UR-433

SOME EFFECTS OF SUPERIMPOSING TWO RADIANT
ENERGY THERMAL BURNS ON BARE PORCINE SKIN

by

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ROCHESTER, NEW YORK

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UR-433

Health and Biology

THE UNIVERSITY OF ROCHESTER
Atomic Energy Project
P. O. Box 287, Station 3
Rochester 20, New York

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Contract W-7401-eng-49 between the U. S. Atomic
Energy Commission and the University of Rochester,
administered by the Department of Radiation Biology
of the School of Medicine and Dentistry.

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Date Completed: 2/17/56

Date of Issue: 3/30/56

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ABSTRACT

The effects of two superimposed radiant thermal energy exposures are synergistic but not additive, and the results are somewhat dependent on the time interval between exposures. A mild burn offers no protection from a more severe burn, but a moderately severe burn occasionally protects against a very severe exposure. Three factors associated with the initial exposure are involved in the final effect: 1) temperature of the tissue, 2) latent, reversible injury of tissue, and 3) changes in the thermal properties of skin.

GENERAL INTRODUCTION

Much work has been done on the effects of radiant thermal energy on bare porcine skin. The relationship between time and intensity (1, 2, 3, 4), the influence of wave length (5, 6, 7), and the effect of skin temperature (8) have been reported. No work has yet been done on another important aspect of the burn problem, the effect of superimposing one such burn upon another. This is of potential military significance since the recipient of one exposure to radiant injury is not necessarily insured against a subsequent insult. Such a study could also give valuable information on the pathology of burns since it involves the exposure to radiant thermal energy of a volume of tissue which may have different thermal properties, a different temperature and different enzymatic reactions from the normal skin.

Only a brief report is available on repeated exposures to any form of thermal energy (9), and this deals with sub-threshold contact burns. It suggests a "latent injury" and a recovery period following a sub-threshold exposure. A subsequent sub-threshold exposure made before the end of this recovery period leads to recognizable damage; one after the recovery period does not produce injury. The work also shows that the greater the initial exposure, the longer the recovery period will be.

One would like to know whether or not there is a similar cumulative effect from exposures to radiant thermal injury and, if there is, something of the nature of the recovery period following the initial exposure. Other important problems also come to mind. Are two exposures, separated by a time interval, additive or merely synergistic? Is the effect of the second exposure due to an initial "latent injury" or to a change in the thermal

properties of the skin, i. e., in the reflectance or transmittance? When two unequal exposures are made, separated by an interval of time, does it make a difference whether the milder or the more severe exposure is delivered first? Can one burn actually protect from a subsequent, more severe burn by altering the thermal properties of the skin?

The following experiments were designed with these questions in mind. The work is presented in three parts. Part I deals with exposures of varying irradiance superimposed at one minute intervals. Part II presents the effects of four exposures, three mild and one moderately severe, superimposed one minute, one hour and six hours after the first exposure. Part III consists of data on the effects of a very severe burn superimposed on a moderately severe burn at one and five hour intervals. A further comparison is made between flash burns and burns of a little longer duration.

METHODS

Young Chester White pigs, anesthetized with intraperitoneal Dial in Urea-urethane (Ciba) in doses of 70 mgm/Kg of body weight, were used as the experimental animal. The hair was removed with electric clippers and the skin was gently washed. The ambient temperature of the room was controlled to decrease variation in skin temperature.

The heat source was a modified 24 inch Army carbon arc searchlight (2, 10).

The exact experimental design will be described separately under the three parts. In each case, however, a simple randomized block was set up to include all irradiances and exposure times used in that part. The burns

were assessed 18 - 24 hours following burning by the criteria previously reported (1, 2, 5). Biopsies of the burns were taken at this time and the tissues were subsequently stained by a method, to be reported at a later date (11), designed to aid in assessing the depth of dermal damage.

PART I THE EFFECTS OF SUPERIMPOSING TWO RADIANT THERMAL
ENERGY EXPOSURES AT AN INTERVAL OF ONE MINUTE.

INTRODUCTION AND EXPERIMENTAL DESIGN

In a study of two superimposed radiant thermal energy exposures it is first of all important to determine whether or not both contribute to tissue injury. If the effect of the two is no greater than that of the more severe single exposure alone, the problem of multiple exposures need no longer concern us. If, however, both do contribute to injury, it is necessary to determine whether their effects are additive or merely synergistic and whether there is a difference between delivering the larger or smaller dose first. The following experiment was designed to answer these questions.

The exposure time of 0.3 sec. was used throughout this part, and the time interval between superimposed doses was maintained at one minute. The irradiance of $6.8 \text{ cal/cm}^2/\text{sec.}$, which will deliver 2.04 calories in 0.3 seconds, was chosen as a "base irradiance" for the double burns. From previous work it was believed that this caloric level would fall well below the median effective exposure for a 2+ burn. For the other half of the double burn, irradiances ranging from $3.6 \text{ cal/cm}^2/\text{sec.}$ to $8.4 \text{ cal/cm}^2/\text{sec.}$ and uniformly separated by 20% increments were selected. For the control each irradiance was used as a single exposure and, in addition to these, four irradiances ranging from $9.34 \text{ cal/cm}^2/\text{sec.}$ to $12.8 \text{ cal/cm}^2/\text{sec.}$ and separated by 10% increments were used to aid in the determination of the median effective exposure of the 2+ burn for the single burns in this experiment.

One group of treatments for the double burns consisted of the more serious burn first, and another group placed the less severe burn first. In all, 18 treatments were necessary, nine for single burns and nine for double burns. Two such treatment blocks could be placed on each side of a pig. This block was replicated 16 times to give a total of 288 burns, and biopsies were taken of eight of these replications (144 biopsies).

RESULTS

The results of surface grading the burns are shown in Tables I, II and III. By subjecting these dose-response data to the simplified graphic method of probit analysis (13) one may obtain the median effective exposure for the 2+ burn ($2+EE_{50}$) for single burns and for double exposures.

The $2+EE_{50}$'s and their 95% confidence limits are given in Table IV. The median effective exposure for the double burns is significantly higher than that of the single burns indicating that, although the two exposures may act synergistically to produce a burn, their effects are not additive. The confidence limits of the median effective exposures for the two methods of delivering double burns overlap. Therefore no significant difference is found between the double burns when the more severe exposure is given first or second.

Table V lists the effects of single exposures and the effects of those same exposures when they have preceded or followed the base exposure. It is readily apparent from these results that both exposures contribute to the result obtained even though their effects are not strictly additive.

Data on the microscopic pathology are presented in Tables VI - IX. Dermal-epidermal separation is chosen as one convenient reference to the

TABLE I

BURNS PRODUCED BY A SINGLE 0.3 SECOND EXPOSURE

Q (cal/cm ²)	0	1+		2+			3+
		Mild	Sev.	Mild	Mod.	Sev.	
3.85				1	7	8	
3.46			1	4	12		
3.11			3	8	3	1	
2.80		1	6	6	3		
2.52		2	6	6	2		
2.04		6	7	3			
1.66		10	5	1			
1.34		15	0	1			
1.09		15	1				

TABLE II

BURNS PRODUCED BY TWO 0.3 SECOND EXPOSURES SEPARATED BY AN INTERVAL OF ONE MINUTE. THE EXPOSURE DELIVERING THE MORE ENERGY IS GIVEN FIRST.

Initial Exposure Q_1 (cal/cm ²)	Second Exposure Q_2 (cal/cm ²)	Total Q (cal/cm ²)	0	1+		2+			3+
				Mild	Sev.	Mild	Mod.	Sev.	
2.52	2.04	4.56			3	8	5		
*2.04	2.04	4.08			5	9	1	1	
2.04	1.66	3.70		1	4	11			
2.04	1.34	3.38		4	7	3	2		
2.04	1.09	3.13		3	5	8			

TABLE III

BURNS PRODUCED BY THREE 0.3 SECOND EXPOSURES SEPARATED BY AN INTERVAL OF ONE MINUTE. THE EXPOSURE DELIVERING LESS ENERGY IS GIVEN FIRST.

Initial Exposure Q_1 (cal/cm ²)	Second Exposure Q_2 (cal/cm ²)	Total Q (cal/cm ²)	0	1+		2+			3+
				Mild	Sev.	Mild	Mod.	Sev.	
2.04	2.52	4.56				7	8	1	
*2.04	2.04	4.08			5	9	1	1	
1.66	2.04	3.70		1	6	8	1		
1.34	2.04	3.38		2	7	7			
1.09	2.04	3.13		5	4	6	1		

*This treatment, which consists of two equal exposures, is shown in both tables for the sake of convenience.

TABLE IV

MEAN EFFECTIVE EXPOSURE (EE_{50}) FOR SINGLE AND DOUBLE BURNS.

Type of Burn	EE_{50} (cal/cm ²)	Confidence Limits
Single Burn	2.5	2.3 - 2.8
Double Burn, More Severe Exposure First	3.3	3.0 - 3.6
Double Burn, Less Severe Exposure First	3.5	3.2 - 3.8
Double Burn, Pooled Data	3.4	3.1 - 3.7

TABLE V

COMPARISON OF SINGLE AND DOUBLE EXPOSURES.

Dose (cal/cm ²)	Response Obtained by Single Dose		Per Cent 2+ Burn	Response Obtained by this Dose Plus Base Dose of 2.04 cal/cm ²		Per Cent 2+ Burn
	1+	2+		1+	2+	
1.09	16	0	0	17	15	47
1.34	15	1	6	20	12	38
1.66	15	1	6	12	20	63
2.04	13	3	19	5	11	69
2.52	8	8	50	3	29	71

pathological change associated with the burns. The fact that there is no separation does not mean that there is no change in the epithelium, but separation does represent a more severe damage than mere vacuolization or other slight structural alteration seen in the epithelial cells. The figure given for depth of dermal damage represents the maximum depth of recognizable change in the dermis. This depth is by no means uniform across the entire burned area and, in the less severely damaged skin it may represent no more than a 20 - 25% area in the center of the burn. This measurement does, however, lead to an accurate expression of the severity of the burn if one understands what it represents.

Tablex VII and VIII compare the effects between delivering the larger and the smaller exposure first. In general, little difference can be found between them. It is of some interest to note the effects on dermal-epidermal separation of the greatest dose used here. When the larger dose is given first, separation is likely to be partial; when the smaller dose is delivered initially, separation is likely to be complete. This difference, however, has little effect on the depth of dermal damage. In the first instance one often sees a severely damaged epithelial layer "stuck" to a damaged dermis.

Table IX compares directly the effect of a single exposure with the effect of that exposure preceding or following the "base exposure" of 2.04 cal/cm². It is apparent that there is no evidence that one burn affords protection from a second burn at the one minute interval. If one compares the effects of the single base exposure of 2.04 cal/cm² with the results of the double exposures, it is seen that adding an exposure of 1.66 cal/cm² or more to the base tends to increase the damage. On the other hand, the

TABLE VI
 MICROSCOPIC PATHOLOGY OF SINGLE BURNS. THE
 EXPOSURE TIME IS 0.3 SECOND THROUGHOUT.

Q (cal/cm ²)	Dermal-epidermal Separation				Dermal Damage		
	None	Partial	Complete		Depth		
					Less than 0.1 mm.	0.1 - 0.2 mm.	0.2 - 0.3 mm.
3.85	0	5	3	2	3	2	1
3.46	0	2	6	2	4	2	0
3.11	0	5	3	2	6	0	0
2.80	0	6	2	6	1	1	0
2.52	1	5	2	7	1	0	0
2.04	2	5	1	7	1	0	0
1.66	6	1	1	8	0	0	0
1.34	8	0	0	8	0	0	0
1.09	6	2	0	8	0	0	0

TABLE VII

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MICROSCOPIC PATHOLOGY OF DOUBLE BURNS. 0.3 SECOND EXPOSURE.
ONE MINUTE BETWEEN BURNS. MORE SEVERE EXPOSURE FIRST.

Q_1 (cal/cm ²)	Q_2 (cal/cm ²)	Total Q	Dermal-epidermal Separation			Dermal Damage			
			None	Partial.	Complete	None	Less than 0.1 mm.	0.1 - 0.2 mm.	0.2 - 0.3 mm.
2.52	2.04	4.45	0	7	1	2	4	2	0
*2.04	2.04	4.08	1	4	3	3	5	0	0
2.04	1.66	3.70	1	6	1	5	3	0	0
2.04	1.34	3.38	1	6	1	7	1	0	0
2.04	1.09	3.13	1	5	2	6	2	0	0

TABLE VIII

MICROSCOPIC PATHOLOGY OF DOUBLE BURNS, 0.3 SECOND EXPOSURES,
ONE MINUTE BETWEEN BURNS. LESS SEVERE EXPOSURE FIRST.

Q_1 (cal/cm ²)	Q_2 (cal/cm ²)	Total Q	Dermal-epidermal Separation			Dermal Damage			
			None	Partial	Complete	None	Less than 0.1 mm.	0.1 - 0.2 mm.	0.2 - 0.3 mm.
2.04	2.52	4.56	0	1	7	3	3	1	0
*2.04	2.04	4.08	1	4	3	3	5	0	0
1.66	2.04	3.70	1	5	2	6	2	0	0
1.34	2.04	3.38	2	5	1	8	0	0	0
1.09	2.04	3.13	1	6	1	7	1	0	0

*This treatment is reproduced in both tables.

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TABLE IX

A COMPARISON OF THE MICROSCOPIC PATHOLOGY OF SINGLE AND DOUBLE BURNS. 0.3 SECOND EXPOSURES. ONE MINUTE INTERVAL BETWEEN DOUBLE EXPOSURES. POOLED DATA ON DOUBLE BURNS.

Q (cal/cm ²)	Dermal-epidermal Separation			Dermal Damage			
	None	Partial	Complete	None	Less than 0.1 mm.	0.1 - 0.2 mm.	0.2 - 0.3 mm.
2.52	1 (13%)	5 (63%)	2 (25%)	7 (88%)	1 (13%)	0	0
2.52 + 2.04	0	8 (50%)	8 (50%)	5 (31%)	7 (44%)	3 (19%)	1 (6%)
2.04	2 (25%)	5 (63%)	1 (13%)	7 (88%)	1 (13%)	0	0
2.04 + 2.04	1 (13%)	4 (50%)	3 (38%)	3 (38%)	5 (63%)	0	0
1.66	6 (75%)	1 (13%)	1 (13%)	8 (100%)	0	0	0
1.66 + 2.04	2 (13%)	11 (69%)	3 (19%)	11 (69%)	5 (31%)	0	0
1.34	8 (100%)	0	0	8 (100%)	0	0	0
1.34 + 2.04	3 (19%)	11 (69%)	2 (13%)	15 (94%)	1 (6%)	0	0
1.09	6 (75%)	2 (25%)	0	8 (100%)	0	0	0
1.09 + 2.04	2 (13%)	11 (69%)	3 (19%)	13 (81%)	3 (19%)	0	0

pathological pictures of the double exposures at the 1.09 cal/cm^2 and 1.34 cal/cm^2 levels show no significant difference from the base exposure. A more meticulous grading of the damage to the epithelium might show some difference, but this would have little practical significance.

The effect of two superimposed exposures separated by a one minute interval is not equal to, but rather somewhat less than, the effect of delivering the total dose at one time. The single dose of 3.11 cal/cm^2 may be considered equivalent in radiant exposure to the double exposure of $1.09 \text{ cal/cm}^2 + 2.04 \text{ cal/cm}^2$ (total 3.13 cal/cm^2). The effects of the single burn are seen to be the more severe of the two. The similarity of the effects from a single exposure of 3.85 cal/cm^2 and a double exposure totaling 4.56 cal/cm^2 illustrates this same point in a different way.

DISCUSSION

The only work which has been found to deal with the cumulative effects of repeated sub-threshold exposures is that of Moritz and Henriques (9). This report contains data on contact burns in which 21 sites were subjected to repeated sub-threshold exposures at timed intervals. Their conclusions were that repeated sub-threshold exposures would produce a burn, a short interval between initial and subsequent exposures would cause injury but a longer recovery period would be followed by less or no injury, and that the recovery from the initial "latent injury" of a shorter exposure time to a given temperature was more rapid than that from a longer exposure time. These were mild contact burns which, at their severest, produced irreversible epidermal necrosis, and at their mildest caused a slight vascular reaction. The problem of dermal injury was not investigated.

This part of the experiment was designed specifically to determine whether or not two exposures to radiant energy, separated by an interval of one minute, would both contribute to the ensuing injury. The answer is that they do, and, as might be expected, this is more readily apparent with the more severe exposures.

The reason for the synergistic effect between two exposures cannot be deduced from this experiment. It could be due to a change in the thermal properties of the skin, to a "latent injury" which would have been reversible had not the second exposure been delivered, or to an increased temperature in the exposed skin. It could be due to a combination of all three factors. If bare porcine skin is exposed to radiant thermal energy of the magnitude used in this experiment an erythema develops after five to ten seconds and persists for at least a few minutes. At the one minute interval used here erythema is fairly prominent. This could well change the effect of the second exposure, but in what manner we do not yet know. The exposed area is not appreciably warmer than the surrounding skin after one minute (with these exposures) but we do not know what temperature change may be present below the surface. Finally, we have no way of knowing the role of "latent injury" in this experiment. It is reasonable to suppose that certain cellular processes are reversibly deranged by the initial exposure. A second exposure might well render this sort of process irreversible.

PART II THE EFFECTS OF SUPERIMPOSING RADIANT THERMAL ENERGY
EXPOSURES AT TIMED INTERVALS FOLLOWING THE INITIAL
EXPOSURE.

INTRODUCTION AND EXPERIMENTAL DESIGN

Since there is a synergistic effect between two radiant thermal energy exposures superimposed at an interval of one minute, the question of the effect of increasing the time between exposures naturally arises. If the synergistic effect is due to heating of the tissue by the initial exposure, a different result might be found at a longer time interval when the tissue temperature has returned toward normal. If the results are due to "latent injury," increasing the time interval might allow for some recovery from this injury. If a change in the thermal properties of the skin has an important role in double exposures, the effects of time might be correlated with a change in these characteristics.

Time intervals between initial and second exposures of one minute, one hour and six hours were selected. If increased tissue temperature is the most important factor, the one minute interval might be expected to reveal results not found at the later times. If latent injury is chiefly responsible for the effect, the results might indicate recovery of the reversibly injured tissue at the longer times. The intervals are also well selected to give an indication of the role of certain thermal characteristics of the skin. For example, after an initial 0.3 sec. exposure to 2.04 cal/cm^2 erythema begins to develop in five to ten seconds and is prominent in one minute. This erythema fades in the next few minutes and is barely noticeable one hour later. However, in four or five hours it reappears and is fairly prominent at the six hour interval. Also, if tissue edema results from the initial exposure, it will be

negligible at one minute, minimal at one hour and greater at six hours.

An exposure time of 0.3 sec. was used throughout this part. The base exposure of 2.04 cal/cm^2 was again used. Exposures of 1.66 cal/cm^2 and 2.52 cal/cm^2 were also carried over from Part I, and a new exposure of 5.86 cal/cm^2 (irradiance of 19.53 cal/cm^2) was added. This more severe exposure was selected because a possible protective effect from initial exposure might be found here when it had not been apparent with subsequent mild exposures. Since this more severe exposure could be expected to result in a deeper dermal damage than did the mild ones, more information could also be gained on the effects of double exposure on this tissue.

METHODS

The treatment block was designed to contain both single and double burns. The single burn treatments consisted of each exposure level used, and the double burn treatments were composed of the base exposure, 2.04 cal/cm^2 , plus exposures of 1.66 cal/cm^2 , 2.52 cal/cm^2 and 5.86 cal/cm^2 . In each instance the second exposure was given at an interval of one minute, one hour and six hours. The treatment block contained 13 separate treatments, four single burns and nine double burns. The treatments were randomly assigned to exposure areas on the sides of the animals and the block was replicated 12 times, making a total of 156 burns. All burns were biopsied.

RESULTS

The results obtained by surface evaluation of the burns are shown in Table X. For convenience they are grouped according to exposure levels, and the base exposure is repeated with each group. The percentage of burns falling under each classification is given in Table XI.

TABLE X

THE EFFECT OF THE TIME INTERVAL BETWEEN SUPERIMPOSED RADIANT THERMAL
ENERGY EXPOSURES ON THE SURFACE APPEARANCE OF THE BURNS PRODUCED.

Q ₁ (cal/cm ²)	Time Between Exposures	Q ₂ (cal/cm ²)	0	1+		2+			3+			4+
				Mild	Sev	Mild	Mod	Sev	Mild	Mod	Sev	
1.66	1 Min. 1 Hr. 6 Hrs.	1.66		10	1	1						
2.04				7	4	1						
2.04				2	7	2	1					
2.04				4	5	3						
2.04				6	5	1						
2.52				6	5	1						
2.04	1 Min. 1 Hr. 6 Hrs.	2.52		7	4	1						
2.04					6	4	2					
2.04					2	7	3					
2.04					6	5	1					
5.86							1		6	1		4
2.04				7	4	1						
2.04	1 Min. 1 Hr. 6 Hrs.	5.86						1	6	2	1	2
2.04									6	3		3
2.04									4	8		

TABLE XI

Q_1 (cal/cm ²)	Time Interval Between Exposures	Q_2 (cal/cm ²)	1+	2+	3+	4+
1.66			92%	8%		
2.04			92%	8%		
2.04	1 Min.	1.66	75%	25%		
2.04	1 Hr.	1.66	75%	25%		
2.04	6 Hrs.	1.66	92%	8%		
2.52			92%	8%		
2.04			92%	8%		
2.04	1 Min.	2.52	50%	50%		
2.04	1 Hr.	2.52	17%	83%		
2.04	6 Hrs.	2.52	50%	50%		
5.86				8%	58%	33%
2.04			92%	8%		
2.04	1 Min.	5.86		8%	75%	17%
2.04	1 Hr.	5.86		0	75%	25%
2.04	6 Hrs.	5.86	0	0	100%	0

It is again noted that exposures of 1.66 cal/cm^2 and 2.52 cal/cm^2 , when superimposed upon a 2.04 cal/cm^2 at one minute, contribute to the injury sustained. There is little difference between one minute and one hour with the $2.04 \text{ cal/cm}^2 + 1.66 \text{ cal/cm}^2$ burn, but at six hours the result is essentially the same as that of the base exposure alone.

When the $2.04 \text{ cal/cm}^2 + 2.52 \text{ cal/cm}^2$ is considered, it is seen that surface evaluation of the burns suggests that the synergistic effect of the exposures is more efficient at one hour than it is at one minute, and is as great at six hours as it is at one minute.

Surface evaluation alone suggests that the effect of an initial exposure of 2.04 cal/cm^2 followed by an exposure of 5.86 cal/cm^2 is little different from that of a single exposure of 5.86 cal/cm^2 . Since no 4+ burns occur from the double exposure at the six hour interval, a protective effect from the first exposure might even be suspected.

Table XII presents the data on the microscopic pathology. The grading system chosen shows no difference between the effects of the base exposure of 2.04 cal/cm^2 alone and with the superimposition of an exposure of 1.66 cal/cm^2 at any of the three times. However, adding an exposure of 2.52 cal/cm^2 to the base exposure leads to a greater injury than is inflicted by either exposure alone. Although surface grading showed a greater difference between single and double exposures at the one hour interval, this result is not confirmed by the biopsies. There is no practical difference in the results obtained at any of the three time intervals between exposures, but the little difference shown indicates less damage at the one hour interval than at one minute and six hours. A comparison between exposures of 5.86 cal/cm^2 alone and in combination with the base exposure certainly shows no indication of a

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TABLE XII

THE MICROSCOPIC PATHOLOGY OF SINGLE AND DOUBLE BURNS. ALL EXPOSURES ARE 0.3 SEC.

Q ₁ (cal/cm ²)	Time Between Burns	Q ₂ (cal/cm ²)	Dermal-epidermal Separation			Dermal Damage						
			None	Partial	Complete	None	Less than 0.1 mm.	0.1- 0.2 mm.	0.2- 0.3 mm.	0.3- 0.4 mm.	0.4- 0.5 mm.	0.5- 0.6 mm.
1.66	1 Min. 1 Hr. 6 Hrs.	1.66	10	2		12						
2.04			6	4	2	10	2					
2.04			5	5	2	11	1					
2.04			7	3	2	11	1					
2.04			6	4	2	11	1					
2.52	1 Min. 1 Hr. 6 Hrs.	2.52	5	4	3	12						
2.04			6	4	2	10	2					
2.04			0	0	12	7	5					
2.04			0	3	9	8	3	1				
2.04			0	0	12	4	6	2				
5.86	1 Min. 1 Hr. 6 Hrs.	5.86	0	0	12	0	0	5	4	2	1	0
2.04			6	4	2	10	2	0	0	0	0	0
2.04			0	0	12	0	0	0	5	3	3	1
2.04			0	0	12	0	0	1	6	4	1	0
2.04			0	0	12	0	0	3	2	5	2	0

protective effect from the initial injury, but rather indicates that the initial exposure does add to the damage produced. There are only slight differences between the results at the three time intervals, the most noticeable one being that injury seems a little more severe at the one minute interval.

DISCUSSION

This part of the experiment was designed primarily to determine the effects of varying the time interval between initial and subsequent exposures to radiant thermal energy. A secondary consideration was the possibility that a mild burn could protect the skin from a subsequent, more injurious exposure.

The role of the time interval between two superimposed exposures can best be evaluated by considering the data on surface grading and on microscopic pathology together. With the mildest double exposure used, the chief differences between single and double exposures was in the severity of the vascular reaction. A single exposure of 2.04 cal/cm^2 produced only five of twelve burns which were more severe than an erythema which blanched completely with pressure. When an exposure of 1.66 cal/cm^2 was added to this at one minute, ten of the twelve burns were more severe than this blanching erythema, and at one hour, eight of the twelve burns were more severe. At six hours, however, there is virtually no difference between the reaction of the double burns and the base exposure alone. Since the difference noted is principally one of vascular reaction, it is not apparent in the data on the biopsies.

When an exposure of 2.52 cal/cm^2 is added to one of 2.04 cal/cm^2 , at any of the three time intervals, a greater injury occurs than results from

either exposure alone. This is most readily seen in the data on dermal-epidermal separation (Table XII). Surface evaluation by itself (Tables X and XI) suggests a greater injury at one hour than at one minute or six hours, but this finding is not confirmed by the biopsies.

How long the base exposure of 2.04 cal/cm^2 contributes to injury from a subsequent exposure seems to be a relative matter. Its effect is very real as long as one hour after initial injury with all three exposures evaluated. It certainly has an effect at six hours when the second dose is 2.52 cal/cm^2 and, at that time, it may contribute something to the damage of a second exposure of 5.86 cal/cm^2 . Its effect, however, seems negligible at six hours when a 1.66 cal/cm^2 dose is superimposed.

The reasons for the synergistic action between two exposures can again be considered. It seems unlikely that at one hour or six hours the temperature of the dermis will have remained significantly elevated from the initial exposure. Presumably a vascular reaction could elevate the temperature slightly, but it should be remembered that at the one hour interval there is considerably less erythema from a 2.04 cal/cm^2 exposure than there is at one minute or at six hours.

Of particular interest is the effect of the base exposure on the results from a subsequent exposure to 5.86 cal/cm^2 (Table XII). At one minute and one hour the depth of dermal damage is definitely greater following the double exposure than it is after a single exposure to 5.86 cal/cm^2 , and there is a similar, though not as definite a tendency at six hours. It is unlikely that increased tissue temperature from the initial exposure causes this result. "Latent injury" could be responsible, but if it is we must assume that the base exposure produces "latent injury" in dermal tissues well below the level at which it causes demonstrable injury. Only two of the twelve base exposures

caused any dermal damage, and in both cases injury extends less than 0.1 mm. in depth. Exposure to 5.86 cal/cm^2 in no instance caused injury less than 0.1 mm. in depth, and the double exposure at one minute caused no injury less than 0.2 mm. in depth. This same general shift toward a greater depth of damage is seen at one hour. It is most tempting to ascribe this finding to a change in the thermal properties of the skin produced by the base exposure. However, if this is the reason, one wonders why there is a return toward the single exposure effect at six hours. It seems just as reasonable to assume deep "latent injury" as it is to suggest that differences in reflectance or diathermancy change toward normal from one minute to six hours.

There is still another possibility. The synergistic effect of two superimposed burns need not be due to the same factor at one minute as it is at one hour or six hours. Latent injury may play a role which decreases with the length of the recovery period. Heating the tissue by the base exposure may well contribute to injury at one minute but not at one hour or six hours. Finally, the thermal characteristics of skin subjected to the base exposure may change with time, and this change might be related to erythema which is prominent at one minute and six hours but not at one hour or to edema formation. The final result may be the product of all these factors playing a varyingly prominent role depending on the time between exposures.

The only suggestion of a protective effect is found in the surface grading data for the most severe double exposure (Table X and XI). One-third of the areas exposed to 5.86 cal/cm^2 responded with a 4+ burn. At the six hour interval, no double burn exceeded the 3+ level. The 4+ burn is a surface phenomenon, a steam bleb. Apparently the base exposure changes the more superficial layers of skin in such a way that a steam bleb is

less likely to occur. The biopsy data (Table XII) certainly do not indicate any protective factor associated with an initial, mild exposure.

It may be said in summary that the effect of two superimposed exposures is dependent on the time interval between exposures. The synergistic effect is probably due to three different factors, and the role of each of these varies with the time interval.

PART III THE EFFECTS OF SUPERIMPOSING TWO SEVERE EXPOSURES
TO RADIANT THERMAL ENERGY.

INTRODUCTION AND EXPERIMENTAL DESIGN

The first two parts of this paper revealed a synergistic effect of superimposed radiant energy exposures. It was shown that an initial exposure may, in some circumstances, contribute to the final injury when there is as long as six hours between exposures, and the initial, mild exposure does not afford protection against a subsequent, severe exposure. However, if protection against radiant thermal energy ever occurs as a result of an initial exposure, this protection must come from a change in the thermal characteristics of the skin. It might therefore be expected that a more severe initial exposure, that is one which would produce a more profound change in the epidermis and superficial dermis or produce more edema, would show an effect different from the milder initial exposure.

Some differences in the effects of superimposed burns would possibly occur as a result of altering the exposure time. A true flash burn, one which occurs in one second or less, tends to produce severe damage to the most superficial layers. A fairly sharp cut-off between damaged and non-damaged dermis is characteristic. Longer exposures penetrate to deeper layers and there is a mixture of damaged and normal tissue in the depths of the injured zone. By an arrangement of double exposures of both the flash burn type and moderate duration type it might be possible to learn something about the penetration of dermis by radiant energy and how this may be altered, either for better or worse.

Two initial exposures were used: 1) an irradiance of 19.53 cal/cm²/sec. for 0.3 seconds (5.86 cal/cm²) and 2) an irradiance of 3.62 cal/cm²/sec. for 3.0 sec. (10.86 cal/cm²). From past experience it was thought that these two exposures would usually produce a 3+ burn. To be superimposed on these, two, more intense irradiances were chosen: 1) 29.77 cal/cm²/sec. for 0.3 sec. (8.93 cal/cm²) and 2) 4.97 cal/cm²/sec. for 3.0 sec. (14.91 cal/cm²). These exposures should more often than not produce a burn greater than the 3+ level. Treatments consisted of each exposure level used as a single dose and of combinations of both second exposures with each of the initial base exposures. One and five hour intervals were maintained between double exposures, it being reasoned that edema was likely to be more prominent at five hours than at one hour. A treatment block therefore consisted of four single exposures and eight double exposures. The treatments were assigned randomly to exposure areas on the sides of the animals and twelve replications were carried out. All burns were biopsied.

RESULTS

Table XIII presents the results obtained by surface grading these burns. All combinations of double exposures raise the level of the surface grade, and there is little difference between the one hour and five hour intervals.

The results obtained by tabulating the microscopic pathology of these burns require a somewhat more elaborate explanation than has been necessary in the previous sections. Table XIV lists the depth of damage produced by the single and double exposures. This reading can, however, be very misleading. Mild flash burns, such as those used in the first two parts of this

TABLE XIII

SURFACE GRADING OF BURNS PRODUCED BY SINGLE AND DOUBLE EXPOSURES.

Q ₁ (cal/cm ²)	Exposure Time (sec)	Time Between Burns	Q ₂ (cal/cm ²)	Exposure Time ₂	3+			4+			5+
					Mild	Mod	Sev	Mild	Mod	Sev	
*5.86	0.3				3	4	0	4	0	0	
8.93	0.3				1	1	0	2	1	5	2
14.91	3.0				0	2	1	0	0	6	3
5.86	0.3	1 Hr.	8.93	0.3	0	0	0	3	4	4	1
5.86	0.3	5 Hrs.	8.93	0.3	0	0	1	0	2	2	7
5.86	0.3	1 Hr.	14.91	3.0	0	0	1	0	0	0	11
*5.86	0.3	5 Hrs.	14.91	3.0	0	0	0	0	0	0	13
10.86	3.0				0	1	7	1	1	0	2
14.91	3.0				0	2	1	0	0	6	3
8.93	0.3				1	1	0	2	1	5	2
10.86	3.0	1 Hr.	8.93	0.3	0	0	2	1	3	1	5
10.86	3.0	5 Hrs.	8.93	0.3	0	0	0	3	3	2	4
10.86	3.0	1 Hr.	14.91	3.0	0	0	0	0	3	0	9
10.86	3.0	5 Hrs.	14.91	3.0	0	0	1	0	0	1	10

*A mistake in exposure assignment accounts for these figures.

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TABLE XIV

MICROSCOPIC PATHOLOGY OF SEVERE DOUBLE AND SINGLE BURNS.

Q ₁ (cal/cm ²)	Exposure Time	Time Between Burns	Q ₂ (cal/cm ²)	Exposure Time	Depth of Damage in Millimeters									
					0.2- 0.4	0.4- 0.6	0.6- 0.8	0.8- 1.0	1.0- 1.2	1.2- 1.4	1.4- 1.6	1.6- 1.8	1.8- 2.0	
5.86	0.3				8	2								
8.93	0.3				5	5	2							
14.91	3.0						3	0	2	2	3			1
5.86	0.3	1 Hr.	8.93	0.3	3	3	5							
5.86	0.3	5 Hrs.	8.93	0.3	4	4	3	0	1					
5.86	0.3	1 Hr.	14.91	3.0				2	2	4	3	0		1
5.86	0.3	5 Hrs.	14.91	3.0			1	2	1	4	1	4		
10.86	3.0				2	0	3	0	3	3	1			
14.91	3.0						3	0	2	2	3			
8.93	0.3				5	5	2							
10.86	3.0	1 Hr.	8.93	0.3	0	1	3	1	2	2	3			
10.86	3.0	5 Hrs.	8.93	0.3	1	2	4	1	2	2				
10.86	3.0	1 Hr.	14.91	3.0			1	2	0	0	5	1		2
10.86	3.0	5 Hrs.	14.91	3.0			1	1	1	3	3	1		2

paper, when they produce a dermal damage at all do not greatly distort the tissues. The structures are recognizable, the dermis is neither shrivelled nor greatly edematous, and one burn can be compared with another on the basis of depth of dermal damaged. As the intensity of the flash burn increases there is an increased tendency for the dermis to shrink in thickness and to lose its structure completely. This type of burn might destroy the full thickness of the dermis, yet the measureable depth of damaged tissue could be no more than one-third the thickness of normal dermis. Burns produced by the 3.0 sec. exposure time may exhibit a variable amount of edema, and the depth of dermal damage here will depend in some measure on the presence of fluid in the interstitial spaces.

It is of practical importance to know whether or not the burn extends through the full thickness of the dermis and how the burn affects the deep hair follicles. Whatever the measureable depth of damaged dermis may be, the burn is a severe one if the whole dermis and the deep hair follicles have been injured. This information has, therefore, been collected and is presented in Table XV. This table also shows certain other characteristics of the burns which require a word of explanation. Intermediate dermal damage refers to the presence of some dermal damage through the full thickness of the dermis but with an intermingling of normal and damaged tissue in the deeper layers. Full-thickness dermal damage means a severe degree of damage of the whole dermis. Shriveled dermis refers to the phenomenon described above; the injured portion of the dermis is compressed to a thickness considerably less than normal. Deep hair follicle damage describes an injury to the hair follicles in the subcutaneous tissue just deep to the dermis. Unusual dermal injury is mentioned only because of its frequent occurrence

with the double exposure; it describes a severe injury of the upper strata of the dermis. In such areas the dermis has completely lost its structure and the tissue has an almost ground glass appearance.

Table XV may now be examined for evidence of both a synergistic effect between double exposures and for a possible protective effect from the initial exposure. The double exposure of 5.86 cal/cm^2 and 8.93 cal/cm^2 , both delivered in 0.3 sec., may occasionally produce a more severe dermal damage than does the heavier exposure alone. However, the double exposure has no greater effect, and may have a milder effect, on the deep hair follicles than does the single exposure. There is less tendency for the more severe exposure to produce a shriveled dermis when it follows an initial, milder exposure than when it is delivered alone. This could possibly represent "protection" by the initial exposure. Although there are, at times, such striking differences in the pathological pictures of single and double burns, the "protective effect" does not seem to be dependable since at the six hour interval deep hair follicle damage and even full-thickness dermal damage are prominent if not the rule.

An initial exposure of 5.86 cal/cm^2 in 0.3 sec. may offer a small measure of protection to the deeper layers of the dermis from a subsequent 14.91 cal/cm^2 exposure in 3.0 sec., but it does not prevent deep hair follicle damage. The upper layers of the dermis often show "unusual dermal injury" when the interval between double exposures is only one hour, but at the six hour interval this is less often seen.

An initial exposure of 10.86 cal/cm^2 in 3.0 sec. may also change the response to an exposure of 8.93 cal/cm^2 in 0.3 sec. With the double exposure, the dermis is less likely to be shriveled, but the upper layers of dermis

TABLE XV

CHARACTERISTICS OF THE MICROSCOPIC PATHOLOGY OF SEVERE SINGLE AND DOUBLE BURNS.

Q_1 (cal/cm ²)	Exposure Time (sec)	Interval Between Exposures	Q_2 (cal/cm ²)	Exposure Time (sec)	Partial Dermal Damage	Inter- mediate Dermal Damage	Full Thickness Dermal Damage	Shrivel- ed Dermis	Deep Hair Follicle Damage	Unusual Dermal Injury
5.86	0.3	1 Hr. 5 Hrs.	8.93	0.3	12	0	0	3	2	0
8.93	0.3				12	0	0	8	5	0
5.86	0.3				11	0	1	3	1	0
5.86	0.3				9	0	3	4	4	0
5.86	0.3	1 Hr. 5 Hrs.	14.91	3.0	12	0	0	3	2	0
14.91	3.0				0	0	12	5	12	2
5.86	0.3				3	1	8	4	12	6
5.86	0.3				1	1	10	1	12	1
8.93	0.3	1 Hr. 5 Hrs.	8.93	0.3	12	0	0	8	5	0
10.86	3.0				4	5	3	2	12	0
10.86	3.0				3	0	9	4	11	4
10.86	3.0				4	0	8	2	11	2
10.86	3.0	1 Hr. 5 Hrs.	14.91	3.0	4	5	3	2	12	0
14.91	3.0				0	0	12	5	12	2
10.86	3.0				0	0	12	2	12	1
10.86	3.0				0	0	12	2	12	1

occasionally lose their structure altogether. The full thickness of the dermis is more likely to be damaged with the double exposure than with either single exposure.

The double exposure of 10.86 cal/cm^2 and 14.91 cal/cm^2 , both delivered in 3.0 sec., results in a very deep burn and there is no evidence of protection from the initial exposure. Shriveling of the dermis follows the double exposure less often than it does the more severe, single exposure.

DISCUSSION

Certain interesting effects are obtained by superimposing two severe radiant energy thermal burns. It is seen that the initial exposure may at times modify greatly the effect of the second exposure, and the double exposure does not always result in the more severe burn. In general it may be said that if the initial exposure has not already completely destroyed the superficial dermal structures, the second exposure will increase the severity of damage here. The effect seems more profound at the one hour interval than at five hours. An initial exposure may so change the epidermis and superficial dermis that a severe second exposure does not penetrate so deeply or bring about such a profound change in the dermis as it might in normal skin. This mechanism could be termed protection, but it is emphasized that the initial injury is itself a severe one and protection by no means invariably results from it.

The burns produced in 0.3 sec. for the most part show a fairly distinct line of demarcation between damaged and normal dermis. The tissue is either severely injured or normal, and there is very little intermingling of the two. Some 3.0 sec. exposures share this characteristic with the flash burns, but most of them show the effects of longer application of energy, a

shading between injured and normal tissue with a zone where the two are found together.

Some double exposures result in deeper dermal damage than do the single exposures alone. This is most easily seen in the third group (10.86 cal/cm² in 3.0 sec. followed by 8.96 cal/cm² in 0.3 sec.) in Table XV and is also apparent in other groups in Table XIV where damage to the subcutaneous tissue is a factor in the measurements. If this finding is due to a change in the absorption or transmission of energy brought about by the initial exposure, it would appear that this change in the thermal properties of the skin at times leads to more severe injury and at times to less injury. It is, perhaps, more reasonable to ascribe the synergistic effect to latent injury of deep tissues.

GENERAL SUMMARY AND CONCLUSIONS

1. Some effects on bare porcine skin of superimposing two exposures to radiant thermal energy have been investigated.
2. The effects of two such exposures are synergistic but not additive.
3. The synergistic effect is still apparent, in most instances, at least six hours after the initial exposure. With milder exposures, separation of the two exposures by intervals of one minute or one hour leads to a more pronounced effect than does a six hour interval.
4. Mild exposures do not protect the dermis from a subsequent more severe exposure. A moderately severe burn, however, at times seems to afford some protection against a subsequent very severe injury. This protection is not at all constant.

5. The synergistic action of superimposed exposures is probably due to three factors associated with the initial exposure: 1) raising the temperature of the tissue, 2) the production of latent injury, i.e., injury which is reversible if a subsequent insult is not forthcoming, and 3) a change in the absorption or transmission of energy by the dermis. The role of any one factor depends on the interval between exposures and on the severity of the initial exposure.

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