DEPARTMENT OF THE AIR FORCE
HEADQUARTERS UNITED STATES AIR FORCE
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MEMORANDUM FOR RADIATION EXPERIMENTS COMMAND CENTER
6801 TELEGRAPH ROAD
ALEXANDRIA VA 22310-3398
ATTN: COL BAILEY

FROM: HQ AFMOA/SGPT
170 LUKE AVENUE, SUITE 400
Bolling AFB, DC 20332-5113

SUBJECT: ***REFERENCE ACHRE REQUEST NO. 031395-E: Benefits of HRE***

Subject request from the ACHRE--to portray the benefits of government sponsored human radiation experiments--was received in our office on 15 Mar 95 with a suspense of 1 Apr 95. Unfortunately, to at the very least obtain a reasonably accurate assessment of experimental benefits of studies performed 20-50 years ago, we felt obligated to contact a multidisciplinary group of scientists. The people we contatcted work in related/similar fields (to previous investigators); we requested they provide a reasonable assessment of the benefits of these many diverse studies. Obviously, this has taken some time; a synopsis of the material we received is as follows:

1. David Grant Medical Center reports on study #7 in Air Force Database (attached):

Note: Much of the "benefits" information provided below would also explain benefits of Study #6.

Major (Dr.) Andrew K. Wong, Medical Corps, Director of Cardiovascular Research, DGMC, explained the benefits as follows:

I have been asked to comment on the scientific and clinical merits of two studies previously completed at DGMC in the early 70's. These two studies were titled "The Effects of Perhexiline Maleate Upon Regional Myocardial Perfusion and Extent of Transient Myocardial Ischemia Assessed by Potassium-43" and "Noninvasive Myocardial Imaging with Potassium-43 and Rubidium-81 in Patients with Left Bundle Branch Block." Both studies involved exposure of patients to medical radiation.

Potassium-43 and Rubidium-81 were the first radionuclide monovalent cations to be applied in the clinical setting. Increased understanding of the active and passive transport mechanisms for concentrating monovalent cations in myocardial tissues led to the exploration of these radioisotopes for the evaluation of regional cardiac perfusion. Intravenous administration of these agents results in their uptake in the myocardium in proportion to the blood flow, cellular integrity, and size of the regional potassium pool. Cardiac pathology producing reductions in regional myocardial blood flow, abnormalities in the cell membrane transport system, and altered cellular energy production or utilization is correlated with diminished uptake of these radionuclide monovalent cations.

The use of potassium-43 was limited by its relatively long half-life and comparatively high radiation exposure to the patient. Technical requirements made imaging interpretation with rubidium-81 difficult. Clinical use of these agents subsequently ceased when thallium-201 emerged as a more suitable imaging radionuclide. Though the clinical use of potassium-43 and rubidium-81 were overshadowed by the development of newer generation agents, the knowledge gained from their study was important in guiding further research in nuclear medicine.

It is difficult to comment specifically on the benefits gained by the individual patients in these studies. However, these projects formed part of the body of work that was pivotal in the development of cardiac nuclear imaging that is currently utilized daily around the world. In summary, I feel that these were valuable investigations in an area that has become a fundamental component of the field of cardiovascular medicine.

2. Wright Patterson AFB (Armstrong Lab), Study #93, #94, and #95 on Air Force Database (attached).

Lt Col Paul Morton of the Crew Systems Directorate at Wright Patterson AFB reported as follows:

Study #93 and #94: These two studies were both based on the same data collection of 411 hand X-rays. The data were used to develop pressure suit gloves for the space program and for Air Force high altitude flights. These products were employed operationally in NASA and the Air Force for many years and continue to be used in NASA SR-71 flights and Air Force U-2 flights. Archived data and study X-rays were destroyed by fire in the 1970's during a Viet Nam War protest by Antiock College Students.

Study #95: The study on "Link System of the Human Torso, X-Rays" was used as part of critical data toward development of the Articulated Total Body Model. This model is very important in the acceleration and impact area for developing protective equipment for both military and commercial use and is the "current state of the art" model. It has been involved in important developments such as seat belt and air bag design and continues to be used by the automotive industry to develop protective equipment and crash worthy tests.

3. Brooks AFB Armstrong Laboratory (AL/AOES) reported on Pre-75 studies as follows:

PART A: GENERAL DESCRIPTION OF STUDY BENEFITS:

a. The following are benefits obtained from the various pre-75 studies conducted at Armstrong Laboratory, USAF School of Aerospace Medicine at Brooks AFB, and USAF School of Aviation Medicine at Randolph AFB. For simplicity, benefits are grouped and the study number follows. Some studies may have several overlapping benefits. Ultimately, the basic research conducted provided information on the effects of physical stressors on humans with particular emphasis on aviators. The information gained was valuable for health care providers in the management of health care for airmen (specifically aircrew members) and assisted planners in the space program.

b. Enhanced our understanding of the effects of radiation on the human body and helped determine protective measures against the deleterious effects of radiation. Study #'s: 21, 22, 31, 32, 38, 40, 77, 78, 80 of the Air Force Database (attached).

c. Improved or maintained the health of Air Force personnel through understanding of effects of physical agents such as high G forces, radiation, high altitude, and temperatures. Information gained helped launch human space travel. Study #'s: 17, 18, 20, 38, 39, 81, 82, 84, 87, 98, 99.

d. Enhanced our understanding of the human body's functions. Various studies were designed to develop methods to measure bodily functions. These new methods were developed to assess the body's ability to adapt to stressors such as physical agents (radiation, high altitude, G-forces, temperature , etc.). Additional studies developed other scientific methods that enabled scientists to extrapolate information from animal studies to humans. Study #'s: 10, 14, 19, 28, 34, 35, 36, 37, 41, 42, 44, 45, 46, 47, 48, 49, 52, 53, 54, 55, 56, 58, 60, 61, 73, 75, 76, 79, 80, 81, 83, 97, 103.

e. Enhanced understanding of the biological effects of cancer radiation treatment.

f. Determined the effects on the human body in an outer space environment. Understanding effects such as weightlessness, confined space, immobility, etc., enabled scientists to plan for human space travel. Study #'s: 12, 13, 15, 61, 63, 64, 65, 66, 67, 104, 106.

g. Determined the effects of medications on aircrew member's performance. This information assisted medical health care providers in managing the clinical health of aircrew, thus enhancing mission support. Study #'s 16, 105.

h. Enhanced basic understanding of the bodily responses of aircrew that may be impacted by physical stressors. Study #'s 30, 33, 68, 69, 70, 71, 72, 74, 85, 86, 96.

PART 2: MORE SPECIALIZED DESCRIPTION OF STUDY BENEFITS: (AL/AOCI, Dr William B Kruyer, MD, FACC, Staff Cardiologist, Internal Medicine Branch, Clinical Sciences Division) Note: Reference to "I" in the following paragraphs refers to Dr. Kruyer

a. Studies 29, 44, and 45 all concern the same project. Studies 29 and 45 are actually journal articles while study 44 is an earlier publication of the same project. This involved development of a time saving, inexpensive and accurate method of determining cardiac output by radioactive indicator dilution curves. Other methods of calculation either involved expensive computer equipment which might have been inaccurate with some curves, a time consuming 20-30 minute process or a quicker, but potentially inaccurate method involving visual estimation of part of the dilution curve. I believe this project was developed by examining several hundred curves from determinations done from previous projects or work; then they validated it prospectively with 25 subjects. It is difficult to assess the benefit as these techniques are no longer used in clinical practice. However, based on the claims made for the procedure in these articles, it would have had significant impact on many of the experiments done here and elsewhere in the 1960's/1970's assessing cardiovascular effects of the manned space flight environment. It would also have had potential impact to any research project throughout the medical community involving measurement of cardiac output by this determination. That would include clinical use in the cardiac catheterization laboratory in the 1970's as indicator dilution curve methods were routinely used then in the catheterization laboratory for determining cardiac output. This has since been replaced by other methods although the principles apply to the currently used thermodilution determination method. So the potential benefit was very wide in scope for both the Air Force and medical/research community at large. I cannot speak to how broadly this particular measurement method was in fact utilized.

b. Study numbers 58-67 were all published in the *Aerospace Medicine Journal.* These projects were all very pertinent to research performed here regarding the manned space flight environment. They all investigated different aspects of the zero gravity, inactive, confined environment experienced in space flight. They all utilized a radioisotope such as I-131 to assess some of the measured parameters. Study 58 utilized bedrest to assess the effect of space environment on adrenal gland function. Studies 59-67 all involved assessment of the cardiovascular effects of manned space flight and some of them investigated different methods to offset the undesirable cardiovascular effects. A space cabin simulator, prolonged chair rest and prolonged bedrest were used to simulate such an environment. Isotonic exercises, lower body negative pressure, Fluorinef therapy, and antigravity suits were methods investigated to offset undesired cardiovascular effects. The radioisotope labels were used predominantly to measure indices such as total blood volume, plasma volume and red blood cell mass. One of the items investigated was differentiating the cardiovascular effects of inactivity and confinement alone as compared to effects of a zero gravity environment. These studies occurred in the 1960's and similar studies were performed at other facilities throughout the United States and the world. Similar research is still ongoing, including with Dr. Convertino at AL/AOCY. It would seem to me that all of these studies had very major impacts on understanding effects on the human system of the manned space environment due to inactivity, confinement and the zero gravity environment. Surely this was incredibly important to the success of our space flights. Much of the research also has implications to the medical community for disease states such as diabetic neuropathy and other conditions that involve prolonged bedrest or ineffective responses to orthostasis.

c. Study numbers 46-52 are School of Aerospace Medicine technical reports. The reports themselves do not contain an impact statement that would allow one to assess benefit. However, they were all projects exploring different methods of studying red blood cell kinetics or ferrokinetics and iron metabolism. Specific parameters examined include plasma volume, extracellular fluid volume, red blood cell mass and red blood cell survival. These studies utilized different radioisotopes of material such as iron, chromium and iodine. They were investigating methods that were either easier, quicker, more accurate, less expensive or able to be done with requirements for fewer blood samples and therefore fewer blood drawings from the subjects or patients. Technically I am unable to make a clear benefit statement, but these same parameters were measured in the manned space flight projects discussed in the previous paragraph. So, if these newer developed methods reported in these technical reports were in fact utilized, they would have had a significant and broad application to numerous experiments performed here and elsewhere as described in the previous paragraph.

d. Dr. Kruyer was unable to find any information on studies 73 and 96.

If you have any questions please call the undersigned at (202) 767-5078.

DANIEL R. BROWN, Lt Col, USAF, BSC
Chief, Clinical Investigations and
Life Sciences Division
Air Force Medical Operations Agency
Office of the Surgeon General

Attachment:
Air Force Database including Pre-75 Experiments