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Research and Development Project Card Progress Report (C)		2. Security Incl	3. Project No. 21-3501-0001 (21-25-029)	
1. Project Title EFFECT OF IRRADIATION OF P ³² UPTAKE BY BONE MARROW			4. Index No. 3250	5. Report Date 28 November 1952
6. Basic Field or Subject Research		7. Sub Field or Subject Sub Group Biochemistry		7a. Tech. Obj. P ³² -12 (102/13)
8. Cognizant Agency Air University		12. Contractor and/or Laboratory Depts of Medicine and Bio-Chemistry, N.W. University Medical School, Chicago, Ill		Contract/W.O. No. Not available
9. Directing Agency USAF School of Aviation Medicine Office Symbol Tp		Prin Invest: Dr. H.L. Allen		
10. Requesting Agency Surgeon General, USAF		13. Related Projects None		17. Est. Compl. Dates Res. Dec 52 Dev. Test Op. Eval.
11. Participation, Coordination, Interest Surgeon General, US Army (I)		14. Date Approved 28 November 1950		18. FY Fiscal Est's (M\$)
		15. Priority 2	16.	51 611 52 111 53 51 54 201
19. This report replaces report on Project No. 21-25-029 dated 30 June 1952.				
20. Requirement and/or Justification In view of the high incidence of radiation casualties anticipated in any future war, it becomes critically important to secure information on the fundamentals of such injury and how it may be combated. Testing of various prophylactic and therapeutic measures has been handicapped by lack of a sensitive quantitative index of radiation damage. Furthermore, to be practical as a screening technique the procedure should be relatively rapid and adaptable to large-scale testing. Preliminary data suggest that such a technique may be developed utilizing the rate of P ³² uptake by marrow.				
21. a. <u>Brief</u> This project will study the effect of nutritional, physiological, and pharmacological variables on the rate of P ³² uptake after irradiation. The study will be carried out first on rats and later on human beings by means of bone marrow aspiration. b. <u>Approach</u> Rigid standardization of the test conditions must first be devised to secure most reproducible results. As soon as				
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1. Project Title EFFECT OF IRRADIATION ON P^{32}
 21. (continued) UPTAKE BY BONE MARROW

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predictable changes in P^{32} uptake after a standardized irradiation can be obtained, the effect of various factors will be studied. These include drugs, hormonal factors, nutritional constituents, environmental conditions, etc. Studies will be conducted to measure both prophylactic and therapeutic effectiveness.

d. Subtasks

None

d. Other Information

This project is funded under the basic project line item No. 670-606.

c. Background History and Progress

(1) Background History

The uptake of P^{32} by bone marrow and spleen was significantly decreased after irradiation with 800 r. Twenty-four hours later the only change noted was an increase in specific activity of deoxyribosenucleic acid (DNA) fractions of marrow and spleen. Animals exposed to 30 hours of intermittent hypoxia (10 hours daily) and irradiated in a hypoxic atmosphere were afforded some protection, as revealed by examination after 24 hours. After 96 hours, the hypoxic protection was evident both in the ribose nucleic acid (RNA) and DNA specific activities in marrow and spleen. At this time, too, the RNA turnover rate was considerably above normal in both tissues and the DNA turnover rate was normal in the spleen and approaching normal in the marrow. Morphologically the bone marrow and spleen 96 hours after irradiation were almost acellular, whereas in the hypoxic protected animals there was some evidence of beginning regeneration although the total cellularity was slight.

(2) Progress

Pilot experiments were developed for the determination of P^{32} uptake under varying X-ray doses. In all previous work, the animals have been submitted to an LD 100 of 800 r. Under the present program, animals are being given X-ray doses varying from 50 r to 400 r. The purpose of the new experiments is threefold. First, is the evaluation of the methods employed as a quantitative measure of the amount of radiation received. Second, to determine the dose of irradiation which will give the most sensitive measure of change when the animals are treated with various protective agents, and third, to separate two important aspects of irradiation injury; that is, to divorce the reversible damage (the temporary cessation of the mitotic activity of cells) from the irreversible changes produced by

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profound alteration of protein metabolism. This third point becomes very important, since protective agents may operate at two distinct levels and one which protects the reversible phase may be quite impotent in the irreversible stage.

Determinations of the phosphorus content of the nucleic acid fractions and rate of incorporation of P³² into the nucleic acids, as well as morphologic examination of both the bone marrow and spleen were carried out at 4, 24, and 48 hours after exposure to X-irradiation. The maximum fall of DNA P³² specific activity is greater with 400 r than 200 r, and from previous work in this laboratory, the maximum fall with 800 r is even greater

f. Future Plans

The nucleic acid metabolism will be extended to smaller doses of X-irradiation. Two reports are in preparation, entitled "Nucleic Acid Metabolism, Bone Marrow and Spleen in the Rat. II. The Effect of X-Ray and the Effect of Anoxia," and Report No. III, "The Combined Effect of X-Ray and Anoxia."

g. References

None

HEADQUARTERS AIR RESEARCH & DEVELOPMENT COMMAND	
APPROVED PROJECT	
DATE OF APPROVAL 28 Nov 50	AUTHENTICATION <i>Petw</i>