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NAVAL MEDICAL RESEARCH INSTITUTE
NATIONAL NAVAL MEDICAL CENTER
BETHESDA, MARYLAND

STUDIES OF EXPERIMENTAL HEAT RASH

Research Project X-479 Report No. 1

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27 December 1945

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SUMMARY

1. Heat rash was produced in every member of four groups of men comprising a total of 27 individuals, by subjecting them to effective temperatures ranging from 88° F. to 90° F. for 24 hours per day, the rash appearing as early as three days after entering the hot environment.

2. When 17 hours or more each day were spent in a cool environment the incidence of heat rash was greatly reduced.

3. Heat rash is a rapidly reversible condition, at least during the first week of exposure to hot environment.

4. Exposure to ultraviolet radiation previous to entering the hot environment inhibited the development of heat rash in all 5 subjects of one experiment, but not in any of 6 subjects in another. The discrepancy is not easily explained.

5. Cold baths appeared to have a slight ameliorating effect on the rash. Neither pressure nor friction, nor the inhibition of sweating by formalin prevented the development of heat rash.

6. Increase in white blood cell counts with relative lymphocytosis was observed in all six participants in the one experiment in which blood counts were made.

7. Change in pH of the sweat is not associated with heat rash.

8. No change in elasticity of the skin, in rate of histamine wheal formation or saline wheal disappearance was found to be associated with the heat rash.

9. These studies are exploratory in nature and serve rather to point the way for further studies than as a basis for drawing conclusions.

*This term is used herein to designate a condition which begins as a papulo-vesicular rash within a few days of exposure to very hot environments.

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BACKGROUND

In the course of studies of the effects of hot environments on man, carried out at this Institute during the period 1943-1945, it was found that heat rash could be produced at will by prolonged exposure to high temperatures (1,2). Heat rash became a serious problem in the Pacific Theater and Project X-479 was therefore formulated specifically for its study.

Two experiments, one in April 1945, and one in June 1945 were carried out for this purpose. In July 1945 the study was prematurely discontinued when it became necessary to dismantle the psychrometric room because of new construction. As a result, the material herein presented is incomplete, but may furnish a basis for further investigation. There are a few clearly established findings, but for the most part the experiments require repetition. Some of the approaches to the problem merit further exploration, whereas others which yielded negative results appear not worth repeating.

OBSERVATIONS AND EXPERIMENTS

Nature of the lesions.- The lesions which have been observed to result fro exposure to hot environments are best described as a papulo-vesicular rash, but morphology varies considerably from individual to individual. Macular erythema usually appears first, raised papules and vesicles developing later. The fluid in the vesicles is clear at first, but becomes cloudy after the first day or two. Culture of the clear fluid of the vesicles did not reveal the presence of bacteria except in rare instances in which the organisms were probably introduced from the surface of the skin. When the vesicles erupt there is opportunity for infection to occur from the outside, and there can be little doubt that this contributes to and complicates the picture observed in later stages. It is remarkable, however, that large papules several millimeters in diameter sometimes appear which one judges to be due to secondary infection but which rapidly regress when the subject is removed to a cooler environment.

In general, the development of the primary lesions appears to be rapidly reversible, a matter which will be illustrated more fully below. This reversibility, the lack of evidence of primary infection, and the universal occurrence of the rash in all subjects when temperature conditions are sufficiently severe lead to the conclusion that heat rash is primarily a physiological process.

The distribution of the lesions as well as the morphology varies widely from individual to individual.

Microscopic studies.- A piece of skin about 30 x 7 mm. in area was removed from the lumbar region of one of the subjects of experiment 5, five days after the first appearance of heat rash. The subject was selected because he showed very severe heat rash on the back in general, but virtually no rash on the area exposed to ultraviolet radiation; the skin removed

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included parts of both areas. To avoid hyperemia, the only precaution taken for sterility was light swabbing with iodine solution. Block anaesthesia was used to avoid swelling of the skin of the biopsy site. The biopsy area was fixed rigidly in a frame to prevent shrinkage, curling or distortion during removal or fixation. Fixation was by freezing and drying. These precautions assure high validity to the measurements of dimensions of skin elements.

After drying, the skin sample was immersed in absolute alcohol, embedded in nitrocellulose and sectioned serially at 24μ. Most of the sections were stained with hematoxlin and eosin and mounted in clarite, but a few were examined unstained to determine the distribution of melanin pigment. Measurements were made on enlarged projection drawings (X300), of the cross-sectional area of the epidermis and of the length of the basal cell layer.

The epidermis of the heat rash area was thickened, as indicated by the greater cross-sectional area in this region as compared to that which was heat rash free (table 1). This is particularly significant because the latter area was no doubt thickened as a result of exposure to ultraviolet radiation. The basal layer is as irregular, if not more irregular, in the heat rash area than in the heat rash free area, even though the latter area probably showed greater irregularity than normal skin. Melanin pigment was more marked in the area which had been exposed to ultraviolet radiation, elaboration of epidermal pigment being one of the results of such exposure. In the heat rash area, small blisters containing wandering cells were visible in the stratum lucidum, and partially healed areas were marked by increased thickness of the stratum lucidum. Neither the thickenings nor the blisters were related to sweat glands or hair follicles. Only one of the sweat glands examined contained polymorphonuclear leucocytes. In a few regions of heat rash, unusually large numbers of wandering cells had infiltrated all layers of the epidermis.

In the dermis, the papillae were edematous in the heat rash area, as indicated by the looseness of the collagen bundles, and were infiltrated with wandering cells. In the deeper layers, the blood vessels in the heat rash area were surrounded by markedly thicker collars of wandering cells. Chromatophores were not greatly different in number in the two areas. The epithelium of the sweat glands of the heat rash area was normal, but the reticular connective tissue of the sweat glands was more edematous than that of the areas which had been exposed to ultraviolet radiation.

The findings on this biopsy may be summarized as follows: The epidermis of the heat rash area is hyperplastic. The blisters have formed in the stratum lucidum, and are not related to the sweat glands or hair follicles. The dermis is edematous, and gives every indication of inflammation. Some of the inflammatory cells have infiltrated the epidermis, and in one case the duct of a sweat gland.

Three more biopsies were taken from subjects of experiment 6. One of these was a large section including an area of skin exposed to ultraviolet radiation, and another area not exposed to this agent. The other two were

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small punch biopsies including only isolated lesions. Unfortunately the heat rash was not as marked in these subjects as in the subject examined from experiment 5 and that which had been present was nearly healed. The findings were, however, in general agreement.

The material examined is of particular interest in that it does not show evidence of primary involvement of the sweat glands, which are generally supposed to be primarily involved in the development of heat rash (3). The material is too limited, however, to permit any generalizations. It is quite possible that the morphological picture varies with the stage of development of heat rash, and that we have studied an earlier or, perhaps, a different stage than have other investigators. More biopsy material of the type we have examined should be collected at different stages in the development of the lesions, from subjects exposed to controlled temperature conditions. This might be an advantageous method of study in contrast to biopsies from the naturally occurring rash produced under uncontrolled conditions, and of unknown duration.

Conditions under which heat rash occurs.- The conditions and results of six experiments are summarized briefly in table 2. In the first four experiments the subjects performed physical work in a hot environment during a part of each day, but spent the remainder of the day and slept at night in quarters having a somewhat different environment (see reference 2 for further details). In experiments 1 and 4, the environment was comfortable, and in both cases the incidence of heat rash was low, only one man in each group developing it, and then only to a slight extent. In experiments 5 and 6 the subjects spent the whole day in a hot environment but did no work; all the subjects developed heat rash.

These experiments do not accurately delimit the temperature conditions which elicit heat rash, since conditions other than temperature were not the same in all. For example, the subjects added to their heat load in some experiments by doing physical work, but not in others. It would be desirable to establish the exact limiting conditions for heat rash by a series of studies in which only the temperature conditions were varied. All the hot environments in experiments 1 to 6 were very humid, and intense sweating without immediate evaporation occurred. The effect of dry heat where the sweat evaporates immediately and the skin remains relatively dry should be studied.

When there is a respite from hot environment during a considerable part of the day, heat rash is not nearly so prevalent (table 2). That heat rash appears to be a relatively reversible condition is also attested by the rapid disappearance of the fully developed rash when the subject is removed to a cool environment.

Attempts at Preventive Measures

Ultraviolet radiation.- Suntanning has been tried widely among the forces in the Pacific area as prophylaxis against heat rash, and there has been some favorable comment. Attempts to study the effect of exposure to ultraviolet radiation under controlled conditions were made in experiments 5 and 6.

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In experiment 5, five subjects were exposed to radiation from a carbon arc using "therapeutic C" carbons, filtered through Corex D glass. Two areas of the back, each approximately 5 x 6 inches, were exposed once each day for five days previous to and two days after entering the hot environment. The dosage was adjusted to the individual erythemal threshold, which was determined by exposure of several small areas to a series of graded doses, on the day before the first exposure of a large area. The exposures for the first few days consisted of doses 25 per cent higher than the threshold; this was raised another 25 per cent on the third or fourth day according to the response of the individual, and in some cases a third raise of 25 per cent was made later. The attempt to produce erythema and tanning without desquamation, was in general successful, although mild desquation occurred in some cases.

In this experiment all five of the subjects developed heat rash, but all showed less rash on the areas of the back which had been exposed to ultraviolet radiation than on the surrounding skin, at least after the first day or two following appearance of the rash. In some cases the difference between the exposed and unexposed areas was striking, and there can be no doubt that in this experiment the exposures to ultraviolet radiation definitely inhibited the development of the heat rash.

The results of experiment 6, which was carried out about two months later than experiment 5, were most surprising because they showed no clear evidence of the inhibiting action of ultraviolet radiation which was so obvious in experiment 5. In some instances the heat rash was more severe on the exposed than on the surrounding areas, in others less.

In the latter experiment (6) the dosages were applied somewhat differently, but this would not seem to account for the striking differences in the results. Areas approximately three inches square on either the back or the abdomen were exposed daily to carbon arc radiation at different periods before entrance into the hot environment (e.g. 4 weeks, 3 weeks, etc.) and radiation from an intermediate pressure and from a low pressure mercury arc, was applied to other areas. The schedules and other details of the exposures for both experiments 5 and 6 are shown in table 3.

While none of the dosages in experiment 6 was exactly comparable to any one of those in experiment 5, a wide range was covered in the latter, and it seems unlikely that the difference in the results of the two experiments is to be accounted for on the basis of dosage. The areas of skin exposed were somewhat smaller in the second experiment, but were amply large to detect any marked difference between the exposed and unexposed skin. There seems no reason to expect that the size of the area exposed should effect the development of heat rash within the area, particularly since in experiment 5 the absence of heat rash was sharply limited to the exposed areas. The exposures to ultraviolet radiation were somewhat shorter in experiment 6 (six days) than in experiment 5 (eight days), and as table 3 shows, none of the doses in the former corresponded exactly with those in the latter.

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It must be remembered, however, that the response of the individual to ultraviolet radiation is quite variable and not subject to exact quantitation so it is difficult to believe that the differences in dosage would produce such sharp differences in results for the two groups of subjects. It also seems improbable that the striking difference in the results of the two experiments is explainable on the basis of individual differences, i.e. that in experiment 5 five individuals happened to be used whose skins were, with regard to some particular character, specifically different from those of the six subjects used in experiment 6. It seems more likely that some seasonal difference was involved, since experiment 5 was carried out in late April before the hot season had commenced, and experiment 6 was performed in mid-June. In experiment 5 the period of exposure to ultraviolet radiation prior to entering the hot environments was comfortably cool, whereas during the corresponding period of experiment 6, the weather was hot, and the men no doubt sweated a good deal. The exact bearing of these conditions on the results of the experiments is a matter of conjecture at present, but it is quite possible that the skins were in different conditions in the two experiments, both during the period of exposure to ultraviolet radiation, and at the beginning of the exposure to hot environment.

From a practical standpoint, the experiments do not suggest that suntanning can have great usefulness in the prevention of heat rash. The doses of ultraviolet radiation obtained by exposure to natural sunlight are necessarily very variable (4), and must represent much greater differences than are to be found between experiments 5 and 6. The same is obviously true if seasonal factors or individual differences account for the differences in the results. Our experiments suggest that quite dramatic inhibition of heat rash may sometimes be obtained as a result of exposures to natural sunlight, which are apt to outweigh in the observer's mind other negative results that may be observed. They also suggest that divergence of opinion with regard to the therapeutic use of ultraviolet radiation in cutaneous diseases may be due to unknown factors such as appear to have affected our experiments.

Certain experiments with ultraviolet radiation, not involving hot environments were carried out subsequent to the experiments discussed above, and will be described briefly. In exploring the effect of heavy doses of ultraviolet radiation considerably above the erythemal threshold, it was found that inhibition of the appearance of erythema occurred when high doses with the longer wavelengths of the erythema spectrum were applied. There results an apparent optimum dose for erythema production, but skin damage does not show such an optimum. The phenomenon seems explainable as due to the inhibition of the response of the minute vessels by the action of the longer wavelength ultraviolet which penetrates to them. With respect to the effect of ultraviolet radiation on the development of heat rash, this phenomenon introduces one more variable to be considered and suggests the possibility that direct action on the minute vessels may be involved. In addition, it renders existing concepts of the erythemal threshold as an index of individual susceptibility to ultraviolet radiation, and as a basis for therapeutic dosage, quite inexact.

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Pressure and friction.- To examine the possible effects of rubbing or pressure of clothing, pressure bandages were placed on the wrists of some subjects, and leather wrist bands on others. There was no evidence that either of these devices markedly diminished or enhanced the heat rash.

Inhibition of sweating by formalin.- In experiment 6 an area approximately three inches square on the thigh of each subject was subjected to formalin caused to enter the skin by electrophoresis, following the method described by Pinson (5). In all cases sweating was inhibited if not completely abolished. Heat rash developed on these areas, to approximately the same extent as on the surrounding untreated skin. This finding is of interest because there is a general tendency to connect heat rash with excessive sweating. The experiment should be repeated before our finding is construed as disproving this hypothesis.

Cold baths.- In both experiments 5 and 6, some of the subjects were permitted to bathe with cold water once a day. These subjects showed on the average somewhat less heat rash than those who did not bathe, but the difference was not great.

Changes Accompanying the Development of Heat Rash

Blood changes.- During the exposure to hot environment, the subjects were allowed to take water and salt *ad libitum*, and there was no evidence of hemoconcentration. In experiment 1, hematocrit and refractive index of plasma were determined and progressive changes were not observed. In experiment 6, hematocrit measurements indicated some hemodilution during the period of exposure to hot environment, and this was also suggested by a corresponding fall in the red cell counts.

White cell counts were made in experiment 6 only. All six subjects showed a rise in white cell count, even though hemodilution occurred. In about five subjects the white counts remained high throughout the exposure to heat. In one subject the count fell to pre-exposure level after initial rise (allowance being made for hemodilution). Slightly raised white cell counts persisted in some subjects 17 days after leaving the hot environment. The data, which are plotted in figure 1, show the rise in white cell counts to have been very great in some subjects. Differential counts showed relative lymphocytosis in all subjects, indicating that the raised white cell count was not a sign of an acute pyogenic condition, but probably a physiological response to heat. Without repetition of this experiment one hesitates to accept this change in white cell count as definitely associated with exposure to hot environment or with heat rash, but this is a lead that should certainly be followed up. Increased white cell count accompanying short exposures to heat has been reported previously (6).

Hydrogen ion concentration of the skin surface.- In experiment 5, the pH of the skin surface was explored with indicator paper, and in experiment 6 this rather rough method was supplemented by measurements with a glass electrode.

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The measurements were made before, during and after entering the hot environment; the areas explored were the axilla, groin, and the foot between the toes, with a smaller number of determinations on the forehead and neck. No consistent change in pH was associated with entrance into the hot environment nor with appearance of the heat rash. There seems no reason to believe that the development of heat rash is associated with change of pH of the sweat.

No consistent difference was found between areas exposed to ultraviolet radiation, and surrounding areas.

Sweat rates.- The loss of water by sweating with the subject standing at rest during periods of two hours was measured as the difference in body weight at the beginning and end of the period. No relationship between the total amount of sweat and the degree of heat rash was found, but the number of subjects was too few to permit a conclusive statement.

Elasticity of the skin.- Measurements of elasticity of the skin of the abdomen, pectoral region and thigh, by means of the tensitometer of Soderman and Burch (7), were made on three subjects at intervals before and after entrance into the hot environment in experiment 6. There was no evidence of change in elasticity of the skin during exposure to the hot environment or development of the heat rash, and the measurements were discontinued, it being concluded that such changes as might occur would not be detected by this method.

Histamine and saline wheals.- Using a "whealometer" devised by Dr. C. C. Pfeiffer for determining the change in volume of wheals with time, the development of wheals resulting from histamine pricks and the disappearance of wheals caused by intradermal injection of saline were studied. The results were quite variable, and do not suggest any definite changes in formation or disappearance of such wheals upon entering a hot environment, nor any progressive changes during exposure to heat or associated with heat rash.

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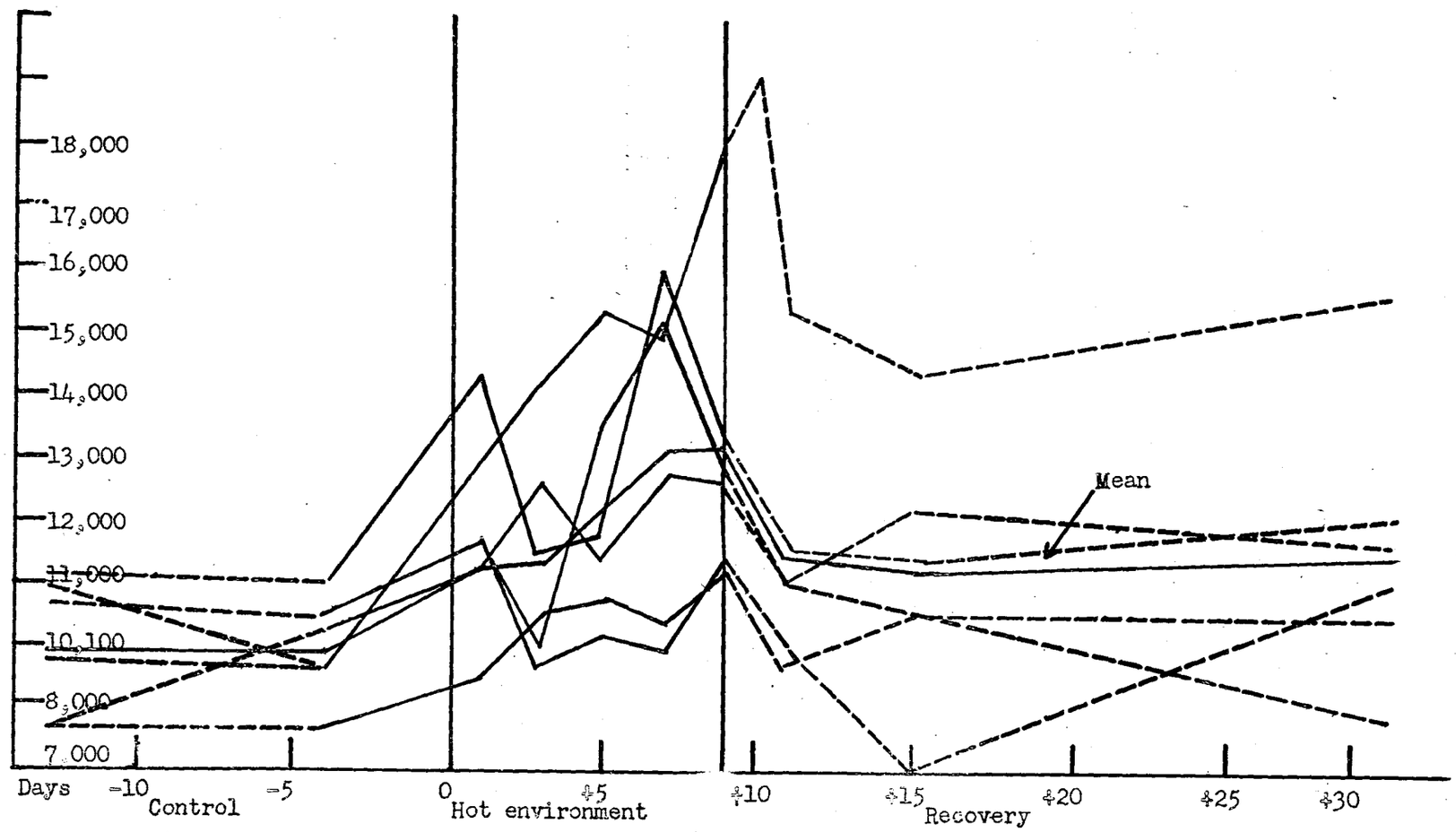

Figure 1.- White blood cell counts, individual and mean for six subjects. Experiment 6.

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Table 1.- Measurements of epidermis in four sections (24 μ thick)

Section No.	Portion of skin	Length of epidermis (cm.)	Length of basal layer (cm.)	Ratio of length of basal layer to length of epidermis	Area of cross-section of epidermis, cm^2	Ratio of cross section of area of epidermis to length of epidermis
1	u.v.*	0.57	0.86	1.51	0.008	1.4
	h.r.**	1.42	2.56	1.80	0.025	1.7
31	u.v.	0.52	0.86	1.65	0.007	1.3
	h.r.	1.02	1.83	1.79	0.019	1.9
71	u.v.	0.78	1.21	1.55	0.010	1.3
	h.r.	1.33	2.11	1.59	0.022	1.7
101	u.v.	0.87	1.48	1.70	0.011	1.3
	h.r.	1.19	1.96	1.65	0.022	1.8

*Area exposed to ultraviolet radiation.

**Area exhibiting heat rash.

Table 2.- Summary of experimental conditions and results of six experiments

Experiment No.	Date	No. of subjects	Average conditions (effective temperatures °F.)		Work in hot environment	Incidence of heat rash (per cent)
			Hottest (work)	Coolest (quarters)		
1	11-27 Aug 1943	10	90° for 7 hr.	87° for 17 hr.*	+	100
2	9-19 Sep 1943	10	90° for 7 hr.	78° for 17 hr.*	+	10
3	13 Nov-12 Dec 1944	6	90° for 4 hr.	85° for 20 hr.**	+	100
4	13 Nov-12 Dec 1944	6	90° for 4 hr.	75° for 20 hr.**	+	17
5	18-26 Apr 1945	5	89.6° for 24 hr.***		-	100
6	11-20 Jun 1945	6	88.0° for 24 hr.†		-	100

*Further details regarding conditions given in ref (1).

**Further details regarding conditions given in ref (2).

***Wet bulb temperature 86.4° F., dry bulb temperature 97.8° F.

†Wet bulb temperature 83.6° F., dry bulb temperature 97.8° F.

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Table 3.- Schedule of exposures to ultraviolet radiation

Experiment No.	Area No.	Approximate size of area	Type of radiation	Days exposed** (inclusive)
5	1	5 x 6 in.	carbon arc**	- 5 to + 1
	2	3 x 5 in.	carbon arc	+ 4 to + 8
6*	1	3 x 3 in.	carbon arc	-28 to -23
	2	3 x 3 in.	carbon arc	-21 to -17
	3	3 x 3 in.	carbon arc	-15 to - 9
	4	3 x 3 in.	carbon arc	- 7 to - 2
	5	3 x 3 in.	carbon arc	0 to + 5
	6	3 x 3 in.	carbon arc	+ 5 to + 8
	7	3 x 3 in.	mercury A***	- 7 to - 2
	8	3 x 3 in.	2537A+	- 7 to - 2

*The position of any given area on the body was different in each subject, to avoid misinterpretation due to greater incidence of heat rash in some areas. All irradiated areas were on the back, thorax or abdomen.

**"Therapeutic C" carbons.

***Intermediate pressure mercury arc.

+Low pressure mercury arc.

++Day 0 is the day of entrance into the hot environment, negative values days before 0, positive values, day after 0.