

## COVER STORY

## THE AGING EYE

...and what can be done to protect it



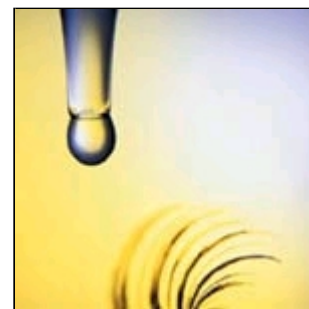
If people live long enough, severe visual impairment or blindness is almost inevitable. The eyes are particularly vulnerable to the effects of aging. Degenerative changes in the eye often begin in middle age. By age 70, a significant percentage of people suffer from macular degeneration, glaucoma and/or cataract. Diabetic retinopathy is also a major cause of visual disability among adults.

A review of the published scientific literature shows that common ocular disorders can be prevented with lifestyle changes. A compelling body of evidence indicates that orally ingested antioxidants and anti-glycating agents (such as carnosine) help to prevent and treat eye disease. Unfortunately, the aging process causes reduced blood flow to the eye, thereby inhibiting the delivery of orally ingested supplements into the eye.

This month, we discuss a new way of administering topical agents directly into the eye to help protect against multiple pathologies related to senile eye disorders.

Few people know that poor vision from cataracts affects 80% of people 75 years of age and older. Cataract surgery costs Medicare more money than any other medical procedure, with 60% of those who initially qualify for Medicare already having cataracts. Taking steps to prevent the disease early in life may mean you are one of those 20% of people who enjoy good eye health and never suffer from cataracts.

A cataract is the clouding of the lens of the eye, which reduces the amount of incoming light and results in deteriorating vision. Often described as similar to looking through a waterfall or a piece of waxed paper, the condition makes daily functions such as reading or driving a car increasingly difficult or impossible. Sufferers may need to change eyeglass prescriptions frequently. It is estimated that 20 million people worldwide suffer from cataracts. More than 350,000 cataract operations are performed in the United States yearly.



Many people are born with minor lens opacities that never progress, while others progress to the point of blindness or surgery. Many factors influence vision and cataract development such as age, nutrition, medications and sunlight exposure. High blood pressure, kidney disease, diabetes or direct trauma to the eye can also cause cataracts.

The aging process itself lends to certain metabolic changes that may predispose the lens to cataract development. Some of this occurs due to low supply of oxygen and nutrients, which leave the eye open to free radical damage. According to a 1983 report from the National Academy of Science, cataracts are initiated by free-radical hydrogen peroxide found in the aqueous humor. Free radicals such as hydrogen peroxide oxidize glutathione (GSH), destroy the energy-producing system of the eye, and allow leakage of sodium into the lens. Water follows the sodium, and the edema phase of the cataract begins. Then, body heat in the lens of the eye oxidizes (cooks) lens protein, and it becomes opaque and insoluble (similar to egg protein).

The good news is that a lot of published research exists showing that the cataract progression can be slowed or prevented by the use of natural therapies and minor lifestyle changes. Researchers at Brigham and Women's Hospital, Harvard Medical School, stated in a scientific research report published in the January/February 1999 issue of *Journal of Association American Physicians* that, "Basic research studies suggest that oxidative mechanisms may play an important role in the pathogenesis of cataract and age-related macular degeneration, the two most important causes of visual impairment in older adults." The researchers recommended that additional research be conducted in the promising area of preventive therapy and treatment. Preserving lens function through adequate antioxidant levels and delaying cataract formation by 10 years would result in saving at least half of the \$3.2 billion spent annually in cataract surgeries and physician visits.[1]

Prevention and treatment of cataracts are probably one of the more scientifically documented and beneficial uses of dietary

supplements. Free-radical action has been directly linked to and accepted as one of the major causes of cataracts and damage to the healthy eye. Numerous well conceived, scientific studies have been conducted to test and document the possible effect of supplements due to their capability to reduce free-radical damage, and in some cases allow the body to reverse the damage done by free radicals.

Although it is difficult to treat cataracts with oral antioxidants since there is only minimal blood circulation within the eye compared to other parts of the body, nutritional supplements have been shown to reduce the risks of cataracts as well as slow or reverse their progression.

A UK study recently reported that plasma antioxidant levels influenced cataract development, independently of age, gender and other risk factors. The study, published in *Ophthalmology* [(2001) 108: 1992-1998], looked at 372 men and women, aged 66 to 75 years, born and still living in Sheffield, England. Results showed that the risk of nuclear, cortical and posterior subcapsular cataracts was lowest in individuals with the highest blood concentrations of carotene and beta-carotene, lycopene and lutein, respectively. A decreased risk was not found in relation to vitamin C, vitamin E or carotenoids (zeaxanthin and  $\beta$ -cryptoxanthin) status. Like other studies that have examined possible preventive links between various antioxidants and age-related eye diseases, such as glaucoma and age-related macular degeneration (AMD), this study helps to pinpoint which nutrients are most helpful for halting specific sight problems. Results also support the argument for supplemental and dietary intake of antioxidants in prevention, and for blood levels being relevant markers for eye disease risk.

### Age-related macular degeneration (AMD)

The macula is the central and most vital area of the retina. It records images and sends them via the optic nerve from the eye to the brain. The macula is responsible for focusing central vision that is needed for seeing fine detail, reading, driving and recognizing facial features.

Age-related macular degeneration (AMD) is the leading cause of blindness in people over the age of 55, affecting more than 10 million Americans. It is a condition in which the central portion of the retina (the macula) deteriorates. It is equally common in men and women and more common in whites than blacks. The cause is unknown, but the condition tends to run in some families. Macular degeneration affects more Americans than cataracts and glaucoma combined.

There are two forms of macular degeneration: atrophic (dry) and exudative (wet). Approximately 85% to 90% of the cases are the dry type. Both forms of the disease may affect both eyes simultaneously. Vision can become severely impaired, with central vision rather than peripheral vision affected. The ability to see color is generally not affected, and total blindness from the condition is rare.

There is little that can be done within conventional medical treatment protocols to restore lost eyesight with either form of the disease. Leading researchers, however, are documenting the benefits of a more holistic approach in the treatment of AMD. Patients are being encouraged to increase physical fitness, improve nutrition (including a reduction in saturated fats), abstain from smoking and protect their eyes from excessive light. Dietary supplementation of trace elements, antioxidants and vitamins is recommended for improving overall metabolic and vascular functioning. Early screening and patient education offer the most hope for reducing the debilitating effects of the disease.

Exposure to light and photochemical damage have been suspected factors in AMD,[2] as well as decreased antioxidant activity responsible for damage control. An age-dependent drop in glutathione blood status, and a significantly lower level of glutathione has been found in older individuals compared to younger ones. Moreover, an increase of oxidized glutathione by-product over time suggests more oxidation and the incumbent higher risk of age-related eye diseases.[3] In the early stages of AMD, glutathione has been found to protect retinal pigment epithelial cells from dying.[4] Glutathione, which is particularly concentrated in the lens, has been shown to have a hydroxyl radical-scavenging function in lens epithelial cells.[5]

### Diabetic retinopathy

One of the leading complications associated with diabetes is blindness or other eye diseases stemming from vascular damage to the eyes caused by high blood sugar. Diabetic retinopathy, the most common form of diabetes eye conditions, happens due to damage of the retinal blood vessels. The damage causes the ruptured vessels to leak fluid, restricting oxygen and blurring sight. As the disease progresses, the eye tries to form new vessels on the surface of the retina, which may also bleed or obscure sight by their mere presence. Diligently controlling blood sugar is a major means of preventing or at least slowing the onset and progression of diabetic retinopathy.



As it is, in diabetics, the vitreous body has been found to change more rapidly than with just normal aging, changes which have been implicated in functional disturbances and retinal detachment. The vitreous body is composed of a fine network of hyaluronan gel, collagen, proteoglycans and fibronectin, all of which are susceptible to free radical damage brought on by light and UV damage and glycation. [6]

A growing body of research shows that oxidation induced by glycation can wreak havoc on the eye. Protein glycation occurs when sugar molecules inappropriately bind to protein molecules, forming crosslinks that distort the proteins and consequently render them useless. Glycation appears to increase oxidative processes, which may explain why both glycation and oxidation simultaneously increase with age. High blood sugar also increases glycation activity, which may also explain the various kinds of tissue damage that characterize advanced diabetes.

In open-angle glaucoma, the common form of the disease, drainage of the aqueous fluid is sluggish, so the backup causes the undue pressure in the eye. The pressure pinches the blood vessels that feed the optic nerve, causing the nerve to die over time.

## Glaucoma

Glaucoma, usually an inherited disease, results from the build-up of pressure in the aqueous humor, the liquid that fills the area between the cornea and the lens. Generally, the condition develops after age 40, although congenital glaucoma and physical injury to the eye can account for earlier age of onset. Figures show that 1 out of every 25 Americans suffers from glaucoma, and over 62,000 are legally blind due to glaucoma.

Age-related losses of antioxidants increase physical stress on the eye, and oxidative damage ensues.[7] For example, diminished antioxidant activity in lacrimal (tear) fluid and blood plasma seems to coincide with progression of glaucoma.[8] It's also proposed that the rate of crystalline damage increases as antioxidant capacity and protease activity declines with age.[9]

In open-angle glaucoma, the common form of the disease, drainage of the aqueous fluid is sluggish, so the backup causes the undue pressure in the eye. The pressure pinches the blood vessels that feed the optic nerve, causing the nerve to die over time, and leading to decreased peripheral vision, tunnel vision and finally blindness. A rarer form of glaucoma is called narrow-angle or congestive glaucoma, whereby the flow of the aqueous liquid is blocked causing pressure to build up.

[Purchase Brite Eyes from the Life Extension Foundation](#)

Continued on Page 2 of 2

[Back to the Magazine Forum](#)

## COVER STORY

### Focus on eye health

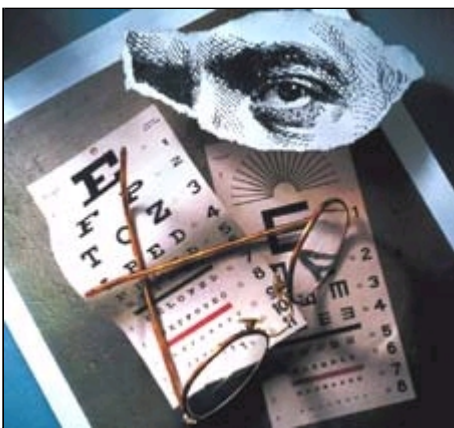
While there is still much speculation about what causes various age-related eye diseases, many possible contributing factors have been examined by scientists. The usual suspect, as with most age-related diseases, is oxidative damage. For example, the lens of the eye, which acts as a light filter for the retina, is under chronic photo-oxidative stress. The retina, meanwhile, is particularly susceptible to the destructive effects of reactive oxygen species (ROS), which are produced in the retina as a result of photochemical reaction, cellular metabolism and high levels of polyunsaturated fatty acids that reactive oxygen species readily oxidize.[10]

Some research suggests that aging processes of the eye may be the result of the breakdown of enzymes that usually metabolize and detoxify hydrogen peroxide and other free radicals found in eye fluids.[11] Free radicals reside in the aqueous fluid and bathe the lens of the eye, destroying enzymes that produce energy and maintain cellular metabolism. Free radicals also break down fatty molecules in membranes and lens fibers, generating more free radicals and creating a cross-linking (denaturing or breakdown) of the laminated-like structural proteins inside the lens capsule. The lens capsule has the ability to swell or dehydrate. In doing so, the increase and/or decrease in pressure can cause breaks in the lens fiber membranes, resulting in microscopic spaces in the eye in which water and debris can reside.

In addition, blood flow within the eye decreases with age, basically depriving it of essential nutrients for proper function and antioxidant activity.[12] An Indiana University study showed that vascular changes occur in the aging eyes of both men and women, which resemble the changes seen in patients with glaucoma or age-related macular degeneration. So such changes as occur typically during normal aging may contribute to the increased risk of these diseases.[13] Meanwhile, German researchers showed that retinal and central retinal artery blood flow significantly decreases with age at approximately 6% to 11% per decade.[14]

### Looking at prevention

While the exact role of individual nutrients and optimum means of delivery (i.e. oral vs. topical) haven't been solidified yet, some useful findings are surfacing about the benefits of antioxidants for eye health. Some research from the USDA Human Nutrition Research Center on Aging has demonstrated that antioxidants such as ascorbate, carotenoids and tocopherol, may protect against cataract formation.[1] A five-year study of over 3000 Wisconsin residents, aged 43 to 86, showed that the five-year risk for cataract was 60% lower among people who reported taking multivitamins or any supplement containing vitamin C or E on a long-term basis (more than 10 years) compared to non-users.[15] Similarly, a survey-based Harvard study of nearly 40,000 men aged 45 to 75 established, at eight-year follow-up, a 19% lower risk of cataract among men in the highest fifth of lutein and zeaxanthin intake compared to men in the lowest quintile.[16]



It's believed that lutein and zeaxanthin, the primary carotenoids concentrated in the macula, counter the free-radical forming action of light and oxygen.<sup>2</sup> The macula is the central part of the retina that's responsible for visual sharpness and detail. It's been suggested that macular pigment protects the retina via a dual role that includes scavenging for free radicals and filtering out blue light, which can cause photochemical damage.[9] Some studies have also suggested a link between dietary carotenoid intake and macular pigment density. In fact, eyes with age related maculopathy (ARM) have revealed significantly lower carotenoid levels in the macula and retina than healthy eyes.[9]

And while a paucity of US-based clinical trials to demonstrate the effectiveness of specific neuroprotective compounds for glaucoma may limit their current therapeutic use, there is evidence slowly mounting to support their effectiveness.[17] A Russian study of 64 patients with primary open-angle glaucoma found that a combined regimen of hyperbaric oxygen and antioxidants over a five-year period stabilized visual function in 80% of patients.[18]

Research from the USDA  
Human Nutrition Research

Center on Aging has demonstrated that antioxidants such as ascorbate, carotenoids and tocopherol, may protect against cataract formation.

Other studies have been examining how antioxidant status relates to the risk of age-related macular degeneration. The Baltimore Longitudinal Study of Aging, for instance, found that tocopherol, and an antioxidant combination of tocopherol, carotene and ascorbate were protective.[10] Researchers have also been looking at the potentially therapeutic role of individual compounds. For example, a study from Sete, France of 2584 inhabitants showed that higher plasma levels of alpha-tocopherol were inversely

related to AMD development and progression.[19]

Another study looked at the topical use of N-acetylcarnosine (NC) for treating cataracts. Carnosine is an endogenous free-radical scavenger and anti-glycating agent. In this six-month study, 49 volunteers (average age 65.3) with cataracts were treated with a 1% solution of NC (2 drops, twice daily), given a placebo composition, or were untreated. Results showed that, compared to baseline measurements, 41.5% of the eyes treated with NC showed a significant improvement in lens clarity at six months, 90% showed gradual improvement in visual acuity, and 88.9% improved in glare sensitivity. Results pointed to NC as a suitable and physiologically acceptable non-surgical treatment for cataracts.[20]

The fact that the macula pigment is heavily comprised of lutein and zeaxanthin, that ascorbic acid (vitamin C) is found in both the aqueous humor and corneal epithelium, that glutathione is highly concentrated in the lens of the eye, and that there is a high content of zinc in the retinal pigment epithelium (RPE-the tissue behind the retina that feeds the rods and cones),[21] there is compelling evidence for the essential need of these antioxidant and anti-glycating agents for maintaining optimal eye function. The question of how to get a sufficient daily intake of these vital eye nutrients is currently under investigation.

A recent study sought to measure dietary amounts of lutein and zeaxanthin by testing 33 various fruits and vegetables, two fruit juices and egg yolk. Surprisingly, results showed that although dark green, leafy vegetables are reputed to contain the highest amounts, lutein and zeaxanthin are also abundantly present in other food choices. Egg yolk and maize had the highest content (more than 85% of total carotenoid content), maize having the highest lutein content (60%) and orange peppers having the highest zeaxanthin content (37%). Substantial amounts were also found in kiwi, grapes, spinach, orange juice, zucchini and various types of squash (30% to 50%).[22] Comparatively, green leafy vegetables actually had 15% to 47% of lutein content but only 0% to 3% of zeaxanthin content. Earlier studies had shown that eating dark leafy vegetables was associated with a 43% lower risk of AMD. Now it seems that some benefit can be derived from other food choices.

One of the current debates about antioxidant intake and eye health is that oral ingestion seems to effectively raise and correlate to blood plasma levels of nutrients, but the intake does not correlate as directly in eye tissues or get reflected in eye health. For example, one study showed that, while oral antioxidant therapy normalized blood levels of antioxidant activity even in advanced cases of glaucoma, it did not help lacrimal antioxidant activity, which argues for locally administered antioxidants perhaps being preferable in glaucoma patients. Another study that tested oral zinc supplementation in 112 subjects with AMD over a two-year treatment period discovered that serum levels of the nutrient were much higher in the supplementation group than controls, but disease progression was similar in both treated and untreated patients.[10]

A recent study carried out by the National Eye Institute, however, had more positive results to report with regards to oral supplementation. The large, multicenter study explored the use of zinc and antioxidant oral supplements containing above the recommended daily requirements to prevent advanced AMD. It examined 3,640 persons aged 55 to 80, who had a high risk of developing advanced AMD, already had it, or had been blinded in one eye by the condition. These participants were randomly assigned to four oral regimen groups and followed up for over a six-year period. Group 1 received daily tablets containing antioxidants (vitamin C, 500 mg; vitamin E, 400 IU; and beta carotene, 15 mg). Group 2 received a zinc supplement, 80 mg, as zinc oxide and copper, 2 mg, as cupric oxide. Group 3 received both the antioxidants and zinc. And group 4 received a placebo. Results showed that those with intermediate disease taking antioxidants plus zinc had a 25% lower risk of developing advanced AMD than those taking a placebo. The vitamin plus mineral regimen also reduced the risk of vision loss by about 19%. The authors, however, were careful not to generalize their findings to suggest an equal benefit of supplementation in everyone, since the supplements showed no effect in people with early-stage AMD.[21]

Scientists are considering the value of topically administered antioxidants as a reasonable option to weigh. Some studies have already shown the success of this direct route of administration, but future evidence will hopefully point to the appropriateness of local and targeted delivery of helpful agents to the eye.

#### Useful Supplements for Eye Health

Vitamin E  
Acetyl-l-carnitine  
Vitamin C  
Carnosine  
Ornithine alpha-ketoglytarate  
Calcium pyruvate  
B complex vitamins  
Glutathione  
Beta carotene  
Zeaxanthin  
Lutein  
Selenium  
Zinc  
Manganese

## References

1. Taylor A. EXS 1992;62:266-279.
2. Schalch W. EXS 1992;62:280-298.
3. Winkler BS, et al. Mol Vis 1999 Nov 3;5:32.
4. Cai J, et al. Prog Retin Eye Res 2000 Mar;19(2):205-221.
5. Giblin FJ. J Ocul Pharmacol Ther 2000 Apr;16(2):121-135.
6. Deguine V, et al. Pathol Biol (Paris) 1997 Apr;45(4):321-330.
7. Dillon J. Doc Ophthalmol 1994;88(3-4):339-344.
8. Makashova NV, et al. Vestn Oftalmol 1999 Sep;115(5):3-4.
9. Taylor A, et al. Free Radic Biol Med 1987;3(6):371-377.
10. Beatty S, et al. Br J Ophthalmol 1999;83:867-877 (July).
11. Green K. Ophthalmic Res 1995;2727:143-149.
12. Ravalico G, et al. Invest Ophthalmol Vis Sci 1996 Dec;37(13):2645-2650.
13. Harris A, et al. Arch Ophthalmol 2000 Aug;118(8):1076-1080.
14. Groh MJ, et al. Ophthalmology 1996 Mar;103(3):529-534.
15. Mares-Perlman JA, et al. Arch Ophthalmol 2000 Nov;118(11):1556-1563.
16. Brown L, et al. Am J Clin Nutr 1999 Oct;70(4):517-524.
17. Ritch R. Curr Opin Ophthalmol 2000 Apr;11(2):78-84.
18. Popova ZS, et al. Vestn Oftalmol 1996 Jan;112(1):4-6.
19. Delcourt C, et al. Arch Ophthalmol 1999 Oct;117(10):1384-1390.
20. Babizhayev MA, et al. Peptides 2001 Jun;22(6):979-994.
21. Ferris, F et al. Arch Ophthalmol 2001;119:1417-1436.
22. Sommerburg O, et al. Br J Ophthalmol 1998;82:907-910 (August).

[Back to the Magazine Forum](#)

All Contents Copyright © 1995-2009 Life Extension Foundation All rights reserved.

**LifeExtension®**

These statements have not been evaluated by the FDA. These products are not intended to diagnose, treat, cure or prevent any disease. The information provided on this site is for informational purposes only and is not intended as a substitute for advice from your physician or other health care professional or any information contained on or in any product label or packaging. You should not use the information on this site for diagnosis or treatment of any health problem or for prescription of any medication or other treatment. You should consult with a healthcare professional before starting any diet, exercise or supplementation program, before taking any medication, or if you have or suspect you might have a health problem. You should not stop taking any medication

without first consulting your physician.