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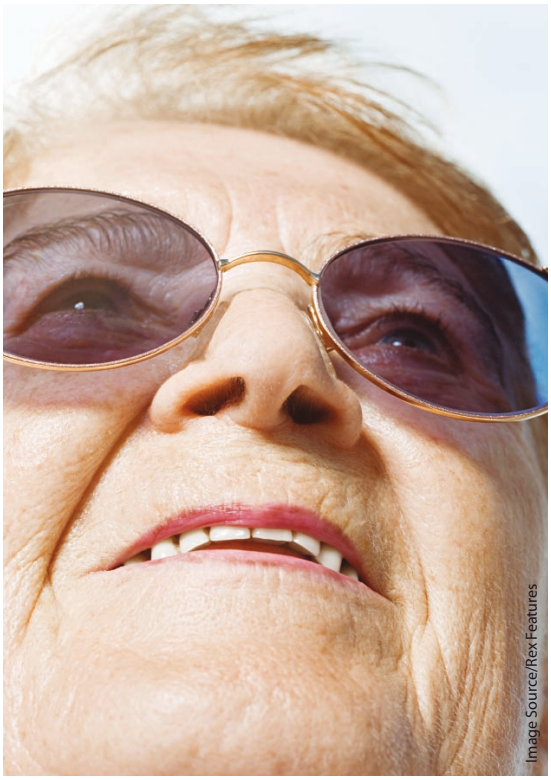
Sunlight and AMD

Dr Frank Eperjesi offers an update on the latest influences upon age-related macular degeneration and its risk factors. Module C14046, one general point for optometrists and DOs

There is now clear evidence from population studies involving large numbers of subjects to prove that age-related macular degeneration is more common in older people[1] (0.3 per cent for those younger than 70 years increasing to 10.1 per cent for those 80 years and above), in those that smoke tobacco, for example[2,3] and for Caucasians[4] (melanin in the iris, RPE and choroid is thought to protect against radiation damage).[5] In contrast the evidence to support a relationship between sunlight exposure and AMD and refractive error and AMD is inconclusive. This article will review evidence linking sunlight exposure to AMD as well as summarise recent developments in the enhancement of macular pigment optical density through the use of nutritional supplements. Links between refractive error and AMD will be discussed in the second article.



People with AMD are advised to wear sunglasses to diminish additional unnecessary damage

Sunlight exposure and AMD

An important public health question can be asked about the potential hazard of long-term exposure to UV and blue light of the visible spectrum. The possibility that long-term exposure to light may be a factor in AMD has been raised and while the role of sun exposure in AMD is less certain than for example cigarette smoking, it still has considerable public health implications regarding the wearing of sunglasses and eye protection.

Glickman[6] described the dual nature of light as capable of enabling vision and destroying it. As visual pigments in the photoreceptors are bleached, excitation energy is transferred to oxygen molecules forming highly reactive singlet oxygen which in the presence of blue light forms hydroperoxides and cholesterol. Recent data has shown that the retina itself along with the RPE is likely the primary site for metabolism of these products and breakdown in this process is likely to lead to retinal disease. The macula is the most metabolically active tissue in the human body. The choroid and the RPE support this high metabolic pace by serving as a heat sink, by quenching free radicals and by phagocytising the photoreceptor outer segments that are continually shed into the RPE in the form of used photoreceptor outer segments. The overload of this phagocytic process causes the build up of lipofuscin (the retinal equivalent of 'age spots') in the RPE.[7] It is well known that the degeneration of RPE cells plays an important role in the progression of AMD and with increased age, the life-long exposure of RPE cells to light may have a significant impact on their degeneration.[8] Lipofuscin is a heterogeneous aggregation of damaged molecules found in RPE cells. Following absorption of UV photons by lipofuscin, radiation is re-emitted into the cytoplasm of the RPE cell at blue and yellow-orange wavelengths[9] and it is likely that there are numerous uncontrolled side-effects resulting from radiation absorption in lipofuscin.[10] This may be of more significance in the older retina since melanin progressively decreases and lipofuscin increases during age.[11] In the RPE of older persons the amount of lipofuscin may exceed that of melanin by five to 10 times.[12]

It has also been shown that visible light induces apoptosis in retinal cells.[13] Blue light of the visible spectrum has been shown to be 30 times more efficient than yellow light in inducing damage to the blood-retinal barrier.[14] Unattenuated sunlight peaks at 470nm and a relatively large proportion of solar energy is concentrated in the blue end of the spectrum.[15]

Wavelengths below 380nm appear to be absorbed almost completely by anterior segment structures but a significant proportion of wavelengths above 380nm are transmitted to the retina. In adults less than 1 per cent of radiation below 340nm and 2 per cent of radiation between 340 and 360nm reaches the retina. Above 380nm transmission increases to as does the incident irradiance (light concentration) so that at 400nm 10 per cent of incident light is transmitted to the retina.[16] Ham et al[15] found that 441.6nm caused retinal damage at thresholds 800 times lower than 1,064nm. This suggests that the threshold for damage would be even lower at 400nm with the possibility of retinal damage despite the low media transmission values at this wavelength. It is also useful to note that the eye focuses incoming light on the retina and this focusing process concentrates light, increasing the power density of light on the retina. Thus, light that delivers a radiant exposure insufficient to produce skin damage may cause eye injury through photochemical damage (changes to the chemical structure or composition of biomolecules) when focused on the retina.[17]

One major problem in undertaking a study to address the relationship between sunlight exposure and AMD is the identification of a population

whose members represent a wide range of lifetime sunlight exposures. Longitudinal studies investigating the relationship sunlight exposure and AMD must resort to questionnaires that gather information on exposure patterns across several decades of each participant's life. Such questionnaires are prone to recall bias or at the very least marginally accurate information because of the need to reconstruct habits that may have changed across a person's lifetime. This means that lifetime exposure questionnaires need to be very detailed.[16] Evans[18] warns that these questionnaires are crude as they attempt to measure lifetime exposure and minute-by-minute exposures can vary enormously depending on the angle of the sun, the position of the head, use of hats, trees and reflective surfaces.

Taylor et al,[19] in a landmark population study, collected work and leisure sunlight exposure data and together with laboratory and field measurements determined yearly ocular exposure to violet, blue and all visible light as well as UVA and UVB for 838 fishermen working in the Chesapeake area of Maryland, USA. When only sunlight exposure for the previous 20 years was considered, a significant association between late AMD and blue light was found. The eight individuals with late AMD had on average 48 per cent higher exposure to blue light than their age-matched controls. The authors postulated that this could be explained by the presence of a defence mechanism that deteriorates with age and may no longer be able to protect the retinal structures against previously non-damaging exposures and irreversible changes start to accumulate. Neither cumulative UVA nor UVB exposure was related to AMD after adjustment for age.

In the epidemiological Beaver Dam Eye study[20] 4,926 participants were reviewed for AMD and sunlight exposure. High levels of leisure time spent outdoors in summer were associated with increased retinal pigment levels in men and late AMD in men and women. Wearing of sunglasses was inversely associated with increased retinal pigment. Participants who wore sunglasses and hats with brims were less likely to have soft indistinct drusen, suggesting a link between exposure to bright sunshine and late AMD. Five years later 3,684 of the original participants were examined again and asked about sunlight-related behaviours during their teenage years (age 13-19) and their 30s (age 30-39).[21] Those who spent five or more hours per day outside in the summertime during their teenage years and 30s appeared to have a greater risk of developing early AMD as older adults compared to people who spent little time outside. No association was found between UV exposure and early AMD in this cohort.[16] Five years later 2,764 participants of the original population were examined and sun exposure information obtained via questionnaires.[22] Controlling for age and gender those participants exposed to the summer sun for more than five hours a day during their teens, 30s and at baseline were at a higher risk of developing increased retinal pigment and early AMD than those exposed to less than two hours per day during the same periods. Interestingly, in those participants reporting the highest summer sun exposure levels in their teens and 30s, the use of hats and sunglasses at least half of the time during the same periods were associated with a decreased risk of developing soft indistinct drusen and RPE depigmentation. No relationships were found for UVB exposure. The authors of this report added that the power to detect relationships between sunlight exposure and late AMD were limited by the rarity of the disease in this cohort.

A study conducted by Delcourt et al[23] on the French Mediterranean coast involved 2,584 residents and a questionnaire was used to gather information on sunlight exposure. Thirty-eight participants had late AMD and this was not associated with any light exposure variable. Counter intuitively, those with high sunlight exposure had a decreased risk of pigmentary abnormalities and fewer early signs of AMD. Subjects who used sunglasses regularly had a decreased risk of soft drusen. The investigators admitted that the small number of cases of late AMD led to a low statistical power to detect any association.

Ten years after obtaining baseline information, 1,952 participants in the Blue Mountains Eye Study were examined for AMD. The investigators used sun-related skin damage as a measure of sunlight exposure and found no relationship with AMD incidence.[24]

In an Australian case-control study, ocular sun exposure was obtained from age five years onwards using structured interviews for 409 cases (328 with wet and 81 with dry AMD) and 286 control cases and controls subjects were assessed

concurrently and the interviewer was masked as to who was a case and who was a control.[25] The data from this study do not support the hypothesis that AMD cases have greater lifetime sun exposure than control subjects. In fact the opposite was found and the investigators concluded that sun exposure was unlikely to be a significant risk factor for AMD.

In another case-control study (446 cases with end stage AMD and 283 spouse controls) sun exposure was determined from the number of years working on an outdoor occupation combined with the number of years when at least two weeks were spent undertaking an outdoor activity and by recording details of skin tumours.[26] The investigators were unable to demonstrate a link between estimated lifetime sun exposure and late AMD.

Howard and Rowe[27] postulate that the differences between these studies (some show a relationship between sun exposure and AMD and some don't) may be related to the participant inclusion criteria. For example, men working outside on water for the Chesapeake study[17] compared to population-based cohort studies.[23,24] The inclusion criteria change the level of sunlight that the participants were exposed to with Chesapeake watermen being exposed to a higher level of light than their counterparts in the general population, albeit this high level would have been more consistent because of their traditional work practices. While epidemiological and case-control studies investigating the impact of light on the retina have produced conflicting results overall, the data appear consistent with the possible harmful effect of light on the retina.

Children are at increased risk of retinal damage from sunlight

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To overcome the inherent problems associated with gathering information on lifetime sunlight exposure through the use of questionnaires, Hirakawa et al[28] used a novel technique of facial wrinkle analysis to determine sunlight exposure. In a case-control study of Japanese men (148 with early or late AMD and 67 controls) facial photographs were taken of the participants. A 'region of interest' was predefined manually on 12 facial landmarks such as corners of the mouth, corners of eye and the bridge of the nose. The length of facial wrinkles in this area was then quantified objectively using image analysis software which automatically located and quantified the total number of wrinkles longer than 5mm and more than 0.16mm wide. The theory being that more wrinkles indicate a greater lifetime exposure to sunlight.[29] The results showed that facial wrinkle length and therefore lifetime sun exposure is positively related to late AMD at least for this group of Japanese men.

Another piece of useful evidence comes from a report on a group of 150 cases of macular lesions. White young males experienced a decline in visual acuity after having worked outside on a tropical island for six months. Conditions were bright and none wore protective lenses. No individuals working inside on the same island suffered from the complaint. Ophthalmoscopy revealed a slight macular oedema, loss of foveal reflex and a mottled pigmentary disturbance within the macular around the fovea similar to that seen in AMD.[30]

Young[10] advises the early use of sunglasses to protect against unnecessary molecular damage. Children are at increased risk of retinal damage

from sunlight because the immature lens transmits more high energy photons than does the adult lens.[31] An observation study set in Honolulu involved two observers monitoring sunglass wear over an 18-month period in parks, outdoor swimming pools and beaches.[32] Interestingly, out of 5,171 people observed, only 33 per cent were wearing sunglasses and 41.6 per cent of adults were observed to wear sunglasses but only 12.3 per cent of children. Since children are likely to spend more time outside, have little lens yellowing and a thinner lens, they are more at risk of actinic related retinal damage. People in parks and swimming pools were more likely to be wearing sunglasses (35.1 per cent and 34.8 percent) compared to beaches (30.4 per cent). It is well known that there is more reflected light from sand and water than from grass.

New research on supplements offering retinal protection

The human macula has a characteristic yellow colour due to the presence of macular pigment (MP) which is composed of two dietary carotenoids lutein and zeaxanthin.[33] As discussed above, sunglasses and brimmed hats may offer extraocular protection from the potential damaging effects of sunlight and evidence is accumulating that MP confers intra-retinal protection against AMD by acting as an optical filter to phototoxic blue light and/or via its powerful antioxidant properties.[34]

Macular pigment has been postulated to preserve[35] and protect[36] the central retina. First, MP absorbs light in the harmful short wavelength end of the spectrum and dissipates it as heat before it renders damage to the foveal tissue.[37] Second, the macular carotenoids are antioxidants able to prevent free-radical reactions that can damage cellular components. It makes sense from the biochemical perspective to maximise levels of MP and thereby maximise endogenous intra-retinal protection.

Two recent studies have reported on the retinal and functional effects of supplementing with carotenoids. Using a non-randomised open label study, Connolly et al[38] investigated the effect of supplementation containing 7.3mg of meso-zeaxanthin (another carotenoid similar to lutein and zeaxanthin found solely in the retina), 3.7mg of lutein and 0.8mg of zeaxanthin daily for eight weeks for five healthy people and five people with early AMD. After just two weeks of supplementation (this is much shorter than previous studies have reported) high values of macular pigment optical density (MPOD) were detected using

TABLE 1

Commonly available nutritional supplements for macular pigment enhancement (in alphabetical order of brand name)

Brand name	Supplier	Lutein (mg per daily dose)	Zeaxanthin (mg per daily dose)	Meso-zeaxanthin (mg per daily dose)
ICaps	Alcon	10	Some but amount unknown	none
Macushield	Bondeye Optical	10	10	2
Nutrof Total	Spectrum-Thèa Pharmaceuticals	10	2	none
Ocuvite plus lutein	Bausch+Lomb	6	unknown	none
Preservision plus lutein	Bausch+Lomb	10	unknown	none
VitEyes	Butterflies online	6	unknown	none
Vitalux Plus	Post Optics online	10	unknown	none

ADVICE TO HEALTHY PATIENTS AND THOSE WITH EARLY SIGNS OF AMD

- Wear sunglasses or photochromic lenses in bright sun light (wraparound if possible) with refractive correction particularly if hyperopic
- Make sure the diet contains fruits and vegetable with lutein and zeaxanthin and if not use nutritional supplements to develop and maintain high levels of MP (see Table 1)
- Wear a brimmed hat in bright sunlight
- Take some moderate exercise (atherosclerosis has been found to be a risk factor for AMD in some studies)
- Check blood pressure with GP and reduce if high (systemic hypertension has been found to be a risk factor for AMD in some studies)

heterochromatic flicker photometry in all subjects. Furthermore, one healthy and three subjects with AMD who had abnormal MPOD profiles prior to supplementation had normal profiles after eight weeks of supplementation.

At the 2010 ARVO meeting Richer et al[39] presented the results from an investigation whereby 60 people with mild to moderate AMD were randomly assigned to one of three dietary supplement carotenoid intervention groups and followed for one year: 8mg zeaxanthin (n=25), or 8mg zeaxanthin with 9mg lutein (n=25) or 9mg lutein (faux placebo-control group n=10). Zeaxanthin alone increased estimated MPOD similarly to lutein, improved 1° foveal shape discrimination, improved 10° kinetic visual field and there was a trend towards significance for improvements in contrast sensitivity and glare recovery. The group taking both zeaxanthin and lutein demonstrated increased MPOD but the combination of carotenoids was not helpful in terms of visual psychophysics, implying carotenoid competition. The authors concluded that these effects make biological sense based on zeaxanthin's foveal location.

Young[10] advocated the wearing of sunglasses to reduce damage to the macula and retard the beginning of cell degeneration.[28] A delay in the onset of AMD by even a few years would significantly lower the prevalence of blindness by allowing many more individuals to complete their lifespan prior to the transition from macular senescence to degenerative diseases. Furthermore, those with AMD should also use sunglasses to diminish additional unnecessary damage, although the earlier sunglasses are put to use the greater the benefits should be. Finally, use of services (eg counselling and rehabilitation) and nutritional supplements and devices identified by questionnaire among 806 individuals with AMD significantly increased as VA decreased. Costs ranged from £345 to £1,104 (converted from US dollars 01.06.10) and increased with AMD severity. Delaying progression of AMD could result in considerable cost savings.[40] ●

MULTIPLE-CHOICE QUESTIONS – take part at opticianonline.net

1 At 400nm, what percentage of incident light is transmitted to the retina?
A None
B 1 per cent
C 10 per cent
D 100 per cent

2 What is the ratio of lipofuscin to melanin in the older retina estimated to be?
A 1 to 1
B 2 to 1
C 5-10 to 1
D 20 to 1

3 Which of the following statements about the Blue Mountains Eye Study is true?
A The study showed poor correlation between skin damage and sun exposure
B There was no relationship between skin damage and AMD
C AMD seems strongly linked with sun exposure
D Skin damage and sun exposure are a useful measure of macular pigment levels

Successful participation in this module counts as one credit towards the GOC CET scheme administered by Vantage and one towards the Association of Optometrists Ireland's scheme.

4 Richer et al have found which of the following to be true of zeaxanthin supplementation?
A An improvement in foval discrimination of 10°
B Improvement in contrast sensitivity
C Reduced glare recovery
D A 1° improved kinetic visual field

5 Which of the following was NOT a finding of the Beaver Dam Study?
A Outdoor activity is associated with late AMD in men and women
B Participants who wear brimmed hats were less likely to have soft drusen
C Wearing sunglasses is inversely associated with increased retinal pigment
D Outdoor activity is associated with increased retinal pigment levels in women

6 Which of the following pieces of advice is NOT appropriate to offer patients with early AMD?
A Wear a brimmed hat in sunlight
B Consider an anti-oxidant rich diet or supplement
C Maintain normal blood pressure levels
D Reduce physical activity

The deadline for responses is July 8 2010

References
A full list of references is available from the clinical editor: william.harvey@rbi.co.uk

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