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well as for controlling carbon dioxide and water vapor concentrations in an efficient and weight-saving manner. In this connection, also, the development of physiological instrumentation and recording devices already was of the utmost interest to other Air Force organizations as well as other agencies, particularly the oxygen and viability sensors, the blood pressure recorder and respiratory flow indicator. The physical performance and maximum work capacity studies produced results that were expected to be extremely valuable to the Air Force with regard to pilot selection and training, the man-in-space programs, the efficiency and health of Air Force personnel, and longevity and the aging process. The fundamental data that were accumulating from the study of carbon monoxide and green plants was expected to be of significant value in helping to understand and solve Air Force problems of the future. Other studies in the Department of a more fundamental and basic nature also offered extremely significant implications.

Meetings. Dr. Robert T. Clark, chief of the Department of Physiology-Biophysics, presented a paper entitled, "Space Biology," at the First International Symposium on Submarine and Space Medicine, New London, Connecticut, on 7 September.

## 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:

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| 7757-2 | Effects of Acute and Chronic X-Ray, Gamma Rays, and Neutron Exposure on Hemopoiesis (Contract with Northwestern University) |
| 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 300-500r 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) |
| 7757-34 | Body Shielding Against Ionizing Radiation (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) |

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| 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) |
| 7757-49 | Radiation Action Caused by Diffusible Agents (Contract with Yale University) |
| 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) |

The development, maintenance, and employment of manned and unmaned 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 postirradiation treatment techniques.

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 resume' of the SAM program in radiobiology:

Fundamental Investigations. The requirement for a classically pure, or fundamental investigation of a general and undirected nature was gaining new recognition and emphasis in the radiobiological research and development program. The pursuit of investigations designed to answer the theoretical and practical questions raised by the nuclear systems (aircraft rockets and/or satellites) was hindered by insufficient information on fundamental mechanisms and relations, and by a lack of the stimulation and incentive which an active basic science program provides. It was accepted that the developmental and applied sciences depend on an active and progressive basic science.

It was desirable therefore to support broad and general research by pre-eminent investigators who were able to take bold, new approaches and develop basic information in particular areas of interest to provide the

stimuli, ideas, and background information required by the applied phases of the program.

Investigation of the Biochemical, Chemical, and Physical Properties of Nucleoproteins. The nucleic acids are vital for the synthesis of proteins and enzymes of living tissue, and their integrity is necessary for the viability of tissues. Their importance in cell division and their genetic influence was well known. Because of a lack of basic information on the biochemistry of nucleic acids and nucleoproteins, it was difficult if not impossible to interpret effects of radiation, anti-tumor agents and the like on tissues and cells.

Dr. S. Gurin of the University of Pennsylvania examined fractions of DNA hydrolyzed by formic acid and new fractions prepared. Also, studies on the absorption of nucleic acid derivatives by the intestine were undertaken. It was hoped these studies would ultimately unveil molecular structures and rearrangements of importance in radiation damage.

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.

The objective of this research was to investigate 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.

Samples of tissue were taken from several areas of the brain of the monkey and cat and planted on suitable media. Cells were grown in these cultures. Some of the cultures were exposed to cosmic radiation during balloon flights 30 miles above sea level, others to massive doses (10,000 roentgens) of gamma radiation, and also neutron exposures were accomplished. Giant cells were photographed as one of the effects of radiation.

Clinical Research. The varied radiation sources in the environment --in the form of weapons, nuclear power or propulsion, or industrial and medical application--made it imperative that everyone concerned with clinical medicine acquaint themselves with the biological effects of ionizing radiation on man. Attempts were made to review and compare all of the accidental human radiation exposures with the therapeutic radiation treatment of cancer patients.

There was a need to define the acute effects of human whole-body exposure to penetrating ionizing radiation and to attempt a realistic evaluation of the facts known to date.

Methods of Rapid Diagnosis and Prognosis in Acute and Chronic Radiation Injury. Under this an in-house subtask by Dr. Herbert Gerstner, entitled "A Study of the Acute Radiation Syndrome in Man," was established. The largest group of persons exposed to radiation was represented by the populations of Hiroshima and Nagasaki. The group of Marshall Islanders exposed in 1954 to a thermonuclear device represent the next largest group, and then case history comparisons could be drawn from the Los Alamos, Argonne, Japanese fishermen, and Russian accidents. From this material, together with the findings obtained on the 263 cancer patients exposed at the M. D. Anderson Hospital to accurately known doses of therapeutic whole-body x-irradiation, the following summary was made: Exposure to a sufficient amount of penetrating x-ray, gamma, and/or neutron irradiation causes in man characteristic clinical sequelae--the acute radiation syndrome. This complex of signs and symptoms unfolding along a rather fixed time schedule, forms a peculiar picture that is as well defined as "lobar pneumonia" or "typhoid fever."

According to their chronologic sequence, four distinct stages of the acute radiation syndrome could be established, namely (1) prodromal, (2) latent, (3) bone marrow depression or hypoplastic anemia, and (4) recovery phase. Of course, the "typical" disease as outlined was subject to variation brought about by several factors--dose, dose rate, type of radiation, and individual susceptibility.

Animal experiments endeavoring to duplicate the exposure conditions of Hiroshima and Nagasaki were continued 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 was entitled, "The Value of the White Blood Cell for Diagnosis and Prognosis of Radiation Injury," carried out also by Dr. Gerstner. If radiation exposure was to be correlated with biological response under certain Air Force operating conditions, methods or measures had to be determined for screening and surveillance of individuals who could be repeatedly exposed to appreciable doses of ionizing radiation. In addition, it was important that information concerning radiation tolerance following previous exposures to ionizing radiation be determined. A first approach to this was to expose animals 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 project was in its third exposure schedule. Daily white cell counts were being plotted, and preliminary results were indicative of remarkable recovery capabilities.

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

men 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. The patients so treated offered an opportunity for studying in human beings the acute reaction to ionizing radiation. Previous experiments at the Hospital involved physical performance of selected psychomotor tests and general clinical examinations reflecting on the physical condition of the patients. Later studies involved clinical observations which demonstrated a pattern comparable to the response in many instances observed among the Japanese, Marshallese, and nuclear accident victims. One major drawback was the inadequate long term study of these patients and lack of follow-up possibility.

Applied Research. Applied research was directed toward developing specific information which was in direct support of Air Force Weapons Systems Programs. Nuclear operations could have required radiation exposures above the tolerance levels. Consequently, continued experimentation toward closer definition and evaluation of permissible exposure levels was necessary.

Analysis of Radiation Hazards in Operational Employment of Atomic Weapons. In-house subtask, "Biological Effects Following Exposure to Nuclear Detonations (Operation Plumbbob)," was established in February 1956.

Animals were taken to the Nevada Test Site and arranged in an exposure pattern so that (a) the dose required to produce 50 percent lethality in 30 days was determined; (b) the range of doses permitted studies on acute clinical symptoms, such as purpura, anorexia, retching, vomiting, epilation, iritis, retinal edema, diarrhea, and fatigue; and (c) a sufficient number of low-dose exposures were obtained so that many animals could be followed for several years to determine the incidence of long-term acute effects, such as cataract production, life shortening, bone-marrow changes, and carcinogenesis.

This study was being continued and being expanded in terms of animal correlation consistent with animal availability and personnel capability.

The final SAM Report, WT-1505, Operation Plumbbob, Project 39.6, was published on 31 December.

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 fasting 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-- five degrees Centigrade, 28 degrees Centigrade, and 35 degrees Centigrade--were done.

Experimental animals were very probably going to be used as passengers in extraterrestrial vehicles. Inasmuch as the satellite program was obviously greatly accelerating, it was deemed advisable to integrate the monkey 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 assumed zero gravity conditions?

It became evident that there may have been certain measurements of value, the instruments for which were probably amenable to minaturization. These measurements were tentatively identified as body temperature, electrocardiograms, blood pressure, electroencephalograms, and possibly a psychologic test of motor coordination. Experiments to obtain the baselines for these parameters were performed, utilizing conventional equipment, and preliminary testing of minaturized equipment was begun.

The baseline work on animal maintenance in a situation of physical confinement was planned. A more refined test apparatus was built simulating conditions of restricted movement more closely, and measurements of the physiological parameters of interest were being accomplished under these conditions.

Effects of High Temperature and Ionizing Radiation on Metabolism and Longevity of the White Rat. Metabolic changes, mortality, and 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, had accumulated a considerable body of data which indicated that the mean survival time of rats and mice was reduced when exposed to doses of 1.1 r per day for the rest of their natural lives. The reason or reasons for the reduced life expectancy seemed to be open to question with possible explanations being inanition, hematopoietic injury, and cancer.

Body Shielding Against Ionizing Radiation. As more exotic weapons systems were conceived, more materials for base hardening were developed,

and hitherto unknown metals and alloys were produced for cabin materials for high altitude and orbit studies, it was important that the effects of high energy particulates (primary and secondary cosmic rays) nuclear power source radiations, and 14 Mev neutrons resulting from nuclear detonations be studied to determine which of the metals and alloys produced the least amount of secondary radiation inside the structure.

A complete survey was made of the various shielding experiments as they applied to the nuclear propulsion program. These studies involved abdominal shielding (of animals) as well as specific organ shielding such as the spleen, kidney-adrenals, liver, stomach-intestine, bone-limb, as well as head-nural-pituitary. Since the relative energy loss and relative biological effectiveness over the wide energy spectrum varied considerably, only general integrated conclusions were possible. These conclusions, however, in terms of shielding, permitted half thickness values for different energy levels to be calculated so that they could be used if necessary in further reducing exposure limits to air-crew members in the nuclear propulsion program. Further studies on shield arrangements were developed.

Application of Dosimetric Techniques 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 and with the completion of the 1958 bomb tests in Nevada--all biological experiments 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 SAM. 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. 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.

Relative Biological Effectiveness of Different Ionizing Radiations. For sometime 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 investigation with Radiobiology-Microbiology, and the Texas Nuclear Corporation had delivered a neutron generator to the School. Experimental work was under preparation. Some neutron work had been completed by Dr. Pomerat and the SAM physics group.

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.

Ionizing radiation was known to cause abnormal effects on the body; therefore, it was of extreme importance to outline these changes and discover their mechanisms of action in order that rational preventive measures and ultimate treatment programs could be developed.

This vast contractual and in-house program produced over one hundred articles each in themselves contributing in some way to a better understanding of radiation and its effects. Specifically, however, several general findings will easily illustrate the significance of the overall study. The care and management of normal animals produced a colony of 1,000 monkeys in various stages of post radiation recovery. Husbandry

had progressed enough to permit aging studies, a modest breeding colony, and studies involving tuberculosis treatment and the effects of too much vitamin D. Additional monkeys were being added to the colony periodically as required by the experimental program.

Gamma Radiation Research. The gamma irradiation experiment using a multikilocurie Cobalt$^{60}$ radiation source was completed and data on the acute effects of gamma radiation in primates were assembled and reported for publication as a SAM report.

So far as radiation versus performance decrement in general was concerned, cognitive functions, sensory functions, motor learning, brightness and color discrimination, perception of distance, vertical activity level, behavior action time, tracking, fatigue, etc., were studied. Even though subtle and interesting changes were noted, it was demonstrated that the recommended dose schedules possible in normal nuclear operations did not demonstrate a performance decrement of significance to thwart accomplishing the flying mission. Performance studies were also extended to space environment conditions.

Physiological Aspects of Ionizing Radiation. A study was begun on nuclear accidents and the possible effects on the lungs. Nuclear accidents involving reactors may produce health hazards by permeating the atmosphere with radioactive particulate matter. These health hazards were not completely understood. For example, how and to what extent was the respiratory apparatus damaged by inhalation of the resulting atmosphere after a possible nuclear accident.

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.

Five of the animals had died. Weight changes were evident in the irradiated groups. Blood changes were typical following radiation. In general, recovery occurred during the first year so that blood values were generally within normal ranges. In view of the paucity of information concerning latent effects of total body irradiation in large animals, the opportunity to observe this group of burros seemed fortunate.

Biological and Medical Aspects of Ionizing Radiation. Dr. K. P. DuBois, University of Chicago, was engaged in research on the development and evaluation of prophylactic and protective measures against radiation effects. 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.

Dr. DuBois tested compounds and certain derivatives of AET which seemingly offered some degree of protection. Other drugs were also being

tested for their protective quality as well as their toxicity.

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, biologic endpoints of performance must be established and then 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. This guide was in the process of revision, taking into consideration new data concerning nuclear aircraft accidents obtained by aircraft company studies.

Bio-Medical Working Group for Aircraft Nuclear Propulsion. On 28 July Col. John E. Pickering was invited to participate as a member of the Bio-Medical Working Group for Aircraft Nuclear Propulsion. The Group was formed to consider engineering details of the various nuclear systems and to suggest biological experimentation desirable in support of their development. The Group was to meet every four to six months for a total time of about ten days annually. Other members were Dr. Donald

M. Ross, Dr. Titus Evans, Dr. L. K. Bustad, and Dr. A. C. Upton, all prominent in radiation research.

Submission of Program for Future Biomedical Testing. On 15 July a proposed program for future biomedical testing was submitted.

Operation Hardtack. A final draft report (WT-1633) on Operation Hardtack was completed. Departmental personnel participated in this project 20 July to 21 August, at the Pacific Proving Ground, Johnson Island, T. H. (Project 4.1, TU-3, Task Group 7.1, Joint Task Force Service).

## SPACE MEDICINE DIVISION

This Division was still in the process of organization during this period. It had not been completely staffed. Most of the work centered around the experiments in the Space Cabin Simulator. The following tasks were assigned to this Division:

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| 7756-1 | The Effect of Drugs Upon Psychological Processes (In-house) |
| 7758-17 | Studies on the Bioclimatology of Space Flight: Studies in the Space Cabin Simulator (In-house) |
| 7758-20 | Studies on the Biological Effect of Sub-Gravity and Zero-Gravity (In-house) |
| 7758-51 | Photosynthetic Gas Exchangers (Contract with University of Texas) |
| 7758-52 | Study of Physical Requirements for Manned Rockets and Artificial Satellites Relating to Specific Vehicles and Weapons Systems (In-house) |
| 7758-117 | Space Medicine Review (Contract--to arrange symposium--with Southwest Research Institute, San Antonio) |