



# Accomplishments and Opportunities at the National Eye Institute

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National Alliance for Eye and Vision Research (NAEVR)

[www.eyeresearch.org](http://www.eyeresearch.org)

## Introduction

The National Eye Institute (NEI) is one of the oldest and most respected Institutes within the National Institutes of Health (NIH). NEI-sponsored basic and translational research—conducted within its Intramural Program and by leading academic and medical centers through its Extramural Program—plays an important role in creating and sustaining healthy and productive lives for all Americans.

Even before a child is born, NEI research has an impact. NEI-sponsored clinical trials have greatly improved treatment for retinopathy of prematurity (ROP), a blinding complication found in low weight, premature infants. As a result, the 3,000 infants affected each year with this condition can be expected to experience 70-80 years of full and productive “sighted” lives. As the “baby boom” generation ages, NEI research into age-related eye diseases has a significant impact. NEI’s Age-Related Eye Disease Study has demonstrated that doses of zinc and three antioxidant vitamins were effective in reducing vision loss in people at high risk for developing Age-related Macular Degeneration (AMD), the leading cause of legal blindness in older-age Americans.

## Current Vision Challenges

NEI estimates the economic and societal cost of eye and vision impairment as \$50 billion annually. This burden to the US is expected to increase dramatically, primarily due to an aging population and the growing prevalence of diseases that result in vision loss. For example:

- Although more than 1.6 million Americans over age 60 currently have Age-related Macular Degeneration, approximately 30 million Americans over age 40 are at risk of developing it.
- Diabetic Retinopathy affects more than 5.3 million Americans age 18 or older, and is now the leading cause of blindness in the industrialized world in people between the ages of 25 and 74.
- About 2.2 million Americans have been diagnosed with glaucoma, a chronic potentially blinding disease that requires life-long treatment to control, and another 2 million Americans do not know they have it.
- Cataracts affect nearly 20.5 million Americans age 65 or older. In the US, a cataract is treatable by removing the natural lens and implanting an intraocular lens (IOL). However, in the rest of the world, cataracts are the leading cause of blindness due to lack of access to adequate care.

These conditions are costly to society since they can result in decreased productivity and the onset of other diseases (e.g. depression and its physical and emotional consequences). Especially with an aging population, adequately spending now on eye and vision research can reduce and potentially prevent future expenditures to the Medicare and Medicaid programs. Funding eye and vision research at the NEI is a cost-effective investment.

## NEI Accomplishments and Opportunities

Because the eye is a complex organ, NEI research is characterized by the portion of the eye affected (e.g. retina, cornea, lens) or by the impairment (e.g. cataract, low vision). Below appears a brief summary of NEI accomplishments during the past five years and the important research that still needs to be done—*which cannot be pursued effectively if additional funding is not forthcoming.*

## **Retinal Diseases**

### *Over the Past 5 Years:*

- More than 130 genes causing inherited retinal diseases have been identified. Identifying mutant genes allows researchers to better understand the causes of blindness and develop therapies.
- Dogs born blind with Leber congenital amaurosis, a severe retinal disease that also affects newborn infants, were successfully treated with a gene replacement therapy that restored their sight. A clinical trial in humans is being planned.
- NEI researchers have discovered an important biological clue in treating uveitis, a blinding autoimmune disease. This finding has sparked therapeutic breakthroughs for a host of autoimmune disease, including colitis and multiple sclerosis.

### *Important Research Still Needs to be Done on:*

- Identifying additional factors that control immune processes and inflammation within the eye in diseases like uveitis to develop better therapeutic approaches.
- Developing strategies to enhance retinal ganglion cell regeneration after damage or loss due to glaucoma and other retinal disease.
- Expanding the initial laboratory success of gene therapy for the wider spectrum of retinal diseases and advance these therapies to clinical trials.
- Exploring the causes of age related macular degeneration and improving the ability to prevent, diagnose, and treat this disease.

## **Corneal Diseases**

### *Over the Past 5 Years:*

- NEI-funded basic research and clinical studies have helped improve the success rate of corneal transplantation to greater than 90 percent. Corneal transplantation has become the most successful and common organ transplant procedure.
- Adult epithelial stem cells grown on membranes outside the body have been successfully transplanted to restore the transparency to the ocular surface damaged by disease or injury. The NEI is pioneering what could become one of the first successful stem cell transplant procedures.
- The NEI-sponsored Herpetic Eye Diseases Study demonstrated that oral acyclovir could reduce potentially blinding recurrence of herpes eye infections by 40 percent. Herpes infection is one of the most common causes of corneal blindness.

### *Important Research Still Needs to be Done on:*

- Identifying and characterizing the stem cells in corneal tissue and determining mechanisms involved in their differentiation into various tissue types.
- Analyzing the causes of corneal graft rejection and uncontrolled growth of new blood vessels into the cornea.
- Developing vaccines and other novel therapeutic interventions for blinding viral, bacterial, fungal, and parasitic corneal and ocular surface diseases.

## **Lens and Cataract**

### *Over the Past 5 Years:*

- NEI-supported studies revealed that a structural component of the lens known as alpha-crystallin acts as a molecular “chaperone” that helps prevent the lens from clouding. Such insight could lead to new therapies that prevent cataract formation, thereby delaying or obviating the need for the millions of cataract surgeries performed each year in older-age Americans. (Note that alpha-crystallin has subsequently been found to play a major role in many diseases, including Alzheimer’s, Parkinson’s, heart

disease, and osteoarthritis.)

- Cell-to-cell communication via gap junctions has been shown to be essential in the lens and is controlled by the structural proteins known as connexins, each of which has unique functions. NEI research has shown that these connexins are necessary to avoid the onset of cataracts.

*Important Research Still Needs to be Done on:*

- Identifying and characterizing genes that, when mutated, cause cataracts.
- Understanding the basis of lens accommodation (near focus) and presbyopia (the loss of near focus with age) at the molecular and mechanistic levels.
- Determining the extent of visual impairment due to cataract.

## **Glaucoma and Optic Neuropathies**

*Over the Past 5 Years:*

- The Ocular Hypertension Treatment Study showed that lowering the intraocular pressure by at least 20 percent in patients with ocular hypertension reduced the probability of developing the most common form of glaucoma by 50 percent over 5 years.
- The Early Manifest Glaucoma Study demonstrated that vision loss in newly diagnosed glaucoma patients progressed less often and more slowly than in untreated patients when the intraocular pressure was reduced at least 20 percent.
- Significant advances have been made in identifying glaucoma-causing or associated genes with mapping of several glaucoma loci and the cloning of a number of the genes. These findings give scientists a new research front to develop more effective therapies.
- Newer/more effective medications for reducing intraocular pressure, developed ultimately from NEI-funded research, have become the mainstays of treatment for glaucoma. Ongoing research in the biology of fluid drainage/pressure regulation in the eye is revealing opportunities for developing more effective drug and gene-based treatment for pressure reduction.

*Important Research Still Needs to be Done on:*

- Determining the mechanisms of optic nerve damage and retinal ganglion cell loss and survival in optic nerve diseases such as glaucoma.
- Developing novel therapeutic approaches to glaucoma and other optic neuropathies, including stem cell therapy, gene therapy, vaccination, and other neuroprotective strategies.
- Developing improved diagnostic measures to detect optic nerve disease onset, progression, and treatment effectiveness.
- Developing additional and still more effective means of reducing intraocular pressure, based on newly acquired knowledge of the basic biology of ocular hydrodynamics.

## **Strabismus, Amblyopia, and Visual Processing**

*Over the Past 5 Years:*

- NEI-supported clinical trials on the treatment of amblyopia, or lazy eye, have made significant progress in optimizing treatment to provide the best visual outcome in affected children.
- Progress has been made in understanding the visual and biochemical cues and genes involved in the regulation of eye growth in myopia. Myopia is by far the most common cause of visual function impairment. Strategies to prevent its onset could prevent the need for correction through glasses and contact lenses.
- A key advance has been in identifying the molecules in developing visual pathways that guide retinal axon growth to the appropriate targets in the developing nervous system.
- NEI researchers have identified biological factors that inhibit regeneration of the central nervous system, giving rise to the possibility of therapies that regenerate lost nerve cells and restore sight.

*Important Research Still Needs to be Done on:*

- Determining how stem cells differentiate in the development of the visual system and how they can be used to understand the molecular logic of cell type-specific identity in the visual system.
- Studying the mechanisms that lead to degeneration and regeneration of the central visual pathways.
- Developing a better understanding of the neural control, biomechanical properties, and anatomical relationships of the tissues around the eye muscles and the roles they play in guiding eye movements.

**Low Vision and Blindness Rehabilitation**

*Over the Past 5 Years:*

- There has been progress in development and deployment of assistive aids such as the global position system-based navigation, talking signs, and auditory signals at street crossings.
- Imaging technologies have increased the understanding of changes in the brain related to visual deficits and impairments.

*Important Research Still Needs to be Done on:*

- Evaluating the effectiveness of existing rehabilitation strategies and programs.
- Developing an understanding of perceptual and cognitive factors involved in the performance of everyday tasks such as driving, other forms of mobility, and reading.

**Conclusion**

The NEI advances noted above come at a time when eye disease—especially in older age Americans—has become a fast-growing but little-known epidemic that threatens to further strain federal resources. The prevalence of age-related eye diseases is increasing at an alarming rate, and many of these conditions still lack effective treatments—although promising discoveries that could lead to treatments are “in the pipeline” at the NEI. As a result, the NEI needs to be adequately funded to ensure that these therapies are available to all Americans so that they may lead healthy and productive lives.