

SGRD-UE-EMT (70)

16 January 1991

MEMORANDUM THRU

Chief, Altitude Physiology and Medicine Division

Acting Chief, ~~Thermal~~ ^{Thermal} Physiology and Medicine DivisionDirector, ^{WR} ~~Environmental~~ ^{Environmental} Physiology and Medicine Division

FOR Commander, USARIEM

SUBJECT: Revisions of the protocol, "Effects of Autologous Erythrocyte Infusion in Sea-Level Residents Rapidly Transported to High Altitude," in response to recommendations by the USARIEM HURC

1. Reference memorandum, SGRD-UE-2A, subject: Report of the USARIEM Human Use Review Committee - TPMD92001-H001 and Decisions and Recommendations, HURC, 14 Jan 92 (copy enclosed)

2. I have considered the comments and recommendations provided by the USARIEM HURC after their review of the subject protocol.

3. I have revised the protocol as detailed below.

a. Both Table 2 in the protocol and the similar table in the consent form have be revised so that the experiments involving arterial catheterization are clearly indicated; there are six such tests. In addition, the table attached to the consent form has been revised so that the tests are indicated using the same wording as used to describe them in the body of the consent form.

b. The risk of experiencing a rash as a result of ingesting NaBr is now addressed in the protocol and the consent form.

c. The risk of allergic reaction to local anaesthetic has now been described in the protocol and the consent form.

d. Although the shift from supine to upright position during the upright tilt maneuver can cause a transient reduction in blood flow and oxygen delivery to the brain, sustained cerebral hypoxia due to syncope is not a hazard of the tilt test procedure. The possibility that the tilt maneuver could cause fainting was already addressed, but the fact that the cause of this is a transient reduction in blood flow and oxygen delivery to the brain is now explicitly stated in the revised protocol. The subject is secured to the tilt table with safety strap to prevent falling, and he will be closely watched for signs of fainting during the maneuver, in which case he will be immediately returned to the supine position. This information

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was contained in the original protocol. The consent form has been revised to advise the subjects to inform the investigators if they begin to feel faint.

e. The consent form has been revised to indicate that the subjects will be allowed to consume only the food and beverages provided by the dieticians during the dietary control periods. It is not entirely clear what the committee meant about a "lock-down." At this time, it is anticipated that the subjects will generally be free to come and go between the laboratory and billeting site as they wish, in accordance with the test schedule requirements and restrictions. The dieticians will serve meals in some central location, yet to be determined. If more restrictive measures are deemed necessary to enforce compliance to the restrictions of the dietary control period, an addendum will be submitted.

f. The consent form has been revised to clarify that the total radiation dosage due to the three blood volume determinations is less than that in a single chest x-ray. Information concerning the clinical use of these procedures does not seem relevant to the experimental use of the procedures; given the length of the consent form as it stands, these details have been omitted.

g. Additional paragraph breaks in the "HAZARDS" section would disrupt the organization of the section without really improving the comprehensibility. Rather, the various adverse outcomes have, at the suggestion of the Chairman, HURC, been highlighted by bolding.

h. The number of venipunctures, arterial catheterizations, and finger pricks have been explicitly stated in the revised consent form, as has been the total amount of blood to be drawn.

i. The consent form has been revised to replace with lay language those terms identified by the HURC as too technical, and to improve the consistency between the wording between the table and the body of the consent form. Also, with one exception, the various minor rewordings specified by the HURC have been incorporated. The HURC suggested describing the amount of CO₂ to be inspired during the hypercapnic sensitivity test relative the amount of CO₂ in expired air rather than inspired air. I don't agree that this is more understandable by the average subject; most people have no appreciation for how much CO₂ they expire, but clearly understand that they normally inspire very little of it. Therefore we feel that saying that the test requires them to

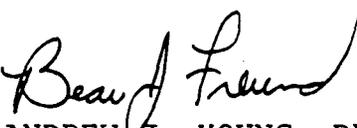
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breath gas containing more than the normal amount of CO₂ is clear.

4. I have reservations with regard to the HURC's directive that I: a) furnish the commanders of the volunteers with copies of AR 70-25, b) brief them on the implications of that and related regulations concerning informed voluntary consent and potential human research subjects, and c) provide written guarantees to HURC that I will comply with this directive. First of all, which level of command is the focus of attention: team, brigade, group? Furthermore, if test subjects are recruited from a variety of different units or military posts, this requirement could be burdensome to meet; certainly if TDY or permanent party soldiers from Natick are recruited, the requirement is not necessary. We appreciate the committee's concern that if Special Forces soldiers are used as subjects, the SOCOM or local SF Headquarters may want the volunteers to come from intact units or teams. If indeed this is the case, team members might be subjected to undo command pressure to volunteer so as to keep the team together. If indeed such a situation appears to be developing, the principle investigator will take all necessary steps to ensure that potential volunteers are not pressured to volunteer, and that only truly consenting volunteers participate as subjects. This, of course, is always the responsibility of the principle investigator, regardless of the type of soldiers serving as research subjects, and I have always met that responsibility in conducting my research.

Encls

for 
ANDREW J. YOUNG, Ph.D.
Research Physiologist

SGRD-UE-ZA (70-1n)

14 January 1992

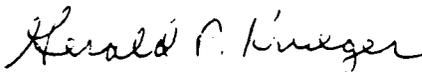
MEMORANDUM THRU Chief, EMT

FOR Dr. A.J. Young

SUBJECT: Report of the USARIEM Human Use Review Committee -
TPMD92001-AP001-H001

1. The USARIEM Human Use Review Committee has reviewed and recommended approval of subject protocol. The decisions and recommendations of the Committee are enclosed.
2. The Committee recommended approval of this study on condition that the points mentioned be appropriately modified or corrected. Following receipt of your revised protocol, I will forward it to the Human Use Office at our Headquarters for their review and determination of final disposition.

Encl


GERALD P. KRUEGER
Colonel, MS
Commanding

CF:
Chrmn, HURC

HUMAN USE REVIEW COMMITTEE
14 January 92
DECISIONS AND RECOMMENDATIONS

TMPD92001-AP001-H001, "Effects of autologous erythrocyte infusion in sea-level residents rapidly transported to high altitude", Dr. A. J. Young, Principal Investigator.

1. The USARIEM Human Use Review Committee reviewed your proposed study at its meeting of 8,9 January 1992, and voted unanimously:

a. to support your request for a waiver of the Type Protocol's upper limit on heart rate of 210/min;

b. to authorize a recommendation of approval to remove two units of blood from up to 24 subjects (but this does not include approval to complete testing of more than 18 subjects), provided that the consent form is revised to state that not all subjects bled will necessarily be tested, and explain why not, and say how they will be used if they are not tested;

c. to direct that copies of the revised Volunteer Agreement Affidavit, on its receipt, be distributed to the Committee for approval; and

d. to recommend approval of your proposed study pending submission to, and approval by, the Commander, USARIEM, of a revised protocol and Volunteer Agreement Affidavit attending to the directives in paragraph 2 and 3, below, and the Committee's approval of the revised Volunteer Agreement Affidavit.

2. The protocol and Volunteer Agreement Affidavit should be revised as follows:

a. Table 2, and the similar table attached to the consent form, should indicate each time that arterial catheterization is to be done.

b. The risks of rash due to NaBr, allergic reaction to local anesthetic, and cerebral hypoxia in the event of syncope during the orthostatic tests should be added to the section "HEALTH HAZARD AND SAFETY CONSIDERATIONS", beginning on p. 41, and the first two should be added to the consent form.

c. The consent form should be revised as follows:

(1) A number of technical terms (e.g., "infused" on p. 2, line 24, "inspired" on p. 8, line 2, and "infusion", "hypoxic", and "hypercapnic" in the table) should be replaced with lay language. Moreover, you should make sure that wording in the table matches that in the text of the consent form.

(2) On p. 2, line 5 of the 2nd paragraph, "relative" should be inserted before "lack", since there is only a relative lack of oxygen at these altitudes.

(3) Since the Red Cross also takes special precautions to be sure that donated blood is labelled properly, it would be better to replace "except that special" with some such words as "and stringent" on p. 3, lines 3 and 4.

(4) In the section "% BODY FAT MEASUREMENT", the next to last sentence should be changed so as not to be misinterpreted to mean that the subject needs to hold his breath only once. This paragraph should say also about how many breath holds will be needed, and how long each breath hold will be.

(5) On p. 4, line 22 "sample" should be inserted after "blood". The consent form should say which artery will be catheterized, and where the catheter will be inserted.

(6) The sentence beginning on p. 5, line 2 should be changed to read "These tests will be separated..."

(7) If during any of the DIETARY CONTROL PERIODS subjects will be confined to quarters or some other restricted area, or if subjects will need to carry urine collection vessels around with them, the consent form needs to say so. Also, in the first line of that section, "fours" seems to be a misprint for "four days", and should be corrected.

(8) In the section "BLOOD VOLUME MEASUREMENTS", it might help subjects to understand better the time course of the elimination of the radiation, if the investigators were to add that therefore 99% will be gone in 7-14 months. Also, it might allay any misgivings of the subjects about taking radioisotopes internally, if the consent form were to state clearly that the total radiation that they will absorb, up to the time that it is all gone, is less than one chest x-ray. Furthermore, the text should be clear as to whether it is one determination, or all determinations in the study, that involve less radiation than one chest x-ray. This section should also say that these isotope dilution procedures are used clinically, and state briefly how.

(9) The section "HAZARDS" should be broken up with more sub-headings and, probably, more paragraph breaks. The problem with the section as it stands is that it seems to invite the reader to skim, and thus pay scant attention to some of the hazards that are "buried" in the section.

(10) On the 7th line from the bottom of p. 7, such words as "to minimize the risk of infection" should be inserted, so as to indicate that sterile procedures are not a guarantee against infection.

(11) Since room air contains such tiny amounts of CO₂, the description on lines 6 and 7 of p. 8 is not very meaningful. It might be better to compare the concentrations to those in exhaled air.

(12) "buildings" on p. 8, line 22 looks as if it should be possessive; if so, it should be corrected.

(13) The word "some" on p. 8, line 32 suggests a misleadingly low incidence of mountain sickness, and should be changed—e.g., to "many". Since subjects are volunteers, there is nothing in the study that they must do. Therefore that word on line 16 should be replaced with something milder, such as "may need to". The approximate incidences of pulmonary and cerebral edema, which are mentioned on lines 38 and 39, in USARIEM's experience on Pikes Peak should be given.

(14) Since risks associated with arterial puncture are greater than those with venepuncture, those risks need to be addressed in the consent form.

(15) The word "befor" on the last line of p. 8 needs a final e.

(16) Breathe as a verb requires a final e, but almost without exception it is spelled like the noun, breath, in the consent form. This should be corrected.

(17) The consent form should have a summary statement giving the total number of finger pricks and venepunctures (arterial punctures having been added to the table), and the approximate total volume of blood that will be taken.

(18) The consent form should say somewhere that subjects will breathe 100% O₂ at some points in the study.

(19) Words to the effect of "without penalty" should be inserted at the end of the very last sentence.

3. Before the subject briefing, you should furnish the prospective subjects' commanding officer with a copy of AR 70-25, and be sure that he understands the nature of, and legal necessity for, voluntary consent; and you should state that you will do so in your memorandum replying to these directives.

4. All testing procedures and safety restrictions conform to the USARIEM Type Protocol, with the following exceptions: (a) autologous erythrocyte reinfusion; (b) measurement of erythrocyte volume by dilution of ⁵¹Cr and plasma volume by dilution of ¹²⁵I; (c) the upright tilt maneuver; and (d) the investigators' request for a waiver of the absolute upper limit of 210/min on heart rate during determination of \dot{V}_{O_2max} .

5. This study is judged to involve more than minimal risk to the participating subjects.

A handwritten signature in black ink, appearing to read "C. Bruce Wenger". The signature is fluid and cursive, with a large, sweeping flourish at the end.

C. BRUCE WENGER, MD, PhD
Chairman, USARIEM HURC