PROPOSED PROGRAM FOR
METALLURGICAL LABORATORY
1945 - 1946
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SECRET

MUC-RSS-353

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To: A. H. Compton

From: Robert S. Stone

In re: Finishing Health Work of Metallurgical Project

In considering the question as to when the Metallurgical Project has completed its task I believe the Health Division's activities should be given special consideration. It is my understanding that in addition to providing DuPont with the information necessary to the successful production of product we are also to provide them safe standards for the health of personnel, which standards are to be based as far as possible on experimental data. We are also to provide them with such means of detecting incipient damage as we can uncover. It is my opinion that we have not fulfilled these obligations.

In particular may I point out that we are just beginning to understand the hazards of product and the levels at which damage may occur. We are just on the threshold of finding out what various fission products may do when in the body in amounts not sufficient to cause acute trouble. We do not yet have a means of detecting radiation effects in their earliest stages. We are still developing instruments for accurate survey purposes, especially of neutrons.

In short, because we could not start testing the actions of fission products until these were available and because we could not get a sufficient portion of the instrument group's time while more pressing problems faced them, we are just now at the point where we should expand our research activities in order to obtain more experimental facts to support our "estimated" tolerances.

The information we can still obtain during this war will, I believe, be of value to the health of the workers at W and Y and elsewhere on D.S.M. projects during this war. The Army and Navy are not discontinuing medical research because the end of the war seems to be in sight. The Metallurgical Project should continue its health research activities as an essential and incomplete part of its program.

SECRET

PROPOSED PROGRAM OF BIOLOGICAL RESEARCH AT ~~SOLVAY~~ LABORATORIES FOR THE PERIOD JULY 1, 1945-JUNE 30, 1946

Proposed Program for Met. Lab

The work of the biological section for the past year has been largely one of developing exposure methods and techniques for the execution of satisfactory biological experiments on the effects of external radiations. A fast neutron source has been developed and calibrated and it has been found that the median lethal dose for mice is 90 n and for rabbits 117 n. Similarly, exposure methods have been worked out for pile slow neutrons, and the median lethal dose for acute killing of mice established as about 1.3×10^{13} neutrons per sq. cm. Gamma ray sources have been developed so that animals may be exposed to any dose up to 1000 r/hr. Beta ray sources and exposure methods have been developed and a number of beta ray studies started. For these different radiations the methods are developed to such an extent that it will be possible to administer accurately monitored doses to several thousand animals per day. In addition, methods have been developed for the separation of pure, carrier free fission products for use in biological work. This group has now been transferred to the chemistry division and charged with the responsibility of producing radioactive materials not only for biological use but for all applications. With the development of exposure methods and as the information on acute effects of these radiations was obtained, the work of the group has been gradually shifting to chronic experiments. It is felt that in the coming period this trend should continue, and in addition new experiments should be started for the purpose of obtaining a better understanding of the mechanism of radiation damage. Thus, as the chronic program becomes established, the responsible investigators will be able to give more and more of their time to the more fundamental aspects of the problem, while still maintaining an active interest in the chronic program.

In order to carry out the proposed program it is estimated that substantially the present personnel will be needed; i.e., 6 research associates; 5 research assistants; 2 technicians; 8 animal caretakers and one secretary. The hematological and histological work is being done by other groups, so that if this work were not done by them, new personnel would have to be added to this section to do this work. It is anticipated that no new buildings and no new major pieces of equipment will be necessary.

The detailed proposed program is given below in three sections. Section I is a service function designed primarily to obtain qualitative information on the hazards likely to be encountered at the Hanford plant. Section II is a research function designed to obtain quantitative information on precautions which will be necessary for the safe operation of the Hanford plant, and also in order that the science of nucleonics may be developed with a full knowledge of the hazards involved. Section III is a research function designed to obtain ideas which will be helpful in estimating the effects of new hazards as they arise and in suggesting prophylactic or therapeutic measures which could be taken if necessary. The work of Section III will also be of considerable interest from the point of view of academic radiobiology.

I. Biological Monitoring.

At present the following monitoring animals are being used. a) Three stations of 12 rabbits each placed at strategic points around the area grounds. b) Six rabbits living next to the pile shield. c) Thirty rabbits living in the pile stack gases, and d) sixteen rats living in a room which has the highest product contamination of any on the plant. These animals will all be maintained, but as they die or are sacrificed they will not be replaced. This cannot be considered as research work. It will require about 2 man-months/month.

II. Chronic effects of external radiations.

This program has been under way since July, 1944, but is being steadily increased as more mice and facilities become available. Many of the more interesting effects will probably become apparent starting in the late spring or summer of 1945. Since these experiments are of vital importance to the future of the project and the science of nucleonics, I feel that this program should by all means continue uninterrupted.

The radiations used in this work are fast neutrons, slow neutrons, gamma rays and beta rays. The doses are of two general classes, a) periodic doses repeated either once a day or once a week, and b) single doses administered while the animals are young adults. In general, mice are used for these experiments except in the case of beta rays where rats will be used almost exclusively. Four different strains of mice are used, although by no means will all points be covered by all four strains. There are two standard strains; namely, CF1 and ABC, which are not particularly susceptible to tumors, and in addition, Strain A, which is highly susceptible to lung tumors, and Strain C58, which is highly susceptible to leukemia. These special strains are being used in an attempt to obtain results sooner than they can be obtained by the use of standard strains. In general, groups of 125 animals are used to establish each point. Animals are sacrificed from each group periodically for histological examination, and blood counts will be taken periodically on a small sub-group within each group. Animals are weighed weekly or bi-weekly. The animals will be kept and treatments will continue in the case of the periodic doses until death occurs or until some gross pathological change such as a tumor can be demonstrated. Schedules are arranged so that as nearly as possible 100 animals will remain in each group for the purpose of obtaining data on longevity. Each animal which is not required for histological or hematological work will be given a thorough gross examination following death and all important tissues will be subjected to histopathological examination.

Fast neutrons are obtained from fission occuring in the Clinton Pile and will be administered in periodic doses ranging from 0.01 n to 1.0 n, and in single doses from 15 to 100 n. Slow neutrons are obtained from the Clinton Pile and the periodic doses will be administered at levels from 0.01% to 10% of the acute lethal dose. The single doses will be from 10

to 100% of the acute lethal dose. Beta rays are administered by means of materials activated in the Clinton Pile and are administered to the entire body surface of the animal. The doses to be given in the chronic series will be determined after preliminary experiments of a semi-acute nature have been performed, but in general they will correspond to the doses chosen for the other radiations. Gamma rays are obtained from sources which have been activated in the Clinton Pile and are administered primarily for the purpose of forming a basis of comparison to which all other radiations may be compared. Doses used will correspond as closely as possible to the doses of the other radiations used.

In addition to the above experiments, a very restricted skin area of rabbits will be subjected to beta rays. Both the delayed effects of a single dose and the effects of periodic doses will be studied. This condition will simulate more closely the hazards met on this project, since in general individuals will be exposed to beta rays on only a restricted skin area.

For all of these external radiations any changes of a chronic nature which occur are carefully examined. It is to be expected, however, that most of these changes will be in the form of tumors, and for this reason special care is being taken to make sure that these tumors get proper diagnosis. Changes in the peripheral blood are being carefully followed. All of the groups are being followed from a histological point of view in order to determine any cellular changes which may be responsible for tumor formation or other later effects. All animals are being examined periodically in an attempt to determine any clinical impression which might be possible such as premature aging, listlessness, nervousness, etc.

III. Mechanism of Radiation Damage.

It is proposed to investigate, insofar as present facilities permit, the more fundamental aspects of the problems of the biological effects of external radiations. It is of course impossible to predict what ideas may occur to any of us, but the definite experiments which are proposed, and for which some information is already at hand, are as follows.

A) Effect of Temperature on Radio-Sensitivity. Mice will be maintained at various environmental temperatures and their later sensitivity tested both for acute and sub-acute exposures in an attempt to determine - 1) how necessary it will be to maintain a constant temperature for all our chronic animals and 2) to determine what mechanisms may be responsible for any differences which may be discovered. Only very preliminary results have been obtained to date, and probably nothing can be started until after July 1.

B) General Metabolism Following Beta Irradiation. Rats will be subjected to various doses to total surface beta irradiation and their general metabolic picture studied following this irradiation. This study will attempt to discover the cause of death of these animals which at the present time is completely unknown. Preliminary experiments are under way, and it will be necessary to await the outcome of these before it will be possible to predict the future course of this experiment.

C) A study of the Circulation Following Beta Irradiation. Rabbits will be exposed to beta irradiation and a study of such circulatory reactions as blood pressure, capillary permeability, etc., will be studied. In addition a microscopic study of the capillary circulation in rats will be undertaken during and after doses of beta rays. It is to be expected that many of the harmful effects of beta rays are primarily on the peripheral circulation, and this study should throw some light on this point. Preliminary experiments are under way, and it will be necessary to await the outcome of these before it will be possible to predict the future course of this experiment.

D) A Study of Recovery Mechanisms Following Beta Irradiation. Rats and mice will be subjected to divided doses of beta rays in an attempt to discover the rate at which recovery takes place following a single dose of beta rays. This information should allow one to calculate the effect of periodic doses of beta rays. No work has been started on this as yet, but it is hoped that preliminary experiments may be started soon, and following them the future course of the experiment can be charted.

E) Comparative Studies on Effects of Beta Rays. Various types and sizes of animals are being treated with beta rays in an attempt to discover a correlation between structure and sensitivity. This information should allow a much more intelligent application of the results of animal experimentation to clinical practice. This experiment is now well under way and it is to be hoped that it can be continued after July 1.

F) Activation of Tissues by Slow Neutrons. Rats and rabbits will be exposed to high doses of slow neutrons and their tissues and excreta examined for the presence of elements which have come activated by the slow neutrons. This is one of the hazards of slow neutrons, and whereas rather accurate calculations can be made of the effects which one would expect to be produced in this way it is essential that these calculations be checked by direct experiment. Only preliminary results have so far been obtained, and it may or may not be possible to complete this study before July 1.

G) Additivity of Beta and Gamma Rays. Rats and mice will be subjected to various proportions of beta and gamma rays in order to determine the biological additivity of these two radiations. This information is necessary since in practice these two radiations are almost always found together and also because this will give an important indication as to the mechanism of damage by radiations in general. It is to be hoped that preliminary experiments may be started soon, and they will undoubtedly want to be extended past July 1.

H) Effect of Age on Radio-Sensitivity. Mice will be kept for varying periods of time and the LD50 determined at various ages. This information will be very important as an aid in the interpretation of the results of the chronic experiments. A certain lot of mice have already been indicated for this experiment, but no work has been started. The experiment will require about 18 months to complete.

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UNIVERSITY OF CALIFORNIA

January 11, 1945

Proposed Biochemical Program at
University of California
J. G. Hamilton

In this letter I have attempted to give you a survey of future work which I feel can be accomplished at Berkeley, As you will note it is divided into two major categories, namely, the health project efforts, which of course, will remain under the diredt supervision of Dr. Stone as it has in the past; and problems relating to the use of the 60" cyclotron. The cyclotron is at the disposal of all interested members of the Metallurgical Laboratory and associated projects for aid to them in their various problems.

Iam of the opinion that the present status of metabolic and toxicity studies with product to date is informative to a considerable degree. However, this information is far from being sufficiently complete to enable those concerned to meet all of the present problems involved in the protection of individuals exposed to product. This aspect of the problem, in my opinion, becomes emphasized upon the consideration of the protection of these individuals after their exposure to this substance.

The phases of experimental efforts with product, most of which I believe to be within the category of research activities useful in winning the war and which we in Berkeley are in a position to render assistance, may be summarized in the following manner: It will be noted that the majority of the different research projects listed below are of such a nature that it is difficult to differentiate between effort that is clearly identified with immediate wartime needs to a program of activity which could be classified as being in the longer range category. I feel that this close relationship between the immediate and longer range phases of our work at Berkeley is advantageous because, first; if the program is either terminated or curtailed at anytime there will be relatively little lost effort, and second; a maximum degree of continuity will exist between the two types of approach to the problems laid out for us here.

1. Further study of the metabolic behavior of product oxide smokes with particular reference to the correlation between particle size and pulmonary retention, and a continuation of the investigation of the rates of elimination of product deposited in the lungs for protracted intervals after exposure ranging up to one year.

2. An investigation of the metabolic behavior of water soluble product compounds following inhalation in the form of find sprays and dusts. This phase of the program at Berkeley is now just getting under way and I feel that long term experiments of this nature should be conducted to aid in evaluating the health hazard of product poisoning arising from the inhalation of certain of its compounds.

3. A study of the metabolic properties of product which has been complexed with agents such as citrate, tartrate and oxalate, etc. The purpose of this particular effort is to a large degree directed to the development of a method of administering product in such a manner as not to have this substance remain in considerable quantities at the site of injection or to suffer entrapment in organs such as the liver following intravenous injection of inorganic compounds which become colloidal at the pH of the body. I believe that any thoroughly satisfactory toxicity studies must await the development of more suitable methods of administration than are now available and the use of complexes would appear to possess a fair possibility of success in this direction. This phase of the program is already under way at Berkeley with investigation of five different complexes.

4. It is planned here at Berkeley to undertake, on a limited scale, a series of metabolic studies with product using humar subjects. This part of our program is awaiting the development of a more satisfactory method of administration of product than is now available. It is hoped that the results of the studies with the complexes will enable us to go ahead with this phase of our work.

5. We expect to initiate a limited number of toxicity experiments using 48 rather than 49 to rule out any question of chemical toxicity which is felt may be present in certain experiments using the heavier isotope of product. The 48 is to be produced by the 60" cyclotron for this purpose and even though both isotopes are produced by the deuteron bombardment of tuballoy the specific activity of this mixture ranges from 40 to 100 fold that of pure 49. If we are successful in producing 48 by proton bombardment with the 60" cyclotron the specific activity for the 48 will be approximately 400 times that of 49. These studies are of necessity limited to a relatively restricted number of small animals such as rats and mice due to the rather low yields of 48 produced by the cyclotron.

6. I believe that a few tracer studies both with human subjects and animals using 48 should be made in as much as it seems desirable that the metabolic behavior of product should be studied using concentrations in the body of the order of 1/100th of a microgram per kilo of body weight. Due to the much lower specific activity of 49 as compared to 48, accurate tracer studies using 49 and with this range of concentration in the body are rendered most difficult. It is entirely possible that significant differences in the metabolic properties of product might exist in the range of 1/100th micrograms per kilo of body weight as compared to the usual tracer studies with 49 in which the concentrations employed for administration is of the order of 25 to 100 micrograms per kilo of body weight. This phase of the problem I believe deserves attention since it is the range from 1/100th to 1/10th of a microgram per kilo of body weight which is of greatest concern from the point of view of exposure to personnel.

7. The decontamination studies which are directed towards the goal for developing methods for either the acceleration of excretion of product deposited in the body or its translocation to less radio-sensitive regions is a phase of our effort which I feel is of importance and should be continued. This problem is by nature long range in character and one from which results of positive practical value cannot be anticipated immediately. In fact it is entirely possible that only a very limited degree of success may be achieved. An example of the unsuccessful realization of such a goal can be cited in the unfortunate state of the problem of radium poisoning. In spite of this somewhat pessimistic outlook it would appear to me that the issues at stake merit a certain amount of effort in this direction. It should be noted in passing that work of this character has been in progress at Berkeley for six months.

8. Radio-autographic studies of appropriate tissues are to be made as an aid to the different programs noted above. It is felt that they will shed additional information upon the questions in hand. The value of this technique has already demonstrated its usefulness as an experimental tool.

9. An investigation of the fixation of product by soils, upon buildings, concrete structure, reserviors, etc. would seem to merit some attention in the future. In addition, the uptake of product from soils by plants seems worthy of some investigation and could well be included in a basic research program after the war.

Even though considerable information has been acquired concerning the general metabolic characteristics of the major members of the fission products possessing half-lives greater than three days, there is obviously much additional data concerning these substances that is of interest to the immediate war effort. Included in the following list of problems are several research projects that can be identified with longer range developments for the future.

1. Considerable information has already been acquired concerning the behavior of fission products when distributed in the air in the form of a smoke of U_3O_8 produced by burning tuballoy rods whose radioactive composition approximated that of the average Clinton slug. However, in view of the fact that this material is now becoming available with a much higher specific activity it would appear desirable to study the behavior in the body of such smokes at a much higher specific activity. It is planned shortly to initiate exposures of rats to product oxide smoke in which the fission product activity is of the order of 1000 fold that of the average material from the Clinton unit. This type of research effort has in mind the simulation on an extremely small scale either a destructive fire at Hanford or an accidental explosion at Y.

2. The distribution in the body of fission products following inhalation as a spary or dust of water soluble compounds would seem to be worthy of devoting some effort by our group here at Berkeley on the basis for a project to be classified as not being identified as urgent in winning the war.

3. The metabolic properties of fission products either possessing relatively short half-lives or of low abundance should be undertaken in the future. This type of effort I believe can be identified with longer range

development projects. Radio-elements in this category include Se, Mo, 43, Rh, Pd, Ag, Cd, Sn, Sb, Nd, 61, and Eu. This project would be patterned closely after the procedures employed for the fission products already studied. It should be noted in passing that the production and isolation of most of these minor members of the fission group in the carrier free form could be best accomplished with the aid of the 60" cyclotron.

4. The study of the fixation of fission products in soils is now well under way with the view of aiding the problem of waste disposal at Hanford and Clinton. It includes an attempt to estimate the hazards that may be expected to arise from the accidental or intnational release to the soil of fission products. Included in this program is the investigation of the absorption of individual radioelements of the major members of the long life fission group in tracer amounts in a selected group of soil clays. A measure of the degree of removal of fission activity from the waste soils percolated through beds of typical Hanford soil samples is being made at present as well as the migration of radioactive tracers in such soils. In order to investigate the possibility of decontamination of active soils, leaching and exchange experiments are to be carried out at some time in the near future.

5. The study of the fixation of fission products on building materials. This is to include measurements of the degree of fixation of radioelements on the surfaces of concrete structures such as reservoirs, etc. wooden building materials and a number of miscelleneous substances such as rubber, glass, metals, plastics, etc. Special attention will be paid to the problem of decontamination of these materials.

6. The study of the agricultural hazards resulting from the absorption of fission products by plants. Measurements of the degree of uptake of radioelements by agricultural plants from active soils is now being carried out in the laboratory and in the greenhouse. The distribution of the absorbed activity within the plant is also being investigated.

7. Fundamental and long-range studies of the chemical factors involved in the absorption of trace elements on clay minerals can be considered as being a part of the plan for future work. Information regarding the adsorption of polyvalent ions either in macro, or micro amounts is virtually non-existent.

8. A detailed study of the chemical factors involved in the fixation and absorption of trace elements by plant roots. The technique of preparing radio-autographs will be of considerable aid in this problem.

9. Immobilizing of agricultural lands by the use fo fission products.

10. It would appear, in my estimation, of value to consider the therapeutic possibilities of several of the long-life fission products for the treatment of malignant conditions. It might be noted in passing that two of the long-life fission products have already demonstrated that they are of therapeutic value, namely, radio-strontium in the treatment of certain types of bone cancers, and radio-iodine for the treatment of hyperthyroidism.

I have not devoted much space in the above discussion concerning fission products to the question of the military use of these substances. Actually the results in hand and those anticipated in the near future can be assembled and interpretated to answer many of the problems that might be expected to arise if such military issues ever present themselves. Moreover, the planning of our fission product work both with the smokes and soil studies has always kept the military aspects in mind. If we were directed tomorrow to reorganize our fission product work to the military needs of radioactive warfare almost all of our past and present efforts with fission products would be directly applicable.

The overhaul period for the 60" cyclotron has unfortunately been prolonged by several technical difficulties. However, we achieved resonance with deuterons at a calculated energy of 23.5 mev three weeks ago. At present the necessary adjustments and trouble shooting is under way to permit us to increase the efficiency to the point where effective and routing bombardment of samples for the Metallurgical Laboratory, siteY, the Rochester group, and Dr. Latimer's section can be initiated. This achievement should be accomplished with the next few weeks.

I have indicated below some of the immediate duties to be performed by the instrument as well as some longer range projects for the future. Obviously there are many other experimental problems for which the cyclotron can be of use but since I am not a physicist I am certain that the following items do not cover other important research problems in this direction.

1. At present one of the most effective uses of the 60" cyclotron would appear, from discussions I have had with various members of the Metallurgical Laboratory and in particular Dr. Seaborg and Dr. Szilard, to be the preparation of certain radioactive isotopes of elements 92 and 96 inclusive. Of course, I am not in a position to state the relative importance of different isotopes that might be thus prepared but it may be of interest to indicate to you some of the possibilities which include: $U^{230, 231}$ $Np^{233,234,235,236}$, $Pu^{235,236,237,240,241,}{}_{95}{}^{239,240}{}_{96}{}^{241,242}$. Many of these isotopes, notably elements 95 and 96, as well as the lighter isotopes of tuballoy, Neptunium and product presumably could only be produced by cyclotron bombardment if they exist. Others such as $Pu^{240,241}$ could be produced with relatively small amounts of Pu^{239} which would considerably simplify many of the investigations it would be desirable to make with these various elements. The amounts produced, of course, would presumably range from 1/10th fo a microgram to 100 micrograms but it is my understanding that these amounts would be adequate for purposes such as determination of the character of radiation, rates of spontaneous fission and a study of the chemical properties of 95 and 96.

2. The increase of energy from 16 mev and 32 mev for deuterons and alpha particles respectively to 23.5mev and 47mev will provide us with a source of faster neutrons than were heretofore available. I have found that several members of the Metallurgical Laboratory, notably Dr. Burton and Dr. Franck, have shown a lively interest in the use of these high energy neutrons for the study of their interaction with such materials as graphite, Be, aluminum, etc. It might be noted in passing that due to the manner in which the external beam is focused, a small area of very high fast neutron intensity is present just adjacent to the target material. Measurements which have been made at various times by different individuals at Berkeley indicate a fast neutron flux of the order of 10^{12} neutrons per second per square centimeter when beryllium is bombarded with 200/μa of 16 mev deuterons. Another possible useful role that these fast neutrons may perform is their application for studying isotopes produced by the n-p and the n-alpha reaction which require very high neutron

energy. It is possible that these fast neutrons can be employed for the purpose of cross bombardment which would be of aid for the identification of certain members of the fission group.

3. The availability of more energetic deuterons and alpha particles will make possible reactions such as the d-alpha type which should also prove of value for purposes of cross bombardment as an aid in identifying various members of the fission group.

4. It is my impression that biological studies concerning the relationship between neutrons of various energies and their relative biological effects would be of interest to various members of the health group. The problem may not be of immediate importance but it would be worthy of consideration for experimental investigation in the future.

5. A very pressing and immediate use of the instrument is the preparation of U^{232} and Pu^{238}. These two isotopes are of current and practical usefulness to both the chemists and biologists.

6. The availability of the 60" cyclotron to both the health group at Berkeley and to Professor Latimer's group has proven in the past to be of considerable assistance and is sure to continue to be in the future. Examples are the production of 48 for tracer work and toxicity studies with product for the health group and the preparation of some of the short lived fission products and Np^{239} for Dr. Latimer's group.

7. For the future there is the very interesting possibility of studying nuclear reactions produced by the acceleration of nuclei of substances such as H^3, Be^9, C^{12}, N^{14}, O^{16}. In the case of O^{16} the accelerated particles would have an approximate energy of 200mev in the 60" cyclotron. This of necessity would require considerable development of a new type of ion source to make possible the production of a sufficient number of stripped atoms to be usable. I might note in passing that Lithium and Boron were intentionally omitted from the list because the presence of these two elements, and in particular Lithium, in the vacuum chamber of the cyclotron would after a short time render operation difficult if not impossible until the apparatus had been thoroughly cleaned. In addition, of course, the possibility of producing protons up to 20mev and deuterons to 40 mev and alpha particles to 80mev exists although here again the successful achievement of this feat would presumably require the expenditure of considerable time and effort and shoudl be considered in the category of future development.

I trust that the above information will serve as an indication of the nature of our various present and future enterprises at the Crocker Laboratory. The staff of the biological group is equivalent to twelve full time workers which includes a secretary and guard. The cyclotron staff is comprised of 14 full time people whose number will be reduced to an operating crew of 10 when our present period of tuning up and adjusting is completed.

J. G. Hamilton, M. D.

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PROPOSED PROGRAM

Health Division of the Metallurgical Laboratory

July 1, 1945 to June 30, 1946

L. O. JACOBSON AND R. S. STONE

The chief responsibility of the Health Division will remain the same as in previous years, namely to protect the health of the personnel working within the Metallurgical and Argonne Laboratories, and the public living in surrounding areas, from all hazards originating in the operation of the laboratories, and to make available to other parts of the Project and to "W" such information as is found to be of value. To achieve this purpose complete medical examinations must be given; attention must be paid to the prevention and treatment of ordinary work connected injuries and diseases; and in addition the hazards peculiar to the laboratory call for special attention. The intelligent and logical approach to the prevention, prophylaxis, detection and treatment of radiation or chemical injury stems from a complete knowledge and understanding of the basic and fundamental mechanism of its production. Such knowledge combined with the development of the ability fo monitor, identify and isolate the chemical or radiation source involved permits us to establish tolerable doses on firmer grounds than before. In the past our efforts have of necessity been directed toward the answering of questions of immediate and practical importance regarding exposure to hazards from the standpoint of the laboratory and all DSM Project personnel and the public at large. Certain of these questions have been answered. Others are still being studied and their solution must be considered as a continuing responsibility of the Health Division to "W" since the information is needed for safe operation.

It seems advisable in view of the potentialities of nucleonics not only in the war but in the future of our country to keep the medical and biological fields astride of the advances being made in chemistry and physics. This can only be done by striving to understand the basic and fundamental problem of radiation damage and directing part of our effort in this direction as well as being familiar with the biological behavior of radioactive materials and chemicals concerned in present and future developments.

Any program proposed for the Metallurgical Laboratory for the fiscal year, July 1, 1945 to June 30, 1946, must, therefore, conclude: (a) Health service activities for any laboratory personnel and (b) Health research activities which have not yet been completed. In addition we feel it would be of great value to (c) extend the fundamental research in the Health fields.

In line with the above introduction the following program for the Health Division of the Metallurgical Laboratory from July 1, 1945 to June 30, 1946 is proposed:

I. Health Service Activity

A. Medical examinations of laboratory personnel; pre-employment, interval, transfer and terminal

B. Routine medical care of personnel

C. Clinical laboratory examinations for various types of damage to personnel exposed to either tolerance or larger doses of radiation of chemicals.

D. Examination of body secretions and excretions for radioactive materials.

E. Monitoring of personnel for general and local exposures.

F. Surveys of laboratories for various degrees and types of radioactive or chemical contamination.

II. Research Activities.

A. Detection of incipient damage to personnel from chemically toxic materials or radiations by a study of metabolic disturbance such as:

(1) Pigment metabolism (Porphyrians) already shown to be applicable to Uranium toxicity in humans.

(2) Leucocyte phospherus metabolism—results of preliminary nature suggest that the alteration after invivo irradiations of various phospherus containing constituents of leucocyte may be a good indicator of incipient damage from irradiation.

B. Development of simpler methods for monitoring excretions and secretions.

C. Further development of methods for studying damage to the hands from radiation.

D. Investigation of methods of prophylaxis and treatment of chemically or radiologically injured personnel.

E. Study of acute radiation effects — external and internal in terms of lethal action, hematological and histological damage and others. These studies will be largely confined to product and fission products except as new materials under consideration become important to the Project. Since the location within the body of the internal radiaters influences the effects, the distribution of these materials will be studied.

F. Study of Chronic radiation effects from external radiation. The object of these studies is to correlate previously known effects with our present series and to establish the tolerance dose on a more quantitative basis. Wherev er piles or large quantities of radio-active solids, liquids or gas are used external radiation is a serious problem.

1. External gamma rays - radium (NCI)
2. External x-rays (Chicago and N.C.I.)
3. External neutron beams (in cooperation with Clinton laboratories)

G. Study of chronic radiation effects from radio-active materials on and in the body. The object here is to find the tolerance dose for such materials according to their localization. To find the tolerance dose one must kno w the minimal effects from doses just above the tolerable dose. Alpha and beta radiations will be used and those which deposits in or on the following organs will be studied.

1. Bone — for Betas, probably Sr^{89}, for Alphas, product and radium.

2. Skin - for Betas, probably Sr^{89}, or P^{32}; for Alphas, product.

3. Digestive tract — since we wish to get the specific effect on this tract without complicating radiations from elsewhere, a poorly absorbed compound of some emitter such as yttrium will be used. When available product will be used as an alpha emitter.

4. Respiratory tract — Product as an alpha emitter and some emitter that is not too readily absorbed through the lung will be used.

The answers to the above four studies are badly needed because wherever product, fission products or other radioactive materials are used they may be inhaled, ingested or deposited on the skin.

H. Chronic effects of material whose toxicity is largely chemical. Various compounds of tuballoy are the main ones with which we are concerned at present but thorium and its compounds and other materials may need study. Such substances should be studied:

1. By ingestion

2. By inhalation

3. By injection

The determination of how these agents act would be a great step forward in discovering tests to demonstrate incipient damage and also in devising means of treating any individuals who may be damaged.

I. Mechanism of radiation and toxicological effects:

1. <u>Physiological Methods such as:</u>

a. Identification of toxic materials secondary to radiation.

b. The changes in the circulatory system.

c. The alteration of water balance.

d. The changes in the endocrine system.

e. The effect of cellular environment on radiation sensitivity.

f. Functional tests of organs by leading to capacity to determine reserve power.

2. <u>Cytological and immunilogical methods, such as:</u>

a. The changes in the lymphocyte and its precursors and their relation to immunological phenomena.

b. The comparative sensitivity of cells.

3. Biochemical methods, such as:

a. The effects upon enzyme systems and other proteins studied both in vivo and in vitro. This is particularly important in the study of carbohydrate and protein metabolism. Nucleic acid metabolism should be given special consideration and should be studied intensively.

b. The use of radioactive tracers in the study of biological phenomenon and particularly with such problems as mentioned above.

J. Development of methods for using the newer radioactive materials as tracers as they become available for use on problems related to the Project as a whole.

K. Consideration of the use of new radioactive materials in treating disease.

L. Research and development studies on instruments and methods for measuring health hazards and the techniques of using same.

The instruments for Health monitoring purposes have not yet reached a satisfactory stage of development and production. Neutron measuring instruments in particular are in an unsatisfactory state. Product monitoring apparatus needs considerable improvement.

III. Personnel and space.

The program outlined above is not appreciably different from that submitted for 1944-1945. Most of the problems are long range ones. Hence the personnal and space requirements are essentially those already requested. The expansion of the laboratory health activities occuring concurrently with some contraction of other Metallurgical Project health activities allows an increase in our laboratory health personnel without an over-all increase in the health program as a whole. The space which we hope to have before July 1, 1945 should be sufficient for the 1945-46 program. It is conceivable that an expansion of activities along a promising line may be indicated and would then require further consideration of space and personnel.

The above constitutes the program anticipated for the next year. Undoubtedly new problems will arise and old ones seem less important. It is our aim to take care of our own problems, to try to foresee those of Hanford and those of other D.S.M. projects that are similar to our own and to cooperate with the medical office of the Manhattan district so as to avoid overlapping of service or research activities.

1/1/45

Clinton Laboratories.

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No. 1 of 9 copies, Series B

To: M. D. Whitaker

From: J. E. Wirth, M. D.

In re: PROJECTED WORK AFTER JUNE 30, 1945

At the Project Council Meeting in December 1944, Mr. Compton requested recommendations for work to be continued after June 30th, 1945. I am forwarding the following recommendations to you from the Medical Div. A copy of this is being sent to Dr. Stone as the Clinton Laboratories part of the over-all medical program.

Required medical services may be summarized as follows:

I. Medical Activities

(a) Pre-employment, interval, termination and transfer physical examinations.

(b) Dispensary service for treatment of sickness and injury occurring on the laboratory's site.

(c) Laboratory examinations.

(d) Observation of personnel exposed to hazards.

(e) Medical surveys of groups in hazardous areas.

(f) Analysis of medical data collected during the project.

II. Health-Physics Activities

(a) Surveys.

1) Personnel. Metering with ionization chambers and films and monitoring for hand, clothing and other personal contamination.

2) Area. Routine surveys for contamination, over-tolerance radiation, and local area air-borne radioactivity of all Laboratories in use. Decontamination laundry monitoring.

3) Atmosphere. Field surveys necessary as long as the pile is in operation.

4) Waste Disposal. Monitoring of effluent waste waters and surveys of activity of adjacent drainage areas. (White Oak Creek drainage system and Clinch River)

5) Maintenance and calibration of survey instruments in use.

III. Projected Medical and Health-Physics Problems

(a) Analysis of medical date collected during the project.

(b) Study of methods of final disposition of contaminated buildings and equipment.

(c) Determination of atmosphere surveys necessary for radioactive materials from newly developed piles or procedures.

(d) Study and determination of a method and necessity of final disposal of and means of protection of persons from radioactive contamination present in the drainage area.

(e) Study of means of final treatment or disposal of contaminated materials in the burial grounds to prevent them from being a future hazard.

(f) Development of new instruments still needed; better alpha counters, portable counter circuits and slow neutron measuring devices.

(g) Determination and study of health hazards connected with research in any new fields under investigation by the laboratories.

All medical and health-physics activities will have to continue at the present level as long as any departments of the laboratories continue to work. It must be remembered that the Medical Division has been understaffed because of the scarcity of trained personnel even for the present routine service work. Expansion is in order even with continuance of the activities of the laboratories at the present level, to the extent of two physicians, two health-physicists, five instrument checkers, one nurse and two medical technicians; a twenty percent increase. If the present activities of the laboratories decrease, health-physics personnel monitoring and surveying these areas may be transferred to inadequately staffed areas. Any new projects undertaken by the laboratories would require a proportionate additional medical and health-physics personnel.

John E. Wirth, M.D.
Medical Director

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