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## Indomethacin blocks arachidonic acid-associated elevation of aqueous humor prostaglandin E.

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Arachidonic acid, a precursor of prostaglandin $E_2$ ($PGE_2$), raised intraocular pressure[1] and aqueous humor protein[2] when applied topically to the eyes of rabbits. Pretreatment with systemic indomethacin or aspirin, inhibitors of prostaglandin synthesis,[3] prevented the elevation of intraocular pressure and aqueous protein induced by arachidonic acid.[1, 2] Topical prostaglandin E (PGE) also elevated intraocular pressure and aqueous protein,[4] but indomethacin failed to block this rise of intraocular pressure.[1, 2] These data suggested that indomethacin inhibited ocular prostaglandin production from arachidonic acid. In order to elucidate the mechanism of these effects of arachidonic acid and indomethacin, similar experiments were carried out measuring aqueous humor PGE.

Albino rabbits, 2 to 3 kilograms, were used. They were being fed Wayne rabbit ration. Arachidonic acid was diluted to 2 per cent in peanut oil. All batches of arachidonic acid were tested in other rabbits for their ability to raise intraocular pressure so as to ensure use of potent preparations. Two drops of arachidonic acid 2 per cent, made up freshly, were applied to one eye and two drops of peanut oil to the other eye. Equal numbers of right and left eyes were employed. Half of the rabbits received indomethacin, 50 mg. per kilogram intraperitoneally, one hour before application of arachidonic acid. Thirty minutes after topical therapy, 0.1 ml. of aqueous humor was withdrawn. A radioimmunoassay, which was capable of detecting as little as 5 pg.,[5, 6] was employed to measure PGE.

The results are summarized in Table I. Topical arachidonic acid 2 per cent to 23 eyes resulted in a mean aqueous humor PGE level of 1,024 ± 297 (S.E.) pg. per milliliter, significantly ($p < 0.05$) higher than the 347 ± 88 pg. per milliliter of fellow eyes treated with peanut oil. The values for aqueous PGE of arachidonic acid-treated eyes were also significantly ($p < 0.005$) higher than the mean PGE of 132 ± 18 pg. per milliliter for 24 animals pretreated with indomethacin, 50 mg. per kilogram intraperitoneally, and then subjected to topical arachidonic acid.

Thirty minutes after topical application of 2 per cent arachidonic acid, therefore, both intraocular pressure[1, 2] and aqueous PGE are elevated. Moreover, both of these rises can be prevented by prior administration of indomethacin. This strongly suggests that the arachidonic acid-induced pressure effect is mediated by a synthesis or release of prostaglandin. It does not answer the questions of whether exogenous precursor is being converted to $PGE_2$ or whether the arachidonic acid is merely a nonspecific stimulus to endogenous synthesis, and where conversion may be taking place. The results do offer direct evidence that ocular prostaglandin production, in vivo, is inhibited by indomethacin. Doses of indomethacin smaller than 50 mg. per kilogram were not employed. However, as little as 2 mg. per kilogram of indomethacin partially blocked the arachidonic acid-induced intraocular pressure elevation in the rabbit eye.[2] This is a useful system for the search for other aspirin-like drugs.

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**Table I.** Effect of indomethacin on the aqueous PGE of rabbit eyes treated with arachidonic acid

| | *Mean PGE ± S.E. at 30 minutes* | | | |
|---|---|---|---|---|
| | *Arachidonic acid (2%)* | | *Peanut oil* | |
| | *pg./ml.* | *No.* | *pg./ml.* | *No.* |
| No indomethacin | 1,024 ± 297*, † | 23 | 347 ± 88 | 22 |
| Indomethacin (50 mg. per kilogram) | 132 ± 18 | 24 | 199 ± 36 | 24 |

*Significant difference between means of eyes treated with arachidonic acid and eyes treated with peanut oil, $p < 0.05$.
†Significant difference between means of eyes of animals treated with and not treated with indomethacin, $p < 0.005$.
The other differences were not statistically significant.

1973; manuscript accepted for publication June 7, 1973.

**Key words:** indomethacin, arachidonic acid, prostaglandin E.

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## Argon laser photocoagulation of ciliary processes and pigmented pupillary membrane in man.

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The purpose of this report is to convey our experience using argon laser photocoagulation to burn pigmented pupillary membranes and ciliary processes of human eyes. Two patients, a man and woman both middle aged, presented with pigmented pupillary membrane following cataract extraction. The man had had an aspiration of a traumatic cataract and the woman an intracapsular removal of a cataract associated with uveitis and rheumatoid arthritis. Both cases had been considered for dissection of the membrane. As an alternative they were offered laser photocoagulation with the full understanding that it was an experimental procedure. In both cases a gonioscopic lens was used to deliver the laser at an angle so that any of the beam passing through the membrane would come to rest in the pars plana area. A 50 micron beam size was used, delivering either 50 or 100 mw. over a period of 1/10 of a second for each treatment. The lady received a total of 0.51 joules and the man 0.16 joules. With the laser burns there was no explosion, rather an opening and retraction of the membrane. No bubble formation occurred. Best corrected vision before treatment for the lady was 20/200 and following treatment was 20/60. The man's vision improved from 20/50 to 20/20. His vision has been maintained to this time. The lady's vision has fluctuated as a function of the degree of inflammation associated with her continuing uveitis, but was stable and in remission for at least three months following the initial treatment. There was no uveitis associated with the laser treatment. Both cases had obvious central openings after treatment which have remained patent to date. Our impression is that the use of argon laser for photocoagulation of such pigmented membranes is worthy of consideration.

The second attempted treatment did not fare as well. In four patients with neovascular glaucoma, argon laser photocoagulation of the ciliary body and ciliary processes was carried out.[1] That was accomplished using a Franklin three-mirror lens which had a 3 mm. plastic ball cemented to the outside rim.[2] The plastic ball served to depress the ciliary body area and bring it into view of the mirror located opposite in the gonioscopic prism. The treatments were done during a number of separate sittings generally using a 200 micron beam at 300 to 500 mw. over 2/10 second. Fifteen processes were treated at a time and eventually all were photocoagulated. The initial hope was to be able to vary the effect depending on the number of processes treated. A treatment was considered complete when all the processes in the area to be treated were white overall the area exposed to view. The processes appeared to stay white over a two to three month period.

The patients were comfortable with only topical