has reported similar observations in a human case of postganglionic Horner’s syndrome.

The clinical application of long posterior ciliary canal cautery has met with equivocal success in the treatment of glaucoma.5-10 We have found it clinically ineffective in secondary glaucoma. Histologic sections of two such eyes did not reveal closure of the long posterior ciliary arteries one month after treatment.

From our experimental results it is clear that closure of the long posterior ciliary vessels is difficult to obtain by cautery in primates. This appears due to difficulty in localizing the vessels, their depth in the suprachoroid, and impermanence of vessel closure. The significant reduction of intraocular pressure noted for at least four weeks in this study is believed to be due to a reduction in blood flow to the ciliary body. The extent to which sympathetic denervation contributed to this intraocular pressure lowering effect is under investigation.

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REFERENCES


The nature of chorioretinal lesions produced by the gallium arsenide laser.*

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Technical modifications of the gallium arsenide laser have recently permitted its emission of sufficient power to produce ocular damage. The emitted radiation at 8,600 A is in the visible spectrum and, hence, primarily damages the retina. Ophthalmoscopically, the lesions are torted of well-defined opacity surrounding small central circles of lesser opacity. The lesions are histopathologically characterized by extensive damage to pigment epithelium and outer retina. The damage is irregular, consisting of extensive damage at the periphery of the burn accompanied by relative sparing of the centers. Furthermore, damaged areas are circular despite an elliptical beam emitted from the laser. The lesions resolve by phagocytic removal of destroyed retina and by reconstitution of pigment epithelium; significant gliosis does not occur. These findings suggest the gallium arsenide laser damages the retina by thermal means, though producing peculiar lesions that are both circular and uneven.

Technical advances have now resulted in development of a gallium arsenide laser which can
emit sufficient energy at a wavelength of 8,600 Å to produce chorioretinal burns. The present communication reports the histologic and ophthalmoscopic character of the burns which have not been heretofore documented.

Irradiation of animals. Details of the laser irradiation facility and animal manipulations are reported elsewhere. In brief, anesthetized rhesus monkeys were placed in a mount; and a helium-neon laser of low output, which was aligned colinearly with the gallium arsenide laser, was focused on their retinas at predetermined loci. The retinas were then exposed for one second to the gallium arsenide laser operating at various levels of power output. The laser produced a pulse-train of 500 nanosecond pulses at a 120 KHz. repetition rate and emitted 20 to 130 milliwatts of power at 8,600 Å.

Preparation of tissues. Retinas from nine rhesus monkeys were exposed to laser pulses, so that lesions were produced at the EDa (level at which 20 per cent of the exposure sites are damaged as judged by ophthalmoscopic observation), EDn, and 2EDn levels of power. Lesions, ranging in age from one hour to 28 days were placed nasal to the optic disc, between the optic disc and the macula, in the macula, and temporal to the macula. Lesions of various types and ages were sampled from all areas and all eyes. Two-hundred fifty lesions from 13 eyes were studied.

Ophthalmoscopy. One hour after exposure to the laser, fundi were viewed through a direct ophthalmoscope (Fig. 1, A). The easily visible lesions, circular and well-circumscribed, had a doughnut shape—a central punched-out area surrounded by a peripheral ring. Retinal arterioles, venules, and capillaries crossed the lesions without apparent interruption. Retinal pigment epithelium as well as choroid in the lesions appeared to have undergone alteration.

Histology at one hour. Damage is centered about pigment epithelium and outer segments (Fig. 2). Centrally, pigment epithelium is generally necrotic or completely destroyed, but occasionally it is only vacuolated or swollen. Outer segments of rods and cones are completely destroyed to form large vacuoles in the subretinal space. Discharged pigment from pigment epithelium floats free in the vacuoles. Inner segments of rods and cones are generally swollen and eosinophilic; but over areas of extensive damage to pigment epithelium, they are necrotic and even completely destroyed. Damage extends into the outer nuclear layer, which is edematous and where nuclei are swollen, shrunken, or even lost. Other retinal layers are unremarkable. Beneath damaged pigment epithelium, Bruch's membrane is swollen, eosinophilic, and pushed into the choroid. The choriocapillaris is generally obliterated and the remaining choroid is slightly inflamed.

The lesions are particularly striking in that many display the most extensive damage at the edges rather than centrally (Fig. 3). In such cases, the centers of the lesions are relatively spared. At the periphery of such lesions, necrosis of pigment epithelium and vacuolization and destruction of rods and cones are prominent. Examination of these eccentric lesions on flat preparations demonstrates a central circle of unremarkable or slightly-swollen pigment epithelium surrounded by a ring of completely destroyed pigment epithelium (Fig. 1, B). Reconstruction of the lesions by serial sections confirms the doughnut configuration. In some eccentric lesions, spared outer retina is overlaid by vacuoles formed by extensive coagulative and lytic necrosis of inner segments and outer nuclear layers; this gives rise to three major foci of damage (Fig. 4). The eccentric configuration was present in 41 out of
Fig. 2. Photomicrograph of an acute chorioretinal lesion. Damage is centered upon pigment epithelium and rods and cones which are mostly necrotic. Note relative sparing of pigment epithelium centrally and complete destruction of pigment epithelium peripherally. (Hematoxylin and eosin, x500.)

59 (70 per cent) acute and one-day-old lesions of all power levels.

Lesions produced by the 2×ED₀ level of power closely resemble the above lesions but are larger (approximately 280 microns as opposed to approximately 160 microns) and characterized by more destruction. Lesions produced at the ED₀ level of power do not conform to the above description. These lesions are difficult to detect and when found are very small (25 microns). They are characterized only by swelling, necrosis, and destruction of a few pigment epithelial cells underlying small vacuoles in the subretinal space.

One day. Lesions now have more necrosis and destruction in the center of the lesions. Pigment epithelium, inner segments, and outer segments are generally necrotic and at the periphery there is definite coagulative necrosis. Vacuoles in the subretinal space are smaller than at one hour and partially filled by necrotic debris and occasional phagocytic cells. A doughnut shape is still discernible but the central cells, which previously appeared to be spared, now display coagulative necrosis and destruction so that the entire width of damaged pigment epithelium is visibly altered.

Three to five days. Lesions are now definitely smaller. The subretinal space is almost completely filled with amorphous, coagulated debris though small irregular vacuoles are still seen. Within the subretinal space are large numbers of ameboid phagocytes, containing phagocytosed pigment and necrotic debris. The thinned overlying outer nuclear layer dips outward into the subretinal space and is edematous. Remaining nuclei in the outer nuclear layer, about half of the normal complement, are small and dark. Pigment epithelium generally has the appearance of regenerating epithelium. Bruch's membrane is still swollen and eosinophilic. The choriocapillaris is still partially obliterated, and leukocytic infiltration into the choroid remains.

Seven days and after. Lesions are considerably smaller than their original size. Pigment epithelium is still rough and irregular. Areas of the subretinal space previously occupied by vacuoles are now filled with amorphous eosinophilic material and phagocytic cells heavily laden with pigment. The overlying outer nuclear layer, which is thinned and depleted of nuclei, dips into the former vacuolar space and its nuclei remain dark and condensed. The inner nuclear layer is thickened and dips toward the depressed outer nuclear layer. The ganglion cell layer shows disruption, loss of ganglion cells, edema, nuclear dropout, and loss of eosinophilic substance. Rods and cones surrounding the lesions appear to have no alterations. After seven days, lesions are relatively inconspicuous. Pigment epithelium is smooth and

Fig. 3. The acute response. This section particularly demonstrates the central sparing. (Hematoxylin and eosin, x337.5.)

Fig. 4. The acute response. This section typifies those lesions characterized by three major loci of damage. Two major loci are centered on the pigment epithelium and a third locus is in the outer nuclear layer and superficial rods and cones. Between the three loci, rods and cones are swollen but not destroyed. Note extension of the damage into the outer plexiform layer. (Hematoxylin and eosin, x500.)
A) lasers have been described. In general, wavelength (8,600 Å) employed in this study, humping or peaking of outer retina into inner retina were not observed in this study. While these differences could result from the different wavelength (8,600 Å) employed in this study, such an explanation is doubtful. First of all, these reactions have been described in lesions produced by wavelengths both below and above the wavelength of the gallium arsenide laser. Second, neither extensive destruction to inner retina or “humping” have been observed in this laboratory in multiple studies of lesions produced by the argon, Ruby, and neodymium lasers. Consequently, we attribute these differences to factors other than the wavelength of the gallium arsenide laser. For example, the fact that animals in this laboratory are routinely perfused intravitaly with fixative before enucleation of the eyes might account for these differences.

The lesions produced by the gallium arsenide laser, however, are quite striking in one regard: their doughnut or eccentric shape of heavy peripheral change and slight central damage. This odd configuration, confirmed by ophthalmoscopy, direct histology, examination of flat preparations, and serial reconstructions of the lesions, is not unique to the gallium arsenide laser. Although it has not been previously described, it has been observed in this lab in lesions induced by the argon laser. The cause of the peculiar configuration is not known, but apparently does not relate to the shape of the beam which has been demonstrated to produce a solid rectangle at the focal plane of any well-behaved optical system. The shape of the lesions could relate to unevenness in heat transfer in the retina. It also could be suggested that an original central vacuole in the subretinal space, presumably filled with steam, acts as a lens to diverge the laser beam. This latter suggestion is supported by the finding of three vacuoles in many lesions. Since the peculiar configuration is also seen in lesions induced by the argon laser, though not in lesions produced by the Q-switched Ruby laser and argon lasers (1,000 and 125 milliseconds, respectively, as compared to the 20 nanoseconds of the Q-switched Ruby laser) may be involved. If so, this also suggests diffraction of the laser beam by the original laser-induced lesions. At present, the eccentric configuration of certain laser-induced lesions remains unexplained.

Lesions produced by the gallium arsenide laser are striking in yet another regard. Although the laser emits a beam in the shape of an elongated ellipse (20 x 170 μ), histopathology and ophthalmoscopy show that the chorioretinal lesions are circular. This is also shown by serial reconstructions and by examination of flat preparations. The present data present no clues which would explain this paradox. It may be speculated that the eye focuses the oval beam on the eye not as such but as a circle, or that retinal factors such as uneven heat transfer and slow thermal relaxation time produce this effect. To date, we have not been able to resolve this question.

Finally, healing of the lesions induced by the gallium arsenide laser takes place by reconstitution of pigment epithelium and filling of subretinal vacuoles with amorphous debris and pigment-laden macrophages. Evidence of significant chorioretinal welding, fibrosis, or gliosis was not found. The present data would not, therefore, encourage use of the gallium arsenide laser as a clinical photoagulator.


*In conducting the research described in this manuscript, the investigators adhered to the Guide for Laboratory Animal Facilities and Care, as promulgated by the Committee on the Guide for Laboratory Animal Facilities and Care of the Institute of Laboratory Animal Resources, National Academy of Sciences, National Research Council.

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Cyclic-AMP in ocular tissues of the rabbit, monkey, and human. Arthur H. Neufeld and Marvin L. Sears.

The ability of various ocular tissues to make cyclic-AMP and release it into the media has been determined. The posterior chamber contains little, if any, cyclic-AMP either before or after administration of epinephrine to the rabbit eye; therefore, neither the lens nor the ciliary body contributes to the aqueous humor of the anterior chamber, the cyclic-AMP which correlates with the intraocular pressure response. In vitro, tissues lining the anterior chamber such as the cornea, iris, and sclera-trabecular tissue make cyclic-AMP in response to various agonists and can release cyclic-AMP into the incubation media. Of particular interest, is the response of the sclera-trabecular tissue with contains the cells lining the channels for the outflow of aqueous humor. Cyclic-AMP in this tissue may play a role in the regulation of intraocular pressure.

Cyclic-AMP is found in the aqueous humor of the rabbit,\(^1\) monkey, and man (unpublished observations). Following the topical administration of adrenergic agonists, a decrease in intraocular pressure occurs that correlates well with an increase in the concentration of cyclic-AMP in the aqueous humor.\(^1\) To understand more fully the mechanism by which adrenergic agonists lower intraocular pressure, we have attempted to determine the tissue of origin of the cyclic-AMP. In this report we compare aqueous humor from the anterior chamber and posterior chamber of the rabbit for cyclic-AMP content and in vitro ocular tissue levels of cyclic-AMP of the rabbit, monkey, and human in response to various adrenergic agonists.

**Anterior and posterior chambers.** The eyes of rabbits, anesthetized with sodium pentobarbital, were proposted and aqueous humor from the anterior chamber and then the posterior chamber was sampled. Cyclic-AMP levels were determined as previously described.\(^1\) Table I compares the cyclic-AMP concentration in aqueous humor from the anterior chamber and the posterior chamber 30 minutes after topical treatment with isotonic saline or with epinephrine (Sigma) in saline.

<table>
<thead>
<tr>
<th>Chamber</th>
<th>Control</th>
<th>30 minutes after 1% epinephrine</th>
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<tbody>
<tr>
<td>Anterior</td>
<td>27 ± 2 (7)(^*)</td>
<td>45 ± 5 (10)</td>
</tr>
<tr>
<td>Posterior</td>
<td>3 ± 2 (7)</td>
<td>4 ± 2 (9)</td>
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*All values in this and succeeding tables are mean ± S.E.M. (number of observations).*