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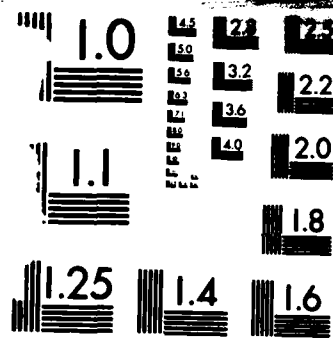
EFFECTS OF SUPPLEMENTARY VITAMINS AND STIMULANTS ON
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**EFFECTS OF SUPPLEMENTARY VITAMINS AND STIMULANTS
ON DARK ADAPTATION**

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MARCH 1983

**LETTERMAN ARMY INSTITUTE OF RESEARCH
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Effects of supplementary vitamins and stimulants on dark adaptation--
O'Mara, Schmeisser, and Weiss

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EFFECTS OF SUPPLEMENTARY VITAMINS AND STIMULANTS ON DARK ADAPTATION-
O'Mara, Schmeisser and Weiss

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It has been claimed recently that a proprietary mixture of vitamins and a stimulant will enhance dark adaptation in normal human subjects. The purported effect occurs following five days of treatment (daily oral doses) and is absent five days after cessation of treatment. An improvement in the rate and degree of dark adaptation was reported. It has been proposed that the effect was due to a synergistic effect of the mixture of compounds. This enhanced dark adaptation could not be demonstrated when the compounds were administered separately.

Night and low-light operations are a fundamental military requirement. Methods for enhancing night vision would benefit soldiers performing in low-light conditions.

The purpose of this investigation was to determine whether the claimed effect can be reproduced under controlled conditions. A double blind technique was used to test the effects on normal volunteers of the test mixture, a placebo, and a no-treatment condition.

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*E.S. Beatrice, M.D., Colonel, Medical Corps, US Army citing classified sources, 1982. Personal communication.

METHODS

Subjects: Eighteen 18- to 40-year-old male military and civilian personnel stationed at the Presidio of San Francisco participated. Each volunteer received a preliminary ophthalmologic examination and filled out a medical information questionnaire to determine if he met the study criteria (Appendix A). Each volunteer was given a briefing concerning the purpose of the study; each person read and signed a volunteer agreement and privacy act statement (Appendices B and C). The Human Use Committee had determined that the participants were "not at risk."

Apparatus: Dark adaptation was tested with the LAIR dark adaptometer (1,2). This device uses red and green light-emitting diode (LED) test displays to derive dark adaptation functions for cones and rods. The adaptometer is automated under microprocessor control. Permanent records for each participant were recorded graphically by a Houston Instrument HiPlot digital plotter.

Drug Preparation: The mixture of test compounds was prepared with the exact dosages outlined in the earlier investigation* (Table). The mixture was placed in gelatin capsules or tablets for oral administration. Placebos contained inert material in the same type of vehicle. Treatments were identified by a code number. Participants and testing personnel did not know the identity of the materials in the coded capsules or tablets.

TABLE
Drug Preparation

Placebo		Drug	
Dosage	Ingredient	Dosage	Ingredient
2 caps	#0 Lactose	8 tabs	50 mg Thiamin
2 caps	#1 Lactose	2 caps	100 mg Vitamin C
2 caps	#21 Blanks (Lilly)	2 caps	25,000 IU Vitamin A
2 caps	100 mg Pyridium	2 caps	No-Doz (caffeine) (Bristol-Myers)

*Ibid.

Procedure: Each volunteer was tested under all three experimental conditions, i.e., placebo, no placebo (control), and vitamin/stimulant conditions. During the first five days, the volunteer received daily one of the three treatments. On the sixth day, a dark adaptation test was given and further experimental treatment was suspended for at least ten days. At the end of the ten-day recovery period, the five-day test, ten-day recovery period was repeated until all three tests had been administered. No dark adaptation tests were conducted after the third recovery period.

Standard test procedures were used. The participant sat in a darkened room in front of a hemisphere containing the red and green stimulus displays. The tests began with a 5 min light adaptation period during which the hemisphere was illuminated at 110 candelas/m². Light adaptation was followed by 20 min of darkness. Dark adaptation testing began with a green stimulus. Each stimulus presentation began with the apparent intensity 0.75 log units below the estimated threshold value. Apparent intensity was then incremented in 0.05 log unit steps every 0.5 s. The participant reported stimulus detection by pressing a response button. Then, the intensity was decremented at the rate of 0.05 log units/0.5 s until the volunteer signaled by releasing the button that it was no longer visible. The absolute threshold for each trial (stimulus presentation) was the average of the log values at which response categories changed during the ascending and descending series. Threshold values were obtained in this manner, alternately for the red and green stimuli throughout the 20 min of dark adaptation.

Experimental Design: Each participant was tested after drug, placebo, and no treatment. With three conditions, there are six possible orders of presentation. Three volunteers were assigned, at random, to each of these orders. The resulting design is a two-factor experiment with repeated measures on treatments and between group comparisons for orders of treatments. The dependent variable is the threshold detection value for the red and green stimuli at 15 min of dark adaptation. Analyses of variance and analyses of covariance for multifactorial designs were used for evaluating treatment, order, and order-by-treatment effects. A significance level less-than-or-equal to 0.05 was used for all tests.

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RESULTS

Figure 1 illustrates a typical output from the LAIR Dark Adaptometer. The five points indicated around the 15-min mark were averaged to form the actual data point submitted to analysis. The analyses of variance and co-variance including repeated measures revealed no significant effects due to group (order of treatment), treatment (drug, placebo, or control), or group by treatment interaction for either red or green LED stimuli. No further statistical analysis was performed.

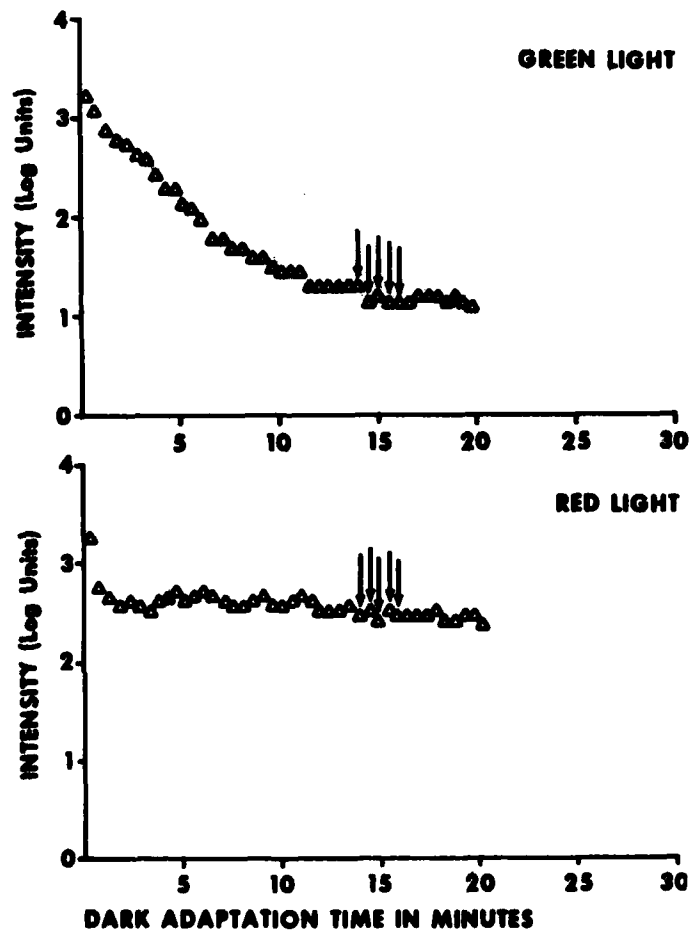


Fig. 1 Dark adaptation curves (response level vs time) showing data points used in the analysis

Cont'd
DISCUSSION

Dark adaptation has been used as a criterion for evaluating the effectiveness of vitamin replacement (3). In such therapy, super-normal dark adaptation curves have not been observed. Tests with normal subjects on vitamin A restricted diets showed effects only after 6 to 8 months (4). Since vitamin insufficiency in normal subjects can decrease the rate and final sensitivity level of dark adaptation, a hypothesis is that the converse is also true, i.e. super-vitamin therapy will produce super-normal results. This has not been substantiated by our results.

CONCLUSION

Supplementary vitamin and caffeine do not demonstrate any significant short-term effects on dark adaptation in normal human volunteers.

RECOMMENDATION

None

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- (1) O'Mara PA, Zwick H, Beatrice ES, Lund DJ. Microprocessor controlled light emitting diode dark adaptometer. Med Biol Electr Comput, 1981 (in press)
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- (3) Carney EA, Russell RM. Correlation of dark adaptation test results with serum vitamin A levels in diseased adults. J Nutr 110: 552-557, 1980
- (4) Sauberlich HE, Hodges RE, Wallace DL. Vitamin A metabolism and requirements in the human studies with the use of labelled retinol. Vitam Horm 32: 251-275, 1974

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APPENDIX A

SCREENING OF TEST SUBJECTS

The volunteers will be requested to bring their medical records with them before being accepted.

QUESTIONNAIRE

YES NO

1. Do you have headaches often?
2. Are you conscious of your heart beat?
3. Have you ever been told you have high blood pressure? .
4. Do coffee, tea, or cola drinks bother you?
5. Do you feel tired all the time?
6. Is your appetite poor?
7. Do you cough frequently?
8. Do you get short of breath easily?
9. Are you bothered by indigestion?
10. Do you get abdominal pains?
11. Is your urination normal?
12. Do your legs swell?
13. Have you ever had kidney stones?
14. Do you have any trouble with your ears?
15. Do you have any trouble with your nose?
16. Do you have any trouble with your throat?
17. Are you prone to skin disorders?
18. Do you have trouble seeing at night?
19. Do you have color deficient vision?
20. Do you have any eye problem (other than glasses)? . . .

21. Are you on a diet? YES NO
22. Do you have difficulty sleeping?
23. Do you feel nervous and jittery?
24. Do you take iron or vitamins containing iron?
25. Do you smoke?
26. Do you drink alcoholic beverages?
27. Do you use tranquilizers?
28. Do you use sleeping pills?
29. Have you consulted a medical practitioner in the
past year for anything but a medical exam?
30. Has a medical practitioner found you to have any
medical problem in the last year?

List all medications, including vitamins and iron, you have taken in the last two weeks and give amounts.

Physical Examinations:

Blood pressure, pulse, best corrected distant visual acuity, slit exam, and ophthalmoscopy. (More examination may be done if indicated by answers to questions.)

The blood pressure and pulse will be repeated before each dose is given and the individuals asked how they feel.

Criteria for exclusion from study:

1. Best corrected visual acuity less than 20/20.
2. Abnormal color vision.
3. Abnormal base line dark adaptation.
4. Abnormal sensitivity to caffeine.
5. History of kidney stones.
6. Takes supplementary iron.
7. Uncontrolled high blood pressure.
8. Presence of major eye problem.
9. Use of psychostimulants or depressants in amounts which, in the opinion of the medical examiner, could mask the effect of the drugs being tested.

GENERAL INFORMATION FOR VOLUNTEERS

The multi-vitamin supplement which you will be given contains a mixture of vitamins and a mild non-prescription stimulant. The exact formulation cannot be revealed in order to protect the proprietary rights of the individual who developed the mixture. Each dose will contain 3 to 19 times the recommended daily allowance (RDA) of a small number of water soluble vitamins. Excess amounts of these compounds are rapidly lost from the body and do not represent a toxic hazard. The mixture also contains vitamin A. This vitamin can accumulate in the fatty tissues of your body. Very high doses of vitamin A taken for long periods of time can produce toxic side effects. These include skin disorders. The amounts of vitamin A which you will receive are 10-13 times the normal dietary intake. This amount is much less than levels which produce toxic effects. The mild stimulant which is used in the preparation is similar to those found in tea, coffee, and certain soft drinks. The amount is equivalent to the amount contained in 1-2 cups of coffee.

APPENDIX B

EXPLANATION OF QUESTIONS RELATING TO
VOLUNTEER AGREEMENT

1. What will be administered to or done to the volunteers?

Prior to beginning the study, you will be given an eye examination to include how well you can see a standard eye chart, your color vision, and how well you can see in the dark. You will be asked to fill out a standard medical information form which included routine questions about your health history and current health. A physician will review your medical history and the results of the visual screening. If your health is normal, you will be asked to participate in a study of the effects of vitamin supplements on your ability to see in the dark. During the study, you will take specially prepared tablets daily for five days. Your ability to see in the dark will be tested after the five-day period. The procedure of taking the tablets will be repeated one more time during the experiment. Your ability to see in the dark will be tested a total of five times over a period of approximately two months.

2. How long will my participation last?

The total duration of the study will be two months. The time you will actually be participating will be approximately four hours. Most of this time will be used to administer the dark adaptation tests to determine how well you see in the dark. Each dark adaptation test lasts 30 min.

3. To what tests or examinations will I be required to submit?

a. Before being accepted into the study, you will be asked to take an eye examination that includes visual acuity, color vision, and dark adaptation.

b. During the study, your dark adaptation will be tested five times. Each test lasts 30 min.

4. Why is the investigation being conducted?

The military often performs operations at night or during low-light conditions. It would be useful to have a means of improving our soldiers' ability to see under low-light conditions. This study will determine whether or not simple dietary vitamin supplements will improve dark adaption.

APPENDIX C

5. Has this particular study been done previously and, if so, with what results?

There is some evidence that the supplements used in this study do improve dark adaptation, but the results of earlier studies need to be confirmed.

6. What inconveniences or discomfort will I experience?

Some of the tablets which you will take during this study contain a mixture of vitamins and a mild non-prescription stimulant. Other tablets will contain only sugar or starch. You will not know which tablets contain the vitamins or starch. The materials used in this experiment are not hazardous. They are normally present in the foods and beverages which you consume every day. These materials will only supplement your normal dietary intake.

The dark adaptation test will require that you remain in a darkened room for approximately 20 min. It is anticipated that considerable attention on your part will be required to produce your best performance on this task.

7. What risks or hazards can be reasonably anticipated?

None.

8. What steps will be taken to prevent or minimize these risks or hazards?

None.

9. What benefits, if any, may I expect from my participation in the study?

You will receive no direct benefits other than the knowledge of the eye examination results.

10. What appropriate alternative procedures, if any, might be more advantageous to me?

There are no alternative procedures of advantage to you.

11. What are my obligations to the project?

Once you have begun the study, we would like you to complete your part in the project. However, you may revoke your consent and withdraw from the project without prejudice.

VOLUNTEER AGREEMENT
(Civilian Adults)

I, _____, having attained my _____, birthday, and otherwise having full capacity to consent, do hereby volunteer to participate in an investigational study entitled "ST-5: The effects of supplementary vitamins and stimulants on dark adaptation."

The implications of my voluntary participation; the nature, duration, and purpose; the methods and means by which it is to be conducted; and the inconveniences and hazards which may reasonably be expected have been explained to me by _____, and are set forth on the reverse side of this Agreement, which I have initialed. I have been given an opportunity to ask questions concerning this investigational study, and any such questions have been answered to my full and complete satisfaction.

I understand that I may at any time during the course of this study revoke my consent, and withdraw from the study without prejudice; however, I may be requested to undergo certain further examinations, if in the opinion of the attending physician, such examinations are necessary for my health or well being.

I understand that I shall not be entitled to any payment for my participation.

I understand that any time spent participating in this study during my regularly scheduled duty hours will be considered as constructive duty for which straight time rates shall be payable. I further understand that any time spent participating in this study during other than my regularly sheduled duty hours, or while in a leave status, will be considered as voluntary overtime for which no payment may be made nor compensatory time granted.

Signature

Date

I was present during the explanation referred to above, as well as the volunteer's opportunity for questions, and hereby witness his signature.

(Witness Signature

Date

PRIVACY ACT STATEMENT
VOLUNTEER AGREEMENT/CONSENT FORM

AUTHORITY

Section 301 of Title, U.S. Code; Section 3101 of Title 44, U.S. Code; Sections 1071-1087 of Title 10, U.S. Code; and Executive Order 9397.

PRINCIPAL PURPOSE(S)

The purpose for requesting personal information is to provide the various types of data needed to satisfy the scientific objectives of the study and to provide the minimum information necessary should you require medical treatment at any future time for a condition proximately resulting from your participation in this investigational study, or so that steps can be taken to contact you should it later be deemed in your best interests to do so.

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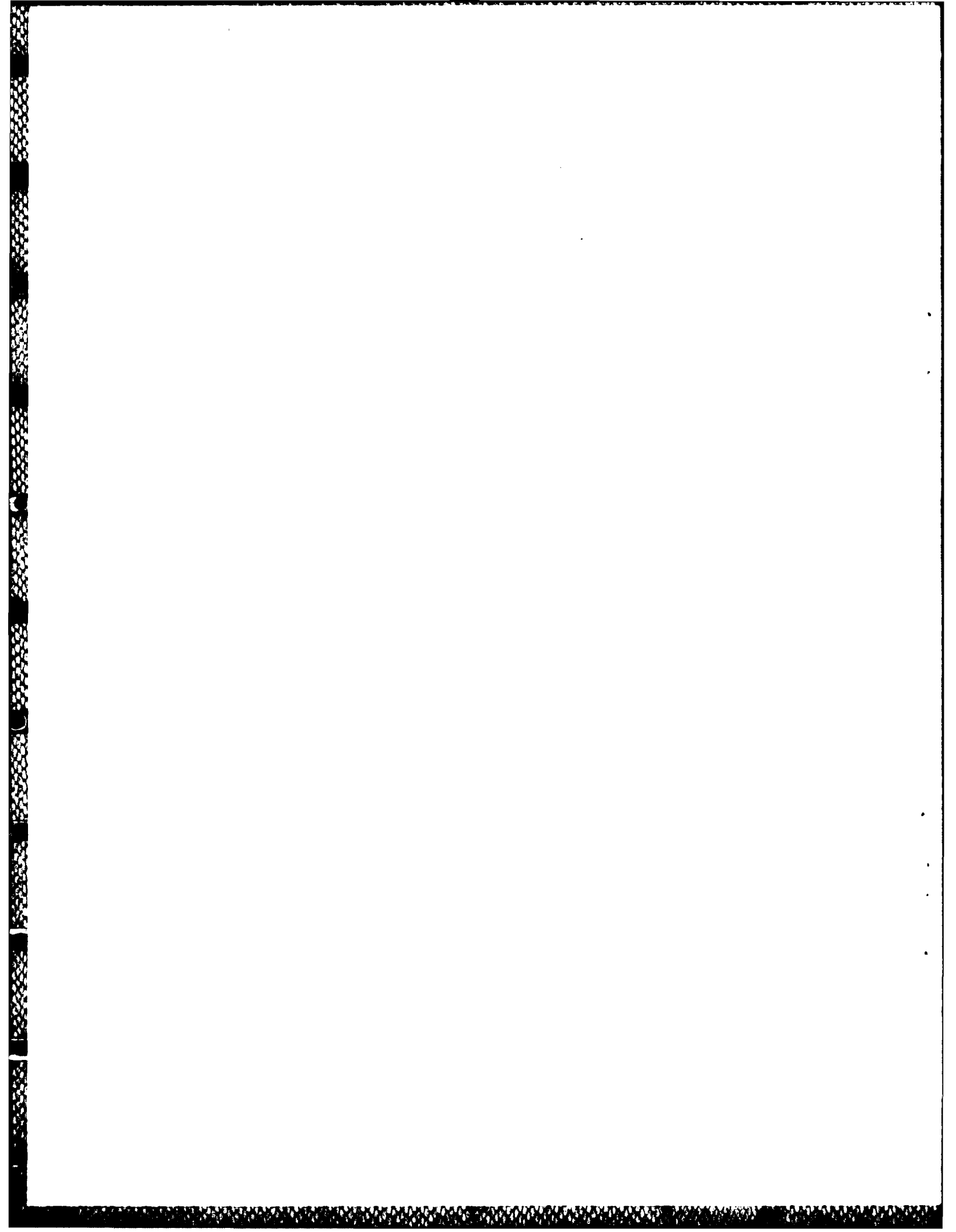
This information will be used to determine the normal values for new vision tests that will be used to screen military personnel and others who build lasers or participate in field exercises where lasers systems are employed. The information may also be used to provide full documentation of investigative studies; conduct further research; teach; compile statistical data; adjudicate claims and determine benefits; and report medical conditions required by law to other Federal, State and local agencies. It may be used for other lawful purposes, including law enforcement and litigation. Even though permitted by law, whenever possible, this personal data will not be released without your consent.

MANDATORY OR VOLUNTARY DISCLOSURE AND EFFECT ON INDIVIDUAL NOT PROVIDING INFORMATION

The disclosure of requested information is voluntary. If the information is not furnished, and/or not available from other sources, your voluntary participation in this investigational study may be precluded.

I understand that a copy of the Volunteer Agreement, together with a copy of this form, may be placed in my health records as evidence of this notification, and that additional copies may be retained permanently by the investigator and by the U.S. Government. I have received or have declined to accept a copy of the Volunteer Agreement and a copy of this form which I may keep.

Signature



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