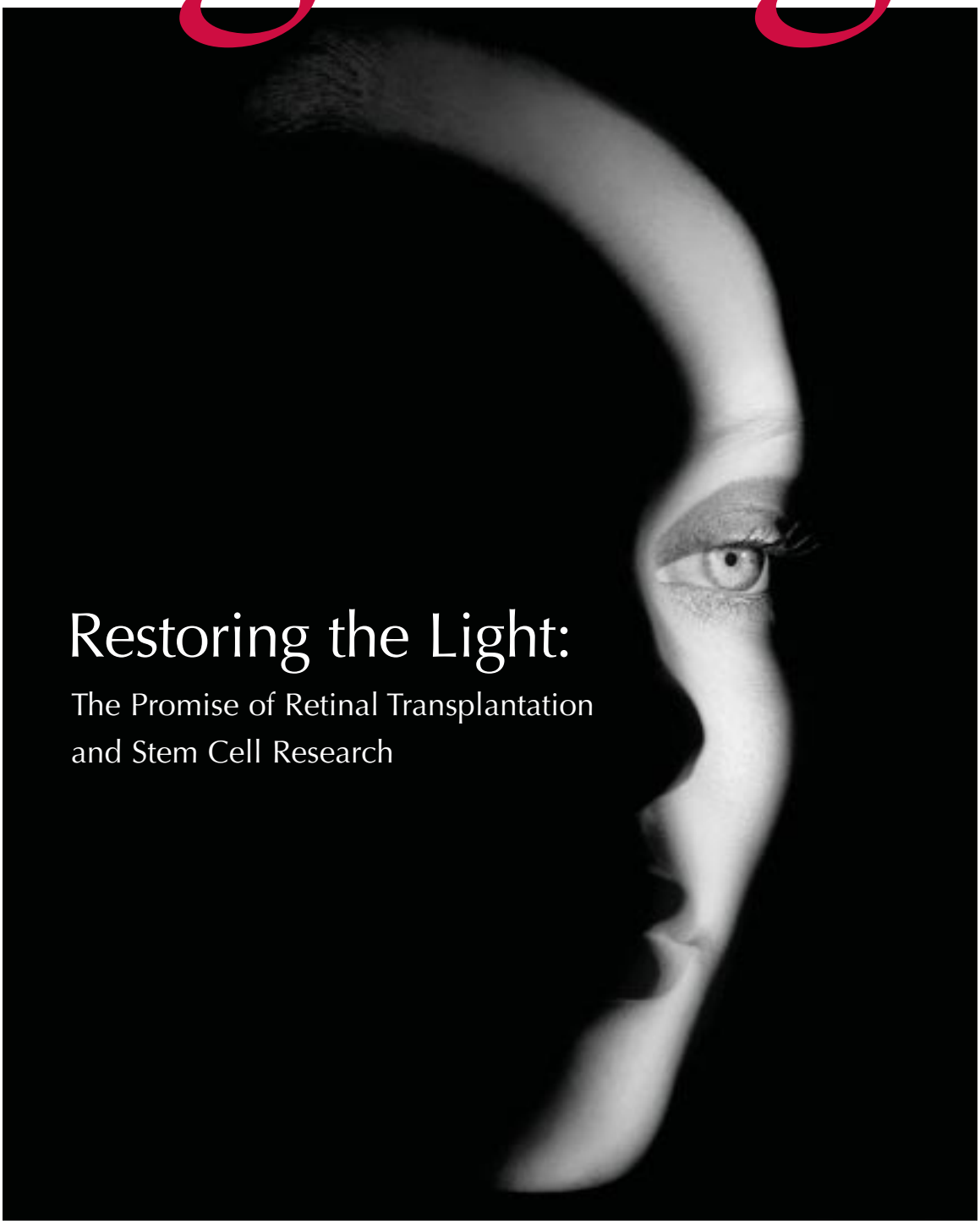
Sightings

Spring 2003



Restoring the Light:

The Promise of Retinal Transplantation and Stem Cell Research

The Schepens Eye
Research Institute

From the President

The last decade bears witness to an ongoing transformation in biomedical research. This is particularly true in the vision sciences and ophthalmology, and no organization better exemplifies this growth than The Schepens Eye Research Institute. During this period of time, federal funding for research at The Schepens has catapulted the Institute to the very forefront of vision research organizations. Simultaneously, the Institute has created powerful collaborative research teams of scientists with diverse skills and talents to attack the most daunting problems that we face: blinding eye diseases that predominantly affect the aging population and for which treatments are unevenly effective and preventions have yet to be found. Glaucoma, macular degeneration, dry eye syndrome, diabetic retinopathy, and chronic eye inflammation are the leading examples of these sight-robbing diseases.

The demographics of an aging "baby boomer" generation in America suggest that an impending "epidemic" of vision loss will occur by 2030 unless novel cures and treatments are discovered. A sense of urgency is in the air! In such a setting, scientists must be allowed to exercise their creativity, and to take risks in order to leapfrog forward in the critical process of discovering new knowledge. Research of this type is not particularly well funded by NIH and the federal government, and therefore, organizations like The Schepens must seek non-governmental, chiefly philanthropic funding to enable its scientists to be daring in their promising research and to take risks that are essential to finding the breakthroughs that will change clinical care and benefit patients.

This issue of *Sightings* highlights the Institute's highly respected and world-class Minda de Gunzburg Retinal Transplantation Research Center, a multi-investigator collaborative research effort that is funded in part through the generosity and forward-thinking of Mr. Charles de Gunzburg and his family. It is easy to imagine how transplantation of retinal tissue could someday restore sight to patients whose retinas have been irreversibly damaged by disease. But it is extremely difficult to develop strategies to accomplish this daunting task. The hurdles that stand in the way include lack of knowledge, lack of technical skills and approaches, and the destructive potential of immune rejection. Based on knowledge available in 1996 (when the Minda de Gunzburg Center was launched), we were filled with anxious optimism that retinal transplantation could be successful in the near or intermediate term. And the Institute and its supporters took the risk to explore the possibilities.

Of course, the potential of stem cells was not on the horizon in 1996, but it is now. Dr. Michael Young, the first Director of the Institute's Minda de Gunzburg Retinal Transplantation Research Center, quickly realized the potential of stem cells upon their discovery in 1998. He was perhaps the first scientist in the world to demonstrate the principle that stem cells derived from brain and retinal tissues, when implanted into eyes of experimental animals with damaged retinas, can repopulate the retina with cells of the type required for vision. The availability of non-federal funds has made it possible to move this research along swiftly, and the results described in this issue of *Sightings* indicate the level of success that is being achieved, and the hope we now have for the future.

Not all high-risk research pays off, and this realization causes some to demur from taking the gamble. The strength and depth of the research team at The Schepens enables this organization to take these gambles — with the endorsement and support of our friends and donors. With these types of partnership we can move forward with confidence that the rate of payoffs will continue to be high in our eye and vision research.

J. Wayne Streilein, M.D., President

Issue Highlights

Restoring the Light

The Promise of Retinal Transplantation and Stem Cell Research

The most fervent wish of people living with retinal disease is for another chance at sight, another chance to appreciate the vision they once had and gradually or rapidly lost. For them — the victims of macular degeneration, retinitis pigmentosa, diabetic retinopathy, even glaucoma and a host of other diseases — the successful regeneration, repair, or transplantation of a human retina would be like coming out of the darkness into the light. An impossible dream.

"If someone told me that I could now have my retinas repaired and regain even part of my vision, my response would be unimaginable. New retinas would dramatically change my life," says Rich Godfrey, volunteer liaison for The Schepens Eye Research Institute, who became legally blind at age 40 from a form of macular degeneration. "My work, my home life, sports — all would be different. But the really big things like reading and driving would mean the most to me. They were the hardest to give up, and would be the most exciting to get back. What a wonderful gift it would be."

For Maureen Murphy from Weymouth, "It would be like being reborn and opening my eyes for the first time." Murphy, diagnosed in her mid-20s with retinitis pigmentosa, says: "It would be the littlest things that would change and make my life and my family's life easier. All the ordinary little things that fully sighted people take for granted, but require extra effort and planning for me. Walking into a store and seeing what is there rather than a whiteout or haze. Being able to see in a dimly lit restaurant and have the ability to see the food in front of me. To recognize familiar faces in social situations instead of listening for the voices. Not having to close my eyes in the sunlight because it causes pain in my eyes. Not needing someone to drive me to baby-sit for my grandchild, going out at night and being able to see in the dark — you have no idea what it would mean to me," she says.

While not an impossible dream, the path to restoring the light for millions by successfully transplanting the human retina has been long and somewhat uneventful until recently.

"Things have never been more hopeful," says Michael Young, Ph.D., assistant scientist and neurobiologist at Schepens. "Five years ago, I couldn't say that. We were all headed in one direction. Now we are being compelled toward a whole new focus," says Young, who is Director of the Institute's Minda de Gunzburg Retinal Transplantation Research Center. Founded in 1997, the Center's mission is to overcome the barriers to retinal transplantation through basic science research.

To meet that goal, Schepens scientists involved in the Center are looking at every aspect of the challenge — exploring the right cells to transplant, the right place to implant them, how to prevent rejection, and how to wire transplanted tissue to the brain so that it actually improves vision.

A BRIEF HISTORY

The concept of transplanting retinas to restore sight has been with us for a hundred years. Initial unsuccessful attempts in mice in the early 1900s put the concept on hold. It was not until the 1970s when many organ transplants were already possible and researchers were experimenting with brain tissue transplants to treat Parkinson's disease that the idea was revived.

A series of studies in the 1980s followed — studies in which retinal tissue was transplanted from one laboratory animal to another. Though quite unsuccessful, these studies did shine a light on the many unexpected, unexplained barriers intrinsic to transplanting this precious tissue from one individual to another.

"If someone told me that I could now have my retinas repaired and regain even part of my vision, my response would be unimaginable …"

THE ANATOMY OF A TRANSPLANT

The retina is the tissue paper-thin film at the back of the eye that captures the light images from the outside and relays these images through the optic nerve to the brain. The retina is made of two layers — the neural retina layer and the retinal pigment epithelial layer. The neural layer consists of an outer shell of light-sensitive cells known as the photoreceptors, an inner shell of ganglion cells, which are the nerve cells that transmit information to the optic nerve and ultimately to the brain, and a middle shell composed of nerve cells that connect the inner and outer shells.

continued on page 4

Restoring the Light
continued from page 3

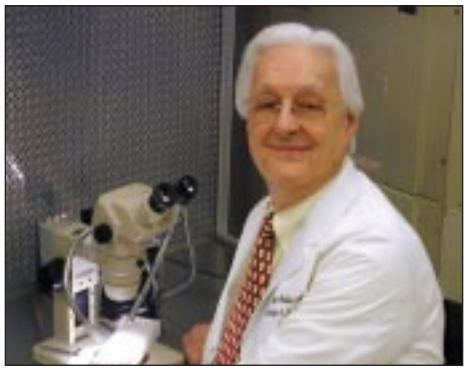
The neural retina layer rests close against the retinal pigment epithelium (RPE) layer, and the cells in this latter layer provide nutrient support for the photoreceptors and carry waste products away. Neither layer can survive without the other. Both are at risk as the retina deteriorates, and both are candidates for transplantation.

Most experimental transplantations have been attempted by placing donor cells in the potential space between the RPE and the neural layer of the retina. The space is known as the subretinal space. Over the years, researchers have placed iris cells, retinal cells, stem cells, and brain cells in this space and then waited and watched for evidence of survival.

Preventing rejection by rescuing immune privilege

With the possible exception of stem cells, and the jury is still out on them, cells transplanted into the subretinal space survive for a while but ultimately succumb to rejection and die. Rejection occurs when the body identifies the transplanted tissue as foreign and signals the immune system to attack and destroy it and, in the process, destroy part of itself as well.

But the eye is a little different. Because of its fragility, and because many eye tissues are unable to regenerate themselves after injury, the eye has evolved a gentler way to deal with foreign invaders. Unlike most other organs and tissues in the body, the eye does not rage all out war. Instead, it picks and chooses its immune battles, and carefully selects the weapons it uses to defend itself. This ability is called immune privilege. Immune privilege allows the eye to tolerate foreign tissue grafts so long as they are harmless. Immune privilege even educates the immune system to recognize foreign tissue grafts as part of itself.



Dr. J. Wayne Streilein

"You would think that this would make transplanting a retina an easy proposition," says J. Wayne Streilein, M.D., President. "But it doesn't seem to work that way. The immune privilege process is complicated enough in the healthy eye, but in a transplant situation we are dealing with an already damaged eye where many processes, including immune privilege, may also be injured," he says.

The focus of Streilein's laboratory, therefore, is to understand why immune privilege fails when it is needed most.

Streilein and his colleagues are convinced that the retinal pigment epithelium layer is responsible for immune privilege in the retina. Therefore, restoring immune privilege is an important goal of Parisa Zamiri, M.D., postdoctoral fellow, and a member of Streilein's team. Zamiri's focus is understanding the characteristics of

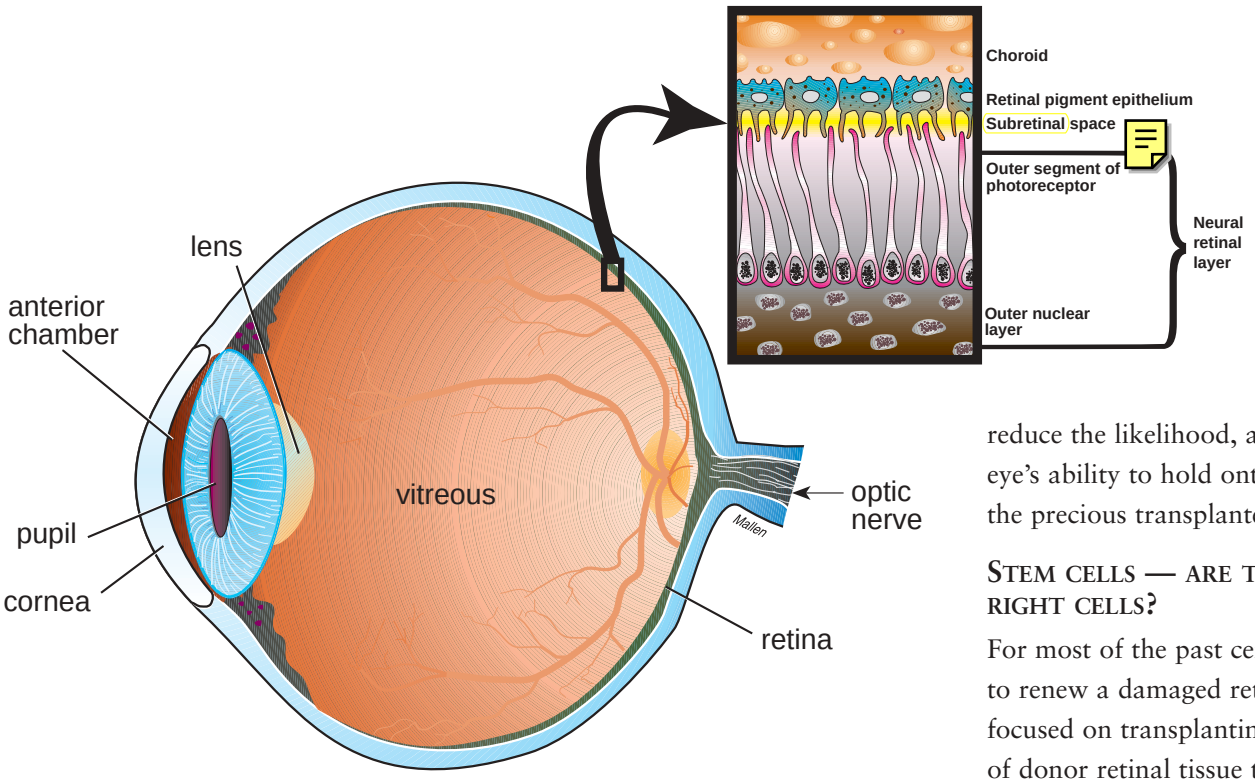
Parisa Zamiri, M.D.

the subretinal space where transplanted tissues are placed. "My question is 'what is the normal healthy state of the subretinal space,' so we can learn what might go right or wrong in a transplant situation," she says.

To determine this, Zamiri has separated the two layers of the retina and placed the RPE layer (the layer known to be immune-privileged) in tissue culture to see what the epithelial cells produce. Her initial findings suggest that RPE produce immune-privileged chemicals similar to those in the aqueous humor, a part of the eye where immune privilege is well understood because of recent Schepens discoveries.

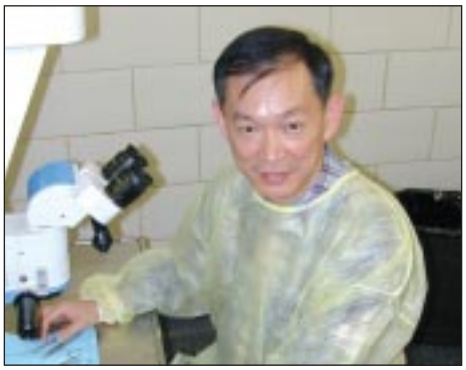
"Knowing what the RPE normally produces and secretes into the subretinal space to maintain immune privilege will help us to re-create the privileged state when the goal is to place a transplant in this space in order to replace a damaged retina," says Zamiri.

Another theory concerning immune privilege in the retina considers a unique group of cells in the retina called microglia. These cells have many functions, including cleaning up debris when the eye is damaged



by too much light, infection or other types of injury. Microglia also play a dual role in the retina's immune response. For example, in some situations microglia tell the immune system to kill a foreign invader and in other situations microglia tell the immune system to consider foreign material as self and protect it. Understanding how these situations differ is an important goal of research.

Tat Fong Ng, Ph.D., investigator, recently completed a training fellowship with Streilein and is now trying to determine whether microglia can influence acceptance or rejection of retinal transplants. He has developed a system of activating microglia by exposing the eye to different levels of light — from non-toxic to toxic levels. Then he places retinal transplants in these eyes. He found that greater light exposure caused greater activation of



Tat Fong Ng, Ph.D.

microglia, and retinas grafted into these eyes suffered greater immune rejection.

Ng concluded that light-toxic damage might activate microglia, triggering them to tell the immune system to "kill" the "invading" transplanted tissue. Diseases of the retina may similarly activate microglia, and if this is the case, then finding ways to block or change the message delivered by microglia to the immune system might reduce the likelihood, and restore the eye's ability to hold onto and nurture the precious transplanted tissue.

Stem Cells — Are They the Right Cells?

For most of the past century attempts to renew a damaged retina have focused on transplanting whole pieces of donor retinal tissue to a recipient eye. Now another type of tissue is showing great promise — the stem cell. Stem cells are undifferentiated cells that can transform into other types of cells. "This is very exciting," says Young, who is pioneering the concept in collaboration with several other laboratories worldwide. "Stem cells," he says, "seem to automatically eliminate some initial barriers to transplantation."

continued on page 14

Michael Young, Ph.D.

Ask a Schepens Scientist

Stephen Burns, Ph.D.

Stephen Burns spent his early childhood in Reading, Massachusetts, where he now lives again. In between, he attended school in New Hampshire, earned a bachelor of science degree at Lehigh University in Pennsylvania, and received a Ph.D. in biophysics at Ohio State University. After completing a postdoctoral fellowship in ophthalmology at the University of Chicago, he served on the faculty of the University of Pittsburgh. He currently is a senior scientist at The Schepens Eye Research Institute and an associate professor at Harvard Medical School. Burns and colleagues recently published "Imperfect optics may be the eye's defense against chromatic blur" in *Nature* (417, 174-6).

Q: I have heard about research that you are doing which may affect LASIK refractive surgery in the future. Can you explain?

A: Each year nearly a million people choose to have LASIK surgery, which uses a laser beam to reshape the cornea of the eye and improves vision for people with myopia (nearsightedness) or hyperopia (farsightedness). In most cases the technique is fairly successful. Most of those who opt for the surgery no longer need glasses for their respective problems. But in some cases, and under specific light conditions, vision can actually be diminished by the procedure. In our work at Schepens, we are trying to understand why and ultimately make suggestions for a more precise technique.

In normal vision, light rays — sent by the object we are looking at — enter the eye through the cornea and then the lens, and are bent or refracted so that all the rays converge in one single point on the retina (the paper-thin film at the back of the eye), which then send a high-quality, clear image to the brain. If the cornea or lens is flawed, such as in farsightedness and nearsightedness, the rays don't converge in one spot on the retina. Instead they come together behind or in front of the retina. The rays are hitting the retina at multiple points and send a confused or blurred image to the brain.

The goal of LASIK surgery is to correct these flaws, which are known as aberrations, in the optics of the eye. These flaws prevent the light coming into the eye from forming a clear image on the retina. These flaws are in the cornea, the clear outer covering of the eye, or in the lens, the eye's focusing device, or in the interaction between the two. In the case of myopia or nearsightedness, for instance, the cornea and the eye are too long. In farsightedness, the eye and the cornea are too short. To correct myopia, a surgeon reshapes the cornea so that it is flattened in the center. In the hyperopic, the surgeon reshapes the cornea so that it has a steeper center.

While LASIK surgery corrects these two straightforward problems, it does not, at the present time, take into account what are known as "higher-order" aberrations, which are smaller and more complex flaws in the cornea or lens. There are numerous higher-order aberrations. Everyone has some, and they impact how each individual sees the world. Though smaller, these flaws in the cornea and the lens are more complicated and can consist of multiple tiny changes in the shape of the cornea or lens.

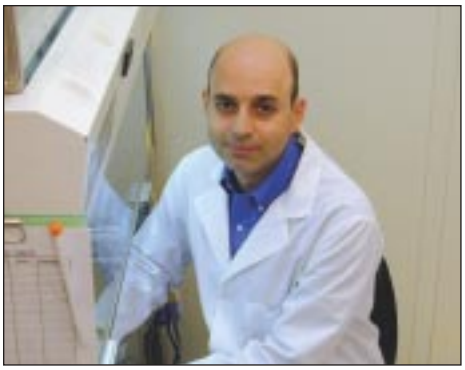
One example of such a flaw is "spherical" aberration, which causes the eye's focus to get worse when the pupil gets larger (such as at night when the pupil expands to take in more light). Because traditional LASIK does not account for this higher-order problem, it actually can make night vision worse than before the surgery for some individuals.

Many in the refractive surgery and technology community are hoping to give people perfect vision by eliminating these more intricate flaws along with the simpler aberrations. They are calling the hoped-for result a "customized" cornea.

However, our research at The Schepens Eye Research Institute is telling us that surgeons and others in the refractive-correction world may need to be cautious. An individual's eye is more complex than we realized. One of our studies, recently published in the jour-

continued on page 11

Clinically Speaking



Kameran Lashkari, M.D.

Kameran Lashkari, M.D., a graduate of Williams College, received his M.D. from New York Medical College. He was an intern at St. Vincent's College, New York, and a resident in ophthalmology at the University of Missouri Eye Foundation of Kansas City. He completed fellowships in retinal disease at The Schepens Eye Research Institute and the Massachusetts Eye and Ear Infirmary (MEEI)/Schepens Retina Associates before joining the staff. He is currently an assistant scientist at Schepens and a vitreoretinal specialist at MEEI.

Q: Retinal transplantation sounds very exciting. What are some diseases that may ultimately be helped by retinal transplantation? Can you tell me what causes them and how they are treated today?

A: When retinal transplantation becomes available, its impact will be dramatic. Thousands of people who are now legally or fully blind may regain partial vision — people with macular degeneration, diabetic retinopathy, retinitis pigmentosa, glaucoma, and numerous other diseases. For some, current treatments can improve vision temporarily or delay progression of the disease. For others, a breakthrough such as retinal transplantation may be the only hope.

Because there are many diseases that damage the retina, I will focus on two conditions — age-related macular degeneration and glaucoma.

Age-related macular degeneration

Age-related macular degeneration (AMD) may be a prime candidate for retinal transplantation. Transplanted cells could replace damaged photoreceptor or light-sensitive cells of the macula, the retina's tiny center, which is destroyed along with central vision and the ability to read, drive, or recognize faces in victims of AMD.

The disease has two forms: dry and wet. In dry macular degeneration, which affects about 90 percent of people with the disease, the cells of the macula break down slowly over a period of years. Vision loss occurs when one or more areas of the retina become scarred. Wet macular degeneration causes more rapid and severe vision loss. This occurs when a collagen-based vascular tissue develops beneath the retina. This scar tissue disturbs the normal anatomy of the back of the eye and causes bleeding, oozing, swelling, and the death of photoreceptors.

No treatment exists for dry AMD, although taking antioxidants like vitamins C and E, lutein, and zinc may reduce the severity. Treatments for wet AMD include laser photocoagulation, which seals the abnormal blood vessels, and photodynamic therapy, a newer drug treatment, which selectively destroys the blood vessels in the scar tissue without damaging the retina. Researchers have also developed compounds that neutralize vascular endothelial growth factor (VEGF), a growth factor that promotes blood vessel growth inside the scar. On the horizon are treatments using these new compounds, possibly in combination with photodynamic therapy.

Glaucoma

Victims of glaucoma may also find relief if retinal transplantation becomes possible. Transplanted cells may one day replace or regenerate damaged ganglion or nerve cells in the retina and the optic nerve.

Glaucoma is actually a group of diseases whose common denominator is damage to the optic nerve, which transmits visual information from the retina to the brain. Contrary to popular belief, high fluid pressure within the eye is only one of several risk factors for glaucoma, since optic nerve damage can occur in eyes with normal pressure.

Most cases in the U.S. are primary open-angle glaucoma, in which the eye appears to be normal but the optic nerve is unusually sensitive to the buildup of fluid pressure in the eye. There can be slow but progressive damage to the optic nerve.

Medications designed to lower fluid pressure within the eye are the first line of defense against glaucoma. Some drugs cause the eye to make less fluid,

continued on page 11

Annual Fund

The Magic of Giving

While there are no magic hats that will instantly produce an answer to blinding eye diseases, Betty and Charles Cohen realized that future treatments and cures for blindness rely on the research of dedicated scientists collaborating on a myriad of different diseases affecting the eye.

Betty, who had been blind in one eye since birth, later developed a cataract, a clouding of the eye's lens that impaired her already limited vision. Currently, the only effective treatment for a cataract is to remove and replace the diseased lens. Betty decided to undergo surgery despite her worry about losing her remaining vision. It was Betty's faith in the role that scientific research plays in perfecting the implantation process that finally convinced her that it was a safe and necessary action.

Despite her limited vision, Betty possessed an appreciation for art. The Cohens' house is an art gallery of sorts, displaying numerous watercolor and acrylic still life and landscape paintings created by Betty over the years.

Prior to meeting Betty, Charles spent ten years performing magic and participating in Vaudeville acts. He was also in a quartet called the Melody Boys. Charles received an early introduction to magic by way of loitering in theatres after performances and talking with the performers. He befriended a few magicians, and they started leaving free tickets so he could serve as a plant in the audience. They would call on him to approach the stage and participate in the performance — unknown to the other spectators — to assist in an array of different tricks. Charles would then rush home to write a description of the tricks and to practice performing each one. Throughout the years, Charles has used this talent in many ways, including volunteer performances for sick children at area hospitals.

Betty and Charles Cohen

For Charles and Betty, when it came to supporting the future of vision research, there were no illusions, mirrors, or slight-of-hand needed to encourage them to give. They were married for 47 years and had many things in common, including a passion for helping those afflicted with vision impairment.

The original decision to support the annual fund at The Schepens Eye Research Institute was rooted in Betty's lifelong experience with visual limits. Together they determined that the most effective role they could play was not that of an audience, but as the catalyst — through financial support — to enable researchers to cure and prevent eye disease.

Despite the devastating loss of his wife to cancer almost two years ago, Charles has not been swayed from his continuing support for his wife's passion for eye research. "Without research, the medical community wouldn't be able to make the advances that people like us reap the benefits of in the clinical setting," said Charles. He is adamant about continuing their commitment to funding eye research that will provide a brighter future for the next generation, in hopes that others don't have to endure the hardship of losing sight.

Philanthropy may not be preceded by the words abracadabra, but the continuous support the Institute has received over the years from Betty and Charles is pure magic.

Please contact Melanie Saunders in the Development Office at (617) 912-2564 to find out how you can contribute to the Annual Fund, or you may donate online by visiting www.eri.harvard.edu.

Focus on Philanthropic Investment

Security in Uncertain Markets

William Wolff Society

The last few years have been anxious times for investors. Gone are the days of double-digit returns in the stock market, replaced by losses in each of the last three years. The go-go '90s are over and most individuals are looking for a safe harbor for their savings and investments. Certificates of Deposit (CDs), the investment vehicle of choice in previous market downturns, have provided little comfort to those seeking a reasonable return on their investment. With interest rates at historically low levels, CDs seem to fare well, only when compared to stashing one's cash under the mattress. Although bonds have been one of the bright spots during this spell, any rise in interest rates could prove devastating to bond investors.

Despite this somewhat gloomy environment, many charitably minded investors have found a haven in Charitable Gift Annuities — a means by which they can receive an attractive income for life, take an income tax deduction, and support their favorite charities. The Schepens Eye Research Institute's Gift Annuity program has been a boon to many of our longtime donors and friends during this volatile time.

How it works

A Charitable Gift Annuity is an agreement between you and The Schepens Eye Research Institute. You agree to give cash or stock to the Institute; we invest your gift and agree to pay you a fixed amount every year for the rest of your life. Married couples may choose payments for the lives of both spouses.

Best of all, the annuity payments stay the same regardless of market fluctuations. In addition to lifetime payments, you receive a tax deduction in the year of your gift.

Attractive annuity rates

The annuity rate you receive depends on your age at the time of the gift. The older you are, the higher your payments will be. The rates for two people of similar ages are slightly lower than they are for one person. Either way, you're likely to find that the rate available to you compares favorably to CDs, money markets, and savings accounts. Take a look at the sample rates below.

Single Person		Married Couple	
Age	Rate	Ages	Rate
65	6.3%	70/70	6.1%
70	6.7%	76/73	6.5%
75	7.3%	81/77	7.0%
80	8.3%	83/80	7.4%
85	9.7%	85/80	7.5%
90+	11.5%	90/85	8.6%

Find out if a gift annuity is right for you

A Charitable Gift Annuity offers many advantages. In addition to the financial and tax benefits, donating to Schepens through a Charitable Gift Annuity makes you eligible for membership in the William Wolff Society. This society recognizes our special friends who have displayed great foresight and generosity by providing for our future research endeavors in their financial and estate plans.

For more information about how you can benefit from a Charitable Gift Annuity, including a personalized gift illustration, please contact George Constant at (617) 912-2572, (877) 724-3736 (toll free), or at constant@vision.eri.harvard.edu.

New Trustees

George Bell

George Bell is the President and CEO of Upromise, a Boston-based early-stage company that aims to make college affordable for every family in America through a free service that brings together a unique coalition of loyalty partners, grocery partners, and a tax-advantaged college savings plan. The company hopes to help solve the crisis of college funding in America.

From 1996–2001, Bell was President and CEO of Excite, one of the Web's first search engines. At his arrival, the company had 22 employees and no revenue. In 1999, Bell oversaw the sale of a profitable Excite to @Home for $7B — at the time, the largest transaction in the history of the Internet. He then became Chairman and CEO of Excite@Home. At its peak, the company had a market capitalization of $46B and employed 3,000 people in 18 offices around the world.

During these years, Bell also chaired California Governor Pete Wilson's Committee on Internet Privacy and Commerce and served on various Internet trade boards.

From 1991–1995, Bell was Senior Vice President at Times Mirror Magazines, acquired by AOL/TW in 2001. At various times, as Group Publisher, he held operating responsibility for *Field & Stream, SKI, Skiing, Trans World SNOWboarding, Salt Water Sportsman* and *Yachting* magazines, as well as the company's multimedia efforts. Bell was instrumental in the 1995 launch of the Outdoor Life Network, a special interest cable channel that now reaches 40 million homes.

Prior to joining Times Mirror Magazines, Bell was a producer and writer of conservation, culture, and adventure documentaries for ABC, CBS, National Geographic, and the Discovery Channel. Altogether Bell has produced films in over 40 countries, from Mt. Everest to Africa's Ituri rain forest. Bell has won four national Emmy Awards.

Bell received his B.A. from Harvard in 1980 and was an All-American squash player. He joined the Schepens Board in 2002 as a member of the public relations committee, and also serves on the boards of the Massachusetts Software and Internet Council and the Advisory Board of Trust for Public Land. He lives in Brookline, Mass., with his wife and three children.

Renee Manger

Renee Manger has made it a priority to carry on her family's tradition of humanitarianism. She was introduced to that philosophy by her father, Ben Manger, who founded the B. L. Manger Foundation. Building on that legacy, Manger expanded her own charitable activities in the New York City and Connecticut areas.

Manger has balanced her charitable activities with her rewarding professional career, earning a B.S. degree at Boston University, School of Management, and subsequently working in the field of human resources for some of the country's leading financial and consumer institutions such as Chase, Priceline.com, and J. Walter Thompson.

Manger has extended the family tradition of philanthropy to include a special relationship with The Schepens Eye Research Institute and is honored to serve on the Board of Trustees as a member of the Public Relations Committee.

Victoria McCullough

Victoria McCullough is the owner of Chesapeake Petroleum, a family-founded business specializing in the distribution of private vehicle lubricants, chemicals, and equipment. The company's extraordinary success is attributed to a commitment to family tradition of service and quality.

McCullough is a graduate of Ohio State University and Cornell University, holding a bachelor of fine arts degree and a dual masters in engineering.

Almost 20 years ago her vision was jeopardized by ill-fitting contact lenses. Although her vision was corrected, she developed a greater appreciation of sight. Ms. McCullough joined The Schepens Board because of her belief that the power of sight is the greatest of gifts and that to join in contributions and efforts to preserve, protect, and restore that gift is a privilege.

McCullough's other commitments include The United AIDS Coalition, The American Institute of Aeronautics and Astronautics, The National Business Aviation Association, Inc., The National Defense Industrial Association, The Society of Women Engineers, Ducks Unlimited, Automotive Trade Association, United States Equestrian Team, American Grand Prix Association, and the Intercollegiate Equestrian Foundation.

McCullough resides in Palm Beach, Florida, where she participates in a myriad of activities such as showing horses, playing golf and tennis, shooting sports, sporting clays and upland game. Her family business has a history of supporting auto racing, and she has a passion for automobiles.

Ask a Schepens Scientist
continued from page 6

nal *Nature,* suggests that while some of these small complex aberrations can be detrimental to vision, other higher-order aberrations may exist for a good reason. So, before we go about eliminating them through a new "cookie cutter" approach to laser surgery, we should understand their roles better.

In our study, we found that some of these complicated individual flaws apparently help individuals see better across a range of incoming wavelengths of light and can, in fact, improve the quality of the image that the brain ultimately receives.

The take-home message of our research is that to refine LASIK surgery for the future, we must have a better understanding of both the simple and the more complex flaws (or perhaps individual differences is a better description). We need to know which flaws harm vision and should be corrected, and which actually help vision and should be left alone or worked around. Taking all this into account in each individual will someday help us create a truly customized cornea that could give an individual the best vision they are capable of.

To assist in that mission, our laboratory at The Schepens Eye Research Institute is continuing its exploration of the intricate optical systems of the eye.

Clinically Speaking
continued from page 7

while others help the fluid leave the eye more efficiently. Laser surgery can stretch open the small channels within the drains, called the trabecular meshwork, but its effects can be short-lived. With conventional surgery, an opening can be created between the anterior chamber and the sclera (the wall of the eye) to allow fluid to exit the eye through a different route. In a new approach to treatment, researchers are using drugs and growth factors to protect ganglion cells from assault and self-destruction. When these treatments fail, retinal ganglion cells die, and these cells are not able to regenerate themselves.

The Promise of Retinal Transplantation

Both AMD and glaucoma are blinding diseases. Current treatments are focused on damage control — damage that has already destroyed precious tissues. The promise of retinal transplantation is damage repair, regeneration of these irreplaceable tissues, and the restoration of vision. (See Restoring the Light: the Promise of Retinal Transplantation and Stem Cell Research on page 3.)

Schepens Welcomes Back an Old Friend

This past December, Dick Donovan returned to the Development Staff at the Institute as the Director of Principal Giving. Donovan first came to the Institute in 1994 from Harvard Medical School. When asked to describe his current role at the Institute, his response was simple: "I raise resources for the best science in the world dedicated to curing blinding eye diseases."

Donovan left two-and-a-half years ago to become the Vice President for Advancement at Emmanuel College in Boston, Mass. Upon his return, Donovan was pleased to see the growth of scientific excellence and the standing of the Institute within the vision research community. Donovan has settled into his new role and has already begun to reengage old friends and create strategic alliances to strengthen the expanding research programs.

Donovan's impressive development career started almost 20 years ago. Among his many accomplishments are a B.A. degree at St. Anselm's College, an M.Ed. from the University of New Hampshire, and an Ed.D. in Educational Leadership from Vanderbilt University.

"The Schepens Eye Research Institute is an organization that one is proud to be associated with. I continue to be impressed with the deep, long-lasting relationships with our donors that began years ago and have continued with our current board of directors, president, and staff," said Donovan.

Dick Donovan

Dick can be reached in the Development Office by calling (617) 912-2542.

Sunglasses: Fashion or Necessity?

Spring has arrived, summer is on its way, and the parade of fashion sunglasses has begun. But sunglasses are not just a warm-weather fad or accessory, they are also necessary for eye health, according to vision experts at The Schepens Eye Research Institute.

Although your eyes have built-in defenses against the sun — squinting, pupil constriction, and filtering by the cornea and the eye's natural lens, sunglasses add comfort and an additional layer of protection against harmful sunlight.

"It is very important to shield your eyes from ultraviolet light," says Kameran Lashkari, M.D., assistant clinical scientist at The Schepens Eye Research Institute. "Wearing sunglasses is always a good idea, but it is essential where there's increased ultraviolet exposure such as on ski slopes or beaches on a bright summer day."

Studies show prolonged exposure to invisible UV and visible blue-UV from the sun may contribute to eye disorders such as cataracts in which the normally clear lens of the eye becomes cloudy, and macular degeneration, a leading cause of blindness.

Most sunglasses now provide UV protection, according to Lashkari, who still suggests carefully checking the labels for "Blocks 100% UV-A and UV-B."

Prescription eyeglass wearers can protect themselves by having an optician apply a UV protective coating to their glasses. Polycarbonate or safety lenses offer complete UV protection in addition to defending your eyes from sports injuries. Polycarbonate glasses are also indicated for individuals who only have vision in one eye.

"After cataract surgery, most implants have UV absorption," says Lashkari. But those who have just undergone cataract surgery should wear wrap-around sunglasses for protection he notes. These are usually given out at the time of surgery.

In addition to wearing sunglasses, Lashkari suggests wearing a wide-brimmed hat to cut glare and add style.

Friends of The Schepens

The New York Friends will host the "Vision for the Future" Luncheon on Wednesday, May 14 at the Harvard Club. Featured speakers are J. Wayne Streilein, M.D.; Ilene Gipson, Ph.D.; and patient liaison Richard Godfrey.

The symposium content will highlight current research on dry eye syndromes and the outreach efforts of the newly formed Women's Eye Health Task Force.

If you are interested in attending, please contact the Development Office at 1-877-724-3736.

The Schepens Eye Research Institute provided vision research education and information to over 4,000 people throughout Florida during its 10th Annual Eye and Vision Research Symposia. Once again this event was open and free to the public, offered as a community service as the result of the generosity of the Institute's friends and supporters.

The symposia series took place on both coasts of Florida, including Boca Raton, Vero Beach, West Palm Beach, Sarasota, Naples, and Ft. Myers. Presentations focused on research progress and current efforts on macular degeneration, the promise of retinal transplantation, and women's eye health.

The following supporters presented in conjunction with scientists and staff from the Institute: Florida Eye Institute, Del Ray Eye Associates, the Sarasota Retina Institute, and the Retina Consultants of Southwest Florida.

J. Wayne Streilein, Judy Grubman, and Charles Castor.

Dr. Layne Nisenbaum, left, and Etonella Christleib.

Judy Grubman, a member of the "Friends of the Schepens," hosted a reception honoring J. Wayne Streilein, M.D., prior to the West Palm Beach symposium.

Doug Regan, J. Wayne Streilein, and Tom Oliveri.

From left to right: Hermé de Wyman Miro, symposium chair; Victoria McCullough, kaleidoscope chair; Judith Grubman, reception chair; Cheryl Gowdy, Palm Beach Friends chair; and Kathryn Vecellio, Florida Friends chair.

Preventing Blindness in Women

The Institute joins forces with top vision experts to form task force

Two-thirds of all legally blind Americans are women. Concerned by this statistic, a group of scientists at The Schepens Eye Research Institute has joined forces with top vision experts throughout the U.S. to form the Women's Eye Health Task Force (WEHTF). Its mission — to increase public awareness of the common eye diseases affecting women and, through education, improve eye health for all Americans.

"As scientists, we don't yet know all the factors involved in these high rates of eye disease in women," says Ilene Gipson, Ph.D., senior scientist at The Schepens Eye Research Institute and chair of the newly formed task force. "Certainly greater longevity among women accounts for part of the problem. Other factors may include nutrition and environment. Although we don't have all the answers, we do know that many eye diseases are preventable and treatable. This is the message we want to get out to women," she says.

Although its message is for women of all ages, the Task Force is particularly interested in reaching older women and women who have young children, not only to educate these women but also to have an impact on the next generation. By targeting women in general, the Task Force also hopes to reach the entire family, since women are the main health care advocates for their husbands and aging parents.

The message, says Gipson, is clear. To protect their vision and that of their families, women may need to make lifestyle changes. First, they must take charge of serious risk factors under their control, such as smoking, which can have a serious impact on eye health. Women must also learn about and be aware of early symptoms of eye diseases. Finally, women should get regular age-appropriate eye examinations for themselves and their families.

From left to right: Hermé de Wyman Miro, Dr. J. Wayne Streilein, and Dr. Ilene Gipson.

The Task Force, which held its first meeting at the Association for Research in Vision and Ophthalmology meeting last spring, kicked off its multifaceted education campaign in November, receiving national press coverage of the issue. The group is also developing eye-health checklists and educational materials for physicians' offices, public service announcements, talks for women's groups, articles in magazines, conferences and symposia, updates for eye specialists, and an informational Web site for the public and professionals. Please visit the site at http://www.eri.harvard.edu/wehtf/.

Restoring the Light
continued from page 5

One barrier is integration. Stem cells, Young has found, automatically migrate to the injured area of the retina. "They seem to have an innate sense of where they are needed most," says Young. Another barrier they overcome is supply. Stem cells are abundant, able to reproduce themselves both in the body and in cultures, he notes. Finally, stem cells appear to be invisible to the immune system, according to Young. "Although this does not mean they can't be rejected, it does mean they have an initial advantage over other tissues," he says.

Young's first experiments were with brain stem cells from young rats trans-

planted into other rats with damaged retinas. In these experiments, the stem cells migrated to the recipient's damaged retina, changed into mature neural cells, and appeared to wire themselves into the optic nerve. Although it is not known whether vision was improved, these results were encouraging.

Next, Young and his colleagues found retinal stem cells in mice that hold more promise. He injected retinal stem cells from one mouse into the eyes of another. The grafted stem cells migrated to where they were needed and developed into retinal cells. Preliminary research to test whether the transplanted cells actually function as retinal cells and improve vision is now underway, with some initial positive results.

Young is now beginning to work with pigs, whose eyes are more similar in size and structure to human eyes. And, he is developing an organized way of delivering the stem cells to the larger eye. This involves the use of tiny scaffolds, made of a biodegradable material called polymers. After using the polymer scaffolds to grow the stem cells into an organized layer of retinal tissue in a culture, the scaffold/stem cell composite is implanted in the eye.

Pigs, according to Young, will bring the exploration closer to human beings. In fact, he believes that human stem cells could also be transplanted into pigs to see if they regenerate themselves in that environment.

Making the final connection — repairing the wiring

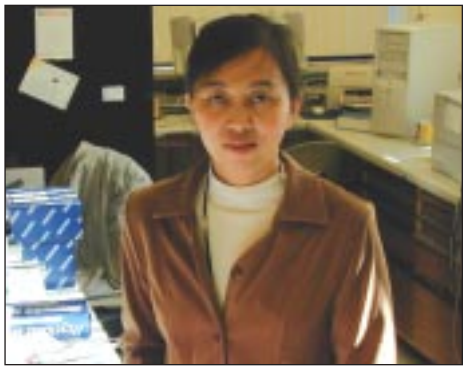
Understanding how transplanted cells make their connections to the optic nerve so that vision is restored is the focus of Dong Feng Chen, Ph.D., assistant scientist at The Schepens Eye Research Institute.

Chen's research has already shed light on the optic nerve itself. She has discovered a gene that is responsible for optic nerve growth and regeneration, and which turns off after the nerve is fully formed. She has also successfully turned the gene back on in animal models, causing nerve growth to resume.

Chen is now in the process of applying her optic nerve insights to the regeneration, and growth of the retina ganglion cells, which lose their connections (axons) to the optic nerve during retinal disease, and, when transplanted, have to grow new axons to wire up to the optic nerve. Chen hopes her optic nerve model will help unlock the genetic barriers to growing these vital new connections.

In addition to the genetic barriers to growing this nerve tissue, Chen has found several other barriers or inhibitors in the tissue surrounding the retina and is working to eliminate those inhibitors.

"If we figure out all the pieces of this puzzle, we can develop the drugs to turn on the right gene, turn off the inhibitors and the barriers, and promote nerve cell replacement therapy," says Chen.



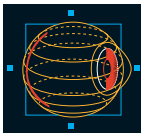
Dong Feng Chen, Ph.D.

The future

"Though the puzzle is not complete, there is now great room for optimism," says Young. "All the progress of the last decade — the human genome project, insight into the molecular workings of the cell, and the breakthroughs we are making here at Schepens — is giving me hope that the cures for retinal diseases will be here in the not too distant future," he says.

These are just a few of the scientists at Schepens Eye Research Institute devoted to finding cures for retinal and other devastating diseases of the eye. Look for others in future issues of Sightings.

The Schepens Eye Research Institute's Web site will soon have a new look. Please visit **www.eri.harvard.edu** in the next few months to view the changes.



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A Father and Daughter on a Mission for Vision

Subhead

Each year, low vision expert Eli Peli, OD, a sSenior sScientist at Schepens Eye Research Institute, and a Professor of Ophthalmology at Harvard Medical School travels to Costa Rica to provide free optometric care along with a group of other vision specialists and volunteers. This year 's trip had special meaning for Peli. His 17-year old daughter, Dana, decided to join him on this medical mission.

"It was a wonderful learning experience for both of us," says Peli.
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Contact: Patti Jacobs 617-912-2544

Newton Father and Daughter Spent Week on Medical Mission in Costa Rica

Boston, MA – "She tried on the glasses and looked up at Patti, the organizer of our trip, and said 'you are really beautiful.' This kind of response was what was so wonderful and rewarding for me," says seventeen-year-old Dana Peli. Dana was describing the excitement of a ninety-year-old Costa Rican woman who could see again thanks to the generosity of a group of optometrists and other volunteers who recently brought vision expertise, a supply of donated glasses and their own big hearts to Costa Rica. A Newton resident and senior at Newton South High School, Dana decided to accompany her father, Dr. Eli Peli, a Professor of Ophthalmology at Harvard Medical School and Senior Scientist at the Schepens Eye Research Institute, on this medical mission. Dr. Peli, who tries to make the trip to Costa Rica each year, wanted his daughter to have this special experience.

The father-daughter team spent a week week last fall in this Central American in Costa Rica this fall working together, examining hundreds ohundreds of f people, many of whom had never had an eye examination before.

The Pelis were part of a group called VOSH (Volunteer Optometric Service to Humanity), a national organization with local chapters which that joins forces with Lions Clubs in the US and in host countries to make these trips possible. For this trip, Dr. Peli and Dana connected with the VOSH and Lions Club from Alabama.

Says Dr. Peli, "It was really wonderful for me to have my daughter along. She learned a lot, andI it was nice seeing how well Dana she interacted with the other professionals, the people we were treating, and the local teenagers who served as our interpreters. She made some great friends."

Dana was very much part of the team. She learned to test visual acuity and helped sort through the hundreds of glasses donated for the trip by Lions Clubs from throughout the US. "It was really pretty easy to learn how to test visual acuity, but the test itself is more complex than it seems on the other side of the examination," says Dana. Dana, along with two other volunteers tested nearly eight hundred patients that week in Costa Rica.

According to Dr. Peli, in addition to examining eight hundred patients, the medical volunteers provided five hundred pairs of glasses and referred numerous patients to Costa Rican specialists. In several instances, Dr. Peli himself diagnosed signs of high blood pressure in patients' eyes and made sure they were referred to local physicians to obtain care and medications once the high after blood pressure was verified by the team's nurses that joint the team as wellnurses.

Patients ranged in age from four to 100. It was the oldest and the youngest that really got to Dana. "There was a little adorable four-year-old girl who came in wearing a pair of glasses that were totally wrong for her. There was no way she could be seeing anything. When we gave her her new pair that actually helped her see only a little bit better, her little face just lit up. That was exciting," says Dana.

"This trip was the most amazing experience I have ever had, and I want to go back again next year," adds Dana, who along with the rest of the volunteers was awarded a special certificate from the Lions Club of Playas del Coco village for her efforts in Costa Rica.

After spending four days conducting eye examinations, the entire group traveled around Costa Rica, andAfter the work was done the Pelis toured the area, and DanaDana, had a special treat. She spent a day joining with one of her new friends at a Costa Rican High high School. "It was so interesting going to high school in another country."

The Pelis hope to go together next year on another VOSH mission, and Dana plans a trip on her own after graduation to see her friends, improve her Spanish, and learn more about the country.

Pictures from the trip are available on Dr. Peli's website: http://www.eri.harvard.edu/faculty/peli/index.html. Go to the "People" section of the site. A link to the VOSH organization is: http://www.vosh.org/home46.html.

Schepens Eye Research Institute is an affiliate of Harvard Medical School and the largest independent eye research Institute in the world.