

ADDRESS ALL REPLIES  
TO THE COMMANDANT

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UNITED STATES AIR FORCE  
AIR UNIVERSITY  
HEADQUARTERS  
SCHOOL OF AVIATION MEDICINE, USAF  
RANDOLPH AIR FORCE BASE  
RANDOLPH FIELD, TEXAS

SAMRSEC

12 June 1956

SUBJECT: Trip Report

TO: Commandant  
School of Aviation Medicine, USAF  
Randolph Air Force Base, Texas

1. In compliance with SAM Regulation 11-13, dated 2 June 1955, the following trip report is submitted.

2. Personnel listed in paragraph a below proceeded to the University of Chicago in accordance with paragraph #6, SO #97, to coordinate research activities of the School of Aviation Medicine. The itinerary was as follows:

Departed Randolph AFB	- 3 June	- 1100 hours
Arrived O'Hare Airport		
Chicago, Ill.	- 3 June	- 1600 hours
Departed O'Hare Airport	- 6 June	- 1415 hours
Arrived Randolph AFB	- 6 June	- 2115 hours

3. a. Monday morning, 4 June, the following personnel met with Dr. DuBois of the University of Chicago:

Colonel H. M. Sweeney  
Colonel L. A. Kossuth  
Lt Colonel A. I. Karstens  
Lt Colonel N. O. Harris  
Colonel J. E. Pickering  
Major Seymour Schwartz  
Captain R. M. Dowben  
Captain R. W. Zellmer  
Dr. W. F. Taylor  
Dr. R. B. Clark  
Lt Colonel R. B. Payne

b. Members of the staff of the University of Chicago included:

Dr. DuBois  
Dr. Doull  
Dr. Peterson  
Dr. Landahl

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The program set up by Dr. DuBois is attached as Inclosure #1.

4. Dr. DuBois opened the discussion by stating that 20 people were working under this contract. In addition graduate students, not charged to the contract, are also participating in the program. Of the 20 people employed 14 are of professional or technical level. The laboratory has the same status as a department at the University of Chicago. The laboratory was started in 1941 by the Army Chemical Corps to accomplish biological screening of poisonous gases. Under the Army Chemical Corps some 2000 compounds were screened. Records on their toxicity and their formulæ are still available and these compounds are anticipated for screening as a part of the work on the effectiveness of drugs for the treatment and prophylaxis of radiation injury. The laboratory was subsequently taken over by the AEC and then by the USAF. The administrative policies affecting the laboratory conform with the regulations of the University of Chicago.

5. The laboratory publishes quarterly reports in 110 copies and distributes them to other laboratories all over the United States. Last year 12 civilian journal publications resulted from the work. Dr. DuBois then discussed the drug testing program and stated that the compounds being screened are furnished by the SAM and the Pharmaceutical companies but more drugs might be available commercially. The initial screening of the drugs are accomplished on animals which have received acute radiation and then if they are effective against acute radiation they are screened on animals chronically radiated.

6. The general discussion of the work of mammalian tissues was then taken up and Dr. DuBois stated that the critical disturbance biochemically in the tissues of animals resulting from radiation had not been found. He stated that this critical disturbance should be evident immediately following radiation.

7. The work on environmental factors studies still require investigation, however in the coming year they will not be continued because of the higher priority being given to the work on the influence of exposure to low level gamma and fast neutron radiation on radiation of mice.

8. Dr. Doull then took up the discussion, particularly the work on the effects of environmental factors on radiation susceptibility. He described the heat studies which required that the animals be maintained at constant temperatures and humidity. A chamber to accomplish this was described and shown on a slide. This chamber is capable of maintaining the animals at a constant temperature plus or minus 1 degree and the humidity plus or minus 5%. The radiation of the animals is accomplished by x-ray at a rate of 35r to 37r per minute with a target distance of 75 centimeters. The ideal temperature for maintaining the animals is 70 degrees and 40% humidity. Prior to exposure the rats

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are subjected to 100 degrees of heat. It was found that the heat had no effect on the radiation effects when compared to the control animals. Temperature of 120 degrees was then used during the exposure to radiation and again no significant effects were found. Animals were then exposed to heat following radiation and this shortened their survival time from 10 days to 6 days. Rectal temperatures taken on animals exposed to heat and radiation showed a rise in this temperature at the end of 5 days. The adrenal ascorbic acid content of rats exposed to heat and radiation was investigated and an increase in this was noted, but the heat exposure in conjunction with radiation did not cause a significant change over that caused by radiation alone. Nucleic acid studies were also carried out in a similar fashion. Studies were carried out in which the rats were exposed to altitude and radiation. The simulated altitude used was 10,000 and 20,000 ft. and groups of animals were exposed to radiation at ground level and altitude; the animals exposed to radiation while at altitude were found to be better able to stand the effects of the radiation, and Dr. Doull stated that x-ray given at 10,000 ft. would be 90% effective as x-ray given at ground level. It is believed that the protective effect is due to hypoxia rather than the decreased pressure, but experiments have not been done to determine specifically whether the protection is due to hypoxia or to the reduced barometric pressure. Studies on the spleens of the animals exposed to altitude and radiation showed no essential differences to that in the control animals. Between now and the end of the present contract they plan to determine whether the protective effect against radiation by altitude is due to hypoxia or the reduced pressure. Dr. Landahl then discussed the effects of heat on rats which had been subjected to 10,000r; work also included the effects of cold. The rats exposed to cold and radiation showed a marked temperature drop during the first 3 days following exposure; rats exposed to heat and radiation showed a temperature drop and then a marked rise in temperature during the 3 days following exposure. Rats exposed to heat and radiation showed a 10% per day drop in oxygen consumption and  $CO_2$  elimination. Some work of a similar nature, using chronic exposure of 50r per day, was carried out. Similar acute studies were accomplished in which the body only, and the head only, of the animal were exposed to radiation. Rectal temperatures in the animals exposed to whole body radiation, radiation of the head alone, and radiation of the body alone were accomplished with rectal temperatures being taken. The average temperature drops resulting from whole body radiation is roughly equal to the average temperature drops resulting from radiation to the body only, plus radiation to the head only.

3. Dr. Peterson then discussed the work of chronic irradiation and the biochemistry of mammalian tissues. The adenosine triphosphatase activity in the spleen and thymus glands were studied in rats exposed to 100, 200, and 400 r. It was noted there was a rise in activities

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in the first 3 days and then a slow drop to normal. From these data it is possible to plot a response curve to various doses of lethal irradiation. Also by giving PAPP and other drugs to the animals prior to irradiation there is a lessening of the reaction in the spleen and thymus. Chronic studies showed that the survival time is increased when the animal is given 25r at spaced intervals over 4 days as against receiving 100r in one day. These studies are still incomplete. Work on the chronic effects have been carried out. In these studies 4 animals were used.

10. Dr. Doull discussed the work of testing of chemical and biological agents for protection against radiation damage. He stated that two methods are used for this testing; these methods are used to study the effect of acute exposure and chronic exposure. In the chronic exposure studies drugs are given 7 days before and after radiation with survival time as the end point. Screening with one method alone has shortcomings, therefore both methods are used on drugs being tested. The drugs are given in water or saline solution when every possible and dosage levels of the drugs are determined prior to radiation. Radiation is from an x-ray source with 800r used in the acute studies rather than LD 50. Using this amount of radiation avoids variation in the results and requires a lesser amount of animals. About 100 compounds have been screened and of these 12 show promise. A list of the drugs screened was furnished each member and discussed at some length; a copy of this list is attached as Inclosure #2. Some of the more promising drugs are those coded XR 31, 32, and 33. These drugs were prepared by Captain Dowben at the SAM.

11. Dr. Peterson took up the discussion of certain drugs which effect the proliferating tissues on the survival of lethally irradiated mice. A list of these drugs studied is attached as Inclosure #3. He stated that within the last 6 months other laboratories report that contrary to past beliefs foreign cells are capable of surviving in irradiated animals. His work involved transplanting of spleen tissue from baby mice in irradiated adult mice. As a result of this transplanting of spleen cells a reduced enzyme activity was shown in the adult mice following irradiation. Embryo liver tissue and bone marrow tissue was also transplanted. These cellular preparations were given one hour prior to the exposure to radiation. Other work involved exposing animals to radiation and allowing them to recover. The animals were then sacrificed and spleen and thymus gland cells were injected into other animals which was subsequently exposed to radiation. This work seems to indicate a method for determining specific cell types. Colonel Sweeney asked about the application of this work in humans, and Dr. DuBois stated that while such a procedure could not be used in humans, the chemical reaction which underlie the work is of importance.

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12. Dr. DuBois then discussed the proposed work on the influence of exposure to low levels of gamma and fast neutron radiation on the life span of the mouse. No work has been started on this problem as it is anticipated in the coming work, however activity on the necessary facilities to carry out the work is under way. Starting shortly the proper strain of mice will be available in suitable quantities. Gamma radiation will be from cobalt 60; the neutron source will be a Po-Be source. An unused underground chemical cave is to be modified to house the neutron source. The funds for the modification of this cave will be from funds remaining from the present contract. The schedule of the radiation to be undertaken and the experimental design was discussed by Dr. Doull and he also described the dosimetry used to calibrate the gamma sources. This is a long term study with longevity and leukemia as end points. At the time of the death of the animals all tissues will be saved and it is hoped that a pathologist who is presently in the Armed Forces will be available to undertake studies of the tissues. Colonel Sweeney asked, the costs for the pathologist as listed in the budget is for what percentage of his time, and Dr. DuBois answered 50%. The rate of exposure schedule was described and Captain Zeller asked about the availability of the animals in the numbers needed. Dr. DuBois answered they had been assured of a source of animals. Major Schwartz asked how long would the experiment be required to carry it to completion and Dr. Doull stated about 2 years, because it is hoped to keep the animals alive for their life span. The irradiation of the first group can be accomplished in 162 days and then the animals must be maintained until they die. A second group will be irradiated. About 800 animals will be required for each group irradiated. A discussion of the statistical aspects brought out that some of the complications in the design were due to the cost of the Po-Be sources which required that as many animals as possible be irradiated during the useful life of the source. The cage effects on longevity was discussed by Dr. Landahl.

13. At this point a tour of the facilities was undertaken. Members of the Council were impressed by the cleanliness of the laboratory and the ingenuity shown by the group in the design of altitude chambers and exposure chambers. It is well to note that many animals are maintained and the animal quarters were considered to be in excellent condition even though only 3 deners are used.

14. The group then reconvened and Captain Zellmer discussed each of the proposals. He stated that the work on the influence of low levels of irradiation to the life span of mice will be correlated with the experiments carried out in monkeys in Austin, and the work is applicable to the ANP. A discussion followed on whether this proposal should be a one or two year proposal with Major Schwartz suggesting that this phase should be a two year phase. The second years work would be a lesser cost because a neutron source and animals would not be required and perhaps the second years work would be \$20,000 to \$25,000 less.

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A discussion of the statistical aspects, between Dr. Taylor and Dr. Doull, followed. It was brought out that statistical assistance is available from the University of Chicago. It was suggested that perhaps in the second year a graduate student could be used to assist with the statistical aspects.

15. Captain Zellmer then discussed the work involving Pharmacological and Toxicological compounds as protective and/or therapeutic agents against radiation. He stated that many of the compounds to be tested will be supplied by Captain Dowben and also from other sources. Colonel Sweeney asked, can the screening of the drugs be increased and Dr. DuBois answered that the drug work could be increased if the cellular screening work were reduced. Dr. DuBois felt that the cellular work could be and perhaps should be reduced. Colonel Kossuth stated that the general screening of drugs is not too satisfactory an arrangement and asked if there are enough leads on present drugs structures which show effectiveness to warrant a speed up of this work. He was assured that there were sufficient leads. Dr. DuBois stated that the work should not be limited to those drugs alone but exploratory work in the areas of new drugs should be allowed and the Council was in agreement with this. Discussion brought out that between 40 and 50 drugs would come from Captain Dowben and similar amounts would come from our contract with Dr. Burger at the University of Virginia and from commercial sources. A total of 150 drugs could be anticipated for screening.

16. Captain Zellmer then discussed the proposal involving the effects of ionizing radiation on the biochemistry of mammalian tissue. He stated that it is proposed to continue the present studies and also to investigate enzyme systems not previously studied. Dr. DuBois pointed out that the biochemical work will point up areas for drug screening work. Also it will elucidate the mechanism of the effects of radiation.

17. Colonel Sweeney then stated that Mr. Pfister will officially check with the University on the salary raises which are included in the proposals and on the balance of funds remaining in the contract. He also stated that he wished to take this opportunity to compliment Dr. DuBois on straightening out the administrative and equipment problems. The cost of sources were discussed and it was brought out that a discount on their cost might be forthcoming in that they were being used in research. Dr. Taylor then brought up the point that perhaps less emphasis on the accomplishment of quarterly reports and more emphasis on scientific reports should be considered. Colonel Pickering stated that the quarterly reports issued by the laboratory are well known and widely circulated and they give an accurate running account of the activities of the laboratory. The quarterly reports were established when the laboratory was known as the Toxicological Laboratory. Further discussion brought out that Dr. DuBois was in favor of the quarterly reporting system, particularly as it provided a means for getting his graduate students to write up their work and he felt they should be continued. Colonel Sweeney then asked, can a good Statement of Work be written from these proposals, and he was

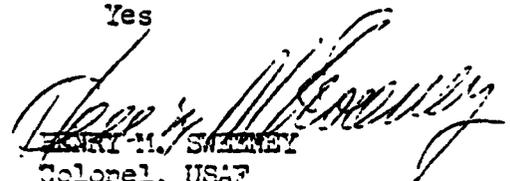
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assured by Colonel Pickering and Captain Dowben and Captain Bellner that it was possible. Dr. Clark discussed the environmental studies with Dr. Doull. Discussion brought out that the environmental studies will be shelved until the gamma-neutron work is finished. This work is not complete but it is at a point where it is reasonable to shelve the work until a later date.

19. At this point the Council held an executive session and discussion immediately arose as to whether this work should be supported for one or two years. Discussion brought out that the work on gamma-neutrons would take 2 years to complete and in order to insure its completion approval for 2 years should be considered. However, it had to be kept in mind that it was unlikely that the University of Chicago would be willing to carry out only one phase of the program and that our support was basically for the overall work of the laboratory. If we were to insure completion of the gamma-neutron work we would have to support the laboratory and the other phases of work for a 2 year period as well. Dr. Clark moved that the Council recommend approval of the work for a period of 2 years; seconded by Colonel Karstens. Colonel Kossuth stated that we basically have 3 separate groups of work going on, one of which is a 2 year program. In order to insure the 2 year program we have to buy all three. He asked if we approved this program for 2 years would we lose our ability to change our emphasis at the end of the first year, or would we be pinned down to a 2 year program or all three packages. Major Schwartz pointed out that this work would more than likely be financed on an annual basis and the second years work would require the submission of a new budget and a new Statement of Work, if that were so indicated. He stated that by passing the proposal for 2 years what we were doing was stating that we would support their work for 2 years but with the details of the actual work of the second year to be worked out by the Contractor, the Director of Medical Research and the Head of the Department of Radiobiology. Colonel Kossuth stated that all he wanted was to be assured that we can control the emphasis of the second years work. The vote to recommend approval was as follows:

Colonel Sweeney	Yes
Colonel Kossuth	Yes
Colonel Karstens	Yes
Lt Colonel Harris	Yes
Colonel Pickering	Yes
Dr. Taylor	Yes
Dr. Clark	Yes
Dt Colonel Payne	Yes

  
SEYMOUR SCHARITZ  
Major, USAF (MSC)  
Research Secretary

  
HENRY M. SWEENEY  
Colonel, USAF  
Director of Medical Research