

AD-A197 703

**Physiological responses wearing MOPP-IV after
atropine and pralidoxime administration in warm and cool environments**

Margaret A. Kolka, Ph.D. and Bruce S. Cadarette, M.S.

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

Running head: Cholinolytic and oxime therapy in protective clothing

Send correspondence to:

**Dr. M.A. Kolka
USARIEM
Kansas Street
Natick, MA 01760-5007**

Unclas

SECURITY CLASSIFICATION OF THIS PAGE

REPORT DOCUMENTATION PAGE

DTIC FILE COPY

Form Approved
OMB No. 0704-0188

AD-A197 703

1b. RESTRICTIVE MARKINGS

3. DISTRIBUTION/AVAILABILITY OF REPORT
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 Med6b. OFFICE SYMBOL
(If applicable)
SGRD-UE-MEP7a. NAME OF MONITORING ORGANIZATION
U.S. Army Res Inst of Env Med

6c. ADDRESS (City, State, and ZIP Code)

Kansas St.
Natick, MA 01760-5007

7b. ADDRESS (City, State, and ZIP Code)

Kansas St.
Natick, MA 01760-50078a. NAME OF FUNDING/SPONSORING
ORGANIZATION
Same as 6a.8b. OFFICE SYMBOL
(If applicable)

9. PROCUREMENT INSTRUMENT IDENTIFICATION NUMBER

8c. ADDRESS (City, State, and ZIP Code)

Same as 6c.

10. SOURCE OF FUNDING NUMBERS

PROGRAM
ELEMENT NO.PROJECT
NO.
3M463751D
993TASK
NO.
993/BCWORK UNIT
ACCESSION NO.
18311. TITLE (Include Security Classification) (U) Physiological responses wearing MOPP-IV after
atropine and pralidoxime administration in warm and cool environments

12. PERSONAL AUTHOR(S)

Margaret A. Kolka, Ph.D. and Bruce S. Cadarette, M.S.

13a. TYPE OF REPORT
Manuscript13b. TIME COVERED
FROM _____ TO _____14. DATE OF REPORT (Year, Month, Day)
April 198815. PAGE COUNT
13

16. SUPPLEMENTARY NOTATION

17. COSATI CODES

FIELD	GROUP	SUB-GROUP

18. SUBJECT TERMS (Continue on reverse if necessary and identify by block number)
anticholinergic, oxime, protective clothing, thermoregulation

+ sub re

19. ABSTRACT (Continue on reverse if necessary and identify by block number)

(U) The effect of cholinolytic and oxime (2 mg atropine + 600 mg pralidoxime) therapy on temperature regulation was evaluated in 8 subjects wearing chemical warfare protective clothing (MOPP-level IV). Subjects were tested in two environments: 35°C, 60% rh and 13°C, 44% rh during very light physical activity (1-2 Met) over a six-hour period. Sweating was suppressed approximately 40% by atropine and pralidoxime, and heart rate increased approximately 30 beats/min with drug treatment. At 13°C, all eight subjects completed 350 minutes of exposure in both drug and control experiments. Exposure time was limited at 35°C, however, averaging 213 (+30) min in control and 190 (+38) min in drug experiments. Rectal temperature (T_{re}) averaged 38.24°C in both treatments when subjects terminated their exposure at 35°C. Mean skin temperature averaged 37.42°C for both groups at termination. T_{sk} was unaffected by treatment at 13°C averaging 36.92°C (+0.15) in control and 36.74°C (+0.10) in drug experiments. T_{sk} was unaffected by treatment averaging 33.10°C (+0.34) and 33.05°C (+0.57), respectively. The treatment of subjects with atropine and pralidoxime

20. DISTRIBUTION/AVAILABILITY OF ABSTRACT

☐ UNCLASSIFIED/UNLIMITED ☒ SAME AS RPT. ☐ DTIC USERS

21. ABSTRACT SECURITY CLASSIFICATION

22a. NAME OF RESPONSIBLE INDIVIDUAL
Margaret A. Kolka22b. TELEPHONE (Include Area Code)
617-651-484922c. OFFICE SYMBOL
SGRD-UE-MEP

19. Abstract (cont'd)

When wearing chemical protective clothing does not adversely affect the length of time individuals can remain in a cool environment during very light work. However, the wearing of chemical protective clothing will decrease exposure time significantly (~~20~~ 40%) in both control and drug treated subjects in a warm environment. Keywords:

Heat Stress Physiology, Human Factors Engineering,
Cholinesterase inhibitors. (AW) *

**Physiological responses wearing MOPP-IV after
atropine and pralidoxime administration in warm and cool environments**

Margaret A. Kolka, Ph.D. and Bruce S. Cadarette, M.S.

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



Running head: Cholinolytic and oxime therapy in protective clothing

Send correspondence to:

**Dr. M.A. Kolka
USARIEM
Kansas Street
Natick, MA 01760-5007**

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

ABSTRACT

The effect of cholinolytic and oxime (2 mg atropine + 600 mg pralidoxime) therapy on temperature regulation was evaluated in 8 subjects wearing chemical warfare protective clothing (MOPP-level IV). Subjects were tested in two environments: 35°C, 60% rh and 13°C, 44% rh during very light physical activity (1-2 Met) over a six hour period after receiving drug or saline control. Sweating was suppressed approximately 40% ($p < 0.05$) by atropine and pralidoxime, and heart rate increased approximately 30 beats $\cdot$ min⁻¹ with drug treatment. At 13°C, all eight subjects completed 350 minutes of exposure in both drug and control experiments. Exposure time was limited at 35°C, however, averaging 213 (± 30) min in control and 190 (± 38) min in drug experiments. Rectal temperature (T_{re}) averaged 38.24°C in both treatments when subjects terminated their exposure at 35°C. Mean skin temperature averaged 37.42°C for both groups at termination. T_{re} was unaffected by treatment at 13°C averaging 36.92°C (± 0.15) in control and 36.74 (± 0.10) in drug experiments. $\bar{T}_{sk}$ was unaffected by treatment averaging 33.10°C (± 0.34) and 33.05°C (± 0.57), respectively. The treatment of subjects with atropine and pralidoxime when wearing chemical protective clothing does not adversely affect the length of time individuals can remain in a cool environment during very light work. However, the wearing of chemical protective clothing will decrease exposure time significantly (~40%, $p < 0.05$) in both control and drug treated subjects in a warm environment.

Key words: anticholinergic, oxime, protective clothing, thermoregulation

INTRODUCTION

The length of time an individual can work in the heat is reduced by both the wearing of protective clothing (5,6) and also by the administration of cholinolytic drugs such as atropine (3,7,8,10). Protective clothing systems compromise thermoregulatory heat loss mechanisms by limiting the transfer of heat from the body surface via the biophysical properties of convection and evaporation. Cholinolytic or anticholinergic drugs, of which atropine is the classic example with almost pure muscarinic action (15), decrease sweat secretion and therefore decrease evaporative heat loss (3,7,8,10). In addition, atropine is associated with increased skin blood flow, which can decrease heat gain from or increase heat loss to the environment, depending on the ambient temperature (8,9). Pralidoxime chloride, an oxime, reactivates bound acetylcholinesterase allowing normal synaptic function (14). The combination of atropine and pralidoxime treatment generally results in similar, albeit, slightly exacerbated effects on sweating and/or skin blood flow than that seen with atropine administered independently (4,11,12,13), that is, decreased time of exposure to a hot environment.

In the present investigation we have examined subjects treated with atropine sulfate and pralidoxime chloride while wearing chemical protective clothing (MOPP-IV) to characterize the combined effect of chemical protective clothing and environmental stress under cholinolytic and oxime therapy. It was hypothesized that the effects of atropine and pralidoxime on thermoregulatory responses, such as decreased sweating and increased heat storage, would not be as marked when wearing chemical protective clothing as the clothing itself is deleterious to the completion of tasks in warm to hot environments. A very light work intensity was used to simulate tasks performed by

soldiers in rear areas (i.e. support or administrative) which are susceptible to NBC (nuclear, biological or chemical) attack.

METHODS

Eight healthy men consented to serve as subjects following approval of all procedures by the local human review committee. The mean ($\pm$ SD) age was 20 ± 3 yr, height 174 ± 5 cm, weight 73 ± 9 kg, DuBois surface area 1.88 ± 0.15 m², percent body fat 15.5 ± 4.5 % and $\dot{V}O_2$ max 3.98 ± 0.48 l $\cdot$ min⁻¹. The eight subjects were tested on four separate days: after the intramuscular injection of 2 mg atropine sulfate (Elkin-Sinn, Cherry Hill, NJ) and 600 mg pralidoxime chloride (Ayerst, NY, NY) and after equal volumes of sterile saline injected intramuscularly (anterior thigh) while wearing Mission Oriented Protective Posture, Level IV (MOPP-IV; clo=2.44; i_m=0.30) in 35°C, 24°C dew-point (rh=54%) and 13°C, 1°C dew-point (rh=44%) environments. The testing order for drug administration and environmental condition was counterbalanced, thus during each exposure at 35°C, four subjects were treated with atropine and pralidoxime and four were completing their control exposure. In this way, the effect of previous environmental exposure or drug treatment could be accounted for.

Subjects were fully oriented to all test procedures in the week before the first test day. Test days were separated by 72 hours to prevent carryover from the various drug treatments or environmental stress. On the day of the experiment the subject reported to the test chamber at 0730 h after a light breakfast. Prior to dressing, each subject was instrumented for rectal temperature measurement (10 cm past the anal sphincter) and a three site mean weighted skin temperature (arm, chest and calf, ref. 2). He dressed in the chemical protective clothing system (MOPP-IV) before resting in

a seated position for 0.5 h. Heart rate was measured by telemetry from chest leads and whole body water loss (sweating) was calculated from the change in body weight before and after the subject entered the test chamber, corrected for water ingested, urine excreted and water trapped in the uniform. Unevaporated sweat (E_{drip}) was not measured.

After a 30 minute period, the physician injected the appropriate drug regimen. On each test day each subject received 3 separate injections, a total fluid volume of 7 ml (either 1ml = 2 mg atropine sulfate and 2 x 3ml = 600 mg pralidoxime chloride or 1ml + 3ml + 3ml sterile saline). Subjects were not informed of the drug injected at the time of administration. However, within 15 to 20 minutes the effects of atropine such as dry mouth and increased heart rate are apparent, so the experiment was not "blind".

The subjects entered the test chamber immediately after they received the three injections, they remained seated for the first half hour followed by approximately 1.5 hours of walking, standing or sitting as they filled out questionnaires, participated in vision testing, evaluation of marksmanship skills and performed tests of dexterity. The energy expended while accomplishing these tasks was 1-2 Met or approximately 100-150 W. The thirty minute seated period corresponded to the time course necessary for intramuscularly injected atropine to reach sufficient plasma levels to elicit the required anticholinergic symptoms (1). The total chamber time attempted for each experiment was 6 hours, as the above cycle of rest and light exercise was repeated three times.

Analysis of variance routines with repeated measures were used for data collected at 0, 30, 60, 120, 240 and 300 minutes of exposure. Tukey's test of critical differences was used whenever a significant F-ratio appeared. Data in the RESULTS are presented as mean $\pm$ SD. All differences are significant at $p < 0.05$.

RESULTS

The mean temperature, heart rate and sweating rate data for the eight subjects wearing MOPP-IV during exposure to 13°C (cool environment) and 35°C (warm environment) are presented in Tables 1 and 2, respectively. The administration of atropine and pralidoxime increased heart rate an average of $27 \text{ b} \cdot \text{min}^{-1}$ ($p < 0.05$) in both the cool and the warm environment by 30 minutes post-injection. Whole body sweating was decreased by ~40% ($p < 0.05$) in the warm environment by cholinolytic and oxime therapy. All eight subjects completed the six hour exposure in the cool environment after saline and atropine/pralidoxime injections. However, neither the saline treated or atropine/pralidoxime treated subjects could complete the six hour exposure in the warm environment. The average exposure times for subjects in the warm environment were $213 (\pm 30)$ min in saline and $190 (\pm 38)$ min in the atropine/pralidoxime experiments, which were significantly less ($p < 0.05$) than the 350 min for both treatments in the cool environment, but not different from each other. In the warm environment, the average rectal temperature was 38.24°C for both drug and saline experiments and the average mean weighted skin temperature was 37.42°C when the subjects terminated their exposure. Rectal temperature decreased with time of exposure in both saline and atropine/pralidoxime MOPP-IV experiments in the cool environment ($p < 0.05$). Mean skin temperature was constant over time for both treatments at 13°C averaging 33.10°C and 33.06°C for control and drug experiments, respectively. In the warm environment, heart rate remained elevated and both T_{re} and $\bar{T}_{sk}$ were higher during exposure in atropine/pralidoxime compared to control ($p < 0.05$). $\bar{T}_{sk}$ and T_{re} were higher in the warm than the cool environment for both control and atropine/pralidoxime treatments ($p < 0.05$).

DISCUSSION

The present study provides evidence that subjects treated with a combination of atropine sulfate and pralidoxime chloride in equal volume to that contained in the MARK-I field autoinjector (self-administered, field use, chemical warfare treatment regimen) can perform light duty tasks for six hours dressed in MOPP-IV in a cool environment. A problem arises when subjects wearing MOPP-IV, either treated with a combination of atropine and pralidoxime or not, are exposed to a warm environment. In this case, even without drug therapy, light work in a warm environment was decreased by an average of 2.5 hours (~40%). When atropine and pralidoxime were administered to the subjects dressed in MOPP-IV, exposure time in this warm environment (35°C) was further decreased (but not significantly) by approximately 25 minutes compared to the MOPP-IV exposure without drug therapy. These observations demonstrate the importance of microclimate cooling for rear area personnel wearing chemical protective clothing in warm environments.

The limitations to exposure to environmental heat stress imposed by the chemical protective clothing layer have been studied previously (6) and the expected heat gain from the environment occurred in the present study even with a very low endogenous (metabolic) heat production. In addition, the results of the present study are in agreement with some of our previous observations (7,10) in that whenever there is a requirement for significant evaporative heat loss to maintain thermal equilibrium, the treatment of subjects with atropine and/or pralidoxime resulted in decreased exposure time; although this decrease was not statistically significant in the present study, it may be operationally significant. Any such barrier to evaporative heat loss, which would include the clothing layers provided by the chemical protective garment affected exposure time in a similar manner.

Exposure to the cool environment in the present study did not cause significant thermal strain as evidenced by the moderate skin temperature and falling rectal temperature during exposure. Thus, these subjects had little, if any, requirement for evaporative cooling so that reduced secretion of sweat in the atropine/pralidoxime treatments was of little consequence. In fact, cooling occurred along the thermal gradient from the skin surface through the uniform. During exposure to the warm environment, heat gain initially occurred through the uniform to the skin surface resulting in elevated core temperature. Sweating occurred but was not associated with adequate evaporative heat loss, the skin surface temperature increased as surface vessels dilated in an attempt to dissipate heat. Unfortunately in the 35°C environment, dry heat exchange was minimized and evaporative heat loss was decreased by the clothing barrier, thus heat storage continued and exposure time was affected. In the atropine treated subjects, heat gain through the skin surface occurred initially causing an increased core temperature. Sweating was inhibited, thus even less evaporative heat loss was possible. The surface vessels dilated (8.9) but little heat was transferred from the body surface to the environment. Heat storage continued and as in the control experiments, exposure time was limited compared to the cool environment.

Based on heart rate responses the effect of atropine was evident by 30 minutes post-injection, as is the normal response (1.15). During exposure to a cool environment, the heart rate returned to normal by 120 minutes, which is consistent with the metabolism of the drug (1). In a hot environment, heart rate remained elevated throughout the exposure, even as atropine (primarily responsible for the cardiac acceleration) was metabolized. The increased skin and core temperatures resulting from

the anticholinergic action at the sweat gland and cutaneous blood vessels, was not reversed in subjects dressed in chemical protective clothing even though the action of the drug was reduced as it was metabolized. Thus, a higher cardiovascular strain as evidenced by the elevated heart rate continued throughout the entire interval of heat exposure.

In the warm environment, the rate of heat storage in the atropine/pralidoxime subjects was 2 times greater (Table 2) than the control experiments due to prevention of evaporative heat loss resulting from the inhibition of sweat gland secretion in the light of increasing core and skin temperatures seen by 60 minutes. However, even in the saline experiments, heat gain from the environment caused rectal temperature to be approximately 0.7°C higher by 120 minutes and 1.4°C higher by 180 minutes of exposure than in the cool exposure.

The current study involved little internal or metabolic heat production from the subjects, and the results presented here impact directly to very light work rates. In this example, subjects can continue heat exposure for approximately 3 hours in a warm environment after atropine and pralidoxime have been injected. Since heat production is proportional to metabolic rate, by increasing heat production through walking on a treadmill at 350W or 3.5 Met, core temperature will increase and combined with heat gained through the skin surface, could limit exposure to approximately an hour based on data collected from previous studies of atropine and heat exposure (7). In summary, if individuals dressed in chemical protective clothing ensembles are administered cholinolytic and oxime therapy, meaningful exposure time to an environment will depend on the work intensity and the environmental conditions.

ACKNOWLEDGEMENTS

The authors acknowledge Dr. J. Kobrick for allowing us to collect this data.

The opinions and/or findings contained in this report are those of the authors and should not be construed as 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. Approved for public release; distribution unlimited.

REFERENCES

1. Berghem, L., Bergman, U., Schildt, B. and Sorbo, B. (1980) Plasma atropine concentrations determined by radioimmunoassay after single-dose i.v. and i.m. administration. *Br. J. Anesth.* 52, 597-600.
2. Burton, A.C. (1935) Human calorimetry II. The average temperature of the tissues of the body. *J. Nutr.* 9, 261-280.
3. Craig, F.N. and Cummings E.G. (1965) Speed of action of atropine on sweating. *J. Appl. Physiol.* 20, 311-315.
4. Cummings, E.G., Craig, F.N., Blevins, W.V. and Bulette, C.R. (1964) Physiological effects of 2-PAMCl on exercising men in temperate and hot environments. CRDLR 3241. Edgewood Arsenal, MD.
5. Gonzalez, R.R., Breckenridge, J.R., Levell, C.A., Kolka, M.A. and Pandolf, K.B. (1986) Efficacy of heat exchange by use of a wettable cover over chemical protective garments. Performance of Protective Clothing ASTM STP900. R.L. Barker and G.C. Coletta, Eds. American Society of Testing and Materials, Philadelphia, 515-534.
6. Henane, R., Bittel, J., Viret, R. and Morino, S. (1979) Thermal strain resulting from protective clothing of an armored vehicle crew in warm conditions. *Aviat. Space Environ. Med.* 50, 599-603.

7. Kolka, M.A., Holden, W.L. and Gonzalez, R.R. (1984) Heat exchange following atropine injection before and after heat acclimation. *J. Appl. Physiol.* 56, 896-899.
8. Kolka, M.A. and Stephenson, L.A. (1937) Cutaneous blood flow and local sweating after systemic atropine administration. *Pflugers Arch.* 410, 524-529.
9. Kolka, M.A., Stephenson, L.A., Allan, A.E. and Rock, P.B. (1987) Atropine lowers body temperature during exercise in a cool environment. *The Physiologist* 30: 147.
10. Kolka, M.A., Stephenson, L.A. and Gonzalez, R.R. (1986) Environmental stress after atropine treatment. *J. Therm. Biol.* 11, 203-207.
11. Kolka, M.A., Stephenson, L.A., Bruttig, S.P., Cadarette, B.S. and Gonzalez, R.R. (1987) Human thermoregulation after atropine and/or pralidoxime administration. *Aviat. Space Environ. Med.* 58: 545-549.
12. Robinson, P.F. and McMichael P.D. (1970) A comparison of the physiological responses to two modes of administration of atropine and 2PAMCl. EATR 4424, Edgewood Arsenal, MD.
13. Stephenson, L.A., Kolka, M.A. and Gonzalez, R.R. (1988) Exercise after atropine and pralidoxime increases the rational effective temperature. *J. Thermal Biol.* 12, 000-000.

14. Taylor, P. (1985) Anticholinesterase agents. In: Gilman, A.G., Goodman, L.S., Rall, T.W. and Murad, F., The Pharmacological Basis of Therapeutics, 7th edition, Macmillan, New York, 120-122.

15. Weiner, N. (1985) Atropine, scopolamine and related antimuscarinic drugs. In: Gilman, A.G., Goodman, L.S., Rall, T.W. and Murad, F., The Pharmacological Basis of Therapeutics, 7th edition, Macmillan, New York, 130-144.

Table 1. Mean ($\pm$ SD) rectal and skin temperatures, heart rates and sweating rates in 8 subjects during exposure to a cool environment (13°C) while wearing mission oriented protective posture (MOPP-IV). Atropine and pralidoxime were administered at time = 0.

Time (min)	<u>CONTROL</u>				<u>ATROPINE</u>			
	T_{re} ($^{\circ}\text{C}$)	$\bar{T}_{sk}$ ($^{\circ}\text{C}$)	HR (b/min)	E_{tot} (g/min)	T_{re} ($^{\circ}\text{C}$)	$\bar{T}_{sk}$ ($^{\circ}\text{C}$)	HR (b/min)	E_{tot} (g/min)
0	37.32 (.28)	33.58 (.72)	84 (9)		37.14* (.28)	33.66 (.76)	95* (21)	
30	37.10# (.28)	33.73 (.49)	71# (11)		36.91*# (.31)	33.96 (.55)	98*# (9)	
60	37.03# (.26)	33.20 (.43)	94# (17)		36.78*# (.31)	33.46 (.76)	106# (6)	
120	37.01# (.30)	33.02 (.56)	80 (9)		36.74*# (.31)	32.88# (.91)	87 (11)	
180	36.88# (.18)	32.86 (.57)	73# (16)		36.64# (.15)	32.89# (.79)	78 (14)	
240	36.81# (.14)	32.91 (.44)	64 (13)		36.70# (.19)	32.73# (.97)	74 (17)	
300	36.70# (.20)	32.85 (.54)	75 (10)	η	36.67# (.07)	32.36# (1.06)	72 (11)	η

η data on all subjects was not available.

* Different from control, $p < 0.05$.

Different from 0 minutes, $p < 0.05$.

Table 2. Mean ($\pm$ SD) rectal and skin temperatures, heart rates and sweating rates in 8 subjects during exposure to a hot environment (35°C) while wearing mission oriented protective posture (MOPP-IV). Atropine and pralidoxime were administered at time = 0.

Time (min)	<u>CONTROL</u>				<u>ATROPINE</u>			
	T_{re} (°C)	$\bar{T}_{sk}$ (°C)	HR (b/min)	E_{tot} (g/min)	T_{re} (°C)	$\bar{T}_{sk}$ (°C)	HR (b/min)	E_{tot} (g/min)
0	37.14 (.18)	34.41 (.49)	81 (17)		37.13 (.24)	34.55 (.23)	92 (14)	
30	37.00 (.13)	35.83# (.31)	81 (17)		36.99 (.24)	36.32# (.23)	108* (14)	
60	37.13 (.14)	35.87# (.35)	109 (.25)		37.35*# (.22)	36.82*# (.42)	131*# (16)	
120	37.68# (.11)	36.76# (.35)	111# (17)		38.23*# (.25)	37.44*# (.32)	139*# (12)	5.6* (2.4)
180	38.24# (.18)	37.39# (.35)	128# (30)	8.8 (1.9)				

* Different from control, $p < 0.05$.

Different from 0 minutes, $p < 0.05$.