Recent Developments in Vision Research:
Light Damage in Cataract

Catherine A. McCarty and Hugh R. Taylor

Cataract is the leading cause of blindness in the world, accounting for nearly half of the 38 million cases of blindness worldwide. Age-related cataract is a multifactorial disease, and the prevalence of cataract approximately doubles with each decade after the age of 30. For this reason, if an intervention were able to delay the onset of cataract by 10 years, the number of cataract operations could be nearly halved. Possible risk factors for cataract include ultraviolet B radiation (UV-B), diabetes, alcohol, smoking, diet, diarrhea, steroid use, and certain medications such as corticosteroids. Matters are complicated because age-related cataract is not a single disease but, rather, three different types of lens changes—cortical, nuclear, and posterior subcapsular (PSC) opacities. Each has its own pathogenic changes, age distribution, and almost certainly different risk factors.

The investigation of UV-B as a risk factor for cataract has received considerable attention and has increased recently for several reasons. Sunlight is the principal source of UV-B for the majority of the world’s population, and depletion of the stratospheric ozone will lead to UV-B exposure of higher intensity. Even if the relative risk for cataract development from UV-B exposure were relatively low, the public health significance could be great because nearly everyone is exposed to UV-B. The changing demographics of the world’s population, caused by the increasing proportion of the elderly, and the thinning of the stratospheric ozone increase the urgency to quantify the possible effect of UV-B on the development and progression of lens opacities. This information is needed so that appropriate public health interventions can be implemented if necessary.

Ultraviolet radiation is usually divided by wavelength into UV-A (400 to 320 nm), UV-B (320 to 290 nm), and UV-C (<290 nm). Incident UV-B varies greatly by time of day, altitude, and season. The ozone layer absorbs almost all UV-C, thus preventing it from reaching the eye lens. Any UV-C that is encountered is usually generated from artificial sources, such as a welder’s arc. This is a well-known cause of severe corneal burn called welder’s arc or flash burn. Almost 60% of radiation at 320 nm is transmitted through the cornea and is absorbed by the lens. Recent research on the action spectrum for UV-A and UV-B in rabbit lens epithelial cells revealed that cytotoxicity was highest at 297 nm (UV-B).

Other suspected sun-related ocular conditions include acute photokeratitis, climatic droplet keratopathy, pinguecula, pterygium, age-related macular degeneration (possibly caused by exposure to blue light or visible light, but not to UV-B), and possibly choroidal melanoma.

QUANTIFICATION OF EXPOSURE AND OUTCOME

The study of the relationship of two variables, such as UV-B exposure and cataract, requires reliable and valid measures of both variables. It is essential to distinguish the three different types of age-related cataract—cortical, nuclear, and PSC. Including all types of cataract or mixed cataract in statistical analyses precludes the ability to discriminate the unique risk factors for each type of age-related cataract.

There are now several grading schemes that allow in vivo assessment of the type, extent, and density of lens opacities. Decimalization of the grading of nuclear opacities has enhanced statistical power in epidemiologic investigations to establish significant associations. The World Health Organization is constructing a simplified grading system, particularly for use in developing countries. In addition to grading actual lens opacities, other factors, such as a standard pupil size, must be considered when quantifying lens opacities for research.

Quantification of UV-B exposure in experimental situations has been relatively straightforward because it is possible to measure UV-B directly in a controlled situation. Quantification of lifetime UV-B exposure in free-living populations is much more challenging because the ocular dose is dependent not only on environmental levels but on personal behaviors as...
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TABLE 1. Effect of Behavior on Relative Personal Ultraviolet B Exposure

<table>
<thead>
<tr>
<th>Behavior</th>
<th>Relative Ultraviolet B Dose (U)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indoor</td>
<td>4</td>
</tr>
<tr>
<td>Outdoor wearing brimmed hat</td>
<td>8</td>
</tr>
<tr>
<td>and sunglasses</td>
<td></td>
</tr>
<tr>
<td>Outdoor wearing sunglasses</td>
<td>17</td>
</tr>
<tr>
<td>Outdoor wearing brimmed hat</td>
<td>47</td>
</tr>
<tr>
<td>Outdoor with no ocular protection</td>
<td>72</td>
</tr>
</tbody>
</table>

well, such as the amount of time spent outdoors and the use of ocular protection such as a brimmed hat or eyewear. Personal behavior can have an 18-fold impact on ocular dose of UV-B (Table 1). This is far greater than the 4-fold global difference in UV-B irradiance by latitude (Fig. 1).

Personal behavior is more important in determining personal ocular UV-B exposure than geographic location. Therefore, it is essential for epidemiologic studies to collect information about personal behavior and to develop an assessment of personal ocular UV-B exposure that incorporates ambient levels of UV-B, outdoor exposure, personal protection and behaviors, and the ocular ambient exposure ratio. The ocular ambient exposure ratio is the proportion of ambient UV-B that actually reaches the eye, considering use of ocular protection, time of year, and ground surface. Studies that do not account for all these factors are likely to result in misclassification of exposure levels, decreasing the power of a study to detect a significant association between UV-B and cataract, and lead to erroneous conclusions.

A detailed, lifetime, personal ocular UV-B exposure questionnaire and model was developed for use in the Chesapeake Bay Watermen Study. This allowed investigators to quantify personal ocular UV-B exposure for every year of life after age 14 years. It was modified slightly for use in the Melbourne Visual Impairment Project by excluding questions regarding winter months because summertime exposure from 9 AM to 5 PM (daylight savings time) accounted for 96% of the annual UV-B exposure. The Salisbury Eye Evaluation project, a population-based study of vision in the elderly under way in Maryland, is using the methodology developed in the Chesapeake Bay Watermen Study to quantify the relationship between UV-B exposure and cataract.

EXPERIMENTAL EVIDENCE

Recently the extensive body of biochemical and experimental evidence relating oxidative stress to cataract was reviewed. Oxidation of lens proteins has been shown to be associated with lens opacification in older people, with a concomitant age-related depletion in glutathione and ascorbate, the major antioxidants in the lens. The initial site of attack by oxidative stress is most likely the epithelium, with later involvement of the lens fibers, which leads to cortical cataract. Ultraviolet light is the primary environmental source of photooxidation, which itself is the major source of oxidative stress to the lens.

EPIDEMIOLOGIC EVIDENCE

The epidemiologic evidence of an association between UV-B and cataract also was reviewed recently. Ecologic studies, in which individual level data are not collected, provided early indications that UV-B might be causally related to the development of cataract because it was noted that cataract rates were higher near the equator. However, without individual data, it was not possible to establish the independent effect of UV-B after accounting for other potential risk factors, such as diet, temperature, and ethnicity. A recent ecologic study conducted in the United States has shown that the cataract surgery rate, ascertained from Medicare data, was strongly related to latitude. After adjusting for many possible confounding factors, cataract surgery rates were twice as high in the south than in the north.

The relationship between UV-B and different types of cataract was examined with data from the 1971-1972 United States National Health and Nutrition Examination Survey (see reference 2). The ecologic assessment of exposure was based on average annual daily UV-B counts at the place of residence derived by the US National Oceanic and Atmospheric Administration. Cortical cataracts were 3.6 times more common in areas with increased UV-B counts. Nuclear and PSC cataracts were not related to ecologic levels of UV-B.

The Lens Opacities Case-Control Study in Boston collected information on personal UV-B exposure, behaviors such as occupational exposure to sunlight, leisure time in the sun, residence, and use of hats, sunglasses, and prescription glasses (see reference 2). How...
However, these separate UV-B-related variables were not incorporated into a personal exposure model. People with high occupational exposure to UV-B were less likely to have nuclear cataract than the other types of cataract (OR = 0.61), and use of prescription glasses increased the likelihood of mixed cataract (OR = 1.44).

The Italian-American Case-Control Study of Age-Related Cataracts was a replicate of the Lens Opacities Case-Control Study (see reference 2). Researchers developed a sunlight index that incorporated information from 14 variables related to general sunlight exposure history. After controlling for age and gender, a significant dose-response effect was found between sunlight exposure index and presence of pure cortical cataracts, as well as of all types of mixed cataract except corticonuclear.

The Chesapeake Bay Watermen Study was the first to incorporate information on ambient levels of UV-B, outdoor exposure, personal protection and behaviors, and the ocular ambient exposure ratio into a model to quantify lifetime personal ocular UV-B exposure. Investigators found that UV-B exposure was significantly related to cortical cataract (OR = 3.30). The association was specific for UV-B; ocular exposure to UV-A, blue light, or visible light was not associated with cataract. A related study showed a similar association between PSC cataract and UV-B exposure. UV-B was not related to nuclear cataract. The difference in findings between this study and the results from the US National Health and Nutrition Examination Survey could be the result of the very different methodologies used. The Chesapeake Bay Watermen Study collected detailed personal sunlight history and did not rely solely on ambient UV-B available in the environment. This should have decreased the chances of misclassification bias.

The Beaver Dam Eye Study in Wisconsin used personal residential history as a surrogate for UV-B exposure and included use of hats and sunglasses as independent terms in a multivariate model, rather than combining them in a personal exposure model as was done in the Chesapeake Bay Watermen Study (see reference 2). They found that men with higher UV-B exposure were 1.36 times more likely to have severe cortical cataract. They found no associations with other wavelengths or the other types of opacities in men. They found no associations between UV-B and cataract in women, although the women in the study had extremely low levels of outdoor exposure and, therefore, the lack of an association is not unexpected.

In summary, the epidemiologic evidence generally supports biologic and experimental evidence suggesting a causal relationship between UV-B and cataract, specifically cortical and possibly PSC opacities. None of the studies suggest an association with nuclear cataract. Some skeptics have interpreted the lack of an association between UV-B exposure and nuclear opacity as an indication that UV-B does not cause cataract. Others think this lack of an association with nuclear cataract strengthens the association with cortical opacities because it demonstrates the ability of these studies to discriminate between these two closely related, but clearly separate, entities.

### SUPPORTING EVIDENCE FROM THE ASSOCIATION OF DIETARY ANTIOXIDANTS AND CATARACT

Because the putative mechanism of UV-B-induced cataractogenesis involves photooxidation, the demonstration of a protective role of antioxidants would add further support to this hypothesis. In vitro and in vivo studies in various animal species have demonstrated a significant protective effect of vitamins C and E against light-induced cataract. The epidemiologic evidence recently was summarized and suggests a role for antioxidants in the protection against all types of cataract.

Two similar cohort studies in the US investigated the association between nutrient intake and risk for cataract extraction. The Physician's Health Study showed a reduced risk for cataract extraction in physicians taking multivitamins (OR = 0.79). In the Nurse's Health Study, the dietary intake of carotene and vitamin A protected against cataract extraction (relative risk = 0.61), and women who took vitamin C supplements had a 45% lower risk for cataract extraction.

The role of dietary antioxidant intake and cataract also was investigated in the Baltimore Longitudinal Study on Aging and in the Beaver Dam Eye Study. In the Baltimore study, plasma beta-carotene levels were not associated with nuclear or cortical opacities. However, higher plasma levels of alpha-tocopherol were associated with a reduced risk for nuclear opacity (OR = 0.52), and middle levels were associated with a reduced risk for cortical opacity (OR = 0.57). An antioxidant index was not associated with cortical or nuclear opacities. The Beaver Dam Eye Study produced confusing results. The regular use of multivitamins for 10 years was associated with decreased risk for nuclear opacities in persons without diabetes (OR = 0.60) but increased risk for cortical opacities (OR = 1.60). In persons with diabetes, past multivitamin use was not associated with nuclear opacities but was related to a decreased risk for cortical opacities (OR = 0.1).

The Linxian Cataract Studies—prospective, randomized, double-masked trials of 5 to 6 years duration in adults in rural China—were designed to test whether nutrient supplements protected against stomach cancer. One study found a 36% reduction in the prevalence of nuclear cataract in people age 65 to 74 years of age who received a multivitamin—mineral supplement. The other trial found that the prevalence of nuclear cataract was significantly lower in persons re-
ceiving riboflavin–niacin, and those in the oldest age group reaped the greatest benefit (44% reduction).

These epidemiologic data support results from biologic studies that suggest low levels of antioxidants are associated with an increased risk for both the development and the progression of lens opacities. The association between antioxidants and cataract also supports the likely importance of oxidation in cataractogenesis, and, as mentioned earlier, UV-B is likely to be the main phototoxidizing agent. Further prospective studies are needed to quantify the relationship of antioxidant intake to lens opacities while controlling for UV-B exposure.

FUTURE DIRECTIONS

Although biologic and epidemiologic evidence generally support an association between UV-B and cortical cataract, more properly conducted studies are needed to confirm this hypothesis. It would be preferable for such studies to be population based, but they must quantify personal lifetime ocular exposure to UV-B. At present, the Chesapeake Bay Watermen Study stands on its own in this field.

Prospective, randomized, controlled trials of antioxidant supplementation are under way in several countries. However, these are long-term studies, and their results will not be available for years to come.

Given the limited data available, many public health administrations and governments are reluctant to initiate major public health campaigns to reduce ocular UV-B exposure. However, with the near universal exposure of the global population to UV-B, even a relatively moderate effect of UV-B in causing cataract would translate into a large number of cataract cases worldwide. While we all wait for information to establish the link between UV-B exposure and cataract definitively, it seems prudent to recommend the reduction of personal ocular UV-B exposure. The best way to do this is to stay out of the summer midday sun. If this is not possible, people should at least protect themselves with the use of a brimmed hat and UV-B absorbing eyeglasses or sunglasses to reduce their ocular UV-B exposure.

Key Words

cataract, exposure assessment, lens, ultraviolet light

References