

Preface: The Aging Eye: Normal Changes, Age-Related Diseases, and Sight-Saving Approaches

Gerald J. Chader¹ and Allen Taylor²

¹Department of Ophthalmology, University of Southern California, Keck School of Medicine, Los Angeles, California

²Laboratory for Nutrition and Vision Research, United States Department of Agriculture, Human Nutrition Research Center on Aging, Tufts University Boston, Massachusetts

Correspondence: Gerald J. Chader, Doheny Eye Institute, 1450 San Pablo Street, Los Angeles, CA 90033; GChader@doheny.org.
Allen Taylor, USDA Human Nutrition Research Center on Aging, Tufts University, 711 Washington Street, Boston, MA 02111; allen.taylor@tufts.edu.

Submitted: August 5, 2013

Accepted: August 7, 2013

Citation: Chader GJ, Taylor A. Preface: the aging eye: normal changes, age-related diseases, and sight-saving approaches. *Invest Ophthalmol Vis Sci*. 2013;54:ORSF1-ORSF4. DOI:10.1167/iivs.13-12993

This volume presents articles based on a workshop held June 14 to 16, 2013 in Rancho Palos Verde, CA sponsored by the Ocular Research Symposia Foundation (ORSF). The mission of the ORSF is to focus attention on unmet needs and current research opportunities in eye research with the objective of accelerating translation of research findings to effective clinical care. In this workshop, the subject of the “The Aging Eye” was addressed, including the prevalence of eye diseases in aging and the economic burden imposed by these diseases. New research work was highlighted on the genetics, biology, biochemistry, neurochemistry, and the impact of nutrition and the environment on function in the older eye. By identifying “low-hanging fruit” (i.e., the best opportunities for successful transition of laboratory research for the prevention of and new treatments and cures for ocular diseases), we seek to spur funding at both the basic research and clinical levels, resulting in sight-saving and sight-restoration measures in the near future.

Keywords: aging, nutrition, eye

THE UNITED STATES AND THE WORLD: AN AGING POPULATION

The United States and other industrialized nations are aging societies with rapidly increasing percentages of populations over the age of 65, and this is the fastest growing segment of society in many countries. In the United States, the number of seniors is projected to more than double from approximately 40 million now to approximately 90 million by 2050. It is everyone's hope to age gracefully and without impairment, but at present this is rarely possible. Most of the major eye diseases are age-related, in that the prevalence of these sight-threatening diseases dramatically increases above 75 years of age. If we look at world estimates overall, there are 285 million people who have some visual impairment, 256 million with low vision, and about 40 million who are blind or have significant visual impairment. Tellingly, 65% of those with visual impairment and 82% of those who are blind are over 50 years of age. In the United States, there are 4.2 million who are blind or have a significant visual impairment, which is up by almost 30% in the last decade.¹ By 2015, it is thought that over 10 million Americans will be blind or have a significant visual impairment. These numbers are staggering in their effects on individuals and on our society in both the costs of healthcare and in lost productivity. As just one example, over 10 million Americans have been diagnosed with some form of retinal degeneration. These currently have poor treatment prospects, yet cost estimates for available treatments are huge, with direct medical costs of retinal disorders in 2013 of approximately \$8.7 billion. Even for treatable disorders such as cataract and refractive errors annual costs in the United States are \$10.7 and \$16.1

billion, respectively. The total annual burden for visual disorders in the United States is estimated to be \$139 billion (<http://costofvision.preventblindness.org/costs/direct-costs/medical-costs-by-disorder>). More specific data for both the prevalence and the economics of age-related eye diseases are given in the individual articles of this volume.

The eye is an amazing organ with the only two clear tissues in the body (Fig.). Its function is to receive and focus light and then transform that photic energy to chemical and electrical signals that are sent to the brain. There, they are recoded into the images that we describe when we talk about our sense of sight and seeing. There are several critical tissues that are directly involved in the visual process and many others that indirectly support this function. Initially, light enters the transparent cornea. From the back of the cornea, it passes through the aqueous humor, the fluid that feeds the lens, and on through the transparent lens. Both the cornea and lens are critical to focusing light on its final destination, the central foveal area of the retina, also called the macula. It is in the retina that the light is converted into chemical and then electrical impulses that are sent down the optic nerve to the brain. Together, the retina and brain constitute our central nervous system.

Time takes its toll on all the tissues of the eye. Common age-related problems at the eye surface include dry eye, and the major age-related disease in the lens is cataract. In the retina, aging is frequently accompanied by macular degeneration. These are discussed below and, in more detail, in the accompanying articles in this issue of *Investigative Ophthalmology & Visual Science*.

There are many other age-related problems that afflict the eye. With age, for example, the jelly-like vitreous body that fills

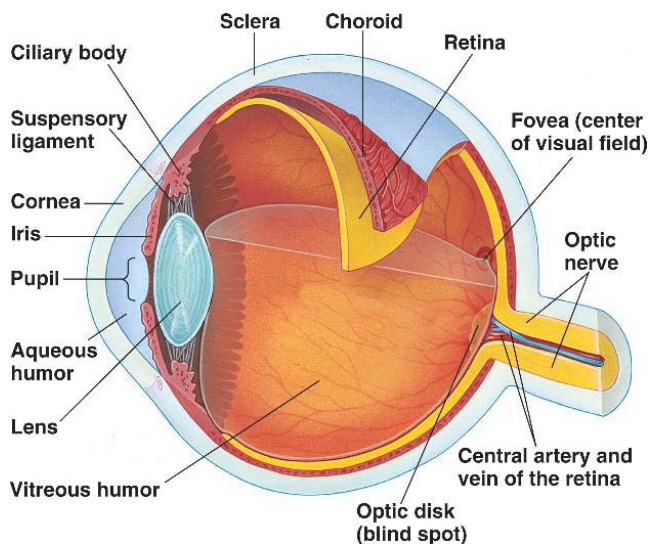


Figure. A schematic view of the tissues of the eye. Light passes through the transparent cornea and the opening in the center of the iris called the pupil. Then, it passes through the clear lens and the vitreous body, which fills the central cavity of the eye. When the optical properties of the cornea and lens are normal, the light is focused on the foveal (macula) area of the neural retina, and is captured by the retinal photoreceptor cells where it is converted into an electrical signal. The electrical signal is processed by other retinal cells and transmitted down the optic nerve to specific brain areas. These areas do the final conversion of the signals into a visual image. Marieb, Elaine N. *Essentials of Human Anatomy & Physiology*. 9th edition. Copyright 2009. Printed and electronically reproduced by permission of Pearson Education, Inc., Upper Saddle River, New Jersey.

the central cavity of the eye liquefies and is able to pull away from its natural attachments to the neural retina. This can lead to the presence of annoying floaters, but is also associated with sight-threatening retinal detachment. Presbyopia is another example of natural aging changes that lead to a diminished ability to focus on near objects. Although usually correctable with eyeglasses, the cumulative optometric costs are high. Significant, age-related cell death in tissues, such as the cornea and retina, can lead to vision loss but, more importantly, set the stage for the onset of age-associated diseases. These are described individually below. Many of these debilities have a genetic component, but they are also induced by environmental factors (e.g., smoking). Some are of unknown etiology. However, they are particularly insidious because they are generally painless in their earlier stages, and thus tend to remain unnoticed and untreated until it is often too late to institute an effective therapy. The National Eye Institute classifies glaucoma, AMD, and diabetic retinopathy in this category of usually asymptomatic, sight-threatening diseases.

THE ECONOMICS OF VISION LOSS

Although the present costs associated with visual impairment are approximately \$139 billion/year in the United States (see above), worldwide, the International Federation on Aging predicts the cost of vision loss by 2020 will reach an alarming \$2.8 trillion with indirect costs adding another \$760 billion (<http://www.ifa-fiv.org/ifa-publication/demographics/the-high-cost-of-low-vision-the-evidence>) (See article by Rein in this volume for additional breakdown of costs associated with specific age-related eye debilities). In the United States, the numbers are not strictly proportional with those worldwide and vary somewhat as to the particular eye

disease as compiled by the American Academy of Ophthalmology in 2011.² Although not the major blinding disease in the United States or much of the developed countries, cataract is the major cause of blindness in lesser developed countries where surgical options are limited. Additionally, risk is different for different age groups. Cataract, for example, affects about 22 million Americans age 40 and older. For those 80 years and above, more than half are affected with cataract, and the other major ocular diseases as considered individually in the next section.

Besides direct medical costs, there is a huge cost to society from related factors, such as the loss of independence, medical costs of secondary sequelae (falls, etc.), the loss of work productivity, and the ability to earn a living. A new analysis shows that indirect costs, such as productivity loss and long-term care “actually exceed direct costs for eye and vision problems.”³ Additional analyses place the costs at orders of greater magnitude⁴; thus, delay of vision loss, improved low vision, or restoration of functional vision to those already blind could have an enormous impact, decreasing the costs of institutionalization and increasing personal productivity and revenue generation. Encouragingly, it is thought that just delaying cataract by only 10 years could eliminate the need for half of the cataractous-lens extractions, and markedly diminish the costs that are associated with the surgery and the loss of vision due to cataract.

MAJOR UNMET NEEDS FOR PREVENTION AND TREATMENT: INDIVIDUAL EYE CONDITIONS

1. **Dry Eye:** This age-related condition is estimated to affect 5 million persons in the United States over the age of 50. About twice as many women are affected with dry eye as men. It is estimated that 70% of Americans over the age of 60 have dysfunction of their meibomian glands, the glands of the eyelid responsible for production of the protective, oily components of tears. The condition is associated with discomfort and pain and may affect vision. Although some short-term treatments are available (eye drops, etc.), there are significant new opportunities here for prevention and better modes of treatment. This is also true in addressing other serious ocular surface problems such as bullous keratopathy, a condition caused by an age-related disease called Fuch's dystrophy that can necessitate a costly corneal transplant. In all of this, there is the potential for significant cost savings with even only modest improvements in current modes of treatment;
2. **Cataract:** It is estimated that cataract affects almost 22 million Americans over the age of 40 and nearly half of US citizens over the age of 80.² Direct costs for treatment are estimated at \$10.7 billion/year. Indirect costs must be added on to this figure, but would be substantially decreased if cataract development could be delayed even a decade or two, or if cataract-induced vision loss could be more fully obviated through other means such as improved surgery, new drugs, optimized nutrition, and so forth. In many developing countries where cataract is more frequent at even earlier ages, the impact would be even greater;
3. **Glaucoma:** Glaucoma is a complex disease with vision loss due to pathologic changes of the neural retina, optic nerve, and brain but also with associated changes in areas of the anterior segment (i.e., the front portion of the eye). The most common forms of primary glaucoma can best be described as age related, possibly even as a disease of premature cellular senescence. There are

approximately 2.3 million Americans over the age of 40 with glaucoma¹ with a total estimate of 3.4 million by 2030. Unfortunately, an equal number have glaucoma without realizing it or it being diagnosed. Available treatments only slow disease progression toward severe vision loss and blindness; even so, the direct costs of glaucoma treatment were estimated to be \$5.8 billion in the United States in 2013. (<http://costofvision.preventblindness.org/costs/direct-costs/medical-costs-by-disorder>). Treatment costs also include the rising costs of required surgery, in some cases, and the cost of visual disability. This will be an increasingly heavy economic burden on American healthcare as our population ages. Recently pinpointed opportunities for novel treatment (including gene therapy and stem cell therapy) could substantially bring down long-term care costs and the costs to society of visual disability due to glaucoma;

4. **Age-Related Macular Degeneration:** Age-Related Macular Degeneration, as the name implies, is an age-related disease most common in those over age 65. It is a complex disease in that has both genetic and environmental components (e.g., long-term smoking substantially increased the risk of developing AMD as it does for cataract). Today, more than 2 million Americans have significant vision loss due to AMD,¹ with up to 8 million more having earlier signs of the disease. In the 40- to 50-year-old age bracket, the prevalence of AMD is around 2% but, startlingly, over 80, it rises to 35%. Overall, AMD is the leading cause of blindness in industrialized nations like the United States. In 2010, the AMD Alliance International estimated the cost of visual impairment due to AMD in the United States at \$4.6 billion/year (<http://costofvision.preventblindness.org/costs/direct-costs/medical-costs-by-disorder>). In spite of these expenditures, there is currently no adequate treatment for the dry form of AMD. In wet AMD, we only have drugs that slow/halt disease progression in some patients, rather than preventing or eliminating the underlying neovascular problem. While useful, the available drugs are expensive (e.g., around \$2000 for one treatment for the leading drug), and the treatment requires repeated injection of the drug into the vitreous body of the eye. With loss of central vision, ancillary costs are high in terms of loss of productivity, loss of independence (housing, driving), and secondary medical expenses due to accidents (falls, etc.) caused by poor vision. Clearly, AMD is also associated with devastating effects on quality of life and often with depression. As with the other problems noted above, quality of life is often compromised during older age. Quality of life would be vastly improved though through elimination of the debilitating effects of AMD. This may soon be possible with therapies such as gene therapy and stem cell treatment that are on the horizon;
5. **Diabetic Eye Complications:** Diabetes can lead to damage of many tissues, including many parts of the eye. Commonly, the retinal blood vessels are damaged, leading to subsequent vision loss and blindness. Diabetic retinopathy affects almost 4.5 million Americans over the age of 40,² and is estimated to cost the US \$500 million annually for its management. Diabetes also markedly increases the risk for cataract and diabetic cataracts develop at earlier ages than in nondiabetics. People with diabetes also have twice the risk of developing glaucoma, relative to nondiabetic persons. Sight-impairing problems with the cornea can also develop. In the retina, macular edema is a major

complication of diabetes. Existing and new, abnormal retinal vessels may leak and fluid accumulates in the central macular region of the retina causing swelling and blurred vision. It has been estimated that up to 1 million Americans have macular edema with accompanying significant vision loss. As we now know, improvement in clinical healthcare as well as better education, including early diagnosis can substantially cut down on all the ocular problems of diabetes. Nevertheless, in part because of the obesity epidemic, the prevalence of diabetes is expected to rise along with the eye problems that are associated with diabetes (i.e., a high risk of severe visual loss). This requires urgent attention as it is an increasing global problem; and

6. **Low Vision:** Low vision is a condition in which a person's vision is poor even with eyeglasses that afford the best correction possible. Low vision may be observed already in early childhood but increases dramatically with aging, mainly due to the eye diseases cited above. It has been estimated that there are 3.6 million Americans, aged 40 and above, who are visually impaired with eyesight at 20/40 or worse even after correction.² Lighthouse International estimates that, because of the rapidly increasing numbers of baby boomers, 61 million Americans are now at risk of serious vision loss due to developing these age-related eye conditions.

OPPORTUNITIES FOR PREVENTION AND TREATMENT

As noted earlier, Prevent Blindness America recently estimated that our national financial burden for eye diseases is \$139 billion annually.² They conclude that "eye disorders and vision loss are among the costliest conditions to the US economy and, based on ever-increasing healthcare costs and an aging population, this cost is set to continue to grow."² On the other hand, it has been recently estimated that 80% of vision loss is preventable and that "vision loss is no longer an inevitable part of the aging process."⁵

How do we control these costs while alleviating the physical and societal problems of the individual suffering from vision loss and blindness, especially in an aging population at much greater risk of eye disabilities? One major step would be to convince governments, healthcare providers, and the general public that many eye diseases can, in fact, be managed or even obviated with early diagnosis. Programs that create early awareness and detection are key elements here with probable and quick success in substantially lowering the vision loss in our country and around the world. Another way is to take advantage of the recent increase in knowledge in understanding the basic biology of these eye diseases, and also new opportunities in translating this knowledge into meaningful preventions, treatments, and cures. Even a decade ago, these pathways to treatment were unknown or unrecognized. Now, they are becoming clearer and better defined, for instance, the "low-hanging fruit" alluded to at the beginning of this introduction. In this issue, readers will find articles that define the problems we currently face as we search for treatments for age-related eye diseases and also opportunities to alleviate these blinding conditions for the sake of both the individual and for our society.

Acknowledgments

Supported by National Institutes of Health Grants R01 021212 and R01 13250, gifts from Alcon and Johnson & Johnson Focused Giving, and USDA contract 1950-510000-060-01A.

Disclosure: **G.J. Chader**, None; **A. Taylor**, None

References

1. Vision Problems in the U.S. Prevent Blindness America Web site. <http://www.preventblindness.org/vision-problems-us>. Updated 2012. Accessed June 21, 2013.
2. Eye Health Statistics at a Glance. *American Academy of Ophthalmology*. <http://www.aao.org/newsroom/upload/Eye-Health-Statistics-April-2011.pdf>. Updated April 2011. Accessed June 21, 2013.
3. Costs of Vision Problems: The Economic Burden of Vision Loss and Eye Disorders in the United States. Prevent Blindness America Web site. <http://costofvision.preventblindness.org>. Updated 2013. Accessed June 21, 2013.
4. Access Economics. *AMD Alliance International. The Global Economic Cost of Visual Impairment*. http://www.amdalliance.org/user_files/documents/Global%20cost%20of%20VI_FINAL%20report.pdf. Published March 16, 2010. Accessed June 21, 2013.
5. The High Cost of Low Vision: Evidence on Aging and the Loss of Sight. *International Federation on Aging*. <http://www.ifa-fiv.org/wp-content/uploads/2013/02/The-High-Cost-of-Low-Vision-The-Evidence-on-Aging-and-the-Loss-of-Sight.pdf>. Published 2013. Accessed June 21, 2013.