Macular Degeneration (AMD) and Retinitis Pigmentosa

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Lifting the darkness

19 June 2009 Julian Cribb

With modern life expectancy increasing, so is the problem of whether our eyesight can indeed last a lifetime. People take it for granted their teeth can be repaired as they age. Hearing can be enhanced electronically. Cosmetic surgery may disguise the external ravages of time. Transplant surgery can replace heart, lungs, liver and kidneys. But when the eye's light-sensitive membrane, the retina, fails there seems little you can do about it – and millions end their lives in darkness. Until now. It may soon be possible to forestall the failure of eyesight in old age and even to repair past damage to the visual system – simply, cheaply and painlessly. Scientist from The Vision Centre (the ARC Centre of Excellence in Vision Science) are reporting striking progress in four highly promising techniques for preventing vision loss and restoring damaged sight, using simple therapies based on light, diet and oxygen. These involve controlling the amount of light received by the eye earlier in life, eating a diet high in healing antioxidants, and repairing damaged eye cells using near-infra-red light or short pulses of oxygen. Their targets are three major diseases: age-related macular degeneration (AMD) which is the most common cause of blindness in old age, age-related degeneration of the retina and retinitis pigmentosa which causes blindness in much younger people. The latter affects one person in every four thousand, sometimes from childhood. AMD affects one person in five, and retinal degeneration affects everyone through the gradual loss of 'rods', the light sensing cells especially important for vision in low light. The age-related loss of retinal function is a growing problem, says the Vision Centre's Professor Jonathan Stone, because the human lifespan is increasing; more and more people are surviving into their 80's and 90's, decades when these conditions can strike. "We lose photoreceptors from our retinas throughout life, and the challenge is to understand the factors which accelerate the loss – and others which can be mobilised to slow the loss. In our animal models, one thing that really causes damage is light itself – the cumulative damage from sunlight or ordinary bright lights clearly regulates the state of the retina in late adulthood." The simple step of restricting light greatly extends retinal life in these models, he says. "This point must be tested rigorously, but there is no reason to expect the human eye to be immune to the same regulation, especially of the last decades of a long life." "That's why I wear dark glasses whenever I go outdoors now," Prof. Stone says. "Furthermore there is evidence from these models that the use of antioxidants will also help stabilise the damage sustained from overexposure to light, and clinical trials have begun." For patients suffering retinitis pigmentosa, which can blind people early in life, studies have revealed the damage is twofold – the death of vision cells, and the damage sustained by surviving vision cells. "We now believe it is possible to de-stress the surviving vision cells by restricting the amount of light they receive." In both cases, Prof Stone considers it will be possible to develop a simple guide that will enable people to control their light exposure through their lives. "Light restriction is a simple remedy, which is what we are after, as people can implement it very easily and manage their own condition. This applies particularly to retinitis pigmentosa sufferers. We seek to provide them with a well-tested protocol, to enable the sufferer to control the rate at which their vision deteriorates – or even to decide to totally protect the vision of one eye so it can be used later in life." Exactly why our vision cells deteriorate with age is not yet known for sure, but there is evidence that damage to their genes caused by oxygen free radicals plays an important role – making antioxidants a possible part of the solution, along with the prevention of further damage. The direct cause of age-related macular degeneration is not known, Prof. Stone says, but smoking is a major risk factor and changes in immune-system genes have been linked to the condition. The disease occurs through the progressive destruction of rods and cones – the eye cells which detect the occurrence and wavelength of light – in the macula, the area of the retina essential for sharp vision. It appears to be driven by an auto-immune response – and so can be controlled by anti-inflammatory treatment. Research by Professor Silvia Bisti of The Vision Centre and University of L'Aquila, Italy, has found the herb saffron taken orally to have remarkable effects on the genes which regulate the performance of the eye's key

vision cells. Prof. Bisti has shown the golden culinary herb made from crocus flowers not only protects mammalian vision cells from damage. So far several hundred changes in gene regulation have been observed in the vision cells due to saffron – but sorting out which of these are key to preventing disease is a major challenge. A clinical trial now taking place in Rome is testing the promise that it may also act to slow and possibly even reverse the course of blinding diseases such as AMD and retinitis pigmentosa. Preliminary data encourage us to hope that the effect will be robust, but the trial is rigorous and (strange description for a trial on vision) is double-blind, she says. "We think we are succeeding in stabilising the condition and maybe even improving it somewhat. We will know more when the results are in later this year," she says. Saffron is a traditional crop in Italy's mountainous Abruzzo country, where fields of crocuses deck the landscape. It was already well-known as an anti-oxidant, although no-one had previously explored its effects on eyesight. "The point about saffron is that it is completely safe and harmless. It has been used in cooking and medicine since Roman times, at least three thousand years," Silvia says. "But saffron is not simply an anti-oxidant. It seems to possess a number of other properties which are protective to vision," she adds. "For example it appears to affect genes which regulate the fatty acid content of the cell membrane, and this makes the vision cells tougher and more resilient. Secondly we have shown in animal models that a saffron diet will protect the eye from the damaging effects of bright light – something we all are vulnerable to whenever we go out in the sun." At the same time, Dr Krisztina Valter's Vision Centre team is producing world-first evidence that eyesight damage caused by exposure to very bright light can be repaired or even prevented with doses of near-infra-red light. "It has been known for some time that infra-red light, at certain wavelengths, can promote healing of various body cells. We decided to carry out a series of experiments to see if it could restore or prevent damage to vision cells that have been exposed to very bright light," she explains. "When an eye cell has been damaged by overexposure to light it usually dies from stress caused by free radicals – but when the cells are stimulated with IR light, they appear to recover significantly and to withstand future damage much better," she says. "This is the kind of damage which could happen to people when their eyes are exposed to excessive light, especially those who live constantly in very bright environments or whose work exposes them to intense lighting. This could cause significant eye damage." Experimental results, carried out in rats, were dramatic – a few minutes exposure to infra-red light at a wavelength of 670 nanometres reduced the amount of eye damage sustained on a typical sunny day significantly. Furthermore it appeared to reduce damage when treatment was given before, during and even after exposure to light. Says Krisztina: "This provides encouraging support for a view that infra-red light can possibly be used to treat people who have suffered from over-exposure to very bright light – or those whose work and living environment exposes them to excessive light over a lifetime and who may be at risk of vision problems due to macular degeneration and other conditions." Clinical trials of the technique are planned to begin shortly. The discovery that near infra-red light assists the body's healing processes was made by astronauts in space tending plants grown under infra-red lighting, she says. "In space wounds heal very slowly, but the astronauts tending plants found small wounds on their hands healed much more quickly," she says. Because the human body consists largely of water, it absorbs most of the spectrum of light. However at wavelengths between 600-1000 nanometres – the near infra-red – specific molecules are able to capture the light and can initiate beneficial changes in certain body cells.. "We believe that what is happening is that the light increases the activity of key enzymes in the body's cells, which make more energy available to the cell. When an eye cell has been damaged by overexposure to light it usually dies from oxygen stress caused by free radicals – but when the cells are stimulated with IR light, they appear to stand up to the damage much better." Dr Valter has also shown that IR treatment also reduces the inflammation that can occur within the eye following overexposure to very bright light. This is important for preventing damage in cases where people know they will be exposed to very bright light – for example eye surgery or examination, or use of bright sources of light. "It seems to assist the healing of the retina and may be able to prevent long-term damage after exposure to excessive light, such as looking straight into welding arcs, sun-gazing, or accidental laser light injury. Our work so far suggests that, for all of these people, infra-red treatment could be protective." One day, the team hopes, it may be possible to hold a wand which emits near-IR light over the eye for a few minutes and so repair or prevent vision damage. The process is known as photobiomodulation, the manipulation of the body's natural responses through the application of light. Like light restriction and dietary supplements, it promises to be easy and painless to administer. Next, there is also promising evidence that loss of vision can be reduced or even reversed by a short-term exposure to high levels of oxygen, says Professor Stone. This can be

carried out in a high-pressure chamber (like that used by divers) with an enriched oxygen atmosphere. While oxidative damage is a major cause of the loss of our vision cells, saturating the eyes with oxygen for a very short time in a hyperbaric chamber can cause vision to improve. “For short periods of time oxygen acts as a tonic for the photoreceptors in the eye, but for longer periods it is a toxin. We are investigating this.” While this technique requires more expensive equipment, it is nevertheless simple and pain-free. Prof. Stone says that the combination of several of these mild treatments may for the first time offer humanity a way to restore or prevent failing eyesight in age. “They are all simple, convenient and painless remedies to administer, especially light restriction and dietary approaches. Our aim is to develop straightforward advice that will help people to adopt them as part of their daily lives.” The director of The Vision Centre Professor Trevor Lamb says the techniques in preventing or repairing vision loss offer new hope for treating conditions that have plagued humanity throughout its existence and still affect billions worldwide. “We’ve learned to care for our teeth so we still have them in old age. We are learning to do the same for our hearts and arteries. Now it’s time to do likewise for our vision. These new techniques offer the prospect of real improvement in quality of life for countless people, as well as reducing the economic costs of vision loss. The fact that they are capable of being delivered through local healthcare services or even self-administered is a major advance when compared with far more costly medical interventions and drug-based therapies. This is an example of what can be achieved when you bring the very best minds and scientific research to bear on a challenge.”