

Sunlight exposure, antioxidant status, and cataract in Hong Kong fishermen

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Abstract

Study objective—The aim was to test whether cataract is associated with higher lifetime exposure to sunlight, and whether antioxidants protect against cataract.

Design—This was a cross sectional survey of eye disease, with assessment of antioxidant status in a subgroup.

Setting—Hong Kong fishing communities in 1989.

Participants—685 men and women aged 55 to 74 years old were included in the study, of whom 367 (54%) attended hospital for detailed examination.

Measurements and main results—At a mobile clinic visual acuity and lens opacities were assessed, and using a questionnaire, occupational history and lifetime exposure to sunlight. At hospital ophthalmic measurements were repeated and blood was taken for measurement of plasma vitamin C, vitamin E, and total carotenoids, and red cell activities of glucose-6-phosphate dehydrogenase, glutathione peroxidase, superoxide dismutase, and catalase. Higher grades of cataract (particularly nuclear cataract) tended to be more common in subjects with the most sun exposure, although not to the point of statistical significance. In contrast to earlier studies, no association was found with antioxidant status.

Conclusions—The findings give some support to the hypothesis that sunlight causes cataract. The absence of a relation to antioxidant status may be because blood levels of antioxidants at one point in time do not adequately reflect a subject's past metabolic state, and particularly the past activity of antioxidants in the lens.

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Cataract is the cause of blindness in an estimated 20-25 million people worldwide.¹ Solar ultraviolet radiation has long been suspected of contributing to the formation of cataract, but its role is not yet firmly established. Ultraviolet irradiation of lens proteins and whole lenses in vitro produces biochemical changes similar to those seen in cataractous lenses,^{2,3} and cortical cataracts have been induced in experimental animals by in vivo exposure to ultraviolet radiation.^{4,5} These laboratory findings are supported by epidemiological studies which have shown associations between cataract and residence in places with higher levels of sunshine.⁶⁻¹¹ However, the relation has been less consistent in geographically localised studies

where differences in sunlight exposure have been inferred from individual behaviour and occupational histories. In a survey of watermen on Chesapeake Bay, a doubling in estimated cumulative exposure to ultraviolet-B was associated with a relative risk of 1.6 for cortical cataract,^{12,13} and a study in Maryland and Delaware found 23% higher sunlight exposure in patients with posterior subcapsular cataract than in controls.¹⁴ On the other hand, two other case-control studies have found only weak and statistically insignificant associations between cataract and sunlight.^{15,16}

The absence of a clear relation in some studies may be partly attributable to difficulties in characterising individual exposure to sunlight retrospectively, particularly if there is little heterogeneity of exposure in the population under study. Also, the sensitivity of the lens to sunlight may depend on nutrition. The biochemical mechanisms whereby ultraviolet radiation is suspected of causing cataract include photo-oxidation of tryptophan residues in lens proteins and the generation of reactive species of oxygen which damage lens protein.¹³ These processes may be counteracted by various dietary dependent antioxidants including vitamin C, vitamin E, carotenoids, and the enzymes glucose-6-phosphate dehydrogenase (G6PD), glutathione peroxidase, superoxide dismutase, and catalase.^{17,18} A case-control study in the United States has suggested that risk of cataract is reduced in subjects with better overall antioxidant status.¹⁸

A recent survey of lifestyle and health in the fishing community of Hong Kong indicated that this might be a good population in which to study the relation of cataract to sunlight exposure.¹⁹ It is a stable population, most of whose members have spent all their lives up to retirement living and working in boats on the South China Sea. At this latitude and on an open sea ultraviolet radiation is relatively intense. However, some methods of fishing are carried out largely at night. Thus marked variation in individual exposure to sunlight might be anticipated.

We report a survey of cataract and sunlight exposure in Hong Kong fishing people in which we have also examined antioxidant status.

Methods

A survey of eye disease was carried out in the 15 main fishing towns and villages of Hong Kong, and was publicised by posters and leaflets distributed through the local fishermen's associations, district boards, and rural committees. Fishermen and women aged 55 years and over were invited to attend a mobile clinic which travelled to each

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centre, with the encouragement that they would be referred for treatment if disease was found.

At the clinic visual acuity was assessed with a Snellen illiterate E chart, and eyes were examined by an ophthalmologist (CHH) in a darkened room with a focused battery hand lamp and loupe, ophthalmoscope, and hand slit lamp. Pupils were not dilated lest this should reduce response rates. Cataract was deemed to be present on this preliminary assessment if the lens had been extracted, if nuclear opacities obscured more than half of the red reflex, or if more than half of the lens cortex or posterior subcapsular area was opacified; and if these changes could not be attributed to trauma.

As well as being examined, all subjects who attended the clinic were interviewed by a second observer (LW) who was unaware of the ophthalmic findings. A structured questionnaire was used to ascertain their lifetime occupational histories with an estimate of the number of hours per day for which they were exposed to sunlight in each job, and details of factors which might modify ocular exposure to ultraviolet radiation (use of hats, canopies, and spectacles).

Following this field survey, all subjects aged 55–74 were asked to attend the outpatient eye clinic of the Prince of Wales Hospital for more detailed examination. Transport was provided for those who needed it. At the hospital visual acuity was again assessed (with corrective lenses if worn)

using a Snellen E chart, and lenses were examined with a slit lamp after dilatation of the pupils with 1% tropicamide and 2.5% phenylephrine. The examinations were carried out by two ophthalmologists who graded cataracts according to the scheme shown in table I. The ophthalmologists were unaware of subjects' occupational histories.

While at the hospital, subjects were also asked to provide 10 ml of blood for analysis of antioxidants. Samples were placed in lithium heparin tubes and stored in the dark on ice for up to two hours before centrifugation for 10 min at 1700 g. Aliquots of plasma were stored at -70°C for analysis of vitamin C,²⁰ vitamin E,²¹ and total carotenoids.²² The packed blood cells were washed twice with ice cold sodium chloride (153 mM) and lysed with saponin. Activities of G6PD,^{23, 24} glutathione peroxidase,²⁵ and superoxide dismutase²⁶ were measured in duplicate based on published methods which were adapted to an automated centrifugal analyser. Catalase activity²⁷ was measured in a temperature controlled spectrophotometer with microprocessor calculated reaction rates. G6PD activity was measured within 1 h of haemolysate preparation and other enzyme activities were measured within 6 h. Aliquots of plasma and haemolysate from one healthy individual were stored at -70°C and used as quality control material throughout the study. However these controls were unsuitable for catalase and G6PD, which were unstable even at -70°C . Throughout the study, the analysts were unaware of subjects' ophthalmic findings. A few samples were insufficient for all of the assays. Also, in some samples glutathione peroxidase could not be measured on the same day due to technical difficulties, and as this enzyme is unstable in haemolysates, a repeat analysis could not be performed. The interassay analytical coefficients of variation of the methods over the six month study period were 11.3% (vitamin C), 7.8% (vitamin E), 2.2% (total carotenoids), 6.5% (glutathione peroxidase), and 11.5% (superoxide dismutase).

Associations of cataract with sunlight exposure and antioxidant status were studied by logistic regression, the analysis being restricted to those subjects who attended hospital. For each type of cataract and for all cataracts combined, subjects were classified according to the highest grade in either eye. Sun exposure was estimated by a score calculated according to the algorithm given in table II. Individual scores were ranked and risks were estimated for the top quintile and middle three quintiles of the distribution relative to the bottom quintile. A similar approach was used to partition vitamin levels and enzyme activities. In addition, summary indices of antioxidant status were derived according to an algorithm devised by Jacques *et al.*¹⁸ The "enzyme index" was considered high if a subject was in the highest quintile for either glutathione peroxidase or superoxide dismutase and not in the lowest quintile for the other enzyme. It was classified as low if the subject was in the lowest quintile for either one of these enzymes and not in the highest quintile for the other. Otherwise it was deemed to be medium. The "vitamin index" was scored high if a subject was in the highest quintile for at least two of the vitamins studied and not in the lowest quintile for the third.

Table I Classification of cataracts

<i>Nuclear cataract</i>	
Grade 0:	Clear red reflex, no opalescence of the nuclear region
Grade 1:	Opacification of the nuclear region obscuring less than $\frac{1}{4}$ of the red reflex in total
Grade 2:	Opacification of the nuclear region obscuring at least $\frac{1}{4}$ but less than $\frac{1}{2}$ of the red reflex
Grade 3:	Opacification of the nuclear region obscuring at least $\frac{1}{2}$ of the red reflex, but with part of the red reflex still visible
Grade 4:	Opacification of the nuclear region obscuring all of the red reflex
<i>Cortical cataract</i>	
Grade 0:	No cortical opacities
Grade 1:	Cortical opacities occupying less than $\frac{1}{8}$ of the lens circumference in total
Grade 2:	Cortical opacities occupying at least $\frac{1}{8}$ and less than $\frac{1}{4}$ of the lens circumference in total
Grade 3:	Cortical opacities occupying at least $\frac{1}{4}$ and less than $\frac{1}{2}$ of the lens circumference in total
Grade 4:	Cortical opacities occupying at least $\frac{1}{2}$ of the lens circumference in total
<i>Posterior subcapsular cataract</i>	
Grade 0:	No posterior subcapsular opacities
Grade 1:	Opacities occupying less than $\frac{1}{8}$ of the posterior subcapsular area in total
Grade 2:	Opacities occupying at least $\frac{1}{8}$ and less than $\frac{1}{4}$ of the posterior subcapsular area in total
Grade 3:	Opacities occupying at least $\frac{1}{4}$ and less than $\frac{1}{2}$ of the posterior subcapsular area in total
Grade 4:	Opacities occupying at least $\frac{1}{2}$ of the posterior subcapsular area in total
Lenses extracted because of cataracts were classified as grade 5	
Lens changes due to trauma were ignored.	

Table 2 Calculation of sun exposure score

A score was calculated for each fishing job as a product of four factors assigned as follows:-

1	<i>Daily sunlight exposure</i>		3	<i>Use of hat</i>	
	> 8 hours	1.0		All the time	0.5
	5-8 hours	0.6		Most of the time	0.6
	1-4 hours	0.3		About half of the time	0.75
	< 1 hour	0.0		Sometimes	0.9
				Rarely or never	1.0
2	<i>Use of canopy</i>		4	<i>Use of glasses</i>	
	All the time	0.5		All the time	0.05
	Most of the time	0.6		Most of the time	0.25
	About half of the time	0.75		About half of the time	0.5
	Sometimes	0.9		Some of the time	0.8
	Rarely or never	1.0		Rarely or never	1.0

Scores were similarly calculated for any land based jobs and periods of retirement, but were reduced by a factor of 0.7 to allow for the higher horizon and lower levels of reflected ultraviolet radiation on land.

The sun exposure score was calculated as a time weighted average of the scores for all jobs and periods of retirement after the age of 10 years.

It was low if the subject was in the lowest quintile for at least one vitamin and not in the highest quintile for either of the other two. Otherwise it was medium. The "combined index" was high if either of the enzyme and vitamin indices was high and neither was low. It was low if either was low and neither was high. Otherwise it was medium.

Table III Distribution of responders by cataract grade. Subjects were classified according to the maximum grade of each type of cataract in either eye.

Type of cataract	Cataract grade			
	0, I	II	III, IV	V
All cataract	164	163	28	12
Nuclear	252	101	14	-
Cortical	250	97	20	-
Posterior subcapsular	361	6	0	-

Table IV Prevalence (%) of cataract by age. Subjects were classified according to the maximum grade of cataract in either eye

Age (years)	No of subjects	All cataracts		Nuclear cataract Grades II, III, IV	Cortical cataract Grades II, III, IV
		Grade II	Grades III, IV, V		
55-59	94	31.9	5.3	20.2	21.2
60-64	95	34.7	3.2	18.9	20.0
65-69	114	51.8	16.7	36.9	38.6
70-74	64	64.1	20.3	56.2	53.1
All ages	367	44.4	10.9	31.3	31.8

Table V Risk of cataract according to sunlight exposure and antioxidant status. Subjects were classified according to maximum grade of cataract of any type in either eye. All odds ratios are relative to grades 0 and I. Each risk factor was examined independently with allowance for age (in five year strata) and sex.

Risk Factor	Cataract grade	0, I		II		III, IV, V	
		n*	OR (95% CI)	n*	OR (95% CI)	n*	OR (95% CI)
Sun exposure score							
Low	(<0.150)	33	1	28	1	6	1
Medium	(0.150-0.418)	90	1.4 (0.7-2.6)	95	1.4 (0.7-2.6)	20	1.7 (0.5-5.3)
High	(>0.418)	32	1.2 (0.6-2.8)	27	1.2 (0.6-2.8)	8	2.1 (0.6-7.9)
G6PD (U/g Hb)							
Low	(<3.29)	26	1	34	1	5	1
Medium	(3.29-4.10)	89	0.8 (0.4-1.6)	84	0.8 (0.4-1.6)	18	1.0 (0.3-3.6)
High	(>4.10)	25	0.9 (0.4-2.1)	23	0.9 (0.4-2.1)	13	2.2 (0.6-8.9)
Glutathione peroxidase (U/g Hb)							
Low	(<36.6)	17	1	25	1	4	1
Medium	(36.6-54.1)	52	0.7 (0.3-1.7)	64	0.7 (0.3-1.7)	21	2.0 (0.5-9.2)
High	(>54.1)	21	0.6 (0.2-1.6)	19	0.6 (0.2-1.6)	6	1.5 (0.3-8.4)
Superoxide dismutase (U/g Hb)							
Low	(<2334)	34	1	21	1	8	1
Medium	(2334-2900)	81	2.2 (1.1-4.5)	92	2.2 (1.1-4.5)	18	1.0 (0.3-2.8)
High	(>2900)	25	2.2 (0.9-5.2)	28	2.2 (0.9-5.2)	10	1.5 (0.4-5.5)
Catalase (U/g Hb)							
Low	(<153)	31	1	28	1	5	1
Medium	(153-195)	78	1.4 (0.7-2.8)	88	1.4 (0.7-2.8)	24	2.1 (0.6-7.1)
High	(>195)	30	1.0 (0.5-2.4)	25	1.0 (0.5-2.4)	7	1.1 (0.3-4.9)
Vitamin C (µmol/litre)							
Low	(<40.9)	21	1	34	1	9	1
Medium	(40.9-80.1)	87	0.9 (0.4-1.7)	83	0.9 (0.4-1.7)	20	0.7 (0.2-2.2)
High	(>80.1)	32	0.7 (0.3-1.6)	24	0.7 (0.3-1.6)	7	0.8 (0.2-3.2)
Vitamin E (µmol/litre)							
Low	(<25.4)	33	1	24	1	8	1
Medium	(25.4-36.4)	76	1.7 (0.9-3.4)	90	1.7 (0.9-3.4)	22	1.0 (0.3-3.2)
High	(>36.4)	30	1.2 (0.5-2.7)	27	1.2 (0.5-2.7)	5	0.4 (0.1-1.8)
Carotenoids (µmol/litre)							
Low	(<0.72)	24	1	29	1	8	1
Medium	(0.72-1.47)	84	0.8 (0.4-1.5)	83	0.8 (0.4-1.5)	18	0.6 (0.2-1.7)
High	(>1.47)	28	1.0 (0.4-2.3)	26	1.0 (0.4-2.3)	6	0.8 (0.2-3.5)
Enzyme index							
Low		28	1	26	1	9	1
Medium		43	1.5 (0.7-3.1)	58	1.5 (0.7-3.1)	13	0.7 (0.2-2.2)
High		19	1.4 (0.6-3.6)	24	1.4 (0.6-3.6)	9	1.5 (0.4-5.6)
Vitamin index							
Low		40	1	47	1	14	1
Medium		77	1.0 (0.5-1.7)	76	1.0 (0.5-1.7)	12	0.4 (0.1-1.2)
High		18	1.0 (0.4-2.5)	15	1.0 (0.4-2.5)	5	1.0 (0.2-4.2)
Combined index							
Low		27	1	44	1	11	1
Medium		37	0.5 (0.2-1.1)	37	0.5 (0.2-1.1)	9	0.3 (0.1-1.2)
High		21	0.8 (0.3-2.0)	24	0.8 (0.3-2.0)	6	1.0 (0.2-4.2)

*Sun exposure scores could not be calculated for 28 subjects because their occupational histories were incomplete. Antioxidant levels were missing for some subjects because they declined to give blood or because of technical problems in the laboratory (see text). G6PD = glucose-6-phosphate dehydrogenase.

Results

The field survey included 685 subjects aged 55-74 years, of whom 367 attended hospital for detailed examination. The attendance rate was similar in men and women, in subjects with high and low sun exposures scores, and in subjects with and without a diagnosis of cataract at the preliminary examination, but it was rather lower in subjects aged 70-74 years (43%) than at younger ages (56%). Of the hospital attenders, 158 were men and 209 were women.

Table III shows the distribution of attenders by cataract grade. Altogether, 40 subjects (11%) had cataracts of grade III or higher, including 12 (3%) who had lens extractions. Almost all of the cataracts observed were cortical or nuclear in type. The prevalence of cataracts was similar in men and women, but increased steeply with age (table IV). Visual acuity was 6/30 or less in 77% of eyes with grade III or IV changes.

Table V shows the overall association of cataract with sun exposure, enzyme levels and vitamin levels when each risk factor was examined independently with allowance for age and sex. The higher grades of cataract tended to be more common in subjects with the highest sun exposure scores, but none of the associations with sun exposure was statistically significant at the 5% level. No clear patterns emerged in relation to antioxidant status. In particular, there was no trend to reduced cataract risk in subjects with the highest enzyme, vitamin, or combined indices. We looked to see whether associations with sun exposure and antioxidant status might be obscured by interconfounding (ie, higher antioxidant levels occurring in subjects with higher sunlight exposure), but found no evidence of such an effect.

When risks were estimated separately for nuclear and cortical cataract, no clear patterns emerged, although the trend to higher risk with increasing sun exposure was if anything stronger for nuclear than for cortical cataract.

Discussion

This study provides limited support for the hypothesis that sunlight is a cause of cataract, but gives no encouragement to the theory that antioxidant status is an important determinant of risk. Our failure to detect associations is unlikely to be related to the selection of subjects for study, but may have been influenced by errors in the grading of cataracts and classification of sun exposure.

We adopted a staged approach to data collection in the hope that during the field survey we would gain the confidence and goodwill of subjects, and thereby promote a better response to our request for hospital attendance. Although only 54% of eligible subjects attended hospital, there was no evidence that the response was biased in relation to cataract prevalence or sunlight exposure. We restricted our main analysis to those who attended hospital because cataract diagnosis in the field survey showed incomplete agreement with the hospital grading, and we felt that the examinations carried out with pupil dilatation and a better slit lamp would be more reliable. Unfortunately, there is no ideal method of assessing cataracts for epidemiological studies. Various grading systems have been explored including some based on

photographic techniques,²⁸ but classifications based on direct observation have been found to be as repeatable as any other.²⁹⁻³⁰ The assessment of cataracts in our study was carried out without knowledge of subjects' occupational histories, and any errors in the grading of cataracts will have tended to obscure associations.

Another possible source of error was our classification of sun exposure. We tried to assist subjects' recall by enquiring about the type of fishing method and time of day when it was carried out, before asking how much they were exposed to the sun in a job. However, their recollections may not have been accurate, particularly for exposures in the distant past. Also the factors by which we modified sun exposure scores to allow for shading and use of spectacles, although partially based on reported measurements,³¹ were inevitably somewhat crude. Again, any errors in misclassification would be expected, if anything, to obscure associations.

We had hoped that the contrast between the sun exposures associated with different fishing methods would compensate for any statistical power lost through misclassification of exposure and disease. As it turned out, the variation in sun exposure within our study sample was less than we had anticipated. Nevertheless, although not statistically significant, our findings on sunlight exposure and cataract are consistent with the associations which have been reported in other studies⁶⁻¹⁴ in that risks were higher in subjects with the highest scores. Different types of cataract may have distinct aetiologies, and previous epidemiological studies have suggested that sunlight particularly increases the risk of cortical¹²⁻¹³ and posterior subcapsular cataracts.¹⁴ In our data, however, the association was if anything stronger for nuclear cataract.

The relation of cataract to antioxidant status has been examined previously in two case-control studies.¹⁸⁻³² Jacques *et al* in the United States found a low risk of the disorder in subjects who scored high on an overall vitamin index and on a combined vitamin and enzyme index, but no clear associations with individual vitamins or enzyme activities.¹⁸ Mohan *et al* in India reported a reduced risk in relation to a different antioxidant index based on glutathione peroxidase, G6PD, vitamin C, and vitamin E, but only for posterior subcapsular cataract (alone or in combination with other cataract types).³² We defined our vitamin and combined indices in the same way as Jacques, but despite studying a larger sample of subjects found no significant association either with cataract overall, or with nuclear and cortical cataract separately. This discrepancy may have occurred because the distribution of vitamin levels and enzyme activities in our study population was different—for example, mean levels of carotenoids were lower than in the US study—or it may have arisen by chance. When considered together, however, the studies of cataract and antioxidant status suggest that any relation to plasma vitamin levels and erythrocyte enzyme activities, once cataract has developed, is weak. This does not necessarily imply that antioxidants have no importance in the pathogenesis of cataract, since blood levels of antioxidants at one point in time may not adequately reflect a subject's past metabolic state, and particularly the past activity of antioxidants in the lens. Further work is needed to find out whether such disparities are likely, and if so, to

establish how antioxidants in the lens can better be monitored.

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