[redacted]

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THE UNIVERSITY OF ROCHESTER

INTRAMURAL CORRESPONDENCE

26 September 1945

TO: Captain David Goldring, Captain Joseph Howland

FROM: Captain P. Dale

RE: Oral Condition of [redacted]

1. A record of the clinical and radiographic oral examination of [redacted] is presented on the attached U.S.A. Medical Department form 55 E-4.

   a- Full mouth extractions were urgently recommended because of an advanced periodontoclastic condition (diffuse alveolar atrophy) which seemed to be a possible focus of infection.

2. The dates, nature of treatments and operations are indicated on U.S.A. Medical Department form 79.

   a- No unusual pre- and post-operative procedures were undertaken other than routine aseptic exodontic measures and topical sulfonamide therapy.

   b- The excellent recovery following the extractions of 3, 4, 6 and 7 teeth together with their respective alveolotomies at approximately weekly intervals is emphasized. The patient fared better than the average subject of seemingly better resistance that had undergone similar dental treatment.

3. The dental radiographs are submitted for filing with the rest of [redacted] data.

Peter P. Dale

Peter P. Dale, Capt., DC AUS

PPD jmp

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Table 1. Urinary Excretion of Plutonium [redacted]
Injected April 9, 1945 with 330,000 c/m (4.7 γ)

	Date and Period	Hrs. in period	c/m in period	c/m per 24 hr. (corrected)	% of inj. dose excr. per 24 hr.
1	4-9 at 4 A.M. to 4-10 at 2:15 P.M.	24 (after inj.)	332.1	332.1	0.101
2	4-10 at 2:15 PM to 4-11 at 2:15 PM	24	340.6	340.6	0.103
3	4-11 at 2:15 PM to 4-12 at 8 AM	17 3/4	214.2	289.5	0.088
4	4-12 at 8 AM to 4-13 at 8 AM	24	256.3	256.3	0.078
5	4-13 at 8 AM to 4-14 at 6:30 AM	22 ½	209.9	209.9	0.068
6	4-14 at 8 AM to 4-15 at 8 AM	24	146.7	146.7	0.044
7	4-15 at 8 AM to 4-16 at 8 AM	24	226.6	226.6	0.069
8	4-16 at 8 AM to 4-17 at 8 AM	24	263.0	263.0	0.080 *
9	4-17 at 8 AM to 4-18 at 8 AM	24	143.0	143.0	0.043
10	4-18 at 8 AM to 4-19 at 8 AM	24	123.7	123.7	0.038
11	4-19 at 8 AM to 4-20 at 1 AM	17	89.4	126.1	0.038 *
12	4-20 at 8 AM to 4-21 at 8 AM	24	90	90.0	0.027 *
13	4-21 at 8 AM to 4-22 at 8 AM	24	98.1	98.1	0.030
14	4-22 at 8 AM to 4-22 at 11:30 PM	15½	83.2	128.8	0.039 *
15	4-23 at 8 AM to 4-24 at 8 AM	24	96.6	96.6	0.029
16	4-24 at 8 AM to 4-25 at 8 AM	24	74.6	74.6	0.023
17	4-25 at 8 AM to 4-26 at 8 AM	24	96.8	96.8	0.029
18	4-26 at 8 AM to 4-27 at 8 AM	24	86.1	86.1	0.026
19	4-27 at 8 AM to 4-28 at 8 AM	24	94.2	94.2	0.029
20	4-28 at 8 AM to 4-29 at 8 AM	24	106.0	106.0	0.032
21	4-29 at 8 AM to 4-30 at 8 AM	24	83.5	83.5	0.025
22	4-30 at 8 AM to 5-1 at 8 AM	24	82.2	82.2	0.025
23	5-1 at 8 AM to 5-2 at 8 AM	24	129.9	129.9	0.039
24	5-2 at 8 AM to 5-3 at 8 AM	24	76.8	76.8	0.023
25	5-3 at 8 AM to 5-4 at 8 AM	24	69.1	69.1	0.021
26	5-4 at 8 AM to 5-5 at 8 AM	24	76.1	76.1	0.023
27	5-5 at 8 AM to 5-6 at 8 AM	24	56.1	56.1	0.017
28	5-6 at 8 AM to 5-7 at 8 AM	24	79.8	79.8	0.024
29	5-7 at 8 AM to 5-8 at 8 AM	24	74.6	74.6	0.023
30	5-8 at 8 AM to 5-9 at 8 AM	24	68.4	68.4	0.021
31	5-9 at 8 AM to 5-10 at 8 AM	24	70.0	70.0	0.021
32	5-10 at 8 AM to 5-11 at 8 AM	24	39.7	39.7	0.012
33	5-11 at 8 AM to 5-12 at 8 AM	24	121.5	121.5	0.037
34	5-12 at 8 AM to 5-13 at 8 AM	24	67.0	67.0	0.020

Table 1. Urinary Excretion of Plutonium [redacted]
Injected April 9, 1945 with 330,000 c/m (4.7 γ)

	Date and Period	Hrs. in period	c/m in period	c/m per 24 hr. (corrected)	% of inj. dose excr. per 24 hr.
35	5-13 at 8 AM to 5-14 at 8 AM	24	85.1	85.1	0.026
36	5-14 at 8 AM to 5-15 at 8 AM	24	60.2	60.2	0.018
37	5-15 at 8 AM to 5-16 at 8 AM	24	74.8	74.8	0.023
38	5-16 at 8 AM to 5-17 at 8 AM	24	60.1	60.1	0.018
39	5-18 at 8 AM to 5-19 at 8 AM	24	68.1	68.1	0.021
40	5-19 at 8 AM to 5-20 at 8 AM	24	61.2	61.2	0.019
41	5-21 at 8 AM to 5-22 at 8 AM	24	43.5	43.5	0.013
42	5-22 at 8 AM to 5-23 at 8 AM	24	43.5	43.5	0.013
43	5-23 at 8 AM to 5-24 at 8 AM	24	50.4	50.4	0.015
44	5-24 at 8 AM to 5-25 at 8 AM	24	50.4	50.4	0.015
45	5-26 at 8 AM to 5-29 at 8 AM	24	57.0	57.0	0.017
46	5-28 at 8 AM to 5-29 at 8 AM	Sample Lost			
47	5-31 at 10 AM to 6-1 at 10 AM	24	50.3	50.3	0.015
48	6-3 at 8 AM to 6-4 at 8 AM	24	57.8	57.8	0.017
49	6-9 at 8 AM to 6-10 at 8 AM	24	51.1	51.1	0.015
50	6-12 at 8 AM to 6-13 at 8 AM	Sample Lost			
51	6-15 a t 8 AM to 6-16 at 8 AM	Sample Lost			
52	6-18 at 8 AM to 6-19 at 8 AM	24	115.0	115.0	0.035
53	6-21 at 8 AM to 6-22 at 8 AM	24	63.7	63.7	0.019
54	6-24 at 8 AM to 6-25 at 8 AM	24	140.7	140.7	0.043
55	6-27 at 8 AM to 6-28 at 8 AM	24	143.0	143.0	0.043
56	6-30 at 9 AM to 6-31 at 8 AM	24	118.0	118.0	0.036
57	7-3 at 8 AM to 7-4 at 8 AM	24	60.0	60.0	0.018
58	7-6 at 8 AM to 7-7 at 8 AM	24	119.0	119.0	0.036

*Values corrected for approximate losses.

Table 2.—Fecal Excretion of Plutonium [redacted] Injected April 9, 1945 with 330,000 c/m (4.7 γ).

Time Interval After Injection Days	c/m/ Sample	Rate of Excretion c/m/24 hrs.
0-2	1830	915
2-3.8	1226	689
3.8-4.7	1110	1270
4.7-8.0	113	35
8.0-11.1	39	12
11.1-12.0	92	110
12.0-13.6	153	97
13.6-15.8	244	110
15.8-18.8	34.8	12
18.8-12.8	503	170
21.8-23.6	94	53
23.6-24.8	118	103
24.8-26.8	94	50
26.8-29.0	103	48
29.0-32.2	69	22
32.2-33.0-	25	34
33.0-34.0	87	87
34.0-34.2	87	362
34.2-35.5	81	72
35.5-37.3	17	9.6
37.3-39.3	96	47
39.3-40.9	lost	
40.0-42.2	29	21
42.2-43.3	24	24
43.3-44.3	17	17
44.3-46.3	37	18

Table 3.--Fecal Excretion of Plutonium on Basis of Even 2 and 4 Day Periods.* [redacted]. Injected with 330,000 c/m (4.7 γ) on April 9, 1945

Time Interval After Injection Days	c/m	% Injected Dose/Period	% Injected Dose/Day
0-2	1830	0.555	0.278
2-4	1473	0.446	0.223
4-6	907	0.275	0.138
6-10	84	0.025	0. 006
10-14	313	0.095	0.024
14-18	225	0.068	0.017
18-22	523	0.158	0.040
22-26	258	0.078	0.020
26-30	162	0.049	0.012
30-34	160	0.048	0.012
34-38	218	0.066	0.017
38-42	Broken in Transit		
42-46	78	0.0247	0.006

*Even periods of 2 and 4 days were obtained by adding the appropriate fraction from the next period.

Table 4.—Plutonium Content of Blood Samples
From [redacted]. Injected with 330,000 c/m (4.7 γ) April 9, 1945

Date of Sample	Time After Injection	Vol. Sample ml.	c/m Sample*	c/m/ 100ml.
4/9	4 hrs.	10	32.5	325
5/10	31	15?	4.7	31.3?
5/25	46 days	15	4.2	28.0
6/1	52 days	10	4.6	46.0
6/19	70 days	10	1.4	14.0

*A blank value of 1 c/m has been subtracted from each result.

Table 5.—Plutonium Content of Bone Samples
From [redacted] Injected with 330,000 c/m (4.7 γ) April 9, 1945

Bone Sample	Date Taken	Weight gms.	c/m/ Sample*
Femur Fragment	4/14	0.065(ash)	0
Patilla	4/14	0.925(ash)	82.3
Fragment from Head of Radius	5/10	0.130(ash)	19.8
Tooth R-1 Ginginal	8/23		1.6
Tooth R-1 Crown	8/23		0
Tooth R-1 Apical	8/23		0.3
Tooth R-2 Gingival	8/23	0.582(wet)	0
Tooth R-2 Crown	8/23	1.161(wet)	0.6
Tooth R-2 Apical	8/23	.160 (wet)	0.4
Tooth R-3 Gingival	8/23	.346 (wet)	0.8
Tooth R-3 Crown	8/23		0.1
Tooth R-3 Apical	8/23	.150 (wet)	0.4
R-2 Gingival Tissue	8/23	.738 (wet)	0.1
R-2 Alvicular Bone	8/23	.047 (wet)	0.7

*A blank value of 1 c/m has been subtracted from each result.

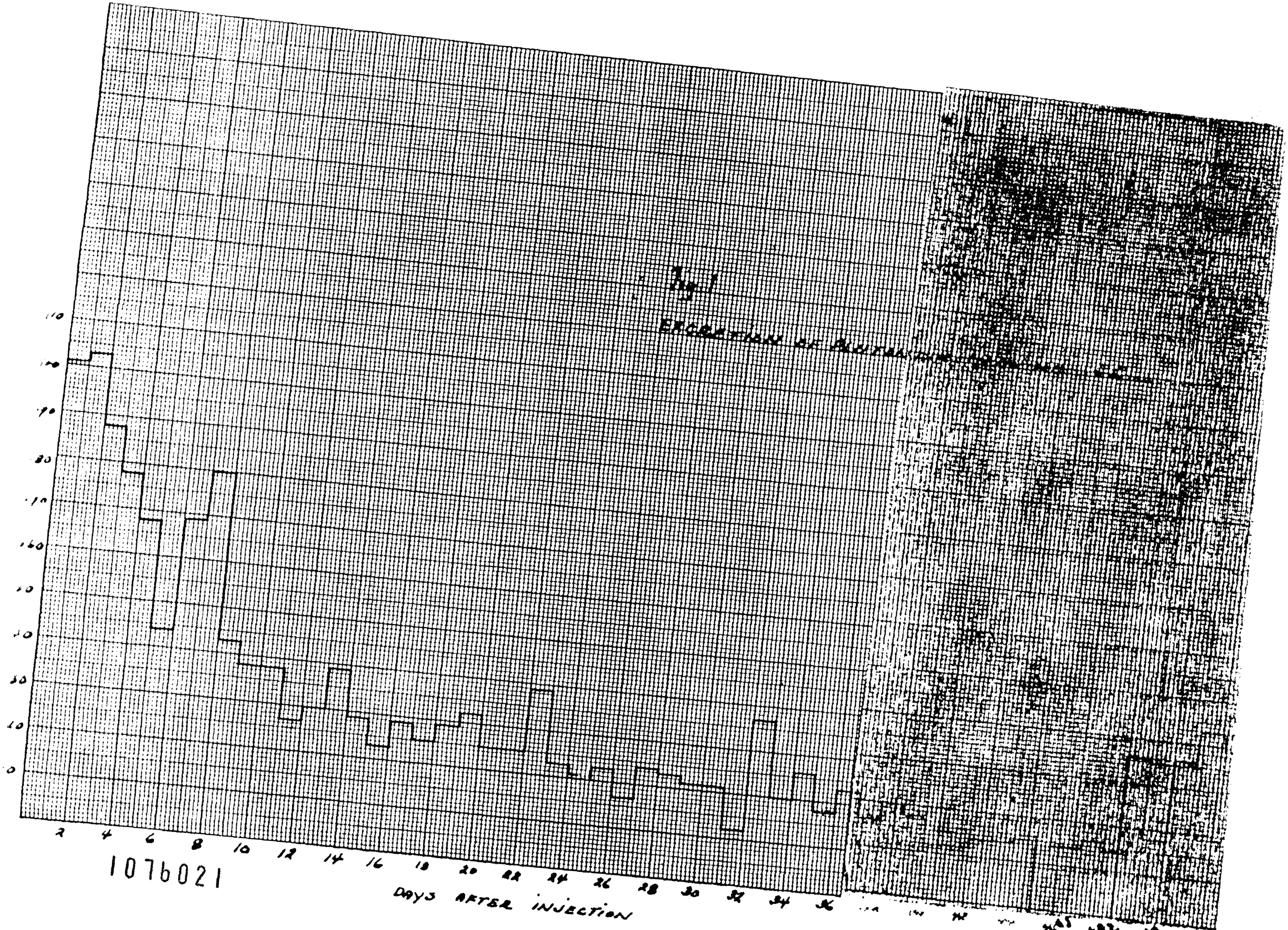
Fig. 1
DAYS AFTER INJECTION
2 4 6 8 10 12 14 16 18 20 22 24 26 28 30 32 34 36

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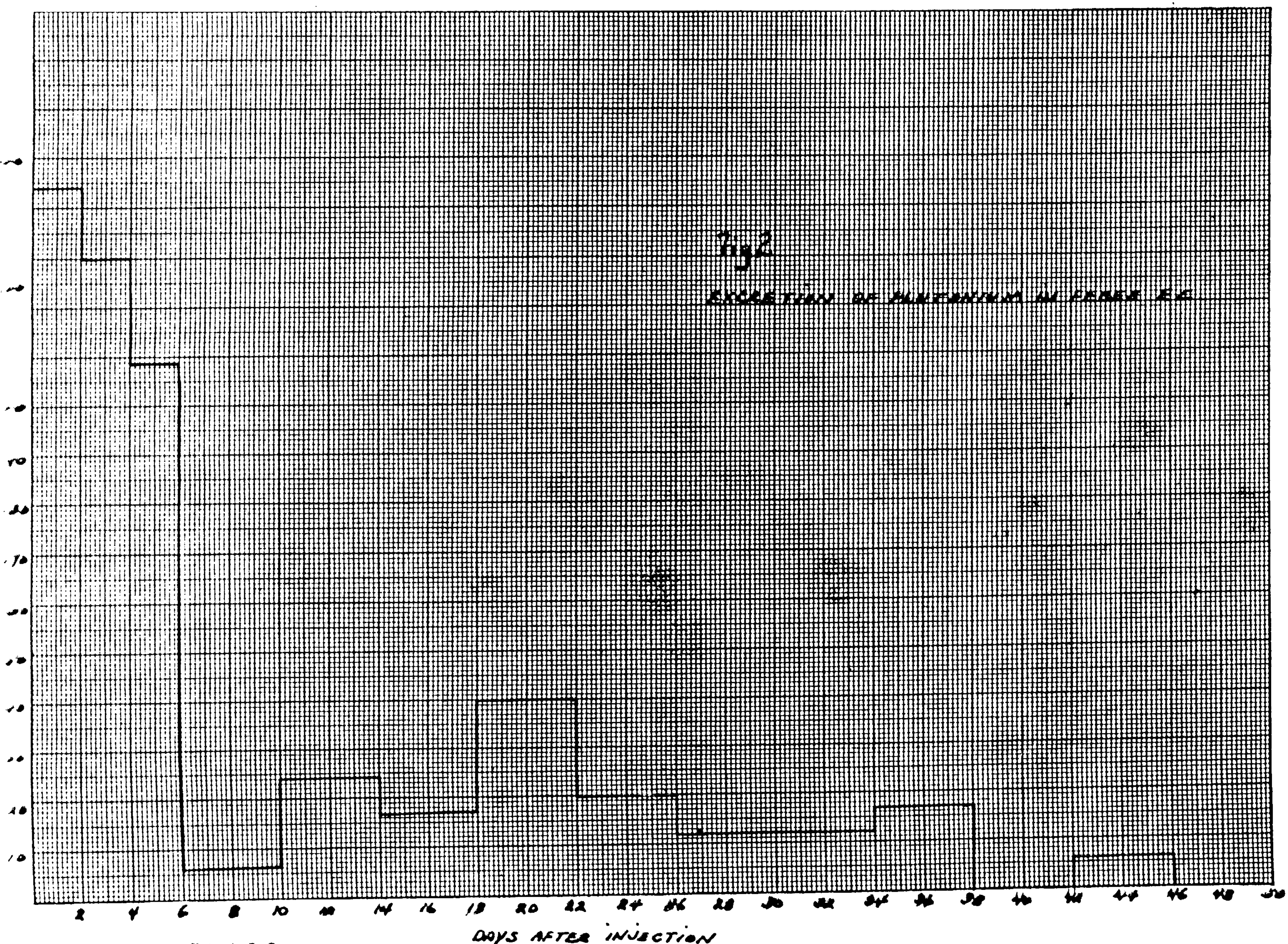

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BIOPHYSICS INSTITUTE

UNIVERSITY OF ROCHESTER

A Coördinated Research Program
Utilizing the Products of Controlled
Nuclear Energy as May Be Applied
to Medical Sciences

Presented by

Andrew H. Dowdy, Director of Rochester Manhattan Project

William F. Bale, Associate Director of Rochester Manhattan Project
and Chief of Division of Special Problems

Harold C. Hodge, Associate Director of Rochester Manhattan Project
and Chief of Division of Pharmacology and Toxicology

Morey J. Wantman, Assistant to the Director of Rochester Manhattan
Project and Chief of Division of Statistics

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INTRODUCTION

The technology of the atomic bomb project, utilizing the fruits which had been harvested and preserved by fundamental scientists during the previous decade, has resulted in a new era. The accomplishment of man-controlled nuclear energy on a mass production scale is both a liability and an asset to humanity. Owing to the exigencies of war the first application of this tremendous power was that of destruction. Consequently our violent introduction to this new giant which was conceived in secrecy and born during a period of national and international unrest and turmoil has caused many to look upon the future with mistrust resulting in some instances to what approaches a national and international hysteria. Such need not be the case. If the proper support is forthcoming from our Federal Government it is not unlikely that the next one to two decades will see many advances made in the fields of medicine, physics, chemistry, biology and industry, resulting in better national health, prosperity and happiness.

The group associated with the war-time program of the Manhattan Project at the University of Rochester is confident that the proper governmental support of a post-war program of research utilizing the products of controlled nuclear energy will result in improved conditions for humanity. It is with this confidence that we wish to present what we believe to be the essentials for the proper conduct of such a program relative to security, duration, organization, sphere of research activities and budget.

ELEMENTS ESSENTIAL FOR SUCCESS OF PROGRAM

Intellectual Freedom:

Science bears its choicest fruits when there is a cross-fertilization of ideas. This condition can be obtained only when there is a minimum restriction placed upon free personal discussion, publication, and participation in scientific meetings. These are the media for the exchange of ideas and the sources of stimuli. It is by granting the greatest possible freedom in this respect that one can hope to retain the interest of the many eminent scientists throughout the country who have been connected with the atomic bomb project for post-war programs under the auspices of a governmental agency.

Long Term Support:

The many fields and branches of science which will be benefited by the production of controlled nuclear energy are so numerous that for the successful exploration it would seem essential that if maximum progress is to be made such an undertaking will have to be sponsored by the Federal Government. Such being the case, in order to retain or secure men of sufficient experience to fill the positions of head of the various departments it will be necessary to provide a minimum assurance of ten years. A ten-year tenure is small in comparison to the assurance given comparable departmental heads in most universities. The nature of the program is such that to insure continuity and correlation of research this minimum is required.

Integration with Medical School and University:

The organization and program to be outlined is to be integrated with the Medical School and University to insure the maximum in results. The department heads, where possible, will be professors of existing or comparable departments in the Medical School or elsewhere in the University. Where this is not possible the department head should be of professorial caliber and as such warrants full professorial rank.

Wherever possible, through coöperation with the Dean of the Graduate School of the University, fellowships will be offered with assignment to problems leading to graduate credit toward advanced degrees.

In order to insure the greatest use of governmental facilities, support and the benefits to be derived from this type of research, it should be the responsibility of the Director of the proposed project to encourage research problems in the various University departments whose talents and facilities are available for problems having a correlative value.

OBJECTIVES

1. To develop quantitative methods for the use of radio-carbon, C_{14}, and radio-hydrogen, H_3, as tracers and their application to the general field of medical and biological sciences.

2. To utilize these new tools in fundamental investigations of general metabolism, degenerative diseases, the aging process and cancer.

3. To study the chemical and radio-active hazards involved in the industrial and in the military use of nuclear energy. The setting of tolerance limits based on the results of these studies, and the instrumentation for implementing these recommendations.

4. To study the pharmacology of the radio-active elements recently made available in quantity; such studies are indispensable prerequisites of the therapeutic application of these elements.

[redacted]

PROGRAM AND BUDGET

OF

DEPARTMENT OF MEDICAL PHYSICS

Department Head, Dr. William P. Sale

DEPARTMENT OF MEDICAL PHYSICS

Metabolic Research With Labelled Elements, Instrumentation

This department has two primary objectives:

I. To develop chemical and physical methods, with the necessary instrumentation, for the easy utilization of labelled elements and other physical tools in medical and biological research.

II. Predominantly but not entirely in coöperative research projects with other departments of the university, to apply these methods and tools to the solution of research problems in medicine, biology and chemistry.

One class of problems to the solution of which this department can make substantial contributions is typified by the contributions of the present Division of Special Problems to the Manhattan Project. These include:

1. Studies on the quantitative metabolic behavior in animals and humans of radioactive elements and compounds.

2. Studies on the toxic properties of these elements.

3. The setting of tolerance limits based upon the results of these studies.

4. Instrumentation for implementing these recommendations.

5. Research on production and analytical problems of interest to the District.

A second class of problems represents work bringing to fulfillment the implied promise of the controlled release of nuclear energy to

the solution of problems in biology and medicine of fundamental importance; problems whose solution gives promise of improved methods of treating disease and prolonging of the useful span of human life. This program is based on the assumption that peace time usefulness as well as military value will be aims of future government sponsored nuclear research. Typical of these problems are:

1. Development of quantitative methods for the use of radio-carbon, C_{14}, and radio-hydrogen, Hg, as tracers in biological research.

2. In coöperation with the Department of Chemistry to develop methods of synthesizing these elements into organic compounds of research interest.

3. In coöperation with the Department of Pathology to study by tracer techniques the role of pertinent compounds in growth and wound healing.

4. In coöperation with the Department of Oncology and other university departments to study the metabolism of aging and tumor growth with appropriately labelled compounds.

5. In coöperation with the Department of Oncology to search for radioactive compounds that will concentrate preferentially in growing tumors and therefore be useful agents in tumor therapy. To give promising compounds clinical therapeutic trial in animals and humans.

6. In coöperation with Pharmacology and other university departments to follow the pathway in the body of therapeutic agents used in the treatment of diseases.

7. To supplement these studies with studies utilizing heavy nitrogen, heavy carbon, and heavy hydrogen in appropriate instances.

8. To develop and utilize other physical tools in medical research.

Tentative Personnel Requirements and Budget

Department Head, (Provisionally, Dr. William F. Bale)		$8 - 12,000
Head - Chemistry Section (Provisionally, Dr. Robert Fink)		5 - 8,000
Head - Physiology Section (Provisionally, Dr. John E. Hursh)		5 - 8,000
Head - Metabolism Section (Provisionally, Dr. Leon Miller)		5 - 8,000
Head - Instrumentation Section (Provisionally, Dr. Theodore Enns)		5 - 8,000
Head - Physics Section		5 - 8,000
Head - Industrial Section (Provisionally, Dr. Luville Steadman)		5 - 8,000
6 Research caliber personnel		3 - 5,000
11 Technicians		2 - 3,000
8 Graduate students	(Total)	8,000
Supplementary personnel Secretary, instrument makers, etc.	(Total)	10,000
	Total average personnel	$118,500
	Materials and supplies	30,000
	TOTAL	$148,500
	Contingency 10%	14,850
	TOTAL YEARLY BUDGET	$163,350

PROGRAM AND BUDGET

OF

DEPARTMENT OF PHARMACOLOGY AND TOXICOLOGY

Department Head, Dr. Harold C. Hodge

DEPARTMENT OF PHARMACOLOGY AND TOXICOLOGY

General Description

A program of research is described herewith based on certain studies in toxicology and including the toxic action of new radioactive substances of great fundamental and practical interest.

Special equipment, laboratories and trained personnel are at hand. These facilities could be profitably devoted to a needed extension of knowledge of the toxicology of the new special materials.

The fundamental program represents a field of investigation of profound scientific interest. Such work might be the keynote of the University Department. The practical program is correlated with the University's interest in industrial hygiene.

A department organization is described capable of furnishing the needed information.

Purpose

The aim of this research is to study the chemical and radioactive hazards involved in the industrial and in the military use of nuclear energy. The program, as presented, attempts to take advantage of the 'know-how' available in the Rochester group of research workers.

Justification

New elements (certainly elements new to industry) are being handled by industrial personnel. A thorough-going fundamental study must be made of the toxicology and pharmacology of these elements in order that industrial hygiene practices may be established on a firm basis.

Department Organization and Personnel

This program would constitute the duties of a department of the School of Medicine and Dentistry of The University of Rochester. Such a department would be known as the Department of Pharmacology and Toxicology. The facilities which are available or which might be needed are described below.

The department would undertake a long term program designed to investigate the fundamental biochemical and pharmacological problems referred to and would serve as a center of consultant toxicologists for the various industries involved.

Department Staff Members

The head of the department would be a man of professor's rank. He would have as his assistants men of nearly equal status, in charge of (a) fundamental toxicology, (b) pharmacology of various special materials and (c) the program of industrial hygiene. The junior members of the department would be selected in part from the young men who have been trained during the past two years in our laboratories on somewhat similar work.

Graduate Students

An essential part of the program would be the selection of men who would come to the department as candidates for graduate degrees and who would receive training in practical industrial hygiene as well as in fundamental health problems related to the industry. These men would be available after a few years for research positions and for industrial health supervision in the plants.

We are fortunate in having at Rochester, practical toxicologists, theoretical biochemists, pharmacologists, biophysicists, experts in cyclotron and other modern techniques who have been working together in a productive fashion, first on studies of radioactive isotopes as biological tracers, and later on various phases of the Manhattan Project. These men represent a potential faculty for the department.

A functioning organization of manifold interests and notable productivity is available. By building on these facilities and utilizing those which fit into the program, the most rapid progress is to be gained.

The personnel required are a few able men plus a technical staff and graduate students. For the fundamental studies only a general field would be indicated; no special assignments would be made. For the practical toxicology the closest cooperation would be maintained with industrial medical supervisors and with technical scientists who had submitted products for study.

Facilities Available

Many government-owned facilities are in use in the studies of acute and chronic toxicity now under way. These represent an investment of thousands of dollars, much of which could be utilized in the continuation of such studies. Special installations are on hand such as the exposure chambers for large groups of animals in carefully controlled atmospheres, special analytical devices for sampling chamber atmosphere containing solids as well as vapors, spectrographic equipment, various alpha counters, Geiger-Mueller counters, particle-size instruments. In addition, in college, medical school and university departments are valuable tools such as the electron microscope, cyclotron, spectrophotometers, Tiselius

Apparatus, polarograph, high vacuum cyclic still, as well as pH meters, colorimeters and the other apparatus of a well-equipped modern laboratory.

Not the least of the facilities is the special 'know-how' developed during the past two years. In addition to the scientists mentioned above, trained personnel are available for kidney function tests, liver function tests, blood clotting characteristics, studies of complexing abilities of metallic ions, studies of pulmonary retention of inhaled dust clouds, ultra-refined chemical methods for T, for proteins, enzymes and lipids, and the standard biochemical and clinical procedures.

Plan of Problems

The most important aspect is that good men should begin fundamental studies to which they might well devote their scientific lifetimes. At the moment, we are attempting to outline the problems that appear to be most interesting to those now engaged in this work, special attention has been given to those problems that appear to have a reasonable change of success in a period of five to ten years. We do not intend that all of the problems mentioned below should be studied in detail, and on the other hand, we do not intend to limit the studies during the five- to ten-year period to the suggestions listed herewith. These problems have come from many persons; they have been edited by Dr. Voegtlin and myself to the extent of discarding unrelated suggestions. The problems are organized in two divisions: first, those having to do with fundamental studies and, second, those dealing with a practical program.

Growing out of our experience with the toxicity of T the problems specifically mentioned deal with the extension and completion of such studies. Investigations of other radioactive elements and the fundamental radiation problems, biochemical and physiological, could follow a comparable development.

Scope of Research

The program described herewith may be considered as embracing two related parts: a fundamental program and a practical program; these studies would be the responsibility of four divisions of the Department of Pharmacology and Toxicology.

Division	Program
	Fundamental
	The fundamental program has 3 main divisions.
I. Toxicology	First, the toxicology of substances of industrial importance and to which industrial exposures exist in the development of atomic power.
II. Mechanism	Second, mechanism of action of toxic compounds and the various therapeutic substances, e.g. the sulfonamide, penicillin and new drugs for therapy of cancer.
III. Pharmacology	Third, the pharmacology of the radioactive elements newly made available in quantity. Such studies include the fate of these elements administered in various forms, knowledge that is an indispensable prerequisite of the therapeutic application of these elements.
IV. Industrial Hygiene	**Practical**
	The practical program has two main divisions.
	First, toxicological studies of industrially important materials under laboratory conditions immediately referable to plant practices.
	Second, methods for surveying plant hazards. This would involve developing and calibrating testing instruments, investigating dust collection and other air sampling procedures as well as recommending sensitive routine methods for detecting incipient poisoning in personnel.

This entire program of fundamental and practical investigations constitutes in one sense a major line of research growing out of and closely associated with the new industry associated with nuclear power. It would be impossible to study all of the possible ramifications of this program simultaneously. A small group such as a University Department which might by steady effort over a period of years investigate key parts of the program.

PROGRAM OF FUNDAMENTAL PROBLEMS

The fundamental studies may be considered under two heads, as follows: I. Toxicity studies of T; II. Pharmacology of radioactive elements.

Each of these topics will be discussed briefly herewith; detailed statements are included in the appended 'Outline of Specific Problems'.

I. Toxicity studies. These are grouped under the following heads: A. Description of Chronic Toxicity; B. Maximum Allowable Concentrations; C. Tolerance to T Poisoning; D. Mechanism of T Poisoning; and E. Methods.

A. Description of Chronic Toxicity. A description of the chronic toxicity of T compounds is probably the most useful immediate extension of present work. Two plans of study are suggested: 1) Lifetime toxicity tests by inhalation of compounds for which Maximum Allowable Concentrations are set, and 2) A study of toxic responses to very high dust concentrations.

B. Maximum Allowable Concentration. Studies on human exposures would be valuable. Laboratory studies of the chronic toxicity of T compounds other than those currently under investigation should be planned.

C. Tolerance to T Poisoning. The mechanism of tolerance needs elucidation, as does the lethal action of high doses of T in tolerant animals. An important question deals with the reversibility of kidney injury, that is, whether repaired and regenerated kidney tissue is in fact normal.

D. Mechanism of T Poisoning. This important field (about which considerable knowledge exists) has been subdivided under the following heads:

Physiological studies, such as clearance tests to help understand the changes in renal function. Physiological function tests of strength and stamina also might be included. Metabolic effects shown by chemical studies are needed.

Effects on tissues, especially the kidney tissues, both as to structure and chemical characteristics, are of the first importance. The liver function tests may be the most sensitive indices of early T poisoning yet available. Blood studies should be continued.

Sensitive tests. Two urinary tests, namely, catalase and amino acid excretion, appear to be most promising.

The effects on various cell constituents and also efforts to develop prophylactic procedures against T poisoning deserve further work.

E. Methods. A number of needed methods have been outlined clearly enough to permit specific suggestions to be made for further work. It must be emphasized that toxicological studies of other elements would be expertly carried out using technics perfected in working on T.

II. Pharmacology of Radioactive Elements. Three main headings are suggested.

A. The fate of these elements in the body.

B. The effect on the body, both of chemical properties and of radiation properties of the elements.

C. Based on such information, a search for suitable means for employing the elements therapeutically.

The general pharmacology of T is a subject for investigation. No such work has been carried out since that of Worochilsky which was done mostly with T tartrates. The nephrotoxic action of tartrates discovered twenty years later makes Worochilsky's work questionable.

One of the most important subjects under investigation is the factors which govern the accumulation deposition of T in bone and its subsequent mobilization.

PROGRAM OF PRACTICAL PROBLEMS

The practical problems may be considered under two heads: I. Toxicity Tests, and II. Industrial Hygiene.

I. Toxicity Tests. At present the Rochester Area of the Manhattan Project is operating the largest toxicity test laboratory in the country. A continuation of some of the present organization would provide (1) adequate facilities, instruments and equipment, and (2) trained and experienced personnel. Additional personnel would include biochemists, analytical chemists and engineers who would work closely with the technical men from the various industries to provide toxicological information which would bear acutely on the problems of industrial health. A sufficient staff of toxicologists would be available to perform short-term experiments (determining approximate toxicities) to indicate the safe limit to inhalation, skin and eye exposures. Facilities should also be available for long-term exposures via inhalation, ingestion, injection, skin and eye.

It is important that the personnel of the toxicology group become intimately acquainted with the manufacturing processes in the plants by personal inspection. A close liaison of this sort would serve to eliminate waste and save money by insuring the production of needed toxicological information.

II. Industrial Hygiene. Methods for dust sampling and the like can be originated de novo or adapted and perfected by this group which is now providing such observations on the atmospheres in which test animals are exposed.

Biochemical or other procedures for monitoring the health of industrial personnel, both laborers and scientists, can be developed, tested and supervised in industrial application by members of this group.

One of the most important aspects of this program is a systemic, periodic checking of industrial exposures. Such a survey program, organized along the lines found suitable by the National Institute of Health, can be centralized here.

A necessary liaison between industry and laboratory is the organization provision of condensed courses for plant personnel and plant safety supervisors. These courses would include a study of toxicity data, of toxicology methods, and of the psychology of health education, the problems of safety control which have to be solved largely by the coöperation of non-medical personnel. This contact would also insure a closer understanding by toxicologists of the exposure problems encountered under industrial conditions.

All toxicity tests would be supervised by a joint committee of Rochester workers together with medical and technical consultants from the industry for which the tests were being made. These contacts would furnish many leads for fundamental studies, for example, it has been recently reported that a sudden acute exposure to PG that produces no other symptoms will occasion a rise in the sedimentation rate to values between 20 and 30; whereas in personnel chronically exposed, the sedimentation rates are frequently low, of the order of 2 or 3. Such an observation brought by the industrial medical personnel to the laboratory is a fruitful source of fundamental research.

TENTATIVE PERSONNEL REQUIREMENTS AND BUDGET

I.	Chief Pharmacologist	1 - 12,000
	Head of Toxicology Division	1 - 8,000
	Sections	
	A. Chief of Inhalation Toxicity Studies	1 - 7,000
	Assistant Chief	1 - 6,000
	6 Unit Heads	3 - 5,000
	12 Assistants	2 - 4,000
	4 Special Problem Workers (Ph.D.)	2 - 4,000
	4 Assistants	2 - 3,000
	B. Chief of Ingestion Toxicity Studies (Maintain-Bronson Avenue)	1 - 7,000
	Assistant Chief	3 - 5,000
	1 Assistant	2 - 3,000
	C. Chief of Analytical Laboratories	1 - 7,000
	2 Analysts	3 - 5,000
	5 Technicians	2 - 4,000
II.	Head of Mechanism Division	1 - 8,000
	6 Biochemists	3 - 5,000
	4 Physiologists	3 - 5,000
	15 Assistants	2 - 4,000
III.	Head of Pharmacology Division	1 - 8,000
	4 Pharmacologists	3 - 5,000
	2 Biochemists	3 - 5,000
	2 Physiologists	3 - 5,000
	12 Assistants	2 - 4,000
IV.	Head of Industrial Hygiene	1 - 8,000
	2 Engineers	3 - 5,000
	1 Electron Microscopist	3 - 5,000
	2 Hygienists	3 - 5,000
	1 Safety Director	3 - 5,000
	1 Industrial Physician	3 - 5,000
	6 Technicians	2 - 4,000

Analytical	$ 28,000
Administration	21,000
Animal Care	32,000
Toxicology	151,000
Mechanism	108,500
Pharmacology	95,500
Industrial Hygiene	69,500
	$503,500
Contingency 10%	50,350
TOTAL ANNUAL BUDGET	$553,850

PROGRAM AND BUDGET

OF

DEPARTMENT OF ONCOLOGY

Department Head, Dr. Andrew H. Dowdy

DEPARTMENT OF ONCOLOGY

In addition to the direction of the research of this Department it would be the function of the department head to encourage correlative research relative to cancer in the various departments of the Project and elsewhere in the Medical School and University. The express aims of this Department would be to stimulate interest in cancer research throughout the University leading to an extensive correlated program directed toward the etiology, physiology, prevention and treatment of cancer. It is likely that a number of the research problems to be listed here will actually be carried out elsewhere in the Medical School or University. It is for this express purpose that a portion of the Department's budget will be allotted. This Department will be closely affiliated with the tumor clinic, radiation therapy clinic and clinical aspects of cancer in the Hospital and Medical School. This would insure the closest integration of the clinical and experimental approach to the field of cancer. It would be the concern of the Department to promote the public health and educational aspects of cancer.

The treatment of cancer clinically is so closely related to irradiation biology and physiology that certain aspects of the research in irradiation is included in this Department of the proposed Project.

The University of Rochester is ideally suited to the philosophy of a correlated approach to the problems as outlined under this Department, in fact as indicated by the organization as a whole.

EXPERIMENTAL PROGRAM

It is impossible to specifically outline in detail a program for ten years. It is possible, however, to state basic fundamental problems which await solution. The following discussion includes a few of these problems. Specific details and techniques will depend upon the particular scientist who elects their study.

I. Basic Cancer Research

Neutron production resulting from the chain-reacting Uranium Pile makes possible the production of radioactive isotopes in an abundance hitherto unheard of. With the production of the long-lived radio-carbon, C_{14} and radio-hydrogen H_3, we are now in a position to attack the basic research on cancer with a renewed hope and vigor. The technique of labelling of amino acids and intermediates in protein metabolism will most surely form the basis for the elucidation of many of the following problems.

Utilization of the dog as an experimental animal for basic cancer research offers many advantages. A wide variety of malignancies corresponding to those occurring in humans occur in dogs. It is also felt that a variety of malignancies can be induced in the dog by one of several methods.

In the hands of many of the Medical School Staff, and especially of Dr. George H. Whipple, the dog has proven to be a valuable research animal. An extensive personal experience with this animal in the study of Gas Gangrene and experiments with dogs of the Rochester Area of the

Manhattan District Project have given us a confidence and satisfaction seldom experienced with other species. Their life span and size permit a continuity and variety of studies not permissible in smaller animals.

Suggested Studies:

1. Protein Metabolism in the normal and cancer bearing patient and animal. Dr. Morton and Dr. Wider have an extensive program centering in this problem.
2. Metabolism of cancer tissue and its relation to corresponding normal tissue metabolism using radioactive isotopes C_{14}, H_3 (Bale).
3. Investigation of various radioactive isotopes in the therapy of cancer and allied diseases. This will include the search for substances having a relative or perhaps a near absolute predilection for cancer tissue.
4. Investigation of possible chemicals or biologicals having a high degree of toxicity to cancer cells relative to normal tissue. Such a substance if found may be enhanced in therapeutic value by labelling with a suitable radioactive isotope.
5. Preliminary work prior to the war by Drs. Heckel and Dowdy indicates a method whereby carcinoma of the uterus or mammary gland in rabbits may be produced at will without the introduction of carcinogenic agents into the body. This technique will provide an extensive field for experimental research. This program is one which will require years to fully explore.

II. Irradiation Biology and Physiology of Normal and Pathological Tissue.

Tolerance limits permissible for chronic exposures have been established and verified during our war-time program. These studies have indicated various limitations especially in reference to the small amount of chronic exposure necessary to produce a reduction or absence of sperm in the seminal fluid (Boche). More knowledge is required relative to the amounts of irradiation required to produce both temporary or permanent sterility and the length of the possible recovery period. The question of sterility based upon sperm motility and a marked reduction in sperm count has not been evaluated. One mechanism of the action of chronic irradiation in reducing the haematopoietic system seems to be reasonably well explained (Boche). Little has been accomplished regarding the action of acute irradiation in general. These and allied problems are pertinent as a Plant Health Hazard in the commercial production of controlled nuclear energy. These same problems, likewise, have a direct bearing upon cancer therapy.

Suggested Problems:

1. Mechanism of the action of irradiation on living cells in general.
2. Mechanism of the action of irradiation on the haematopoietic system. Dr. John S. Lawrence has done a considerable amount of work in this field prior to and during the war. Investigations to date have revealed the life span of the W.B.C. and are suggestive for that of the platelets.

3. Mechanism of the action of irradiation on infections. At present there is no adequate explanation. Work on the Project makes it seem unlikely that previously published explanations are tenable. It is at least certain from previous experiments (S.L.Warren) that the action is not a direct action of irradiation upon the bacteria per se.

4. Action of irradiation upon proteins and enzymes.

5. Study of irradiation toxicity, its causation and therapy.

6. Investigations of irradiation induced mutations in plants, bacteria and fungi.

This would include a careful study of symbiosis and antagonistic or antipathetic symbiosis. This study would be directed toward new therapeutic measures in the treatment of infections.

7. Tolerance rates and recovery from irradiation with special emphasis on ovary and testis. Study of the effects of measured amounts of irradiation upon gestation in each trimester.

III. Betatron

The betatron offers new avenues in cancer therapy, provided the beam can be controlled. It offers the possibility of delivering a predetermined dose of radiation to deep-seated tumors with minimal effects to the superficial layers of tissue. It is proposed that the following studies should be conducted.

1. Animal and plant experimentation.

2. Clinical studies in the treatment of cancer and allied diseases.

TENTATIVE LIST OF COOPERATING MEDICAL SCHOOL AND UNIVERSITY DEPARTMENTS

Tumor Clinics:	Drs. Samuel Stubins, Forrest Young, Karl Wilson, Roger Harvey and Andrew H. Dowdy
Surgery:	Clinical and Fundamental Research Drs. J. J. Morton and B. Mider
Medicine:	Clinical and Fundamental Research Dr. John S. Lawrence
Gynecology and Obstetrics:	Clinical and Fundamental Research on Hormones Dr. George Hockel

Tentative List of Consultants:

Surgery:	Dr. John J. Morton Jr.
Medicine:	Dr. John S. Lawrence
Gynecology & Obstetrics:	Dr. Karl M. Wilson
Pediatrics:	Dr. William L. Bradford
Radiology:	Dr. George H. Ramsey
Hospital Administration:	Dr. Basil C. MacLean
Physics:	Dr. Lee A. DuBridge
Chemistry:	Dr. W. Albert Noyes Jr.
Biology:	Dr. Curt Stern
Economics:	Dr. Donald W. Gilbert
Rochester Health Bureau:	Dr. Albert D. Kaiser

TENTATIVE PERSONNEL REQUIREMENTS AND BUDGET

Department Head (Provisionally, Dr. Andrew H. Dowdy)	$8 - 12,000
Head of Physics Division	5 - 8,000
2 assistants	3 - 5,000
Head of Biology Division	5 - 8,000
2 assistants	3 - 5,000
Head of Chemistry Division	5 - 8,000
1 assistant	3 - 5,000
Head of Bacteriology Division	5 - 8,000
1 assistant	3 - 5,000
Head of Therapy Research Division	5 - 8,000
1 assistant	3 - 5,000
Head of Radiology Division	5 - 8,000
1 assistant	3 - 5,000
12 technicians	2 - 3,000
6 animal caretakers	1800 - 2,400
7 secretaries	1800 - 2,400
Total average salaries	$138,300
Materials and supplies	50,000
Correlative research in University	30,000
	$218,300
Contingency 10%	21,830
Total annual budget	$240,130
Betatron 100 M.E.V. (approximately)	$200,000
Building to house Betatron "	$100,000

BIOPHYSICS INSTITUTE
ORGANIZATIONAL CHART

Director

Administrative Assistant In Charge Of

- Personnel
- Purchasing
- Accounting
- Inventory
- General Shop
- Maintenance

Administrative Assistant In Charge Of

- Scientific Records
- Library
- Photography
- I.B.M. Installation
- Technical Aide

Administrative Assistant In Charge Of

- Health
- Central Laboratories
  - Pathology
  - Hematology
  - Bacteriology
- Veterinary

Departments

Medical Physics

- Chemistry
- Physiology
- Metabolism
- Instrumentation
- Physics
- Industrial

Pharmacology & Toxicology

- Toxicology
  - Inhalation
  - Ingestion
  - Analytical
- Mechanism
- Pharmacology
- Industrial Hygiene

Oncology

- Physics
- Biology
- Chemistry
- Bacteriology
- Therapy
- Radiology

BIOPHYSICS INSTITUTE

ANNUAL BUDGET

Director ($15,000 - 20,000)		$ 17,500
Administrative Assistants (3) ($8,000 - 12,000)		30,000
Personnel, Purchasing, Accounting, Inventory, General Shop, Maintenance		190,000
Library, Photography, IBM Installation, Technical Aide		75,000
Health, Central Laboratory (Pathology, Hematology, Bacteriology)		143,000
Veterinary		
Medical Physics		148,500
Pharmacology and Toxicology		503,500
Oncology		218,300
	Total	$1,325,800
	10% contingency	132,580
	Annual Budget	$1,458,380
	Primary expense (see page 30)	300,000
	Initial Year's Budget	$1,758,380

AIR MAIL

FINAL-1

BMB/rl

23 April 1946.

Subject: Employment of Geneticist.

To: The Area Engineer, Rochester Area, Rochester, New York.

(Attention: Dr. Andrew H. Dandy)

1. Your attention is called to the inclosed letter with Colonel Warren's answer to your original request. Colonel Warren has requested that you initiate whatever measures are necessary to employ the geneticist on a salary basis as provided by your office.

2. As you will note, Colonel Warren has indicated his approval of this arrangement.

For the District Engineer:

1 Incl.:
Ltr., 4/10/46

RICHARD M. BRUNDAGE,
Captain, MC
Exec. Off., Med. Sect.

Cc: Col. Warren

1076057

The University of Rochester
School of Medicine and Dentistry
P. O. BOX 287, CRITTENDEN STATION
Rochester 7, N. Y.

C C P Y

1o April 1946

Col. Stafford L. Warren
Building 2001, Oakland Army Base
14th and Ferry Streets
Oakland, California

Dear Col. Warren:

I have just learned from Dr. Donald Charles that he knows a Ph. D. who has had considdrable experience in human gjenetics, and who is available. Are you still interested in investigating the problem which you had in mind sometime ago regarding compiling data in human genetics from hospital records, etc. If so, would you please let us know promptly, with as must detail as possible regarding the job, since we might then contact this man with the idea of interesting him in the problem.

Sincerely yours,

/s/ Andrew H. Dowdy
ANDREW H. DOWDAY

AHD:deh

(Note from Col. Warren)

To Lt. Col. Friedell or Capt. Brundage:

This should be instituted.

1. It is probable that the MED will have to defend suits brought by former employees who have a defective child, monster or fre-miscarrages or sterility and claim that this is the result of the one or both parent's exposure to radiation or toxic materials.

The medical secfion thus have as good information as can be obtained of the frequency of such occurrences in the normal industrial population in the various district in which the MED had operations during the war. Such data should be gotten where ever it can be found, and from insurance companies Maternal Health Organizations, etc. and the records of representative hospitals, etc., should be surveyed.

2. Leukemieas, Hodgkins Disease, bone tumor and perhaps the caner frequencies should also be obtained from similar sources.

s/s Staff

SCOPE OF PROGRAM FOR 1946-1947

The objectives of the Manhattan Program to be carried on at Rochester will be to conduct research for the Manhattan District along four general lines.

1. Investigation of problems which are directly referable to the health of plant employees as pertains to specific current problems in relation to uranium and other chemical toxicity and radiation hazards

   Examples:

   (1) relationship between dust particle size and toxicity
   (2) continuation of PO studies
   (3) chronic alpha exposure in animals
   (4) chronic radon exposure in large animals
   (5) extension of chronic sperm studies
   (6) high density roentgen exposure levels for animals
   (7) human cases (McCann, Bassett)
   (8) picture of chronic uranium toxicity

2. The maintenance of a service division in charge of a liaison physician who will correlate the operational problems with the research and service personnel of the local Project (all legal responsibility rests with the District)

   Examples:

   (1) Urine examination for Fluoride
   (2) Breath samples and air samples for radon
   (3) Film monitoring
   (4) Urine and blood analysis for Po
   (5) Instrumentation (electronics)
   (6) Spot analysis on the ground (plant)

3. Research on request from the District referable to various legal problems as they arise

   Examples:

   (1) Fluoride and other exposure

4. Research along very broad basic lines leading to the evaluation of

(1) the mechanism of radiation reaction on biological systems and tissues
(2) early detection of radiation damage
(3) the mechanism and pharmacology of uranium and uranium compounds
(4) the metabolism of various radioactive elements and fission products
(5) the purification and measurement of radioactive isotopes
(6) the establishment of the biological life (in contrast to the half life)
(7) the distribution, metabolism and establishment of the safety factors in the production and use of the various radioactive isotopes

In order to insure a continued interest in the program by professional talent of a high order and to insure the best service to the District, it will be necessary to convert the Project from a production status to that of an academic one with a close integration with the respective departments of the Medical School and University. The Project will be organized as a Medical School Department with all the privileges pertaining thereto for the personnel, including graduate credit to qualified advanced students who may participate in the program. Wherever possible specific problems will be assigned to permanent University personnel who are particularly qualified to carry out basic research in the field in question.

Examples:

(1) effect of irradiation upon female reproductive system
Heckel (Gyn and Ob)
(2) effects of irradiation on haematopoietic system
Lawrence (Medicine)
(3) effects of irradiation upon the male reproductive system
Mason (Anatomy and Histology)
(4) Genetics and General Biology
Stern (Biology)
(5) effects of irradiation upon protein metabolism
Morton, Mider, Dounce, Whipple, Bale, Alling