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CHAMBER TESTS WITH HUMAN SUBJECTS

XX HYPERSENSITIVITY TO H AS DEMONSTRATED
BY PATCH TESTS BEFORE AND AFTER
CHAMBER EXPOSURE TO H VAPOR

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ABSTRACT

A series of sensitivity tests on men before and after exposure to H vapor is described in this report. Doses of 1, 1/2, 1/4 and 1/8 micrograms of H in mineral oil, worn as closed patches on the forearm for four hours, represented a satisfactory subvesicant level for determining altered sensitivity. The intensity of reaction to patch tests by previously unexposed men showed a marked variation directly proportional to the outside effective temperature at the time the patches were worn. In addition to erythema, edema and/or folliculitis were observed in only 2 of 230 men tested prior to exposure to H vapor. After exposure, 26% of 169 men manifested edema and/or folliculitis to patch tests. These men were arbitrarily considered "sensitized". This sensitized group also showed a more intense erythema for each dose and a lower threshold dose for perceptible erythema than the non-sensitized group. Cases of abnormal generalized skin reaction following exposure to H vapor in the man-chamber are discussed. Eight kodachrome prints, illustrating pertinent features, are included.

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INTRODUCTION

A. Authorization

1. This work was authorized under Project No. 547/41, "Maintenance, Bureau of Ships" dated 16 December 1940.

The problems which were proposed for study were given in BuShips letter S-S77-2(dz), serial 811 of 17 December 1940.

2. Participation of volunteer Naval personnel in the tests for the study of vesicant gases, was approved by the Secretary of the Navy (Acting Sec. Nav. ltr. to OSRD dated 8 May 1942). Performance of such tests at the Naval Research Laboratory was approved by the Chief of the Bureau of Medicine and Surgery (BuMed ltr. Serial No. 446 X:OA All/EN10(430320)(SC) dated 20 March 1943.

B. Statement of Problem

3. A method for the quantitative estimation of the variation in skin sensitivity to H would be useful not only for testing previously unexposed individuals but also for investigating possible changes in sensitivity as a result of exposure to H vapor in the man-chamber. Reports on several different tests are available in the literature but there is considerable variation in the results obtained, especially as regards the threshold dosage for erythema in normal or in sensitized men. It was felt that the men employed as test subjects for testing protective clothing against H who usually sustained an intense generalized erythema would be excellent subjects for sensitivity tests. Such data would be obtained incidental to and with no interference with the clothing testing program; and since these tests would be carried out during varying outdoor and indoor climatic conditions, it might be possible to evaluate the effect of such conditions on the results of the sensitivity tests. Most of the studies in the literature describe tests on exposed men as compared with similar tests on an unexposed control group. Very few large-scale studies are reported in which tests were carried out on the same individuals before and after exposure to H. It was felt that the chamber testing program at NRL offered a unique opportunity to carry out such tests on the same individuals.

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C. Known Facts Bearing on the Problem

4. Well known is the fact that the skin of certain individuals will not tolerate contact with amounts of various substances which are used with impunity by the majority of the population. Such individuals are said to be hypersensitive to these substances. Although many maintain that previous exposure is necessary to develop hypersensitivity, such a history is not always evident.

5. Equally definite is the fact that some individuals, through known repeated contacts with a substance, may become sensitized to it and no longer tolerate these contacts. Such hypersensitivities are manifested in increasing order of reaction intensity by erythema, edema, vesiculation, crusting and the other concomitants of dermatitis venanata.

6. The possibility of the development of hypersensitivity to H is a generally accepted fact. It has been reported for casualties of World War I as well as for laboratory and factory workers who have been repeatedly exposed. A review of the literature and original observations are presented by Sulzberger, et al, in Volume III of the Fasciculus on Chemical Warfare Medicine prepared for the CMR by the Committee on Treatment of Gas Casualties, 1945. According to them "the incidence of hypersensitivity subsequent to exposure varies from about 30% to about 65%".

7. During the course of the program for testing protective clothing in the man-chamber at this Laboratory, occasional individuals were observed who sustained abnormal reactions following exposure to H vapor. In view of these cases, which will be further discussed below, it became evident that a method of testing for hypersensitivity to H would be highly desirable.

D. Theoretical Considerations

8. The patch test, in which suitable dilutions or amounts of a substance are worn in contact with the skin for varying lengths of time, offers one of the simplest means of testing for epidermal hypersensitivity. A positive response consists of erythema, edema, vesiculation, and crusting in increasing order of intensity of reaction.

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9. Most substances tested by the allergist provoke little or no reaction in the so-called normal skin so that interpretation of positive tests is relatively simple. However, in sufficient amounts, H causes reactions on the skin of any individual which resemble, or appear identical with, those of a positive patch test. Hence, development of a suitable patch test for H will require a critical adjustment of dosages to be able to detect small changes of threshold or increase in sensitivity as distinct from the normal reaction.

10. Since cutaneous reactions to H are influenced very markedly by external conditions, especially temperature and relative humidity, these factors should be given careful consideration in the interpretation of the results. Evidence was presented in NRL Report No. P-2579, dated 14 August 1945, which indicates that the effects of temperature and relative humidity on the susceptibility of the skin to H vapor are exerted indirectly -- apparently by the influence which they exert on the sweating mechanism.

1. Terminology

11. In NRL Report No. P-2579, the term "susceptibility" was used throughout to refer to the relative vulnerability of the skin to the effects of H vapor under varied conditions of temperature and relative humidity. The terms "sensitivity" and "hypersensitivity" were assiduously avoided because of their usual connotation in the field of allergy. However, in the present report, it is felt that some of the changes in vulnerability are closely related to a true sensitization so the liberty is taken of using these terms. The justification for this is reconsidered in the DISCUSSION. Variations in reaction caused by alterations of temperature and relative humidity are still referred to as changes in "susceptibility". Thus, theoretically, both a normal and a hypersensitive individual might show variation in susceptibility under altered physiological conditions.

EXPERIMENTAL

Part I. PROCEDURE

4. Test Subjects

12. It was not considered practicable to expose a sufficiently large series of men to H vapor under

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uniform conditions solely for the purpose of determining possible alterations in reactions to patch tests. But it was felt that by performing routine tests, before and after chamber exposure, on the men employed in testing the various types of protective clothing, sufficiently useful data could be obtained to warrant the procedure worthwhile.

13. The men who participated in these tests were volunteer Naval personnel from USNTC, Bainbridge, Maryland, and were usually seamen, second class, from eighteen to twenty years of age who had just completed their "boot" training. Drafts (i.e. groups) 75 to 82, each consisting of about thirty men, were employed in these tests during the period from 28 May 1945 to 5 September 1945 (Table 1).

B. Chamber Tests

14. The procedure for the chamber tests with H vapor has been described in detail in NRL Reports No. P-2208 dated 22 December 1943 and No. P-2579 dated 14 August 1945. Since the data for these test subjects as related to protective clothing, etc., has been presented in other reports from this Laboratory, only data pertinent to the main thesis of this report will be included.

15. The chamber tests in which these subjects participated were of two main types: (1) basic, in which masks and dungarees were worn; or (2) tests of protective clothing of various types. In the second class, protective suits (either CC-2 impregnated or carbon types), CC-2 impregnated gloves and socks were worn as well as masks. All the subjects included in this report wore CC-2 impregnated shorts during exposure in the chamber. The type of test, the CT employed, the number of exposures, and the resulting reactions are listed in Table I.

C. Chamber Test Readings and their Evaluation

16. The men were inspected daily by a medical officer for four to eight days or longer after exposure. A list of the abbreviations employed is presented in Table X and the maximum reading on any part of a given area is listed in Table I. These readings were assigned arbitrary values according to the scale in current use at this Laboratory:

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- 0 = no reaction
- 1 = mild erythema
- 2 = moderate erythema
- 3 = intense erythema
- 4 = a. erythema with edema
 - b. dry scaling of scrotum
 - c. maceration of axillary skin
- 5 = a. vesicle
 - b. numerous pinpoint vesicles
 - c. crusting or ulceration of scrotum or axilla.

These data are presented in Tables II and III according to the following categories: (1) Maximum reading for the individual regardless of area; (2) Total reaction, which represents the sum of the readings listed for any of the 18 areas; (3) Per A.A., which represents the average reaction per area affected by the H vapor, or, in other words, the total reaction divided by the number of areas affected. Readings listed in Table I for the various body areas which are underlined indicate that not only an erythema of that intensity was present but that it was accompanied by a follicular reaction.

D. Patch Tests (Sensitivity Tests)

17. Solutions of redistilled thiodiglycol mustard (H) in mineral oil were prepared so that one (1) drop as delivered by a blunt No. 26 gauge hypodermic needle contained one (1), one-half (1/2), one-fourth (1/4), and one-eighth (1/8) micrograms (gamma) of H respectively. The size of the drops delivered by each needle was calibrated gravimetrically and the same needles were used for all the tests. Solutions were prepared fresh before each test and were applied within an hour of preparation. One drop of each solution was placed on a separate disc of filter paper one (1) centimeter in diameter which was then worn for four (4) hours on the volar surface of the forearm covered by a strip of adhesive tape one inch wide (closed patch). The test doses were applied in sequence so that the largest dose was applied proximally and the smallest

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distally. Initial tests were always performed on the right arm; finals, on the left.

E. Reading of Patch Tests

18. The tests were read at approximately twenty-four (24) and forty-eight (48) hours after application of the patches. At the time of removal of the patches, the skin was not treated in any way. Since the graded test doses employed usually gave a range of readings on the initial tests of intense erythema to questionable erythema, it was decided to assign numerical values to the readings proportional to the fraction of a microgram of H employed. Erythema accompanied by edema, that is, a visible or palpable elevation of the skin, was arbitrarily given a value of double that for intense erythema.

16 = erythema accompanied by edema

8 = intense erythema

4 = moderate erythema

2 = faint erythema

1 = questionable erythema

0 = no reaction (left blank in Table 1)

An underlined numeral in Table I signifies that the erythema was accompanied by a follicular type of reaction, that is, erythema located mainly at the hair follicles with intermediate skin little or less affected.

F. Evaluation of Patch Tests

19. In Tables II and III, the sum of the readings (each of which was maximum at 24 or 48 hours for a given dose) are presented for the initial (I) and final (F) tests. In order to give follicular reactions additional weight, the underlined figures, indicating follicular reaction, were arbitrarily doubled in value in taking this sum except in those cases where edema was also present. It was felt that in this latter case the factor of possible sensitization had been given additional weight already. In order to obtain a value for the final test which did not include additional weighting for edema or folliculitis, a value

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Fx was calculated in which readings of 16 were assigned their erythema value of 8 and underlined figures were not doubled in value. These Fx values are listed in Table IV.

G. Thresholds for Reaction of Intensity 2

20. The lowest dosages to give a faint erythema (value of 2) are taken as the threshold and are listed in Tables II and III. If a figure is preceded by an L, meaning "less than", it indicates, as shown in Table I, that the lowest reading (except 1) was greater than a 2. Since in this case the threshold is probably lower, such subjects were included in the group having a threshold of next lower dosage. For example, if on a given subject the 1/8 microgram dose produced a moderate erythema (value of 4), the threshold for this subject was arbitrarily taken as 1/16 micrograms of H.

H. Temperatures at which Patch Tests were Performed

21. The indoor and outdoor temperature and relative humidity were determined hourly during the period in which the patches were worn and are listed in Table V. Since variations in temperature and relative humidity both influence sweating which, in turn, influences susceptibility to H, the effective temperature (outdoor, for wind velocity = 0), as employed by heating and ventilating engineers, was used in considering the effects of temperature and relative humidity on the reactions to patch tests (Table V).

Part II. RESULTS

A. Introductory Remarks

22. The results of the tests have been collated under the following main headings:

A. General Remarks

B. Average Total Reactions to Patch Tests.

1. Initial
2. Final
3. Second Pre-exposure (Repeated Initial) Tests.

C. Differences in Average Total Arm Reactions as Compared with Differences in Effective Temperatures at the Time the Tests were Performed

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- D. Average Reactions for a Given Test Dose
- E. Changes in Threshold
- F. Abnormal Skin Reactions Following Chamber Exposure to H Vapor.

B. General Remarks

23. The reactions to the test doses employed were always within the range of erythema with edema (16) to questionable erythema (1). In no case was vesication observed on either an initial or a final test following the technic for patch tests described above. Maximum reactions (i.e. maximum at either the 24 or 48 hour readings) for all patch tests are listed in Table I.

24. An illustration showing the general type of response to initial patch tests is presented in Plate 1; however, the erythema is not reproduced quite as intensely as it actually was. Far more accurate are the illustrations in Plates 2 and 3 showing the reactions of a hypersensitive individual to patch tests. This degree of edema is as great, or greater than, that observed in any other individual tested.

25. Of 230 men who received initial tests, only two showed erythema accompanied by edema. One of these subjects manifested a similar reaction on his final test; the other did not. Since this is definitely an atypical reaction to an initial test, these values are not included in the averages.

26. A total of 169 men received patch tests both before and after exposure to H vapor in the chamber. Edema and/or folliculitis were present in 44, absent in 125 of the final tests. Of these 44 tests, 25 were accompanied by edema, 15 by edema with associated folliculitis, while 4 manifested folliculitis alone. In subsequent discussion and in the tables, these 44 men are arbitrarily referred to as "Sensitized" whereas those 125 are designated as "Non-sensitized". The validity of such terminology is further considered in the DISCUSSION.

27. The intervals between the last chamber exposures and the final patch tests are listed in Table 1. These show an average of 15 days for the sensitized as compared with 14.5 days for the non-sensitized.

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Thus the two groups show no appreciable difference in this respect.

28. Most of the men considered in these tests were subjected to repeated chamber exposures wearing masks and a given type of protective clothing until they sustained an intense erythema (i.e. until the suit "broke"). Almost all the men who later showed edema and/or folliculitis on the patch test had sustained a moderate or intense generalized erythema from the chamber test; however, there was no apparent correlation between the intensity of chamber reaction and subsequent development of hypersensitivity. It should be added that an adequate series with graded intensities of chamber reactions was not available in this series of patch tests.

C. Average Total Reactions to Patch Tests

1. Initial

29. The average total reactions of the groups to initial (Pre-exposure) patch tests are listed in Table V with the dates on which these tests were performed and the average outdoor effective temperatures prevailing during the four hour period during which the patches were worn. The values for these reactions are plotted chronologically on Plate 9; and there appears to be a trend toward more intense reactions during the midsummer months for the initial tests.

30. However, if these same initial reaction values are plotted against the effective temperatures, as on Plate 10, it can be seen that the intensity of reaction shows a very definite relationship to the effective temperature at the time the patch is worn. Since each point on this curve represents the average value for patch tests on about thirty men, it is felt that this result is fairly well established. According to this curve, a rise in effective temperature of one (1) degree results in an increase in average total intensity of reaction of 0.4 unit. This applies to initial tests on men who have had no previous exposure to H.

2. Final

31. The reaction values for final (Post-exposure) patch tests are divided into two categories: those on men showing no evidence of sensitization (i.e. no edema or folliculitis); and those showing evidence of

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such sensitization. In comparing these two classes of men, the Fx values are employed for the men showing evidence of sensitization. This Fx value has been defined in paragraph 19 and the values have been listed in Table IV. Briefly, it represents a score in which no additional weighting is added for edema or folliculitis, only erythema of varying degrees being assigned value. It facilitates comparison of initial and final tests with regard to possible differences in intensity of erythema. When plotted chronologically, as in Plate 9, the values for the unsensitized men lie in fairly close proximity to those for the initial tests whereas those for the sensitized men are consistently higher. The points on the curve for the final tests do not represent as many men as those for the initial so that these points are not as firmly established.

32. On Plate 11, the final reactions are plotted against the effective temperatures. The slope line for the initial tests (Plate 10) is included. The values for the unsensitized men are fairly close to those for the initial tests. Some temperature effect is evident but is not as consistent as for the initial tests. The final tests on the sensitized men show consistently higher values than those for the initial tests or for those on the non-sensitized men. No consistent temperature effect is evident.

33. It is of paramount importance to compare the values for the initial tests on the men who subsequently became sensitized with those who did not to see if there was any fundamental difference before chamber exposure. These two categories of initial tests are listed in Table V and averaged in Table VII. The values of 11.7 for the non-sensitized as compared with 11.0 for the sensitized are considered sufficiently close to indicate that both groups started from the same initial baseline. The average temperatures at which the patches were worn were 77° F. and 75° F., respectively.

3. Second Pre-exposure (Repeated Initial) Tests

34. Initial tests were performed on a group of men and were then repeated about two weeks later with no exposure to H in the chamber during the intervening period. These results are presented in Table VI. The difference between the first (average = 15.8, at 85° F.) and the second (average = 13.2, at 78° F.) are adequately explained by the differences in temperature since both these points lie in proximity

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to the temperature curve established on Plate 10. If the correction of 0.4 unit change in reaction per degree rise in temperature (Paragraph 30) is applied to the 13.2 value, it becomes 16.0 which is in complete agreement with the results obtained at 85°F. Thus, the responses of this group of men to the patch tests were not appreciably altered by living about two weeks under the conditions maintained at the Laboratory and without exposure to H vapor, nor was there any apparent sensitization caused by the first patch test.

D. Differences in Average Total Reactions to Patch Tests as Compared with Differences in Effective Temperatures at the Times the Tests were Performed

35. Because of the individual variation in intensity of reaction to initial patch tests and because of the very definite relation of the intensity of reaction to temperature, it was felt that the most significant analysis of these data would be one in which the differences between an individual's reaction before and after chamber exposure would be compared with the differences in the temperatures at which the patch tests were performed. These differences are listed for the sensitized men in Table III and for the non-sensitized men in Table II. The overall averages for these differences for the various categories of men are listed in Table X and have been plotted on Plate 12.

36. It is evident that differences in temperature exert a definite influence on the intensities of reaction. If the average differences for the men showing a positive change in reaction and for those showing a negative change in reaction are calculated, a line may be drawn which shows the average change in reaction per degree (°F.) change in temperature. This change for the initial tests is 0.39 units/degree which is in very good agreement with the value of 0.4 obtained in paragraph 27. The values for the sensitized men are 0.28 if the F values are used and 0.31 if the Fx values are used. Thus changes in temperature influence the reactions of sensitized as well as non-sensitized men.

37. It is evident in Plate 12 that the curve for the sensitized men lies well above that for the non-sensitized for any given temperature difference. This would be expected since the scoring system gives increased value for edema or folliculitis. But if

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the Fx values are used, no such extra value is given; and the line still lies well above that for the initial tests. The sensitized men show an average increase in intensity of reaction as shown by erythema alone without considering edema and folliculitis.

38. The values for the patch tests on the men who were exposed in the chamber to HN3, but actually received little or no reaction, lie near the line for the non-sensitized men (Plate 12). It should be reiterated that the reactions of these men to HN3 were too mild to draw any conclusions as to the presence or absence of cross sensitization to H.

E. Average Reactions for a Given Test Dose

39. The average reactions for a given test dose are presented in Table XI and plotted on Plate 14. A nice gradation in intensity of reaction proportional to the size of the dose is evident. The reactions for the initial tests on either the sensitized or non-sensitized men are nearly identical. The reactions to the final tests of the non-sensitized men lie in close proximity although slightly above those of the initial tests. On the other hand, the final reactions of the sensitized men are markedly greater for any given dose than for the non-sensitized. Since the maximum scoring value used was 8 (only intensity of erythema was considered with no extra value for edema and/or folliculitis), the curve for the finals on the sensitized men shows an apparent falling off as it approaches 8. This is an artefact dependent on the arbitrary scoring system. Since the overall average temperatures at which the tests were performed were identical for the sensitized and the non-sensitized men, these average reactions may be compared as above without correction for temperature effects.

F. Changes in Threshold

40. The threshold doses to cause an erythema of intensity 2 are listed in Table II for the non-sensitized and Table III for the sensitized men. These data are summarized in Table VIII and are compared with similar data for chamber reactions, total reactions to patch test, and temperatures in Table VII. The data from Table VIII have been summarized in Table IX to show the percentages of the men reacting to a given dose with an intensity of 2 or more. These percentages are plotted on Plate 13.

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41. From Table VII, it can be seen that the average initial thresholds were 0.36 micrograms (at 75°F.) for the nonsensitized and 0.35 micrograms (at 79°F.) for the sensitized men. Hence, the thresholds of the two groups of men before exposure to H in the chamber were as nearly identical as could be expected. The thresholds for the final tests were 0.28 (at 76.5°F.) for the non-sensitized and 0.14 (at 76.5°F.) for the sensitized men. The average threshold had been lowered for both groups but especially in the case of the sensitized men. The average temperatures at which the tests were performed were quite comparable for the two groups and do not provide an adequate explanation for the marked changes in threshold.

42. From Plate 13, it is also evident that the thresholds expressed as percentages reacting are approximately identical for the two groups initially. The final tests on the non-sensitized men show a slight lowering of threshold whereas there is a marked lowering for the sensitized men. The level at which 50% of the men show a faint erythema is below 1/8 microgram for this latter group, indicating that most of the men in this group showed a reaction of greater than 2 to the 1/8 microgram dose.

G. Abnormal Skin Reactions Following Chamber Exposure to H Vapor

43. The usual ("normal") reaction to H vapor was a relatively uniform generalized erythema. In the more intense reactions, the erythema was accompanied by edema; but the reaction was again uniform. On the other hand, some individuals manifested a maculopapular follicular type of reaction which was distinctly different from the above. This follicular type of reaction can be seen by close scrutiny of the illustrations in Plates 4-8.

44. While there was no difficulty in recognizing the two types of extremes described above, there was considerable difficulty with very mild follicular type of reactions. These were accompanied by very little edema, frequently became confluent, and subsequently appeared like the "normal" reactions. Such reactions were commonest in the popliteal and cubital fossae. Their classification varied somewhat with the examining medical officer. Cases like those in the illustrations offered no difficulty and all agreed they were atypical reactions.

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45. Available data do not permit a satisfactory correlation of the atypical chamber reactions with the subsequent final patch tests. Patch tests were initiated quite late in the chamber testing program and relatively few of the men observed with marked follicular type of reactions had patch tests. Some of the subjects in Table I designated as having follicular reactions to chamber tests actually had very mild ones. Of 169 men who received pre- and post-H-exposure patch tests, 25 men (15%) had shown some follicular reaction following their chamber tests. Of these 25 men, 11 (44%) showed edema and/or folliculitis on patch tests. Hence the patch tests, performed about two weeks after the chamber tests, do not correlate well with the abnormal reactions to chamber tests. It is felt that the data as regards time to develop an abnormal reaction to patch test and the time of persistency of this abnormal reaction are inadequate to permit conclusions on this point.

46. Most of the test subjects employed in the NRL clothing tests were subjected to repeated exposures in the chamber wearing protective clothing and masks. When the man sustained an intense erythema on any part of the body, the suit was considered to have "broken" after that many exposures. Almost all of the men who developed follicular types of reactions were in this type of clothing test, i.e. subjected to repeated exposures (2-12) and received repeated small doses through the clothing until the erythema level was reached. The follicular reaction was usually not evident until 48 to 96 hours after the last chamber exposure. These reactions might occur on any part of the body or be generalized (See Plates 4 and 5), but were most frequent in the cubital fossae, popliteal fossae, lateral and ventral thorax. From the above illustrations, it is evident that these reactions were usually observed on sites which had sustained an erythema from H and were not conspicuous on the more protected, unaffected skin. In Figure 4, it is evident that the areas covered by the protective shorts and suspenders, and the interscapular area on which the cannister of the Navy mask rested, are free from the maculopapular erythema.

47. It may be added here, parenthetically, that most of the men who were tested wore CC-2 impregnated protective gloves which covered the forearms on which the patch tests were run. The forearms were much less affected by the chamber tests than the rest of the body.

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It is not clear whether hypersensitivity to patch tests (forearm) is due to the effect of a mild local reaction to H from leakage through the impregnated gloves or whether it represents an effect transferred to the skin of the forearm from the more seriously affected areas.

48. Although most of the generalized follicular types of reactions to chamber tests occurred in men who had received several exposures, such reactions also occurred in a few men who had received only one exposure (i.e. in basic tests or after wearing a protective suit which "broke" after only one exposure). Such men had always sustained at least a moderate or intense erythema. The atypical reactions developed 48 to 96 hours following the chamber exposure.

DISCUSSION

49. While there is almost universal agreement that true sensitization to H may occur, the methods and criteria for determining this have been somewhat varied. From the most recent review on this subject by Sulzberger, et al, (paragraph 6), it is evident that the most frequently used method of testing is the "drop" method, i.e. the application of drops of various dilutions to the skin and allowing them to remain there without cover. The solvent used has frequently been benzene although absolute alcohol or mineral oil have also been used. Sulzberger, et al, have used patch tests in testing for hypersensitivity to lewisite.

50. Regardless of the test, the criteria for hypersensitivity are critical. Most workers have employed the threshold dose for erythema as the baseline from which to reckon an individual's susceptibility or sensitivity. Subjects who react to a dilution significantly below that to which normals just react, are said to be hypersensitive or to have been sensitized. According to Sulzberger, et al, almost all normals react to a dilution of 1:500 (benzene) and strong reactions to dilutions of greater than 1:5000 indicate a very sensitive skin.

51. It is evident that the closed patch test causes a much more intense reaction for a given dilution than the open drop test. This would be expected since the agent is held in close contact with the skin, the evaporation of the agent (H) is greatly hindered, and the sweat beneath the patch undoubtedly increases the susceptibility.

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Converting our dosages into units comparable to those of other workers leads to the following approximate scale:

1 microgram	=	1:5000	Weight/Weight*
1/2 microgram	=	1:10,000	"
1/4 microgram	=	1:20,000	"
1/8 microgram	=	1:40,000	"

Since our threshold for unsensitized men was about 0.35 micrograms (1:15,000) on the average (and less than 0.25 micrograms (1:20,000) as determined by the 50% method on Plate 13), it is evident that the patch test leads to a somewhat lower threshold than the "drop" test.

52. In interpreting the patch tests, we have emphasized edema and/or folliculitis as being good criteria for sensitization. In the first place, these were observed in only 2 of 230 pre-exposure patch tests (0.9%). But of 169 men who had pre- and post-H-exposure patch tests, 44 manifested edema and/or folliculitis on their final patch tests (26%). These are criteria which are readily observable and do not require the differentiation of fine degrees of erythema. For any individual test, edema is probably a simpler criterion than a change in erythema.

53. The more frequent association of folliculitis with edema than the occurrence of folliculitis alone on the patch tests, and the fact that the follicular type of reaction is conspicuous in the abnormal (probably sensitized) reactions from chamber tests, have been the reasons for considering both these symptoms as evidence of sensitization. It is well understood that most dermatologists emphasize that for routine patch tests, only edema is to be considered as indicating sensitization whereas folliculitis does not. It is felt that in the case of H, available evidence indicates that follicular types of reaction with or without edema probably also represent a sensitization.

* Some workers employ volumetrically prepared solutions.

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54. Further justification for these criteria is the fact that, if a group of men is selected according to these criteria, there appears in that group a very significant change in threshold. This threshold represents an expression of increased reaction as determined by erythema alone.

55. The occurrence of edema and/or folliculitis definitely represents an altered response in some of the men following chamber exposure and probably indicates a more intense response. As to whether this edema is caused by the same mechanism as the urticaria observed in other patch tests for other hypersensitivities or as to whether it represents merely a more intense response to the vesicant action of H, being analagous to the prevesication edema observed following exposure to H, cannot be stated. It is not inconceivable that the two mechanisms are closely related.

56. It is impossible to comment on the practical significance of these tests. It can merely be said that about two weeks after chamber exposure under the conditions employed, about one-fourth of the men showed an abnormal reaction to patch tests probably indicating an increased sensitivity to H. How long this sensitivity persists or what it would mean in terms of combat using H are questions which would require further tests.

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SUMMARY AND CONCLUSIONS

1. Doses of 1, 1/2, 1/4 and 1/8 micrograms of H in mineral oil, worn as closed patches on the forearm for four hours, represented a satisfactory subvesicant level for determining altered sensitivity to H.
2. The total reactions to patch tests on previously unexposed men showed a marked variation proportional to the outdoor effective temperature at the time the patches were worn.
3. Edema and/or folliculitis were observed in only 2 of 230 men previously unexposed to H vapor. On the other hand, of 169 of these men, tested after chamber exposure to H vapor, 44 (26%) showed edema and/or folliculitis on patch tests. These 26% were arbitrarily designated as "sensitized" and the others as "non-sensitized".
4. The "sensitized" men also showed a more intense erythema or reaction to any given dose and also showed a lowered threshold for the appearance of a faint erythema as compared to the "non-sensitized" men.

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RECOMMENDATIONS

1. It is recommended that if, in the future, any program be initiated in which men are exposed to H under controlled conditions, that some type of pre- and post-H-exposure sensitivity tests be performed. The test presented in this report is suggested as one such possible test.
2. It is recommended that the effects of temperature and humidity on the responses to patch tests of any type be given more consideration than they have in the past.

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ACKNOWLEDGEMENT

Human Volunteers

This program could not have been carried out without the men who bravely volunteered to participate in the tests knowing the personal inconvenience which might result. For service definitely beyond the call of duty they are deserving of the greatest praise. This Laboratory wishes to express great appreciation for the cooperation of the Commandant of the U. S. Naval Training Center, Bainbridge, Maryland in permitting volunteer personnel to take part in these tests. An index of all men who volunteered for chemical warfare tests at this Laboratory is on file with the Physical Qualifications and Medical Records Section of the Bureau of Medicine and Surgery.

The authors are indebted to Dr. Herbert D. Landahl of the University of Chicago Toxicity Laboratory for many cogent suggestions pertinent to the interpretation of these data.

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TABLE I (continued)

Abbreviations employed for body regions.

ne	neck
ash	anterior shoulders
ax	axillae
aarm	anterior arms
cf	antecubital fossae
parm	posterior arms
psh	posterior shoulders
sc	scapulae
dth	dorsal thorax
lth	lateral thorax
vth	ventral thorax
uabd	upper abdomen
athi	anterior thighs
kn	knees
al eg	anterior legs
pthi	posterior thighs
pop	popliteal fossae
pleg	posterior thighs

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Table II. Summary of Data on Men Showing No Evidence of Sensitization by Patch Test.

Draft Man No.	No.	Chamber Reaction			Sensitivity			Threshold			Effective Temp. °		
		Max.	Total	Per A. A.	I	F	F-I	I	F	F-I	I	F	F-I
75	1	3	10	0.2	7	7	0	1/2	1/2	0	78	75	-3
	2	3	12	1.2	7	11	+4	1/2	1/2	0	78	75	-3
	3	3	32	2.3	8	14	+6	1/2	1/4	-1/4	78	75	-3
	4	5	13	1.4	8	15	+7	1/2	1/4	-1/4	78	75	-3
	5	3	19	1.9	7	24	+17	1/2	1/8	-3/8	78	79	+1
	6	2	13	1.3	7	7	0	1/2	1/2	0	78	79	+1
	8	3	26	2.2	7	15	+8	1/2	1/4	-1/4	78	79	+1
	9	3	31	1.8	5	14	+9	L 1	1/4	-1 3/4	78	75	-3
	10	3	18	1.6	7	10	+3	1/2	1/4	-1/4	78	75	-3
	11	3	34	2.1	7	22	+15	1/2	1/8	-3/8	78	75	-3
	12	3	31	2.1	7	15	+8	1/2	1/4	-1/4	78	75	-3
	14	3	24	1.7	11	8	-3	1/2	1/4	-1/4	78	75	-3
	15	3	18	2.3	8	14	+6	1/2	1/2	-G 0	78	79	+1
	16	3	28	2.0	5	7	+2	1	1/2	-1/2	78	79	+1
	17	3	39	2.3	7	14	+7	1/2	1/2	-G 0	78	75	-3
	18	3	24	1.8	10	7	-3	L 1/2	1/2	-L 0	78	75	-3
	19	3	38	2.2	7	7	0	1/2	1/2	0	78	75	-3
	20	3	27	1.9	12	12	0	1/2	1/2	0	78	75	-3
	21	3	34	2.0	8	7	-1	1/2	1/2	0	78	75	-3
	22	3	28	1.8	7	7	0	1/2	1/2	0	78	75	-3
	25	3	30	2.1	5	18	+13	L 1	1/8	-1 7/8	78	79	+1
	27	3	31	2.1	7	16	+9	1/2	1/8	-3/8	78	79	+1
	28	3	32	2.3	7	9	+2	1/2	1/2	-G 0	78	79	+1
	29	3	36	2.4	8	15	+7	1/2	1/4	-1/4	78	86	+8
76	31	3	41	2.4	5	12	+7	L 1	1/2	-1 1/2	62	75	+13
	32	0	0	0	9	7	-2	L 1	1/2	-1 1/2	62	75	+13
	33	3	29	1.8	7	18	+11	1/2	1/8	-3/8	62	79	+17
	34	3	29	2.2	6	15	+9	1/2	1/4	-1/4	62	79	+17
	35	3	34	2.1	4	16	+12	1/2	1/6	-3/6	62	79	+17
	36	3	24	1.7	6	9	+3	1/2	1/4	-1/4	62	79	+17
	37	3	42	3.0	3	16	+13	1	1/8	-7/8	62	79	+17
	38	3	39	2.6	7	7	0	1/2	1/4	-1/4	62	79	+17
	40	3	36	2.4	7	6	-1	1/2	1/2	0	62	79	+17
	42	3	31	2.1	7	7	0	1/2	1/2	0	62	75	+13
	43	2	6	1.2	7	9	+2	1/2	1/4	-1/4	62	75	+13
	44	3	34	2.1	5	18	+13	1/2	1/8	-3/8	62	79	+17
	46	3	32	2.1	7	15	+8	1/2	1/4	-1/4	62	79	+17
	47	3	32	2.3	12	16	+4	1/4	1/8	-1/8	62	79	+17
	54	2	20	1.3	5	20	+15	1/2	1/8	-3/8	62	79	+17
	55	5	43	2.4	7	22	+15	1/2	L 1/8	-G 3/8	62	77	+15
	56	3	41	2.3	5	14	+9	L 1	1/6	-1 7/8	62	77	+15
	57	3	44	2.4	3	15	+12	1	1/4	-3/4	62	86	+24
	59	3	10	2.0	3	15	+12	1	1/4	-3/4	62	77	+15
	60	3	17	2.1	3	17	+14	1	L 1/4	-G 3/4	62	77	+15
77	61	3	16	2.7	14	15	+1	1/4	1/4	0	75	79	+4
	62	3	14	1.8	7	16	+9	1/2	1/8	-3/8	75	77	+2
	63	3	21	2.3	7	14	+7	1/2	L 1/2	-G 0	75	86	+11
	64	3	16	2.3	8	13	+5	1/2	1/4	-1/4	75	77	+2
	67	3	16	2.7	8	14	+6	1/2	L 1/2	-G 0	75	86	+11
	68	3	11	2.2	13	8	-5	L 1/2	1/2	+G 0	75	86	+11
	70	3	17	2.1	17	15	-2	L 1/4	1/4	+G 0	75	77	+2
	71	3	20	2.5	11	16	+5	1/2	1/8	-3/8	75	77	+2
	72	3	15	2.5	6	14	+8	1/2	L 1/2	-G 0	75	77	+2
	75	3	11	2.2	13	15	+2	L 1/2	1/4	-1 1/4	75	86	+11
	76	5	8	2.0	14	15	+1	1/4	1/4	0	75	86	+11
	78	3	11	2.7	15	15	0	1/4	1/4	0	75	86	+11
	80	3	10	2.5	7	16	+9	1/2	1/8	-3/8	75	79	+4
	82	5	20	2.5	13	15	+3	L 1/2	1/4	-1 1/4	75	79	+4
	83	2	5	1.7	15	11	-4	1/4	1/4	0	75	77	+2
	85	5	11	2.2	14	14	0	1/4	1/4	0	75	86	+11
	86	3	13	2.6	13	13	0	1/4	L 1/2	+1 1/4	75	86	+11
	87	3	3	3.0	11	15	+4	L 1/2	1/4	-1/4	75	86	+11
	88	2	2	2.0	11	18	+7	1/2	1/8	-3/8	75	86	+11
	89	3	13	2.6	19	15	-4	1/4	1/4	0	75	72	-3
	90	3	24	1.7	15	7	-8	1/4	1/2	+1 1/4	75	69	-6

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Table II (cont'd) Summary of Data on Men Showing No Evidence of Sensitization by Patch Test.

Draft No.	Man No.	Chamber Reaction			Sensitivity			Threshold			Ineffective Temp.		
		Max.	Total	Fer A. A.	I	F	F-I	I	F	F-I	I	F	F-I
78	91	3	45	2.8	11	10	-1	1/2	1/4	-1/4	79	69	-10
	92	0	0	0	8	11	+3	1/2	1/2	0	79	72	-7
	96	3	45	3.0	15	15	0	1/4	1/4	0	79	72	-7
	100	3	33	1.9	14	4	-10	L1/2	1	+3 1/2	79	69	-10
	101	3	30	2.7	15	13	-2	1/4	L1/2	+L1/4	79	69	-10
	102	3	27	2.1	15	11	-4	1/4	1/2	+1/4	79	69	-10
	103	3	41	2.7	16	7	-9	1/8	1/2	+3/8	79	69	-10
	104	3	31	2.2	15	25	+10	1/4	L1/4	-G 0	79	69	-10
	105	4	42	2.6	13	10	+3	L1/2	L1	+1/2	79	69	-10
	106	3	36	2.6	25	15	-10	L1/4	1/4	+G 0	79	72	-7
	107	4	46	3.1	15	15	0	1/4	1/4	0	79	69	-10
	108	3	46	2.9	13	15	+2	L1/2	1/4	+L1/4	79	69	-10
	111	3	31	2.4	14	11	-3	L1/2	1/2	+G 0	79	72	-7
	112	3	33	2.5	16	15	-1	1/8	1/4	+1/8	79	72	-7
	114	4	45	2.8	16	15	-1	1/8	1/4	+1/8	79	72	-7
	115	5	23	2.1	16	16	0	1/8	1/8	0	79	72	-7
	119	4	36	2.1	16	16	0	1/8	1/8	0	79	85	+6
	120	3	26	2.2	15	21	+6	1/4	L1/4	-G 0	79	72	-7
79	121	0	0	0	15	11	-4	1/4	1/2	+1/4	86	72	-14
	123	3	23	1.4	7	11	+4	1/2	1/4	-1/4	86	76	-10
	124	2	22	1.4	15	14	-1	1/4	1/4	0	86	76	-10
	125	3	24	1.4	19	10	-9	1/4	1/2	+1/4	86	76	-10
	126	3	28	1.6	14	6	-8	1/4	L1	+L3/4	86	72	-14
	127	3	21	1.4	15	16	+1	1/4	1/8	-1/8	86	72	-14
	128	3	30	1.8	14	9	-5	1/4	1/4	0	86	72	-14
	129	3	35	2.2	14	6	-8	1/4	1/2	-1/4	86	76	-10
	130	3	30	1.8	14	13	-1	L1/2	L1/2	0	86	85	-1
	132	3	33	2.2	14	14	0	1/4	1/4	0	86	76	-10
	133	3	27	1.9	16	15	-1	1/8	1/4	+1/8	86	72	-14
	135	4	26	1.9	18	15	-3	1/8	1/4	+1/8	86	72	-14
	136	4	36	2.6	16	16	0	1/8	L1/4	+L1/8	86	72	-14
	137	4	32	2.3	18	11	-7	1/8	1/2	+3/8	86	85	-1
	138	4	35	2.5	14	20	+6	1/4	1/8	-1/8	86	85	-1
	139	3	23	1.6	11	4	-7	1/2	L1	+L1/2	86	85	-1
	140	3	23	1.6	15	15	0	1/4	1/4	0	86	76	-10
	141	3	13	1.6	16	12	-4	1/8	1/4	+1/8	86	72	-14
	143	2	20	1.5	15	14	-1	1/4	1/8	-1/8	86	85	-1
	144*	0	0	0	12	14	+2	1/2	1/4	0	86	88	-18
	145*	2	7	1.2	18	4	-12	1/8	1/4	+1/8	86	88	-18
	146*	2	2	2.0	15	12	-3	1/4	1/4	0	86	88	-18
	147*	3	13	1.4	15	6	-9	1/4	1/4	0	86	88	-18
	148*	2	4	2.0	17	12	-5	L1/4	1/2	+G 1/4	86	88	-18
	149*	2	2	2.0	17	15	-2	L1/4	1/4	+G 0	86	88	-18
	150*	0	0	0	15	-	-	1/4	-	-	86	-	-
80	151*	0	0	0	12	17	+5	1/8	L1/4	+L1/8	85	88	-17
	152*	0	0	0	7	8	+1	1/2	L1	+L1/2	85	88	-17
	153*	0	0	0	20	9	-11	L1/8	L1	+7/8	85	88	-17
	154*	0	0	0	14	14	0	1/2	L1/8	-G 3/8	85	88	-17
	155*	0	0	0	15	4	-11	1/4	1/2	+1/4	85	88	-17
	156*	0	0	0	24	13	-11	L1/8	L1/4	+1/8	85	88	-17
	157*	0	0	0	8	8	0	1/4	1/4	0	85	88	-17
	158*	0	0	0	14	8	-6	1/4	1/4	0	85	88	-17
	159*	0	0	0	8	5	-3	L1/2	L1	+1/2	85	88	-17
	160*	0	0	0	10	12	-7	1/4	L1/2	+L1/4	85	88	-17
	161	5	54	3.0	15	18	+3	1/4	L1/2	-L1/4	85	88	-17
	162	3	51	2.6	19	12	-7	1/4	L1/2	+L1/4	85	88	-17
	163	3	40	2.5	15	8	-7	1/4	L1/2	+L1/4	85	88	-17
	164	3	21	2.1	16	10	-6	1/2	1/4	+1/8	85	88	-17
	165	0	0	0	15	9	-6	1/4	L1/2	+L1/4	85	88	-17
	166	3	14	1.6	15	10	-5	1/4	L1	+L3/4	85	88	-17
	167	5	49	3.1	15	23	+10	1/4	L1/4	-G 0	85	88	-17
	168	3	50	2.6	15	19	+4	1/4	1/4	0	85	88	-17
	169	3	40	2.5	11	12	+1	1/4	1/2	0	85	88	-17
	170	3	13	2.6	19	8	-11	1/4	L1/2	+L1/4	85	88	-17
	171	3	47	2.6	14	12	-2	L1/2	L1/2	0	85	88	-17
	173	3	47	2.9	22	9	-13	1/8	L1	+L7/8	85	88	-17

* Chamber tests were with R103 - very mild reaction.

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Table II (cont'd) Summary of Data on Men Showing No Evidence of Sensitization by Patch Test.

Draft No.	Man No.	Chamber Reaction			Sensitivity			Threshold			Effective Temp.°		
		Max.	Total	Per A. A.	I	F	F-I	I	F	F-I	I	F	F-I
80	175	3	42	2.5	16	16	0	1/8	1/8	0	85	83	- 2
	176	4	44	2.9	16	15	-1	1/8	1/4	+1/8	85	76	- 9
	177*	0	0	0.0	16	-	-	1/8	-	-	85	-	-
	178	-	-	-	20	-	-	1/8	-	-	85	-	-
	179	-	-	-	10	-	-	1/8	-	-	85	-	-
	180	-	-	-	19	-	-	1/4	-	-	85	-	-
81	181*	0	0	0.0	7	7	0	1/2	1/2	0	80	76	- 4
	182*	2	8	1.6	18	8	-10	1/4	1/4	0	80	76	- 4
	183*	2	6	1.5	14	14	0	1/4	1/4	0	80	76	- 4
	184*	2	16	1.8	17	6	-11	L1/2	L1	+1/2	80	76	- 4
	185	3	23	2.6	20	10	-10	1/8	1/4	+1/8	80	76	- 4
	186	3	32	2.1	13	14	+1	L1/2	1/4	-L1/4	80	76	- 4
	187	3	14	1.8	16	14	- 2	1/8	1/4	-1/8	80	76	- 4
	188	3	45	2.8	16	8	- 8	1/8	1/4	-1/8	80	76	- 4
	189	3	36	2.4	14	16	+ 2	L1/2	1/8	-L3/8	80	76	- 4
	190	3	38	2.5	13	12	- 1	L1/2	1/4	-L1/4	80	76	- 4
	191	3	23	1.8	15	9	- 6	1/4	1/4	0	80	76	- 4
	192	3	34	2.3	13	14	+ 1	L1/2	1/4	-L1/4	80	76	- 4
	194	3	30	2.3	19	13	- 6	1/4	1/4	0	80	76	- 4
	199	-	-	-	15	-	-	1/4	-	-	80	76	- 4
	200	-	-	-	14	-	-	L1/2	-	-	80	-	-
	201	-	-	-	20	-	-	1/8	-	-	80	-	-
	202	-	-	-	14	-	-	1/4	-	-	80	-	-
	203	-	-	-	12	-	-	1/4	-	-	80	-	-
	204	-	-	-	13	-	-	L1/2	-	-	80	-	-
	205	-	-	-	18	-	-	1/4	-	-	80	-	-
	206	-	-	-	15	-	-	1/4	-	-	80	-	-
208	-	-	-	16	-	-	1/8	-	-	80	-	-	
210	-	-	-	13	-	-	L1/2	-	-	80	-	-	
82	211	-	-	-	9	-	-	1/4	-	-	89	-	-
	212	-	-	-	4	-	-	L 1	-	-	89	-	-
	213	-	-	-	11	-	-	1/4	-	-	89	-	-
	214	-	-	-	15	-	-	1/4	-	-	89	-	-
	215	-	-	-	9	-	-	1/4	-	-	89	-	-
	216	-	-	-	5	-	-	1/2	-	-	89	-	-
	217	-	-	-	5	-	-	L 1	-	-	89	-	-
	218	-	-	-	10	-	-	L 1	-	-	89	-	-
	219	-	-	-	7	-	-	1/8	-	-	89	-	-
	220	-	-	-	1	-	-	-	-	-	89	-	-
	221	-	-	-	11	-	-	1/2	-	-	89	-	-
	222	-	-	-	6	-	-	L 1	-	-	89	-	-
	223	-	-	-	6	-	-	L 1	-	-	89	-	-
	224	-	-	-	16	-	-	1/8	-	-	89	-	-
225	-	-	-	17	-	-	L1/2	-	-	89	-	-	
226	-	-	-	6	-	-	L 1	-	-	89	-	-	
227	-	-	-	4	-	-	1/2	-	-	89	-	-	
228	-	-	-	14	-	-	1/4	-	-	89	-	-	
229	-	-	-	14	-	-	1/8	-	-	89	-	-	
230	-	-	-	9	-	-	1/4	-	-	89	-	-	
231	-	-	-	9	-	-	1/4	-	-	89	-	-	
232	-	-	-	12	-	-	1/4	-	-	89	-	-	
233	-	-	-	12	-	-	L1/2	-	-	89	-	-	
234	-	-	-	3	-	-	1/2	-	-	89	-	-	

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Table III. Summary of Data on Men Showing Evidence of Sensitization by Patch Test.

Draft Man No.	No.	Chamber Reaction			Sensitivity			Threshold			Effective Temp.			
		Max.	Total	Per A.A.	I	F	F-I	I	F	F-I	I	F	F-I	
75	7	5	35	2.5	7	64	+57	1/2	L1/8	-G3/8	78°	79°	+1°	
	13	3	29	1.8	7	17	+10	1/2	L1/2	-G 0	78°	75°	-3°	
	23	3	40	2.5	4	40	+36	1	L1/8	-G7/8	78°	75°	-3°	
	24	3	31	2.1	4	56	+52	1	L1/8	-G7/8	78°	75°	-3°	
	26	3	33	2.1	9	44	+35	1/4	1/8	- 1/8	78°	79°	+1°	
	30	5	42	2.3	6	50	+44	L 1	1/8	-L7/8	78°	77°	-1°	
76	39	3	38	2.2	15	29	+14	1/4	L1/4	-G 0	62°	75°	+13°	
	41	3	40	2.5	5	56	+51	1/2	L1/8	-G3/8	62°	79°	+17°	
	45	3	27	1.9	7	30	+23	1/2	1/8	- 3/8	62°	79°	+17°	
	48	3	41	2.9	7	64	+57	1/2	L1/8	-G3/8	62°	79°	+17°	
	49	3	35	2.7	8	52	+44	1/4	1/8	-L1/8	62°	79°	+17°	
	50	3	47	2.6	7	38	+31	1/2	1/8	- 3/8	62°	77°	+15°	
	51	5	56	3.1	7	56	+49	1/2	L1/8	-G3/8	62°	86°	+24°	
	52	5	54	3.0	11	64	+53	1/2	L1/8	-G3/8	62°	72°	+10°	
	53	5	55	3.0	8	49	+41	1/2	L1/4	-G1/4	62°	76°	+14°	
	58	3	46	2.6	5	24	+19	L 1	L1/2	- 1/2	62°	86°	+24°	
	77	65	3	20	2.5	12	40	+28	1/4	L1/8	-G1/8	75°	77°	+ 2°
66		3	22	2.8	14	35	+21	1/4	1/4	0	75°	86°	+11°	
69		3	14	2.3	11	21	+10	1/2	1/4	-1/4	75°	77°	+ 2°	
73		3	24	2.7	6	41	+35	1/2	L1/4	-G1/4	75°	86°	+11°	
74		3	15	2.1	14	29	+15	1/4	L1/4	-G 0	75°	86°	+11°	
77		3	16	2.3	15	48	+33	1/4	L1/4	-G 0	75°	86°	+11°	
79		3	11	2.2	7	30	+23	1/2	1/8	-3/8	75°	79°	+ 4°	
81		5	9	3.0	13	32	+19	L 1/2	L1/8	-3/8	75°	79°	+ 4°	
84		2	5	1.3	13	23	+10	L 1/2	1/4	-L1/4	75°	77°	+ 2°	
78		93	3	43	2.7	12	35	+23	1/4	1/4	0	79°	72°	- 7°
	94	3	48	2.7	15	48	+33	1/4	L1/4	-G0	79°	72°	- 7°	
	95	3	50	2.9	16	52	+36	1/8	L1/8	-G0	79°	72°	- 7°	
	98	3	41	2.7	15	42	+27	1/4	1/8	-1/8	79°	72°	- 7°	
	109	3	36	2.6	10	26	+16	1/4	1/4	0	79°	69°	-10°	
	110	3	48	3.0	16	56	+40	1/8	L1/8	-G0	79°	72°	- 7°	
	113	4	38	2.9	16	52	+36	1/8	L1/8	-G0	79°	76°	- 3°	
	116	3	42	2.5	15	23	+ 8	1/4	1/4	0	79°	76°	- 3°	
	117	3	36	2.4	15	19	+ 4	1/4	1/4	0	79°	76°	- 3°	
	118	3	43	2.5	13	38	+25	1/4	1/8	-1/8	79°	76°	- 3°	
	79	122	5	50	2.9	10	35	+25	1/2	1/4	-1/4	86°	76°	-10°
		131	3	21	1.8	17	41	+24	L1/4	L1/4	0	86°	76°	-10°
		134	3	29	2.1	15	27	+12	1/4	1/4	0	86°	72°	-14°
142		4	28	2.0	14	64	+50	1/4	L1/8	-G1/8	86°	72°	-14°	
80	172	3	20	2.2	22	50	+28	1/8	1/8	0	85°	68°	-17°	
	174	4	39	2.4	14	56	+42	L1/2	L1/8	-3/8	85°	68°	-17°	
81	193	3	27	2.1	17	16	- 1	L1/4	L1/2	+1/4	80°	76°	- 4°	
	195	3	35	1.9	14	50	+36	1/4	1/8	-1/8	80°	76°	- 4°	
	197	3	24	1.8	16	40	+24	1/8	L1/4	-L1/8	80°	76°	- 4°	

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Table IV. Total Reactions to Final Patch Tests (F_x values)*

<u>Draft No.</u>	<u>Man No.</u>	<u>Reaction</u>	<u>Average</u>
75	7	32	26
	13	13	
	23	28	
	24	32	
	26	22	
	30	26	
76	39	21	26
	41	32	
	45	22	
	48	32	
	49	26	
	50	22	
	51	32	
	52	32	
	53	25	
	58	16	
77	65	28	22
	66	19	
	69	19	
	73	25	
	74	21	
	77	24	
	79	22	
	81	24	
	84	15	
78	93	19	23
	94	24	
	95	28	
	98	26	
	109	18	
	110	32	
	113	28	
	116	15	
	117	15	
	118	22	
79	122	19	23
	131	21	
	134	19	
	142	32	
80	172	26	29
	174	32	
81	193	12	19
	195	26	
	197	20	
Overall Average			23.7

* No extra value added for edema or folliculitis.

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Table V. Average Temperatures and Relative Humidities during Time Patches were worn. Average Total Reactions to Patch Tests.

Date	Draft No.*	Indoor		Outdoor		Outdoor Effective Temperature	Initial Patch Tests				Final Patch Tests							
		T. °F.	RH%	T. °F.	RH%		Nonsen.		Sens.		Combined		Nonsen.		Sens.		Sens. Fx	
							No. Men	Av.	No. Men	Av.	No. Men	Av.	No. Men	Av.	No. Men	Av.	No. Men	Av.
5-28	75	83	67	83	68	78	24	7.5	6	6.2	30	7.2						
6-4	76	75	42	65	50	62	20	5.9	10	8.0	30	6.6						
6-11	77	82	55	80	57	75	21	12.0	9	12.0	30	12.0						
6-20	-	82	55	80	57	75							19	10.8	4	36	4	24
6-25	78	86	66	84	69	79	18	14.9	10	14.3	28	14.7	22	14.2	8	47	8	27
6-27		82	43	85	43	77							10	15.4	5	35	5	22
7-2	79	92	59	94	57	86	26	14.9	4	16.0	30	14.8	12	14.2	6	39	6	23
7-11		78	46	74	53	69							10	11.7	1	26	1	18
7-18		78	72	74	82	72							17	13.8	8	49	8	27
7-19		81	79	77	91	76							6	11.7	7	37	7	21
7-26	80	90	75	90	75	85	28	15.7	2	16.0	24	15.8	6	13.0	0	0	0	0
8-7		85	61	84	62	78	33	13.0			33	13.0						
8-13	81	85	61	86	61	80	23	15.0	3	16.0	26	15.0						
8-27	82	75	47	73	49	69	24	9.0			24	9.0	22	9.7**	2	53	2	29
8-29	-	-	-	92	50	83							7	15.0***	0	0	0	0
9-5		81	61	80	65	76							14	11.4****	3	35	3	19

* Draft. Nos. apply only to Initial Patch Tests. Finals were not run according to drafts but when men were available.

** This includes 14 men who were exposed to HN3 in chamber, sustained little or no reaction from chamber test.

*** This includes 2 HN3 men.

**** This includes 4 HN3 men.

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Table VI. Second Pre-exposure Patch Tests.

Draft No.	Man No.	First Pre-exposure Patch Test					Second Pre-exposure Patch Test									
		Date	E.T.°	1	1/2	1/4	1/8	Tot.	Date	E.T.°	1	1/2	1/4	1/8	Tot.	
79	145	7- 2	86	8	4	4	2	17	8- 7	78	8	4	2	1	15	
	146			8	4	2	1	15			8	4	4		16	
	147			8	4	2	1	15			8	4	2		14	
	148			8	4	4	2	18			8	4	2		14	
	149			8	4	4	1	17			8	4	2		14	
80	151	7-26	85	4	4	2	2	12			8	4	2	1	15	
	152			4	2	1		7			4	2	2	1	9	
	153			8	4	4	4	20			8	4	2		14	
	154			8	4	1	1	14			8	4	2		14	
	155			8	4	2	1	15			1	1			2	
	156			8	8	4	4	24			8	4	2	1	15	
	157			4	2	2		8			4	2	2	1	9	
	158			8	4	2		14			2	1	1		4	
	159			4	4			8			8	2	1		11	
	160			8	8	2	1	19			8	2	2	1	13	
	161			8	4	2	1	15			8	4	2	1	15	
	162			8	8	2	1	19			8	2	2	1	13	
	163			8	4	2	1	15			8	4	4		16	
	164			8	4	2	2	16			2	2	1		5	
	165			8	4	2	1	15			8	4	2	1	15	
	166			8	4	2	1	15			8	2	2	1	13	
	167			8	4	2	1	15			8	4	2		14	
	168			8	4	2	1	15			8	4	2	1	15	
	169			4	4	2	1	11			4	2	2		8	
	170			8	8	2	1	19			8	2	2		12	
	171			8	4	1	1	14			8	4	2		14	
	172			8	8	4	2	22			8	4	2	1	15	
	173			8	8	4	2	22			8	4	2	2	16	
	174			8	4	1	1	14			16	4	2		22	
	175			8	4	2	2	16			8	4	2	1	15	
	176			8	4	2	2	16			8	8	4		20	
	177			8	4	2	2	16			8	4	2	1	15	
	178			8	8	2	2	20			8	4	2	1	15	
	180			8	8	2	1	19			8	2	2		12	
Average								15.8	13.2							

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**

TABLE IX. Percentages of men reacting to a given dose with intensity of 2 or more.

<u>Group</u>	<u>No. Men</u>	<u>Test</u>	<u>Test Dose</u>				
			<u>1</u>	<u>1/2</u>	<u>1/4</u>	<u>1/8</u>	<u>1/16 *</u>
NONSENSITIZED	125	Initial	100%	96%	57%	15%	0%
	125	Final	100%	99%	77%	22%	2%
SENSITIZED	44	Initial	100%	95%	61%	16%	0%
	44	Final	100%	100%	100%	73%	32%

* Although a dosage of 1/16 microgram H was not used, if at 1/8 a man reacted with a greater intensity than 2 (mild erythema), his threshold was arbitrarily considered as 1/16.

** This represents a summary of the data in Table VIII and has been plotted on Plate 13.

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TABLE X. Relation of Change in Effective Temperature to Change in Total Reaction to Patch Test.

Type of Men	No. Men	E.T.f. - E.T.i. ($^{\circ}$ F.)		Change in Reaction (F-I)		Av. React. Change/ $^{\circ}$ E.T. Change
		Av.	Range	Av.	Range	
Nonsensitized	49	+ 10 $^{\circ}$	+ 1 $^{\circ}$ to +24 $^{\circ}$	+5.6	-5 to +17	0.39
"	76	-7.5 $^{\circ}$	-1 $^{\circ}$ to -17 $^{\circ}$	-1.25	-13 to +15	
Sensitized	21	+10.9 $^{\circ}$	+1 $^{\circ}$ to +24 $^{\circ}$	+33	+10 to +57	0.28
"	23	-7 $^{\circ}$	-1 $^{\circ}$ to -17 $^{\circ}$	+28	+ 4 to +52	
Sensitized (Calculated with F _x).	21	+10.9 $^{\circ}$	+1 $^{\circ}$ to +24 $^{\circ}$	+15.5	+2 to +27	0.31
	23	-7 $^{\circ}$	-1 $^{\circ}$ to -17 $^{\circ}$	+9.9	-5 to +28	
Nonsensitized (Exposed to HN ₃ in chamber)	20	-13 $^{\circ}$ *	-2 $^{\circ}$ to -18 $^{\circ}$	-4.8	-14 to +5	-

* No men were exposed to HN₃ when E.T.f. - E.T.i. was plus.

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TABLE XI

Average Reactions per Test Dose.

NON-SENSITIZED	Draft No.	No. Men	Initial Test				Final Test			
			1	1/2	1/4	1/8	1	1/2	1/4	1/8
	75	24	4.3	2.0	0.9	0.3	6.3	3.5	1.8	0.7
	76	20	3.7	1.7	0.6	0.0	6.6	3.4	2.1	1.6
	77	21	6.8	3.2	1.5	0.4	7.4	3.7	1.8	1.0
	78	18	7.8	4.0	2.0	1.1	7.2	3.7	2.0	0.7
	79	19	7.8	4.0	2.0	0.9	7.2	3.0	1.6	0.5
	80	14	7.7	4.9	2.0	1.3	6.1	4.9	1.6	0.5
	81	9	<u>8.0</u>	<u>4.9</u>	<u>1.6</u>	<u>1.0</u>	<u>6.7</u>	<u>3.1</u>	<u>2.0</u>	<u>0.4</u>
Weighted Aver.			6.3	3.3	1.5	0.6	6.8	3.6	1.8	0.8
SENSITIZED	75	6	3.3	1.5	1.2	0.2	8.0	7.3	6.2	4.0
	76	10	4.6	2.1	1.1	0.2	8.0	8.0	6.0	4.0
	77	9	7.1	3.1	1.3	0.1	8.0	7.1	5.1	1.7
	78	10	7.2	3.8	2.0	1.3	8.0	7.2	5.2	2.3
	79	4	8.0	3.5	2.0	0.5	8.0	8.0	4.0	2.8
	80	2	8.0	6.0	2.5	1.5	8.0	8.0	8.0	5.0
	81	3	<u>8.0</u>	<u>4.0</u>	<u>2.7</u>	<u>1.0</u>	<u>8.0</u>	<u>6.7</u>	<u>4.0</u>	<u>0.7</u>
Weighted Aver.			6.2	3.0	1.6	0.6	8.0	7.5	5.4	2.8

* Values for Final Tests were calculated with F_x i.e. no extra value for edema or folliculitis.

These data have been plotted on Plate 14.

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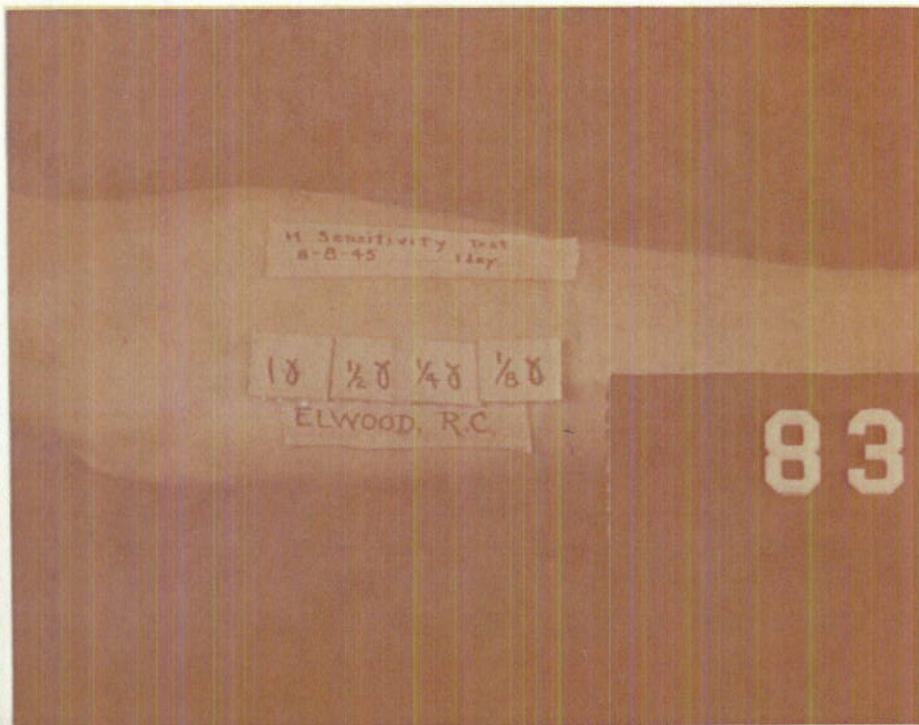


FIG. 1

SECOND PRE-EXPOSURE PATCH TEST ON SUBJECT 163. E.T. 78° F.
READINGS WERE 8-4-4-0. FIRST PRE-EXPOSURE TEST HAD BEEN 8-4-2-1.
THE ERYTHEMA WAS CONSIDERABLY MORE INTENSE THAN SHOWN BY THIS
PICTURE.

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PLATE I

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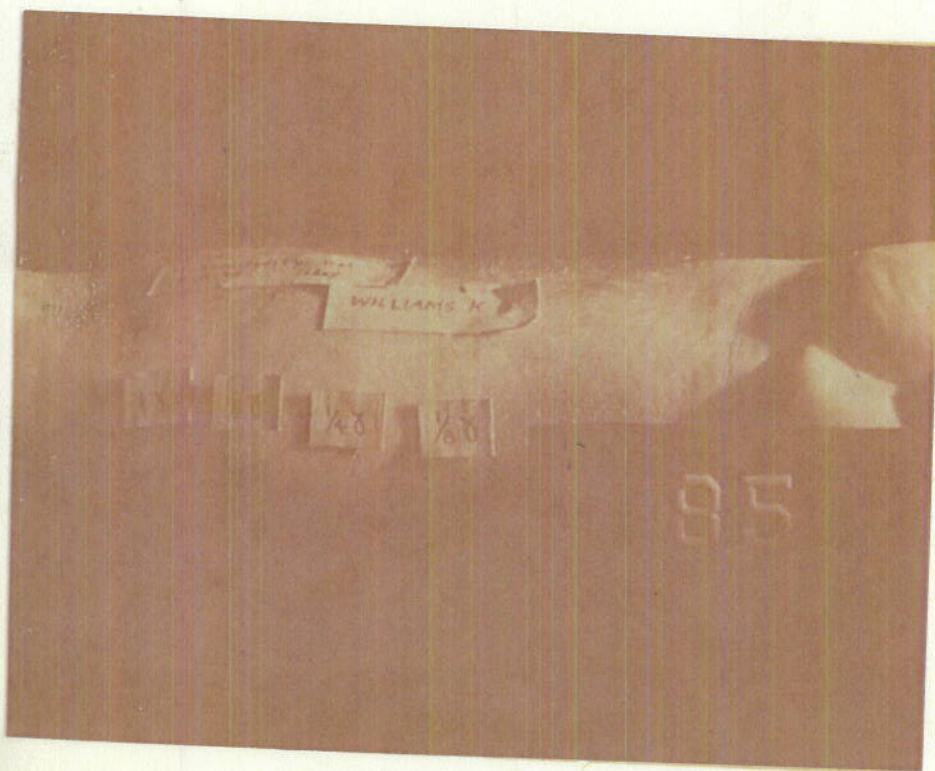


FIG. 2

SUBJECT K.W. 24 HOURS AFTER PATCH TEST. E.T. 78° F.
READINGS AT 24 HOURS WERE 16-16-16-8; 48 HOURS, 16-16-16-4.
NO OTHER INDIVIDUAL SHOWED A TEST AS STRONGLY POSITIVE.
K.W., A CHEMIST, HAD SUSTAINED ABOUT 15 MINOR BURNS FROM H
DURING A 3 YEAR PERIOD, ABOUT 10 OF WHICH WERE ACCOMPANIED
BY VESICATION; AND HE WAS AWARE OF AN INCREASING SENSITIVITY
TO H. HE HAS NO KNOWN HYPERSENSITIVITY TO OTHER SUBSTANCES,
NO ALLERGY TO FOOD, NO HAY FEVER.

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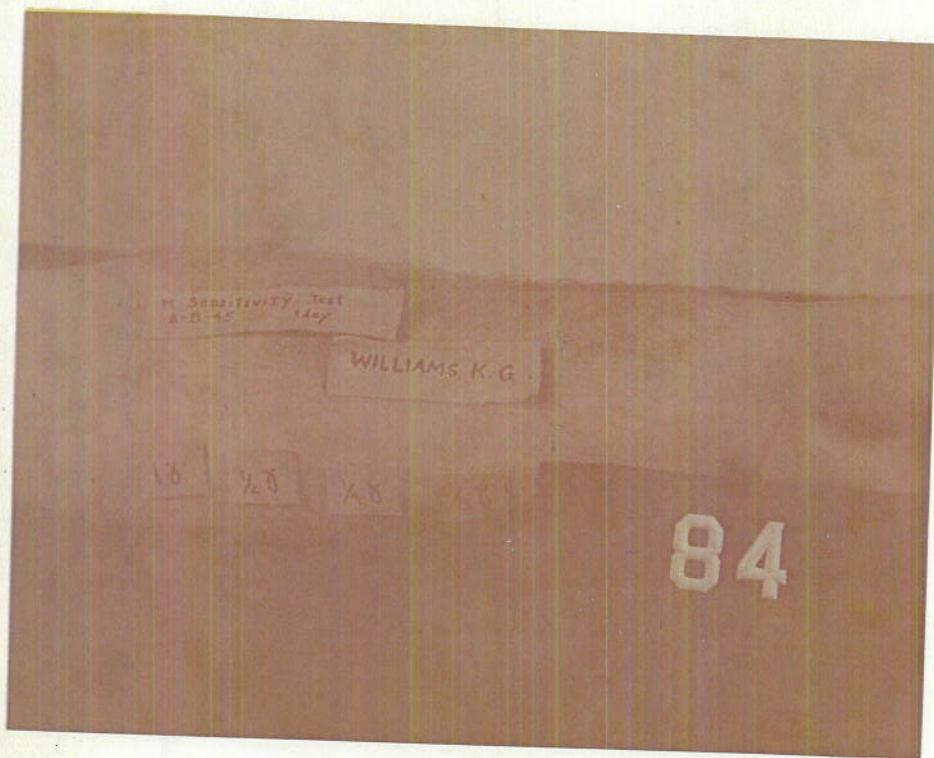


FIG. 3

SAME SUBJECT AS SHOWN IN FIG. 2 BUT PHOTOGRAPHED SO AS TO EMPHASIZE ERYTHEMA RATHER THAN EDEMA.

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PLATE 3

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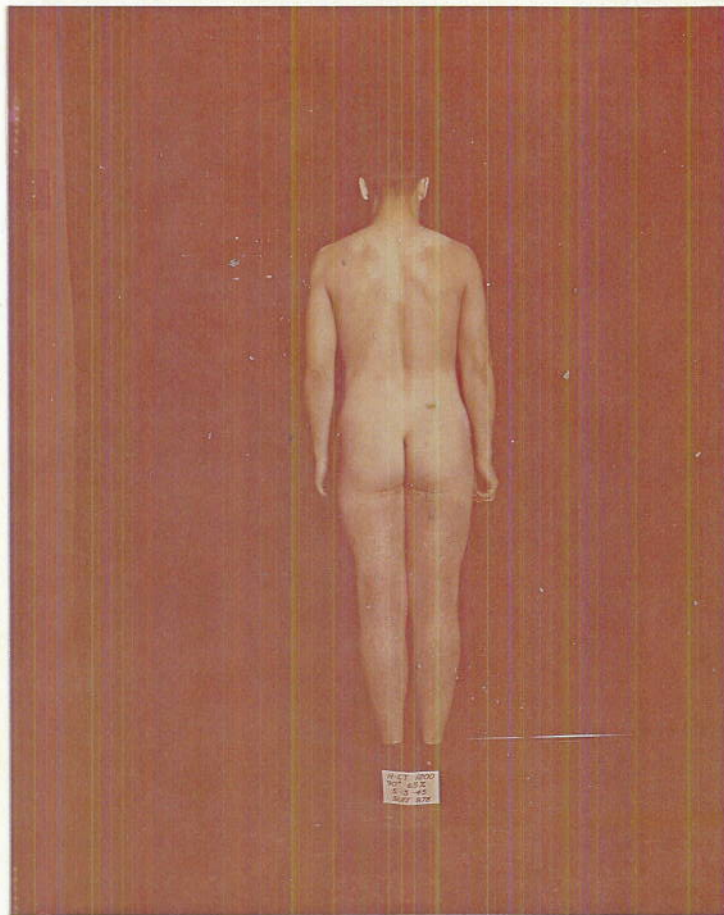


FIG. 4

SUBJECT 878 WORE $1\frac{1}{2}$ LAYER STANDARD CC-2 IMPREGNATED SUIT PLUS CC-2 IMPREGNATED SHORTS FOR 4 EXPOSURES TO H VAPOR AT CT 1200, 90° F., 65% RH. 24 HOURS AFTER THE LAST EXPOSURE, HE MANIFESTED A GENERALIZED MACULOPAPULAR ERYTHEMA WITH MARKED EDEMA. PICTURE TAKEN 5-5-45, 48 HOURS AFTER THE LAST EXPOSURE. (NOTE THAT THE INTERSCAPULAR AREA, SUBJACENT TO THE CANNISTER OF THE NAVY MASK, WAS SPARED.)

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PLATE 4

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FIG. 5

SAME SUBJECT WAS IN FIG. 4. NOTE THE MARKEDLY PAPULAR CHARACTER OF THE RASH ON THE ANTERIOR THIGHS AND THE SPARING OF THE AREAS COVERED BY THE IMPREGNATED GLOVES, SHORTS, AND SOX. SOME DEGREE OF PROTECTION WAS AFFORDED BY THE UNIMPREGNATED SKIVVY SHIRTS.

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PLATE 5

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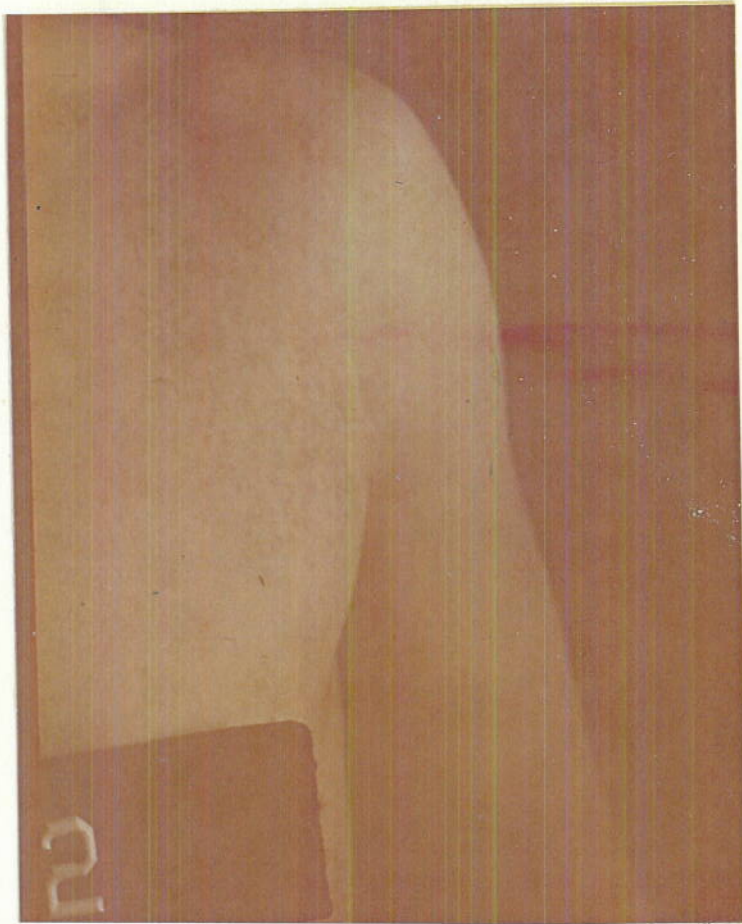


FIG. 6

SAME SUBJECT AS IN FIGS. 4 AND 5. CLOSEUP OF THE ANTERIOR SHOULDER SHOWING THE MACULOPAPULAR RASH. TAKEN THE SAME TIME AS THE OTHER PICTURES.

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PLATE 6

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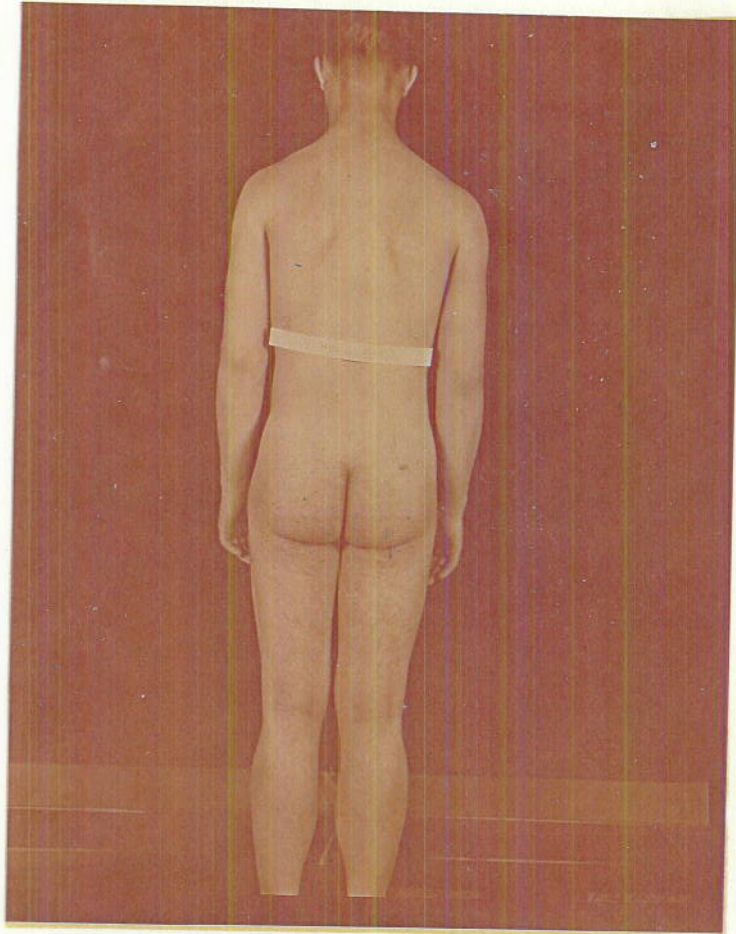


FIG. 7

SUBJECT D.L.H., SUIT NO. 89. WORE 2 LAYER CC-2 IMPREGNATED (ZnO, SOLVENT) SUIT DURING 10 EXPOSURES TO H VAPOR AT CT 1200, 90° F., 65% RH. 24 HOURS AFTER THE LAST EXPOSURE, HE MANIFESTED A GENERALIZED MACULOPAPULAR ERUPTION. PICTURE WAS TAKEN 2-5-44, 48 HOURS AFTER THE LAST EXPOSURE.

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PLATE 7

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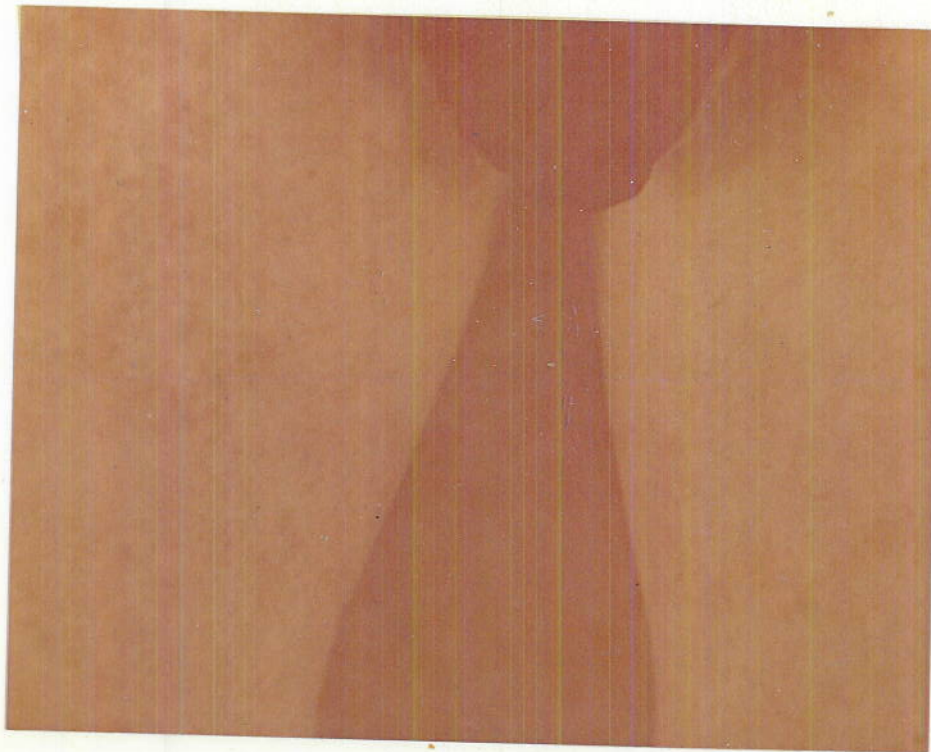


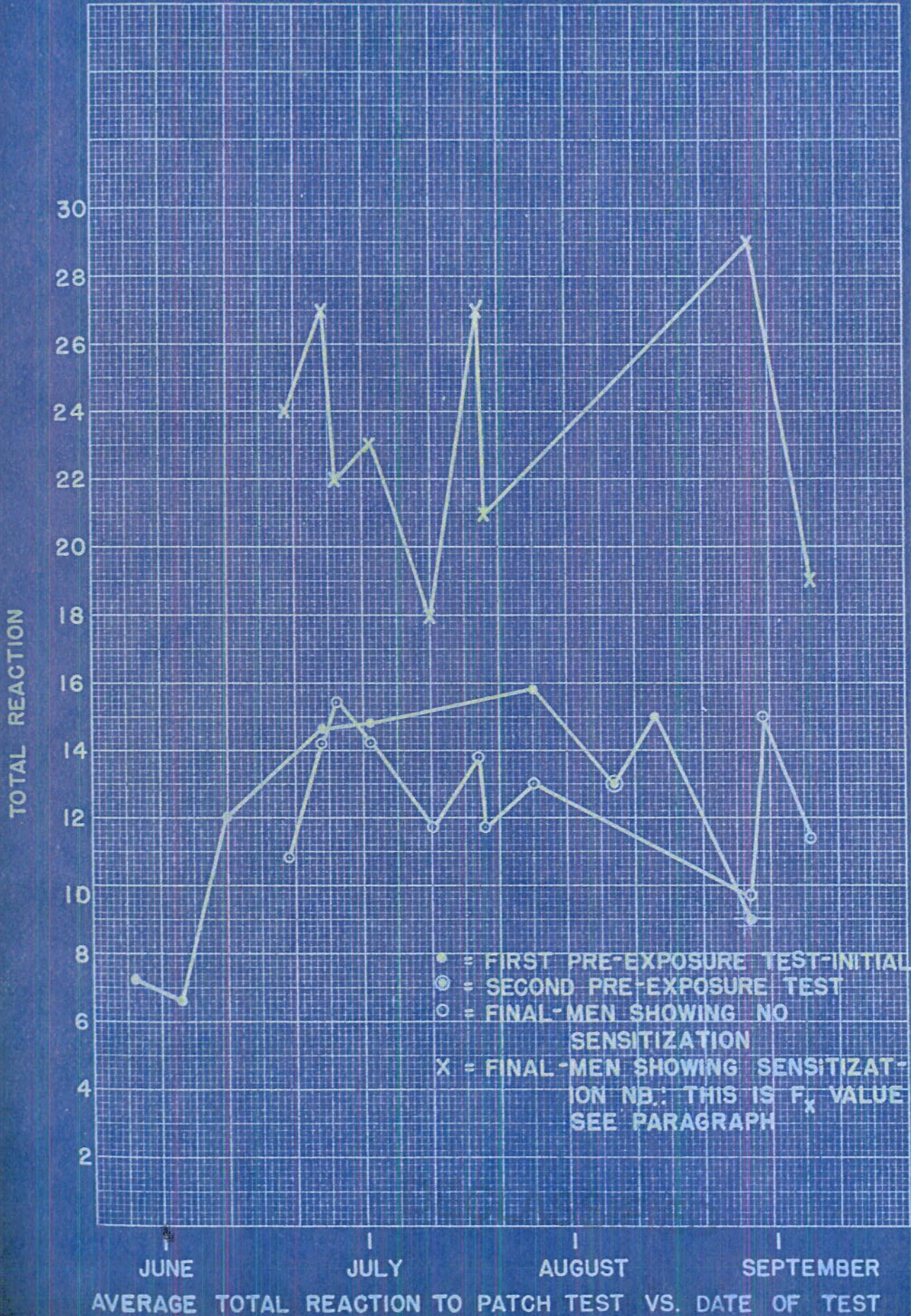
FIG. 8

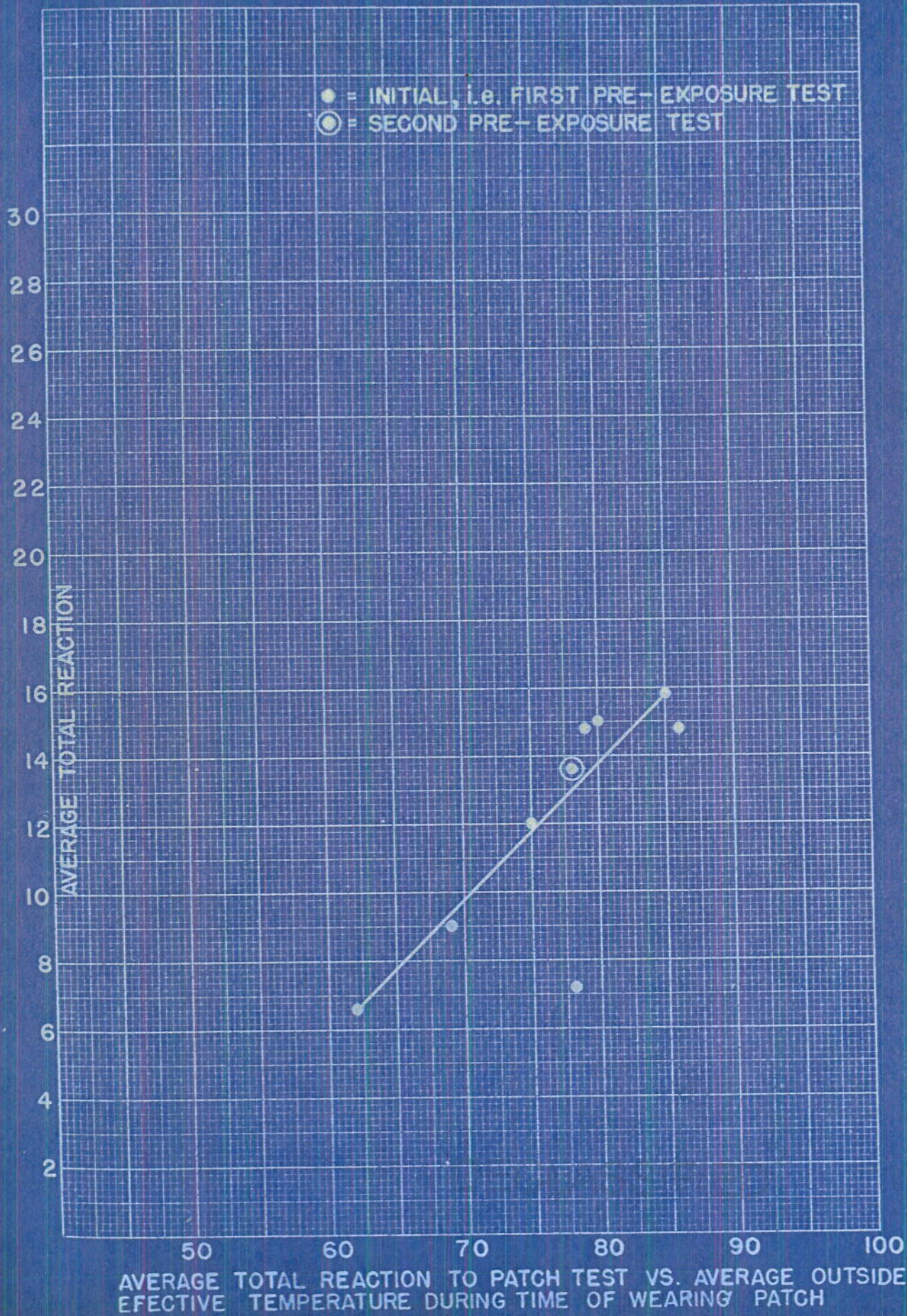
SUBJECT 515 WORE DUNGAREES AND CC-2 IMPREGNATED SHORTS DURING ONE EXPOSURE TO H VAPOR AT CT 600, 60° F., 65% RH. THE PICTURE WAS TAKEN 1-19-45, 8 DAYS AFTER EXPOSURE, AND SHOWS A MACULO-PAPULAR ERUPTION OF THE ANTERIOR SURFACE OF THE THIGHS.

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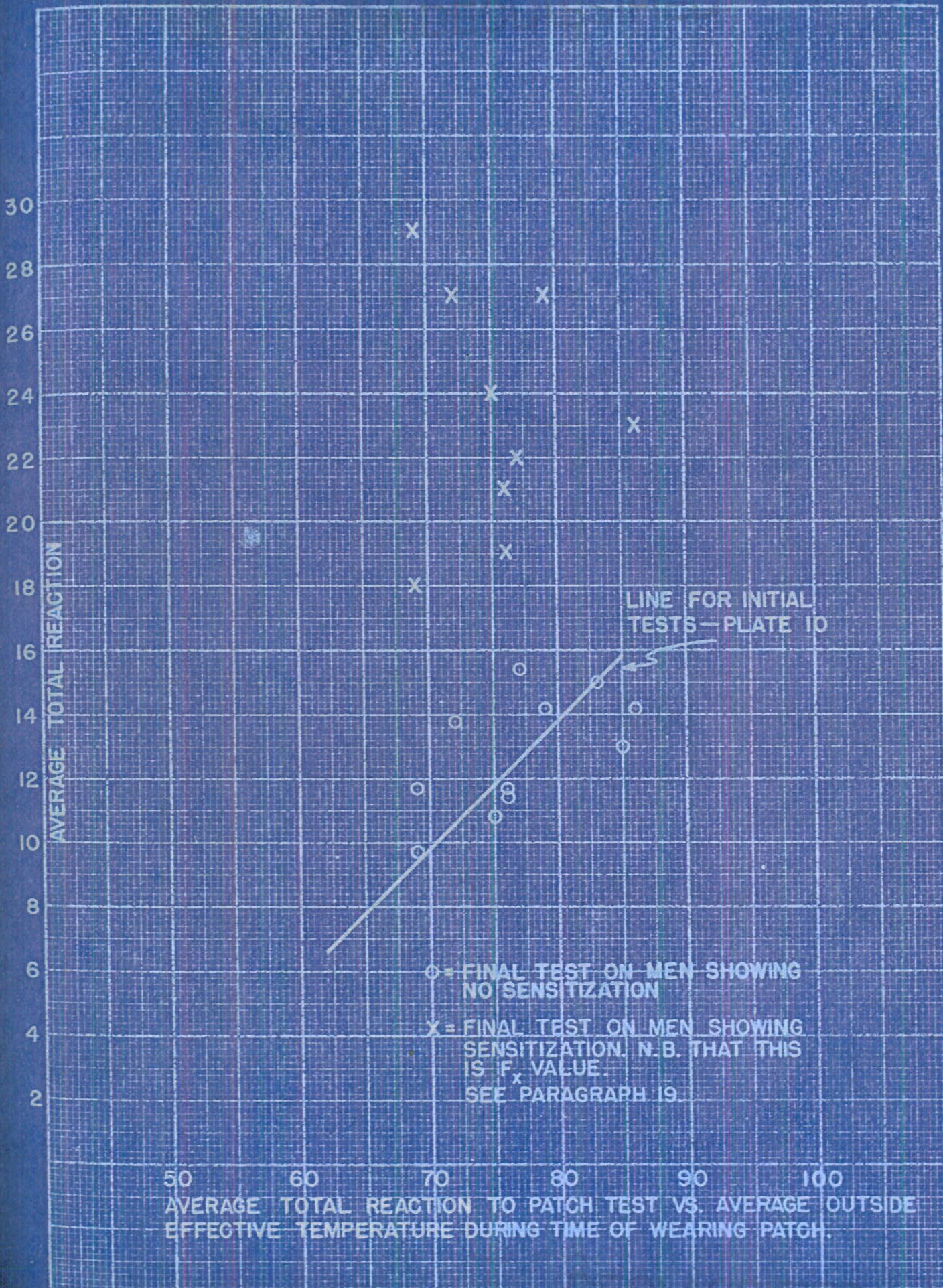
CONFIDENTIAL

PLATE 8

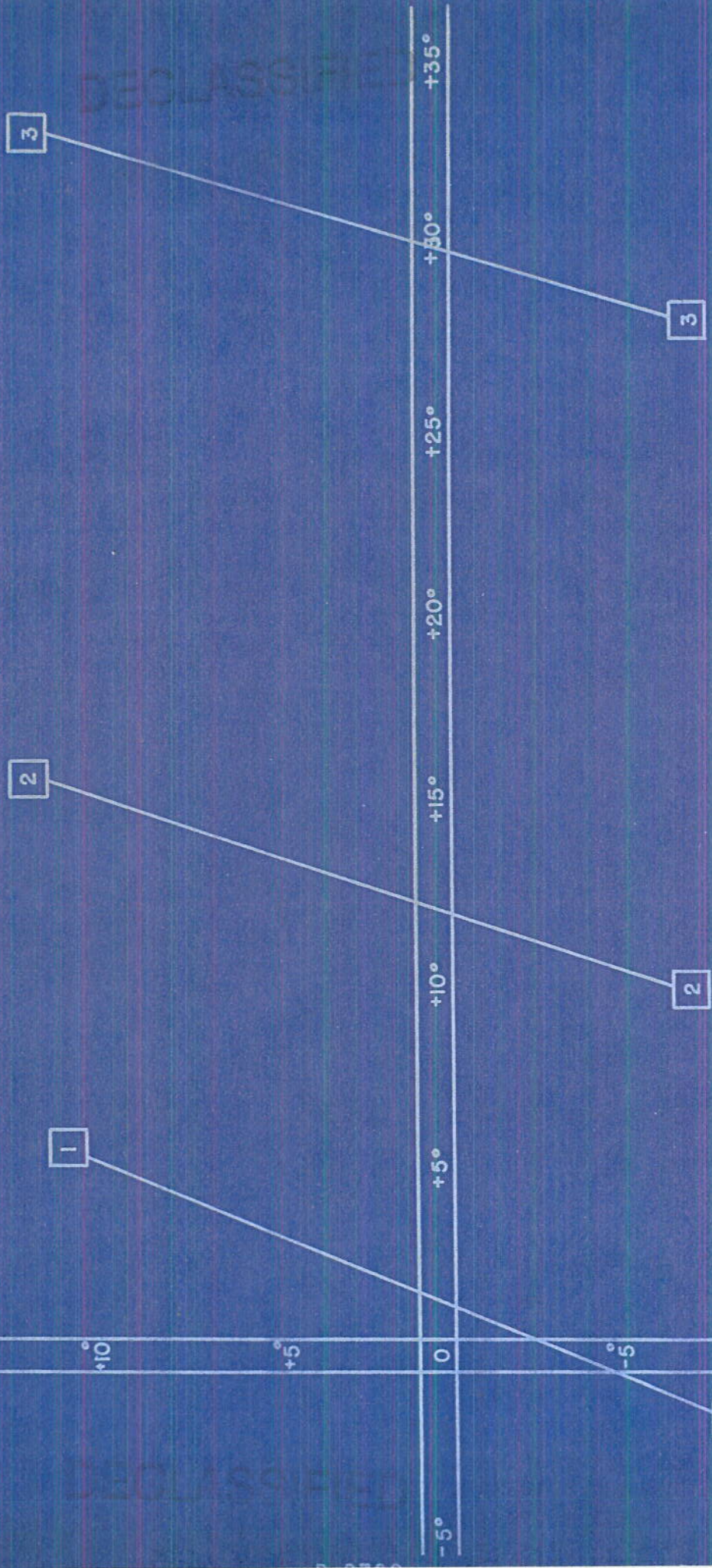




AVERAGE TOTAL REACTION TO PATCH TEST VS. AVERAGE OUTSIDE EFFECTIVE TEMPERATURE DURING TIME OF WEARING PATCH



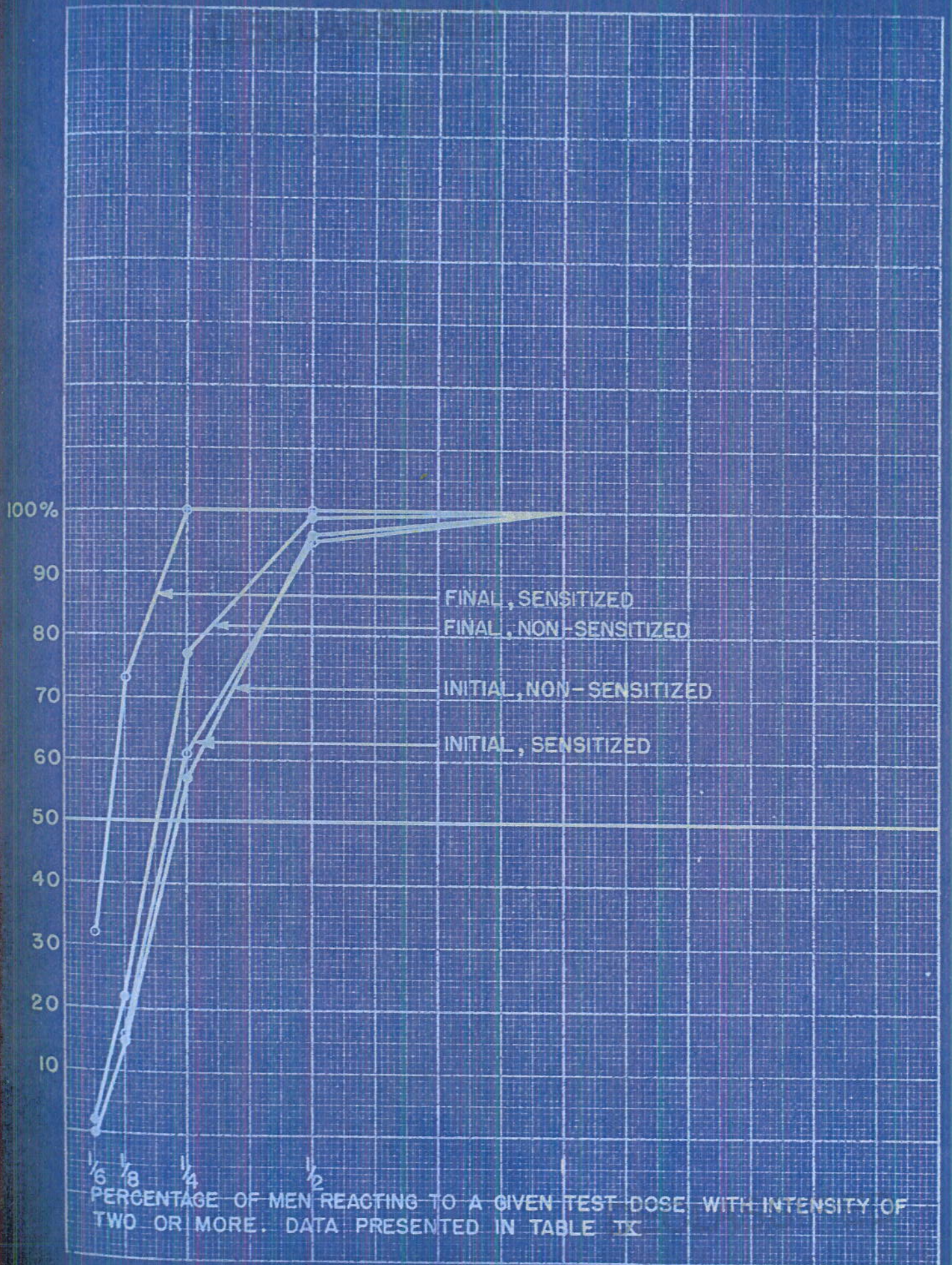
AVERAGE TOTAL REACTION TO PATCH TEST VS. AVERAGE OUTSIDE EFFECTIVE TEMPERATURE DURING TIME OF WEARING PATCH.

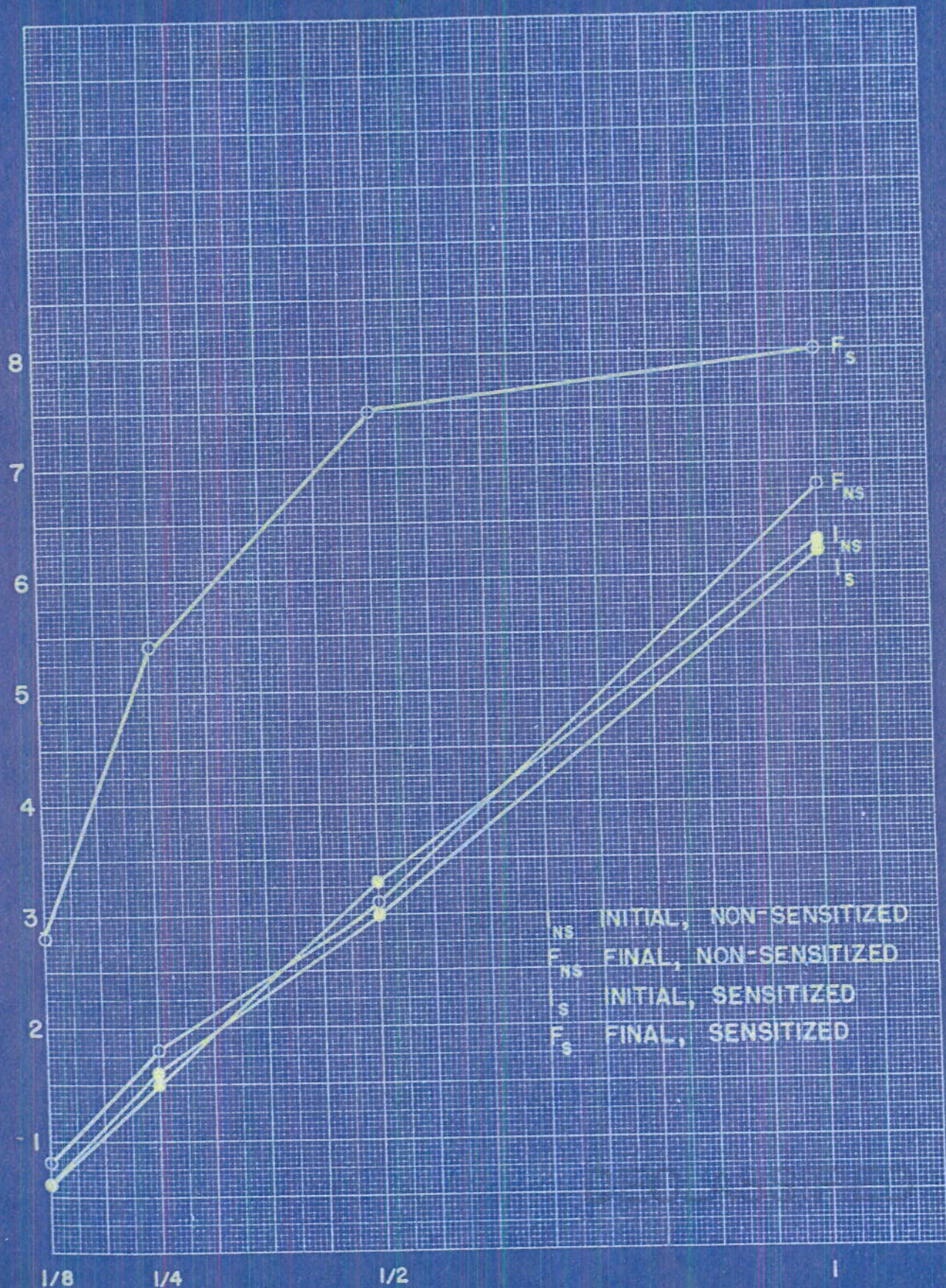


1-1 NONSENSITIZED
 2-2 SENSITIZED (F_X)
 3-3 SENSITIZED (TOTAL F
 4 NONSENSITIZED (HN3)

DIFFERENCES IN EFFECTIVE TEMPERATURES (°F.) AT WHICH PATCH TESTS WERE DONE VS. DIFFERENCE IN TOTAL REACTIONS TO PATCH TESTS

(FINAL - INITIAL = DIFF.) DATA IN TABLE X.





AVERAGE REACTIONS PER TEST DOSE (DATA IN TABLE XI)

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DISTRIBUTION

BuShips	7
BuMed	2
ORI	2
CO, Naval Unit, EA	1
CWS, Tech. Div.	4
CWS, Med. Div.	1
CWS, Med. Div. EA	1
NMRI, Bethesda, Md.	1
UCTL, Chicago, Illinois	1
MFRL, Camp Lejeune	1

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