higher blood-glucose, and very low pancreatic and serum IRI-levels. The metabolic state of this group corresponds almost to the ketonuric, catabolic diabetic group with a strongly reduced life expectancy as described by Junod and co-workers.  

In conclusion, therefore, the results of our study suggest that BMT in induced diabetes may be a consequence of long-standing hyperglycemia and subsequent metabolic disorders due to the β-cytotoxic effect of streptozotocin.

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From the Hopital Cantonal, Clinique Universitaire d’Ophthalmologie, Geneva, Switzerland. This study has been supported by the SNSF Grant No. 3.1150.73. Submitted for publication Feb. 25, 1975.

Key words: diabetic microangiopathy, streptozotocin, retina, Acomys cahirinus, basement membrane thickening, morphometry, spontaneous diabetes, electron microscopy.

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The relationship between pre-exposure fundus temperature and the temperature rise which produces a threshold burn was examined in rabbit eyes exposed to an Argon c. w. laser (4,880 A) for 10 seconds. The posterior pole of the eye was surgically exposed and a 20-micron tip diameter probe was inserted into the ocular fundus to measure temperature rises. The temperature rise for threshold burns linearly increased as pre-exposure fundus temperature decreased, implying a constant threshold temperature. Threshold temperature was indirectly predicted to be 52.4° C. using a system with an estimated error of ± 0.4° C.

The need for understanding the nature of retinal injury from intense light increases each year. Consequently, development of a reliable model of retinal damage has been actively pursued. However, such a model requires accurate temperature measurement associated with retinal lesion formation. Such temperature measurements have been made in rabbit and monkey eyes with thin-film copper-nickel microthermocouples specifically designed for measuring temperature transients in tissue at The University of Texas. These temperature measurements have shown good agreement with temperatures predicted with a finite difference solution to the heat conduction equation in the retina.

The threshold lesion temperatures (temperatures associated with formation of a minimum ophthalmoscopically visible lesion) measured with these microthermocouples have also shown agreement with computed temperatures based upon corneal power necessary to produce a threshold burn. Ward and Bruce estimated threshold lesion temperatures by correlating body temperature with threshold retinal irradiance. They assumed a linear relation between retinal irradiance and body temperature. Furthermore, they predicted that a threshold lesion due to a 100 ms. exposure would require a fundus temperature at the site of the burn of 44° C. This would represent a temperature rise of 7° C. with respect to normal body temperature.
The recently developed capability of measuring temperatures in the retina in vivo allowed us to test their hypothesis and obtain direct evidence for examining the relationship between threshold temperature rise and pre-exposure fundus temperature. Microthermocouples 10 to 20 microns in diameter were used to measure the temperature rise necessary to produce a threshold ophthalmoscopically visible lesion five minutes after a 10-second Argon laser exposure. Such measurements were recorded for various pre-exposure ocular fundus temperatures.

Experimental procedure.

Apparatus. The temperature output was amplified and displayed on a Clevite Brush Mark 200 8-channel strip chart recorder. The overall bandwidth of the system was about 90 Hz. Near steady-state temperature rises were accurate to approximately ± 5 per cent (assuming a minimum of 10° C. rise for lesion production).

The eye was irradiated by a Spectra-Physics Model 166-03 Argon laser, tuned to a primary wavelength of 4,880 A. Pulse length was controlled with an electronic shutter, from Vincent Associates, Model 23XDB2X5, in conjunction with a Devices Sales Ltd. digital timer. The ocular fundus was viewed with a Zeiss Fundus Camera. Mounted immediately beyond the fundus camera lens was a beam splitter to allow viewing of the fundus while half the energy from the Argon laser was directed into the eye. The fundus camera was used to observe image location and lesion formation on the fundus.

Radiant energy was measured with an EG & G Model 580 Radiometer with a narrow beam adapter and 25A Detector Head. Neutral density filters were placed in the laser beam path to control intensity. Retinal images 200 μm in diameter were obtained by placing a 30 cm. focal length lens in the laser beam to produce a near Maxwellian view to the rabbit eye.

Laboratory procedure. Mixed breed, pigmented rabbits were anesthetized and the posterior pole of the left eye was surgically exposed. The surgical procedure and insertion of the microthermocouple has been reported elsewhere. In addition to measuring fundus temperature, both body temperature and tissue temperature at the back of the eye were monitored. A Sears heat lamp was used to control fundus temperature prior to laser irradiation.

The tip of the microthermocouple was moved just beyond the retinal layers into the vitreous (to minimize conduction effects), and 5 ms. laser pulses were applied to the eye. The animal was rotated until the probe was in the center of the image (presumably the point of maximum direct absorption for the sensor in an image with a Gaussianly distributed intensity profile). A measurement of the intensity distribution of the retinal image was obtained by rotating the animal through the beam. Temperature due to direct absorption of light by the probe was measured for 5 ms. laser pulse. Rotation about the center of the lens system resulted in minimal movement of the image in space at the plane of the fundus.

After the relative intensity of the retinal image had been measured, the laser beam was moved approximately 1 mm. away from the sensor, and an irradiation series was conducted to determine the minimum corneal power for producing an ophthalmoscopically visible lesion. Locations within 1 mm. of the sensor were irradiated at decreasing power levels for 10-second intervals, until the minimum power that produced a lesion within five minutes after exposure was obtained. The animal was then rotated to impinge the laser upon the thermocouple and the sensor was retracted to the center of the pigment epithelium (PE). This position was obtained experimentally by applying short nondestructive 50 ms. laser pulses and adjusting the position of the sensor until the location of maximum temperature rise was achieved which theoretically occurs in the center of the beam and center of the PE. A ten-second pulse at one-fourth the power necessary for a threshold lesion was applied and temperature rise was recorded on the Brush Recorder.

The sensor was repositioned to correct possible movement of the animal or shift of the image, and full threshold power was delivered to the site. All experimental subthreshold temperature rises were kept below 8° C.

The temperature rises associated with the subthreshold laser pulses were linearly extrapolated with respect to the corneal power that produced a threshold lesion. Thus, when subthreshold and threshold temperatures were measured, two threshold temperatures were obtained—one from the extrapolated subthreshold temperature, and one from the threshold exposure. This relationship was based on the linearity between corneal power and temperature in the ocular fundus reported by Cain and Welch.5

Results. Data were taken from twenty rabbits, three of which had two sensor insertions and a fourth of which had three insertions. In addition to threshold measurements, subthreshold measurements were obtained from nine of these rabbits (including two of the double insertions and the triple insertion). These subthreshold measurements were extrapolated to threshold temperatures. A total of twenty-seven usable measured and extrapolated thresholds temperatures were obtained during this research.

Fig. 1 is a plot of threshold temperature rise vs. fundus temperature before laser irradiation. Minimum and maximum fundus temperatures were 30° C. and 44.5° C., respectively. The data best fit (in a least squares sense) a straight
Fig. 1. Threshold temperature rise vs. pre-exposure fundus temperature.

line of slope $m = -1.15$ and x-intercept 52.4° C. Threshold temperatures determined by extrapolation of subthreshold temperatures are depicted by open circles. The dashed line indicates linear extrapolation beyond the data to the abscissa.

Discussion. Fundus temperature prior to laser exposure and threshold temperature rise appear to be linearly related (see Fig. 1). However, the data are insufficient for accurate definition of the relationship between these two variables. Nevertheless, if one assumes a linear relationship, extending to the abscissa, a fundus temperature of 52.4° C. is predicted as the threshold temperature for lesion production.

Though the validity of such a linear extension of the data is questionable, especially for elevated pre-exposure fundus temperatures, agreement with existing data is good. The authors have measured 10-second exposure threshold temperatures in rabbits with a 54° C. mean and 3.1° C. standard deviation. Also, Priebe, Cain, and Welch have obtained 10-second exposure threshold temperatures in Rhesus monkeys with 61° C. mean. Agreement such as this lends support to the supposition of a linear relation between threshold temperature rise and pre-lesion fundus temperature within a moderate range of pre-exposure fundus temperature. Consequently, threshold temperature appears to remain constant throughout this range.

However, the range of pre-exposure fundus temperature presented in this research is only 7° C. below and 7.5° C. above body temperature. One would expect that a critical pre-exposure temperature could be exceeded such that the tissue temperature would contribute to the formation of thermal damage.

Conclusions. The conclusions of this research are that within a moderate range (14.5° C.) of pre-exposure fundus temperature, measured threshold temperature increases linearly as pre-lesion fundus temperature is decreased. Consequently, threshold temperature appears to remain constant. Finally, linear extrapolation of the pre-exposure fundus temperature vs. threshold temperature rise relationship suggests a threshold fundus temperature of 52.4° C.

Key words: Ocular burn, thermal damage, photocoagulation, retina, retinal temperature, model, microprobe, thermocouple, Argon laser, temperature.

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Full-thickness eye wall biopsy. II. In primates. Golam A. Peyman, Paul Homer, Richard Kasbeek, and Joseph Vlcek.

We devised a technique to perform an intact full-thickness eye wall biopsy in primates. An eye basket is sutured to the eye wall for stabilization. Trephines demarcate and incise a 4 to 7 mm. circumferential area of sclera; diathermy deepens the incision until perforation is achieved. The biopsy specimen is removed and immediately fixed for histologic evaluation, and the eye wall defect is covered by a 7 mm. scleral homograft. Our results showed that histologically excellent biopsies can be obtained with minimal damage to the eye.

Diseases such as retinitis pigmentosa and uveitis are visible and well described clinically but are poorly understood pathogenetically. We felt that chorioretinal pathology could be studied more precisely if there were a method to take a small biopsy specimen of the eye wall without disturbing ocular function. In light of recent successful whole wall resections in animals and humans and good preliminary eye wall biopsy results in rabbits, we attempted to do biopsies on specious monkey eyes.

Materials and methods. Eight eyes from five specious monkeys were used in this study. The monkeys were sedated with intramuscular phencyclidine and anesthetized with intravenously administered thiamylal. Proparacaine hydrochloride was dropped onto the eye for anesthesia as needed. The pupil was dilated with 1 per cent cycloplegic hydrochloride and 10 per cent phenylephrine hydrochloride. A large temporal canthotomy and peritomy were performed. The side arms of the eye basket were positioned perilumbally beneath the superior and lateral rectus muscles and sutured to the sclera with 8-0 running black silk. A scleral incision was made to the choroid with a 7 mm. trephine. Another incision was made centrally within the first one with a 4 mm. trephine. Diathermy was applied between these two incisions until perforation was achieved. The specimen was excised with corneal scissors and immediately fixed in a neutral buffered solution of 1 per cent formaldehyde - 1 per cent glutaraldehyde. Small amounts of vitreous (0.2 to 3 ml.) protruding through the biopsy site were cut with scissors. A scleral homograft (7 mm. in diameter) that had been presoaked in 8 μg per milliliter of gentamicin sulfate was sutured to the area of resection, using running 7-0 chromic suture. Intraocular pressure was restored with 8 μg per milliliter of gentamicin sulfate in normal saline. The conjunctiva and canthotomy were closed with 5-0 chromic gut.

The monkeys received systemic oxytetracycline (Terramycin) for five days. They were observed daily for the first week following the procedure, and weekly thereafter. Prior to death, electroretinograms were done and compared to those of unoperated contralateral eyes. They were killed at intervals from four to twelve weeks.

All eyes were enucleated and immediately fixed in a neutral buffered 1 per cent formaldehyde-1 per cent glutaraldehyde solution. Seven of the eight eyes from which biopsies were taken were dehydrated in ethanol and chloroform, then embedded in paraaffin. Histologic sections were cut on a microtome. The sections were stained with hematoxylin and eosin and examined by light microscopy.

The eighth eye and all of the biopsy specimens were prepared for electron microscopy as previously described. Results. Seven of eight eyes tolerated the procedure well (Table 1) with minimal loss of vitreous and little or no hemorrhage at the site of the graft.

Eye No. 5, which received a friable scleral graft that detached while intraocular pressure was being restored, had large vitreal loss and the graft had to be resutured. It never regained its preoperative configuration.

The seven eyes were quiet, the fundi clear, and intraocular pressures normal at the time of death. They had well demarcated white scleral grafts surrounded by chorioretinal scar (Fig. 1) formation. Indirect ophthalmoscopic examination before and after the biopsies revealed no evidence of retinal detachment or degeneration.