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January 3, 1949

Memorandum to: Dr. Henry A. Blair

From: William F. Bale

Subject: Dr. Shields Warren's Request for Information Concerning Polonium Research

When the production of polonium in large quantities was undertaken during the war years, the Medical Section of the Manhattan District assigned to the Rochester Project the responsibility for any research necessary for the safety of the production personnel at Dayton. No useable information existed concerning the metabolism or toxicity of this element. The reports of Lacassagne and coworkers were rapidly demonstrated to be in a quantitative sense completely unreliable.

Following the development of reliable methods for polonium analysis, work at Rochester was first concentrated on a study of polonium distribution and of excretory rates in rats following intravenous injection. This work was later supplemented by a study of polonium excretion in six human subjects (victims of leukemia) and a large scale study of the comparative toxicity of polonium, radium, and plutonium in rats following single intravenous injections.

From this work it was possible to arrive at a correlation between the body polonium content of human subjects and the rate of urinary excretion. This method has been in continual use at Dayton for monitoring the body polonium content of production plant personnel. From the comparative toxicity studies, plus calculations based upon the body distribution of radioactivity as experimentally determined, estimates of permissible body content were made.

Preliminary work was also carried out on absorption of polonium through the skin, by way of the gastro-intestinal tract, following inhalation into the lungs, etc.

Several instruments constructed at Rochester were provided the Dayton plants for monitoring purposes.

Results of this research are given in several reports of very limited distribution and are summarized in a Survey Volume for the National Nuclear Energy Series (Division VI, Volume III) which is presumably now awaiting publication as a classified volume.

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To: Dr. Henry A. Blair January 3, 1949

At the Dayton plant it was found that exposure to polonium was so great that numerous individuals had, in fact, greater body concentrations of polonium than our research indicated ought to be permitted. Although by improved methods exposure to polonium has decreased considerably, individuals at Dayton still carry polonium concentrations in their bodies close to the maximum allowable on the basis of our research. A careful survey of the Present Status of Polonium Tolerance Estimations may be found in our recent report under that title (UR-44, October 14, 1948).

Recent and Present Research at Rochester - During the past two years research on polonium has continued at Rochester. It has been found in preliminary work that BAL (British Anti-Lewisite) and related substances somewhat increase polonium excretion in experimental animals and also reduce toxicity as measured by lethal effects. Also we have found that kidney lesions are demonstrable in rats following single doses lower than we had previously realized exerted deleterious effects upon this organ. This lesion, demonstrated histologically, may become a limiting factor in permissible dosage calculations since it is considerably more marked than any permanent blood changes at the same dosage level.

It has also been found that the distribution and excretion of polonium after oral administration may be qualitatively and quantitatively quite different than following administration by the intravenous route. In particular, following oral administration polonium shows a pronounced tendency to accumulate in circulating erythrocytes.

Work Planned for the Future - Work that will be carried out at Rochester in the future is dependent upon what the Medical Section of the Atomic Energy Commission decides is the essential work to be done and where it wishes to assign responsibility for the carrying out of this work. In view of the fact that exposure of plant personnel to polonium still remains relatively high, and is difficult to reduce without further great increases in production costs, there may be considerably more work indicated.

Almost all toxicity studies to date have been carried out on rats, and following single intravenous injections. Perhaps such work should be broadened to include other species, particularly the longer lived dog, should include other than intravenous routes of administration, and should include experiments with repeated administration of polonium more closely simulating the chronic exposure of human subjects. Perhaps blood changes, possible production of sterility, and tumor induction should be investigated more completely.

Little is yet really known about the magnitude of polonium absorption through the lungs, or concerning any detrimental changes

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such as tumor induction that may be induced in this organ at the present permitted exposure levels.

Further studies may be someday indicated on polonium excretion in human subjects following administration at non-toxic levels. The patients with leukemia studied may not be representative of human subjects as a whole.

Additional work perhaps should be carried out on methods of increasing polonium excretion and decreasing toxicity, to the point that the utility of optimal methods are known as applied to cases of accidental human over-exposure.

Biological research so far conducted has been almost entirely on an empirical basis to answer specific health problems with little attention paid to the chemical nature of polonium or to the nature of polonium metabolism. Such basic work on the metabolism of polonium in the body is perhaps indicated to provide a more sure foundation of basic biochemical and physiological knowledge on which to build an ultimate determination of a safe exposure level.

Finally polonium, because of its relative ease of handling and quantitative measurement, because of its wide and, compared with most other alpha emitting elements, relatively uniform distribution in the body, and because of its convenient half-life, may provide the best tool for a general investigation of alpha ray toxicity. Its acute toxicity, for example, is, on a radioactivity basis, some ninety times as great as radium. This is because radium is rapidly transported and stored in calcified areas where its acute toxicity is not high. Polonium, on the other hand, remains largely in soft tissues.

Future Assignment of Research Responsibility - The unit of the Monsanto Chemical Company engaged in polonium production is in the process of moving to greatly enlarged facilities for the production of polonium. A laboratory to be devoted to biological research in connection with the polonium hazard is included in the plant facilities. On the basis of informal discussions between representatives of the medical group at Dayton, headed by Dr. Svirbely, and the group at Rochester, I believe it was generally agreed that large scale toxicity can better be undertaken in Dayton rather than in Rochester, while Rochester is likely to be better equipped for studies on some aspects of pathological physiology, physiology, pathology, therapeutic methods, and metabolism.

Research on polonium at Rochester now represents the only work underway on toxicity due to alpha radiation. It may be desirable to have such investigative work continue in this Project to provide

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experienced personnel for consultative work and to aid in our teaching program.

A disadvantage of work on polonium has been and perhaps will continue to be its classified nature, so that work on this subject does not promise to the investigator the rewards associated with the normal publication of research findings.

Distribution of Reports - The limited distribution of reports on biological studies with polonium mentioned earlier means that in most of the operational and research areas of the Atomic Energy Commission no information is available on the results of the investigative work at Rochester. Some of these results are certainly of interest not only to workers with polonium but to persons interested in other alpha emitting elements and in radiation toxicology in general. This suggests that it is perhaps advisable either to expedite the publication of the classified volume of the National Nuclear Energy Series in which the results of this work is contained, or alternatively to issue the contents of this volume as a classified report from the Rochester area. It is a manuscript of some 700 typewritten pages.

Assignment of Responsibility at Rochester - Work on polonium at Rochester was originally centered in the Division of Special Problems. When a concentration of Rochester Research Divisions occurred about two years ago, this Division was consolidated with the Division of Radiology and renamed the Division of Radiology and Biophysics. They have had the general responsibility of research on medical aspects of ionizing radiations and of materials toxic because of radioactivity.

WFB:mt William F. Bale

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