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REPORT NO T10-92

VALIDATION OF TWO TEMPERATURE
PILL TELEMETRY SYSTEMS IN HUMANS DURING
MODERATE AND STRENUOUS EXERCISE

October 1992

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REPORT DOCUMENTATION PAGE			Form Approved OMB No. 0704-0188	
Public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington, VA 22202-4302, and to the Office of Management and Budget, Paperwork Reduction Project (0704-0188), Washington, DC 20503.				
1. AGENCY USE ONLY (Leave blank)	2. REPORT DATE October 1992	3. REPORT TYPE AND DATES COVERED Technical Report		
4. TITLE AND SUBTITLE Validation of Two Temperature Pill Telemetry Systems in Humans during Moderate and Strenuous Exercise		5. FUNDING NUMBERS		
6. AUTHOR(S) Lou A. Stephenson, Mark D. Quigley, Laurie A. Blanchard, Deborah A. Toyota and Margaret A. Kolka				
7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) US Army Research Institute of Environmental Medicine Kansas Street Natick, MA 01760-5007		8. PERFORMING ORGANIZATION REPORT NUMBER		
9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES) Same as Block 7.		10. SPONSORING/MONITORING AGENCY REPORT NUMBER		
11. SUPPLEMENTARY NOTES				
12a. DISTRIBUTION/AVAILABILITY STATEMENT Approved for public release; distribution is unlimited.		12b. DISTRIBUTION CODE		
13. ABSTRACT (Maximum 200 words) This study examined how two core temperature telemetry pill systems (Konigsberg Instruments, KI (T_{ki}) and Human Technologies, HTI (T_{hi})) compared to esophageal temperature (T_{es}) and rectal temperature (T_{re}) during exercise/rest cycles. T_{es} (17.8 ± 8.1 min), T_{ki} (17.8 ± 8.4 min) and T_{hi} (22.5 ± 9.9 min) were at steady state faster during moderate exercise ($p \leq 0.001$) than T_{re} (35.7 ± 5.3 min). The change in core temperature per time (slope) was greater for T_{es} ($0.073 \pm 0.037^\circ\text{C} \cdot \text{min}^{-1}$) than T_{ki} ($0.039 \pm 0.023^\circ\text{C} \cdot \text{min}^{-1}$) and T_{hi} ($0.018 \pm 0.005^\circ\text{C} \cdot \text{min}^{-1}$) and T_{re} ($0.049 \pm 0.029^\circ\text{C} \cdot \text{min}^{-1}$) was greater than T_{es}. The total change in core temperature was larger ($p \leq 0.01$) for T_{es} ($0.93 \pm 0.21^\circ\text{C}$) and T_{hi} ($0.90 \pm 0.24^\circ\text{C}$) than T_{ki} ($0.63 \pm 0.25^\circ\text{C}$). The change in T_{ki} was not different from T_{re} ($0.76 \pm 0.25^\circ\text{C}$). T_{ki} did not respond as fast as T_{es} and did not measure large changes in core temperature like T_{es} or T_{hi}. T_{hi} was more responsive than T_{re} and T_{ki} responded like T_{re}. The concept of using a temperature sensor in a pill as a clinical thermometer is good, but mobility of the pill makes it less suitable as a research tool than esophageal or rectal temperature measurements.				
14. SUBJECT TERMS Temperature Regulation; Telemetry; Exercise		15. NUMBER OF PAGES 76		
		16. PRICE CODE F36		
17. SECURITY CLASSIFICATION OF REPORT Unclassified	18. SECURITY CLASSIFICATION OF THIS PAGE Unclassified	19. SECURITY CLASSIFICATION OF ABSTRACT Unclassified	20. LIMITATION OF ABSTRACT	

TECHNICAL REPORT

NO. T10-92

**VALIDATION OF TWO TEMPERATURE PILL TELEMETRY SYSTEMS IN HUMANS
DURING MODERATE AND STRENUOUS EXERCISE**

by

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October 1992

U.S. Army Research Institute of Environmental Medicine
Natick, Massachusetts 01760-5007

DTIC QUALITY INSPECTED 2

Acquisition For	
DTIC 02/91	☒
DTIC 143	☐
(Unannounced)	☐
Justification	
By	
Distribution/	
Availability Codes	
Dist	Avail and/or Special
A-1	

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FOREWORD

The Joint Working Group of the Physiological and Psychological Effects of the NBC Environment and Sustained Operations on Systems in Combat (P²NBC²) identified a need for a temperature telemetry system which accurately measured core temperature in soldiers involved in P²NBC² studies in the field. The temperature telemetry system had to be precise enough to be used as a clinical index of core temperature to reduce the risk of heat injury in volunteers participating in field studies. In order to routinely use temperature telemetry during field tests, the telemetry systems used were compared with esophageal and rectal temperature in a laboratory test described in this report. Two telemetry systems were tested; one made through a collaborative effort of Walter Reed Army Institute of Research (WRAIR) and P²NBC² based on a contract with the developer, Konigsberg Instruments, Inc. (Pasadena, CA), and the other made by Human Technologies, Inc. (CorTemp™; St. Petersburg, FL). Both systems included an ingestible temperature sensor/pill, a receiver, and a data storage system. Each system was expected to reliably measure and store core temperature data from individual soldiers involved in lengthy field studies.

ACKNOWLEDGEMENTS

The authors are indebted to the volunteers who performed in these experiments. We gratefully acknowledge the technical support provided by Ms. P. Burgoon, Mr. B. Cadarette, Ms. L. Levine, SGT W. Latzka, Ms. D. Cohen, Ms. A. Tarentino, and Ms. G. Carrubba. We also thank the medical monitors, CPT J. Cook, MAJ M. Reardon and LTC W. Curtis.

Both temperature telemetry systems were supplied by COL Redmond, Chief, Special Studies Branch, Department of Behavioral Psychology, WRAIR, in support of the funding agency, P²NBC². COL Redmond also advised us in the use of the telemetry systems, in particular the KI system, as did MAJ J. Leu and SSG F. Gutierrez (Special Studies Branch, WRAIR). We also thank SSG Gutierrez for quickly providing USARIEM with additional supplies as needed during the study.

Funding for this study was provided, in part, by the Joint Working Group of the Physiological and Psychological Effects of the NBC Environment and Sustained Operations on Systems in Combat (P²NBC²) program of the U.S. Army Chemical School.

EXECUTIVE SUMMARY

This study examined how two core temperature telemetry pill systems (Königsberg Instruments, KI (T_{ki}) and Human Technologies, HTI (T_{hi})) compared to esophageal temperature (T_{es}) and rectal temperature (T_{re}) during exercise/rest cycles. Two hours after swallowing both pills, eight volunteers exercised on a cycle ergometer ($T_a=29^\circ\text{C}$, $T_{re}=11^\circ\text{C}$) for 40 min at 40% peak $\dot{V}O_2$, rested 15 min, then completed 3 cycles of 5 min of exercise at 80% peak $\dot{V}O_2$ and 5 min of rest. T_{es} , T_{re} , T_{ki} and T_{hi} were recorded every 30 s. T_{es} (17.8 ± 8.1 min), T_{re} (17.8 ± 8.4 min) and T_{hi} (22.5 ± 9.9 min) were judged to be at steady state faster during moderate exercise ($p\leq 0.001$) than T_{ki} (35.7 ± 5.3 min). The change in T_{es} with change in activity (rest/exercise/recovery) was significantly less than the change in T_{re} , T_{ki} and T_{hi} ($p\leq 0.001$). However, the mean change in core temperature during steady-state moderate exercise was not significantly different ($p=0.12$) among the four core temperature indices. The change in core temperature per time (slope) was greater for T_{es} ($0.073\pm 0.037^\circ\text{C}\cdot\text{min}^{-1}$) than T_{re} ($0.039\pm 0.023^\circ\text{C}\cdot\text{min}^{-1}$) and T_{ki} ($0.018\pm 0.005^\circ\text{C}\cdot\text{min}^{-1}$). In addition, this slope was greater for T_{hi} ($0.049\pm 0.029^\circ\text{C}\cdot\text{min}^{-1}$) than T_{re} . However, the T_{hi} slopes were not different from T_{es} slopes. The total change in core temperature (peak - rest) was larger ($p\leq 0.01$) for T_{es} ($0.93\pm 0.21^\circ\text{C}$) and T_{hi} ($0.90\pm 0.24^\circ\text{C}$) than T_{re} ($0.63\pm 0.25^\circ\text{C}$). The change in T_{re} was not different from T_{ki} ($0.76\pm 0.25^\circ\text{C}$). The majority of the T_{re} data indicates that it does not respond as fast as T_{es} , but responds just as quickly as T_{hi} . T_{re} during a 1.0°C change in core temperature lagged by nearly 0.4°C . Therefore, T_{re} did not measure large changes in core temperature as effectively as T_{es} or T_{hi} . The HTI pill detected the total change in core temperature better than the KI pill ($p\leq 0.01$). Overall, T_{hi} tracked dynamic changes in core temperature significantly faster than T_{re} , although T_{hi} did not track dynamic changes as well or as consistently as T_{es} . T_{hi} was an effective index of the total change in core temperature ($\sim 1^\circ\text{C}$) during the experiment. T_{hi} was a more responsive index of core temperature than T_{re} , and T_{re} responded like T_{ki} . Finally, T_{es} tracked core temperature more quickly than the telemetry pills did, and T_{re} and T_{ki} showed a faster response to changing core temperature than did T_{hi} . The concept of using a temperature sensor in a pill may be useful clinically, but mobility of the pill makes this temperature measurement less suitable for research than esophageal or rectal temperature measurements.

INTRODUCTION

Thermoregulatory strain occurs in soldiers during field and laboratory tests of military equipment and systems. In laboratory tests, either rectal or esophageal temperature of the volunteers is monitored to ensure that internal body temperature (core temperature) does not exceed safe clinical limits. Each of these core temperature indices is reproducible and not biased by environmental temperature (2,8,14); however, the slow response time of rectal temperature is well known (7,8,11,15,16). Esophageal temperature measurements are not used in the field, but are routinely used in laboratory tests which are concerned with the study of thermoregulation. Rectal temperature measurements are used as a index of core temperature in the field and in some types of laboratory studies of exercise and heat stress responses. In the field, it is not always practical to monitor core temperature because volunteers reject the use of rectal probes as a clinical thermometer or the current portable system requires that a medical observer be close to the volunteer at all times. This methodology interferes with field exercises and requires large numbers of medical observers. For example, a medical observer would effectively disrupt the military mission of a tank crew while he monitors the core temperature of each crew member. A solution to monitoring core temperature during field exercises would be to monitor core temperature at an accepted internal site and to transmit the core temperature responses some distance from the body using telemetry. In this way, the medical observer could communicate to the crew or individual when core temperature limits have been exceeded. Alternatively, the individual could carry a temperature telemetry data logger that contained an alarm which would be activated if a core temperature safety limit were exceeded during the field exercise.

STATEMENT OF PURPOSE

The purpose of this study was to compare how well two different temperature telemetry systems tracked rapid and absolute changes in core temperature compared with esophageal and rectal temperatures during exercise. The temperature telemetry systems tested were 1) a prototype using the ingestible temperature sensor/transmitter developed by Konigsberg Instruments, Inc. (Pasadena, CA) under the supervision of COL Redmond, WRAIR [as part of the Chemical Defense User Safety System

(CDUSS; 19), the Biomedical Safety Monitoring System (BSMS; 19) and the Biomedical Field Monitoring System (BFMS; 18)], and 2) the CorTemp™ ingestible temperature sensor and data logger (HTI; Human Technologies, Inc., St. Petersburg, FL). Specific questions investigated were:

1. Are rapid changes in core temperature measured as accurately by the temperature telemetry systems as they are by esophageal temperature?
2. How does core temperature measured by the temperature telemetry systems compare to rectal temperature during rapid changes in core temperature?
3. How effectively do the temperature telemetry systems measure absolute changes in core temperature?

Esophageal measurements were included as the "gold standard" for comparison purposes. Rectal temperature measurements were included because they are often used as the core temperature index for field studies. It was hoped that the temperature telemetry pills would be as reproducible as esophageal and rectal temperature measurements, but could also demonstrate faster responses than rectal temperature measurements.

BACKGROUND

The Joint Working Group of the Physiological and Psychological Effects of the NBC Environment and Sustained Operations on Systems in Combat (P²NBC²) identified a need for the development of a temperature telemetry system which accurately measured core temperature in soldiers involved in P²NBC² studies in the field. The development of radio telemetry systems which measure body temperature has been outlined recently by Redmond *et al.* (19). Mackay, who was involved in the development of radio telemetry of physiological data, described the principles of that technology in detail (13). In an attempt to validate temperature telemetry, which has been routinely used during field tests, those telemetry systems were compared to esophageal and rectal temperature measurements in a laboratory test. The first system was designed to operate from within armored vehicles and over considerable

distance [this system (KI) was developed through a collaborative effort of Walter Reed Army Institute of Research (WRAIR) and P²NBC² (12, 19) by Konigsberg Instruments, Inc.]. The second telemetry system tested was a commercially available system marketed by Human Technologies, Inc. (CorTempTM; St. Petersburg, FL) developed at the Applied Physics Laboratory of Johns Hopkins University. Both systems included an ingestible temperature sensor/pill, a receiver, and a data storage system and were expected to reliably measure and store core temperature data from individual soldiers involved in field studies.

Before telemetry systems for monitoring core temperature can be judged as an appropriate replacement for other indices of core temperature, they must be compared to those measures of core temperature which are currently accepted as accurate by thermal physiologists and clinicians. Brengelmann (2) reviewed the criteria required for an accurate and reliable measure of core temperature as cited by earlier investigators (7, 8, 20). The measurement must accurately reflect the hypothalamic temperature because the hypothalamus is the site of the thermoregulatory controller. The site where core temperature is measured must also respond rapidly and accurately to changes in brain temperature and must not be influenced by environmental temperature changes. This is particularly important because rapid heat gain and loss by individuals in field studies must be measured so that heat injury to participants in field studies can be prevented. Finally, the measurement should be reliable, easy to use in the field and harmless to the test volunteer.

The first of these criteria, that the measured temperature reflect brain temperature, has been addressed by several investigators (1, 2, 7, 22, 23). In 1951, Eichna *et al.* (7) reasoned that the temperature of blood in the left ventricle would be the best approximation of what they called "critical deep tissue" temperature. They equated critical deep tissue temperature with the temperature of the central thermoreceptors in the brain (7). Historically, the U. S. Army Research Institute of Environmental Medicine (USARIEM) and other research groups have used rectal temperature as an equilibrated or "steady state" index of internal body temperature. Eichna *et al.* (7) noted that rectal temperature was not a satisfactory index of internal temperature because changes in T_{re} occurred after changes had already occurred in heat loss or heat production effectors during body heating or cooling. These investigators (7)

concluded that the use of rectal temperature as an index of deep body temperature was appropriate during "steady state" conditions. Both oral and esophageal temperature responded rapidly enough to changes in body temperature to be used as an index of brain temperature (8). Furthermore, there was a highly significant relationship between heat elimination and oral temperature, which Gerbrandy *et al.* (8) interpreted as evidence that oral and esophageal temperature reflect the temperature at the central thermoreceptors. Esophageal temperature is the best method of tracking blood temperature in the right heart, and consequently, it responds very quickly to dynamic changes in deep body temperature (2,8,20,22,23).

Tympanic or auditory meatus temperature has also been used by some groups as an index of internal body temperature in laboratory studies (1, 9, 21-23). Initially tympanic temperature was used because it responded similarly to brain temperature in the monkey and the cat (1). It has been proposed that tympanic temperature is the best core temperature index in humans because it more accurately reflects hypothalamic temperature and would also account for selective brain cooling (3,5,6), but the existence of selective brain cooling in humans has not been proven and remains highly controversial (5, 17, 25). In fact, Jessen and Kuhnen (10) have since reported evidence against selective brain stem cooling in humans. The interpeak latencies for evoked brain stem potentials, which depend on brain stem temperature, did not change during face fanning in hyperthermic humans. Also, esophageal temperature did not change significantly during face fanning while tympanic temperature decreased slightly and forehead temperature decreased significantly (10). The main detractor for using tympanic temperature is that it more reliably tracks skin temperature than core temperature in humans (9, 21, 22). This bias makes tympanic temperature an unreliable index of brain temperature (23), while esophageal temperature effectively tracks brain temperature. The disagreement among researchers is in part due to the effective insulation around the tympanic thermocouple. In animal experiments, the tympanic thermocouple was carefully insulated and implanted (1), techniques not possible in humans. Brinnet and Cabanac (3) presented evidence that tympanic temperature tracks esophageal temperature if the tympanic thermocouple is situated on the lower anterior quarter of the tympanic membrane and properly insulated from the rest of the ear canal. This technique is risky in that the tympanic membrane might be punctured when the thermocouple is

placed against it. However, Shiraki *et al.* presented data from a human case study which showed that tympanic temperature did not track brain temperature as did esophageal temperature (23).

The current study was designed to use changes in activity state (rest→exercise→recovery→heavy exercise→recovery) to force many changes in core temperature during the experiment. Esophageal temperature was used as the most rapidly responding index of hypothalamic temperature in this study.

METHODS

VOLUNTEERS

Eight males volunteered to serve as test subjects after they were informed of the purpose, procedures, and known risks of this study. Each signed a consent form describing the study which was approved by the USARIEM Human Use Review Committee and the Surgeon General's Human Use Review Office. Each volunteer was given a medical examination and granted medical clearance before participating in the study. Investigators adhered to guidelines established for research on humans in USARIEM M 40-68, AR 70-25 and USAMRDC 70-25 Use of Volunteers in Research. The physical characteristics of the volunteers are described in Table 1.

PEAK AEROBIC POWER TEST

Peak aerobic power (peak $\dot{V}O_2$) was determined for each volunteer during exercise on a cycle ergometer which was modified so that the volunteer pedalled the ergometer as he sat in a chair attached behind the ergometer (Table 1). The procedure began with a five min warm-up period during which the volunteer exercised at a work intensity that elicited a heart rate of approximately 125 beats per min. After a few minutes rest, peak aerobic power was determined (Sensormedics 2900) during continuous resistance work. The work load was increased approximately 30 W every two min until the volunteer could no longer continue pedalling at 60 revolutions per min or when he voluntarily quit pedalling. Peak $\dot{V}O_2$ was designated when oxygen

Table 1
Test Volunteer Characteristics

Volunteer	Height (cm)	Weight (kg)	Age (years)	A ₀ (m ²)	Peak V _{O₂} (ml·kg ⁻¹ ·min ⁻¹)
A	183	72	23	1.9	50
B	178	82	19	2.0	41
C	163	72	19	1.8	45
D	185	76	19	2.0	47
E	173	80	18	1.9	47
F	170	65	20	1.8	53
G	180	93	19	2.1	45
H	186	97	19	2.2	36
MEAN	177	80	20	2.0	46
SD	8	11	2	0.1	5

uptake did not change more than 150 ml with increased ergometer resistance. Individual peak $\dot{V}O_2$ was used to calculate the relative work intensity for each experiment.

EQUIPMENT/ INSTRUMENTS

The four methods of measuring core temperature included rectal temperature (T_{re}), esophageal temperature (T_{es}), CorTemp™ (Human Technologies, Inc., St. Petersburg, FL) ingestible temperature sensor (HTI, T_{in}) and the ingestible temperature sensor developed by Konigsberg Instruments, Inc. (Pasadena, CA) under the supervision of COL Redmond, WRAIR, as part of CDUSS, BSMS and BFMS (KI, T_{in}). Rectal temperature was measured at a depth of 10 cm past the anal sphincter in the rectum using an YSI thermistor (Yellow Springs, OH). The J-type thermistor was calibrated in a water bath prior to use. Esophageal temperature was measured at a predetermined location in the esophagus deemed the "hot spot". The "hot spot" was located by systematically determining temperature in the esophagus beginning at approximately 25% of each volunteer's height until the temperature was at a peak presumably due to the anatomical proximity to the great vessels of the heart. Once the site of peak temperature in the esophagus was found, the T_{es} probe was marked and was inserted to this depth. In order to eliminate the cooling of the T_{es} probe, volunteers did not swallow saliva during these experiments. Esophageal temperature was measured using a 28-gauge copper-constantan thermocouple encased in PE-200 polyethylene tubing (Clay-Adams) which was sealed at one end with dental epoxy. This probe was calibrated in a water bath prior to use. Both the thermocouple and thermistor data were collected using a programmable volt meter (Hewlett-Packard 3497A) and stored on floppy disks by a computer (Hewlett-Packard 9816).

The CorTemp™ telemetry system included an ingestible temperature sensor (2 cm by 1.3 cm in diameter), FM antenna and data recorder system. In this system, temperature modifies a continuous, low-frequency radio wave (19). The temperature sensor included a silver oxide battery (1.5 V) which provided the power for sensing and transmitting temperature. The components of the sensors were encapsulated in epoxy and covered with silicone rubber. Temperature was transmitted through the body to a double bandoleer-type antenna and recorded by a data logger. A 9 V

alkaline battery (Radio Shack) provided power sufficient for data collection for four hours while temperature was measured every 30 s.

The CDUSS system used was described in a report to the U.S. Navy (12). Rather than continuous radio wave transmission, this system encodes temperature data by pulse interval modulation of the bursts of low power radio waves in the FM Band which are characteristic for each transmitter (19). For this study, the KI system was used in a prototype configuration of software and hardware which included the temperature telemetry transmitter (T2D), receiver (TR6B) and antenna communicating directly with a computer (Zenith Supersport or Zenith portable 286) by an RS232 interface. The temperature transmitter (~2.5 cm by 1.5 cm in diameter) included a 1.5 V silver oxide battery, two circuit boards and an antenna embedded in epoxy and coated with silicone rubber. The coating of the temperature transmitter was a material approved previously by the FDA. The components used in the TR6B receiver included a transceiver, a microreceiver controller, two I/O boards and a power supply which were contained in an aluminum case. DC power was supplied to the power supply board by four lithium batteries (1.5 V each). The TR6B locked on radio frequency transmission from the T2D as picked up by an antenna wrapped around the volunteer. Redmond *et al.* documented the performance of the CDUSS system (19) which used different software than the KI system used in this study. They reported that pill temperature correlated well with oil bath temperature when the oil temperature was measured as it cooled from 40°C to 36°C.

Calibration

All calibrations were performed by biomedical engineers in the Biophysics and Biomedical Modelling Division and Thermal Physiology and Medicine Division, USARIEM. Rectal thermistors and esophageal thermocouples were calibrated prior to use to ensure that temperature measurement in body temperature range was accurate to the standards of the National Bureau of Standards (NBS). HTI pills were calibrated in a water bath to a NBS thermometer for a range of temperatures between 36 and 39°C. Only those pills that were highly correlated (correlation coefficient > 0.98) to the NBS thermometer were used in the study (Appendix). Seven of the 19 HTI pills calibrated were not used because they were not highly correlated to NBS temperature.

The KI pills were calibrated in a stirred water bath to a range of temperatures between 36 and 39.5°C (Appendix). There were many problems in calibrating these pills, the most severe being inability to collect data using the prototype BSMS system during calibration. Calibration was attempted on 36 KI pills, but a signal could be detected consistently during the calibration procedure in only 11 KI pills. These problems were documented in depth in correspondence to COL Redmond (USARIEM Memoranda SGRD-UE-UEZ (70) dated 3 JUL 1990 and SGRD-UE-MEP (70) dated 26 SEP 1990) and included 1) the use of the temperature pills beyond their shelf life, 2) significant interference of the FM bands used in the 88-92 MHz frequency by commercial radio stations in the Boston area, and 3) software problems in the data acquisition program. These problems limited the number of KI pills available for the laboratory test, therefore reducing the number of volunteers in which the KI pills were tested. Also, calibration problems prevented the exclusion of KI pills which did not correlate with water bath temperature.

PROTOCOL

Two volunteers were studied each test day, although the exercise test times were staggered so that one volunteer at a time could be studied during exercise. The first volunteer arrived at the laboratory at 0700 h and the second volunteer arrived at 0900 h. Upon arrival at the laboratory the volunteer swallowed both telemetry pills with water. He then ate a light breakfast consisting of two pieces of toast with about 200 ml of juice. After breakfast, the volunteer inserted the rectal and esophageal temperature probes. Two (± 0.5) hours after swallowing the pills the volunteer was taken to the environmental test chamber to complete the exercise experiment.

Experimental Procedures and Environmental Conditions

The ambient temperature in the environmental test chamber was $29.5 \pm 0.6^\circ\text{C}$ and the dew point temperature was $11.4 \pm 1.0^\circ\text{C}$. Upon entering the test chamber the volunteer was weighed and the antennae for the telemetry systems were attached to his torso. He then sat in a chair which was positioned behind the cycle ergometer while all other instruments were attached. T_{re} , T_{es} , T_{sk} , and T_{ms} were measured every 30 s throughout the experiment. Heart rate was measured at 5 min intervals by

electrocardiography. A 15 min rest period preceded exercise.

After rest the volunteer exercised for 40 min at 40% peak $\dot{V}O_2$. When T_{re} stabilized during moderate exercise, the volunteer drank 100 ml of water so that it could be determined whether the HTI and KI pills were still in the stomach. Volunteers A and B were given drinks at ~15 and 30 min of exercise, but the remaining six volunteers drank only once, at ~20 min of exercise.

Following moderate exercise there was another 15 min rest period. To test whether the telemetry systems accurately tracked rapid changes in core temperature, there were three cycles of intense exercise (80% peak $\dot{V}O_2$) for 5 min interspersed with 5 min rest periods. During intense exercise, heart rate was measured every minute.

After the experiment, the volunteers lived in a laboratory which served as a dormitory until it could be verified that the telemetry pills had passed through their digestive tracts. In those cases in which the signal was not detected periodically, the stools of the volunteer were collected until the pills were identified. The length of time it took for passage of the pills through the digestive system of each volunteer is shown in Table 2.

Data Analysis

The tracking responses of the four indices of core temperature are subjectively described to assess how suitable T_{re} and T_{ms} were for detecting the rapid changes in core temperature elicited by exercise or recovery. There were several other approaches used to ascertain differences in tracking characteristics, as well as steady-state responses among the core temperature indices. First, the steady-state temperatures during rest and moderate exercise, and peak temperature during heavy exercise were tabulated along with the time it took to reach these values (Table 3). Second, the change in core temperature for each activity level was calculated. The magnitude of the change was constrained to the period of exercise or recovery as shown in Table 4. In addition, the time it took for each core temperature index to increase or decrease 0.1°C in response to activity changes was compiled for each individual experiment (Table 5). In order to compare tracking responses of the four

Table 2
Protocol Variation Between Individual Volunteers

Volunteer	Time After Ingestion When Volunteer in Test Chamber (h:min)	Experiment Duration (min)	KI Pill Passage Time (h)	HTI Pill Passage Time (h)
A	1:00 - 2:40	95 ¹	47.5	31.5
B	2:00 - 3:40	100	25	44.5
C	2:15 - 3:43	88 ²	12.5	31.5
D	2:00 - 3:40	100	7	29.5
E	2:00 - 3:40	100	28	28
F	3:00 - 4:40	100	12.5	12.5
G	2:00 - 3:40	100	8	30
H	2:30 - 4:10	100	-. ³	36

¹Volunteer A ate breakfast before arriving at the laboratory. During exercise he experienced what appeared to be gastric reflux into the esophagus from his description of "heartburn" and what was observed in the T_{es} data. Testing was halted at 95 min by the investigator due to volunteer discomfort. For all other volunteers the protocol was modified to that described above so that a light breakfast was eaten immediately after pill ingestion. None of the other volunteers experienced "heartburn".

²Volunteer C had severe muscular cramping in the gluteus maximus during the first intense exercise bout so the experiment was terminated when the cramping persisted after eight min of rest.

³Volunteer H did not ingest a KI pill because a signal could not consistently be detected from any of the KI pills available at the time of calibration for this experiment.

indices of core temperature to changes in heat production and dissipation due to the exercise/rest cycle of the experiment, regression equations were generated from the temperature changes as a function of time during both increasing and decreasing temperatures. The slopes (Table 6) of the individual regression equations were compared by analysis of variance with repeated measures. T_{re} , T_{sk} and T_{ce} were compared to T_{co} during those times when all data were available, in this case, when core temperature was increasing during exercise and in five volunteers. Because we were able to collect more temperature data from the HTI system than the KI system, we were able to compare those data more extensively with T_{re} and T_{sk} . As described in the DISCUSSION the experimental protocol differed for Volunteers A and C, and there were no T_{re} data for Volunteers G and H, therefore, all the analyses could not be done for all volunteers and all core temperature indices. As many volunteers and data as possible were used in the analyses of variance with repeated measures which determined differences among the indices of core temperature. When significant differences were identified by analysis of variance ($p < 0.05$), Tukey's test of critical differences was used for *post hoc* comparison.

RESULTS AND DISCUSSION

All data on human test subjects were collected in the spring of 1990 (April - June).

The prototype KI telemetry system was used in only seven of the eight experiments because only nine of 36 KI pills were suitably calibrated and responsive prior to consumption by the volunteer as discussed in the METHODS. Two of these pills were used in other experiments. For Volunteer C, the T_{re} data were so sporadic after ingestion that T_{re} was useless as a core temperature index during exercise. Although Volunteer G ingested a KI pill, the signal could not be detected at all after ingestion. The data for the seven KI pills used in this study are presented in the Appendix (Figures 9-12). The bench calibrations done in this study indicated that the KI sensor, as a thermometer, was not as accurate as reported when the calibration was done using an oil bath which was allowed to cool from 40°C to 36°C ($\pm 0.05^\circ\text{C}$; (19)). Seven of nineteen HTI pills, for which a water bath calibration was attempted, were eliminated because of either too much fluctuation around calibrated water bath

temperature or difficult signal detection. Four HTI pills were used in another study and two HTI pills were calibrated during preliminary tests of the HTI telemetry system. The calibration data for the HTI pills used in the current study are presented in the Appendix (Figures 13-16).

Figure 1 shows the core temperatures and heart rate responses for Volunteer A. The experimental protocol was different for this volunteer than the others (Table 2) because he experienced what he described as "heart burn" and what appeared to be gastric reflux as indicated from the T_{es} data (Figure 1). This volunteer swallowed the pills without eating a light meal. The heart rate response in Figure 1 demonstrates the changes in exercise intensity during the experiment. After 16 min of rest, Volunteer A began exercising at a moderate intensity (40% peak $\dot{V}O_2$). Approximately 100 ml of water (room temperature) was ingested at mins 34 and 52 which corresponded to 18 and 36 min of moderate exercise. These times can be identified in Figure 1 by the dramatic decrease in T_{es} as water cooled the esophageal probe. The quick recovery of T_{es} from cooling is also apparent. Both T_{re} and T_{sk} show the decrease in temperature due to drinking water which indicated that both pills were in the stomach. The absolute temperature and the time at which each index was judged to have reached steady state are shown for rest, moderate exercise, and heavy exercise in Table 3. Moderate exercise ended at 56 min and the change in core temperature is shown in Table 4. These data were compiled from the time when each core temperature index was judged to have reached a steady state temperature. The T_{es} data collection was temporarily interrupted due to a malfunction of the thermocouple connector during the recovery from moderate exercise until approximately minute 70, so T_{es} data were collected only for the last minute of the 15 min recovery period. T_{es} decreased by 75% and T_{re} decreased by 68% during that period. During this recovery period, T_{sk} decreased more than it had increased during exercise (Tables 4 and 5). This might be due to the KI pill moving in the gastrointestinal (GI) tract during the 55 min of moderate exercise and recovery, or to the response characteristics of this particular KI pill to change in temperature (Appendix). T_{es} decreased only slightly during this recovery period (Table 4). Heavy exercise (80% peak $\dot{V}O_2$) began at minute 71. Table 4 shows the change in the core temperature indices at the end of the 5 min work period. T_{es} increased by 0.8°C, but the other core temperature indices changed less dramatically during the time of heavy exercise. Additionally, Figure 1 shows that

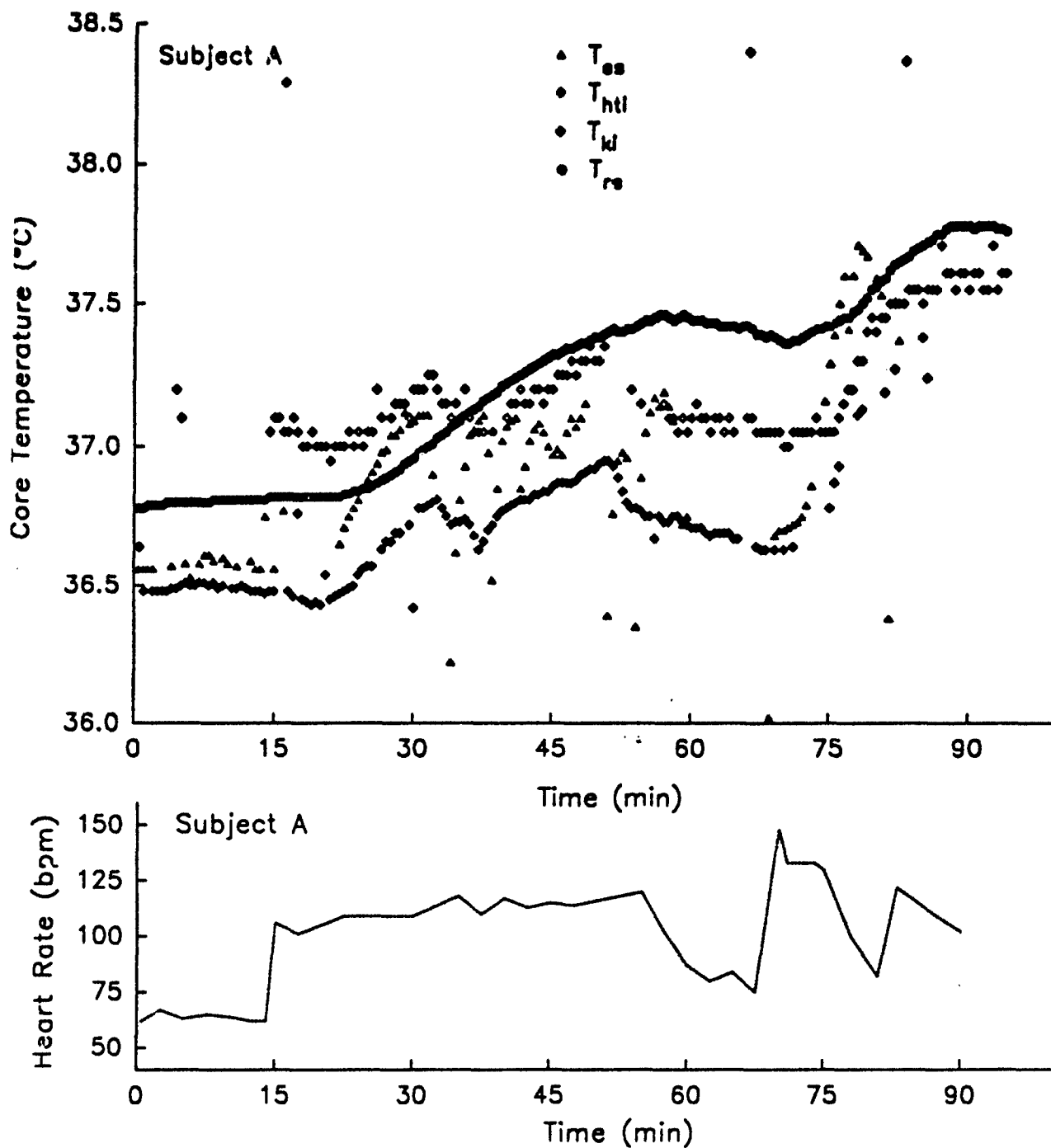


Figure 1 Core temperature and heart rate responses during rest and bouts of moderate and heavy intensity exercise.

after exercise stopped at 76 min, while T_{re} continued to increase for another 90 s. T_{re} , T_{sk} and T_{ce} continued to increase longer during recovery, when those indices finally reached a peak value. T_{re} responded much more rapidly to the change in core temperature during heavy exercise and recovery from heavy exercise than did the other three core temperature indices in this experiment. The volunteer's indigestion and technical difficulties that occurred with the T_{re} thermocouple did not obscure the more rapid response of T_{re} to change in core temperature than the other three core temperature indices.

The experimental protocol was standard for Volunteer B (Table 2) as reflected in the core temperature and heart rate responses (Figure 2). During rest, T_{re} decreased by 0.4°C although both T_{re} and T_{sk} data indicate that Volunteer B was close to thermal equilibrium at this time. In this case it appears that the HTI pill moved in the GI tract from a hot location, perhaps adjacent to the liver, to a cooler location. A change in temperature of that magnitude is comparable to the change that occurs during moderate exercise (Table 4) and highlights the argument that pill mobility could easily undermine research which uses temperature pill telemetry as an index of core temperature. Had the pill moved when moderate exercise began (minute 15) the increase in core temperature might have been missed. The brief plateau in T_{re} at minute 17 through minute 19 might be due to pill movement. The T_{sk} data appear to indicate that the KI pill also moved in the GI tract during rest, although these data are more scattered than the T_{re} data. Approximately 100 ml of water (room temperature) was ingested at mins 30 and 45 which corresponded to 15 and 30 min of moderate exercise (Figure 2). T_{re} decreased both times when Volunteer B drank water, but T_{re} cooled only after the second drink. T_{sk} may have decreased after both drinks but it is hard to determine that with any degree of certainty because of the variability in that measure (Figure 2). Apparently, the pills were in the GI tract at some point beyond the stomach as it took a greater volume of water (two drinks) to effect a temperature change than was observed for Volunteer A. The absolute temperature and the time at which each index was judged to have reached steady state are shown for rest, moderate exercise, and heavy exercise in Table 3. Moderate exercise ended at 55 min and the change in core temperature is shown in Table 4. During recovery from moderate exercise, T_{re} responded quickly and decreased by nearly the same degree as it increased during moderate exercise (Table 4). Both the T_{re} and T_{sk} data, although

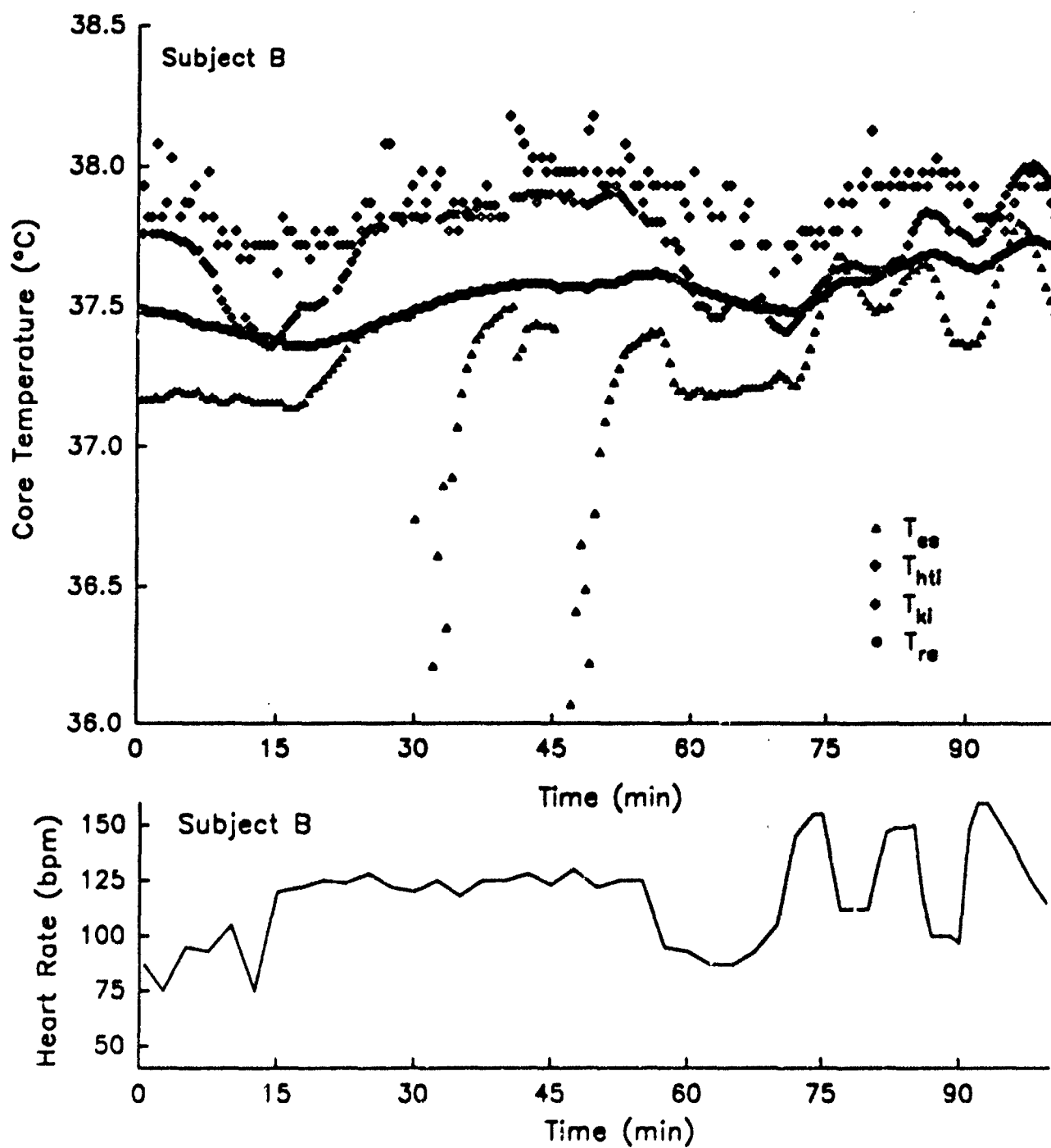


Figure 2 Core temperature and heart rate responses during rest and bouts of moderate and heavy intensity exercise.

not as rapidly responding as T_{re} , also decreased during recovery by almost the same magnitude as they increased during moderate exercise. T_{re} decreased by 50% of the initial increase during this recovery period (Table 4). The heavy exercise (80% peak $\dot{V}O_2$) work/recovery cycles began at minute 70. Figure 2 shows that both T_{re} and T_{ms} responded quickly to the change in work, and to some extent parallel the change in heart rate. Both T_{re} and T_{ms} have a damped response to the heavy work and recovery during the first two cycles, although T_{re} responds more like T_{ms} during the third cycle. The T_{ms} response is still damped during the final cycle of heavy work and recovery. For this experiment, T_{ms} responded much more rapidly to the change in core temperature during the moderate exercise bout than the other three indices of core temperature, but during the heavy exercise and recovery cycles both T_{re} and T_{ms} responded quickly. Perhaps, during the last 30 min of the experiment the HTI pill did not move in the GI tract. The T_{re} data could indicate that this pill did move in the GI tract because it became more responsive during the last heavy exercise/recovery cycle.

The experimental protocol was modified for Volunteer C (Table 2) so that he only performed one cycle of heavy work and recovery from that work (Figure 3). During rest, some T_{re} data were collected and used in Tables 4 and 5, but during exercise only sporadic readings were made (Figure 3). T_{re} increased rapidly during moderate work and T_{re} and T_{ms} data indicated that those core temperature indices lagged behind T_{ms} . T_{ms} decreased abruptly when Volunteer C drank 100 ml of water (room temperature) at 38.5 min which corresponded to 23.5 min of moderate exercise (Figure 3). T_{re} did not respond to this drink. The absolute temperature and the time at which each index was judged to have reached steady state are shown for rest, moderate exercise, and heavy exercise in Table 3. Moderate exercise ended at 55 min and the change in core temperature is shown in Table 4. During recovery from moderate exercise, T_{re} responded quickly and decreased by about 70% of the increase in T_{re} during the moderate exercise (Table 4). T_{ms} had a slower response time than T_{re} but returned to pre-exercise level. T_{ms} decreased only slightly during this recovery period (Figure 3, Table 4). The one heavy exercise (80% peak $\dot{V}O_2$) work/recovery cycle began at minute 70. Figure 5 shows that both T_{re} and T_{ms} responded quickly to the change in core temperature due to work. T_{re} does not increase during heavy exercise mainly because at 5 min of heavy exercise it is still

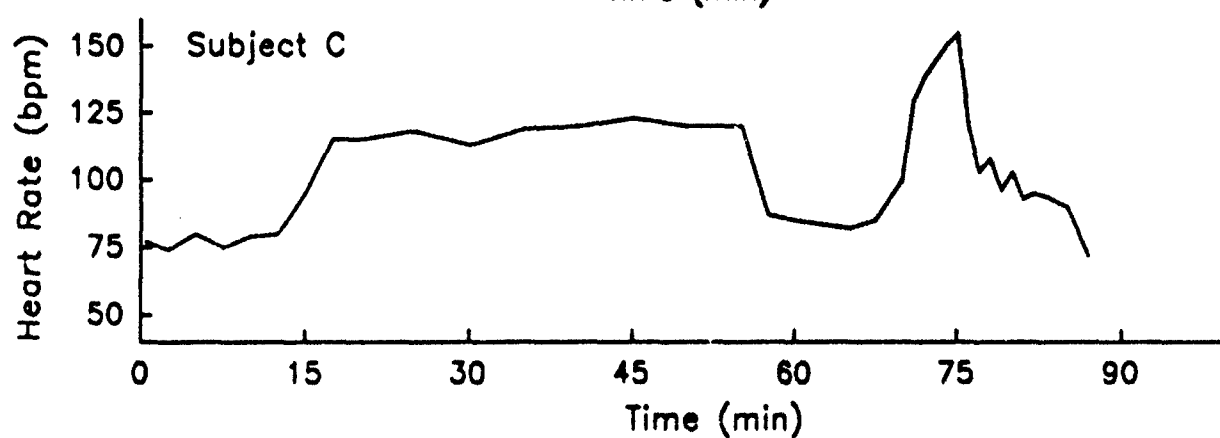
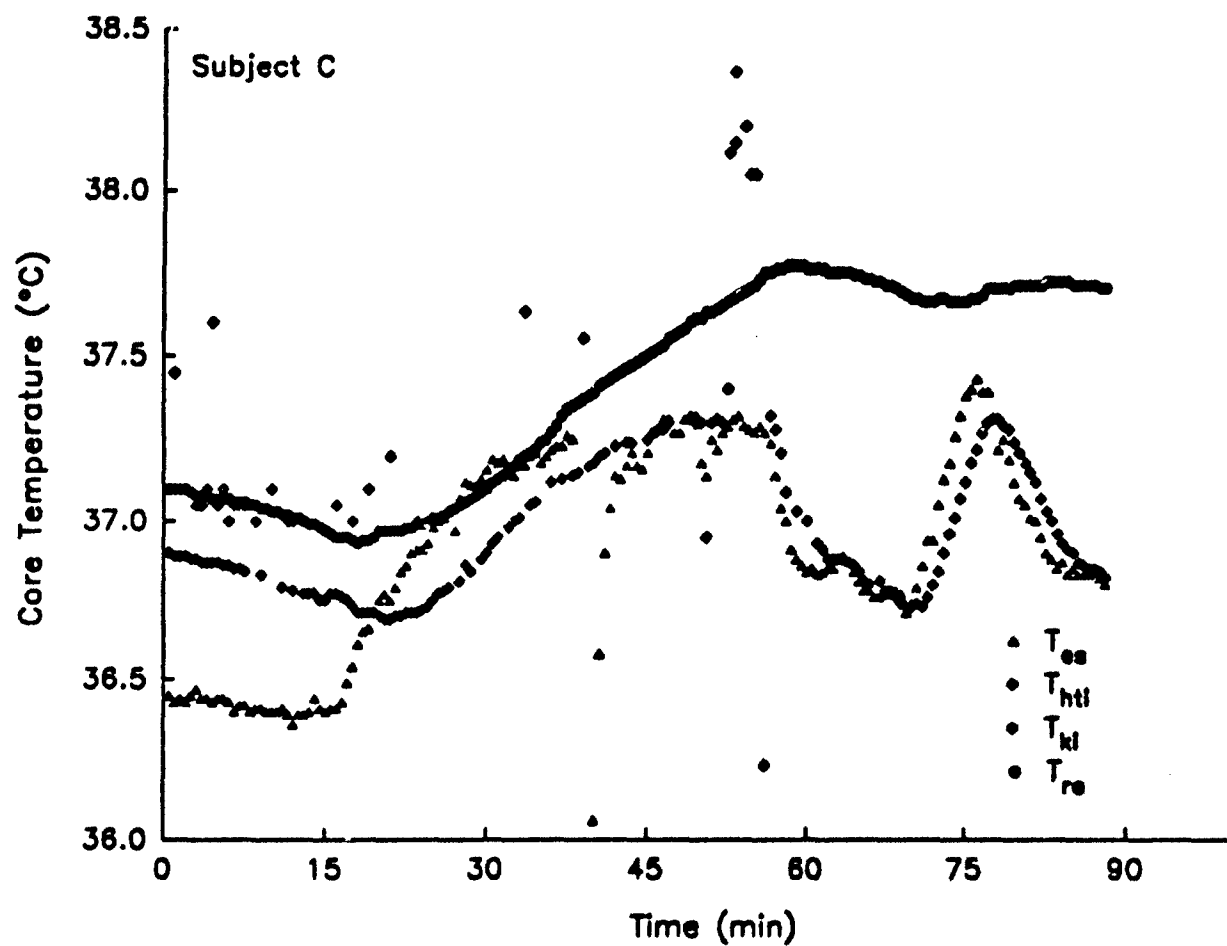


Figure 3 Core temperature and heart rate responses during rest and bouts of moderate and heavy intensity exercise.

decreasing in response to the previous recovery period. Five minute of recovery from heavy work was not long enough for T_{re} to reflect the increased heat stored during the exercise session.

Volunteer D performed the standard experimental protocol (Table 2) and the core temperature and heart rate responses are shown (Figure 4). During rest, all four indices of core temperature are fairly stable and by the beginning of moderate exercise Volunteer D was in thermal equilibrium. During moderate exercise Volunteer D drank 100 ml of water (room temperature) at 30 min which corresponded to 15 min of work (Figure 4). T_{re} and T_{ms} decreased transiently after the drink. The data indicate that the HTI pill, but not the KI pill, was in the stomach or upper small intestine. The absolute temperature and the time at which each index was judged to have reached steady state are shown for rest, moderate exercise, and heavy exercise in Table 3. The changes in all indices of core temperature are shown in Table 4. During recovery from moderate exercise, T_{re} responded more quickly than the other three indices (Figure 4). T_{ms} , T_{ms} and T_{ms} , although not as rapidly responding as T_{re} , also decreased to some extent during recovery (Table 4). The heavy exercise/recovery cycles began at minute 70. Figure 4 shows that both T_{re} and T_{ms} responded quickly to the increase in core temperature caused by exercise. During recovery and subsequent work/recovery cycles T_{re} responded quickly to change in core temperature. T_{ms} was blunted during the last two heavy exercise recovery cycles. Both T_{ms} and T_{ms} were damped compared to the T_{re} response to the heavy work and recovery during all cycles of heavy work and recovery. In this experiment, T_{re} responded much more rapidly to the change in core temperature during the moderate exercise bout than the other three indices of core temperature. During the first heavy exercise and recovery cycle both T_{re} and T_{ms} responded quickly. However, during the last 2 cycles of heavy exercise and recovery the T_{ms} response was more like T_{ms} and T_{ms} than T_{re} . The change in T_{ms} response characteristics might indicate that the HTI pill was moving through the GI tract during the experiment.

Volunteer E also performed the standard experimental protocol (Table 2). The core temperature and heart rate responses are presented in Figure 5. During rest, the indices of core temperature are fairly stable by the last 5 min before moderate exercise. Volunteer E drank 100 ml of water (room temperature) at 40 min which

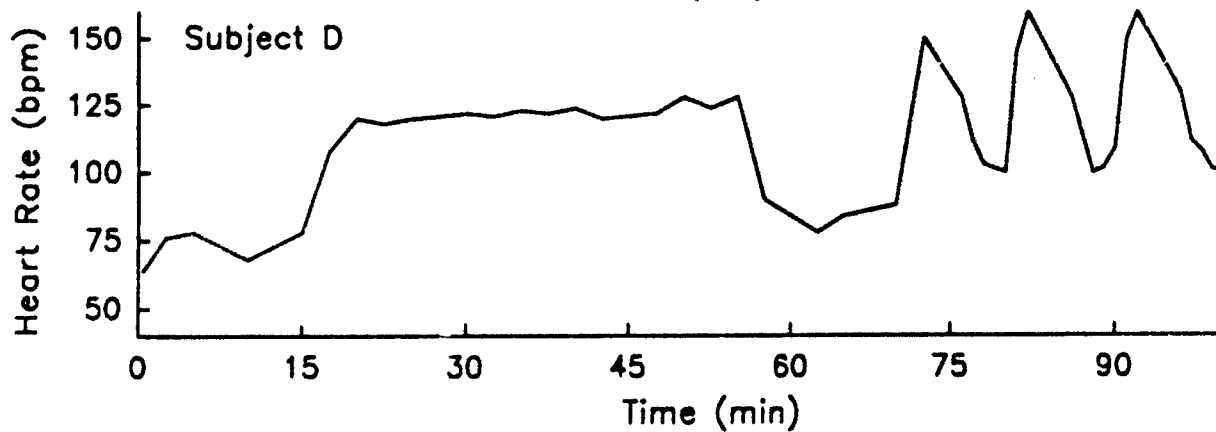
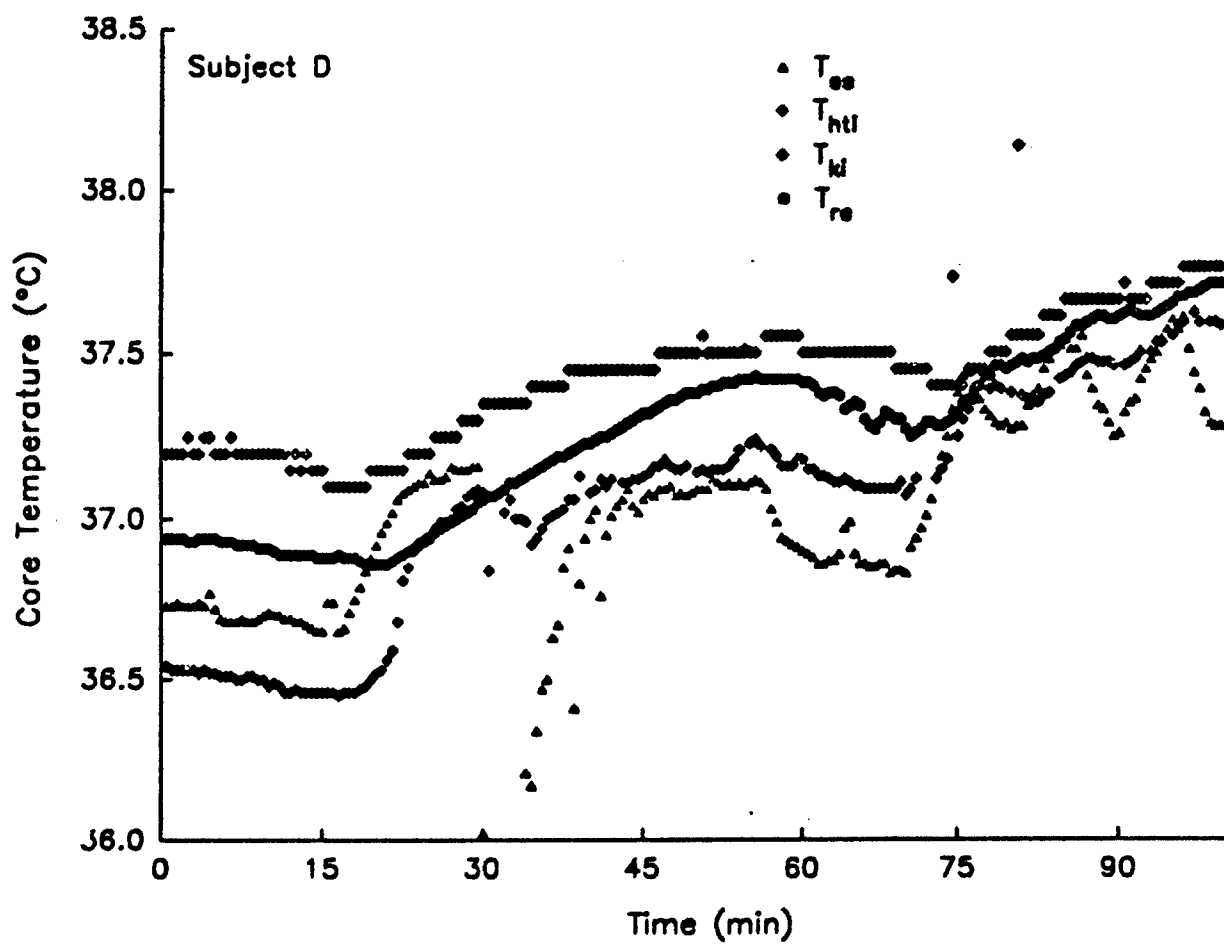


Figure 4 Core temperature and heart rate responses during rest and bouts of moderate and heavy intensity exercise.

corresponded to 20 min of work (Figure 5). T_{re} , T_{ms} and T_{sk} decreased transiently after the drink, indicating that both the HTI and KI pills were in the stomach. The absolute temperature and the time at which each index was judged to have reached steady state are shown for rest, moderate exercise, and heavy exercise in Table 3. The changes in all indices of core temperature are shown in Table 4. During moderate exercise, T_{re} , T_{ms} and T_{sk} responded more quickly than T_{co} (Figure 5). However, during recovery from moderate exercise T_{ms} and T_{sk} responded less quickly than T_{re} , but more quickly than T_{co} (Figure 5, Table 4). When the heavy exercise/recovery cycles began, both T_{re} and T_{ms} responded quickly to the initial work, while T_{sk} lagged behind those two indices. During recovery and subsequent work/recovery cycles T_{re} continued to respond quickly to change in core temperature, while both T_{ms} and T_{sk} responses were blunted during the last two heavy exercise recovery cycles. Both T_{ms} and T_{sk} were much more dynamic in response than T_{co} in this experiment. Both the KI and HTI pills were presumably located in the stomach or upper small intestine during this experiment and showed a more dynamic response to changing core temperature than the experiments in which the pill changed only slightly, if at all, when water was consumed (Volunteers B, D, and H; Figures 2, 4, and 8).

The core temperature and heart rate responses (Figure 6) to the standard experimental protocol (Table 2) for Volunteer F are shown. Volunteer F was in thermal equilibrium prior to moderate exercise (Figure 6). At the beginning of moderate exercise, there is a transient decrease in T_{re} and T_{ms} , and perhaps in T_{sk} and T_{co} , before core temperature increases as heat production increases. This phenomenon at the onset of exercise is due to shunting of cooler blood from the skin to the core caused, presumably, by transient catecholamine vasoconstrictor action on cutaneous blood vessels. The absolute temperature and the time at which each index was judged to have reached steady state are shown for rest, moderate exercise, and heavy exercise in Table 3. The changes in all indices of core temperature are shown in Table 4. During moderate exercise, T_{re} and T_{ms} responded more quickly than T_{sk} , and T_{sk} responded faster than T_{co} (Figure 6). When Volunteer F drank 100 ml of water at 40 min, which corresponded to 25 min of work, T_{re} , T_{ms} and T_{sk} decreased transiently which indicated that the HTI and KI pills were in the stomach. During recovery from moderate exercise, T_{re} decreased sooner than T_{ms} and T_{sk} , but the two pill temperatures responded much faster than T_{co} (Figure 6, Table 4). During the heavy

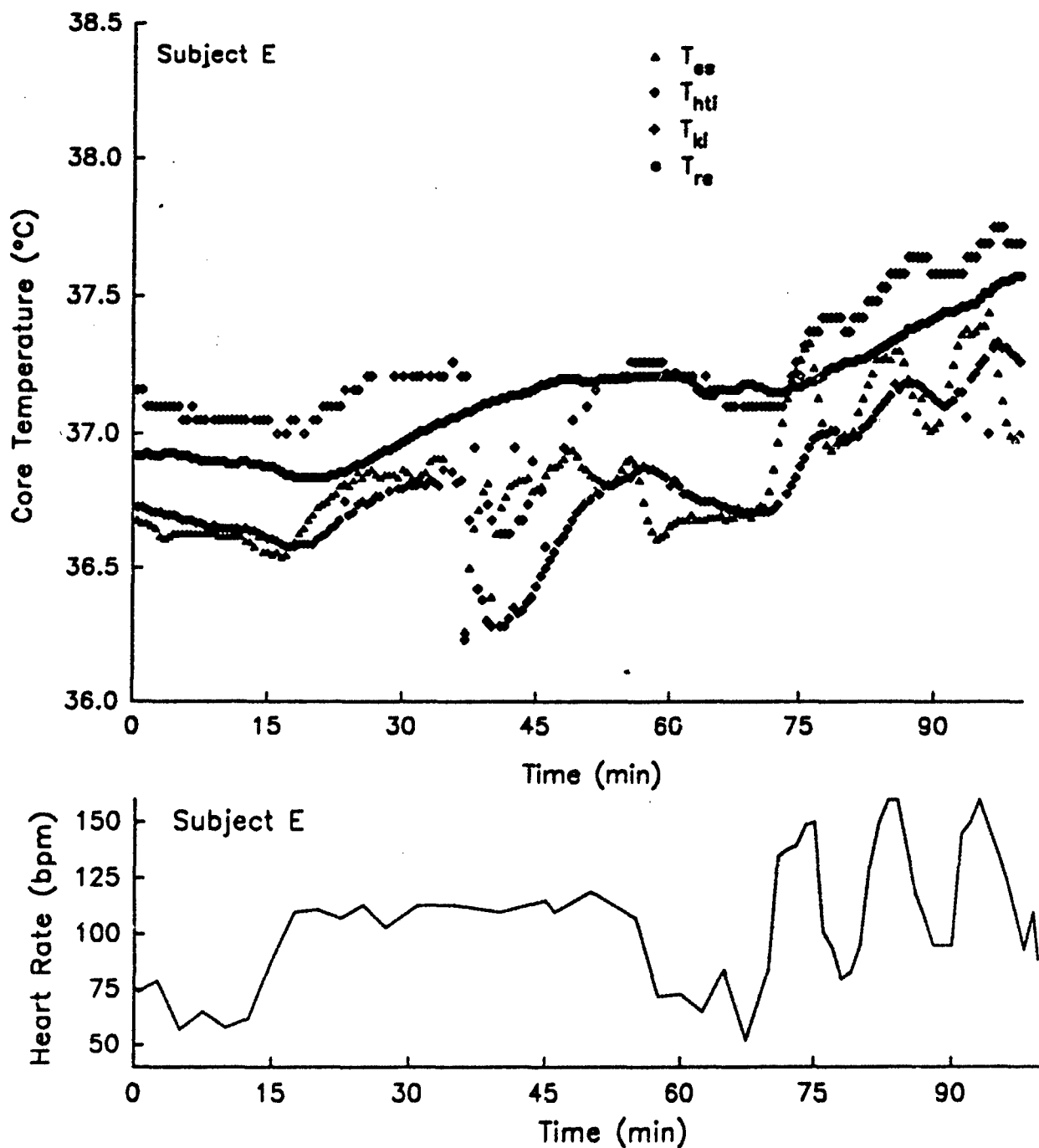


Figure 5 Core temperature and heart rate responses during rest and bouts of moderate and heavy intensity exercise.

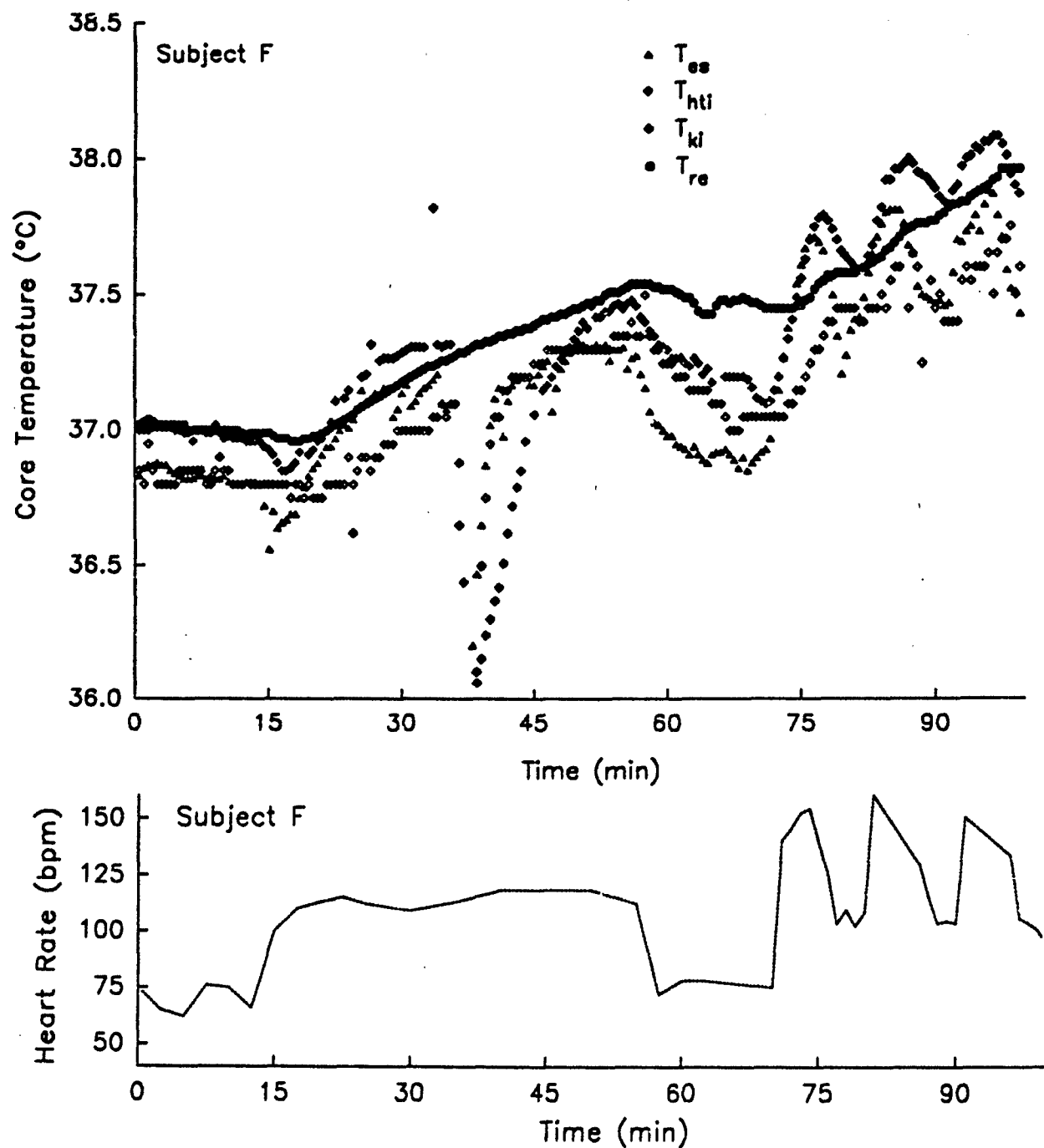


Figure 6 Core temperature and heart rate responses during rest and bouts of moderate and heavy intensity exercise.

exercise/recovery cycles, both T_{re} and T_{ms} responded quickly to the initial work, while T_{sk} lagged behind those two indices. During recovery and subsequent work/recovery cycles, T_{re} continued to respond quickly to changes in core temperature, while responses of both T_{sk} and T_{ms} were somewhat blunted during the last two heavy exercise recovery cycles. Both T_{sk} and T_{ms} were again more responsive than T_{re} in this experiment. This experiment is another example which shows that when both the KI and HTI pills were presumably located in the stomach, they exhibited a more dynamic response to changing core temperature than those experiments in which the pill temperature changed only slightly, if at all, when water was consumed (Volunteers B, D, and H; Figures 2, 4, and 8). The difference in the responses of the pill temperatures between the two types of experiments is apparently due to the location of the pills in the GI tract.

The core temperature and heart rate responses (Figure 7) to the standard experimental protocol (Table 2) for Volunteer G are shown. T_{sk} was not measured in this experiment due to the inability of the data acquisition system to detect the KI pill signal. Volunteer G was in thermal equilibrium prior to moderate exercise (Figure 7). The absolute temperature and the time at which each index was judged to have reached steady state are shown for rest, moderate exercise, and heavy exercise in Table 3. The changes in the three indices of core temperature are shown in Table 4. During moderate exercise, T_{re} responded more quickly than T_{ms} and T_{sk} (Figure 7). The sluggish response of T_{ms} during moderate exercise was different than observed in the other experiments. The HTI pill might have been in the volunteer's stomach in water (200 ml) which was swallowed before the experiment when he placed the esophageal probe. Perhaps the water was absorbed more slowly from the stomach of Volunteer G than from the other volunteers' stomachs so that water remained in the stomach ~1 h after being consumed. Otherwise, the response characteristics of this HTI pill were different during the first twenty min of moderate exercise in this volunteer than the other pills. When Volunteer G drank water at minute 40, T_{re} decreased transiently while T_{ms} decreased for about 10 min, then it increased fairly rapidly toward the end of moderate exercise. The sluggish response of T_{ms} to the drink of water is consistent with the HTI pill being in water in the stomach. During recovery from moderate exercise T_{re} decreased sooner than T_{ms} , but the T_{ms} response was more dynamic than its earlier responses, and was much faster than T_{sk} (Figure 7, Table 4). During the

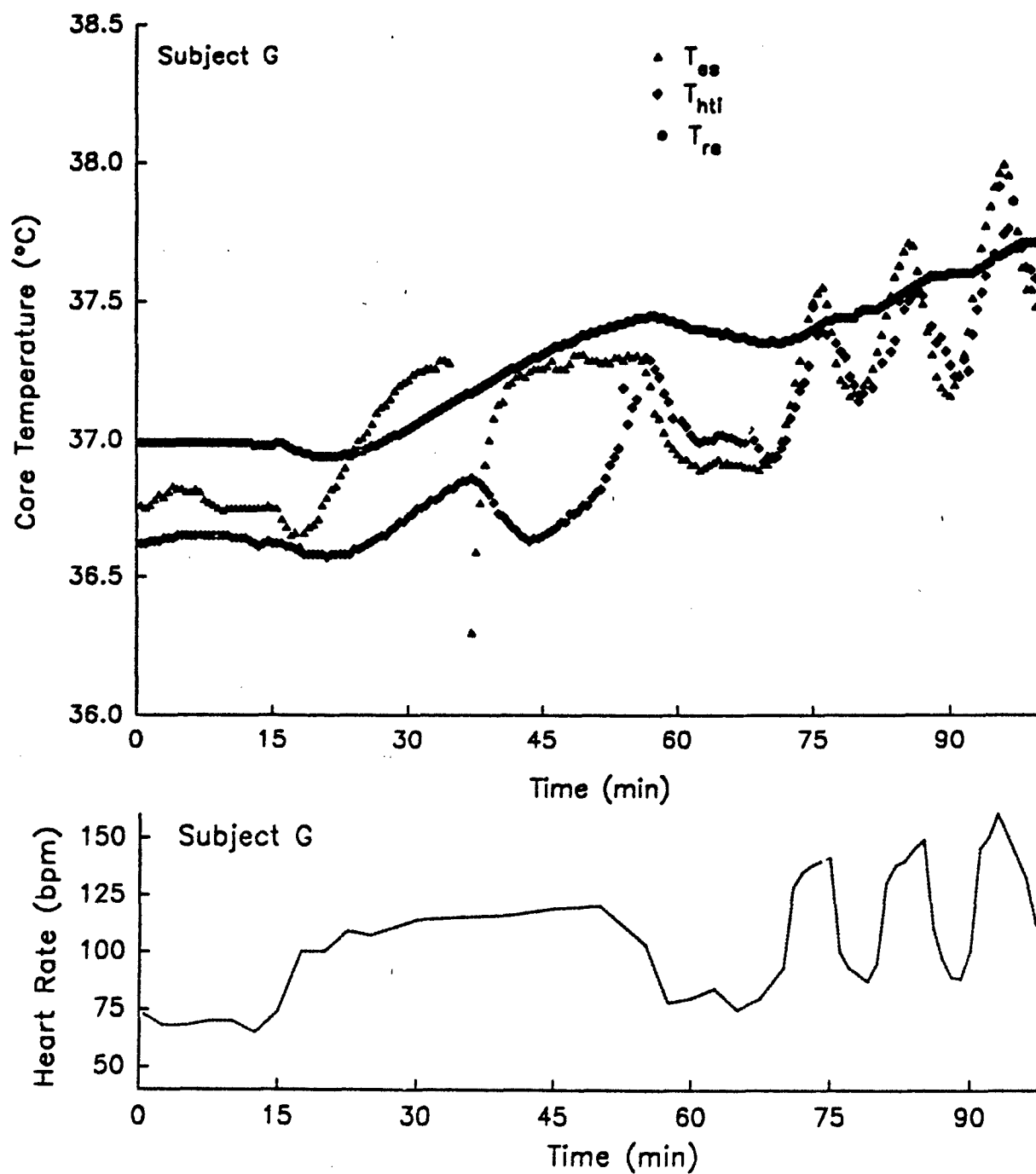


Figure 7 Core temperature and heart rate responses during rest and bouts of moderate and heavy intensity exercise.

heavy exercise/recovery cycles, both T_{re} and T_{ms} responded quickly and similarly to all changes in core temperature. The response of the HTI pill during heavy exercise/recovery cycles was different than during moderate exercise and was the most like T_{re} of any experiment. T_{ms} responses during the heavy work/recovery cycles were not dynamic enough to detect the change in core temperature during recovery, but did measure an overall increase during the cycles. This experiment showed a problem with using T_{ms} when the HTI pill was presumably located in the stomach because it responded sluggishly during moderate exercise and when water was consumed. However, for some reason, perhaps absorption of water in the stomach or movement of the pill out of the stomach, the response of T_{ms} was greatly improved during the heavy work/recovery cycles.

The core temperature and heart rate responses (Figure 8) to the standard experimental protocol (Table 2) for Volunteer H are shown. For reasons cited in the METHODS, T_{ms} was not measured in this experiment. By the end of the rest period the three indices of core temperature were stable (Figure 8). The time at which each index of core temperature was judged to have reached steady state are shown for rest, moderate exercise, and heavy exercise in Table 3. Core temperature changes are shown in Table 4. During the whole experiment, T_{re} responded as dynamically as seen in all other experiments. In this experiment, T_{ms} and T_{es} responded in near synchrony (Figure 8). The sluggish response of T_{ms} during this experiment was another variation of response description for the HTI pill. An explanation of its response is that it was in a location in the GI tract which was more thermally insulated than observed in other experiments. For example, the HTI pill might have been in the large intestine. This assumption would explain why T_{ms} characteristics were so similar to T_{re} characteristics.

Although much information can be derived from the above description of T_{re} and T_{ms} during each individual experiment, only intuitive conclusions can be drawn from the individual experiments. Intuitive conclusions alone are important as decisions can be made about the usefulness of a pill temperature sensor in measuring core temperature, however by analyzing the common features of the individual experiments more statistically powerful conclusions can be drawn. There were several approaches used to ascertain differences in response time among the core temperature indices.

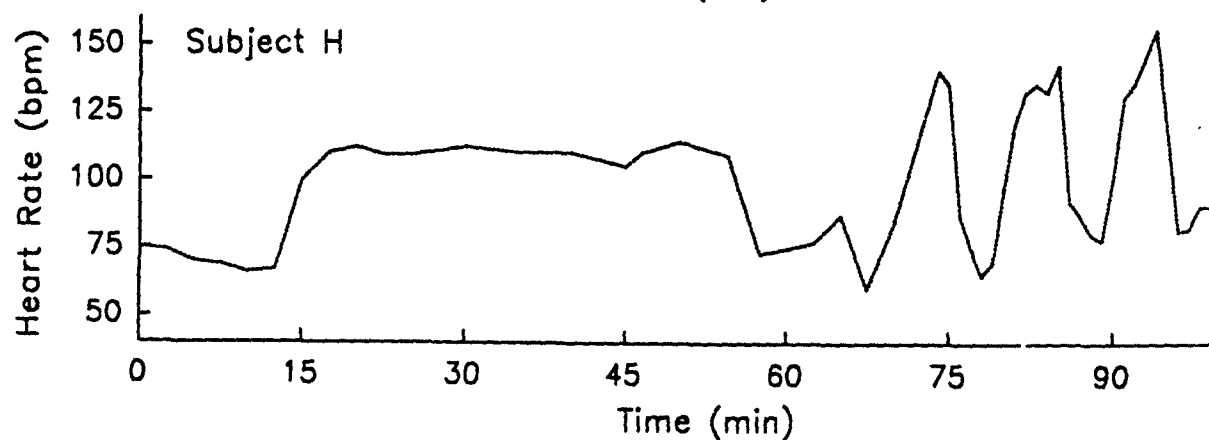
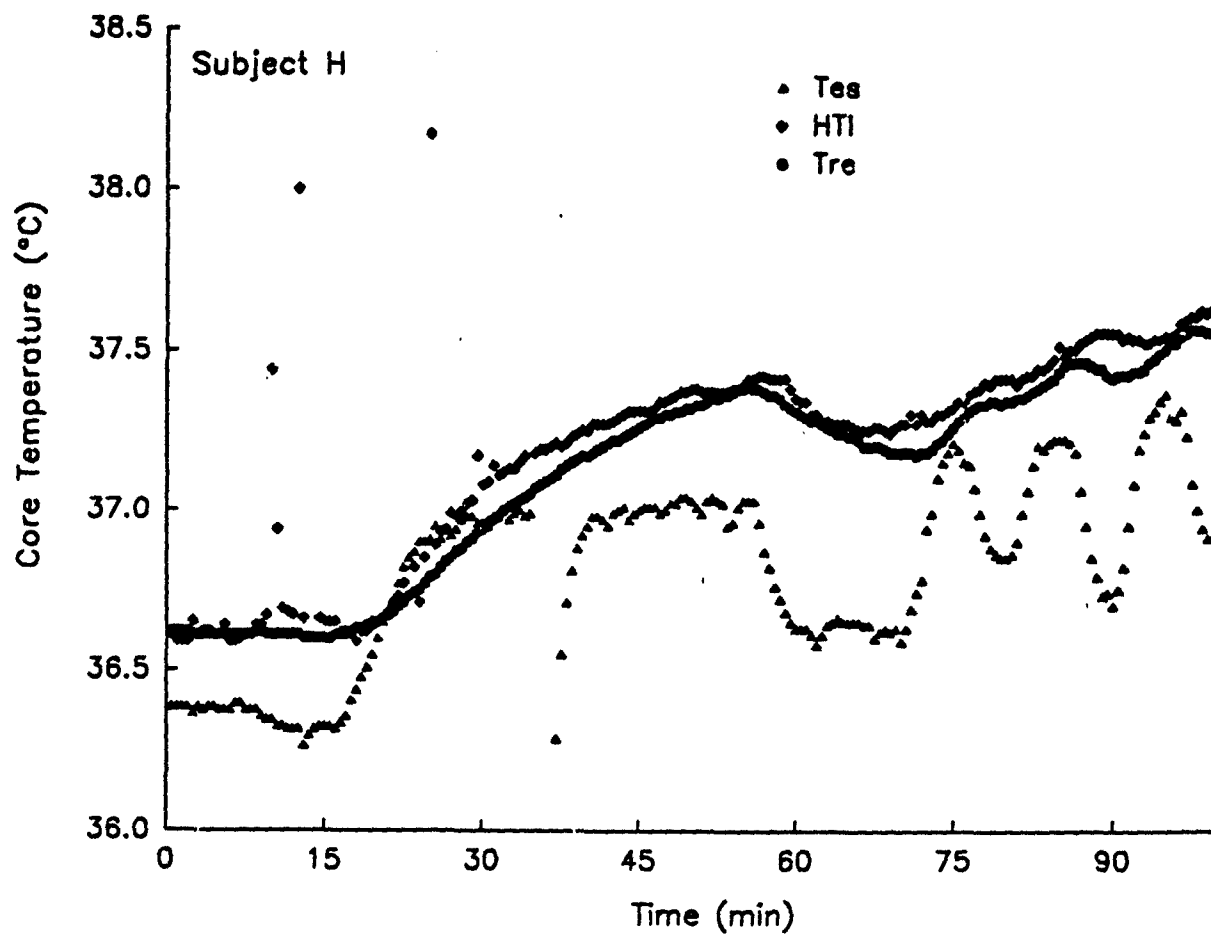


Figure 8 Core temperature and heart rate responses during rest and bouts of moderate and heavy intensity exercise.

First, the steady-state core temperatures during rest and moderate exercise, and the peak core temperature during heavy exercise, along with the time it took to reach these core temperatures were tabulated (Table 3). Second, the change in core temperature for each activity level was calculated. The magnitude of the change was constrained to the period of exercise or recovery as shown in Table 4. The change in core temperature during steady-state moderate exercise was examined alone because that condition in the experiment would be analogous to those field exercises in which service members would be exercising at a moderate work pace, in thermal equilibrium. In addition, the time it took for each core temperature index to increase or decrease 0.1°C in response to a change in activity was compiled for each individual experiment (Table 5) and the slope of each increase or decrease in core temperature was calculated when possible (Table 6). Finally, the total change in core temperature during the experiment (peak - rest) was calculated (Table 7) to determine whether large changes in core temperature could be measured effectively with the two telemetry pills.

The two-way analyses of variance with repeated measures indicated a significant main effect of activity state, as changes in activity state were used to force changes in core temperature. In general, the analyses indicated significant interaction between the core temperature indices and the activity states. Neither the significant main effect of activity state nor the significant interaction between core temperature indices and activity will be discussed further as each was an expected result of the experimental design of the study. The entire focus of the data analyses was on the comparisons of the core temperature indices.

The intent of the study was to compare T_{re} and T_{ms} to two accepted indices of core temperature (T_{es} and T_{ms}). Because the experimental protocol differed for Volunteers A and C, and there were no T_{re} data for Volunteers G and H, and limited T_{ms} data for Volunteer C, not all analyses could be done for all volunteers and all core temperature indices. However, by limiting the volunteer number to five, as well as by limiting the activity states, analysis of variance with repeated measures were done to compare all four core temperature indices (Tables 3-6). To fully present the remaining data, and to examine the relationship of T_{re} with T_{es} and T_{ms} in greater detail than could be done with T_{re} data, as many volunteers ($n \geq 6$) as possible were used in the data analyses

to compare T_{re} , T_{ms} and T_{ce} .

The equilibrated core temperature during rest (Table 3) was different among the four indices ($n=6$). T_{re} averaged $36.70(\pm 0.3)^{\circ}\text{C}$ which was significantly less ($p \leq 0.01$) than T_{ce} ($37.14 \pm 0.3^{\circ}\text{C}$) and T_{ms} ($36.99 \pm 0.2^{\circ}\text{C}$), but not different from T_{ms} ($36.78 \pm 0.3^{\circ}\text{C}$). T_{ce} was also significantly greater ($p \leq 0.01$) than T_{ms} . When only three indices (T_{re} , T_{ms} and T_{ce}) were compared using all eight volunteers (Table 3), both T_{re} ($36.66 \pm 0.3^{\circ}\text{C}$) and T_{ms} ($36.75 \pm 0.3^{\circ}\text{C}$) were significantly lower ($p \leq 0.01$) than T_{ce} (36.94 ± 0.2).

When the four core temperature indices were compared during moderate steady state exercise (Table 3; $n=5$) there were no significant differences among indices ($p=0.06$). However, when the analysis was limited to T_{re} , T_{ms} and T_{ce} and included all eight volunteers, T_{re} ($37.18 \pm 0.2^{\circ}\text{C}$) and T_{ms} ($37.20 \pm 0.3^{\circ}\text{C}$) were lower ($p \leq 0.01$) than T_{ce} ($37.46 \pm 0.2^{\circ}\text{C}$). This confirms the report of Sparling *et al.* (24) that T_{re} is lower than T_{ce} during rest and exercise, although the difference between the two indices averaged between approximately 0.4 - 0.8°C in that study. The differences between T_{re} and T_{ce} in the current study were much less than that report (24) and may indicate the merit of giving the volunteers a light meal after ingesting the HTI pill and waiting 2 h before initiation of exercise.

The peak temperatures (when obviously not aberrant points, as seen in many of the core temperature figures, and not constrained to a specific activity state) measured during the experiment were not different among the four indices ($n=5$; $p=0.65$) or among T_{re} , T_{ms} and T_{ce} ($n=8$; $p=0.61$). That is, the differences previously observed for equilibrated temperatures during rest and moderate exercise were no longer apparent. This observation is noteworthy because it indicates both the magnitude of the variation among individuals in the change in core temperature with activity state changes (Table 4) and the slow response time of T_{re} and T_{ms} (Table 3).

The time it took for each of the four core temperature indices to reach steady state during moderate exercise (Table 3) was also compared using a one-way analysis of variance with repeated measures ($n=5$). T_{re} (17.8 ± 8.1 min), T_{ce} (17.8 ± 8.4 min) and T_{ms} (22.5 ± 9.9 min) were judged to be at steady state faster during moderate exercise ($p \leq 0.001$) than T_{ms} (35.7 ± 5.3 min). When all eight volunteers were used in the analysis

Table 3
Individual Core Temperatures (°C) and Time Observed (min)

Volunteer	Steady-State Rest							
	T_{re}	T_{ra}	T_{ms}	T_{re}	T_{re}	T_{ra}	T_{ms}	T_{re}
A	36.56	37.10	36.48	36.81	13-15	15	12.5-15	12-14.5
B	37.16	37.72	37.36	37.38	12.5-15	12.5-14.5	14-15	14-15
C	36.39	37.00	36.77	36.98	11.5-13	11-12	13-14	14.5
D	36.65	37.15	36.46	36.88	14-15	14-15	11.5-15	14-15
E	36.62	37.05	36.65	36.89	9.5-12	7-15	8.5-12.5	10.5-14
F	36.81	36.80	36.96	36.99	10.5-14	11-15	12.5-14	12-15
G	36.75	-	36.62	36.98	10-14	-	13-15	13-15
H	36.32	-	36.66	36.60	11.5-12.5	-	14.5	13-15

Table 3 (cont.)
Individual Core Temperatures (°C) and Time Observed (min)

Volunteer	Steady-State Moderate Exercise (40% Peak $\dot{V}O_2$)							
	T_{re}	T_{ra}	T_{re}	T_{ra}	T_{re}	T_{ra}	T_{re}	T_{ra}
A	37.11	37.25	36.95	37.44	30.5	31.5	50.5	55.5
B	37.46	38.08	37.79	37.58	27.5	28.5	26.0	41.5
C	37.31	-	37.30	37.71	46.5	-	47	55
D	37.16	37.50	37.16	37.42	27	48.5	46	52
E	36.91	37.21	36.82	37.20	33.5	26	32	52
F	37.21	37.10	37.32	37.51	34	34.5	34	53.5
G	37.29	-	36.86	37.43	33.5	-	37	54.5
H	37.00	-	37.37	37.38	31.5	-	49	54.5

Table 3 (cont.)
Individual Core Temperatures (°C) and Time Observed (min)

Volunteer	80% Peak $\dot{V}O_2$ (Third Bout)							
	T_{re}	T_{ra}	T_{re}	T_{ra}	T_{re}	T_{ra}	T_{re}	T_{ra}
A	37.71	37.71	37.38	37.78	78	87	85	88
B	37.79	38.98	38.01	37.74	96	96.5	97	97
C	37.43	-	37.31	37.72	76	-	77.5	82.5
D	37.61	37.76	37.62	37.71	96	96	97	98.5
E	37.44	37.75	37.33	37.57	96	96.5	97	99
F	37.88	37.75	38.08	37.96	96	98.5	96.5	97.5
G	37.99	-	37.86	37.71	96	-	97	98
H	37.36	-	37.62	37.56	95	-	98.5	97.5

to compare T_{re} , T_{ms} and T_{ss} , the time it took T_{re} (37.17 ± 1.58 min) to reach steady state temperature was greater ($p \leq 0.001$) than T_{ms} (17.75 ± 2.19 min) and T_{ss} (25.06 ± 3.17 min). In this analysis, T_{ss} was at steady state before T_{ms} ($p \leq 0.001$). When the time it took to reach peak core temperature for heavy exercise was compared among the four indices ($n=5$), there were no significant differences found ($p=0.06$) when changes were not confined to a specific activity state. Yet, when only T_{re} , T_{ms} and T_{ss} were compared ($n=8$; $p \leq 0.01$), T_{re} peaked earlier (91.1 ± 8.7 min) than T_{ms} (94.8 ± 6.1 min). Peak T_{ms} (93.2 ± 7.7) was not different from either T_{re} or T_{ss} (Table 3).

There were significant differences among changes in core temperature with change in activity state (Table 4). The analysis ($n = 5$; Volunteers A, B, D, E, F) comparing all four indices of core temperature by change in activity state (rest $\rightarrow$ 40% peak $\dot{V}O_2$; 40% peak $\dot{V}O_2 \rightarrow$ recovery; recovery $\rightarrow$ 80% peak $\dot{V}O_2$) indicated that the change in T_{re} was significantly less than the change in T_{ms} , T_{ss} and T_{ss} ($p \leq 0.001$). When the number of volunteers was reduced by one (Volunteer A) to include all the changes in activity state for the experiments (Table 4), the analysis indicated that the change in T_{re} was greater than the other three core temperature indices ($p \leq 0.001$). When only T_{re} , T_{ms} and T_{ss} were compared ($n = 7$; Volunteers B-H) for the first four changes in activity state (Table 4), the change in T_{re} was greater than T_{ms} ($p \leq 0.05$) and T_{ss} ($p \leq 0.001$) and the change T_{ms} was greater than the change in T_{ss} ($p \leq 0.01$). When Volunteer C was eliminated from the analysis, which allowed comparisons of more activity states with the three indices of core temperature, the change in T_{re} was greater than T_{ms} and T_{ss} ($p \leq 0.001$). The statistical analyses for the change in the core temperature indices with change in activity state, in general, confirm the descriptive analyses for the individual experiments. That is, T_{re} tracked core temperature more quickly than the telemetry pills did, and T_{ms} and T_{ss} showed a greater response to changing core temperature than did T_{re} .

In order to examine the portion of the experiment which was most like a field exercise during which the soldiers would be exercising at a moderate pace for a long enough time to be in steady-state, the change in core temperature for the four indices of core temperature were compared during steady-state moderate exercise ($n=5$; Table 4). The mean change in core temperature as measured by T_{re} ($0.41 \pm 0.12^\circ\text{C}$), T_{ms} ($0.26 \pm 0.10^\circ\text{C}$), T_{ss} ($0.43 \pm 0.19^\circ\text{C}$), and T_{ss} ($0.44 \pm 0.19^\circ\text{C}$) was not significantly

Table 4
Change in Core Temperature Indices (°C) With Activity State Changes

Rest → 40% Peak $\dot{V}O_2$				
Volunteer	T_{re}	T_{in}	T_{ms}	T_{rs}
A	0.55	0.15	0.47	0.63
B	0.30	0.36	0.43	0.20
C	0.92	-	0.53	0.73
D	0.51	0.35	0.70	0.54
E	0.29	0.16	0.17	0.31
F	0.40	0.30	0.36	0.52
G	0.54	-	0.24	0.45
H	0.58	-	0.71	0.78

40% Peak $\dot{V}O_2$ → Recovery				
Volunteer	T_{re}	T_{in}	T_{ms}	T_{rs}
A	-0.41	-0.25	-0.32	-0.08
B	-0.28	-0.36	-0.33	-0.10
C	-0.60	-	-0.56	-0.03
D	-0.33	-0.05	-0.09	-0.15
E	-0.30	-0.11	-0.11	0.01
F	-0.33	-0.10	-0.20	-0.08
G	-0.40	-	0.13	-0.07
H	-0.42	-	-0.13	-0.20

Table 4 (cont.)
Change in Core Temperature Indices (°C) with Activity State Changes

Recovery → 80% Peak $\dot{V}O_2$ (1)				
Volunteer	T_{re}	T_{te}	T_{me}	T_{se}
A	0.80	0.10	0.30	0.08
B	0.40	0.15	0.14	0.07
C	0.67	-	0.38	-0.02
D	0.55	-0.05	0.18	0.05
E	0.66	0.11	0.16	-0.04
F	0.79	0.15	0.44	0.05
G	0.61	-	0.39	0.15
H	0.63	-	0.08	0.08

80% Peak $\dot{V}O_2$ (1) → Recovery				
Volunteer	T_{re}	T_{te}	T_{me}	T_{se}
A	-	-	-	-
B	-0.10	0.06	0.03	0.05
C	-0.31	-	0.09	0.05
D	-0.11	0.15	0.13	0.14
E	-0.33	0.16	0.10	0.09
F	-0.46	0.30	0.10	0.10
G	-0.37	-	-0.24	0.06
H	-0.36	-	0.07	0.08

Table 4 (cont.)
Change in Core Temperature Indices (°C) with Activity State Changes

Recovery → 80% Peak $\dot{V}O_2$ (2)

Volunteer	T_{re}	T_{in}	T_{ms}	T_{re}
A	-	-	-	-
B	0.17	0.05	0.20	0.09
C	-	-	-	-
D	0.27	0.11	0.05	0.08
E	0.33	0.21	0.16	0.07
F	0.60	0.10	0.28	0.09
G	0.51	-	0.33	0.07
H	0.37	-	0.10	0.09

80% Peak $\dot{V}O_2$ (2) → Recovery

Volunteer	T_{re}	T_{in}	T_{ms}	T_{re}
A	-	-	-	-
B	-0.29	-0.11	-0.08	0.04
C	-	-	-	-
D	-0.29	0.0	0.03	0.07
E	-0.25	0.0	-0.02	0.09
F	-0.34	-0.10	-0.03	0.10
G	-0.52	-	-0.20	0.07
H	-0.52	-	0.04	-0.01

Table 4 (cont.)
Change in Core Temperature Indices (°C) with Activity State Changes

Recovery → 80% Peak $\dot{V}O_2$ (3)				
Volunteer	T_{re}	T_{in}	T_{ms}	T_{se}
A	-	-	-	-
B	0.41	0.0	0.21	0.07
C	-	-	-	-
D	0.35	0.05	0.09	0.04
E	0.37	0.11	0.13	0.07
F	0.32	0.15	0.14	0.11
G	0.75	-	0.40	0.06
H	0.66	-	-0.01	0.08

80% Peak $\dot{V}O_2$ (3) → Recovery				
Volunteer	T_{re}	T_{in}	T_{ms}	T_{se}
A	-	-	-	-
B	-0.34	-0.05	-0.06	0.0
C	-	-	-	-
D	-0.32	0.05	0.03	0.06
E	-0.39	0.0	0.01	0.08
F	-0.36	-0.10	-0.16	0.08
G	-0.43	-	-0.09	0.05
H	-0.45	-	0.08	0.05

different ($p=0.12$). Also, when the change in T_{re} , T_{ms} , and T_{sk} during moderate exercise only were compared ($n=8$; Table 4), there was no difference among those indices ($p=0.48$). During moderate exercise, and when the volunteers were in thermal equilibrium, a similar change in core temperature was measured by each of the four indices.

The time of an observable change in core temperature (0.1°C) with a change in activity state (Table 5; $n=4$) was faster ($p\leq 0.001$) for T_{re} (2.5 ± 1.1 min) than T_{ms} (4.8 ± 1.6 min), T_{sk} (5.6 ± 3.0 min), and T_{te} (6.7 ± 3.2 min). However, T_{ms} response was faster than T_{sk} ($p\leq 0.001$). When only T_{re} , T_{ms} , and T_{sk} were compared (Table 5; $n=6$) the T_{re} response (2.4 ± 1.2 min) was faster ($p\leq 0.001$) than T_{ms} (5.0 ± 2.3 min) and T_{sk} (6.7 ± 3.3 min) responses. The response of T_{ms} was faster than the T_{sk} response ($p\leq 0.001$). These data indicate that T_{re} tracked changes in core temperature faster than the other three indices. In addition, T_{ms} tracked core temperature better than T_{sk} , although T_{sk} response was not different from T_{re} .

The slopes, Δ core temperature/ Δ time, ($n=5$; Table 6) with changes in activity state (rest $\rightarrow$ moderate exercise $\rightarrow$ recovery $\rightarrow$ heavy exercise) for the four core temperature indices were greater for T_{re} ($0.073\pm 0.037^{\circ}\text{C}\cdot\text{min}^{-1}$) than T_{sk} ($0.039\pm 0.023^{\circ}\text{C}\cdot\text{min}^{-1}$) and T_{te} ($0.018\pm 0.005^{\circ}\text{C}\cdot\text{min}^{-1}$). Also, the slopes for T_{ms} ($0.049\pm 0.029^{\circ}\text{C}\cdot\text{min}^{-1}$) were greater than T_{te} . However, the T_{sk} slopes were not different from T_{te} slopes. To evaluate an additional activity state (moderate exercise $\rightarrow$ recovery) and to include data which potentially might have an associated hysteresis, T_{re} , T_{ms} , and T_{sk} were compared for 5 volunteers (Table 6). T_{re} slopes ($0.035\pm 0.080^{\circ}\text{C}\cdot\text{min}^{-1}$) were greater ($p\leq 0.01$) than T_{sk} slopes ($0.008\pm 0.015^{\circ}\text{C}\cdot\text{min}^{-1}$) and T_{ms} slopes ($0.027\pm 0.043^{\circ}\text{C}\cdot\text{min}^{-1}$) were not different from the slopes of either T_{re} or T_{sk} . The comparison of the slopes of the core temperature indices also indicates that T_{re} responded to changes in core temperature faster than T_{sk} and T_{ms} .

The total change in core temperature (peak - rest; Table 7) was significantly different among the four indices ($n=5$; $p\leq 0.01$). Both T_{re} ($0.93\pm 0.21^{\circ}\text{C}$) and T_{ms} ($0.90\pm 0.24^{\circ}\text{C}$) changes were greater than T_{sk} ($0.63\pm 0.25^{\circ}\text{C}$) changes. The change in T_{sk} was not different from T_{te} ($0.76\pm 0.25^{\circ}\text{C}$). When T_{re} , T_{ms} , and T_{sk} were compared ($n=8$), the total change in core temperature was greater ($p\leq 0.05$) for T_{re} ($0.99\pm 0.18^{\circ}\text{C}$)

Table 5
Time (min) to Observe 0.1°C Change in Core Temperature Indices
With Activity State Changes

Rest → 40% Peak $\dot{V}O_2$

Volunteer	T_{re}	T_{in}	T_{ex}	T_{re}
A	9.0	12.0	0.5	12.5
B	5.5	9.50	2.5	13.5
C	2.0	-	13.0	13.0
D	3.0	10.5	6.0	11.0
E	4.0	8.5	8.5	15.0
F	1.5	9.0	7.0	10.0
G	7.5	-	15.0	16.5
H	3.0	-	7.5	7.0

40% Peak $\dot{V}O_2$ → Recovery

Volunteer	T_{re}	T_{in}	T_{ex}	T_{re}
A	3.0	2.5	11.0	15.0
B	3.0	4.0	3.5	11.0
C	2.0	-	3.0	15.0
D	2.5	15.0	6.5	11.0
E	2.0	11.5	10.5	15.0
F	2.0	4.5	3.5	9.0
G	2.0	-	6.5	15.0
H	2.0	-	7.5	6.5

Table 5 (cont.)
Time (min) to Observe 0.1°C Change in Core Temperature Indices
With Activity State Changes

Recovery → 80% Peak $\dot{V}O_2$ (1)

Volunteer	T_{re}	T_{in}	T_{ms}	T_{re}
A	2.0	5.5	4.0	5.0
B	3.5	5.0	3.0	5.0
C	1.0	-	2.5	5.0
D	1.0	10.0	4.0	5.0
E	2.0	4.0	4.0	5.0
F	2.0	4.5	3.0	5.0
G	2.0	-	2.5	5.0
H	1.0	-	7.0	5.0

80% Peak $\dot{V}O_2$ (1) → Recovery

Volunteer	T_{re}	T_{in}	T_{ms}	T_{re}
A	-	-	-	-
B	5.0	0.5	5.0	5.0
C	3.0	-	5.0	5.0
D	4.0	5.0	5.0	5.0
E	2.0	5.0	5.0	5.0
F	3.5	5.0	5.0	5.0
G	2.0	-	0.5	5.0
H	2.0	-	5.0	5.0

Table 5 (cont)
Time (min) to Observe 0.1°C Change in Core Temperature Indices
With Activity State Changes

Recovery → 80% Peak $\dot{V}O_2$ (2)

Volunteer	T_{re}	T_{in}	T_{ms}	T_{re}
A	-	-	-	-
B	3.0	5.0	3.5	5.0
C	-	-	-	-
D	2.0	5.0	5.0	5.0
E	1.5	2.5	4.0	5.0
F	0.5	5.0	3.5	5.0
G	1.5	-	2.5	5.0
H	1.5	-	5.0	5.0

80% Peak $\dot{V}O_2$ (2) → Recovery

Volunteer	T_{re}	T_{in}	T_{ms}	T_{re}
A	-	-	-	-
B	2.0	5.0	5.0	5.0
C	-	-	-	-
D	2.0	5.0	5.0	5.0
E	2.5	5.0	5.0	5.0
F	2.5	2.0	5.0	5.0
G	2.0	-	3.5	5.0
H	2.0	-	5.0	5.0

Table 5 (cont.)
Time (min) to Observe 0.1°C Change in Core Temperature Indices
With Activity State Changes

Recovery → 80% Peak $\dot{V}O_2$ (3)

Volunteer	T_{re}	T_{tr}	T_{ss}	T_{re}
A	-	-	-	-
B	2.5	5.0	3.5	5.0
C	-	-	-	-
D	1.5	5.0	5.0	5.0
E	1.5	5.0	4.5	5.0
F	2.0	3.0	3.5	4.5
G	1.5	-	2.5	5.0
H	1.0	-	5.0	5.0

80% Peak $\dot{V}O_2$ (3) → Recovery

Volunteer	T_{re}	T_{tr}	T_{ss}	T_{re}
A	-	-	-	-
B	3.0	5.0	5.0	5.0
C	-	-	-	-
D	2.0	5.0	5.0	5.0
E	2.0	5.0	5.0	5.0
F	3.0	1.5	4.0	5.0
G	2.5	-	5.0	5.0
H	2.0	-	5.0	5.0

Table 6
Individual Slopes and Intercepts from Linear Regression Equations Generated From
Observed Temperature as a Function of Time

Rest → 40% Peak $\dot{V}O_2$

Volunteer	Intercept			Slope		
	T_{re}	T_a	T_{re}	T_{re}	T_a	T_{re}
A	35.56	36.46	35.89	0.053	0.024	0.028
B	36.70	35.78	36.62	0.028	0.027	0.037
C	35.49	-	36.14	0.054	-	0.026
D	35.89	36.80	35.39	0.050	0.017	0.060
E	35.77	36.73	36.26	0.040	0.17	0.018
F	35.76	36.87	36.23	0.049	0.020	0.036
G	35.60	-	36.07	0.052	-	0.021
H	35.16	-	36.45	0.072	-	0.019
						0.022

Table 6 (cont.)
Individual Slopes and Intercepts from Linear Regression Equations Generated From
Observed Temperature as a Function of Time

40% Peak $\dot{V}O_2 \rightarrow$ Recovery

Volunteer	Intercept			Slope				
	T_m	T_a	T_{re}	T_m	T_a	T_{re}	T_m	T_a
A	43.14	-	-	-	-	-0.069	-	-
B	41.26	40.71	39.71	38.14	-0.031	-0.068	-0.022	-0.010
C	42.81	-	39.35	38.39	-	-0.072	-0.038	-0.010
D	37.91	-	37.75	38.25	-	-0.016	-0.009	-0.014
E	43.34	-	37.76	-	-	-0.117	-0.016	-
F	39.89	38.44	38.53	38.23	-0.025	-0.049	-0.020	-0.013
G	40.91	-	38.45	37.93	-	-0.067	-0.022	-0.008
H	40.83	-	38.32	38.19	-	-0.069	-0.016	-0.015

Table 6 (cont.)
Individual Slopes and Intercepts from Linear Regression Equations Generated From
Observed Temperature as a Function of Time

Recovery → 80% Peak $\dot{V}O_2$ (1)

Volunteer	Intercept			Slope				
	T_{∞}	T_u	T_m	T_{∞}	T_u	T_m		
A	35.56	32.45	32.78	35.55	0.049	0.062	0.055	0.026
B	30.11	31.74	34.70	35.87	0.100	0.064	0.038	0.022
C	28.19	-	30.34	-	0.121	-	0.090	-
D	29.35	35.71	33.55	36.29	0.107	0.023	0.050	0.014
E	27.95	32.23	33.18	35.85	0.123	0.067	0.049	0.018
F	27.92	32.15	28.38	35.76	0.128	0.067	0.122	0.022
G	27.64	-	30.02	36.37	0.130	-	0.098	0.014
H	26.88	-	36.19	35.20	0.138	-	0.015	0.027

Table 6 (cont.)
Individual Slopes and Intercepts from Linear Regression Equations Generated From
Observed Temperature as a Function of Time

80% Peak $\dot{V}O_2$ (1) $\rightarrow$ Recovery

Volunteer	Intercept			Slope		
	T_{∞}	T_0	T_m	T_{∞}	T_0	T_m
A	-	-	-	-	-	-
B	40.37	42.20	-	-0.035	-0.044	-0.013
C	44.32	-	41.51	-0.090	-	-0.054
D	40.48	-	-	-0.040	-	-
E	50.51	-	39.63	-0.175	-	-0.028
F	51.37	42.32	41.95	-0.178	-0.054	-0.054
G	46.93	-	41.67	-0.125	-	-0.056
H	44.50	-	-	-0.097	-	-0.019

Table 6 (cont.)
Individual Slopes and Intercepts from Linear Regression Equations Generated From
Observed Temperature as a Function of Time

Recovery → 80% Peak $\dot{V}O_2$ (2)

Volunteer	Intercept			Slope		
	T_{∞}	T_u	T_m	T_{∞}	T_u	T_m
A	-	-	-	-	-	-
B	34.50	-	33.38	35.77	0.037	0.052
C	-	-	-	-	-	-
D	32.36	-	35.82	-	0.061	0.019
E	31.27	34.37	33.74	-	0.070	0.040
F	27.51	35.14	30.68	-	0.121	0.085
G	27.87	-	31.54	-	0.115	0.070
H	29.15	-	35.73	35.46	0.086	0.019
						0.021

Table 6 (cont.)
Individual Slopes and Intercepts from Linear Regression Equations Generated From
Observed Temperature as a Function of Time

Recovery $\rightarrow$ 80% Peak $\dot{V}O_2$ (3)

Volunteer	Intercept			Slope		
	T_{∞}	T_u	T_m	T_{∞}	T_u	T_m
A	.	.	.	.	.	.
B	28.17	.	32.96	0.101	.	0.052
C	.	.	.	.	.	.
D	32.02	.	35.29	0.058	.	0.024
E	30.23	33.97	34.47	0.075	0.039	0.029
F	30.41	34.04	33.88	0.077	0.037	0.044
G	22.35	.	22.73	0.163	.	0.158
H	23.69	.	.	0.145	.	.

Table 7
Change in Core Temperature (°C) from Rest Temperature to Peak Temperature

Volunteer	T _{re}	T _u	T _{pe}	T _{te}
A	1.15	0.61	0.90	0.97
B	0.63	0.26	0.65	0.36
C	1.04	-	0.54	0.74
D	0.96	0.61	1.16	0.83
E	0.82	0.70	0.68	0.68
F	1.07	0.95	1.12	0.97
G	1.24	-	1.24	0.73
H	1.04	-	0.96	0.96

than T_{re} ($0.78 \pm 0.19^\circ\text{C}$). The total change in T_{re} ($0.91 \pm 0.24^\circ\text{C}$) was not different from T_{sk} or T_{ms} . The sluggish response of T_{re} and T_{sk} was probably part of the reason for these differences, but the total change in T_{sk} was an average of 0.36°C lower than T_{re} ; perhaps the KI sensors are not as effective as thermocouples. On the other hand, the other choice for monitoring core temperature in field studies is T_{ms} and the total change in T_{ms} was not significantly different from T_{re} . The poor showing of the T_{sk} was not inherent to a temperature sensor/pill *per se*, as the change in T_{ms} was not different from T_{re} .

T_{re} , as an index of core temperature, is useful when an individual is in thermal equilibrium (7, 8, 11, 15, 16) and data from the current study indicate that T_{re} lags behind T_{sk} by 12-25 min (Tables 3-6). Even though the moderate exercise period was 40 min (rest→moderate exercise; Table 3), T_{re} was not always equilibrated by the end (Figures 6,12,14,16). However, the mean change in core temperature during moderate exercise was measured as effectively by T_{re} as any other core temperature index (Table 4). On the other hand, Table 4 also shows that T_{re} response during rapid changes in core temperature was often changing opposite to T_{sk} . During heavy exercise in a hot environment, a delay in detecting a substantial increase in core temperature might contribute to heat injury.

The primary purpose of this study was to evaluate whether or not the temperature pill telemetry systems were reliable and accurate indices of core temperature. The evaluation of the KI system (CDUSS, BSMS and BFMS) was of special interest because its development had been funded, in part by the US Army (P²NBC² program) with the intention to use the KI system as a clinical index of core temperature to prevent heat injury in field studies (12, 18, 19). Specifications of this system predict that core temperature can be transmitted for 150 meters, or up to two km if a relay system is used (18). However, the KI telemetry system used in the current study could not transmit even one meter in USARIEM, so the relay portion of the telemetry was not used in this study. The data collected with the prototype KI system were unreliable to the extent that substantial data were lost. Some statistical analysis were possible, although the small volunteer number ($n=5$) limited the interpretation to the population used in the study. Not only was the prototype KI telemetry system unreliable in the current study, the KI pill as a temperature sensor was inaccurate as shown by the extensive water bath calibration data for two KI pills (Figure 17). For example, for a water bath temperature of 38.05°C

38.08°C, the temperature of KI Pill #70 ranged between 35.45-37.75°C. The temperature of KI Pill #121 ranged between 36.05-37.59°C for a water bath temperature of 38.05-38.08°C. If the KI pill is this inaccurate in a water bath calibration, when the sensors equilibrated for 8.5 min as data were collected, it may not be suitable for use as a clinical index of core temperature. Rigorous bench tests of the KI sensor should be made to determine the nature of its response to changing water bath temperature to discount the possibility that the data shown in Figure 17 are representative of all KI pills. These bench tests should be conducted before the KI sensor is used as a clinical thermometer.

Equilibrated T_{re} during rest and moderate exercise, was similar to T_{ms} . There were also some outliers in the T_{re} data as shown in the figures, but the bigger problem in the KI system was an inability to detect the KI pill signal. Peak T_{re} was not different from any of the other core temperature indices. These observations indicate that T_{re} ($37.79 \pm 0.11^\circ\text{C}$) was as effective as T_{ms} ($37.75 \pm 0.14^\circ\text{C}$) when used to measure the peak temperature during the heavy exercise/rest cycles (Table 3). Further, T_{re} ($0.63 \pm 0.25^\circ\text{C}$) was as effective an index as T_{ms} ($0.76 \pm 0.25^\circ\text{C}$) when used to measure the change in core temperature from rest to peak, although the change in T_{re} was significantly less ($p \leq 0.01$; Table 7) than T_{ms} ($0.93 \pm 0.21^\circ\text{C}$) and T_{ms} ($0.90 \pm 0.24^\circ\text{C}$). When the quickness of response of T_{re} was evaluated (Tables 4, 5 and 6), the average time it took for T_{re} to reach an equilibrated temperature during moderate exercise was 18 min faster than for T_{ms} to reach an equilibrated temperature. During heavy exercise the time it took T_{re} to reach the highest temperature during the exercise or recovery period was not different than any other index. This was mainly because the time was constrained to the five min periods and the temperatures were not necessarily equilibrated (Figures 1-8).

The change in T_{re} with change in activity state was greater than the change in T_{ms} ($n=4$; 3 activity states; Table 4), while the change in T_{re} was less than T_{ms} ($n=4$; 8 activity states). Although T_{ms} changed more during changes in activity state than T_{re} , the change in T_{re} was greater than T_{ms} . The time it took for a 0.1°C change in T_{re} was about the same as the time it took T_{ms} , and it was about three min slower than T_{ms} ($p \leq 0.001$; Table 5). The slope changes with activity state changes were much less for T_{re} compared to T_{ms} (Table 6), but T_{re} slopes were not different from the slopes of T_{ms} . The weight of the data for T_{re} response indicates that it is not as fast as T_{ms} , but just as quickly responding as T_{ms} . Although the absolute peak temperature of T_{re} was not different from T_{ms} , T_{ms} , or T_{ms} during heavy

exercise, the total change in T_{re} ($0.63^{\circ}\text{C} \pm 0.20$) was significantly less ($p \leq 0.01$; Table 7) than in T_{so} ($0.99 \pm 0.18^{\circ}\text{C}$) and T_{ms} ($0.91 \pm 0.19^{\circ}\text{C}$). T_{re} during a 1.0°C change in core temperature, lagged by nearly 0.4°C . Therefore, T_{re} did not measure large changes in core temperature as effectively as T_{so} or T_{ms} . Part of the lag in T_{re} might be due to an apparent inconsistency in the response characteristics of the KI pill. In the Appendix, Figure 17 (KI pill #70 and KI pill #121) shows extensive calibration data (> 3 h). There was a large and obvious hysteresis for both KI pill #70 (Volunteer A) and KI pill #121 (Volunteer B). The hysteresis may or may not explain the smaller total change in T_{re} compared to T_{ms} .

T_{ms} could be compared to T_{so} and T_{re} more extensively than could be done with the KI telemetry system because fewer data were lost with the HTI telemetry systems. There were sporadic outlying points in T_{ms} data as can be seen from the figures of the individual data, as occurred with T_{re} data. Table 3 shows that the steady state rest T_{ms} was not different from T_{so} , but was 0.2 and 0.26°C lower than T_{so} and T_{re} , respectively. During moderate exercise, T_{ms} was not different from T_{re} or T_{so} but averaged 0.26°C lower than T_{so} . The difference between T_{ms} and T_{re} averaged 0.2°C and 0.3°C at rest and during moderate exercise, respectively. The only published report (24) comparing T_{ms} with T_{re} indicated that the difference between T_{ms} and T_{re} for rest and exercise was about 0.4°C and 0.8°C , respectively. The differences between the two temperatures were much greater as reported by Sparling *et al.* (24) than in the current study, but that may be due to experimental design, variation in pill mobility, whether there was water in the gut, or whether a small meal was eaten after pill ingestion. Figure 7 shows that T_{ms} was abnormally low during moderate exercise, presumably because there was water in the gut. Later in the experiment T_{ms} response improved markedly, presumably because the HTI pill moved out of the stomach. Also, in one volunteer (B), T_{ms} was greater than T_{re} throughout the experiment (Figure 2). In this study, peak T_{ms} was not different than the other three core temperature indices during heavy exercise. However, the total change in T_{ms} averaged 0.28°C greater than T_{re} and was not significantly different from T_{so} and T_{ms} (Table 7). The HTI pill detected the total change in core temperature better than the KI pill ($p \leq 0.01$). This difference between the two pills might be due to the hysteresis detected during calibration of the KI pills (Figure 17). The HTI calibration data are presented in Figures 13-16. A heated water bath interfered with HTI signal transmission. Consequently, the calibration was done only on decreasing water temperature without

checking for hysteresis, but the correlation coefficients for the HTI pill calibration were much better than those for the KI pill calibrations (Figures 9-12). During moderate exercise (Table 3) T_{re} equilibrated 12 min faster than T_{so} , although T_{so} equilibrated about 7 min faster than T_{re} . During heavy exercise, the time at which the peak T_{re} occurred was not different from the time of peak T_{so} or T_{re} . During changes in activity state, the change in T_{re} was greater than the change in T_{so} , but less than the change in T_{re} . The time of an observable change (0.1°C) in core temperature with a change in activity state (Table 5) for T_{re} was 2-3 min faster than T_{so} , but 2-2.5 min slower than T_{re} ($p \leq 0.001$). Using this method of analysis, T_{re} tracked core temperature better than T_{so} while T_{re} was not different from T_{so} . In the slope analysis from two changes in activity state indicated that T_{re} slopes were greater than T_{so} , but not different from T_{re} . By contrast, the T_{re} slopes were not different from T_{so} slopes, but less than T_{re} slopes (Table 6). Again, by using this analysis, T_{re} was a more responsive index of core temperature than T_{so} , yet T_{re} responded as did T_{so} . Overall, these analyses indicated that T_{re} tracked rapid changes in core temperature significantly faster than T_{so} , although T_{re} did not track dynamic changes as well or as consistently as did T_{re} . T_{re} was an effective index of the total change in core temperature (~1°C) during the experiment (Table 7).

CONCLUSIONS

In our hands, T_{re} was not reliable due to many problems, as detailed in the **METHODS**. The KI sensor itself, when calibrated extensively in a water bath, was inaccurate. When the prototype KI telemetry system was functioning, we obtained limited data ($n=5$) pertaining to the use of T_{re} as an index of core temperature. In some cases, T_{re} responded better to dynamic changes in core temperature than T_{ms} , but T_{ms} was undeniably more reliable than T_{re} . T_{ms} was a better index of core temperature than T_{re} in that it was more reliable, more responsive and more accurate.

The reliability of the HTI telemetry system as a data acquisition system was far better than the prototype KI telemetry system. However, screening, by water bath calibration, was still required to ensure that the HTI sensor measured temperature accurately. As a core temperature index, T_{ms} , for the most part was accurate with some drawbacks: 1) mobility of the pill in the GI tract caused changes in insulation and absolute temperature and made T_{ms} less reliable than T_{re} and T_{ms} ; and 2) the response characteristics of the HTI pill did change several times which is probably related to pill mobility or water in the GI tract.

The concept of using a temperature sensor in a pill (26) may be useful clinically, but mobility of the pill makes this temperature measurement less suitable for research than esophageal or rectal temperature measurements. If new evidence indicates the KI pills are reliable and accurate, further testing should be initiated to test the KI telemetry system when used in conjunction with the KI pills before the KI telemetry system is used as a clinical index of core temperature. Field use of T_{ms} would still require a medical observer in close proximity to the soldiers since the pill transmits a signal to a receiver worn on the body and is not relayed further by telemetry. However, the HTI system is equipped with an audio alarm that may be activated when safe temperature limits have been exceeded.

RECOMMENDATIONS

Before the KI pill is used as a clinical thermometer, it is recommended that the KI temperature sensors be rigorously tested in a bench test to determine the nature of the KI pill response to changing water bath temperature (as measured by a thermometer calibrated to National Bureau of Standards specification). The bath temperature should be changed as fast as the human body can store heat during vigorous exercise ($\sim 0.6^{\circ}\text{C}$ in 5 min at 80% peak $\dot{V}\text{O}_2$). Finally, the bench test should include both increasing and decreasing water bath temperatures over the range of human core temperature.

Due to the high failure rates observed during water bath calibrations of both the HTI and KI pills, it is recommended that a suitable water bath calibration be done on each pill by the investigator within a day or two of human ingestion.

Temperature pills should not be used for research from which decisions will be made regarding heat storage differences between different uniforms, uniform/systems, microclimate cooling, and other personal equipment for the soldier such as sleeping bags. This recommendation is based on the variable and sometimes sluggish pill temperature responses due to the changing anatomical location of the pill during these 100 min experiments. A change of $0.2\text{--}0.3^{\circ}\text{C}$ due to changing pill location could confound findings.

In this study the HTI telemetry system was tested in the laboratory and the instrument was protected from excessive wear as much as necessary. Under field conditions, additional precautions to protect the HTI data logger might be necessary. The HTI telemetry system has been tested under field conditions recently (4) and found to operate successfully in extreme environments.

REFERENCES

1. Baker, M. A., R. A. Stocking, and J. P. Meehan. Thermal relationship between tympanic membrane and hypothalamus in conscious cat and monkey. *J. Appl. Physiol.* 32: 739-742, 1972.
2. Brengelmann, G. L. Dilemma of body temperature measurement. In: *Man in Stressful Environments. Thermal and Work Physiology.* edited by K. Shiraki, and M. K. Yousef. Springfield, IL: Charles C. Thomas, 1987, p. 5-22.
3. Brinnet, H., and M. Cabanac. Tympanic temperature is a core temperature in humans. *J. Therm. Biol.* 14:47-53, 1989.
4. Bruckart, J. E., J. R. Licina, B. Olding, and M. Quattlebaum. Test and evaluation report of the Human Technology Ambulatory Cortemp Recorder Model COR-124. USAARL Report No. 92-19, March, 1992, Fort Rucker, Alabama 36362-5292.
5. Cabanac, M. Keeping a cool head. *News Physiol. Sci.* 1:41-44, 1986.
6. Cabanac, M., and M. Caputa. Natural selective cooling of the human brain: evidence of its occurrence and magnitude. *J. Physiol. (Lond.)* 286:255-264, 1979.
7. Eichna, L. W., A. R. Berger, B. Rader, and W. H. Becker. Comparison of intracardiac and intravascular temperatures with rectal temperatures in man. *J. Clin. Invest.* 30:353-359, 1951.
8. Gerbrandy, J., E. S. Snell, and W. I. Cranston. Oral, rectal and oesophageal temperatures in relation to central temperature control in man. *Clin. Sci.* 13:615-624, 1954.
9. Greenleaf, J. E., and B. L. Castle. External auditory canal temperature as an estimate of core temperature. *J. Appl. Physiol.* 32: 194-198, 1972.

10. Jessen, C., and G. Kuhnen. No evidence for brain stem cooling during face fanning in humans. *J. Appl. Physiol.* 72: 664-669, 1992.
11. Kolka, M. A., L. A. Stephenson, S. P. Bruttig, B. S. Cadarotte, and R. R. Gonzalez. Human thermoregulation after atropine and/or pralidoxime administration. *Aviat. Space Environ. Med.* 58: 545-549, 1987.
12. Konigsberg, E. Dispersed telemetry system for measurement of body temperatures. Final Report to Naval Supply Systems Command and Navy Clothing and Textiles March, 1990.
13. Mackay, R. S. Bio-Medical Telemetry. Second Ed., New York: John Wiley & Sons, Inc., 1970, p. 154-159.
14. Mead, J., and C. L. Bonmarito. Reliability of rectal temperatures as an index of internal body temperature. *J. Appl. Physiol.* 2:97-109, 1949.
15. Mittleman, K. D., and I. B. Mekjavic. Effect of occluded venous return on core temperature during cold water immersion. *J. Appl. Physiol.* 65:2709-2713, 1988.
16. Molnar, G. W., and R. C. Read. Studies during open-heart surgery on the special characteristics of rectal temperature. *J. Appl. Physiol.* 38:333-336, 1974.
17. Nadel, E. R. Comments on "Keeping a cool head" by M. Cabanac. *News Physiol. Sci.* 2: 33, 1987.
18. Redmond, D., J. R. Leu, K. A. Popp, S. W. Hall, C. Galinski, and P. E. Gutierrez. Medical monitoring: Assessment of physiological changes in military personnel during field studies. In: Banderet *et al.* Proceedings of a symposium--Consequence of wearing the chemical protective ensemble: illustrative assessment approaches. U.S. Army Research Institute of Environmental Medicine Technical Note 9-92, Natick, Massachusetts March, 1992 p. 31-40.
19. Redmond, D. P., J. R. Leu, K. A. Popp, P. E. Gutierrez, Jr., and S. W. Hall, Jr.

The Walter Reed temperature pill: Evaluations for clinical and investigational usage. WRAIR Technical Report Aug, 1990.

20. Rowell, L. B. Cardiovascular adjustments to thermal stress. In: Handbook of Physiology-The Cardiovascular System III, edited by J. T. Shepherd, and F. M. Abboud. Bethesda: Am. Physiol. Soc., 1983, Chapter 27, p.967-1023.
21. Sharkey, A., P. Elliott, J. M. Lipton, and A. H. Giesecke. The temperature of the air within the external auditory meatus compared with esophageal temperature during anaesthesia and surgery. *J. Therm. Biol.* 12: 11-13, 1987.
22. Shiraki, K., N. Konda, and S. Sagawa. Esophageal and tympanic temperature responses to core blood temperature changes during hyperthermia. *J. Appl. Physiol.* 61:98-102, 1986.
23. Shiraki, K., S. Sagawa, F. Tajima, A. Yokota, M. Hashimoto, and G. L. Brengelmann. Independence of brain and tympanic temperatures in an unanesthetized human. *J. Appl. Physiol.* 65: 482-486, 1988.
24. Sparling, P. B., T. K. Snow, and M. Millard-Stafford. Monitoring core temperature during exercise: ingestible sensor vs rectal thermistor (abstract). *Med. Sci. Sports Exerc.* 24:S153, 1992.
25. Wenger, C. B. More comments on "Keeping a cool head" by M. Cabanac. *News Physiol. Sci.* 2: 150, 1987.
26. Wolff, H. S. The radio pill. *New Scientist* 16:419-421, 1961.

**APPENDIX
CALIBRATIONS**

**Table 8. Telemetry Pill Identification and Calibration Correlation Coefficients
for Esophageal and Rectal Temperatures**

Volunteer	KI Pill #	HTI Pill #	T _{es} Calibration (r)	T _{re} Calibration (r)
A	70	901439	1.00	0.999
B	121	904310	0.990	0.990
C	140	901444	0.990	0.988
D	159	901426	0.990	0.989
E	48	904809	0.990	0.988
F	75	904817	0.990	0.989
G	204	904751	0.990	0.988
H	None	904753	0.990	0.989

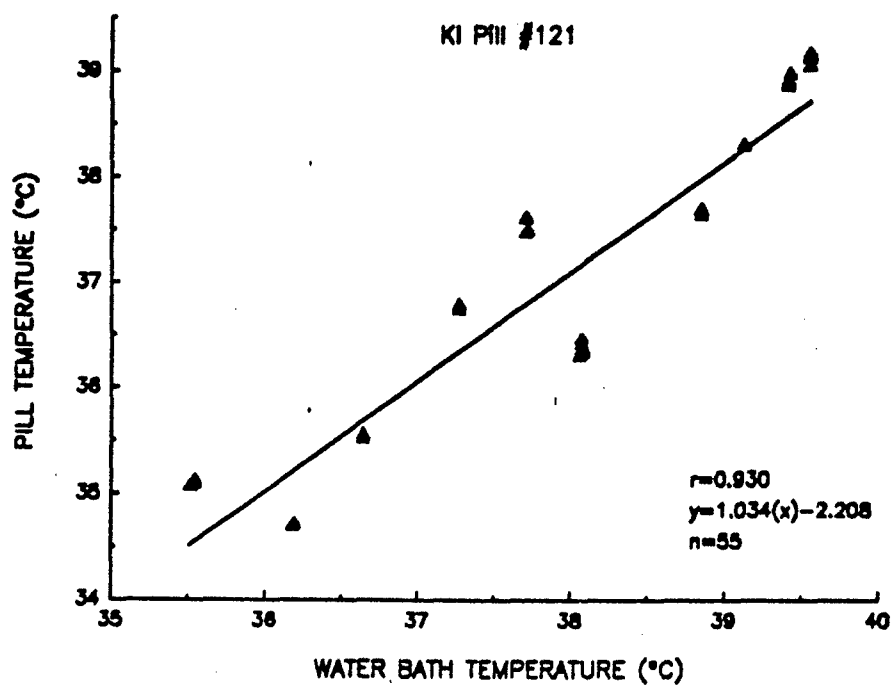
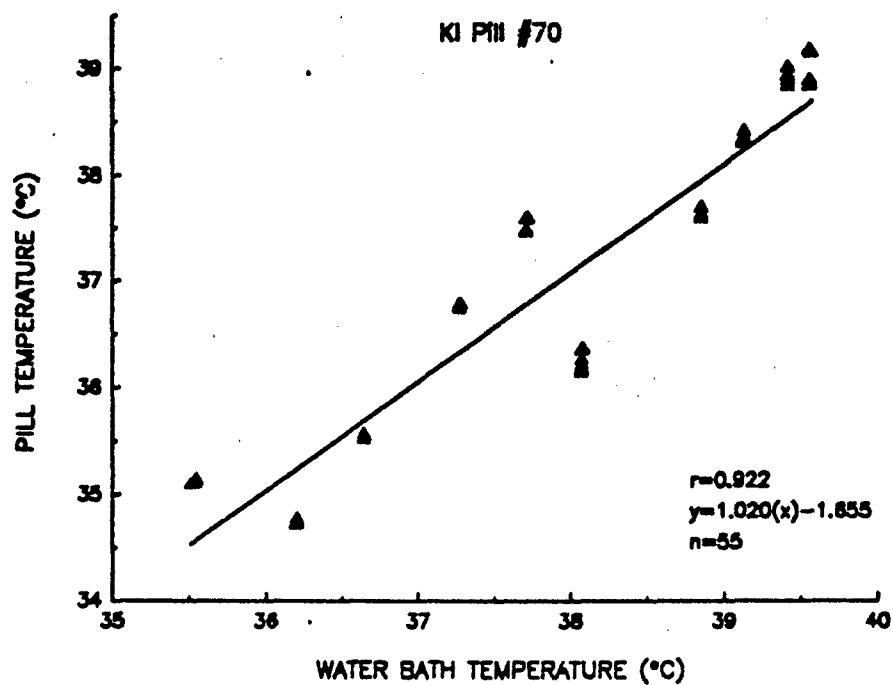


Figure 9 Correlation coefficients for KI pills ingested by Volunteers A and B.

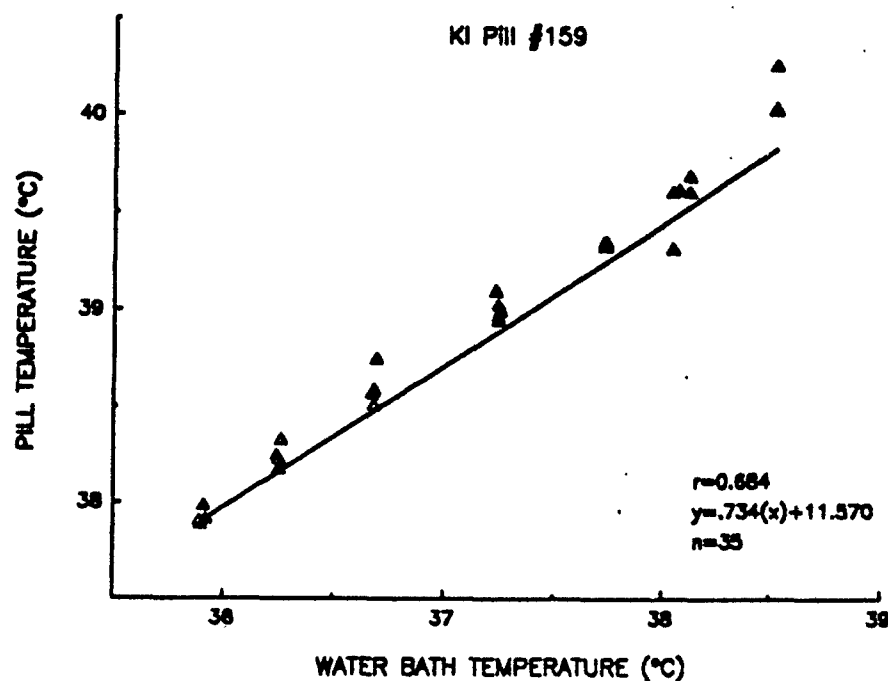
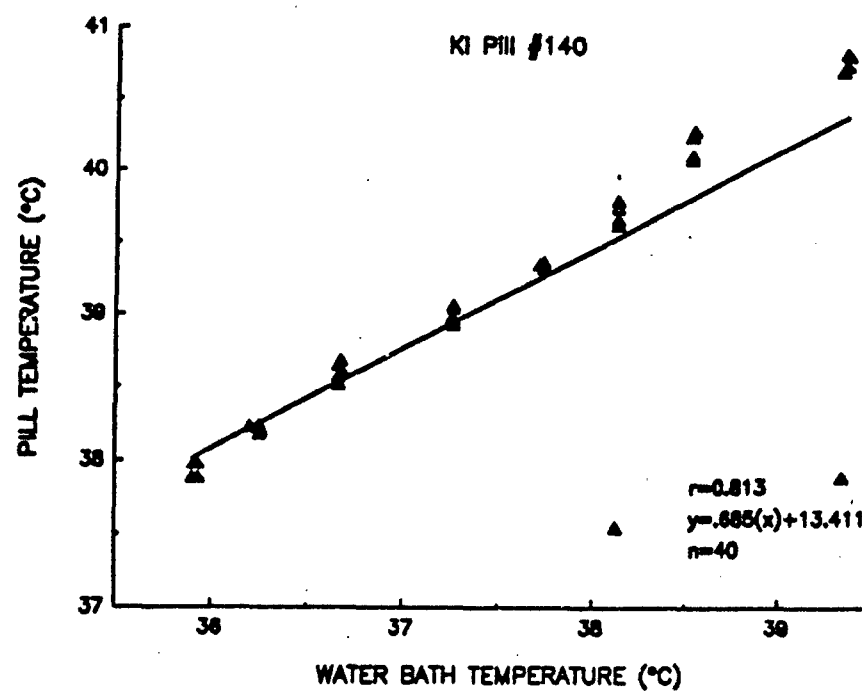


Figure 10 Correlation coefficients for KI pills ingested by Volunteers C and D.

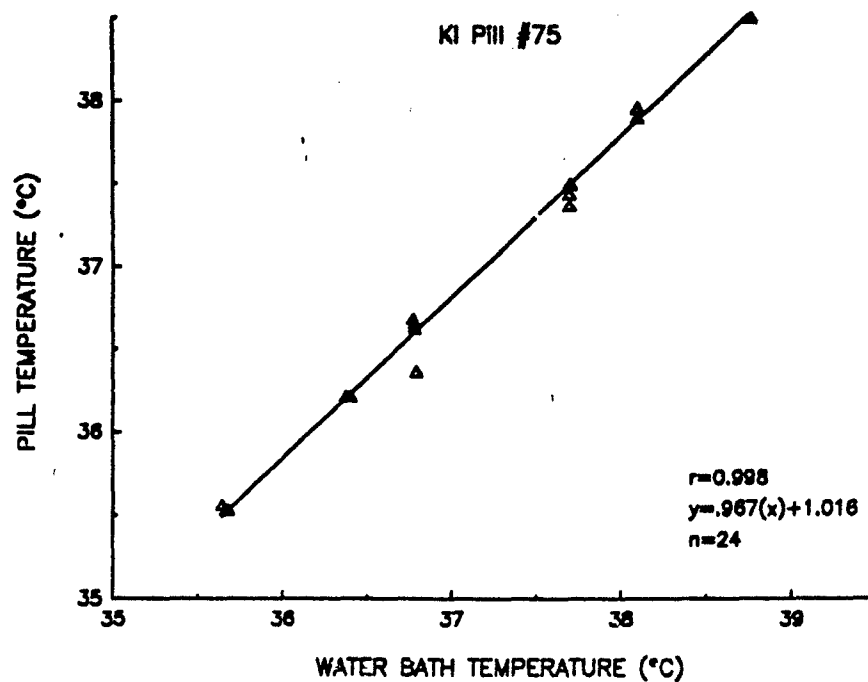
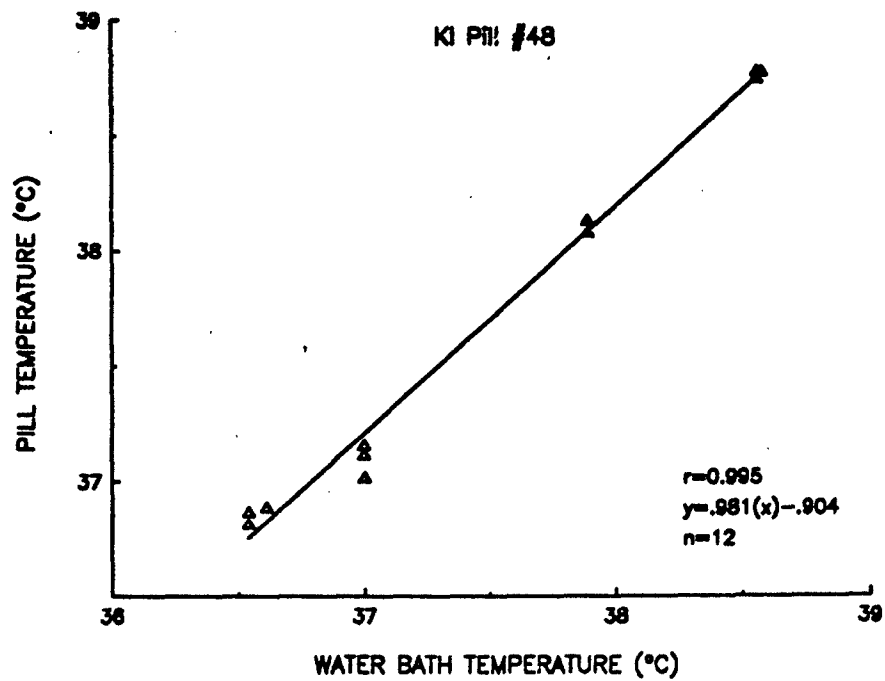


Figure 11 Correlation coefficients for KI pills ingested by Volunteers E and F.

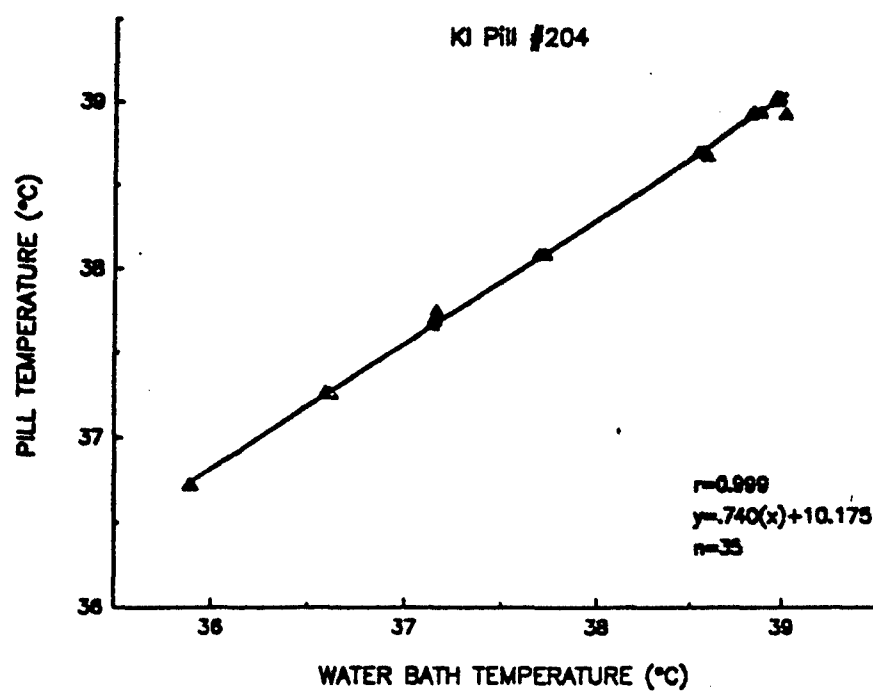


Figure 12 Correlation coefficients for KI pill ingested by Volunteer G.

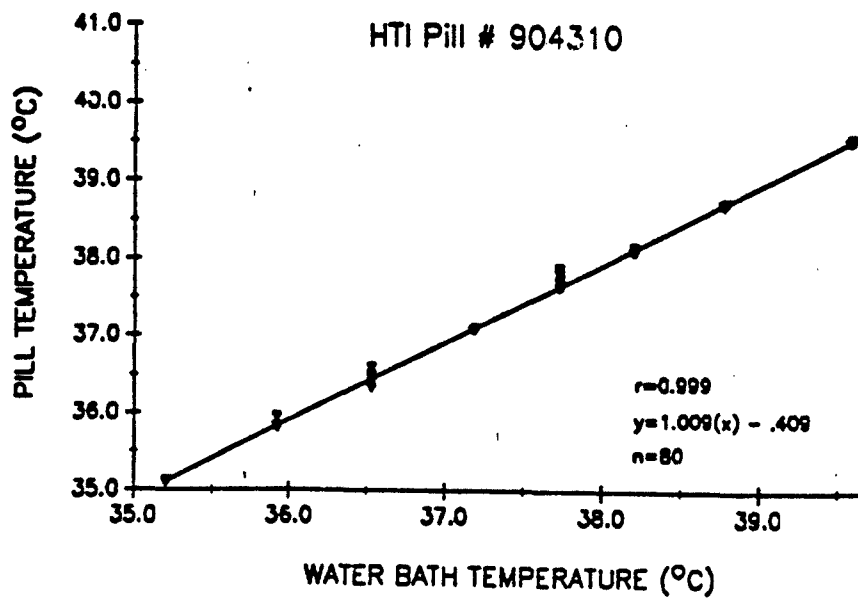
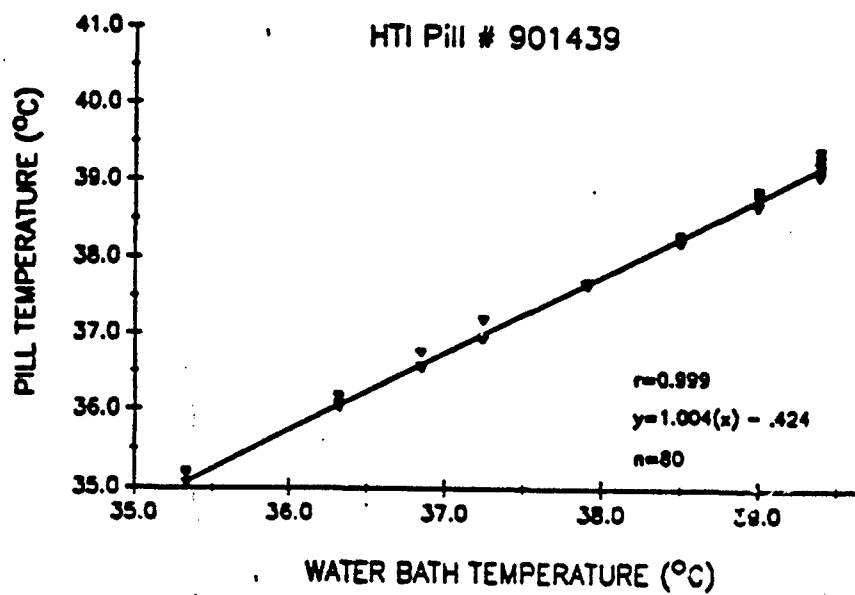


Figure 13 Correlation coefficients for HTI pills ingested by Volunteers A and B.

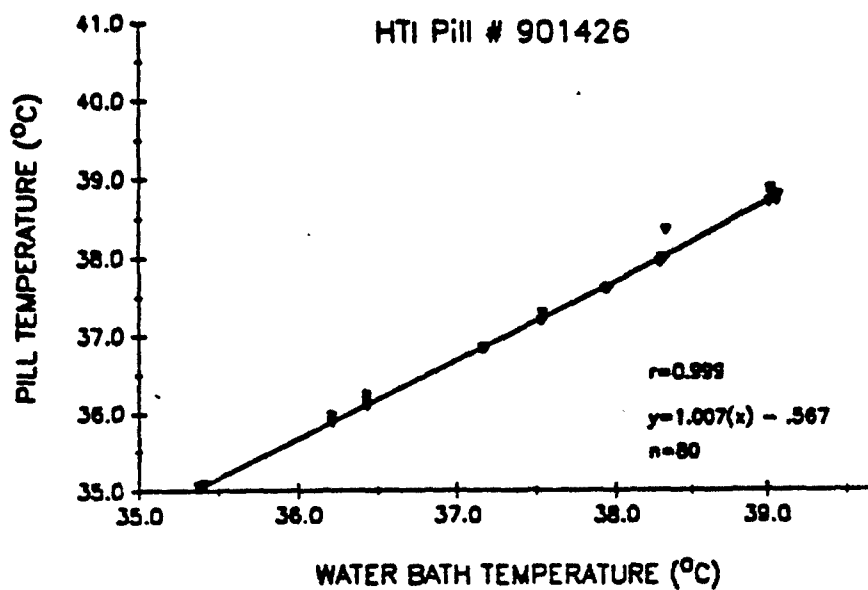
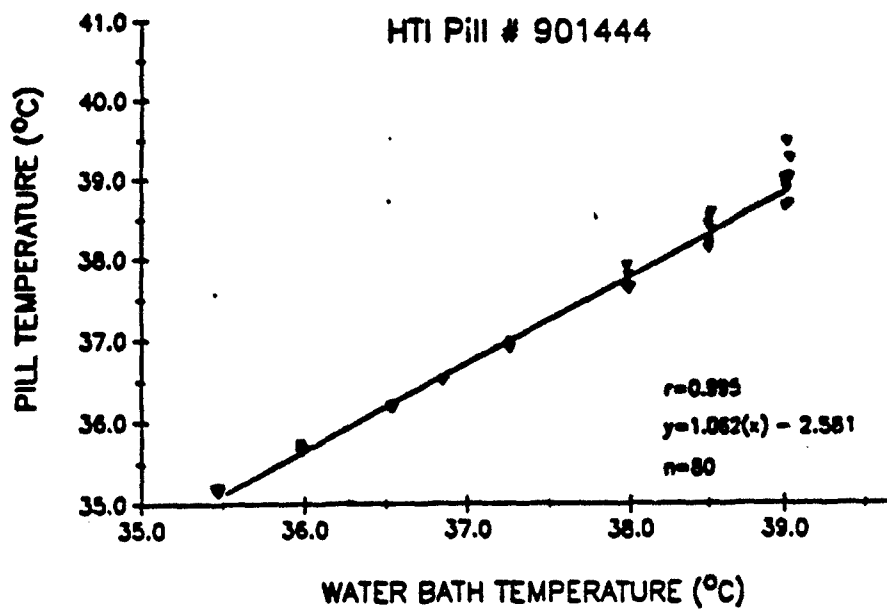


Figure 14 Correlation coefficients for HTI pills ingested by Volunteers C and D.

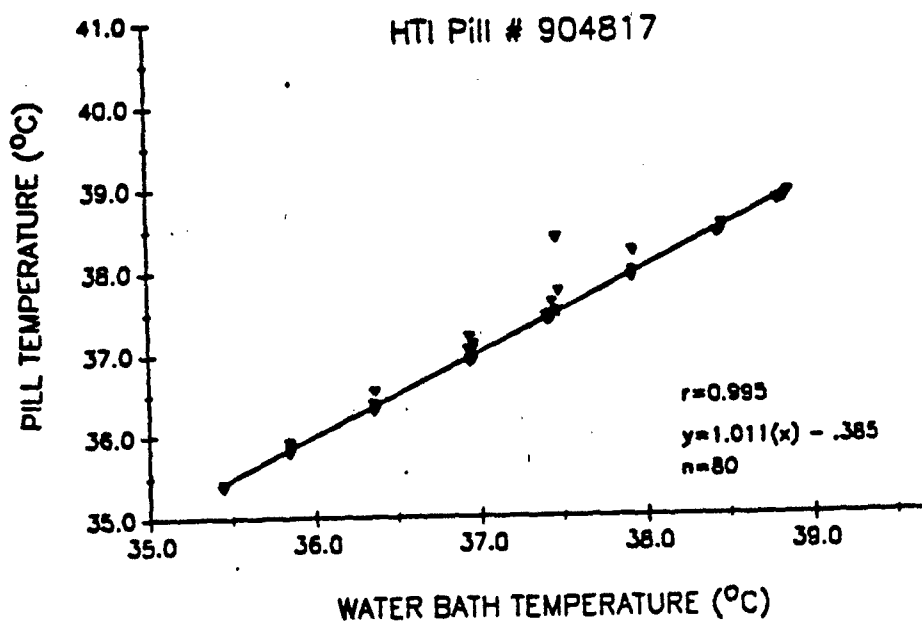
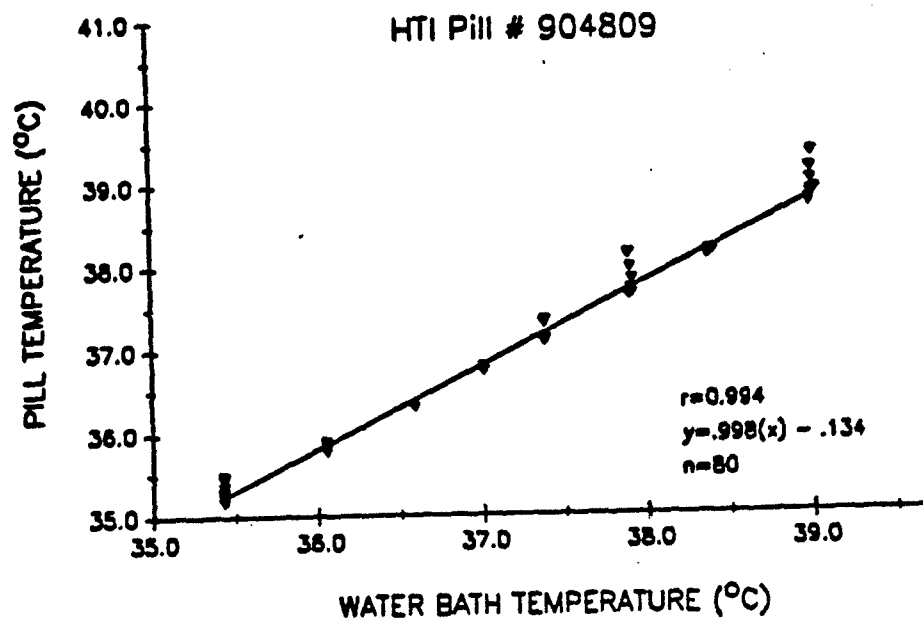


Figure 15 Correlation coefficients for HTI pills ingested by Volunteers E and F.

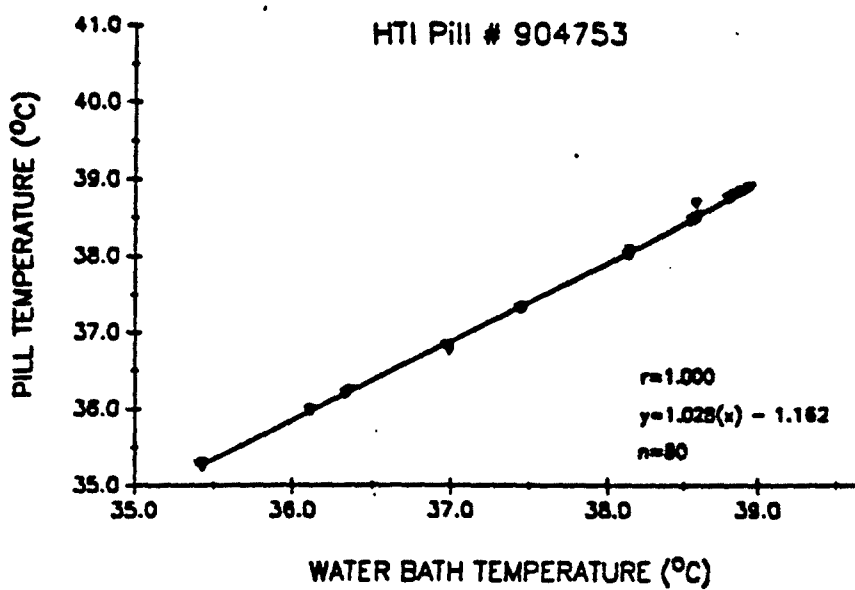
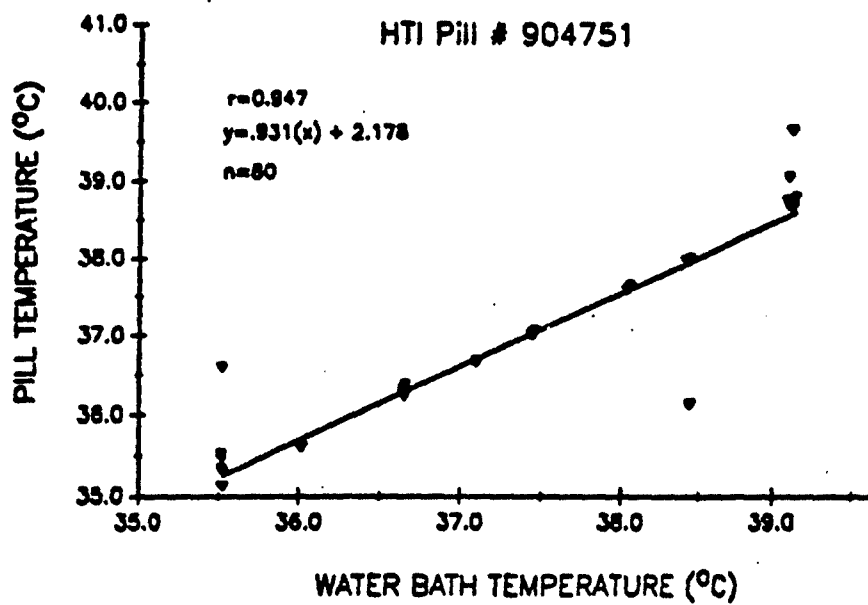


Figure 16 Correlation coefficients for HTI pills ingested by Volunteers G and H.

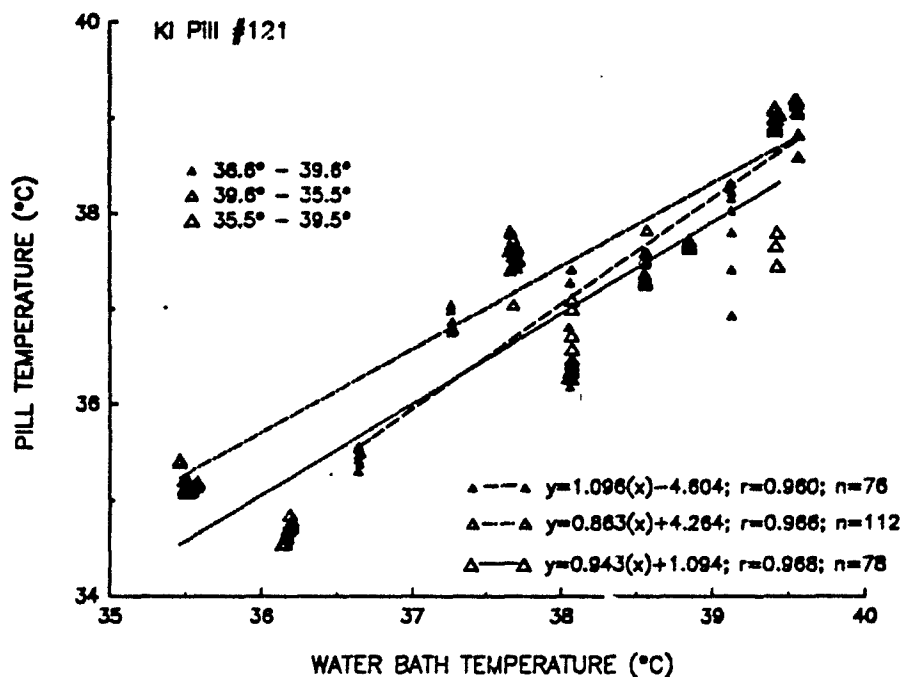
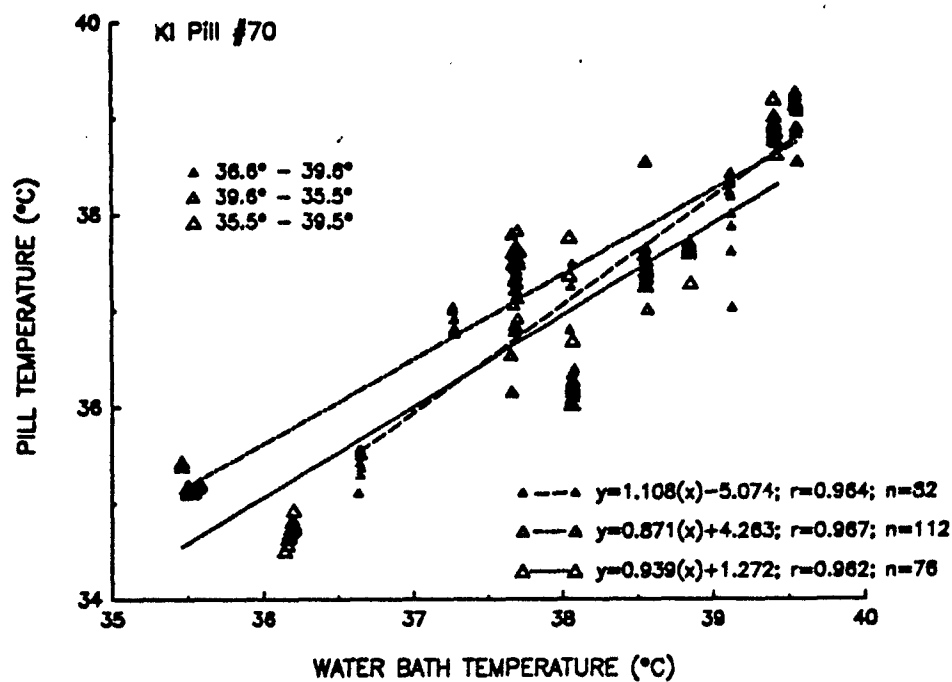


Figure 17 Hysteresis seen during calibration of KI pills ingested by Volunteers A and B.

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