

UNCLASSIFIED

AD NUMBER
AD853967
NEW LIMITATION CHANGE
TO Approved for public release, distribution unlimited
FROM Distribution authorized to U.S. Gov't. agencies only; Administrative/Operational Use; MAY 1969. Other requests shall be referred to US Army Edgewood Chemical Biological Center, Attn: SMUEA-RMC, Edgewood Arsenal, MD 21010.
AUTHORITY
EA, d/a ltr, 14 Aug 1973

THIS PAGE IS UNCLASSIFIED

AD

AD853967

**EDGEWOOD ARSENAL
TECHNICAL REPORT**

EATR 4252

**AN EVALUATION OF THE IRRITANT
POTENTIAL OF CS AEROSOLS ON HUMAN
SKIN UNDER TROPICAL CLIMATIC CONDITIONS**

by

Alfred Hellreich, CPT, MC
Millard M. Mershon
John T. Weimer
Kragg P. Kysor
Nicholas G. Bottiglieri, COL, MC

May 1969

MAY 1969



COLOR ILLUSTRATIONS REPRODUCED
IN BLACK AND WHITE

Limited number of copies containing color
other than black and white are available until
stock is exhausted. Reproductions will be
made in black and white only.

**DEPARTMENT OF THE ARMY
EDGEWOOD ARSENAL
Research Laboratories
Medical Research Laboratory
Edgewood Arsenal, Maryland 21010**

Distribution Statement

Each transmittal of this document outside the agencies of the US Government must have prior approval of the Commanding Officer, Edgewood Arsenal, ATTN: SMUEA-TSTI-T, Edgewood Arsenal, Maryland 21010.

Disclaimer

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

Destroy this report when no longer needed. Do not return it to the originator.

ACCESSION NO.	
CLASS.	
DATE	
BY	
POSTED	
3	

EDGEWOOD ARSENAL TECHNICAL REPORT

EATR 4252

AN EVALUATION OF THE IRRITANT POTENTIAL OF
CS AEROSOLS ON HUMAN SKIN UNDER TROPICAL
CLIMATIC CONDITIONS

by

Alfred Hellreich, CPT, MC
Millard M. Mershon
John T. Weimer
Kragg P. Kysor
Nicholas G. Bottiglieri, Col, MC
Clinical Research Department

May 1969

Each transmittal of this document outside the agencies of the US Government must have prior approval of the Commanding Officer, Edgewood Arsenal, ATTN: SMUEA-TSTI-T, Edgewood Arsenal, Maryland 21010.

Task 1B662706A09710

DEPARTMENT OF THE ARMY
EDGEWOOD ARSENAL
Research Laboratories
Medical Research Laboratory
Edgewood Arsenal, Maryland 21010

FOREWORD

The work described in this report was authorized under Task 1B662706A09710. "Defense Medical Aspects of Chemical Agents, Incapacitating and Riot Control Agents." This work was started in December 1966 and completed in February 1967.

The volunteers in these tests are enlisted US Army personnel. These tests are governed by the principles, policies, and rules for medical volunteers as established in AR 70-25.

Reproduction of this document in whole or in part is prohibited except with permission of the Commanding Officer, Edgewood Arsenal, ATTN: SMUEA-TSTI-T, Edgewood Arsenal, Maryland 21010; however, DDC is authorized to reproduce the document for US Government purposes.

The information in this document has not been cleared for release to the general public.

Acknowledgments

The authors wish to express their appreciation to Mrs. Marion P. Royston for editorial assistance, to Dr. Edmund G. Cummings, and Mr. William V. Blevins for photoelectric plethysmography, and to Mr. Moses Stewart and Mr. Ray Clawson, the photographers. The authors are also indebted to Mr. Edmund J. Owens for design of the exposure chamber, to Mr. Thomas L. Hess for the analyses of CS, and to Mr. Harold L. Feller, Mr. Thomas A. Ballard, and Mr. Ronald P. Merkey for operation of the exposure facility.

DIGEST

An attempt was made to quantitate the irritant potential of (*o*-chlorobenzylidene) malononitrile (CS) aerosols on human skin. A "negative patch test" was devised to expose small areas of the forearm to the agent in a subchamber assembly simulating tropical and temperate climates. Graded responses were obtained by unsheathing the areas at intervals, and responses were read 24 hours after exposure.

It was found that it is virtually impossible to predict the dose of CS that will cause minimal erythema in an untested individual under tropical conditions because the variations among individuals are so great. It is estimated that 50% of a large group of men will develop some degree of erythema when the Ct of CS is 3500 ± 1500 mg min/cu m and the air is moist and warm. It was also found that CS can produce sensitization and delayed skin response.

CONTENTS

	Page
I. INTRODUCTION	7
II. EXPERIMENTAL DESIGN	7
A. Subjects	7
B. Apparatus	7
C. Analysis of Chamber Concentrations of CS	9
D. Patch Testing	9
E. Response and Follow-Up	10
F. Special Procedures	10
III. RESULTS AND DISCUSSION	12
A. Clinical Observations	12
B. Analysis of Results	12
C. Effect of Temperature and Humidity	16
D. Sensitizing Potential of CS	16
E. Fluorescent Aerosol	20
F. Photoelectric Plethysmography	20
G. Other Factors	24
IV. CONCLUSIONS	24
DISTRIBUTION LIST	27

LIST OF FIGURES

Figure		Page
1	Experimental	8
2	Patch Test Sleeve Assembly	11
3	Example of Graded Deposition of CS Powder Depending on Length of Exposure (Volunteer No. 4490)	11
4	Vesicular Reaction and Erythema (Volunteer No. 4469) Photograph was taken 3 days after exposure	11
5	Dose-Response Data Under Tropical Conditions	15
6	Log Dose vs. Response to CS Under Tropical Conditions (probit analysis) ...	17
7	Dose vs. Response to CS Under Tropical Conditions (linear)	17
8	Sensitization by CS	
	A. Delayed Primary Reaction Which Subsequently Disappeared	
	B. Eczematous Allergic Flare-up Which Started 10 Days After Exposure Subject was exposed on 6 February 1967	19
9	Demonstration of Leakage With Fluorescent Dye	
	A. Fluorescence Under UV Light Immediately After Termination of Exposure to CS (the irregularity of the boundaries of the exposure sites indicates leakage)	
	B. Subsequent Reaction to CS (erythema was much less apparent when the 24-hour reading were taken)	21
10	Photoelectric Plethysmograms Before and After Erythema and Blisters. Pulsation Amplitude Is Expressed in Arbitrary Units. (Tracings also reflect transient variations in blood pressure.)	22
11	Photoelectric Plethysmogram of Volunteer No. 4509 Showing Pulse Amplitude Increased Sixfold With the Primary Skin Response (8/2/67) and Fourteenfold With the Subsequent Allergic Response	23

LIST OF TABLES

Table		Page
I.	Subchamber CS Concentrations by Ultraviolet vs. Colorimetric Analysis ...	9
II.	Individual Skin Site Responses to CS Under Simulated Tropical Conditions (98°F, 98% RH)	13
III.	Grouped Data on Skin Responses to CS Under Tropical Conditions	16
IV.	Responses at Temperate Climatic Conditions	18
V.	Table of Intercorrelations	25
VI.	Scores Used in Intercorrelations	26

AN EVALUATION OF THE IRRITANT POTENTIAL OF CS AEROSOLS ON HUMAN SKIN UNDER TROPICAL CLIMATE CONDITIONS

I. INTRODUCTION.

Studies conducted with thermally generated (*o*-chlorobenzylidene) malononitrile (CS) aerosols under conditions of high temperature and humidity have demonstrated their potential for irritating human skin.* Generally, the volunteers most susceptible to sunburn (e.g., blue-eyed blondes) displayed the most severe reactions. It was also noted that areas covered by dry clothing were not affected, whereas the CS penetrated wet clothing rather readily, producing severe second-degree burns.

Before evaluation of topical protectants against CS burns can proceed, a reliable measure of the dose that will cause minimal erythema and a preliminary estimation of human and environmental variables must be available. These were the purposes of this study.

II. EXPERIMENTAL DESIGN.

A. Subjects.

Twenty-eight US Army Medical Volunteers were used in this study. They consisted of 24 Caucasians with light to dark complexions and four non-Caucasians; their ages ranged from 18 to 30 years. The subjects were divided into seven groups of four men each, four being the maximum number that could be handled simultaneously in the aerosol chamber. None of those selected had a history of being atopic or was taking any medication at the time of testing.

B. Apparatus.

The aerosols were generated by firing M7 CS thermal grenades in a 20,000-liter chamber at 7- to 10-minute intervals. The agent cloud was then drawn through a subchamber where the right or left arms of four volunteers were exposed to the moving (5 mph) air stream. (Figure 1 shows the experimental setup; however, these subjects are not wearing the plastic sleeves described below.) The agent concentration was maintained at about 300 mg min/cu m. The introduction of steam with the agent cloud simulated tropical conditions (98°F and 98% relative humidity). The other arms of three groups of volunteers were also exposed to CS under temperate conditions.

*Hellreich, A., Goldman, R.H., Bottiglieri, N.G., and Weimer, J.T. EATR 4075. The Effects of Thermally-Generated CS Aerosols on Human Skin. January 1967. UNCLASSIFIED Report.



Figure 1. Experimental

C. Analysis of Chamber Concentrations of CS.

All airborne samples of CS were analyzed by two methods: ultraviolet analysis at 300 m μ * and dinitrobenzene colorimetric analysis.** Agreement between the two methods was generally good. Table I gives values from a typical series of analyses performed on airborne samples drawn during one set of exposures.

Table I. Subchamber CS Concentrations by Ultraviolet vs. Colorimetric Analysis

Sample	Ultraviolet	Colorimetric
	mg/cu m	
1	308	308
2	353	368
3	490	458
4	340	338
5	373	390
6	340	358
7	310	348
8	425	400
9	398	410

D. Patch Testing.

A new patch test method that prevents exposing excessive areas of the skin to the aerosol was devised. One arm of each subject was encased in a protective sleeve† that had been modified to allow sequential exposure of 1-1/2-inch diameter areas of skin on the flexor aspect

*Housely, S. Nancekuke Report No. 51. The Estimation of *o*-Chlorobenzal-malononitrile by Ultraviolet Absorption. September 1952. UNCLASSIFIED Report.

**Master, I. and Sass, S. CWL Tech Memo 13-7. Colorimetric Determination of Trace Quantities of EA 1779 (T 792, CS). February 1959. UNCLASSIFIED Report.

†"JP" suits, plastic-covered, disposable, protective suits. Snyder Manufacturing Co., Philadelphia, Ohio.

of the forearm (figure 2). The modification consisted of inserts of prepunched, 2-in.-h wide adhesive plastic tape* which adhered to the skin. The holes were covered with paper discs, and the discs were covered with waterproof adhesive tape.** While their arms were in the chamber, the subjects peeled a patch off each other when told. Thus, six to eight sites on each arm could receive different doses (Ct's, concentration x time) depending on length of exposure to the relatively constant concentration of CS (figure 3). The subjects wore rubber gloves to protect their hands.

E. Response and Follow-up.

Immediately after each series of exposures, the protective sleeve assemblies were removed and any remaining CS was washed off the forearm with cold water. As we noted in previous studies, there was a temporary stinging sensation and erythema on the exposed sites. A response was considered positive only if delayed or sustained erythema was evident 24 hours postexposure. Responses were graded as negative to 4+ erythema, and every positive reaction was closely followed for possible subsequent vesiculation. Effective treatment, which has been described†, was available in case of untoward reactions.

F. Special Procedures.

In an attempt to improve the objectivity of our readings, two special procedures were included in the experimental design.

1. Fluorescent Aerosol.

Since air-tightness is a requirement of this type of patch test, we checked leakage in the sleeve assembly with an inert fluorescent aerosol. With each unsheathing of a new exposure area, 100 mg/cu m of the sodium salt of 8-anilino-1-naphthalenesulfonic acid was introduced into the subchamber for 10 seconds. The subjects' forearms were subsequently viewed under ultraviolet light, revealing the exact sites of contact with the agent. Even after thorough washing this fluorescence was visible for at least 48 hours. The aerosol by itself in much higher concentration has not produced any inflammation or erythema.§

2. Photoelectric Plethysmography.

An objective method for measuring inflammatory responses of capillaries in the skin was tested§§ on a few subjects. A photoelectric plethysmograph was used to reveal changes in

*Polyethylene tape, catalog No. 32-7999, Sears, Roebuck and Co., Philadelphia, Pa.

**Blenderm tape, Minnesota Mining and Manufacturing Co., St. Paul, Minn.

†Hellreich et al., op cit.

§Owens, E. J., Aerosol Branch, unpublished data.

§§ Performed by Dr. E.G. Cummings and Mr. W. V. Blevins of the Applied Physiology Branch. This method is described in EATR 4223, Cummings, E.G. Temperature and Concentration Effects on Penetration of *N*-octylamine through Human Skin *in situ*. January 1960. UNCLASSIFIED Report.

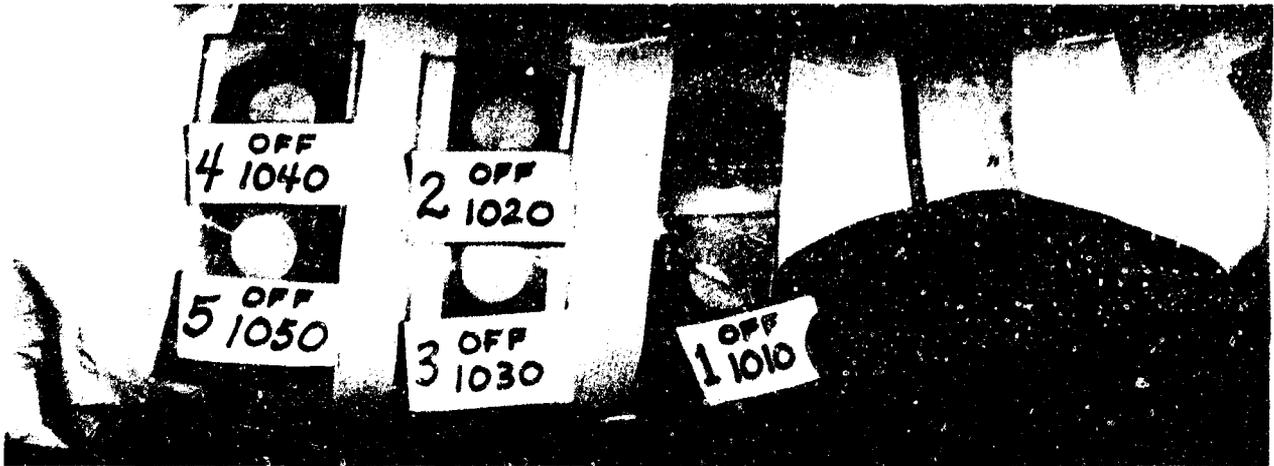


Figure 2. Patch Test Sleeve Assembly.

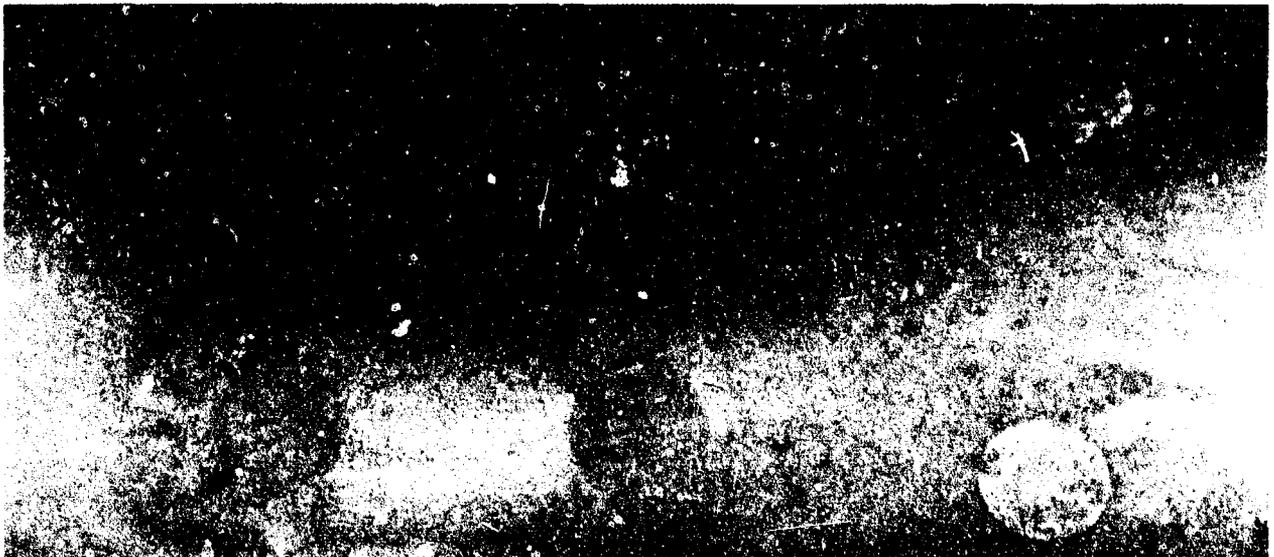


Figure 3. Example of Graded Deposition of CS Powder Depending on Length of Exposure. (Volunteer No. 4490)



Figure 4. Vesicular Reaction and Erythema (Volunteer No. 4469)
Photograph was taken 3 days after exposure.

blood flow at individual sites of exposure. This instrument detects pulsation of superficial blood vessels by measuring variations in light absorption with the ebb and flow of red blood cells. These variations are recorded as tracings on moving paper. The distances between peaks and valleys for pulses on such tracings indirectly indicate the proportion of the capillary bed that is carrying blood at the moment. Because many more capillaries are open during inflammation than under normal conditions, this method provides an objective confirmation of visual assessment of erythema, which is subject to variation in interpretation with the observer.

III. RESULTS AND DISCUSSION.

A. Clinical Observations.

A total of 211 skin sites exposed to doses ranging from 1,515 to 33,120 mg min/cu m were read. (Data on three subjects were discarded because of evidence of leakage.) Responses were recorded as negative, erythema (minimal [\pm] to 4+), and vesicular.

Table II is a summary of the skin responses observed under simulated tropical conditions. There was such individual variation that the dose which caused minimal erythema (\pm) ranged from less than 1,515 to 23,040 mg min/cu m.

Three subjects developed blisters (second-degree chemical burns). They were all fair-skinned Caucasians who sunburn easily, although a moderately high dose (3,030 mg min/cu m) caused only minimal erythema in one subject (No. 4531).

Volunteer No. 4522 developed blisters in the antecubital region, but other sites (which received higher Ct's) on this subject were only erythematous. This confirms the common observation that the antecubital area is the most reactive site on the forearm and should not be used as an exposure site.

Volunteer No. 4469, who was red-haired and freckled, had a history of frequent blistering following exposure to sun. A blister was seen forming 65 minutes after the exposure of this subject was begun (figure 4), and he was immediately removed from the apparatus.

All the blisters were small and no treatment was required. Healing was complete within 5 days.

B. Analysis of Results.

It is clear from table II that the threshold susceptibility to CS and the intensity of the inflammatory response vary so widely from individual to individual that it is impossible to predict with any degree of accuracy the dose of CS that would produce minimal erythema in an untested individual. Therefore, several methods of statistical analysis were used to arrive at an MED50, the dose at which half of the sites exposed developed at least minimal erythema.

In figure 5, the degrees of response under tropical conditions are plotted against Ct. It can be seen that there is an extremely wide dose range at each response level.

Table II. Individual Skin Site Responses to CS Under Simulated Tropical Conditions (98°F, 98% RH)

Ct mg min/cu m	Responses			
	4391 ^a	4422		
4,600	0	0		
7,800	0	0		
12,200	+	0		
15,700	++	0		
	4446	4450		
1,800	0	0		
5,400	0	0		
9,800	0	0		
13,400	+	+		
	4415	4438		
2,930	0	0		
5,390	0	0		
8,310	0	0		
10,920	+	++		
13,600	++	+++		
	4496	4490	4481	4532
11,040	++	+	++	No reading
14,840	++	++	++	++
18,400	++	++	++	+
22,620	++	++	++	++
26,600	++	+++	+++	++
29,760	++	+++	+++	+++
	4528	4546 ^b	4543	4548
2,480	0	0	+	0
6,000	±	0	++	+
8,340	±	±	++	+
11,560	+	±	+++	+
14,000	±	±	+++	+
15,960	+	+	+++	+
	4518 ^c	4522	4531	4519 ^c
1,515	0	+	0	0
3,030	0	++vd	+	0
5,720	±	++	+	0
9,000	0	++	+	0
16,200	+	+++	+	0
23,040	+	+++	++++vd	±

Table II. Continued

Ct mg min/cu m	Responses		
	4509	4539	4482
1,650	0	0	0
3,300	±	0	+
5,600	+	+	+
8,610	++	++	++
15,000	+	++	++
27,540	+++	+++	+++
	4483	4537 ^c	4540
1,550	0	0	±
3,600	±	+	+
5,400	+	±	+
7,460	++	+	++
10,950	+	+	+
18,250	+++	++	+++
33,120	+++	++	++
	4469		
1,550	±		
9,125	+		
23,725	++++ ^v d		

- a Volunteer number
- b Mexican-American
- c Negro
- d Vesiculation

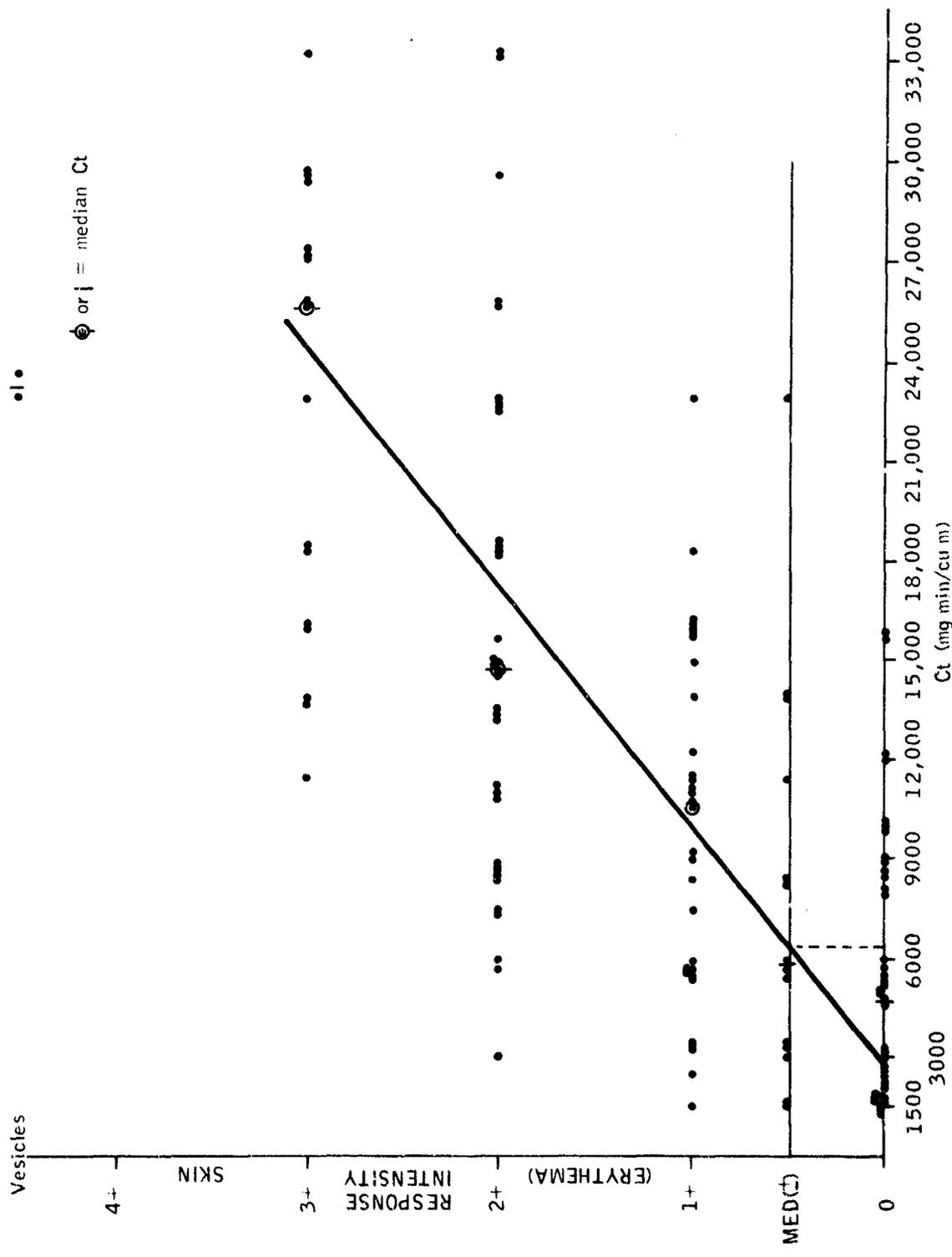


Figure 5. Dose-Response Data Under Tropical Conditions

For ease of analysis, the doses were grouped into discrete categories (table III). The percentage of positive (erythema) responses was then determined for each dose category and plotted for both linear- and log-dose vs probit-response (figures 6 and 7). A best visual-fitting line drawn through the partial response points on the linear dose plot (figure 6) yielded an MED50 of approximately 4,500 mg min/cu m. However, when the same data are analyzed by the standard computer program that utilizes the log of the dose, the MED50 is approximately 3,500 (\pm 1,500) mg min/cu m (figure 7). Consequently, any figure between 2,000 and 5,000 mg min/cu m could be the MED50.

Table III. Grouped Data on Skin Responses to CS Under Tropical Conditions

Dose Range mg min/cu m	Midpoint	No. Positive (Erythema)	Total Exposed Areas	Positive Total
0-4000	2000	11	30	0.37
4000-8000	6000	15	25	0.60
8000-12000	10000	22	30	0.73
12000-16000	14000	24	27	0.89
16000-20000	18000	7	7	1.00
20000-24000	22000	9	9	1.00
24000-28000	26000	7	7	1.00
28000-32000	30000	4	4	1.00
32000-36000	34000	3	3	1.00

C. Effect of Temperature and Humidity.

Table IV lists the responses obtained with the subchamber at temperate climatic conditions. The doses of CS required to produce erythema under these conditions are significantly higher than in a tropical environment. This is evident when the responses of the same subjects are compared under tropical (table II) and temperate conditions. The lowest effective doses were 1,515 (tropical) and 21,060 (temperate) mg min/cu m.

Moisture on the skin surface (from sweat or water vapor) may enhance irritancy by helping CS to dissolve in stratum corneum made susceptible to diffusion by hydration of the corneum. High environmental temperatures and increased peripheral circulation may also play a part in enhancing skin reactions to CS in troops or civilians in hot, humid environments.

D. Sensitizing Potential of CS.

As illustrated by figure 8, one of the volunteers (No. 4509) developed a classical, delayed, eczematous, hypersensitivity reaction 10 days after a single exposure to the aerosol

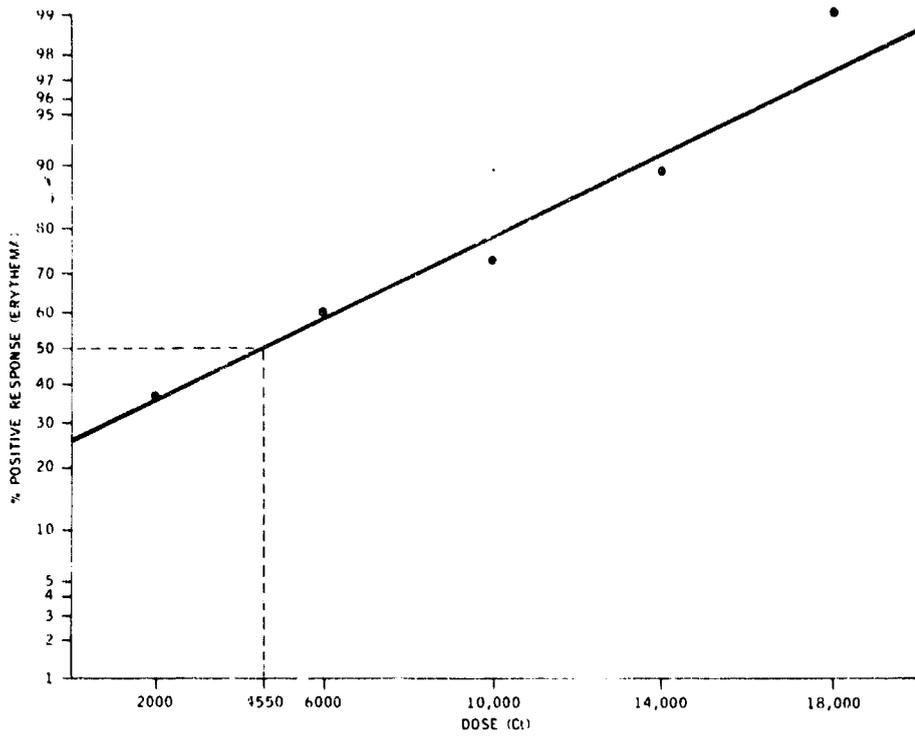


Figure 6. Log Dose vs. Response to CS Under Tropical Conditions (probit analysis)

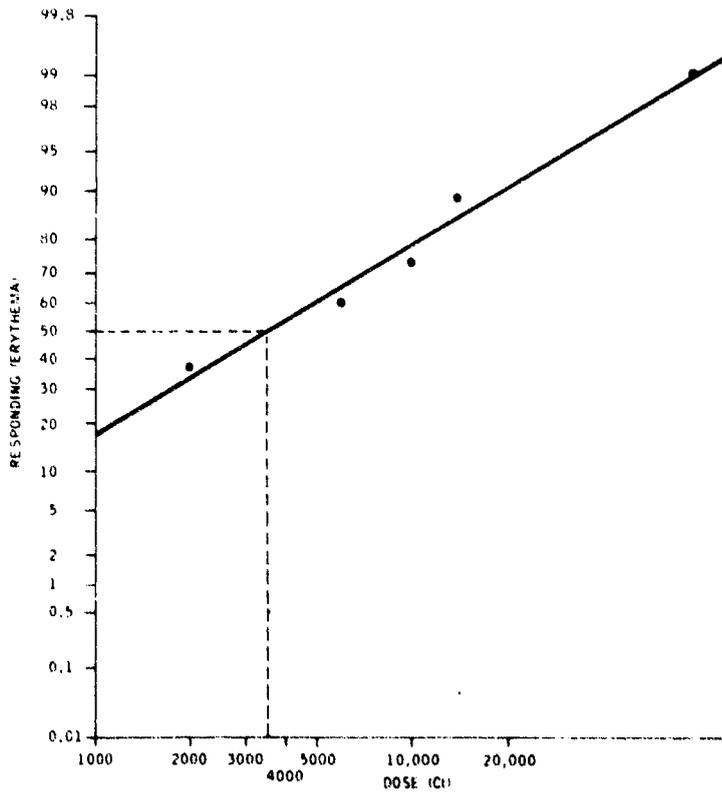
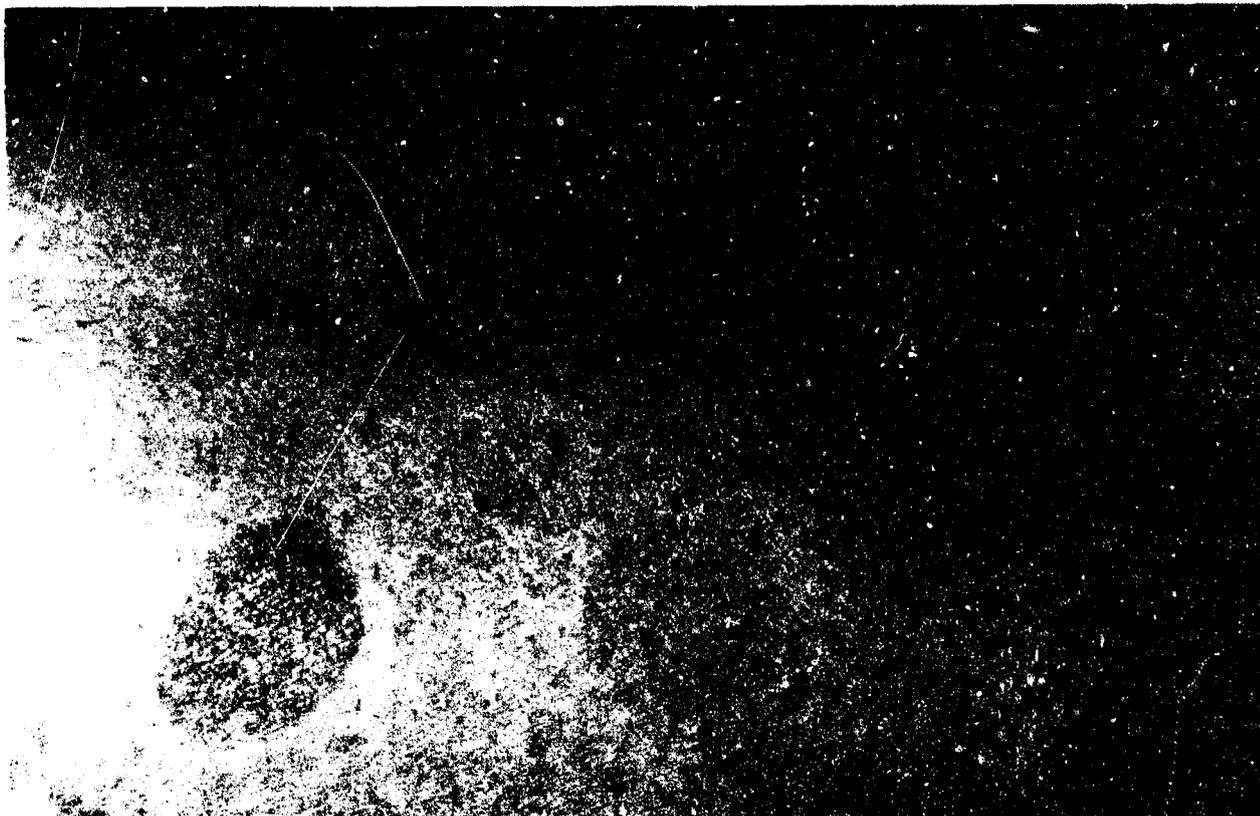


Figure 7. Dose vs. Response to CS Under Tropical Conditions (linear)

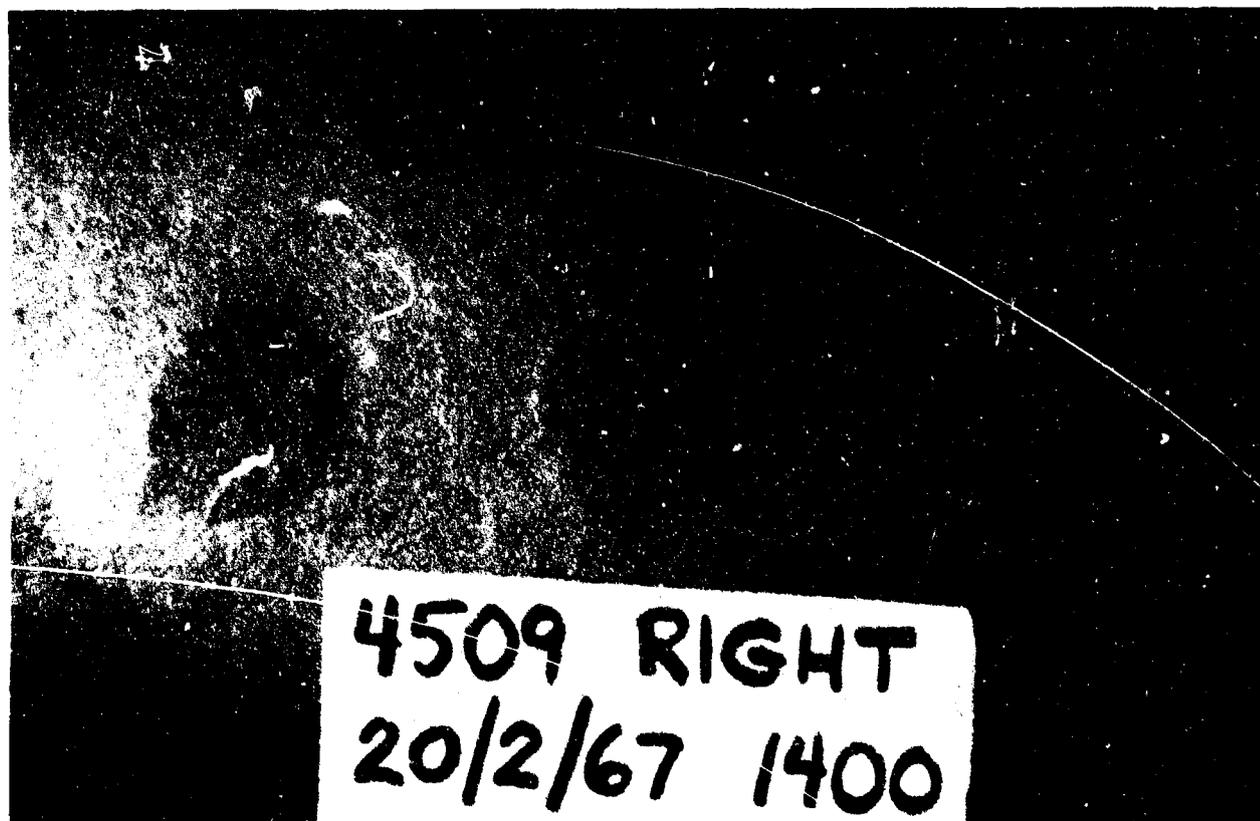
Table IV. Responses at Temperature Climatic Conditions

Ct mg min/cu m	Responses (57°F, 41% RH)			
		4391*	4422	4446
4,200	0	0	0	0
7,100	0	0	0	0
9,500	0	0	0	0
11,400	0	0	0	0
13,300	0	0	0	0
15,900	0	0	0	0
		(68°F, 95% RH)		
	4496	4490	4481	4532
4,470	0	0	0	0
10,410	0	0	0	0
15,885	0	0	0	0
21,060	0	0	±	0
26,025	0	0	+	±
30,240	+	±	+	+
		(72°F, 72% RH)		
	4528	4546	4543	4548
4,620	0	0	0	0
9,300	0	0	0	0
13,680	0	0	0	0
18,840	0	0	0	0
23,175	0	0	0	0
25,560	0	0	0	0

*Volunteer number.



A. Delayed Primary Reaction Which Subsequently Disappeared



B. Eczematous Allergic Flare-up Which Started 10 Days After Exposure
Figure 8. Sensitization by CS. Subject was exposed on 6 February 1967.

under tropical conditions. As well as could be determined, this was his first exposure to either CS or the fluorescent dye. Cases of sensitization have been reported in CS plant workers* but the true sensitizing potential of CS can only be determined by large numbers of patch tests. Preliminary screening by Kligman** suggests that CS is a potent skin-sensitizer as well as a photosensitizer. Since sensitization to the dye has not been reported, CS is considered the probable cause of the delayed allergic response of volunteer No. 4509.

E. Fluorescent Aerosol.

Leakage in the sleeve assembly was detected on the left forearm of volunteer No. 4546, as illustrated by figure 9. This was severe enough to produce some coalescence of two exposure sites (on the right side of the photographs). The areas of fluorescence corresponded with subsequent areas of erythema.

Readings from three volunteers had to be discarded because of significant leakage. Fortunately, leakage was uncommon, even when exposure was as long as 90 minutes.

F. Photoelectric Plethysmography.

The correlation between clinical observations and serial plethysmograph recordings is illustrated by figures 4, 10, and 11. The red coloration of the blistered area in figure 4 is an indication of increased blood volume. However, color alone does not indicate whether the blood is pooled or moving. It is assumed that the blood is flowing if the area becomes blanched under light pressure and then rapidly returns to the reddened condition. The photoelectric plethysmograph records clearly show pulsations associated with blood flow and also indicate the degree of filling of the capillary bed.

Figures 10 and 11 show differences in pulse amplitudes that probably represent normal blood flow in a few of the available capillaries (low amplitude tracings) and flow in a fully-functional capillary bed (highest amplitude). Pulse amplitudes from the blistered area on volunteer No. 4469 vary from low (pre-exposure control, 5 units) to high (35 units subsequent to loss of blister covering). The exceptionally high amplitude is probably caused by the severe inflammatory effects of tissue products released from cells damaged by dehydration.

The late, allergic, eczematous reaction of volunteer No. 4509 visually appeared to be more severe than his primary response to CS (figure 8); this difference is confirmed in figure 11. Pulse amplitudes after the allergic reaction occurred were approximately twice as high as those recorded 2 days after exposure.

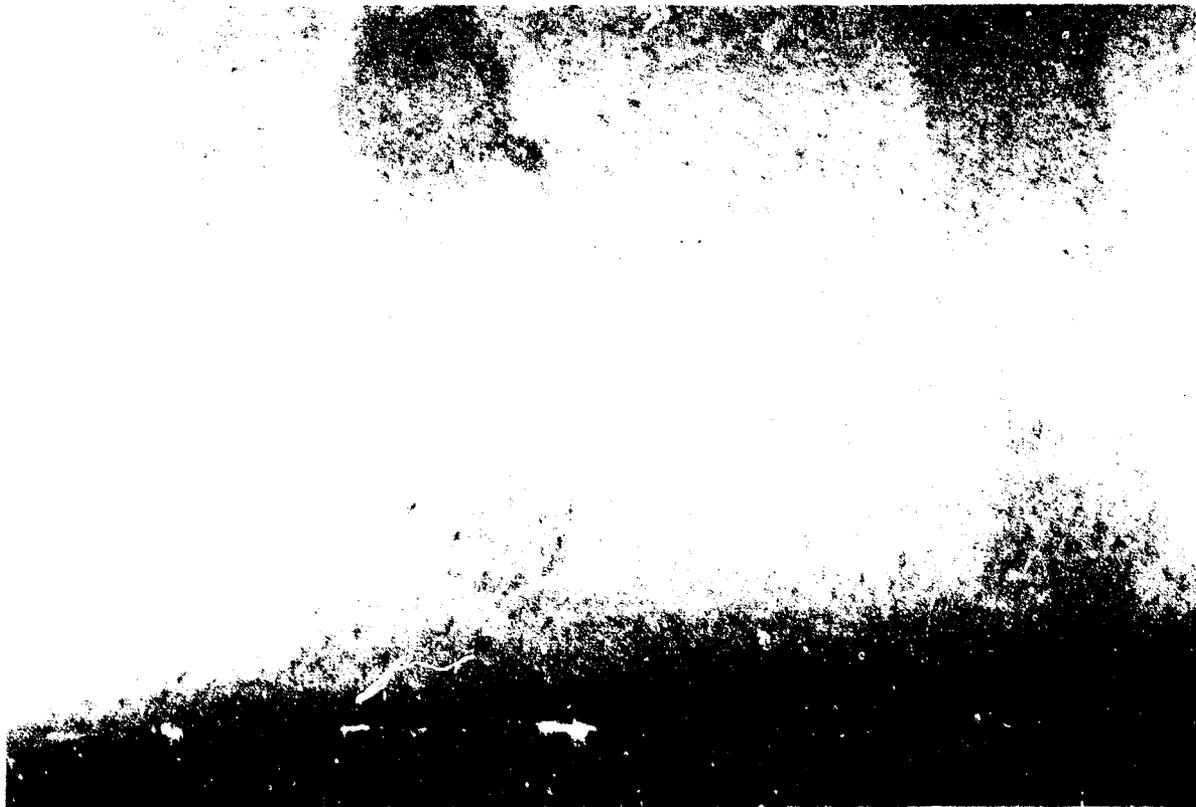
As expected, no conclusion could be drawn from comparing plethysmograms of different sites because of each area's individual pattern of underlying vasculature.

*Bowers, M. B., Owens, E. J., and Punte, C. I. CWL Tech Memo 24-50. Interim Report of CS Exposures in Plant Workers. June 1960. UNCLASSIFIED Report.

**D. Albert Kligman, University of Pennsylvania, personal communication.



**A. Fluorescence Under UV Light Immediately After Termination of Exposure to CS
(the irregularity of the boundaries of the exposure sites indicates leakage)**



**B. Subsequent Reaction to CS (erythema was much less apparent
when the 24-hour readings were taken)**

Figure 9. Demonstration of Leakage With Fluorescent Dye

VOLUNTEER NO. 4469, RIGHT ARM

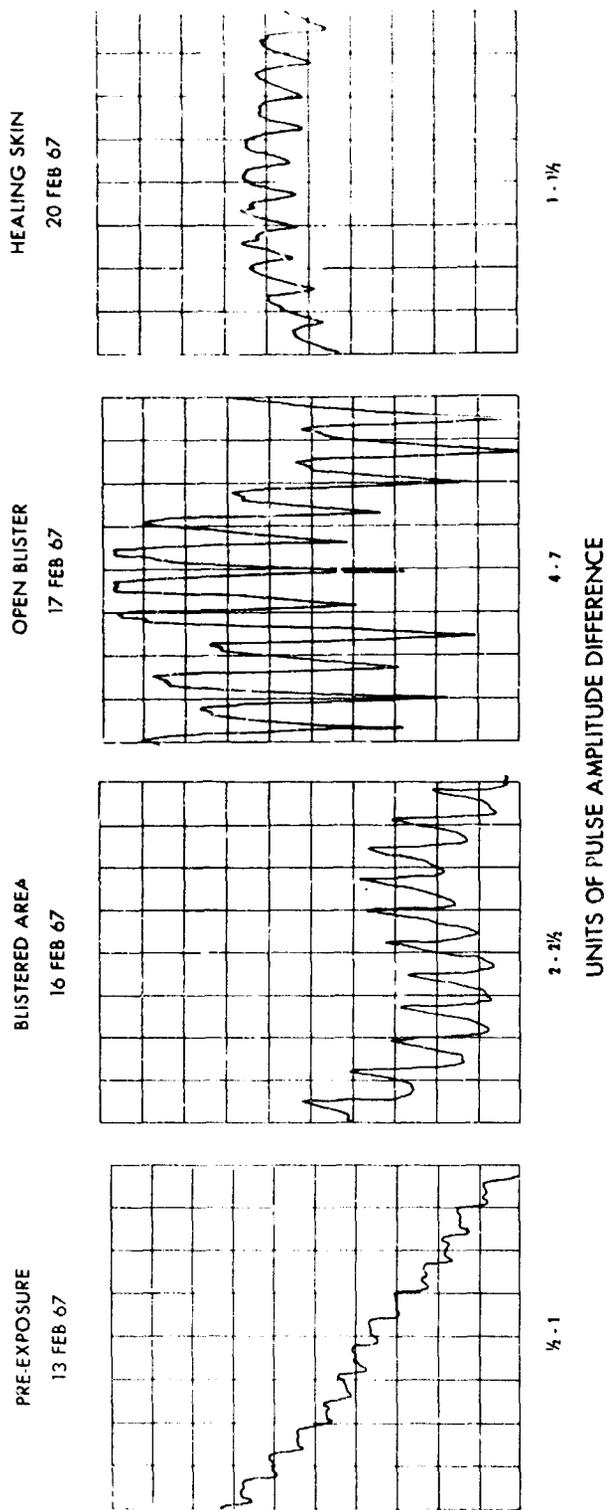
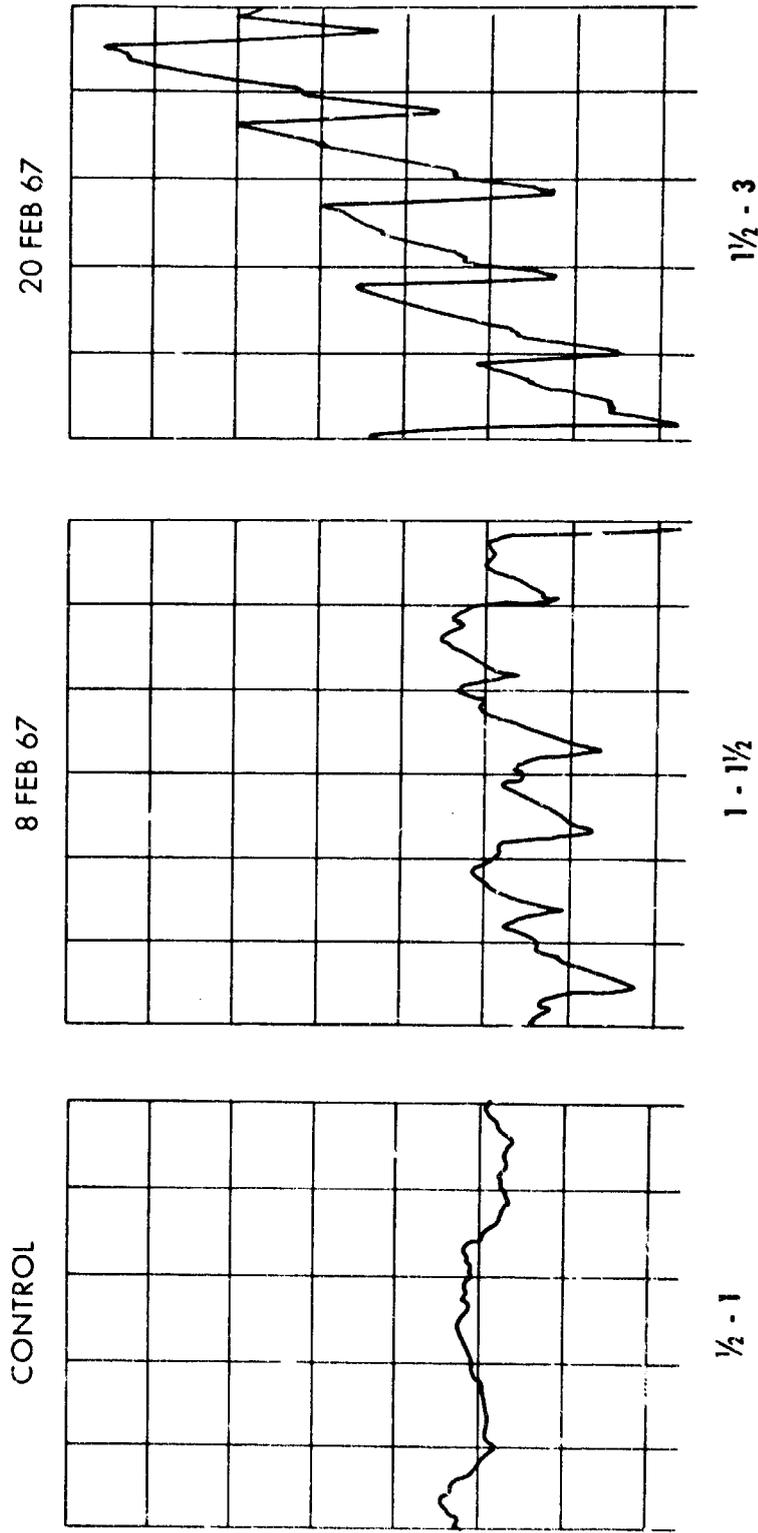


Figure 10. Photoelectric Plethysmograms Before and After Erythema and Blisters. Pulsation Amplitude Is Expressed in Arbitrary Units. (Tracings also reflect transient variations in blood pressure.)

VOLUNTEER NO. 4509, RIGHT ARM



UNITS OF PULSE AMPLITUDE DIFFERENCE

Figure 11. Photoelectric Plethysmogram of Volunteer No. 4509 Showing Pulse Amplitude Increased Sixfold With the Primary Skin Response (8/2/67) and Fourteenfold With the Subsequent Allergic Response.

G. Other Factors.

To better define the individual factors which influence susceptibility to CS-induced skin burns, each volunteer was rated as to his eye color, natural hair color, general complexion, history of susceptibility to sunburn, "incubation" time (the total number of minutes his arm was exposed to tropical climatic conditions), dose causing minimal erythema (estimated by extrapolating his own dose-response curve to this level), and the maximum response to the agent (see tables V and VI).

Each factor was then compared with the other six factors to determine whether any are significantly interrelated. The table of intercorrelation (table V) demonstrates that which has been well known, the highly significant intercorrelation of eye color, hair color, complexion, and susceptibility to sunburn.

It can be seen that the dose to cause minimal erythema correlates with sunburn susceptibility, incubation time, and maximum response. However, the maximum response of each subject correlates significantly with eye color along with the same factors that correlate with the minimal erythema dose. The presence of this additional significant factor implies that it might be easier to predict whether or not a subject will react severely to the agent than it is to predict at what dose he will begin to show a reaction.

The intercorrelations evident from this study must be considered in designing any future studies.

IV. CONCLUSIONS.

From this study, it is concluded that:

1. It is impossible to predict the dose of CS that will cause minimal erythema in an untested individual under tropical conditions because the variations among individuals are so great.
2. Fifty percent of a large group of men will develop some degree of erythema when the Ct of CS is 3500 ± 1500 mg min/cu m and the climate is tropical.
3. CS may produce sensitization and delayed skin response.

Table V. Table of Intercorrelations^a

	Eyes	Hair	Complexion	Susceptibility to Sunburn	Incubation Time	Minimal Erythema Dose	Maximum Response
Eyes	-						
Hair		.66b	.69b	.74b	.12	.29	-.47c
Complexion			.78b	.81b	.19	.05	-.29
Susceptibility to sunburn				.87b	.10	.11	-.27
Incubation time					-.11	.52c	-.52c
Minimal erythema dose						-.53c	.48
Maximum response							-.69b

SCORING SYSTEM:

Eyes	Hair	Complexion	Susceptibility to Sunburn	Incubation Time	Minimal Erythema Dose	Maximum Response
Blue	1 Red	1 Light	++++2°	Minutes - no scale	0-2,000	1 Neg
Light hazel	2 Blonde	2 Light, freckled	+++		2,000-4,000	2 ±
Green	3 Sandy blonde	3 Fair	++		4,000-6,000	3 +
Hazel	4 Light brown	4 Medium, light	+		6,000-9,000	4 ++
Brown	5 Brown	5 Medium	Some		9,000-13,000	5 +++
Dark brown	6 Dark brown	6 Medium, dark	±		13,000-18,000	6 +++V
	7 Black	7 Dark, Cau	No		>18,000	7 ++++V
		8 Dark, Mex				
		9 Dark, Negro				

a Spearman Rank Correlation Coefficients

b $p < .05$.

c $p < .01$.

Table VI. Scores Used in Intercorrelations

Subject No.	Eyes	Hair	Complexion	Susceptibility to Sunburn	Incubation Time Min	Minimal Erythema Dose	Maximum Response
4391	5	6	7	7	40	4	3
4422	5	3	4	5	40	6	1
4446	5	5	5	7	34	5	2
4450	1	5	5	7	34	5	2
4496	5	7	4	6	80		2
4490	1	2	3	3	80	4	4
4481	4	2	3	1	80		4
4532	1	2	3	1	80		4
4442	5	5	7				
4415	1	3	1		50	4	3
4385	5	5	6				
4438	4	5	5		50	3	4
4429	5	7	7				
4528	4	2	3	2	60	3	2
4546	6	7	8	7	60	4	2
4543	3	7	6	4	60	1	4
4548	5	5	4	6	60	3	2
4518	6	7	9	7	80	3	2
4522	1	2	3	2	80	1	6
4531	2	5	5	3	80	2	6
4519	5	7	9	7	80	7	1
4483	4	5	5	4	90	2	4
4537	5	7	9	7	90	2	3
4540	5	5	7	7	90	1	4
4469	1	1	2	1	65	1	7
4509	4	4	4	3	90	2	4
4539	4	4	3		90	3	4
4482	5	5	5		90	2	4
4470	5	5	5				

UNCLASSIFIED

Security Classification

DOCUMENT CONTROL DATA - R & D		
<i>(Security classification of title, body of abstract and indexing annotation must be entered when the overall report is classified)</i>		
1. ORIGINATING ACTIVITY (Corporate author) CO, Edgewood Arsenal ATTN: SMUEA-RMC Edgewood Arsenal, Maryland 21010		2a. REPORT SECURITY CLASSIFICATION UNCLASSIFIED
3. REPORT TITLE QUANTITATIVE EVALUATION OF THE IRRITANT POTENTIAL OF CS AEROSOLS ON HUMAN SKIN UNDER TROPICAL CLIMATIC CONDITIONS (U)		2b. GROUP NA
4. DESCRIPTIVE NOTES (Type of report and inclusive dates) This work was started in December 1966 and completed in February 1967.		
5. AUTHOR(S) (First name, middle initial, last name) Hellreich, Alfred, CPT, MC, Mershon, Millard M., Weimer, John T., Kysor, Kragg P., and Bottiglieri, Nicholas G., COL, MC		
6. REPORT DATE May 1969	7a. TOTAL NO. OF PAGES 31	7b. NO. OF REFS 5
8a. CONTRACT OR GRANT NO.	9a. ORIGINATOR'S REPORT NUMBER(S) EATR 4252	
b. PROJECT NO. 1B6627206A097 c. Task No. 1B662706A09710 d.	9b. OTHER REPORT NO(S) (Any other numbers that may be assigned this report)	
10. DISTRIBUTION STATEMENT Each transmittal of this document outside the agencies of the US Government must have prior approval of the Commanding Officer, Edgewood Arsenal, ATTN: SMUEA-TSTI-T, Edgewood Arsenal, Maryland 21010.		
11. SUPPLEMENTARY NOTES Defense Medical Aspects of Chemical Agents, Incapacitating and Riot Control Agents (U)	12. SPONSORING MILITARY ACTIVITY	
13. ABSTRACT (U) An attempt was made to quantitate the irritant potential of (o-chlorobenzylidene)malononitrile (CS) aerosols on human skin. A "negative patch test" was devised to expose small areas of the forearm to the agent in a subchamber assembly simulating tropical and temperate climates. Graded responses were obtained by unsheathing each area at intervals, and responses were read 24 hours after exposure. It was found that it is virtually impossible to predict the dose of CS that will cause minimal erythema in an untested individual under tropical conditions because the variations among individuals are so great. It is estimated that 50% of a large group of men will develop some degree of erythema when the Ct of CS is 3,500 ± 1,500 mg min/cu m and the climate is tropical. It was also found that CS may produce sensitization and delayed skin response.		
14. KEYWORDS CS Tropical climatic conditions Temperate climatic conditions Human skin Exposure Ct Sensitization Erythema o-(chlorobenzylidene)malononitrile Ultraviolet analysis Colorimetric analysis Plethysmograph Fluorescent dye Vesiculation		

DD FORM 1473
1 NOV 66

REPLACES DD FORM 1473, 1 JAN 64, WHICH IS OBSOLETE FOR ARMY USE.

UNCLASSIFIED

Security Classification

SUPPLEMENTARY

INFORMATION

DEPARTMENT OF THE ARMY
Headquarters, Edgewood Arsenal
Aberdeen Proving Ground, Maryland 21010

ERRATUM SHEET

28 SEP 1973

AD-853967L

Report No.: EATR 4252
Title: An Evaluation of the Irritant Potential of CS Aerosols
on Human Skin Under Tropical Climatic Conditions
Authors: Alfred Hellreich, Millard M. Mershon, John T. Weimer,
Kragg P. Kysor, Nicholas G. Bottiglieri
Date: May 1969
Classification: UNCLASSIFIED

This report was forwarded to your installation in May 1969.

Please make the following changes:

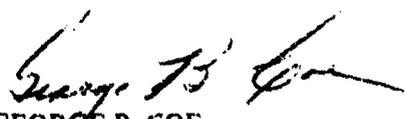
1. Add the following sentence to the last paragraph in the digest, page 3, and to the first paragraph on page 16.

"It should be noted that a Ct of 3500 ± 1500 mg min/cu m is extremely high and is likely to be encountered only under unusual conditions, e.g., the conditions used in this study."

2. Change the distribution statement on inside of front cover, title page, and DD Form 1473 to read:

"Approved for public release; distribution unlimited."

3. Delete the word "not" in the fourth paragraph of the foreword on page 2.


GEORGE B. COE
COL, CmlC
Director of Technical Support