

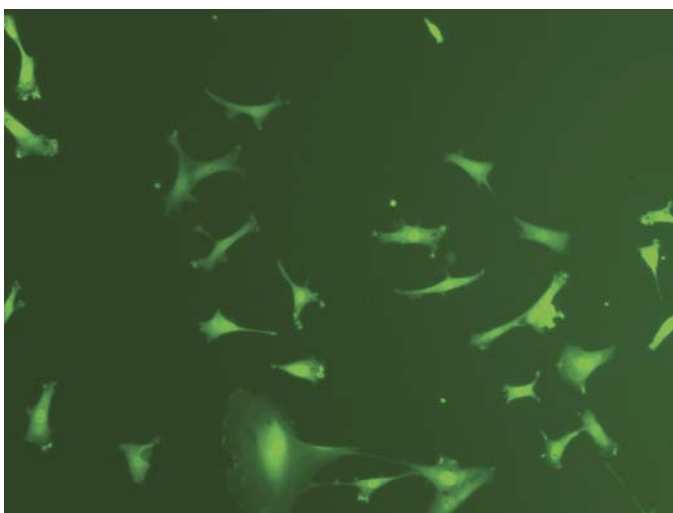
# CURE GLAUCOMA



THE WILMER OPHTHALMOLOGICAL INSTITUTE GLAUCOMA SERVICE

Winter 2006

## New Nerve Cells for Glaucoma Eyes



Stem cell research has in one form or another begun in many areas of medicine. The eye is a particularly interesting place in which the placement of new nerve cells could potentially restore sight lost through disease. For glaucoma patients, it is often heard that sight cannot be replaced once it's gone, so it is necessary to protect what is still there.

The future may hold hope that we will be able to improve sight in glaucoma eyes by transplanting cells that would reconnect the tissues lost from the disease. Drs. Quigley and Zack, working with colleagues in the laboratory, investigated a number of possible sources of new cells. Stem cells, or embryonic germ line cells, come from fetuses, and have features that make them less likely to become new eye cells. In addition, there are ethical issues and limitations related to the use of such stem cells.

Instead, Dr. Quigley has developed methods first suggested by researchers in Canada. He has found that new cells, called progenitor cells, are present in the eye of the person who needs them. This avoids the problem of where to find cells. In fact, adult eyes are now known to have cells that can be transplanted. The work is still in early stages in the laboratory. Wilmer researchers are developing a method to direct the new cells to become the type that is needed to replace those cells lost from glaucoma.

## American Glaucoma Society Clinician Scientist Award

Dr. Sameer Ahmad, Assistant Professor of Ophthalmology and the newest member of the Glaucoma Division received the prestigious Clinician Scientist Award from the American Glaucoma Society for his proposal entitled, "Glaucoma in the Himalayas: A clinic-based survey in Kashmir, India". The award was announced on March 3rd at the annual American Glaucoma Society meeting held in Charleston, South Carolina.

During recent travel to India, Dr. Ahmad visited various ophthalmology clinics in Srinagar, the capital of Kashmir. Through his meetings with

local ophthalmologists, he found a high reported prevalence of pseudoexfoliation glaucoma among Kashmiri natives that has not been previously reported in the Western literature. Pseudoexfoliation (PEX) is the most common identifiable cause of secondary open angle glaucoma worldwide. In addition to the research benefits of higher rates of familial diseases, research dollars may be used more productively in India due to lower manpower and infrastructure costs.

The specific aims of his study are 1) to identify potential open angle glaucoma (OAG) and

*Continued on page 2*

## Dr. David S. Friedman Chairs Angle Closure Glaucoma Consensus Panel

Dr. Friedman led a group of nearly 100 glaucoma specialists from across the globe in developing a document that arrives at consensus statements regarding the definitions, mechanisms, screening, and treatment for angle closure glaucoma. The document also makes important recommendations about areas of research that require attention. The consensus panel used the interconnectivity of the World Wide Web to hash out initial drafts on the internet. The group then convened this May during one of the major eye disease research conferences to finalize the report. The final document will be published this month in book form and the key consensus statements will be available to all at the website of the Association of International Glaucoma Societies.

Angle closure glaucoma is responsible for nearly half the blindness caused by glaucoma around the world. It is more common in Asian populations, but affects all groups. Many cases of angle closure glaucoma could be prevented with laser surgery. More research is needed to determine which individuals are most likely to benefit from this procedure, and to improve the effectiveness of current screening procedures. New devices have been developed that appear promising, and Dr. Friedman and colleagues have been studying them in Singapore and south China.

## Clinician Scientist Award

*Continued from page 1*



**Dr. Tejit Singh, Professor of Ophthalmology, Government Medical College, Srinagar, Kashmir with Dr. Sameer Ahmad, Assistant Professor**

pseudoexfoliation (PEX) patients that can be randomized to various treatment protocols such as medication, laser, or filtration surgery and to prospectively follow the response of these interventions; 2) to develop a grading scheme for patients with PEX to see if specific clinical findings correlate with risk of glaucoma or disease severity; and 3) to identify potential families with OAG and PEX for future genetic studies.

The American Glaucoma Society started the Clinician Scientist research fellowships in 1997 to encourage the development of new investigators in glaucoma research with the hope of seeing these start-up grants lead to projects that may merit future funding by larger agencies such as the National Eye Institute.

## Wilmer Glaucoma Physicians

### Harry Quigley, MD

A. Edward Maumenee Professor of Ophthalmology and Director of the Glaucoma Service and the Dana Center for Preventive Ophthalmology

### Sameer Ahmad, MD

Assistant Professor

### David Friedman, MD, MPH

Associate Professor

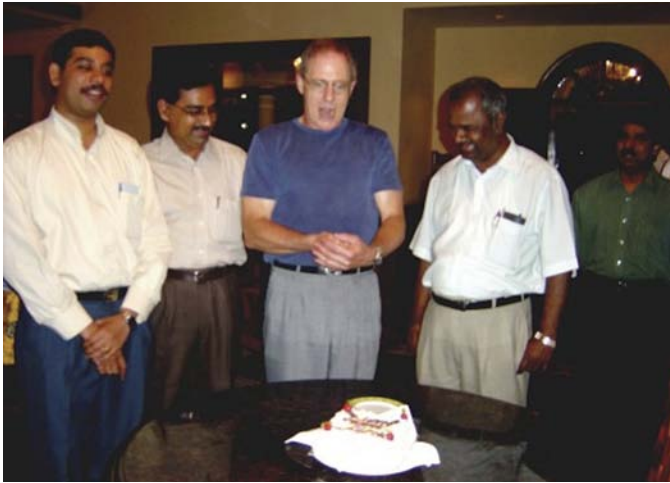
### Henry Jampel, MD, MHS

Odd Fellows Professor of Ophthalmology

### Donald Zack, MD, PhD

The Guerrieri Family Professor in Genetic Engineering and Molecular Ophthalmology

## Study of Glaucoma Treatment in India Completed



**Dr. Quigley celebrates a birthday with colleagues in India.**

Drs. Friedman and Quigley have worked for nearly five years with coworkers in India to study how we can best treat the many in India with glaucoma. India is a country with a newly expanding economy and health care system, with both urban and rural segments. With well over one billion citizens, India has the third largest number of glaucoma patients, after China and Europe/USA. During the next 15 years, India's glaucoma problem will grow faster than in any other part of the world, according to a study published by Dr. Quigley in the British Journal of Ophthalmology last year.

Since there is such diversity in India, with highly urbanized areas and poor agrarian zones, it has not been clear what might be the best treatment to offer persons there. Should daily

eyedrop treatment be introduced initially as most often is done in the U.S.? Will the eyedrops be administered as prescribed? Will the eyedrops work as effectively in the Indian population?

Such a study was carried out in the U.S., led by Dr. Jampel, and is described in this newsletter. For Americans, initial surgery and initial eyedrops were both equally effective in preventing progressive loss of vision from glaucoma. The data from the Indian study is equally encouraging.

It was a concern that persons with little experience in health care and traditional medicines would not be able to take and continue eyedrop treatment. Likewise, patients might not agree to the offer of surgery for a disease that does not often cause discernable injury from the patient's point of view. In order to reduce the question to what might work under ideal conditions, medicines and surgery were given free for the study.

Initial results suggest that patients in India take and continue their medications, and have reasonable responses to surgery in newly diagnosed glaucoma. Eye pressures fell in both groups and side effects and complications were no greater than expected. We hope to follow up with these persons for longer periods of time if funding can be obtained for the study. The cost of the work has been largely supported by Wilmer Glaucoma donations. Thanks to those of you who have contributed to this worthy effort.

## Older Persons have High Rates of Glaucoma

As principal investigator of a National Eye Institute funded study, Dr. Friedman examined persons 74 years of age and older living on the Eastern Shore of Maryland. Subjects were identified from the community (not the clinic), so the estimates of glaucoma rates are felt to be unbiased. He found that nearly 10% of white persons and 20% of black persons over the age of 75 had glaucoma. Previous studies had not enrolled a sufficient number of black and white people in this age range to make accurate estimates.

The findings point to a need for active screening for glaucoma in these older age ranges. Dr. Friedman is also assessing how glaucoma affects motility and independence in this population. All subjects had to walk a course, climb stairs, and walk a straight line. Preliminary results indicate that persons with glaucoma in both eyes had substantial decreases in walking speed through the course and reported greater difficulty with daily tasks.

## Helping Doctors to Make the Right Decisions

The Glaucoma Service is working with a brilliant new Wilmer faculty member, Dr. Michael Boland, to develop methods that will improve care for our patients. In Boland's program, all the available information on how glaucoma develops, what influences it, and how medicines work are put into computer databases, and helpful summary values are produced. These numbers are referred to as "risk calculations", and work somewhat as do prediction approaches used by insurance companies.

For example, imagine you are a suspect for glaucoma, but don't have it. If the new risk calculation predicted that your risk of developing glaucoma was 12% (one chance in eight) over the next five years, would you want to use eye drops every day to decrease that risk? If you said yes, how low would your risk need to be before you would not want to use eye drops? If you said no, how high would your risk need to be before you would want to start treatment?

These questions are the type of research that Dr. Boland is doing so that doctors can better inform patients about the true risks and benefits of treatment for early glaucoma. In subsequent work, he will study choices made by those with established glaucoma who are already being treated.

Historically, we have had to rely on clinical judgments made by experienced doctors who care for large groups of people. This is not an unbiased approach for scientific calculations. As more and more research is done on diseases like glaucoma, we are better able to make predictions in a scientific way. This allows a personal risk estimate to be calculated for each patient.

Using the results of large research clinical trials, we are working toward a goal of giving a specific estimate of risk to each patient based on their unique situation. Since this information is individualized to each patient, the doctor and patient are better able to work together to decide whether the patient should undergo treatment, and if so, which treatment is most appropriate.

## Computer Games for Doctors

With internet interactions taking a front row seat in all our lives, Dr. Quigley and colleague Dana Blumberg, M.D. (now practicing in Washington, DC) have designed initial teaching material for doctors about glaucoma that is somewhat like a computer game. It is "interactive;" the doctor must ask for information and give answers. It is very practical, and in many ways the system almost acts like a virtual patient.

Part of the motivation for developing this modular, computer-based text is to test whether the method teaches physicians new things that they don't now know about how to take care of glaucoma patients. When we read books, we can "doze off" and miss the main points. It is rare that someone tests the actual skills of the physician in real life settings. This project hopes to do that, for the benefit of doctors and patients.

During the learning process, sets of questions are presented that assess how well the doctor knew the material at the start. Then, after passing through the various stages of learning, a subsequent test is given to see how much improvement there has been. In this way, we can test the system itself to see if it truly teaches effectively.

It is quite possible that such an approach would be so successful that it would partially replace heavy textbooks and lectures as a method by which doctors learn. More likely, our Skills Transfer System will become an additional approach that some doctors will find useful.

We wish to thank the many patients who have (anonymously, but with permission) had portions of their eyes video-taped for this new teaching venture. As always, there are many ways for patients to help with our research efforts. In this case, no one but a glaucoma patient can donate anything that looks like an eye with glaucoma for our photography. Thanks again!



## Henry D. Jampel, M.D., M.H.S. Is Appointed Odd Fellows Professor of Ophthalmology



On May 6th, in a festive ceremony in Hurd Hall at Johns Hopkins Hospital, Dr. Jampel, Professor of Ophthalmology, and a member of the Glaucoma Division for the past 18 years, was installed as the Odd Fellows Professor of Ophthalmology at the Wilmer Institute.

Receiving an endowed chair is one of the highest academic honors that can be bestowed upon a faculty member. Dr. Jampel becomes the second member of the Glaucoma division to hold an endowed professorship, joining division director Harry Quigley, M.D., the A. Edward Maumenee Professor of Ophthalmology.

Endowed chairs provide a stream of revenue that allow faculty the opportunity to pursue research interests that they might otherwise not have the time or resources to explore. This endowed chair was started more than 40 years ago with a generous donation to the Wilmer Institute by the Odd Fellows and Rebekahs, an organization that for more than 200 years has been dedicated to the betterment of humankind.

In his speech accepting the chair, Dr. Jampel stated, "I am thrilled to be named the third Odd Fellows Professor of Ophthalmology at the Wilmer Eye Institute. This endowed chair is a marriage of two great missions, that of the Odd Fellows to give aid to those in need and that of the Wilmer Eye Institute to reduce suffering from blindness through leadership and excellence in research, education, and patient care. I will work my hardest to be a worthy recipient of this gift from the Odd Fellows to Wilmer and Johns Hopkins."

## Dr. Ahmad to Head Wilmer Pediatric Glaucoma Center

There have been many recent studies looking at adult glaucoma that have improved our understanding on glaucoma management in this population. However, there are virtually no large studies looking at childhood glaucoma. About one in a thousand children has a form of glaucoma developing early in life.

There have been numerous classification systems proposed for childhood glaucoma, but the lack of a consistent way to group and study them complicates the research on these diseases in children. As a result there are no clear standard guidelines for treatment.

In other childhood eye diseases, there have been significant advances in diagnosis and management through multi-center national and international collaborative efforts. Dr. Sameer Ahmad of the Wilmer Glaucoma Service will be spearheading efforts to formalize the Wilmer Pediatric Glaucoma Center with a major aim to initiate similar multi-center collaborations for the study of pediatric glaucoma. A team of national and international experts in the field will convene at Wilmer in the future to discuss the establishment of classification standards and future prospective studies for the various pediatric glaucomas.

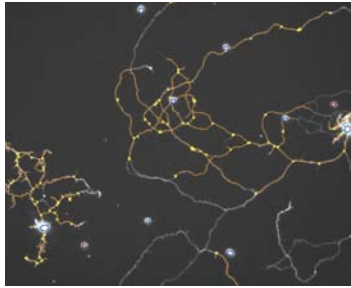
The Wilmer Pediatric Glaucoma Center will serve as the major care center for childhood glaucomas in the region and provide 24/7 access for easy referrals by pediatricians and ophthalmologists in the community. While we have cared for children with glaucoma for many years, this new initiative will mean that the most difficult problems in this area will have a central place for evaluation.

## Discovery of Molecules that Promote Retinal Ganglion Cell Survival

The retina is the part of the eye that detects light — it is like the film in a camera. Retinal ganglion cells (RGCs) are the nerve cells of the retina that transmit visual information from the eye to the brain. RGCs can be thought of as the telephone system (or perhaps the internet) of the body that tells the brain what the eye is “seeing.” Fibers, known as axons, from these cells form the optic nerve. It is damage and death of RGCs that causes visual loss and blindness in glaucoma. In advanced glaucoma, although the retina can still sense light, the patient cannot see because the phone line is dead.

One of the major goals of glaucoma therapy is to prevent, or at least reduce, further damage and death of RGCs. The traditional way of doing this is to lower eye pressure, by eye drops, laser treatment, or surgery. Although such treatment is often effective, sometimes it is not possible to safely lower eye pressure, and sometimes damage continues even after eye pressure is reduced. Therefore, scientists are trying to discover other and hopefully more powerful approaches for preserving and protecting RGCs. Such approaches are often referred to as “neuroprotection.”

Researchers at Wilmer are leaders in this effort to develop novel neuroprotective treatment strategies. In one set of studies, Donald J. Zack, M.D.,



Ph.D., Guerrieri Professor of Genetic Engineering and Molecular Ophthalmology, Harry A. Quigley, M.D., A. Edward. Maumenee Professor of Ophthalmology, and the members of their labs are working together to discover small molecules (chemicals) that can prolong the survival of RGCs. They are doing this by growing RGCs in special culture plates. A photograph of these cells is shown at left.

The cells grow “in culture” for several days but then die. In order to identify chemicals with neuroprotective activity, they add test molecules to the culture plates and measure survival of RGCs. This is done with a special robotic microscope. If the cells live longer, or function better, with the chemical than without the chemical, then the chemical tested is a potential neuroprotective agent.

Using this state-of-the-art high throughput approach, over 2,500 molecules have already been tested, and several with interesting activity have been identified. Screening is ongoing, with the goal of eventually testing 100,000 molecules. The positive “hits” are being retested and further analyzed. The availability of additional funding will make possible the acceleration and expansion of this screening program. Hopefully, one of the molecules discovered by this program will some day lead to a new and more effective medicine for the treatment of glaucoma.

## Adherence to Therapy Can Be Monitored

Recent work by Drs. Friedman and Quigley has demonstrated that many patients fail to take their eyedrops as prescribed. It is estimated that on average about 70% of prescribed doses are taken, with some taking more and others taking less. This is similar to what has been seen with other chronic diseases such as high cholesterol and high blood pressure. If patients do not take eyedrops as prescribed, the eye pressure will stay higher than needed, and glaucoma is more likely to get worse.

One company has developed a device that can keep track of when eyedrops are adminis-

tered, and Dr. Friedman confirmed that the device is accurate. He called 20 patients twice a day and waited while they used the device and then compared the results from the device to his own diary and found that the device records virtually all doses. These results were recently published in the American Journal of Ophthalmology. We are now recruiting subjects in a study to look at patterns of using drops by patients and hope to design approaches to improving adherence to medication recommendations.

## Medicare Prescription Drug Plan

Many of you, our patients, have Medicare insurance coverage, and those of you with Medicare and no other health insurance have been painfully aware of the costs of our commonly prescribed eye drops for glaucoma. With the enactment of Medicare Part D, or the Medicare Prescription Drug Plan, many of you have surely grappled with whether or not to sign up for the plan, and if so, which plan to sign up for.

Now is the time to start thinking about selecting (or not selecting) a plan for 2007. In making a decision, there are a few points that you should keep in mind. First, there are many plans to choose from. Some may offer your specific glaucoma medications and some may not. Keep in mind that if you and your doctor change eye drops, the new eye drop may not be covered by your particular plan. Second, although glaucoma medications are expensive, if eye drops are the only prescription medications that you use, it is unlikely that enrollment in the Medicare Prescription Drug Plan will make financial sense. This is because of the monthly premiums, deductibles, and co-pays that are part of this insurance plan. However, if you are taking two or more medications for your general health, in addition to eye drops for glaucoma, it is likely that participation in a program will save you money. Finally, you can get assistance with your questions by contacting the Medicare Prescription Drug Plan from Medicare at [www.medicare.gov](http://www.medicare.gov) or by calling 1-800-MEDICARE.

Your glaucoma doctors here at Wilmer are dedicated to removing the barriers that make it difficult for you to fill your prescriptions and use your medications. We want to know if paying for your eye drops is a problem for you, so please don't hesitate to discuss it with us.

## Update on the Collaborative Initial Glaucoma Treatment Study

Clinical research is an important aspect of what we do on the Glaucoma Service. Many of our patients continue to participate in the Ocular Hypertensive Treatment Study, which has proven once and for all that lowering eye pressure can prevent the development of glaucoma. Many others participated in the Collaborative Initial Glaucoma Treatment Study (CIGTS), in which patients with glaucoma, who had never been treated, were either initially treated with eye drops or operating room surgery. The CIGTS was completed in 2004, and it is time to review some of its more important findings.

- 1) The patients who had surgery did well. In fact, among the 300 patients who had surgery, there were no instances where the surgery itself caused permanent loss of vision. In this group of patients, surgery was safe.
- 2) Over the course of five years, in both the medicine and surgery groups, there was on average almost no vision loss. The CIGTS protocol required dramatic lowering of eye pressure. The inference is that if the eye pressure is dramatically lowered in glaucoma patients, most of the time disease progression can be halted.
- 3) Assessment of quality-of-life was an important aspect of the CIGTS. Patients had an extensive telephone interview twice a year. For the first two years of the study, surgery patients had more complaints than medicine patients, but after two years there was no difference in the quality of life reported among the surgery and the medicine groups.

The take home message from the CIGTS at this point is that when either surgery or medicines successfully lower eye pressure substantially, most patients don't lose vision from glaucoma. Surgery for glaucoma should not be considered a "last resort" and there is no reason to feel that just because your doctor is discussing surgery with you that your situation is desperate.

## Genetics and Glaucoma

Glaucoma is a disease in which there is a significant genetic component. This means that someone who has a family history of glaucoma (brothers, sisters, parents, aunts, uncles or other relatives with glaucoma) is more likely to develop glaucoma, and to have more progressive glaucoma, than someone without a family history. The molecular basis for this increased susceptibility to glaucoma lies in the genes we inherit from our parents. Humans have about 30,000 genes, and for the vast majority of them we have two copies, one from mom and one from dad. Genes are made of DNA, and they contain the information (the blueprint) that makes us who we are. However, genes are not the whole story — the environment is also important. In fact, interactions between genes and the environment are not only very important, they are also very complex.

Glaucoma is almost certainly the result of interactions between our genes and our environment. Understanding the genetic and environmental factors that determine if a person develops glaucoma would likely aid in the development of new diagnostic and treatment approaches for glaucoma. Unfortunately, however, very little is known about these factors. Research

underway at the Wilmer Glaucoma Service is trying to change this situation. This work is a partnership between our faculty and our patients. We are asking our patients to help in two ways. For those patients with siblings, parents, or children with glaucoma, or patients who had glaucoma start when they were 55 years of age or younger, we would like to invite you to participate in the Wilmer Glaucoma Genetics Study. This involves giving a sample of blood (for extraction of DNA), answering some questions about family and environmental factors, and allowing us to use your medical record for analysis. The genetic studies we perform on patients' DNA are very sophisticated - we use special microarray chips that can measure one million different parts of one's DNA at the same time. Unfortunately, these chips, and their analysis are very expensive. Your financial support would help us accomplish our research goals. By working together to learn more about the genetic and environmental causes of glaucoma, we will be able to develop novel and more effective strategies for glaucoma diagnosis, prevention, and treatment.

If you would like to participate in this study please contact Vanessa Kellner at (410) 502-5732 for more information.

---

## CURE GLAUCOMA

**Cure Glaucoma** is an initiative to advance glaucoma research leading to improvements in eye care through philanthropic support. We are grateful for past gifts and ask others to consider including Cure Glaucoma in their charitable gift planning. Gifts to Cure Glaucoma can be made in many ways, including an outright gift of cash or stock, a pledge payable over a period of years, a life-income gift, such as a charitable remainder trust or annuity, or a bequest.

All gifts should be made payable to Johns Hopkins University/Wilmer Eye Institute and should include Cure Glaucoma on the memo line of your check or in supporting correspondence. For further information on how to contribute to Cure Glaucoma, please contact:

Terri Meekins  
Office of Development  
Wilmer Eye Institute  
600 North Wolfe Street, Wilmer 112  
Baltimore, MD 21287  
410-955-2020  
tmeekin1@jhmi.edu

To remove your name from our mailing list, please call 410-955-2020.