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To: Department of Defense Agencies on Distribution List for Report

Subj: U. S. Naval Radiological Defense Laboratory report; forwarding of

Encl: (1) U. S. Naval Radiological Defense Laboratory report entitled "Thermal, and Combined Thermal and Ionizing Radiation, Effects on Biological Systems -- 1 July to 31 December 1954. (Semi-annual Progress Report for Armed Forces Special Weapons Project)."

1. The subject program report covers the period 1 July to 31 December 1954.

2. This letter is unclassified when separated from enclosure (1)

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THERMAL, AND COMBINED THERMAL AND IONIZING RADIATION, EFFECTS ON BIOLOGICAL SYSTEMS -- 1 JULY TO 31 DECEMBER 1954.

(Semi-annual Progress Report for Armed Forces Special Weapons Project)

E. L. Alpen

AFSWP-735

Thermal Injury Branch
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Scientific Director
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U. S. NAVAL RADIOLOGICAL DEFENSE LABORATORY
San Francisco 24, California

31 December 1954

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PRINCIPAL INVESTIGATORS

During this reporting period the principal investigators were Edward L. Alpen, A. Kennon Davis, Elly M. Jacobsen, D. M. Jones and William Lee.

COLLABORATORS

Working with the principal investigators were John A. Alexander, HM1, Basil Scofidio, HM1, and Charles Haggerty, HM1 (to 19 October 1954).

OBJECTIVES

On 1 February 1954 a new program proposal oriented towards the local effects of high intensity thermal radiation was submitted and approved by AFSWP. The phases of this program are as follows:

Phase 1. Basic Considerations on the Interaction of Fabrics and High Intensity Radiant Energy with Reference to Effects on Skin.

The primary objective of this task is the evaluation of all parameters having an effect on the protective influence provided by fabric combinations against the effects of high intensity radiant thermal energy.

Phase 2. Studies on the Relationship of Severity and Nature of Burn Damage and Certain Parameters of Biological Effectiveness.

As a natural adjunct to Phase 1 it becomes imperative to ascertain the biological effectiveness of certain types of burn lesions. Under certain conditions of exposure to radiant energy through fabric combinations either pure radiant energy burns, flame burns or contact burns will arise. The objective of this task is the evaluation of relationships between these various types of lesions and some biological endpoint should be

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evaluated. The two subtasks of this phase as presently outlined are:

a) study of mortality and body area -- body size relationship, and

b) study of acute red blood cell destruction as a function of burn intensity and type.

Phase 3. Studies of the Effects of the Local Burn Lesion on Erythrocyte Production and Survival.

The objective of this task is the investigation of the relationship between erythrocyte production in the burned animal and the time course of inflammatory processes in the local lesion.

1. PHASE 1. PROGRESS

1.1 Fabric Studies. Critical Energies for Skin Behind Standard 9 oz. Sateen.

The Quartermaster Corp of the Army has made available to this Laboratory a series of fabrics in which the reflectivity is varied by incorporation of graded amounts of carbon black in a carboxymethyl cellulose binder. The critical energies for these fabrics have been measured at 1 second square wave exposures at contact and at spacings of 2 mm or 5 mm. The results of these measurements are given in Table 1.

It has not been possible with the peak irradiance of the Mitchell source to produce burns at 5 mm spacing except where long exposures are used which produce destruction of the fabric. The 60 cal/cm^2 exposure at 5 mm spacing in Table 1 represents a 2.75 sec full beam exposure.

1.2 Temperature Measurements.

A thermocouple for intradermal use has been developed in this Laboratory of 0.8 mil constantan upon which a silver junction has been plated. The maximum diameter of the couple is 1.2 mil over the region of silver plating. Measurements have been made with these couples in the fabric skin systems and on bare fabric. Figures 1, 2, and 3 are typical time temperature histories for bare skin, white fabric in contact with skin, and dark grey fabric in contact with skin. It is evident that in the case of white fabric the time-temperature history of the subcutaneous couple at a depth of 200 microns is quite similar to that of the same couple on bare skin. The peak temperature attained and the duration of hyperthermia are quite similar. However, in the case of the dark grey fabric the subcutaneous temperature history is quite different. The rise is slow and prolonged with the three couples attaining equal temperatures in about 10 seconds.

1.3 Spectral Measurements.

In an effort to explain certain discrepancies between critical energies for skin determined on various radiant energy sources in this Laboratory and to elucidate the effect of fabrics in their role as selective spectral filters a study has been pursued on the critical energy for burn production with various filters. Work has been completed with a series of four filters on normal and blackened rat skin. These data are presented in Figure 4. These filters are: Filter A, 0.4 - 0.6 μ, Filter B, 0.6 - 0.9 μ, Filter C, 0.8 - 1.9 + μ (peak at 1.1 μ), Filter D, 1.0 - 2.0 + μ

(peak at 1.5 μ). The critical energies for all but Band "B" are in the range 3.8 - 4.5 cal/cm^2 for a minimal white burn at 2.0 sec exposure. The B filter has a critical energy of 28 cal for a 6 second exposure. Shorter exposures at full beam irradiance failed to produce a burn. Reciprocity failure at this level of skin damage would, however, not alter this figure by more than 10 - 20% in the downward direction for the 2.0 sec burn.

On blackened skin the critical energy is, as would be predicted, independent of wave length. The value for production of a minimal white burn is 2.4 cal/cm^2.

The conclusions from these data are that the white fabric acts as a neutral transmission filter without its own temperature being remarkably elevated, and the black fabric acts as a heat transferring medium without direct transmission of an appreciable proportion of radiant energy. From Figure 3 it can be seen that a burn behind black fabric is essentially equivalent to a contact type burn.

1.4 Human Studies.

A comparison has been made of the critical energy for first degree burn production on the human forearm at simulated weapon yields of 100 kt and 10 mt. These have been found to be 4 cal/cm^2 and 6 cal/cm^2, respectively. The data is as yet incomplete but these figures are considered to be correct within $\pm$ 0.5 cal.

1.5 Pulse Shape Studies.

Studies on the critical energy for rat skin as a function of weapon

yield over the range 20 kt to 40 mt have been completed and the report published. Studies are now in progress on the effect of "cutting of the tail" of the pulse, or in other words simulating evasive action. Studies at the 250 kt yield have been completed. The data are presented in Table 2. It can be seen from this table that even a three second cutoff succeeds in making a small difference in effective radius for production of a minimal white burn and that a 1.0 second cutoff makes an appreciable difference. From column two of this table the efficiency of the three pulse shapes can be directly compared.

The parameters used for the nuclear pulse are those presented in Streets (AFSWP 503). Ten tp is taken as a nominal full pulse even though only 80% of the energy is delivered in this interval. Correction for this factor must be made in extrapolation to true pulses.

It must be recognized that certain assumptions are made in these studies which do not hold for the field condition. Two of the most important of these are: a) the spectral distribution of energy does not change with time, and b) the energy reaching the individual is not appreciably scattered.

2. PHASE 2. PROGRESS

2.1 Acute Red Blood Cell Destruction.

Studies on acute red blood cell destruction are nearly completed at this time. The data are presented in Figures 5 to 8.

The destruction measured for 12 or 16 cal/cm^2 given in 1 sec are 20

[redacted]

and 24% respectively at 24 hours after exposure. Destruction is apparently increased by the shortest exposure time (0.5 sec) but unaffected by increasing to 2.0 sec. Over the range of area involvement studied, 15 to 22%, no significant differences are detected. It is obvious from the data that heat injured cells are not completely removed in 4 hours for in nearly every measurement destruction at 24 hours is increased.

It has been demonstrated that the early anomalous results obtained in this Laboratory with $Cr^{51}O_4$ labeled erythrocytes were because of the interference of ether anesthesia with CrO_4 labeling. Fe^{59} labeled cells are not subject to this shortcoming.

The report on this phase is in preparation.

2.2 Severity-Mortality Studies.

Work temporarily suspended on this phase.

2.3 Area-Mortality Studies.

Work temporarily suspended on this phase.

3. PHASE 3. PROGRESS

3.1 Iron Utilization and Survival of Autologous Cells.

Studies on rats are now complete and have been reported in USNRDL unclassified report 433. This same data has appeared in the January 1955 issue of the Journal of Clinical Investigation.

The studies on dogs have progressed to the point that preliminary statements may now be made. It is apparent that a rapid hemolytic process exists in the dog quite similar to that seen in the rat. Figure 9

[redacted]

[redacted]

indicates the apparent uptake of radioiron into the erythrocytes of burned dogs. Because control uptakes are done before burning, there is a measurable amount of radioactivity in the blood, and therefore if destruction is more rapid than formation of cells it is possible to obtain "negative" or less than zero uptakes. This is the case in several instances in 15% third degree burns on our dogs. Accompanying these hemolytic phenomena is a depressed serum iron turnover in the early phase followed by increased serum iron turnover in the post infection stage. The tissues of these animals show evidence of active extramedullary hematopoiesis.

3.2 Survival of Transfused Red Cells.

This study is complete and the report is in preparation. No changes in the data presented in the last semi-annual progress report are required.

3.3 Plasma Hematopoietic Factor Studies.

In the course of the studies on the burn anemia in the rat, interest was stimulated in the factors controlling blood volume. The work of Borsook et al on the hematopoietic factor seen in the serum of anemic rabbits was used as a point of departure. It has been possible to prepare a plasma fraction with erythropoietic stimulating activity. During this reporting period all effort has been on preparation of active plasma fractions by both the hemorrhagic method and the method used by the original authors, i.e. injection of phenyl hydrazine. In our hands it has been possible to prepare active plasma fractions from rabbits made anemic with phenyl hydrazine, but in every case where rabbits were made equally anemic by bleeding no hematopoietic activity was found in the plasma. Certain observations

[redacted]

have been made that provide partial explanation for this phenomenon. In rabbits bled on successive days until the hematocrits were equal to the paired animal made anemic by phenyl hydrazine, there is, nevertheless, a lower oxygen carrying capacity in the phenyl hydrazine treated animals. The latter have methemoglobin concentrations amounting to 20% of the total blood pigment, while in the bled animals the methemoglobin concentration is practically zero. In addition, it has been observed that active preparations are seen in phenyl hydrazine treated rabbits only when accompanied by a cirrhotic liver. The conclusion to be drawn is that the factor is produced only when the effective hematocrit is below about 12 to 15% and when the liver is not capable of rapid destruction of the factor.

4. PLANS FOR NEXT PERIOD

4.1 Phase 1.

4.1.1 Fabric Studies.

As soon as the 4 oz white underwear is made available it is planned to measure critical energy as a function of weapon yield for the 4 oz white -- 9 oz OG 107 combination in contact and with 2 mm spacing. In addition, studies on effect of fabric water content are planned for the near future.

4.1.2 Temperature Measurements.

These studies will continue as outlined in the progress section. In addition, it is planned to make some exploratory studies in the comparative temperature response of skin and the NHL simulant.

4.1.3 Spectral Measurements. A new expanded series of filters are available which will be used in the same fashion as the earlier group. These filters are as follows:

Maximum λ	Maximum Irradiance
0.4 μ	5.0 cal/cm^2/sec
0.6 μ	5.3 cal/cm^2/sec
0.7 μ	7.8 cal/cm^2/sec
0.9 μ	4.7 cal/cm^2/sec
1.2 μ	7.3 cal/cm^2/sec
1.7 μ	2.5 cal/cm^2/sec.

In addition another longer wavelength filter of coated AgCl is on order from Harshaw Chemical Company.

4.1.4 Human Studies.

An analysis of critical energy for human skin as a function of yield from 30 kt to 10 mt is planned. It is not possible to go to lower yields The end points used will be 1° and 2° burns on the volar surface of the forearm.

4.1.5 Pulse Shape Studies.

These will continue as outlined in the progress section covering the range 250 kt to 10 mt.

4.2 Phase 2.

4.2.1 Acute Red Blood Cell Destruction.

It is planned to terminate this phase and issue a report in the next reporting period.

[redacted]

4.2.2 Severity-Mortality Studies.

This study will be activated again during the coming reporting period.

4.2.3 Area-Mortality Studies.

This study will be activated again during the coming reporting period.

4.3 Phase 3.

4.3.1 Iron Utilization and Survival of Autologous Cells.

Studies will be continued in dogs with emphasis on the role of infection in depressing red cell production.

4.3.2 Survival of Transfused Red Cells.

The report on this phase will be complete shortly.

4.3.3 Plasma Hematopoietic Factor Studies.

Studies aimed at preparation of an active substance will continue. When the plasma factor is obtained in high enough potency it will be applied in burned rats to measure its effect on iron metabolism in the burned animal.

5. REPORTS AND PUBLICATIONS DURING THIS REPORTING PERIOD.

1. E. L. Alpen, J. A. Alexander and A. K. Davis. Combined Effects of Total Body X-Irradiation and Radiant Energy Thermal Burns on the Osmotic and Mechanical Fragility of the Erythrocyte. Am. J. Physiol. (in press).

2. W. M. Davis, A. K. Davis, W. Lee and E. L. Alpen. The Combined Effects of Thermal Burns and Whole-Body X Irradiation. III. Study of Blood

[redacted]

Coagulation. Annals of Surgery (in press).

3. William M. Davis, Edward L. Alpen and A. K. Davis. Studies of Radio-iron Utilization and Erythrocyte Life Span in Rats Following Thermal Injury. J. Clin. Invest. 34, 67, 1955.

4. W. Lee, A. K. Davis, C. Entenman and G. E. Sheline. Phospholipide Changes in Rat Skin after Exposure to Radiant Thermal Energy. Arch. of Biochem. and Biophysics (in press).

5. A. K. Davis, E. L. Alpen and G. E. Sheline. The Combined Effects of Thermal Burns and Whole-Body X Irradiation. II. Anemia. Ann. Surg. 140, 726, 1954.

6. William Mabon Davis, Janette D. Bigelow and Edward L. Alpen. Changes in Red Cell Volume and Osmotic Fragility of Erythrocytes in the Rat Following Acute Blood Loss. Am. J. Physiol. 178, 17, 1954.

7. Edward L. Alpen and Glenn E. Sheline. The Combined Effects of Thermal Burns and Whole Body X Irradiation on Survival Time and Mortality. Ann. Surg. 140, 113, 1954.

8. P. R. Kuhl, G. E. Sheline and E. L. Alpen. Blister Formation and Tissue Temperature in Radiant Energy and Contact Burns. Am. J. Path. 30, 695, 1954.

[redacted]

TABLE 1

FABRIC CRITICAL ENERGY FOR MINIMAL WHITE BURN PRODUCTION (1 SECOND EXPOSURE)
Mitchell Carbon Arc

Fabric (9 oz Sateen)	Critical Energy for Minimal White (cal/cm^2)		
	Contact	2 mm	5 mm
Bleached	16.5	21.5	Flaming with severe skin lesion at 60 cal/cm^2
Light Gray	10.3	----	----
Medium Gray	5.6	----	----
Dark Gray	6.2	----	Flaming with severe skin lesion at 11.0 cal/cm^2

[redacted]

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TABLE 2

EFFECT OF PULSE CUTOFF ON EFFECTIVENESS FOR BURN PRODUCTION ("EVASION")

Time of Cutoff (sec.)	Q for min. white burn (cal/cm^2)	Ratio $\frac{Q_p}{Q_{co}}$	Q_p	D (miles) (vis. = .98)
none	6.9	1.0	6.9	5.6
3.0	6.7	.89	7.6	5.4
1.0	5.8	.57	10.2	4.7

Q_p = total nuclear pulse energy

Q_{co} = total energy delivered up to cutoff point

D = critical energy radius for minimum white burn

$\frac{Q_p}{Q_{co}}$ = fraction of total energy in pulse to time of cutoff

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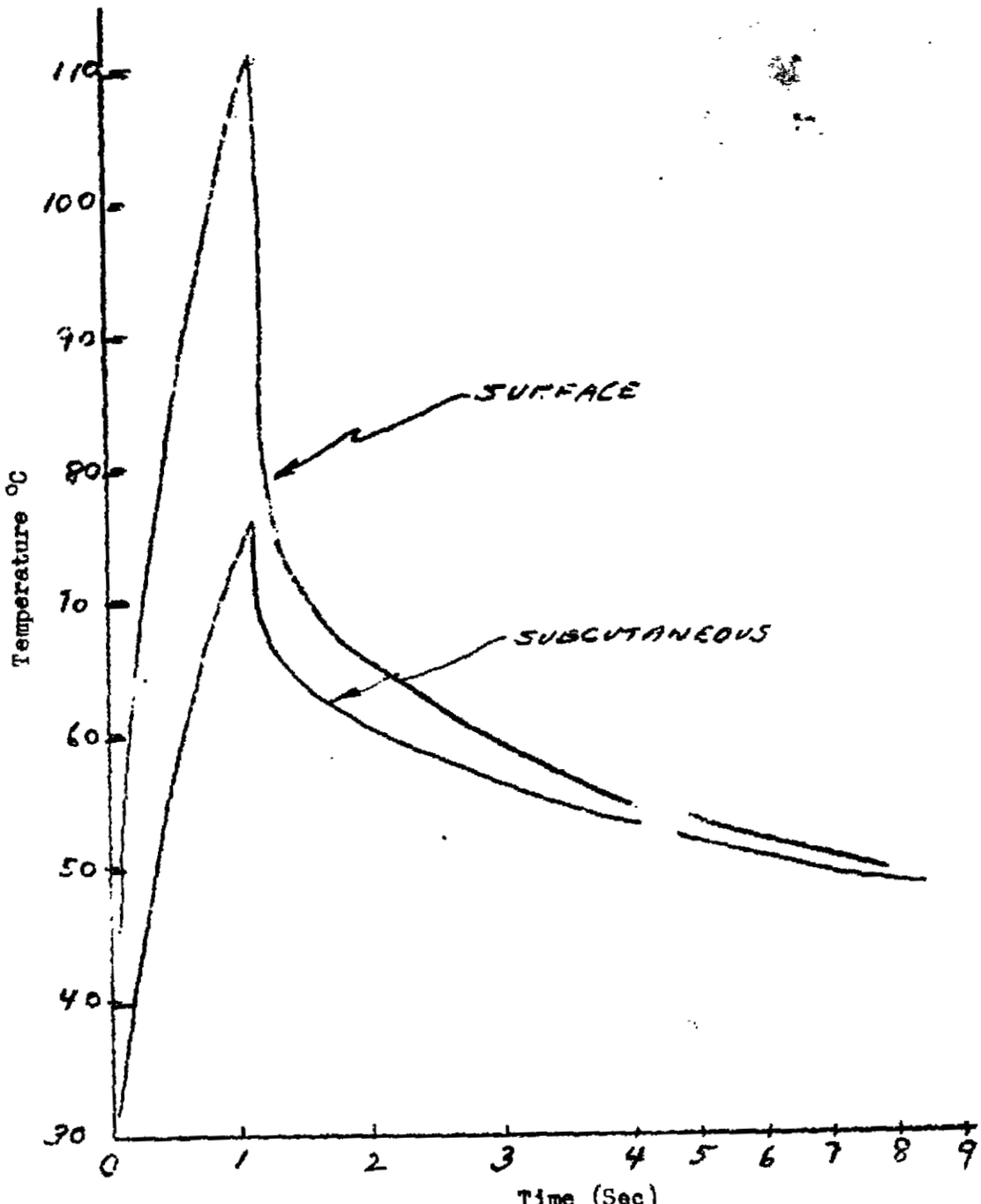

Fig. 1. Time-Temperature Record -- bare skin, minimal white burn -- 1.1 sec exposure, Q = 6.6 cal/cm^2.

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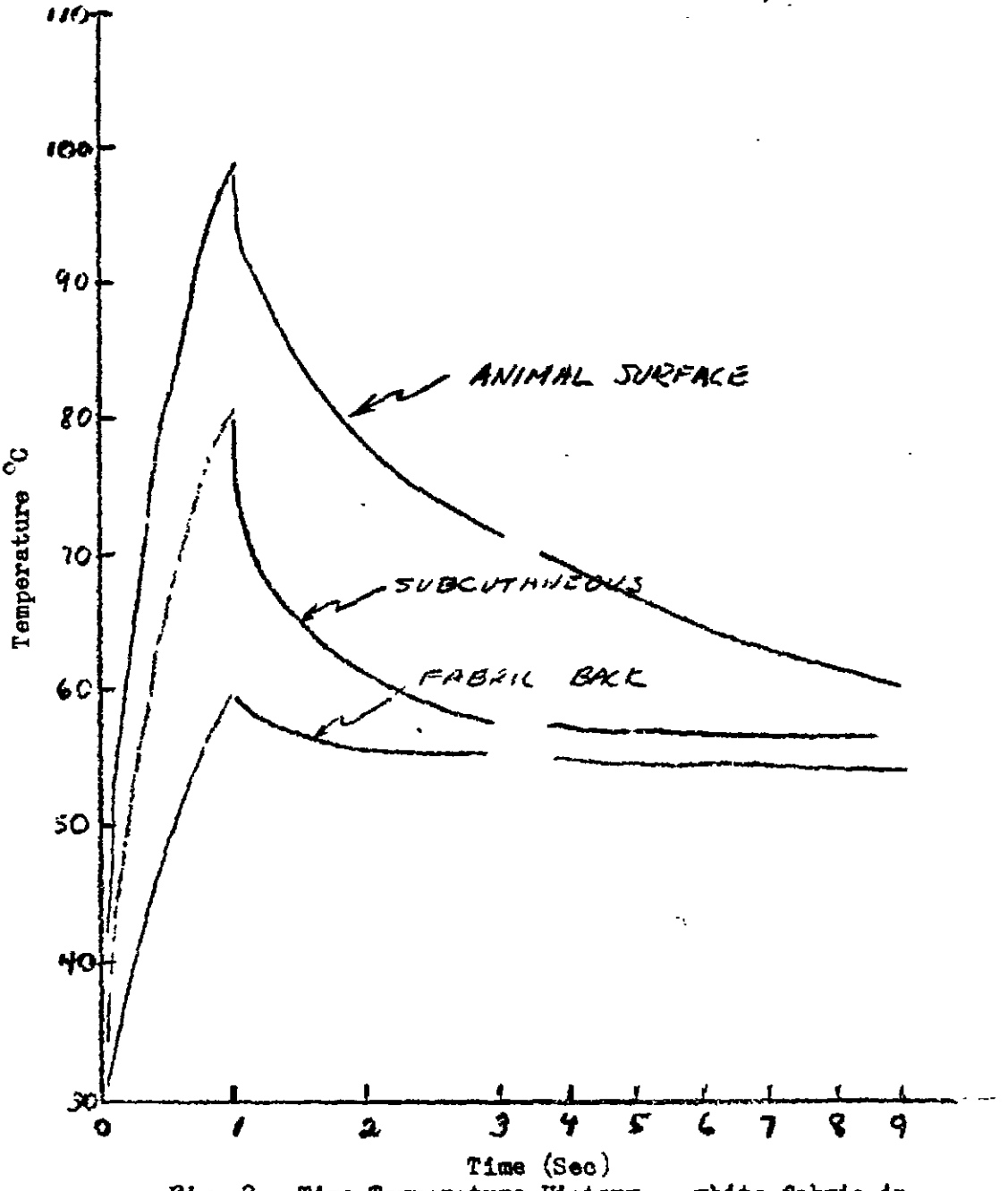

Fig. 2. Time-Temperature History -- white fabric in contact 1.0 sec exposure -- Q = 19.1 cal/cm^2.

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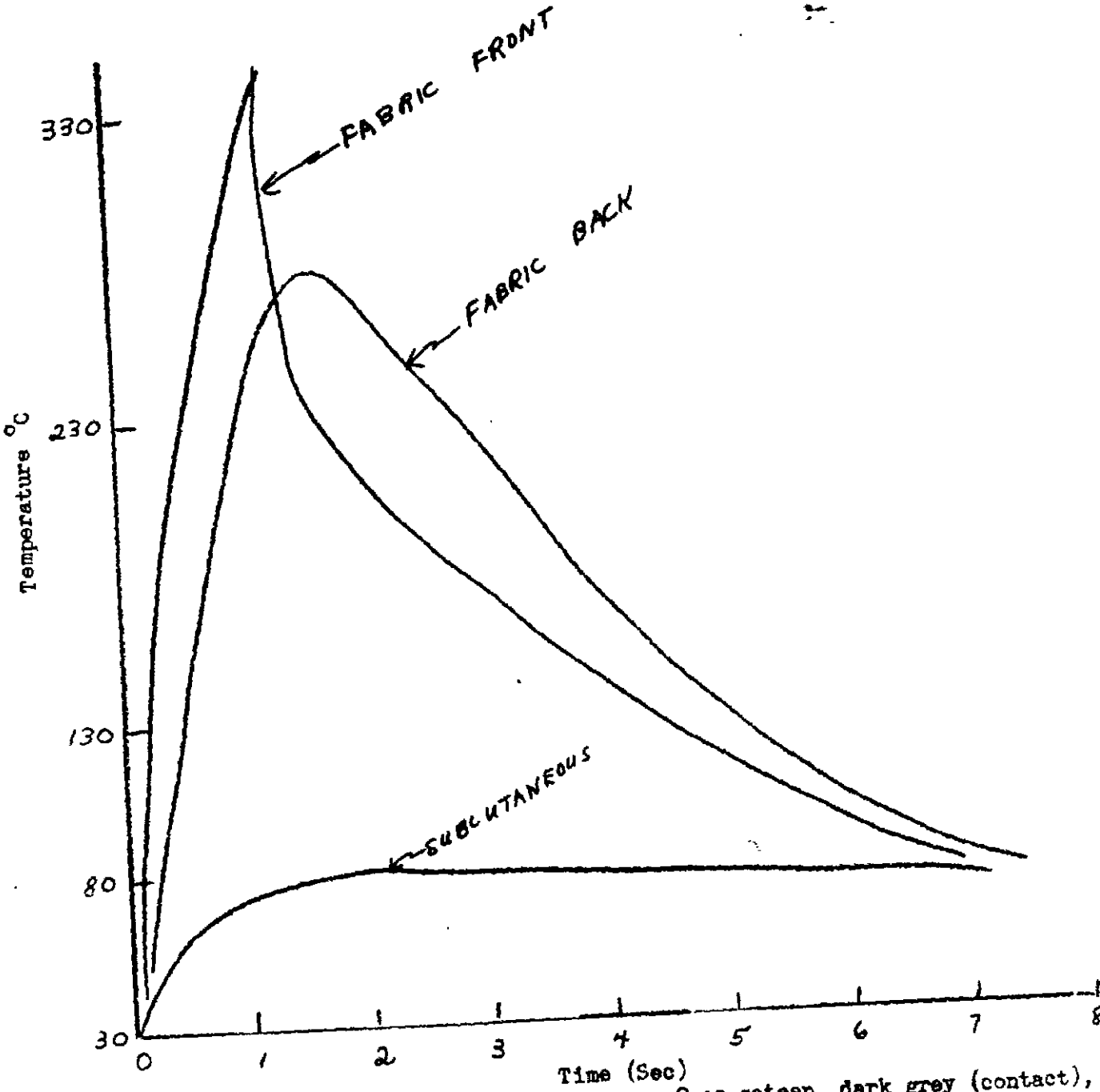

Fig. 3. Time-Temperature History -- 9 oz sateen, dark grey (contact), Q = 6.4 cal/cm^2, t = 1.2 sec.

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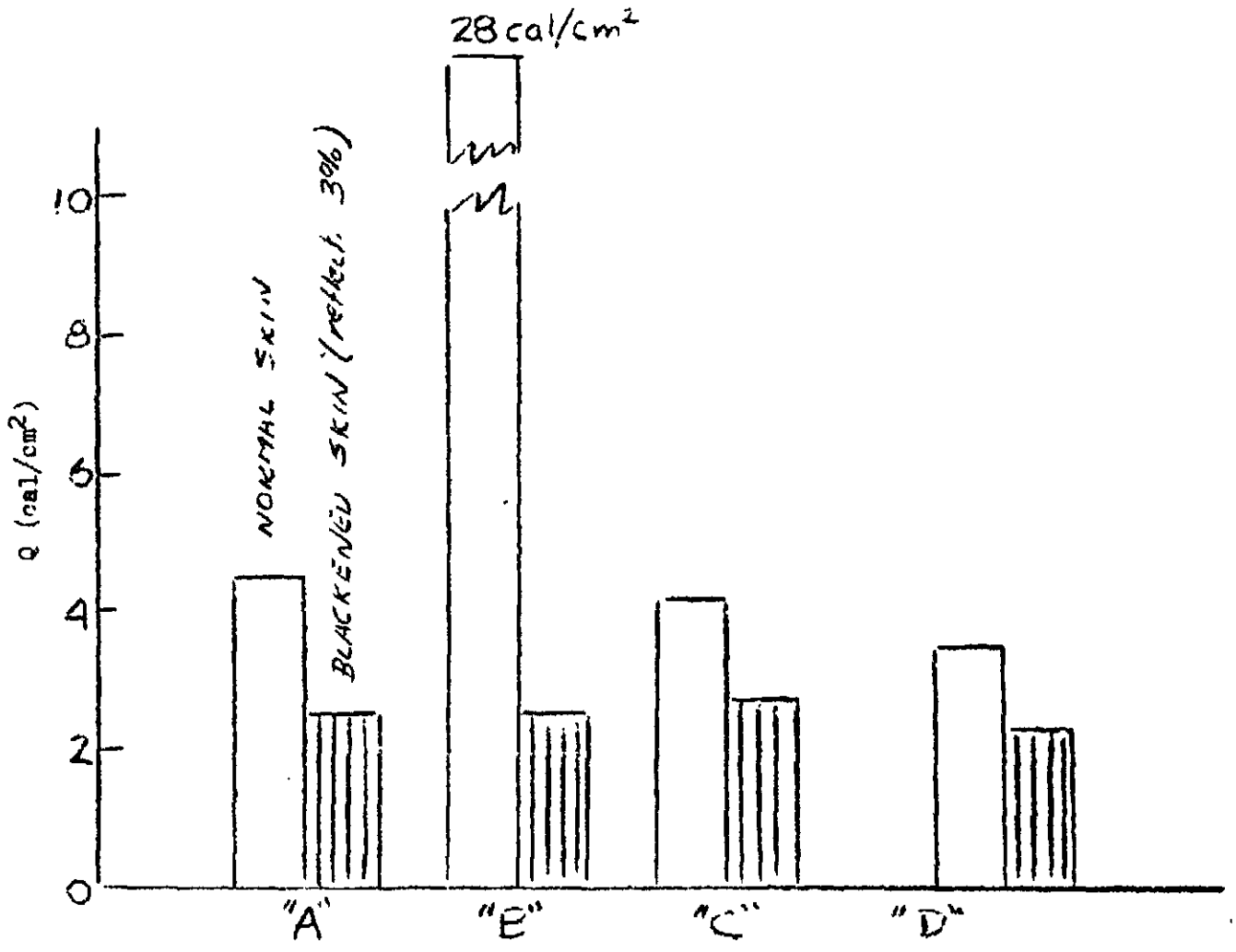

Fig. 4. Energy for Minimal White Burn with Various Spectral Regions (exposure time 2 second except "B").

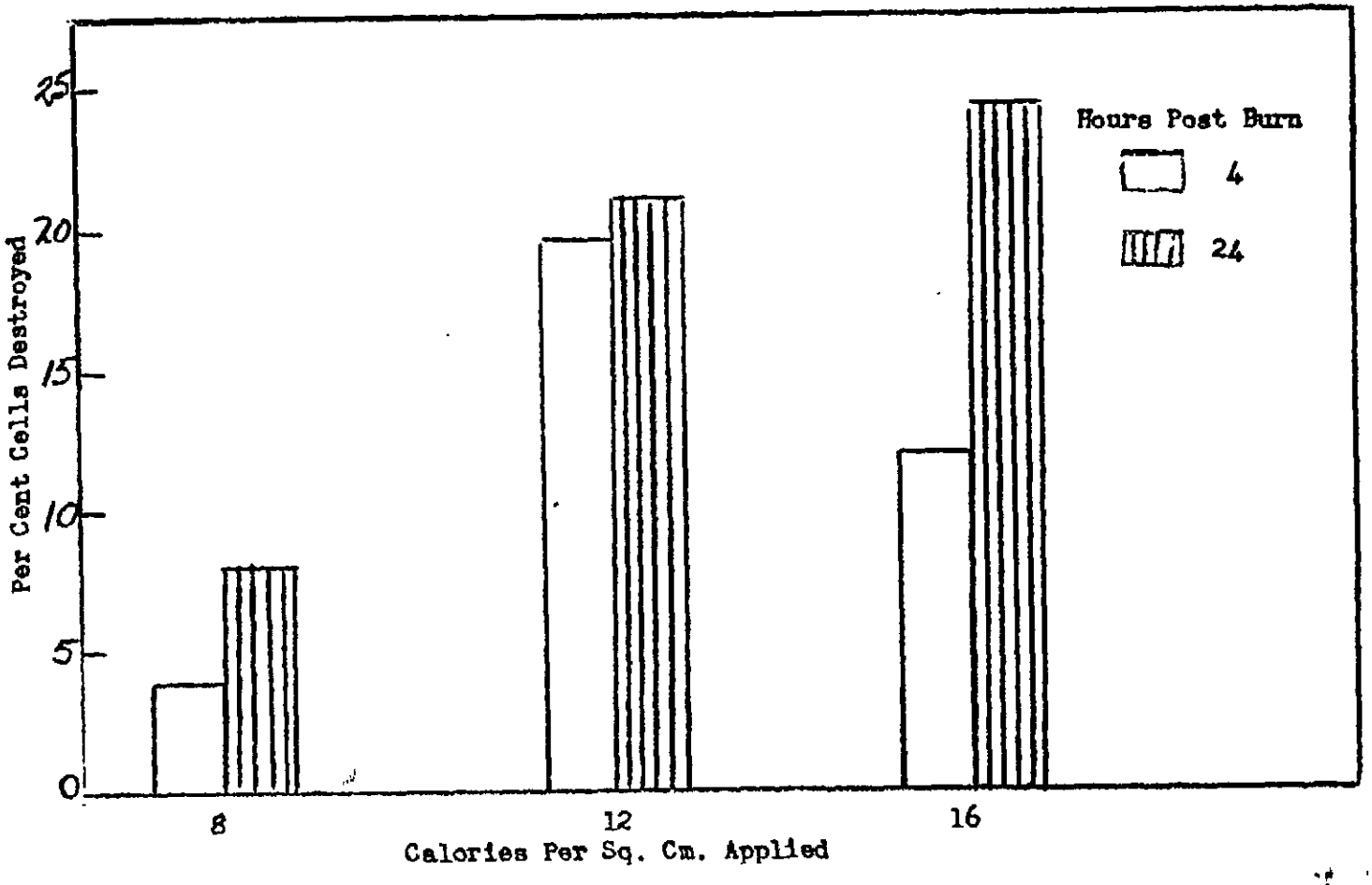

Fig. 5. Relationship Between Intensity of Thermal Radiation Burn and Destruction of Red Blood Cells.

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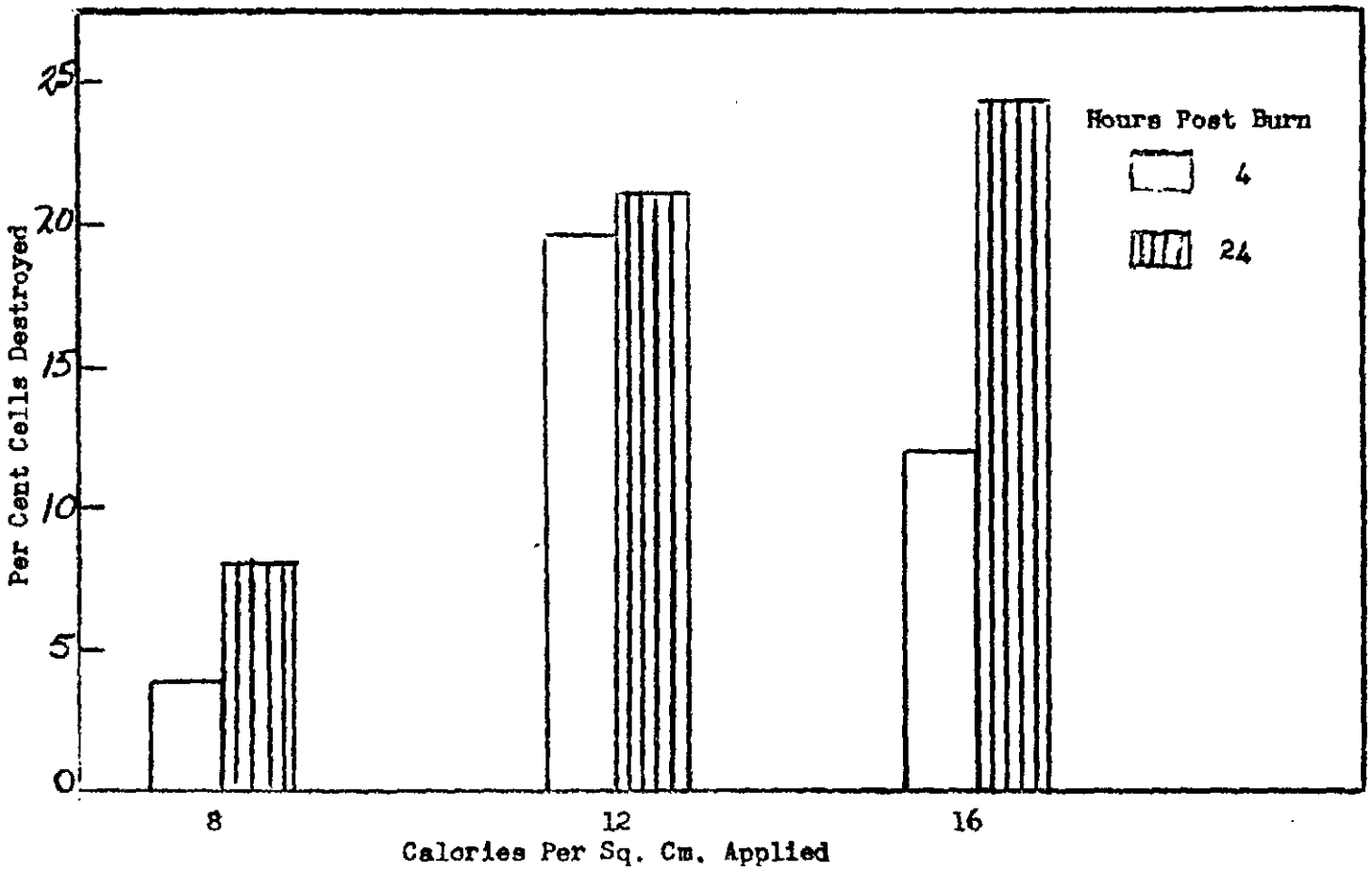

Fig. 5. Relationship Between Intensity of Thermal Radiation Burn and Destruction of Red Blood Cells.

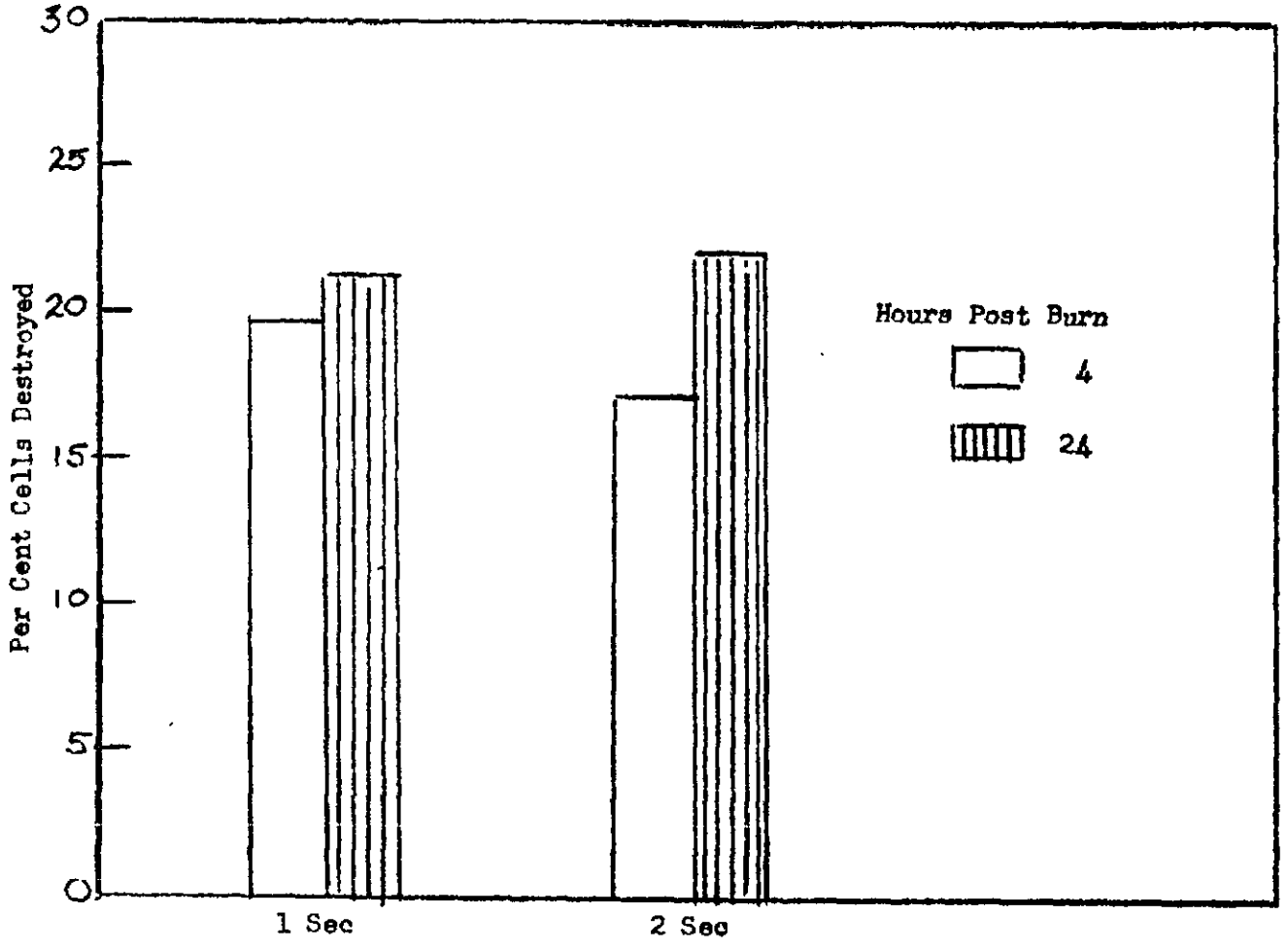

Fig. 6. The Effect of Exposure Time Upon the Acute Destruction of Red Blood Cells (12 cal/cm^2, 15% body area burn).

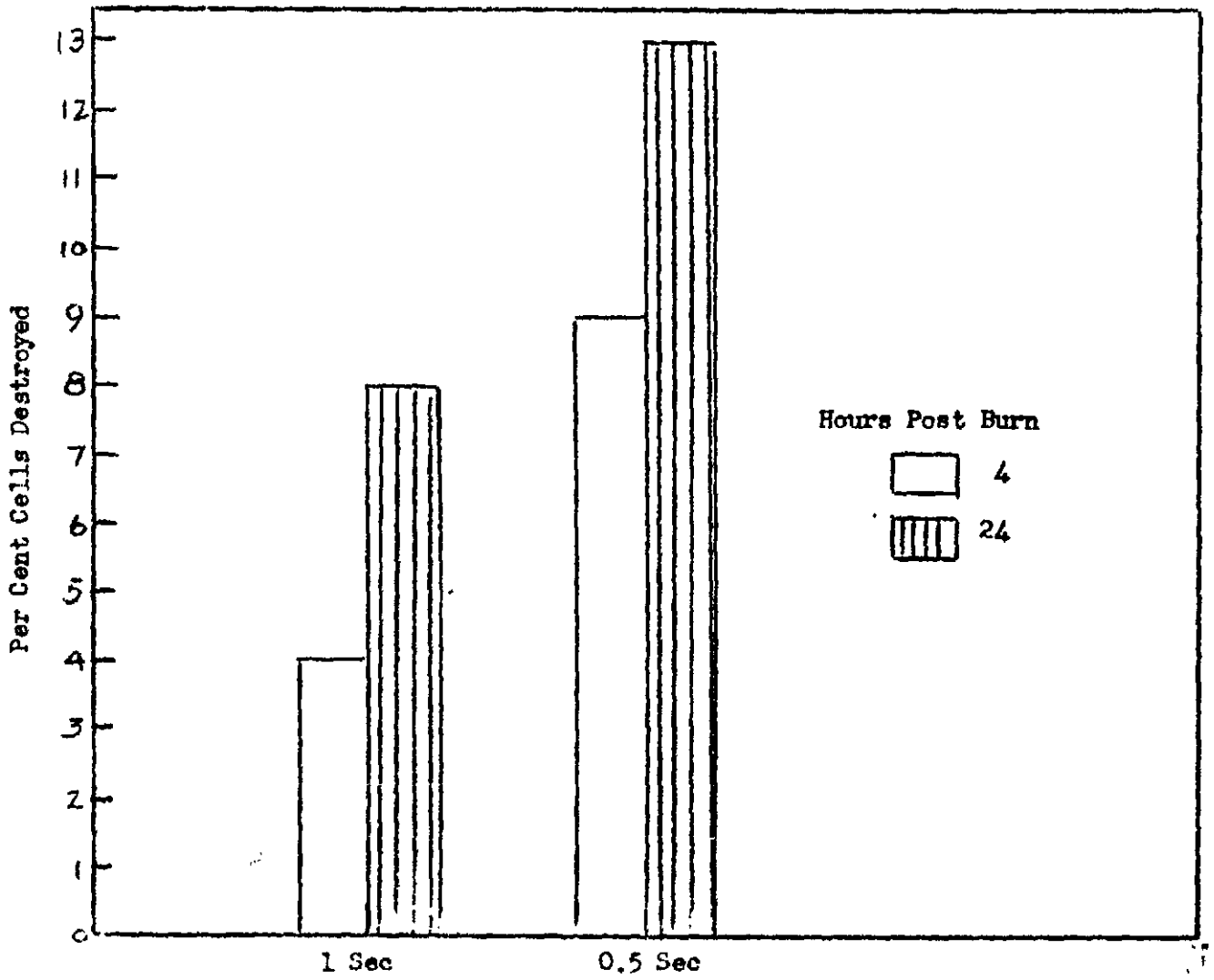

Fig. 7. The Effect of Exposure Time Upon the Acute Destruction of Red Blood Cells (8 cal/cm^2, 15% body area burn).

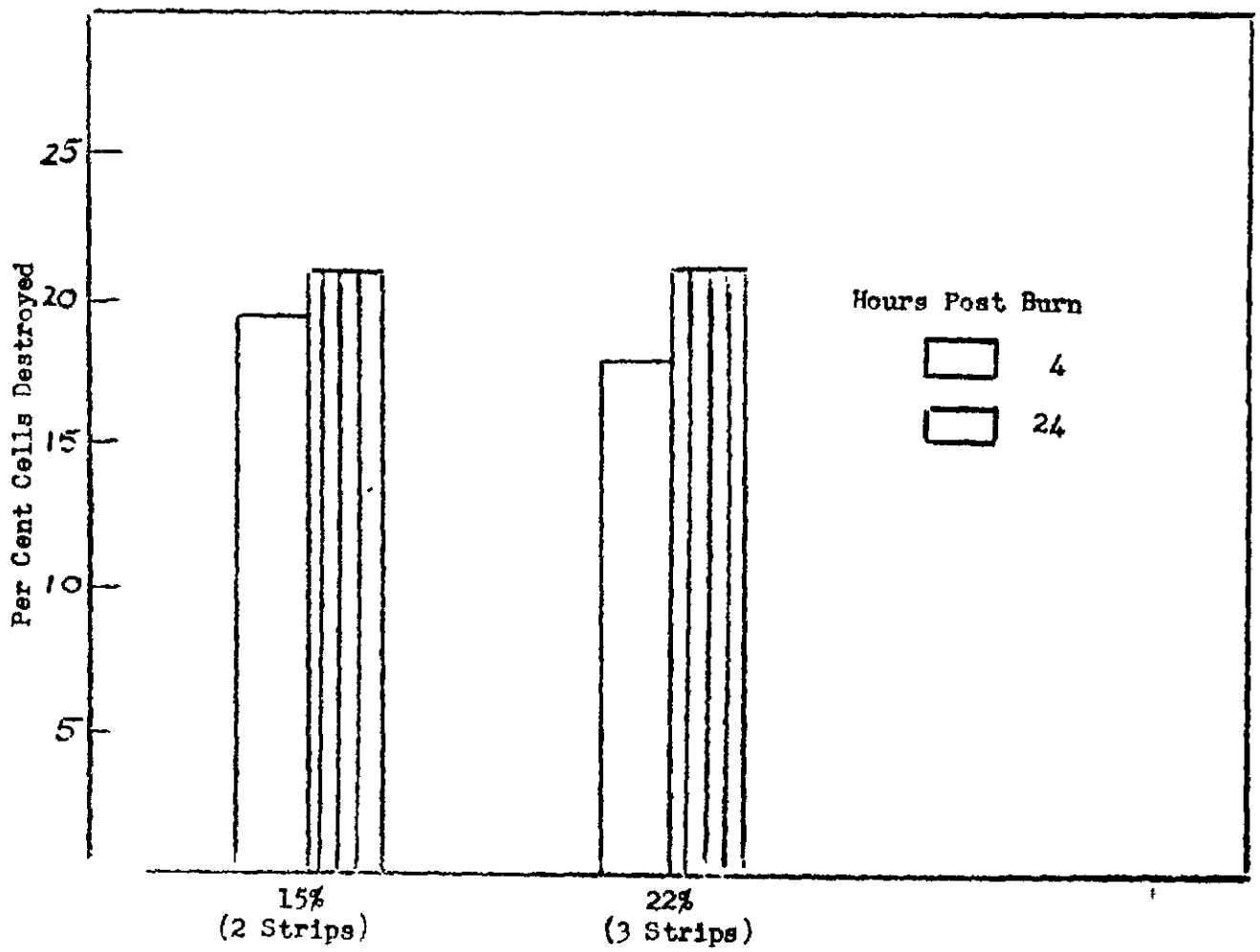

Fig. 8. The Effect of Burn Area Upon the Acute Destruction of Red Blood Cells (12 cal/cm^2, 1 second exposure time).

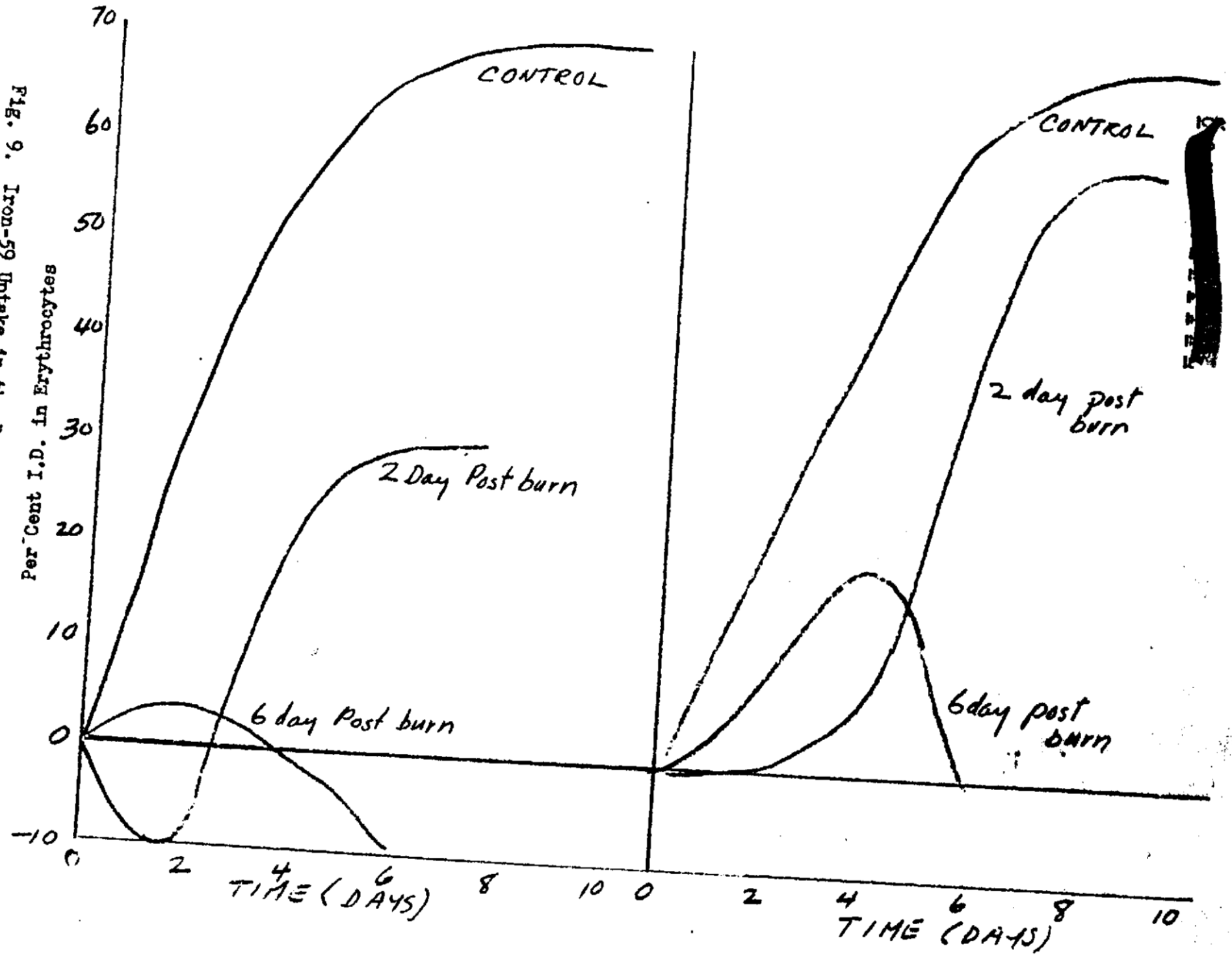

Fig. 9. Iron-59 Uptake in the Burned Dog.

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