The environment and the lens

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SUMMARY The association of various personal, occupational, and environmental factors with cataracts and pseudoexfoliation of the lens (PXF) was examined in a group of Australian Aborigines. Cataracts occurred more commonly in the elderly but were also associated with high levels of ultraviolet radiation and sunlight and were more commonly seen in lower latitudes. PXF was also seen more commonly in the elderly, especially among males. PXF occurred particularly commonly in stockmen and was related to latitude and global radiation. It was positively associated with the occurrence of cataract and with climatic droplet keratopathy. It is suggested that senile cataracts are related to the amount of ultraviolet radiation and PXF to global radiation.

The eyes of Australian Aborigines in outback Australia are exposed during waking hours to an atmosphere of low humidity and often of high temperature, and in particular to intense solar irradiation. Both senile cataracts and pseudoexfoliation of the lens (PXF) have been reported as occurring commonly in Australian Aborigines.^{1,2} While it has been suggested that senile cataracts, in particular nuclear sclerosis, may be related to environmental factors, including solar radiation,³⁻⁵ no epidemiological studies have demonstrated a clear association with ultraviolet radiation. PXF has a marked regional variation in its distribution,^{1,6-9} but the possibility of an environmental cause had not been considered.

The following study investigated the role of a number of personal and environmental factors in the causation of these 2 conditions. It was conducted as a separate study in conjunction with the routine field work performed by the National Trachoma and Eye Health Programme (NTEHP).

Materials and methods

The methods used to select people for inclusion in this study and the examination procedure have been described in detail.^{2,10,11} Briefly, 350 Aborigines over the age of 30 were studied. They were selected from either a sampling of 2 aboriginal communities or were included in a case-control study of blindness. A detailed personal history was obtained and

slit-lamp examination performed. Intraocular pressure was measured with either a Goldmann or Perkins applanation tonometer.

The presence of lens opacities was determined by slit-lamp examination. The severity of lens opacities was graded according to the degree of reduction of visual acuity attributable to those opacities: grade 1, visual acuity correctable to 6/6; grade 2, visual acuity correctable to better than 6/60 but less than 6/6; grade 3, visual acuity correctable to 6/60 or less. The data presented in this study are for grade 2 and grade 3 opacities. In bilateral cases the patient was classified according to the poorer eye.

Environmental data for the place of residence for each person were obtained from published records.¹²⁻¹⁵ The test of statistical significance used throughout was the chi-square test. For simplicity only the P values are presented in the text. It must be remembered that the associations of many variables were tested.

Results

SENILE CATARACTS

In the 350 individuals studied 116 people (64 males and 52 females) were found to have lens opacities other than traumatic cataract. One hundred and three of these cataracts were either nuclear or mature cataracts, and a further 7 were hypermature. No significant sex correlation was found, but this may have been masked by the matching used in the case-control study of blindness.

The finding of cataracts was strongly age related (Table 1, Fig. 1). No correlation was found between

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Fig. 1 Histograms showing the prevalence of senile cataracts in 350 Aborigines by age (years), latitude (degree), annual mean daily hours of sunlight, annual mean ultraviolet-B radiation (mean erythemal doses); the latter is also shown for 315 Aborigines over the age of 40.

Table 1 Distribution of cataract by age in 350 Aborigines*

Age (years)	Cataract		
	Present	Absent	Total
Below 40	1	34	35
40-59	13	92	105
Above 60	102	108	210
Total	116	234	350

* χ^2 , 2DF=57.5; $P \leq 0.001$.

occupation, a history of alcohol intake, or ocular trauma, either in the group as a whole or for each age and sex group.

For both those aged 40-59 and those over the age of 60 years no relation was found between the severity of trachoma signs and cataracts (Table 2).

Table 2 Distribution of cataract by severity of trachoma and trichiasis in 315 Aborigines over the age of 40

	Age 40-59 years			Age 60+ years		
	Cataract			Cataract		
	Present	Absent	Total	Present	Absent	Total
Trachoma scarring						
Index ¹⁰						
Nil	0	0	0	1	2	3
Negligible	3	14	17	1	10	11
Mild	5	48	53	37	36	73
Severe	5	30	35	63	60	123
Trichiasis	2	2	4	12	18	30
Total	13	92	105	102	108	210

A strong association was found between cataracts and latitude, with cataracts being more common at lower latitudes (Table 3, Fig. 1). A trend existed for cataracts to be associated with a greater number of hours of sunlight per day (Table 3, Fig. 1), those with less than 8 hours of sunlight having fewer cataracts than those with 8.5 hours or more. A trend was also found for cataracts to occur more often in areas with higher annual mean ultraviolet-B radiation levels (Table 3, Fig. 1). This association was statistically significant when those over the age of 40 were examined separately (Table 4, Fig. 1). Only 1 person under the age of 40 had a cataract.

No relation was found to exist between the presence of cataract and the following environmental factors: maximum temperature, evaporation rate, relative humidity, and total global radiation for January or the year, or annual rainfall. There was no age correlation with these factors.

In all, 14 cases of traumatic cataract were seen. These have not been included in the preceding analysis. All these traumatic cataracts were unilateral. Ten occurred in males and 4 in females. Nine cases followed blunt trauma, 2 followed penetrating trauma, and in 3 the nature of the trauma was unknown. Four occurred in childhood, 3 in adolescence, 6 in young adults, and only 1 over the age of 40. The ages of the patients seen ranged from 22 to about 70 years. The causes of blunt trauma included: fights, stones, and being

Table 3 *Distribution of cataract in 350 Aborigines according to latitude, mean daily hours of sunlight, and annual mean ultraviolet radiation (mean erythemal doses)**

	Cataract			Relative risk
	Present	Absent	Total	
<i>Latitude</i>				
20°-24°	23	20	43	2.2
25°-29°	76	181	257	0.8
Above 30°	17	33	50	1.0
<i>Sunlight hours</i>				
8 or less	2	14	16	1.0
8.5-9	38	93	131	2.9
9.5 or more	76	127	203	4.2
<i>Ultraviolet dosage</i>				
2000	30	81	111	1.0
2500	52	103	155	1.3
3000	34	50	84	1.8
Total	116	234	350	

*Latitude: χ^2 , 2DF = 9.53; P = 0.009. Sunlight: χ^2 , 2DF = 5.78; P = 0.06. Ultraviolet: χ^2 , 2DF = 3.92; P = 0.14. χ^2 , 1DF (<2500 vs. 3000) = 2.74; P = 0.09.

Table 4 *Distribution of cataract in 315 Aborigines over the age of 40 according to annual mean ultraviolet radiation (mean erythemal dose)**

Ultraviolet dosage	Cataract			Relative risk
	Present	Absent	Total	
2000	30	71	101	1.0
2500	51	93	144	1.3
3000	34	36	70	2.3
Total	115	200	315	

* χ^2 , 2DF = 6.49; P = 0.04. χ^2 , 1DF (<2500 vs. 3000) = 5.65; P = 0.02.

hit by a whip. The types of penetrating injury included injury from a stone, from chopping wood, and from tree branches.

PSEUDOEXFOLIATION OF THE LENS

Thirty-four cases of pseudoexfoliation of the lens capsule (PXF) were seen. Twenty-six cases occurred in males and 8 in females, and the sex correlation was statistically significant (P < 0.001, Fig. 2). Twenty-nine of the patients were over the age of 60 years, and this increase in prevalence with age was statistically significant (Table 5, Fig. 2). There was no tribal clustering of PXF.

In only 1 case was the intraocular pressure elevated. This occurred in a 66-year-old male who has unilateral PXF with a hypermature cataract and with an open angle. The presence of the cataract prevented examination of his disc. Because of examination conditions detailed visual-field assessment was not possible, but his fields appeared full on confrontation testing. The unilateral elevation of intraocular pressure may have been related to the hypermature cataract.

Occupation was related to the finding of PXF; there was a much higher prevalence of PXF among stockmen than in those who had other occupations or who had not worked (P = 0.006; Table 6, Fig. 2).

PXF was seen more often in the lower latitudes; those living in the more northern areas had a significantly higher prevalence of PXF than those living further south (P = 0.03; Table 7, Fig. 2). The annual total global radiation level was also associated with PXF (Table 8); persons receiving more than 600 mW/h/cm² had more cases of PXF than those living in areas receiving less irradiation (P = 0.07 for the group as a whole; P = 0.06 for males over the age of 60; Fig. 2). Males over the age of 60 were examined separately because PXF occurred most frequently in this group.

No consistent association existed between the environmental factors of maximum temperature,

Table 5 Distribution of pseudoexfoliation by age* in 350 Aborigines

Age (years)	Pseudoexfoliation		
	Present	Absent	Total
0-39	0	35	35
40-59	5	100	105
60 and over	29	181	210
Total	34	316	350

* χ^2 , 1DF (less than 59 vs. 60 and over) = 10.04; P=0.001.

Table 6 Distribution of pseudoexfoliation by occupation in 350 Aborigines

Occupation	Pseudoexfoliation		
	Present	Absent	Total
Not employed	20	195	215
Stockman	9	33	42
Station hand	3	35	38
Other	2	53	55
Total	34	316	350

* χ^2 , 1DF (stockmen vs. others) = 7.47; P=0.006.

evaporation rate, relative humidity, annual rainfall, hours of sunlight, or ultraviolet radiation. This was true for analyses using the annual means, mid-summer (January) and midwinter (July) values of these variables.

Pseudoexfoliation and climatic droplet keratopathy were significantly linked when the group as a whole was examined (P=0.002). Because both conditions were found frequently in stockmen, this association may have been factitious. However, when stockmen were analysed for the occurrence of pseudoexfoliation and climatic droplet kerato-

Table 7 Relation between pseudoexfoliation and latitude (degrees) in 350 Aborigines*

Latitude	Pseudoexfoliation		
	Present	Absent	Total
20-24	8	35	43
25-29	25	232	257
30-35	1	49	50
Total	34	316	350

* χ^2 , 2DF=7.27; P=0.03.

Pseudoexfoliation Associated With:

Fig. 2 Histograms showing the prevalence of pseudoexfoliation in 350 Aborigines by age (years), sex, occupation, latitude (degree), annual mean daily total global radiation (mW/h/cm²); the latter is also shown for 104 males over the age of 60.

Table 8 Relation between pseudoexfoliation and annual total global radiation ($mW/h/cm^2$) for 350 Aborigines and for 104 males over the age of 60*

Global radiation	All ages			Males 60+ years		
	Pseudoexfoliation			Pseudoexfoliation		
	Present	Absent	Total	Present	Absent	Total
500 or less	0	12	12	0	2	2
550	3	57	60	2	20	22
600 or more	31	247	278	21	59	80
Total	34	316	350	23	81	104

* χ^2 , 1DF (550 or less vs. 600 or more) = 3.18; $P=0.07$ (all ages); = 3.44, $P=0.06$ (men over 60).

Table 9 Relation between pseudoexfoliation and climatic droplet keratopathy in 42 stockmen*

Climatic droplet keratopathy	Pseudoexfoliation		
	Present	Absent	Total
Present	7	11	18
Absent	2	22	24
Total	9	33	42

* χ^2 , 1DF = 5.70; $P=0.02$.

Table 10 Relation between pseudoexfoliation and cataract in 210 Aborigines over the age of 60*

Cataract	Pseudoexfoliation		
	Present	Absent	Total
Present	20	82	102
Absent	9	99	108
Total	29	181	210

* χ^2 , 1DF = 5.60; $P=0.02$.

pathy (Table 9), this significant correlation still remained ($P=0.02$).

Pseudoexfoliation was also significantly associated with the presence of cataracts. Because both these conditions were more common in the elderly, those over the age of 60 were examined separately (Table 10). Pseudoexfoliation and cataracts were still significantly associated in those over the age of 60 ($P=0.02$).

Discussion

CATARACT

Although many specific disorders are known to be associated with cataract formation, these account for only a small proportion of the total number of cataracts. The majority of cataracts fall into the

so-called 'senile' group, for which no cause is known.

The global distribution of cataracts is difficult to determine.¹⁶ This is in part due to the variation in definition of cataracts, and is also due to the samples that have been studied. Kahn *et al.*¹⁷ defined cataract as lens opacities, excluding certain small embryonal and dot opacities, in eyes with a best visual acuity of 20/30 or less. Kornzweig *et al.*¹⁸ classified cataracts on a different set of visual acuity gradings and excluded eyes with associated glaucoma or macular diseases. Milne and Williamson¹⁹ defined cataract as any opacity in the lens of either eye. Brennan and Knox²⁰ used the criterion of lens opacities that caused people to present for cataract surgery, whereas Chatterjee²¹ based his diagnosis on the 'simultaneous diminution of the fundal glow with diminished visual acuity'.

The populations studied have also varied greatly—from large population surveys²¹ to small, carefully selected random samples,^{17,19} the occupants of old people's homes,¹⁸ outpatients attending an eye clinic,²² or inpatient surgical cases.²⁰

The present analysis examined data collected for two previous studies.^{2,10} Because of the selection methods used, no inference can be drawn about the overall prevalence of cataracts or PXF in the population studied, although investigation into the role that personal and environmental factors play in causation of these 2 conditions is valid.

The obvious relation between the prevalence of cataract and ageing was clearly shown in this study. Cataracts were found to occur as commonly in males as in females. In previous studies no consistent sex difference has been found. Reports finding both more males with cataracts¹⁷ and more females¹⁹ have been published.

The relation between cataract and latitude, hours of sunlight, and ultraviolet radiation (UV-B) is of greater interest. In general, ultraviolet radiation increases directly with hours of sunlight and indirectly with latitude. Therefore latitude and sunlight act as indirect markers of ultraviolet radiation. The relationship between these 3 parameters and cataract shows a clear and consistent dose-response with a progressive increase in relative risk. This indicates the validity of the association, though all did not reach statistical significance by chi-square testing. Although both ultraviolet radiation and global radiation tend to be positively related to latitude and sunlight, they have different distributions in the area studied. As cataract was not related to global radiation, the specificity of the association with ultraviolet radiation is strengthened.

The data on the distribution of ultraviolet

radiation in Australia have only recently become available.¹⁵ As yet comparable data do not exist for any other continent.

Several previous epidemiological studies have indicated that some forms of radiant energy, particularly sunlight, may be associated with cataract formation.^{4 23} Similar evidence comes from studies of the prevalence of cataracts in different areas. Cataracts are particularly common in tropical areas.^{3 16 21 22 24 25} In northern temperate areas it appears that cataracts are found in about 20% of those aged between 65 and 75 years^{17 19} and that they are seen even more uncommonly in more northern subarctic areas.^{26 27}

The study of Chatterjee²¹ is particularly interesting. He found a higher prevalence of cataracts in the Punjabi plains of India than in the higher altitudes of the Himalayas. Many factors may play a role in this difference, including genetic variation and environmental effects such as the mineral content of water, yoghurt consumption, and socioeconomic variables. (Richter and Duke²⁸ produced cataracts in rats fed on commercially manufactured yoghurt which had a high galactose content.) As altitude increases, there is usually an increase in the radiant energy, especially ultraviolet radiation, and Chatterjee's figures have been used to suggest that ultraviolet radiation is not related to the development of cataracts. However, Chatterjee himself mentions that the middle Himalayan area often has a heavy cloud cover. Although a light cloud cover does not block a significant amount of ultraviolet radiation, a heavy cloud cover may.²⁹ The data are not available on either the hours of sunlight or the ultraviolet radiation levels in the areas studied by Chatterjee, and the significance of his findings as they relate to the effect of radiation cannot yet be determined. Interestingly, Vines³⁰ found a higher prevalence of cataracts in the highlands of New Guinea than he found in the lower plains.

Pirie⁵ has demonstrated that human lens proteins turn brown in direct sunlight, and that this is the result of photo-oxidation. She showed that this photo-oxidation was caused by light of wavelengths between 300–320 nm (i.e., ultraviolet-B radiation). There exists in the lens a reducing system to reverse this photo-oxidation of the lens proteins. The reducing substances of most importance are thought to be glutathione and ascorbic acid.³¹ It may be that this reducing system, or at least its efficiency, decreases with age. If the photo-oxidised proteins are not reduced, they form covalent bonds, especially disulphide bonds, with other lens proteins. This cross-linkage formation between lens proteins leads to the formation of insoluble protein com-

plexes.^{31 32} It has also been possible to produce lens changes with ultraviolet light in short-term in-vitro experiments.^{33 34}

Although there is biochemical evidence suggesting that senile cataracts may be caused by the cumulative ultraviolet-induced photo-oxidation and cross-linkage of lens proteins, no previous study was found that had examined the association between environmental ultraviolet levels and cataract. Thus the finding of an association between cataract and ultraviolet radiation in this study provides this epidemiological evidence.

The effect of nutrition on cataractogenesis is uncertain. Pirie³⁵ suggested that poor nutrition, especially a riboflavin deficiency, may be important in the formation of cataracts, but others have believed that nutrition is less important in this regard.^{21 25} The diet and nutritional status of the Aborigines examined in this study were essentially uniform. It is noteworthy that riboflavin deficiency is not uncommon in alcoholics,³⁶ and it is the author's experience that young people with senile cataracts are often alcoholic. This observation has also been made by Hollows (personal communication). In this study, however, no association was found between the presence of cataracts and alcohol consumption.

It has been suggested by some that diabetics have a higher incidence of senile cataracts than non-diabetics,^{35 37 38} but others have disagreed with this finding,³⁹ or suggested that diabetics are only more likely to have cataract surgery.^{40 41} Australian Aborigines have a high prevalence of diabetes, but this has not been associated with an increased prevalence of cataracts.^{42 43}

Several interesting correlations with the presence of senile cataract were found in the Framingham Eye Study.¹⁷ As a group, people with cataract were found to have had a lesser amount of education, to have a higher blood sugar, higher blood pressure, a smaller vital capacity, decreased mean grip strength, and to be of shorter height as compared to those without cataracts. It is possible that the reduction in height, vital capacity, and grip strength are all related, inasmuch as they are all known effects of ageing. The association of an elevated casual blood sugar, hypertension, and elevated phospholipid levels may all be secondary associations with diabetes, ageing, or even alcoholism. A lower level of education may have caused these people to seek a manual or outside occupation and thus result in their being exposed to higher levels of sunshine and thus an increased risk of developing cataract. The exact relevance of these findings is not yet clearly understood, though they open up an interesting field for further study.

PSEUDOEXFOLIATION

The prevalence of pseudoexfoliation of the lens capsule (PXF) was found to increase with increasing age. This association between PXF and ageing has been previously described.⁶ The common finding of cataract with PXF and the infrequent finding of glaucoma with this condition in the Australian Aborigines have been previously reported.¹ The infrequency with which glaucoma is found is even more striking, as it has been suggested that glaucoma is common in eyes with trachoma.⁴⁴ This study has confirmed the earlier findings related to PXF in Aborigines and has quantified the frequent association with cataract.

The association of PXF with various environmental factors—in particular those factors relating to radiation effects such as latitude and yearly global radiation levels—was unexpected. After examination of previous reports,⁹ the possibility of an environmental factor such as radiation does not seem so unusual, because the highest prevalence of PXF reported by Forsius was found in the Lapps, who live around the Arctic Circle. Lower prevalences were found in more southerly areas of northern Europe, although Forsius and Luukka⁴⁵ felt that PXF was not related to latitude. Similarly, the relatively high prevalence of PXF in the African Bantus⁸ and the lower prevalence of PXF in the American Negroes⁷ could possibly be explained by environmental factors, because these groups share a common genetic background. The association observed between PXF and senile cataract and climatic droplet keratopathy would also suggest that PXF may be radiation induced.

The PXF material is known to be banded fibrillary protein^{46–48} and that it is histochemically, immunologically, and ultrastructurally similar to amyloid^{46,49} and is not derived from collagen.⁵⁰ It has been suggested that the material is an altered basement-membrane protein,^{48,51} possibly elaborated by the pre-equatorial lens epithelium.

Seland⁵² has shown that the abnormal material can definitely be elaborated by the lens epithelium. Others have pointed out that the material is also seen in the iris, ciliary body, and subconjunctiva, and that the formed material could not migrate there because of its size.^{51,53,54} Eagle and co-authors⁴⁸ have also demonstrated the likelihood that the PXF material, or precursor, is elaborated by iris and ciliary epithelium. It has been postulated that a circulating substance in the aqueous is somehow stimulated to form the PXF material.^{53,55} Sugar and others⁵¹ considered that ageing alone was the stimulus, while Dark and co-workers⁴⁶ have postulated that some as yet unidentified lysozymal enzyme may be responsible. It may well be that the causative stimulus is provided by radiation.

It is postulated, therefore, that basement-membrane precursors are elaborated by the epithelial cells lining the anterior segment of the eye. These diffuse into the aqueous and are denaturated by irradiation. These denatured proteins then polymerise and are deposited on the intraocular surfaces particularly the lens capsule. Some denatured proteins also pass into the extracellular spaces of the adjacent structures (the iris, ciliary body, and subconjunctiva) and form agglomerations there. An alternative pathway may be that these epithelial cells produce abnormal basement-membrane precursors as a result of radiation-induced changes. These precursors may then polymerise spontaneously.

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