Experimental glaucoma in the rhesus monkey. DOUGLAS GAASTERLAND AND CARL KUPFER.

Repeated, circumferential argon laser photocoagulation of the trabecular meshwork area of the anterior chamber angle of normal Rhesus monkeys causes a sustained elevation of the intraocular pressure and marked reduction of the outflow facility. During the observation period of this study, cupping of the optic nervehead developed. Preliminary histopathologic examination revealed localized scarring of the anterior chamber angle structures. Retinal and optic nerve changes, similar to those seen in human chronic, open-angle glaucoma, were seen. The method to produce this experimental glaucoma is reported.

To allow in-depth study of the physiology and pharmacology of glaucoma, an experimental animal model is required. A number of attempts have been made in this direction.1-7 In each case, the methods used have produced either a generalized damage to the eye or a pressure rise of insufficient duration to cause selective loss of retinal ganglion cells.

The present report describes a new method for the production of sustained, elevated intraocular pressure in the Rhesus monkey. This is accomplished by specific alteration of the outflow pathways induced by argon laser photocoagulation. Six Rhesus monkeys, weighing 3 to 4 kilograms each, were used. Baseline examination, under phencyclidine (Sernylan) catalepsia, showed eyes with normal anterior chamber angles, normal intraocular pressure (11 to 14 mm. Hg, Perkins applanation tonometer), clear ocular media, and normal optic nerveheads. One monkey served as a control. Following baseline examination, each of the remaining five monkeys was anesthetized with systemic pentobarbital and placed in front of the slit lamp delivery system of the argon laser (Coherent Radiation). Both eyes of each of the five monkeys were treated with topical proparacaine 0.5 per cent (Ophthaine) and photocoagulated using a modified Koeppe-type goniolens (Jocson modification, Hansen Optical Instruments, Iowa City, Iowa) with hydroxypropyl methylcellulose 2.5 per cent as the filling fluid. Approximately 200 laser applications were made to each eye, aimed at the middle of the trabecular meshwork, using a 50 μ beam diameter, 0.2 to 0.5 second duration and 0.4 to 0.8 watts of power. Power selection was based upon adequate tissue reaction being observed immediately after initial applications. Slit lamp and fundus examinations and measurement of intraocular pressure levels were repeated under phencyclidine catalepsia every five to eight days. Retreatment of the anterior chamber angle with the laser was done if there was no clinical evidence of anterior chamber inflammation for two weeks, and the intraocular pressure remained normal. In three eyes this aspect of the protocol was not strictly followed. Instead, in these non-inflamed eyes after two treatments no additional photocoagulation was done.

Table I. Intraocular pressures before and during intervals after laser photocoagulation of entire circumference of the monkey anterior chamber angle. Outflow facility after photocoagulation.

<table>
<thead>
<tr>
<th>Monkey</th>
<th>Eye</th>
<th>Before treatment</th>
<th>After laser photocoagulation of angle</th>
<th>Outflow facility* (μl min⁻¹ mm. Hg⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Intraocular pressure (mm. Hg)</td>
<td>First</td>
<td>Second</td>
</tr>
<tr>
<td>1</td>
<td>RE</td>
<td>10-12</td>
<td>11-50</td>
<td>0.05</td>
</tr>
<tr>
<td>2</td>
<td>LE</td>
<td>11</td>
<td>4-10</td>
<td>8-16</td>
</tr>
<tr>
<td>3</td>
<td>RE</td>
<td>12</td>
<td>9-12</td>
<td>7-11</td>
</tr>
<tr>
<td>4</td>
<td>LE</td>
<td>12</td>
<td>2-14</td>
<td>10-14</td>
</tr>
<tr>
<td>5</td>
<td>RE</td>
<td>14</td>
<td>7-11</td>
<td>6-10</td>
</tr>
<tr>
<td>Control</td>
<td>LE</td>
<td>12</td>
<td>4-7</td>
<td>7-8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>13</td>
<td>10-30</td>
<td>12-50</td>
</tr>
<tr>
<td></td>
<td>LE</td>
<td>11</td>
<td>10-20</td>
<td>20-42</td>
</tr>
<tr>
<td></td>
<td>RE</td>
<td>12</td>
<td>5-10</td>
<td>11-19</td>
</tr>
<tr>
<td></td>
<td>LE</td>
<td>12</td>
<td>5-11</td>
<td>12-23</td>
</tr>
</tbody>
</table>

* Determined by in vivo perfusion four to 12 weeks after last laser photocoagulation of anterior chamber angle.

† Range of pressures during interval.
done despite near normal intraocular pressure. Four to ten weeks after the last photocoagulation treatment, in vivo perfusion of the anterior chamber was performed in all monkeys by a constant-pressure method similar to that used by Grant for enucleated eyes.⁴ ⁵

The observation period reported here was four to twelve weeks after the last photocoagulation treatment. Results are summarized in Table I. The eyes underwent two to four treatments. The usual inflammatory reaction was one-plus flare and cells in the anterior chamber on the second day after treatment. This declined to no reaction by ten to twelve days. The maximum inflammatory reaction, observed in one eye, was three-plus flare and cells in the anterior chamber on the fifth day after treatment. This took three weeks to resolve.

Seven out of ten eyes in the five treated monkeys developed elevated intraocular pressure. In four of these eyes, the onset of the elevation occurred during the first eight days after treatment. In one eye, onset occurred between five and...
eleven days after treatment. In two eyes, onset occurred between four and 25 days after treatment. In these seven eyes, pressure ranged from 24 mm Hg to slightly more than 50 mm Hg. (The upper limit of the Perkins tonometer is 50 mm Hg.)

Cupping of the optic nervehead developed during the observation period in six out of the seven eyes.

In one monkey, the pressure in one eye ranged from 6 to 16 mm Hg after two photocoagulation treatments. The eye was not inflamed. In a second monkey, the pressure in one eye was 20 mm Hg seven days after the second treatment. This subsequently fell to normal values. The pressure in the other eye of the same animal was 12 mm Hg seven days after the second treatment; it rose to 24 mm Hg by 30 days after the second treatment, but was normal at 40 and 50 days. No change of the optic nervehead from normal occurred in these three eyes.

Outflow facility, determined in vivo, was impaired in all treated eyes. The values obtained ranged from 0.02 to 0.11 μl min⁻¹mm⁻²mmHg⁻¹ (normal values: 0.33 to 0.75 μl min⁻¹mm⁻²mmHg⁻¹).

Histopathologic specimens have been prepared from the two control eyes and from four eyes which had developed elevated intraocular pressure and cupping of the optic nervehead. Preliminary examination has shown trabecular scarring with obliteration of the canal of Schlemm in the treated eyes (Fig. 1). In the retina, a selective loss of ganglion cells and thinning of the nerve fiber layer has been observed (Fig. 2). Cupping of the optic nervehead, with posterior bowing of the lamina cribrosa, has been verified (Fig. 2). No extensive cavernous degenerative change was seen in the optic nerves.

The experimental ocular hypertension presented here differs from previous models in several ways. First, the sustained elevation of intraocular pressure is produced by use of a noninvasive technique. Second, the mild to moderate initial inflammation, caused by the photocoagulation, is transient, usually lasting less than two weeks. Third, the primary alteration induced in the eye is localized to the region of the aqueous humor outflow pathways. That this experimental ocular hypertension is a glaucoma is indicated by the observed development of cupping of the optic nervehead and by the selective loss of retinal ganglion cells in histopathologic specimens.

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REFERENCES


Permeability of the isolated rabbit cornea to corticosteroids. DAVID S. HULL, JAMES E. HINE, HENRY F. EDELHAUSER, AND ROBERT A. HYNDIUK.

Isolated rabbit corneas were mounted in a perfusion chamber, and the corneal permeability of four tritiated corticosteroids was determined. With the epithelium intact, corneal permeability to dexamethasone sodium phosphate was significantly lower than to prednisolone sodium phosphate, prednisolone acetate, and fluorometholone. With the epithelium removed, the corneal permeability to dexamethasone sodium phosphate and prednisolone sodium phosphate increased three- to four-fold while the corneal permeability