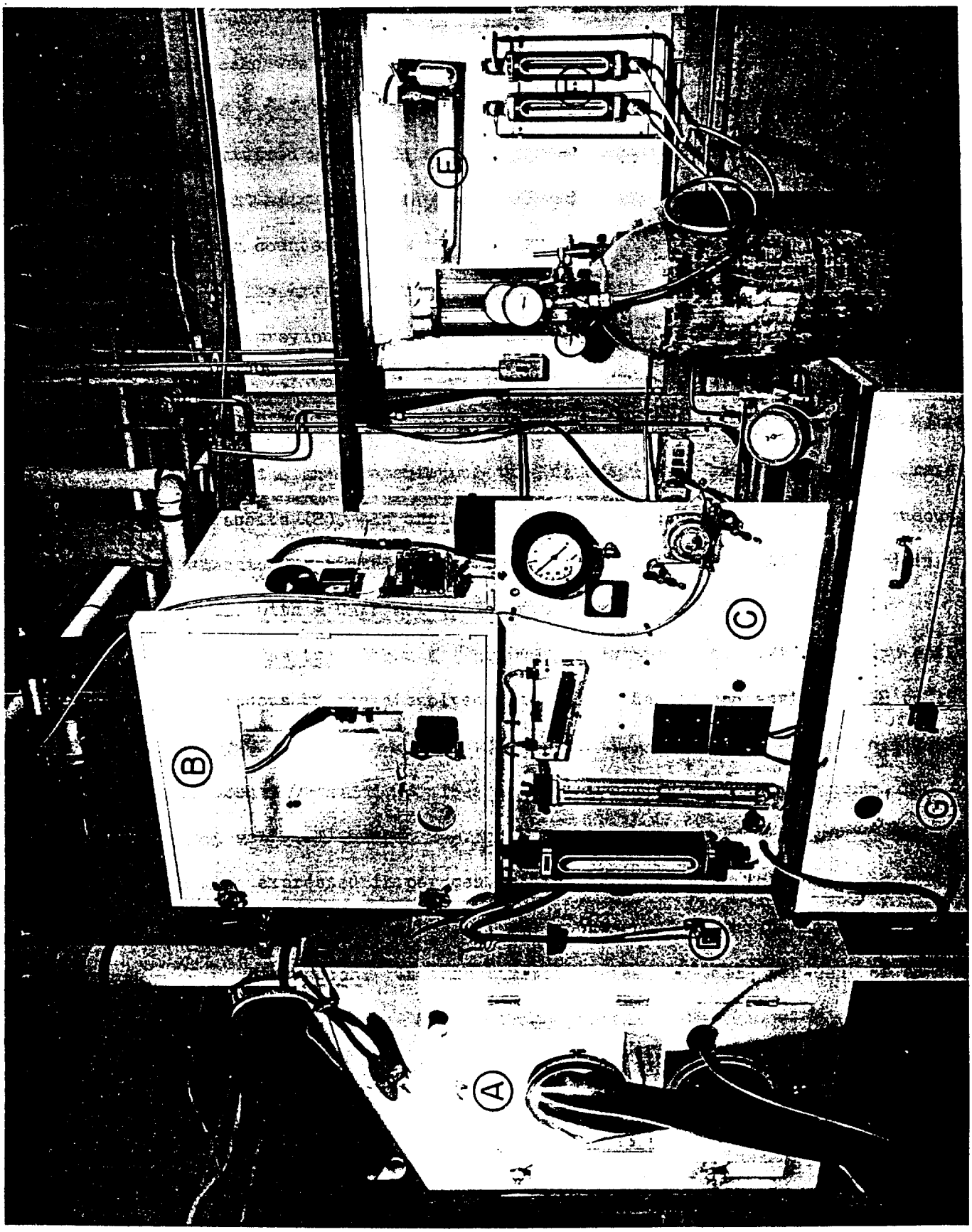


Figure 2b. Inhalation Exposure Unit Showing Position of (A) Exposure Chamber (B) Fume Feed Hood (C) Chamber and Feed Control Panel Board (D) Filter Paper Sampler (E) Inclined Manometer for Venturi Meter (F) Argon and Oxygen Flow Meters (G) Vacuum Pump Compartment

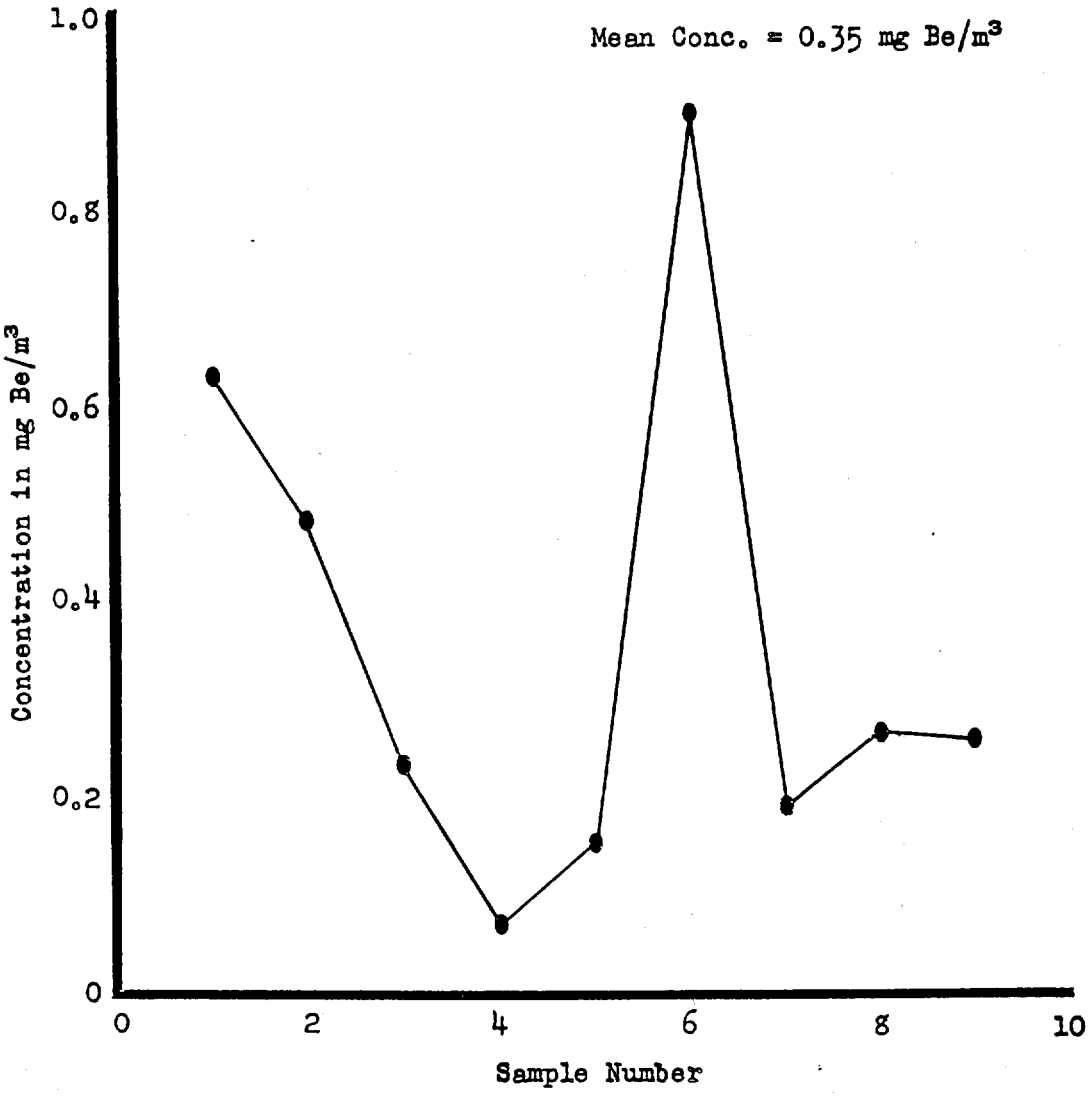
50,500x

Figure 3. Beryllium Fume Produced by Arcing Two Beryllium Electrodes in an Argon - Air Atmosphere. 2-9-51

FIGURE 4

CONCENTRATION VARIATION OF Be FUME OVER

THE COURSE OF A FOUR HOUR EXPOSURE



Program Code: Be. (BERYLLIUM)

Problem Code: Be.4 (Fate)

Section Code: 460

Author: R. E. Gosselin

The Failure of Hexametaphosphate to Influence the Renal Excretion of Radioberyllium (Be^7).

Introduction: For over a year this laboratory has studied the influence of various polyphosphates on the excretion and toxicity of uranium salts in laboratory animals (1). This interest has inevitably extended to other toxic metals. The availability of a small quantity of isotopic beryllium (Be^7) prompted a pilot study to determine what influence, if any, a polyphosphate compound has on the excretion of tracer doses of beryllium. Although the quantity of isotope was too small for an entirely conclusive demonstration, the negative results reported here are sufficiently convincing to cancel plans for a more elaborate experiment of this type.

Methods: Each milliliter of the isotope solution contained 6920 counts/min. of Be^7 (counting efficiency less than 1 per cent) in dilute HCl and 0.24 mg citric acid at a final pH of 4.5. Each of four adult male albino rats (average body weight 291 g) received intravenously (femoral v.) 1.00 ml of this solution once. In one rat this injection was followed immediately by a single subcutaneous injection of calcium hexametaphosphate (Ca-HMP). On the second day, one of the control animals was given subcutaneously a similar dose of Ca-HMP. Each animal was kept in a separate all-glass metabolism cage, from which urine was collected without appreciable fecal contamination. These rats ate

a standard chow ration ad libitum. At the end of each 24-hour period, each cage was carefully rinsed with 500 ml of dilute nitric acid. These washings were added to the specimens of urine, evaporated to small volumes, and oxidized with HNO_3 and H_2O_2; the final volume of each sample was 10 ml. Two 2-ml aliquots of each sample were assayed for gamma activity by a dipping counter tube.

The preparation of calcium hexametaphosphate (Ca-HMP) has been described previously (2). The calcium product is made from a commercial sodium salt, which is known to consist of a mixture of linear phosphate polymers with 6 atoms of phosphorus in the average molecule. The toxicity, hydrolysis, and excretion of this material have been described in rats and rabbits (2). As employed here, the calcium salt was in an aqueous suspension, containing approximately 30 mg labile P (100 mg P/kg) in two ml, with a Ca/P mol ratio of 0.5, and with a final pH of 7.4

Results: Table 1 (page 119) summarizes the observed gamma activity in aliquots of the dissolved urine ash. Background activity (12 to 15 counts/min.) has been subtracted from each datum, and a small correction has been introduced for loss of radioactivity by natural decay. The total activity in each 24-hour urine specimen is indicated, and the latter is also expressed in per cent of the original dose (given on the first day). Three consecutive days are represented in the table.

Discussion: In this limited series, 11 to 15 per cent of an intravenous tracer dose of Be^7 was recovered in rat urine collected in the first 24 hours, 1 to 2 per cent in the second, and less than 1 per cent in the third. Because of the limited quantity of isotope available, doses of Be^7 were small and urine assays were correspondingly inexact, especially after

TABLE 1

DAILY URINE ANALYSES FOR Be^7

Rat Number		1	2	3	4
1) First Day					
	Be^7 i.v. (counts/min)	6920	6920	6920	6920
	Ca-HMP s.c. (mg P)	30.1	0	0	0
Urine	Activity in aliquot (counts/mm)	155	168	210	182
Urine	Total Activity (counts/mm)	775	840	1050	910
Urine	Per cent of Be^7 given	11.2	12.2	15.2	13.2
2) Second Day					
	Ca-HMP s.c. (mg P)	0	31.5	0	0
Urine	Activity in aliquot (counts/mm)	17	19	24	29
Urine	Total Activity (counts/min)	75	95	120	145
Urine	Per cent of Be^7 given	1.1	1.4	1.7	2.1
3) Third Day					
	Ca-HMP s.c.	0	0	0	0
Urine	Activity in aliquot (counts/min)	8	12	12	-
Urine	Total Activity (counts/min)	40	60	60	-
Urine	Per cent of Be^7 given	0.6	0.9	0.9	-

the second day. Employing carrier-free Be^7 given to rats in doses about 10 times higher, Scott, Neuman, and Allen (3) observed renal excretions over 30 per cent in the first 24 hours, and about 1.2 per cent in the second.

As seen in Table 1, commercial calcium hexametaphosphate in a subcutaneous dose of 100 mg P/kg (equivalent to about 1/2 LD50) failed to exert an appreciable influence on the urinary excretion of intravenous Be^7. It did not matter whether polyphosphate were administered simultaneously with beryllium or 24 hours later. Since no information is available about the in vitro stability of any chelate-complex between hexametaphosphate and ionic beryllium, any speculative explanation of these excretion data is not justifiable.

Summary and Conclusions: In a pilot study, carrier-free Be^7 was given intravenously to rats. At the same time or 24 hours later, a calcium salt of commercial hexametaphosphate was administered subcutaneously. The urinary excretion of Be^7 was not appreciably modified by this treatment with polyphosphate. In spite of the small number of observations reported here, the results indicate that a more complete study in unwarrented.

Bibliography

1. Gosselin, R. E., Rothstein, A., Berke, H., Miller, G., and Meier, R., UR-142 Quarterly Technical Report, July 1 - Sept. 30, 1950

2. Gosselin, R. E., Rothstein, A., Berke, H., Miller, G., Tidball, C., and Meier, R., UR-163 Final A.E.C. Report, May 3, 1951

3. Scott, J. K., Neuman, W. F., and Allen, R., J. Biol. Chem., 182, 291 (1950)

Program Code: I.N. (INSTRUMENTATION, SPECTROSCOPY, ELECTRON MICROSCOPY, X-RAY AND NUCLEAR RADIATION DETECTORS, X-RAY DIFFRACTION, ELECTRONICS)

Problem Code: I.N.2 (Service)

Section Code: 350

Author: L. T. Steadman

Spectrographic Service Analyses

The following services were performed by the Spectroscopy Section:

1. 128 air dust samples were analyzed for beryllium.
2. 127 animal tissues were analyzed for beryllium.
3. 63 blood plasma samples were analyzed for copper.
4. 32 animal tissues were analyzed for thorium.
5. 45 animal tissues were analyzed for vanadium.
6. 1 snow sample was analyzed for all contaminating elements present.

Program Code: Educational Program

Problem Code: Ed.

Section Code: 610

Author: J. N. Stannard

Radiological Physics: The group of A.E.C. Fellows in Radiological Physics completed their formal course work in June.

The curriculum during the last quarter included the courses in Tracer Chemistry, lecture outline (Page 123), Practical Radiological Physics, lecture and experiment outlines (Pages 124, 125), completion of the course in Statistical Methods given in this Department, and Research in various phases of Radiological Physics.

Practical training for the Radiological Physics Fellows is being continued at Brookhaven National Laboratory.

Industrial Medicine: The courses offered in this joint curriculum were concluded by a series of lectures on the Practice of Industrial Medicine. A schedule of these lectures is attached (Pages 126-128). Dr. James H. Sterner, Medical Director of the Eastman Kodak Company, organized this curriculum and, it will be noted, secured the cooperation of a number of outstanding workers in the field of Industrial Medicine.

General Summary of Graduate Training Programs: During the academic year 1950-51, the graduate training activities of the Department developed along many lines. A tabular summary of these activities indicating both their status in May, 1951, and a cumulative total (since this has never been set down before) is included in the following pages (129-131). This summary does not include short courses offered in connection with civil defense programs.

SCHEDULE

RADIATION BIOLOGY 252

INTRODUCTION TO TRACER CHEMISTRY

April 10 to May 3, 1951

Lecture No.	Title	Lecturer
1	Introduction. Scope of Course. Isotopy	L. L. Miller
2	Stable Isotopes. Properties. Methods of Preparation. Methods of Assay	L. L. Miller
3	Radioactive Isotopes. Properties. Methods of Preparation. Methods of Assay	L. L. Miller
4	General Tracer Chemistry Methodology	L. L. Miller
5	Special Methods - Isotope Dilution	L. L. Miller
6	The Design of Tracer Experiments	L. L. Miller
7	Applications of Tracer Chemistry to Inorganic, Analytical, and Physical Chemistry	L. L. Miller
8	Applications of Tracer Chemistry to Organic Chemistry	J. Richmond
9	The Synthesis of Tracer Labeled Organic Compounds	L. L. Miller
10-12	Applications of Tracer Chemistry to Biological Chemistry and Physiology	K. I. Altman
13	Applications of Tracer Chemistry to Clinical Medicine	T. R. Noonan
14	Applications of Tracer Chemistry to Engineering and Agriculture	J. Richmond
15	The Future of Tracer Chemistry	J. Richmond

Five major experiments were conducted as follows:

Experiment No. 1 - Determination of the Solubility Product of Silver Iodide

Experiment No. 2 - Determination of the Iodine Content of an Unknown Solution by the Isotope Dilution Principle

Experiment No. 3 - Measurement of the Circulating Blood Volume by the Isotope Dilution Principle

Experiment No. 4 - A Study of the Distribution of Radioactive Phosphate ($P^{32}O_4$) in the Rat

Experiment No. 5 - The Separation of Amino Acids by Paper Partition Chromatography

LECTURE SCHEDULE

RADIATION BIOLOGY 210

PRACTICAL RADIOLOGICAL PHYSICS

May 8 to June 12, 1951

Tuesday and Thursday - 9:00 A.M. Wednesday and Friday - 11:00 A.M.

Lecture No.	Title	Lecturer
1	Introduction, Outline of Course	H. Mermagen
2	Dosimetry	G. H. Whipple, Jr.
3	Dosimetry	G. H. Whipple, Jr.
4	Dosimetry, Bragg-Gray Principle	G. H. Whipple, Jr.
5	Dosimetry, Practical	G. H. Whipple, Jr.
6	Health Physics Organization	*C. M. Patterson
7	Maximum Permissible Exposure	H. Mermagen
8	Design and Calibration of Instruments	H. Mermagen
9	Instruments (Continued)	H. Mermagen
10	Personnel Meters	H. Mermagen
11	Survey Methods	H. Mermagen
	Mid-Term Examination	
12	Shielding I	J. Shapiro
13	Shielding II	J. Shapiro
14	Safeguards and Recommendations for X-Ray Laboratories	H. Mermagen
15	Hot Laboratory Design	G. H. Whipple, Jr.
16	Waste Disposal	H. Mermagen
17	Plant Health Physics Methods	H. Mermagen
18	Plant Health Physics Methods	H. Mermagen
	Final Examination	

* DuPont de Nemours & Company

RADIATION BIOLOGY 210

PRACTICAL RADIOLOGICAL PHYSICS

EXPERIMENT SCHEDULE

1951

5/8	5/10	5/15	5/17	5/22	5/24	5/29	5/31	6/5
I. γ ,n Cal. Inst.			I. γ,n Cal.Inst.			I.γ,n Cal.Inst.		
II.β,γ,α Cal. Inst. Cal. Phot.	I. Survey		II.β,γ,α Cal.Inst. Cal.Phot.	I Survey		II.β,γ,α Cal.Inst. Cal.Phot.	I. Survey	
III. X-Ray Cal. Inst. Cal. Phot.	II. Survey	I. Survey	III. X-Ray Cal.Inst. Cal.Phot.	II. Survey	I. Survey	III. X-Ray Cal. Inst. Cal. Phot.	II. Survey	I. Survey
	III. Survey	II. Survey		III. Survey	II. Survey		III. Survey	II. Survey
		III. Survey			III. Survey			III. Survey

Instructors and Assistants

I. G. H. Whipple, Jr. - R. Koontz

II. R. Koontz - J. Hilcken

III. H. Mermagen - J. Shapiro

Instruments

I. Methane Counter, C. P. Meter

II. C. P., Juno, GM Survey Meters

III. Victoreen R Meter, C. P., GM

- Film Badges, Pencil Chambers

(I, II, III) (I, II, III)

INDUSTRIAL MEDICINE 203

THE PRACTICE OF INDUSTRIAL MEDICINE

March 19 to June 30, 1951

Number of Lectures	Title of Lecture	Lecturer
1	History of Industrial Medicine	Dr. G. M. Hemmett, Medical Director, Hawk-Eye Works, Eastman Kodak Company
1	The Development and Principles of Industrial Medical Practice	Dr. W. A. Sawyer, Medical Consultant, Eastman Kodak Company
1	The Role of Industry in the Community and Nation	Mr. M. Brugler, President, Pfaudler Company, Rochester, New York
10	The Functions of an Industrial Organization	
	a. Employment	Mr. R.C. Welch, Eastman Kodak Company
	b. Wage Standards	Dr. C. I. Miller, Eastman Kodak Company
	c. Public Relations	Mr. T. F. Robertson, Eastman Kodak Company
	d. Accounting	Mr. J. M. Richey, Eastman Kodak Company
	e. Operating Departments	Mr. R. Hahn, Works Manager, Rochester Products Corp.
	f. Engineering and General Service	Mr. C. H. Brown, Eastman Kodak Company
	g. Industrial Relations	Mr. C. P. Cochrane, Eastman Kodak Company
	h. Employee Benefits	Mr. M. V. Dill, Eastman Kodak Company
	i. Management	Mr. A. B. Gates, Eastman Kodak Company
	j. Training	Mr. N. D. Hubbell, Eastman Kodak Company

INDUSTRIAL MEDICINE 203 (Continued)

Number of Lectures	Title of Lecture	Lecturer
2	The Organization of a Medical Service in Industry	Dr. W. A. Sawyer
1	Medical Records	Dr. C. I. Miller
1	Statistics	Mr. J. F. Teegardin, Eastman Kodak Company
4	Management of Non-Occupational Disabilities and Injuries	Dr. J. L. Norris, Medical Director of Kodak Park, Eastman Kodak Company
	"	Dr. F. M. Hoskins, Eastman Kodak Company
2	Rehabilitation and Management of the Handicapped	Dr. R. B. Crain, Eastman Kodak Company
2	Special Examinations	Dr. M. A. Barnard, Eastman Kodak Company
	"	Dr. C. I. Miller
2	Mental Hygiene	Dr. R. C. Collins, Eastman Kodak Company
3	Workmen's Compensation	
	a. The History, Principles, and Philosophy	Miss Mary Donlon, Chairman, Workmen's Compensation Board, N.Y. State Department of Labor
	b. The Job of the Industry Workmen's Compensation Officer	Mr. T. J. Carney, Eastman Kodak Company
	c. The Job of the Physician	Dr. G. M. Hemmet
1	Source Material in Industrial Medicine and Industrial Hygiene	Dr. J. H. Sterner, Medical Director, Eastman Kodak Company
1	Research in Industrial Medicine	Dr. D. W. Fassett Eastman Kodak Company
1	Industrial Nursing	
1	Nutrition	Dr. W. A. Sawyer

INDUSTRIAL MEDICINE 203 (Continued)

Number of Lectures	Title of Lecture	Lecturer
1	Sanitation	Dr. E. K. Chaffee, Eastman Kodak Company
1	Community Health and Welfare Agencies	Mr. O. W. Kuolt, Director, Council of Rochester Social Agencies
1	Relation to other Community Medical Activities	Dr. J. L. Norris
2	The Safety Department Program	Mr. E. D. Carson, Safety Director, Camera Works, Eastman Kodak Co.
2	Governmental Agencies in Industrial Health	Dr. L. W. Greenburg, Chief, Division of Industrial Hygiene, N.Y. State Dept. of Labor
2	The Safety Department Program	Mr. A. L. Cobb, Safety Director, Kodak Park Works, Eastman Kodak Company
1	Community Medico-Legal Agencies	Dr. F. S. Winslow, Examining Physician for the Coroner, Monroe County, New York State
4	Public Health in Industrial Medicine	Dr. A. D. Kaiser, Director, Department of Public Health, Rochester, N. Y.
2	The Attitudes and Role of Labor in Industrial Medicine	Dr. Leo Price, Medical Director, I.L.G.W.U.
1	Special Problems Relating to Women in Industry	Dr. J. D. Watkeys, Eastman Kodak Company

SUMMARY OF GRADUATE STUDENTS AND GRADUATE DEGREES, MAY, 1951

I. Degrees granted.

Degree	Year	Number	Field	Thesis Title
M.S.	1948	1	Pharmacology	The ratio of urinary amino acid nitrogen to creatine as a sensitive test for uranium poisoning in the rabbit.
M.S.	1950	4	Pharmacology	Physico-chemical studies of the Beryllium-citrate complex.
			"	A kinetic study of normal and uranium-inhibited hexose metabolism in yeast.
			"	The relation of particle-size to toxicity.
			"	Calcium exchange as the mechanism for the uptake of radioactive calcium by bone.
		1	Physics	A proportional counter for carbon 14.
M.S.	1951 (expected)	6	Radiation Biology	Studies concerning the effects of radiation on the biosynthesis of hemoglobin.
			"	Spectrographic determination of cerium.
			"	Spectrographic determination of columbium.
			"	Electron microscopy of lung containing particulate matter.

Degree	Year	Number	Field	Thesis Title
M.S.	1951 (expected)		Radiation Biology	Effect of diet on X-ray sensitivity of rats.*
			"	The effects of X-rays on polycythemic rats.
		1	Pharmacology	The deposition of fluoride in glyco-ashed bone.
		3	Applied Physics	A quenching circuit for Geiger-Müller counting of carbon 14 as carbon dioxide.
			"	Cadmium sulphide crystal counter for in vivo detection of radio-activity.
Total M.S. Degrees		15		
Ph.D.	1949	1	Biochemistry	The isolation of microquantities of uranium by precipitation with protein prior to fluorometric determination.
Ph.D.	1950	1	Biochemistry	Studies on Ferritin.
Ph.D.	1951 (expected)	2	Biophysics	A chemical dosimeter for ionizing radiation.
			"	Electron microscope: Histology of normal and irradiated rat testis.

*Done in cooperation with the National Institutes of Health.

Degree	Year	Number	Field	Thesis Title
Ph.D.	1951 (expected)	4	Pharmacology	A new pneumotachograph: Its application in the study of human and canine respiration.
			"	Studies of the deposition of airborne submicron UO_2F_2 dust in the respiratory tract of rabbits during normal respiration.
			"	Studies on the chemistry of beryllium.
			"	Physico-chemical mechanisms of uranium transport in the body.
		1	Biochemistry	Contributions to the analytical chemistry of beryllium. Studies on the renal excretion of beryllium.
		1	Anatomy	A study of x-irradiation injury and repair in the germinal epithelium of male rats.
		—		

Total Ph.D. Degrees 10

II. Current Graduate Students (excluding those expecting degrees in 1951 and new registrants for 1951-52).

Field	Number	Type
Anatomy	1	Part-time employee
Biochemistry	6	Part-time employees of local project
Biophysics	10	A.E.C. Predoctoral Fellows and part-time employees of local project
Industrial Medicine	1	A.E.C. Fellow in Industrial Medicine
Pathology	1	A.E.C. Postdoctoral Fellow
Pharmacology	10	A.E.C. Predoctoral Fellows and part-time employees
Physiology	1	Part-time employee
Radiological Physics and Radiation Biology	27	A.E.C. Fellows in Radiological Physics, Service Officers, part-time employees
Total --	57	

TECHNICAL REPORTS ISSUED FOR DISTRIBUTION

April 1, 1951 thru June 30, 1951

Report No.	Title	Authors	Subject Category
UR-159	Cross Circulation Studies on the Irradiated Dog (UNCLASSIFIED) Issued: May 10, 1951	Rekers, et al	Health and Biology
UR-161	Effect of Single Doses of X-ray on the Survival of Rats (UNCLASSIFIED) Issued: May 10, 1951	T. R. Noonan F. Van Slyke J. B. Hursh	Health and Biology
UR-162	Observations on the Role of Phosphatase in Calcification (UNCLASSIFIED) Issued: May 10, 1951	W. F. Naumen V. DiStefano B. J. Mulryan	Health and Biology
UR-163	Observations on the Metabolism of a Soluble Sodium Phosphate Glass and Its Calcium (UNCLASSIFIED) Issued: May 28, 1951	Rothstein Burke, Meier Miller Tidball Gosselin	Health and Biology
UR-164	Quarterly Technical Report January 1, 1951 thru March 31, 1951 (UNCLASSIFIED) Issued: June 18, 1951	Blair	Health and Biology
UR-166	A Partial Bibliography on Uranium and its Compounds with Especial Reference to Pharmacology and Toxicology (UNCLASSIFIED) Issued: May 16, 1951	LaFrance	Health and Biology
UR-169	A Note on the Synthesis of Fatty Acids in Bone Marrow Homogenates as Affected by X-radiation (UNCLASSIFIED) Issued: June 12, 1951	Altman Richmond Salomon	Health and Biology
UR-170	The Separation of Beryllium from Biological Material (UNCLASSIFIED) Issued: June 12, 1951	Toribara Chen	Health and Biology