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Editorials

Cigarettes and cataract: cadmium or a lack of vitamin C?

Cigarette smoking and cadmium have been identified as risk factors for cataract, and vitamin C (ascorbate) has been proposed as a protective factor.[1] In this issue Ramakrishnan *et al* (p 202) bring together all three in a single study of cataract in Madras, India. The smoking component was of beedies which are smaller than cigarettes and have the tobacco wrapped in a dry leaf rather than paper. The tobacco from beedies has a high nicotine content.

The link between smoking and cataract has been established by a series of epidemiological studies, first in Edinburgh[2] then Oxford,[3 4] London,[5] and the United States.[6–9] Some of these studies have been on patients having cataract surgery,[3 4 9] others on other visually impairing cataracts,[8] but some have been on any types of lens opacity however minor.

The later studies indicate that smoking is a risk specifically for nuclear opacity.[5–8] Although heavy smoking may double the risk of cataract it probably accounts for only about 3% of cataracts in Western countries.[10] Smoking appears to increase the risk of cataract in type 2 diabetics.[11]

Tobacco leaves contain significant amounts of cadmium and it has been shown in Hungary that the level of cadmium is much higher in human cataracts than in normal lenses.[12] Ramakrishnan *et al* provide evidence that cadmium in the tobacco reaches the lens. They show that cataract lenses from smokers contain much more cadmium than those from non-smokers. Smokers with or without cataract had higher cadmium levels in blood. So cadmium could be the toxic agent in tobacco smoke that causes cataract. There are, however, other factors to consider.

Smokers have low plasma levels of vitamin C, vitamin E, and β carotene which might explain their propensity to develop cataract.[8 9] Studies of the role of vitamins in human cataract give a rather confused picture, but in two recent American studies where data for smokers and non-smokers were analysed separately it was found that the apparent benefit was present only in smokers.[13 14] Both the studies were of users of supplements. Ramakrishnan *et al* did not find decreased blood levels of vitamin C in smokers among either the cataract or non-cataract population; nor did they find decreased levels of vitamin C in the cataract lenses of smokers. Their results make it less likely that the causal pathway from smoking to cataract is via vitamin C. It could be via the other vitamin supplements associated with protection against cataract,[13 14] but it seems possible that American smokers who use vitamin supplements are an unusual subset of both smokers and of vitamin users.

Ramakrishnan *et al* favour the idea that cadmium accumulating in the lens directly causes the damage. They have the cadmium data to support that hypothesis, but other components of tobacco smoke and their products in blood may play a role. Cyanide and thiocyanate levels are raised in the blood of smokers; and cigarette smoke is rich in free radicals and aldehydes.[15] The radicals probably cause their damage before reaching the lens but isocyanate, formed from cyanide, and aldehydes might find their way to the lens to attack enzymes and other proteins.[16] Isocyanate can cause lens opacification in vitro.[17] Both aldehydes and isocyanate can modify lens proteins causing changes similar to those seen in human cataract.[18–20]

The interactions of cadmium with various components of the lens have yet to be explored. Plasma membranes, structural proteins, channels, enzymes, receptors, etc are obvious candidates for study. If cadmium is playing a major role in the link between smoking and cataract then workers exposed to high cadmium levels in the cadmium plated steel industry, or those consuming cadmium enriched food – for example, rice in some parts of Japan, might have an increased risk of cataract.

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Automated perimetry in glaucoma – room for improvement?

The objective of static threshold automated perimetry in glaucoma is the efficient detection of visual field defects and the accurate measurement of progressive field loss.

Automated perimetry is a psychophysical test of visual function necessarily dependent upon the subjective response of the patient. The test involves the detection of a stimulus the luminance of which is greater than that of the background of a given constant luminance. Threshold static perimetry expresses the minimum detectable stimulus brightness at individual locations within the visual field in terms of sensitivity units (decibels) and provides a contour of the height and shape of the hill of vision. The numerical information, which is an estimate of the true threshold, is usually compared with that from a database of normal individuals of the same age. Abnormality of the visual field at any single examination can be expressed by a variety of graphical techniques such as the grey scale plot, and by statistical procedures such as the visual field indices,[1 2] cluster analysis,[3] the total and pattern probability plots,[4] and the glaucoma hemifield test.[5] Visual field progression can be evaluated for the field as a whole, for any region of the field, or for any stimulus location in terms of comparison with results from previous examinations by using regression analysis techniques.[2 6 6a] The change in sensitivity at a given stimulus location can also be compared with the expected variation in stable glaucoma patients.[5] The explanation for any statistically proved progressive field loss should always be compatible with the clinical assessment.

Automated perimetry is limited by the fact that the outcome of any given examination is affected by a large number of factors including those specific to the patient and/or technician and those particular to the measurement technique. Such factors determine the absolute value of sensitivity at the given location and also the variability in the response at that location both within a single visual field examination (that is, the short term fluctuation) and between examinations (that is, the long term fluctuation),[7 8] and can limit the usefulness of automated perimetry for the evaluation of visual field progression. Indeed, the level of fluctuation can be such that it is often impossible from inspection of the results of two sequential visual field examinations to determine whether progression has occurred. Confirmation of progression often necessitates a repeat examination with the consequent resource implications. Indeed, progression is frequently deemed to have occurred only by retrospective examination of a large series of field plots.

Some factors can be controlled by the clinician, such as the pupil size[9 10] and the correction of refractive error,[11 12] but other factors may be more difficult to eliminate. Indeed, the coexistence of cataract (which may be progressing) also affects the quality of the recorded information and confounds interpretation of the data at any given examination and during follow up.[13 14] Probably the single most important factor influencing the quality of the visual field examination, and yet largely ignored by current perimetric software, is the interaction of the nature of the patient response with the demands of the examination procedure. Some evidence as to the quality of patient performance is given by the reply to the catch trials which assess the number of fixation losses, and the number of false positive and false negative responses. Nevertheless, the performance of the patient is likely to be governed by factors such as motivation and anxiety. Furthermore, the current psychophysical determination of perimetric threshold using a bracketing technique is generated from substantially more stimulus presentations than the clinical ideal. Indeed, the initial lack of familiarity with the requirements of the task and the relatively long duration of the examination have been manifested in the learning and fatiguing effects respectively. The learning effect – namely, an improvement in sensitivity at a given stimulus location, can occur within a single examination of a given eye,[15] between eyes at the same visit,[15] and between subsequent examinations.[15 16] The improvement is particularly noticeable over short follow up periods, and is more pronounced at the extremities of the central 30 degree field.[4 17] The fatiguing effect, whereby sensitivity decreases during the examination, becomes more pronounced as the length of the examination increases,[18 19] is greater in the second eye examined,[20] and increases with age.[21]

To date, attempts to enhance the quality of the patient response have largely centred on the development of methods for improving data acquisition. The introduction of faster thresholding strategies has reduced the duration of the perimetric examination largely at the expense of increased variability compared with the standard threshold strategy.[22–25] Other approaches for improving data acquisition have included the use of fewer stimulus locations,[26] larger stimuli,[27 28] or repeated thresholding of the given stimulus locations.[29] No attempt has been made to enhance the quality of the recorded data. The contribution of Fitzke and colleagues, published in this issue (p 207), illustrates the potential of filtering techniques (frequently used in image processing) to reduce the variability, inherent in static threshold automated perimetry and hence improve the quality of the data. Indeed the index of spatial variability, also reported in this issue by Crabb and colleagues (p 213), based on filtering techniques, provides a further statistical tool for the evaluation of glaucomatous loss. The advent of new thresholding strategies based on