

ONR COMBINED PROJECT DESCRIPTION AND PROJECT PROGRESS REPORT, 1952

2:1 JUL 1952

RESEARCH AND DEVELOPMENT PROJECT CAPD (NEW PROJECTS)		1 SEC. U	3. PROJ. NO. NR 117-000	
1. PROJECT TITLE Effects and Use of Radiation in the Study of the Living Organisms			4. INDEX NO. ---	5. REPORT DATE 1 Jan 52
6. BASIC FIELD OR SUBJECT Biological Sciences		7. SUB FIELD OR SUBJECT SUB GROUP Biophysios AW 06601		
8. COGNIZANT AGENCY Office of Naval Research		12. CONTRACTOR AND/OR LABORATORY See para. 21.e below		CONTRACT/W. O. NO. ---
9. DIRECTING AGENCY Research Group Physiology Branch, Code 441				
10. REQUESTING AGENCY Office of Naval Research		13. RELATED PROJECTS NR 182-000		17. EST. COMPL. DATES
11. PARTICIPATION AND/OR COORDINATION See para. 21.d below		14. DATE APPROVED 15 March 1950		RES. Cont'd DEV. --- TEST --- OP. EVAL. ---
		15. PRIORITY IC	16. MAJ. CAT. ---	Fy 18. FISCAL EST'S. 52 23M 53 24M
19. This card supersedes NR 117-000 dtd 1 April 1951				
20. REQUIREMENT AND/OR JUSTIFICATION With increased knowledge and use of electromagnetic radiations and nuclear radiations, the requirement for investigation of the biological effects of such radiations is of recognized military importance. In addition, use of the new radiation techniques in biological fields may lead to scientific accomplishments heretofore unattainable by classical methods.				
21. BRIEF OF PROJECT AND OBJECTIVE a. <u>Brief:</u> This project is concerned with an investigation of the effects of ionizing and non-ionizing radiations on the biological system as well as the use of these radiations as a research tool. The radiations include the electromagnetic spectrum of cosmic rays, gamma rays, x-rays, ultraviolet, visible, infrared, and microwaves. The use of isotopes in biological experiments is included in this category. b. <u>Approach:</u> The general approach to this project will be emphasis of those important aspects of radiation research which have had relatively little support or scientific investigation. Since A.E.C. denotes a large percentage of research funds to biological effects of nuclear radiations, it is not planned to accelerate research in this field. The modern theories and techniques of electromagnetic radiations seem to show strong promise of significant results if the key to their biological effects can be found. In the field of the physical sciences, for example, many advances have been made in the theory and use of microwaves, yet application of this knowledge in the biological fields has been far from adequate. c. <u>Tasks:</u> See para. 21.e below d. <u>Participation and Coordination:</u> A.E.C. - NR 117-196, Plasma Proteins with Labeled Amino-Acids, \$15,000				
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22. J. RDR NR-32208		K & P. 49-42		X I C

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21.d (Cont'd)

NR 117-203, Studies of the Biological Effects of Radiation Syndrome, \$8,000
A.E.C. - NR 117-581, Biological Effects of High Voltage Radiation, \$45,000 (fiscal 1949 funds)

- e. NR 117-196: Plasma Proteins with Labeled Amino Acids (Unclassified)
Contractor: University of Rochester, Rochester, New York
Annual Rate: \$15,000 (outside funds, \$15,000)
Contract: N6ori-12608 (9/1/46 to 6/30/52)
Investigator: G. H. Whipple

Problem: The fate of parenteral plasma proteins and their inter-relationship to protein metabolism in general will be studied. Conditions in which this study is of importance are (1) protein repletion -- plasma and blood transfusions; (2) severe bleeding, shock, edema, protein depletion; (3) presence of infection; and (4) administration of cortisone under varying conditions of diet and protein depletion.

Reports: (1 April 1951 - 1 January 1952)

1. McKee, F. W., Yuile, C. L., Lamson, B. G., Whipple, G. H., "Relative Rates of Interchange between Plasma and Ascetic Fluid Studied with C¹⁴ Labeled Proteins", J. Exp. Med., Vol. 95, p. 161.
2. Miller, L. L., Bly, C. G., Watson, M. L. and Bale, J. F., "The Dominant Role of the Liver in Plasma Protein Synthesis", J. Exp. Med., Vol. 94, No. 5 (1951)
3. Yuile, C. L., Lamson, B. G., Miller, L. L. and Whipple, G. H., "Conversion of Plasma Protein to Tissue Protein Without Evidence of Protein Breakdown", J. Exp. Med., Vol. 93, No. 6 (1951)
4. Claus, C. J., and Morgenthau, J. L., "A New Method for the Conversion of Nitrites to Aldehydes", Comm. to Ed. Jour. Amer. Chem. Soc. Vol. 73, No. 10, October (1951)

NR 117-105: Isotope Research (Unclassified)
Contractor: Harvard University, Cambridge, Massachusetts
Annual Rate: \$1.00

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NR 117-000, Effects and Use of Radiation in the Study of the Living Organisms

21.e (Cont'd)

Contract: Nonr-01900 (2/1/50 to 9/30/52)
Investigator: A. B. Hastings

Problem: This is a fixed price contract at a token cost of \$1.00 per year to allow the contractor retention of equipment originally provided under contract N5ori-76, T.O. VII, which expired 30 September 1949. The Atomic Energy Commission is supporting this research program under contract AT (30-1) - 609.

Reports: (1 April 1951 - 1 January 1952) - None

NR 117-203: Basic Studies in Endocrinologic Aspects of the Radiation syndrome
Contractor: U. S. Naval Radiological Defense Laboratory, San Francisco, California
Annual Rate: (\$8,000 outside funds)
Contract: Allotment No. 41191 (10/15/51 to 6/30/52)
Investigator: D. J. Kimeldorf

Problem: It is proposed to determine the alterations in hormone production and tissue sensitivity to hormones which may occur during radiation sickness. The alterations in endocrine integration will be revealed and localized by means of intra-ocular implant techniques.

Reports: (1 April 1951 - 1 January 1952) - None

NR 117-681: Biological Effects of High Voltage Radiation (Unclassified)
Contractor: Union College, Schenectady, New York
Annual Rate: (Outside funds, \$15,000)
Contract: N8onr-53401 (6/1/48 to 5/31/52)
Investigator: L. B. Clark

Problem: The effect of very high X-ray radiations of the order of one hundred million volts on enzyme systems of cells is not well known. It is hoped that in this study the effects of these high-voltage X-rays may improve our present understanding of their effects on various biological processes.

Reports: (1 April 1951 - 1 January 1952) - None

f. Accomplishments: The research on task NR 117-196 is divided between the Chemistry Department, the Pathology Department, and the Department of

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12. The Department of Radiation Biology in the City of the Living Organisms

21.4 (Cont'd)

Department of Biology. Dr. Yuile of the Department of Pathology is particularly concerned with the general problem of parenteral plasma protein metabolism. This problem is particularly well suited to investigation by the radioisotope technique being used by Dr. Yuile. By feeding labelled amino acids to donor dogs it is possible to obtain labelled plasma proteins which in turn can be injected into experimental animals. The work of the Chemistry Department in synthesizing these amino acids, particularly lysine E-C¹⁴ of exceptionally high activity, has contributed greatly to the success of these experiments. One great point of interest in these experiments is the question of whether plasma proteins are completely broken down to the amino acid stage before being incorporated into the tissue proteins or whether they are only partially broken down. The research done so far on this task seems to favor the theory of partial as opposed to complete catabolism.

A few experiments have been done on the effects of inflammation (sterile turpentine abscesses) on protein metabolism. Preliminary results indicate that the turnover and breakdown of plasma proteins is somewhat accelerated in the presence of acute inflammation. Experiments are underway on the study of the fate of intravenous injections of dextran labelled with C¹⁴ in dogs.

The Department of Radiation Biology is primarily concerned with the role of the liver in regard to protein synthesis. The experimental method of using the isolated intact liver perfused with homologous oxygenated blood, in conjunction with the use of lysine-E-C¹⁴ has given some significant results in regard to protein synthesis in mammalian tissue. The most important of these is that the liver synthesizes practically all the plasma fibrinogen, the albumin fraction and probably more than 80 per cent of the plasma globulin fraction. The response of the isolated perfused liver seems to be both qualitatively and quantitatively analogous to that of the intact animal. Their latest results with this technique indicates that the amino acid level is the determining factor in the quantitative albumin-globulin ratio of the plasma proteins produced. This data affords a basis for a working hypothesis which will account for the disturbances in plasma protein metabolism noted in protein starvation and hepatic cirrhosis.

Considerable experimentation is underway on task HR 117-581. Some of the results are summarized below:

Continuation of studies on the residual effect of X-radiation from 124 KV and 60 Kev. machines on mice, substantiate previous findings that there are no consistent biological differences between the two kinds of radiation.

Depth dose studies on rats exposed to 124KV X-radiation are almost complete. The findings will be used in a comparison of similar observations

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Project 117-196: Effects and Mechanism of Radiation in the Study of the Living Organisms

21.2 (Cont'd)

on rats exposed to 50 Mr. X-radiation where a different ionization gradient will occur in the body.

Some additive protective action has been demonstrated for mixtures of folic acid, B₆, B₁₂, and streptomycin against radiation death.

g. Future Plans: In addition to continued studies along the lines indicated under (h) on task NR 117-196 it is hoped that time and material will permit completion of work started several years ago on the passage of C¹⁴ across the placenta in dogs after injection of labeled plasma into the maternal circulation and that an approach may be made to the problem of proteinuria with the use of labeled protein. Research will continue on the effort to produce a new synthesis of lysine-E-C¹⁴ which possesses the advantage of introducing the radioactive carbon at a late stage of synthesis in order to obtain a highly active yield.

h. Other Operational Requirements which are Strongly Supported by this Project:

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SR 13801
BR 03800

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