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REFER TO FILE NO.

CORPS OF ENGINEERS
OFFICE OF THE DISTRICT ENGINEER
MANHATTAN DISTRICT
OAK RIDGE, TENNESSEE

5 March 1946

HRE-0580

Subject: Proposed Medical Research Program, 1946-47.

MEMORANDUM to: Brigadier General K. D. Nichols.

1. Attached is a brief outline of the program and proposed budget for the next budgetary period.

2. The figures given for last year's expenditures are approximations because so many of the medical programs were merged with the physics and chemical research programs and the real figures could not be obtained.

3. Estimates for 1946-47 will be fairly close to the programs agreed upon to date, except that no estimate has been received from the Berkeley group. The figure of $250,000 is this officer's guess of what it may be from the rough outline presented in January.

STAFFORD L. WARREN,
Colonel, Medical Corps,
Chief, Medical Section.

Incl.:
Outline.

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PROPOSED MEDICAL RESEARCH PROGRAM - 1946-47

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PROPOSED MEDICAL RESEARCH PROGRAM

I Introduction

During the past three years the Medical Section of the Manhattan District has organized and supervised an extensive research program aimed at the diagnosis and control of those hazards peculiar to the development of atomic energy. These include those injurious effects produced through accidental exposure to radiations emitted by various radioactive materials during experimental or processing operations as well as the chemical toxicity or localized radiation from such materials deposited within the body.

Considerable experimental and clinical information has been obtained by this research program during this period of time. The injurious effects following single exposures to large amounts of radiation have been determined experimentally; the changes following prolonged chronic radiation exposure have been observed; the biological effects which follow the introduction of various toxic and radioactive materials into the body have been demonstrated. Such studies have been useful in the determination of tolerance levels of radiation or toxic materials to which personnel can be safely exposed for a period of time, and the control of such hazards by the prevention of such exposures.

While the above information has been extremely useful in this work it immediately becomes obvious that many critical problems of far reaching scope remain to be solved. Information concerning the method of production of these injurious effects in body tissues is almost completely lacking. No methods are available which might stop or delay the development of radiation injuries. No therapeutic measures are at hand to use following accidental injury to radiation or radioactive materials. It immediately becomes obvious that such problems relate to the fundamental nature of living matter and demand the careful and continued attention of competently trained scientists.

At the present time the above program which is advocated has been hampered and its continuance seriously threatened by the fact that personnel in key and subordinate positions are leaving the project and cannot be replaced. Examination of the cause of this exodus reveals the following inherent weaknesses in the present Manhattan District Medical program which must be itemized:

1. The investigators have no assurances of length of tenure.

2. Many have no academic association or affiliations which would furnish personal security.

3. The work being performed was not undertaken by personal choice, but carried out because of the urgent demands of the war.

4. Following achievement of victory, no specific objective for the individual problem has been stated.

It is obvious that continued success of the research program as established and maintained by this organization demands first of all the immediate correction of each and all of the above-mentioned personnel problems. Otherwise the individual programs will deteriorate rapidly with the final destruction of the nucleus of scientists on which such a successful program largely depends.

It must be emphasized that this program would not necessarily be limited in its applications to atomic problems alone, because, as it has already been shown, the techniques developed will yield information of great importance to almost every branch of biology and medicine. Organized effort again will successfully develop additional new tools which can be used in the attack on fundamental medical problems.

A slightly more detailed outline of the field is given below.

II General Studies of Radiation

The radiations encountered in nuclear fission as well as those encountered from naturally radioactive substances divide themselves into the following types: Alpha rays, beta rays, gamma rays and neutrons. Information available from the literature on previous studies indicates a rather extensive knowledge of the biological effects of X-rays and gamma rays and very little information on alpha and beta rays and neutrons.

The programs were and are organized using the following basic outlines:

A. The Physical Measurement of Radiation of various types - Here it is necessary to develop methods of accurately measuring and standardizing the dosage of radiation to be used in the biological experimentation and measurement of the extent of any hazardous radiation which might be found in a plant area.

B. The Biologic Effects of Radiation. Because of the known deleterious effect of radiation on the animal organism, it becomes necessary to determine the effect of controlled dosages of the various types of radiation on various animal species, so that such observations can be used in the control of possible human exposure.

The types of biological effect possible to study are:

(1) The Survival Time or percentage that the effect of a given dose will reduce the normal life span of different animal species.

(2) The Genetic Effects of radiation as manifested in the development of abnormal individual types from changes in the hereditary mechanism.

(3) Histopathological Changes as demonstrated by abnormal changes in the makeup of the various body tissues.

(4) Physiological Changes produced by the alteration of the normal functioning of animal tissues following radiation.

(5) Biochemical and Enzymatic disturbances which are the potential source of these physiological abnormalities.

C. Methods for the Detection of Minimal Radiation Damage are developed directly from observation of the above types and are applied to study of the human individual or worker. These include studies on:

(1) Biochemical and Enzymatic Changes which may be detected and which, if measurable, can be corrected before irreversible damage has taken place. Examples of such change would be effects on the metabolism of coproporphyrins, excretion of abnormal substances in the urine and the like.

(2) It has been known that radiation depresses the function of the hematopoetic system and detailed study is indicated to detect early changes under controlled dose radiation withall blood elements under continuous observation.

(3) The Production of Anatomical Changes such as epilation, skin erythema, and alterations in the integrity of the skin and the like must likewise be studied under controlled dosage.

D. Studies are likewise indicated on methods for the prevention of radiation injuries. These include:

(1) Methods of physical detection of external radiation by the development of sensitive direct reading instruments capable of the detection of amounts of radiation well below those necessary for demonstrable injury to the animal subjects.

(2) Methods for the determination of harmful amounts of radioactive dusts and gases in air, in water and the like. Many radioactive materials like radium are deposited in the body and in such locations produce injury to tissue. Methods based on the determination of dangerous amounts of these substances by examination of the excreta and direct measurement of the body itself are necessary.

E. Protective Measures. Studies on the efficiency of shielding against radioactive materials, the efficiency of exhaust and ventilating systems against dangerous amounts of dusts, the development of protective clothing and devices, and the development of remote control processing methods have been extremely important in the Manhattan District protection program to date and will continue into the future.

F. The possible therapeusis of radiation damage by the use of replacement therapy for the damaged bodily elements, as well as the reduction in the exposure following deposition of radioactive materials in the body deserves considerable study. Replacement of the damaged hematopoetic elements destroyed by severe radiation exposure offers one possibility; detection and neutralization of unknown toxic substances produced by radiation and other such difficult problems deserve consistent and detailed study.

All the above studies are necessary on alpha, beta and gamma rays and neutrons of varying intensity. In addition, the radiation from the radioactive substances to be discussed has likewise to be considered. Also, the effects of acute and chronic exposure must be determined because of their dissimilarity.

III Hazards Due to Special Materials

For brevity it is preferable to discuss the potential toxicity of special materials by first indicating the type of study to be carried out, followed by the presentation of these materials on which studies have been necessary.

A. First, an actual determination of the toxicity of a substance must be made indicating how poisonous it may be in both acute and chronic exposure. In this way the toxic levels may be avoided in laboratory and plant environments.

(1) The mode of entrance into the body by ingestion, inhalation and skin absorption must be studied as different manifestations and degrees of toxicity may be produced by each route employed.

(2) A careful analysis must be made as to the character of the biological changes with the production of physiological, histopathological and biochemical evidences of damage incurred.

(3) The nature of these injuries and the mechanism by which they occur must likewise be studied inasmuch as this affords information as to the necessary protection and indicated therapy after exposure.

B. Preventative measures require study.

(1) The effectiveness of physical methods for the removal of hazardous dusts, reduction in skin contact and prevention of ingestion must be measured, and methods for accurate determination of such hazards must be developed and used. The use of certain chemicals, ointments, and the like as protective measures must be studied as to their efficiency.

(2) Protective devices such as respirators and clothing must be tested on required substances against which they will be used.

(3) Finally, appropriate investigation of therapeutic measures to be used in the treatment of both acute and chronic poisoning states should they occur in industrial exposure must be made.

Completion of all phases of the above program on a variety of substances provides complete information as to the medical aspects necessary to be considered in protection of the worker, prevention of injury and treatment of injury should it occur.

C. Substances on which studies of this type are necessary are:

(1) Uranium and its compounds

a. Uranium metal and its chemical compounds, oxide, nitrate, chloride, bromide, tetra and hexafluoride, sodium and ammonium sulfates.

b. Uranium chain of heavy metals

Uranium X1
Uranium X2
Radium
Polonium

c. Fission products of cleavage of U-235 and plutonium

d. Artificial isotopes of uranium - 232, 234, etc.

(2) Thorium and its chain

(3) Plutonium

(4) Special Accessory Materials

a. Fluorocarbons

b. Fluorine

IV Production Hazards

The results of studies made on the materials discussed above are applied for the prevention and control of industrial hazards arising in the large manufacturing areas where these materials are used in large amounts.

A. In the Electromagnetic and Diffusion Methods for the isolation of uranium 235 the major hazards are from the uranium compounds, the concentration of uranium X1 and X2, and the special accessory materials and by products formed in the process of manufacture.

B. In the graphite pile where plutonium (239) is produced on a large scale, the hazards are from the alpha, beta and gamma rays, neutrons, the plutonium metal and its compounds, the various radioactive fission products resulting from the pile operation.

C. The chemical isolation of polonium following its formation in the pile incorporates hazards from alpha radiation following absorption into the body.

D. Study of the medical aspects of plant programs aside from the determination of the effect of radiation and chemical toxicity, include additional information obtained from plant investigations as from:

1. Clinical survey of all exposed personnel

2. Monitoring of hazards by special instruments and methods

3. Surveys of new types of graphite piles and production equipment

V Hazards of Military Use

A. Ordnance - assembly of the necessary dangerous radioactive materials into bombs incorporated similar hazards to those of plant production.

B. Atomic Explosion

(1) Immediate Effects

a. Radiation - the radiation occurring at the time of the explosion coupled with blast and heat causes biological effects which may differ from those occurring following other acute known effects from gamma and neutron radiation, and demand study.

b. Blast - the blast of atomic explosion is so intense and may have totally different types of shock waves, recoil waves with other unique biological effects which should be investigates.

c. Heat - The intense burns from actinic type of radiation have not been studied. This also includes the combination effect of all three items in this group: blast, radiation and heat.

d. Tactical - methods of use of bomb for most personnel effect; protection of own assault troops; application of other types of atomic explosion and their biological effects and the like.

(2) Delayed Effects

a. Protective Devices - study of methods of protection against the radioactivity deposited at the time of blast.

b. Decontamination - methods of decontamination of soil and the like must be worked out for cleaning up active areas.

c. Investigative Equipment - special equipment must be developed and tested for use in investigating bombed areas.

d. Study of casualty effects - field study of fission clouds, possible injury to water supply, soil and the like, human damage by population surveys.

e. Study of treatment of all immediate effects such as radiation, heat and blast.

(3) Preparation of pertinent information in proper form for use by strategic forces.

VI Considerations on Organization and Budget

To implement such a medical research program it would seem feasible to model it after one suggested by the present Manhattan District medical program. This has certain advantages in that the main laboratories are located in Medical Centers in the East, Midwest and West. With such a national scope teaching institutions may be utilized and work stimulated in all parts of the U. S.; these men and their laboratories also offer facilities of use to the Manhattan District in emergencies and for medico legal consultation.

Below is a breakdown of the approximate current 1 July 1945-30 June 1946 budget. These funds are for fundamental, applied medical and biological research over a one-year period:

	1945-46	1946-47
University of Chicago	$2,500,000	$1,000,000
University of Rochester	1,700,000	1,200,000
University of California	250,000	250,000
Biochemical Research Foundation	120,000	25,000
Columbia University	80,000	75,000
University of Seattle	60,000	50,000
Los Alamos	100,000	100,000
Clinton Laboratories		200,000
Other Installations for Miscellaneous Problems as Appropriate	100,000	1,000,000
TOTAL	$4,910,000	$3,880,000

It is believed that approximately $5,000,000 per annum is an appropriate budget for a program as difficult and as broad as this must be.

It is proposed to distribute the major portion of the budget among three large universities, one in the east, one in the midwest, and one in the west (University of Rochester, University of Chicago, and University of California, respectively). These three are particularly designated because of their past experience and fitness in dealing with the problems involved. Lesser but still substantial grants for

additional work would be assigned to other institutions throughout the country, a few of which are listed above.

This program should be correlated with the general Atomic Energy program and should be carefully integrated in its control with however, freedom for the various institutions to pursue their individual research problems.

Summary and Recommendations

1. A brief review of the proposed research program is submitted.

2. A listing is made of the difficulties arising at the present time, largely of a personnel nature. It is suggested that official action be taken toward the statement of the proposed research problem on a long-term basis (10 years). When such an action is taken it will be possible to correct these defects by (1) acquiring people who have chosen to pursue this type of work; (2) acquiring people who may be offered academic appointments of some type in universities and other educational institutions; (3) acquiring people who will be provided with a definite estimate of the length of tenure.

Failure to correct these weaknesses will seriously curtail, if not doom, the satisfactory culmination of the work.