DISPOSITION FORM

For use of this form, see AR 340-15; the proponent agency is TAGO.

REFERENCE OR OFFICE SYMBOL	SUBJECT
SGRD-UE-MEP	Addendum to Protocol (HURC #276)

TO Dir, Mil Div

FROM C, Physiol Br, ME Div DATE 22 Sep 87 CMT

TO Commander, USARIEM /phd/5141

1. DF, SGRD-UE-MEP, 10 Sep 87, Subject: Consent Form for Methodology Testing (ME-1-87) and CMT 2, SGRD-UEZ, 17 Sep 87 (Encl 1).

2. The approved protocol, "Interaction of Aerobic Fitness and the Hypohydration Response During Exercise-Heat Stress," requires that total body water measurements be performed by determining the volume of distribution of intragastric ethanol. Our preliminary testing indicates that the total body water values obtained by this method are inconsistent and not suitable for our research purposes.

3. The inconsistent total body water measurements may be due to inadequate or prolonged absorbtion of alcohol from the gut region. As a result, the intravenous infusion of ethanol (by a physician) may represent a more accurate and reliable method of determining its volume of distribution and therefore total body water.

4. I would like to amend the protocol, HURC #276 to include the venous infusion of ethanol to measure total body water according to the methods of Wilkinson et al. (see reprint, Encl 2). Ethanol, suitable for intravenous use, will be injected into sterile saline bags to elicit an 8% V/V ethanol solution. The sterile solutions will be administered at a rate of ~6 ml/min by continuous intravenous infusion. Each subject will be infused until 0.35 g of ethanol per kg of body weight has been administered or for ~1 h. Blood samples will be periodically drawn from an indwelling catheter both during and following the infusion for the subsequent determination of blood ethanol concentration.

5. Enclosed is a new Human Test Volunteer Agreement to reflect the measurement of total body water by the venous infusion of ethanol (Encl 3).

6. Actually, before this methodology is employed as a part of HURC #276, it will be evaluated to insure that satisfactory resolution can be obtained for total body water measurements. However, this addendum is required (see DF, 10 Sep 87, Encl 1) prior to this methodology evaluation.

Michael N. Sawka

3 Encl
as

MICHAEL N. SAWKA, Ph.D.
Chief, Physiology Branch

DISPOSITION FORM

For use of this form, see AR 340-15, the proponent agency is TAGO.

REFERENCE OR OFFICE SYMBOL	SUBJECT
SGRD-UE-MEP	Consent Form for Methodology Testing (ME-1-87)

TO ~~THRU C, Physiol Br~~ ~~Dir, Mil Erg Div~~ FROM P. Darrell Neufer, Physiol Br, Mil Erg Div DATE 10 Sep 87 CMT 1 /phd/4834

TO ~~Commander, USARIEM~~

The determination of total body water is critical for an upcoming scheduled study, "Interaction of aerobic fitness and the hypohydration response during exercise-heat stress," ME-1-87. However, preliminary testing of the volume of distribution of intragastric ethanol as a measure of total body water has given inconsistent results, unsuitable for research purposes. In addition, estimation of body water following intragastric administration of ethanol has been shown to overestimate the total body water in anesthetized dogs due to a delayed gastrointestinal absorption. In view of these findings, we would like to evaluate the technique of infusing ethanol for the determination of total body water according to the methods of Wilkinson et al.*(ref. below). This work does not represent a pilot study. We wish only to evaluate this methodology in preparation for the protocol mentioned above.

Encl

P. DARRELL NEUFER
Research Physiologist

*Wilkinson, P.K., A.J. Sedman, E. Sakmar, R.H. Earhart, D.J. Weidler and J.G. Wagner. Blood ethanol concentrations during and following constant-rate intravenous infusion of alcohol. Clin. Pharmacol. Ther. 19:213-223, 1976.

SGRD-UEZ(SGRD-UE-MEP, dtd 10 Sept 87)

THRU ~~Dir, Mil Erg Div~~
TO C, Physiol Br FROM Commander DATE 17 September 1987 CMT 2 /atw/4811

1. No pretesting of this methodology may be conducted without human use approval. Please resubmit as an amendment to the protocol with a revised consent form. I will refer the request to the USARIEM HURC for review and determination of level of risk, because your request does involve an invasive procedure. If judged to be more than minimal risk, I will have to refer the matter to the OTSG HURO for final approval.

2. Upon approval, if you desire to pretest the method with additional volunteer subjects, you will need to submit a request for a pilot study which I will most likely be able to approve locally.

3. Please advise if there has been a change in Primary Investigator for this protocol.

DAVID D. SCHNAKENBERG
Colonel, MS
Commanding

CF: Dr. Knuttgen

VOLUNTEER AGREEMENT AFFIDAVIT

For use of this form, see AR 40-38; the proponent agency is the Office of the Surgeon General

THIS FORM IS AFFECTED BY THE PRIVACY ACT OF 1974

1. **AUTHORITY:** 10 USC 3012, 44 USC 3101 and 10 USC 1071-1087.

2. **PRINCIPAL PURPOSE:** To document voluntary participation in the Clinical Investigation and Research Program. SSN and home address will be used for identification and locating purposes.

3. **ROUTINE USES:** The SSN and home address will be used for identification and locating purposes. Information derived from the study will be used to document the study; implementation of medical programs; teaching; adjudication of claims; and for the mandatory reporting of medical condition as required by law. Information may be furnished to Federal, State and local agencies.

4. **MANDATORY OR VOLUNTARY DISCLOSURE:** The furnishing of SSN and home address is mandatory and necessary to provide identification and to contact you if future information indicates that your health may be adversely affected. Failure to provide the information may preclude your voluntary participation in this investigational study.

PART A - VOLUNTEER AFFIDAVIT

VOLUNTEER SUBJECTS IN APPROVED DEPARTMENT OF THE ARMY RESEARCH STUDIES

Volunteers under the provisions of AR 70-25 are authorized all necessary medical care for injury or disease which is the proximate result of their participation in such studies.

I, _____ (last, first, middle) SSN _____ having full capacity to consent and having attained my _____ birthday, do hereby volunteer to participate in

Interaction of Aerobic Fitness and the Hypohydration Response During Exercise-Heat Stress
(research study)

under direction of Michael N. Sawka, Ph.D. (617) 651-5141 conducted at US Army Research Institute of Environmental Medicine, Natick, MA
(name of institution)

The implications of my voluntary participation; the nature, duration and purpose of the research study; the methods and means by which it is to be conducted; and the inconveniences and hazards that may reasonably be expected have been explained to me by

Dr. Michael N. Sawka

I have been given an opportunity to ask questions concerning this investigational study. Any such questions were answered to my full and complete satisfaction. Should any further questions arise concerning my rights on study-related injury I may contact

Office of the Chief Counsel (617) 651-4322

at US Army Natick Research, Development and Engineering Center, Natick, MA
(name and address of hospital & phone number (include area code))

I understand that I may at any time during the course of this study revoke my consent and withdraw from the study without further penalty or loss of benefits however, I may be ☐ required (military volunteer) or ☐ requested (civilian volunteer) to undergo certain examination if, in the opinion of the attending physician, such examinations are necessary for my health and well-being. My refusal to participate will involve no penalty or loss of benefits to which I am otherwise entitled.

PART B - TO BE COMPLETED BY INVESTIGATOR

INSTRUCTIONS FOR ELEMENTS OF INFORMED CONSENT: (Provide a detailed explanation in accordance with Appendix E, AR 40-38 or AR 70-25.)

See Reverse.

Encl 3

(CONTINUE ON REVERSE)

This study will examine the effect of physical fitness on your ability to exercise in the heat when dehydrated. We wish to determine if high levels of physical fitness will enable dehydrated individuals to perform more exercise and at a lower body temperatures than their less fit counterparts. This study will be conducted at USARIEM and USANRDEC facilities located in Natick, MA, and at the Naval Blood Research Laboratory in Boston, MA.

Prior to experimental testing, your physical fitness and percent body fat will be determined as well as your energy cost to walk (3.5 or 4.5 mph) on a treadmill. You will then complete a 4 to 10 day heat acclimation program. For this you will attempt daily 2-h walks (3.5 or 4.5 mph, 2% treadmill grade) in a hot-dry (120°F, 20% rh) environment. After completing the heat acclimation program, your total body water will be measured on one day, and the volume of water in your blood will be measured on another day. You will then attempt four Heat Stress Tests during the next two weeks. You will also complete several additional heat acclimation sessions between the Heat Stress Tests. The tests and procedures are described below.

% Body Fat. To estimate your body fat, you will be weighed on a scale underwater while you hold your breath. The gas in your lungs will be measured by having you breathe oxygen through a snorkel-like apparatus. This procedure takes about 45 minutes.

Maximal Effort Exercise. You will first practice walking and running on a treadmill. For the maximal effort exercise test, you will run on the treadmill and the treadmill grade will be increased (by 2 1/2%) at 1.5-minute intervals until you can no longer continue. This test takes about 30 to 90 minutes.

Total Body Water: Alcohol (ethanol), suitable for intravenous use, will be injected into sterile salt water (saline solution) and infused slowly into an arm vein. You will receive ~0.35 grams of ethanol per kilogram of body weight (e.g., if you weigh 150 lbs. you will receive 0.84 ounces of alcohol) over approximately 1 hour. Venous blood samples will be obtained from your arm over the next three hours while you are seated. This test takes about four to five hours.

Blood Volume Measurement. This test will be performed at the Naval Blood Research Laboratory in Boston. A small sample of blood (less than one ounce) will be taken from your arm vein. Radioactive material will be added, and then it will be reinjected into your arm. You will receive a very small amount of radioactive material. Small samples of blood will then be taken at intervals during the next several hours. This test will take about three hours.

Heat Stress Tests. You will be asked to limit your food and fluid intake for about two days before the two dehydration Heat Stress Tests. The day before each Heat Stress Test, you will report at 1200 h. You will first be weighed, then you will enter a Climatic Chamber, which will be 104°F (20% humidity). In the chamber, you will rest and exercise so that you sweat. If this is the day before a normal hydration Heat Stress Test, you will be given water to fully replace your sweat. If this is the day before a dehydration Heat Stress Test, you will not be given water. Once you have lost the desired body weight, you will go to a comfortable room and remain there until the

SIGNATURE OF VOLUNTEER	DATE SIGNED	SIGNATURE OF LEGAL GUARDIAN (If volunteer is a minor)
PERMANENT ADDRESS OF VOLUNTEER	TYPED OR PRINTED NAME AND SIGNATURE OF WITNESS	DATE SIGNED

next morning. During the night and next morning, you will be allowed to eat fresh fruit, but only in the amount that your weight allows. In the morning you will enter the chamber for the the Heat Stress Test. It will be 120°F (20% Humidity). You will try to walk for three hours at a moderate exercise intensity. You will attempt four Heat Stress Tests; two with normal body water levels, two when dehydrated by 8% of your total body water. An 8% reduction in total body water will correspond to a 4% to 6% reduction of your body weight. These tests will be separated by at least 2 days.

During all exercise tests, you will wear shorts and tennis shoes. You will have several electrodes taped to your chest so that we can monitor your heart rate. During the Heat Stress Tests, we will measure your skin and rectal temperatures. Also, your rectal temperature will be measured during the acclimation sessions. The rectal thermometers are flexible probes which may be somewhat unpleasant to insert the first time, but are not harmful. During the Heat Stress Tests (and total body water measurements) you will have a sterile plastic catheter in your arm vein so that we can take blood samples. A total of ~3 ounces of blood will be obtained for each Heat Stress Test.

Potential Risks and Hazards

The primary risks of participating in this study are those associated with (a) physical exercise, (b) hyperthermia, (c) hypohydration and (d) venous catheterization, and the additional risks of the combinations of these. The stress of exercise, and especially maximal effort, increases the potential for uncovering and/or aggravating pre-existing cardiac problems, notably ischemia, conduction defects and ectopic beats. Therefore, the electrocardiogram will be displayed on an oscilloscope and periodically monitored. Muscle soreness, cramps, nausea and general fatigue may also result from exercise; this pain and discomfort is temporary and not deemed harmful. Misjudgement or accident (i.e., falling on treadmill) can result in bodily injury during physical exercise. The risk of this is probably less during the supervised activities used in a study than in unsupervised exercise, free play or competitive sports. Also, breathing in water is a risk associated with the underwater weighing procedure.

High body temperatures are expected in the acclimation sessions and Heat Stress Tests; so both skin temperature and rectal temperature will be closely monitored. During the Heat Stress Tests, you will be weighed every 50 min and provided water to maintain the desired hydration level. Also, a schedule for programmed drinking will be used during the exercise bouts as well as after the Heat Stress Tests. Testing will be discontinued, and you will be removed to a cool environment should your rectal temperature exceed 104.0°F, if the rate of temperature increase exceeds 1.1°F in five minutes or if your heart rate exceeds 180 beats per minute for 10 consecutive minutes. For this study the core temperature end-point criterion has been extended from 103 to 104°F on a case-by-case basis. However, the medical monitor will pay particular attention to this physiological variable during the Heat Stress Tests. Even if the above limit has not been reached, symptoms and signs of impending heat illness, such as confusion, coordination difficulties, excessive breathing and/or faintness will result in discontinuation of testing and your removal to a cool environment. Testing will also be terminated if the medical monitor so requests. During all testing, a staff

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member will be stationed near you to observe and assist you should the need arise. Testing will be discontinued if you show any signs of unusual distress during the work. It is recognized that overexposure to heat may led to heat injury, "heat exhaustion", or "heat stroke". However, under this protocol safeguard tolerance limits are placed on responses to provide a margin of safety and reduce the risk to your health.

Within the past four years, we have conducted approximately 120 exercise-heat experiments on subjects dehydrated and experienced no serious adverse physical effects. The primary risk of hypohydration is that of the subsequent high body temperature during exercise-heat stress, and these risks have been discussed.

Needle punctures and catheterization of veins in the extremities will be performed by skilled technicians with sterile techniques. These procedures involve extremely little risk of any injury beyond possible bruising and temporary discomfort. Blood volume measurements with the labelled radioactive chromium and albumin methods are performed routinely in the United States, and the low level of radiation is associated with no known risks.

There are no known health risks associated with small, dilute amounts of ethanol. The ethanol has the risk of short-term intoxication; however, this feeling will subside before you are released. There is always a risk of infusates inadvertently becoming contaminated. However, pathogen free ethanol suitable for intravenous infusion and sterile saline will be used to make up solutions. It is also possible that infusion of an alcohol solution may result in some irritation around the needle site.

The benefits of this study to you are only indirect. You will be able to find out your percent body fat and physical fitness level. Both of these measurements are of value to individuals interested in assessing the state of their physical conditioning program. All data and medical information obtained about you as an individual will be considered privileged and held in confidence; you will not be identified in any presentation of the results. Complete confidentiality cannot be promised, particularly to subjects who are military personnel because information bearing on your health may be required to be reported to appropriate medical or command authorities, and applicable regulations note "the possibility that the Food and Drug Administration and U.S. Army Medical Research and Development Command officials may inspect the records".

This study requires a considerable time and energy commitment from you. Please take your commitment seriously and plan to complete all testing if you volunteer. However, you are free at any time to withdraw from the study without prejudice.

SIGNATURE OF VOLUNTEER	DATE SIGNED	SIGNATURE OF LEGAL GUARDIAN (If volunteer is a minor)
PERMANENT ADDRESS OF VOLUNTEER	TYPED OR PRINTED NAME AND SIGNATURE OF WITNESS	DATE SIGNED