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to safeguard the workers in all cases.

(2) Clinton Laboratories. - The Clinton group had an industrial research section similar to the one at Chicago. This group assumed responsibility for the medical supervision and protection of all workers at Clinton Laboratories, both by monitoring the plant and making physical and laboratory studies of the workers at frequent regular intervals.

(3) The University of Rochester. - The University of Rochester also had an industrial research section. Film and instrument monitoring methods and protective devices were developed, for the protection of the workers exposed to uranium and other special materials (See App. B 6). Actual monitoring of the plant areas, under the supervision of the District Medical Section, was done to detect dangerous amounts of radioactive substances. Consultant service was provided, for the determination of the extent of the radioactive hazard in the individual industry.

5-7. Reports on Research Activities. - The various research sections kept in close contact with the Office of the Medical Section through the medium of progress reports. The Chicago, Clinton Laboratories, University of California, and National Cancer Institute reports are filed with the District and are designated as the CH and CK reports. The University of Rochester and Biological Foundation reports are also filed in the Office of the Medical Section and are designated as M reports. The reports from the University of Washington are filed in the same office and are designated as Fish Program Reports and Charts.

5-8. Organization.

a. Manhattan District Personnel. - The District Engineer was required to approve all contracts of the Manhattan District, including

those for medical research. The Chief of the Medical Section, Colonel Stafford L. Warren, acted in a staff capacity to the District Engineer, to provide information on the District requirements for biological research and to report the progress of the program. Colonel Warren organized, supervised, and integrated the medical research program. In this task he was aided by Lt. Col. H. L. Friedell. In March 1945, Lt. Col. Friedell was appointed Head of the Division of Biological and Health Physics Research of the Medical Section. Capt. J. W. Howland was selected as Assistant Division Head, and, with Capt. David Goldring, acted as liaison officer to the research organizations. The relationship of the Division of Biological and Health Physics Research to the civilian research agencies is illustrated in the attached chart (See App. C 22).

b. University of Chicago. - The Health Program of the Metallurgical Laboratory of the University of Chicago was directed by Dr. Robert S. Stone, formerly professor of radiology at the Medical School of the University of California. Dr. Stone joined the Metallurgical Project as Associate Project Director for Health, in June 1942. He was charged with the responsibility of protecting the health of all of the individuals engaged in the pile process. To discharge this obligation he was required to procure the necessary personnel, to set up safety standards and safe-operating procedures for the pile process, and to plan and supervise the research necessary to insure intelligent formulation of the standards of health protection. Dr. Leon Jacobson, a member of the staff of the University of Chicago Clinics, had been assigned previously the task of clinical care of project employees, first as a consultant in January 1942 and later as an assistant (November 1942) in that capacity with

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Dr. Stone. Dr. Simeon T. Cantril, previously Director of the Radiological Department of Swedish Hospital, Seattle, Washington, became Dr. Stone's assistant in August 1942, and, with Dr. H. M. Parker, an expert in radiation dosimetry, instituted the industrial hazards section, charged specifically with the responsibility of instituting safe-operating practices for radiation and radioactive substances (Both Dr. Cantril and Dr. Parker were transferred to Clinton Laboratories in August 1943, to head the Health Program and Instrument Section respectively). Dr. E. W. Hollan, Assistant Professor of Physics, University of Chicago, aided in the development of monitoring instruments and in the design of the shielding required by operation of the pile. After Dr. Cantril left the staff, Dr. L. O. Jacobson became assistant to Dr. Stone. The activities of the organization were divided into the following groups, headed by the persons listed:

1) Clinical Medicine - Dr. L. O. Jacobson

2) Biological Research - Dr. K. S. Cole

3) Industrial Hazards - Dr. J. J. Nickson

Dr. Cole had been Associate Professor of Physiology, College of Physicians and Surgeons, Columbia University, and performed experiments on toxicology of radioactive substances. He was assisted in this work by Dr. R. E. Zirkle, Professor of Botany, University of Indiana, Dr. C. L. Prosser, Assistant Professor of Zoology, University of Illinois, and Dr. A. M. Brues, Associate Physician, Huntington Memorial Hospital, Boston, Mass. Dr. Albert Tannenbaum, of the research staff of Michael Reese Hospital, Chicago, Illinois, performed the feeding experiments to determine the toxicity of uranium compounds for mice. The Industrial Hazards Section, after Dr. Cantril's departure, was headed by Dr. J. J. Nickson (serving directly

under Dr. Jacobson) who was assisted by Dr. John E. Rose. Assisting in the Section on Clinton Medicine were Dr. Samuel Schwartz, who was in charge of biochemistry, and Dr. E. S. G. Barron, Associate Professor of Medicine, University of Chicago, who directed studies of enzyme Chemistry. The Pathology Section was headed by Dr. William Bloom, Professor and chairman of the Department of Anatomy, at the University of Chicago. Dr. Bloom was assisted by Dr. Herman Lesco. Dr. C. Failla, Professor of Radiology and Director of the Radiological Research Laboratory, College of Physicians and Surgeons, Columbia University, Dr. W. H. Talliaferro, Dean, Division of Biological Sciences, University of Chicago, and Dr. J. Watson, Professor and Head of the Department of Medicine, University of Minnesota, acted as consultants to the project. The organisation grew in size as the research program expanded, until approximately 215 persons were employed at the period of greatest activity. This does not include the 90 people employed in the clinical group. Not included in this total are persons in the Instrument Section who worked full or part time on the development and maintenance of instruments required by the Health Program.

c. Clinton Laboratories. - The health program at Clinton Laboratories, under the supervision of Dr. R.S. Stone, was directed by Dr. Simeon Cantril, from its inception in July 1943 to September 1944. He was replaced at this time by Dr. John Firth, who had been previously at the National Cancer Institute. Dr. Firth, in addition to his duties as director, supervised the clinical medicine section of Clinton Laboratories. Dr. H. J. Curtis, formerly Assistant Professor of Physiology, College Physicians and Surgeons, of Columbia University, was in charge of biological research. Dr. K. Z. Morgan, previously a research physicist

at the University of Chicago, was in charge of the instrument section. At the peak of employment, a total of approximately 100 persons were employed by the Clinton Laboratories Health program.

d. The University of Rochester. - The Biological and Health Physics Research project of the University of Rochester was inaugurated in April 1943, with Dr. Stafford L. Warren, Chairman of the Department of Radiology, in charge. He organized and supervised the project, which was divided into the following major sections, headed by the individuals listed:

1) Radiology - Dr. Andrew H. Dowdy.

2) Pharmacology - Dr. Harold Hodge.

3) Instruments and Special Problems - Dr. William F. Dale.

All of these men were members of the staff of the University of Rochester at the start of the project. Dr. Dowdy was associate professor of radiology, Dr. Hodge was associate professor of biochemistry and pharmacology, and Dr. Dale was associate in radiology. As Dr. Warren became more and more concerned with activities of the Manhatten District, Dr. Dowdy became assistant director and, in November 1943, was appointed director. He continued to supervise the radiology section, until Dr. Robert Roche (Research Fellow University of Pennsylvania Medical School) was added to the staff, in the spring of 1944, to head the department. Dr. Dowdy was assisted in the administration of the project by Dr. Maury Wantman, who also was in charge of the statistics section. Other individuals who supervised research groups included:

(a) Dr. George Boyd - - Head of Cyclotron and Nuclear Research Department, Biochemical Research Foundation, Newark, Del., in charge of

special studies of the toxicity of certain radioactive substances.

(b) Capt. Fred Bryan -- Formerly instructor in the School of Medicine and Dentistry, University of Rochester, in charge of hematology (subsequently replaced by Dr. George Suter, also instructor in Medicine, at the University of Rochester).

(c) Dr. Alexander Bounce -- Instructor in Biochemistry at the University of Rochester, who was responsible for enzyme chemistry.

(d) Dr. Francis Haven -- Associate in Biochemistry at the University of Rochester, who was in charge of the mechanism group.

(e) Capt. Roger Metcalf -- Who was responsible for the pathology of the experimental work.

(f) Dr. L. T. Steadman -- Associate in Radiology at the University of Rochester, in charge of spectrochemistry.

(g) Dr. Herbert E. Stokinger -- Immunochemist, University of Rochester, who was responsible for supervision of inhalation experiments.

(h) Mr. David Tiedemann -- Who replaced Dr. Mantman as head of the statistical section.

(i) Capt. Paul Rekers -- Conducted special hematological research in radiation exposures.

(j) Capt. William Valentine -- Conducted similar hematological research in radiation exposures as Capt. Paul Rekers.

(k) Dr. Carl Voegtlin -- Retired Chief of the National Cancer Institute, an authority on toxicology, served as full time consultant to the pharmacology section.

Other part-time consultants to this section included:

(l) Dr. H. H. Schrenk -- Associate Toxicologist of the Bureau

of mines.

(m) Dr. J. F. Treon - - Instructor in Toxicology, Kettering Laboratory of Applied Physiology, Cincinnati, Ohio.

As the research program expanded, especially trained individuals were added to the staff until a peak of approximately 200 persons was reached.

e. University of California. - The medical research program at Berkeley was under the direction of Dr. Joseph G. Hamilton, Assistant Professor of Medicine and Radiology, Radiation Laboratory, University of California. Dr. Hamilton was assisted by Dr. Louis Jacobson, Dr. Ray Overstreet and Dr. Kenneth S. Scott. The program was closely correlated with that of the University of Chicago. Approximately 16 persons were employed at the peak of operations.

f. National Cancer Institute. - The work at National Cancer Institute was under the direction of Dr. R. R. Spencer, Chief of the National Cancer Institute of the U. S. Public Health Service. He was assisted by Drs. E. Lorenz, A. D. Eschenbrenner, M. Deringer, W. E. Heston, and approximately 6 others.

g. Columbia University. - The research performed at Columbia University was integrated with the radiation program of the University of Rochester and was under the direction of Dr. U. Failla, Professor of Radiology and Director of Radiologic Research Laboratory, College of Physicians and Surgeons, Columbia University. He was assisted by Dr. T. C. Evans. Approximately 6 additional persons were employed on this project.

h. Biochemical Research Foundation. - The program of research at the Biochemical Research Foundation, Franklin Institute, Newark,

Del., was directed by Dr. Ellice McDonald, Director of the Foundation. He was assisted in this work by Dr. Harold M. Terrell. Approimately 14 other persons were employed in the program.

i. University of Washington. - The fish program conducted by the University of Washington was headed by Dr. Lauron Donaldson, assisted by Mr. Richard Foster. Approximately 4 other individuals were employed in the performance of this experimental work. Mr. Hanford Thayer acted as CSRD consultant to the project.

j. The Cost. - In most cases the research projects in the foregoing paragraphs were carried out in areas where types of research other than medical were being performed. Because of this fact, costs for the medical research alone are not available, since all costs have been lumped into one sum for each project.

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SUPPLEMENT TO MEDICAL HISTORY ON MEDICAL RESEARCH

Introduction

During the period from 1 July 1946 to 1 June 1947, the activities of the Medical Research Groups of the M.E.D. was occupied in the following three ways:

1. Termination of the research problems of the period 1942-1946.

2. Writing of final reports and chapters for the medical volumes of the M.P.T.S.

3. Reorganization of the research projects in many instances under new research directors, and the setting up of new programs directly applicable to the peace-time application of atomic energy.

To aid in the overall correlation of the research program, an interim medical advisory committee under the direction of Dr. S. L. Warren, (formerly Col. S. L. Warren) was set up at the request of the District Engineer. Action of this committee toward the shaping of present policy and program as well as future recommendations will be considered in greater detail later. For clarity the activities of this committee will be considered in the resume as their recommendations shape the general policy, rather than as a separate section.

Report of Past Activities

As mentioned above, a very major effort during this period was in the termination of research problems and the writing of reports, both as final reports and portions of the M.P.T.S. soon to be released. In a program of such a size, even the summarized accounts are of such magnitude that it becomes impossible to summarize it in any brevity. During this six-month

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period the research branch of the Medical Division has prepared a medical research summary of some 160 pages containing all the pertinent findings of all associated projects. (This may be included as a portion of the history if desirable).

In the early part of this period it was requested that the Research Division prepare for future use a formal statement of the general scope of the entire research project which would cover all past and future activities. This was modified from previously prepared material and was approved by the medical advisory committee at their September meeting. This scope is as follows:

SCOPE OF RESEARCH PROJECT

I 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 outline:

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 make-up 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 with all 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 measurements 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.

II 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 studies 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 studies 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 hexa-fluoride, 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
c. Beryllium
d. Others

III 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.

IV Hazards of Atomic Catastrophe in Production Areas.

A. Immediate Effects

(1) 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.

(2) 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 investigated.

(3) 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.

B. Delayed Effects

(1) Protective Devices - study of methods of protection against the radioactivity deposited at the time of blast.

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

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

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

(5) Study of treatment of all immediate effects such as radiation, heat and blast.

(C) Preparation of pertinent information in proper form for use by catastrophe units in production areas.

Organization

The research branch of the Medical Division has continued under the supervision of Major J. W. Howland working closely with the Advisory Group under Col. S. L. Warren (now Dr. S. L. Warren) following his return from Operations Cross Roads where he acted as Chief of the Radiological Safety Section. Lt. R. V. Randall replaced Capt. D. Goldring, AUS who was discharged in July 1946.

Several changes have occurred involving changes in directorship of the Research Groups, however. In July 1946 Dr. A. M. Brues succeeded Dr. L. Jacobson as head of the Medical Group of the newly formed Argonne National Laboratory which supplanted the previous Metallurgical Group of the University of Chicago.

Dr. Paul Henshaw acted as head of the Clinton Laboratory Medical Group under the Monsanto Chemical Company for a short time, until an agreement was made between the United States Public Health Service and the Monsanto Group in October 1946, at which time Dr. A. Hollaender was appointed director and Dr. Henshaw placed in charge of the radiation studies already being investigated. With the change in supervision, a definite modification of program at the Clinton Laboratories is taking place.

New medical research programs have been instituted at the Monsanto Chemical Company at Dayton under the direction of Dr. Joseph Svirbely and at the Western Reserve University at Cleveland under Dr. H. L. Friedell. The Dayton program relates to further investigations of the polonium problem. The Western Reserve program is investigating thorium toxicity and certain special aspects on the fundamental nature of biological action of radiation.

New contracts have been approved for workers at the U. of California at Berkeley. Dr. R. S. Stone, formerly medical supervisor of the Metallurgical

Project has assumed directorship of the program on whole body radiation in human and biological effect of radioactive iodine. Dr. John H. Lawrence is working on certain fundamental aspects of radio isotope research.

Dr. Lauren Donaldson of the University of Washington has expanded his program to meet certain findings pertinent to the project welfare and re-emphasized as a result of the Cross Roads Operation. His program now includes experiments both at the Hanford Engineering Works Project and at the Seattle Laboratories of the University of Washington.

Finally, two new programs have been submitted by the University of Virginia under Dr. Alfred Chanutin specializing in protein chemistry, and by the University of Tennessee under Dr. Henry Mills specializing in kidney physiology. Both of these were approved by the medical advisory committee in December 1946 but have not as yet been given formal approval of the District Engineer.

Research Program 1946 - 1947

With the termination of a large number of research problems the changes in the research allottments and a shifting of personnel back to their peace-time jobs it was also necessary for the directors of the various medical projects to shape up new research programs to meet all of these conditions. In addition new problems requiring investigation followed modification of the research and production programs and it was deemed necessary to set up additional programs to speed the work, (beryllium and thorium toxicity being two of the major items). For convenience, and clarity it seems wise to list all the programs giving specific experiments by title. At this time no results can be given inasmuch as very few problems have been under investigation sufficiently long to produce positive results. This program was approved by the Medical Committee on December 5 and can be listed as that recommended to the AEC for continuation.