702001

FILE DESIGNATION 3225

FROM: [illegible] Hilberry
Argonne

DATE 5/18/49

NO. 123443

NO REPLY

ANSWERED

REMARKS

CR

SUBJECT:
Material for 6th semiannual report to Congress.

DO NOT REMOVE THIS COPY

REFERRED TO: MILLER

DATE 5/19/49

RFRD.

CHARGED TO

PREVIOUS CORRESPONDENCE

ATTACHED

NO RECORD

PERMANENT FILE COPY

FORM OCS-6

013458

D. Warren
VIA AIR MAIL 3/13

Argonne National Laboratory
P.O. BOX 5207
CHICAGO 80, ILLINOIS
BUTTERFIELD 8-5200

May 18, 1949

Dr. Shields Warren
Director, Division of Biology & Medicine
U. S. Atomic Energy Commission
1901 Constitution Avenue, N.W.
Washington 25, D. C.

Dear Dr. Warren:

Enclosed is the material for the Sixth Semi-Annual Report to Congress which has been prepared by the Biology Division of Argonne National Laboratory.

The material from Argonne's Division of Medicine will be transmitted at a later date.

No

3W

Sincerely yours,

N Hilberry

N. Hilberry
Deputy Director

NH:cy

cc S. M. Skinner, COO, AEC wo/enc

2 Argonne Lab.

by Austin M. Brues

003225

The Biology Division of Argonne National Laboratory carries on a broad research program in the biological effects of radiations. The aims of this program are twofold: to establish the basis for "permissible" radiation exposures, including all types of radiation and radioactive isotopes, and to discover the nature of radiation sensitivity of various organisms, particularly in relation to radiation sickness and its prevention and treatment. These aims are important alike to industrial and military problems and to the proper scientific and clinical use of isotopes. They are of particular importance in connection with the program of Argonne National Laboratory, which has been given primary responsibility for reactor development. The staff of the laboratory recognize that, in carrying out the program, developments in biophysics and cellular and theoretical biology, and in particular, basic understanding of growth, cancer and ageing are an integral part of the approach.

In addition to this, the Division has in common with the other regional laboratories, its share of responsibility for training in radiation biology, especially in the midwestern area. Due to the fact that the division is still confined to small temporary quarters it has been impossible to offer any formal course work, but its members have collaborated actively in courses in radiobiology and cancer given at the University of Chicago. It has been possible to offer training to 12 visiting investigators and post-doctoral fellows, usually for periods of a year, and this program will be extended as space becomes available. Special equipment of the laboratory is accessible to investigators from other institutions on a collaborative basis. In one such project which is now in progress, neutron irradiation of animal tissue has been used in the chemical determination of iodine in very small quantities. Irradiations are done in the Argonne heavy water pile,

Activation analysis

and the radioactive iodine (I^{128}) created by the neutron activation of normal iodine is measured by a counter. Because of the high neutron flux of the pile this method is sensitive to less than a millionth ~~for~~ of a gram of the element, which gives it a considerable advantage in sensitivity and speed over chemical methods of analysis. The possibilities of this method for the determination of other trace elements in tissue are being examined. By the neutron activation method, analysis can be done while leaving the material intact, which has many obvious advantages over more destructive methods.

The division is available to the laboratory for advice in special problems relating to safe conduct of laboratory operations, particularly where experimental work is required.

In order that realistic "permissible" levels of radiation can be established, it is necessary to define clearly the lowest amount of radiation which can be considered harmful to man. Large numbers of animals are being exposed to X rays and other external radiations and injected with radioactive elements to gain exact information on the nature of injury following various amounts of radiation exposure. During the war, these experiments were begun using plutonium and various radioactive products of nuclear fission; at present, other isotopes such as $phosphorus^{32}$, $hydrogen^{3}$, and $carbon^{14}$, which are of peacetime value, are being studied in the same way.

Most of our present knowledge is based on the observation that the life-span is shortened and that cancer arises in areas which have been radiated. We have gained valuable information regarding the amounts and timing of radiation treatment which induce cancer, but a great deal of further investigation is required and will have important bearing on the cancer problem as well as on radiation toxicity. By the same token, those studies which relate to the shortening of life following radiation will bear on the problem of ageing. These studies require the collaboration of pathologists, chemists, and physicists, and an important role is being assumed by mathematicians, who are interested in organizing our experimental knowledge in such a way that it brings as much reliability as possible ~~with~~ to predictions.

Typical studies related to the chronic effects of low level radiation include experiments aimed at discovering whether radiation produces cancer by chemical effects (since cancer can be induced by many chemical agents) or by other types of injury to the cell or its parts which may cause these cells to give rise to malignant growth. The pile is being used as a source of heavy irradiation of normal body ~~constituents~~ chemicals in an effort to discover the nature and biological action of their irradiation products.

One of the puzzling questions regarding the production of cancer and other changes is the meaning of the long period of time which elapses between radiation and the appearance of the tumor. This is being attacked by careful examination of the chemical and structural state of irradiated tissue during this interval. Many changes must occur which are invisible by ordinary means of examination; for instance, the changes in the lens of the eye responsible for cataracts after neutron exposure might be missed if they occurred in tissues, such as muscle or the internal organs, which are not transparent.

Along with the studies on radioisotope toxicity the laboratory is conducting investigation of the exact localization of the isotopes in cells and tissues. Through the properly coordinated use of analytical and photographic methods, it is entirely possible to reach a high degree of accuracy, but these methods require a great deal of further development. An illustration of the importance of this is seen in the case of carbon^{14}, which may form many compounds in the body and may become concentrated in certain cells within an organ, although it is being rapidly lost from other tissues. The wise clinical use of this isotope demands a fairly complete picture of the finer details of its lodging places. This study is going on at the present time, together with a rather complete investigation of the fate of those other isotopes which lodge in the skeleton. Since bone is apparently highly susceptible to radiation damage, this group of isotopes has been given the first priority in this program.

The removal of isotopes which have been absorbed into the body forms a subject of investigation which has attracted the attention of experimenters in both the Biology and Medical Divisions. It has been found that radioactive isotopes of calcium and of the chemically similar elements are absorbed so rapidly from the blood stream into bone that the uptake by the skeleton must be measured in minutes rather than hours. The skeleton then holds on to these elements very tenaciously and, as has been discovered in cases of human radium poisoning, efforts toward removal have been singularly disappointing. Studies in the removal of deposited radioelements is considered an important phase of the program.

The chain reacting piles at the Argonne National Laboratory afford an opportunity of studying effects of neutrons which it is the duty of the laboratory to utilize. A program has therefore been outlined which will utilize the experimental methods already developed for a study of neutron damage, again with the primary aim of determining the more subtle, or occasional, effects of radiations which determine the conditions under which they must be used.

It is also important to discover what differences there are between the effects of isotopes generally, and those which form part of a chemical molecule that may be of critical importance. The cell nucleus contains phosphorus, carbon, hydrogen, and sulfur, and radioactive isotopes of all these elements are in use. Experiments have shown that the one-celled Paramecium, whose genetic behavior is well understood, is more sensitive to radiation from radiophosphorus than to certain other radiations. This is presumably due to the fact that the Paramecium stores the phosphorus in its body and that the radiation therefore originates from the substance of the cell itself. Similar studies on other biologically important isotopes are planned for the immediate future.

Sensitivity to radiation forms the other major topic of study. When we contrast the extremely large amounts of radiation which are required to injure many of the simpler forms of life, and indeed most of the cells and organs of the animal body, it is clear that only the specially sensitive nature of certain critical cells can explain death in the higher animals.

Physiological studies begun in this laboratory during the war have painted in clear outlines the general nature of radiation sickness, and more recent work has focussed on some of the systems which appear to be most significant in the study of sensitivity. The mechanism of blood clotting has been subjected to a systematic study and it has been found that substances like heparin, which normally prevent blood from clotting within the circulation, appear in greatly increased amounts, resulting in the marked bleeding tendency which is one of the serious features of radiation sickness. This new understanding of the mechanism of a serious symptom has resulted in the discovery of two chemicals which stop bleeding by neutralizing the excess heparin.

The effects of radiation on the circulation of the blood are being studied by observing the wing of a small bat which occurs in great profusion in limestone caves. The thickness of the wing is slightly over one-thousandth of an inch, so that the flow of blood and lymph can be observed under highest magnification with the microscope. Striking changes occur after X ray treatment, including slowing of the circulation and blocking of the vessels by cells and debris.

Much attention has been given to the various blood cells and the part which they play in radiation sickness. By irradiating animals with different degrees of sensitivity to radiation, it has been found that certain of the white blood cells are much more essential to survival than others. Since transfusions of white blood cells are uniformly unsuccessful, other means must be sought for protecting them or substituting for their functions. While blood formation ordinarily occurs in the bone marrow, it has been found that the spleen very rapidly takes over this function in some animals where the bone marrow alone has been irradiated, thus exerting a protective effect.

Studies on the sensitivity of blood cells and their relation to radiation sickness are important in many fields of medical research. As the relation is subjected to further scrutiny, it is expected that important knowledge in the nature of immunity to infectious diseases will result. At present, the relation of the blood cells to immune reactions are being studied in irradiated animals, and the part played by bacterial infection in radiation death is likewise under study.

The endocrine glands have also been implicated in radiation sickness and a detailed study of the response of an animal's adrenals is being made. Definite chemical changes occur in these glands even after moderate amounts of radiation. In some cases, these changes can be prevented by treatment with adrenal hormones, but the treatment fails to improve the survival of the irradiated animal to any considerable extent.

Two means of treatment of irradiation sickness have, however, appeared to be of definite value in enhancing the survival of X-rayed rats and mice. The female sex hormone has been found protective when it is given a week or ten days before X ray. Studies of the white blood cells in these animals points out that the hormone depresses them, and their subsequent regeneration probably accounts for the protection, which occurs during this recovery phase. A similar observation was made previously in the case of the red blood cells, which appear to be more resistant to radiation when they are being rebuilt, following an experimentally induced anemia.

Another partially protective agent was discovered through consideration of the fact that hydrogen peroxide and similar oxidizing substances appear in irradiated water. Cysteine, a normal body constituent which can neutralize these oxidants, was found to be protective when it was given immediately prior to irradiation. It was found ineffective five minutes after irradiation, suggesting that the critical damage is done almost at once, although serious symptoms require days to develop.

Studies in radiation biochemistry are being carried on through the irradiation of substances which occur in the body and perform important functions, such as enzymes and proteins. A clear definition of the nature of the more radiosensitive enzymes has been made, and it is found that the sensitive ones are those which are most easily oxidized, in accordance with the suggestion made above. Studies are in progress in an attempt to relate sensitivity of these chemical parts of cells to cell sensitivity itself. Similar studies are being pursued in which body cells and organs are cultivated separately, and important cell structures such as the chromosomes are being isolated and studied under the electron microscope. These investigations are an integral part of the radiosensitivity program, yet they have important implications for biology in general.

The question of the radiation sensitivity of plants is given an important place in this program and has wide implications. Since plant growth hormones have been considered especially sensitive, this group of substances is being studied in the first phases of the work.

Finally, environmental conditions are being altered in a search for further information. It has been found that frogs, if kept chilled after being given a fatal dose of X ray, will survive for many months. If, however, they are removed to room temperature, they proceed to die as they would have in the first place. It was hoped that while living on time thus borrowed, some reparative processes might take place, but it appears that destructive and reparative processes alike are retarded by cooling the body.

Plans for the future are implicit in the present program, which in its development requires the coordinated effort of scientists trained in varied disciplines. The basic importance of the various problems posed by this program, as indicated in its presentation, touches on our understanding of such elusive subjects as growth, and of the functions of the various elements of the body. This program requires also that full use be made of the special equipment of the laboratory and implies close contact with physical scientists and their problems. This will be greatly facilitated when the Division finds adequate quarters at the new laboratory site.

While many toxic and environmental factors are known or suspected to result in disabilities, in cancer, and perhaps in a certain shortening of life span ~~in small degree and difficult to detect~~, only in the field of atomic energy is this matter being faced squarely by a serious determination to reduce damage to the vanishing point. The experimental approach to this problem presents a challenge in the development of new techniques and the exploration of some of the most basic branches of biological science. This approach should prove to be a pattern for the attack on many other important fields now neglected.

AMB/fs 5/17/49