

Prevalence of posterior subcapsular lens opacities in patients with retinitis pigmentosa

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SUMMARY We clinically evaluated 338 patients with various genetic types of retinitis pigmentosa (RP) for the presence of posterior subcapsular (PSC) lens opacities. Of these, 180 (53%) had PSC lens changes or were bilaterally aphakic. Patients with X-linked recessive RP showed a greater prevalence and patients with autosomal dominant RP a lesser prevalence of PSC lens changes compared with autosomal recessive or isolated cases.

Previous authors have presented data or observations on cataracts in patients with retinitis pigmentosa (RP). These reports have varied from descriptions of ultrastructural changes^{1,2} to advantages of cataract surgery³ to data on the prevalence of posterior subcapsular (PSC) lens changes in RP.^{4,5}

This paper records the prevalence of PSC cataract in 338 patients with various genetic types of RP and emphasises the patient's age and genetic type as relevant factors in the determination of PSC lens opacities in RP patients. These data extend and modify those from previous investigations.

Patients and methods

All patients with RP seen by one of us (G.A.F.) between January 1977 and August 1982 were included in this study. Of these 338 patients 173 (51.2%) were male and 165 (48.8%) were female. Their mean age was 38.7 years, median 37 years, range 4 to 77 years. An assessment of racial distribution showed 249 (73.7%) were white, 64 (18.9%) were black, and 25 (7.4%) were Hispanic or Oriental. A determination of the genetic types demonstrated that 96 (28.4%) of the patients were autosomal dominant, 62 (18.3%) were autosomal recessive, 40 (11.8%) were X-linked recessive, and 140 (41.4%) were isolated cases.

Each patient was personally examined by one of us (G.A.F.) and was given a complete ocular examination, including an external evaluation and slit-lamp

biomicroscopy of the cornea, anterior chamber, lens, and vitreous. Examination of the lens was done after the instillation of a mydriatic. Ocular pressures were checked by applanation tonometry, and the fundus was examined by both direct and indirect ophthalmoscopy. Patients were further assessed by visual field examination, electroretinography, and fundus photography. In selected cases dark adaptometry was also performed with a Goldmann-Weekers dark adaptometer.

The diagnosis of RP was based on a history of night blindness, various degrees of bilateral peripheral visual field loss, reduction or absence of rod function, and in most cases reduction or absence of cone function determined by electroretinography and fundus changes. In most cases the fundus changes included attenuated retinal vessels, variable amounts of pigment clumping with anterior migration in the form of bone spicule pigmentation, and hypopigmentation of the retinal pigment epithelium, most apparent in the midperipheral retina. 'Wax' disc atrophy was also noted, but not in all patients. We excluded patients considered to have sector, unilateral, or other 'atypical' forms of RP, such as a localised or 'delimited' type⁶; those with congenital deafness (Usher's syndrome) or with syndromes associated with RP, such as the Bassen-Kornweil syndrome, Refsum's syndrome, or the Bardet-Biedl syndrome; and patients categorised as having a cone-rod dystrophy, choroideremia, or gyrate atrophy of the choroid and retina. A review of family pedigrees facilitated the classification of patients with specific genetic types based on criteria for categorisation previously described.⁷

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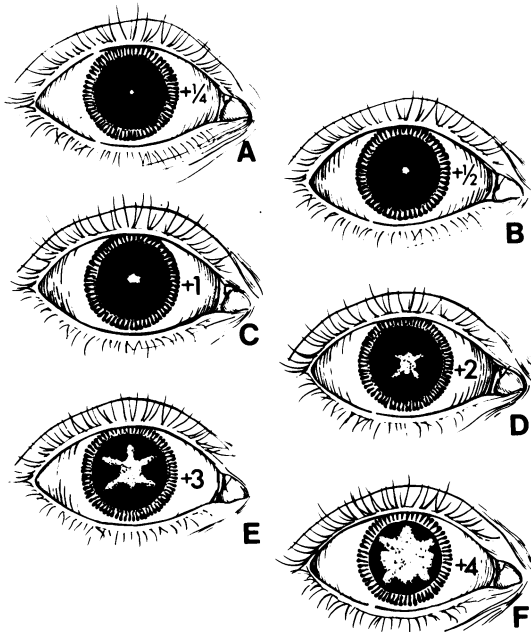


Fig. 1 Clinical grading system used to quantitate the degree of posterior subcapsular (PSC) lens opacities.

The presence of PSC cataracts was determined by one of us (G.A.F) with the aid of a slit-lamp biomicroscope. An attempt was made to quantitate the degree of lens alteration by an arbitrary grading system of +1/4 to +4 (Fig. 1). For the purpose of analysis bilaterally aphakic patients were included among those having a cataract (17 patients). Mild opacities were considered as $\leq +1$, moderate as +2, and marked as $\geq +3$. Asymmetry in lens changes between eyes was occasionally apparent. In 13 patients the PSC changes were exclusively monocular. Although the development of anterior subcapsular opacities would also appear to be associated with the presence of RP, their incidence is considerably less than that of PSC lens changes, and so they were not recorded in our series of patients.

Results

Table 1 summarises the age spectrum and number of patients within each type of RP. Based on the Scheffé multiple comparisons procedure, with $\alpha = 0.05$, an analysis showed no differences of mean age among autosomal dominant, autosomal recessive, and isolated cases; however, the average age of X-linked recessive patients was younger than that of the other groups. Table 2 denotes the average age of subjects in three age groups for each genetic type of RP. Of our 338 RP patients 180 (53%) showed a PSC lens opacity

Table 1 Distribution of subjects, age, and genetic group

Age group (yr)	Dominant	X-linked	Isolated	Recessive
0-9	3	5	1	2
10-19	5	12	15	4
20-29	27	9	28	11
30-39	17	6	26	10
40-49	10	4	25	11
50-59	17	4	30	14
60-69	9	0	11	4
70-79	8	0	4	6
Total	96	40	140	62
Mean age	40.4	26.2	39.7	41.8

Table 2 Average age of subjects, and genetic group

Age group	Dominant	X-linked	Isolated	Recessive
0-19	12.7	12.0	14.3	12.2
20-39	28.8	29.5	29.7	28.2
40+	57.1	50.2	53.2	55.1

(or were bilaterally aphakic). There was no difference between males and females in the prevalence of cataract as a function of age once the genetic group was taken into account. This was tested by determining whether the terms in a logistic regression model that involved the sex variable (that is, main effect or any interactions) were jointly significant.⁸ The results indicated clearly no difference between the sexes in this context ($\chi^2 = 2.98$, 6 df, $p = 0.81$).

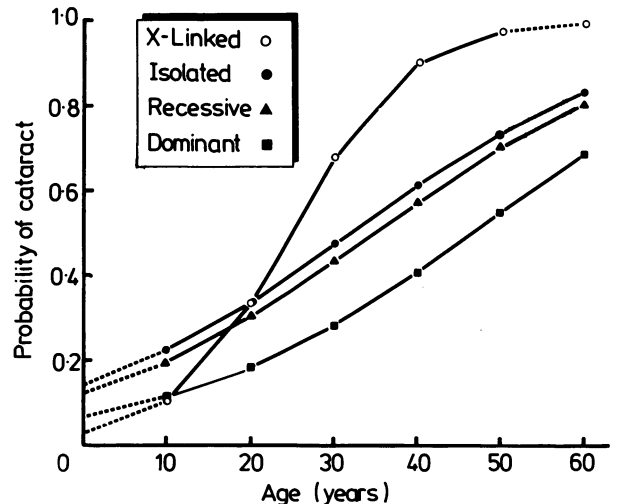


Fig. 2 Logistic regression analysis describes the probability of posterior subcapsular (PSC) lens opacities with age for patients with different genetic types of retinitis pigmentosa. Dotted lines reflect less precision in estimating the probability of PSC changes at the upper and lower limits of the observed ages due to small sample sizes.

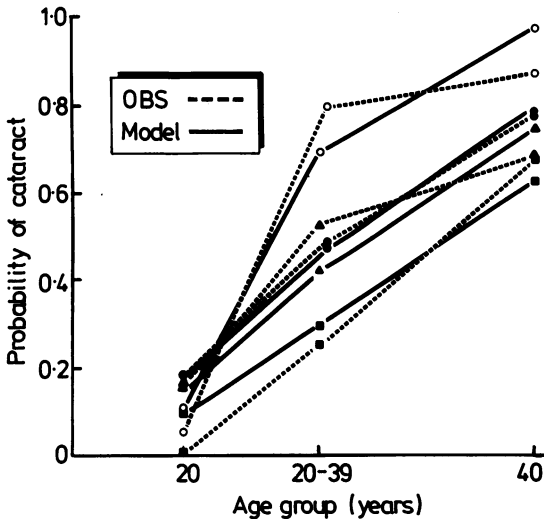


Fig. 3 Probability of posterior subcapsular lens opacities in retinitis pigmentosa patients separated into three age groups. The solid line is determined from a logistic regression analysis model, while the dotted line is a plot of actual data (OBS). Note the close fit of the predictive model with actual data. The symbols for the different genetic types are the same as in Fig. 2.

Further analysis showed that the prevalence of cataract changed with age, as expected. However, while the rate of change of the prevalence was about the same for the autosomal dominant, autosomal recessive, and isolated groups ($\chi^2=2.71$, 2 df, $p=0.26$), it was appreciably greater for the X-linked group (Fig. 2). The results depicted in Fig. 2 have been used to infer, for example, that the probability of a person with autosomal recessive disease having a cataract by age 40 years is about 57%, while the probability would be about 90% for a person with X-linked recessive disease, and about 41% for one with the autosomal dominant form of the disease. Further inspection of the regression equation indicated, as we might have expected, that the curves for autosomal recessive and isolated patients were not significantly different ($\chi^2=0.24$, 1 df, $p=0.62$). Yet additional analysis showed that not only was the X-linked recessive group distinct in terms of its greater rate of change in prevalence of lens opacities, but the autosomal dominant group was distinct in its lesser prevalence of lens opacities ($\chi^2=6.76$, 1 df, $p=0.009$). We also performed an analysis of lens opacities within genetic types grouped into three age categories similar to those used in reports by other investigators.^{4,5} The results with this approach were equivalent to those described in our analysis when age was used as a continuous variable (Fig. 3). Finally, we noted an expected general trend for an

increase in severity of lens opacities with age within each genetic type (Cochran–Mantel–Haenszel statistic (using scored data) = 63.05, 1 df, $p \ll 0.001$).⁹

Discussion

Heckenlively⁵ analysed frequency and severity of PSC cataracts in 291 patients with various forms of hereditary retinal degeneration and found an overall frequency of PSC changes in 41%. His study was not directly comparable to ours, because he included patients with cone-rod degeneration, Usher's syndrome, choroideremia, and 'typical' RP. Interestingly, he reported that PSC cataracts were most common in patients with autosomal dominant RP, a finding contrary to that of our own study. The nature of this disparity is uncertain, though the difference in population samples is a possibility. Also in contrast to our findings, Heckenlively noted a significant sex preference ($p < 0.002$) in his group with 'sporadic' (isolated) RP in which there was a female preponderance.

Berson and coworkers⁴ found a significantly greater prevalence of cataracts in X-linked recessive RP patients as compared with isolated cases in their 20–39-year age group. However, unlike our study they found no substantial differences in other age-specific group prevalences between X-linked recessive RP and isolated cases or between other genetic types such as autosomal dominant and autosomal recessive RP patients. As in our study they showed an increase in the prevalence of PSC cataracts in both eyes with age for all genetic types.

Our results stress the importance of the patient's age and genetic type in the analysis of data on the prevalence of PSC lens opacities. X-linked recessive patients appear to develop opacities more frequently and at a faster rate than patients with other genetic types of RP. As a group, patients with the autosomal dominant trait show PSC lens changes less frequently when compared with other genetic types of RP. In this regard Fig. 2 is helpful in providing specific information on the expected prevalence of PSC lens changes among the different genetic RP types with age.

This report does not resolve the pathogenetic mechanisms responsible for the development of PSC lens opacities. It does, however, point to the overall prevalence rates of lens opacities with age in a group of RP patients with different genetic types. Without consideration for genetic type our data suggest that approximately 50% of a given RP population will have PSC lens opacities or be bilaterally aphakic.

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References

- 1 Eshaghian J, Rafferty NS, Goossens W. Ultrastructure of human cataract in retinitis pigmentosa. *Arch Ophthalmol* 1980; **98**: 2227–30.
- 2 Eshaghian J, Rafferty NS, Goossens W. Human cataract complicata: clinicopathologic correlation. *Ophthalmology (Rochester)* 1981; **88**: 155–63.
- 3 Bastek JV, Heckenlively JR, Straatsma BR. Cataract surgery in retinitis pigmentosa. *Ophthalmology* 1982; **89**: 880–4.
- 4 Berson EL, Rosner B, Simonoff E. Risk factors for genetic typing and detection in retinitis pigmentosa. *Am J Ophthalmol* 1980; **89**: 763–75.
- 5 Heckenlively J. The frequency of posterior subcapsular cataract in the hereditary retinal degenerations. *Am J Ophthalmol* 1982; **93**: 733–8.
- 6 Marmor MM. The electroretinogram in retinitis pigmentosa. *Arch Ophthalmol* 1979; **97**: 1300–4.
- 7 Fishman GA. Retinitis pigmentosa: genetic percentages. *Arch Ophthalmol* 1978; **96**: 822–6.
- 8 Schlesselman JJ. *Case-control studies: design, conduct, analysis*. New York, Oxford University Press, 1982: chapter 8.
- 9 Landis JR, Heyman ER, Koch GG. Average partial association in three-way contingency tables: a review and discussion of alternative tests. *Int Statistical Rev* 1978; **48**: 237–54.