

Research
Program

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BOX No. 5

FOLDER December 1944

Dr. Leon Jacobson
Associate Director of the Health Division
Metallurgical Laboratory

Dear Dr. Jacobson:

The personnel of the Health Division working in my laboratory under my direction is concerned with studies on the effect of radiations and heavy metals on enzyme systems, on tissue metabolism, and on proteins. This work had its real start on June of this Year. In these few months we have made a survey of the effect of X rays on tissue metabolism and have demonstrated that single doses of X rays will affect it immediately after radiation. Respiratory inhibition was observed even in tissues (kidney) where no microscopic alterations were noticed. We have demonstrated that one of the effects of X rays is the inhibition of -SH enzymes by oxidation of the -SH groups of the protein component. In fact, succinoxidase was inhibited by X rays and reactivated on addition of glutathione. We have shown that T acts on enzyme systems by combining reversibly with the protein moiety. In fact T inhibitions were reversed on addition of alpha hydroxyaspartic acid and citric acid. We have shown that the effect of product on the metabolism of tissues is profoundly altered and that these alterations are more complex than those observed in T poisoning or X ray radiation. We have started a comprehensive study on the alterations of proteins produced by radiations and by heavy metals. This last part of the program has unfortunately being considerably delayed for lack of apparatus.

In our opinion, without a serious study of these three points (enzymes, tissue metabolism, proteins) it will be impossible to have an understanding of the mechanism of action of radiation and of heavy metals on the human body. Furthermore we believe that such an approach might provide for a better therapy and for more logical protective measures. Unfortunately the road for this approach to disease is hard and full of difficulties. It requires the continuous preparation of proteins of diverse structure and size. And all these steps require not only meticulous care but also personnel trained for a long time in this specialized field of biochemistry.

The effect of radiations, and to some extent of heavy metals seems to depend on the amount of radiation. Small amounts confine their action to the enzymes responsible for cellular division; by increasing the dose, destruction of -SH enzymes ensues and finally we have irreversible denaturation of proteins with the dramatic and non specific symptoms which occur on radiation with lethal doses. It is the effect of these graded doses of radiations that we would like to study, for these effects are of primary importance in our project. We have only make a start and we are, like you, aware of the complexities of the problem which has occupied scores of investigators for scores of

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years without, as yet a satisfactory solution. We are requesting now an extension of our contract for the following purpose.

1. The metabolism of nucleoproteins and the effect of radiations. For this work we intend to use normal and cancer tissues. We feel this work might have applications not only for the discovery of the mechanism of action of small doses of radiation but also for the mechanism of abnormal growth.
2. The effect of radiations other than X rays on enzyme systems and on biochemical reactions in general.
3. The effect of radiations and heavy metals on proteins. For this purpose we intend to prepare pure proteins and study the mode of action of these agents.
4. The effect of radiations and of heavy metals on the metabolism of blood producing organs.
5. We shall attempt during the course of our work to apply the results of our findings for curative and protective measures.

We have lost one coworker in our laboratory. We request his replacement by one not subject to sudden call.

Sincerely yours,

ESGB:CC

E. S. Guzman Barron

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