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ATOMIC ENERGY PROJECT

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Health and Biology

THE UNIVERSITY OF ROCHESTER
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Submitted by: Henry A. Blair
Director

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INTRODUCTION

The scientific work presented herein has been coded at the program and problem levels according to the scheme given on Pages 7 and 8. In the report all contributions to a given problem have been assembled together without regard to the administrative organization except that the number of the section which did the work is prefixed in each case. By using this number, it can be found on Page 12 what administrative officer can be approached for information about particular work.

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.

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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 in 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 or chemical toxicity of uranium, for example, has been broken down into problems according to the divisions commonly employed by toxicologists.

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. The administrative organization will be ignored in making this quarterly report of our research and service activities, all material being assembled according to the program and problem codes. The contribution of each section to a Quarterly Technical Report will be prefixed by the section number, however, to permit reference to the administrative organization if necessary.

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.

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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

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- 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

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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

[redacted]

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VIII. Zr. ZIRCONIUM

Zr.1 Physical and Chemical Properties

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

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

Zr.4 Fate (distribution and excretion)

Zr.5 Mechanism of Toxic Effect

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IX. S.M. SPECIAL MATERIALS

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

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I.S.3 Therapy

XI. O.S. OUTSIDE SERVICES

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H.P.1 Research and Development

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XIV. C.S. SPECIAL CLINICAL SERVICE

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

I.N.1 Research and Development

I.N.2 Service

I.N.3 Instrumentation for Outside Organizations

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3130	Radiation Tolerance	John B. Hursh
3136	Radiation Physiology	John B. Hursh
3140	Radiation Chemistry	Kurt Salomon
3150	Spectroscopy	Luville T. Steadman
3160	Radiation Mechanics	Michael Watson
3170	Radiation Toxicology	J. Newell Stannard
3171	Radioautography	J. Newell Stannard

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PROGRAM X.R.

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

Problem Code: X.R.1 (Tolerance Studies)

Section Code: 3130

Author: G. W. Casarett

Effects of X-rays on Spermatogenesis in Dogs.

Background. From previous experiments initiated under the direction of Dr. Andrew H. Dowdy and Dr. Robert Boche, it is known that chronic x-radiation (total-body) at dosage levels of 1.0 r or greater per day produce a condition of aspermia in dogs within one year. A dose of 0.5 r per day produces a lowered sperm concentration in dog semen with complete aspermia in some cases. Sperm counts were made on dogs exposed to 0.1 r per day of x-irradiation and a small, but statistically significant depression in sperm concentration occurred.

These studies were not of primary consideration in the experiments involved and were of necessity incomplete and not extensive.

We have initiated and are carrying out a chronic study on dogs in an endeavor to discover the lowest dosage level at which significant changes in sperm and sperm concentration can be induced. Young male beagles are being used, with litters represented in each dosage group insofar as is possible. When daily irradiation is begun it is planned to continue such exposures over the reproductive lifetime of these animals or until significant results have been obtained at the lowest radiation levels.

The dosage levels which will be used for this extensive study of dog semen and spermatozoa are:

Controls - 20 dogs

0.05 r / day - 20 dogs

0.10 r / day - 10 dogs

0.50 r / day - 10 dogs

Total - 60 dogs

The dogs used for this study are being carefully assembled. Litters of 3 or 4 thoroughbred beagle puppies are being assigned to experimental groups in such a fashion as to permit satisfactory statistical handling of the results.

If the results of radiation studies on spermatozoa of dogs can be transferred to man, the significance in setting a permanent permissible human exposure level of radiation is apparent.

However, in terms of sterility and fertility of the male, spermatozoa concentration alone, except when drastically reduced, has little meaning. That is, fertility may be greatly reduced without great change in sperm concentration. Therefore, other seminal and spermatozoal factors influencing male fertility are important subjects for study.

Purpose. To determine:

1. The minimal chronic dose of x-radiation which will depress the concentration of spermatozoa in dog semen or effect other changes in spermatozoa;

2. The effect of chronic x-radiation at the proposed dosage levels on motility, viability, and morphology of spermatozoa;

3. The effect of chronic x-radiation at these dosage levels on the relationship between hyaluronidase and sperm concentrations in the semen;

4. The ability of the semen and sperm to recover at various intervals of time from changes which may be produced at certain dosage levels.

Methods. Since even the oldest dogs have not yet reached a point of

stability and uniformity with regard to sexual excitability, ease and regularity of collection of semen, volume of ejaculate, and production of spermatozoa, radiation has not begun.

Collections of semen are first attempted at the age of 8 months and at weekly intervals thereafter. The oldest dogs at the present time are only 11 months old. Volumes of ejaculate are often very small and do not permit accurate or complete analysis of semen.

For these reasons the beginning of x-radiation is not yet indicated, and no quantitative results will be presented here. However, extensive work has been done on the methods and techniques and on the elimination of as much of the personal and experimental error as possible.

Techniques and measurement methods have been developed for determining an index of potential fertility in the male. Some of the analytical methods of E. J. Farris have been modified for our use.

Any change in a property of a spermatozoon which prevents the spermatozoon from reaching an ovum is in effect as important in fertility and sterility as the existence or nonexistence of a spermatozoon, i.e., factors preventing the function of spermatozoa are at least as important in a determination of fertility as a determination of sperm concentration alone.

Sperm concentration, except when drastically lowered, means very little in terms of fertility without a knowledge of the other factors discussed below.

Collection of Semen Samples. Collection of semen samples from the dogs is accomplished by masturbation, i.e., the production of orgasm and emission by manipulation of the genitals by hand. Just prior to masturbation, the male dog is placed with a female dog until he becomes excited enough to mount the female. A stall table for collection of semen during the mounting procedure

is to be built shortly. The ejaculate is collected in a graduated tube and the volume and time recorded.

If the bitch is in heat, the sexual excitement and active participation of the male dog are greater, and the ejaculate more complete and copious. Female dogs come into heat only twice a year, usually in the spring and fall. Samples are more difficult to obtain without the aid of a bitch in heat, and those obtained thus were often incomplete. In order to overcome this problem, hormone treatment was used in an attempt to bring about at least the excitatory phases of the heat period in a female dog out of season.

It was found that the intramuscular injection of 30 mg. of stilberstrol in saline, 10 mg. in each of three injections spaced two days apart, in a female dog which had had its heat period 5 or 6 weeks before, was followed, after a period of several days by all of the external signs of an intensive "heat" period, with tumescence of the external genitals, secretion of fluids, and great sexual excitement on the part of the female and also on the males exposed to her. It is not known as yet whether ovulation has actually taken place. This dog has now been in heat for 8 or 9 days so far. Other female dogs which have completed their spring heat cycle are being given the same treatment, and repetition and substantiation of this result is being awaited.

At the present time there is no way of showing by direct means that masturbation or this form of "interruptus coitus" provides a sample identical with that supplied in copulation, since there is no objective evidence concerning the content of the ejaculation during normal coitus. It seems reasonable to assume, however, that the ejaculate provided by coitus interruptus compares favorably with that resulting from uninterrupted coitus, and Farris has determined that for the human, masturbation gives approximately the same results

as coitus interruptus. The consistent and successful results obtained by Farris' methods, which hinge upon the use of masturbation to get semen samples, tends to support the view that for all practical purposes the specimen resulting from masturbation is representative of the semen deposited in intercourse.

In the present dog experiment, now that it seems possible to obtain samples consistently from highly excited, cooperative dogs, it is reasonable to assume that the samples so obtained will be sufficiently similar to those produced in normal coitus to allow, upon analysis, a good means for prediction of the degree of fertility in the dogs.

The period of time between emissions in a sexually mature dog for the spermatozoa count to reach its maximum level has not yet been worked out satisfactorily, not only because the dogs do not yet show indisputable evidence of sexual maturity on the basis of spermatozoa production, but because until recently the lack of excitatory means made consistent collection of good samples difficult. With the aid of the bitch in heat the number of dogs sampled successfully, as well as the volume and sperm population of the specimens, has increased. Sampling attempts had been made at weekly intervals, but two-week intervals seem indicated at the present time. Increased volumes of ejaculate will now tend to allow application of all analytical procedures to each sample.

Motility. The "absolute motility" or the number of moving spermatozoa in the total ejaculate is of prime importance, since only moving spermatozoa are likely to effect fertilization of ova.

Locke's fluid is used to dilute the semen in order to keep the spermatozoa alive, active, and normal, thereby permitting a differential count of both the active and inactive spermatozoa.

A known dilution of well-mixed semen is made by the addition of Locke's

fluid. The spermatozoa are counted in five groups of 16 small squares in the red field of an haemocytometer, routinely the four corner groups and the center group. The spermatozoa in both chambers are counted and averaged.

The counting chamber is sealed with vaseline after loading, in order to prevent evaporation from the sample. The spermatozoa retain their motility for many hours in this sealed preparation. The counting, however, is done at an early interval after collection and dilution of semen.

A systematic count of active and inactive cells is made in order to obtain the per cent of motile cells.

Volume of ejaculate multiplied by number of motile cells per cubic centimeter equals total number of moving cells in the ejaculate ("absolute motility").

Fertility bears a more direct relationship to absolute motility than to the concentration of motile spermatozoa per ml. of semen.

Concentration of Spermatozoa. A dilution of the semen is made with a fixing and staining solution which renders all cells immotile and easily visible. A solution of methyl green is now in use, but other dyes are being tested. The spermatozoa count is made like a blood count on the red field of an haemocytometer. A 16 mm. objective is used for counting.

The count of the fixed cells should not vary greatly from that of the motile and nonmotile cells in the Locke's fluid preparation, and thereby serves as a check on the motile spermatozoa count.

Speed of Spermatozoa. In order to obtain some measurement of this fertility factor, five of the fastest spermatozoa in each of the five blocks of squares on the red field of the haemocytometer are timed. The Locke's fluid preparation is used for this determination, and the measurements are made at

certain times after collection of the sample, the condition of temperature being kept constant. The time for each of the spermatozoa to cross a large square is determined by means of a stopwatch, and the speeds of the 25 spermatozoa are averaged. Only fast progressive spermatozoa are timed.

It is to be realized that if the speed of spermatozoa is drastically reduced, an animal may be infertile despite the presence of large numbers of motile spermatozoa.

Both the type of motility and the speed will have a definite bearing on the probability that any one spermatozoon will ever find its way to an ovum.

The speed of rapid, progressive dog spermatozoa seems to be about the same as that reported by Farris for the human, i.e., about .5 to .9 second for .05 mm. distance.

Character of Motility. Spermatozoa must not only move to complete fertilization, but they must move with definite forward progression.

Normal spermatozoa are usually the only ones which travel with definite forward progression, but in all directions from the point of deposit.

The characteristic types of motility which have been found are:

1. Progressive (rapid, moderate, and sluggish)
2. Oscillating
3. Circling

Spermatozoa with oval heads usually show a progressive type of motility. The other spermatozoa, representing various types of abnormalities, do not progress normally as a rule, but are sluggish, oscillating, or moving in circles. If a spermatozoon cannot move progressively, it cannot reach and fertilize an ovum. The speed must be adequate and the direction definite. Spermatozoa which move sluggishly, oscillate, or move in circles do not contribute to fertility.

Morphology. It is not possible to classify semen specimens without knowing the important characteristics of the normal spermatozoon under investigation.

All of the male dogs produce some spermatozoa that are abnormal in appearance, and it is expected that the concentrations of abnormal forms may vary with irradiation. In the past in this laboratory increased numbers of abnormal spermatozoa, with abnormal motility, have been noted following acute irradiation in rats.

By phase microscopy and also by means of morphological stains, the details of both active and inactive cells have been studied.

The normal dog spermatozoon has an oval, somewhat flattened head, which in profile is rather pyriform in shape. The head is about 6 micra in length, about 4 micra in width, and about $1\frac{1}{2}$ micra at the thickest part. The nucleus is in the posterior half of the head. A cap covers a little more than half of the anterior part of the head.

The neck is a slight constriction, about $\frac{1}{2}$ micron in length, between the head and the middle piece.

The middle piece is made up of a spiral filament of 0.2 micron or less in diameter, coiled about an axial fiber or thread to form a cylinder, the whole being about 8 micra long and less than a micron in diameter.

The tail tapers slightly from the middle-piece to its terminal thread. The average thickness of the tail appears to be about 1/3 micron and its length about 45 micra. The tail has the appearance of a long, smooth, flexible structure with an external sheath, and showing slight density variations throughout its length. It has an abrupt termination, where its diameter is about 0.2 micron, and its terminal filament, with a length of several microns, is about 0.1 micron thick.

The abnormal cells are classified primarily by their variations in shape, and seem to be present in greater numbers in samples with low concentrations of spermatozoa.

The abnormal forms notes are:

1. Giant heads
2. Small heads
3. Round heads
4. Double tails
5. Double heads
6. Separation of head and tail (tailless and headless)
7. Heads attached at abnormal angles
8. Cytoplasmic appendages

Three hundred individual cells are examined under oil immersion, are classified, and percentages of abnormal forms calculated.

Viability. A nigrosin-eosin stain for differentiating viable and non-viable spermatozoa has been perfected to a point where it may now be used. Spermatozoa which are dead before application of the stain, take the stain. Spermatozoa which are alive at the time of application of the stain do not take the stain.

Differential viability counts have been begun on our samples.

Now that many of the technical problems of accurate semen analysis have been met, this laboratory has begun to accumulate quantitative control data which are considered to be dependable. When the oldest animals reach an unquestionable state of sexual maturity, probably well within a few months, irradiation will be started. Irradiation cannot be begun hastily because the age at which any dog begins exposure should be an age at which all dogs in the

experiment will certainly have reached sexual maturity by all criteria used.

It is felt necessary to emphasize that data obtained until recently on these young animals which were without, during most the time, adequate stimulation for true ejaculation of semen are considered too undependable and erratic for this report.

Summary. The structure of a life-long experiment on the effects of low x-irradiation on spermatogenesis in dogs has been presented along with a description and discussion of the general methods of semen analysis employed. Certain qualitative data have been reported but the incomplete and erratic data obtained on the immature dogs to date are not dependable enough for reporting quantatively.

Problem Code: X.R.2 (Mechanism of Effects)

Section Code: 3140

Author: B. W. Gabrio

A Paper Chromatographic Study of Ferritin and Apoferritin Hydrolysates.

Background. During the course of experimentation on some chemical properties of the iron-protein, ferritin, and the role of ferritin it seemed desirable to obtain more detailed information about the amino acid composition of ferritin, and its protein moiety apoferritin. Conflicting data concerning the amino acid components of ferritin and apoferritin have been reported from the laboratories of Kuhn et al (1) and Tria (2). Recently, however, Mazur and Shorr (3) reported the partial amino acid composition of horse spleen ferritin and apoferritin, which showed identical amino acid values on the basis of nitrogen content.

Methods. The two dimensional chromatographic method used in these studies was essentially that of Consden, Gordon, and Martin (4) as modified by Dent (5). The solvents employed were phenol, saturated with water, and a mixture of 2,4,6-collidine and 2,4-lutidine, saturated with water. Whatman #1 filter paper was used. The amino acids were detected by spraying the papers with 0.1% ninhydrin in n-butanol to which an excess of water had been added. The color was allowed to develop for 24 hours, and the amino acids were identified by their relative positions and by comparison with a reference map prepared by Dent (6).

The chromatogram thus obtained with 50 µl. of horse spleen apoferritin hydrolysate equivalent to 0.8 mg. of protein is shown in Figure 1 (Page 25). The hydrolysis was carried out with 6N HCl at 100° C for 18 hours. The following amino acids were present as ninhydrin-reactive substances: tyrosine, phenylalanine, the leucines, valine, glutamic acid, aspartic acid, glycine, serine, arginine, lysine, cystine, (as cysteic acid) and methionine. Threonine was observed in trace amounts on chromatograms employing larger quantities of protein. Histidine was not observed in Figure 1 because of its low sensitivity to the ninhydrin reagent, although its presence is reported by Mazur and Shorr (3). The relative quantitative estimations are in agreement with those of Mazur and Shorr (3) except that in addition to those listed by the latter authors, aspartic acid, glycine, serine, and threonine were detected chromatographically.

Paper chromatography of horse spleen ferritin showed the same amino acid composition as that of apoferritin, but in addition it was observed that some of the iron, liberated by hydrolysis, had migrated in the phenol direction as a definite yellow spot. A chromatogram of ferric iron alone did not show this movement. It was found that the migration of iron on the chromatogram of the

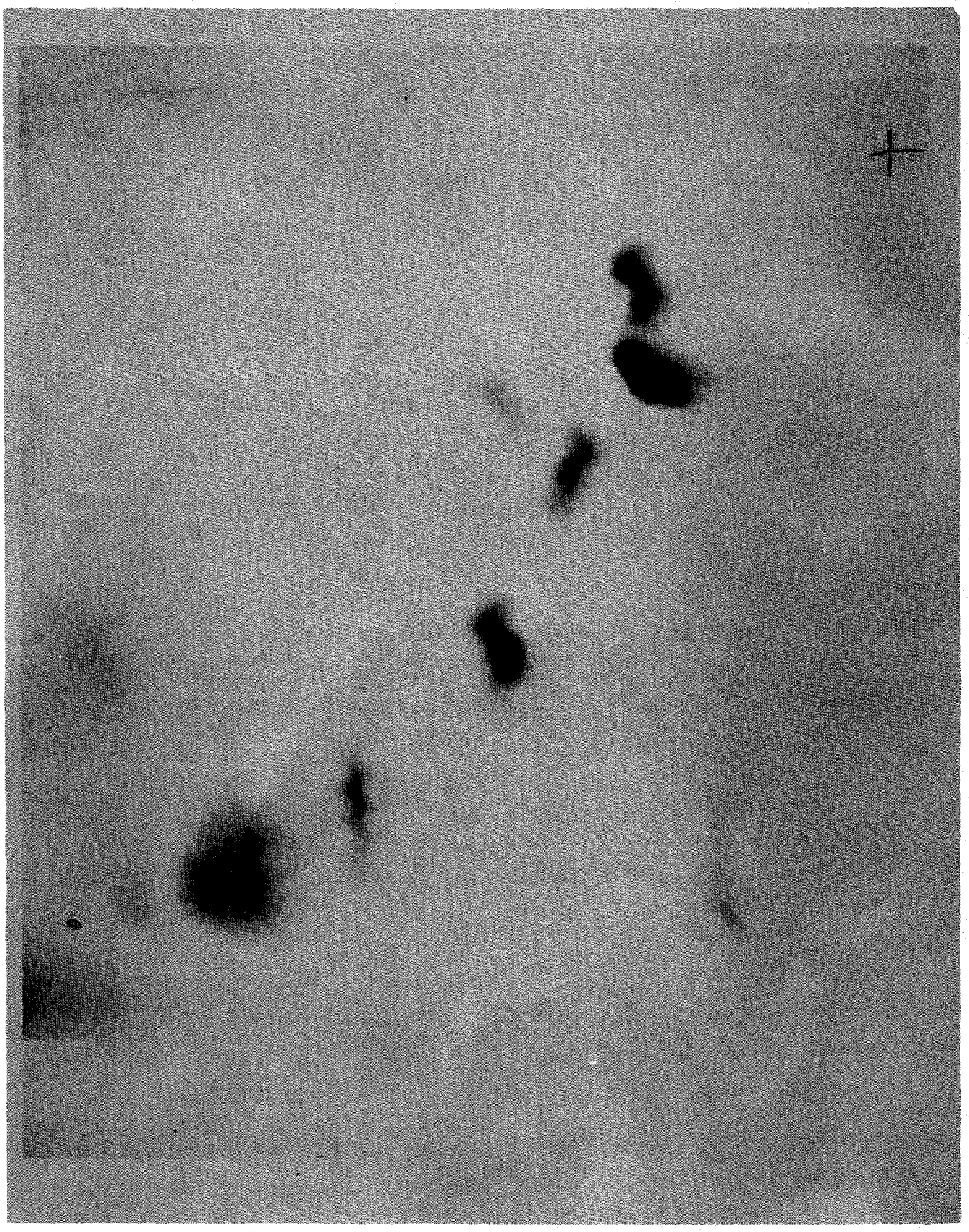

Figure 1. Chromatogram obtained with 50 µc
of horse spleen apoferritin hydrolysate equivalent to 0.8 mg of protein.

ferritin hydrolysate was not characteristic of ferritin, for identical movement was seen in a paper chromatogram run on amigen (commercial pancreatic casein hydrolysate) to which ferric iron had been added in amounts approximating that contained in ferritin. However, in all of these chromatograms the amino acids moved to their relative positions with the collidine-lutidine solvent while the iron remained on the phenol abscissa. Thus the iron appears to be conjugated with one or more of the amino acids in the phenol run, but the association is disrupted by the collidine-lutidine solvent.

One dimensional chromatograms (phenol solvent) of several single amino acids with added iron showed that all of the amino acids tested were capable of moving iron from the starting point in varying degrees. Each amino acid could be classified according to the amount of iron it carried. This information is tabulated below in Table 1. The system of grading of++++ to + is used to designate the amount of iron carried by the amino acid.

TABLE 1

Amino Acid	Amount of Iron Carried by the Amino Acid
Histidine	++++
Alanine	++
Arginine	++
Isoleucine	++
Leucine	++
Lysine	++
Phenylalanine	++
Tyrosine	++
Valine	++
Threonine	+
Serine	+
Aspartic acid	+
Glutamic acid	+
Glycine	+
Control-iron	No Migration

Thus, the iron spot, noted on the paper chromatograms of hydrolysed ferritin and amigen+iron, is probably due to the fact that such amino acids as histidine, the leucines, arginine, lysine, phenylalanine, and valine are associated with a considerable amount of iron and move to about the same position in phenol.

It is also apparent from Table 1 (Page 26) that histidine conjugates a greater quantity of ferric iron than the other amino acids. Furthermore, the strong affinity of histidine for iron has been reported (7). It is possible that a correlation might be found between the histidine content of proteins and their iron-binding capacity.

Results. The amino acid composition of ferritin was studied by means of two-dimensional chromatographic analysis. The ability of amino acids to carry iron was investigated on a one-dimensional chromatograph.

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Problem Code: X.R.3 (Therapy)

Section Code: 2606

Authors: F. W. Furth and J. Shrier

Effect of Aureomycin on Coagulation Time.

Background. It has been reported that certain antibiotic substances (1,2) shorten the whole blood coagulation time, and a recent reference (3) reports that aureomycin has a similar effect. In studies on the effect of antibiotics on the radiation syndrome being carried on in our laboratory it became of interest to determine if aureomycin did have any effect on blood coagulation mechanisms. To this end the following experiments were done.

Method. A series of six coagulation times done by the Lee White method with blood drawn from the external jugular vein were performed during a one week period, on four normal healthy mongrel dogs. All coagulation times are reported in minutes. After these control values had been obtained the dogs were given aureomycin capsules orally every six hours, day and night, for the next fifteen days. The dose of aureomycin was approximately 100 mg./kg./24 hours (one 250 mg. capsule q. six hours) which is two to four times the recommended oral dose for humans. Coagulation times were then done on these dogs each morning approximately three hours after a dose of aureomycin. The results are shown in Table 1 below.

TABLE 1

	Control Days						Days After Starting Aureomycin Administration										
Dog No.	1	2	3	4	5	6	1	2	3	4	7	8	9	10	11	14	15
1	7	3	5	9	9	8	8	11	9	8	9	10	10	11	10	10	6
2	7	8	10	9	10	9	11	12	9	9	8	11	10	12	10	11	9
3	7	7	13	12	10	10	11	13	10	10	10	13	7	10	9	11	3
4	10	8	10	8	12	11	11	11	10	10	5	8	11	11	8	8	6

Serum levels of aureomycin were done on these dogs on three occasions and found to be between 2 and 16 micrograms/cc (averaging 5 mcg./cc) which covers the range of levels reported in humans receiving aureomycin. The effect on the coagulation time of a single, very large oral dose of aureomycin (200 mg/kg) is shown in Table 2 below.

TABLE 2

Dog No.	Control	Control	Control	2 Hours After Aureomycin	3 Hours After Aureomycin
1546	10	9	8	9	8
1505	10	7	6	9	10

It was also of interest to know if intravenous aureomycin had any effect on coagulation time. With this route of administration higher and more prolonged serum levels of aureomycin can be obtained. Seven normal healthy adult mongrel dogs were used for this experiment. A series of three control coagulation times were done on each dog during a period of thirty minutes previous to injection of 100 mg. of aureomycin HCl (Lot No. 7-5554) with 100 mg. sodium glycinate dissolved in 20 cc of sterile normal saline. This solution was injected in the external jugular vein over a period of sixty seconds. Coagulation times were taken on the dogs at intervals after injection, and the results are shown in Table 3 (Page 30).

An attempt was made to determine if aureomycin had any effect on coagulation time in vitro. Measured quantities of aureomycin buffered with sodium glycinate and dissolved in 0.5 cc of saline were placed in the small tubes used for the coagulation time. Whole blood drawn from a normal dog was placed in these tubes and the time for coagulation to occur was measured.

TABLE 3

Dog No.	Controls			Time After Aureomycin Administration						
				15 min.	30 min.	1 hour	2 hours	3 hours	4 hours	5 hours
1443	6	8	7	60+	60	60	60+	30	10	12
1445	10	10	9	10	10	9	8			
1286	8	3	5	300+	285+	240+	180+	30	21	6
1498	4	4	3	120+	52	19	7			
1564	11	10	5	2	3	7	8	9	8	
1490	10	8	3	3	3	8	8	8	8	
1530	8	9	3	240+	240+	195+	70	16	7	

The results are shown in Table 4 below.

TABLE 4

	Trial No. 1	Trial No. 2
Control without saline	6	10
Control with saline	17	10
Aureomycin 5 mcg./cc.	15	13
Aureomycin 10 mcg./cc.	15	11
Aureomycin 200 mcg./cc.	15	

Discussion. According to the experiments reported here oral aureomycin in therapeutic doses has no effect on the whole blood coagulation time. As shown in Table 3 above the intravenous administration of aureomycin in this dosage produced a marked prolongation of the coagulation time in four of the seven dogs. Most of the dogs which showed a prolonged coagulation time, also

exhibited a shock-like state for five to fifteen minutes immediately after injection which was characterized by lethargy, staggering gait, and vomiting. It was felt that this represented a "peptone shock" phenomenon and that a heparin-like substance was released into the blood by the same reaction (4). It was not determined whether this was due to the aureomycin HCl, or the sodium glycinate used as a buffering agent. In an attempt to determine this by administering an equal quantity (200 mg.) of aureomycin HCl without buffer intravenously such profound hemolysis ensued that gross hemoglobinuria occurred and the dog succumbed within 48 hours after injection. The administration of such a concentrated solution of aureomycin HCl-sodium glycinate in a relatively short period of time may also have provoked the shock reaction. The mixing of aureomycin with blood after it was drawn had no apparent effect on the coagulation time.

Conclusions.

1. Aureomycin administered orally in amounts which produce therapeutic blood levels, has no effect on the whole blood coagulation time in dogs.

2. Intravenous aureomycin HCl buffered with sodium glycinate may produce a markedly prolonged coagulation time. This effect may be related to a "peptone-shock" phenomenon.

3. In vitro, aureomycin has no effect on the blood coagulation time.

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Problem Code: X.R.3 (Therapy)

Section Code: 2606

Authors: F. W. Furth and M. Coulter

Effect of Aureomycin and Terramycin on the Mortality and Diarrhea of the X-radiated Rat.

Background. Preliminary experiments done in this section during the past year indicated that certain of the antibiotic and chemotherapeutic agents are effective in reducing the incidence of diarrhea and possibly affect the mortality of rats which have received large doses of whole body x-radiation. These experiments have involved the use of a variety of therapeutic agents including penicillin, streptomycin, chloramphenical, and several sulfonamide compounds. None of these were found to influence the morbidity and mortality of the x-radiated rat as favorably as aureomycin and terramycin. Although earlier experiments with these two drugs involving smaller groups of rats have been done, only the most recent experiment which shows results typical of all the experiments will be reported here.

Method. A total of 180 adult female Wistar rats weighing 160 - 180 gms. were used in this experiment. They were divided into 4 groups of 45 each. Each rat was housed in an individual cage. The rats were weighed, and examined for evidence of diarrhea, daily for 7 days prior to radiation. These same observations were continued for 28 days post-radiation. Each rat was offered 15 grams of feed each day, and the amount left from the previous day was weighed so that a measure of the appetite could be made. Those rats which received the drugs were offered 15 gms of feed daily with which the drug had been admixed. The groups which received the drug in the feed only were offered 60 mg. (approximately 350 mg./kg.) of aureomycin or terramycin during

the first 5 days post-radiation when the anorexia was most marked. Thereafter until the 28th day post-radiation they were offered 22.5 mg. (approximately 100 mg/.kg.) of the drug each day. 50 mg.% of aureomycin-sodium glycinate was added to the drinking water of one group for the first 5 days post-radiation and the amount of water drunk during each 24 hours measured. These rats were also offered 22.5 mg. of aureomycin in the feed each day during the entire post-radiation period. All the drugs were started immediately after radiation.

The rats were given a total of 700 r of whole body x-radiation at the rate of 18 r/minute administered by a 250 KV Picker machine at 15 m.a. with a parabolic aluminum filter and 0.5 mm. of copper. The target skin distance was 25 inches. They were radiated in groups of 15 which were arranged to include rats from each experimental group.

Results. The diarrhea which is typical of radiation sickness in the rat appeared on the third day post-radiation. In the control group the percentage of rats with diarrhea was much higher than many of the treated groups, as shown in Graph 1 (Page 34). Coincident with the diarrhea was a profound anorexia and weight loss. This anorexia and weight loss was equally severe in control and treated groups until the 5th day post-radiation when the treated groups began to eat more and regain weight more rapidly. The surviving treated rats regained their pre-radiation weight more rapidly than the surviving control rats. The rats in the groups which received aureomycin and terramycin in the feed presented a better appearance during the first ten days post-radiation with smoother coats and greater activity. The mortality in the group which received the aureomycin only in the feed approximated that of the controls as shown in Graph 2 (Page 35). In the group which received supplementary aureomycin in the drinking water the rate of mortality and 28 day mortality

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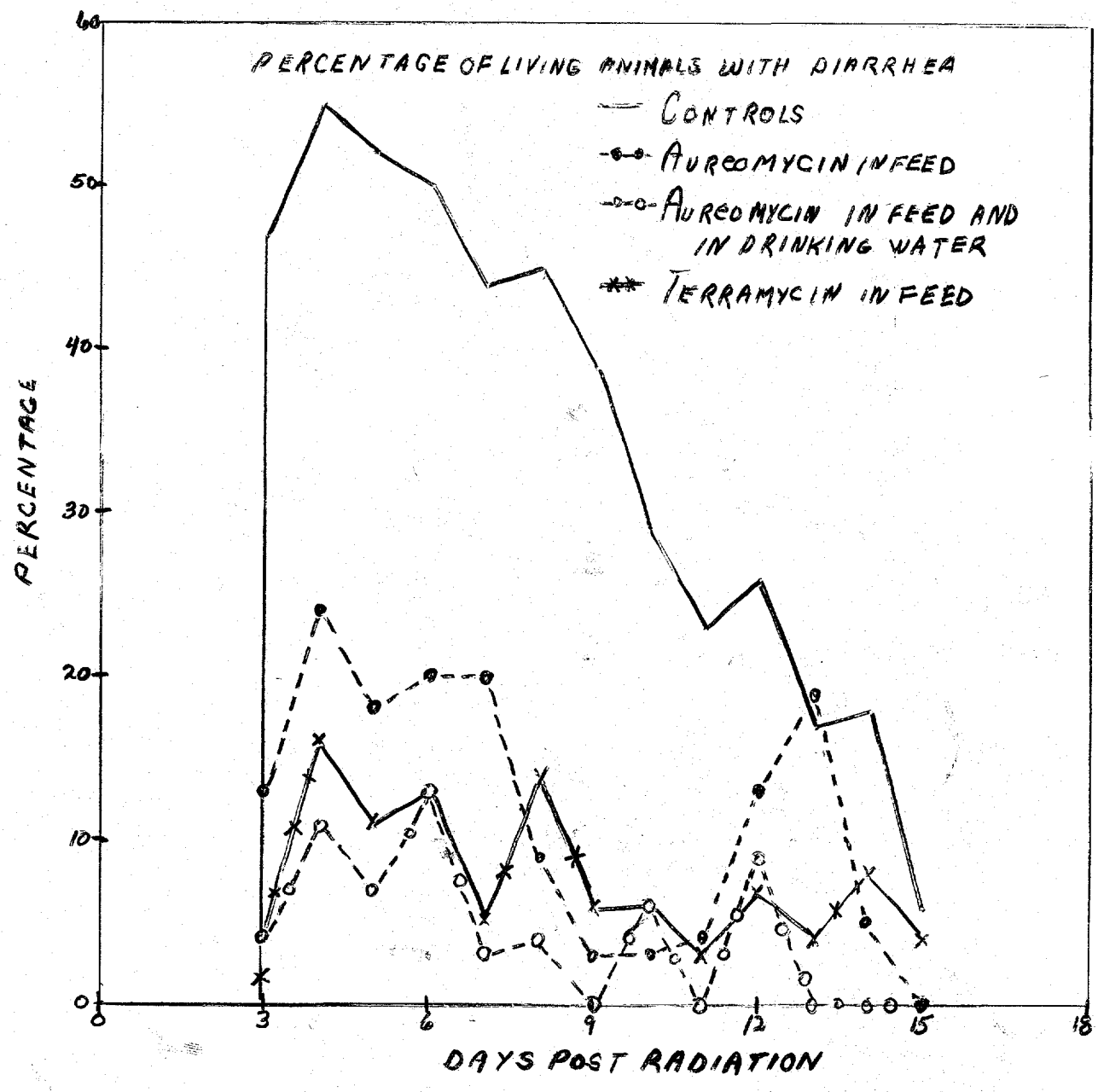
GRAPH 1



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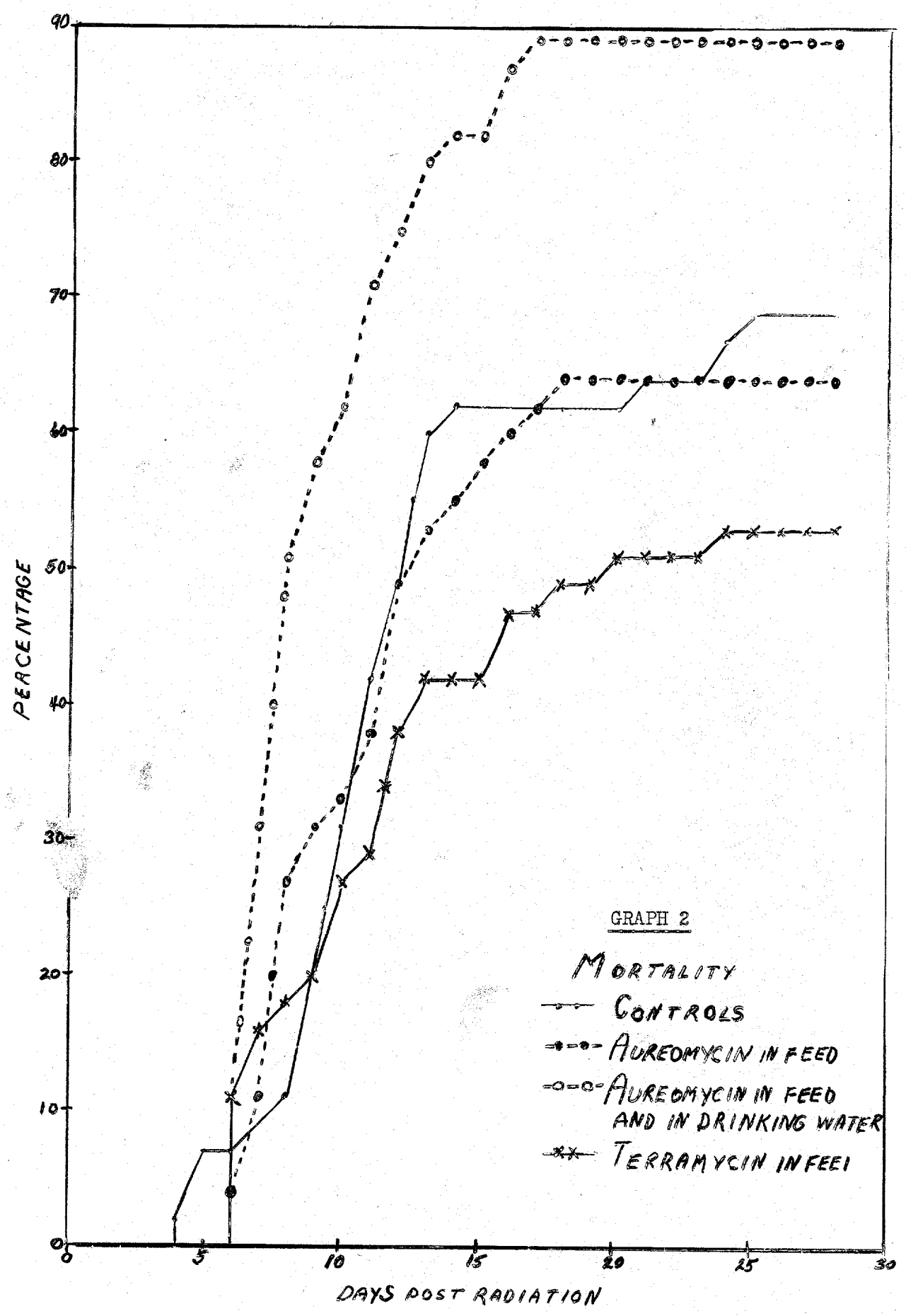

was higher than in the control group. The terramycin-treated group showed a mortality which was less than the controls.

Discussion. The decrease in diarrhea associated with the administration of aureomycin and terramycin to the x-radiated rat may have several explanations. Since both of these drugs are potent antibiotics, effective against both gram-positive and gram-negative organisms, it is conceivable that the bulk of the feces may be diminished by decreasing the numbers of bacteria within the gastro-intestinal tract. It is also possible that this decrease in bacterial flora may diminish the irritating effect that the bacteria may have on the injured epithelium of the gastro-intestinal tract. It is also possible that this decrease in bacterial flora may diminish the irritating effect that the bacteria may have on the injured epithelium of the gastro-intestinal tract. The possibility that either of these drugs may exert a specific inhibitory effect of peristalsis through parasympathetic paralysis seems remote since we have found that other antibiotics such as penicillin and streptomycin also diminish the diarrhea following x-radiation in the rat. The cause of the more rapid regain of weight in the treated rats may in part be explained by the alteration in intestinal flora. It has been recently reported (1), that aureomycin fed to normal rats causes an augmented weight gain and growth, but an adequate explanation of this phenomonen has not been advanced. Miller and his co-workers (2), report a markedly diminished mortality in x-radiated mice given streptomycin and/or terramycin. They also report (3) that the incidence of positive blood cultures in x-radiated mice can be reduced by the administration of these antibiotics. We have been unable to substantiate these results in rats as far as mortality is concerned using streptomycin, aureomycin or terramycin. In this experiment terramycin seemingly did decrease the mortality.

It may be that if blood stream infection plays a role in the mortality following x-radiation in the rat, there exists an organism in our strain of rats which is resistant to the antibiotics used and which may produce a generalized sepsis and death. Studies on the bacterial flora of the strain of rats used in these experiments are contemplated. The increased mortality in the group which received the supplementary aureomycin in the drinking water would seem to indicate that the toxic dose of aureomycin was exceeded. By measurement the rats received no more than 25 mg. of aureomycin per day (160 mg./kg.) which does not exceed the oral toxic dose reported (4) for rats. However, the injured epithelium may be more permeable and allow a toxic amount of aureomycin to be absorbed. This may in part account for the absence of effect on mortality observed in the dog. In addition, following x-radiation the normal detoxification mechanisms may be altered, so that smaller doses may produce toxicity.

Summary.

1. Orally administered aureomycin and terramycin markedly diminishes the incidence of diarrhea in the rat which has received a large dose of whole body x-radiation.

2. Oral aureomycin and terramycin accelerate the regain of weight following x-radiation in the rat.

3. Oral terramycin may diminish the mortality following large doses of x-radiation in the rat.

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Problem Code: X.R.4 (Hematology)

Section Code: 3351

Author: M. Ingram

The Incidence of Unusual Lymphocytes in the Blood of Dogs Exposed to Radiation from the 130-inch Cyclotron.

Previous Quarterly Reports have indicated that the relationship between the incidence of lymphocytes with bilobed nuclei in the peripheral blood and exposure to radiation from the cyclotron was being studied in an experiment utilizing dogs. Specifically, three healthy mongrel dogs have been studied before and after three different exposures to small amounts of radiation from the 130 inch cyclotron. Quantitative interpretation of the experimental results is now essentially complete and it is possible to report additional details of the relationship between the exposures and the incidence of the abnormal cells.

The entire experiment extended over a period of approximately one year. Blood examinations were made approximately daily during a control period of approximately two months prior to the first exposure. During this period a total of 180 coverslip blood smears was examined. A like number was examined during each first post-exposure week, and thereafter approximately 30 smears were examined each week.

For convenience in interpreting results each blood smear has been classified according to whether or not it contains one or more of the abnormal

lymphocytes, and the frequency of occurrence of "positive" smears has arbitrarily been chosen as an index of the incidence of lymphocytes with bilobed nuclei. In all, approximately 3.4×10^6 white blood cells were examined during the entire experiment. The experimental results are presented briefly in Table 1 (Page 40). They indicate a marked increase in the occurrence of lymphocytes with bilobed nuclei following exposure to radiation from the cyclotron. The incidence was maximal during an approximately two-week period following each of the three exposures. Thereafter the incidence decreased fairly steadily. The slightly higher frequency of positive blood smears after the first exposure probably indicates that a greater dose of radiation was received in that exposure. This assumption is supported by the fact that a slight but definite decrease in the white blood cell counts occurred concomitantly with the increased incidence of lymphocytes with bilobed nuclei in this instance. No reduction in the total leukocyte count was noted after the second and third exposures.

At this time it is not possible to indicate the relative effectiveness of the various components of radiation from the cyclotron in inducing the increased incidence of the unusual lymphocytes, however studies designed to provide such information are currently being undertaken.

TABLE 1

FREQUENCY OF BLOOD SMEARS CONTAINING ONE OR MORE LYMPHOCYTES WITH BILOBED NUCLEUS
(Dogs exposed to radiation from 130" cyclotron)

	Control Period*	Post-exposure Period				
		1st week	2nd week	3rd & 4th weeks	5th & 6th weeks	After 6th week
1st exposure	0.00(6)	0.22**	0.37**	0.11	0.02	- - -
2nd exposure	"	0.16	0.13	0.06	0.03	0
3rd exposure	"	0.19	0.07	0.11#	- - - - -0.03#- - - - -	

* Control counts represent a period of approximately two months before the first exposure
** Associated with a slight depression in the total white blood cell count
\# Counts were done only once a week after the third week, and only three days during 3rd week
Based on counts done once a week from the 4th through the 17th post-exposure weeks

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PROGRAM U.

URANIUM

Problem Code: U.4 (Fate)

Section Code: 3210

Authors: H. E. Stokinger, H. B. Wilson, G. E. Sylvester and S. P. Dzuiba*

Lobar Partition of Inhaled U_3O_8 Particles.

A review of the toxicologic literature on the deposition and retention of particulate matter reveals considerable information on the amount of: (1) deposition in the entire respiratory system; (2) nasal filtration and penetration; (3) alveolar deposition - as a function of particle size, shape, solubility, breathing rate and other factors in the human and laboratory animal.

This information has unquestionable merit in defining the amount of contaminant of known characteristics that will be retained on inhalation and where particles of a given size may be expected to lodge in the respiratory tree, but it is insufficient to form a sound basis for evaluation of more localized tissue injury from the inhalation of chemically toxic or radioactive particles at any particular site in the lung. Previous data assume a uniform deposition of particulate matter throughout the lung.

The present study was undertaken to supply quantitative information as to whether an even distribution of dust occurred uniformly in all lobes and in gross sections of the lungs under normal conditions of inhalation in animals.

Procedure. Twenty albino rats of similar age and weight (261-314 g) were exposed in individual, compartmentalized cages continuously for one, 6-hour period to U_3O_8 dust of known particle size. The mass-median size determined by

* With the technical assistance of R. E. Root

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Cascade Impactor samples of the exposure atmosphere was 2.6 μ with a standard deviation of 2.6; the atmospheric concentration averaged 84 mg U_3O_8/m^3 with a range of from 80-87 as sampled by the filter paper dust sampler with a Whatman #41 paper and quantitatively determined by acid ferrocyanide.

In order to allow opportunity for the particles to be cleared from the larger air passages (1), the rats were not killed until the following morning. The group of 20 rats was divided at random in 2 groups of 10 each; from one group of 10 rats, the lung was divided into its 5 natural lobes, namely, left, post-caval, superior, median and inferior left lobes; from the other 10 rats, 3 equal, transverse sections were taken from each rat from the left lobe which we termed the upper, middle and lower sections. The weight of each fresh section was determined to the nearest milligram on an analytical balance; the body weights of the rats were obtained at death in order to permit comparison of the lung to body weight, which value gives an indication of the condition of the lung. Analyses for uranium were made in quadruplicate by the fluorophotometric method of Neuman (2) and the results analyzed statistically by Dr. S. Lee Crump.

Results. The uranium analyses in μg U/g fresh tissue of the 5 lobes and transverse sections with the respective rat body-weights are given in Tables 1 and 2 (Page 43). It is apparent from these tables that particulate uranium is deposited in the upper right lung lobe in from 1.5-2 times the amount of that found in any other lobe on a concentration basis. No differences in deposition among any other lobes were found. The difference in deposition cannot be due to differences in lobar size as the upper right lobe is as small as any other section in the rat lung (Table 3, Page 44).

When tables utilizing the data of Tables 1 and 2 were prepared to ascertain whether the amount of uranium in the segments were determined by

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TABLE 1

PARTITION OF INHALED U_3O_8 DUST IN LUNGS OF RATS

Results in μg U/g Tissue, Particle Size 2.6 μ, σ 2.6, 6-hour Exposure

Rat No.	Left	Post Caval (Median)	Upper Right	Median Right	Lower Right	Rat Weights
2	19.6	13.2	9.1	4.7	15.0	295
7	23.8	23.9	41.7	22.8	21.1	273
9	18.8	27.4	40.5	29.2	25.4	296
11	16.1	12.2	23.2	12.2	13.2	268
13	23.0	24.3	36.3	21.9	21.1	281
14	31.7	33.9	54.2	27.3	30.8	282
16	18.8	16.2	32.7	16.5	13.8	281
17	32.0	27.9	50.0	24.4	31.7	256
18	20.9	21.0	30.7	20.4	12.5	273
19	32.4	31.4	47.0	28.5	34.8	393
Sum	237.1	231.4	365.4	207.9	219.4	
Av.	23.71	23.14	36.54	20.79	21.94	

TABLE 2

PARTITION OF INHALED U_3O_8 DUST IN TRANSVERSE SECTION OF LEFT LOBE OF LUNG OF RATS

Results in μg U/g Tissue, Particle Size 2.6 μ, σ 2.6, 6-hour Exposure

Rat No.	Upper	Middle	Lower	Rat Weights
1	28.3	21.5	25.0	312
3	30.0	32.6	33.3	314
4	20.4	4.6	18.9	261
5	22.0	16.8	22.9	279
6	27.3	22.6	22.6	305
8	44.9	37.7	48.7	275
10	19.3	11.8	26.6	300
12	13.8	32.8	12.7	295
15	30.6	26.7	28.4	285
20	43.8	34.3	37.2	267
Sum	280.4	241.4	276.3	
Av.	28.04	24.14	27.63	

[redacted]

TABLE 3

AVERAGE LOBE WEIGHT OF RATS*
(in milligrams)

Post Caval	134
UPPER RIGHT	136
Median Right	172
Lower Right	385
Left	438

* Rat weights averaged 280 g

either: (1) the tissue mass of the segments; or (2) by the lung weight and body weight as co-variants, no correlation of either sort was obtained. Moreover, lung weight to body weight showed a ratio of all specimens below 0.6% indicating no pathologic process was present that might influence the results; the normal lung to body weight ratio averages 0.5% for rats of our colony.

The importance of finding differences in lobar deposition is obvious in permitting a better estimate of tissue injury from inhaled particulates especially of radioactive character.

Conclusions.

1. A non-uniform deposition of particles of mass-median size 2.6 μ has been demonstrated in the lung of the rat after a single, 6-hour inhalation of U_3O_8; 1.5 to 2 times as much was deposited in the upper right lobe as in any other lobe of the lung.

2. Deposition was uniform in the other 4 lobes.

3. No appreciable differences in deposition were found in gross, transverse sections of the large left lobe.

[redacted]

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Problem Code: U.4 (Fate)

Section Code: 3210

Authors: C. W. LaBelle and J. M. Dohl

Radioactive Dust as a Tracer in the Study of Lung Transport Mechanisms. I. Analytical Methods.

A sample of radioactive dust is available which it is believed will facilitate the study of the transport of particulate material within the lung, provided that an assay method can be developed. The two requirements for such an assay method are first, that it be sufficiently rapid to permit measurement of a larger number of samples per day, and second, that it involve no assumptions as to the chemical species associated with the radioactivity, especially with respect to the solution and transfer of samples. The precision of the method, although important, is secondary to these other requirements. As a corollary requirement, it is desirable that the assay method be such as to permit decontamination of the apparatus and containers used in the process. It is believed that the methods described below offer satisfactory solutions to these problems.

Experimental. Preliminary tests showed that the following technique is adequate for the destruction of organic matter in a biological sample of the size contemplated, and in addition permits of the rapid handling of large

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numbers of samples with minimal attention.

The sample, weighing up to 2 grams on the wet basis, is removed from the animal and placed in a #0, low form, porcelain crucible. The tissue is covered with concentrated nitric acid, of which the volume may be varied to suit the size of the sample taken, and allowed to stand overnight. At this point the crucible contains a clear yellow liquid with only an occasional fat globule remaining of the original tissue. This liquid is evaporated at a low temperature (70-90°C) to a pasty residue which is finally charred on a hot plate until no more nitrous fume is seen. The crucible is then placed in a furnace at 700-750°C for one hour, at which time the ash is normally completely colorless or at least free of unburned carbon.

An adaptor was constructed by which crucibles could be inserted into the shielded counting chamber in such a way that the upper rim of the crucible occupied the position normally occupied by the foils used in conventional counting techniques. One milliliter of radioactive dust suspension was pipetted into each of nine crucibles, evaporated to dryness and counted. Each crucible was then re-evaporated with one milliliter of distilled water, evaporated with 5 milliliters of concentrated nitric acid and finally ignited for one hour at 700°C, counting each crucible between each operation. Finally, a series of nine foils were prepared from one milliliter samples of the original suspension, dried and counted in the conventional manner. The results are shown in Table 1 (Page 47).

The differences between foils and crucibles are due mostly to the completely different geometries involved in the two methods of counting and are no greater than might be expected. The difference between the crucibles before and after the chemical treatment represents a shift of $\frac{3602 - 3343}{\sqrt{192 \times 297 \times 9}} = 3.4$

[redacted]

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TABLE 1

USE OF PORCELAIN CRUCIBLES AS SAMPLE CARRIERS N = 9 SAMPLES

	Foils	CRUCIBLES			
		Orig. Count	Evaporated with Water	Evaporated with Acid	Ignited 1 hr. at 700° C
Mean counts per min.	9221	3602	3568	3710	3343
σ, 1 sample, cpm	618	192	175	168	297
Coefficient of variation* for 1 sample, %	6.7	5.3	4.9	4.5	8.9
Coefficient of variation* for 3 samples, %	3.9	3.1	2.8	2.6	5.1
Coefficient of variation* for 5 samples, %	3.0	2.4	2.2	2.0	4.0
Coefficient of variation* for 9 samples, %	3.2	1.8	1.6	1.5	3.0

* 100 x standard deviation/mean

STANDARD deviations and is probably just significant.

A further series of measurements was made in which twenty samples of dust of 0.3 milliliters each were pipetted into crucibles, and entire rat lungs added to ten of the samples. All twenty crucibles were ignited as described above and counted. The results are shown in Table 2 (Page 48).

The coefficient of variation of these samples is comparable to that of the preceeding series. Again there is a difference between the means which is just significant for groups of ten samples. In order to analyze this situation further, additional samples were prepared until a total of twenty activity-plus-tissue samples were available covering a range of 0.00 to 2.50 grams of tissue. The coefficient of correlation between recovery and tissue weight was computed

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TABLE 2

RECOVERY OF ACTIVITY IN THE PRESENCE OF RAT LUNG TISSUE, N = 10 SAMPLES EACH.

	Crucibles Only	Crucibles Plus Lung
Mean, counts per min.	866	796
Standard deviation, cpm	61	71
Coefficient of variation, %	7.0	8.9
Difference between means in standard deviation units	3.3	

and found to be:

$$r = \pm 0.15 \text{ , } (N = 20)$$

This implies that 15% of the variance is due to the effect of the added tissue, hence the variance not so accounted for is:

$$(71)^2(1.00 - 0.15)$$

$$= (71)^2(0.85)$$

$$= 4280$$

If the effect of the tissue were completely eliminated the standard deviation would be

$$\sigma = \sqrt{\text{variance}} = \sqrt{4280} = 65$$

Therefore we may conclude that the effect of added tissue on the scatter is negligible.

Finally, a series of measurements were made on the lungs, livers and kidneys of control rats to determine the normal radioactivity content as measured by this technique. The results are shown in Table 3 (Page 49).

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TABLE 3

RADIOACTIVITY IN LUNGS, LIVERS AND KIDNEYS OF CONTROL RATS

Organ	No. of Samples	Net Counts Per Minute	% of Background
Lung	10	1.2	6
Liver	10	2.1	10
Kidney	12	1.8	9

After the crucibles have been counted, they are treated according to the following schedule. Each contaminated crucible is rinsed with water and dropped into a bath of boiling 10% sodium carbonate solution for one hour. At the end of this time the crucible is rinsed and placed in a bath of warm 6 N HCl, where it remains overnight. The following day it is boiled in the same bath for 2-3 hours, changing the bath if it becomes badly stained. Finally, the crucibles are rinsed with hot water, polished and dried.

This procedure will reduce the activity in most crucibles to less than 50 counts per minute, of which about 25 counts per minute arise from contamination originally present in the porcelain. It is a curious fact that neither solvent bath alone, nor both together in the reverse order, will accomplish an adequate decontamination. When used as described the process leads to the following results.

Net mean count, original crucibles	24	
Net mean count before decontamination	3343	cpm
Net mean count after decontamination	51	cpm
Background	23	cpm

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Conclusions. A method is available by which the radioactivity from diverse sources present in a soft tissue may be measured with a precision of 6-8%. Recovery is slightly low, being about 90-92% on the average, but is probably as high or higher than could be obtained by other methods, because the method described here is largely independent of the chemical properties of the radioactive species which may be present.

A procedure is described by which the crucibles used may be decontaminated.

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PROGRAM F.

FLUORIDE

Problem Code: F.4 (Fate)

Section Code: 3210

Authors: F. A. Smith, D. E. Gardner, J. DeVoldre, R. E. Root, and D. Wing

Blood Fluoride Levels Following Exposure to Hydrogen Fluoride.

Previous studies on dogs exposed to hydrogen fluoride (UR-70) have indicated a considerable variation among maximal blood fluoride concentrations attained under comparable conditions of exposure; 11 to 53-fold increases above normal were noted, with maximal fluoride concentrations of 140-630 µg F/100 ml occurring on the 4-7 exposure days. Because of this somewhat wide variation, it was considered desirable to carry out a third exposure study in order to accumulate additional data relative to the variations to be expected among different dogs. Accordingly, two dogs were exposed for five consecutive days to an atmosphere containing approximately 19 mg HF/m^3. An aspirator-type feed system similar to that described by Stokinger, et al., (UR-68) was used. Blood fluoride determinations were made at regular intervals throughout the exposure period, and for 59 days thereafter. The data resulting are shown in Table 1 (Page 52).

It is again evident that maximal blood concentrations are reached only after exposure has continued for at least two days. It is apparent also that these peak levels are of the same order of magnitude as were encountered in previous exposures, being 18-27 times greater than the mean pre-exposure concentrations. Similarly, the post-exposure data are comparable to those obtained in the preceding ten-day exposure study; a minimum 60-day post-exposure interval

is necessary before the blood-fluoride concentrations are restored to pre-exposure levels. It is interesting to note that an interval of this magnitude is required in spite of the fact that the exposure period was only half as great as in the 10-day study.

TABLE 1

FLUORIDE CONTENT OF BLOOD OF DOGS EXPOSED TO HYDROGEN FLUORIDE 19 mg HF/m^3

Time Interval, Days	Microgram F per 100 ml Blood	
	Dog No. 1517	Dog No. 1534
Pre-Exposure Period		
-6	9.0	21.2
-4	19.4	9.2
Exposure Period		
+1	46.2	
2		391
3	267	
4		357
5	175	75.8 (not exposed)
Post-Exposure Period		
1	61.6	48.6
2	83.8	39.4
3	65.2	38.2
4	53.4	29.0
5	49.6	45.2
7	23.0	34.0
10	27.8	32.8
12	27.8	29.0
14	26.0	25.8
18	34.6	33.4
25	23.4	26.6
32	22.0	16.6
40	13.6	3.4
47	10.2	19.8
59	20.8	18.4

Problem Code: F.4 (Fate)

Section Code: 3210

Authors: F. A. Smith and D. E. Gardner,

Fluoride Levels in Blood and Urine of Industrial Personnel.

Continuing investigations into the toxicology of fluorides have now been extended to include a study of the concentrations of fluoride in the blood and urine of personnel engaged in the industrial production of fluoride compounds. Through the courtesy of Dr. Elmer R. Swanson of the Harshaw Chemical Co., Cleveland, there were obtained twelve spot blood and urine specimens from workers in that company's fluoride plants, together with an equal number of samples from office and laboratory personnel with none or negligible exposure to fluorides. The concentrations of fluoride found in these samples are indicated in Table 1 (Page 54). The mean concentration of blood fluoride in the control group was found to be 11.5 μg F/100 ml, with a standard deviation of 4.4, whereas the corresponding value for the exposed personnel was 30.4 μg F/100 ml, S.D. 10.8. The mean control urinary fluoride level was 0.30 mg F/l, S.D. 0.18 while that for the exposed groups was 11.3 mg F/l, S.D. 6.2.

The mean urinary fluoride level of 0.30 mg F/l for the control group is in reasonable agreement with the value of 0.38 mg F/l predicted from the data of McClure and Kinser (U.S. Pub. Health Rept., 50, 1575, 1944) for a concentration of 0.1 mg F/l in the community water supply. The mean concentration for four samples of Cleveland water was analyzed as 0.1 mg/l.

The blood fluoride concentrations for the control group are in general somewhat higher than have been encountered in control data collected in this community; in only four instances, however, are they greater than the maximal normal level previously noted (10 μg F/100 ml) for Rochester residents. In only

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TABLE 1

FLUORIDE CONTENT OF BLOOD AND URINE OF CERTAIN PERSONNEL OF HARSHAW CHEMICAL COMPANY, CLEVELAND, OHIO

Sample No.	Job Classification		Blood μg F/100 ml	Urine mg F/l
		CONTROL		
1		Physician	18.0	0.22
2	plant	analyst	14.5	0.12
3	plant	analyst	20.2	0.16
4	plant	accounting office	8.3	0.34
5	plant	accounting office	10.0	0.31
6	plant	accounting office	10.4	0.10
7	plant	accounting office	10.9	0.10
8	main office	main office	14.2	0.38
9	main office	research laboratory	9.5	0.74
10	main office	research laboratory	6.0	0.35
11	main office	research laboratory	9.2	0.45
12	main office	research laboratory	6.8	0.28
		EXPOSED		
13	plant	process man	25.3	20.4
14	plant	process helper	54.9	13.8
15	plant	maintenance helper	30.0	10.9
16	plant	chief process man	27.4	7.2
17	plant	process man	38.8	15.0
18	plant	process man	40.9	16.9
19	plant	chief process man	24.4	15.2
20	plant	process man	26.9	9.3
21	plant	process man	34.4	17.9
22	plant (hex area)	chief process man	25.3	4.8
23	plant (hex area)	chief process man	24.6	4.0
24	plant (hex area)	loader	11.8	0.57

Cleveland water sample (main gate)	#1 0.09 mg F/l	first group
" " " (in plant)	#2 0.11 mg F/l	of samples
Cleveland water sample	I 0.10 mg F/l	second group
" " "	II 0.09 mg F/l	of samples

one instance was the blood fluoride content of an exposed individual within the range (6.0-20.2 μg F/100 ml) noted for the control group.

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It is evident that there are significant differences between the means for the fluoride contents of the bloods and urines of the two groups of Harshaw personnel. The increased concentrations found for the exposed groups may be attributed to the greater concentration of fluorides present in the plant atmospheres in which these men work.

Problem Code: F.4 (Fate)

Section Code: 3210

Authors: F. A. Smith, H. E. Stokinger, L. T. Steadman and D. E. Gardner

Deposition of Fluoride and Beryllium in Animal Tissues Following Exposure to 2 mg BeF_2/m^3.

Analyses for fluoride and beryllium contents have now been completed in certain tissues of animals exposed to 2 mg BeF_2/m^3 (mist) for intervals ranging from 422 to 854 exposure hours. Beryllium and fluoride in blood were determined serially in each of four dogs during the course of the exposure, and fluoride determinations have been completed for the epiphysis, kidney, lung and liver at termination of the exposure (854 exposure hours). Similar determinations were carried out on skeletal and soft tissues of the cat after 422 hours of exposure. Fluoride determinations also have been completed on skeletal and soft tissues of rabbits taken at intervals up to 2.5 months after cessation of 422 exposure hours. A discussion of the results obtained follows. Descriptions of the exposure methods, together with the mortality, hematologic and biochemical findings have been reported previously (cf. R. H. Hall, et al., UR-116).

In Table 1 (Page 56) are listed the fluoride and beryllium contents found for serial blood samples of four dogs during the exposure interval

TABLE 1

FLUORIDE AND BERYLLIUM CONTENT OF BLOOD OF DOGS EXPOSED TO 2 mg BeF_2/m^3

Exposure Hours	Dog #1437		Dog #1518		Dog #1537		Dog #1538	
	µg F/ 100 ml	µg Be/ 100 ml	µg F/ 100 ml	µg Be/ 100 ml	µg F/ 100 ml	µg Be/ 100 ml	µg F/ 100 ml	µg Be/ 100 ml
368.1	26.4	-	37.2	-	22.4	-	42.7	-
398.1	8.1	-	23.8	-	15.2	-	17.8	-
458.1	21.1	2.2	14.4	2.7	16.9	3.8	15.1	7.3
512.1	1.1	-	10.4	-	6.5	-	20.6	-
614.1	23.6	8.3	20.9	5.6	19.0	14.0	15.3	13.0
668.1	16.9	3.8	17.8	3.5	15.0	3.2	14.2	4.5
704.1	16.0	4.4	11.7	4.2	10.0	4.5	22.9	6.1
722.1	18.3	6.4	20.4	8.5	12.7	5.3	17.8	5.5
848.1	22.5	4.0	26.3	4.5	22.6	3.1	20.6	4.8

207 calendar days of exposure

368-848 exposure hours.

It is evident that there is no progressive increase in either fluoride or beryllium content with continuing exposure. Because pre-exposure blood fluoride determinations were not made on these dogs, it is not possible to state to what extent these latter values are increased over the normal levels. However, during the past three years, 98 blood fluoride determinations have been made on normal dogs. These levels have ranged between 0 and 35 µg F/100 ml blood, with a mean level of 6 µg/100 ml; moreover, only 5 per cent of the values have been greater than 20 µg/100 ml and 72 per cent have been 10 or less µg/100 ml. Using these control data, it is apparent that exposure to 2 mg BeF_2/m^3 probably has elevated the blood fluoride levels of these dogs to some extent. However, only 2 of the total of 36 determinations are greater than the higher normal levels.

Were the beryllium fluoride inhaled by these dogs to be transported as the nondissociated compound, it would be expected that the quantities of beryllium and fluoride would be present (on a weight basis) in the ratio of

1:4. For dog 1437, it will be noted that the average weight ratio of beryllium to fluoride is 1:4.8, while for dog 1518, the ratio is 1:4.2. The agreement with the theoretical ratio is not quite so excellent for dogs 1537 and 1538 where the ratios are 1:3.4 and 1:2.9, respectively. The average ratio for the entire group of analyses is approximately 1:3.9. It will be noted that this computation is based on the total fluoride present, i.e., that fluoride present as a result of the exposure to BeF_2, together with that normally present from the dietary intake. Thus the actual ratio may not be as high as the calculated value indicates. These data suggest the possibility that the beryllium fluoride inhaled by these dogs may be transported in the blood in part as the nondissociated compound.

Table 2 below lists the fluoride contents found for the femoral epiphysis and kidney, lung and liver of these four dogs at sacrifice. Only one control

TABLE 2

TERMINAL FLUORIDE CONTENT OF TISSUES OF DOGS EXPOSED TO 2 mg BeF_2/m^3

Dog No.	FLUORIDE CONTENT IN PARTS PER MILLION			
	Epiphysis	Kidney	Lung	Liver
1437	4190	1.8	1.3	0.5
1518	2280	2.0	2.3	1.5
1537	2470	1.6	4.0	1.0
1538	2380	1.8	2.1	1.0

207 calendar days
142 exposure days
854.1 exposure hours

Nos. 1518, 1538:
11 day interval between end of sacrifice and exposure
Nos. 1437, 1537:
12 day interval

femoral epiphysis, and no soft tissues from control dogs are available for comparison. A single analysis of a control epiphysis showed 1930 ppm F (ash); dogs 1518, 1537 and 1538 are slightly higher in fluoride content; whether or not this is significant cannot be said in the absence of data relative to the variation to be expected among control dogs. Dog 1437 probably has a significantly greater fluoride content in the epiphysis.

The fluoride contents found for the kidney, lung and liver of the dogs do not differ significantly from those found for the exposed cats and rabbits (Tables 3 and 4, Pages 59 and 60). Moreover, all of these levels agree reasonably well with normal values for liver and kidney of the cow, guinea pig and calf as reported by McClure (Public Health Repts., 64, 1061, 1949).

Fluoride and beryllium contents of hard and soft tissues of cats at sacrifice are shown in Table 3; comparable fluoride data for one normal cat are also included here. The fluoride contents of the soft tissues of the treated cats do not differ significantly from those of the one control cat. The femurs of the exposed animals, however, show a definite increase in stored fluoride, as might be expected; the average increase is approximately two-fold over the one control femur available. No significant differences are noted among the fluoride contents of the soft tissues of the control and experimental animals. It may be shown that there is no molar relation of fluoride to beryllium in the lung, femur, liver and kidney.

The fluoride contents of hard and soft tissues of rabbits sacrificed serially after termination of the exposure are given in Table 4 (Page 60). The fluoride contents of the diaphyses do not change significantly with increasing post-exposure time. Because of the great variations noted between the epiphysis of the two rabbits at each post-exposure interval, no clear-cut downward trend

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TABLE 3

FLUORIDE AND BERYLLIUM CONTENTS OF TISSUES OF CATS EXPOSED TO 2 mg BeF_2/m^3(a)

No. and	001 3.6 kg		002 3.3 kg		604 2.9 kg		1204 3.0 kg		1426 2.6 kg		
Body Wt.	Be	F	Be	F	Be	F	Be	F	Be	F	Normal
Lung	7.1	10.9	5.1	1.4	5.3	1.3	17.6	0.9	6.8	0.5	0.9
Femur	1.2	950	2.64	840	2.2	920	2.2	1170	2.2	1380	560
Liver	0.66	0.3	1.83	0.3	0.45	0.8	0.65	0.6	0.57	0.7	0.5
Kidney	0.05	1.2	0.02	0.7	0.04	2.6	0.04	0.7	0.05	2.0	1.1

	BERYLLIUM		FLUORIDE		Calc. F from
	Mean	Range	Mean	Range	Mean Be
Lung	8.4	5.1 -17.6	3	5 - 11	36
Femur	2.1	1.2 - 2.6	110	56-164[b]	8.9
Liver	0.8	0.45- 1.8	0.5	0.3-0.8	3.4
Kidney	0.04	0.02-0.05	1.4	0.7-2.6	0.17

(a) Be expressed as μg/g fresh tissue; F expressed as μg/g fresh soft tissue, μg/g ash femur
(b) Excess from normal on wet weight basis

is apparent during the post-exposure period under study. Also, no control data are available for these tissues in this species.

The soft tissues show no significant differences, either among themselves or among comparable tissues of normal cows, calves and guinea pigs (McClure, loc.cit.).

Conclusions.

1. Exposure of dogs for 848 hours to BeF_2 at a concentration of 2 mg/m^3 produces a slight increase in circulating blood fluoride. Small quantities of beryllium are also encountered in this tissue. No progressive increase is noted, however, for either fluoride or beryllium with increasing exposure.

TABLE 4

FLUORIDE CONTENT OF TISSUES OF RABBITS EXPOSED TO 2 mg BeF_2/m^3

Rabbit No.	Post-Exposure Interval	FLUORIDE CONTENT IN PARTS PER MILLION				
		Epiph	Diaph	Kidney	Lung	Liver
300	Terminal	3900	2900	-	1.9	-
354	"	5470	3910	-	1.4	-
353	3 weeks	4900	3050	1.7	1.0	0.9
352	"	4030	2760	5.2	1.9	0.8
351	1.5 mos.	3710	3420	2.3	1.7	1.9
350	"	3630	2890	1.6	1.2	1.8
349	2.5 mos.	3870	2830	1.2	1.5	0.6

102 calendar days
70 exposure days
422.1 exposure hours

Nos. 300, 354: 4 day interval between end of exposure and sacrifice

2. The data suggest that inhaled BeF_2 may be transported in part in the blood in the molar ratio resembling that of the inhaled compound.

3. No significant changes from the normal are noted in the fluoride contents of soft tissues of dogs exposed for 848 hours, and of cats and rabbits exposed 422 hours to 2 mg BeF_2/m^3. Beryllium is found in the tissues of these animals, but no molar relationships can be demonstrated for the two elements in these tissues.

4. Increased deposition of fluoride is noted in the skeletal tissue of the dog and cat, and probably of the rabbit. However, there are insufficient data for control animals to permit an estimation of the magnitude of this increase.

5. The difficulty of interpreting these data quantitatively indicates the need for more such analyses of tissues of control or nonexposed animals.

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PROGRAM Zr.

ZIRCONIUM

Problem Code: Zr.3 (Toxic Limits)

Section Code: 3210

Authors: C. J. Spiegl, S. Laskin, and M. Calkins.

Current Status of Industrial and Experimental Zirconium Toxicity.

Summary of Findings from Spot Industrial Surveys of Two Zirconium Plants.

The current interest in zirconium and its compounds and the lack of literature on the toxicity of these materials has prompted further toxicologic investigations. Recent papers by DuBois (Arch. Ind. Hyg. and Occup. Med., 1, 637, 1950) and by Schubert (Science, 105, 389, 1947) (J. Lab. & Clin. Med., 34, 313, 1949) confirm previous reports as to the low order of acute toxicity of zirconium compounds administered orally or intraperitoneally.

TITANIUM ALLOY MANUFACTURING DIVISION OF NATIONAL LEAD (T.A.M.)*

In brief, the manufacturing processes employed at T.A.M. are the following:

I. Ore Cleaning - Crude Florida or Australian Ti-Zr sand is freed of ordinary SiO_2 sand at the mine.

II. Ore Separation - Electromagnetic-static separation is used for separation of ilmenite, rutile and zircon. Typical zircon (zirconium silicate) products are:

A. Crude

1. Zirconite sand "A"

2. Zirconite flour

* The T.A.M. plant in Niagara Falls was visited by Drs. Stokinger, Spiegl, Messrs. DeVoldre and Calkins for the purpose of observing the manufacture of zirconium compounds. Mr. R. A. Easton, Plant Manager, and Dr. Urban, Research Director, gave the group a background of the chemical and medical aspects of zirconium and arranged a comprehensive inspection of the production areas.

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B. Refined

1. "G" zircons

2. TAM zircons

3. Zircopax and superpax (small particle-size products)

Mixed products of zircon are also made. These are combinations with oxides of barium, calcium, magnesium or zinc tumbled together in a dry ball mill. Typical product - barium zirconium silicate.

III. Production of Zirconium Oxide from Zircon

A. Weighed amounts of zircon and coke are intermittently shoveled by hand during a 36-40 hour period into an open graphite-electrode crucible furnace until the furnace becomes full. This is a process evolving immense heat and copious quantities of smoke and fumes. The chemical reactions taking place include the conversion of carbon and silicon to their monoxides and burning of the monoxides to the dioxides. The zirconium silicate becomes zirconium cyanonitride (or a mixture of zirconium carbide and nitride).

B. The hot melt is treated in one of two ways:

1. It is covered and allowed to cool completely and is sent as the cyanonitride to another company for chlorination.

2. The melt is allowed to harden but while still red hot is placed on open grates where air by convection produces oxidation and decrepitation of the zirconium cyanonitride to crude zirconium oxides.

C. Crude zirconium oxide is heated in a rotating oil-heated furnace to remove residual carbon.

D. The oxide is ball-mill ground to various sieve sizes. Typical products are opax, treopax and CP zirconium oxide.

E. The oxide is mixed with oxides of barium, calcium or magnesium.

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Typical product is barium zirconate (ticon BZ).

IV. Zirconium chemicals are produced from the zirconium tetrachloride (Step B1) by hydrolysis of the compound and addition of the appropriate acid. These are vat processes producing zirconium sulfate, acetate, hydrate and hydrated carbonate.

Typical uses of zirconium compounds are:

1. In enamels and glazes
2. For production of refractories
3. Electrical insulators and dielectrics
4. Support for catalyst
5. Preparation of water repellent compounds for textiles and furs.
6. Possible future use as deodorant, poison ivy ointment and radio-opaque substance

Plant Samples. The major sites of possible atmospheric contamination at this plant were the furnace area and the cyanonitride oxidation room. Concentration samples were collected with a Filter Paper Dust Sampler and those for particle size with a Cascade Impactor. Sampling rates for both methods were 14 liters per minute. Analysis of the samples was made by the spectrographic method for zirconium. The filter paper samples were also analyzed for silicon content.

Ten-minute samples were taken by each of the methods in the furnace area under conditions that were considered typical. The filter paper dust sample showed a total of 190 micrograms of zirconium and only 6 µg (3.1%) of silicon. The calculated zirconium air concentration value was 1.4 mg/m^3. In comparison with this value, the air concentration level determined from total sample collected with the Cascade Impactor was of the same order of magnitude (1.9 mg/m^3). The results of the particle size analysis showed a typically normal distribution

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with a mass-median diameter of 1.51 μ, with a corresponding geometric standard deviation of 2.85.

The zirconium cyanonitride oxidation room was also sampled under typically normal conditions. The concentration data showed higher values with 3.6 mg/m^3 obtained by a filter paper sample and 7.8 mg/m^3 determined from the total sample collected with the Cascade Impactor. A total of 500 μg of zirconium was obtained on the filter paper sample but in this case less than 1 μg or approximately 0.14% silicon was found. Significantly larger particle size was present in this area. The distribution was typically normal for a mass-median diameter of 3.4 μ and a corresponding geometric standard deviation of 2.52.

If the particle size data are examined in terms of the sizes representing the physiologically toxic range of less than 1 μ (an assumption based on our experiemnts relating to the physiologic effects of small particles), the sample collected in the furnace area showed 35% of the mass concentration to be present in sizes below 1 μ, whereas the sample collected in the cyanonitride oxidation area showed only 7% of the mass concentration to be present below 1 μ. Recalculation of the probable effective air concentration, therefore, indicates values of the same order of magnitude for both areas, namely, 0.7 and 0.6 mg/m^3, respectively.

Four zirconium bulk samples were also obtained from the plant and subjected to physical analysis. The particle size and specific surface data obtained on these samples are shown in Table 1 (Page 65). The samples showed large differences in particle size as determined by optical microscope measurements, varying from a mass-median size of 2.39 μ for the pure $ZrCl_4$ to a value of 9.0 μ for the mass size of the zirconium cyanonitride. Since this latter value was so much higher than those of the other samples, the optical microscope measurement for cyanonitride was repeated. In this case a value of 8.8 μ was obtained for the

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TABLE 1

SPECIFIC SURFACE AND RELATED DATA FOR BULK ZIRCONIUM COMPOUNDS (a)

Sample Description	PARTICLE SIZE (c)				SPECIFIC SURFACE, m^2/g		Porosity
	Mass Median, μ	Geo. Stand. Dev. of Mass Median	Count Median, μ	Surface Median, μ	Calc. from Particle Diameter	By Ethane Adsorption	
TAM $ZrCl_4$, Z-135	2.4	2.1	0.38	1.4	0.29	(b)	
TAM ZrO_2, C, P, Z-135	3.5	1.9	0.90	2.3	0.13	3.8	29
TAM Superpax ZrO_2SiO_2 Fines	3.0	1.9	0.73	2.0	0.20	3.2	16
Dust from Bag Filter (d)	9.0	2.2	0.86	5.7	0.047	5.2	111

(a) Samples obtained from Titanium Alloy Mfg. Div., National Lead Co., Niagara Falls, N. Y.
(b) This sample was found to decompose under the high vacuum degassing required prior to ethane adsorption.
(c) Measurements by optical microscope based on a count of 1000 particles per sample.
(d) Air from zirconium cyanonitride burning room.

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mass median size, thus checking the original determination. Electron micrographs of these samples showed no unusual structure and in general confirmed the particle-size measurements by the optical microscope.

Specific-surface determinations by low-temperature adsorption of ethane are reported for all samples except $ZrCl_4$. The surface value of this compound could not be determined by the adsorption method because it decomposed under the high vacuum degassing treatment which is required prior to ethane adsorption. The specific-surface values of the remaining three zirconium compounds were in close agreement. It might be expected that the surface value for the Zr cyanonitride sample would be extremely low due to the large particle size; however, this sample showed the highest value of the three, indicating a relatively high "internal" surface. No evidence of such structure, however, could be demonstrated at an increased magnification to 18,500x. A porosity value of 111 for this sample indicates an internal surface at least 4 times as great as those of the ZrO_2 and $ZrO_2 \cdot SiO_2$ samples which showed porosities of 29 and 16, respectively.

Medical Histories. According to Dr. Urban, the incidence of illness among plant workers is rather low and does not differ from that of any other typical manufacturing plant in the industry. At present, a program of yearly x-ray examinations is in effect. Although this program has not been in effect during the entire 30 years of plant operation, only 2 cases of lung damage, of unproven origin, have been reported during this time. Working personnel averages approximately 200.

Summary and Conclusions. No unusual industrial hazard problems were found at this plant. Although zirconium concentrations of 1.4 and 3.6 mg/m^3 were found by the Filter Paper Dust Sampler under typical conditions, calculations showed that these concentrations represent values of only approximately 0.6 and

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0.7 mg/m^3 of probable physiologically-active material. The low incidence of industrial disease under these plant conditions does not suggest that a major, acute toxicity problem exists with these compounds.

FOOTE MINERAL COMPANY*

Processes employed by this firm are the following:

I. Formation of the $POCl_3$ Complex - zirconium tetrachloride obtained either from the local plant or from other sources is placed into a round-bottom, pyrex flask and is allowed to react with liquid $POCl_3$. Exposure to zirconium tetrachloride is minimized by providing adequate air ventilation and exposure to $POCl_3$ is essentially prevented by using a closed system.

II. Distillation - the $ZrCl_4 \cdot POCl_3$ complex is distilled in a large glass column at a head temperature of 355-360 C. During the 30-hour period of a cycle various fractions are collected; and by re-cycle and re-distillation a special high-purity, low Hf fraction is obtained.

III. Production of $Zr(OH)_4$ - Propyl alcohol (C_3H_7OH) is introduced under N_2 pressure into a pyrex flask containing purified complex at 80 C. Nitrogen pressure forces the liquid into a vat containing hot water. The addition of NH_4OH, with a stirring, causes precipitation of zirconium hydroxide. After settling, the $Zr(OH)_4$ is washed three or four times with distilled water and placed into silica trays.

IV. Formation of ZrO_2 - the silica trays containing the zirconium hydroxide are placed in a furnace, having ventilation, to form the oxide.

Plant Samples. The major site of possible atmospheric contamination at both the research and pilot plant was in the area of the distillation column

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* Drs. Stokinger, Spiegl, Messrs. DeVoldre and Calkins visited the research laboratory of the Foote Mineral Company at Berwyn, Pa., and the manufacturing plant at Paoli, Pa. Dr. S. G. Ogburn, Manager of Research and Development, and his associate, Mr. Fisher, made arrangements for us to discuss the processes and to visit appropriate sampling sites.

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head. Samples for both concentration and particle size were collected with the Cascade Impactor at a sampling rate of 14 liters per minute. The atmospheric contaminant appeared to be an occasional wisp of cloud, indicating mist or vapor. Although the actual compound present may be a $ZrCl_4 \cdot POCl_3$ complex, or a hydrolysis product, the samples were analyzed spectrographically only for zirconium content.

In the laboratory at the still head of a research-scale process, a sampling time of 65 minutes was needed. An atmospheric concentration of 0.034 mg/m^3 was determined from the total sample collected. A normal particle size distribution was found with a mass median diameter of 1.25 μ and a corresponding geometric standard deviation of 2.08. Thirty-nine per cent of the mass concentration was found to be below 1 μ particle size. The probable physiological effective air concentration was therefore calculated as 0.013 mg/m^3. A corresponding sample was taken at the still head of the large-diameter glass distillation column used in the pilot plant. In this area, a sampling time of 32 minutes was used. The air concentration of 0.044 mg/m^3 obtained was not considered significantly higher than that obtained in the research area. Particle sizes were larger, however, with a mass median diameter of 2.29 μ and a corresponding geometric standard deviation of 2.26. For this sample, only 16% of the mass concentration was present in sizes below 1 μ, resulting in a probable physiologically effective concentration of 0.007 mg/m^3.

In order to provide a sample of momentarily high concentration typifying a still block or blow, a one-minute sample was taken during a deliberately simulated condition. For this sample, an atmospheric concentration of 20.6 mg/m^3 was obtained in the immediate vicinity of the still head. Particle size distribution showed that the increase in concentration was accompanied by the production of larger particulates. A mass median diameter of 4.30 μ and a

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corresponding geometric standard deviation of 1.91 was obtained. The percentage of mass concentration below 1 μ was very low (1%), resulting in a physiologically effective value calculated as 0.206 mg/m^3.

Medical. The operations are carried out under adequate ventilation. Any exposures that may occur result mainly from leaks at joints or accidental breakage of apparatus. The principle hazard appears to include exposure to $POCl_3$ at the still head; this has caused minor throat irritation and symptoms typical of a common "head cold" that may persist for two or three days. Exposures to Zr compounds are limited to the vapor of the complex at the still head, to periodic charging of still-pot with $ZrCl_4$ and to the manual handling of the insoluble zirconium hydroxide and oxide. During December, the process was entirely on a pilot plant scale.

Summary and Conclusions. Because of the newness of the process and the relatively small number of people employed, no adequate estimate can be made of the hazards involved. Concentrations in both research laboratory and pilot plant areas indicated extremely low values in the order of 40 μg/m^3. Smaller particle sizes were indicated in the research laboratory areas than in the pilot plant (MMD 1.25 - 2.29 μ).

EXPERIMENTAL RESULTS ON THE INHALATION OF ZIRCONIUM COMPOUNDS.

Animal inhalation experiments with a concentration of zirconium tetrachloride considerably greater (20.5 mg/m^3) than that found in the plants confirms the preliminary estimate of the relatively low acute toxicologic hazard of zirconium compounds.

Zirconium tetrachloride was chosen for the initial 60-day inhalation study because of its widespread industrial usage, solubility in water and relative ease of analysis by the spectrographic method. Time-consuming difficulties with

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dry dust feeds forced the use of an aerosolizer and a solution of $ZrCl_4$. Presumably, this solution contained $ZrOCl_2$ instead of $ZrCl_4$, but probably represents an approximation of the behavior of $ZrCl_4$ in air. The atmospheric concentration of $ZrCl_4$ was maintained at a level of 20 mg/m^3 and an average mass median diameter of 0.57 μ and standard deviation of 2.62.

The operation of the chamber followed established Rochester procedure. Animals were exposed for 6 hours on each week-day. During this time, hourly filter paper dust samples were weighed as a guide to atmospheric concentrations. In addition, one sample daily was analyzed spectrographically for the Zr content. Weekly Cascade Impactor samples were analyzed spectrographically for the size-distribution of the zirconium in the chamber air.

A total of 8 dogs, 4 cats, 20 rabbits, 20 guinea pigs and 72 rats were exposed. Of these, 4 dogs, 20 rats and 10 rabbits will later also be exposed to ZrO_2 in an attempt to utilize the cumulative effects of acute exposures to simulate a chronic.

Weekly urinary protein determinations on 4 dogs and 4 rabbits gave only slight, variable results.

Weekly blood nonprotein nitrogen studies on the same 4 dogs and 4 rabbits gave inconclusive results. The dog blood fibrinogen levels similarly were normal.

The 4 dogs examined hematologically semi-monthly showed progressive decreases in the count of the red blood cells and an increase in mean corpuscular volume. Maximal blood changes in dogs were seen at periods as early as 10 days and as late as 52 days after the start of exposure; decreases of red cell counts approximated 1.5×10^6 cells/cu mm; hemoglobin decreased about 4 gm; mean corpuscular volume increased 11 to 16 cu μ. One month after exposure, blood

[redacted]

[redacted]

values were within the normal range. Other variables appeared to change at random. Weekly weight records showed little except for a transient loss of weight among the guinea pigs. No histologic pathology is yet available on the 44 animals of 5 species sacrificed terminally nor on 15 rats sacrificed serially during exposure. Grossly, the only evidences of damage were hemorrhage and consolidation of the lung of a few dying rats and guinea pigs. Members of a group of 20 rats are being sacrificed at intervals up to 48 weeks after exposure to determine tissue repair rate and zirconium disappearance rate. The tissues being studied histologically include a complete autopsy for the dog, cat and rat. Lung, liver and kidney only are being taken from the rabbit and guinea pig.

Analyses for zirconium are being made of the lung, liver and kidney of all animals plus the pulmonary lymph node and femur from dogs, cats and rats.

A group of 10 rats and 10 rabbits was handled in a manner similar to that of the exposed animals with the exception that these received no zirconium aerosol. These animals serve as a base-line level for control of unknown factors influencing the criteria studied.

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UNCLASSIFIED

PROGRAM I.S.

ISOTOPES

Problem Code: I.S.3 (Therapy)

Section Code: 3310 and 3340

Authors: W. B. Mason and J. R. Hayes

Approximately nine months ago a cooperative program was instituted which would make radio-isotopes available to private physicians in the community. Briefly this plan is for private physicians to refer patients for diagnostic studies or therapy to the radiology departments of the cooperating hospitals. The patient's case is then reviewed by the Isotope Committee of that hospital, and the necessary isotope is requested in a form suitable for administration to the patient. To date, most of the work has been with I^{131} and the Clinical Chemistry Section, in addition to standardizing the isotope and preparing it for administration, has also carried out the laboratory work necessary for urinary I^{131} studies, with the understanding that this portion of the work will be taken over by the cooperating hospitals as soon as conditions permit.

The present brief report deals only with the laboratory part of the program. During the last six months approximately 160 requests for I^{131} have been filled, and urine studies have been done in almost all instances. The usual practice is to collect three urine specimens, corresponding to 0-12 hours, 12-24 hours, and 24-48 hours after administration of the isotope. The I^{131} content is determined by a procedure involving comparison with I^{131} standards. This technique eliminates decay corrections, and is advantageous in other respects.

During the course of the present program, repeat urinary excretion

studies have been done on a fair number of patients, and on the basis of these cases it is possible to arrive at a tentative estimate of the reliability of urinary I^{131} measurements. The data are from 26 patients receiving both tracer and therapeutic amounts of I^{131}, who showed no clinical evidence of thyroid instability over the period of less than two months between the two studies. These patients all had the tracer dose (usually 50 microcuries) before the therapeutic dose (6-20 millicuries), and there was no reason to suspect incomplete urine collections. The data are not otherwise selected. The standard deviation between the two values for the total 48 hour urinary I^{131} for these patients is 11%. Perhaps a more useful form of this figure is that the mean urinary I^{131} for a given patient will be within ± 20% of the reported figure in 90% of the cases. An example or two will make the application clear. Suppose that 15% of a tracer dose of I^{131} is recovered in the urine collected during the first 48 hours following administration. In the absence of evidence to suggest incomplete urine collection, there is a 90% chance that the mean urine output of I^{131} lies between 12% and 18%, and interpretation is quite clear provided the clinical picture is not strongly against the diagnosis of hyperthyroidism. In another instance, suppose 40% of the tracer dose is recovered in 48 hours. Here there is a 90% chance that the mean output lies between 32% and 48%, and interpretation will depend a great deal on the clinical picture. As more data are collected it may be necessary to modify the above figures, but for the present they are useful.

In an attempt to detect the presence of possible aberrent or metastatic thyroid tissue, I^{131} urinary excretion studies have been carried out on a patient during the early postoperative period following total thyroidectomy for carcinoma. Eighty microcuries of I^{131} were administered and the patient had

an in-dwelling catheter to insure complete collection of urine. I^{131} studies under such circumstances are relatively uncommon, and the data are reported in full.

Collection Period	Urine Volume	I^{131} Recovered
1st 6 hrs.	667 ml.	39.5%
2nd 6 hrs.	610	27.1
2nd 12 hrs.	385	17.3
3rd 12 hrs.	588	10.0
4th 12 hrs.	300	2.5
	Total	96.4%

The uncertainty in the determinations is believed to be in the neighborhood of 10%, and the results are compatible with complete absence of active thyroid tissue.

A laboratory training program has recently been conducted for the interested personnel of the cooperating hospitals, and these groups are now gradually taking over the determination of I^{131} in urines. The Clinical Chemistry Section will continue to do the standardizations and prepare the I^{131} for administration to the patients, as well as to check the urine determinations from time to time.

UNCLASSIFIED

PROGRAM I.N.

INSTRUMENTATION (SPECTROSCOPY, ELECTRON MICROSCOPY, X-RAY AND NUCLEAR RADIATION DETECTORS, X-RAY DIFFRACTION, ELECTRONICS)

Problem Code: I.N.1 (Research and Development)

Section Code: 3110

Author: A. H. Dahl

Quality Evaluation of X-ray Beams by Metal-walled Ionization Chambers.

Background. For several years the writer has been thinking about developing a simple, reliable system for quality evaluation of a heterogenous beam of x-rays. The systems of half-value-layer, effective wavelength, and effective energy at best give information only about the primary beam and not the primary plus scattered beam which is actually producing the exposure. In addition, the process of obtaining an absorption curve presents many pitfalls to anyone but the experienced radiologist and physicist. This was clearly demonstrated to the writer in reviewing some selected past results at Rochester where special studies were made to obtain low intensities and as monochromatic a beam as possible with high amounts of filter (results not published). In attempting to obtain the half-value-layer under these high amounts of filtration, the results showed high values; and the recent estimation of the effective energy from the former results showed that the effective energy would calculate to be much higher than the peak voltage of the x-ray machine. This was obviously not possible. The reason for this error was that a considerable portion of the exposure recorded by the ionization chambers was produced by photons which had been scattered around the filters. These errors were not detected since an effort was made only to obtain the "half-value-layer" and the effective energy was not calculated. This also emphasizes

the fact that the half-value-layer can, in some cases, be very unreliable and that in many cases the half-value-layer may have no real significance to the person making the study.

Method. The system of quality evaluation under consideration by the writer is that of determining the ratios of readings from ionization chambers containing inner linings of various materials. During the early days of quantity measurement of x-ray beam output much effort was expended in determining the criteria for fabricating energy independent ionization chambers. In fact, the standardized use of ionization chambers in quantity measurement of x-rays was delayed for nearly two decades due to the energy dependence of the various chambers used in addition to the poor quality of accessory voltage-measuring devices. The proposed method of quality evaluation makes use of the energy dependence of chambers which incorporate metal liners of average atomic number greater than 11.

The first studies were made using x-ray machines operated in the range of 100 k.v. peak to 250 k.v. peak. Liners of aluminum and copper were placed in some 0.25 r condenser r meter chambers purchased from the Victoreen Instrument Company. In the case of aluminum liners the metal thickness of 1 mil, 2 mil, and 5 mil were used and the liners were constructed so that they would fit snugly against the inner walls of the condenser r meter chambers. In the case of copper liners the thicknesses used were 1.5 mil, 2.5 mil, and 4.5 mil. Comparison of the readings of the chambers with the aluminum liners to the readings from condenser r meter chambers which had no liners and could be considered as "air-wall", showed that as filter was added in the port below the x-ray tube the ratio first increased when the thinnest filter was placed in the port and then the ratio decreased gradually. It had been expected that

the ratio would decrease continually from no filter to heavy filtration since the ratio of absorption of x-rays by aluminum to that of carbon, nitrogen, and oxygen (characteristic of tissue and air absorption) would decrease with increasing effective energy of the x-ray beams. The first increase in ratio from no filter to light filtration was considered to be due to the fact that, under conditions of no filter external to the tube, the effective energy of the x-ray beam was very low. Since the chambers were approximately $1\frac{1}{2}$ inches in diameter and the range of the electrons released from the chamber walls was less than the chamber diameter, we did not have total wall effect in the chambers. In order to have the system work properly the wall effect must be greater than 90 per cent of the effect producing the ionization in the chambers.

For this reason pocket personnel chambers which were purchased from the Victoreen Instrument Company were reamed out such that metal liners could be inserted into the chambers. The liners were made such that the inside diameter of the liners were equal to the original inside diameter of the pocket chambers. With these chambers it was found that the greater share of the ionization produced within the chambers was produced by the electrons released from the walls in the range of x-ray peak voltages from 100 k.v. to 250 k.v. and filter thicknesses greater than 0.25 mm of copper. Even at low filtration most of the ionization in the chamber was produced by electrons released from the walls. Therefore, ionization chambers with inside diameters less than one centimeter could be used in this type of quality evaluation in the x-ray peak energy range of 100 to 250 k.v.

In studying the results of the ratio of aluminum-lined chambers to "air-wall" chambers it was noted that the ratio increased with decrease in the effective energy of the x-ray beam, as was expected theoretically. The purpose

of using the metal liners in the chambers was that theoretically the number of electrons released from the aluminum lining would be proportional to the x-ray energy absorbed and this in turn would bear a relation to the effective mass absorption coefficient provided that the liner thicknesses were approximately equal to the range of the most energetic electrons released from the aluminum. In addition the electrons released into the "air-wall" chamber would bear a relation to the effective mass absorption coefficient for air. In the range of 100 to 250 k.v. peak the optimum thickness of aluminum liner was found to be 2 mil with the 1 mil and the 5 mil liners each giving 5 to 10 per cent less ionization within the chamber.

At present the method of quality evaluation, which is being utilized in studying filter and scatter conditions under peak x-ray energies of 100 to 250 k.v., consists of determining the ratio of readings from a 2 mil aluminum-lined chamber to an "air-wall" chamber and using the ratio only as an indication of the effective energy. Further studies are continuing in an attempt to assign an effective energy to the ratio of the chamber readings. Experiments to date have also indicated that in the range of 100 to 250 k.v. peak, copper liners should not be used since the copper gives excessive weight to low energy photons and also the ratio of copper to "air-wall" chambers becomes so high under certain conditions that the ratio cannot be determined very accurately with one simultaneous exposure. Studies have also indicated that the system is not very useful in the range below 100 k.v. peak due to the short range of the electrons released from the walls. However, for therapeutic uses most x-ray machines will be operated well above 100 k.v. peak and some filter is also used with the machine. In quality evaluation around the 100 k.v. peak x-ray machine ratios of copper-lined to "air-walled" chambers were used at

first and recently the ratio of tin-lined to copper-lined chambers have also been used to avoid the excessive weight the copper or tin liners give to the low energy photons relative to the weight given by "air-wall" chambers.

Results. The primary application for the system was found to be in the quality evaluation of the 1000 k.v. peak x-ray machine. There the problem of reducing the radiation around the filters in making an absorption study is multiplied several fold since the energy of the radiation is so high. In the studies an absorption curve was first made with the filter near the end of the x-ray tube. However, it was mounted approximately 4 inches below the one foot thick concrete ceiling which surrounded the x-ray tube. As shown on curve A of Figure 1 (Page 80), a straight line portion could not be obtained on a semi-log plot of the absorption curve even up to 1½ inches of lead. Simultaneous with the gathering of data for the absorption curve, the ratio of readings of a copper-lined chamber to an "air-wall" chamber was obtained and the results are shown in curve A of Figure 2 (Page 80).

As previously stated, the lower the ratios of readings of the copper-wall to "air-wall" chambers, the higher is the effective energy producing the exposure on the chambers. As shown by curve A of Figure 2, the first ¼ inch of lead filter made the beam slightly higher in effective energy. However, further additions of lead filter made the effective energy much lower. This indicated that curve A of Figure 1 was not a reliable absorption curve since considerable scatter was coming around the side of the filters. An attempt was then made to reduce the scatter around the filter and this was first done by moving the filter close to the x-ray tube such that the bottom lead filter was flush with the bottom of the concrete ceiling. Curves B of Figures 1 and 2 resulted. Following this a one foot wide, ½ inch thick strip of lead was

Figure 1. - Absorption curve for lead on 1000 k.v.p. machine

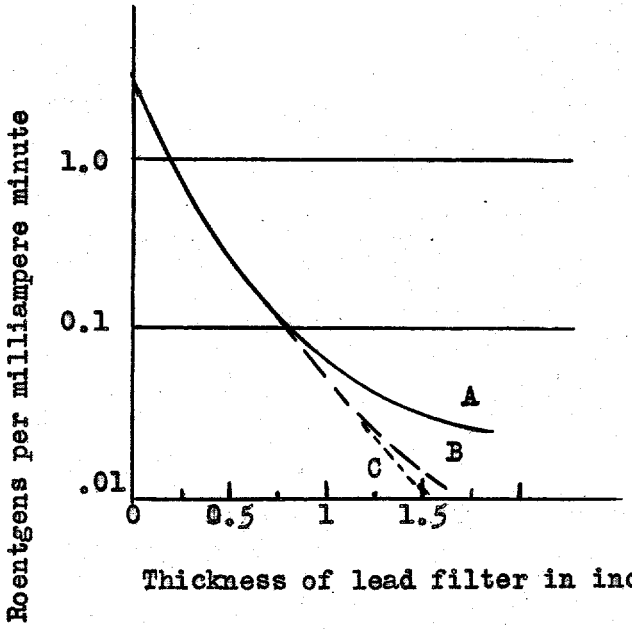
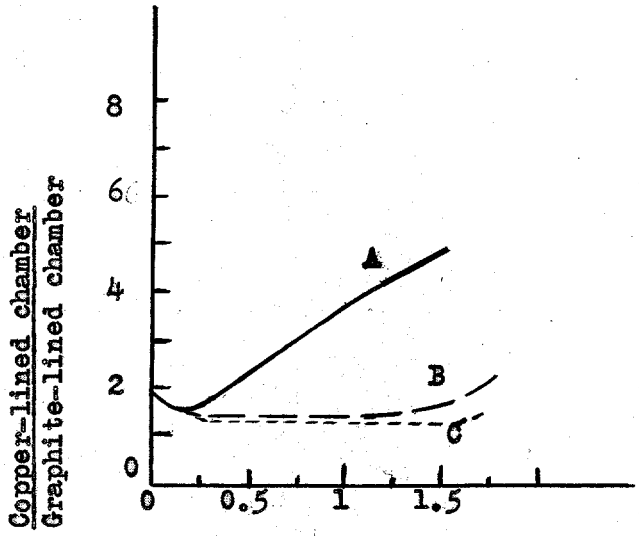


Figure 2. - Ratio of copper-lined chamber readings to graphite-lined chamber readings



mounted on the concrete ceiling around the port opening into the exposure room. Below this a $\frac{1}{2}$ inch thick sheet of lead was mounted over the port with a 6 inch diameter centered hole thereby acting as a diaphragm for the x-ray beam entering the exposure room. The absorption curve was then determined with the filters mounted above the diaphragm and curves C of Figures 1 and 2 (Page 80) were obtained.

In another application a study was made of the effective energy variation between locations near the diaphragm mounted on the ceiling and the various positions between the ceiling and the concrete floor of the exposure room (the exposure room being approximately 9 feet high). The ratios of tin-lined chambers to copper-lined chambers varied from 1.2 near the diaphragm to 1.6 on the floor. There was a continuous increase in these ratios as the chambers were moved from the ceiling to the floor of the exposure room. This indicated that the floor was producing a great deal of scatter. Four feet by four feet pieces of lead of various thicknesses were placed directly beneath the metal chambers which were mounted one foot above the floor; and it was found that 1/8 inch of lead reduced the ratio from 1.54 to 1.34. Further thicknesses of lead on the floor would not decrease this ratio thus indicating that lead of 1/16 inch maximum thickness would be very helpful in reducing the scatter from the floor and making the exposuring beam the hardest possible for any one condition.

Conclusions. The above results demonstrate that using the ratio of readings from chambers having different metal liners can be of great assistance in assuring that the maximum effective energy of an exposing x-ray beam is obtained. The ratios alone can be used as a measure of the hardness of the exposing beam similar to the use of the half-value-layer. It is felt that

through further studies the ratio of chamber readings can be correlated with a "biological effective energy". A preliminary report will be released in the near future giving more details of the theory of the system.

Problem Code: I.N.1 (Research and Development)

Section Code: 3110

Authors: J. W. Kanwisher and W. F. Bale

Ionizing Radiation Dosimeter.

Background. This report indicates the feasibility of a new type of high range ionizing radiation dosimeter, commonly known as a casualty dosimeter. This dosimeter is based upon the increase in conductivity in the water layer of a water-carbon tetrachloride or water-chloroform system sealed in a fountain-pen-sized, light-opaque, pyrex-glass-lined capsule. Dosage is read by a portable electronic device based upon the Q-meter in principle, increasing conductivity following irradiation produces correspondingly greater electrical losses in the meter circuit. These losses are read on a dial calibrated in r units.

This instrument is frankly based upon the colorimetric dosimeter developed by Taplin and Douglas (1,2). Taplin and Douglas have developed, in a preliminary form, a dosimeter based upon the reported linear relationship between the acid evolved from chloroform and the energy absorbed by it. A two phase system measures the acid produced colorimetrically. After radiation, the acid liberated diffuses into the aqueous phase, reducing the pH and changing the color of the dye (brom cresol purple). Compared with its Taplin and Douglas prototype it has several probable advantages and at least one potential

disadvantage.

1. In the Taplin and Douglas instrument the color change occurs chiefly at one value of dosage. Thus a separate chamber must be included for each dosage that it is desirable to measure. In contrast one liquid chamber in our instrument is sufficient to measure any radiation dose from 50 to 1,000 r.

2. Our instrument has the light excluded even during dosage reading. It contains only two components, water plus chloroform or carbon tetrachloride. In contrast the prototype Taplin-Douglas instrument contains in addition a pH sensitive dye and must be observed visually for reading purposes. It has not yet been conclusively proven that this dosimeter is stable for periods of months or years under these conditions. The simple two phase system with light excluded has potentially a longer period of usefulness.

3. Our instrument reported here needs an auxillary electronic instrument for reading purposes, not required with the visually read Taplin-Douglas instrument. Such a reader, it is believed, can be developed that will not be expensive to construct, light weight, and easy and rapid to use, possessing the advantage of giving exposure directly on a calibrated meter. With one meter many dosimeters can be read, probably as rapidly as 5 seconds per individual dosimeter.

Method. This work was based upon the idea that the developmental program of Taplin and Douglas on a dosimetric dosimeter might be usefully supplemented if a reader could be produced independent of visual observation and without the incorporation of a dye. It was felt that these two factors might limit the stability and accuracy of the Taplin and Douglas instrument.

Our initial idea was that pH or conductivity might be read by electrodes permanently sealed into a glass capsule containing the two liquids. Both of

these effects are of a magnitude subject to easy measurement. For example, our measurements in preliminary experiments showed a change in pH of the water layer from 6.05 to 3.4 when approximately one to one ratios of water and chloroform were irradiated with 500 r of x-rays from a 200 peak k.v. generator. Similar experiments with C Cl_4- water filled tubes gave pH changes of 6.1 to 4.0 following 500 r. Such order of magnitude results are consistent with data reported by Taplin and Douglas.

Measurements of conductivity in water following the irradiation with a 450 r dose of equal volume mixtures of $CHCl_3$ and water show changes in conductivity of from 30,000 ohms for non-irradiated controls to 400 ohms following irradiation.

As a means of reading electrical conductivity of prototype dosimeter tubes with built-in electrodes, a light portable battery-powered AC bridge was constructed. A 1,000 cycle oscillator utilized a 1S4 tube. Detection of bridge unbalance was made with earphones. No amplification was necessary. This reader, complete with batteries, weights about one pound.

The problem of a design of dosimeter with built-in conductivity electrodes, cheap and easy to manufacture, has, however, not been solved. The apparent necessity of using platinum electrodes, fabricated with fair precision and sealed in pyrex glass, suggested that this dosimeter may be somewhat more expensive to produce than is desirable.

When preliminary experiments indicated that by utilizing radio-frequencies in the neighborhood of 10 megacycles, the use of internal electrodes might be entirely eliminated, work was extended in this direction.

Studies on Radiofrequency Detection of Conductivity. To achieve maximum usefulness an individual casuality-type dosimeter ought to be cheap,

manufacturing cost under a dollar and preferably not more than a few cents, easily manufactured, rugged and with a long "shelf" life. Providing a satisfactory "reading" apparatus can be developed, a dosimeter in which conductivity is read by radiofrequency means without electrodes sealed into the liquid compartment has distinct advantages. The dosimeter is reduced to the simple form of a small pyrex glass tube, probably encased in a thin envelope of opaque plastic to prevent exposure to visible and ultraviolet light and to add ruggedness to the dosimeter.

To investigate the feasibility of radiofrequency conductivity measurements a commercial type radiofrequency bridge was utilized with a standard signal generator and receiver equipped with an "S" meter. Typical of capsules tested were pyrex tubes 10 inches long, 1 inch in diameter, 7/8 filled with equal parts of carbon tetrachloride and water. A typical frequency used was 5 megacycles. The water phase was placed inside a coil, 30 turns and 4 inches long which made up the unknown arm of the bridge. Separate readings of L and R were obtained. The L readings, in general, were constant for a given coil and geometry of dosimeter tube. The R reading obtained depended upon the radiation dose that the dosimeter has received. It seemed obvious that a reader of this type could be developed sensitive to a radiation dose of 25 r or less. It probably would be entirely feasible to develop portable reading apparatus based upon this principle.

Study of a Q-Meter Type of Detector. It was noticed that the L and R readings on the bridge could be interpreted in terms of the Q of the coil in which the dosimeter is inserted. Changes in conductivity give rise to changes in Q. The feasibility was, therefore, investigated of constructing a dosimeter reader based upon the principles of the Q-meter such as Boontown

model. In principle such a reader consists of a radiofrequency oscillator feeding a signal into a coil into which the dosimeter tube fits. With the dosimeter in the coil and the coil circuit tuned to resonance, the voltage developed across the coil is the original fed voltage multiplied by Q. This final voltage is read by a high impedance vacuum tube voltmeter. Increases in dosimeter fluid conductivity would be indicated as decrease in this output voltage read by the vacuum tube voltmeter.

A dosimeter reader based upon this principle has been developed and found to have adequate sensitivity for the desired purpose. Figure 1 (Page 87) gives schematically the circuit now in use. Figure 2 (Page 88) shows the first portable model constructed. The oscillator is a feedback type employing a 1S4 tube. Coupling to a low impedance load is accomplished by a single turn on the coil form. The oscillator frequency is 10 megacycles.

The coil in which the dosimeter tube is inserted is $1\frac{1}{2}$ inches long and wound on a 1/32 inch wall polystyrene form with a $\frac{1}{2}$ inch center hole. Winding is 22 gauge enameled wire. Dosimeter tubes now in use are fabricated from standard 10 millimeter pyrex tube. They are $4\frac{1}{2}$ inches long, filled 7/8 full with equal parts carbon tetrachloride and water or chloroform and water. The tube is inserted until the water phase, which floats on the chloroform or carbon tetrachloride, occupies the space within the coil.

A standard electrometer type of circuit was adapted for use as the vacuum tube voltmeter. This provides the necessary high impedance input to prevent loading down the coil. The tube is biased well below cut-off. Changes in the electrometer tube bias can be used to vary the sensitivity of the meter in terms of indicated radiation. Conductivity changes produced by radiation doses of 50 r can be easily measured with this unit.

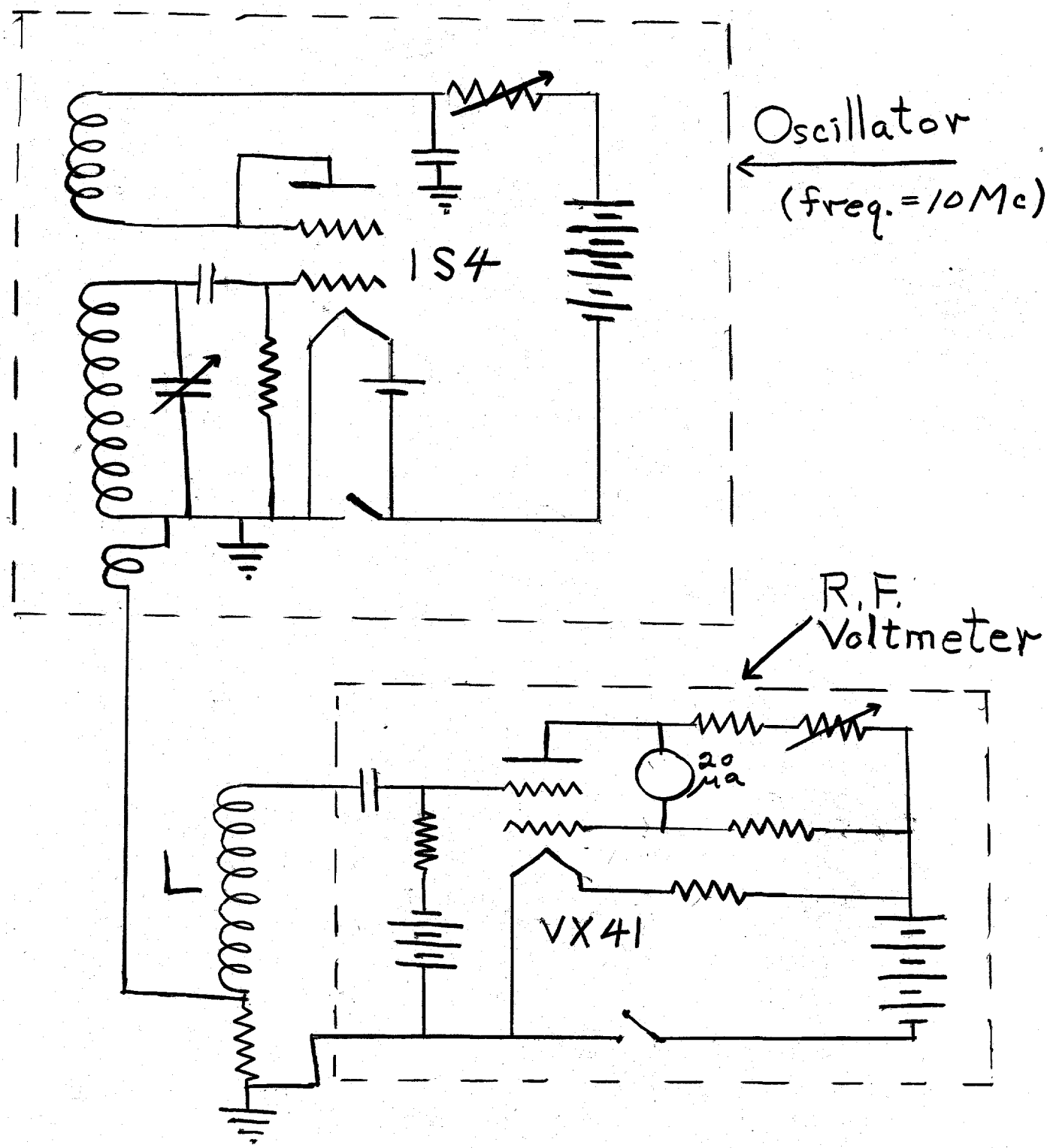


Figure 1

Q Meter Circuit. The change in "q" of the coil L is interpreted in terms of dose received by the capsule inserted in L.

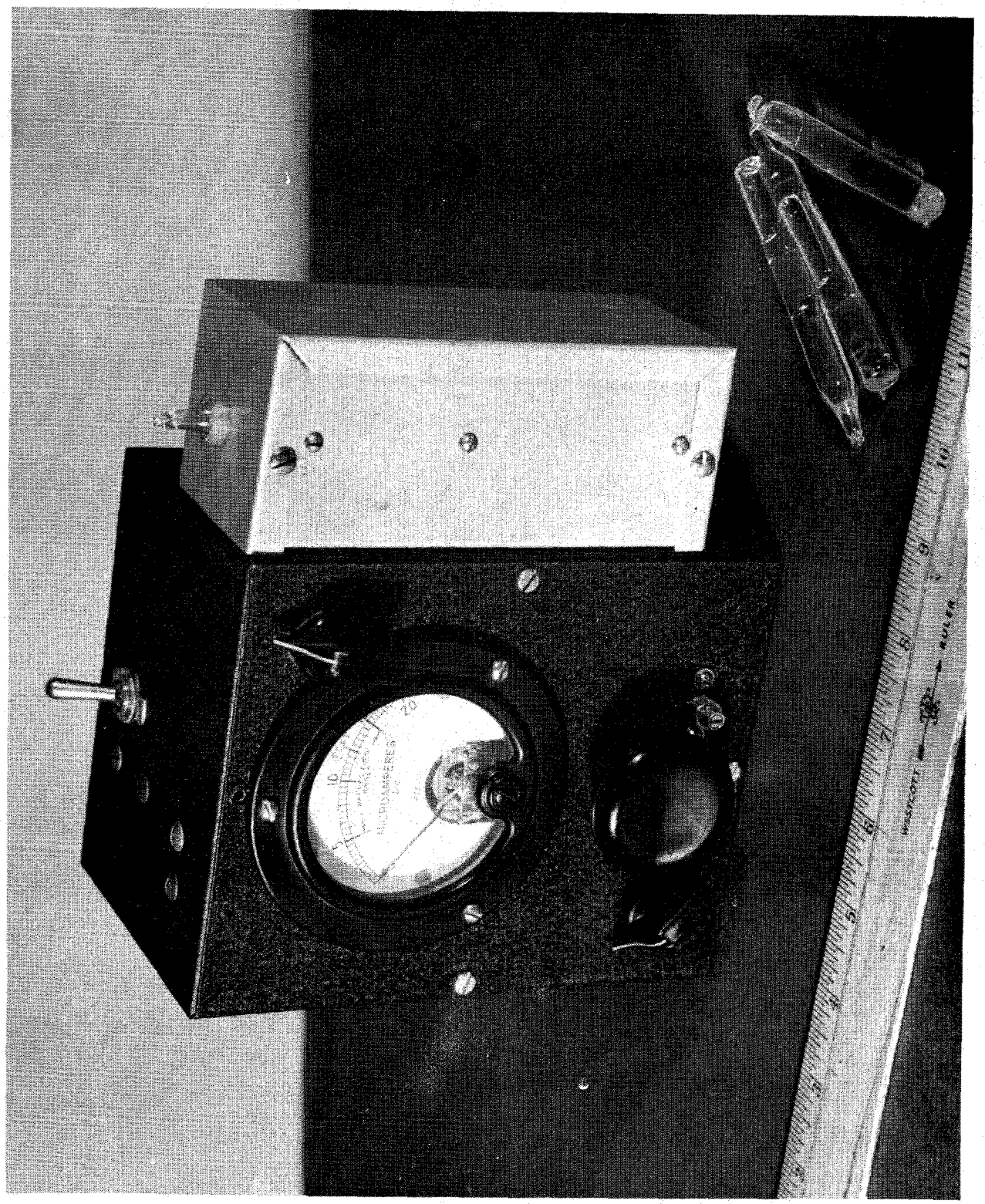


Figure 2

It appears feasible to design a small, rugged, light weight, and relatively inexpensive dosimeter reader based upon this principle. The unit illustrated in Figure 2 (Page 88) is 4x6x6 inches and weighs under three pounds. It is the first experimental unit constructed and no great effort has been expended to increase sensitivity and portability.

Bibliography

1. Taplin, George V. and Douglas, Clayton H., UCLA-58, December 29, 1949

2. Taplin, George V. and Douglas, Clayton H., RA-DET, Vol. 3, No. 5, P. 3, May 1950

Problem Code: I.N.2 (Service)

Section Code: 3150

Author: L. T. Steadman

1. 73 chamber air samples were analyzed for zirconium
2. 4 air dust samples were analyzed for beryllium
3. 212 animal tissues were analyzed for beryllium
4. 4 animal food samples were analyzed for beryllium
5. 15 human autopsy samples were analyzed for uranium and beryllium
6. 25 chamber air samples were analyzed for thorium
7. 7 miscellaneous samples were analyzed for constituent elements

EDUCATIONAL PROGRAM

Problem Code: None

Section Code: 3480

Author: J. N. Stannard

Radiological Physics Course. During this quarter the final phases of the academic program were completed. A course entitled Practical Radiological Physics was given under the direction of Assistant Professor Mermagen and Mr. Hoyt Whipple. An outline of lectures and laboratory exercises follow (Pages 91-92). It will be noted that this course takes up in order the more urgent practical health problems resulting from the preparation and use of fissionable materials in the release of nuclear energy. In addition, some instruction in meeting hospital x-ray and radium problems is included.

The practical training for five of the group is being continued at Brookhaven National Laboratory this summer under the auspices of their Health Physics Division. Owing to lack of housing at Brookhaven, those students with families are remaining in Rochester this summer to pursue research problems.

All students began preliminary research investigations during the quarter. A list of these is attached (Page 93).

Educational Facilities. Transfer of nearly all educational activities to a new addition to the Medical School building was completed during this quarter. Equipment requirements for each course were determined in detail by the responsible instructors and the task of fitting up laboratories for an expanded student body is under way.

UNCLASSIFIED

PRACTICAL RADIOLOGICAL PHYSICS

LECTURE SCHEDULE

Monday and Friday - 10:30 A.M., Tuesday and Thursday - 9:00 A.M.

May 1 to June 9, 1950

	Topic	Lecturer
1.	Introduction and History	Mermagen
2.	Maximum Permissible Exposure	Mermagen
3.	Units	Whipple
4.	Bragg-Gray Principle	Whipple
5.	Principles of Measurement	Mermagen
6.	Factors in Design and Use of Instruments	Whipple
7.	Survey Instruments	Dahl
8.	Survey Methods	Whipple
9.	Radioactive Laboratory Design	Andrews
10.	Excretory Methods for Bio-Assay	Stannard
11.	Hematological Bio-Assay Methods	Ingram
	Discussion	Staff
	Quiz	
12.	Waste Disposal	Bale
13.	X-ray Installation Safeguards	Mermagen
14.	Plant Health Physics Methods	Mermagen
15.	Correction of Substandard Conditions	Whipple
16.	Shielding	Whipple
17.	Atomic Disaster	Howland
18.	Seminar: Experiment Summaries	Students

Topic	Lecturer
Summary, Review and Discussion	Staff
Examination	

LABORATORY SCHEDULE

Tuesday and Thursday - 1:00 - 5:00 P.M.

1. Photographic Dosimetry
2. Photographic Dosimetry
3. Instrument Calibration
4. Beta Activity Analysis
5. Decontamination
6. Practical Laboratory Survey
7. Cyclotron Neutron Measurements
8. X-ray Calibration of Low and High Voltage Generators
9. X-ray Shielding

UNCLASSIFIED

A.E.C. RADIOLOGICAL PHYSICS FELLOWS

RESEARCH ASSIGNMENTS

February 24 through June 9, 1950

Student	Problem	Instructor
Geo. M. Angleton	Spectrochemical methods for determination of fission products	Steadman
Wm. J. Bair	Protein synthesis with radioactive amino acids	Miller
Robt. F. Barker	Extension and amplification of current tolerance calculations for internal emitters	Stannard
Stuart C. Black	Depth dose determinations	Mermagen
John C. Gallimore	Aggregates and radio-colloids as factors affecting distribution of radioactive materials in the body (Autoradiographic attack)	Boyd-Stannard
Paul D. Shandley	Radium-radon determinations	Hursh
Geo. A. Simon	Spectrochemical methods for determination of fission products (different substances than used by Angleton)	Steadman
Lawrence Thomas	Aggregates and radio-colloids as factors affecting distribution of radioactive materials in the body (correlative physical measurements)	Stannard-Boyd
Theodore Watanabe	Electronmicroscopy of soft tissue with particular reference to the respiratory system	Laskin
Donald Morken	Development of an analytical fluorophotometer for the study of project metals	Neuman

UNCLASSIFIED

[redacted]

TECHNICAL REPORTS ISSUED FOR DISTRIBUTION

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April 1, 1950 thru June 30, 1950

Report No.	Title	Authors	Subject Category
UR-103	Quarterly Technical Report for October 1, 1949 thru December 31, 1949 (FOR OFFICIAL USE ONLY) Issued: April 11, 1950	Blair	Health and Biology
UR-108	"The Removal of Uranium Compounds from Cloth, A Laundry Problem" (UNCLASSIFIED) Issued: June 19, 1950	Carlson Neuman	Health and Biology
UR-109	"Beryllium Complexes with Naphthazarin and Alkannin" (UNCLASSIFIED) Issued: April 4, 1950	Underwood Toribara Neuman	Chemistry General
UR-110	"Bone as a Problem in Surface Chemistry" (UNCLASSIFIED) Issued: April 19, 1950	Neuman	Health and Biology
UR-111	"The Isolation of Morin as a Reagent for Be Analysis" (UNCLASSIFIED) Issued: April 19, 1950	Bonner	Chemistry General
UR-113	"Pilot Experiments on Indications of Radiation Sickness and Comparison of Lethal Doses of X-rays for Rats and Dogs at Intensities of 160 r per Hour and When Delivered in 24 Hours" (UNCLASSIFIED) Issued: May 23, 1950	Casarett	Health and Biology
UR-114	"The Surface Chemistry of Bone II. Fluoride Deposition" (UNCLASSIFIED) Issued: June 1, 1950	Neuman et al	Health and Biology
UR-115	"Effect of Polonium^{210} and Selenium^{75} in Experimental Schistosoma Mansoni Infection in Mice" (FOR OFFICIAL USE ONLY)(Declassified) Issued: June 2, 1950	Watts McConnell	Health and Biology

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Report No.	Title	Authors	Subject Category
UR-116	Quarterly Technical Report for January 1, 1950 thru March 31, 1950 (FOR OFFICIAL USE ONLY) Issued: June 29, 1950	Blair	Health and Biology
UR-117	"A Kinetic Study of Normal and Uranium Inhibited Hexose Metabolism in Yeast" (FOR OFFICIAL USE ONLY)(Declassified) Issued: June 2, 1950	Hurwitz	Health and Biology
UR-119	"The Radium Content of the Body for Individuals with no Known Occupational Exposures" (UNCLASSIFIED) Issued: June 30, 1950	Hursh Gates	Health and Biology
UR-120	"The Relationship of the Cell Surface to Metal. VII. The Chemical Nature of Uranium-Complexing Groups to the Cell Surface" (CONFIDENTIAL) (Declassified) Issued: June 23, 1950	Rothstein et al	Health and Biology

END DATE

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