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Report of Activities under the Finney-Howell Foundation Fellowship

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In July, 1938, when I became a Fellow of the Finney-Howell Foundation I had just found that it is possible to localize the effect of fast neutrons. Hitherto it had been considered a difficult problem to collimate these penetrating, uncharged particles. After conducting a number of physical tests which showed that neutrons could not only be confined to a beam but that they could deliver a depth dose suitable for the treatment of deep neoplasms, I began a series of skin tests on rabbits with both neutrons and x-rays to establish a dose of neutrons that would be safe to try on patients.

The tests on rabbits indicated that the neutron beam could be used safely on patients. It was also determined that the intensity of neutrons from our present cyclotron would allow clinical tests to be made on patients in times comparable to those used with x-rays. In view of the practicability of undertaking clinical tests with the present cyclotron it was decided not to wait till our large, new, medical cyclotron is completed but to gain some clinical information with the present machine to expedite an effective use of the new one. I then arranged a treatment set-up which could be fitted to the cyclotron and used for tests on the upper regions of the body. On the new cyclotron, which is being designed for medical uses, a much more flexible arrangement will be possible. Some pictures accompany this report showing the present irradiation arrangement.

On September 26th fast neutrons were first administered to a patient. Since then once each week the cyclotron is used for the clinical tests. Such a limited schedule is necessary at present in order not to curtail the many other researches in progress. The usual daily, divided dose therapy is hence not undertaken, but single or weekly-spaced doses are given. This preliminary work is to be considered more as a test of skin, mucosal, and neoplastic reactions than as therapy, although beneficial results are being obtained. The patients are watched carefully for the time of appearance and the degree of the various phases of the reactions. Comparisons are made to the results obtained with similarly conducted exposures using million volt and 200 kilovolt x-radiation. The combined information not only will serve as a basis for a neutron therapy procedure with the new cyclotron but should yield results concerning the dependence of the radiation reactions upon various factors.

Besides aiding in the clinical tests, I have cooperated in several lines of biological experimentation. Dr. Marshak, who is an expert at the study of chromosomes, has come to our laboratory as a Guggenheim Fellow and is carrying out studies on the effects of radiation on chromosomes with the aid of a grant by the National Research Council. We have been irradiating mouse tumors in vivo with both neutrons and x-rays. Dr. Marshak then observes the decrease in mitoses and the number of abnormal mitoses of the tumor cells. We have used Sarcoma 180, a

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lymphosarcoma, and a mammary carcinoma. It is planned to use freshly excised human neoplastic tissue in these studies. A study is also being made of the chromosomal changes induced by neutrons and x-rays in the fast dividing cells of the root tips of sprouting beans, peas, and tomatoes. These various cells have different numbers and sizes of chromosomes as well as different sensitivities to radiation. The object is to see whether a correlation can be made between the total length of chromosomes (chromonemia) in a cell and its sensitivity ro radiation and whether this relation is dependent on the radiation. The indications are that total chromosome length and radiosensitivity are directly related and there are some differences in the action of neutrons and x-rays. This work promises to give worthwhile information for the prediction of radiosensitivity and for an explanation of the processes of cell alteration by irradiation as well as an insight into the nature of chromosomes.

Dr. Spear, Assistant Director of the Strangeways Research Laboratories, Cambridge, England, has recently come to our laboratory through the aid of the Rockefeller Foundation to study the effect of neutrons on embryonic tissues and upon tissue cultures. We have irradiated young rats and Dr. Spear has observed the changes in mitoses and the rate of recovery of cell development in the embryonic tissues. A great deal of work has been done in this field at the Strangeways Laboratory using gamma rays; consequently a comparison can be made with the results obtained here. We have also irradiated two types of bacteria and will soon start irradiations of tissue cultures and further embryonic tissues. This work is related to the problems of the irradiation of neoplasms in that dividing cells and the recovery of cells from radiation are studied.

For the proper administration of neutrons and for an interpretation of the biological experiments, a number of physical experiments have been done. Experiments on the collimation of neutrons were reported at the meetings of the Physical Society in Washington last December. An abstract of this paper has been sent to the Secretary of the Finney-Howell Foundation. Dr. Gladys Anslow, head of the Department of Physics at Smith College, and I have investigated two problems regarding the ionization produced by neutron irradiation. Part of this work will be reported at the New York Meetings of the Physical Society on February 24th (an abstract of this is enclosed), and it is hoped to report the balance at the Annual Meetings at Washington in April.

Unfortunately all of the work discussed has been undertaken so recently that there has not yet been time for publication of results and in most cases the data are still being accumulated. I am now writing up three papers and in a few more months there should be some definite results to report on the work in progress. The work on the Medical Cyclotron is being pushed, and it is hoped that in several months a 16 million volt beam will be obtained. No doubt later in the year I will be setting up an arrangement for neutron irradiation with the new cyclotron and possibly regular neutron therapy will then be undertaken.

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I want to express my appreciation for the opportunity to engage in such stimulating work with the feeling of assurance that has been afforded me by this year's fellowship, and as I look forward to the exciting things that may arise from the rapid developments here, I hope I may be reassured in my work by the continued support of the Finney-Howell Foundation.