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USAF School of Aerospace Medicine (AFSC)
Brooks Air Force Base, Texas 78235

Minutes of the USAFSAM Research Committee

29 March 1966

1. Place: Bldg. 170, Brooks AFB, Texas

2. Time: 0900

3. Chairman: Dr. Hans G. Clamann

4. Members present: Col Robert L. Johnson
Col Arthur J. Stumpf
Dr. Billy E. Welch
Lt Col Fritz M. G. Holmstrom
Maj Irving Davis, Recorder

(Col Holmstrom required to leave meeting prior to conclusion.)

5. Proposed RDT&E protocol reviewed (see Atch 1):

a. Title: The prevention of altitude sickness with Acetazolamide (Diamox). Project 7758, Task 775801, Work Unit 775801003.

b. Principal investigators: Capt Richard S. Kronenberg and Dr. Stephen M. Cain.

c. Responsible medical officers: Capt Kronenberg (supervising physician) and assisting Major Robert G. McIver, Capt Howard G. Iger, Capt Allen Greenwald, and Major William Brown.

d. Technical objectives: To evaluate the chemoprophylactic effects of Diamox relative to altitude-induced incapacitation. Measurements will include physiological and biochemical parameters and clinical observations. Experimental protocol will include modifications contained in the principal investigator's letter of 21 Mar 66.

e. Discussions: Dr. Clamann provided some background information on recent studies with Diamox which provided the rationale for the planned protocol. He further made mention of the complementary studies of Severinghause and his associates on acclimatization to high altitude. Col Holmstrom disclosed that the Army is planning to run a major study with Diamox this summer with a large number of

Atch 1

individuals (over 100) at altitude. In order to provide answers to several questions that were raised, the Committee requested Capt Kronenberg to meet with it. One question raised by Dr. Welch and answered by Capt Kronenberg concerned the lag time for physiological and biochemical indices between material from arterial puncture and lumbar puncture. He explained that this lag was approximately four hours but indeed offered no definite evidence as to ventral surface of the brain, that is the central chemoreceptors. He expressed the opinion, however, that changes on the central chemoreceptors would occur earlier than those changes appearing in the spinal fluid following lumbar puncture. Capt Kronenberg further pointed out that recent work done by Severinghause and his associates on acclimatization to high altitude indicates that the most important compensatory changes in respiratory pattern are governed by the central chemoreceptors on the ventral surface of the medulla. These chemoreceptors are sensitized to changes in the hydrogen ion concentration in the spinal fluid. The importance, therefore, for determining composition of cerebrospinal fluid is underscored. To a question from Col Johnson regarding how intracranial and lumbar spine pathology would be determined on the potential subjects, Capt Kronenberg stated that a medical history and neurological examination of each subject was planned. Col Johnson suggested that it would be wise to have x-rays of the lower back taken, primarily for medical-legal protection. Further discussions with Capt Kronenberg revealed that 20 human subjects from Brooks AFB have already volunteered. This raised the question regarding the need for other kinds of volunteers as stated in the original letter requesting human subjects, specifically recruits from Lackland and Fort Sam Houston and Federal prisoners. Capt Kronenberg agreed that these sources were not necessary at this time.

f. Recommendations of the Committee: The Committee members present unanimously recommend the following to the Commander:

(1) Lower back x-rays be made on all human subjects prior to their use as subjects, primarily for medical-legal protection.

(2) Human volunteers for this protocol be limited to volunteering personnel from Brooks AFB.

(3) Approval for the use of human volunteers on the proposed research.

Irving Davis

IRVING DAVIS, Major, BSC, USAF
Recorder

Hans G. Clamann

HANS G. CLAMANN, M.D.
Chairman

APPROVED:

Harold V. Ellingson

HAROLD V. ELLINGSON, Colonel, MC, USAF
Commander, USAF School of Aerospace Medicine

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1. Cy SMBPP Ltr 21 Feb 66
2. SMBP Ltr 21 Mar 66

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DEPARTMENT OF THE AIR FORCE
USAF SCHOOL OF AEROSPACE MEDICINE (AFSC)
BROOKS AIR FORCE BASE, TEXAS 78235

SMBP 21 March 1966

Request for Human Subjects--Modification of Original Experimental Protocol

TO SMBP SMB SMG

1. Title of experiment: The prevention of altitude sickness with Acetazolamide (Diamox). Original human subject request submitted on 21 Feb 1966.

2. Methods: The original experimental protocol will be modified as follows: Each group of four subjects will be placed in the low pressure chamber one time only for a period of 24 rather than 48 hours. This 24-hour period will be spent either at ground level or 14,000 feet (447 mm. Hg). Preexperimental control runs will no longer be necessary. Approximately 2 hours prior to the conclusion of the flight, an arterial puncture will be made with the subjects at rest. Simultaneously with the arterial puncture, a lumbar puncture will be done and approximately 10 cc. of cerebral spinal fluid withdrawn. These samples will be analyzed for P_{O_2}, P_{CO_2}, pH, lactate, and standard bicarbonate. The subjects will also be asked to breathe into a CO_2 meter for analysis of their end-tidal P_{CO_2} periodically during the flight and at the time of the arterial puncture and spinal tap. Other measurements as outlined in the original protocol will remain unchanged.

3. Potential Hazards: In addition to those hazards outlined in the original protocol, certain new hazards associated with the arterial puncture and spinal tap will be incurred. The dangers of arterial puncture are principally those of hemorrhage and occlusion of the circulation. A pressure dressing will be applied for a minimum of 5 minutes following the puncture to prevent hemorrhage. Arterial occlusion is a rare complication which would require hospital treatment if it should occur. Wilford Hall USAF Hospital is available for this purpose. A carefully-done spinal tap under sterile conditions presents no serious hazard to the healthy individual. The presence of intracranial and/or lumbar spine pathology will be ascertained before the flight and will be cause for elimination of that subject. In approximately 1 - 6% of individuals a severe, incapacitating headache, lasting up to 7 days, will occur following a spinal tap. This can be uniformly relieved by having the subject lie down. It is hoped that this complication can be kept to a minimum by using a small diameter needle and keeping the subjects horizontal for a minimum of 2 hours after the tap.

4. Type of subjects needed: No change from original protocol.

5. The individuals responsible for the planning of the experiment: No change from the original protocol.

6. Responsible medical officers: William Brown, Major, MC, USAF, is to be added to the list of assisting physicians.

R. S. Kronenberg

RICHARD S. KRONENBERG, Capt, MC, USAF
Performance Physiology Section
Physiology Branch

Copy for Maj. Davis

SMBPP 21 Feb 1966

Request for Human Subjects

SMGP SMR SMO

1. Title of Experiment: The prevention of altitude sickness with Acetazolamide (Diamox), Project 7758, Task 77580103.

2. Methods: Four subjects will be placed in a low pressure chamber at 14,000 feet (447 mm.) for 48 hours without supplemental oxygen. Two of the subjects will have taken 750 mg. of acetazolamide during the 12 hours prior to entering the chamber. The other two subjects will have taken glucose as a placebo. The drugs will be administered in a double blind fashion. During the 48 hours at altitude records will be made of the subjects' EEG's and respiration rate and pattern during sleep. Twenty-four hour urines will be collected and analyzed for Na, K, Cl, creatinine, catechol amines and 17-OH steroids. The subjects may also be asked to perform various standardized treadmill exercises during which arterial blood samples would be taken. During the study the subjects will be independently observed by four physicians and ranked individually as to their state of well-being. One week prior to going to altitude, the subjects will be required to spend the night in the chamber at ground level during which time EEG and respiration will be recorded and a 24-hour urine collected. Acetazolamide or placebo will be taken the night before this control run. Three weeks after the first experimental run, a second control run will take place with the subjects getting the drug and placebo being reversed. This will be followed one week later with a second 48-hour period at altitude.

3. Potential Hazards: It is expected that the placebo treated subjects will be quite uncomfortable for the first 24 hours at altitude. This discomfort will take the form of severe headache, lethargy, breathlessness and occasionally nausea and vomiting. Rarely, people taken abruptly to high altitude will develop an acute illness resembling pulmonary edema. This will readily respond to treatment with O_2 and digitalization. In addition, hyperbaric O_2 will be available if needed.

4. Type of subjects needed: A total of 25 - 30 subjects will be needed. Each subject will be required for a total period of 6 weeks. These subjects should have the following qualifications:

a. A wide range of ages from 18 - 40.

b. Pass Class III physical examination.

c. Level of training: None required.

d. Because of the discomfort involved, they should be highly motivated and well disciplined.

e. They should be able to forego smoking for 48 hours.

The ideal subjects to fulfill these criteria would be on-base personnel. Unfortunately the experiment requires an excessive amount of time spent away from assigned duties. Moreover, the discomforts involved are well known to the base personnel from previous experiments, making it virtually impossible to get highly motivated volunteers. Therefore, it is suggested that the following sources of subjects be explored. These are listed in order of preference:

a. Recruits from Lackland Military Training Center and/or Fort Sam Houston.

b. Federal prisoners.

c. On-base personnel.

5. The individuals responsible for the planning of the experiment: Richard Kronenberg, Capt, MC, USAF, and Stephen M. Caiu, Ph.D.

6. Responsible medical officers: Dr. Kronenberg will be the supervising physician. Assisting him will be: Robert G. McIver, Major, MC, USAF, Howard G. Iger, Captain, MC, USAF, and Allan Greenwald, Captain, MC, USAF.

RICHARD S. KRONENBERG, Captain, MC, USAF
Performance Physiology Section
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