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above 14,000 feet. At various times, some of these individuals (Peruvian Indians) were brought down to sea level for adaptation studies, and others who had lived for a number of years at sea level were taken to an altitude above 14,000 feet where the same type clinical work-up was made. A number of small, separate investigations on acclimatized Indians were in progress.

Carbon Dioxide Absorbers. Different methods for removing carbon dioxide from sealed capsules was under study. The recovery, recycling and purification of waste water in manned life support systems was also being attempted.

New Contracts. Three new contracts were in effect, tasks 7756-145, 7758-132, and 7758-133.

Tasks Terminated. Five tasks were terminated, as follows: 7752-10, "Field Test on the Uptake of Carbon Monoxide by Tissues," 7758-72, "The Effect of Acclimatization on Enzyme Reaction Rates," 7758-73, "The Physiological Effects of Ozone," 7758-76, "Adaptation to Hypoxia Stress at the Tissue Level," and 7758-77, "The Effect of Great Internal Cold in Man."

Department of Radiobiology

In addition to its facilities at Randolph, this Department staffed and operated the Radiobiological Laboratory, Balcones Research Center, Austin, Texas. This Laboratory was established in March 1950, and was a joint undertaking between the University of Texas and the School of Aviation Medicine.

The following tasks were under study by this Department in support of the biomedical effects of atomic weapons and nuclear propulsion systems:

7757-3	Effects of Ionizing Radiation Upon Physiological and Psychological Functions of Various Species (Contract with University of Texas)
7757-5	Biological and Medical Aspects of Ionizing Radiation (Contract with University of Chicago)
7757-19	Effects of High Temperature and Ionizing Radiation on Metabolism and Longevity of the White Rat (Contract with Washington University)
7757-20	Sustained Observations of Occurrence of Latent Effects in Burros Surviving 300-500 r Total-Body Gamma Radiation (Joint Project with U. S. Atomic Energy Commission)
7757-23	Effect of Radiation on Neurons and Glial Cells by Tissue Culture Method (Contract with University of Texas)
7757-32	Analysis of Radiation Hazards in Operational Employment of Atomic Weapons (In-house)
7757-35	Effects of Ionizing Radiation and other Stresses of Importance in Air Force Operations (In-house)
7757-36	Methods of Rapid Diagnosis and Prognosis in Acute and Chronic Radiation Injury (In-house)
7757-37	Physiological Aspects of Ionizing Radiation (In-house)
7757-38	Relative Biological Effectiveness of Different Ionizing Radiation (In-house)
7757-39	Application of Dosimetric Techniques and Equipment in Biological Dose Studies (In-house)
7757-41	Analysis of Ionizing Radiation Hazards to Aircrews in Operation and Maintenance of Nuclear Propelled Aircraft (In-house)

7757-42	Biological Effects of Cosmic Rays at Extremely High Altitude Air Force Operations (In-house)
7757-43	The Mechanism of Action of the Thiouronium Class of Radiation Protective Agents (Contract with Albert Einstein Medical Center)
7757-50	Effect of Total Body and Local Irradiation on the Metabolism of the Hematopoietic System in Humans (Contract with University of Texas Medical Branch)
7757-51	Radiation Biological Effectiveness Studies on Delayed Biologic Effects of Exposure to Fast Neutron versus Gamma Radiation (Contract with Atomic Energy Commission, transfer of funds)
7757-53	Pharmacology, Toxicology, and Biochemistry of Protective Compounds for Aircrews (In-house)
7757-54	The Study of Radiation-Induced Radicals in Chemical and Biological Systems (Contract with Southwest Research Institute, San Antonio)
7930-9	Radiobiological Effects of Simulated Primary Cosmic Radiation (Contract with Yale University)

The development, maintenance, and employment of manned and unmanned nuclear weapons systems, the requirements of space travel, and the possibilities of nuclear power, presented the Air Force with a host of radiobiologic problems which were not yet sufficiently defined and understood. Continued analysis of anticipated radiation hazards led to the SAM investigations of acute and chronic effects. In certain instances long term clinical observation was required before delayed radiation effects could be completely revealed. Complementing the animal experiments were the continuing efforts to collect, evaluate, and correlate biomedical data on nuclear accidents and the Japanese casualties. Corollary efforts were devoted to a characterization of radiation

sickness and injury. New emphasis was placed on the search for compounds which would protect against or modify radiation effects, methods and means of vital dosimetry, and rationale and evaluation of post-irradiation treatment technics.

The varied types, ratios, energies, and schedules of nuclear radiation demanded for research represented an array of experimental radiation sources beyond the capabilities of any given installation or facility. Consequently, the challenges of the SAM program were met by utilizing a combination of in-house and contract studies, by collaboration between Air Force and Atomic Energy Commission facilities, and through participation at the Nevada and Pacific Proving Grounds. The following is a resumé of the SAM program in radiobiology:

The Mechanism of Action of the Thiouronium Class of Radiation Protective Agents. The development of protective drugs against radiation injury was an important task in nuclear propulsion operations and in development of effective handling of an atomic disaster. The mechanism of these drugs, their toxicity, and their protective form and stability were of paramount importance.

Dr. Bernard Shapiro, Albert Einstein Medical Center, was investigating the mode by which thiouronium salts (AET) protected animals against the damaging action of radiation. Such information would greatly facilitate the discovery of drugs more effective in protecting against radiation damage and also which had less toxicity than the current agents (amineothylisothiuronium salts). Also this

research had the potential to yield basic information on the mechanism by which radiation produces its ill effects on animals.

Effect of Radiation on Neurons and Glial Cells by Tissue Culture Methods. Dr. C. M. Pomerat, University of Texas Medical School, searched for more information on the effect of radiation on the neutron and glial cells of the central nervous system. This was an important area of radiobiology which had not been adequately explored. The purpose of Dr. Pomerat's work was to grow neurons and glial cells by tissue culture and study the effect of irradiation on the cells as a means of better understanding basic mechanisms.

Considerable progress was made toward maintaining the neutron and glial cells using a newly developed cellophane as a cover. Cytological changes resulting from irradiation were being studied with special reference to giant cell formation.

Methods of Rapid Diagnosis and Prognosis in Acute and Chronic Radiation Injury. Dr. Herbert Gerstner, under an in-house subtask entitled, "A Study of the Acute Radiation Syndrome in Man," accomplished an important piece of research. Dr. Gerstner studied the accumulated data on the Hiroshima-Nagasaki survivivors, the group of Marshall Islanders accidentally exposed in 1954 to a thermonuclear device, and the case history comparisons of the Los Alamos, Argonne, Japanese, and Russian accidents. From this material, together with the findings obtained on 263 cancer patients exposed to known doses of therapeutic whole-body x-irradiation at the M. D. Anderson Hospital, Houston, Texas, Dr. Gerstner described the four distinct stages of typical acute radiation sickness.

Animal experiments endeavoring to duplicate the exposure conditions of Hiroshima and Nagasaki were conducted and the subjects were being observed for long term effects of ionizing radiation. Early clinical symptoms as well as long term effects were to be compared with the data from the Atom Bomb Casualty Commission.

Another subtask under 7757-36, entitled "The Value of the White Blood Cell for Diagnosis and Prognosis of Radiation Injury," was also being accomplished by Dr. Gerstner. Operation and maintenance of nuclear powered vehicles and weapons required that crews and maintenance men be repeatedly exposed to appreciable doses of ionizing radiation. Therefore, it became necessary to determine the effects of previous exposure on human tolerance to subsequent radiation. The first approach to this was to expose rabbits to x-ray doses between 100 roentgens (r's) and 500 r, and to run daily white blood cell counts. Then after complete recovery, the animals were re-exposed to the same doses, and when reaction to the second radiation exposure was followed by complete recovery, a third exposure was performed. The results showed that repeated radiation exposure to relatively high doses would not lead to enhanced damage (as indicated by the white blood cell count) when the interval between exposures was long enough to allow complete recovery of the bone marrow.[21] New experimentation with several chemical agents was in progress.

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21. Gerstner, H. B., and H. A. Gorman, "Effect of Repeated Whole-Body X-Irradiation on the Peripheral White Blood Cell Count of Rabbits," SAM Report 59-52, February 1959.

Effect of Total Body and Local Irradiation on the Metabolism of the Hematopoietic System in Humans. Dr. W. C. Levin, University of Texas Medical School, investigated this problem. If the biological response in man to ionizing radiations was to be more accurately understood, it could only come from measuring that response in man. The use of whole-body radiation therapeutically offered one such means of adding to that understanding of human response, especially since in this case the dose could be measured with all desirable accuracy.

Whole-body x-irradiation was used therapeutically at the M. D. Anderson Hospital, Galveston, Texas, in certain cases of cancer, such as leukemia and metastatic tumors. Twenty patients had been treated with either 175 r or 200 r whole-body irradiation. Data on their hematologic response and initial reaction was near completion.

Effect of Ionizing Radiation and Other Stresses of Importance in Air Force Operations. Flying involved many conditions of stress normally not encountered in ground operations. It was important that the Air Force know which of these physiological conditions were detrimental or beneficial when combined with ionizing radiation. It was known that fatigue, cold, heat, noise, hypoxia, fasting, and the absence of noise had an effect on aircrew performance. These combined with radiation may have caused loss of crew efficiency.

Studies were done to determine the effect of hypoxia, cold, one hundred percent oxygen, prolonged simulated flights, and fastings on survival and performance before and after exposure to ionizing

radiation. Animals acclimatized to 18,000 feet simulated altitude for six months survived 880 r of x-irradiation. Carbon monoxide acclimatization studies were also performed. Monkeys were droned through atomic clouds at altitudes of 30,000 feet to study the effects of internal versus external radiation and the differences between inhalation plus ingestion of radioactive materials. Furthermore, studies on metabolism plus radiation under conditions of cold were done.

Biomedical Support of Project Mercury. Experimental animals were very probably going to be used as passengers in extraterrestrial vehicles. Inasmuch as the satellite program was greatly accelerated, it was decided that the monkey should be integrated into this research as rapidly as possible in order to have the animals available, trained, and baselined if the opportunity to participate in a space flight involving experimental animals presented itself.

Accordingly, several monkeys were in training for this purpose and a program had been initiated (jointly with the Department of Physiology) in which answers to the following questions were being obtained: (1) What are the minimum caloric and fluid requirements for a maintenance situation? (2) What is the best method of confining a monkey for an extended period of time? (3) What is the oxygen requirement per unit time? (4) Can a monkey be conditioned to feed himself under zero gravity conditions? (5) What is the best method of waste disposal under zero gravity conditions?[22]

Effects of High Temperature and Ionizing Radiation on Metabolism and Longevity of the White Rat. Metabolic changes, mortality, and

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22. "Primates in Space," Bioastronautics, Advances in Research, Special SAM Report, March 1959, 58-72.

histological changes resulting from or associated with gamma irradiation at low dose rate at constant environmental temperatures were important in nuclear planning. Dr. L. D. Carlson, University of Washington, conducted a study designed to determine the effect of a relatively large dose of gamma radiation on aircrews that had previously received background irradiation in nuclear powered aircraft. He exposed rats and mice to daily low doses of ionizing radiation, then challenged them with larger doses in order to observe their response.

Application of Dosimetric Technics and Equipment in Biological Dose Studies. Of extreme importance in determining radiation damage was the accurate correlation of biologic response with physical dose. Standardization of dosimetry was begun in 1956 at the School of Aviation Medicine. All biological experiments at the 1958 bomb tests in Nevada were monitored by physical dosimetry provided by the School of Aviation Medicine. Methods of single and two-phase chemical systems for differential gamma ray and neutron dosimetry were developed at the School. The temperature dependence, sensitivity, stability, and reliability of these chemical dosimeters was such that they were the method of choice for gamma dosimetry in the field, and probably in the laboratory also. A portable, field-type spectrophotometer dose-reader had been partially developed. Coupled with the fission foil system of neutron dosimetry utilized by the Oak Ridge National Laboratory Group, these systems provided neutron and gamma ray dosimetry for almost any situation. SAM dosimetric development was coordinated with the Los Alamos Scientific Laboratory.

Relative Biological Effectiveness of Different Ionizing Radiations. For some time it had been realized that different types of radiation produced a different degree of biological responses over the same identical time period with the same dose of radiation. Because all types of radiation could be expected in most Air Force operations, it was imperative that the relative biological effects of each of these radiations be well defined. This was of particular importance in nuclear propulsion for manned systems since shielding characteristics would be different for various radiation environments, and also for ground handling construction and for any nuclear power program.

Monkeys were exposed to fast neutrons, thermal neutrons, Cobalt^{60} gamma rays in acute situations and a mixture of Cobalt and PoBe for chronic long term exposures to various neutron and gamma ratios. This project involved the long term collection of data and would later be extended to include the fission products, unfissioned materials, as well as the prompt radiations associated with reactors and nuclear devices.

Biological Effects of Cosmic Rays in Extremely High Altitude Air Force Operations. Although a primary cosmic ray source was not available as a laboratory device, it was believed possible to simulate the same tissue effect using other high energy sources. Preliminary work was under way in the Departments of Radiobiology and Microbiology and the Texas Nuclear Corporation. A neutron generator had been acquired and was in use. Investigators planned to use microbeams to simulate in the laboratory the effects of energetic heavy particles in cosmic radiation.

Monitorship of a contract with Yale University to study, "Radiobiological Effects of Simulated Primary Cosmic Radiation," was transferred from Holloman Air Development Center to the Department of Radiobiology.

The Effects of Ionizing Radiation on Biochemical, Physical, and Psychological Functions in Various Species. In the development of low dose chronic radiation designed to support permissible levels of exposure in excess of Atomic Energy Commission established limits, long term effects were of controlling importance. A large scale, thorough animal husbandry program obviously became a prime requirement. Accurate baseline data on normal animals were necessary so that subtle changes following radiation exposure could be measured.

At the Austin laboratory, the care and management of animals had produced a colony of over 700 monkeys in various stages of post radiation recovery. The monkey was chosen as the experimental animal because the findings could be more readily extrapolated to man.

The animals were trained to take performance tests in order to determine radiation effects on their coordination, sensory perception, learning ability, color discrimination, behavior action time, and fatigue. Even though subtle and interesting changes were noted, it was demonstrated that a dose equal to that expected in normal nuclear operations did not cause a performance decrement of significance to thwart accomplishing the flying mission. Biochemical studies encompassed every phase of the radiation exposures. A biologic dosimeter, such as changes in the enzyme system, blood, or tissue, was sought.

The follow-up of such a large primate colony of both normal and irradiated animals lent tremendous value to the radiation studies involving Japanese casualties of Hiroshima-Nagasaki and furnished excellent prediction data for accidents which were expected to occur in the ever expanding nuclear industry.

Sustained Observations of Occurrence of Latent Effects in Burros Surviving 300-500 r Total Body Gamma Radiation. Fifty-nine burros surviving total body irradiation by a gamma source were being maintained at the University of Tennessee-AEC Farm. Under a joint agreement, SAM was allowed to participate in these studies. Some of the animals were irradiated in 1951, and others in 1953. The clinical history of these burros, including records of irradiation, progressive hematological values, many biochemical measurements, and ophthalmic examinations, was carefully maintained.

Biological and Medical Aspects of Ionizing Radiation. Dr. K. P. Dubois, University of Chicago, was engaged in research on the development and evaluation of radiation protection compounds. For a number of years various investigators had tested a myriad of chemical compounds for their efficacy in preventing or treating acute radiation disease. No compound *per se* had been successful in preventing the syndrome if given after irradiation, but several compounds gave some measure of protection if administered prior to exposure. However, no startling new group of chemical agents had been found.

Dr. Dubois also traced the effects of low dose gamma and fast neutron irradiation on the life span of the mouse. Preliminary

findings indicated fast neutrons were some four to five times more effective in causing certain aspects of radiation damage.

Attemptiong to find a biological dosimeter, Dr. Dubois observed the effects of ionizing radiation on the biochemistry of mammalian tissues. Enzyme changes were noted, but no single system adequate for measuring radiation injury was found.

Analysis of Ionizing Radiation Hazards to Aircrews in Operation and Maintenance of Nuclear Propelled Systems. The application of nuclear energy in aircraft, rocket, or satellite propulsion subjected Air Force personnel to cumulative doses of radiation (through normal operation and maintenance, crashes, meltdowns, etc.). The probability of operating under existing levels of permissible exposure recommended by the National Committee of Radiation Protection was extremely low. Consequently, it was mandatory that biologic endpoints of performance be established and the threshold doses determined. Data from accidental exposures clearly defined the areas of concern. Fast and thermal neutron, Cobalt^{60} gamma, bomb and reactor mixtures of neutron-gamma radiation, fallout, radiation, and selected fission products were all being investigated.

A basic radiobiology guide of mission dose schedules, ground handling doses as well as inhalation concentrations under various conditions of release was published in 1958. Study and evaluation were continued, with correlation of hazards, developments, and using requirements.