Hypoperfusion of the Iris and its Consequences in Anterior Segment Pigment Dispersal Syndrome

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ABSTRACT
The effects of changes in iris perfusion in anterior segment pigment dispersal syndrome (ASPDS) were examined by iris fluorescein angiography in 29 patients (20 men and 9 women; mean age, 49 ± 14 years; range, 23 to 77 years). All showed hypoperfusion, with mild to moderate microneovascularization. There was a significant relationship between the degree of hypoperfusion and pigment scatter (\(P < .05\)), and between the level of intraocular pressure (IOP) and angle pigmentation (\(P < .01\)). No statistically significant relation was found between hypoperfusion and iris leak, nor between the level of IOP and iris hypoplasia, hypoperfusion, leakage of dye, pigment scatter, or iris processes. These findings suggest that iris hypoplasia and hypoperfusion are the underlying causes of ASPDS with a congenital etiology.

Pigmentary glaucoma occurs in some cases of anterior segment pigment dispersal syndrome (ASPDS), presumably due to the effect on aqueous outflow of a heavy deposition of pigment granules in the trabecular meshwork. The etiology of the pigment dispersion in ASPDS remains unclear. The transillumination defects in the iris pigment epithelium, one of the characteristics of the condition, strongly suggest that the source of the pigment is the iris pigment epithelium. Campbell has suggested that the posterior iris, rubbing against packets of lens zonules, mechanically liberates pigment granules from the iris pigment epithelium; electron microscopy studies have lent some support to this theory. Sugar proposed that radial folds of iris pigment epithelium, rubbing against the lens capsule, may have a similar effect. Others have theorized that an inherent abnormality of the iris is the underlying cause of the condition, with changes in the iris pigment epithelium and hyperplasia of the dilator muscle. Iris angiography has provided evidence of hypoperfusion of the iris and often microneovascularization, suggesting that a long-standing defect of the iris is the underlying mechanism producing instability of the iris pigment epithelium.

To explore the possible relationship between hypoperfusion of the iris and the development of pigmentary glaucoma in ASPDS, we assessed the relationship between hypoperfusion and pigment scatter, angle pigmentation, iris processes, iris hypoplasia, leakage of dye, and level of intraocular pressure (IOP).

MATERIALS AND METHODS
The study was approved by the Human Research Ethics Committee of the hospital, and informed consent was obtained from all patients.

The principal criterion of ASPDS we used was heavy deposition of pigment in the trabecular meshwork along the line of Schlemm's canal. Other evidence was used to confirm the diagnosis, including Krukenberg spindles, light reflux through the outer iris on transillumination, pigment scatter in the iris stroma, and pigment deposition on Wiegert's ligament. Marked iris processes were often associated with the condition.
Twenty-nine patients (20 men and 9 women; mean age, 49 ± 14 years; range, 29 to 77 years) underwent iris angiography as described previously. The angiographic findings were then compared with the other features of ASPDS.

Based on the iris angiography, the degree of hypoperfusion was classified as mild, moderate, or marked. It was judged to be mild (Fig 1) if the appearance time of the dye in the iris was normal, the arteriovenous time was somewhat lengthened, the number and caliber of radial vessels were somewhat reduced, and there was mild pupillary leak of dye but only slight additional evidence of microneovascularization, with leaks at no more than three sites in the iris stroma.

Hypoperfusion was considered moderate (Fig 2) if the appearance time of the dye was delayed, the arteriovenous time was lengthened, and there was a more marked reduction in the radial arterioles, with moderate attenuation of the vessels. Additional criteria were: more evidence of microneovascularization with moderate pupillary and peripupillary leak, scattered stromal neovascular tufts, and sometimes opening up of the lesser vascular circle of the iris and of peripheral vascular loops.

Hypoperfusion of the iris was considered marked (Fig 3) if the dye appeared extremely late, the arteriovenous time was greatly lengthened, and radial vessels were extremely reduced and attenuated, often with the absence of vessels from large segments of the iris. These features were usually accompanied by marked evidence of microneovascularization, with heavy pupillary and peripupillary leak, more complex plexuses, and more common tufts of microneovascularization, usually with numerous peripheral loops and a well-developed lesser circle.

Leakage of fluorescein dye from iris microneovascularization was assessed similarly: no leak at all, mild, moderate, or heavy.

A leak from the pupil margin and one or two stromal points was considered mild. Profuse leakage from the pupil and peripupillary area as well as from scattered tufts in the iris stroma was regarded as heavy. Leakage intermediate between mild and heavy was judged moderate.

Pigment scatter in the anterior segment was assessed as mild, moderate, or marked, based on the degree of light reflex on retroillumination through the peripheral iris, the amount of posterior corneal pigment (usually as a spindle), and the amount of pigment granules scattered through the iris stroma.

Angle pigmentation also was assessed as mild, moderate, or marked: mild if there was only slight
deposition of pigment in the angle; and marked if there was heavy deposition of pigment in the trabecular meshwork, particularly along the line of Schlemm’s canal all around the angle. Pigment amounts intermediate between these two extremes were considered moderate.

Lichter’s 0 to 4 grading system was used to assess the iris processes.

The relationship of leakage of dye to hypoperfusion and of hypoperfusion to pigment scatter also were studied, as was the relationship between the level of IOP and these various changes (with IOP classified as 20 mm Hg or less, greater than 20 and less than 30 mm Hg, and 30 mm Hg or more).

In most cases, the data were assessed using Pearson’s correlation coefficient (r). However, where the comparisons were dichotomous, maximum-likelihood chi-square statistics were used.

RESULTS
Details of hypoperfusion, leak, pigment scatter, angle pigmentation, iris processes, and iris hypoplasia are shown in Table 1.

Some degree of hypoperfusion of the iris was present at least in the more affected eye in all of the patients undergoing angiography for ASPDS.

There was a significant relationship between hypoperfusion of the iris and the degree of pigment scatter in the anterior segment of the eye ($P < .05$) (Table 2). However, although there was a trend for leakage of dye to be related to hypoperfusion, this tendency was not statistically significant based on the criteria we used.

There was a statistically significant relationship between elevated IOP and the degree of angle pigmentation ($P < .01$): elevated IOP was much more common among patients with marked angle pigmentation (Table 3). However there was no significant relation between level of IOP and the degree of iris hypoplasia, hypoperfusion, leakage of dye, pigment scatter, or iris processes.

DISCUSSION
In this series of patients with ASPDS, there was a significant relationship between iris angiography and hypoperfusion of the iris and dispersal of pigment. There was also a significant relationship between the degree of pigment deposition in the angle and the elevated IOP common in the syndrome.

Based on our finding that all of the cases studied had hypoperfusion of the iris (at least in the worse eye) and that there was usually a hypoplastic iris stroma, we propose that the underlying cause of ASPDS is a congenital hypoplasia of the iris, with accompanying hypoperfusion.

We believe that this hypoplasia and hypoperfusion initially is relatively low-grade, but probably pro-
progresses slowly throughout life, causing secondary changes in the pigment epithelium of the iris, increasing the likelihood that cells will break up and release pigment. This hypothesis is consistent with the findings of Rodrigues, Spaeth, et al., who demonstrated degenerative changes in the pigment epithelium of the iris in ASPDS.

Campbell has proposed that the release of pigment in ASPDS is due to mechanical rubbing of the iris on zonular packets in predisposed eyes, and that this occurrence is more likely in myopia, which is common in these patients. However, not all myopes develop pigment dispersion and not all patients with ASPDS are myopic. We found only 24 myopes in a series of 68 patients. Thus, it is likely that some other factor operates to make pigment cells liable to develop degenerative changes resulting in pigment release.

It may be significant that the shedding of pigment is most marked in the outer iris, where the dilator muscle inserts into pigment epithelium and its action would be likely to cause susceptible cells to shed their pigment. Rodrigues, Spaeth, et al. found changes in the dilator muscle in ASPDS.

Congenital hypoplasia of the iris stroma in ASPDS also would be compatible with the frequent occurrence of dense iris processes in the angle of the eye in ASPDS, since it is possible that both are due to a congenital ectodermal defect.

Overall, the sequence would be as follows: a congenital defect of the iris stroma and iris perfusion causes changes in the iris pigment epithelium. Consequently, these cells break down, with release of pigment and its dispersal in the anterior segment of the eye. Due to slow progression of the hypoperfusion, this condition worsens with aging. The deposition of pigment in the trabecular meshwork of the eye then causes IOP to rise due to interference with a trabecular meshwork that may be less able to accommodate the abnormal degree of pigment release. In late life, the process may regress as the amount of available pigment declines and the pupil becomes less mobile.

REFERENCES