EXPERIMENTAL PRODUCTION OF FLASH BURNS IN THE RABBIT RETINA *

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INTRODUCTION

UNTIL THE FIRST atomic bomb exploded over Hiroshima, Verhoeff and Bell's statement made in 1916 (1), "No artificial illuminant can fairly be considered dangerous from the standpoint of thermal radiation on the retina," held true. Since the advent of the atomic bomb, however, this statement is no longer factual. The known effects of thermal radiation on the eye have been studied extensively, but only recently has the hazard of chorioretinal damage from nuclear explosions been recognized (2). While only one case of retinal injury has been reported following the Hiroshima explosion (3), it has been shown experimentally by Byrnes, Rose, and Cibis (4) in 1952 that such injury could be produced in rabbits exposed out to distances of 42.5 miles from an atomic explosion, and in the past years, six cases of thermal injury to the retina as a result of atomic explosions have been reported (5). It has, therefore, become important to determine as accurately as possible the threshold dose necessary to produce irreversible burns of the retina. This study was undertaken in an effort to shed some light on the problem, and this paper is a preliminary report of work still in progress under United States Air Force sponsorship.

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Retinal damage can be produced at distances far in excess of those at which flash burns are observed, because of the optical system of the eye. As one moves away from the fireball, the intensity of radiation at the cornea decreases as the square of the distance; at the same time, however, the area of the retinal image of the fireball also decreases in the same proportion. Hence, if scattering and attenuation are neglected, the intensity of thermal energy on the retina remains constant, regardless of distance from the fireball, until that distance is reached where the eye can no longer resolve the image of the fireball.

LABORATORY EQUIPMENT

Previous work in this laboratory had demonstrated the usefulness of a 24-inch Army searchlight equipped with an ellipsoidal reflector for the production of flash burns in animals and human volunteers (6, 7). It was possible to produce thermal intensities of 22–23 cal/cm^2/sec. over a diameter of 0.5 inch, using standard 10-mm. high intensity carbons. However, this arrangement, while excellent for studies on flash burns to the skin, is not suitable for producing small retinal burns because the highly converging cone of radiation (28 degree solid angle) would produce a retinal burn covering a large part of the fundus. By employing a second ellipsoidal mirror to focus the real image from the first mirror, we obtain a cone of radiation having a solid angle of about 7 degrees which more nearly simulates the atomic fireball viewed at an appreciable distance. For example, viewing the 6-inch diameter cone of light reflected from the second mirror at a distance of 51 inches is equivalent to viewing a fireball 900 feet in diameter at a distance of 1.45 miles. On the assumption that the rabbit eye may be approximated by a lens of 1 cm. focal length, the retinal image of the fireball would have a diameter of about 1.2 mm. It must be emphasized, however, that the thermal dose delivered in one second by the fireball of a 20 KT weapon would be about seven to ten times the thermal dose delivered by the laboratory source described here. In this respect, our simulation of the fireball is not realistic at distances where atmospheric attenuation can be neglected. However, as the distance from the fireball is increased to many miles, attenuation by absorption and scattering becomes appreciable in reducing radiation intensity. This attenuation is not present in the laboratory. Moreover, at great distances from the fireball, only those photons which have not undergone absorption or scattering will contribute to a well-defined image of the fireball on the retina. Scattered photons will be distributed more

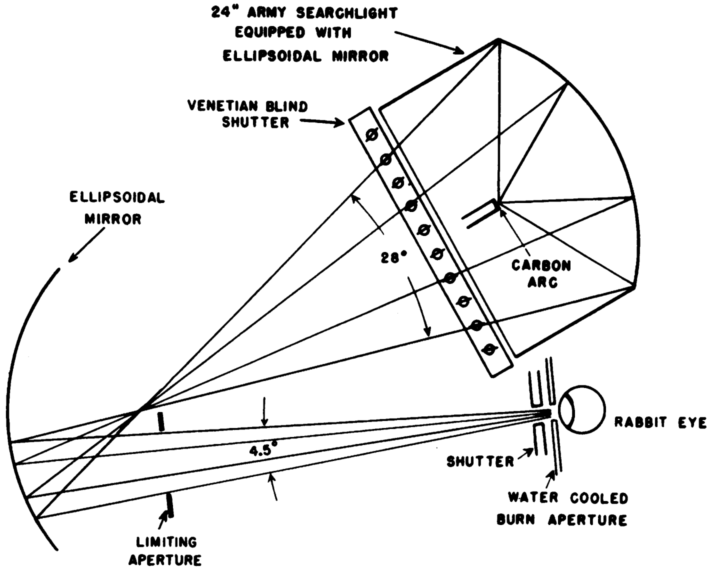

FIGURE 1. SCHEMATIC DIAGRAM OF OPTICAL SYSTEM EMPLOYED IN PRODUCING RETINAL BURNS

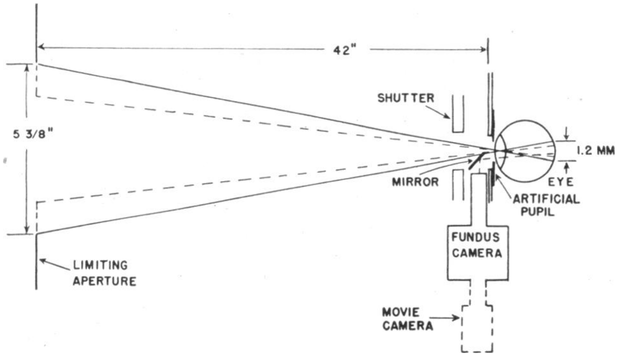

FIGURE 2. DETAILED SCHEMATIC DIAGRAM OF OPTICAL SYSTEM AT THE BURN APERTURE

or less uniformly over the entire retina. To put it another way, the thermal intensity measured by an uncollimated black body receiver is greater than the intensity incident on the cornea which contributes to a retinal image of the fireball. Thus, as we proceed to great distances from the fireball, the thermal intensity available for a definitive retinal image can be more closely approximated by a laboratory source, since the latter provides a constant thermal intensity on the retina, regardless of image size.

A limiting diaphragm or aperture placed eight inches from the second reflecting mirror, as shown in Figure 1, serves as a method for controlling the retinal image size. As the diameter of this aperture is reduced, the solid angle subtended by the rabbit eye becomes smaller, but at the expense of the thermal intensity incident on the cornea in direct proportion to the area of the radiation cone excluded. These two factors, solid angle and thermal intensity incident on the cornea, cancel out to maintain a constant thermal intensity on the retina (Figure 2). Under experimental conditions with a source of finite size, where the shadow of the carbon arc

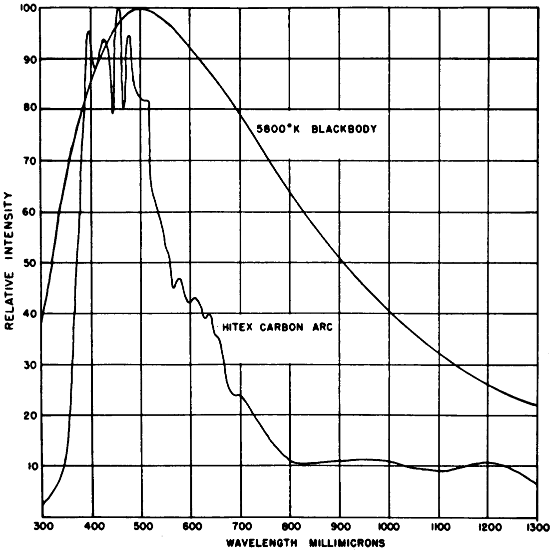

FIGURE 3. GRAPH OF SPECTRAL DISTRIBUTION OF HITEX CARBON ARC SUPERIMPOSED ON THE SPECTRAL DISTRIBUTION FROM A BLACK BODY AT 5800° K.

mount is focused on the retina, there are practical limitations to the size of burns which can be produced.

Visual alignment of the rabbit is accomplished with a Bausch and Lomb fundus camera and a tiny mirror placed in the beam entering the eye. A 16-mm. movie camera can be substituted for the eye piece, allowing photography of lesion production (Figure 2). Exposure time is controlled by a Compur shutter, and is measured by means of a photomultiplier, an electronic gating circuit, a 10 KC oscillator, and a scaler. The photomultiplier tube operates the gating circuit, which allows 10 KC pulses to feed into the scaler. The scaler indicates exposure time directly to 0.1 milliseconds.

In the retinal burn studies, National Carbon Company 10 mm. diameter Hitex positive carbons and Orotip negative carbons operated at 140 amperes D.C. have been utilized. Figure 3 illustrates the special distribution obtained with a Bausch and Lomb grating spectrometer and an Eppley thermopile. A 5800-degree black body curve is shown for comparison. The carbon arc distribution is deficient in near infrared, as compared to the black body at 5800 degrees K.

Thermal intensity has been measured with a water flow calorimeter. The intensities available at the burn aperture range from 1.2 to 1.4 cal/cm^2/sec. Insertion of the mirror used with the fundus camera reduced this intensity about 10 percent. A Venetian blind type of shutter mounted on the searchlight housing provides a means of reducing intensity to any desired level (Figure 1).

EXPERIMENTAL PRODUCTION OF RETINAL BURNS

Mature Chinchilla gray and New Zealand black rabbits, weighing from 3,000 to 5,000 grams, were used in these studies. Refractive error and corneal curvature were measured in all animals used in order to assure ocular uniformity. The geometric axis also was measured in a number of enucleated eyes. Animals with too much variation in pigmentation of the fundus were eliminated from the study. Sodium Nembutal (60 mg/5 lbs. body weight) was used for intraperitoneal anesthesia; the pupils of all animals were dilated with atropine prior to exposure and the nictitating membrane excised.

The animal to be exposed was then rested on an adjustable platform and the eye held against a plastic annulus inserted in the burn aperture; an aperture 8 mm. in diameter was used to define the pupillary diameter. The animal's dilation was greater than 8 mm. in all cases. The fundus was then viewed through the fundus camera with the Venetian blind shutter almost closed. When the radiation was on a desired spot, the exposure was given by the operator of the fundus camera. At the same time a motion picture of the exposure was taken at approximately 70 frames per second.

Exposures of 500–1,000 milliseconds produced, immediately after the burn, round or slightly oval lesions of a dense white appearance. A few minutes later a small halo appeared around this white lesion; the halo was less dense and more yellowish in color than the lesion. Over the next three to four days the central bright area became smaller with consequent enlargement of the halo. A slight vitreous haze was seen sometimes immediately after exposure, but this usually disappeared on the third or fourth day. After four or five days, fine granules of pigmentation were visible around the burn, and eschar formation took place in much the same manner as in a retinochoroidal inflammatory lesion or in an electric current induced diathermy puncture.

In the motion picture, the first few frames showed the illuminated area on the fundus. Then, usually in an area below the center, there appeared the white blanching of the coagulated tissue. This area spread constantly during exposure, and at the end of a 1-second exposure it usually exceeded the originally illuminated area.

With exposure times from 50 to 250 milliseconds, clinically less severe lesions were observed. The color of these lesions was yellow rather than white, and in the short exposure times (50 to 100 milliseconds), the lesion appeared only after two or three minutes in much the same manner as the halo around the more severe burns; also, the shape of these lesions was different from that of the more severe burns, for they were kidney or bean shaped, because of the image of the carbon holder on the retina. Presumably, conduction of heat into the shadow area took place only partially during these short exposures.

The clinical course of these mild lesions was very much the same as that of the big ones, pigmentation and, ultimately, scarification taking place from four to fourteen days after exposure. There was no noticeable change in the appearance of these lesions after two weeks, when they were usually barely visible; follow-up periods were terminated four to five weeks after exposure.

PATHOLOGY AND HISTOLOGY OF THE LESIONS

Routine colloidin sections and HE stains of exposed rabbit globes were examined microscopically. These globes were examined at various intervals after the burn exposure. A number of globes that received exposures of from 500 to 1,000 milliseconds in our experiments with fundus motion picture photography were used for histologic studies. In those globes enucleated and fixated immediately after the burn (within five to ten minutes) the burn in the retina is readily seen in the sections (Figure 4). There is moderate swelling of the nerve fiber layer and marked pyknosis of all the nuclei in the inner and outer nuclear layers. In the ganglion cell layer, the cells appear structureless and show pyknotic or no nuclei. The structure of rods and cones is lost or modified in the burned area. The nuclei in the pigment epithelium show marked pyknosis, fragmentation, or chromatolysis. There are few or no changes in the choroid immediately after burn.

In sections of eyes enucleated three to four days after burn, the changes in the retina were not much different from those described above, but there was marked choroidal hyperemia, but very little leucocyte infiltration around the burn. In several severe burns produced by 1-second exposures, the inner layers of the sclera suffered, appearing homogeneously red and without nuclei in the area underlying the burn. Moderate pigment proliferation at the edges was seen in some sections as early as four days after exposure (Figure 5).

The few sections that we have obtained so far of lesions produced with exposure times from 50 to 100 milliseconds show a very similar picture (Figures 6 and 7). The damage seems to be confined mostly to the pigment epithelium, rods and cones, and the inner nuclear layer of the retina. The rod-and-cone layer shows a dark red appearance, and structures can be made out only vaguely. The outer nuclear layer in these mild lesions is grossly disarranged, most of the nuclei being pyknotic. There is space formation in this

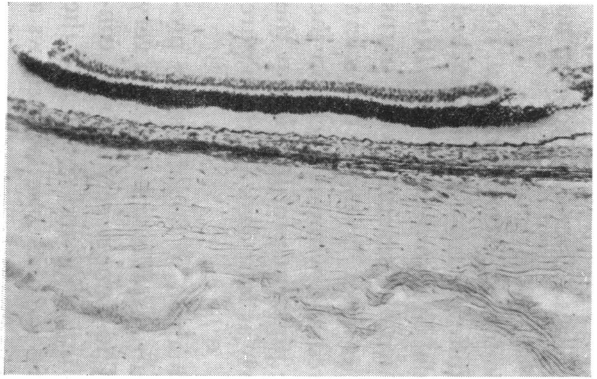

FIGURE 4. HISTOLOGIC SECTION OF A SEVERE BURN
Globe fixated within 10 minutes of burn.

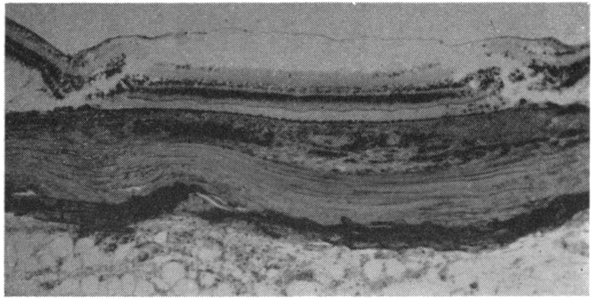

FIGURE 5. HISTOLOGIC SECTION OF A SEVERE BURN
Globe fixated 4 days after burn.

FIGURE 6. HISTOLOGIC SECTION OF A MINIMAL BURN LESION
Globe fixated within 10 minutes of burn.

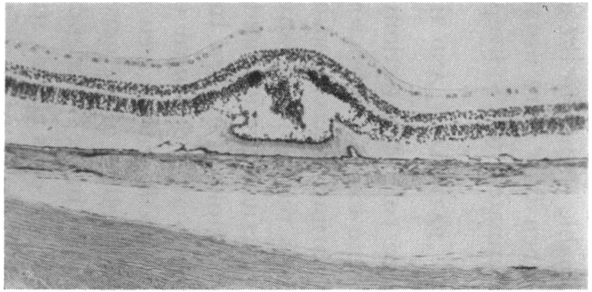

FIGURE 7. HISTOLOGIC SECTION OF A MINIMAL BURN LESION
Globe fixated within 10 minutes of burn.

layer, causing the retina to bulge slightly outward. The other retinal layers show no, or only mild, cellular changes, the nerve fiber and ganglion cell layer appearing normal.

No follow-up histologic slides on these short exposure burns are available as yet. The histologic appearance of the lesions produced in this laboratory is very similar to those described by Verhoeff and Bell (1).

EVALUATION OF THERMAL DOSE AT THE RETINA

In order to calculate the thermal dose incident on the retina, the following factors must be known: the thermal intensity incident on the cornea, the pupillary diameter, the average transmission coefficient through the optic media, the area of the image on the retina, and the exposure time. Reliable data for the thermal intensity in $\text{cal/cm}^2\text{/sec.}$ incident on the cornea were provided by the water calorimeter, which was cross calibrated against other laboratory standards. The pupillary diameter is defined accurately by means of an 8-mm. limiting aperture adjacent to the cornea. The transmission of radiant energy through the ocular media has been shown in another study of this laboratory, using the same strain of rabbits, to be approximately 78 percent (8). In order to calculate the image area, we have taken the average distance from the nodal points to the retina of the rabbit eye to be 10 mm. Knowing the solid angle of the incident cone of radiation on the cornea and the distance from the limiting diaphragm to the cornea, one can calculate the image diameter produced on the retina. The greatest source of error in this calculation is the distance from the nodal points to the retina. This error has been minimized by carefully selecting animals with little variation in measurable ocular constants. Fundus photography of the illuminated cone of radiation on the rabbit retina under the same experimental conditions provided an accurate check on this method of determining image size. The following formula for calculating the retinal thermal dose is used:

$$\frac{\text{cal/cm}^2\text{/sec. at cornea} \times (\text{pupillary diameter})^2 \times \text{transmission coefficient} \times \text{exposure time in seconds}}{(\text{true image diameter})^2 \times \text{image shape factor}}$$

The image shape factor of 0.82 in the denominator takes account of the decrease in image area on the retina due to the shadow of the carbon holder. It is essential that the irradiated area on the retina be used, and not the size of the burn lesion as determined subsequently by ophthalmoscope, fundus photography, or gross anatomic measurement, since we have noted that the size of the burn lesion depends to a marked extent upon the exposure time.

Fundus photography at the rate of 70 frames per second during the burn exposure was employed as one means of determining the thermal energies needed to produce irreversible retinal lesions. Blanching of the retina as seen after several exposed frames was taken as a criterion for an irreversible lesion. Table 1 summarizes the data obtained on 10 animals, 6 gray and 4 black rabbits. The lowest values were obtained with a 4½-inch limiting aperture producing an image diameter of 1.1 mm., and they ranged from 2.8 to 5.1 cal/cm^2. The average thermal dose for 14 burns on 10 animals was 3.6 ± 0.7 cal/cm^2. For the 3-inch aperture producing an image diameter of 0.7 mm., the average thermal dose was 4.9 ± 1.3 cal/cm^2, while the 1⅝-inch aperture producing an image diameter of 0.4 mm. required an average dose of 5.6 ± 1.3 cal/cm^2. These figures show that the thermal dose required for a thermal lesion increases markedly as the retinal image size decreases. This is probably due to increased conduction in the smaller lesion, as previously noted by Verhoeff and Bell in 1916 (1).

TABLE 1. SUMMARY OF BURN DATA OBTAINED BY FUNDUS PHOTOGRAPHY

Rabbit Number	*4½" Aperture Thermal Dose cal/cm^2*	*3" Aperture Thermal Dose cal/cm^2*	*1⅝" Aperture Thermal Dose cal/cm^2*	*1" Aperture Thermal Dose cal/cm^2*
135B	3.8	—	—	—
136B	3.0	5.5	5.7	—
136B	4.5	—	—	—
145G	3.5	5.5	—	—
144G	2.8	4.0	4.0	—
140G	3.1	3.0	5.1	—
141G	4.1	—	3.9	—
141G	4.0	—	—	—
141G	3.0	—	—	—
129G	3.0	5.1	6.5	9.0
130B	3.0	4.4	6.3	—
130B	—	4.5	—	—
126G	3.5	7.4	7.9	—
131B	3.4	—	—	—
131B	5.1	—	—	—
Average	3.56 ± .65	4.93 ± 1.33	5.63 ± 1.32	9.0

More recently we have found that a minimal lesion on the retina may be produced by very short exposure times (50–100 milliseconds). These lesions are not always seen immediately with the ophthalmoscope, but take from two to three minutes to develop. This observation led us to question the validity of the motion picture photography technique to determine the thermal energy to produce a minimal irreversible lesion. It is also a matter of subjective judgment to decide just at which frame the first signs of blanching occur. Accordingly, we have abandoned the fundus motion picture photography method in favor of the more difficult but sensitive method of varying the exposure time from burn to burn and waiting several minutes to evaluate the result of the exposure. This method involves a hit-or-miss technique which is ideally suited to the type of statistical analysis known as the probit method. We still employ the fundus camera, however, to align the eye properly.

TABLE 2. PRELIMINARY BURN DATA BY SHORT EXPOSURE TIME TECHNIQUE
(*Using the 4½″ diameter limiting aperture*)

Rabbit Number	*Exposure Time in Milliseconds*	*Thermal Dose in cal/cm²*	*Burn*
141G	.0551	2.40	No
"	.0652	2.86	No
"	.1061	4.68	Yes
144G	.0649	2.73	No
"	.0590	2.48	No
"	.0829	3.47	Yes
"	.0825	3.46	Yes
145G	.0902	4.26	Yes
"	.0717	3.38	Yes
"	.0491	2.32	Yes
"	.0487	2.30	No
135B O.S.	.0267	1.25	No
" O.S.	.0483	2.19	Yes
" O.S.	.0685	3.09	Yes
" O.S.	.0664	3.00	Yes
" O.D.	.0961	4.34	Yes
" O.D.	.0672	3.05	Yes
" O.D.	.0500	2.26	No
" O.D.	.0490	2.21	No
" O.D.	.0919	4.15	Yes

Average for lowest "yes" value of each eye: 3.14 ± 0.81 Standard Deviation: 0.81

In Table 2 are summarized a limited number of short exposure experiments on 4 animals, placing several burns on each eye. Success or failure to produce an observable lesion after waiting at least five minutes is indicated by "yes" or "no" in the column headed *burn*. In these experiments only the 4½-inch limiting aperture has been used to date. The lowest thermal dose which has produced an observable lesion is 2.2 cal/cm^2. Most of the minimal lesions observed required 3–4 cal/cm^2, which is in the same range as that determined by the fundus photography method. Nonetheless it seems preferable to depend on the statistical method for further evaluation of threshold and reciprocity, since it is inherently more sensitive.

SUMMARY

A technique has been evolved in this laboratory for the production and study of small retinal burns in the rabbit eye. A 24-inch carbon arc searchlight equipped with an aluminized ellipsoidal mirror has been utilized as the source of radiation. A second ellipsoidal mirror is used to reduce the angle of convergence of the radiation in order to simulate the fireball of an atomic weapon viewed at appreciable distances. Intensities of 1.2–1.4 cal/cm^2/sec., as measured by a waterflow calorimeter, are available at the cornea of the rabbit eye. Provision is made for motion picture photography of the burn.

The ophthalmoscopic and histologic appearance of lesions produced by various exposure times is described. Two methods of evaluating the thermal dose for a minimal irreversible retinal lesion are compared. The dose for such a lesion is a function of retinal image size during the burn. Up to the present, the dose required to produce a minimal burn lesion in the rabbit retina has been found to range between 2 and 4 cal/cm^2.

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DISCUSSION

Dr. Irving H. Leopold. Man's body is so ordered that each tolerable challenge has the property of calling forth activities to compensate for, nullify, or repair resulting disturbances. They constitute the adaptive talents which have permitted man to endure a hostile world.

The harm done to human beings by physical agents, such as heat, is profoundly influenced by many variables. The intricacies of man's inner mechanisms are not reducible to simple equations.

Doctors Guerry, Wiesinger, and Ham have been well aware of many uncontrollable variables in their carefully designed attempt to determine the minimal thermal energy necessary to produce the minimal irreversible retinal lesion. In other words, they have studied a physical force, its measurement, and the disorders it produces on the retina.

They found that the average dose required for a minimal irreversible lesion, using the 4½-inch diameter aperture, is 3–4 cal/cm^2. The damage occurred mostly to the rods and cones and inner nuclear layers. The choroid showed little change.

The establishment of such a standard unit is important for future studies that will attempt to evaluate internal adaptations and external protective measures which may prevent the disabling effects, and for therapeutic means to alleviate or correct the damage which could result.

Most successful research activities stimulate questions, and this well-planned report is no exception.

What is the influence of choroidal pigment content on the thermal energy required for the production of the irreversible retinal lesion? Is the energy required greater or less in the albino rabbit?

Was there any histologic evidence of retinal change after exposure without associated detectable ophthalmoscopic evidence?

What are the capacities of the same or adjacent retinal tissue to respond to a second exposure, particularly if the initial exposure produced only reversible alteration?

The study of the influence of thermal energy on the retina and choroid is timely, important, and complex. The present investigations of Dr. Guerry and his associates represent an important initial step toward the accumulation of useful information.

DR. F. H. VERHOEFF. I was pleased to hear the essayists refer to Verhoeff and Bell. Dr. Guerry started out by quoting our statement that no commercial illuminant was a source of danger as regards the thermal effect on the retina, and said we would now have to change that because of atomic explosions. I would not call an atomic explosion a commercial illuminant, so I do not think the statement has to be changed.

Dr. Guerry has shown some pictures of experimental thermal burns of the retina as seen macroscopically and also microscopically. He did not state that we had produced these thermal burns experimentally and studied them microscopically. Perhaps he said that in the paper, but he did not say so in his talk, so I am going to say that we did produce them, and also that I do not see that he has found out anything about the histology of these burns that we did not find out. If he did, I would like to know what it was. We pointed out that the heat effect was chiefly in the outer retinal layers, and we produced lesions in which only the pigment epithelium was affected. In his pictures, I think the lesions look very much like those we produced.

DR. CHARLES A. PERERA. I had the experience of examining the eyes of one of the Hiroshima girls who were brought over to this country. Twenty-five of these Japanese girls, who were fourteen-year-old schoolchildren at the time of the atomic bomb explosion, and who were all within a mile of the explosion, were brought here for plastic surgery by the surgeons of New York's Mount Sinai Hospital. Only one of the girls was looking at the plane carrying the bomb and saw the flash. The others were in the school building. This young girl has extensive scarring of the cornea in one eye, and most of the vision has been lost. In the second eye, the cornea is clear, but there is a defect in the central vision, due to a burn in the macular region. I understand in talking to Dr. Guerry that this case was reported in the literature.

DR. WILLIAM T. HAM, JR. (BY INVITATION). I am honored to be invited to appear before you. I am not an M.D., but a physicist, and I am afraid there is very little I can contribute to this discussion. Certainly I can contribute nothing to what Dr. Verhoeff said. I do not think that Dr. Guerry, Dr. Wiesinger, or I felt that we obtained any new histologic data. We are mainly concerned with the very short duration of the thermal flash that comes with a nuclear explosion. To what extent does the amount of energy required to produce a retinal lesion depend upon the speed with which it is delivered? This sort of physical problem is best handled by a team of people working together, namely, ophthalmologists, physicists, and electronic people. Our hope is that we will be able to define the amount of energy needed to produce retinal lesions under the conditions in which it will be delivered by an atomic or hydrogen weapon, so that we can calculate what the hazards may be for all of us in the event of nuclear warfare, which I hope and pray we will never have to experience.

DR. HERBERT WIESINGER (BY INVITATION). I would first like to thank the discussers for their most stimulating thoughts on the subject. I will also make an attempt to answer some of the questions, as far as this is possible at the present stage of our work.

We have not yet exposed any albino rabbits to thermal flashes to study the influence of choroidal pigmentation upon the production of lesions. We have deliberately utilized pigmented strains in order to more closely simulate the human eye. We have, however, used two kinds of pigmented strains, gray and black ones, and if one rules out from the study the animals with too much individual variation in pigmentation of the fundus, there seems to be no significant difference in the amount of energy required to produce lesions in either strain.

In regard to Dr. Leopold's second question, we have been unable to detect any lesions histologically that we had not observed before with the ophthalmoscope.

As to the influence of refractive error upon the lesion, one can only speculate. All the animals we used had a refractive error of between one and two diopters hyperopia, which produces only an unappreciable enlargement in the retinal image area, too small for us to assume from it any change in energy required to produce a lesion. Dr. Leopold's question as to whether reexposure to a previous sublethal dose to the retina lowers the threshold is very difficult to answer. In our limited experiments in this direction, we have not found any conclusive evidence to that effect, but we are at the present time in no situation to make a definite statement.

We have planned future work on as many as possible of the variables that are encountered in this project, such as the influence of speed of delivery, image area, and spectral distribution on the amount of energy required for production of thermal lesions.

I should also like to apologize to Dr. Verhoeff for not mentioning his earlier results here. Only lack of time has prevented our doing so. I believe that the lesions we produce with our apparatus are very similar to, if not identical with the ones he has reported in his monograph on the subject in 1916. The statement that we have quoted from Dr. Verhoeff's paper is "No artificial illuminant can fairly be considered dangerous from the standpoint of thermal injury to the retina." I believe that one can consider the atom bomb an artificial illuminant, but agree with Dr. Verhoeff that, fortunately, it is as yet not commercially available.