Lens thickness in early cataract

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SUMMARY The search for environmental factors associated with cataract has produced conflicting evidence and one possible reason may be that environmental influences are initiating events occurring perhaps for short periods many years before loss of sight from cataract. It is important, therefore, to be able to detect the earliest changes of cataract formation so that epidemiological studies have a better chance of detecting environmental factors. Two possible indicators of early cataract are delayed growth of the lens and abnormalities of the anterior subcapsular clear zone of the lens as observed on slit-lamp microscopy. A series of patients with early lens changes was compared with control subjects in respect to these two factors. Lens thickness was measured by a simple optical method. The mean thicknesses of the lens in patients with early cortical or posterior subcapsular lens changes were significantly less than that of age matched controls. 60% of lenses with early cataract of all types were found to have a deficient or absent anterior subcapsular clear zone. Lens thickness and the appearance of the anterior subcapsular clear zone are easy to measure and observe through an undilated pupil. Although the prognostic value of the results is uncertain in individual cases owing to the rather wide scatter of results in normal eyes, such observations could be of value in comparative studies of populations.

Cataract is a major cause of blindness and ocular morbidity throughout the world, and any means of delaying or preventing its onset would have enormous social and economic benefits. If age is the sole determinant of cataract formation, there may be little we can do to realise this goal, but if environmental factors are involved there is the possibility of reducing the risk by eliminating adverse environmental conditions.

Two main observations suggest environmental factors. First, the prevalence of cataract is higher in some regions of the world and the age of onset is earlier. Weale¹ has plotted the risk of cataract against age for populations in India and South-east Asia and compared the distribution with that in European populations, and his graphs clearly show that for a given age group the risk is up to 400 times greater for the Asian populations. This does not prove an environmental influence, as genetic factors could produce the same result, but such large differences are certainly suggestive of environmental factors.

Secondly, epidemiological studies have suggested that exposure to solar radiation, particularly in the

ultraviolet range, dietary deficiency, or dehydrating conditions such as recurrent severe diarrhoea may be involved.² Taylor,³ for example, from surveys on Australian aborigines showed a strong association between cataract and latitude and a trend for cataracts to occur more often in areas with higher annual mean ultraviolet-B radiation levels. Other studies have attempted to link sunlight exposure by comparing populations from areas with different intensities of solar radiation. The difficulties involved in the assessment of exposure to ultraviolet radiation for varying geographic conditions have been well reviewed by Sliney.⁴

Typically such research has looked at the environment of patients with relatively advanced cataract causing severe visual disability. Cataract is thought to be multifactorial, and, if environmental factors are involved, they may be initiating events which occurred many years before its manifestation as visual loss. The latency period—the time from the initiation of disease to the time of its first clinical symptom—for cataract is poorly defined. One possible clue to this latency period is the thickness of the lens. The continuous growth of the lens throughout life was recognised as early as 1883 by Priestley Smith and has

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been amply confirmed by many later studies, notably those of Jansson,⁵ Goldmann,⁶ Babel *et al.*,⁷ Brown,⁸ and many others. There is a linear relationship between the anteroposterior thickness of the lens and age, so that the mean thickness of a normal lens in 20-year-old subjects is about 3.8 mm and that of 80-year-old subjects is about 5.2 mm. This increase in size is due to the continuous laying down of new lens fibres modified to some extent by the compaction of the older fibres, as demonstrated by the observation by Brown⁸ that traumatic opacities are seen to sink into the lens at approximately twice the speed at which the lens is growing. This linear relationship between lens thickness and age makes it possible to compare the thickness of a given lens to the expected thickness for the age of the subject.

There is some evidence of racial differences in lens thickness, as Young and Leary⁹ found the lenses of Eskimos to be slightly thicker than those of Caucasians. The influence of refraction on lens thickness is still uncertain, and it has been suggested that the lens of myopes is thinner and that of hypermetropes thicker than normal, but Jansson⁵ and Luyckx and Delmarcelle¹⁰ found no significant difference, and Franceschetti and Luyckx¹¹ and François and Goes¹² found no significant difference in lens thickness in the two eyes of anisometropic subjects.

We have just completed an epidemiological survey of 160 patients admitted for cataract extraction and an equal number of controls matched for sex and age (within one year) seen at the Department of Ophthalmology, University of Iowa.¹³ A questionnaire was administered by a trained interviewer which included a detailed history of residence, occupation, lifetime sunlight exposure, acute and chronic skin reactions to sunlight, the use of glasses, sunglasses, and head covering, exposure to agricultural chemicals, and diet. In addition height and weight were recorded, and the subjects were asked for any history of alcohol abuse, diabetes, hypertension, rheumatic disease, cancers or tumours, and a history of glaucoma, retinal detachment, or other ocular conditions, and any medications such as corticosteroids, tranquilisers, antidepressants, antihypertensives, and glaucoma medication. Any family history of cataract was noted, and the refractive error, presence of pinguecula, and arcus senilis recorded. The type of cataract was classified by a modification of the classification recommended by the American Cooperative Cataract Research Group.¹⁴

The results of this study will be reported in detail but can be briefly summarised as follows. We could find no association with working environment or occupation, and there was no difference between the cases and controls in lifetime sunlight exposure or the

use of protective devices such as glasses or sunglasses which would be expected to reduce the ocular exposure to ultraviolet light.

There were, however, three findings which were suggestive of some sunlight-senile cataract association. First, an acute skin response to sunlight was found to be significantly associated with nuclear cataract. This could, however, suggest a genetic association with light-skinned subjects or a secondary effect of sunburn rather than a direct effect on the lens. Secondly, there was a trend for fewer cataracts in men who wore head coverings. And, thirdly, there was a higher incidence of skin neoplasms in the subjects than in the controls which approached statistical significance.

There was little evidence, therefore, in this population that direct exposure of the eye to sunlight was a cause of cataract. In addition, there is one ocular condition which is almost certainly due to ultraviolet light and that is pinguecula. Pathologically the changes in pinguecula are very similar to those seen in actinic elastosis of the skin. It would be expected, therefore, that there would be a higher incidence of cataract in patients with pinguecula if cataract resulted from ultraviolet light exposure to the lens, but in this series, as in a previously published series,¹⁵ we could find no association between pinguecula and cataract, and there was no significant difference in the incidence of pinguecula in the cataract patients and controls.

This study therefore failed to show any marked environmental factors associated with cataract in this population. Cataract is almost certainly multifactorial in origin, and in other parts of the world, the effect of age, heredity, refraction, hypertension, and glaucoma may be supplemented by dietetic deficiencies, chronic or acute intestinal disease, and environmental factors associated with the geographical area. It is possible that environmental influences initiate events occurring perhaps for short periods many years before the lens becomes opaque and the patient seeks treatment. There may be a long latent period between the onset and recognisable clinical disease, in which case it would be difficult to elicit the relevant environmental history responsible by questioning the patient when the disease is manifest.

After completion of our survey in Iowa, I realised that many of the cataract patients had had intraocular lenses implanted, and in order to estimate the power of the implant they had had preoperative ultrasound examinations. Analysis of the ultrasound measurements of lens thickness kindly provided by the Division of Ultrasonography yielded the following results.

The mean lens thickness of 87 cataractous lenses

Table 1 Type of cataract and lens thickness

Type of Cataract	No.	Mean age	Mean lens thickness (SD), mm	Expected lens thickness, mm	Difference	p Value
Posterior subcapsular	16	65.3	3.93±0.50	4.85	0.92	<0.001
Nuclear	23	70.0	4.45±0.67	4.97	0.52	<0.001
Cortical and subcapsular	6	62.7	4.10±0.33	4.80	0.70	<0.001
Cortical and nuclear	6	69.3	4.45±0.59	4.97	0.52	<0.046
PSC and nuclear	25	70.8	4.00±0.615	5.05	1.05	<0.001
Mature	11	67.8	3.94±0.75	4.96	1.01	<0.001

PSC=posterior subcapsular.

was 4.13 mm (SD 0.8). The mean age of the patients was 68.5 years, and according to Luyckx¹⁶ the normal mean thickness for persons of this age would be 5 mm, which is highly significantly different ($p<0.001$). The cataracts were classified according to their slit-lamp appearance into predominantly cortical, posterior subcapsular, nuclear, or a mixture of two of these three components. When all three types of lens change were present, it was classified as a mature cataract. In Table 1 the type of cataract, the number in each group, the mean patient age, and the mean thickness of the lens are recorded and compared with the expected thickness.

There was no significant correlation between lens thickness and age in the cataract patients, and although patients with posterior subcapsular changes were younger than those with nuclear or those with posterior subcapsular and nuclear changes, there were significant differences in lens thickness (posterior subcapsular versus nuclear, $p=0.046$; posterior subcapsular versus posterior subcapsular with nuclear, $p=0.001$).

In adults the lens increases in thickness by approximately 0.2 mm every 10 years, so that the thickness of the cataractous lenses corresponds to that of the normal lens 25 to 30 years previously. Similar results have been reported.^{6,7,17,18} Shibata *et al.*¹⁹ noted that lenses with wedge-shaped opacities or posterior subcapsular opacities do not show any increase in lens thickness with age. If this failure to reach a normal thickness for age is due only to cessation of lens growth, it would imply that the cataractous lenses stopped growing 25 to 30 years before the cataract was extracted, and it could be inferred that the initiating process in cataract formation, which could be environmental, also occurred at this time.

It cannot be assumed, however, that the small size of the cataractous lens is only due to cessation of growth. Some degree of compaction of lens fibres is a normal feature⁸ of lens maturation, and the changes in the cataractous lens may be the result of a combination of slower growth and greater compaction. At the moment there are no data to estimate the time scale of these processes, but it is known that the

diminution of thickness is due to cortical thinning and that the nucleus is not involved. Does this occur only as a late change? The diminution of thickness of the cortex is paralleled by a diminution in the weight and volume of the lens and alterations in the structure of the proteins.²⁰ These authors remark that early cortical changes result in a change in refraction of the cortex which may cause the refraction of the eye to become more hypermetropic.

If we wish to look at aetiological factors in cataractogenesis, the results reported above indicate that it is essential to know more about the latent period of cataract, so that investigations can be aimed at the critical period when the disease starts.

Other methods of detecting early changes in the formation of cataract depend on changes in the optical quality of the lens. They include the disappearance of the anterior subcapsular clear zone, fluorescence of the lens, spectroscopic studies of the lens protein, and nuclear magnetic resonance.

Of these methods slit-lamp observation and photography are the simplest and most easily available techniques. Slit-lamp microscopy of the lens shows a number of clearly defined zones in the lens. Brown and Tripathi²¹ have shown that the normal clear zone immediately beneath the lens capsule may be thinned or absent in cataract, and such lenses are usually thinner than expected for the age of the patient. A defective anterior subcapsular clear zone was almost always seen with posterior subcapsular cataract and in older patients with nuclear sclerosis. Senile cortical lens changes were not associated with changes in the anterior subcapsular clear zone. They postulate that the loss is due to a primary defect in the lens epithelium of the equatorial region which is failing to produce normal lens fibres, which also results in defective lens growth.

Examination of the subcapsular clear zone may therefore be a very useful method for detecting the early changes in the lens which lead to cataract formation. This, combined with measurement of lens thickness, could provide suitable methods of screening.

The ideal study for this purpose would be a

Table 2 Age distribution of all subjects

Age	0-9	10-19	20-29	30-39	40-49	50-59	60-69	70-79	80-89	90+	Totals
Clear lenses	3	10	12	10	16	16	23	10	1	0	101
Cataract	1	0	3	6	4	12	25	34	16	3	104

longitudinal study of individuals over many years. Unfortunately this is hardly practicable, but a cross-sectional study of different age groups and different stages of cataract formation should supply useful information.

The present study was designed to measure lens thickness and to note the presence or absence of the anterior subcapsular clear zone in a series of subjects with normal lenses and those with early cataract.

Material and methods

The subjects were patients attending the outpatient clinics of the Department of Ophthalmology at the University of Iowa Hospitals and Clinics in Iowa City. Anterior chamber depth and lens thickness were measured by an optical method which has been shown to correlate closely with ultrasonic measurements.²² In this method the movement of the slit-lamp is measured when the focus of the slit is moved from the anterior surface of the cornea to the anterior surface of the lens. This apparent distance can be converted to real distance by Linstedt's formula. The sagittal thickness of the lens is measured by the movement of the slit-lamp required to focus from the anterior surface of the lens to the posterior capsule.

The anterior subcapsular clear zone was recorded as present, reduced in width, or absent, and any cataractous changes found after dilatation of the pupil were recorded. These changes were classified as cortical, nuclear, posterior subcapsular, combined cortical and nuclear, and those with posterior subcapsular changes combined with cortical or nuclear changes. The severity of the lens changes was classi-

fied as mild, moderate, or severe. In no case was the cataract interfering with vision enough to warrant cataract extraction.

Additional measurements of anterior chamber depth and lens thickness were made in some subjects with a Stortz ultrasonic A-20/20 instrument. The refractive error in spherical equivalents was also recorded for each subject.

Results

The age distribution of the subjects is shown in Table 2. As would be expected, there was a preponderance of older subjects with cataract.

A comparison between ultrasonic and optical measurements of lens thickness showed a good correlation ($r=0.86$, $p<0.001$) for clear lenses and a somewhat lower correlation for cataractous lenses ($r=0.69$, $0.02>p>0.01$). This may be partly due to the smaller number of subjects with cataractous lenses measured (11) compared with 26 subjects with clear lenses, but it is possible that refractive changes in the cataractous lenses caused errors in both methods of measurement resulting in a greater scatter.

The mean lens thickness by the optical method of clear lenses in subjects aged 60 and over is compared with the mean lens thickness for different types of cataract in Table 3. Lenses with cortical opacities were significantly thinner than clear lenses in patients of similar age. Lenses with posterior subcapsular changes combined with either nuclear or cortical changes were also thinner than clear lenses but the difference was not statistically significant. Lenses with nuclear changes were very similar in mean thickness to normal lenses.

Linear regression analysis of age and lens thickness showed a highly significant relationship in subjects with clear lenses but no significant linear relationship in any of the groups of patients with lens changes. This lack of linear relationship between age and lens thickness in cataractous lenses may be partly due to the shorter age range of the patients with cataract but does also suggest that cataractous changes alter the normal growth characteristics of the lens.

There was no significant difference in the slope of the age versus thickness curve for males and females with clear lenses or between myopes and other refractive states.

Table 3 Mean lens thickness (right eye) in mm

Subjects	Mean thickness	SD	No.	Probability of difference from clear lenses
Clear lenses aged 60 and over	4.90	± 0.44	34	
Cortical lens changes	4.50	± 0.45	16	<0.01
Nuclear lens changes	4.84	± 0.41	23	>0.1
Cortical and nuclear	4.73	± 0.38	29	$=0.1$
PSC and other	4.52	± 0.30	5	$<0.05>0.01$

PSC=posterior subcapsular.

Table 4 The anterior subcapsular clear zone in normal and early cataractous lenses

Lens	Subcapsular clear zone			Total
	Normal	Reduced	Absent	
Clear lenses	166 (85.1%)	26 (13.3%)	3 (1.5%)	195
Early cataract	50 (40.3%)	52 (41.9%)	22 (17.7%)	124

The results of assessment of the anterior subcapsular clear zone are shown in Table 4, and it will be seen that 60% of the cataractous lenses had a deficient or absent subcapsular clear zone. However, 15% of apparently normal lenses also showed some abnormality of the subcapsular clear zone, but it is impossible to say that this represents a 15% false positive rate, as it is conceivable that these lenses may be showing the earliest sign of cataractous change. The high false negative rate (40%) in the cataractous lenses is disappointing and was approximately the same for each type of lens opacity.

81% of the cataractous changes were recorded as slight and the remainder as moderate. An abnormal clear zone was present more frequently in the lenses recorded as having moderate lens changes, but the difference was not statistically significant.

Discussion

The purpose of this study was to see whether changes in lens thickness or the appearance of the anterior subcapsular clear zone could be used as an indication of early cataract formation. The results, though not as dramatic as those from patients with more advanced cataract, did show that lenses with cortical changes were significantly thinner than would be expected from the age of the patient. Lenses with nuclear changes only did not differ from normal lenses in their thickness. The difference between the thickness of clear lenses and those with cortical changes in subjects aged 60 or over was 0.42 mm, a difference which could be detected by either ultrasonic or optical methods.

Measurement of lens thickness, therefore, could be a useful parameter in population studies in association with an analysis of environmental influences. Unfortunately the scatter of lens thickness versus age is such that a difference of 0.4 mm in lens thickness is approximately equal to the standard deviation of lens thickness in normal subjects of the same age. Lens thickness cannot be used as an indicator of early cataract in individual subjects unless the difference from the expected value for age is marked.

In the hope of being able to define the limits of

normal lens thickness more closely, the correlations between age and lens thickness were calculated for males and females separately, but there was no significant difference in the slope of the curve between males and females. Similarly, no significant difference could be found between myopic and non-myopic eyes.

A reduced or absent anterior subcapsular clear zone was noted much more frequently in patients with lens changes of any type than in subjects with clear lenses and abnormality of the subcapsular clear zone is strongly suggestive of early cataract (Table 4). Unfortunately, the clear zone was present in approximately 40% of patients with early cataract, so that a normal clear zone does not exclude the possibility of lens changes.

All lenses with cortical lens changes and absent or reduced subcapsular clear zone were thinner than would be expected for age (mean difference -0.66 mm). Lenses with nuclear changes only and abnormal subcapsular clear zone were little different from the expected thickness (mean difference +0.05 mm). Ten lenses with cortical and nuclear changes out of 14 were thinner than expected (mean difference -0.32 mm). Out of 14 clear lenses with an abnormal subcapsular clear zone, seven were thicker than expected and seven thinner (mean difference -0.01 mm).

In summary, lenses with cortical lens changes are thinner than would be expected for age and an abnormal subcapsular clear zone is also associated with a reduced lens thickness. Nuclear lens changes are not accompanied by thinning of the lens, but abnormalities of the anterior subcapsular clear zone do occur with this type of cataract. Lens thickness and the appearance of the anterior subcapsular clear zone are easy to measure and observe through an undilated pupil with a slit-lamp microscope, and, although their prognostic significance is uncertain in individual lenses owing to the normal variation (particularly in lens thickness), these observations could be of value in comparative studies of populations as an indication of early cataract.

This research was supported in part by an unrestricted grant from Research to Prevent Blindness.

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Accepted for publication 5 March 1987.