

# Reducing the Release of Pigment

Methods for decreasing pigment particles in the anterior chamber in exfoliation syndrome and pigment dispersion syndrome.

BY WISAM SHIHADDEH, MD, AND ROBERT RITCH, MD

**T**he release of pigment into the anterior chamber is a well-known phenomenon in both exfoliation syndrome and pigment dispersion syndrome. The deposition of pigment in the trabecular meshwork is an underlying cause of elevated IOP and glaucoma. This article describes what triggers the release of pigment and suggests methods for reducing the problem.

## EXFOLIATION SYNDROME

### Overview

Exfoliation syndrome is the most widespread, classifiable cause of open-angle glaucoma worldwide.<sup>1</sup> In this age-related disorder, fibrillar extracellular materials are produced by and accumulate in various ocular tissues (Figure 1). Friction between the anterior lens capsule and the iris disrupts the iris pigment epithelium, dispersing pigment throughout the anterior chamber. The result is corneal pigmentation, iris sphincter transillumination defects (Figure 2), and a characteristic increase in the trabecular meshwork's pigment (Figure 3). Pigment dispersion may occur before the physician even detects exfoliation syndrome with a slit-lamp examination.<sup>2</sup>

The release of pigment into the anterior chamber is common and profuse after pupillary dilation in patients with exfoliation syndrome.<sup>3-8</sup> Subsequent increases in IOP can be as high as 30 mm Hg above baseline and may peak as many as 2 or 3 hours after dilation.<sup>9</sup> It is particularly important for physicians to measure IOP and assess the degree of pigment release in the anterior chamber after pupillary dilation. If the spread of pigment is extensive, the clinician

should continue follow-up until the patient's IOP is safely under control. Unrecognized pressure spikes may exacerbate glaucomatous damage, particularly in patients whose disease is moderate to severe. We have seen a patient with exfoliative glaucoma who suffered a central retinal vein occlusion and an IOP spike to 55 mm Hg after pupillary dilation.

### Drug Therapy

In patients with exfoliation syndrome, inhibiting the release of pigment should slow glaucomatous progression by blocking the mechanism most responsible for elevated IOP in these eyes. Theoretically, miotics should be the first line of treatment. Decreasing pupillary movement may reduce iridolenticular friction and thus avert the liberation of iris pigment, slow the progression of trabecular blockage, and perhaps allow the meshwork to clear.

Although physicians' use of pilocarpine decreased upon the introduction of newer classes of IOP-lowering medications, this agent may still have a role in exfoliation syndrome. One drop of pilocarpine 2% daily may be sufficient to reduce pupillary reactivity for 24 hours without severely constricting the pupil.<sup>10</sup> Other IOP-lowering agents may be

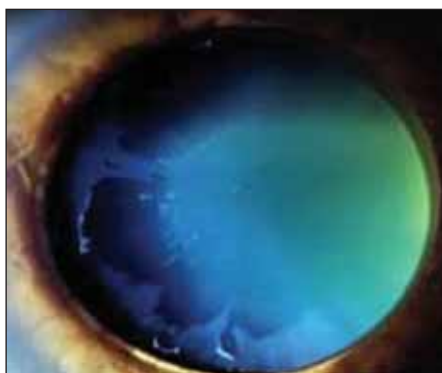


Figure 1. Three zones are present on the anterior lens capsule in exfoliation syndrome. Note the clear area between the central disc and the peripheral zone.

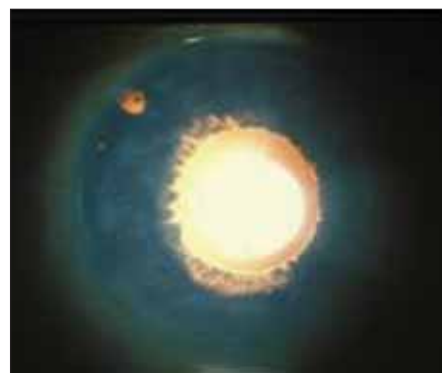


Figure 2. Iris sphincter transillumination defects in exfoliation syndrome result from the dispersion of pigment into the anterior chamber.



**Figure 3.** Sampaolesi's line and hyperpigmentation of the trabecular meshwork in exfoliation syndrome are visible.



**Figure 4.** Krukenberg's spindle is one of the clinical signs of pigment dispersion syndrome.

used concomitantly as needed. After undergoing treatment for sufficiently long periods with miotic therapy, we observed an early pigment reversal sign,<sup>10</sup> which indicates that pigment has cleared from the trabecular meshwork.

## PIGMENT DISPERSION SYNDROME

### Overview

The onset of pigment dispersion syndrome, which is an autosomal dominant disorder, typically occurs when patients are in their early 20s, but the condition begins to regress with increasing age, enlargement of the lens, and the loss of accommodation due to the onset of presbyopia. The mechanism underlying IOP elevation in patients with pigment dispersion syndrome and pigmentary glaucoma is analogous to that in exfoliation syndrome. In pigment dispersion syndrome and pigmentary glaucoma, the iris insertion is typically posterior, and the peripheral iris configuration tends to be concave. Iridozonular contact during accommodation as well as during normal pupillary constriction and dilation disrupts the iris pigment epithelium and results in the deposition of pigmentary granules throughout the anterior segment. The classic diagnostic triad consists of corneal pigmentation (Krukenberg's spindle); slit-like, radial, midperipheral iris transillumination defects; and dense trabecular pigmentation (Figures 4 to 6).

Patients with pigment dispersion syndrome or pigmentary glaucoma can also experience sudden IOP spikes after pupillary dilation. The examination and treatment of these patients is similar to that de-

scribed earlier for exfoliation syndrome.<sup>5,8,11</sup> Although exercise may cause the shedding of pigment and a subsequent pressure spike in some patients with pigment dispersion syndrome,<sup>12,13</sup> the majority of patients do not appear to be affected.<sup>13,14</sup> Pigmentary shedding is most commonly associated with jogging or bouncing. Ultrasound biomicroscopy indicates that cycling increases the iris' concavity in both healthy eyes<sup>15</sup> and those with pigment dis-

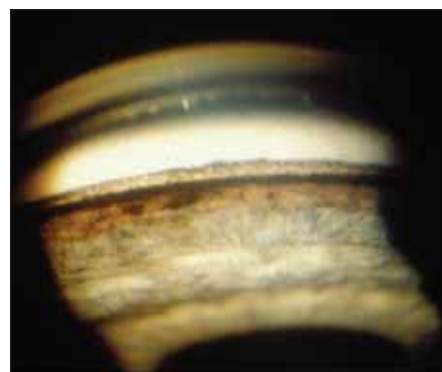
persion syndrome.<sup>16</sup> The effect was eliminated in the latter by laser iridotomy. Vibration-induced increases in trabecular pigmentation have also been reported in rock drillers.<sup>17</sup>

### Drug Therapy

Because miotics both constrict the pupil and increase aqueous outflow, they are, in principle, first-line therapy. In practice, pilocarpine completely stops the exercise-induced release of pigment and elevation of IOP,<sup>12,13,18,19</sup> whereas dapiprazole has a lesser effect<sup>20</sup> and iridotomy provides incomplete inhibition.<sup>21</sup> Miotics convert the concave iris configuration (Figure 7A) to a convex one and eliminate iridozonular friction (Figure 7B). Pilocarpine drops are poorly tolerated, however, because of accommodative spasm and induced myopia in younger patients. Pilocarpine Ocuserts were ideal for patients with pigment dispersion syndrome or pigmentary glaucoma, because these drugs were well tolerated and effective at both lowering IOP and inhibiting pigmentary release. Unfortunately, they are no longer manufactured, which has created a serious problem for our younger patients.



**Figure 5.** Midperipheral iris transillumination defects occur in pigment dispersion syndrome.



**Figure 6.** Hyperpigmentation of the trabecular meshwork occurs in patients with pigment dispersion syndrome.

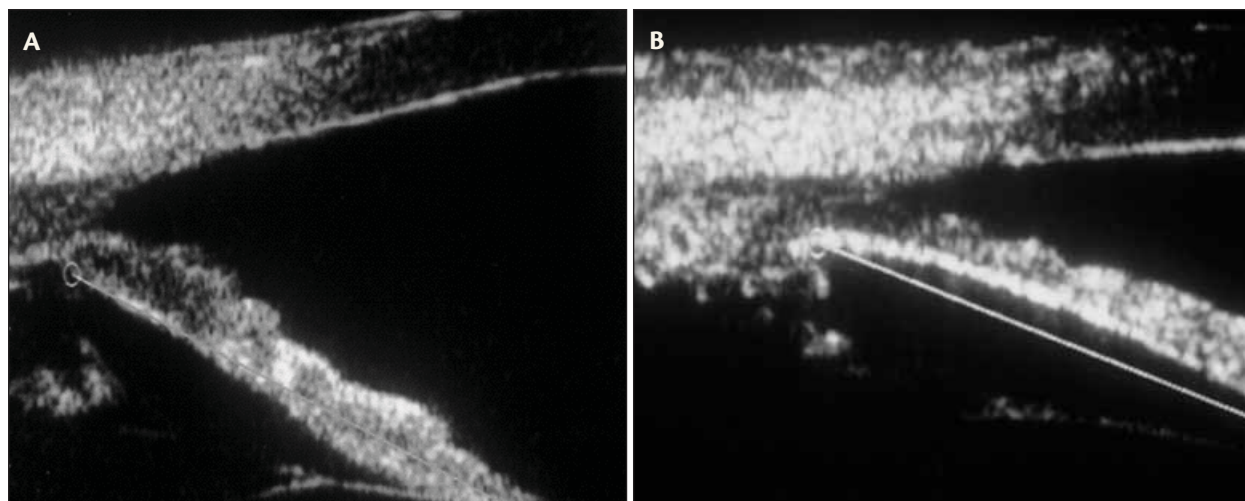


Figure 7. In a patient with pigment dispersion syndrome (A), the iris' concavity changes after treatment with pilocarpine (B).

### Laser Intervention

Laser iridotomy can eliminate reverse pupillary block, flatten the iris' contour (Figure 8), and reduce the extent of iridolenticular contact.<sup>22</sup> The technique also appears to prevent the accentuation of the iris' concavity that accompanies accommodation.<sup>23</sup> Moreover, it decreases the number of melanin granules present in the anterior chamber.<sup>24</sup> Although iridotomy may relieve IOP spikes, it does not lower baseline IOP, because it takes years for pigment to clear from the trabecular meshwork. Wang et al<sup>25</sup> conducted a review of 23 patients with pigment dispersion syndrome and elevated IOP who had no or only mild glaucomatous damage and who had undergone laser iridotomy. The investigators found no significant difference

in the long-term reduction of IOP in the lasered eyes compared with the medically treated fellow eyes. The latter had mostly received treatment with pilocarpine Ocuserts and latanoprost. Now that Ocuserts are no longer available, the use of laser iridotomy will probably increase.

By preventing the liberation of pigment from the iris, laser iridotomy should allow the trabecular meshwork to clear itself and avoid further pigmentary deposition. Candidates for the procedure, therefore, are in the pigment-liberation stage. In such individuals, pupillary dilation likely will lead to the release of pigment into the anterior chamber. Patients with uncontrolled glaucoma are poor candidates for laser iridotomy, since clearing of the meshwork and the subsequent IOP reduction requires a long time after the laser iridotomy.

As a rule of thumb, we restrict iridotomy to patients under 45 years of age who have elevated IOP, demonstrate no early glaucomatous damage, and experience a release of pigment upon pharmacologic dilation or spontaneously after exercise. Because not all patients with pigment dispersion syndrome develop elevated IOP, and because the iridotomy procedure itself results in a significant release of pigment, we do not currently advocate treating normotensive eyes.

### CONCLUSION

The release of pigment into the anterior chamber and the subsequent deposition on the trabecular meshwork constitutes a major mechanism in IOP elevation and glaucoma in patients with exfoliation syndrome and pigment dispersion syndrome. Reducing the release of pigment may slow the progression of these diseases and may even lead to a clearing of the trabecular meshwork. □

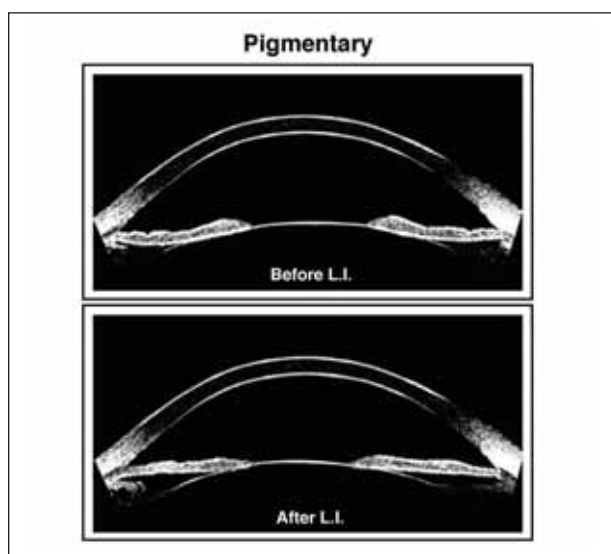


Figure 8. Laser iridotomy flattens the iris' contour in an eye with pigment dispersion syndrome.



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1. Ritch R. Exfoliation syndrome: the most common identifiable cause of open-angle glaucoma. *J Glaucoma*. 1994;3:176-178.
2. Prince AM, Streten BW, Ritch R, et al. Preclinical diagnosis of pseudoexfoliation syndrome. *Arch Ophthalmol*. 1987;105:1076-1082.
3. Aggarwal JL, Beveridge B. Liberation of iris pigment in the anterior chamber. *Br J Ophthalmol*. 1971;55:544-549.
4. Kristensen P. Pigment liberation test in open-angle glaucoma. *Acta Ophthalmol*. 1968;46:586-599.
5. Mapstone R. Pigment release. *Br J Ophthalmol*. 1981;65:258-263.
6. Prince AM, Ritch R. Clinical signs of the pseudoexfoliation syndrome. *Ophthalmology*. 1986;93:803-807.
7. Tarkkanen A. Pseudoexfoliation of the lens capsule. *Acta Ophthalmol*. 1962;71:1-98.
8. Valle O. The cyclopentolate provocative test in suspected or untreated open-angle glaucoma: III. The significance of pigment for the result of the cyclopentolate provocative test in suspected or untreated open-angle glaucoma. *Acta Ophthalmol*. 1976;54:654-664.
9. Shihadeh W, Ritch R, Scharf B, Liebmann JM. Delayed intraocular pressure elevation after pupillary dilation in exfoliation syndrome (ARVO abstract). *Invest Ophthalmol Vis Sci*. (suppl). In press.
10. Ritch R, Schlötzer-Schrehardt U. Exfoliation syndrome. *Surv Ophthalmol*. 2001;45:265-315.
11. Kristensen P. Mydriasis-induced pigment liberation in the anterior chamber associated with acute rise in intraocular pressure in open-angle glaucoma. *Acta Ophthalmol*. 1965;43:714-724.
12. Schenker HL, Luntz MH, Kels B, Podos SM. Exercise-induced increase of intraocular pressure in the pigmentary dispersion syndrome. *Am J Ophthalmol*. 1980;89:598-600.
13. Haynes WL, Johnson AT, Alward WLM. Effects of jogging exercise on patients with the pigment dispersion syndrome and pigmentary glaucoma. *Ophthalmology*. 1992;99:1096-1103.
14. Smith DL, Kao SF, Rabbani R, Musch DC. The effects of exercise on intraocular pressure in pigmentary glaucoma patients. *Ophthalmic Surg*. 1989;20:561-567.
15. Haagaard B, Jensen PK, Kessing SV, Nissen OI. Exercise and iris concavity in healthy eyes. *Acta Ophthalmol Scand*. 2001;79:277-282.
16. Jensen PK, Nissen O, Kessing SV. Exercise and reversed pupillary block in pigmentary glaucoma. *Am J Ophthalmol*. 1995;120:110-112.
17. Mansour AM, Uwaydat SH, Khouri AS. Ocular sequelae of pneumatic drills. *Eye*. 2000;14:64-66.
18. Campbell DG. Improvement of pigmentary glaucoma and healing of transillumination defects with miotic therapy. *Invest Ophthalmol Vis Sci*. 1983;23(suppl):173.
19. Haynes WL, Johnson AT, Alward WLM. Inhibition of exercise-induced pigment dispersion in a patient with the pigment dispersion syndrome. *Am J Ophthalmol*. 1990;109:599-601.
20. Mastropasqua L, Carpineto P, Ciancaglini M, Gallenga PE. The effectiveness of dapiprazole in preventing exercise-induced IOP increase in patients with pigmentary dispersion syndrome. *Int Ophthalmol*. 1995-1996;19:359-362.
21. Haynes WL, Alward WLM, Tello C, et al. Incomplete elimination of exercise-induced pigment dispersion by laser iridotomy in pigment dispersion syndrome. *Ophthalmic Surg Lasers*. 1995;26:484-486.
22. Breingan PJ, Esaki K, Ishikawa H, et al. Iridolenticular contact decreases following laser iridotomy for pigment dispersion syndrome. *Arch Ophthalmol*. 1999;117:325-328.
23. Pavlin CJ, Macken P, Trope G, et al. Accommodation and iridotomy in the pigment dispersion syndrome. *Ophthalmic Surg Lasers*. 1996;27:113-120.
24. Küchle M, Mardin CY, Nguyen NX. Quantification of aqueous melanin granules in primary pigment dispersion syndrome. *Am J Ophthalmol*. 1998;126:425-431.
25. Wang JC, Liebmann JM, Ritch R. Long-term outcome of argon laser iridotomy in pigment dispersion syndrome. *Invest Ophthalmol Vis Sci*. 2001;42(suppl):S560.

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