Laser-Induced Primate Glaucoma

I. Progression of Cupping

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• Sustained intraocular pressure elevations were induced in 15 monkey eyes by argon laser photocoagulation of the trabecular meshwork. Large fluctuations of IOP resulted. Posttreatment gonioscopy revealed an open angle with scattered low peripheral anterior synechiae. Optic disc cupping progressed during pressure elevations, manifested first as posterior bowing of the optic nerve head and peripapillary tissues. Reversal of this early phase of cupping occurred in eight eyes during spontaneous normalization of IOP. In most eyes, as cupping evolved from saucerization to a deeper cup, the cup remained round. In four eyes, focal sloping of the cup to the inferotemporal rim occurred with nerve fiber layer defects. Total cupping with undermining of the rim occurred in five eyes with prolonged IOP elevation. Laser-induced primate glaucoma has features in common with juvenile human glaucoma and is a useful model for the study of cupping of the optic nerve head.

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Argon laser photocoagulation of the trabecular meshwork has recently gained favor in the treatment of open-angle glaucoma.[1] If the entire circumference of the trabecular meshwork is treated, approximately 10 joules of energy are used. However, laser photocoagulation can induce glaucoma in monkey eyes if more than 50 joules are applied to the trabecular meshwork.[2,3] Laser-induced primate glaucoma is typified by large fluctuations in intraocular pressure, allowing for study of the progression and reversal of cupping.[4] To our knowledge, the clinical features of optic disc changes have not been described. The present report describes the clinical features of laser-induced glaucoma in the monkey, with special emphasis on the development of cupping of the optic nerve head.

See also pp 1604, 1626, 1629, 1693, and 1699.

MATERIALS AND METHODS

Fourteen monkeys, ten rhesus and four cynomolgus, initially weighing 2.5 to 7.1 kg, were used in this study. Pretreatment optic disc photographs and IOP measurements were made. With the use of pentobarbital sodium anesthesia, 15 eyes underwent argon laser photocoagulation of the trabecular meshwork with an argon laser photocoagulator (Coherent model 900) using a small Koeppe lens or single-mirror Goldmann goniolens. Laser settings were as follows: 50 μm, 700 to 850 mW, 0.5 to 1.0 s, and 38 to 115 spots (average, 71 spots). Confluent laser burns were made on the light-gray trabecular meshwork. The laser spot was moved circumferentially, in a "painting" fashion, during the burn. If no IOP elevation occurred within several months, the treatment was repeated.

All eyes were examined weekly, when possible, with the use of intramuscular ketamine hydrochloride anesthesia. Tests included slit-lamp examination, IOP measurement with a tonometer (Perkins), and optic disc photographs with a fundus camera (Zeiss). The animals were killed at varying intervals to obtain representative samples for histopathologic determinations.

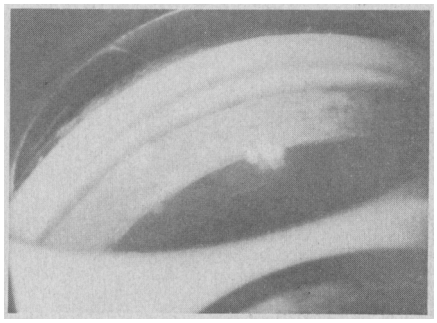

Fig 1.—Gonioscopic appearance of angle structures two months following laser photocoagulation of trabecular meshwork. Irregular pigmentation of trabecular meshwork is noted, with several low peripheral anterior synechiae.

RESULTS

Prior to the laser treatment, no animal exhibited appreciable optic disc cupping. A small-diameter, shallow depression was sometimes noted in the center of the optic disc, measuring less than 0.1 cup-disc ratio. All animals had pretreatment IOPs between 10 and 20 mm Hg.

During the laser treatment, the trabecular meshwork would blanch markedly, with visible swelling and bubble formation. Because of the long duration of the laser burn, the area of blanching would expand onto the ciliary body band, which was more heavily pigmented than the trabecular meshwork. Immediately following the laser treatment, mild iridocyclitis developed in all eyes, with anterior chamber flare and cells (+1 on a scale of 1 to 4). The anterior chamber reaction cleared within three to four weeks. Frequently the IOP fell for about one week. If the IOP subsequently rose, it occurred one to two

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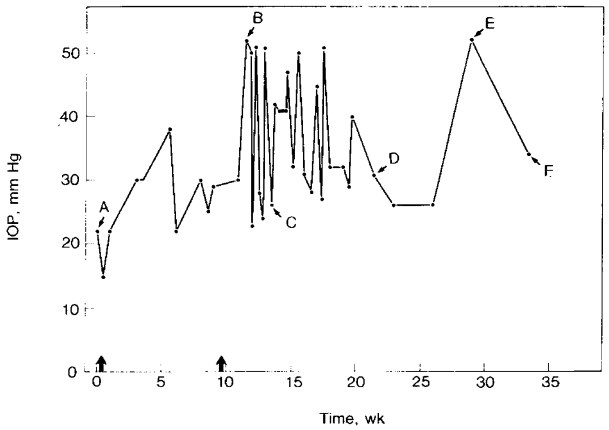

Fig 2.—Intraocular pressure of monkey eye 6, with disc photographs shown in Fig 4. Letters A through F correspond to Fig 4, A through F. Solid arrows indicate laser treatments.

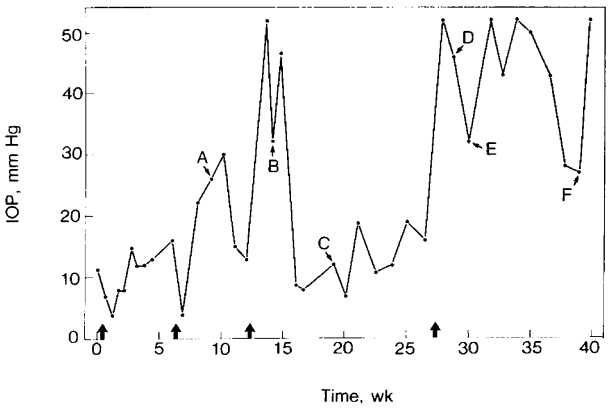

Fig 3.—Intraocular pressure of monkey eye 13, with disc photographs shown in Fig 5. Letters A through F correspond to Fig 5, A through F. Solid arrows indicate laser treatments.

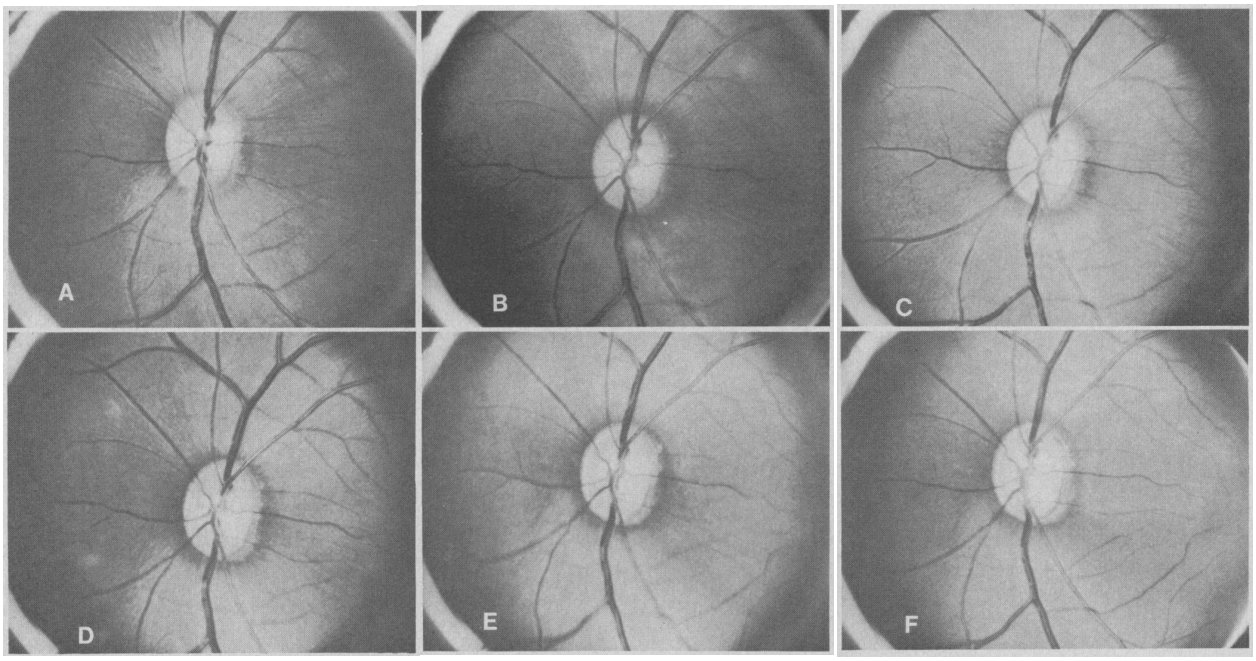

Fig 4.—Disc photographs for monkey 6: A, pretreatment; B, following laser treatment, slight saucerization, and peripapillary shadow; C, reversal of cupping and loss of peripapillary shadow; D, minimal increase in cupping; E, more cupping; F, more extensive cupping, with nerve fiber layer thinning inferiorly.

weeks following the laser treatment. Gonioscopic examination after laser treatment in all eyes revealed an open angle, with indistinct angle structures, pigment mottling of the trabecular meshwork, and scattered, low, tentlike peripheral anterior synechiae (to ciliary body or scleral spur) (Fig 1). More than one laser treatment was usually required to produce a permanent IOP rise. The IOP rise was rapid, followed by alternating periods of normal and elevated IOP (Figs 2 and 3).

Fixed mydriasis, with absent light reflex, occurred in all eyes following prolonged pressure elevation. This condition was not due to stretching of the iris by peripheral anterior synechiae. Corneal edema developed during periods of extremely high IOP, occasionally interfering with adequate optic disc photographs. Since the upper limit of IOP measurement with the tonometer we used is 50 mm Hg, IOPs above that level were designated as greater than 50 mm Hg. The mean fluctuation in IOP (highest recorded IOP to lowest) was 41 mm Hg.

Progression of optic disc cupping only occurred following IOP elevations above 39 mm Hg. One eye showed no cupping, but had a maximum IOP of 37 mm Hg, with a total of only four weeks of IOP above 30 mm Hg. Cupping in the other 14 eyes typically began as conical or funnel-shaped saucerization, the change being best detected with stereoscopic viewing. Posterior bowing of the optic nerve head and peripapillary region was noted in 11 of 15 eyes. A peripapillary "shadow," detectable without stereoscopic viewing, was observed in those eyes; it was due to an increase in posterior sloping of the peripapillary region (Fig 4, B). With normalization

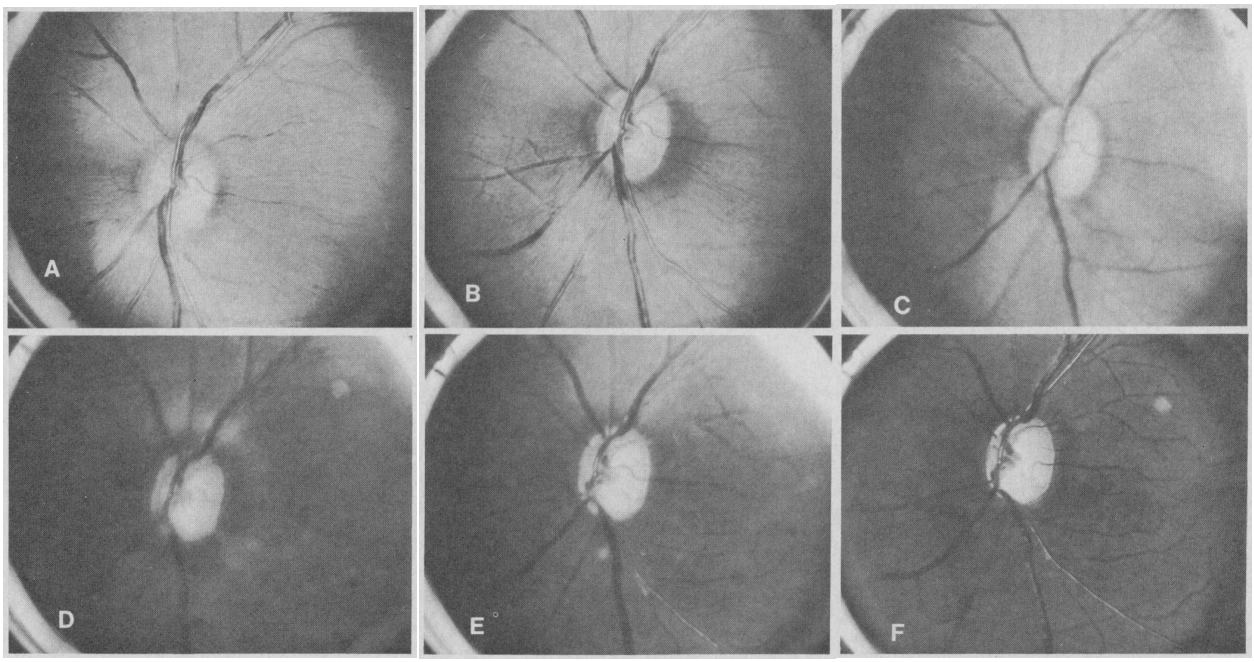

Fig 5.—Disc photographs for monkey 13: A, pretreatment; B, following laser treatment, moderate saucerization; C, early nerve fiber layer defect inferiorly; D, increased cupping and nerve fiber layer defect; E, cup extends to rim inferiorly; F, virtually total cupping, with undermining of rim and development of collateral vessel in base of cup.

Clinical Features of Monkey Eyes After Sustained Elevation of Intraocular Pressure*

Eye	Saucer-ization	Reversal of Cupping	Nerve Fiber Layer Defect	Peripapillary Shadow	Duration of Experiment, mo	No. of Laser Treatments	Total Energy, Joules	IOP Needed for Cupping, mm Hg	Final Vertical Cup-Disc Ratio
1	–	–	–	–	9	3	71	. . .	0.0
2	+	+	+	+	6	1	65	50	0.4
3	+	+	–	+	6	1	69	50	0.5
4	+	+	–	+	21	3	76	>50	0.6
5	+	–	–	–	15	2	53	>50	0.7
6	+	–	+	+	15	2	47	>50	0.8
7	+	+	–	+	10	4	110	50	0.8
8	+	+	+	+	9	4	80	39	0.8
9	+	+	–	+	6	3	137	43	0.9
10	+	+	–	+	9	4	114	43	0.9
11	+	–	–	–	8	3	63	43	1.0
12	+	–	–	–	10	5	114	47	1.0
13	+	+	+	+	9	4	90	50	1.0
14	–	–	–	+	9	3	65	40	1.0
15	–	–	–	+	6	1	60	>50	1.0
Total	12	8	4	11	. . .	. . .	. . .	. . .	. . .
Mean	. . .	. . .	. . .	. . .	10	3	81	. . .	. . .

*Plus indicates noted; minus, not noted.

of IOP (which periodically occurred spontaneously), reversal of saucerization was noted in eight of 15 eyes (Fig 4, C). After the initial phases of cupping, a gradual increase in saucerization of the optic nerve head was noted, resulting in a deeper cup with steeper walls, and an increase in the area of pallor (Fig 4, E). The cup remained round during this phase, and definite vertical ovalization of the cup was not observed. Reversal of cupping did not occur during this stage of cupping. Nerve fiber layer defects were noted in four of 15 eyes (Figs 4 and 5). Those eyes in which nerve fiber layer defects developed had corresponding thinning of the rim tissue, resulting in a slightly vertically oval cup. If the IOP elevation remained extremely high for a considerable time, total cupping with undermining of the rim ultimately occurred (Fig 5, F). No flame-shaped hemorrhages or notches of the neural rim were noted in any eye during the study. Other clinical features are summarized in the Table. The cup-disc ratio in the Table is the contour ratio, determined by stereoscopic viewing of optic disc photographs.

Discernible enlargement of the globe was often noted following IOP elevation. Immediately following removal of the eyes for histopathologic evaluation, the globe dimensions were measured. The mean (±SD) antero-

posterior dimension of ten globes was 20.7 ± 1.1 mm and the horizontal dimension was 20.2 ± 0.9 mm. Comparable dimensions of six normal monkey eyes were 18.8 ± 1.2 and 17.8 ± 0.3 mm, respectively.

COMMENT

Although several reports have outlined the technique for creating laser-induced primate glaucoma, to our knowledge the clinical features have not previously been detailed.[2-4] Primate glaucoma differs from human open-angle glaucoma in several respects. Although the angle is open in primate glaucoma, scattered, low, peripheral anterior synechiae are present. They do not extend over the trabecular meshwork and may be due to postlaser iridocyclitis from absorption of laser energy by the darkly pigmented ciliary body. Fixed mydriasis, noted in all eyes, may also be due to laser-induced damage of ciliary nerves that pass through the ciliary body and innervate the iris sphincter.

Another difference between human and primate glaucoma is the variability of the IOP. Although a direct statistical comparison cannot be made, the IOP fluctuation in primate glaucomas (41 mm Hg) is greater than in untreated human primary open-angle glaucoma, which has an average IOP fluctuation of about 15 mm Hg.[5] The IOP fluctuation in untreated human secondary open-angle glaucoma is unknown but would offer a more direct comparison.

In the early phases of cupping in laser-induced primate glaucoma, posterior bowing of the optic nerve head and peripapillary tissues was frequently observed. The posterior displacement was of sufficient magnitude to produce a characteristic shadow around the optic disc (Fig 4, B). Viewed stereoscopically, this feature was saucerization of the optic disc and surrounding tissues, creating a sloping margin, visible as a shadow. Presumably the thin monkey sclera allows the entire region to stretch posteriorly. This characteristic is not observed in older patients with open-angle glaucoma but has been described in younger patients.[6] In the early phases of glaucoma in the monkey, reversal of saucerization was observed during periods of lower IOP. This change is well described in infantile glaucoma[7] and has been noted in young adults.[6] Additional similarities between infantile human glaucoma and primate glaucoma include enlargement of the globe and corneal edema with markedly elevated IOP.

Symmetrical expansion of the cup, with later development of localized thinning of the disc rim tissue, has been noted in a longitudinal study of cupping in human adult glaucoma.[8] Similar observations were made in the present study. If the IOP remained elevated, a definite round cup would develop after the phase of saucerization. The rim tissue of the optic nerve head remained symmetrical in most eyes, but in four monkey eyes localized thinning of the disc rim tissue developed in association with nerve fiber layer defects (Figs 4 and 5).

A follow-up study of patients with childhood glaucoma found visual field defects similar to those found in adult open-angle glaucoma.[9] This finding suggests a similar mechanism of optic nerve damage in infantile and adult human glaucoma. Since primate glaucoma resembles infantile human glaucoma, by inference the primate model should be useful for studying the pathogenesis of cupping of both infantile and adult human glaucoma.

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Key Words.—Argon laser photocoagulation; experimental glaucoma; intraocular pressure; monkey eye; optic disc cupping.

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