

AD_____

AD-A187 730

REPORT NO T1-88

HEAT EXCHANGE THROUGH
CUTANEOUS VASODILATION
AFTER ATROPINE TREATMENT
IN TWO ENVIRONMENTS

U S ARMY RESEARCH INSTITUTE
OF
ENVIRONMENTAL MEDICINE
Natick, Massachusetts

OCTOBER 1987

DTIC
SELECTE
NOV 30 1987
S E D



Approved for public release; distribution unlimited

UNITED STATES ARMY
MEDICAL RESEARCH & DEVELOPMENT COMMAND

The findings in this report are not to be construed as an official Department of the Army position, unless so designated by other authorized documents.

DISPOSITION INSTRUCTIONS

Destroy this report when no longer needed.

Do not return to the originator.

Unclas

SECURITY CLASSIFICATION OF THIS PAGE

H187 730

REPORT DOCUMENTATION PAGE				Form Approved OMB No. 0704-0188	
1a. REPORT SECURITY CLASSIFICATION Unclassified			1b. RESTRICTIVE MARKINGS		
2a. SECURITY CLASSIFICATION AUTHORITY			3. DISTRIBUTION / AVAILABILITY OF REPORT		
2b. DECLASSIFICATION / DOWNGRADING SCHEDULE			Approved for public release; distribution is unlimited		
4. PERFORMING ORGANIZATION REPORT NUMBER(S)			5. MONITORING ORGANIZATION REPORT NUMBER(S)		
6a. NAME OF PERFORMING ORGANIZATION U.S. Army Res Inst of Env Med		6b. OFFICE SYMBOL (If applicable) SGRD-UE-MEP	7a. NAME OF MONITORING ORGANIZATION U.S. Army Research Institute of Environmental Medicine		
6c. ADDRESS (City, State, and ZIP Code) Kansas Street Natick, MA 01760-5007			7b. ADDRESS (City, State, and ZIP Code) Kansas Street Natick, MA 01760-5007		
8a. NAME OF FUNDING / SPONSORING ORGANIZATION Same as 6.a.		8b. OFFICE SYMBOL (If applicable)	9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER		
8c. ADDRESS (City, State, and ZIP Code) Same as 6.c.			10. SOURCE OF FUNDING NUMBERS		
			PROGRAM ELEMENT NO.	PROJECT NO. BM263764 D994	TASK NO. 995/DC
					WORK UNIT ACCESSION NO. 141
11. TITLE (Include Security Classification) (U) Heat exchange through cutaneous vasodilation after atropine treatment in two environments					
12. PERSONAL AUTHOR(S) Margaret A. Kolka and Lou A. Stephenson					
13a. TYPE OF REPORT Technical Report		13b. TIME COVERED FROM _____ TO _____		14. DATE OF REPORT (Year, Month, Day) October 1987	
				15. PAGE COUNT 22	
16. SUPPLEMENTARY NOTATION					
17. COSATI CODES			18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)		
FIELD	GROUP	SUB-GROUP			
			anticholinergic, dry heat exchange, sweating, thermoregulation, vasodilation		
19. ABSTRACT (Continue on reverse if necessary and identify by block number) (U) This report summarizes two tightly controlled laboratory studies in which the thermoregulatory effects of an intramuscular injection of atropine sulfate (2 mg) were compared with a placebo injection of sterile saline during two environmental conditions. Four subjects were tested in each environmental condition (22°C or 30°C) during seated cycle exercise at a moderate exercise intensity (55% $\dot{V}O_2$ peak). Esophageal temperature (T_{es}), mean weighted skin temperature (T_{sk}), and forearm sweating rate ($\dot{m}$) were continuously measured during 30 minutes of rest and 35 minutes of exercise. Skin blood flow (FBF) from the forearm was measured twice each minute by venous occlusion plethysmography. The expected decrease in whole body and local sweating rate (-60%) occurred in both environments in the atropine treated subjects. During exercise, FBF was 85% greater at 30°C and 95% greater at 22°C after treatment. The increased skin blood flow compensated for the suppression in sweating increasing dry heat loss in the atropine experiments. At 22°C, core temperature actually decreased 0.2°C in the atropine treated subjects during exercise as a result of					
20. DISTRIBUTION / AVAILABILITY OF ABSTRACT ☒ UNCLASSIFIED/UNLIMITED ☒ SAME AS RPT ☐ DTIC USERS			21. ABSTRACT SECURITY CLASSIFICATION Unclas		
22a. NAME OF RESPONSIBLE INDIVIDUAL Margaret A. Kolka, Ph.D.			22b. TELEPHONE (Include Area Code) 617-651-4849		22c. OFFICE SYMBOL SGRD-UE-MEP

DD Form 1473, JUN 86

Previous editions are obsolete.

SECURITY CLASSIFICATION OF THIS PAGE

Unclas

19. Abstract (Cont'd)

enhanced dry heat exchange. The atropine-induced vasodilation, based on regression analysis of the $FBF:T_{es}$ relationship during changing T_{es} was due to an elevated slope (27.7 vs 15.0 at 30°C; 8.1 vs 2.3 at 22°C) with an unchanged T_{es} threshold for vasodilatory onset. The T_{es} for onset of $\dot{m}_s$ was increased 0.3°C at both 22 and 30°C by the atropine treatment, with no change in the slope of the regression equation. The atropine-induced vasodilation was widespread as skin temperatures increased at all sites measured. These results suggest that the peripheral modification of cutaneous blood flow which occurs in atropine treated subjects is sufficient to alter heat exchange in both warm and cool environments.

The views, opinions, and/or findings contained in this report are those of the authors and should not be construed as an official Department of the Army position, policy or decision unless so designated by other official documentation.

Human subjects participated in these studies after giving their informed voluntary consent. Investigators adhered to AR 70-25 and USAMRDC Regulation 70-25 on Use of Volunteers in Research.

Citations of commercial organizations and trade names in this report do not constitute an official Department of the Army endorsement or approval of the products or services of these organizations.

Accession For	
NTIS GRA&I	☒
DTIC TAB	☐
Unannounced	☐
Justification	
By	
Distribution/	
Availability Codes	
Dist	Avail and/or Special
A-1	



ACKNOWLEDGEMENTS

The authors acknowledge the expertise of T.J. Doherty in data collection and statistical programming, the assistance provided by Drs. A.E. Allan, P.B. Rock, R.R. Gonzalez and S.P. Bruttig and Mr. B.S. Cadarette during the experiments.

Heat exchange through cutaneous vasodilation
after atropine treatment in two environments

Margaret A. Kolka and Lou A. Stephenson
USARIEM, Natick, MA 01760-5007

October 1987

PREFACE

The methodology and findings of these studies as described and referenced in this report have been submitted to the open literature as follows:

Kolka, M.A. and L.A. Stephenson. Cutaneous blood flow and local sweating after atropine administration. Pflugers Archiv. (in press).

Kolka, M.A., L.A. Stephenson, A.E. Allan and P.B. Rock. Atropine-induced cutaneous vasodilation decreases core temperature during exercise. J. Appl. Physiol. (in review).

Kolka, M.A., L.A. Stephenson, S.P. Bruttig, B.S. Cadarette and R.R. Gonzalez. Human thermoregulation after atropine and/or pralidoxime administration. Aviat. Space and Environmental Medicine 58:545-549, 1987.

TABLE OF CONTENTS

Preface	iii
List of Figures	v
List of Tables	vi
Abstract	vii
Introduction	1
Military Relevance	1
Minimizing Risks to Subjects	2
Methods	3
Results	6
Discussion	17
Summary	18
References	19
Distribution List	20

LIST OF FIGURES

Figure 1. Esophageal temperature plotted over time during rest, exercise and recovery at 30°C for a representative subject in both saline (control) and atropine experiments. Exercise was initiated at 30 minutes and ended at 65 minutes.

Figure 2. Forearm blood flow plotted over time during an experiment at 30°C for a representative subject in saline and atropine experiments.

Figure 3. Esophageal temperature versus time for a representative subject in saline (control) and atropine experiments at 22°C . Exercise began at time = 0.

Figure 4. Forearm blood flow over time in saline and atropine experiments for a representative subject at 22°C . Exercise began at time = 0.

Figure 5. Mean forearm blood flow graphed against esophageal temperature during the exercise transient at both 22°C and 30°C .

Figure 6. Mean forearm sweating rate plotted against esophageal temperature during the exercise transient at 22°C and 30°C .

LIST OF TABLES

Table 1. Characteristics of the eight subjects used in the two experimental protocols. The mean ($\bar{X}$) and standard deviation (sd) of each parameter are also presented.

Table 2. The mean ($\pm$ sd) temperature parameters for subjects 1 through 4 at rest and during moderate exercise in a 30°C environment.

Table 3. The mean ($\pm$ sd) temperature parameters for subjects 5 through 8 at rest and during moderate exercise in a 22°C environment.

Table 4. The individual slopes for arm sweating: T_{es} ($\text{mg} \cdot \text{cm}^{-1} \cdot \text{min}^{-2} \cdot ^\circ\text{C}^{-1}$) and forearm blood flow: T_{es} ($\text{ml} \cdot 100\text{ml}^{-1} \cdot \text{min}^{-1} \cdot ^\circ\text{C}^{-1}$) and esophageal temperature thresholds for arm sweating and forearm vasodilation ($^\circ\text{C}$) for subjects 1 through 4 during the exercise transient at 30°C. The mean ($\bar{X}$) and standard deviation (sd) of each parameter are also presented.

Table 5. The individual slopes for arm sweating: T_{es} ($\text{mg} \cdot \text{cm}^{-2} \cdot \text{min}^{-1} \cdot ^\circ\text{C}^{-1}$) and forearm blood flow: T_{es} ($\text{ml} \cdot 100\text{ml}^{-1} \cdot \text{min}^{-1} \cdot ^\circ\text{C}^{-1}$) and esophageal temperature thresholds for arm sweating and forearm vasodilation ($^\circ\text{C}$) for subjects 5 through 8 during the exercise transient at 20°C.

ABSTRACT

This report summarizes two tightly controlled laboratory studies in which the thermoregulatory effects of an intramuscular injection of atropine sulfate (2 mg) were compared with a placebo injection of sterile saline during two environmental conditions. Four subjects were tested in each environmental condition (22°C or 30°C) during seated cycle exercise at a moderate exercise intensity (55% $\dot{V}_{O_2}$ peak). Esophageal temperature (T_{es}), mean weighted skin temperature ($\bar{T}_{sk}$), and forearm sweating rate ($\dot{m}_s$) were continuously measured during 30 minutes of rest and 35 minutes of exercise. Skin blood flow (FBF) from the forearm was measured twice each minute by venous occlusion plethysmography. The expected decrease in whole body and local sweating rate (-60%) occurred in both environments in the atropine treated subjects. During exercise, FBF was 85% greater at 30°C and 95% greater at 22°C after atropine treatment. The increased skin blood flow compensated for the suppression in sweating increasing dry heat loss in the atropine experiments. At 22°C, core temperature actually decreased 0.2°C in the atropine treated subjects during exercise as a result of enhanced dry heat exchange. The atropine-induced vasodilation, based on regression analysis of the FBF: T_{es} relationship during changing T_{es} was due to an elevated slope (27.7 vs 15.0 at 30°C; 8.8 vs 2.3 at 22°C) with an unchanged T_{es} threshold for vasodilatory onset. The T_{es} for onset of $\dot{m}_s$ was increased 0.3°C at both 22 and 30°C by the atropine treatment, with no change in the slope of the regression equation. The atropine-induced vasodilation was widespread as skin temperatures increased at all sites measured. These results suggest that the peripheral modification of cutaneous blood flow which occurs in atropine treated subjects is sufficient to alter heat exchange in both warm and cool environments.

INTRODUCTION

The anticholinergic effect of systemic atropine treatment on the eccrine sweat gland is well known and the inhibition of sweat secretion during exercise and heat stress is well documented in the scientific literature (1, 2, 7, 8, 10, 11, 13). We have consistently observed a 45 to 65% decrease in evaporative heat loss through the inhibition of sweat secretion during exercise in the heat following systemic atropine treatment (7, 8, 10, 11, 13).

The intramuscular injection of small doses of atropine sulfate (2 mg) is associated with widespread cutaneous vasodilation appearing thirty to forty-five minutes after treatment (10, 11). We have reported a decreased dry heat gain in hot environments associated with this increased cutaneous vasodilation (7,8). These observations indicated that atropine altered the thermal gradient from the body surface to the environment and implied that excessive dry heat loss would occur in a cooler environment. In the current report, the cutaneous blood flow response was estimated by venous occlusion plethysmography, rather than calculated as changes in dry heat loss from the heat balance equation. Particular attention was given to the change in cutaneous perfusion during times when core temperature was changing in order to evaluate the vasomotor effector response.

Military Relevance

Current U.S. Army doctrine instructs soldiers to self-administer atropine when exposed to organophosphate poisoning; however, it is possible that atropine could be used in the absence of a nerve agent challenge. In our past evaluations, we have consistently shown atropine was a cutaneous vasodilator which significantly altered heat

exchange in warm to hot environments. Recently, the combined challenge of atropine and pralidoxime was evaluated with similar vasodilatory effects as atropine administered singularly. Consequently, the problems associated with heat exchange in warm and cool environments after antidote administration can be adequately addressed by using atropine alone and eliminating the subjects' exposure to any more risk than absolutely necessary (i.e., treatment with pralidoxime also). The regulation of body temperature in a cool environment may be compromised with the enhanced heat loss associated with atropine-induced cutaneous vasodilation. This evaluation will provide information which will aid our predictive efforts on soldier performance following pre-treatment or treatment drug administration.

Minimizing risks to subjects

With the exception of the administration of atropine, all of the procedures in these studies fell within the framework, restrictions and safety limitations of the Type Protocols for Human Research Studies Thermal Stress and Exercise and Physical Training March 1984.¹ To minimize risks associated with atropine, volunteers were given medical examinations prior to acceptance as subjects. No one with a history of asthma, glaucoma or intraocular injury, peptic ulcer, or adverse reactions to previous atropine administration (as in the form of eye drops, antispasmodics or decongestants) was used as a subject. Fatalities from atropine alone are rare; the lethal dose is unknown (it may be as low as 65 mg for some individuals, or greater than 1000 mg for others). Central nervous system manifestations (emotional instability, anxiety,

1./ Approved 5 March 1984. The type protocol provides information and explanations about conditions, standards and safeguards, in order to serve as an encompassing framework for specific in-house studies in its general subject area. It is to be used as a reference to facilitate the understanding and review of specific study protocols which conform to its provisions, and thus do not exceed the degree of risk, and safety limits herein stipulated (reference para 19, USAMRDC Reg 70-25, 27 April 1981).

hallucinations) are usually mild or not seen with less than a 5 mg dose. Fatigue, headache, lightheadedness and non-coordinated movement can be expected in at least 25% of subjects receiving a 2 mg dose (4).

METHODS

Eight healthy male subjects were evaluated during seated cycle exercise in one of two environmental temperatures ($n=4$ per environment). All experimental procedures were identical with two exceptions; subjects were exposed to either 22°C or 30°C (ambient water vapor pressure = 1.0 kPa in both environments), and within a specific environment the subjects were studied on one occasion after 2 mg atropine sulfate (Elkins-Sinn, Cherry Hill, NJ) was injected into the vastus lateralis and once following a sterile saline placebo, injected in an identical manner. Subjects were not informed of the drug being injected and treatment order (drug or placebo) was counterbalanced. All procedures had been approved by the local human review committee.

The subject reported to the environmental chamber having not eaten for the previous twelve hours. He was weighed and then sat in a chair placed behind the pedals of a cycle ergometer, such that when pedalling his legs would be parallel to the floor. He swallowed an esophageal catheter containing a copper-constantan thermocouple and adjusted it to heart level for the measurement of esophageal temperature (T_{es}). Eight surface thermocouples (copper-constantan) were placed on the skin to estimate a mean weighted (12) skin temperature ($\bar{T}_{sk}$). Local sweating rate ($\dot{m}_s$) was measured from the left forearm with a small dew-point sensor (5, 9). Skin blood flow (FBF) was measured from the right forearm by venous occlusion plethysmography as described by Whitney (14) and modified by Hokanson (6). Whole

body sweating ($\dot{M}_s$) was determined from body weight before and after the exercise bout. Heart rate was measured from the EKG, and mean arterial pressure (MAP) was measured by an auscultatory technique and calculated as 1/3 systolic pressure and 2/3 diastolic pressure.

At this point, the physician injected the atropine or the sterile saline. On-line data collection began. Metabolic heat production was evaluated from oxygen consumption measurements made during the 35 minute rest period and during exercise. Exercise began at 55% of each subjects previously determined $\dot{V}_{O_2}$ peak and continued for 30 minutes.

The experiments at 30°C were completed on subjects 1-4 in November of 1985 and were followed by the 22°C exposures in February of 1987 for subjects 5-8 (Table 1). The data were analyzed within a given ambient temperature by analysis of variance with repeated measures.

TABLE 1. SUBJECT CHARACTERISTICS

	AGE (yr)	Ht (cm)	Wt (kg)	SA (m ²)	$\dot{V}_{O_2}$ peak ¹ (l·min ⁻¹)	Body Fat ² (%)
1	22	185.4	88.3	2.13	4.11	16.8
2	20	177.8	67.0	1.79	3.47	13.4
3	19	170.2	87.0	2.06	3.97	23.1
4	24	181.0	82.8	2.12	3.28	21.4
5	19	180.3	77.1	2.00	3.83	9.7
6	24	172.7	78.9	1.93	3.81	17.0
7	18	188.0	64.0	1.87	3.29	13.5
8	18	182.9	66.5	1.87	3.76	13.4
$\bar{x}$	20.5	179.8	76.5	1.97	3.69	16.0
sd	(2.5)	(6.1)	(9.6)	(0.13)	(0.31)	(4.5)

¹ Measured while seated behind the pedals of a cycle ergometer

² Hydrostatic weighing

RESULTS

The thermoregulatory and cardiovascular responses of the subjects at rest and during exercise in either 30°C or 22°C are presented in Tables 2 and 3. Heart rate was significantly increased during rest in 22°C and exercise in both environments ($p < 0.05$) after atropine administration. During exercise in the atropine treated subjects, sweating was significantly depressed ($p < 0.05$) and forearm blood flow was enhanced ($p < 0.05$) in both environments. Specifically, at 30°C, both forearm sweating and whole body sweating were reduced 60%. Forearm blood flow increased 86% after atropine during steady-state exercise resulting in a 2.1°C ($p < 0.05$) increase in $\bar{T}_{sk}$ compared to the control experiment. T_{es} was significantly increased during steady-state exercise after atropine administration ($p < 0.05$). A typical response for esophageal temperature and forearm blood flow during rest, exercise and recovery from exercise at 30°C is shown in Figures 1 and 2 for a representative subject. In the cooler environment, body temperature actually decreased during exercise in the atropine experiment resulting from the increased dry heat loss, as shown in Figure 3 for a representative subject. The forearm blood flow response for a representative subject is presented in Figure 4 during rest and exercise at 20°C. Forearm blood flow continued to increase throughout the exercise bout after atropine administration, but during the control experiment, FBF stabilized during steady-state exercise. In the experiments conducted at 20°C, whole body sweating was decreased an average of 57% and local (forearm) sweating was depressed an average of 68%. The 98% increase in forearm blood flow seen during steady-state exercise in 20°C in the atropine experiments (Table 3) resulted in a significantly higher $\bar{T}_{sk}$ (1.55°C, $p < 0.05$).

TABLE 2. MEAN ($\pm$ sd) TEMPERATURE PARAMETERS FOR SUBJECTS 1-4 AT REST AND DURING EXERCISE AT 30°C.

	T_{es} (°C)	$\bar{T}_{sk}$ (°C)	FBF (ml·100ml ⁻¹ ·min ⁻¹)	$\dot{m}_s$ (mg·cm ⁻² ·min ⁻¹)	HR (b·min ⁻¹)	MAP ¹ (torr)	$\dot{M}_s$ (g·min ⁻¹)
REST							
Saline	36.67 (0.15)	34.04 (0.28)	1.8 (0.8)	0.16 (0.06)	67 (8)	92 (11)	—
Atropine	36.61 (0.18)	34.06 (0.30)	1.8 (0.5)	0.15 (0.04)	59 (13)	83 (5)	—
EXERCISE							
Saline	37.37 (0.15)	33.62 (0.51)	9.2 (0.4)	1.08 (0.30)	130 (5)	103 (3)	13.2 (3.7)
Atropine	37.78* (0.18)	35.72* (0.49)	17.1* (5.8)	0.43* (0.14)	158* (4)	101 (13)	5.5* (1.4)

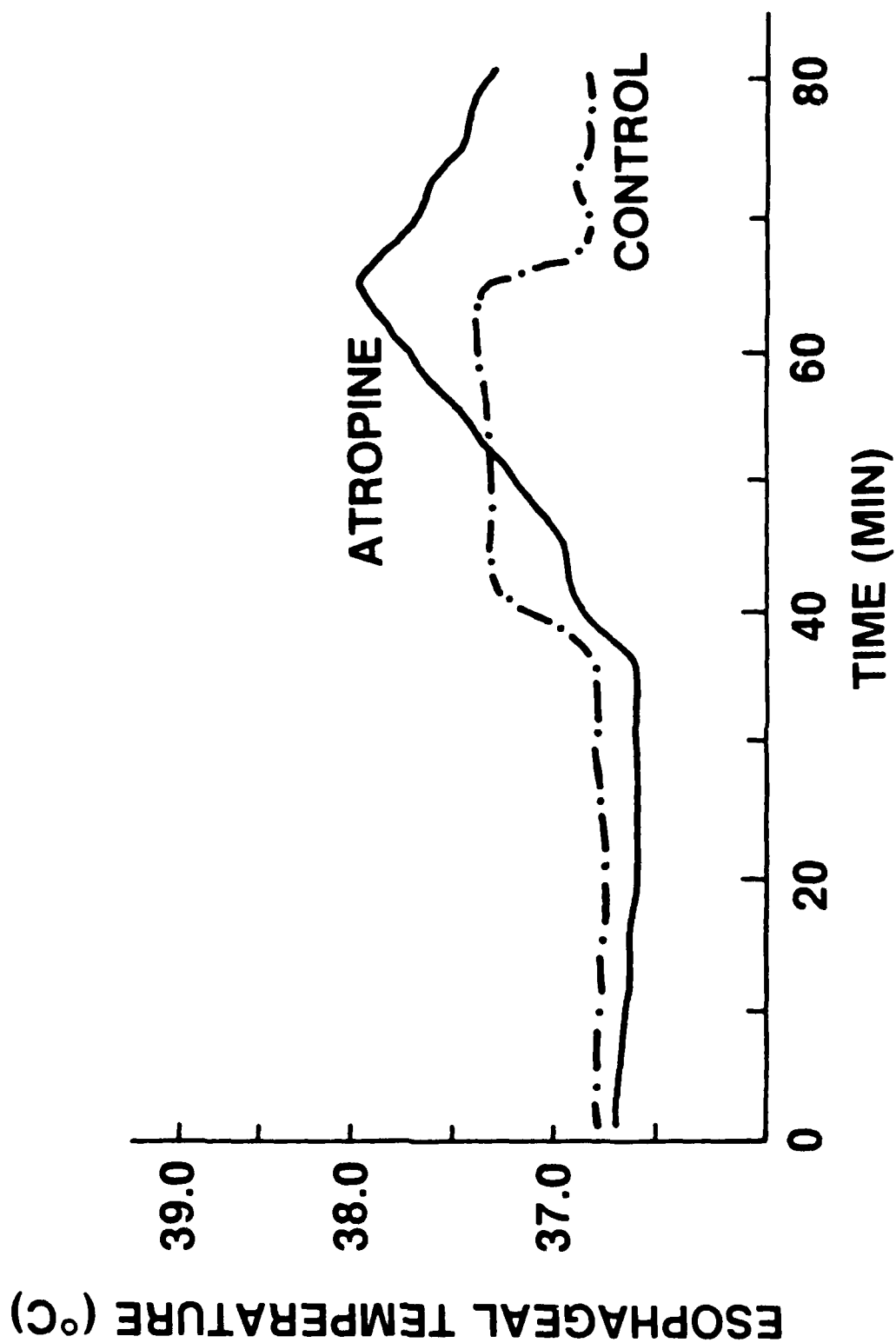
¹ MAP, mean arterial pressure

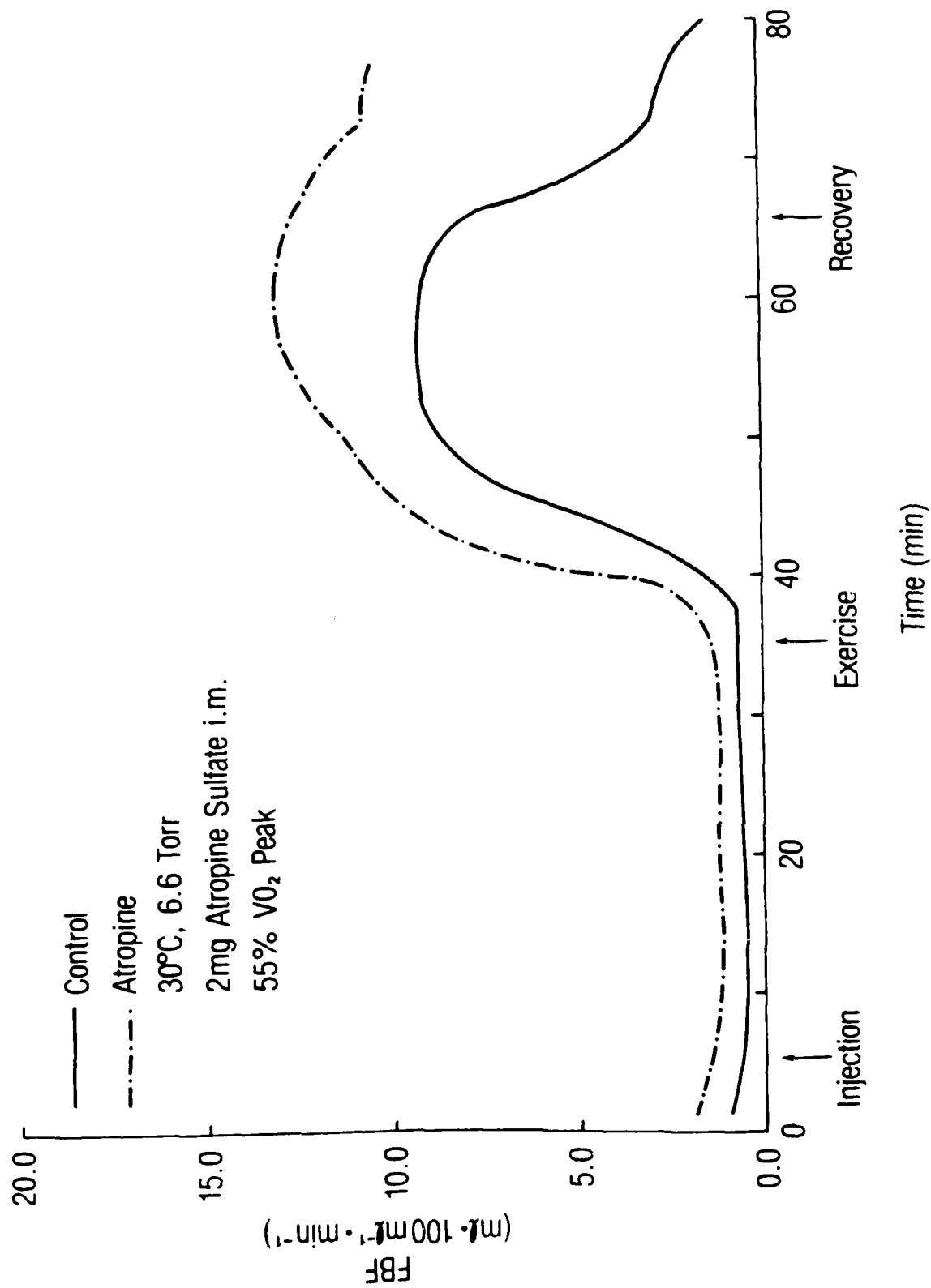
* $p < 0.05$, different from saline

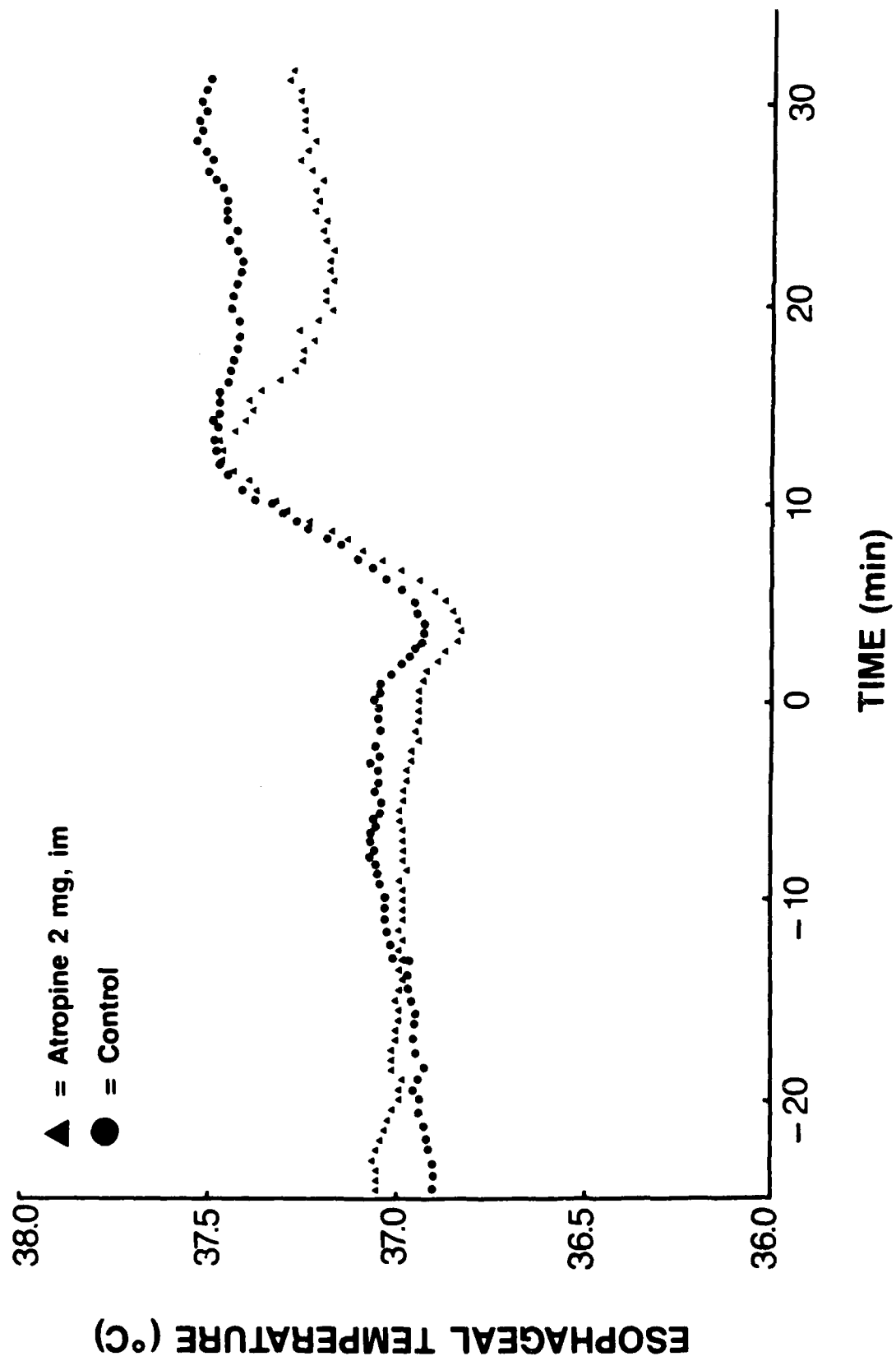
TABLE 3. MEAN ($\pm$ sd) TEMPERATURE PARAMETERS FOR SUBJECTS 5-8 AT REST AND DURING EXERCISE AT 22°C.

	T_{es} (°C)	$\bar{T}_{sk}$ (°C)	FBF (ml·100ml ⁻¹ ·min ⁻¹)	$\dot{m}_s$ (mg·cm ⁻² ·min ⁻¹)	HR (b·min ⁻¹)	$\dot{M}_s$ (g·min ⁻¹)
REST						
Saline	36.79 (0.20)	30.29 (0.51)	0.4 (0.1)	0.07 (0.01)	69 (18)	—
Atropine	36.81 (0.15)	30.14 (0.31)	0.4 (0.1)	0.07 (0.01)	86* (18)	—
EXERCISE						
Saline	37.36 (0.10)	31.01 (0.33)	4.1 (3.3)	0.77 (0.23)	138 (16)	9.4 (3.3)
Atropine	37.26 (0.22)	32.56* (0.87)	8.1* (3.6)	0.25 (0.17)	162* (13)	4.0* (2.7)

* $p < 0.05$, different from saline







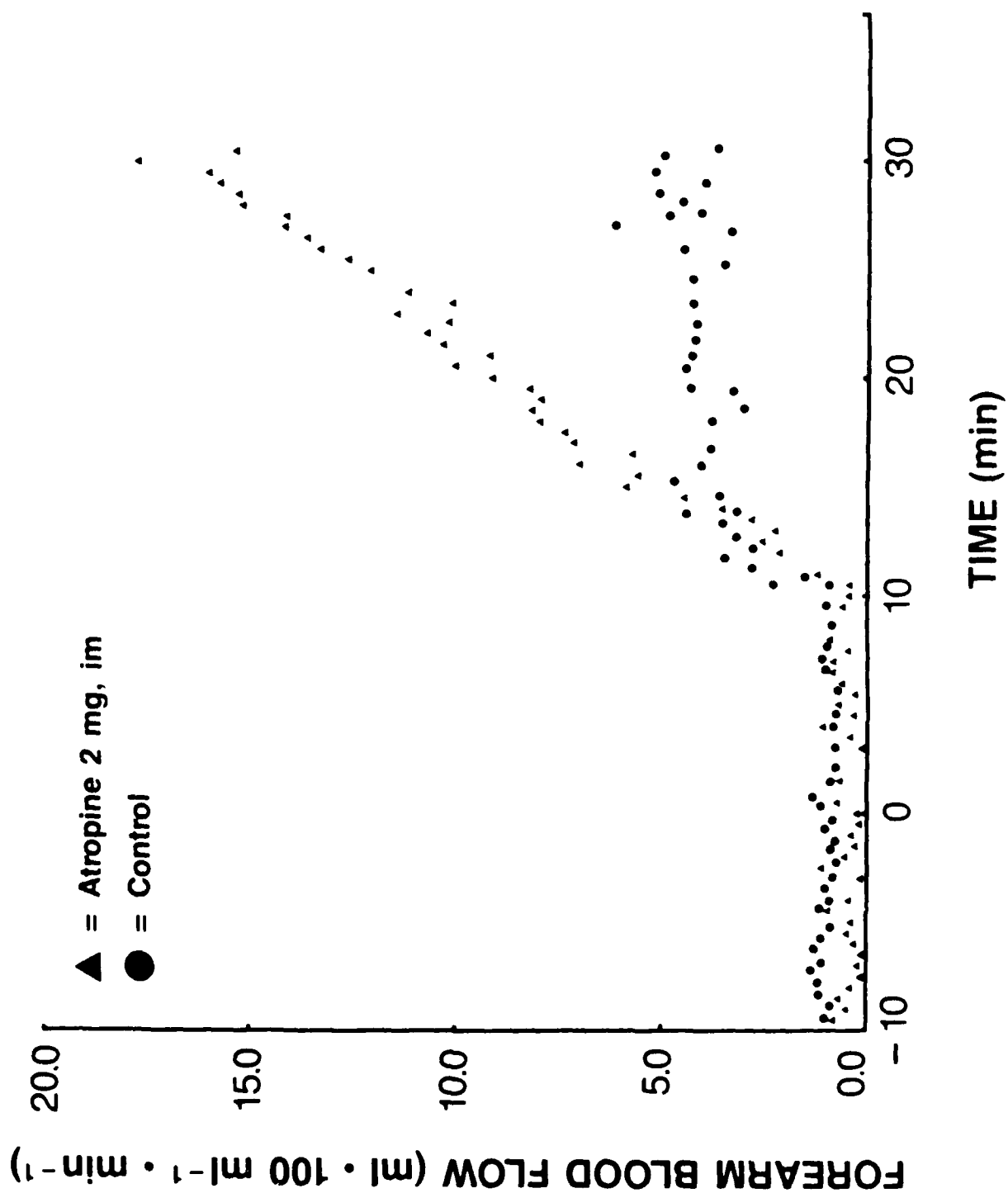


TABLE 4. INDIVIDUAL SLOPE AND T_{es} THRESHOLD ($^{\circ}\text{C}$) FOR ARM SWEATING ($\text{mg}\cdot\text{cm}^{-2}\cdot\text{min}^{-1}\cdot^{\circ}\text{C}^{-1}$) AND FOREARM BLOOD FLOW ($\text{ml}\cdot 100\text{ml}^{-1}\cdot\text{min}^{-1}\cdot^{\circ}\text{C}^{-1}$) FOR SUBJECTS 1-4 DURING THE EXERCISE TRANSIENT AT 30°C .

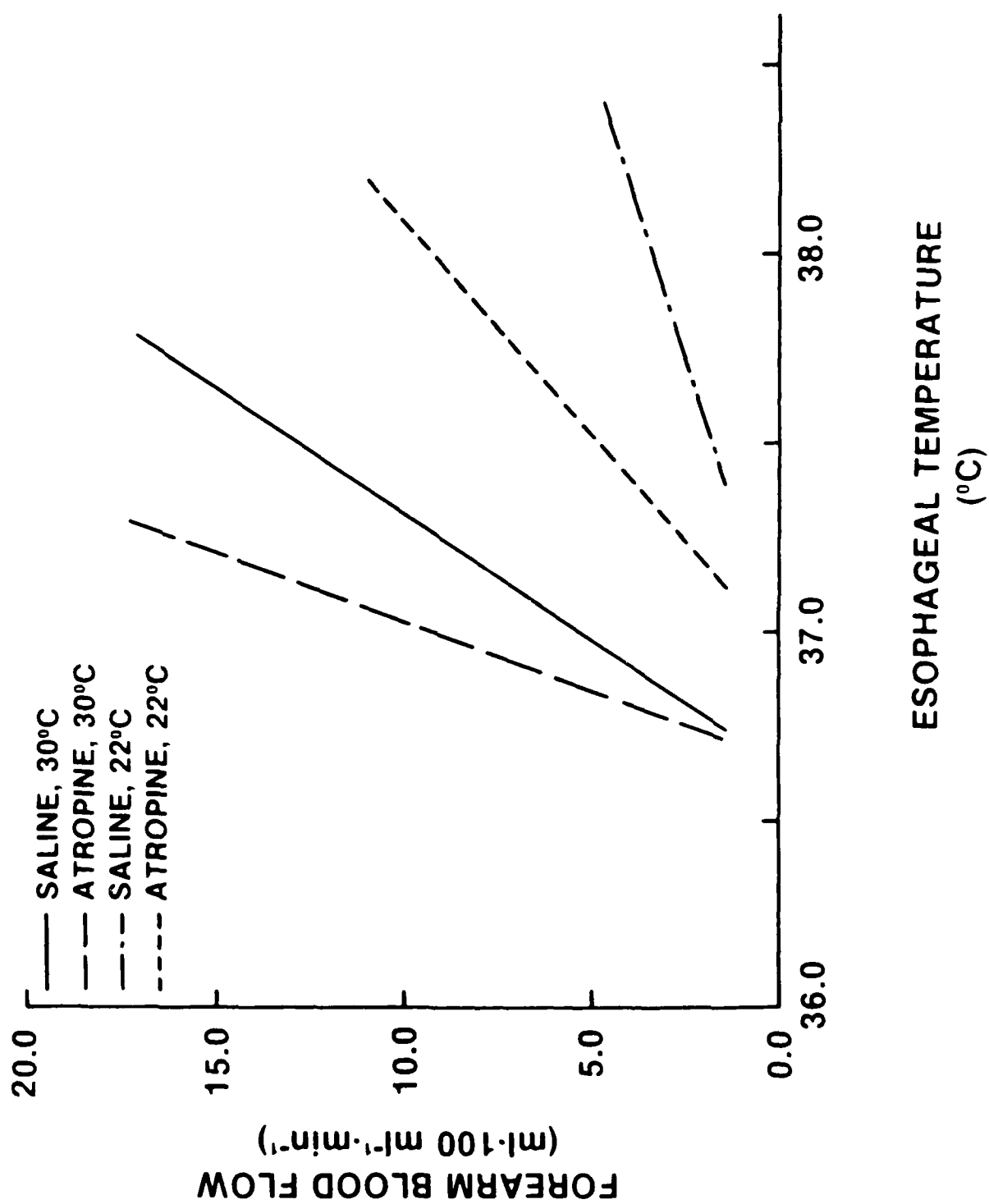
	$\dot{m}_s$ slope	$\dot{m}_s$ threshold	FBF slope	FBF threshold
SALINE				
1	1.31	36.78	18.90	36.92
2	0.82	36.37	7.17	36.14
3	0.84	36.26	13.00	36.86
4	1.38	36.54	21.00	37.09
$\bar{x}$	1.09	36.49	15.02	36.75
sd	(0.30)	(0.23)	(6.23)	(0.42)
ATROPINE				
1	1.18	36.81	25.39	36.67
2	0.82	36.51	26.50	36.54
3	0.75	36.85	26.90	36.80
4	0.45	37.06	32.10	36.90
$\bar{x}$	0.80	36.81*	27.72*	36.73
sd	(0.30)	(0.23)	(2.99)	(0.16)

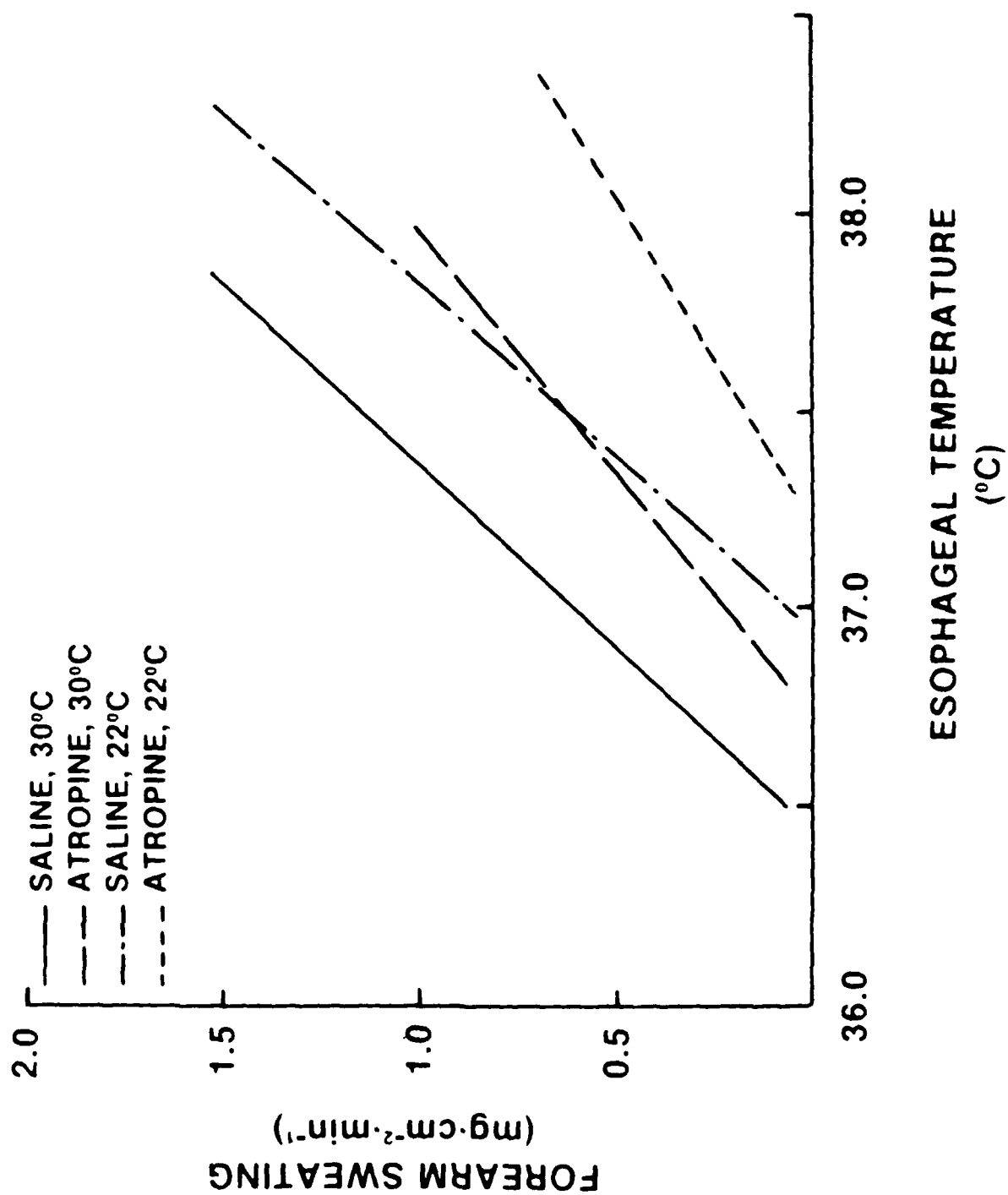
* $p < 0.05$, different from saline

TABLE 5. INDIVIDUAL SLOPE AND T_{es} THRESHOLD ($^{\circ}\text{C}$) FOR ARM SWEATING ($\text{mg}\cdot\text{cm}^{-2}\cdot\text{min}^{-1}\cdot^{\circ}\text{C}^{-1}$) AND FOREARM BLOOD FLOW ($\text{ml}\cdot 100\text{ml}^{-1}\cdot\text{min}^{-1}\cdot^{\circ}\text{C}^{-1}$) FOR SUBJECTS 5-8 DURING THE EXERCISE TRANSIENT AT 22°C .

	$\dot{m}_s$ slope	$\dot{m}_s$ threshold	FBF slope	FBF threshold
SALINE				
5	0.94	36.8	1.03	37.3
6	1.25	36.8	1.92	37.2
7	1.09	37.0	2.90	37.5
8	1.25	37.2	3.33	37.4
$\bar{x}$	1.13	37.0	2.30	37.4
sd	(0.15)	(0.19)	(1.03)	(0.13)
ATROPINE				
5	0.62	37.1	7.25	37.2
6	1.26	37.1	8.19	37.1
7	0.46	37.3	10.23	37.3
8	0.25	37.5	9.36	36.6
$\bar{x}$	0.65	37.3*	8.76*	37.1
sd	(0.43)	(0.19)	(1.31)	(0.31)

* $p < 0.05$, different from saline





An evaluation of how atropine affected thermoregulatory control is presented as the T_{es} threshold for sweating or vasodilatory onset and the slope of the linear regression equation of sweating to T_{es} and FBF to T_{es} in Tables 4 and 5 for the 30°C and 22°C environments, respectively. The similar responses of all subjects in atropine experiments, independent of environmental temperature is evident in this presentation. Specifically, there was a latency in the onset of forearm sweating compared to the placebo experiments which was coupled with a tendency for the suppression of the sensitivity of the relationship. Conversely, the onset of cutaneous blood flow occurred at a lower temperature with an increased sensitivity. Hence in the 30°C environment, this enhanced cutaneous perfusion increased surface temperature and greater dry heat exchange occurred compared to the placebo experiments. At 20°C, this increased cutaneous perfusion greatly increases heat loss from the skin surface resulting in decreased core temperature even in the face of a relatively high endogenous heat production (~ 700 W or $390 \text{ W} \cdot \text{m}^{-2}$). The control of forearm blood flow during increasing esophageal temperature is shown in Figure 5 as the mean regression line for all of the subjects tested in a specific environment. For each pair of regression lines (either 30 or 22°C), treatment with atropine resulted in an increase in the slope or sensitivity of the regression line. These changes result in the increased forearm blood flow during steady-state exercise as shown in Tables 2 and 3. No change in the esophageal threshold for the onset of forearm vasodilation was apparent in the atropine experiments. In a similar manner the control of forearm sweating to changing esophageal temperature is shown in Figure 6. Again, the regression lines for each pair of experiments for a specific environment represent the mean response for the subjects. The consistent response after atropine treatment is a higher core temperature threshold for the initiation of sweating with no change in the slope or sensitivity of the

regression equation. Care must be taken to not rigorously compare the results from the two environments as the same subjects were not tested at both 22°C and 30°C. However, the response to atropine was similar in both environments.

DISCUSSION

The systemic administration of atropine sulfate in a volume equal to that contained in one field applicable auto-injector is sufficient to alter heat exchange in soldiers performing moderate exercise in a warm and in a cool environment. The self-administration of this anti-cholinergic agent without exposure to a nerve agent challenge may occur in field situations due to fear or confusion. A series of studies at numerous levels of environmental stress or thermoregulatory strain have been conducted by USARIEM to evaluate the effectiveness of a soldier's performance following this inappropriate or accidental atropine administration (7, 8, 10, 11, 13).

The current study has extended our observations of the effects of atropine on thermoregulation by including the direct assessment of the vasomotor and local sudomotor responses to the whole body sweating responses. During exercise in a 30°C environment, the depressed sweat secretion and subsequent decreased evaporative heat loss would have led to a large heat storage in the subjects thereby limiting exercise at that intensity. However, the increased blood flow to the skin surface increased the surface temperature and widened the thermal gradient between the skin and the ambient air providing for greatly enhanced dry heat loss from the subjects. This increase in cutaneous perfusion at 30°C compensated in part for the decrease in evaporative heat loss, and the subjects did not experience substantially large increases in heat storage, which would have interfered with the completion of the exercise bout.

In the cool environment, this increased cutaneous perfusion actually caused core temperature to decrease by 0.2°C after T_{es} had stabilized at approximately 10 minutes of exercise. The cutaneous vasodilation and the consonant dry heat loss seen in atropine treated subjects, in the absence of an anticholinergic nerve agent exposure, was sufficient to decrease body temperature. Further experiments will have to be done to more fully evaluate the implications of this increased convective and radiative heat loss in cold environments.

It is important to note here that the subjects were clothed in running shorts, shoes and socks to enable the appropriate measurements of heat exchange properties to occur. This is not the clothing that a soldier would wear in the field, however, in ongoing studies at very low exercise levels, in soldiers dressed in BDU and MOPPIV configurations core temperature decreased over time at both 12°C (MOPPIV) and 22°C (BDU) after systemic atropine administration.

SUMMARY

1. The anticipated decrease in sweating and increase in heart rate occurred with the systemic administration of 2 mg of atropine sulfate.
2. Atropine caused widespread cutaneous vasodilation in healthy male subjects during moderate exercise in both a warm and a cool environment. This increased cutaneous perfusion is manifested in enhanced dry heat exchange in these environments.
3. During exercise in a cool environment, the increased cutaneous vasodilation is sufficient to lower the body temperature.

REFERENCES

1. Craig, F.N. Effects of atropine, work and heat on heart rate and sweat production in man. *J. Appl. Physiol.* 4:826-833, 1952.
2. Davies, C.T.M., J.R. Brotherhood and E. Zeidifard. Effects of atropine and β -blockade on temperature regulation and performance during prolonged exercise. *Eur. J. Appl. Physiol.* 38:225-232, 1978.
3. Gaskell, P. The effect of intra-arterial atropine infusions on the blood flow through the human hand and forearm. *J. Physiol. (London)* 142:219-232, 1958.
4. Goodman, A.G., L.S. Gillman, T.W. Rall and F. Murad. The Pharmacological Basis of Therapeutics 7th Edition. New York: MacMillan Co., 1985, pp 120-122.
5. Graichen, H., R. Rascati and R.R. Gonzalez. Automatic dewpoint sensor. *J. Appl. Physiol.* 52:1658-1660, 1980.
6. Hokanson, D.E., D.S. Sumner and D.E. Strandess, Jr. An electrically calibrated plethysmograph for direct measurement of limb blood flow. *IEEE Trans. Biomed. Eng.* 22:25-29, 1975.
7. Kolka, M.A., W.L. Holden and R.R. Gonzalez. Heat exchange following atropine injection before and after heat acclimation. *J. Appl. Physiol.* 56:896-899, 1984.
8. Kolka, M.A., L.A. Stephenson and R.R. Gonzalez. Environmental stress after atropine treatment. *J. Thermal Biol.* 11:203-207, 1986.
9. Kolka, M.A., L.A. Stephenson, P.B. Rock and R.R. Gonzalez. Local sweating and cutaneous blood flow during exercise in hypoxic environments. *J. Appl. Physiol.* 62:2224-2229, 1987.
10. Kolka, M.A. and L.A. Stephenson. Cutaneous blood flow and local sweating after atropine administration. *Pflugers Archiv* (in press).
11. Kolka, M.A., L.A. Stephenson, A.E. Allan and P.B. Rock. Atropine-induced cutaneous vasodilation decreases core temperature during exercise. *J. Appl. Physiol.* (in review).
12. Nishi, Y. and A.P. Gagge. Direct evaluation of convective heat transfer coefficient by naphthalene sublimation. *J. Appl. Physiol.* 28:830-838, 1970.
13. Stephenson, L.A., M.A. Kolka and R.R. Gonzalez. Exercise after atropine and pralidoxime increases the rational effective temperature. *J. Thermal Biol.* (in review).
14. Whitney, R.J. The measurement of volume changes in human limbs. *J. Physiol. (London)* 121:1-27, 1953.

DISTRIBUTION LIST

- 2 Copies to:
Commander
U.S. Army Medical Research and Development Command
SGRD-RMS
Fort Detrick
Frederick, MD 21701-5012
- 12 Copies to:
Defense Technical Information Center
ATTN: DTIC-DDA
Alexandria, VA 22304-6145
- 1 Copy to:
Commandant
Academy of Health Sciences, U.S. Army
ATTN: AHS-COM
Fort Sam Houston, TX 78234
- 1 Copy to:
Dir of Biol & Med Sciences Division
Office of Naval Research
800 N. Quincy Street
Arlington, VA 22217
- 1 Copy to:
CO, Naval Medical R&D Command
National Naval Medical Center
Bethesda, MD 20014
- 1 Copy to:
HQ AFMSC/SGPA
Brooks AFB, TX 78235
- 1 Copy to:
Director of Defense Research and Engineering
ATTN: Assistant Director (Environment and Life Sciences)
Washington, DC 20301
- 1 Copy to:
Dean
School of Medicine Uniformed Services
University of Health Sciences
4301 Jones Bridge Road
Bethesda, MD 20014

DISTRIBUTION LIST

- 2 Copies to:
Commander
U.S. Army Medical Research Institute of Chemical Defense
Aberdeen Proving Ground, MD 21010-5425
- 2 Copies to:
Commander
U.S. Army Chemical R&D Center
Aberdeen Proving Ground, MD 21010-5423
- 2 Copies to:
Commandant
U.S. Army Chemical School
Ft. McClellan, AL 36205-5000
- 2 Copies to:
Commander
U.S. Army Medical Research and Development Command
ATTN: SGRD-PLE
Ft. Detrick
Frederick, MD 20701-5012
- 2 Copies to:
Commander
USAF School of Aerospace Medicine
Brooks Air Force Base, TX 78235
- 2 Copies to:
Commander
Naval Health Research Center
P.O. Box 85122
San Diego, CA 92138-9174
- 2 Copies to:
Commander
U.S. Army Biomedical Research and Development Laboratory
Ft. Detrick
Frederick, MD 21701-5010
- 2 Copies to:
Commander
U.S. Army Medical Materiel Development Laboratory
Ft. Detrick
Frederick, MD 21701-5009
- 2 Copies to:
Commander
U.S. Army Natick Research, Development and Engineering Center
Natick, MA 01760-5000

2 Copies to:

Commander

10th Special Forces (ABN)

1st Special Forces Group Headquarters

Fort Devens, MA 01433